Appendix F: Full evidence tables – review questions 1 - 10

F.1 Review question 1 full evidence tables

Review question 1: What are the key components and organisations of hospital care to ensure optimal management of people with diabetic foot problems?

Title: Critical Pathway Approach to Diabetic Pedal Infections in a Multidisciplinary Setting.

Study type	No. of people	Prevalence / incidence	Patient characteristics	Type of test	Reference standard	Results
ID: 2506 Author: Crane et. al (1999) Study type: Cohort Level of evidence: (+)	Study group: CP (critical pathway)-60 NP(non pathway)-25 Conventional Group(1993)-30 Control group: Non pathway people Study period: 18 month (1995 to 1996) Setting: Roger Williams Medical Center	N/A	Inclusion /Exclusion(study group): All people admitted from January to June 1993, January to June 1995, and October 1995 to September 1996, with the applicable diagnostic codes [ICD-9(The data were searched using *International Classification of Diseases, 9th revision* diagnostic codes) codes 250.xx (Diabetes Mellitus) and its complications 707.1 (chronic ulcer, foot) and/or 785.4 (gangrene)] were included in this retrospective study. Those people in whom pedal disease was a secondary diagnosis were excluded. Characteristics of	To evaluate, utilizing clinical and financial outcomes, the critical pathway approach to diabetic foot infections in an inpatient setting. In our program, the path is initiated in the emergency department utilizing committee-approved standing physician's orders and clinical progress records to facilitate transitions between departments. The critical pathway, during the first 6 months of this investigation, was a voluntary podiatry-only logarithmic approach to emergency room people admitted with diabetic pedal infections. After the preliminary results were evaluated by the Critical Pathway Committee, the entire medical staff, regardless of specialty, were "highly encouraged" to admit their people to the pathway	Conventional treatment	**Table 1: Comparison of patient populations** Year / N / Male (%) / Avg Age / Avg LOS / Readmissions / Major Amputations / Minor Amputations 1993 / 30 / 60% / 72.6 (53-91) / 14.4 (2-43) / 20% / 27% / 30% 1995 / 38 / 60% / 66.1 (32-95) / 6.1 (1-16) / 11% / 18% / 13% 1996 / 47 / 52% / 65,1 (41 - 89) / 5.1 (1-22) / 15% / 4% / 38% 1995 CP / 27 / 68% / 63.0 (32-93) / 5.4 (2-11) / 7% / 15% / 11% 1995 NP / 11 / 50% / 73,8 / 7.8 / 18% / 27% / 18%

			cases: Refer to table 1. Baseline Measurements: Not applicable.	from the emergency room. This, however, was not mandatory. The 1993 group was defined as the conventional methodology group and the 1995-1996 group was further stratified to either a critical pathway group or nonpathway group. Clinical outcomes were defined by amputation level, [i.e., toe, transmetatarsal (TMA), below knee (BKA), or above knee (AKA)] and readmission within 6 months for the same problem.		

			(66-95)	(3-16)			
1996 CP	33	56%	64.2 (41 - 89)	3.6 (1-8)	15%	0%	45%
1996 NP	14	42%	67.4 (42-87)	8.7 (3-22)	15%	14%	21%
Total CP	60	61%	63.7 (32-93}	4.4 (2-11)	12%	7%	30%

CP-Critical pathway people; NP-non-pathway people; LOS-length of hospital stay. Data are presented as average (range)

There was a significant decrease in the length of stay (LOS) and charges for people treated using the critical pathway in 1995 and 1996 compared to people treated in 1993 and to people treated in 1995 and 1996 in which the pathway was not used ($p < .05$).

In addition, there was a significant decrease in the proportion of major amputations (BKA or AKA) in 1995 and 1996 as compared to baseline values (1993 = 23%, 1995-1996 = 7%, $p = .02$).

Likewise, there was a significant decrease in the proportion of major amputations during 1995 and 1996 for people treated with the pathways model compared to people who were not treated with this approach (pathway = 7%, nonpathway — 29%, $p < .001$).

There was not a significant difference in minor amputations (toe, ray, or transmetatarsal) or in people who did not require

						amputation in pathway versus nonpathway people in 1995-1996 versus 1993 (minor amputations: 1995-1996 = 38%, 1993 = 33%; no amputation: 1995-1996 = 54%, 1993 = 43%). There was also not a significant decrease in the proportion of people who required readmission in pathway versus nonpathway people (1993 = 20%, 1995-1996= 10%, $p = x$ .17).
Additional comments:						

Reference:

Crane, M. and Werber, B. 1999, "Critical Pathway Approach to Diabetic Pedal Infections in a Multidisciplinary Setting." *Journal of Foot and Ankle Surgery,* vol. 38, no. 1, pp. 30-33.

Title: Benefits of a Multidisciplinary Approach in the Management of Recurrent Diabetic Foot Ulceration in Lithuania

Study type	No. of people	Prevalence / incidence	Patient characteristics	Type of test	Reference standard	Results
ID: 2624 Author: Dargis et. al (1999)	Study group: Total-145 diabetic participants Control group: Patients presenting in the other cities formed the standard treatment group	N/A	Inclusion /Exclusion(study group): Diabetic patients with a history of previous ulceration (Wagner grades I and II) living in the Kaunas region were referred to the rehabilitation hospital. Characteristics of cases: Variable | Intervention group | Standard treatment	To assess the ability of a multidisciplinary approach to diabetic foot care to reduce the incidence of recurrent ulceration and amputations compared with standard care. The clinic is staffed by a	N/A	The intervention group had significantly fewer recurre n t ulcers during the 2-year period than the standard treatment group (30.4 vs. 58.4%, respectively;

Study type: Cohort Level of evidence: (-)	<u>Study period:</u> Not mentioned <u>Setting:</u> Not mentioned		<table><tr><td></td><td></td><td>group</td></tr><tr><td>Sex (F/M)</td><td>2 9 / 2 7</td><td>4 7 / 4 2</td></tr><tr><td>Age (years)</td><td>59.2 ± 13.4</td><td>58.5 ± 11.5</td></tr><tr><td>Diabetes duration (years)</td><td>14.0 ± 7.1</td><td>15.6 ± 7.8</td></tr><tr><td>NDS</td><td>8.1 ± 1.4</td><td>7.9 ± 1.7</td></tr><tr><td>VPT (V)</td><td>31.1 ± 12.1</td><td>33.9 ± 11.2</td></tr><tr><td>ABPI</td><td>1.14 ± 0.14</td><td>1.10 ± 0.17</td></tr><tr><td>Previous ulcers (n)</td><td>2.3 ± 0.9</td><td>2.1 ± 1.0</td></tr></table> Data are means ± SD, %, or *n*. NDS-Neuropathy disability score VPT- Vibratory perception threshold ABPI- Ankle brachial pressure index. <u>Baseline Measurements:</u> Not applicable.	multidisciplinary team consisting of a diabetologist, a rehabilitation physician, a podiatrist, orthopaedic surgeons, and shoemakers. The intervention group received podiatry, education, and specialty footwear at the Kaunas centre for 2 years. The standard treatment subjects were all screened at the baseline visit by visiting staff from Kaunas who also provided identical standard foot care education and advice at this first visit.		Odds ratio [95% CI] 0.31 [0.14–0.67], x2 10.86, *P* , 0.001) and Fewer amputations (7% [3 minor and 1 major] versus 13.7% [8 minor and 4 major], respectively). The recurrent ulceration rate was thus almost halved.
<u>Additional comments:</u> Did not consider randomizing patients to intensive or standard treatment groups to be ethical because previous single-centre studies have demonstrated the effectiveness of intensive treatment and education programs							

Reference:
Dargis, V, Pantelejeva, O, Jonushaite, A, Vileikyte, L, Boulton, AJ Benefits of a multidisciplinary approach in the management of recurrent diabetic foot ulceration in Lithuania: a prospective study. *Diabetes Care* 1999; 22: 1428-31.

Title: Decreasing Incidence of Major Amputation in Diabetic Patients: a Consequence of a Multidisciplinary Foot Care Team Approach?						
Study type	No. of people	Prevalence / incidence	Patient characteristics	Type of test	Reference standard	Results
ID: 6065 Author: Larsson et. al (1995) Study type: Cohort Level of evidence: (-)	Study group: Total-294 diabetic participants Control group: Participants treated prior to 1983. Study period: Not mentioned Setting: Health care districts of Lund and Orup in southern Sweden	N/A	Inclusion /Exclusion(study group): Amputations in patients not residing in the Lund/ Orup health care district *(n* = 349), and amputations performed for reasons other than vascular disease and/or diabetes *(n* = 89), were excluded. Characteristics of cases: Male- 144 Female- 150 Median age- 77 (range- 32 to 94 years) Baseline Measurements: Not applicable.	To evaluate the changes in diabetes-related lower extremity amputations following the implementation of a multidisciplinary programme for prevention and treatment of diabetic foot ulcers. The instrument for implementing this programme is a team consisting of a diabetologist and an orthopaedic surgeon assisted by a diabetes nurse, a podiatrist, and an orthotist and working in close cooperation with the Department of vascular surgery and the Department of infectious diseases. A programme for patient and staff education was also started. The patients were followed by the same team both as in- and out-patients and throughout the process a high degree of continuity and accessibility was maintained.	N/A	The total annual incidence of primary amputations decreased by 49 %. The incidence of major amputations decreased by 78% from 16.1 to 3.6/100 000 inhabitants (p<0.001). The decrease was most marked in the oldest age group. The proportion of amputations at all levels performed in patients over 80 years of age decreased from 43% to 26% *(p<0.05)* between the first and last 3-year period. In patients younger than 60 years, few amputations were performed and no change in incidence could be demonstrated in this age group. Calculated per 1000 diabetic subjects, with a 2.4% prevalence of diabetes, the total incidence of amputation decreased from 7.9 to 4.1 and the incidence of major amputations from 6.7 to 1.5.

Additional comments:

Did not consider randomizing patients to intensive or standard treatment groups to be ethical because previous single-centre studies have demonstrated the effectiveness of intensive treatment and education programs

Reference:
Larsson, J, Apelqvist, J, Agardh, CD, Stenstrom, A Decreasing incidence of major amputation in diabetic patients: a consequence of a multidisciplinary foot care team approach? *Diabetic Medicine* 1995; 12: 770-776.

Title: Diabetes- and Nondiabetes-Related Lower Extremity Amputation Incidence Before and After the Introduction of Better Organized Diabetes Foot Care.						
Study type	No. of people	Prevalence / incidence	Patient characteristics	Type of test	Reference standard	Results

ID: 2008 Author: Canavan et. al (2008) Study type: Cohort Level of evidence: (-)	Study group: Total-454 LEA (lower extremity amputation) 223-diabetic related Control group: Non-DRLEA Study period: July 1995 to June 2000 Setting: South Tees, UK	N/A	Inclusion /Exclusion(study group): Not mentioned Characteristics of cases: Not mentioned Baseline Measurements: Not applicable.	The aim was to present data on trends in DRLEAs (Diabetic Related Lower Extremity Amputation) and non-DRLEAs in the South Tees area over a continuous 5-year period. The Global Lower Extremity Amputation Study (GLEAS) group through collaboration developed a standard protocol for LEA data collection and can be used to arrive at population-based diabetes-related (DR) LEA and non-DRLEA rates for their own particular areas. Four independent data sources (operating theatre records, limb fitting centre records, hospital discharge data, and community diabetes register) were used to identify patients. LEAs were categorized as first and repeat, major and minor, diabetes related, and nondiabetes related. The denominator populations for non-DRLEAs were 1996 midyear estimates based on 1991 U.K. census data less the population with diabetes.	N/A	**All LEAs (i.e., major, minor, first, and repeat)** LEA rates went from 564.3 of 100,000 persons with diabetes in the first year to 176.0 of 100,000 persons with diabetes in the fifth year. For non-DRLEAs there was an increase from 12.3 to 22.8 of 100,000 persons without diabetes. The relative risk of a person with diabetes undergoing any LEA went from being 46 times that of a person without diabetes at the start of the study to being only 7.7 times that of a person without diabetes at the end of the 5 years.
Additional comments:						

Reference:
Canavan, RJ, Unwin, NC, Kelly, WF, Connolly, VM Diabetes- and nondiabetes-related lower extremity amputation incidence before and after the introduction of better organized diabetes foot care: continuous longitudinal monitoring using a standard method. *Diabetes Care* 2008; 31: 459-63.

Title: Reducing Amputation Rates in Patients With Diabetes at a Military Medical Center. The Limb Preservation Service model.						
Study type	No. of people	Prevalence / incidence	Patient characteristics	Type of test	Reference standard	Results
ID: 2932 Author: Driver et. al (2005) Study type: Cohort Level of evidence: (-)	Study group: Total-128 diabetic Control group: Not mentioned Study period: 1999 to 2003 Setting: Madigan Army Medical Centre (MAMC)	N/A	Inclusion /Exclusion(study group): Not mentioned Characteristics of cases: Not mentioned Baseline Measurements: Not applicable.	The aim was to evaluate the Limb Preservation Service (LPS), a multidisciplinary, state-of-the-art, foot care clinic for patients with diabetes. And the effect on LEAs. High-risk diabetic foot care has become a focused specialty providing standard and advanced care modalities in one setting. This includes prevention and education, wound care, infection management, surgical and hospital management, research and grant development, community and regional education, and the creation of orthotics, prosthetics, and shoes.	N/A	During this period, the number of diagnosed diabetic patients at MAMC increased 48% from 3,340 in 1999 to 4,940 in 2003. Concurrent with the increase in patients with diabetes at MAMC was a decrease in the number of inpatient LEAs from 33 in 1999 to just 9 in 2003. The incidence rate of LEAs in patients with diabetes at MAMC dropped from 9.9/ 1,000 to 1.8/1,000 over 5 years.
Additional comments:						

Reference:

Driver, VR, Madsen, J, Goodman, RA Reducing amputation rates in patients with diabetes at a military medical center: the limb preservation service model. *Diabetes Care* 2005; **28:** 248-53.

F.2 Review question 2 full evidence tables

Table 1: National diabetes inpatient audit 2012

<table>
<tr><td>Title and reference</td><td>National diabetes inpatient audit 2012.
Health and Social Care Information Centre 2013. Key findings about the quality of care of inpatients with diabetes in England and Wales. Available from www.ic.nhs.uk</td></tr>
<tr><td>Study type</td><td>Clinical audit</td></tr>
<tr><td>Objective</td><td>To assess national service arrangements and quality of care provided for people admitted to hospital who have diabetes.</td></tr>
<tr><td>Population</td><td>Adult inpatients in hospital for any reason and a diagnosis of diabetes who had been admitted for more than 24 hours at the time of data collection.
Excluding obstetric or paediatric wards, mental health wards, A&E, day case wards, day surgery wards, observation or surgical short stay wards (if patients have been admitted for less than 24 hours), palliative care centres, community hospitals.</td></tr>
<tr><td>Methods</td><td>Prospective clinical audit undertaken on one nominated day in September 2012
Data collection via three questionnaires on patient experience, patient clinical data and hospital characteristics
199 audit sites in England (136 Trusts) and 17 audit sites in Wales (6 Local Health Boards).</td></tr>
<tr><td>Results</td><td>England
30.2% of participating hospitals in England (60 of 199) did not have a multidisciplinary foot team as defined by the NICE CG119. A total of 9.2% of all people with diabetes admitted to hospital for any reason had active diabetic foot disease and of these, 53.9% were seen by a member of the multidisciplinary foot team within 24 hours.
Composition of multidisciplinary foot teams, England 2012:
<table>
<tr><td></td><td colspan="3">Percentage of sites</td></tr>
<tr><td></td><td>Foot team member</td><td>Not member but accessible</td><td>No access</td></tr>
<tr><td>Vascular surgeon</td><td>56.6</td><td>40.9</td><td>2.5</td></tr>
<tr><td>Diabetologist</td><td>81.3</td><td>18.2</td><td>0.5</td></tr>
<tr><td>Specialist podiatrist</td><td>82.2</td><td>11.7</td><td>6.1</td></tr>
<tr><td>Diabetes specialist nurse</td><td>59.6</td><td>36.9</td><td>3.5</td></tr>
<tr><td>Interventional radiologist</td><td>9.7</td><td>75.9</td><td>14.4</td></tr>
</table></td></tr>
</table>

	Orthopaedic surgeon	25.4	69.0	5.6
	Tissue viability nurse	26.2	69.7	4.1
	Microbiologist	24.9	74.1	1.0
	Orthotist	36.3	57.0	6.7

Wales

52.9% of participating hospitals in Wales (9 of 17) did not have a multidisciplinary foot team as defined by the NICE CG119. A total of 10.1% of all people with diabetes admitted to hospital for any reason had active diabetic foot disease and of these, 46.6% were seen by a member of the multidisciplinary foot team within 24 hours.

Composition of multidisciplinary foot teams, Wales 2012:

	Percentage of sites		
	Foot team member	Not member but accessible	No access
Vascular surgeon	35.3	64.7	0.0
Diabetologist	64.7	35.3	0.0
Specialist podiatrist	76.5	23.5	0.0
Diabetes specialist nurse	56.3	43.8	0.0
Interventional radiologist	0.0	68.8	31.3
Orthopaedic surgeon	18.8	75.0	6.3
Tissue viability nurse	31.3	68.8	0.0
Microbiologist	12.5	75.0	12.5
Orthotist	23.5	64.7	11.8

Comments	Commissioned by the Healthcare Quality Improvement Partnership England and Wales data presented separately to allow comparison to previous audits in which Wales did not participant.

Table 2: Williams (2012)

Reference	Williams,D.T.; Majeed,M.U.; Shingler,G.; Akbar,M.J.; Adamson,D.G.; Whitaker,C.J. A diabetic foot service established by a department of vascular surgery: an observational study. Annals of Vascular Surgery 2012;26(5):700-06.
Study type	Observational study (prospective cohort)
Objective	To assess whether an integrated diabetic foot service was associated with changes in outcomes for those with diabetic foot problems and factors that influenced this.

Population	People with diabetes referred to a secondary care diabetic foot service attached to a district general hospital in the UK. Service established by a vascular unit.
Methods	Prospective data collection for 4 years (2006-2009) of all people referred to the multidisciplinary unit compared to retrospective data collected in the 2 years prior to the service (2004 - 2005).
Results	Multidisciplinary foot service consisted of: Consultant vascular surgeon Vascular nurse specialist Podiatrist with an interest in diabetic foot disease Nurses with an interest in lower limb wound care Orthotist

Table 3: Sampson (2007)

Reference	Sampson,M.J.; Brennan,C.; Dhatariya,K.; Jones,C.; Walden,E. A national survey of inpatient diabetes services in the United Kingdom. Diabetic Medicine 2007;24(6):643-49.
Study type	Survey
Objective	To assess national service provision for people admitted to hospital who have diabetes.
Population	Diabetes specialist teams in UK acute hospitals.
Methods	Structured questionnaire sent to the senior consultant diabetologist and senior diabetes specialist nurse in each acute hospital in the UK. The survey was completed between 18 May 2005 and 1 March 2006. Survey comprised 63 questions in five sections. No previous validated survey used to guide development.
Results	239 (91.2%) responses to the questionnaire from 262 specialist teams Sixty hospitals (25.1%) had no guidelines for the immediate management of the diabetic foot and also did not refer these patients to the diabetes team on admission. Of 228 responding hospital teams, 96 (42.2%) of 227 hospital teams reported that they had access to a podiatrist for in-patients with diabetes.

Table 4: Housley (2006)

Rreference	Housley, A., Betts, C. and Rajbhandari, S. (2006), Diabetes foot health in Chorley and South Ribble: a step in the right direction. Pract Diab Int, 23: 161–165. Doi: 10.1002/pdi.934
Study type	Clinical audit
Objective	To assess provision and quality of care provided for people with diabetic foot problems in Chorley and South Ribble .
Population	The podiatry department of Chorley and South Ribble Primary Care Trust works closely with the Chorley and South Ribble District General Hospital of

	Lancashire Teaching Hospitals NHS Trust serving a population of approximately 210 000. Around half of the podiatry department's activity involves the management of patients with diabetes mellitus.
Methods	Clinical audit.
Results	16 podiatrists (14.1 whole time equivalent), one diabetes specialist podiatrist and a foot care assistant work with district nurses and the community tissue viability nurse to provide a foot care service in the community. The hospital specialist foot clinic is led by the consultant diabetologist with a special interest in feet working closely with community diabetes specialist podiatrist, clinic nurses, diabetes specialist nurses, orthotist, plaster technician, vascular surgeons, radiologists and microbiologists. In addition, community podiatrists attend this clinic in rotation mainly for training to ensure continued high quality diabetes care.
Comments	Lack of clarity however it is assumed that the community podiatry services mentioned are not specific to people with diabetes

Table 5: El Sakka (2006)

Reference	El,Sakka K.; Fassiadis,N.; Gambhir,R.P.; Halawa,M.; Zayed,H.; Doxford,M.; Greensitt,C.; Edmonds,M.; Rashid,H. An integrated care pathway to save the critically ischaemic diabetic foot. International Journal of Clinical Practice 2006;60(6):667-69.
Study type	Prospective cohort study
Objective	Evaluating the efficacy of an integrated care pathway by a multidisciplinary team for the management of the critically ischaemic diabetic foot patient
Population	People with lower limb ischaemia referred to a multidisciplinary team at King's College Hospital, UK.
Methods	Prospective data collection between January 2002 and June 2003.
Results	128 patients seen by the multidisciplinary team. Multidisciplinary team consisted of a consultant vascular surgeon, vascular registrar, diabetes consultant, consultant podiatrist and radiology procedure coordinator.

Table 6: Jude (2003)

Reference	Jude,E.B.; Oyibo,S.O.; Millichip,M.M.; Boulton,A.J.M. A survey of physicians' involvement in the management of diabetic foot ulcers in secondary health care. Practical Diabetes International.20 (3) (pp 89-92), 2003.Date of Publication: April 2003. 2003;(3):89-92.
Study type	Survey
Objective	To investigate the management of diabetic foot ulcers in different secondary care centres in the UK.
Population	Consultant diabetologists in secondary health care
Methods	Postal survey of 160 consultant diabetologists in the UK
Results	50% response rate recorded 67.1% of respondents had a designated foot clinic. Availability of vascular surgery was reported by 91.1% of physicians. Availability of podiatry services was reported by 92.4% of physicians. Availability of orthotist services was reported by 77.2% of physicians.
Comments	Unclear as to original selection of sample, unlikely to be total number of consultant diabetologists in the UK. No definition given for "foot clinic".

Table 7: Winocour (2002)

Reference	Winocour,P.H.; Morgan,J.; Ainsworth,A.; Williams,D.R.; Association of British Clinical Diabetologists: survey of specialist diabetes care services in the UK, 2000. 3. Podiatry services and related foot care issues. Diabetic Medicine 2002;19():Suppl-8.
Study type	Survey
Objective	To establish the national levesl of input of podiatric services into diabetes services
Population	All secondary care diabetes services in the UK
Methods	Paper survey sent to secondary care providers of diabetes services in 2000. Of 456 questionnaires sent to 238 acute NHS trusts / units, 77% completed documents were subjected to full analysis
Results	97% of diabetes services had a state registered chiropodist attached. In 75% of responses care was provided by a designated chiropodist, whereas a ‘pool’ of chiropodist sprovided care in 20% of responses 44% of diabetes services reported chiropodists present in all diabetic clinics 49% of diabetes services had a separate diabetic foot clinic >90% of diabetes services recorded access to plaster technician 66.5% of diabetes services reported access to orthotists (majority at stated times)

	46% of diabetes services reported had a dedicated foot surgeon in hospital

Table 8: Gooday 2013

Bibliographic reference	**Gooday, C., Murchison, R., & Dhatariya, K. (2013). An analysis of clinical activity, admission rates, length of hospital stay, and economic impact after a temporary loss of 50% of the non-operative podiatrists from a tertiary specialist foot clinic in the United Kingdom. Diabetic foot & ankle, 4.**
Study type	Observational, prospective study
Study quality	Summary Location: United Kingdom, Norfolk, specialist diabetes foot service Intervention: Presence of podiatrists within a multidisciplinary foot care team prior to loss of 50% of non-operative podiatry team for almost 7 months. Comparison: There was a 50% reduction in specialist podiatry staff members in 2010. Replacement of podiatry footcare team members with non-specialist community non-operative podiatrists for some of this time. Specialist staffing levels and activity levels were eventually restored more than 7 months after the original loss. This study shows the effect of the loss of these staff in a diabetic foot clinic. Population: Foot clinic activity increased from 4197 to 5270 people seen between the years 2005 and 2012. Acute diabetic foot complications were triaged by the clinic and team of podiatrists. Outcome: Hospital bed days, hospital admissions, resource use and cost. 1. The method of allocation to intervention groups was unrelated to potential confounding factors (the reason for participant allocation to intervention is not expected to affect the outcome under study)? Controls were taken from before the period that the service was established. Unclear if any other confounding factors may have affected the results during this time. 2. Attempts were made with the design or analysis to balance the comparison groups for potential confounders? There were no attempts to balance groups for confounders 3. The groups were comparable at baseline, including all major confounding factors? Unclear if groups were comparable at baseline including major confounding factors 4. The comparison groups received the same care and support apart from the interventions studied? Unclear if comparison groups received comparable care other than due to the changes implemented by the programme. See intervention section for other changes of care that may have occurred over this time period. 5. Participants receiving care and support were kept blind to intervention allocation? Participants were not blinded to intervention allocation. 6. Individuals administering care and support were kept blind to intervention allocation?

Bibliographic reference	**Gooday, C., Murchison, R., & Dhatariya, K. (2013). An analysis of clinical activity, admission rates, length of hospital stay, and economic impact after a temporary loss of 50% of the non-operative podiatrists from a tertiary specialist foot clinic in the United Kingdom. Diabetic foot & ankle, 4.**
	Individuals administering care were not blinded to intervention allocation 7. All groups were followed for an equal length of time, or analysis was adjusted to allow for differences in length of follow up? Observational period was over 7 years. Unclear if participants were observed for an equal length of follow up. 8. Groups were comparable for intervention completion? Unclear if groups were comparable for compliance or intervention completion or for general adherence to treatment. 9. The groups were comparable with respect to the availability of outcome data? There was no loss to follow up reported. 10. The study had an appropriate length of follow up? Observation period was appropriate 7 years, data was recorded prospectively from participants who had been seen during this period of time. 11. The study used a precise definition of outcome? Good definitions of outcomes were described. 12. A valid and reliable method was used to determine the outcome? A valid and reliable method was used to determine outcome. 13. Investigators were kept blind to participant's exposure to the intervention? Investigators were not kept blinded to exposure to the intervention 14. Investigators were kept blind to other important confounding factors? Investigators were not kept blinded to other important confounding factors .
Number of patients	Total patients (per year) 2008= 4,197 2009= 4,799 **2010= 4,058** 2011= 4,294 2012= 5,270
Patient characteristics	Inclusion: Patients seen at a specialist foot clinic Exclusion: Not stated

<table>
<tr><th>Bibliographic reference</th><td>Gooday, C., Murchison, R., & Dhatariya, K. (2013). An analysis of clinical activity, admission rates, length of hospital stay, and economic impact after a temporary loss of 50% of the non-operative podiatrists from a tertiary specialist foot clinic in the United Kingdom. Diabetic foot & ankle, 4.</td></tr>
<tr><td></td><td>Baseline characteristics:
Not stated</td></tr>
<tr><td>Intervention</td><td>Presence of podiatrists within a multidisciplinary foot care team prior to loss of 50% of non-operative podiatry team for almost 7 months.</td></tr>
<tr><td>Comparison</td><td>There was a 50% reduction in specialist podiatry staff members in 2010. Replacement of podiatry footcare team members with non-specialist community non-operative podiatrists for some of this time. Specialist staffing levels and activity levels were eventually restored more than 7 months after the original loss. This study shows the effect of the loss of these staff in a diabetic foot clinic.</td></tr>
<tr><td>Length of follow up</td><td>5 year observation period</td></tr>
<tr><td>Location</td><td>United Kingdom</td></tr>
<tr><td>Outcomes measures and effect size</td><td>Rates (and recurrent rates) of foot ulceration, infection and gangrene resulting from diabetes
Not reported

Resource use and costs (including referral rates)

At this institution a hospital bed day costs £275
The increase in hospital admissions and length of stay during the staff shortage equated to 327 extra bed days compared to the 12 months prior to service disruption.
The increased expenditure for this year equated to £89,925

Rates of hospital admission for foot problems resulting from diabetes

<table>
<tr><th>Year</th><th>Clinical activity (number of people seen)</th><th>Number of admissions</th><th>Admissions as a % of total activity</th><th>Total bed days</th><th>Mean length of hospital stay (±SD)</th></tr>
<tr><td>2005</td><td>2835</td><td>30</td><td>1</td><td>515</td><td>17.2 (9.2)</td></tr>
<tr><td>2006</td><td>2921</td><td>43</td><td>1.5</td><td>775</td><td>17.2 (19.2)</td></tr>
<tr><td>2007</td><td>3325</td><td>39</td><td>1.1</td><td>570</td><td>14.6 (11.3)</td></tr>
<tr><td>2008</td><td>4197</td><td>50</td><td>1.2</td><td>919</td><td>18.4 (16.8)</td></tr>
</table>
</td></tr>
</table>

Bibliographic reference	**Gooday, C., Murchison, R., & Dhatariya, K. (2013). An analysis of clinical activity, admission rates, length of hospital stay, and economic impact after a temporary loss of 50% of the non-operative podiatrists from a tertiary specialist foot clinic in the United Kingdom. Diabetic foot & ankle, 4.**

2009	4799	58	1.2	867	14.7 (11.3)
2010	**4058**	**72**	**1.8**	**1194**	**16.5 (12.3)**
2011	4294	41	0.95	838	20.4 (16.6)
2012	5270	45	0.89	733	16.2 (15.1)

Length of hospital stay

See table above, which shows the drop in number of people seen when the number of staff dropped, but a corresponding increase in the proportion of people admitted, and an increase in their hospital length of stay. (see year 2010)

Following staffing and activity levels returning to normal it took more than a year to reduce the number of hospital admissions directly from the diabetic foot clinic back to 45 in 2012 which reflected the average of the 5 years preceding the staff loss.

Rates and extent of amputation

Not reported

Health related quality of life

Not reported

Source of funding	No funding recieved
Comments	This study shows the drop in number of people seen when the number of staff dropped, but a corresponding increase in the proportion of people admitted, and an increase in their hospital length of stay. (see year 2010). This supports the importance of the specialist podiatrist in the multidisciplinary team and the cost of disrupting this system within this clinic.

F.3 Review question 3 full evidence tables

Table 9: Gooday 2013

Bibliographic reference	**Gooday, C., Murchison, R., & Dhatariya, K. (2013). An analysis of clinical activity, admission rates, length of hospital stay, and economic impact after a temporary loss of 50% of the non-operative podiatrists from a tertiary specialist foot clinic in the United Kingdom. Diabetic foot & ankle, 4.**
Study type	Observational, prospective study
Study quality	Summary Location: United Kingdom, Norfolk, specialist diabetes foot service Intervention: Presence of podiatrists within a multidisciplinary foot care team prior to loss of 50% of non-operative podiatry team for almost 7 months. Comparison: There was a 50% reduction in specialist podiatry staff members in 2010. Replacement of podiatry footcare team members with non-specialist community non-operative podiatrists for some of this time. Specialist staffing levels and activity levels were eventually restored more than 7 months after the original loss. This study shows the effect of the loss of these staff in a diabetic foot clinic. Population: Foot clinic activity increased from 4197 to 5270 people seen between the years 2005 and 2012. Acute diabetic foot complications were triaged by the clinic and team of podiatrists. Outcome: Hospital bed days, hospital admissions, resource use and cost. 1. The method of allocation to intervention groups was unrelated to potential confounding factors (the reason for participant allocation to intervention is not expected to affect the outcome under study)? Controls were taken from before the period that the service was established. Unclear if any other confounding factors may have affected the results during this time. 2. Attempts were made with the design or analysis to balance the comparison groups for potential confounders? There were no attempts to balance groups for confounders 3. The groups were comparable at baseline, including all major confounding factors? Unclear if groups were comparable at baseline including major confounding factors 4. The comparison groups received the same care and support apart from the interventions studied? Unclear if comparison groups received comparable care other than due to the changes implemented by the programme. See intervention section for other changes of care that may have occurred over this time period.

Bibliographic reference	**Gooday, C., Murchison, R., & Dhatariya, K. (2013). An analysis of clinical activity, admission rates, length of hospital stay, and economic impact after a temporary loss of 50% of the non-operative podiatrists from a tertiary specialist foot clinic in the United Kingdom. Diabetic foot & ankle, 4.**
	5. Participants receiving care and support were kept blind to intervention allocation? Participants were not blinded to intervention allocation. 6. Individuals administering care and support were kept blind to intervention allocation? Individuals administering care were not blinded to intervention allocation 7. All groups were followed for an equal length of time, or analysis was adjusted to allow for differences in length of follow up? Observational period was over 7 years. Unclear if participants were observed for an equal length of follow up. 8. Groups were comparable for intervention completion? Unclear if groups were comparable for compliance or intervention completion or for general adherence to treatment. 9. The groups were comparable with respect to the availability of outcome data? There was no loss to follow up reported. 10. The study had an appropriate length of follow up? Observation period was appropriate 7 years, data was recorded prospectively from participants who had been seen during this period of time. 11. The study used a precise definition of outcome? Good definitions of outcomes were described. 12. A valid and reliable method was used to determine the outcome? A valid and reliable method was used to determine outcome. 13. Investigators were kept blind to participant's exposure to the intervention? Investigators were not kept blinded to exposure to the intervention 14. Investigators were kept blind to other important confounding factors? Investigators were not kept blinded to other important confounding factors .
Number of patients	Total patients (per year) 2008= 4,197 2009= 4,799 **2010= 4,058** 2011= 4,294 2012= 5,270
Patient characteristics	Inclusion: Patients seen at a specialist foot clinic

<table>
<tr><th>Bibliographic reference</th><td>Gooday, C., Murchison, R., & Dhatariya, K. (2013). An analysis of clinical activity, admission rates, length of hospital stay, and economic impact after a temporary loss of 50% of the non-operative podiatrists from a tertiary specialist foot clinic in the United Kingdom. Diabetic foot & ankle, 4.</td></tr>
<tr><td></td><td>Exclusion:
Not stated

Baseline characteristics:
Not stated</td></tr>
<tr><td>Intervention</td><td>Presence of podiatrists within a multidisciplinary foot care team prior to loss of 50% of non-operative podiatry team for almost 7 months.</td></tr>
<tr><td>Comparison</td><td>There was a 50% reduction in specialist podiatry staff members in 2010. Replacement of podiatry footcare team members with non-specialist community non-operative podiatrists for some of this time. Specialist staffing levels and activity levels were eventually restored more than 7 months after the original loss. This study shows the effect of the loss of these staff in a diabetic foot clinic.</td></tr>
<tr><td>Length of follow up</td><td>5 year observation period</td></tr>
<tr><td>Location</td><td>United Kingdom</td></tr>
<tr><td>Outcomes measures and effect size</td><td>Rates (and recurrent rates) of foot ulceration, infection and gangrene resulting from diabetes
Not reported

Resource use and costs (including referral rates)

At this institution a hospital bed day costs £275
The increase in hospital admissions and length of stay during the staff shortage equated to 327 extra bed days compared to the 12 months prior to service disruption.
The increased expenditure for this year equated to £89,925

Rates of hospital admission for foot problems resulting from diabetes

<table>
<tr><th>Year</th><th>Clinical activity (number of people seen)</th><th>Number of admissions</th><th>Admissions as a % of total activity</th><th>Total bed days</th><th>Mean length of hospital stay (±SD)</th></tr>
<tr><td>2005</td><td>2835</td><td>30</td><td>1</td><td>515</td><td>17.2 (9.2)</td></tr>
</table>
</td></tr>
</table>

Bibliographic reference	Gooday, C., Murchison, R., & Dhatariya, K. (2013). An analysis of clinical activity, admission rates, length of hospital stay, and economic impact after a temporary loss of 50% of the non-operative podiatrists from a tertiary specialist foot clinic in the United Kingdom. Diabetic foot & ankle, 4.

2006	2921	43	1.5	775	17.2 (19.2)
2007	3325	39	1.1	570	14.6 (11.3)
2008	4197	50	1.2	919	18.4 (16.8)
2009	4799	58	1.2	867	14.7 (11.3)
2010	**4058**	**72**	**1.8**	**1194**	**16.5 (12.3)**
2011	4294	41	0.95	838	20.4 (16.6)
2012	5270	45	0.89	733	16.2 (15.1)

Length of hospital stay

See table above, which shows the drop in number of people seen when the number of staff dropped, but a corresponding increase in the proportion of people admitted, and an increase in their hospital length of stay. (see year 2010)

Following staffing and activity levels returning to normal it took more than a year to reduce the number of hospital admissions directly from the diabetic foot clinic back to 45 in 2012 which reflected the average of the 5 years preceding the staff loss.

Rates and extent of amputation
Not reported

Health related quality of life
Not reported

Source of funding	No funding recieved
Comments	This study shows the drop in number of people seen when the number of staff dropped, but a corresponding increase in the proportion of people admitted, and an increase in their hospital length of stay. (see year 2010). This supports the importance of the specialist podiatrist in the multidisciplinary team and the cost of disrupting this system within this clinic.

Table 10: Patout 2000

Bibliographic reference	**Patout, C. A., Birke, J. A., Horswell, R., Williams, D., & Cerise, F. P. (2000). Effectiveness of a comprehensive diabetes lower-extremity amputation prevention program in a predominantly low-income African-American population. Diabetes Care, 23(9), 1339-1342.**
Study type	Observational, prospective study
Study quality	Summary Location: USA, enrolment in a comprehensive diabetes lower-extremity amputation prevention programme Intervention: Population as below, all patients receive an initial diabetes foot screen to identify the individuals relative risk for foot injury. Patients at low risk are provided foot care education, assistance in the selection of proper fitting and designed foot wear, and routine follow up to manage simple problems. Patients at high risk are provided custom molded inserts orthoses and prescription footwear to reduce foot pressure and are followed at a more frequent interval. Molded orthoses and footwear modifications are fabricated on site by a certified pedorthist. Patients with foot injuries such as ulceration or Charcot osteoarthropathy are provided the highest priority with would debridement, moist dressings, contact casts and other custom offloading appliances used to promote healing. Surgical intervention is provided via consultation through the state hospital system. (see paper for breakdown of risk and management by risk category.) Comparison: Comparison with standard care outcomes 1 year prior to enrolment in the LEAP program described above. Standard care consisted of non-co-ordinated treatment of foot problems provided in primary care clinics, in emergency rooms, and in wound care, surgical and podiatry clinics. Population: Accepts all patients with a diagnosis of diabetes or related disorders with neuropathic foot complications referred from local and regional physicians within the Louisiana State Hospital system. Outcome: Hospital bed days, hospital admissions, emergency room admissions, ulcer days.
Number of patients	Total n= 197 patients
Patient characteristics	Inclusion: All patients with a diagnosis of diabetes or related disorder with neuropathic foot complications Exclusion: Not stated Baseline characteristics: No baseline characteristics reported

Bibliographic reference	**Patout, C. A., Birke, J. A., Horswell, R., Williams, D., & Cerise, F. P. (2000). Effectiveness of a comprehensive diabetes lower-extremity amputation prevention program in a predominantly low-income African-American population. Diabetes Care, 23(9), 1339-1342.**
Intervention	Population as below, all patients receive an initial diabetes foot screen to identify the individuals relative risk for foot injury. Patients at low risk are provided foot care education, assistance in the selection of proper fitting and designed foot wear, and routine follow up to manage simple problems. Patients at high risk are provided custom molded inserts orthoses and prescription footwear to reduce foot pressure and are followed at a more frequent interval. Molded orthoses and footwear modifications are fabricated on site by a certified pedorthist. Patients with foot injuries such as ulceration or Charcot osteoarthropathy are provided the highest priority with would debridement, moist dressings, contact casts and other custom offloading appliances used to promote healing. Surgical intervention is provided via consultation through the state hospital system. (see paper for breakdown of risk and management by risk category.)
Comparison	Comparison with standard care outcomes 1 year prior to enrolment in the LEAP program described above. Standard care consisted of non-co-ordinated treatment of foot problems provided in primary care clinics, in emergency rooms, and in wound care, surgical and podiatry clinics.
Length of follow up	1 year follow up
Location	USA
Outcomes measures and effect size	Rates (and recurrent rates) of foot ulceration, infection and gangrene resulting from diabetes Comparison of 1 year of standard foot care and 1 year of comprehensive lower extremity prevention programme in 197 patients for the outcome of number of ulcer days rate per patient year (mean ± SD): Standard care period: 73.944 ± 17.245 CD-LEAP period: 37.513 ± 10.179 % change (paired t test comparison): 49% Resource use and costs (including referral rates) Comparison of 1 year of standard foot care and 1 year of comprehensive lower extremity prevention programme in 197 patients for the outcome of number of missed workdays rate per patient year (mean ± SD): Standard care period: 17.538 ± 9.356 CD-LEAP period: 5.273 ± 5.094 % change (paired t test comparison): 70%

Bibliographic reference	**Patout, C. A., Birke, J. A., Horswell, R., Williams, D., & Cerise, F. P. (2000). Effectiveness of a comprehensive diabetes lower-extremity amputation prevention program in a predominantly low-income African-American population. Diabetes Care, 23(9), 1339-1342.**
	Rates of hospital admission for foot problems resulting from diabetes Comparison of 1 year of standard foot care and 1 year of comprehensive lower extremity prevention programme in 197 patients for the outcome of number of number of hospitalisations rate per patient year (mean ± SD): Standard care period: 0.3517 ± 0.106 CD-LEAP period: 0.0401 ± 0.031 % change (paired t test comparison): 89% Comparison of 1 year of standard foot care and 1 year of comprehensive lower extremity prevention programme in 197 patients for the outcome of number of emergency room visits rate per patient year (mean ± SD): Standard care period: 0.487 ± 0.236 CD-LEAP period: 0.091 ± 0.057 % change (paired t test comparison): 81% Length of hospital stay Comparison of 1 year of standard foot care and 1 year of comprehensive lower extremity prevention programme in 197 patients for the outcome of number of hospital days rate per patient year (mean ± SD): Standard care period: 3.756 ± 1.530 CD-LEAP period: 0.371 ± 0.366 % change (paired t test comparison): 90% Rates and extent of amputation Comparison of 1 year of standard foot care and 1 year of comprehensive lower extremity prevention programme in 197 patients for the outcome of number of lower extremity amputations rate per patient year (mean ± SD): Standard care period: 0.096 ± 0.048 CD-LEAP period: 0.020 ± 0.020 % change (paired t test comparison): 79% Health related quality of life

Bibliographic reference	**Patout, C. A., Birke, J. A., Horswell, R., Williams, D., & Cerise, F. P. (2000). Effectiveness of a comprehensive diabetes lower-extremity amputation prevention program in a predominantly low-income African-American population. Diabetes Care, 23(9), 1339-1342.**
	Not reported
Source of funding	Not stated
Comments	This study showed a large reduction in foot-related ulcer days, hospitalisations, hospital stays, hospitalisations, emergency room visits, amputations and missed workdays after the first year of comprehensive foot care.

Table 11: Rith-Najarian 1998

Bibliographic reference	**Rith-Najarian, S., Branchaud, C., Beaulieu, O., Gohdes, D., Simonson, G., & Mazze, R. (1998). Reducing lower-extremity amputations due to diabetes. Application of the staged diabetes management approach in a primary care setting. The Journal of family practice, 47(2), 127-132.**
Study type	Observational, prospective study
Study quality	Summary Location: USA, rural primary care clinic amongst American Indians. Intervention: A two year staged diabetes management period during which comprehensive guidelines for diabetic foot management were adapted by primary care clinicians to their practice and were systematically implemented. A foot care team was formed consisting of a family physician, two clinic nurses, a home care nurse, a nutritionist and a registrar. The team met monthly to develop co-ordinated strategies for improving access to and utilization of appropriate foot care services. Flow sheets based on staged diabetes management algorithms were produced and a copy placed in each patient's charts. Standing orders and standardised ulcer assessment and management protocols for each risk category were implemented. (see in paper for details and treatment flow pathways). Comparison: A three year period in which patients received standard care during which patients received foot care at the discretion of the primary care provider. A three year period during which patients were screened for foot problems and high-risk individuals received foot care education and protective footwear. Population: 639 American Indians with diabetes in a rural primary care clinic Outcome: amputation.
Number of patients	Total n= 639 American Indians Standard care period= 428

<table>
<tr><th>Bibliographic reference</th><td>Rith-Najarian, S., Branchaud, C., Beaulieu, O., Gohdes, D., Simonson, G., & Mazze, R. (1998). Reducing lower-extremity amputations due to diabetes. Application of the staged diabetes management approach in a primary care setting. The Journal of family practice, 47(2), 127-132.</td></tr>
<tr><td></td><td>Public health period= 449
Staged diabetes management period= 475</td></tr>
<tr><td>Patient characteristics</td><td>Inclusion:
Amputations defined as the loss of any part of the lower limb
Patients hospitalised at IHS, and HIS contracted facilities

Exclusion:
Amputations among individuals seeking care outside the IHS system.

Baseline characteristics:

<table>
<tr><td></td><td>Standard care</td><td>Public Health</td><td>Staged Diabetes Management</td></tr>
<tr><td>Number of patients</td><td>428</td><td>449</td><td>475</td></tr>
<tr><td>Person years</td><td>1465</td><td>1543</td><td>1313</td></tr>
<tr><td>Mean age, y (SD)</td><td>53.9 ±12.9</td><td>53.6 ±13.1</td><td>54.2 ±13.0</td></tr>
<tr><td>Sex, % female</td><td>54.4</td><td>56.8</td><td>56.8</td></tr>
<tr><td>Diabetes duration, y (SD)</td><td>8.3 ± 6.5</td><td>8.5 ± 6.4</td><td>9.7 ± 7.2</td></tr>
</table>
</td></tr>
<tr><td>Intervention</td><td>A two year staged diabetes management period during which comprehensive guidelines for diabetic foot management were adapted by primary care clinicians to their practice and were systematically implemented. A foot care team was formed consisting of a family physician, two clinic nurses, a home care nurse, a nutritionist and a registrar. The team met monthly to develop co-ordinated strategies for improving access to and utilization of appropriate foot care services. Flow sheets based on staged diabetes management algorithms were produced and a copy placed in each patient’s charts. Standing orders and standardised ulcer assessment and management protocols for each risk category were implemented. (see in paper for details and treatment flow pathways).</td></tr>
<tr><td>Comparison</td><td>A three year period in which patients received standard care during which patients received foot care at the discretion of the primary care provider. A three year period during which patients were screened for foot problems and high-risk individuals received foot care education and protective footwear.</td></tr>
<tr><td>Length of follow up</td><td>Data provided in diabetic person-years, 11 year study period</td></tr>
<tr><td>Location</td><td>USA</td></tr>
<tr><td>Outcomes measures and effect size</td><td>Rates (and recurrent rates) of foot ulceration, infection and gangrene resulting from diabetes</td></tr>
</table>

Bibliographic reference	**Rith-Najarian, S., Branchaud, C., Beaulieu, O., Gohdes, D., Simonson, G., & Mazze, R. (1998). Reducing lower-extremity amputations due to diabetes. Application of the staged diabetes management approach in a primary care setting. The Journal of family practice, 47(2), 127-132.**

Not reported

Resource use and costs (including referral rates)
Not reported

Rates of hospital admission for foot problems resulting from diabetes
Not reported

Length of hospital stay
Not reported

Rates and extent of amputation
Amongst 639 American Indians contributing 4322 diabetic person years during 11 years of observation

Average annual incidence of lower-extremity amputation among patients by intervention period

Period	Person-years at risk	No. of cases of lower extremity amputation	Lower extremity amputations/1000 diabetic person-years	% change	P value
Standard care					
Any LEA	1464	42	29	-	
First LEA	1414	30	21	-	
Major LEA	1464	16	11	-	
Public Health					
Any LEA	1543	33	21	-28	0.20
First LEA	1467	18	12	-43	0.06
Major LEA	1543	12	8	-27	0.37
Staged Diabetes Management					
Any LEA	1313	20	15	-48	0.016

Bibliographic reference	**Rith-Najarian, S., Branchaud, C., Beaulieu, O., Gohdes, D., Simonson, G., & Mazze, R. (1998). Reducing lower-extremity amputations due to diabetes. Application of the staged diabetes management approach in a primary care setting. The Journal of family practice, 47(2), 127-132.**

First LEA	1246	7	6	-71	0.0006
Major LEA	1313	11	8	-27	0.49

Incidence rates of Lower-extremity amputation, by intervention period and selected risk groups
Rates per 1000 person-years

Risk group	Standard care	Public Health	Staged diabetes Management
Male	34	36	20
Female	25	11	12
Age <55 years	17	11	13
Age ≥55 years	41	33	18
Diabetes duration <10 years	9	3	1
Diabetes duration ≥10 years	59	47	32

For patients aged ≥ 55 years, Diabetes duration <10 years, Diabetes duration ≥10 years were found to be significantly different when the staged diabetes management period was compared to the baseline rate.

Health related quality of life
Not reported

Source of funding	Not stated
Comments	This study showed at baseline amputations were a frequent complication in this patient group. Reductions in amputation rate were associated with the public health period in which patients were screened for high risk foot problems and then targeting with simple interventions. More substantial reductions in amputation rates were observed with the formation of a foot care team, development of consensus guidelines, use of flow sheets and standing orders, a tracking system for patient follow up and programme evaluation.

Table 12: Birke 2002

Bibliographic reference	**Birke, J. A., Horswell, R., Patout Jr, C. A., & Chen, S. L. (2002). The impact of a staged management approach to diabetes foot care in the Louisiana public hospital system. The Journal of the Louisiana State Medical Society: official organ of the Louisiana State Medical Society, 155(1), 37-42.**
Study type	Observational, retrospective study
Study quality	Summary Location: USA, a disease management initiative started at all Louisiana State public hospitals Intervention: The diabetes disease management initiative implemented standards and targeted goals for the medical care of patients with diabetes in the hospital system. This included annual, comprehensive foot exams and the implementation of Lower Extremity Amputation Prevention programmes at all State hospitals. The five-part LEAP programme recommends: annual foot screening of all patients with diabetes; ongoing foot care education; assistance in the selection of appropriate foot wear; daily foot self-inspection and management of simple problems (nail, callus and skin care). LEAP is designed to reduce foot amputations in diabetes by identifying at-risk feet, focusing efforts on the prevention of foot injuries and managing early lesions. The diabetes foot Program provided regional referral care for high-risk foot problems. The program provides treatment for foot ulcerations or Charcot fractures within 24 hours of referral. The diabetes foot programme uses staff including a physician, nurse practitioner, physical therapists, registered nurse, pedorthist, cast technicians and other support staff. In the staged management approach, all patients receive an initial foot screen to identify the individuals relative risk for foot injury. Patients with loss of protective sensation are considered at risk for developing foot injury and are provided foot care, education, assistance in the selection of proper fitting and designed foot wear and routine follow up to manage simple problems. For higher risk patients wound debridement, moist dressings, contact casts and other specially designed, custom offloading appliances are used to promote healing. (see paper for breakdown of risk and treatment). The programme is designed to provide long term follow up for all patients of increased risk. Comparison: In contrast the standard care in the State hospital system frequently provides poorly co-ordinate treatment of foot problems by primary care, podiatry, surgical and wound care clinics and emergency room providers. Population: all diabetic patients within the Louisiana State University Health Care Services Division Hospitals, data given per 100 person years. Outcome: amputation, hospitalisation.
Number of patients	Total not stated, data given per 100 diabetic patient years
Patient characteristics	Inclusion: All diabetic patients through the staged management approach (although the diabetes foot program provides regional referral care for high-risk foot problems)

Bibliographic reference	**Birke, J. A., Horswell, R., Patout Jr, C. A., & Chen, S. L. (2002). The impact of a staged management approach to diabetes foot care in the Louisiana public hospital system. The Journal of the Louisiana State Medical Society: official organ of the Louisiana State Medical Society, 155(1), 37-42.**
	Exclusion: Not stated Baseline characteristics: Not stated
Intervention	The diabetes disease management initiative implemented standards and targeted goals for the medical care of patients with diabetes in the hospital system. This included annual, comprehensive foot exams and the implementation of Lower Extremity Amputation Prevention programmes at all State hospitals. The five-part LEAP programme recommends: annual foot screening of all patients with diabetes; ongoing foot care education; assistance in the selection of appropriate foot wear; daily foot self-inspection and management of simple problems (nail, callus and skin care). LEAP is designed to reduce foot amputations in diabetes by identifying at-risk feet, focusing efforts on the prevention of foot injuries and managing early lesions. The diabetes foot Program provided regional referral care for high-risk foot problems. The program provides treatment for foot ulcerations or Charcot fractures within 24 hours of referral. The diabetes foot programme uses staff including a physician, nurse practitioner, physical therapists, registered nurse, pedorthist, cast technicians and other support staff. In the staged management approach, all patients receive an initial foot screen to identify the individuals relative risk for foot injury. Patients with loss of protective sensation are considered at risk for developing foot injury and are provided foot care, education, assistance in the selection of proper fitting and designed foot wear and routine follow up to manage simple problems. For higher risk patients wound debridement, moist dressings, contact casts and other specially designed, custom offloading appliances are used to promote healing. (see paper for breakdown of risk and treatment). The programme is designed to provide long term follow up for all patients of increased risk.
Comparison	In contrast the standard care in the State hospital system frequently provides poorly co-ordinate treatment of foot problems by primary care, podiatry, surgical and wound care clinics and emergency room providers.
Length of follow up	Varied, data given per 100 diabetic person years
Location	USA
Outcomes measures and effect size	Rates (and recurrent rates) of foot ulceration, infection and gangrene resulting from diabetes Not reported Resource use and costs (including referral rates)

Bibliographic reference	**Birke, J. A., Horswell, R., Patout Jr, C. A., & Chen, S. L. (2002). The impact of a staged management approach to diabetes foot care in the Louisiana public hospital system. The Journal of the Louisiana State Medical Society: official organ of the Louisiana State Medical Society, 155(1), 37-42.**

Not reported

Rates of hospital admission for foot problems resulting from diabetes

Foot related hospitalisation rates among Louisiana State University Health Care services Hospitals before 1998 and after 1999, the implementation of a disease management initiative with and without access to a diabetes foot program.

Facility	1998 Hospitalisation Rate (per 100 person-years)	1999 Hospitalisation rate (per 100 person-years)	Percent change
1	2.52	1.93	-23%
2	2.50	1.03	-59%
3	1.22	0.19	-84%
4	2.46	2.31	-6%
5	4.09	2.36	-42%
6	2.71	2.34	-14%
7	3.95	3.05	-23%
8	1.07	1.57	+47%
Facility group:			
DMI and DFP	2.44	1.37	-44%
DMI alone	2.71	2.29	-15%

Length of hospital stay
Not reported

Rates and extent of amputation

Foot-related

Foot related amputation rates among Louisiana State University Health Care services Hospitals before 1998 and after 1999,

Bibliographic reference	**Birke, J. A., Horswell, R., Patout Jr, C. A., & Chen, S. L. (2002). The impact of a staged management approach to diabetes foot care in the Louisiana public hospital system. The Journal of the Louisiana State Medical Society: official organ of the Louisiana State Medical Society, 155(1), 37-42.**
	the implementation of a disease management initiative with and without access to a diabetes foot program.

Facility	1998 Amputation Rate (per 100 person-years)	1999 Amputation rate (per 100 person-years)	Percent change
1	0.92	0.90	-2
2	0.71	0.33	-54
3	1.22	0.00	-100
4	0.78	0.23	-71
5	2.32	0.99	-67
6	0.84	0.70	-17
7	1.94	1.56	-20
8	0.48	0.76	+58
Facility group:			
DMI and DFP	0.84	0.56	-33
DMI alone	1.13	0.80	-29

Health related quality of life
Not reported

Source of funding	Not stated
Comments	This study showed mean diabetes foot related hospitalisation rates were lower in 1999 (1.96 per 100 person-years) compared to 1998 (2.61 per 100 person-years) (P<0.001). Diabetes related lower-extremity amputation rates were also lower in 1999 (0.72 per 100 person years) compared to 1998 (1.03 per 100 person-years) (P<0.001). The reduction in the rate of foot-related hospitalisations was greater (P<0.001) in patients after DMI and access to the diabetes foot program (-44%) compared to patients after DMI without access to the DFP (-15%). The reduction in lower extremity amputations in this case however was non-significant.

Table 13: Armstrong 1998

Bibliographic reference	**Armstrong, D. G., & Harkless, L. B. (1998). Outcomes of preventative care in a diabetic foot specialty clinic. The Journal of foot and ankle surgery, 37(6), 460-466.**
Study type	Observational, prospective study
Study quality	Summary Location: USA, University of Texas health science centre Intervention: A multidisciplinary diabetic foot care team, which included aggressive foot care and consistent treatment-based risk classification. Available specialties include general internal medicine, podiatry, endocrinology, opthalmology, diabetes nurse education and nutritional and social services with an active vascular consultancy. (see paper for treatment and follow up algorithm also diagnosis of lower extremity vascular insufficiency) Comparison: Non-compliance was defined as missing >50% of scheduled appointments in any calendar year (n=30) Population: 341 people with diabetes all assessed by University of Texas Foot Classification system. 118 fell into category 0 (protective sensation intact), 98 category 1 (loss of protective sensation), 77 into category 2 (loss of protective sensation with deformity, 48 into category 3 (loss of protective sensation, deformity, previous history of ulcer or amputation). Patients were stratified based on their compliance to follow up appointments and foot category. Observation period was over 3 years. No subjects falling into category 4 (noninfected ulcer/Charcot) or 5 (infection) were enrolled. Outcome: ulceration, reulceration and amputation
Number of patients	Total n= 341
Patient characteristics	Inclusion: Presence of diabetes mellitus Evaluation by medicine service within the past 3 months at the time of enrolment HbA1c performed in the past 3 months Age 18-80 years of age Exclusion: Not stated Baseline characteristics: Male: 57.8% Mean age: 53.2 ± 11.8 years

Bibliographic reference	**Armstrong, D. G., & Harkless, L. B. (1998). Outcomes of preventative care in a diabetic foot specialty clinic. The Journal of foot and ankle surgery, 37(6), 460-466.**
	Compliant group: Time with diabetes mellitus: 7.5 ± 6.3 Vibration pressure threshold: 29.7 ± 14.2 HbA1c at enrolment: 9.1 ± 1.9 Non-compliant group: Time with diabetes mellitus: 9.0 ± 6.1 Vibration pressure threshold: 28.6 ± 4.0 HbA1c at enrolment: 9.2 ± 1.7
Intervention	A multidisciplinary diabetic foot care team, which included aggressive foot care and consistent treatment-based risk classification. Available specialties include general internal medicine, podiatry, endocrinology, opthalmology, diabetes nurse education and nutritional and social services with an active vascular consultancy. (see paper for treatment and follow up algorithm also diagnosis of lower extremity vascular insufficiency)
Comparison	Non-compliance was defined as missing >50% of scheduled appointments in any calendar year (n=30) Population: 341 people with diabetes all assessed by University of Texas Foot Classification system. 118 fell into category 0 (protective sensation intact), 98 category 1 (loss of protective sensation), 77 into category 2 (loss of protective sensation with deformity, 48 into category 3 (loss of protective sensation, deformity, previous history of ulcer or amputation). Patients were stratified based on their compliance to follow up appointments and foot category. Observation period was over 3 years. No subjects falling into category 4 (noninfected ulcer/Charcot) or 5 (infection) were enrolled.
Length of follow up	3 year observation period
Location	USA
Outcomes measures and effect size	Rates (and recurrent rates) of foot ulceration, infection and gangrene resulting from diabetes When comparing the higher risk patients in each cohort (category 3), those in the non-compliant group were approximately 54 times more likely to ulcerate than patients who returned regularly for their scheduled care. (81.8% ulcer prevalence vs 5.4% p<0.0001) Odds ratio 54.0 Confidence interval 7.5-1,425.0)

<table>
<tr><th>Bibliographic reference</th><th>Armstrong, D. G., & Harkless, L. B. (1998). Outcomes of preventative care in a diabetic foot specialty clinic. The Journal of foot and ankle surgery, 37(6), 460-466.</th></tr>
<tr><td></td><td>Resource use and costs (including referral rates)
Not reported

Rates of hospital admission for foot problems resulting from diabetes
Not reported

Length of hospital stay
Not reported

Rates and extent of amputation

When comparing the higher risk patients in each cohort (category 3), those in the non-compliant group were over 20 times more likely to receive amputation than category 3 compliant patients. (45.5% amputation prevalence vs 2.7% p<0.002) Odds ratio 2.5-819.0)

Health related quality of life
Not reported

<table>
<tr><th>Group</th><th>Compliant group, n</th><th>Incidence of ulceration/1000/year</th><th>Incidence of amputation/1000/year</th><th>Non compliant group, n</th><th>Incidence of ulceration/1000/year</th><th>Incidence of amputation/1000/year</th></tr>
<tr><td>Foot category 0</td><td>108</td><td>0</td><td>0</td><td>10</td><td>0</td><td>0</td></tr>
<tr><td>Foot category 1</td><td>94</td><td>0</td><td>0</td><td>4</td><td>83.3</td><td>0</td></tr>
<tr><td>Foot category 2</td><td>72</td><td>3.5</td><td>0</td><td>5</td><td>66.6</td><td>0</td></tr>
<tr><td>Foot category 3</td><td>37</td><td>18.0</td><td>9.0</td><td>11</td><td>272.7</td><td>151.5</td></tr>
<tr><td>total</td><td>311</td><td>3.1</td><td>1.1</td><td>30</td><td>122.2</td><td>5.5</td></tr>
</table>
</td></tr>
<tr><td>Source of funding</td><td>Not stated</td></tr>
<tr><td>Comments</td><td>This study showed that a multidisciplinary care team may be effective in reducing ulceration and amputation. Patient noncompliance to this service seems to be associated with a significantly higher prevalence of amputation and ulceration.</td></tr>
</table>

Table 14: Schraer 2004

Bibliographic reference	**Schraer, C. D., Weaver, D., Naylor, J. L., Provost, E., & Mayer, A. M. (2004). Reduction of amputation rates among Alaska Natives with diabetes following the development of a high-risk foot program. International journal of circumpolar health, 63.**
Study type	Observational, retrospective study
Study quality	Summary Location: USA, Alaska, high risk foot programme Intervention: Initially involving a surgical podiatrist who provided training to local staff and performed preventive and reconstructive surgery on several patients with impending amputations. The programme then provided training for a physiotherapist to become a pedorthist who established long-term maintenance by conducting diabetic foot clinics routinely at a referral centre in anchorage. A system was established in a common database management program to track the patient's foot conditions. Patient education was emphasised. A risk category system was found useful in planning follow up for diabetic foot care. The physiotherapist/pedorthist provided routine foot examination, toenail and callus trimming, evaluation and fitting for custom shoes, and orthotics. This person also worked in consultation with Orthopaedics, Vascular Surgery and the Diabetes Clinic to provide conventional wound care management and offloading as indicated. The programme also provided training for village aids. Comparison: Before and after inception of the foot care programme. Non-systemised foot services before this period. Population: Alaska's Indian, Eskimo and Aleut populations. Half of this population do not have road access to hospitals or physicians, presenting a challenge in the attempt to prevent lower extremity amputations. Outcome: amputation
Number of patients	Total person years: Pre-program= 4226.5 Post-program= 5908
Patient characteristics	Inclusion: Diabetes and diabetes related lower extremity amputations Exclusion: Not stated Baseline characteristics:

Bibliographic reference	**Schraer, C. D., Weaver, D., Naylor, J. L., Provost, E., & Mayer, A. M. (2004). Reduction of amputation rates among Alaska Natives with diabetes following the development of a high-risk foot program. International journal of circumpolar health, 63.**
	Not reported
Intervention	Initially involving a surgical podiatrist who provided training to local staff and performed preventive and reconstructive surgery on several patients with impending amputations. The programme then provided training for a physiotherapist to become a pedorthist who established long-term maintenance by conducting diabetic foot clinics routinely at a referral centre in anchorage. A system was established in a common database management program to track the patient's foot conditions. Patient education was emphasised. A risk category system was found useful in planning follow up for diabetic foot care. The physiotherapist/pedorthist provided routine foot examination, toenail and callus trimming, evaluation and fitting for custom shoes, and orthotics. This person also worked in consultation with Orthopaedics, Vascular Surgery and the Diabetes Clinic to provide conventional wound care management and offloading as indicated. The programme also provided training for village aids.
Comparison	Before and after inception of the foot care programme. Non-systemised foot services before this period.
Length of follow up	6 year observation period
Location	USA
Outcomes measures and effect size	Rates (and recurrent rates) of foot ulceration, infection and gangrene resulting from diabetes Not reported Resource use and costs (including referral rates) Not reported Rates of hospital admission for foot problems resulting from diabetes Not reported Length of hospital stay Not reported Rates and extent of amputation All diabetes related amputations amongst all Alaska Natives with Diabetes 1996-2001

Bibliographic reference	**Schraer, C. D., Weaver, D., Naylor, J. L., Provost, E., & Mayer, A. M. (2004). Reduction of amputation rates among Alaska Natives with diabetes following the development of a high-risk foot program. International journal of circumpolar health, 63.**

Ethnic group	Pre-program (1996-1998)			Post-program (1999-2001)			Reduction %	P value
	Diabetic person years	Amputations	Incidence per 1000	Diabetic person-years	Amputations	Incidence per 1000		
Eskimo	1355	9	6.6	1979.5	4	2.0	70%	0.047
Indian	1950	7	3.6	2655.5	8	3.0	16%	0.94
Aleut	921.5	16	17.4	1273	4	3.1	82%	<0.001
All Native	4226.5	32	7.6	5908	16	2.7	64%	<0.001

All diabetes related amputations amongst all Alaska Natives with Diabetes ≥10 years duration 1996-2001

Ethnic group	Pre-program (1996-1998)			Post-program (1999-2001)			Reduction %	P value
	Diabetic person years	Amputations	Incidence per 1000	Diabetic person-years	Amputations	Incidence per 1000		
Eskimo	405.5	7	17.3	501.5	4	8.0	54%	0.235
Indian	610.5	7	11.5	742	6	8.1	29%	0.722
Aleut	326	8	24.5	384.5	1	2.6	89%	0.01
All Native	1342	22	16.4	1628	11	6.8	59%	0.021

Health related quality of life
Not reported

Source of funding	Not stated

Bibliographic reference	**Schraer, C. D., Weaver, D., Naylor, J. L., Provost, E., & Mayer, A. M. (2004). Reduction of amputation rates among Alaska Natives with diabetes following the development of a high-risk foot program. International journal of circumpolar health, 63.**
Comments	This study showed that in populations living in an isolated region, diabetic amputations can be prevented by a co-ordinated system to identify high-risk feet and provide preventive treatment and education in the context of a comprehensive diabetes management program in an integrated health system.

Table 15: Lavery 2005

Bibliographic reference	**Lavery, L. A., Wunderlich, R. P., & Tredwell, J. L. (2005). Disease management for the diabetic foot: effectiveness of a diabetic foot prevention program to reduce amputations and hospitalizations. Diabetes research and clinical practice, 70(1), 31-37.**
Study type	Observational, prospective study
Study quality	Summary Location: USA, diabetic foot disease management program Intervention: Implementation of a lower extremity disease management program consisting of screening and treatment protocols diabetic members in a managed care organization.Screening consisted of evaluation of neuropathy, peripheral vascular disease, deformities, foot pressures and history of lower extremity pathology. Patients were stratified into high and low risk groups and implemented preventive or acute care protocols. Utilization was tracked for 28 months and compared to 12 months of historic data prior to implementation of the disease management program. Staff included pedorthist and podiatrist care. (more information on risk classification, screening criteria and interventions can be found in paper) Comparison: Before and after establishment of the disease management program. Population: 2738 persons with diabetes Outcome: amputation, diabetic foot related admissions, average length of stay for acute bed days
Number of patients	Total n= 2738 Baseline= 1708 Disease management programme= 2738
Patient characteristics	Inclusion: All diabetic members in a managed care organisation

Bibliographic reference	**Lavery, L. A., Wunderlich, R. P., & Tredwell, J. L. (2005). Disease management for the diabetic foot: effectiveness of a diabetic foot prevention program to reduce amputations and hospitalizations. Diabetes research and clinical practice, 70(1), 31-37.**
	Exclusion: Not stated Baseline characteristics: Average age: 67.2 ± 8.5 years (range 23-90) Mexican America: 42.8% Non-hispanic white: 53.2% African American: 4.0% Duration of diabetes: 11.2 ± 9.5 years (range 0-32)
Intervention	Implementation of a lower extremity disease management program consisting of screening and treatment protocols diabetic members in a managed care organization.Screening consisted of evaluation of neuropathy, peripheral vascular disease, deformities, foot pressures and history of lower extremity pathology. Patients were stratified into high and low risk groups and implemented preventive or acute care protocols. Utilization was tracked for 28 months and compared to 12 months of historic data prior to implementation of the disease management program. Staff included pedorthist and podiatrist care. (more information on risk classification, screening criteria and interventions can be found in paper)
Comparison	Before and after establishment of the disease management program
Length of follow up	Utilisation tracked for 28 months and compared to 12 months of historical data
Location	USA
Outcomes measures and effect size	Rates (and recurrent rates) of foot ulceration, infection and gangrene resulting from diabetes Not reported Resource use and costs (including referral rates) Not reported Rates of hospital admission for foot problems resulting from diabetes The number of foot-related hospital admissions decreased 37.8% from 22.86 per 1000 members per year to 14.23 (37.8%)

Bibliographic reference	**Lavery, L. A., Wunderlich, R. P., & Tredwell, J. L. (2005). Disease management for the diabetic foot: effectiveness of a diabetic foot prevention program to reduce amputations and hospitalizations. Diabetes research and clinical practice, 70(1), 31-37.**
	The number of skilled nursing facility admissions per 1000 members per year decreased 69.8% Length of hospital stay The average inpatient length of stay was reduced 21.7% from 4.75 to 3.72 (p=<0.05) The length of skilled nursing facility bed days decreased 38.2% from 8.72 to 6.52 (p<0.05) Rates and extent of amputation After the implementation of the health disease management program the incidence of amputations decreased 47.4% from 12.89 per 1000 diabetics per year to 6.18 (P=<0.05) Health related quality of life Not reported
Source of funding	Not stated
Comments	This study showed that the disease management model and protocol to screen, risk stratify and provide prevention service for high-risk patients was effective in reducing lower extremity amputations, hospitalisations and length of hospitalisation in a health maintenance organisation.

Table 16: Dargis 1999

Bibliographic reference	**Dargis, V., Pantelejeva, O. L. G. A., Jonushaite, A. L. A. N. T. A., Vileikyte, L. O. R. E. T. T. A., & Boulton, A. J. (1999). Benefits of a multidisciplinary approach in the management of recurrent diabetic foot ulceration in Lithuania: a prospective study. Diabetes care, 22(9), 1428-1431.**
Study type	Observational, prospective study

<table>
<tr><th>Bibliographic reference</th><th>Dargis, V., Pantelejeva, O. L. G. A., Jonushaite, A. L. A. N. T. A., Vileikyte, L. O. R. E. T. T. A., & Boulton, A. J. (1999). Benefits of a multidisciplinary approach in the management of recurrent diabetic foot ulceration in Lithuania: a prospective study. Diabetes care, 22(9), 1428-1431.</th></tr>
<tr><td>Study quality</td><td>Summary
Location: Lithuania, a single rehabilitation hospital. Patients were referred from 7 outpatient clinics and were compared to patients treated in 7 outpatient clinics in other cities.
Intervention: A multidisciplinary foot clinic. The intervention group was followed by a multidisciplinary team of physicians, nurse and podiatrists with regular podiatry and re-education every 3 months and the provision of specialty footwear as required. Staff consisted of a diabetologist, rehabilitation physician, orthopaedic surgeon, podiatrist, and shoe makers.
Comparison: The standard treatment participants were provided with identical standard foot care education and advice, all patients were seen at 3 month intervals. Subjects in this group received education provided by the local endocrinologist or nurse and follow up review examinations from local physicians every 3 months.
Population: A total of 145 patients with a past history of neuropathic foot ulcers but no evidence of peripheral vascular disease were followed for 2 years. Patients with Charcot foot or history of amputation were excluded.
Outcome: amputation, ulceration</td></tr>
<tr><td>Number of patients</td><td>Total n= 145</td></tr>
<tr><td>Patient characteristics</td><td>Inclusion:

Previous neuropathic ulceration
Neurological disability score ≥6 and/or vibratory perception threshold ≥25 V
Ankle brachial pressure index ≥0.9 and ≥1 palpable pulse per foot

Exclusion:
Past history of amputations
Charcot neuropathy
Cannot follow simple instructions

Baseline characteristics:
<table>
<tr><td></td><td>Intervention group</td><td>Standard treatment group</td></tr>
<tr><td>Sex F/M</td><td>29/27</td><td>47/42</td></tr>
<tr><td>Age y</td><td>59.2 ±13.4</td><td>58.5 ±11.5</td></tr>
<tr><td>Diabetic duration, y</td><td>14.0 ± 7.1</td><td>15.6 ± 7.8</td></tr>
</table></td></tr>
</table>

<table>
<tr><td>Bibliographic reference</td><td>Dargis, V., Pantelejeva, O. L. G. A., Jonushaite, A. L. A. N. T. A., Vileikyte, L. O. R. E. T. T. A., & Boulton, A. J. (1999). Benefits of a multidisciplinary approach in the management of recurrent diabetic foot ulceration in Lithuania: a prospective study. Diabetes care, 22(9), 1428-1431.</td></tr>
<tr><td></td><td>
<table>
<tr><td>Type of diabetes type 2/1</td><td>47/9</td><td>67/22</td></tr>
<tr><td>Insulin/oral</td><td>40/16</td><td>71/18</td></tr>
<tr><td>Neurological disability score</td><td>8.1 ± 1.4</td><td>7.9 ± 1.7</td></tr>
<tr><td>Vibratory perception threshold</td><td>31.1 ± 12.1</td><td>33.9 ± 11.2</td></tr>
<tr><td>Ankle brachial pressure index</td><td>1.14 ± 0.14</td><td>1.10 ± 0.17</td></tr>
<tr><td>Previous ulcers</td><td>2.3 ± 0.9</td><td>2.1 ± 1.0</td></tr>
<tr><td>Foot deformities</td><td>87.5</td><td>85.4</td></tr>
</table>
</td></tr>
<tr><td>Intervention</td><td>A multidisciplinary foot clinic. The intervention group was followed by a multidisciplinary team of physicians, nurse and podiatrists with regular podiatry and re-education every 3 months and the provision of specialty footwear as required. Staff consisted of a diabetologist, rehabilitation physician, orthopaedic surgeon, podiatrist, and shoe makers.</td></tr>
<tr><td>Comparison</td><td>The standard treatment participants were provided with identical standard foot care education and advice, all patients were seen at 3 month intervals. Subjects in this group received education provided by the local endocrinologist or nurse and follow up review examinations from local physicians every 3 months.</td></tr>
<tr><td>Length of follow up</td><td>2 years</td></tr>
<tr><td>Location</td><td>Lithuania</td></tr>
<tr><td>Outcomes measures and effect size</td><td>Rates (and recurrent rates) of foot ulceration, infection and gangrene resulting from diabetes

New recurrent ulceration presentations
New ulcers and ulcers appearing at a previous ulcer site are included in the term recurrent ulcers, only the first recurrence was counted.
Intervention group (n=56)= 30.4%
Standard care group (n=89)= 58.4%
Odds ratio (95% CI)= 0.31 (0.14-0.67), P<0.001 i.e. significant difference

Resource use and costs (including referral rates)</td></tr>
</table>

Bibliographic reference	**Dargis, V., Pantelejeva, O. L. G. A., Jonushaite, A. L. A. N. T. A., Vileikyte, L. O. R. E. T. T. A., & Boulton, A. J. (1999). Benefits of a multidisciplinary approach in the management of recurrent diabetic foot ulceration in Lithuania: a prospective study. Diabetes care, 22(9), 1428-1431.**
	Not reported Rates of hospital admission for foot problems resulting from diabetes Hospitalisation Intervention group (n=56)= 2 patients Standard care group (n=89)= 8 patients Length of hospital stay Not reported Rates and extent of amputation Amputations Intervention group (n=56)= 7% (3 minor and 1 major) Standard care group (n=89)= 13.7% (8 minor and 4 major) Health related quality of life Not reported
Source of funding	
Comments	This study showed significantly fewer recurrent ulcerations in the group treated with multidisciplinary care including provision of specialist footwear over those who received standard care.

Table 17: Driver 2010

Bibliographic reference	**Driver, V. R., Goodman, R. A., Fabbi, M., French, M. A., & Andersen, C. A. (2010). The impact of a podiatric lead limb preservation team on disease outcomes and risk prediction in the diabetic lower extremity: a retrospective cohort study. Journal of the American Podiatric Medical Association, 100(4), 235-241.**
Study type	Observational, retrospective cohort study
Study quality	Summary Location: a military regional tertiary care hospital serving a beneficiary population of approximately 350000 individuals. Population: random sample of 540 patients with diabetes mellitus from a population of 8,422 with diabetes. A random selection of patients being referred to the limb preservation team were included if follow up was at least 3 years. Intervention: The referral to a limb preservation team Outcome: hospitalization, infection, amputation, ulceration and survival 1. The method of allocation to intervention groups was unrelated to potential confounding factors (the reason for participant allocation to intervention is not expected to affect the outcome under study)? There was no allocation between groups. Groups were split by those who were referred to a limb preservation team and those who were not. 2. Attempts were made with the design or analysis to balance the comparison groups for potential confounders? There were no attempts to balance groups for confounders 3. The groups were comparable at baseline, including all major confounding factors? Groups were not comparable at baseline including all major confounding factors. The group referred to the limb preservation team had a greater proportion of participants with ulceration and those who had a higher grade of ulcer. There were a greater proportion of patients with infection in the limb preservation group. More of these patients also had a history of ulcer, pedal deformity, callus and neuropathy. 4. The comparison groups received the same care and support apart from the interventions studied? Unclear if comparison groups received comparable care other than due to the changes implemented by the foot protection team. 5. Participants receiving care and support were kept blind to intervention allocation? Participants were not blinded to intervention allocation 6. Individuals administering care and support were kept blind to intervention allocation? Individuals administering care were not blinded to intervention allocation 7. All groups were followed for an equal length of time, or analysis was adjusted to allow for differences in length of follow up? Data was taken retrospectively, including only participants who had at least a 3 year follow up available. Data was split by patient quarter in analysis. 8. Groups were comparable for intervention completion? Unclear if groups were comparable for compliance or intervention completion or for general adherence to treatment. 9. The groups were comparable with respect to the availability of outcome data?

Bibliographic reference	**Driver, V. R., Goodman, R. A., Fabbi, M., French, M. A., & Andersen, C. A. (2010). The impact of a podiatric lead limb preservation team on disease outcomes and risk prediction in the diabetic lower extremity: a retrospective cohort study. Journal of the American Podiatric Medical Association, 100(4), 235-241.**
	There was no loss to follow up reported. Participants were only included if 3 years of follow up were available. 10. The study had an appropriate length of follow up? Observation period was appropriate (at least 3 years) 11. The study used a precise definition of outcome? The study did use a clear definition of amputation and ulceration. 12. A valid and reliable method was used to determine the outcome? A valid and reliable method was not used, data was taken retrospectively through electronic chart review 13. Investigators were kept blind to participant's exposure to the intervention? Investigators were not kept blinded to exposure to the intervention 14. Investigators were kept blind to other important confounding factors? Investigators were not kept blinded to other important confounding factors .
Number of patients	Total n= 485 diabetic patients Number of people seen under podiatric specialist service=311 Number seen by non-limb preservation team service= 174
Patient characteristics	Patients taken from: USA Inclusion: Diabetes mellitus Mean follow up was at least 3 years Seen between June 1999 and June 2004 Exclusion: Not stated Baseline characteristics: No baseline characteristics provided between treatment groups Overall: age (>70 years)= not reported

Bibliographic reference	**Driver, V. R., Goodman, R. A., Fabbi, M., French, M. A., & Andersen, C. A. (2010). The impact of a podiatric lead limb preservation team on disease outcomes and risk prediction in the diabetic lower extremity: a retrospective cohort study. Journal of the American Podiatric Medical Association, 100(4), 235-241.**
	Requiring insulin= not reported Oral hypoglycaemics alone= not reported Male: 305 White: 393 History of amputation 45 History of ulceration: 64 Cause of foot lesion: not reported Peripheral neuropathy: not reported Wagner grade 3-4: not reported Hypertension: not reported Smoking: not reported Coronary disease: 73% Chronic renal insufficiency: not reported End stage renal failure: not reported Extent of ulcers >2.5 cm: not reported Depth of tissue loss >2 mm: not reported Groups were not comparable at baseline including all major confounding factors. The group referred to the limb preservation team had a greater proportion of participants with ulceration and those who had a higher grade of ulcer. There were a greater proportion of patients with infection in the limb preservation group. More of these patients also had a history of ulcer, pedal deformity, callus and neuropathy. Wound classification: university of Texas Limb protection team group No ulceration: 196 Grade 1: 53 Grade 2: 19 Grade 3: 40 Total 311 Non limb protection team group No ulceration: 151 Grade 1: 14 Grade 2: 2 Grade 3: 7 Total 174

Bibliographic reference	**Driver, V. R., Goodman, R. A., Fabbi, M., French, M. A., & Andersen, C. A. (2010). The impact of a podiatric lead limb preservation team on disease outcomes and risk prediction in the diabetic lower extremity: a retrospective cohort study. Journal of the American Podiatric Medical Association, 100(4), 235-241.**
Intervention	Referral to the limb protection team: Employing: Podiatric and vascular surgery, a orthotist, a wound care nurse and a research unit. These patients received comprehensive inpatient and outpatient evaluation and care, including advanced wound care management, medical and surgical management of infection, at least a quarterly clinical visit, ongoing education programmes, orthotic devices, and extra depth custom shoes as required.
Comparison	Non- limb preservation team service (non-specialty, no further details)
Length of follow up	mean follow up 3.8 ± 1.5 years
Location	USA
Outcomes measures and effect size	Rates (and recurrent rates) of foot ulceration, infection and gangrene resulting from diabetes Ulceration Limb preservation team group= mean 1.8 per year Non-limb preservation team group= mean 2.7 ulcers per year Not statistically significant Rates of hospital admission for foot problems resulting from diabetes No data provided Rates and extent of amputation Minor amputation Limb preservation team group= 52 of 311 patients (17%) Non-limb preservation team group= 27 of 174 patients (15%) P=0.0006 i.e. significant difference

Bibliographic reference	**Driver, V. R., Goodman, R. A., Fabbi, M., French, M. A., & Andersen, C. A. (2010). The impact of a podiatric lead limb preservation team on disease outcomes and risk prediction in the diabetic lower extremity: a retrospective cohort study. Journal of the American Podiatric Medical Association, 100(4), 235-241.**
	Health related quality of life Survival Limb preservation team group= 7.7% died Non-limb preservation team group= 19.5% died P=0.0001 i.e. significant difference
Source of funding	Unclear source of funding
Comments	Among patients treated in a speciality multidiscipline podiatric medical setting, the proportion of amputations that were minor was significantly increased and survival was significantly improved. Participants who received the specialty podiatric care had a higher proportion of risk factors. NB see in paper for clues to higher risk groups (referral criteria?)

Table 18: Carrington 2001

Bibliographic reference	**Carrington, A. L., Abbott, C. A., Griffiths, J., Jackson, N., Johnson, S. R., Kulkarni, J., ... & Boulton, A. J. (2001). A foot care program for diabetic unilateral lower-limb amputees. Diabetes care, 24(2), 216-221.**
Study type	Observational, prospective study
Study quality	Summary Location: United Kingdom, subregional rehabilitation center for prosthetic care Intervention: Focused foot care program. Peripheral vascular and nerve assessment, education and podiatry were provided for each patient. Comparison: Matched patients without the program. Patients who had been referred to the Disablement Services Centre between January 1990 and December 1991 before the establishment of the diabetes amputee foot clinic.(n=148) These patients received the same prosthetic care but did not have access to the specialist foot care programme. Population: 143 diabetic lower-limb unilateral amputees referred to a subregional rehabilitation clinic for prosthetic care. Patients were observed for a 2 year period after initial assessment. Outcome: contralateral limb amputation.

<table>
<tr><th>Bibliographic reference</th><th>Carrington, A. L., Abbott, C. A., Griffiths, J., Jackson, N., Johnson, S. R., Kulkarni, J., ... & Boulton, A. J. (2001). A foot care program for diabetic unilateral lower-limb amputees. Diabetes care, 24(2), 216-221.</th></tr>
<tr><td>Number of patients</td><td>Total n= 291</td></tr>
<tr><td>Patient characteristics</td><td>Inclusion:
All new diabetic unilateral lower-limb amputee referrals to the rehabilitation centre

Exclusion:
None stated

Baseline characteristics:

<table>
<tr><td></td><td>Patients referred before the clinic</td><td>Patients seen in the clinic</td></tr>
<tr><td>n</td><td>148</td><td>143</td></tr>
<tr><td>Age, y</td><td>67.81 ± 9.99</td><td>65.20 ± 11.07</td></tr>
<tr><td>Diabetes duration, y</td><td>12.56 ± 12.70</td><td>14.35 ± 11.91</td></tr>
<tr><td>Sex M/F</td><td>105/43</td><td>101/42</td></tr>
</table>
</td></tr>
<tr><td>Intervention</td><td>Focused foot care program. Peripheral vascular and nerve assessment, education and podiatry were provided for each patient.</td></tr>
<tr><td>Comparison</td><td>Matched patients without the program. Patients who had been referred to the Disablement Services Centre between January 1990 and December 1991 before the establishment of the diabetes amputee foot clinic.(n=148) These patients received the same prosthetic care but did not have access to the specialist foot care programme.</td></tr>
<tr><td>Length of follow up</td><td>2 year follow up after initial assessment</td></tr>
<tr><td>Location</td><td>United Kingdom</td></tr>
<tr><td>Outcomes measures and effect size</td><td>Rates (and recurrent rates) of foot ulceration, infection and gangrene resulting from diabetes
Not reported

Resource use and costs (including referral rates)
Not reported

Rates of hospital admission for foot problems resulting from diabetes
Not reported</td></tr>
</table>

<table>
<tr><th>Bibliographic reference</th><th>Carrington, A. L., Abbott, C. A., Griffiths, J., Jackson, N., Johnson, S. R., Kulkarni, J., ... & Boulton, A. J. (2001). A foot care program for diabetic unilateral lower-limb amputees. Diabetes care, 24(2), 216-221.</th></tr>
<tr><td></td><td>Length of hospital stay
Not reported

Rates and extent of amputation

Major amputation rate (above or below knee)

<table>
<tr><th></th><th>Patients referred before the clinic (n=148)</th><th>Patients seen in the clinic (n=143)</th><th>P value</th></tr>
<tr><td>Bilateral amputations</td><td>21 (14.2%)</td><td>22 (15.4%)</td><td>NS</td></tr>
<tr><td>Number of deaths</td><td>39</td><td>27</td><td>NS</td></tr>
<tr><td>Bilateral amputation and death</td><td>3</td><td>1</td><td>NS</td></tr>
</table>

Health related quality of life
Not reported</td></tr>
<tr><td>Source of funding</td><td>Department of Health, London UK</td></tr>
<tr><td>Comments</td><td>This study did not show a significant reduction in bilateral amputations in diabetic unilateral amputees, despite the establishment of the foot clinic at the rehabilitation centre.</td></tr>
</table>

Table 19: Nason 2013

Bibliographic reference	Nason, G. J., Strapp, H., Kiernan, C., Moore, K., Gibney, J., Feeley, T. M., ... & Tierney, S. (2013). The cost utility of a multi-disciplinary foot protection clinic (MDFPC) in an Irish hospital setting. Irish journal of medical science, 182(1), 41-45.
Study type	Observational, prospective study (audit, cost effectiveness)

Bibliographic reference	**Nason, G. J., Strapp, H., Kiernan, C., Moore, K., Gibney, J., Feeley, T. M., ... & Tierney, S. (2013). The cost utility of a multi-disciplinary foot protection clinic (MDFPC) in an Irish hospital setting. Irish journal of medical science, 182(1), 41-45.**
Study quality	Summary Location: An Irish university hospital. Intervention: a dedicated bi-weekly consultant led multidisciplinary foot protection clinic employing vascular surgery, endocrinology, orthopaedic surgery, podiatry, orthotics, tissue viability established in a Irish university hospital as part of an integrated foot protection service. Population: 313 referrals seen during a 2 year study period Outcome: amputations, hospitalisation, length of hospitalisation 1. The method of allocation to intervention groups was unrelated to potential confounding factors (the reason for participant allocation to intervention is not expected to affect the outcome under study)? Controls were taken from before the period that the clinic was established. Unclear if any other confounding factors may have affected the results during this time. 2. Attempts were made with the design or analysis to balance the comparison groups for potential confounders? There were no attempts to balance groups for confounders 3. The groups were comparable at baseline, including all major confounding factors? Unclear if groups were comparable at baseline including all major confounding factors 4. The comparison groups received the same care and support apart from the interventions studied? Unclear if comparison groups received comparable care other than due to the changes implemented by the foot protection clinic. 5. Participants receiving care and support were kept blind to intervention allocation? Participants were not blinded to intervention allocation 6. Individuals administering care and support were kept blind to intervention allocation? Individuals administering care were not blinded to intervention allocation 7. All groups were followed for an equal length of time, or analysis was adjusted to allow for differences in length of follow up? Data was taken prospectively for 2 years. Observational period was over 4 years. Unclear if participants were followed for an equal length of follow up. 8. Groups were comparable for intervention completion? Unclear if groups were comparable for compliance or intervention completion or for general adherence to treatment. 9. The groups were comparable with respect to the availability of outcome data? There was no loss to follow up reported. 10. The study had an appropriate length of follow up? Observation period was appropriate 4 years, length of follow up was most likely variable and may not have been appropriate in

Bibliographic reference	Nason, G. J., Strapp, H., Kiernan, C., Moore, K., Gibney, J., Feeley, T. M., ... & Tierney, S. (2013). The cost utility of a multi-disciplinary foot protection clinic (MDFPC) in an Irish hospital setting. Irish journal of medical science, 182(1), 41-45.
	all cases. 11. The study used a precise definition of outcome? The study used a clear definition of amputation and hospitalisation length of stay. 12. A valid and reliable method was used to determine the outcome? Unclear if a valid and reliable method was used to determine outcome. Data was taken from hospital databases that may not have been accurate in all cases. 13. Investigators were kept blind to participant's exposure to the intervention? Investigators were not kept blinded to exposure to the intervention 14. Investigators were kept blind to other important confounding factors? Investigators were not kept blinded to other important confounding factors .
Number of patients	Total n= 251 patients at high risk of foot ulceration (neuropathy or absent pulses with deformity), with active ulceration or previous minor amputations. 131 in the control period 120 in the study period
Patient characteristics	Patients taken from: Ireland Inclusion: patients at high risk of foot ulceration (neuropathy or absent pulses with deformity), with active ulceration or previous minor amputations. Exclusion: Not defined Baseline characteristics: Not provided
Intervention	Treatment under a dedicated bi-weekly consultant led multidisciplinary foot protection clinic employing vascular surgery,

Bibliographic reference	Nason, G. J., Strapp, H., Kiernan, C., Moore, K., Gibney, J., Feeley, T. M., ... & Tierney, S. (2013). The cost utility of a multi-disciplinary foot protection clinic (MDFPC) in an Irish hospital setting. Irish journal of medical science, 182(1), 41-45.
	endocrinology, orthopaedic surgery, podiatry, orthotics, tissue viability established in an Irish university hospital as part of an integrated foot protection service. All diabetic patients at high risk of foot ulceration (neuropathy or absent pulses with deformity), with active ulceration or previous minor amputations are referred to the clinic for structured assessment. (skin and soft tissue sensation, perfusion and structural deformity. Patients are streamlined into two categories, those for preventive management and those for intervention In patients considered to be high risk for ulceration, intervention is focused on the prevention of ulceration and diabetic foot complications. Glycaemic control and cardiovascular risk factors are optimised by the endocrinology service. Patients are treated with best medical management, educated regarding personal foot care and hygiene and advised regarding smoking cessation and lifestyle. Patients are then provided with footwear and casted insoles as required. Patients with active ulceration are treated more aggressively, have more frequent clinic visits, including debridement of calluses, infected and necrotic tissue, assessment with a view to early admission from clinic for high dose intravenous antibiotics and further intervention for revascularisation such as angioplasty in order to expediate wound healing in those with associated arterial disease.
Comparison	Care before establishment of the above clinic and treatment pathway (undefined care)
Length of follow up	4 years observation period, 2 years before and after the establishment of the clinic.
Location	Ireland
Outcomes measures and effect size	Rates (and recurrent rates) of foot ulceration, infection and gangrene resulting from diabetes No outcomes reported Rates of hospital admission for foot problems resulting from diabetes The establishment of the foot protection clinic coincided with a reduction in the median length of stay for each admission with

Bibliographic reference	**Nason, G. J., Strapp, H., Kiernan, C., Moore, K., Gibney, J., Feeley, T. M., ... & Tierney, S. (2013). The cost utility of a multi-disciplinary foot protection clinic (MDFPC) in an Irish hospital setting. Irish journal of medical science, 182(1), 41-45.**
	diabetic foot complication as the presenting complaint under diabetic foot clinic= 12 days (range 1-258) Control period= 15 days (range 4-194) Rates and extent of amputation Number of above knee amputations Under diabetic foot clinic period= 3 amputations Control period= 8 amputations Number of below knee amputations Under diabetic foot clinic period= 4 amputations Control period= 4 amputations Health related quality of life No data reported
Source of funding	Unclear source of funding
Comments	The number of major amputations decreased from 12 during the control period to 7 in the study period. There was also an overall saving of 114063 euros associated with the introduction of the foot protection clinic.

F.4 Review question 4 full evidence tables

1.1 Evidence tables: Assessment tests

Table 20: included studies for assessment tests

Study	ID	Number of patients	Patient characteristics	Prognostic test	Length of follow-up	Outcome measures	Results	Comments
Nather (2008) Prospective cohort Singapore	1820	202 patients treated in outpatient multi-disciplinary hospital setting for diabetic foot problems Jan 2005 to May 2006	Mean age 60 years (range 21-91 years) Mean duration of diabetes range 1 to 48 years Male 50% Ethnicity: Chinese 45.5% Malay 32.7% Indian 17.8% Other 4% No exclusions stated	Prognostic test of interest: 5.07 Semmes-Weinstein monofilament. Other prognostic factors examined in univariate and multivariate analysis including patient characteristics, comorbidities, life style risk factors, complications.	Not stated	Lower extremity amputation	Limb loss in 30/202 patients (14.8%) OR 2.0 (1.1-3.8) P=0.029 Monofilament sensitivity not significant in multivariate analysis. Only PVD and infection were significant predictors of limb loss.	Authors conclude that sensory neuropathy by monofilament is a univariate predictive factor for limb loss. However, monofilament sensitivity not significant in step-wise logistical regression.
Boyko (2006)	2285	1285 patients. Recruited	Male 98% Mean duration of diabetes >10	Prognostic tests of interest: 5.07	Mean follow up 3.38 years	Foot ulcer occurrence	In total, 216 / 1285 patients developed foot ulcer. Of 93 patients with monofilament insensitivity, 60 developed foot ulcer.	Authors conclude that a risk prediction

Study	ID	Number of patients	Patient characteristics	Prognostic test	Length of follow-up	Outcome measures	Results	Comments
Prospective cohort USA		from general internal medicine clinic at a Veterans Affairs Medical Center. 210 died 277 lost to follow up	years Mean age 62 years Exclusions: current foot ulcer, bilateral foot amputation, inability to walk.	Semmes-Weinstein monofilament. Other prognostic factors examined in univariate and multivariate analysis including patient characteristics, comorbidities, life style risk factors, complications.			Univariant analysis of monofilament insensitivity HR 3.10 (2.36-4.07) P=<0.001. Final multivariable model of independent predictors of foot ulcer, HR 2.03 (1.50-2.76) for monofilament insensitivity (P=<0.001). Sensitivity 60% and specificity of 67% in predicting foot ulcer.	model (combining clinical characteristics and history) is more accurate than monofilament testing
Abbott (2002) Prospective cohort UK	3235	9710 patients receiving community healthcare in 6 districts. 6613 responding to follow-up 2300 non-responders	Responders: Mean age 61.7 (+/-13.3 SD) Mean duration of diabetes 8.6 (+/- 10.4 SD) Male 53.2% Ethnicity: White 89.8% African-Caribbean 2.4% South Asian 7.6% Other 0.2%	Prognostic tests of interest: NSS NDS Pain sensation (Neurotip) Vibration score (128Hz tuning fork) Temperature score (warm and cool rods) 10g monofilament Foot deformity	2 year (+/- 6 weeks)	Foot ulcer occurrence	New ulcer occurrence in 291/6613 patients. Univariate analysis of predictors of foot ulcer RR (95% CI) Abnormal NSS 1.94 (1.54-2.43) Abnormal NDS 6.28 (4.93-7.99) Abnormal vibration score one side 2.41 (1.69-3.43) Abnormal vibration score both sides 4.95 (3.83-6.39) Abnormal temperature sensation one side 2.66 (1.97-3.59) Abnormal temperature sensation both sides 3.94 (2.99-5.19) Abnormal pain sensation one side 2.03 (1.40-2.95)	Authors conclude that NDS and/or 10g monofilament plus foot palpation can identify high risk patients and predict foot ulcer occurrence.

Study	ID	Number of patients	Patient characteristics	Prognostic test	Length of follow-up	Outcome measures	Results	Comments
			Populations similar for all baseline variables of responders and non-responders apart from ethnicity (more South Asian in non-responders) and age (lower age for non-responders)	score Achilles tendon reflex (hammer) Other prognostic factors examined in univariate and multivariate analysis including patient characteristics, comorbidities, life style risk factors, complications.			Abnormal pain sensation both sides 5.05 (3.94-6.48) 10g monofilament insensitivity 4.82 (3.82-6.07) Abnormal foot deformity score 2.04 (2.04-3.22) Achilles tendon reflex score: 1 = 0.48 (0.12-1.98) 2 = 2.88 (1.88-4.39) 3 = 4.86 (2.77-8.53) 4 = 5.12 (3.75-6.98) Multivariate analysis of independent predictors of foot ulcer RR (95%CI) Abnormal NDS 2.32 (1.61-3.35) 10g monofilament insensitivity 1.80 (1.36-2.39) Abnormal foot deformity score 1.57 (1.22-2.02) Achilles tendon reflex score: 1 = 0.40 (0.10-1.65) 2 = 1.99 (1.26-3.12) 3 = 2.25 (1.24-4.10) 4 = 1.55 (1.01-2.36)	
Carrington (2002) Prospective cohort UK	3143	169 patients consecutively attending routine clinic at a diabetes centre. 22 people without	51 with diabetes without DN. Mean age 53 (IQR 47-60). Male 51%. 67 with diabetes and DN. Mean age	Prognostic tests of interest: Motor Nerve Conduction Velocity PPT (dorsum) PPT (plantar)	Follow up yearly until Dec 2000. Median time: First ulcer / study end 67.9 months	Foot ulceration Amputation Mortality	63 / 169 patients developed foot ulcer. Predictors of new foot ulceration: PPT (dorsum) normal: Univariate RR 1.00, P 0.003 PPT (dorsum): Univariate RR 2.53 (1.37-4.67), P -	Authors conclude that MNCV is the best predictor new foot ulceration. PPT was the test with best predictive of amputation.

<table>
<tr><th>Study</th><th>ID</th><th>Number of patients</th><th>Patient characteristics</th><th>Prognostic test</th><th>Length of follow-up</th><th>Outcome measures</th><th>Results</th><th>Comments</th></tr>
<tr><td></td><td></td><td>diabetes recruited from staff members, friends and relatives)
Recruited 1994 and 1995.</td><td>58 (IQR 48-62). Male 51%.
34 with diabetes and history of ulcer. Mean age 55 (IQR 49-59). Male 68%.
17 with diabetes and Charcot arthropathy. Mean age 54 (IQR 48-62). Male 65%.
22 without diabetes (control group). Mean age 50 (IQR 46-60). Male 68%.
Exclusions: Aged <20 or >75.

Exclusions: Intermittent claudication
Active foot ulcer
Amputation
Major disability.</td><td>VPT (Neurothesiometer)

Other prognostic factors examined in univariate and multivariate analysis including ABPI, $TcpO_2$ and clinical history.</td><td>(range 0.6 to 79.9)
Amputation / study end 69.7 months (range 7.3-79.9)
Death / study end 69.5 months (range 0.2-79.9)</td><td></td><td>
<table>
<tr><td>abnormal</td><td></td><td></td></tr>
<tr><td>PPT (plantar) normal</td><td>1.00</td><td><0.001</td></tr>
<tr><td>PPT (plantar) abnormal</td><td>4.12 (2.49-6.84)</td><td>-</td></tr>
<tr><td>VPT</td><td>1.05 (1.04-1.07)</td><td><0.001</td></tr>
<tr><td>MNCV</td><td>0.88 (0.83-0.94)</td><td><0.001</td></tr>
</table>
Multivariate analysis showed MNCV RR 0.90 (0.84-0.96) P=0.001

19 / 169 patients had foot amputation. Predictors of amputation:
<table>
<tr><td></td><td>Univariate RR</td><td>P</td></tr>
<tr><td>PPT (dorsum) normal</td><td>1.00</td><td>0.005</td></tr>
<tr><td>PPT (dorsum) abnormal</td><td>4.06 (1.54-10.69)</td><td>-</td></tr>
<tr><td>PPT (plantar) normal</td><td>1.00</td><td><0.001</td></tr>
<tr><td>PPT (plantar) abnormal</td><td>5.34 (2.03-14.05)</td><td>-</td></tr>
<tr><td>VPT</td><td>1.05 (1.01-1.08)</td><td>0.011</td></tr>
<tr><td>MNCV</td><td>0.86 (0.76-0.97)</td><td>0.015</td></tr>
</table>
Multivariate analysis showed PPT at plantar RR 5.18 (1.96-13.68) P=0.001

30 / 169 patients died.</td><td>MNCV was the test with best predictive of mortality.</td></tr>
</table>

<table>
<tr><th>Study</th><th>ID</th><th>Number of patients</th><th>Patient characteristics</th><th>Prognostic test</th><th>Length of follow-up</th><th>Outcome measures</th><th>Results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>Predictors of mortality:
<table><tr><td></td><td>Univariate RR</td><td>P</td></tr><tr><td>PPT (dorsum) normal</td><td>1.00</td><td>0.001</td></tr><tr><td>PPT (dorsum) abnormal</td><td>3.82 (1.74-8.40)</td><td></td></tr><tr><td>PPT (plantar) normal</td><td>1.00</td><td>0.012</td></tr><tr><td>PPT (plantar) abnormal</td><td>2.54 (1.23-5.26)</td><td></td></tr><tr><td>VPT</td><td>1.05 (1.02-1.08</td><td><0.001</td></tr><tr><td>MNCV</td><td>0.87 (0.79-0.95)</td><td>0.002</td></tr></table>Multivariate analysis showed MNCV RR 0.84 (0.73-0.97) P=0.016</td><td></td></tr>
<tr><td>Kastenbauer (2001) Prospective cohort</td><td>3405</td><td>187 patients recruited from a diabetes centre</td><td>Type 2 diabetes 100%
Inclusion:
<75 years age
Normal gait

Exclusions
Type 1 diabetes
Past or current foot ulcer
History of amputation
PAD
Any other</td><td>Prognostic tests of interest:
VPT by biothesiometer
10g monofilament
Plantar pressure (Novel SF platform device)

Other prognostic factors</td><td>Mean follow-up 3.6 years</td><td>Ulcer occurrence</td><td>10 / 187 patients developed 18 ulcers.
70% had sensory neuropathy but none lacked perception of 10g monofilament (not included in multi-variant analysis).
Multiple Cox proporational hazards regression analysis showed elevated VPT to be strongest independent predictor of ulceration (RR 25.4 [3.1-205 95%CI]). Elevated mean plantar pressure also significant risk factor for ulceration (RR 6.3 [1.2-32.7 95%CI])</td><td>Authors conclude that elevated VPT is strongest independent predictor of ulceration.</td></tr>
</table>

<table>
<tr><th>Study</th><th>ID</th><th>Number of patients</th><th>Patient characteristics</th><th>Prognostic test</th><th>Length of follow-up</th><th>Outcome measures</th><th>Results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td>peripheral neuropathy
Charcots foot</td><td>examined in univariate and multivariate analysis including patient characteristics and clinical history.</td><td></td><td></td><td></td><td></td></tr>
<tr><td>Pham (2000)

Prospective cohort

USA</td><td>3624</td><td>248 patients consecutively enrolled from 3 foot care centres
Exclusions: none stated</td><td>Mean age 58 (+/- 12 SD)
Mean duration of diabetes 14 (+/-11 SD)
Male 50%</td><td>Prognostic tests of interest:
NSS
NDS
VPT (Biothesiometer)
Monofilament
F-scan mat (plantar foot pressure)
Goniometer (joint mobility)</td><td>Mean follow up 30 months (range 1-60 months)</td><td>Foot ulcer occurrence</td><td>Foot ulcers developed in 95 (19%) feet or 73 (29%) patients. 22 (9%) developed ulcers in both feet.
Univariate analysis:<table><tr><th></th><th>Se</th><th>Sp</th><th>PPV</th><th>OR</th></tr><tr><td>High NDS</td><td>92</td><td>43</td><td>28</td><td>8.1 (3.8-17.3)</td></tr><tr><td>High VPT</td><td>86</td><td>56</td><td>32</td><td>8.2 (7.4-18.4)</td></tr><tr><td>High SWF</td><td>91</td><td>34</td><td>25</td><td>5.4 (2.6-11.6)</td></tr><tr><td>High foot pressure</td><td>59</td><td>69</td><td>31</td><td>3.2 (2.0-5.1)</td></tr><tr><td>High NDS and/or VPT</td><td>94</td><td>38</td><td>26</td><td>9.0 (3.9-21.1)</td></tr><tr><td>High NDS and/or SWF</td><td>99</td><td>22</td><td>23</td><td>26.2 (3.6-190.0)</td></tr></table></td><td>Authors conclude that NDS obtained in clinical examination provides best sensitivity in identifying patients at risk of ulceration, whereas high VPT, inability to feel SWF and high foot pressures were independent risk factors.</td></tr>
</table>

<table>
<tr><th>Study</th><th>ID</th><th>Number of patients</th><th>Patient characteristics</th><th>Prognostic test</th><th>Length of follow-up</th><th>Outcome measures</th><th>Results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>
<table>
<tr><td>High SWF and/or VPT</td><td>98</td><td>28</td><td>24</td><td>17.7 (4.3-73.0)</td></tr>
<tr><td>High NDS and/or foot pressure</td><td>58</td><td>78</td><td>38</td><td>-</td></tr>
</table>
Multivariate analysis:
High NDS OR 3.1 (1.3-7.6)
High VPT OR 3.4 (1.7-6.8)
High SWF OR 2.4 (1.1-5.3)
High foot pressure OR 2.0 (1.2-3.3)</td><td></td></tr>
<tr><td>Adler (1999)
Prospective cohort
USA</td><td>3715</td><td>776 veterans in a general medicine clinic at a Veterans Affairs Medical Center</td><td>Male 98%
Mean duration of diabetes 9 years
Mean age 65 years
Exclusions: current foot ulcer, bilateral foot amputation, inability to walk.</td><td>Prognostic tests of interest:
10g monofilament
Other prognostic factors examined in univariate and multivariate analysis including patient characteristics and clinical history.</td><td>Median 3.3 years (0.5-8)</td><td>Lower extremity amputation</td><td>30 / 776 patients had lower limb amputation
Multivariant analysis of peripheral neuropathy using models with various methods of measuring PVD (HR 95% CI)
AAI model 2.2 (0.8-6.2)
TcPO2 model 2.9 (1.1-7.8)
Pulse model 2.5 (0.9-6.8)</td><td>Authors conclude that peripheral neuropathy as measured by 10g monofilament is an independent predictor of lower extremity amputation.</td></tr>
<tr><td>Boyko (1999)</td><td>3714</td><td>749 patients recruited from</td><td>Male 98%
Mean duration</td><td>Prognostic tests of</td><td>Mean follow-up</td><td>Full thickness ulcer</td><td>162 ulcers in 1483 limbs.
Univariant analysis RR (95% CI):</td><td>Authors conclude that foot sensory</td></tr>
</table>

<table>
<tr><th>Study</th><th>ID</th><th>Number of patients</th><th>Patient characteristics</th><th>Prognostic test</th><th>Length of follow-up</th><th>Outcome measures</th><th>Results</th><th>Comments</th></tr>
<tr><td>Prospective cohort

USA</td><td></td><td>general internal medicine clinic at a Veterans Affairs Medical Center.</td><td>of diabetes 11.4 years
Mean age 63 years
Exclusions: current foot ulcer, bilateral foot amputation, inability to walk.</td><td>interest:
5.07 monofilament
128-Hz tuning fork
Achilles tendon reflex

Other prognostic factors examined in univariate and multivariate analysis including patient characteristics, ABPI, TcpO2 and clinical history.</td><td>3.7 years</td><td>occurrence</td><td>Insensitivity to 5.07 monofilament 3.37 (2.45-4.63) P=<0.001
Absent tendon reflex 1.40 (1.03-1.90) P=0.030
Absent vibration sensation 2.33 (1.66-3.28) P=<0.001
Final multivariant model analysis showed foot insensitivity to 5.07 monofilament RR 2.17 (1.52-3.08) P=<0.001
Absent tendon reflex and diminished vibration sensation did not provide additional predictive power over and above monofilament testing.</td><td>neuropathy as measured by 5.07 monofilament emerged as the test most predictive of foot ulcer risk.</td></tr>
<tr><td>Litzelman (1997)

Prospective cohort

USA</td><td>7391</td><td>352 patients with NIDDM receiving primary care from a university affiliated general medicine practice.

395 originally enrolled, 43 did not</td><td>Mean age 60.4 (+/-9.6 SD)
Male 29%
African-American 76%
Median duration of diabetes 9.9 years (+/-8.1 SD)
Exclusions: <40 years old
<ideal body weight
Diagnosed with</td><td>Prognostic tests of interest:
10g monofilament
Thermal sensitivity (Sensortek)

Other prognostic factors examined in univariate and</td><td>12 month</td><td>Foot wound occurrence</td><td>63 had blister or wound graded minor injury (41), superficial ulcer (0), partial thickness (2) and full thickness (1).

Univariate analysis of predictors of foot lesion:<table><tr><td></td><td colspan="2">Seattle wound class</td></tr><tr><td></td><td>>=1.2</td><td>>=1.3</td></tr><tr><td>Monofilament</td><td>3.37 (1.95-5.80) P=<0.0001</td><td>5.46 (2.39-12.45) P=<0.0004</td></tr><tr><td>Thermal insensitivity</td><td>2.82 (1.52-5.25)</td><td>3.04 (1.17-7.88)</td></tr></table></td><td>Authors conclude that monofilament insensitivity is an important predictor of wounds, even when minor injuries included in the definition. Thermal insensitivity was also a strong univariate predictor but did</td></tr>
</table>

Study	ID	Number of patients	Patient characteristics	Prognostic test	Length of follow-up	Outcome measures	Results	Comments
		complete the study.	NIDDM before aged 30 Pregnancy Major psychiatric illness Renal failure Terminal illness	multivariate analysis including patient characteristics and clinical history.			<table><tr><td></td><td>P=0.001</td><td>P=0.02</td></tr></table> Multivariate analysis of predictors of foot lesion: <table><tr><td></td><td colspan="2">Seattle wound class</td></tr><tr><td></td><td>>=1.2</td><td>>=1.3</td></tr><tr><td>Monofilament</td><td>2.75 (1.55-4.88) P=<0.001</td><td>5.23 (2.26-12.13) P=<0.001</td></tr><tr><td>Thermal insensitivity</td><td>2.18 (1.13-4.21) P=0.02</td><td>NS</td></tr></table>	not enter the multivariate model for wound score >=1.3.
Young (1994) Prospective cohort UK	4445	469 patients consecutively recruited between 1988 and 1989 in a diabetic or diabetic foot clinic	Mean age 54 (range 17-85 Male 49% Type 1 41% Mean duration of diabetes 12.4 years (0-60) Exclude: no history of foot ulcer	VPT by biothesiometry	4 years	Foot ulcer occurrence	48 / 469 patients developed foot ulcer Adjusted OR for 4-year cumulative incidence of foot ulceration in VPT>25 vs VPT <15 = 6.82 (2.75-16.92) P=<0.01 Analysis adjusted for duration of diabetes.	Authors conclude that VPT can predict those patients at increased risk of foot ulceration and that a VPT >25V carries a seven fold risk of ulceration compared to <15V
Rith-Najarian (1992) Prospective cohort USA	-	358 examined in primary care setting 19 died 2 lost to follow up	Native American population. Mean age 55 (+/-12.3) Mean duration of diabetes 12.3 (+/-6.7) 44% male	Prognostic test of interest: 5.07 Semmes-Weinstein monofilament Other prognostic factors examined in	32 month follow up period	Foot ulcer occurrence Foot amputation	42 patients developed foot ulceration and 14 had an amputation. Insensitivity to monofilament in 70 patients (19%). Among this group, odds ratio of subsequent ulceration 9.9 (95% CI 4.8-21.0) and amputation 17 (95% CI 4.5-95.0)	Authors conclude that presence of deformity and history of lower extremity event can identify high risk patients. However, ulceration and amputation still

Study	ID	Number of patients	Patient characteristics	Prognostic test	Length of follow-up	Outcome measures	Results	Comments
				analysis included clinical examination and history.				occurred in people sensate to monofilament testing.
Leese (2013) cohort UK	Rerun search	15, 938 were identified between 2004 and 2006 Over 3 years follow up 670 people developed new foot ulcers	UK population with diabetes. Mean age 64.44 ± 15.72 Mean duration of diabetes 8.79 years ± 8.04	Prognostic test of interest: Lack of 10g monofilament sensation was defined as absence of three or more plantar sites out of ten assessed (five in each foot)	3 year follow up period	Foot ulcer occurrence Foot amputation	670 patients developed foot ulceration and 99 proceeded to amputation. Known insensitivity to foot monofilament in 464 patients, unknown in 2,160. Among this group, odds ratio of subsequent ulceration 6.46 (95% CI 4.96-8.41) and amputation 2.52 (95% CI 1.24-5.10)	Authors concluded risk factors for foot ulceration were age, previous ulcer, absent foot pulses, absent sensation to monofilaments, insulin use, duration of diabetes, previous retinal laser treatment and social deprivation.

1.2 Evidence tables: Stratification systems

Table 21: Included studies for stratification systems

Study	Number of patients	Patient characteristics	Prognostic system	Length of follow-up	Outcome measures	Results	Comments

Study	Number of patients	Patient characteristics	Prognostic system	Length of follow-up	Outcome measures	Results	Comments
Monteiro-Soares (2012) Retrospective cohort study Portugal	364 patients Inclusion: patients with diabetes attending a podiatry section Jan 2008 to Dec 2010. Exclusions: Patients with active diabetic foot ulcer. Inability to walk Follow up less than 1 year	Mean age 64 (19 to 94 years) 49% male 99.7% type II diabetes 42% used insulin Mean diabetes duration 17 years (range 1 to 52 years)	Five systems used on all patients: UT ADA Modified IWGDF SIGN Seattle risk score Neuropathy measurement varied according to the system PVD assessed though direct pulse palpation	Median follow up 12 months (range 1 to 12)	Diabetic foot occurrence (full thickness defect to the malleoli requiring more than 14 days to heal)	Diagnostic accuracy AUC values: UT 0.73 (0.63-0.83) ADA 0.83 (0.79-0.88) Modified IWGDF 0.86 (0.81-0.91) SIGN 0.75 (0.68-0.82) Seattle 0.82 (0.75-0.89)	Authors conclude that all systems are equally and highly accurate. Trend observed for increased DFU occurrence in higher risk groups. All systems presented <30% PPV – of those classified as at risk more than 70% will not develop a DFU. For highest risk group (or highest + medium risk) excellent negative predictive values. Almost all patients developing a foot ulcer are predicted by the systems.

Study	Number of patients	Patient characteristics	Prognostic system	Length of follow-up	Outcome measures	Results	Comments
Monteiro-Soares (2010) Retrospective cohort study Portugal	360 All patients attending the podiatry section of a diabetic foot clinic from 2002 to 2008. (435 initial patients, 75 patients excluded if unable to walk)	Median age 65 years 98% Type II diabetes 45% male	Boyko stratification model (Seattle Risk Score) Four risk categories: Lowest risk Next to lowest risk Next to highest risk Highest risk Neuorpathy tested using monofilament. PVD assessed through palpation	Median follow-up of 25 months Range 3 to 86 months. Follow up ended on first ulcer occurrence	Foot ulcer development (full thickness requiring >14d healing)	Highest risk: Se% 61 (51-70) Sp% 87 (83-91) LR+ 4.7 (3.33-6.76) LR- 0.45 (0.35-0.58) Next to highest risk Se% 84 (75-90) Sp% 70 (65-75) LR+ (2.83 (2.34-3.47) LR- 0.23 (0.14-0.36) Next to lowest risk Se% 95 (88-98) Sp% 50 (44-56) LR+ 1.88 (1.65-2.13) LR- 0.10 (0.05-0.25) PPV % 62 (57-67) NPV % 60 (55-65)	People excluded if unable to walk (in line with original Boyko model). PPV calculated for highest risk group and NPV for the lowest risk group Authors conclude that the Boyko system is an excellent discriminating instrument for foot ulcer prediction in patients with diabetes. Inclusion of footwear variable may improve the model.

Study	Number of patients	Patient characteristics	Prognostic system	Length of follow-up	Outcome measures	Results	Comments
Leese (2006) Prospective cohort study UK	3526 patients attending for routine diabetes care in hospital and community	Mean age 64.7 years (range 15-101) 91% Type 2 Mean diabetes duration 8.8 years	SIGN system Low – No risk factor Moderate – One risk factor (PVD or DN or FD or VI or PI) without callous High – History of FU/LEA, or (PVD and DN) or more than one risk factor and callous or deformity. Neuropathy assessed through monofilament testing PVD assessed through foot pulse palpation	Mean follow up 1.7 years (+/- 0.9)	Development of ulcer	Kappa statistic for agreement 0.95 High-risk Se% 84 (83-86) Sp% 90 (89-91) PPV% 29 (28-31) High and mod risk Se% 95 (95-96) Sp% 67 (65-68) Low risk NPV% 99.6 (99.5-99.7)	System modified by Authors conclude that the main value of tool in identifying patients at low risk of ulceration

Study	Number of patients	Patient characteristics	Prognostic system	Length of follow-up	Outcome measures	Results	Comments
Peters (2001) Prospective case control study USA	236 patients 23 lost to follow up	Female 53.5% Type 2 diabetes 93.8% Mean age 52.6 (+/- 10.4 SD) Mean diabetes duration 11 years (+/- 9.3 SD)	IWGDF system 0 No neuropathy 1 DN 2 DN and FD or PVD 3 History of ulcer Neuropathy assessed through vibration perception threshold (biothesiometer) and monofilament PVD assessed by foot pulse or defined as <0.8 ABI	Mean follow up 30 months	Ulcer occurrence Lower extremity amputation	Group 3 patients 17.8 times more likely to develop an ulcer than groups 0 to 2 combined. Group 3 patients 52.2 times more likely to receive an LEA than groups 0 to 2 combined. Variant classification – patients with previous amputation 100 times (95% CI 20.4-491.0) more likely to ulcerate Diagnostic accuracy calculated by 8750: Group 3 Se% 74 (62-86) Sp% 86 (81-92) LR+ 5.35 (3.52-8.14) LR- 0.30 (0.19-0.47) PPV 64 (58-70) Groups 3 and 2: Se% 87 (78-96) Sp% 58 (51-66) LR+ 2.10 (1.70-2.59) LR- 0.22 (0.11-0.45)	Authors conclude that the system is effective in predicting groups that are more likely to develop foot complications.

Table summarising the diagnostic accuracy measures (ulcer prediction)

System	Paper	Risk group	Se (95% CI)	Sp (95% CI)	LR+ (95% CI)	LR- (95% CI)	PPV (95% CI)	Accuracy (95% CI)
IWGDF	Peters (2001)	3	74 (62-86)	86 (81-92)	5.35 (3.52-8.14)	0.30 (0.19-0.47)	64 (58-70)	83 (78-88)
		3+2	87 (78-96)	58 (51-66)	2.10 (1.70-2.59)	0.22 (0.11-0.45)	NA	66 (59-72)
Modified IWGDF	Monteiro-Soares (2012)	3A+3B	88 (77-99)	71 (66-76)	3.00 (2.40-3.70)	0.20 (0.07-0.40)	23 (16-30)	-
		2A+2B+3A+3B	100 (NC)	45 (39-50)	1.80 (1.60-1.90)	NC	15 (11-20)	-
		1+2A+2B+3A+3B	100 (NC)	38 (33-44)	1.60 (1.50-1.80)	NC	14 (10-18)	-
SIGN	Monteiro-Soares (2012)	High	100 (NC)	52 (46-57)	2.10 (1.80-2.30)	NC	17 (12-22)	-
		High + moderate	100 (NC)	9 (6-12)	1.10 (1.00-1.10)	NC	10 (6-12)	-
	Leese (2006)	High	84 (79-90)	90 (89-91)	8.41 (7.45-9.49)	0.17 (0.12-0.25)	31 (29-33)	90 (89-91)
		High + moderate	95 (92-98)	67 (65-68)	2.97 (2.70-3.04)	0.07 (0.04-0.14)	NA	68 (67-70)
Seattle	Monteiro-Soares (2012)	Highest	70 (54-85)	83 (79-87)	4.20 (3.00-5.80)	0.40 (0.20-0.60)	30 (19-40)	-
		Highest + next to highest	85 (73-97)	70 (65-75)	2.80 (2.20-3.50)	0.20 (0.10-0.50)	22 (15-29)	-
		Highest + next to highest + next to lowest	94 (86-100)	44 (39-49)	1.70 (1.50-1.90)	0.10 (0.04-0.50)	14 (10-19)	-
	Monteiro-Soares (2010)	Highest	61 (51-70)	87 (83-91)	4.7 (3.33-6.76)	0.45 (0.35-0.58)	62 (57-67)	80 (76-84)
		Highest + next to highest	84 (75-90)	70 (65-75)	2.83 (2.34-3.47)	0.23 (0.14-0.36)	NA	74 (69-79)
		Highest + next to highest + next to lowest	95 (88-98)	50 (44-56)	1.88 (1.65-2.13)	0.10 (0.05-0.25)	NA	61 (56-66)
ADA	Monteiro-Soares (2012)	3	91 (81-100)	70 (66-75)	3.10 (2.50-3.70)	0.10 (0.04-0.40)	23 (16-31)	-
		2+3	100 (NC)	56 (51-61)	2.30 (2.00-2.60)	NC	18 (13-24)	-
		1+2+3	100 (NC)	13 (9-17)	1.10 (1.10-1.20)	NC	10 (7-14)	-
UT	Monteiro-Soares (2012)	3	58 (41-74)	85 (81-89)	3.70 (2.50-5.50)	0.50 (0.30-0.70)	27 (17-38)	-
		2+3	64 (47-80)	73 (68-78)	2.30 (1.70-3.20)	0.50 (0.30-0.80)	19 (12-26)	-
		1+2+3	73 (58-88)	66 (61-71)	2.10 (1.60-2.80)	0.40 (0.20-0.70)	18 (11-24)	-

NC= not calculable

F.5 Review question 5 full evidence tables

No evidence was identified for this review

F.6 Review question 6 full evidence tables

Table 22: Lavery 2007

Bibliographic reference	Lavery, Lawrence A., et al. "Preventing Diabetic Foot Ulcer Recurrence in High-Risk Patients Use of temperature monitoring as a self-assessment tool." Diabetes care 30.1 (2007): 14-20.
Study type	Randomised control trial
Study quality	Summary Population: USA, participants with severe peripheral vascular disease were excluded Intervention: Structured foot examination, Enhanced therapy (temperature monitoring) Standard of care: Evaluation every 8 weeks, education, insoles and footwear. Comparison: Standard care alone Outcome: incidence of ulceration, adherence, adverse events 1) Has an appropriate method of randomisation been used? Appropriate method of randomisation was used 2) Was there adequate concealment of allocation? Patient allocation was sealed in opaque envelope and opened following randomisation. 3) Were the groups comparable at baseline for all major confounding/prognostic factors? Groups appear similar at baseline for all major confounding factors although P values were not provided. No significant differences were found for age, duration of diabetes, history of amputation, severity of sensory neuropathy, or activity level among the three treatment groups. 4) Did the comparison groups receive the same care apart from interventions studied? General diabetic foot care was standardised for all participants and included lower extremity examination by a physician every 8 weeks, regularly scheduled podiatry assessments to see if footwear required replacing or repairing, video education and pedometer provided. 5) Were participants receiving care kept blind to treatment allocation? Participants were not blinded to treatment allocation. 6) Were the individuals administering care kept blind to treatment allocation? Individuals administering care were blinded to treatment allocation, patients were instructed not to discuss treatment group assignment with the treating physician however it is unclear how well there was adhered to.

Bibliographic reference	**Lavery, Lawrence A., et al. "Preventing Diabetic Foot Ulcer Recurrence in High-Risk Patients Use of temperature monitoring as a self-assessment tool." Diabetes care 30.1 (2007): 14-20.**
	7) Were groups comparable with respect to availability of outcome data and for how many participants were no outcome data available? Groups appeared similar for loss to follow up and availability of outcome data. Intention to treat analysis was used. 8) Did the study have an appropriate length of follow up? 15 month length of follow up was employed, this was appropriate. 9) Did the study use a precise definition of outcome? Precise and clear definitions of ulceration were used. 10) Was a valid and reliable method used to determine that outcome? Valid and reliable methods were used 11) Were investigators kept blind to participant's exposure to the intervention? Investigators were kept blind to participant's exposure to the intervention. 12) Were investigators kept blind to other important confounding and prognostic factors? Unclear if investigators were kept blind to other important confounding and prognostic factors.
Number of patients	Randomised= 173 Standardised therapy group= 58 Structured foot exam group= 56 Enhanced therapy group= 59
Patient characteristics	Patients taken from: USA Inclusion: Aged 18-80 years History of foot ulceration Diagnosis of diabetes Ability to provide informed consent Ankle brachial index ≥0.70 Exclude: Open ulcers or open amputation sites Active osteoarthropathy

Bibliographic reference	**Lavery, Lawrence A., et al. "Preventing Diabetic Foot Ulcer Recurrence in High-Risk Patients Use of temperature monitoring as a self-assessment tool." Diabetes care 30.1 (2007): 14-20.**

Severe peripheral vascular disease
Foot infection
Dementia
Other conditions that would preclude active participation

Baseline characteristics: Unclear if significant differences. P values not provided in study.

Characteristics	Standard therapy group	Enhanced therapy group	Structured foot examination
Age	65.0 ± 9.6	65.4 ± 9.3	64.2 ± 8.6
Sex	53.4	55.9	51.7
Race (White/Mexican/African American)	31/24/3/56	32/22/3/55	30/10/12/4
Type 2 diabetes	56	55	53
Duration of diabetes, y	13.7 ± 10.3	12.7 ± 9.7	13.8 ± 11.5
Ulcer history (hallux/toes/submetatarsal/medfoot-heel)	7/29/21/3	4/35/17/7	8/30/21/5
History of previous amputation	18	13	14
History of vascular surgery Lower extremity bypass Lower extremity angioplasty Coronary artery bypass Cardiac angioplasty	 3 0 2 0	 0 0 1 0	 0 1 0 2
Foot deformity Hallux rigidus Hallux valgus Claw toe/hammer toe	 50 23 33	 51 33 41	 46 12 41
Ankle brachial index R L	 1.1 ± 0.4 1.2 ± 0.5	 1.1 ± 0.4 1.1 ± 0.6	 1.1 ± 0.6 1.2 ± 0.6
Activity (steps per day)	3,817 ± 3,364	3,489 ± 2,706	3963 ± 2363
Time prescribed shoes worn <4 4-8 >8-12	 1 5 33	 2 8 31	 0 15 19

Bibliographic reference	**Lavery, Lawrence A., et al. "Preventing Diabetic Foot Ulcer Recurrence in High-Risk Patients Use of temperature monitoring as a self-assessment tool." Diabetes care 30.1 (2007): 14-20.**
	>12 | 19 | 18 | 22
Intervention	Structured foot exam: n= 56 Standard therapy as below and training to conduct a structured foot inspection twice a day using a mirror and recording findings in a log book with a checklist of elements to be included in self-examination.
	Enhanced therapy: n= 59 Standard therapy as below and training to use a digital infrared thermometer to measure and record temperatures on each foot. Foot temperature taken over 6 sites and recorded in a logbook. Subjects with amputation were given alternative sites. If the skin temperatures were elevated by >4°F (2.2°C) compared with the corresponding site on the opposite foot for two consecutive days subjects were instructed to contact the research nurse and decrease activity until temperatures normalised.
Comparison	Standard therapy alone: n=58 lower extremity examination by a physician every 8 weeks, regularly scheduled podiatry assessments to see if footwear required replacing or repairing, video education and pedometer provided.
Length of follow up	Length of follow up was 15 months
Location	USA
Outcomes measures and effect size	Rates of foot ulceration/infection Number who developed foot ulceration Defined using American Diabetes Association criteria Structured foot exam= 17 of 58 participants Enhanced therapy= 5 of 59 participants Standard therapy alone= 17 of 56 participants Odds ratio of enhanced therapy group vs standard therapy group= 4.48 (95% CI 1.53-13.14) P= 0.008 i.e. significant difference Odds ratio of enhanced therapy group vs structured foot examination group= 4.71 (95% CI 1.60-13.85)

Bibliographic reference	Lavery, Lawrence A., et al. "Preventing Diabetic Foot Ulcer Recurrence in High-Risk Patients Use of temperature monitoring as a self-assessment tool." Diabetes care 30.1 (2007): 14-20.
	P=0.0061 i.e. significant difference Time to develop ulceration (Kaplan-Meier survival) Structured foot exam= 377.3 ± 18.4 days Enhanced therapy= 429.5 ± 11.9 days Standard therapy alone= 378.5 ± 18.6 days Enhanced therapy group vs standard therapy group P= 0.0059 i.e. significant difference Enhanced therapy group vs structured foot examination group P=0.0055 i.e. significant difference Rates of gangrene resulting from diabetes No data available Rates of amputation No data available Rates of A&E/ Hospital admission for foot problems resulting from diabetes No data available Resource use and costs No data available
Source of funding	Grant from National Institutes of Health
Comments	

Table 23: Armstrong 2007

Bibliographic reference	**Armstrong, D. G., Holtz-Neiderer, K., Wendel, C., Mohler, M. J., Kimbriel, H. R., & Lavery, L. A. (2007). Skin temperature monitoring reduces the risk for diabetic foot ulceration in high-risk patients. The American journal of medicine, 120(12), 1042-1046.**
Study type	Randomised control trial
Study quality	Summary Population: USA, veteran population, International Foot Risk Classification System; risk group 2 and 3. Intervention: Infrared skin thermometer, measuring temperatures on 6 sites on the skin twice a day Standard of care: Therapeutic footwear, diabetic foot education and regular foot care Comparison: Standard care alone Outcome: incidence of ulceration, 1) Has an appropriate method of randomisation been used? Appropriate method of randomisation was used 2) Was there adequate concealment of allocation? Patient allocation was sequentially assigned to a randomisation list by a biostatistician presumably without knowledge of the participant's clinical state, however this is unclear. 3) Were the groups comparable at baseline for all major confounding/prognostic factors? Groups appear similar at baseline for all major confounding factors and P values were provided. 4) Did the comparison groups receive the same care apart from interventions studied? General diabetic foot care was standardised for all participants and included therapeutic footwear, diabetic foot education and regular foot care. All subjects were instructed to perform a structured foot inspection daily and record their findings in a logbook. 5) Were participants receiving care kept blind to treatment allocation? Participants were not blinded to treatment allocation. 6) Were the individuals administering care kept blind to treatment allocation? Individuals administering care were blinded to treatment allocation, patients were instructed not to discuss treatment group assignment with the treating physician however it is unclear how well this was adhered to. 7) Were groups comparable with respect to availability of outcome data and for how many participants were no outcome data available? Unclear if groups were comparable for availability of outcome data. No information on loss to follow up was provided. The study did not provide information on the number of participants in each group and this was calculated from percentages provided in the results section. It appears 4 participants were not included in the results but unclear from which groups these participants were lost. 8) Did the study have an appropriate length of follow up?

Bibliographic reference	**Armstrong, D. G., Holtz-Neiderer, K., Wendel, C., Mohler, M. J., Kimbriel, H. R., & Lavery, L. A. (2007). Skin temperature monitoring reduces the risk for diabetic foot ulceration in high-risk patients. The American journal of medicine, 120(12), 1042-1046.**
	18 month length of follow up was employed, this was appropriate. 9) Did the study use a precise definition of outcome? Precise and clear definitions of ulceration were used. 10) Was a valid and reliable method used to determine that outcome? Valid and reliable methods were used 11) Were investigators kept blind to participant's exposure to the intervention? Investigators were kept blind to participant's exposure to the intervention. 12) Were investigators kept blind to other important confounding and prognostic factors? Unclear if investigators were kept blind to other important confounding and prognostic factors.
Number of patients	Randomised= 225 Standardised therapy group= 115 Thermometry monitoring group= 106
Patient characteristics	Patients taken from: USA Inclusion: Aged 18-80 years Southern Arizona VA Health Care System Category 2 or 3 of the International Diabetic Foot Risk Classification System Exclude: Open ulcers or open amputation sites Active Charcot neuropathy Severe peripheral vascular disease Ankle brachial pressure index <0.8 on either extremity Foot infection Dementia Active drug abuse or alcoholism within 1 year Sight impaired

<table>
<tr><th>Bibliographic reference</th><td>Armstrong, D. G., Holtz-Neiderer, K., Wendel, C., Mohler, M. J., Kimbriel, H. R., & Lavery, L. A. (2007). Skin temperature monitoring reduces the risk for diabetic foot ulceration in high-risk patients. The American journal of medicine, 120(12), 1042-1046.</td></tr>
<tr><td></td><td>Unable to walk without the assistance of wheelchair or crutches

Baseline characteristics: No significant differences found, P values provided in the study

<table>
<tr><th>Characteristics</th><th>Thermometry, n=106</th><th>Standard therapy group, n=115</th></tr>
<tr><td>Age</td><td>68.2 ± 9.6</td><td>69.7 ± 10.4</td></tr>
<tr><td>Sex</td><td>98.2</td><td>94.7</td></tr>
<tr><td>Race (White/African American/Hispanic/Asian/native american) %</td><td>72.97/4.50/20.72/0.00 /1.80</td><td>71.05/8.77/17.54/1.75/ 0.88</td></tr>
<tr><td>Type 2 diabetes</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Duration of diabetes, y</td><td>13.6 ± 11.6</td><td>12.6 ± 9.1</td></tr>
<tr><td>Ulcer history</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>History of previous amputation</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>History of vascular surgery</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Foot deformity</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Ankle brachial index</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Activity (steps per day)</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Time prescribed shoes worn</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Diabetic foot risk classification %
Risk 2
Risk 3</td><td>
84.7
15.3</td><td>
82.5
17.5</td></tr>
<tr><td>Neuropathy %</td><td>100</td><td>100</td></tr>
<tr><td>Retinopathy %</td><td>23.4</td><td>34.2</td></tr>
</table>
</td></tr>
<tr><th>Intervention</th><td>Thermometry monitoring: n= 106

Participants used an infrared skin thermometer to measure 6 sites on the foot twice a day. Temperature differences greater than 2.2°C between left and right corresponding sites triggered patients to contact the study coordinator and reduce activity until their temperatures normalised.</td></tr>
<tr><th>Comparison</th><td>Standard therapy alone: n=115</td></tr>
</table>

Bibliographic reference	**Armstrong, D. G., Holtz-Neiderer, K., Wendel, C., Mohler, M. J., Kimbriel, H. R., & Lavery, L. A. (2007). Skin temperature monitoring reduces the risk for diabetic foot ulceration in high-risk patients. The American journal of medicine, 120(12), 1042-1046.**
	General diabetic foot care was standardised for all participants and included therapeutic footwear, diabetic foot education and regular foot care. All subjects were instructed to perform a structured foot inspection daily and record their findings in a logbook.
Length of follow up	Length of follow up was 18 months
Location	USA
Outcomes measures and effect size	Rates of foot ulceration/infection Number who developed foot ulceration Defined as the full thickness loss of epidermis and dermis or involvement of deeper structures Thermometry group= 5 of 106 participants Standard therapy alone= 14 of 115 participants Odds ratio of thermometry group vs standard therapy group= 3.0 (95% CI 1.00-8.5) P= 0.038 i.e. significant difference Time to develop ulceration (Kaplan-Meier survival) Difference between groups was found to be significant in favour of the treatment group. (P value= 0.04). Individual mean times to ulceration between groups were not provided. Rates of gangrene resulting from diabetes No data available Rates of amputation No data available Rates of A&E/ Hospital admission for foot problems resulting from diabetes No data available

Bibliographic reference	**Armstrong, D. G., Holtz-Neiderer, K., Wendel, C., Mohler, M. J., Kimbriel, H. R., & Lavery, L. A. (2007). Skin temperature monitoring reduces the risk for diabetic foot ulceration in high-risk patients. The American journal of medicine, 120(12), 1042-1046.**
	Resource use and costs No data available
Source of funding	Merit award from Veterans Affairs
Comments	

Table 24: Lavery 2004

Bibliographic reference	**Lavery, L. A., Higgins, K. R., Lanctot, D. R., Constantinides, G. P., Zamorano, R. G., Armstrong, D. G., ... & Agrawal, C. M. (2004). Home monitoring of foot skin temperatures to prevent ulceration. Diabetes care, 27(11), 2642-2647.**
Study type	Randomised control trial
Study quality	Summary Population: USA, International Foot Risk Classification System; risk group 2 and 3. Intervention: Infrared skin thermometer, measuring temperatures on 6 sites on the skin twice a day Standard of care: Therapeutic footwear, diabetic foot education and foot evaluation by a podiatrist every 10-12 weeks Comparison: Standard care alone Outcome: incidence of ulceration, infections, charcot fractures and amputations 1) Has an appropriate method of randomisation been used? Unclear if appropriate method of randomisation was used 2) Was there adequate concealment of allocation? Unclear if there was adequate allocation concealment 3) Were the groups comparable at baseline for all major confounding/prognostic factors? Groups appear similar at baseline for all major confounding factors although specific P values were not provided 4) Did the comparison groups receive the same care apart from interventions studied? General diabetic foot care was standardised for all participants and included Therapeutic footwear, diabetic foot education and foot evaluation by a podiatrist every 10-12 weeks 5) Were participants receiving care kept blind to treatment allocation? Unclear if participants were blinded to treatment allocation.

Bibliographic reference	**Lavery, L. A., Higgins, K. R., Lanctot, D. R., Constantinides, G. P., Zamorano, R. G., Armstrong, D. G., ... & Agrawal, C. M. (2004). Home monitoring of foot skin temperatures to prevent ulceration. Diabetes care, 27(11), 2642-2647.**
	6) Were the individuals administering care kept blind to treatment allocation? Individuals administering care were blinded to treatment allocation. 7) Were groups comparable with respect to availability of outcome data and for how many participants were no outcome data available? Three participants in the standard therapy group and four patients in the thermometry group were lost to follow up. Further details were not provided. Intent to treat analysis was employed and it is therefore likely that groups were comparable with respect to availability of outcome data. 8) Did the study have an appropriate length of follow up? 6 month length of follow up was employed, this was appropriate. 9) Did the study use a precise definition of outcome? No definition for ulceration was provided 10) Was a valid and reliable method used to determine that outcome? Unclear if valid and reliable methods were used 11) Were investigators kept blind to participant's exposure to the intervention? Investigators were kept blind to participant's exposure to the intervention. 12) Were investigators kept blind to other important confounding and prognostic factors? Unclear if investigators were kept blind to other important confounding and prognostic factors.
Number of patients	Randomised= 85 Standardised therapy group= 41 Thermometry monitoring group= 44
Patient characteristics	Patients taken from: USA Inclusion: Aged 18-80 years Diagnosis of diabetes Category 2 or 3 of the International Diabetic Foot Risk Classification System Exclude:

<table>
<tr><th>Bibliographic reference</th><td>Lavery, L. A., Higgins, K. R., Lanctot, D. R., Constantinides, G. P., Zamorano, R. G., Armstrong, D. G., ... & Agrawal, C. M. (2004). Home monitoring of foot skin temperatures to prevent ulceration. Diabetes care, 27(11), 2642-2647.</td></tr>
<tr><td></td><td>Open ulcers or open amputation sites
Active Charcot neuropathy
Peripheral vascular disease
Ankle brachial pressure index <0.8 on either extremity
Foot infection
Dementia
Active drug abuse or alcoholism within 1 year

Baseline characteristics: No significant differences found, P values not provided in the study

<table>
<tr><td>Characteristics</td><td>Standard therapy group, n= 44</td><td>Thermometry, n=41</td></tr>
<tr><td>Age, years</td><td>54.8 ± 9.6</td><td>55.0 ± 9.3</td></tr>
<tr><td>Sex, Male %</td><td>52.3</td><td>48.8</td></tr>
<tr><td>Race</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Type 2 diabetes</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Duration of diabetes, y</td><td>12.7 ± 10.0</td><td>14.8 ± 11.5</td></tr>
<tr><td>Ulcer history</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>History of previous amputation</td><td>1</td><td>1</td></tr>
<tr><td>History of vascular surgery</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Foot deformity</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Ankle brachial index</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Activity (steps per day)</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Time prescribed shoes worn</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Diabetic foot risk classification %
Risk 2
Risk 3</td><td>
26
18</td><td>
24
17</td></tr>
<tr><td>Neuropathy %</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Retinopathy %</td><td>Not reported</td><td>Not reported</td></tr>
</table>
</td></tr>
<tr><th>Intervention</th><td>Thermometry monitoring: n= 41

Participants used an infrared skin thermometer to measure 6 sites on the foot twice a day. Temperature differences greater than 2.2°C between left and right corresponding sites triggered patients to contact the study coordinator and reduce activity until their</td></tr>
</table>

Bibliographic reference	**Lavery, L. A., Higgins, K. R., Lanctot, D. R., Constantinides, G. P., Zamorano, R. G., Armstrong, D. G., ... & Agrawal, C. M. (2004). Home monitoring of foot skin temperatures to prevent ulceration. Diabetes care, 27(11), 2642-2647.**
	temperatures normalised.
Comparison	Standard therapy alone: n=44 General diabetic foot care was standardised for all participants and included Therapeutic footwear, diabetic foot education and foot evaluation by a podiatrist every 10-12 weeks
Length of follow up	Length of follow up was 6 months
Location	USA
Outcomes measures and effect size	Rates of foot ulceration/infection Number who developed foot ulceration Definition unclear Thermometry group= 1 of 41 participants Standard therapy alone= 7 of 44 participants P value = <0.05 i.e. significant difference Rates of gangrene resulting from diabetes No data available Rates of amputation Number who required amputation following infection Definition unclear Thermometry group= 0 of 41 participants Standard therapy alone= 2 of 44 participants

Bibliographic reference	**Lavery, L. A., Higgins, K. R., Lanctot, D. R., Constantinides, G. P., Zamorano, R. G., Armstrong, D. G., ... & Agrawal, C. M. (2004). Home monitoring of foot skin temperatures to prevent ulceration. Diabetes care, 27(11), 2642-2647.**
	P value not provided Rates of A&E/ Hospital admission for foot problems resulting from diabetes Number who developed Charcot fracture Definition unclear Thermometry group= 0 of 41 participants Standard therapy alone= 2 of 44 participants P value = >0.05 i.e. not significant difference Resource use and costs No data available
Source of funding	Grant from National Institutes of Health
Comments	There is some overlap of authors between the above three papers however it seems that none of the results were shared between studies.

Table 25: Gershater 2011

Bibliographic reference	**Annersten Gershater, M., Pilhammar, E., Apelqvist, J., & Alm-Roijer, C. (2011). Patient education for the prevention of diabetic foot ulcers. Interim analysis of a randomised controlled trial due to morbidity and mortality of participants.**
Study type	Randomised control trial
Study quality	Summary Population: Sweden, International Foot Risk Classification System; risk group 3 (all had previous ulcers) Intervention: Education: Diabetes specialist nurse lead sessions for 60 minutes in which participants actively participated in discussions. Standard of care: adjusted shoes and individually fitted insoles for indoor use, and recommended regular chiropody. All patients received standard information provided by a registered nurse working at the foot clinic.

Bibliographic reference	**Annersten Gershater, M., Pilhammar, E., Apelqvist, J., & Alm-Roijer, C. (2011). Patient education for the prevention of diabetic foot ulcers. Interim analysis of a randomised controlled trial due to morbidity and mortality of participants.**
	Comparison: Standard care alone Outcome: incidence of ulceration 1) Has an appropriate method of randomisation been used? An appropriate method of randomisation was used however groups were adjusted to make the male/female ratio more evenly distributed, one man received standard information as the other members of his group did not turn up to their session. This is not strictly true randomisation. 2) Was there adequate concealment of allocation? There was adequate allocation concealment using numbered envelopes 3) Were the groups comparable at baseline for all major confounding/prognostic factors? Groups were not similar for all aspects as with the male and female distribution above. P values were not provided for any of the other baseline characteristics recorded and it is unclear if groups were comparable. 4) Did the comparison groups receive the same care apart from interventions studied? General diabetic foot care was standardised for all participants and included adjusted shoes and individually fitted insoles for indoor use, and recommended regular chiropody. All patients received standard information provided by a registered nurse working at the foot clinic. 5) Were participants receiving care kept blind to treatment allocation? Participants were not blinded to treatment allocation. 6) Were the individuals administering care kept blind to treatment allocation? Individuals administering care were not blinded to treatment allocation. 7) Were groups comparable with respect to availability of outcome data and for how many participants were no outcome data available? Loss to follow up was comparatively quite large in both groups. 21 were lost to follow up in the intervention group and 22 were lost to follow up in the control group. Unclear if groups were comparable for the reasons for loss to follow up. 8) Did the study have an appropriate length of follow up? 6 month length of follow up was employed, this was appropriate although the original study was planned for 24 months. 9) Did the study use a precise definition of outcome? A precise definition of ulceration was employed using the Wagner system. The definition for type 1 or type 2 diabetes however was dubious. Diagnosed at age 30 or above was deemed to be type 2 diabetes. Participants below age 30 were deemed to be type 1 diabetes. 10) Was a valid and reliable method used to determine that outcome? Valid and reliable methods were used. 11) Were investigators kept blind to participant’s exposure to the intervention?

<table>
<tr><th>Bibliographic reference</th><th>Annersten Gershater, M., Pilhammar, E., Apelqvist, J., & Alm-Roijer, C. (2011). Patient education for the prevention of diabetic foot ulcers. Interim analysis of a randomised controlled trial due to morbidity and mortality of participants.</th></tr>
<tr><td></td><td>Investigators were kept blind to participant’s exposure to the intervention assessing photographs taken by individuals administering care.
12) Were investigators kept blind to other important confounding and prognostic factors?
Unclear if investigators were kept blind to other important confounding and prognostic factors.</td></tr>
<tr><td>Number of patients</td><td>Randomised= 131
Intervention group= 40
Standard therapy group= 58</td></tr>
<tr><td>Patient characteristics</td><td>Patients taken from: Sweden

Inclusion:
Previously known diabetes mellitus
Signs of sensory neuropathy
Aged 35-79 years
Healed index ulcer (Wagner grade 1 or more) below the ankle

Exclude:
Present ulcer on foot/feet below the ankle
Co-morbidity that inhibited participation and follow up
Previous major amputation (transtibial or higher)
Reliance on an interpreter

Baseline characteristics: No significant differences found, P values not provided in the study

<table>
<tr><td>Characteristics</td><td>Intervention n=61</td><td>Standard therapy, n=70</td></tr>
<tr><td>Age, years, median (range)</td><td>64 (37-78)</td><td>64 (35-79)</td></tr>
<tr><td>Sex, Male/female</td><td>46/15</td><td>50/20</td></tr>
<tr><td>Race</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Type 2 diabetes</td><td>39</td><td>49</td></tr>
</table>
</td></tr>
</table>

Bibliographic reference	**Annersten Gershater, M., Pilhammar, E., Apelqvist, J., & Alm-Roijer, C. (2011). Patient education for the prevention of diabetic foot ulcers. Interim analysis of a randomised controlled trial due to morbidity and mortality of participants.**
	<table><tr><td>Duration of diabetes, y</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Ulcer history</td><td>All</td><td>All</td></tr><tr><td>History of previous amputation</td><td>16</td><td>16</td></tr><tr><td>Peripheral vascular disease</td><td>13</td><td>16</td></tr><tr><td>Foot deformity</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Ankle brachial index</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Activity (steps per day)</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Time prescribed shoes worn</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Diabetic foot risk classification % Risk 2 Risk 3</td><td>All risk 3</td><td>All risk 3</td></tr><tr><td>Neuropathy %</td><td>14</td><td>15</td></tr><tr><td>Retinopathy %</td><td>54</td><td>62</td></tr><tr><td>HbA1c</td><td>65 ± 19</td><td>70 ± 18</td></tr><tr><td>Current smoker</td><td>8</td><td>15</td></tr></table>
Intervention	Education: n= 40 Diabetes specialist nurse lead sessions for 60 minutes in which participants actively participated in discussions. Each participant took part in one of the group sessions. All participants received standard care.
Comparison	Standard therapy alone: n=58 General diabetic foot care was standardised for all participants and included adjusted shoes and individually fitted insoles for indoor use, and recommended regular chiropody. All patients received standard information provided by a registered nurse working at the foot clinic.
Length of follow up	Length of follow up was 6 months
Location	Sweden
Outcomes measures and effect size	Rates of foot ulceration/infection Number who developed foot ulceration Definition taken from Wagner grade 1 ulcer or above. Intervention group group= 19 of 40 participants (48%)

Bibliographic reference	**Annersten Gershater, M., Pilhammar, E., Apelqvist, J., & Alm-Roijer, C. (2011). Patient education for the prevention of diabetic foot ulcers. Interim analysis of a randomised controlled trial due to morbidity and mortality of participants.**
	Standard therapy alone= 22 of 58 participants (38%) no significant difference found (p value not provided) Kaplan-Meier analysis of ulcer free days did not show a significant difference between the two groups. Rates of gangrene resulting from diabetes No data available Rates of amputation No data available Rates of A&E/ Hospital admission for foot problems resulting from diabetes No data available Resource use and costs No data available
Source of funding	Grant from Diabetes Association in South West Skane; Shoe business Branch's Research foundation, Swedish Nurses Association
Comments	

Table 26: McMurray 2002

Bibliographic reference	**McMurray, S. D., Johnson, G., Davis, S., & McDougall, K. (2002). Diabetes education and care management significantly improve patient outcomes in the dialysis unit. American journal of kidney diseases, 40(3), 566-575.**
Study type	Randomised control trial
Study quality	Summary Population: USA, participants with end stage renal failure, undergoing renal replacement therapy (haemodialysis or peritoneal dialysis Intervention: An education programme followed up by a care manager who provided self-management education, diabetes self-care monitoring/management, motivational coaching and foot checks.

Bibliographic reference	**McMurray, S. D., Johnson, G., Davis, S., & McDougall, K. (2002). Diabetes education and care management significantly improve patient outcomes in the dialysis unit. American journal of kidney diseases, 40(3), 566-575.**
	Standard of care: after baseline assessments were completed, the control group had no further contact with the diabetes care manager until end of study evaluations were initiated. They received standard diabetes care from the dialysis facility as directed by the physician. This included monitoring random blood glucose and quarterly HbA1c levels Comparison: Standard care as above Outcome: incidence of amputation, quality of life, hospital admissions, self-knowledge, behaviour, glycaemic control and foot care. 1) Has an appropriate method of randomisation been used? An appropriate method of randomisation was not used and subjects were split by day of the week in which they attended the clinic. This did have some purpose however in order to avoid knowledge sharing between patient groups. 2) Was there adequate concealment of allocation? Unclear if there was adequate allocation concealment. 3) Were the groups comparable at baseline for all major confounding/prognostic factors? Groups were comparable for major confounding factors and P values were provided however many important factors were not reported. 4) Did the comparison groups receive the same care apart from interventions studied? General diabetic foot care was standardised for all participants who received the same care from the same physician at the same facility, however it is difficult to glean which particular service was most effective in the study group since the study group seemed to receive a large variety of different treatments over the standard care group. It will be difficult therefore to prove any one aspect of management caused a benefit. 5) Were participants receiving care kept blind to treatment allocation? Participants were not blinded to treatment allocation. 6) Were the individuals administering care kept blind to treatment allocation? Individuals administering care were not blinded to treatment allocation. 7) Were groups comparable with respect to availability of outcome data and for how many participants were no outcome data available? Loss to follow up was comparatively quite large in both groups. 21 were lost to follow up in the intervention group and 22 were lost to follow up in the control group. Unclear if groups were comparable for the reasons for loss to follow up. Four participants were excluded from each group due to refusal to complete all baseline assessments. The other 35 patients excluded from the study chose not to participate in the project. It is unclear if loss to follow up effected one group more than another. 8) Did the study have an appropriate length of follow up? 12 month length of follow up was employed, this was appropriate. 9) Did the study use a precise definition of outcome? A precise definition of outcomes were used 10) Was a valid and reliable method used to determine that outcome?

<table>
<tr><th>Bibliographic reference</th><th>McMurray, S. D., Johnson, G., Davis, S., & McDougall, K. (2002). Diabetes education and care management significantly improve patient outcomes in the dialysis unit. American journal of kidney diseases, 40(3), 566-575.</th></tr>
<tr><td></td><td>Valid and reliable methods were used.
11) Were investigators kept blind to participant’s exposure to the intervention?
Investigators were not kept blind to participant’s exposure to the intervention
12) Were investigators kept blind to other important confounding and prognostic factors?
Unclear if investigators were kept blind to other important confounding and prognostic factors.</td></tr>
<tr><td>Number of patients</td><td>Randomised= 126
Intervention group= 45
Standard therapy group= 38</td></tr>
<tr><td>Patient characteristics</td><td>Patients taken from: USA

Inclusion:
End stage renal failure requiring renal replacement therapy with either haemodialysis or peritoneal dialysis
Diagnosis of type 1 or type 2 diabetes

Baseline characteristics: No significant differences found, P values not provided in the study

<table>
<tr><td>Characteristics</td><td>Study group n=45</td><td>Control group, n=38</td></tr>
<tr><td>Age, years</td><td>60.9 ± 11.7</td><td>63.0 ± 13.5</td></tr>
<tr><td>Sex, Male/female</td><td>21/17</td><td>24/21</td></tr>
<tr><td>Race</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Type 2 diabetes</td><td>34</td><td>38</td></tr>
<tr><td>Duration of diabetes, y</td><td>22.0 ± 11.7</td><td>20.5 ± 13.0</td></tr>
<tr><td>Ulcer history</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>History of previous amputation</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Peripheral vascular disease</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Foot deformity</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Ankle brachial index</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Activity (steps per day)</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Time prescribed shoes worn</td><td>Not reported</td><td>Not reported</td></tr>
</table>
</td></tr>
</table>

Bibliographic reference	**McMurray, S. D., Johnson, G., Davis, S., & McDougall, K. (2002). Diabetes education and care management significantly improve patient outcomes in the dialysis unit. American journal of kidney diseases, 40(3), 566-575.**

Diabetic foot risk classification % Risk 2 Risk 3	Not reported	Not reported
Neuropathy %	Not reported	Not reported
Retinopathy %	Not reported	Not reported
HbA1c	Not reported	Not reported
Current smoker	Not reported	Not reported
Moths on dialysis therapy	33.2 ± 24.2	32.4 ± 22.8

Intervention	Intervention group, n=45 An education programme followed up by a care manager who provided self-management education, diabetes self-care monitoring/management, motivational coaching and foot checks. Participants also received nutrition counselling with a dietician and follow up reminders from the diabetes case manager.
Comparison	Standard therapy alone: n=38 After baseline assessments were completed, the control group had no further contact with the diabetes care manager until end of study evaluations were initiated. They received standard diabetes care from the dialysis facility as directed by the physician. This included monitoring random blood glucose and quarterly HbA1c levels
Length of follow up	Length of follow up was 12 months
Location	USA
Outcomes measures and effect size	Rates of foot ulceration/infection No data available Rates of gangrene resulting from diabetes No data available Rates of amputation Number who developed lower extremity amputation Definition unclear Intervention group group= 0 of 45 participants

Bibliographic reference	McMurray, S. D., Johnson, G., Davis, S., & McDougall, K. (2002). Diabetes education and care management significantly improve patient outcomes in the dialysis unit. American journal of kidney diseases, 40(3), 566-575.
	Standard therapy alone= 5 of 38 participants P value: <0.05 i.e. significant difference Rates of A&E/ Hospital admission for foot problems resulting from diabetes Number who required hospitalisation With vascular or diabetes related admissions Intervention group group= 1 of 45 participants Standard therapy alone= 10 of 38 participants P value: <0.002 i.e. significant difference Resource use and costs No data available
Source of funding	Renal Care Group and a grant from The Kidney Foundation of Indiana
Comments	

Table 27: Bloomgarden 1987

Bibliographic reference	Bloomgarden, Z. T., Karmally, W., Metzger, M. J., Brothers, M., Nechemias, C., Bookman, J., ... & Brown, W. V. (1987). Randomized, controlled trial of diabetic patient education: improved knowledge without improved metabolic status. Diabetes care, 10(3), 263-272.
Study type	Randomised control trial
Study quality	Summary Population: USA, amongst insulin treated patients in one clinic Intervention: 9 education sessions were offered to each patient in the education group. 82 participants in the education group attended at least 7 of these educational sessions. Standard of care: patients had a contact at each visit with their physician and a nurse who reviewed medications and specific problems. Patients in the education group attended 5.7 ± 2.7 clinic visits, those in the control group attended 5.2 ± 2.7 clinic visits

Bibliographic reference	**Bloomgarden, Z. T., Karmally, W., Metzger, M. J., Brothers, M., Nechemias, C., Bookman, J., ... & Brown, W. V. (1987). Randomized, controlled trial of diabetic patient education: improved knowledge without improved metabolic status. Diabetes care, 10(3), 263-272.**
	during follow up period. Comparison: Standard care alone as above Outcome: incidence of ulceration/amputation, self-knowledge, Hba1c, behaviour, other lab measurements, body mass index, foot lesion score. 1) Has an appropriate method of randomisation been used? Unclear if an appropriate method of randomisation was used, the clinic randomised the entire patient list before finding out which participants could take part which resulted in a large drop out post randomisation. 2) Was there adequate concealment of allocation? Unclear if there was adequate allocation concealment. 3) Were the groups comparable at baseline for all major confounding/prognostic factors? Groups were not comparable for all major confounding factors. Foot lesions had occurred more frequently in the control group, fasting blood glucose and number of hospitalisations in the previous year were higher in the education group. 4) Did the comparison groups receive the same care apart from interventions studied? Patients had a contact at each visit with their physician and a nurse who reviewed medications and specific problems. Patients in the education group attended 5.7 ± 2.7 clinic visits, those in the control group attended 5.2 ± 2.7 clinic visits during follow up period. Participants were treated and monitored in the same clinic. 5) Were participants receiving care kept blind to treatment allocation? Participants were not blinded to treatment allocation. 6) Were the individuals administering care kept blind to treatment allocation? Individuals administering care were not blinded to treatment allocation. 7) Were groups comparable with respect to availability of outcome data and for how many participants were no outcome data available? Loss to follow up was comparatively quite large in both groups. Post randomisation 404 participants were lost to follow up. Twenty-seven percent of non-participants were >70 years old. A greater proportion on non-participants than participants were men. 8) Did the study have an appropriate length of follow up? Length of follow up also varied between groups 1.5 ± 0.3 years in the control group and 1.6 ± 0.3 years in the in the education group 9) Did the study use a precise definition of outcome? A precise definition of outcome was not used for foot lesions, outcomes were grouped into severe, minor and none. This included groups of complications which was not helpful for separating for outcomes of interest. 10) Was a valid and reliable method used to determine that outcome? Unclear if valid and reliable methods were used.

<table>
<tr><th>Bibliographic reference</th><td>Bloomgarden, Z. T., Karmally, W., Metzger, M. J., Brothers, M., Nechemias, C., Bookman, J., ... & Brown, W. V. (1987). Randomized, controlled trial of diabetic patient education: improved knowledge without improved metabolic status. Diabetes care, 10(3), 263-272.</td></tr>
<tr><td></td><td>11) Were investigators kept blind to participant’s exposure to the intervention?
Investigators were not kept blind to participant’s exposure to the intervention
12) Were investigators kept blind to other important confounding and prognostic factors?
Unclear if investigators were kept blind to other important confounding and prognostic factors.</td></tr>
<tr><td>Number of patients</td><td>Randomised= 749
Education group= 165
Standard therapy group= 180</td></tr>
<tr><td>Patient characteristics</td><td>Patients taken from: USA

Inclusion:
Insulin treated patients
Mount Sinai Medical Center Diabetes Clinic

Baseline characteristics:

<table>
<tr><th>Characteristics</th><th>Education group n=127</th><th>Control group, n=139</th></tr>
<tr><td>Age, years</td><td>56 ± 12</td><td>59 ± 13</td></tr>
<tr><td>Sex, female</td><td>77</td><td>67</td></tr>
<tr><td>Race
White
Black
Hispanic</td><td>
7
52
40</td><td>
9
40
49</td></tr>
<tr><td>Type 2 diabetes</td><td>96</td><td>91</td></tr>
<tr><td>Duration of diabetes, y</td><td>13 ± 8</td><td>14 ± 9</td></tr>
<tr><td>Ulcer or amputation</td><td>6</td><td>9</td></tr>
<tr><td>History of previous amputation</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Peripheral vascular disease</td><td>Not reported</td><td>Not reported</td></tr>
</table>
</td></tr>
</table>

Bibliographic reference	**Bloomgarden, Z. T., Karmally, W., Metzger, M. J., Brothers, M., Nechemias, C., Bookman, J., ... & Brown, W. V. (1987). Randomized, controlled trial of diabetic patient education: improved knowledge without improved metabolic status. Diabetes care, 10(3), 263-272.**
	<table><tr><td>Foot deformity</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Ankle brachial index</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Activity (steps per day)</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Time prescribed shoes worn</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Diabetic foot risk classification % Risk 2 Risk 3</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Neuropathy</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Retinopathy</td><td>21</td><td>29</td></tr><tr><td>HbA1c</td><td>6.8 ± 2.1</td><td>6.6 ± 2.0</td></tr><tr><td>Current smoker</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Abnormal renal function</td><td>12</td><td>10</td></tr><tr><td>Hospitalizations/yr</td><td>0.5 ± 0.8</td><td>0.3 ± 0.5</td></tr></table>
Intervention	Education group, n=127 9 education sessions were offered to each patient in the education group. 82 participants in the education group attended at least 7 of these educational sessions. All participants received standard therapy.
Comparison	Standard therapy alone: n=139 Patients had a contact at each visit with their physician and a nurse who reviewed medications and specific problems. Patients in the education group attended 5.7 ± 2.7 clinic visits, those in the control group attended 5.2 ± 2.7 clinic visits during follow up period.
Length of follow up	Length of follow up also varied between groups 1.5 ± 0.3 years in the control group and 1.6 ± 0.3 years in the in the education group
Location	USA
Outcomes measures and effect size	Rates of foot ulceration/infection Number who developed ulcer or amputation who had not had either at initial evaluation Definition unclear Intervention group= 4 of 127 participants Standard therapy alone= 5 of 139 participants Results calculated from the data provided, 7 participants from the education group and 13 participants from the control group had

Bibliographic reference	**Bloomgarden, Z. T., Karmally, W., Metzger, M. J., Brothers, M., Nechemias, C., Bookman, J., ... & Brown, W. V. (1987). Randomized, controlled trial of diabetic patient education: improved knowledge without improved metabolic status. Diabetes care, 10(3), 263-272.**
	had ulceration or amputation already at initial evaluation. Study found no significant differences between groups Rates of gangrene resulting from diabetes No data available Rates of amputation See above Rates of A&E/ Hospital admission for foot problems resulting from diabetes No data available Resource use and costs No data available
Source of funding	Supported in part by grants from the Mount Sinai Hospital Auxiliary Board, the New York State Bureau of Health, the Centres for Disease Control and the Alexander foundation
Comments	

Table 28: Lincoln 2008

Bibliographic reference	**Lincoln, N. B., Radford, K. A., Game, F. L., & Jeffcoate, W. J. (2008). Education for secondary prevention of foot ulcers in people with diabetes: a randomised controlled trial. Diabetologia, 51(11), 1954-1961.**
Study type	Randomised control trial
Study quality	Summary Population: UK, three specialist diabetes clinics Intervention: footcare education programme with one to one targeted education Standard of care: no structured education, many patients were discharged to the care of their general practitioner, with or without

Bibliographic reference	**Lincoln, N. B., Radford, K. A., Game, F. L., & Jeffcoate, W. J. (2008). Education for secondary prevention of foot ulcers in people with diabetes: a randomised controlled trial. Diabetologia, 51(11), 1954-1961.**
	input from a community podiatrist. Any education regarding prevention of ulcer recurrence was unstructured and opportunistic. Participants were provided with regular podiatry and suitable orthoses when appropriate. Their overall medical care followed UK guidelines. Comparison: Standard care alone as above Outcome: incidence of ulceration/amputation, mood, quality of life, behaviour 1) Has an appropriate method of randomisation been used? An appropriate method of randomisation was used with a computer generated random allocation sequence that had been prepared in advance. 2) Was there adequate concealment of allocation? Allocation was concealed from the clinical researcher 3) Were the groups comparable at baseline for all major confounding/prognostic factors? Groups were likely comparable for all major confounding factors, no differences were reported however no P values were provided. 4) Did the comparison groups receive the same care apart from interventions studied? Patients received the same care apart from intervention provided however treatment was split across 3 different centres and care may have varied between depending on the physician and general practitioners involved with care. 5) Were participants receiving care kept blind to treatment allocation? Participants were not blinded to treatment allocation. 6) Were the individuals administering care kept blind to treatment allocation? Individuals administering care were not blinded to treatment allocation. 7) Were groups comparable with respect to availability of outcome data and for how many participants were no outcome data available? Loss to follow up was 6 in the education group and 12 in the control group. Unclear if this difference significantly effected results. Intention to treat analysis was employed. 8) Did the study have an appropriate length of follow up? Length of follow up was 12 months. This was appropriate. 9) Did the study use a precise definition of outcome? A precise definition of outcome was unclear for ulceration and amputation. A precise definition was used for the other outcomes of mood, behaviour and quality of life. 10) Was a valid and reliable method used to determine that outcome? Unclear if valid and reliable methods were used. Questionnaires were used to gather results and these were cross checked with medical and hospital records and podiatry in some cases. Occasional discrepancies concerning ulcer occurrence and amputation were found between medical records but these errors were resolved by reading the medical records in detail.

Bibliographic reference	**Lincoln, N. B., Radford, K. A., Game, F. L., & Jeffcoate, W. J. (2008). Education for secondary prevention of foot ulcers in people with diabetes: a randomised controlled trial. Diabetologia, 51(11), 1954-1961.**
	11) Were investigators kept blind to participant's exposure to the intervention? Investigators were kept blind to participant's exposure to the intervention 12) Were investigators kept blind to other important confounding and prognostic factors? Unclear if investigators were kept blind to other important confounding and prognostic factors.
Number of patients	Randomised= 172 Education group= 87 Standard therapy group= 85
Patient characteristics	Patients taken from: UK Inclusion: Patients attending specialist foot clinics in Nottingham and Derby Diabetes mellitus Recently healed ulcers of the foot (on or below the malleoli) Remained ulcer free for 28 days Excluded Lived in institutional care Documented history of dementia Other serious medical problems Non-english speaking without English speaking carer Distance more than 50 miles Enrolled in a different study Withheld consent Members of the focus groups used in developing the educational programme Baseline characteristics:

Characteristics	Education group n=87	Control group, n=85

Bibliographic reference	**Lincoln, N. B., Radford, K. A., Game, F. L., & Jeffcoate, W. J. (2008). Education for secondary prevention of foot ulcers in people with diabetes: a randomised controlled trial. Diabetologia, 51(11), 1954-1961.**

Age, years	63.5 ± 12.1	64.9 ± 10.9
Sex, female	24	32
Race UK white Other	 83 4	 82 3
Type 2 diabetes	64	69
Duration of diabetes, y	Not reported	Not reported
Previous Ulcer	All	All
History of previous amputation	26	18
Pulses palpable (both feet) One palpable	30 39	33 28
Foot deformity	Not reported	Not reported
Ankle brachial index	Not reported	Not reported
Activity (steps per day)	Not reported	Not reported
Fitted footwear	38	30
Diabetic foot risk classification % Risk 2 Risk 3	Not reported	Not reported
Neuropathy	Not reported	Not reported
Retinopathy	53	50
HbA1c	Not reported	Not reported
Current smoker	Not reported	Not reported
Nephropathy	25	19
Hospitalizations/yr	Not reported	Not reported

Intervention	Education group, n=87 Footcare education programme with one to one targeted education. A single 1 hour session within 4 weeks of randomisation. All participants received standard therapy.
Comparison	Standard therapy alone: n=85 No structured education, many patients were discharged to the care of their general practitioner, with or without input from a community podiatrist. Any education regarding prevention of ulcer recurrence was unstructured and opportunistic. Participants were provided with regular podiatry and suitable orthoses when appropriate. Their overall medical care followed UK guidelines.
Length of follow up	Length of follow up was 12 months

Bibliographic reference	**Lincoln, N. B., Radford, K. A., Game, F. L., & Jeffcoate, W. J. (2008). Education for secondary prevention of foot ulcers in people with diabetes: a randomised controlled trial. Diabetologia, 51(11), 1954-1961.**
Location	UK
Outcomes measures and effect size	Rates of foot ulceration/infection Number who developed ulcer within 6 months Definition unclear Education group= 26 of 87 participants Standard therapy alone= 18 of 85 participants Relative risk: 0.890 (0.746-1.061) i.e. no significant difference Number who developed ulcer within 12 months Definition unclear Education group= 36 of 87 participants Standard therapy alone= 35 of 85 participants Relative risk: 0.997 (0.776-1.280) i.e. no significant difference Rates of gangrene resulting from diabetes No data available Rates of amputation Number who developed amputation within 6 months Definition unclear Education group= 3 of 87 participants Standard therapy alone= 0 of 85 participants Relative risk: 0.966 (0.928-1.005) i.e. no significant difference Number who developed amputation within 12 months Definition unclear Education group= 9 of 87 participants

Bibliographic reference	**Lincoln, N. B., Radford, K. A., Game, F. L., & Jeffcoate, W. J. (2008). Education for secondary prevention of foot ulcers in people with diabetes: a randomised controlled trial. Diabetologia, 51(11), 1954-1961.**
	Standard therapy alone= 9 of 85 participants Relative risk: 1.003 (0.905-1.111) i.e. no significant difference Rates of A&E/ Hospital admission for foot problems resulting from diabetes No data available Resource use and costs No data available
Source of funding	Supported by Diabetes UK
Comments	

Table 29: Malone 1989

Bibliographic reference	**Malone, James M., et al. "Prevention of amputation by diabetic education." The American journal of surgery 158.6 (1989): 520-524.**
Study type	Randomised control trial
Study quality	Summary Population: USA, two clinics: podiatry and vascular surgery clinic. A mix of patients with uninfected foot ulcers or previous amputation. Intervention: foot care education programme including a review of slides of infected/amputated limbs and a simple set of instructions for foot care: 1 hour educational session per patient. Standard of care: routine diabetic teaching with respect to diet, weight, exercise and medication. Comparison: Standard care alone as above and in the respective clinics, further details unclear. Outcome: incidence of ulceration, amputation, infection 1) Has an appropriate method of randomisation been used? An unusual method of randomisation was used using the odd and even numbers from a participants social security number to split

Bibliographic reference	Malone, James M., et al. "Prevention of amputation by diabetic education." The American journal of surgery 158.6 (1989): 520-524.
	the groups. 2) Was there adequate concealment of allocation? Unclear if allocation was concealed 3) Were the groups comparable at baseline for all major confounding/prognostic factors? Groups were not comparable for all major confounding factors, as participants in the treatment group were stated to have a higher incidence of foot callus. Otherwise there was stated to be no statistical difference between groups for the incidence of foot deformities, neuropathy, gangrene, prior foot amputation, prior foot ulceration, hypertrophic nails, medical management of diabetes, prior diabetic foot education, vascular reconstruction or level of distal pulses. No further differences were found however data was no provided nor P values. Many important variables were not reported. It appears that some included participants may have already had foot ulceration and it is therefore also uncertain how these factors were spread between groups. 4) Did the comparison groups receive the same care apart from interventions studied? Unclear if participants received the same care. Participants were split across two different clinics, podiatry and vascular. The study stated both groups received routine diabetic teaching with respect to diet, weight, exercise and medication however it is not clear if there were any further differences in diabetic foot care. Results were not stratified per clinic. 5) Were participants receiving care kept blind to treatment allocation? Participants were not blinded to treatment allocation. 6) Were the individuals administering care kept blind to treatment allocation? Individuals administering care were not blinded to treatment allocation. 7) Were groups comparable with respect to availability of outcome data and for how many participants were no outcome data available? Loss to follow up was 13 in the education group and 8 in the control group. Groups seem similar for availability of outcome data. 8) Did the study have an appropriate length of follow up? Length of follow up varied between participants: for Group 1 the range of follow up was 1-26 months, mean 13.2 months for group 2 the range of follow up was 1-26 months, mean 9.2 months. The study states that overall there was no statistically significant difference in follow up between groups. 9) Did the study use a precise definition of outcome? Definition of outcomes was unclear. 10) Was a valid and reliable method used to determine that outcome? Unclear if valid and reliable methods were used. Follow up included a careful clinical assessment and evaluation of the limb at risk but no further details were provided. 11) Were investigators kept blind to participant’s exposure to the intervention? Investigators were not kept blind to participant’s exposure to the intervention 12) Were investigators kept blind to other important confounding and prognostic factors? Unclear if investigators were kept blind to other important confounding and prognostic factors.

<table>
<tr><th>Bibliographic reference</th><th>Malone, James M., et al. "Prevention of amputation by diabetic education." The American journal of surgery 158.6 (1989): 520-524.</th></tr>
<tr><td></td><td></td></tr>
<tr><td>Number of patients</td><td>Randomised= 203
Education group= 90
Standard therapy group= 92</td></tr>
<tr><td>Patient characteristics</td><td>Patients taken from: USA

Inclusion:
Patients referred to either the vascular surgery or podiatry clinic
Diabetic
Stable patients with uninfected foot ulcers or prior amputation
Excluded participants below who had received definitive surgical treatment

Excluded
Patients requiring wound debridement, formal incision and drainage of foot infections, amputation or vascular reconstruction

Baseline characteristics:

<table>
<tr><th>Characteristics</th><th>Education group n=90</th><th>Control group, n=92</th></tr>
<tr><td>Age, years</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Sex, female</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Race
UK white
Other</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Type 2 diabetes</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Duration of diabetes, y</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Previous Ulcer</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>History of previous amputation</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Pulses palpable (both feet)
One palpable</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Foot deformity</td><td>Not reported</td><td>Not reported</td></tr>
</table>
</td></tr>
</table>

Bibliographic reference	**Malone, James M., et al. "Prevention of amputation by diabetic education." The American journal of surgery 158.6 (1989): 520-524.**
	<table><tr><td>Ankle brachial index</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Activity (steps per day)</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Fitted footwear</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Diabetic foot risk classification % Risk 2 Risk 3</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Neuropathy</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Retinopathy</td><td>Not reported</td><td>Not reported</td></tr><tr><td>HbA1c</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Current smoker</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Nephropathy</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Hospitalizations/yr</td><td>Not reported</td><td>Not reported</td></tr></table>
Intervention	Education group, n=90 Foot care education programme including a review of slides of infected/amputated limbs and a simple set of instructions for foot care: 1 hour educational session per patient. Standard care.
Comparison	Standard therapy alone: n=92 Routine diabetic teaching with respect to diet, weight, exercise and medication. Standard care otherwise unclear.
Length of follow up	Length of follow up varied between participants: for Group 1 the range of follow up was 1-26 months, mean 13.2 months; for group 2 the range of follow up was 1-26 months, mean 9.2 months. The study states that overall there was no statistically significant difference in follow up between groups.
Location	USA
Outcomes measures and effect size	Rates of foot ulceration/infection Number who developed ulcer on follow up Definition unclear Education group= 8 of 177 limbs Standard therapy alone= 26 of 177 limbs P value ≤0.005 i.e. significant difference

Bibliographic reference	**Malone, James M., et al. "Prevention of amputation by diabetic education." The American journal of surgery 158.6 (1989): 520-524.**
	Number who developed infection on follow up Definition unclear Education group= 2 of 177 limbs Standard therapy alone= 2 of 177 limbs i.e. no significant difference Rates of gangrene resulting from diabetes No data available Rates of amputation Number who developed amputation on follow up Definition unclear Education group= 7 of 177 limbs (1 toe, 1 foot, 5 below knee,) Standard therapy alone= 21 of 177 limbs (1 toe, 2 foot, 14 below knee, 4 above knee) P value ≤0.025 i.e. significant difference Rates of A&E/ Hospital admission for foot problems resulting from diabetes No data available Resource use and costs No data available
Source of funding	Supported by Veterans Administration, Washington D.C
Comments	

Table 30: Litzelman 1993

Bibliographic reference	**Litzelman, D. K., Slemenda, C. W., Langefeld, C. D., Hays, L. M., Welch, M. A., Bild, D. E., ... & Vinicor, F. (1993). Reduction of lower extremity clinical abnormalities in patients with non-insulin-dependent diabetes mellitusA randomized, controlled trial. Annals of Internal Medicine, 119(1), 36-41.**
Study type	Randomised control trial
Study quality	Summary Population: USA, the study was conducted in an academic practice that provided care predominantly to poorly educated and indigent women of black ethnicity with type 2 diabetes. The practice is split into 4 primary care teams each with its own nursing and clerical staff Intervention: The intervention was multifaceted: Patients received foot-care education and entered into a behavioural contract for desired self-foot care, which was reinforced through telephone and postcard reminders. Health care providers were given practice guidelines and informational flow sheets on foot related risk factors for amputation in diabetic patients. In addition, the folders for intervention patients had special identifiers that prompted health care providers to 1) ask that patients remove their foot wear, 2) perform foot examinations and 3) provide foot-care education Standard of care: undefined Comparison: Standard care alone further details were not defined. Outcome: incidence of foot lesions (non-separable for ulceration), amputation, behaviour, physician/health care professional behaviour 1) Has an appropriate method of randomisation been used? An unusual method of randomisation was used; the practice was subdivided into 4 primary care teams each with its own nursing and clerical staff. Two teams were randomly assigned to the intervention group and two teams to the control group. Method of randomisation was unclear. This method may introduce confounding factors since care may vary between teams. 2) Was there adequate concealment of allocation? Unclear if allocation was concealed 3) Were the groups comparable at baseline for all major confounding/prognostic factors? Groups were not comparable for all major confounding factors, as participants in the treatment group were stated to have a higher HbA1c value at baseline. Groups were comparable for other baseline measures recorded. Some important variables were not reported. 4) Did the comparison groups receive the same care apart from interventions studied? Unclear if participants received the same care as standard care is not stipulated. The multifaceted nature of the intervention itself which targeted both participants and healthcare professionals also meant that it would be difficult to tell which aspect of care caused

Bibliographic reference	**Litzelman, D. K., Slemenda, C. W., Langefeld, C. D., Hays, L. M., Welch, M. A., Bild, D. E., ... & Vinicor, F. (1993). Reduction of lower extremity clinical abnormalities in patients with non-insulin-dependent diabetes mellitusA randomized, controlled trial. Annals of Internal Medicine, 119(1), 36-41.**
	any effect. By the end of the study participants in the intervention group were found to be examined more frequently and have the examinations recorded more frequently and in more detail. Physicians exposed to the intervention were also more likely to refer patients to the podiatry clinic. 5) Were participants receiving care kept blind to treatment allocation? Participants were not blinded to treatment allocation. 6) Were the individuals administering care kept blind to treatment allocation? Individuals administering care were not blinded to treatment allocation. 7) Were groups comparable with respect to availability of outcome data and for how many participants were no outcome data available? Loss to follow up was 44 in total. It is unclear however how many participants were lost to each group and whether groups were comparable for outcome data available. 8) Did the study have an appropriate length of follow up? Length of follow up was 12 months, this was appropriate for the purpose of the study. 9) Did the study use a precise definition of outcome? A precise definition of outcomes was used. No definition of amputation was given, however, or information on the extent of amputation. 10) Was a valid and reliable method used to determine that outcome? Unclear if valid and reliable methods were used. A blinded nurse-clinician took information on outcomes from an audit of the medical charts and medical records. This was helpful to provide information on how well documented examinations were however it adds an extra element of uncertainty in interpreting the original findings of the physician. 11) Were investigators kept blind to participant's exposure to the intervention? Investigators were kept blind to participant's exposure to the intervention (observer blinded) 12) Were investigators kept blind to other important confounding and prognostic factors? Unclear if investigators were kept blind to other important confounding and prognostic factors. There is possibly some issues regarding generalizability of this data since the inclusion criteria only included those diagnosed after 30 years of age, greater than 40 years of age currently and type 2 diabetes.
Number of patients	Randomised= 396 Intervention group= 191 Standard therapy group= 205

Bibliographic reference	**Litzelman, D. K., Slemenda, C. W., Langefeld, C. D., Hays, L. M., Welch, M. A., Bild, D. E., ... & Vinicor, F. (1993). Reduction of lower extremity clinical abnormalities in patients with non-insulin-dependent diabetes mellitusA randomized, controlled trial. Annals of Internal Medicine, 119(1), 36-41.**
Patient characteristics	Patients taken from: USA Inclusion: Type 2 diabetes Seen at least 2 times in the preceding year by the same provider Aged >40 years Diagnosis of diabetes after 30 years of age Diagnosis of diabetes based on National Diabetes Data Group criteria Disease requiring medication for the control of hyperglycaemia Intention to obtain care at the general medical practice for the next 2 years Body weight either ideal or heavier than ideal Excluded Pregnancy Major psychiatric illness Terminal illness likely to cause death within 1 year Renal failure Previous bilateral amputations above or below the knee Inability to provide any self-care Patients of investigators involved in the study Baseline characteristics: P values provided, HbA1c found to be significantly different between groups

Characteristics	Intervention group n=191	Control group, n=205
Age, years	60.9 ± 9.8	59.9 ± 9.4
Sex, female %	82	80
Ethnicity Black %	75	77
Type 2 diabetes	All	All
Duration of diabetes, y	9.6 ± 8.0	10.1 ± 8.1

Bibliographic reference	**Litzelman, D. K., Slemenda, C. W., Langefeld, C. D., Hays, L. M., Welch, M. A., Bild, D. E., ... & Vinicor, F. (1993). Reduction of lower extremity clinical abnormalities in patients with non-insulin-dependent diabetes mellitusA randomized, controlled trial. Annals of Internal Medicine, 119(1), 36-41.**

Previous Ulcer	Not reported	Not reported
History of previous amputation	Not reported	Not reported
Pulses palpable (both feet) One palpable	Not reported	Not reported
Foot deformity	Not reported	Not reported
Ankle brachial index	Not reported	Not reported
Activity (steps per day)	Not reported	Not reported
Fitted footwear	Not reported	Not reported
Diabetic foot risk classification % Risk 2 Risk 3	Not reported	Not reported
Neuropathy	Not reported	Not reported
Retinopathy	Not reported	Not reported
HbA1c	10.5 ± 2.3	10.0 ± 2.6
Current smoker	Not reported	Not reported
Nephropathy	Not reported	Not reported
Hospitalizations/yr	Not reported	Not reported

Intervention	Intervention group, n=191 The intervention was multifaceted: Patients received foot-care education and entered into a behavioural contract for desired self-foot care, which was reinforced through telephone and postcard reminders. Health care providers were given practice guidelines and informational flow sheets on foot related risk factors for amputation in diabetic patients. In addition, the folders for intervention patients had special identifiers that prompted health care providers to 1) ask that patients remove their foot wear, 2) perform foot examinations and 3) provide foot-care education
Comparison	Standard therapy alone: n=205 Unclear definition of usual care
Length of follow up	Length of follow up was 12 months
Location	USA
Outcomes measures and	Rates of foot ulceration/infection

Bibliographic reference	**Litzelman, D. K., Slemenda, C. W., Langefeld, C. D., Hays, L. M., Welch, M. A., Bild, D. E., ... & Vinicor, F. (1993). Reduction of lower extremity clinical abnormalities in patients with non-insulin-dependent diabetes mellitusA randomized, controlled trial. Annals of Internal Medicine, 119(1), 36-41.**
effect size	No data available Rates of gangrene resulting from diabetes No data available Rates of amputation Number who required amputation by 1 year Definition unclear Intervention group= 1 of 191 participants Standard therapy alone= 4 of 205 participants Study states that neither the sample size nor the length of follow up was adequate to show that these interventions can reduce the incidence of lower extremity amputations in this study i.e. non-significant (P values not provided) Rates of A&E/ Hospital admission for foot problems resulting from diabetes No data available Resource use and costs No data available
Source of funding	Supported by Division of Diabetes Translation, Centers for Disease Control and Prevention
Comments	

Table 31: Armstrong 2005

Bibliographic reference	**Armstrong, D. G., Holtz, K., & Wu, S. (2005). Can the use of a topical antifungal nail lacquer reduce risk for diabetic foot ulceration? results from a randomised controlled pilot study. International wound journal, 2(2), 166-170.**
Study type	Randomised control trial
Study quality	Summary

Bibliographic reference	**Armstrong, D. G., Holtz, K., & Wu, S. (2005). Can the use of a topical antifungal nail lacquer reduce risk for diabetic foot ulceration? results from a randomised controlled pilot study. International wound journal, 2(2), 166-170.**
	Population: USA, International Diabetes Foot Classification risk category 2 or 3 Intervention: preventive foot care program using daily self-inspection with the use of antifungal nail lacquer (ciclopirox 8%) Standard of care: Patients were followed every 3 months for 12 months or until ulceration in a multidisciplinary high-risk diabetic foot clinic. Patients were also given contact information for a foot hotline that was staffed 24 hours a day by a clinician familiar with the care and status of these patients. Clinicians could appoint patients into pre-assigned emergency visit slots in each daily clinic schedule. Comparison: Standard care as above and instructions for self inspection. Outcome: incidence of ulceration, hyperkeratosis, tinea pedis 1) Has an appropriate method of randomisation been used? An appropriate method of randomisation was used with a computer generated randomisation schedule 2) Was there adequate concealment of allocation? Unclear if allocation was adequately concealed 3) Were the groups comparable at baseline for all major confounding/prognostic factors? Groups were comparable for all major confounding factors, however many important variables were not reported. 4) Did the comparison groups receive the same care apart from interventions studied? Patients received the same care apart from intervention provided, care was provided at the same multidisciplinary clinic. 5) Were participants receiving care kept blind to treatment allocation? Participants were not blinded to treatment allocation. 6) Were the individuals administering care kept blind to treatment allocation? Individuals administering care were not blinded to treatment allocation. 7) Were groups comparable with respect to availability of outcome data and for how many participants were no outcome data available? Unclear if there was loss to follow up; intention to treat analysis was used. 8) Did the study have an appropriate length of follow up? Length of follow up was 12 months. This was appropriate. 9) Did the study use a precise definition of outcome? A precise definition of outcome was unclear for ulceration. A precise definition was used for other variables. 10) Was a valid and reliable method used to determine that outcome? Unclear if valid and reliable methods were used. No details were provided of how and when ulcerations were diagnosed. 11) Were investigators kept blind to participant’s exposure to the intervention? Investigators were not kept blind to participant’s exposure to the intervention 12) Were investigators kept blind to other important confounding and prognostic factors?

<table>
<tr><td>Bibliographic reference</td><td>Armstrong, D. G., Holtz, K., & Wu, S. (2005). Can the use of a topical antifungal nail lacquer reduce risk for diabetic foot ulceration? results from a randomised controlled pilot study. International wound journal, 2(2), 166-170.</td></tr>
<tr><td></td><td>Unclear if investigators were kept blind to other important confounding and prognostic factors.</td></tr>
<tr><td>Number of patients</td><td>Randomised= 70
Education group= 34
Standard therapy group= 36</td></tr>
<tr><td>Patient characteristics</td><td>Patients taken from: USA

Inclusion:
International Diabetes Foot Classification risk category 2 or 3

Excluded
Unable to ambulate without the assistance of a wheelchair or crutches
Sight impaired to the extent that they were legally blind
Unwilling or unable to give consent to participate

Baseline characteristics:

<table>
<tr><td>Characteristics</td><td>Intervention group n=34</td><td>Control group, n=36</td></tr>
<tr><td>Age, years</td><td>69.5 ± 13.6</td><td>70.3 ± 9.3</td></tr>
<tr><td>Sex, male %</td><td>100</td><td>94.4</td></tr>
<tr><td>Race
UK white
Other</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Type 2 diabetes</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Duration of diabetes, y</td><td>12.8 ± 9.0</td><td>11.2 ± 8.2</td></tr>
<tr><td>Previous Ulcer</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>History of previous amputation</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Pulses palpable (both feet)</td><td>Not reported</td><td>Not reported</td></tr>
</table>
</td></tr>
</table>

Bibliographic reference	**Armstrong, D. G., Holtz, K., & Wu, S. (2005). Can the use of a topical antifungal nail lacquer reduce risk for diabetic foot ulceration? results from a randomised controlled pilot study. International wound journal, 2(2), 166-170.**
	One palpable Foot deformity: Not reported / Not reported Ankle brachial index: Not reported / Not reported Activity (steps per day): Not reported / Not reported Fitted footwear: Not reported / Not reported Diabetic foot risk classification % Risk 2 Risk 3: Not reported / Not reported Neuropathy: Not reported / Not reported Retinopathy: Not reported / Not reported HbA1c: Not reported / Not reported Current smoker: Not reported / Not reported Nephropathy: Not reported / Not reported Hospitalizations/yr: Not reported / Not reported
Intervention	Antifungal Nail Lacquer group, n=34 Preventive foot care program using daily self-inspection with the possible use of antifungal nail lacquer (ciclopirox 8%). All participants received standard therapy.
Comparison	Self-inspection instruction: n=85 Patients were followed every 3 months for 12 months or until ulceration in a multidisciplinary high-risk diabetic foot clinic. Patients were also given contact information for a foot hotline that was staffed 24 hours a day by a clinician familiar with the care and status of these patients. Clinicians could appoint patients into pre-assigned emergency visit slots in each daily clinic schedule..
Length of follow up	Length of follow up was 12 months
Location	USA
Outcomes measures and effect size	Rates of foot ulceration/infection Number who developed ulcer within 12 months Definition unclear Intervention group= 2 of 34 participants Standard therapy alone= 2 of 36 participants

Bibliographic reference	**Armstrong, D. G., Holtz, K., & Wu, S. (2005). Can the use of a topical antifungal nail lacquer reduce risk for diabetic foot ulceration? results from a randomised controlled pilot study. International wound journal, 2(2), 166-170.**
	P value= 0.9 i.e. no significant difference Rates of gangrene resulting from diabetes No data available Rates of amputation No data available Rates of A&E/ Hospital admission for foot problems resulting from diabetes No data available Resource use and costs No data available
Source of funding	Supported by Aventis/Dermik Investigator Initiated Merit Award
Comments	

Table 32: Lemaster 2008

Bibliographic reference	**LeMaster, J. W., Mueller, M. J., Reiber, G. E., Mehr, D. R., Madsen, R. W., & Conn, V. S. (2008). Effect of weight-bearing activity on foot ulcer incidence in people with diabetic peripheral neuropathy: feet first randomized controlled trial. Physical Therapy, 88(11), 1385-1398.**
Study type	Randomised control trial
Study quality	Summary Population: USA, among patients with peripheral neuropathy and diabetes mellitus Intervention: Intervention involved leg strengthening and balance exercises; a graduated, self-monitored walking program followed by motivational telephone calls every 2 weeks apart. Standard of care: both groups received diabetic foot care education, regular foot care and 8 sessions with a physical therapist. Participants received usual medical care from their own providers. Project staff referred all participants to local orthotists or podiatrists to obtain therapeutic footwear at enrolment. Comparison: Standard care as above Outcome: incidence of ulceration, foot lesions, activity , adverse events

Bibliographic reference	**LeMaster, J. W., Mueller, M. J., Reiber, G. E., Mehr, D. R., Madsen, R. W., & Conn, V. S. (2008). Effect of weight-bearing activity on foot ulcer incidence in people with diabetic peripheral neuropathy: feet first randomized controlled trial. Physical Therapy, 88(11), 1385-1398.**
	1) Has an appropriate method of randomisation been used? An appropriate method of randomisation was used; randomisation was by type of clinical site as care may vary between sites. Block randomisation was used within sites. 2) Was there adequate concealment of allocation? Allocation was adequately concealed using opaque sealed envelopes. 3) Were the groups comparable at baseline for all major confounding/prognostic factors? Groups were comparable for all major confounding factors. During the study however it was recognised that the study was not designed primarily to detect foot ulcer incidence and that any inferences regarding the effect of physical activity on foot ulcer risk are dependent on the change in weight-bearing physical activity. 4) Did the comparison groups receive the same care apart from interventions studied? Patients received the same care apart from intervention provided, however participants in the control group did not receive motivational calls from the study nurse and may not have been as engaged in the study as participants in the intervention group. This could have led to reduced reporting of minor foot lesions by the control group. 5) Were participants receiving care kept blind to treatment allocation? Participants were not blinded to treatment allocation. 6) Were the individuals administering care kept blind to treatment allocation? Individuals administering care were not blinded to treatment allocation. 7) Were groups comparable with respect to availability of outcome data and for how many participants were no outcome data available? Loss to follow up was 6 in the intervention group and 3 in the control group by 12 months; intention to treat analysis was used. 8) Did the study have an appropriate length of follow up? Length of follow up was 12 months. This was appropriate. 9) Did the study use a precise definition of outcome? A precise definition of outcome was clear for all outcomes. 10) Was a valid and reliable method used to determine that outcome? Valid and reliable methods were used. Photographs of lesions were independently examined by an independent panel of dermatologists. 11) Were investigators kept blind to participant's exposure to the intervention? Investigators were kept blind to participant's exposure to the intervention (observer blind) 12) Were investigators kept blind to other important confounding and prognostic factors? Unclear if investigators were kept blind to other important confounding and prognostic factors.

Bibliographic reference	**LeMaster, J. W., Mueller, M. J., Reiber, G. E., Mehr, D. R., Madsen, R. W., & Conn, V. S. (2008). Effect of weight-bearing activity on foot ulcer incidence in people with diabetic peripheral neuropathy: feet first randomized controlled trial. Physical Therapy, 88(11), 1385-1398.**
Number of patients	Randomised= 70 Education group= 34 Standard therapy group= 36
Patient characteristics	Patients taken from: USA Inclusion: Aged 50 years and over Received diabetes or foot care at primary care, endocrinology, or podiatry practices in central Missouri Inactive (did not engage in moderately intense activity more than twice per week for more than 20 minutes per session Diagnosed type 1 or 2 diabetes mellitus Absent sensation 5.07 Semmes-Weinstein monofilament sensation on at least one of 10 points on the foot and loss of vibratory sensation. Excluded Lacked telephone access Medical conditions that may contra-indicate exercise Baseline characteristics:

Characteristics	Control group n=38	Intervention group, n=41
Age, years	64.8 ± 9.4	66.6 ± 10.4
Sex, female %	53	47
Race Non-white %	8	7
Type 2 diabetes %	92	95
Duration of diabetes, y	11.2 ± 8.5	10.8 ± 8.3
Number of Ulcers in past year	0.6 ± 1.5	0.37 ± 1.3
History of previous amputation	Not reported	Not reported

Bibliographic reference	**LeMaster, J. W., Mueller, M. J., Reiber, G. E., Mehr, D. R., Madsen, R. W., & Conn, V. S. (2008). Effect of weight-bearing activity on foot ulcer incidence in people with diabetic peripheral neuropathy: feet first randomized controlled trial. Physical Therapy, 88(11), 1385-1398.**

Ankle brachial pressure index	1.01 ± 0.1	1.05 ± 0.1
Foot deformity	Not reported	Not reported
Foot pulses present	Not reported	Not reported
Activity (steps per day) (SEM)	3,350 ± 247	3,335 ± 246
Fitted footwear	All	All
Diabetic foot risk classification % Risk 2 Risk 3	Not reported	Not reported
Neuropathy	All	All
Retinopathy	Not reported	Not reported
HbA1c	Not reported	Not reported
Current smoker %	13	5
Nephropathy	Not reported	Not reported
Hospitalizations/yr	Not reported	Not reported

Intervention	Weight bearing activity, n=41 Intervention involved leg strengthening and balance exercises; a graduated, self-monitored walking program followed by motivational telephone calls every 2 weeks apart.
Comparison	Standard care alone: n=38 Both groups received diabetic foot care education, regular foot care and 8 sessions with a physical therapist. Participants received usual medical care from their own providers. Project staff referred all participants to local orthotists or podiatrists to obtain therapeutic footwear at enrolment
Length of follow up	Length of follow up was 12 months
Location	USA
Outcomes measures and effect size	Rates of foot ulceration/infection Number who developed ulcer within 6 months Full thickness disruption Intervention group= 8 of 41 participants (incidence rate= 0.41 lesions/person year) Standard therapy alone= 4 of 38 participants (incidence rate= 0.21 lesions/person year)

Bibliographic reference	**LeMaster, J. W., Mueller, M. J., Reiber, G. E., Mehr, D. R., Madsen, R. W., & Conn, V. S. (2008). Effect of weight-bearing activity on foot ulcer incidence in people with diabetic peripheral neuropathy: feet first randomized controlled trial. Physical Therapy, 88(11), 1385-1398.**
	Rate ratio: 1.93 (0.58-6.42) i.e. no significant difference but cannot rule out important effect Number who developed ulcer within 12 months Full thickness disruption Intervention group= 9 of 41 participants (incidence rate= 0.21 lesions/person year) Standard therapy alone= 9 of 38 participants (incidence rate= 0.22 lesions/person year) Rate ratio: 0.96 (0.38-2.42) i.e. no significant difference but cannot rule out important effect Rates of gangrene resulting from diabetes No data available Rates of amputation Number who required amputation within 12 months No definition Intervention group= 0 of 41 participants (incidence rate= 0.21 lesions/person year) Standard therapy alone= 0 of 38 participants (incidence rate= 0.22 lesions/person year) No significant difference Rates of A&E/ Hospital admission for foot problems resulting from diabetes Number of ulcers required hospitalisation for infection within 12 months No definition Intervention group= 0 of 41 participants (incidence rate= 0.21 lesions/person year) Standard therapy alone= 0 of 38 participants (incidence rate= 0.22 lesions/person year) No significant difference Resource use and costs No data available
Source of funding	Supported by Robert Wood Johnson Foundation Generalist Physician Faculty Scholars program

Bibliographic reference	**LeMaster, J. W., Mueller, M. J., Reiber, G. E., Mehr, D. R., Madsen, R. W., & Conn, V. S. (2008). Effect of weight-bearing activity on foot ulcer incidence in people with diabetic peripheral neuropathy: feet first randomized controlled trial. Physical Therapy, 88(11), 1385-1398.**
Comments	

Table 33: Cisneros 2010

Bibliographic reference	**Cisneros, L. L. (2010). Evaluation of a neuropathic ulcers prevention program for patients with diabetes. Brazilian Journal of Physical Therapy, 14(1), 31-37.**
Study type	Randomised control trial
Study quality	Summary Population: Brazil, among patients with peripheral neuropathy and diabetes mellitus Intervention: Intervention involved therapeutic education with weekly group meetings (4 meetings of 90 minutes in groups of up to 8 participants) and provision of two pairs of special protective shoes. The participants could choose their colour and model. Standard of care: All participants maintained the routine care assistance offered by the unit where the study was conducted. Both groups were monitored by the researcher through foot inspection to survey the incidence and recurrence of neuropathic injury. The control group received instructions on foot care and use of footwear when requested during individual consultations with the researcher. Participants who had neuropathic injuries during the study received medical and nursing care and instructions on how to reduce loads on the affected limb. Comparison: Standard care as above Outcome: incidence of ulceration, and recurrence 1) Has an appropriate method of randomisation been used? Unclear method of randomisation was used; 2) Was there adequate concealment of allocation? Allocation was stated to be blinded, unclear method used. 3) Were the groups comparable at baseline for all major confounding/prognostic factors? Groups were comparable for all major confounding factors. Many important factors were not reported however. More than this it is unclear to what extent the loss to follow up affected the composition of the groups comparatively since a large proportion of participants from each group were lost to follow up. 4) Did the comparison groups receive the same care apart from interventions studied? Patients received the same care apart from intervention provided, however the intervention provided was both education and the provision of footwear and it is therefore difficult to see which of these interventions had the greater effect if any. Unclear how

Bibliographic reference	Cisneros, L. L. (2010). Evaluation of a neuropathic ulcers prevention program for patients with diabetes. Brazilian Journal of Physical Therapy, 14(1), 31-37.
	adherence may have affected the occurrence of ulceration as information on adherence was not used for analysis for association with outcomes. 5) Were participants receiving care kept blind to treatment allocation? Participants were not blinded to treatment allocation. 6) Were the individuals administering care kept blind to treatment allocation? Individuals administering care were not blinded to treatment allocation. 7) Were groups comparable with respect to availability of outcome data and for how many participants were no outcome data available? Loss to follow up was 7 in the intervention group and 7 in the control group by 24 months; intention to treat analysis was not used. The composition of the intervention and control group involved those of high and lower risk of ulceration therefore it is unclear to what extent the outcomes were affected as a result of the loss to follow up. 8) Did the study have an appropriate length of follow up? Length of follow up was 24 months. This was appropriate. 9) Did the study use a precise definition of outcome? A precise definition of outcome not provided for outcomes. There was no definition of ulceration or a clear definition of what is considered a recurrent ulcer and a primary ulcer. 10) Was a valid and reliable method used to determine that outcome? Unclear if valid and reliable methods were used. We know that both groups were monitored by a researcher but it is unclear what criteria he/she was using. The study states that adherence was monitored but it is unclear how since participants were presumably not seen daily for 24 months. 11) Were investigators kept blind to participant's exposure to the intervention? Investigators were not kept blind to participant's exposure to the intervention 12) Were investigators kept blind to other important confounding and prognostic factors? Unclear if investigators were kept blind to other important confounding and prognostic factors. Sample size was small and authors indicate a high probability of type II error in the present study.
Number of patients	Randomised= 53 Education group= 30 Standard therapy group= 23
Patient characteristics	Patients taken from: Brazil

<table>
<tr><th>Bibliographic reference</th><td>Cisneros, L. L. (2010). Evaluation of a neuropathic ulcers prevention program for patients with diabetes. Brazilian Journal of Physical Therapy, 14(1), 31-37.</td></tr>
<tr><td></td><td>Inclusion:
Diabetes mellitus and peripheral neuropathy

Baseline characteristics: No significant differences found

<table>
<tr><th>Characteristics</th><th>Intervention group, n=21</th><th>Control group, n=14</th></tr>
<tr><td>Age, years</td><td>64.4 ± 9.2</td><td>59.8 ± 9.0</td></tr>
<tr><td>Sex, male</td><td>21</td><td>12</td></tr>
<tr><td>Race Non-white</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Type 2 diabetes</td><td>29</td><td>22</td></tr>
<tr><td>Duration of diabetes, y</td><td>14 ± 10</td><td>15 ± 10.5</td></tr>
<tr><td>Number of Ulcers in past year</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>History of previous amputation</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Ankle brachial pressure index</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Foot deformity</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Foot pulses present</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Activity (steps per day) (SEM)</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Fitted footwear</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Diabetic foot risk classification
Risk 1
Risk 2
Risk 3
Risk 4</td><td>
6
15
3
6</td><td>
10
7
3
3</td></tr>
<tr><td>Neuropathy</td><td>All</td><td>All</td></tr>
<tr><td>Retinopathy</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>HbA1c</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Current smoker</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Nephropathy</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Hospitalizations/yr</td><td>Not reported</td><td>Not reported</td></tr>
</table>
</td></tr>
<tr><th>Intervention</th><td>Footwear and education, n=21

Intervention involved therapeutic education with weekly group meetings (4 meetings of 90 minutes in groups of up to 8 participants) and provision of two pairs of special protective shoes. The participants could choose their colour and model.</td></tr>
<tr><th>Comparison</th><td>Standard care alone: n=14</td></tr>
</table>

Bibliographic reference	**Cisneros, L. L. (2010). Evaluation of a neuropathic ulcers prevention program for patients with diabetes. Brazilian Journal of Physical Therapy, 14(1), 31-37.**
	All participants maintained the routine care assistance offered by the unit where the study was conducted. Both groups were monitored by the researcher through foot inspection to survey the incidence and recurrence of neuropathic injury. The control group received instructions on foot care and use of footwear when requested during individual consultations with the researcher. Participants who had neuropathic injuries during the study received medical and nursing care and instructions on how to reduce loads on the affected limb.
Length of follow up	Length of follow up was 24 months
Location	Brazil
Outcomes measures and effect size	Rates of foot ulceration/infection Number who developed a first ulcer Unclear definition Intervention group= 8 of 21 participants Standard therapy alone= 8 of 14 participants P value 0.317 i.e. no significant difference Number who developed a recurrent ulcer following first ulcer Unclear definition Intervention group= 1 of 8 participants Standard therapy alone= 5 of 8 participants P value 0.119 i.e. no significant difference (although unclear statistical working) Kaplan-Meier survival function was not significantly different between groups (p=0.362) Rates of gangrene resulting from diabetes No data available Rates of amputation No data available

Bibliographic reference	**Cisneros, L. L. (2010). Evaluation of a neuropathic ulcers prevention program for patients with diabetes. Brazilian Journal of Physical Therapy, 14(1), 31-37.**
	Rates of A&E/ Hospital admission for foot problems resulting from diabetes No data available Resource use and costs No data available
Source of funding	Unclear source of funding
Comments	

Table 34: Reiber 2002

Bibliographic reference	**Reiber, G. E., Smith, D. G., Wallace, C., Sullivan, K., Hayes, S., Vath, C., ... & LeMaster, J. (2002). Effect of therapeutic footwear on foot reulceration in patients with diabetes: a randomized controlled trial. Jama, 287(19), 2552-2558.**
Study type	Randomised control trial
Study quality	Summary Population: USA, among patients with previous history of foot ulcer Intervention: There were 2 groups: Participants were randomly assigned to receive 3 pairs of therapeutic shoes and 3 pairs of customised medium-density cork inserts with a neoprene closed cell cover; or 3 pairs of therapeutic shoes and 3 pairs of prefabricated, tapered polyurethane inserts with a brushed nylon cover. Standard of care: All shoes and inserts in the two treatment groups were fitted by the same study pedorthist who manufactured the custom inserts, performed shoe-fitting adjustments and replaced footwear based on wear patterns. Four visits occurred within 1 month of enrolment to ensure proper footwear fit in the in the intervention groups. Thereafter, visits were scheduled every 17 weeks to collect information. To prevent contamination of the footwear interventions by patient education or clinical care, no participants received such education or care at the study site. Comparison: Usual footwear and standard care. Outcome: incidence of ulceration, foot lesions, footwear use, physical foot and diabetes characteristics. 1) Has an appropriate method of randomisation been used? Good method of randomisation was used; computer generated block randomisation according to health care organisation and sex. 2) Was there adequate concealment of allocation?

Bibliographic reference	**Reiber, G. E., Smith, D. G., Wallace, C., Sullivan, K., Hayes, S., Vath, C., ... & LeMaster, J. (2002). Effect of therapeutic footwear on foot reulceration in patients with diabetes: a randomized controlled trial. Jama, 287(19), 2552-2558.**
	Unclear if allocation was adequately concealed. 3) Were the groups comparable at baseline for all major confounding/prognostic factors? Groups were not comparable for all major confounding factors. All but the incidence of moderated foot deformity were non-significant between groups. This was found to be significantly lower in the group with prefabricated inserts compared to the two other groups. 4) Did the comparison groups receive the same care apart from interventions studied? Patients received the same care apart from intervention provided. Care may have varied between study site however this was adjusted for in the randomisation process. 5) Were participants receiving care kept blind to treatment allocation? Participants were not blinded to treatment allocation. 6) Were the individuals administering care kept blind to treatment allocation? Individuals administering care were not blinded to treatment allocation. 7) Were groups comparable with respect to availability of outcome data and for how many participants were no outcome data available? Loss to follow up was 17 in the cork inserts group, 23 in the prefabricated inserts group and 26 in the control group by 24 months; intention to treat analysis was used. Loss to follow up seems similar between groups. 8) Did the study have an appropriate length of follow up? Length of follow up was 24 months. This was appropriate. 9) Did the study use a precise definition of outcome? A precise definition of outcome was provided for all outcomes.. 10) Was a valid and reliable method used to determine that outcome? Valid and reliable methods were used. Final ulcer classification was determined by a panel of 3 foot care specialists blinded to study group. 11) Were investigators kept blind to participant's exposure to the intervention? Investigators were kept blind to participant's exposure to the intervention for the determination of final ulcer classification. 12) Were investigators kept blind to other important confounding and prognostic factors? Unclear if investigators were kept blind to other important confounding and prognostic factors. Among control participants 30% purchased therapeutic shoes and over-the-counter inserts over the 2 year follow up.
Number of patients	Randomised= 400 Therapeutic shoes and custom cork inserts= 121 Therapeutic shoes and prefabricated polyurethane inserts= 119 Usual footwear group=160

Bibliographic reference	**Reiber, G. E., Smith, D. G., Wallace, C., Sullivan, K., Hayes, S., Vath, C., ... & LeMaster, J. (2002). Effect of therapeutic footwear on foot reulceration in patients with diabetes: a randomized controlled trial. Jama, 287(19), 2552-2558.**
Patient characteristics	Patients taken from: USA Inclusion: Diabetes mellitus Aged 45-84 years Men from either Veterans Affairs Puget Sound health Care System or Group Health Cooperative Women from Group Health Cooperative (there were few female veterans meeting eligibility) History of full thickness foot lesion or foot infection requiring antibiotic treatment Ability to walk 1 block and climb 1 flight of stairs per day Shoe size 8-12.5 for men, 7-10.5 for women Willingness to consent to randomisation and study footwear provisions Exclusion: Foot deformities requiring custom shoe Prior lower-extremity amputation of more than 1 digit Presence of either unhealed or healed lesion in the prior month Requirement of boots, custom shoes or non-traditional footwear for daily activities Non ambulatory status Terminal illness that would make 2 year survival unlikely. Severe foot deformities and Charcot foot. Baseline characteristics: Moderate foot deformity found to be significantly different (P=<0.03)

Characteristics	Cork inserts group, n=121	Prefabricated inserts group, n=119	Usual footwear group, n=160
Age, years	61 ± 10.1	62 ± 10.1	63 ± 10.0
Sex, female %	22	23	23
Race % White Black Other	 79 12 8	 82 10 8	 74 14 12
Type 1 diabetes %	7	5	8

Bibliographic reference	Reiber, G. E., Smith, D. G., Wallace, C., Sullivan, K., Hayes, S., Vath, C., ... & LeMaster, J. (2002). Effect of therapeutic footwear on foot reulceration in patients with diabetes: a randomized controlled trial. Jama, 287(19), 2552-2558.

Duration of diabetes, y % < 6 6-24 ≥ 25	 35 11 54	 35 8 57	 30.2 14.4 55.4
Previous ulcers	All	All	All
History of previous amputation	Not reported	Not reported	Not reported
Ankle brachial pressure index	Not reported	Not reported	Not reported
Moderate foot deformity %	36	22	35
No foot pulses present %	1	1	2
Activity (steps per day) (SEM)	Not reported	Not reported	Not reported
Fitted footwear	All	All	30% by 2 years
Diabetic foot risk classification Risk 1 Risk 2 Risk 3 Risk 4	Not reported	Not reported	Not reported
Neuropathy %	59	66	52
Retinopathy	Not reported	Not reported	Not reported
HbA1c	Not reported	Not reported	Not reported
Current smoker	Not reported	Not reported	Not reported
Nephropathy	Not reported	Not reported	Not reported
Hospitalizations/yr	Not reported	Not reported	Not reported
Body Mass Index	33 ± 6.8	32 ± 6.9	33 ± 7.2

Intervention	Therapeutic shoes and custom cork inserts n= 121 Participants were randomly assigned to receive 3 pairs of therapeutic shoes and 3 pairs of customised medium-density cork inserts with a neoprene closed cell cover. All shoes and inserts in the two treatment groups were fitted by the same study pedorthist who manufactured the custom inserts, performed shoe-fitting adjustments and replaced footwear based on wear patterns.
	Therapeutic shoes and prefabricated polyurethane inserts n= 119 Participants were randomly assigned to receive 3 pairs of therapeutic shoes and 3 pairs of prefabricated, tapered polyurethane inserts with a brushed nylon cover. All shoes and inserts in the two treatment groups were fitted by the same study pedorthist who manufactured the custom inserts, performed shoe-fitting adjustments and replaced footwear based on wear patterns.
Comparison	Usual footwear group n=160

Bibliographic reference	**Reiber, G. E., Smith, D. G., Wallace, C., Sullivan, K., Hayes, S., Vath, C., ... & LeMaster, J. (2002). Effect of therapeutic footwear on foot reulceration in patients with diabetes: a randomized controlled trial. Jama, 287(19), 2552-2558.**
	All participants maintained the routine care assistance offered by the health care system they were under. As well as this; four visits occurred within 1 month of enrolment to ensure proper footwear fit in the in the intervention groups. Thereafter, visits were scheduled every 17 weeks to collect information. To prevent contamination of the footwear interventions by patient education or clinical care, no participants received such education or care at the study site
Length of follow up	Length of follow up was 24 months
Location	USA
Outcomes measures and effect size	Rates of foot ulceration/infection Number of ulcers per group A cutaneous erosion extending into or through the dermis to deeper tissue or other cuts that do not heal within 30 days. Therapeutic shoes and custom cork inserts= 26 Therapeutic shoes and prefabricated polyurethane inserts= 31 Usual footwear group=38 Number of ulcers per person (≥1 ulcer) A cutaneous erosion extending into or through the dermis to deeper tissue or other cuts that do not heal within 30 days. Therapeutic shoes and custom cork inserts= 18 of 121 participants (risk ratio: 0.88 CI 0.51-1.52) Therapeutic shoes and prefabricated polyurethane inserts= 17 of 119 participants (risk ratio: 0.85 CI 0.48-1.48) Usual footwear group=27 of 160 participants (reference standard 1.00) No significant difference Cumulative incidence per person: Therapeutic shoes and custom cork inserts= 0.15 (0.09-0.22) Therapeutic shoes and prefabricated polyurethane inserts= 0.14 (0.09-0.22) Usual footwear group= 0.17 (0.11-0.24) Incidence per person-year Total ulcers: incidence rate (rate ratio) Therapeutic shoes and custom cork inserts= 0.11 (0.06-0.19) (risk ratio: 0.87 CI 0.43-1.75) Therapeutic shoes and prefabricated polyurethane inserts= 0.14 (0.08-0.23) (risk ratio: 1.09 CI 0.56-2.13)

Bibliographic reference	Reiber, G. E., Smith, D. G., Wallace, C., Sullivan, K., Hayes, S., Vath, C., ... & LeMaster, J. (2002). Effect of therapeutic footwear on foot reulceration in patients with diabetes: a randomized controlled trial. Jama, 287(19), 2552-2558.
	Usual footwear group=0.13 (0.08-0.20) (reference standard 1.00) No significant difference Number of ulcer episodes per group Multiple ulcers occurring on the same day on the same foot Therapeutic shoes and custom cork inserts= 25 Therapeutic shoes and prefabricated polyurethane inserts= 22 Usual footwear group=37 Incidence per person-year Ulcer episodes: incidence rate (rate ratio) Therapeutic shoes and custom cork inserts= 0.11 (0.06-0.17) (risk ratio: 0.86 CI 0.45-1.63) Therapeutic shoes and prefabricated polyurethane inserts= 0.10 (0.06-0.17) (risk ratio: 0.80 CI 0.41-1.56) Usual footwear group=0.12 (0.08-0.18) (reference standard 1.00) No significant difference Rates of gangrene resulting from diabetes No data available Rates of amputation No data available Rates of A&E/ Hospital admission for foot problems resulting from diabetes No data available Resource use and costs The customised cork inserts with neoprene covers required considerably more time, equipment and expense to produce than did the tapered polyurathene and brushed nylon inserts which performed similarly but were far less expensive.
Source of funding	Rehabilitation Research and Development, Health Services Research and Development, The Epidemiology Research and Information Centre, Department of Veterans Affairs, National Institute of Diabetes and Digestive and Kidney Disease, and the

Bibliographic reference	**Reiber, G. E., Smith, D. G., Wallace, C., Sullivan, K., Hayes, S., Vath, C., ... & LeMaster, J. (2002). Effect of therapeutic footwear on foot reulceration in patients with diabetes: a randomized controlled trial. Jama, 287(19), 2552-2558.**
	Centres for Disease Control and Prevention.
Comments	

Table 35: Lavery 2012

Bibliographic reference	**Lavery, L. A., LaFontaine, J., Higgins, K. R., Lanctot, D. R., & Constantinides, G. (2012). Shear-reducing insoles to prevent foot ulceration in high-risk diabetic patients. Advances in skin & wound care, 25(11), 519-524.**
Study type	Randomised control trial
Study quality	Summary Population: USA, among patients with previous history of foot ulcer and/or loss of protective sensation and foot deformity. Intervention: Shear reducing insole with elastic binders and two thin Teflon sheets. Standard of care: Standard therapy consisted of foot and lower extremity evaluation by a physician every 10-12 weeks, an education program that focused on foot complications and self-care practices, and therapeutic shoes and insoles. If study patients identified an area of concern on their feet they were instructed to contact the study nurse. All patients were provided with the same brand of therapeutic shoes. Insoles were replaced every 4 months and shoes once a year. Comparison: Standard care alone as above Outcome: incidence of ulceration, adherence. 1) Has an appropriate method of randomisation been used? Unclear method of randomisation was used; 2) Was there adequate concealment of allocation? Unclear if allocation was adequately concealed. 3) Were the groups comparable at baseline for all major confounding/prognostic factors? Groups were stated to be comparable for all major confounding factors reported although P values were not provided. 4) Did the comparison groups receive the same care apart from interventions studied? Patients received the same care apart from intervention provided. Care was over three sites and there is potential for some variance in care between sites. 5) Were participants receiving care kept blind to treatment allocation? Participants were not blinded to treatment allocation. 6) Were the individuals administering care kept blind to treatment allocation?

Bibliographic reference	**Lavery, L. A., LaFontaine, J., Higgins, K. R., Lanctot, D. R., & Constantinides, G. (2012). Shear-reducing insoles to prevent foot ulceration in high-risk diabetic patients. Advances in skin & wound care, 25(11), 519-524.**
	Individuals administering care were blinded to treatment allocation. (physician blinded/single blind) 7) Were groups comparable with respect to availability of outcome data and for how many participants were no outcome data available? Unclear if groups were comparable for loss to follow up or outcome data available, this information was not provided. Intention to treat analysis was employed. 8) Did the study have an appropriate length of follow up? Length of follow up was 18 months. This was appropriate. 9) Did the study use a precise definition of outcome? A precise definition of outcome was provided for all outcomes. 10) Was a valid and reliable method used to determine that outcome? Valid and reliable methods were used. 11) Were investigators kept blind to participant's exposure to the intervention? Investigators were kept blind to participant's exposure to the intervention for the determination of final ulcer classification. (physician) 12) Were investigators kept blind to other important confounding and prognostic factors? Unclear if investigators were kept blind to other important confounding and prognostic factors. .
Number of patients	Randomised= 299 Shear reducing insole= 149 Standard therapy group= 150
Patient characteristics	Patients taken from: USA Inclusion: Diabetes mellitus 18-80 years of age Informed consent History of foot ulceration and/or presence of sensory neuropathy with loss of protective sensation and foot deformity Exclusion: Open ulcers or open amputation site Charcot arthropathy Unable or unwilling to use over the counter shoe

Bibliographic reference	**Lavery, L. A., LaFontaine, J., Higgins, K. R., Lanctot, D. R., & Constantinides, G. (2012). Shear-reducing insoles to prevent foot ulceration in high-risk diabetic patients. Advances in skin & wound care, 25(11), 519-524.**

Severe peripheral vascular (ankle brachial pressure index <0.70)
Transmetatarsal foot amputation or higher
Active foot infection
Dementia
Impaired cognitive function
History of drug or alcohol abuse within one year of the study
Investigators clinical judgement

Baseline characteristics: No significant differences found

Characteristics	Shear reducing insole, n=149	Standard insole, n=150
Age, years	69.4 ± 10.04	71.5 ± 7.9
Sex, male	102	100
Race % White Black Other	Not reported	Not reported
Type 1 diabetes %	Not reported	Not reported
Duration of diabetes, y	13.0 ± 8.7	12.0 ± 4.9
Previous ulcers	40	38
History of previous amputation	18	13
Ankle brachial pressure index L R	 0.95 ± 0.11 0.97 ± 0.11	 0.99 ± 0.12 0.98 ± 0.13
Foot deformity	Not reported	Not reported
No foot pulses present	Not reported	Not reported
Activity (steps per day) (SEM)	Not reported	Not reported
Fitted footwear	All	All
Diabetic foot risk classification Risk 1 Risk 2 Risk 3 Risk 4	Not reported	Not reported

Bibliographic reference	**Lavery, L. A., LaFontaine, J., Higgins, K. R., Lanctot, D. R., & Constantinides, G. (2012). Shear-reducing insoles to prevent foot ulceration in high-risk diabetic patients. Advances in skin & wound care, 25(11), 519-524.**
	<table><tr><td>Neuropathy %</td><td>100</td><td>100</td></tr><tr><td>Retinopathy</td><td>Not reported</td><td>Not reported</td></tr><tr><td>HbA1c</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Current smoker</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Nephropathy</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Hospitalizations/yr</td><td>Not reported</td><td>Not reported</td></tr><tr><td>Body Mass Index</td><td>Not reported</td><td>Not reported</td></tr></table> There was not a significant difference in self-reported frequency of shoe and insole usage in either group.
Intervention	Shear reducing insole n= 149 Standard therapy and shear reducing insole with elastic binders and two thin Teflon sheets.
Comparison	Standard therapy group n=150 Standard therapy consisted of foot and lower extremity evaluation by a physician every 10-12 weeks, an education program that focused on foot complications and self-care practices, and therapeutic shoes and insoles. If study patients identified an area of concern on their feet they were instructed to contact the study nurse. All patients were provided with the same brand of therapeutic shoes. Insoles were replaced every 4 months and shoes once a year.
Length of follow up	Length of follow up was 18 months
Location	USA

Bibliographic reference	**Lavery, L. A., LaFontaine, J., Higgins, K. R., Lanctot, D. R., & Constantinides, G. (2012). Shear-reducing insoles to prevent foot ulceration in high-risk diabetic patients. Advances in skin & wound care, 25(11), 519-524.**
Outcomes measures and effect size	Rates of foot ulceration/infection Incidence of ulceration Full thickness loss of epidermis and dermis or involvement of deeper structures Shear reducing insole group= 3 of 149 participants Standard therapy group= 10 of 150 participants Odds ratio: 3.47 95% confidence interval 0.94-12.89 P value= 0.04 i.e. significant difference Rates of gangrene resulting from diabetes No data available Rates of amputation No data available Rates of A&E/ Hospital admission for foot problems resulting from diabetes No data available Resource use and costs No data provided
Source of funding	National Institute of Health.
Comments	

Table 36: Uccioli 1995

Bibliographic reference	**Uccioli, L., Faglia, E., Monticone, G., Favales, F., Durola, L., Aldeghi, A., ... & Menzinger, G. (1995). Manufactured shoes in the prevention of diabetic foot ulcers. Diabetes care, 18(10), 1376-1378.**

Bibliographic reference	**Uccioli, L., Faglia, E., Monticone, G., Favales, F., Durola, L., Aldeghi, A., ... & Menzinger, G. (1995). Manufactured shoes in the prevention of diabetic foot ulcers. Diabetes care, 18(10), 1376-1378.**
Study type	Randomised control trial
Study quality	Summary Population: Italy, among patients with previous history of foot ulcer. Intervention: Therapeutic shoes with custom mold insoles Standard of care: Standard therapy consisted of the same educational guidelines on foot care and general information on the importance of appropriate footwear (i.e. proper size, durability, and sole) Comparison: The patients in the control group were free to wear ordinary shoes unless clearly dangerous. The same follow up protocol was applied to both groups. Outcome: incidence of ulceration, adherence. 1) Has an appropriate method of randomisation been used? Unclear method of randomisation was used; 2) Was there adequate concealment of allocation? Unclear if allocation was adequately concealed. 3) Were the groups comparable at baseline for all major confounding/prognostic factors? Groups were stated to be comparable for all major confounding factors reported although many important variables were not reported.. 4) Did the comparison groups receive the same care apart from interventions studied? Unclear if patients received the same care apart from intervention provided. Care was over multiple sites and there is potential for some variance in care between sites. Also the study did not provide details of standard care. 5) Were participants receiving care kept blind to treatment allocation? Participants were not blinded to treatment allocation. 6) Were the individuals administering care kept blind to treatment allocation? Individuals administering care were not blinded to treatment allocation. 7) Were groups comparable with respect to availability of outcome data and for how many participants were no outcome data available? Unclear if groups were comparable for loss to follow up or outcome data available. 8) Did the study have an appropriate length of follow up? Length of follow up was 12 months. This was appropriate. 9) Did the study use a precise definition of outcome? A precise definition of outcome was not provided for all important outcomes. 10) Was a valid and reliable method used to determine that outcome? Unclear if valid and reliable methods were used. The study was lacking in details.

<table>
<tr><th>Bibliographic reference</th><th>Uccioli, L., Faglia, E., Monticone, G., Favales, F., Durola, L., Aldeghi, A., ... & Menzinger, G. (1995). Manufactured shoes in the prevention of diabetic foot ulcers. Diabetes care, 18(10), 1376-1378.</th></tr>
<tr><td></td><td>11) Were investigators kept blind to participant’s exposure to the intervention?
Investigators were not kept blind to participant’s exposure to the intervention
12) Were investigators kept blind to other important confounding and prognostic factors?
Unclear if investigators were kept blind to other important confounding and prognostic factors. .</td></tr>
<tr><td>Number of patients</td><td>Randomised= 69
Therapeutic shoes with custom mold insoles= 33
Standard therapy group= 36</td></tr>
<tr><td>Patient characteristics</td><td>Patients taken from: Italy

Inclusion:
Previous foot ulceration and those considered to be at high risk of foot ulceration

Exclusion:
Absence of ulceration
Absence of previous minor or major amputation
Absence of major foot deformities such as Charcot joints

Baseline characteristics: No significant differences found

<table>
<tr><th>Characteristics</th><th>Therapeutic shoes with custom mold insoles, n=33</th><th>Standard therapy group, n=36</th></tr>
<tr><td>Age, years</td><td>59.6 ± 11</td><td>60.2 ± 8.2</td></tr>
<tr><td>Sex, male</td><td>20</td><td>23</td></tr>
<tr><td>Race %
White
Black
Other</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Type 1 diabetes %</td><td>8</td><td>9</td></tr>
<tr><td>Duration of diabetes, y</td><td>16.8 ± 12.7</td><td>17.5 ± 8</td></tr>
<tr><td>Previous ulcers</td><td>All</td><td>All</td></tr>
</table>
</td></tr>
</table>

Bibliographic reference	**Uccioli, L., Faglia, E., Monticone, G., Favales, F., Durola, L., Aldeghi, A., ... & Menzinger, G. (1995). Manufactured shoes in the prevention of diabetic foot ulcers. Diabetes care, 18(10), 1376-1378.**

History of previous amputation	Not reported	Not reported	
Ankle brachial pressure index	0.95 ± 0.2	1 ± 0.2	
Foot deformity	Not reported	Not reported	
No foot pulses present	Not reported	Not reported	
Activity (steps per day) (SEM)	Not reported	Not reported	
Fitted footwear	Not reported	Not reported	
Diabetic foot risk classification Risk 1 Risk 2 Risk 3 Risk 4	Not reported	Not reported	
Neuropathy	Not reported	Not reported	
Retinopathy	Not reported	Not reported	
HbA1c	Not reported	Not reported	
Current smoker	Not reported	Not reported	There was not a significant difference in self-reported frequency of shoe and insole usage in either group.
Nephropathy	Not reported	Not reported	
Hospitalizations/yr	Not reported	Not reported	
Body Mass Index	Not reported	Not reported	

Intervention	Therapeutic shoes with custom mold insoles, n=33 And standard therapy
Comparison	Standard therapy group n=36 Standard therapy consisted of the same educational guidelines on foot care and general information on the importance of appropriate footwear (i.e. proper size, durability, and sole)
Length of follow up	Length of follow up was 12 months
Location	Italy
Outcomes measures and effect size	Rates of foot ulceration/infection Incidence of relapse (ulceration) over 1 year The incidence of an ulcer was taken as the incidence of first ulcer relapse only.

Bibliographic reference	**Uccioli, L., Faglia, E., Monticone, G., Favales, F., Durola, L., Aldeghi, A., ... & Menzinger, G. (1995). Manufactured shoes in the prevention of diabetic foot ulcers. Diabetes care, 18(10), 1376-1378.**
	Therapeutic shoes with custom mold insoles = 9 of 33 participants Standard therapy group = 21 of 36 participants Data calculated from percentages provided Odds ratio: 0.26 95% confidence interval 0.2-1.54 P value= 0.009 i.e. significant difference Rates of gangrene resulting from diabetes No data available Rates of amputation No data available Rates of A&E/ Hospital admission for foot problems resulting from diabetes No data available Resource use and costs No data provided
Source of funding	This study was supported in part by Buratto S.p.a. Italy who supplied the therapeutic shoes and insoles
Comments	

Table 37: Rizzo 2012

Bibliographic reference	**Rizzo, L., Tedeschi, A., Fallani, E., Coppelli, A., Vallini, V., Iacopi, E., & Piaggesi, A. (2012). Custom-made orthesis and shoes in a structured follow-up program reduces the incidence of neuropathic ulcers in high-risk diabetic foot patients. The international journal of lower extremity wounds, 11(1), 59-64.**
Study type	Randomised control trial
Study quality	Summary Population: Italy, among patients with peripheral vascular disease or deformities associated with sensory neuropathy or if previous

Bibliographic reference	**Rizzo, L., Tedeschi, A., Fallani, E., Coppelli, A., Vallini, V., Iacopi, E., & Piaggesi, A. (2012). Custom-made orthesis and shoes in a structured follow-up program reduces the incidence of neuropathic ulcers in high-risk diabetic foot patients. The international journal of lower extremity wounds, 11(1), 59-64.**
	diabetic foot ulcers or amputations. (International Consensus on Diabetic Foot risk category 2 and 3.) Intervention: Standard therapy and custom made orthesis and shoes Standard of care: Standard therapy consisted of in-depth education on how to prevent ulceration and advice to use comfortable shoes with non-traumatizing characteristics. A list of suitable shoes was delivered to patients and their features were discussed to be sure that patients would understand properly. In case of new diabetic foot ulcer, patients of both groups were requested to refer to our clinic for an urgent consultation within 24 hours, otherwise patients were seen quarterly for 12 months for assessment of feet and footwear condition. Comparison: Standard therapy alone as above Outcome: incidence of ulceration at 1 year, 3 years and 5 years. Cost and patient satisfaction. 1) Has an appropriate method of randomisation been used? Clear method of randomisation was used; Computer generated randomisation. 2) Was there adequate concealment of allocation? Unclear if allocation was adequately concealed. 3) Were the groups comparable at baseline for all major confounding/prognostic factors? Groups were stated to be comparable for all major confounding factors reported although many important variables were not reported. 4) Did the comparison groups receive the same care apart from interventions studied? Patients received the same care apart from intervention provided. Care was under the same clinic. No measure of adherence to therapy was recorded. 5) Were participants receiving care kept blind to treatment allocation? Participants were not blinded to treatment allocation. 6) Were the individuals administering care kept blind to treatment allocation? Individuals administering care were not blinded to treatment allocation. 7) Were groups comparable with respect to availability of outcome data and for how many participants were no outcome data available? Unclear if groups were comparable for loss to follow up or outcome data available. There was no reported loss to follow up over the 12 month period. Following this there were 88 lost to follow up in the standard care group and 97 lost to follow up in the intervention group. Since it is unclear how this large loss to follow up affected the characteristics of the populations under study this makes interpreting the results at 3 and 5 years follow up problematic. 8) Did the study have an appropriate length of follow up? Length of follow up was 12 months-5 years. This was appropriate. 9) Did the study use a precise definition of outcome?

<table>
<tr><th>Bibliographic reference</th><th>Rizzo, L., Tedeschi, A., Fallani, E., Coppelli, A., Vallini, V., Iacopi, E., & Piaggesi, A. (2012). Custom-made orthesis and shoes in a structured follow-up program reduces the incidence of neuropathic ulcers in high-risk diabetic foot patients. The international journal of lower extremity wounds, 11(1), 59-64.</th></tr>
<tr><td></td><td>A clear definition of ulceration was not stated
10) Was a valid and reliable method used to determine that outcome?
Valid and reliable methods were used: foot deformities and presence of active ulcerations were evaluated by an experienced podologist.
11) Were investigators kept blind to participant’s exposure to the intervention?
Investigators were not kept blind to participant’s exposure to the intervention
12) Were investigators kept blind to other important confounding and prognostic factors?
Unclear if investigators were kept blind to other important confounding and prognostic factors. .</td></tr>
<tr><td>Number of patients</td><td>Randomised= 334
Custom made orthesis and shoes = 148
Standard therapy group= 150</td></tr>
<tr><td>Patient characteristics</td><td>Patients taken from: Italy

Inclusion:
Patients with peripheral vascular disease or deformities associated with sensory neuropathy or if previous diabetic foot ulcers or amputations. (International Consensus on Diabetic Foot risk category 2 and 3.)

Exclusion:
Patients with active or recent (<3 months) ulcers
Active Charcot foot
Local ischaemia (lack of pulses and/or ankle-brachial pressure index <0.7)
Inability to stand or walk without help
Life expectancy less than 1 year

Baseline characteristics: No significant differences found

<table><tr><td>Characteristics</td><td>Standard therapy group, n=150</td><td>Custom made orthesis and shoes n=148</td></tr><tr><td>Age, years</td><td>66.2 ± 9.4</td><td>68.1 ± 14.1</td></tr></table></td></tr>
</table>

Bibliographic reference	**Rizzo, L., Tedeschi, A., Fallani, E., Coppelli, A., Vallini, V., Iacopi, E., & Piaggesi, A. (2012). Custom-made orthesis and shoes in a structured follow-up program reduces the incidence of neuropathic ulcers in high-risk diabetic foot patients. The international journal of lower extremity wounds, 11(1), 59-64.**

Sex, male	Not reported	Not reported
Race % White Black Other	Not reported	Not reported
Type 1 diabetes	27	21
Duration of diabetes, y	17.4 ± 10.9	18.1 ± 12.1
Previous ulcers	Not reported	Not reported
History of previous amputation	Not reported	Not reported
Ankle brachial pressure index	Not reported	Not reported
Foot deformity	Not reported	Not reported
No foot pulses present	Not reported	Not reported
Activity (steps per day) (SEM)	Not reported	Not reported
Fitted footwear	Not reported	Not reported
Diabetic foot risk classification Risk 1 Risk 2 Risk 3 Risk 4	Not reported	Not reported
Neuropathy	Not reported	Not reported
Retinopathy	Not reported	Not reported
HbA1c	8.7 ± 1.1	8.6 ± 1.4
Current smoker	Not reported	Not reported
Nephropathy	Not reported	Not reported
Hospitalizations/yr	Not reported	Not reported
Body Mass Index	Not reported	Not reported

Intervention	Custom made orthesis and shoes n=148 And standard therapy
Comparison	Standard therapy group, n=150 Standard therapy consisted of in-depth education on how to prevent ulceration and advice to use comfortable shoes with non-traumatizing characteristics. A list of suitable shoes was delivered to patients and their features were discussed to be sure that patients would understand properly. In case of new diabetic foot ulcer, patients of both groups were requested to refer to our clinic for

Bibliographic reference	**Rizzo, L., Tedeschi, A., Fallani, E., Coppelli, A., Vallini, V., Iacopi, E., & Piaggesi, A. (2012). Custom-made orthesis and shoes in a structured follow-up program reduces the incidence of neuropathic ulcers in high-risk diabetic foot patients. The international journal of lower extremity wounds, 11(1), 59-64.**
	an urgent consultation within 24 hours, otherwise patients were seen quarterly for 12 months for assessment of feet and footwear condition.
Length of follow up	Length of follow up was 12 months, 3 years and 5 years
Location	Italy
Outcomes measures and effect size	Rates of foot ulceration/infection Incidence of ulceration over 1 year (per person) Patients developing diabetic foot ulcers. Custom made orthesis and shoes = 17 of 148 participants (20 diabetic foot ulcers total) Standard therapy group = 58 of 150 participants (75 diabetic foot ulcers total) P value= <0.0001 i.e. significant difference Then after significant loss to follow up: Incidence of ulceration over 3 years (per person) Patients developing diabetic foot ulcers. Custom made orthesis and shoes = 9 of 51 participants Standard therapy group = 38 of 62 participants Data calculated from percentages provided P value= <0.0001 i.e. significant difference Incidence of ulceration over 3 years (per person) Patients developing diabetic foot ulcers. Custom made orthesis and shoes = 12 of 51 participants Standard therapy group = 45 of 62 participants Data calculated from percentages provided P value= <0.0001 i.e. significant difference

Bibliographic reference	**Rizzo, L., Tedeschi, A., Fallani, E., Coppelli, A., Vallini, V., Iacopi, E., & Piaggesi, A. (2012). Custom-made orthesis and shoes in a structured follow-up program reduces the incidence of neuropathic ulcers in high-risk diabetic foot patients. The international journal of lower extremity wounds, 11(1), 59-64.**
	Rates of gangrene resulting from diabetes No data available Rates of amputation No data available Rates of A&E/ Hospital admission for foot problems resulting from diabetes No data available Resource use and costs The cost for the orthesis and shoes manufacturing for the 1 year follow up amounted to €99,900 or €675 per patient per year The study calculated that an estimated €107 505 was saved when taking into account the diabetic foot ulcers prevented
Source of funding	The authors received no financial support for the research.
Comments	

Table 38: Scire 2009

Bibliographic reference	**Scire, V., Leporati, E., Teobaldi, I., Nobili, L. A., Rizzo, L., & Piaggesi, A. (2009). Effectiveness and safety of using Podikon digital silicone padding in the primary prevention of neuropathic lesions in the forefoot of diabetic patients. Journal of the American Podiatric Medical Association, 99(1), 28-34.**
Study type	Randomised control trial
Study quality	Summary Population: Italy, among patients with peripheral neuropathy and deformity or preulcerative conditions in the forefoot Intervention: Digital off-loading silicone padding made to measure with standard therapy. There were two types of orthotic treatment depending on the presentation of the treated patient they were either given corrective or protective types of orthosis. Details are provided in study. Standard of care: Standard therapy consisted of clinical examination to find and treat areas of hyperkeratosis using mechanical keratolysis. Patients were then prescribed an accommodating soft insole and extra deep shoe.

Bibliographic reference	**Scire, V., Leporati, E., Teobaldi, I., Nobili, L. A., Rizzo, L., & Piaggesi, A. (2009). Effectiveness and safety of using Podikon digital silicone padding in the primary prevention of neuropathic lesions in the forefoot of diabetic patients. Journal of the American Podiatric Medical Association, 99(1), 28-34.**
	Comparison: Standard therapy alone as above. The study states participants in this group were not fitted with orthotic protection but it is presumed that they did receive the accommodating soft insole and extra deep shoe. Outcome: incidence of ulceration at 3 months 1) Has an appropriate method of randomisation been used? Clear method of randomisation was used; Computer generated randomisation list. 2) Was there adequate concealment of allocation? Unclear if allocation was adequately concealed. 3) Were the groups comparable at baseline for all major confounding/prognostic factors? It appears that groups were comparable at baseline although this is never stated and P values were not provided. 4) Did the comparison groups receive the same care apart from interventions studied? Patients probably received the same care apart from intervention provided. Care was under the same clinic. The study states that participants in the control group underwent all the exams and procedures as in the intervention group except that they were not fitted with orthotic protection. It is unclear if this includes the accommodating soft insole and extra deep shoe. 5) Were participants receiving care kept blind to treatment allocation? Participants were not blinded to treatment allocation. 6) Were the individuals administering care kept blind to treatment allocation? Individuals administering care were not blinded to treatment allocation. 7) Were groups comparable with respect to availability of outcome data and for how many participants were no outcome data available? No participants were lost to follow up in either group. 8) Did the study have an appropriate length of follow up? Length of follow up was 3 months, this may not have been appropriate to capture the differences between groups. 9) Did the study use a precise definition of outcome? A clear definition of ulceration was not stated 10) Was a valid and reliable method used to determine that outcome? Valid and reliable methods were used: evaluations performed were well defined 11) Were investigators kept blind to participant's exposure to the intervention? Investigators were kept blind to participant's exposure to the intervention (observer blind) 12) Were investigators kept blind to other important confounding and prognostic factors? Unclear if investigators were kept blind to other important confounding and prognostic factors. .

Bibliographic reference	**Scire, V., Leporati, E., Teobaldi, I., Nobili, L. A., Rizzo, L., & Piaggesi, A. (2009). Effectiveness and safety of using Podikon digital silicone padding in the primary prevention of neuropathic lesions in the forefoot of diabetic patients. Journal of the American Podiatric Medical Association, 99(1), 28-34.**
Number of patients	Randomised= 167 Digital off-loading silicone padding = 89 Standard therapy group= 78
Patient characteristics	Patients taken from: Italy Inclusion: Aged older than 18 years Diagnosis with diabetes mellitus for at least 5 years Peripheral neuropathy and deformity or preulcerative conditions of the forefoot Exclusion: Active ulcerative lesions Peripheral macroangiopathy Systemic symptoms of infection Clinically visible symptoms of rhagades or dyshidrosis Charcot's neuroarthropathy in an active or stabilising phase "presence of peripheral neuropathies other than peripheral neuropathy" Baseline characteristics: No significant differences reported, no p values provided

Characteristics	Digital off-loading silicone padding = 89	Standard therapy group, n=78
Age, years	58.2 ± 17.1	54.9 ± 18.2
Sex, male	Not reported	Not reported
Race % White Black Other	Not reported	Not reported
Type 1 diabetes	12	8
Duration of diabetes, y	15.2 ± 8.9	16.4 ± 9.4
Previous ulcers	Not reported	Not reported

Bibliographic reference	**Scire, V., Leporati, E., Teobaldi, I., Nobili, L. A., Rizzo, L., & Piaggesi, A. (2009). Effectiveness and safety of using Podikon digital silicone padding in the primary prevention of neuropathic lesions in the forefoot of diabetic patients. Journal of the American Podiatric Medical Association, 99(1), 28-34.**

History of previous amputation	Not reported	Not reported
Ankle brachial pressure index	Not reported	Not reported
Foot deformity %	6	8
No foot pulses present	Not reported	Not reported
Activity (steps per day) (SEM)	Not reported	Not reported
Fitted footwear	Not reported	Not reported
Diabetic foot risk classification Risk 1 Risk 2 Risk 3 Risk 4	Not reported	Not reported
Neuropathy	Not reported	Not reported
Retinopathy	Not reported	Not reported
HbA1c	8.2 ± 1.7	7.9 ± 0.9
Current smoker	Not reported	Not reported
Nephropathy	Not reported	Not reported
Hospitalizations/yr	Not reported	Not reported
Body Mass Index	Not reported	Not reported

Intervention	Digital off-loading silicone padding = 89 And standard therapy
Comparison	Standard therapy group, n=78 Standard therapy consisted of clinical examination to find and treat areas of hyperkeratosis using mechanical keratolysis. Patients were then prescribed an accommodating soft insole and extra deep shoe. The study states participants in this group were not fitted with orthotic protection but it is presumed that they did receive the accommodating soft insole and extra deep shoe.
Length of follow up	Length of follow up was 3 months
Location	Italy
Outcomes measures and effect size	Rates of foot ulceration/infection Incidence of ulceration over 3 months

Bibliographic reference	**Scire, V., Leporati, E., Teobaldi, I., Nobili, L. A., Rizzo, L., & Piaggesi, A. (2009). Effectiveness and safety of using Podikon digital silicone padding in the primary prevention of neuropathic lesions in the forefoot of diabetic patients. Journal of the American Podiatric Medical Association, 99(1), 28-34.**
	Definition unclear Digital off-loading silicone padding = 1 of 89 participants Standard therapy group = 12 of 78 participants P value= <0.001 i.e. significant difference Rates of gangrene resulting from diabetes No data available Rates of amputation No data available Rates of A&E/ Hospital admission for foot problems resulting from diabetes No data available Resource use and costs No data on cost available
Source of funding	The authors received no financial support for the research.
Comments	

Table 39: Ronnemaa 1997

Bibliographic reference	**Rönnemaa, T., Hämäläinen, H., Toikka, T., & Liukkonen, I. (1997). Evaluation of the impact of podiatrist care in the primary prevention of foot problems in diabetic subjects. Diabetes Care, 20(12), 1833-1837.** **Hämäläinen, H., Rönnemaa, T., Toikka, T., & Liukkonen, I. (1998). Long-term effects of one year of intensified podiatric activities on foot-care knowledge and self-care habits in patients with diabetes. The Diabetes Educator, 24(6), 734-740.**
Study type	Randomised control trial
Study quality	Summary

Bibliographic reference	**Rönnemaa, T., Hämäläinen, H., Toikka, T., & Liukkonen, I. (1997). Evaluation of the impact of podiatrist care in the primary prevention of foot problems in diabetic subjects. Diabetes Care, 20(12), 1833-1837.** **Hämäläinen, H., Rönnemaa, T., Toikka, T., & Liukkonen, I. (1998). Long-term effects of one year of intensified podiatric activities on foot-care knowledge and self-care habits in patients with diabetes. The Diabetes Educator, 24(6), 734-740.**
	Population: Finland, patients without recent visits to podiatrist and without an obvious need for foot care Intervention: Podiatric care group: education and primary prevention measures. Patients were visited by a podiatrist during the 12 month period after the baseline examination as many times as judged appropriate by the podiatrist. Education was given individually to every patient, taking into account each patient's age, occupation, earlier foot care habits etc Standard of care: Unclear Comparison: Patients in the control group received written instruction only Outcome: incidence of ulceration, amputation Trouble finding original paper cited from 1993 (awaiting) 1) Has an appropriate method of randomisation been used? Unclear method of randomisation. Randomisation was conducted separately for women and men and for those greater and younger than 20 years of age. 2) Was there adequate concealment of allocation? Unclear if adequate allocation concealment 3) Were the groups comparable at baseline for all major confounding/prognostic factors? Unclear if groups were comparable at baseline for all major confounding factors 4) Did the comparison groups receive the same care apart from interventions studied? The control group received only written instruction and fewer podiatry visits. Further information on the definition of standard care was unclear. 5) Were participants receiving care kept blind to treatment allocation? Participants receiving care were not blinded to treatment allocation 6) Were the individuals administering care kept blind to treatment allocation? Participants administering care were not blinded to treatment allocation 7) Were groups comparable with respect to availability of outcome data and for how many participants were no outcome data available? Loss to follow up was 34 in the podiatrist care group and 37 in the control group at 1 year. At 7 years 64 participants were lost to follow up in the podiatric group and 63 in the control group. This is a significant loss to follow up and intention to treat analysis was not employed. 8) Did the study have an appropriate length of follow up?

Bibliographic reference	**Rönnemaa, T., Hämäläinen, H., Toikka, T., & Liukkonen, I. (1997). Evaluation of the impact of podiatrist care in the primary prevention of foot problems in diabetic subjects. Diabetes Care, 20(12), 1833-1837.** **Hämäläinen, H., Rönnemaa, T., Toikka, T., & Liukkonen, I. (1998). Long-term effects of one year of intensified podiatric activities on foot-care knowledge and self-care habits in patients with diabetes. The Diabetes Educator, 24(6), 734-740.**
	The study had an appropriate length of follow up 9) Did the study use a precise definition of outcome? Definition of ulceration and amputation was unclear 10) Was a valid and reliable method used to determine that outcome? Follow up examinations were performed at follow up by a podiatrist, collecting data about previous foot problems, unclear if this podiatrist was unaware of the patient's treatment group allocation. Unclear if results of the interview were cross checked with clinical notes. 11) Were investigators kept blind to participant's exposure to the intervention? Unclear if investigators were kept blind to the participants exposure to the intervention 12) Were investigators kept blind to other important confounding and prognostic factors? Investigators were blinded to the previous results of baseline examination and interview The low incidence of ulceration and serious foot lesions in this study could have been because all patients who were estimated to be at a higher risk for major foot problems were all referred to podiatric care and excluded from this randomised study.
Number of patients	Randomised= 530 Referral to podiatrist = 267 Written instructions= 263
Patient characteristics	Patients taken from: Finland Inclusion: Type 1 and type 2 diabetes Exclusion: Visit to the podiatrist within the prior 6 months Obvious need for podiatry (referred and excluded) Baseline characteristics: No significant differences reported, no p values provided

<table>
<tr><td>Bibliographic reference</td><td>Rönnemaa, T., Hämäläinen, H., Toikka, T., & Liukkonen, I. (1997). Evaluation of the impact of podiatrist care in the primary prevention of foot problems in diabetic subjects. Diabetes Care, 20(12), 1833-1837.

Hämäläinen, H., Rönnemaa, T., Toikka, T., & Liukkonen, I. (1998). Long-term effects of one year of intensified podiatric activities on foot-care knowledge and self-care habits in patients with diabetes. The Diabetes Educator, 24(6), 734-740.</td></tr>
<tr><td></td><td>
<table>
<tr><td>Characteristics</td><td>Podiatrist group
n=267</td><td>Written instructions
n=263</td></tr>
<tr><td>Age, years</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Sex, male</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Race %
White
Black
Other</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Type 1 diabetes</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Duration of diabetes, y</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Previous ulcers</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>History of previous amputation</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Ankle brachial pressure index</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Foot deformity %</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>No foot pulses present</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Activity (steps per day) (SEM)</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Fitted footwear</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Diabetic foot risk classification
Risk 1
Risk 2
Risk 3
Risk 4</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Neuropathy</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Retinopathy</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>HbA1c</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Current smoker</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Nephropathy</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Hospitalizations/yr</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Body Mass Index</td><td>Not reported</td><td>Not reported</td></tr>
</table>
</td></tr>
<tr><td>Intervention</td><td>Podiatrist group = 267

Standard therapy otherwise unclear. Podiatric care group: education and primary prevention measures. Patients were visited by a</td></tr>
</table>

Bibliographic reference	**Rönnemaa, T., Hämäläinen, H., Toikka, T., & Liukkonen, I. (1997). Evaluation of the impact of podiatrist care in the primary prevention of foot problems in diabetic subjects. Diabetes Care, 20(12), 1833-1837.** **Hämäläinen, H., Rönnemaa, T., Toikka, T., & Liukkonen, I. (1998). Long-term effects of one year of intensified podiatric activities on foot-care knowledge and self-care habits in patients with diabetes. The Diabetes Educator, 24(6), 734-740.**
	podiatrist during the 12 month period after the baseline examination as many times as judged appropriate by the podiatrist. Education was given individually to every patient, taking into account each patient's age, occupation, earlier foot care habits. The first visit lasted 45 minutes and focused mainly on education including proper use of footwear, hygiene, toenail cutting, emollient cream, foot exercises and avoidance of high risk situations. In addition certain preventive measures were available, including preparation of individual insoles, treatment for ingrown toenails and gentle trimming of callosities provided free of charge.
Comparison	Written instruction, n=263 Standard therapy otherwise unclear
Length of follow up	Length of follow up was 7 years
Location	Finland
Outcomes measures and effect size	Rates of foot ulceration/infection Incidence of ulceration at 1 year Definition unclear Podiatry care = 1 of 233 participants Written instruction = 0 of 226 participants no significant difference Incidence of ulceration at 7 years Definition unclear Podiatry care = 1 of 169 participants Written instruction = 1 of 163 participants P value= 0.499 i.e. no significant difference Rates of gangrene resulting from diabetes No data available

Bibliographic reference	**Rönnemaa, T., Hämäläinen, H., Toikka, T., & Liukkonen, I. (1997). Evaluation of the impact of podiatrist care in the primary prevention of foot problems in diabetic subjects. Diabetes Care, 20(12), 1833-1837.** **Hämäläinen, H., Rönnemaa, T., Toikka, T., & Liukkonen, I. (1998). Long-term effects of one year of intensified podiatric activities on foot-care knowledge and self-care habits in patients with diabetes. The Diabetes Educator, 24(6), 734-740.**
	Rates of amputation Incidence of amputation at 1 year Definition unclear Podiatry care = 0 of 233 participants Written instruction = 0 of 226 participants i.e. no significant difference Incidence of amputation at 7 years Definition unclear Podiatry care = 2 of 169 participants Written instruction = 0 of 163 participants P value= 1.00 i.e. no significant difference Rates of A&E/ Hospital admission for foot problems resulting from diabetes No data available Resource use and costs No data on cost available
Source of funding	Unclear source of funding
Comments	

Table 40: McCabe 2009

Bibliographic reference	**McCabe, C. J., Stevenson, R. C., & Dolan, A. M. (1998). Evaluation of a diabetic foot screening and protection programme. Diabetic Medicine, 15(1), 80-84.**

Bibliographic reference	**McCabe, C. J., Stevenson, R. C., & Dolan, A. M. (1998). Evaluation of a diabetic foot screening and protection programme. Diabetic Medicine, 15(1), 80-84.**
Study type	Randomised control trial
Study quality	Summary Population: UK, patients seen within a specialist diabetic foot clinic Intervention: Primary and secondary screening programmes followed by foot protection programme for those patients found to be high risk. Standard of care: Usual care consisted of 2 years of follow up through the general diabetes out-patients clinic. Comparison: The control group consisted of 1000 patients who were silently tagged and continued to attend the general out-patients clinic but received no special care. Outcome: incidence of ulceration, minor and major amputation, compliance, cost effectiveness 1) Has an appropriate method of randomisation been used? Unclear method of randomisation. Four participants with active diabetic foot ulcers were not randomised but automatically entered into the screening and treatment group side of the trial. Unclear how this would have affected the results. 2) Was there adequate concealment of allocation? Unclear if allocation was adequately concealed. 3) Were the groups comparable at baseline for all major confounding/prognostic factors? It is never stated in this study if groups were comparable at baseline for all confounding factors. Some patients were shared with another study by Klenerman et al however this study appears only to provide information on those who were entered into the screening side of the trial. No further data is provided in the present study. Non-attendance was greater in the control group which could suggest that there were some unknown differences between groups. 4) Did the comparison groups receive the same care apart from interventions studied? Patients probably received the same care apart from intervention provided. Care was under the same clinic. Intervention on the screening group side however involved care under the foot protection programme for high risk patients. Groups were statistically similar for use of chiropody service. 5) Were participants receiving care kept blind to treatment allocation? Participants were not blinded to treatment allocation. 6) Were the individuals administering care kept blind to treatment allocation? Individuals administering care were not blinded to treatment allocation. 7) Were groups comparable with respect to availability of outcome data and for how many participants were no outcome data available? For those in the screening side of the trial 33 patients did not complete the full programme. In the full 2 year follow up 531 patients in the control group and 323 participants in the screening group did not attend appointments, outcome data for these patients were found by reviewing hospital case records. By the end of 2 years, in the treatment group, 37 participants died and 2 were lost to follow up. Unclear for how many no outcome data was available for the control group.

<table>
<tr><th>Bibliographic reference</th><th>McCabe, C. J., Stevenson, R. C., & Dolan, A. M. (1998). Evaluation of a diabetic foot screening and protection programme. Diabetic Medicine, 15(1), 80-84.</th></tr>
<tr><td></td><td>8) Did the study have an appropriate length of follow up?
Length of follow up was 2 years, this was appropriate..
9) Did the study use a precise definition of outcome?
A clear definition of primary outcomes amputation and ulceration was not stated
10) Was a valid and reliable method used to determine that outcome?
Valid and reliable methods were not always used. For those participants who did not attend follow up clinics; data on ulcers and amputations depended on hospital patient records which may have been unreliable.
11) Were investigators kept blind to participant’s exposure to the intervention?
Investigators were not kept blind to participant’s exposure to the intervention
12) Were investigators kept blind to other important confounding and prognostic factors?
Unclear if investigators were kept blind to other important confounding and prognostic factors. (unlikely)</td></tr>
<tr><td>Number of patients</td><td>Randomised= 2001
Screening and foot protection programme = 1001
Control group= 1000</td></tr>
<tr><td>Patient characteristics</td><td>Patients taken from: UK

Inclusion:
Diabetic patients at a diabetic specialist clinic

Exclusion:
No exclusion criteria stated

Baseline characteristics: No baseline characteristic reported

<table>
<tr><th>Characteristics</th><th>Screening and foot protection = 1001</th><th>Control group, n=1000</th></tr>
<tr><td>Age, years</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Sex, male</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Race %
White</td><td>Not reported</td><td>Not reported</td></tr>
</table>
</td></tr>
</table>

Bibliographic reference	McCabe, C. J., Stevenson, R. C., & Dolan, A. M. (1998). Evaluation of a diabetic foot screening and protection programme. Diabetic Medicine, 15(1), 80-84.

Black Other		
Type 1 diabetes	Not reported	Not reported
Duration of diabetes, y	Not reported	Not reported
Previous ulcers	Not reported	Not reported
History of previous amputation	Not reported	Not reported
Ankle brachial pressure index	Not reported	Not reported
Foot deformity %	Not reported	Not reported
No foot pulses present	Not reported	Not reported
Activity (steps per day) (SEM)	Not reported	Not reported
Fitted footwear	Not reported	Not reported
Diabetic foot risk classification Risk 1 Risk 2 Risk 3 Risk 4	Not reported	Not reported
Neuropathy	Not reported	Not reported
Retinopathy	Not reported	Not reported
HbA1c	Not reported	Not reported
Current smoker	Not reported	Not reported
Nephropathy	Not reported	Not reported
Hospitalizations/yr	Not reported	Not reported
Body Mass Index	Not reported	Not reported

Intervention	Screening and foot protection = 1001 Standard therapy as below if not high risk patient. All in the intervention group received primary foot screening examination using Semmes-Weinstein monofilaments, biothesiometer and palpation of pedal pulses. Patients found to have a significant deficit in any of these areas were given an appointment for a second examination which repeated the above tests and also calculated ankle brachial pressure index, subcutaneous oxygen levels, foot pressure and x-rays were taken. Patients with foot deformities, or a history of foot ulceration or an ankle brachial pressure index of ≤0.75 were judged to be high risk of ulceration and were entered into the foot protection programme. The foot protection programme provided chiropody, hygiene maintenance, support hosiery, and protective shoes for patients in the high risk category. Clinic was weekly and patients received advice and were allowed to contact the clinic whenever they felt necessary.

Bibliographic reference	**McCabe, C. J., Stevenson, R. C., & Dolan, A. M. (1998). Evaluation of a diabetic foot screening and protection programme. Diabetic Medicine, 15(1), 80-84.**
Comparison	Control group, n=1000 The control group consisted of 1000 patients who were silently tagged and continued to attend the general out-patients clinic but received no special care.
Length of follow up	Length of follow up was 2 years
Location	UK
Outcomes measures and effect size	Rates of foot ulceration/infection Incidence of ulceration over 2 years Definition unclear Screening and foot protection programme = 24 of 1001 participants Control group = 35 of 1000 participants P value= >0.14 i.e. no significant difference Rates of gangrene resulting from diabetes No data available Rates of amputation Incidence of all amputation over 2 years Definition unclear Screening and foot protection programme = 7 of 1001 participants Control group = 23 of 1000 participants P value= <0.04 i.e. significant difference Incidence of minor amputation over 2 years Definition unclear Screening and foot protection programme = 6 of 1001 participants Control group = 13 of 1000 participants P value= >0.15 i.e. no significant difference

Bibliographic reference	McCabe, C. J., Stevenson, R. C., & Dolan, A. M. (1998). Evaluation of a diabetic foot screening and protection programme. Diabetic Medicine, 15(1), 80-84.
	Incidence of major amputation over 2 years Definition unclear Screening and foot protection programme = 1 of 1001 participants Control group = 12 of 1000 participants P value= <0.01 i.e. significant difference Rates of A&E/ Hospital admission for foot problems resulting from diabetes No data available Resource use and costs Crude estimates found the foot clinic to be cost effective in terms of amputations averted. Total cost of the two year programme was £100,375, with a mean cost per patient of approximately £100. £12,000 was taken as a mean estimate of the cost of a major amputation.
Source of funding	The study was financed by the Department of Health
Comments	

Table 41: Plank 2003

Reference	Plank, J., Haas, W., Rakovac, I., Gorzer, E et al (2003)Evaluation of the impact of chiropodist care in the secondary prevention of foot ulcerations in diabetic subjects, Diabetes Care 26 (6) 1691-1695
Study type & aim	A single centre parallel group randomised controlled trial to evaluate the influence of regular chiropodist care on the recurrence rate of diabetic foot ulcers within 1 year.
Quality assessment	1) Has an appropriate method of randomisation been used? Appropriate method of randomisation used 2) Was there adequate concealment of allocation? Allocation was adequately concealed.

Reference	**Plank, J., Haas, W., Rakovac, I., Gorzer, E et al (2003)Evaluation of the impact of chiropodist care in the secondary prevention of foot ulcerations in diabetic subjects, Diabetes Care 26 (6) 1691-1695**
	3) Were the groups comparable at baseline for all major confounding/prognostic factors? Groups were comparable for all reported confounding factors 4) Did the comparison groups receive the same care apart from interventions studied? Patients probably received the same care apart from intervention provided. Care was under the same clinic. Participants in the control group could choose to pay for chiropody care if they wished. 5) Were participants receiving care kept blind to treatment allocation? Participants were not blinded to treatment allocation. 6) Were the individuals administering care kept blind to treatment allocation? Individuals administering care were not blinded to treatment allocation. 7) Were groups comparable with respect to availability of outcome data and for how many participants were no outcome data available? There was no apparent loss to follow up. Intent to treat analysis was used. 8) Did the study have an appropriate length of follow up? Length of follow up was 1 year, this was appropriate. 9) Did the study use a precise definition of outcome? A clear definition of primary outcomes amputation and ulceration was not stated 10) Was a valid and reliable method used to determine that outcome? Valid and reliable methods were used. 11) Were investigators kept blind to participant's exposure to the intervention? Investigators were not kept blind to participant's exposure to the intervention 12) Were investigators kept blind to other important confounding and prognostic factors? Unclear if investigators were kept blind to other important confounding and prognostic factors. (unlikely)
Number of participants & patient characteristics	**Total number of participants:** Out of 93 eligible participants, 91 adult patients receiving routine outpatient care at a diabetic foot clinic were randomised (after their foot ulcer had healed) to receive either routine chiropodist care at least once a month or to a control group where chiropodist care was not specifically recommended. 47 patients were randomised to the intervention group; 44 patients were randomised to the control group. **Inclusion criteria:** All patients had type 1 or type 2 diabetes and neuropathy. **Exclusion criteria:** Not reported **Patient characteristics:**

Reference	**Plank, J., Haas, W., Rakovac, I., Gorzer, E et al (2003)Evaluation of the impact of chiropodist care in the secondary prevention of foot ulcerations in diabetic subjects, Diabetes Care 26 (6) 1691-1695**

There was no difference between the groups in terms of general clinical or foot related features such as amputation status, peripheral circulation or use of therapeutic shoes. Baseline characteristics are shown below.

	Intervention group (n=47)	**Control group (n=44)**
Age (y)	64 ± 10	65 ± 11
Women (n)	25	26
Ethnicity: Caucasian (%)	100	100
Type 1 diabetes (n)	3	3
Duration of diabetes (years)	18 ± 11	14 ± 10
BMI (kg/m^2)	28.4 ± 4.5	28.6 ± 4.3
HBA1c (%)	8.5 ± 1.6	8.4 ± 1.6
RR systolic/diastolic (mmHg)	147/80	144/80
Insulin therapy (n)	38	29
Retinopathy (n)	28	25
Nephropathy (n)	21	19
Peripheral vascular disease (n)	22	20
Therapeutic shoes (n)	28	26
Amputation major* (n)	12	13
Amputation minor**(n)	2	3

*Above ankle; **Below ankle

Monitoring information & definitions

Monitoring:

Chiropodists kept a record of patient's visits throughout the trial. Patients were advised to contact the outpatient foot clinic if they suspected a new foot ulcer, inter-current hospitalisation for foot related complications or other relevant clinical features. Medical records were requested from other health care institutions if needed.

The activities of the trial were carried out until the end of the observation period, or death of a patient.

Outcome measures: The clinical endpoints were ulceration, amputation and death

Data for both the intention to treat (ITT) population and per protocol (PP) population were analysed. The ITT population covered all patients included in each treatment group of the trial. The PP population included all patients who had at least one chiropodist visit every 5 weeks (regardless of which treatment group. Concomittant illness and treatment were also considered.

<table>
<tr><td>Reference</td><td>Plank, J., Haas, W., Rakovac, I., Gorzer, E et al (2003)Evaluation of the impact of chiropodist care in the secondary prevention of foot ulcerations in diabetic subjects, Diabetes Care 26 (6) 1691-1695</td></tr>
<tr><td>Intervention</td><td>Patients in the intervention group were asked to see a chiropodist at least once a month. The cost was remuneration free.</td></tr>
<tr><td>Comparator:</td><td>Patients in the control group were not specifically recommended to see a chiropodist, although, they could choose to visit a chiropodist if they wished to and they were required to pay for their attendance.</td></tr>
<tr><td>Length of follow-up</td><td>Follow up was 12 months (median follow up equated to 368 days)</td></tr>
<tr><td>Outcome measures & effect sizes</td><td>
Ulceration (ITT):
Ulceration recurred in 18 patients in the intervention group compared to 25 patients in the control group (HR 0.60, 0.32-1.09, p=0.09)
Ulceration also recurred in 20 feet within the intervention group compared to 32 feet in the control group (RR 0.52, CI, 0.29-0.93, p=0.03)
Ulceration (PP):
4 patients in the control group received chiropodist care (at least every 5 weeks) and 15 patients in the intervention group had infrequent/ no care. Therefore 36 patients (71 lower limbs) had frequent care by a chiropodist and 55 patients (106 lower limbs) did not.13 patients with frequent visits developed a new lesion; 30 patients with infrequent/ no visit developed a new lesion (HR 0.53; 0.30-1.01, p = 0.05)
15 lower limbs with regular care developed a new lesion whereas 37 lower limbs without regular care developed a lesion (RR 0.46; 0.24- 0.9 , p=0.02)

Results for recurrence of ulceration are shown below
<table>
<tr><th>Analysis</th><th>Intervention n (%)</th><th>Control n (%)</th><th>Cox RR/HR</th><th>95%CI</th><th>P value</th></tr>
<tr><td>Feet (ITT)</td><td>92 (22%)</td><td>85 (38%)</td><td>0.52</td><td>0.30-0.93</td><td>0.03</td></tr>
<tr><td>Feet (PP)</td><td>71 (22%)</td><td>106 (35%)</td><td>0.46</td><td>0.24-0.90</td><td>0.02</td></tr>
<tr><td>Patient (ITT)</td><td>47 (38%)</td><td>44 (56%)</td><td>0.60</td><td>0.32-1.08</td><td>0.09</td></tr>
<tr><td>Patient (PP)</td><td>36 (36%)</td><td>55 (55%)</td><td>0.53</td><td>0.30-1.01</td><td>0.05</td></tr>
</table>

Amputation and death:
2 patients in the intervention group required minor amputation compared to one minor amputation in control group.
2 patients in the intervention group and 4 patients in the control group died (due to cardiovascular events)

Aggregate end point:
Aggregated end points showed a significant overall reduction in the ITT population for ulceration, amputation and death (18 vs 29 events (HR 0.54 0.30-0.96; p=0.03) and for the PP population 13 vs 34 events (0.49; 0.28-0.91; p=0.02)
</td></tr>
</table>

Reference	**Plank, J., Haas, W., Rakovac, I., Gorzer, E et al (2003)Evaluation of the impact of chiropodist care in the secondary prevention of foot ulcerations in diabetic subjects, Diabetes Care 26 (6) 1691-1695**
Study location	Austria
Authors conclusion	Regular chiropodist care was effective in preventing secondary ulceration
Source of funding	Supported by the Styrian government
Comments	None

Table 42: Ulbrecht 2014

Bibliographic reference	**Ulbrecht, J. S., Hurley, T., Mauger, D. T., & Cavanagh, P. R. (2014). Prevention of Recurrent Foot Ulcers With Plantar Pressure–Based In-Shoe Orthoses: The CareFUL Prevention Multicenter Randomized Controlled Trial. Diabetes care, DC_132956.**
Study type	Randomised control trial
Study quality	Summary Population: USA amongst patients with recently healed foot ulcers Intervention: orthoses initially designed to be similar to shape only insole and then modified using a computer-aided design process according to defined algorithms based on the peak barefoot plantar pressure distribution contours. Standard of care: in all cases subjects received three pairs of identical orthoses to be rotated while using the primary study footwear according to a written rotation protocol. Patients received education and motivation to encourage adherence. Comparison: foot shape obtained using foam boxes and sent to the manufacturer of the control insoles, no plantar pressure based adjustments made Outcome: ulceration 1) Has an appropriate method of randomisation been used? YES 2) Was there adequate concealment of allocation? YES 3) Were the groups comparable at baseline for all major confounding/prognostic factors? NO There were some differences at baseline between groups. At baseline mean ankle brachial pressure index was higher in the control group (P=0.02), and subjects in the control group showed a trend towards higher scores on avoiding foot damaging behaviour. Both of these biases would favour better outcomes in the control group however. 4) Did the comparison groups receive the same care apart from interventions studied? YES

Bibliographic reference	**Ulbrecht, J. S., Hurley, T., Mauger, D. T., & Cavanagh, P. R. (2014). Prevention of Recurrent Foot Ulcers With Plantar Pressure–Based In-Shoe Orthoses: The CareFUL Prevention Multicenter Randomized Controlled Trial. Diabetes care, DC_132956.**
	5) Were participants receiving care kept blind to treatment allocation? NO 6) Were the individuals administering care kept blind to treatment allocation? NO 7) Were groups comparable with respect to availability of outcome data and for how many participants were no outcome data available? YES 8) Did the study have an appropriate length of follow up? YES 9) Did the study use a precise definition of outcome? YES 10) Was a valid and reliable method used to determine that outcome? YES 11) Were investigators kept blind to participant's exposure to the intervention? YES (investigator blinded only) 12) Were investigators kept blind to other important confounding and prognostic factors? UNCLEAR
Number of patients	Randomised= 130 Pressure customised footwear= 66 Shape customised footwear= 64
Patient characteristics	Patients taken from: USA Inclusion: Men and women ≥18 years of age Diabetes and loss of protective sensation (inability to feel the 10-g monofilament at one or more sites) At least one recently healed foot ulcer (>1 week but < 4 months) Plantar MTH-related foot ulcer Peak barefoot plantar pressure in the area of this previous ulcer >450 kPa Community ambulatory No current ulcer below the malleoli Partial foot amputation of no greater than two MTHs or rays per foot Ability to comply with protocol Exclusion: Ankle-foot orthosis Existing footwear intervention more complex than would be available through the study footwear and orthotic options

Bibliographic reference	**Ulbrecht, J. S., Hurley, T., Mauger, D. T., & Cavanagh, P. R. (2014). Prevention of Recurrent Foot Ulcers With Plantar Pressure–Based In-Shoe Orthoses: The CareFUL Prevention Multicenter Randomized Controlled Trial. Diabetes care, DC_132956.**

Baseline characteristics:

Characteristics	Customised pressure based orthosis n=66	Shape customised orthosis n=64
Age, years	60.5 ± 10.1	58.5 ± 10.7
Sex, male	50	52
Race % White African American Other	 55 10 1	 51 11 2
Type 1 diabetes	Not reported	Not reported
Duration of diabetes, y	Not reported	Not reported
Previous ulcers	All	All
History of previous amputation	21	24
Ankle brachial pressure index	1.05 ± 0.16	1.13 ± 0.18
Foot deformity index	28.4 ± 14.6	28.9 ± 17.3
No foot pulses present	Not reported	Not reported
Activity (steps per day) (SEM)	Not reported	Not reported
Fitted footwear	All	All
Diabetic foot risk classification Risk 1 Risk 2 Risk 3 Risk 4	Not reported	Not reported
Neuropathy	All	All
Retinopathy	Not reported	Not reported
HbA1c	Not reported	Not reported
Current smoker	6	12
Nephropathy	Not reported	Not reported
Hospitalizations/yr	Not reported	Not reported
Body Mass Index	32.3 ± 7.1	31.4 ± 5.5

Bibliographic reference	**Ulbrecht, J. S., Hurley, T., Mauger, D. T., & Cavanagh, P. R. (2014). Prevention of Recurrent Foot Ulcers With Plantar Pressure–Based In-Shoe Orthoses: The CareFUL Prevention Multicenter Randomized Controlled Trial. Diabetes care, DC_132956.**
Intervention	Pressure customised footwear= 66 Orthoses initially designed to be similar to shape only insole and then modified using a computer-aided design process according to defined algorithms based on the peak barefoot plantar pressure distribution contours. In all cases subjects received three pairs of identical orthoses to be rotated while using the primary study footwear according to a written rotation protocol. Patients received education and motivation to encourage adherence.
Comparison	Shape customised footwear= 64 Foot shape obtained using foam boxes and sent to the manufacturer of the control insoles, no plantar pressure based adjustments made. In all cases subjects received three pairs of identical orthoses to be rotated while using the primary study footwear according to a written rotation protocol. Patients received education and motivation to encourage adherence.
Length of follow up	Length of follow up was 15 months
Location	USA
Outcomes measures and effect size	Rates of foot ulceration/infection Incidence of ulceration after 1 year follow up Ulcers were judged to be present if the integrity of both the epidermis and dermis were broken. Pressure customised orthosis group = 6 of 66 participants Shape customised orthosis group = 16 of 64 participants Hazard ratio was 3.4 (95% CI 1.3-8.7) i.e. significant difference Rates of gangrene resulting from diabetes Outcome not reported Rates of amputation Outcome not reported Rates of A&E/ Hospital admission for foot problems resulting from diabetes Outcome not reported

Bibliographic reference	**Ulbrecht, J. S., Hurley, T., Mauger, D. T., & Cavanagh, P. R. (2014). Prevention of Recurrent Foot Ulcers With Plantar Pressure–Based In-Shoe Orthoses: The CareFUL Prevention Multicenter Randomized Controlled Trial. Diabetes care, DC_132956.**
	Resource use and costs Outcome not reported
Source of funding	Grant from the National Institutes of Health
Comments	

Table 43: Bus 2013

Bibliographic reference	**Bus, S. A., Waaijman, R., Arts, M., de Haart, M., Busch-Westbroek, T., van Baal, J., & Nollet, F. (2013). Effect of Custom-made Footwear on Foot Ulcer Recurrence in Diabetes A multicenter randomized controlled trial. Diabetes care, 36(12), 4109-4116.**
Study type	Randomised control trial
Study quality	Summary Population: Netherlands amongst patients with recently healed foot ulcers Intervention: custom-made footwear of which the offloading properties were improved and subsequently preserved based on inshoe plantar pressure measurement and analysis Standard of care: see below Comparison: custom-made footwear that did not undergo improvement based on in-shoe pressure measurement I.e usual care Outcome: ulceration 1) Has an appropriate method of randomisation been used? YES 2) Was there adequate concealment of allocation? YES 3) Were the groups comparable at baseline for all major confounding/prognostic factors? NO There were differences between groups for the baseline characteristics of diabetes duration, barefoot peak plantar pressure at baseline and in-shoe peak pressure at footwear delivery. 4) Did the comparison groups receive the same care apart from interventions studied? UNCLEAR Footwear design was not enforced by any protocol and there were differences in footwear design between patients. Unclear how these differences of footwear design affected patients across groups. 5) Were participants receiving care kept blind to treatment allocation? NO

Bibliographic reference	**Bus, S. A., Waaijman, R., Arts, M., de Haart, M., Busch-Westbroek, T., van Baal, J., & Nollet, F. (2013). Effect of Custom-made Footwear on Foot Ulcer Recurrence in Diabetes A multicenter randomized controlled trial. Diabetes care, 36(12), 4109-4116.**
	6) Were the individuals administering care kept blind to treatment allocation? NO 7) Were groups comparable with respect to availability of outcome data and for how many participants were no outcome data available? YES 8) Did the study have an appropriate length of follow up? YES 9) Did the study use a precise definition of outcome? YES 10) Was a valid and reliable method used to determine that outcome? YES 11) Were investigators kept blind to participant's exposure to the intervention? YES (investigator blinded only) 12) Were investigators kept blind to other important confounding and prognostic factors? UNCLEAR
Number of patients	Randomised= 171 Pressure customised footwear= 85 Shape customised footwear= 86
Patient characteristics	Patients taken from: Netherlands Inclusion: ≥18 years of age Confirmed type 1 or type 2 diabetes Loss of protective foot sensation as a result of peripheral neuropathy A healed plantar foot ulcer (in the 18 months preceding randomisation A new prescription of custom-made footwear Exclusion: Bilateral amputation proximal to the tarsometatarsal joint Use of walking aids that offload the foot Severe illness that would make 18 month survival unlikely Inability to follow the study instructions Baseline characteristics:

<table>
<tr><td>Bibliographic reference</td><td colspan="3">Bus, S. A., Waaijman, R., Arts, M., de Haart, M., Busch-Westbroek, T., van Baal, J., & Nollet, F. (2013). Effect of Custom-made Footwear on Foot Ulcer Recurrence in Diabetes A multicenter randomized controlled trial. Diabetes care, 36(12), 4109-4116.</td></tr>
<tr><td></td><td colspan="3">
<table>
<tr><td>Characteristics</td><td>Customised pressure based orthosis n=85</td><td>Shape customised orthosis n=86</td></tr>
<tr><td>Age, years</td><td>62.6 ± 10.2</td><td>63.9 ± 10.1</td></tr>
<tr><td>Sex, male</td><td>82.3</td><td>82.6</td></tr>
<tr><td>Race, Caucasian</td><td>97.6</td><td>93.0</td></tr>
<tr><td>Type 2 diabetes</td><td>67.1</td><td>75.6</td></tr>
<tr><td>Duration of diabetes, y</td><td>19.9 ± 15.1</td><td>14.7 ± 11.2</td></tr>
<tr><td>Previous ulcers</td><td>All</td><td>All</td></tr>
<tr><td>History of previous amputation</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Ankle brachial pressure index</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Foot deformity absent %</td><td>4.7</td><td>2.3</td></tr>
<tr><td>Peripheral arterial disease %</td><td>28.8</td><td>37.5</td></tr>
<tr><td>Activity (steps per day) (SEM)</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Fitted footwear</td><td>All</td><td>All</td></tr>
<tr><td>Diabetic foot risk classification
Risk 1
Risk 2
Risk 3
Risk 4</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Neuropathy (monofilament) %</td><td>94.1</td><td>91.9</td></tr>
<tr><td>Retinopathy</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>HbA1c %</td><td>7.5 ± 1.4</td><td>7.6 ± 1.5</td></tr>
<tr><td>Current smoker</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Nephropathy</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Hospitalizations/yr</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Body Mass Index</td><td>30.9 ± 6.4</td><td>30.2 ± 4.9</td></tr>
</table>
</td></tr>
<tr><td>Intervention</td><td colspan="3">Pressure customised footwear= 85

Custom-made footwear of which the offloading properties were improved and subsequently preserved based on inshoe plantar pressure measurement and analysis</td></tr>
<tr><td>Comparison</td><td colspan="3">Shape customised footwear= 86

Custom-made footwear that did not undergo improvement based on in-shoe pressure measurement i.e usual care</td></tr>
</table>

Bibliographic reference	**Bus, S. A., Waaijman, R., Arts, M., de Haart, M., Busch-Westbroek, T., van Baal, J., & Nollet, F. (2013). Effect of Custom-made Footwear on Foot Ulcer Recurrence in Diabetes A multicenter randomized controlled trial. Diabetes care, 36(12), 4109-4116.**
Length of follow up	Length of follow up was 18 months
Location	Netherlands
Outcomes measures and effect size	Rates of foot ulceration/infection Incidence of ulceration after 18 months follow up Ulcers were defined as cutaneous erosions through the dermis Pressure customised orthosis group = 33 of 85 participants Shape customised orthosis group = 38 of 86 participants Odds ratio was 0.80 (0.44 to 1.47) i.e. no significant difference Rates of gangrene resulting from diabetes Outcome not reported Rates of amputation Outcome not reported Rates of A&E/ Hospital admission for foot problems resulting from diabetes Outcome not reported Resource use and costs Outcome not reported
Source of funding	Grants from the Dutch Diabetes Research Foundation, Dutch Foundation for the Development of Orthopaedic Footwear, and the Dutch Organisation for Health Research and Development
Comments	

F.7 Review question 7 full evidence tables

Table 44: Evidence table - Classification tools

Study	Participants	Characteristics	Tool	Follow up	Outcomes	Results	Comments
Erdman (2012) Retrospective cohort USA Review ID 134	77 people (101 feet) with foot ulcer and suspected infection undergoing ^{99m}Tc-WBC SPECT/CT. Large municipal hospital setting. Jan 2007 to Jul 2009.	None given Patients included if there was documented follow up of at least three months and technically satisfactory image.	Composite Severity Index (CSI) for foot infection in conjunction with ^{99m}Tc-WBC SPECT/CT. CSI scored on number of lesions, stage and intensity.	Median 325.4d (+/-148.8d)	Healing Failure to resolve symptoms or recurrence of symptoms requiring amputation or hospitalisation	CSI accuracy (AUC 0.79) Prediction of favourable outcome: CSI 0 = PPV 92% declining incrementally to 25% for CSI >=7 Odds ratio for people with CSI >2, 15.1 (4.4-51.5 CI 95%)	Clinical management did not vary by grade or stage (retrospective study). Authors conclude that a standardised system incorporating wound infection parameters gained from ^{99m}Tc-WBC SPECT/CT, has prognostic value in DFI.
Beckert (2009) Prospective cohort Germany Review ID 1325	2019 consecutive people with lower extremity ulcers attending an outpatient wound care unit. Dec 1997 to April 2004	Male 58% Median age 70y (15-98) 45.3% had more than one ulcer Median wound history 65d (15-21229) If the patient had multiple ulcers, the highest graded	MAID severity score. Grades 0 to 4 based on pedal pulses, wound area, wound duration and number of ulcers. Pulse presence determined by palpation. Wound	Median time to follow up 73d (2-365)	Healing Follow up infection Hospitalisation	With increasing MAID score, the probability of healing at 365d decreased from 84% (grade 0) to 31% (grade 4)(P<0.0001; x^2=191.230). Increase of one point score reduced chances of healing by 37% Chance of hospitalisation increased 34% to 67%. Follow up infection more likely in higher MAID group even though little difference at presentation (P=0.001;	Clinical management was not varied by grade or stage. Treatment protocol consisted of debridement, local surgical procedures, moist wound therapy, off-loading. Authors conclude that the ulcer score provides a valuable diagnostic tool for anticipating probability of healing.

Study	Participants	Characteristics	Tool	Follow up	Outcomes	Results	Comments
		was selected as index. Exclusion: people with less than two visits during the observation period.	area measured by photoplanimetry. Wound duration established in interview with patient.			x2=18.654). In multivariate analysis of parameters influencing healing: Multiple ulcer HR 0.729 (0.697-0.835), P=0.0001. Wound >4cm2 HR 0.455 (0.388-0.535), P=0.0001. Duration >130d HR 0.641 (0.547-0.752), P=0.0001 Non-palpable pulse HR 0.827 (0.723-0.947), P=0.01.	
Abbas (2008) Retrospective cohort Tanzania Review ID 1816	326 people (479 ulcers) referred to specialist multidisciplinary foot clinic. 74 lost to follow-up. 252 people (375 ulcers) in final analysis. Jan 2003 to Sep 2005.	Male 67.1% Mean age 54.7y +/- 11.5	Wagner University of Texas S(AD) SAD PEDIS Single specialist assessed all patients Modified S(AD) SAD neuropathy assessment Depth determined by visual inspection and sterile probe. Infection determined by clinical criteria. PAD diagnosed by absence of	Median duration 36 days (range 0-973)	Healing Amputation Death	230 (61.3%) ulcers healed 69 (18.4%) unhealed 58 (15.5%) resolved by minor or major amputation 18 (4.8%) resulted in death Strongest significant statistical association (x^2 trend) observed between healing and: Wagner score (82.923) Depth of ulcer (S(AD) SAD, PEDIS and UT grade, 70.558), Infection (S(AD) SAD 61.774, PEDIS 37.924) UT Stage (32.929)	Clinical management was not varied by grade or stage (retrospective study). Large drop-out rate. Authors conclude that the factors most closely associated with outcome are dependent on the population. This has implications for the classification systems chosen.

<table>
<tr><th>Study</th><th>Participants</th><th>Characteristics</th><th>Tool</th><th>Follow up</th><th>Outcomes</th><th>Results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td>pedal pulse.

Single observer.</td><td></td><td></td><td></td><td></td></tr>
<tr><td>Ince (2008)
Retrospective cohort
UK
Germany
Tanzania
Pakistan</td><td>449 people referred to a specialist clinic in UK.
Germany 239
Tanzania 479
Pakistan 173
Total 1340</td><td>UK: Male 64%, Age 68y (+/- 13)
86% type 2.

Germany: Male 59%, Age 69y (+/- 11)
90% type 2.

Tanzania: Male 67%, Age 55y (+/- 11)
98% type 2.

Pakistan: Male 67%, Age 53y (+/- 12)
99% type 2.</td><td>SINBAD

Ischemia determined by pulse palpation with reduced tissue perfusion. Infection classified according IDSA and IWGDF. Neuropathy determined by neurotips or 10g monofilament.</td><td>UK: 91d (6-1344).

Germany: 70d (1-967).

Tanzania: 30d (0-973).

Pakistan: 60d (1-1088).</td><td>Time to healing
Amputation
Death</td><td colspan="3">Time to healing in days (range) for ulcers that healed showed significant difference between scores (x2 37.324, P=0).
Multi variate analysis showed significant independent association between variables and outcome (healing v non-healing, death and amputation).
Data 95% CI (P value). Data not presented for Pakistan as only one variable significant on univariate analysis.
<table><tr><td></td><td>UK</td><td>Germany</td><td>Tanzania</td></tr><tr><td>Site</td><td>-</td><td>-</td><td>0.340-0.894 (0.016)</td></tr><tr><td>Ischemia</td><td>2.046-7.484 (0)</td><td>2.695-14.228 (0)</td><td>-</td></tr><tr><td>Neuropathy</td><td>-</td><td>-</td><td>1.466-9.345 (0.006)</td></tr><tr><td>Bacteria</td><td>-</td><td>1.963-20.325 (0.002)</td><td>1.596-7.781 (0.002)</td></tr><tr><td>Area</td><td>1.436-4.461 (0.001)</td><td>-</td><td>-</td></tr><tr><td>Depth</td><td>1.322-5.009 (0.005)</td><td>3.950-49.970 (0)</td><td>-</td></tr></table></td><td>Variable duration of follow up period.

Authors conclude that time to healing increases between those scoring 2 and 3 and that those grade 3 and above are at particular risk. Authors also conclude the scoring system could be applied worldwide.</td></tr>
<tr><td>Parisi (2008)
Prospective cohort</td><td>105 consecutive people with diabetic foot</td><td>Male 61%
Mean age 57.61y (SD 12.44, range</td><td>University of Texas
Wagner
S(AD) SAD</td><td>1 to 4 week intervals
6 months minimum</td><td colspan="2">Primary: Ulcer healing
Secondary: Major and minor</td><td>Baseline data incomplete for 11 and excluded, 94 in final analysis.

Clinical management did not very by grade or stage. Treatment consisted of debridement, off-loading and</td></tr>
</table>

Study	Participants	Characteristics	Tool	Follow up	Outcomes	Results	Comments
Brazil Review ID 1635	ulcers. Specialist multi-disciplinary unit in an Endocrinology Division Dec 2003 to Dec 2005.	13-89) Mean duration of diabetes 16.9y (SD 8.16) If the patient had multiple ulcers, the most significant was selected as index. Each patient included once only.	Ischemia assessed by palpation of pulses Infection diagnosed by clinical signs. Osteomyelitis diagnosed on probe to bone. Depth judged on inspection. Sensation determined by VPT, monofilament and ankle reflex.	follow up (or death / amputation) None lost to follow up or death.	amputation	51% of ulcers healed without surgery 12% underwent minor amputation No major amputation UT, chance of healing: Stage A v Stage D OR=4.6, 95%CI 1.37-15.49, P=0.014. Stage B v Stage D OR=1.68, 95%CI 0.46-6.11, P=0.433. Stage C v Stage D OR=2.26, 95%CI 0.62-8.32, P=0.219. Grade 1 v Grade 2+3 OR=2.87, 95%CI 1.08-7.64, P=0.035. Wagner chance of healing: Grade 1 v Grade 2+3 OR=3.48, 95%CI 1.38-8.76, P=0.008 S(AD) SAD chance of healing: Score <=9 v >10 OR=7.64, 95%CI 2.72-21.45, P<0.0001.	revascularisation. Authors conclude that the three classifications performed equally well but that systems of classification, which are validated in one group, may not be applicable to others (regional differences).

Study	Participants	Characteristics	Tool	Follow up	Outcomes	Results	Comments
Lavery (2007) Prospective cohort USA and Netherlands Review ID 2093	247 consecutive people with diabetic ulcer in a diabetes management programme foot clinic. Time period not stated.	No infection: mean age 59.8y, male 53.6%, duration of diabetes 12.8 +/- 9.6 Mild infection: mean age 63.4, male 53.5%, duration of diabetes 13.2 +/- 9.3 Moderate infection: mean age 50.0y, male 48.1%, duration of diabetes 16.3 +/- 10.8 Severe infection: mean age 51.9y, male 63.0%, duration of diabetes 14.4 +/- 12.0	IDSA IWGDF Infection classification system Infection diagnosed using clinical criteria	Unclear intervals Average follow-up length 27.2 months.	Lower extremity complication including hospitalisation and amputation	61% developed foot infection. With an increasing IDSA-IWGDF severity there was a trend toward increased risk of amputation (x^2 trend 108.00, P<0.001), an increased atomic level of amputation (x^2 trend 113.3, P<0.001) and an increased need for lower extremity related hospitalisation (x^2 118.6, P<0.001).	Unclear if treatment differed by grade of infection. Authors conclude there is value of the IDSA-IWGDF classification in predicting clinical outcomes. Persons with mildly infected or non-infected wounds are highly unlikely to require hospitalisation, develop osteomyelitis or undergo amputation.
Beckert (2006) Prospective cohort Germany Review ID 2310	1000 consecutive people attending an out-patient wound care. Dec 1997 to April 2004.	Median age 69 (range 26-95) Male 67.5% In patients with multiple ulcers, the wound with the highest grading was	Diabetic ulcer severity score (DUSS) Score 0 to 4 based on pedal pulses, bone involvement, site and number of	365 days or until healing or amputation Median follow-up 68 days, range 3-365.	Healing Hospital admission Surgery (debridement, resection, amputation)	9.9% had minor amputation 2.6% had major amputation 93% probability of healing for uncomplicated ulcer (score 0), decreasing to 57% for score 4	Clinical management was not varied by grade or stage. Treatment protocol consisted of debridement, local surgical procedures, moist wound therapy, off-loading. Authors conclude that this new severity scoring system provides an easy

Study	Participants	Characteristics	Tool	Follow up	Outcomes	Results	Comments
		selected as for analysis. Exclusion: people with less than two visits.	ulcers. Pulse presence determined by palpation. Bone involvement established by probe to bone.			(P<0.0001) Multivariate analysis of parameters reducing chances of healing (OR, 95%CI) : Multiple ulcer 0.648 (0.540-0.778) P=0.001 Probing to bone 0.777 (0.623-0.968) P=0.025 Location 0.483 (0.402-0.580) P=0.001 Non palpable pulses (0.723 (0.603-0.868) P=0.001 Increasing probability of amputation with increasing DUSS score. Score 0 = no risk Score 1 = 2.4% Score 2 = 7.7% Score 3 = 11.2% Score 4 = 3.8% Not statistically significant.	diagnostic tool for anticipating the probability of healing, hospital admission and surgery.
Gul (2006) Retrospective cohort Pakistan Review ID 2136	383 people with diabetic foot ulcer visiting a foot clinic. Complete data only available for 200.	Male 65% Mean age: Male, 53.04y (SD 10.33) Female 51.14y (SD 9.94) Ulcer type: 45%	University of Texas Wagner Ischemia assessed by palpation of pulses	Average duration of treatment: Males 109.68 days (+/- 82.26 days)	Complete healing, major/minor amputation or death.	72.5% completely healed 24% healed with amputation 3.5% died. Wagner system. More likely to have amputation if Grade 4 or 5 compared	Clinical management was not varied by grade or stage (retrospective assessment). Authors conclude that healing time had a positive relationship with Wagner grade and UT

Study	Participants	Characteristics	Tool	Follow up	Outcomes	Results	Comments
	Jan 1997 to Dec 2003	neuropathic 55% neuro-ischaemic <1% pure ischemic	Infection diagnosed by presence of purulent discharge and other clinical signs. Osteomyelitis diagnosed on probe to bone and radiological signs.	Females 85.10 days (+/- 61.97)		to 1 (OR 45.5, 95%CI 3.48-594.68) UT system. Grade 2 v Grade 1: OR 2.9, 95%CI 0.37-23.93. Grade 3 v Grade 1: OR 9.5, 95%CI 1.15-77.27. Stage C and D v A and B: OR 2.7, 95%CI 1.31-5.41.	grade and stage. Significant difference in the amputation rate was noted as the grade or stage increased.
Treece (2004) Prospective cohort UK Review ID 2726	302 consecutive people with diabetic foot ulcer. Multi-disciplinary clinic at a hospital. Jan 2000 and July 2002.	Male 64.6% Mean age 66y +/-13y If more than one ulcer, the most significant was chosen as index ulcer	S(AD) SAD Area measured by ruler. Depth judged by inspection (probe not used). Vascular supply by palpation of pulses. Sensation by Neurotip. Infection judged by clinical signs and purulent discharge. Assessment by one of two clinicians (consultant or trainee)	1 to 4 week intervals 6 month follow up None lost to follow up	Healing Amputation Death	2 patients excluded from final analysis because of lack of data Ulcers healed 69.7% Unhealed 9.7% Amputation 10% Death 10.7% Differences in outcome according to: Area x^2 = 25.9, P<0.001 Depth x^2 = 33.8, P<0.001 Sepsis x^2 = 13.5, P=0.004 Arteriopathy x^2 = 33.7, P<0.001 Denervation x^2 = 5.1, P=0.16 Strength of association confirmed by Somers d: Area r_s = -0.24, P<0.001 Depth r_s = -0.32, P<0.001	Clinical management was not varied by grade or stage. Usual clinical management unaltered (antibiotics, off-loading, podiatric input and revascularisation as appropriate). Authors conclude that four factors used in classification are significantly associated with ulcer healing, and that three independently contribute to outcome (area, depth and arteriopathy).

Study	Participants	Characteristics	Tool	Follow up	Outcomes	Results	Comments
						Sepsis r_s = -0.15, P<0.01 Arteriopathy r_s = -0.30, P<0.001 Denervation r_s = -0.10, P=0.08	
Oyibo (2001) Prospective cohort UK and USA Review ID 3480	194 people presenting with a new foot ulcer to two specialist diabetic foot centres (one in USA and one in UK). 1998 to 1999.	Mean age 56.6 (SD 12.6) Male 77% Mean duration of diabetes 15.4y (SD 9.9) Type 2 diabetes 89%	University of Texas Wagner Infection diagnosed by clinical criteria. Osteomyelitis diagnosed by probe to bone and radiography. Ischemia diagnosed by clinical signs and/or ABPI.	Weekly appointments. Minimum length of follow up 6 month. No loss to follow up reported	Complete healing Amputation	65% healed completely 15% had amputation 16% not healed at study completion 4% died Wagner system (grade) showed a positive trend with increased number of amputations (x2 trend= 21.0, P <0.0001). UT system showed positive trend for grade (x2 trend 23.7, P<0.0001) and stage (x2 trend = 15.1, P=0.0001) with increased number of amputations.	Clinical management was not varied by grade or stage. Usual care consisted of debridement, dressing, off-loading, orthoses, antibiotics and vascular expert input (if necessary). Authors conclude that the grade and stage affect the outcome of diabetic foot ulcers. The higher the grade, the greater the number of amputations performed. The presence of infection and/or ischemia increased the risk of amputation. They also state that the UT system show greater association with increased risk of amputation and prediction of healing than the Wagner system.
Armstrong (1998) NEW Retrospective cohort USA	360 people with diabetic foot wound in a multidisciplinary tertiary care diabetic foot clinic.	Mean age 53.9y +/-10.4 Male 68.6% Mean duration of diabetes 14y +/- 9.2y	University of Texas Infection diagnosed by clinical criteria.	6 months	Amputation	Of all patients, 28.6% had some form of lower extremity amputation. Trend assessed using x^2 test for trend. Overall trend towards	Clinical management was not varied by grade or stage (retrospective assessment). Original validation of UT system.

Study	Participants	Characteristics	Tool	Follow up	Outcomes	Results	Comments
Review ID X1	Jan 1994 to July 1996		Osteomyelitis diagnosed by bone biopsy. Ischemia diagnosed by clinical signs and ABI.			increased prevalence of amputation as wounds increased in depth (x^2 trend = 143.1, P<0.001) and stage (x^2 trend = 91, P<0.001). Patients 11 times more likely to receive midfoot or higher amputation if wound probed to bone (grade 3) (18.3 v 2.0%, P<0.001, x^2 trend 31.5, OR 11.1 [CI 4-31.3]) Patients 90 times more likely to receive midfoot or higher amputation if stage D compared to lower stages (76.5 v 3.5%, P<0.001, x^2 trend 133.5, OR 89.6 [CI 25-316])	Authors conclude that outcomes deteriorate with increasing grade and stage of wounds as measured by UT classification system.
Wukich (2013) RERUN Retrospective cohort USA	100 patients hospitalised for diabetic foot infection January 2006 to December 2011	Mean age 58.0y +/- 11.6 Male 78% Mean duration of diabetes 14.9y +/- 9.6	IDSA IWGDF Infection classification system Severe diabetic foot infection was diagnosed as having two or more objective findings of systemic toxicity and/or metabolic	Retrospective observation period of 5 years	Amputation and hospital length of stay, limb salvage rates	Amputations were more common among patients with a severe diabetic foot infection (55%) than those with moderate diabetic foot infection (42%) but this was non-significant (P=0.22) Hospital length of stay was longer in those with severe infection (median 8 days) than for those with moderate infection (median 5 days)	Authors conclude length of stay was significantly longer for those with severe infection with a non-significant trend indicating higher rates of limb salvage in patients with moderate infections compared to patients with severe infections.

Study	Participants	Characteristics	Tool	Follow up	Outcomes	Results	Comments
			instability at the time of initial assessment			(P=0.021) Limb salvage was greater in those with moderate infections (94%) when compared to those with severe infections (80%) but the difference was non-significant (P=0.081)	
Tsai (2013) RERUN Retrospecti ve cohort	658 diabetic patients admitted to the diabetic foot care centre Between January 2009 and December 2010	Mean age 65 ± 13 years Male 55.0% Mean duration of diabetes: 12.4 ± 8.9 years	Wagner grade 4 or 5 vs 1,2 or 3 Ischaemia was diagnosed by duplex ultrasound scan and ankle brachial pressure index.	Retrospecti ve over 1 year	Lower extremity amputation	Of all patients 16.7% experienced major lower extremity amputation defined as any amputation through or proximal to the ankle joint. Risk of major lower limb amputation was found to be significantly greater in those with Wagner grade 4 or 5 when compared to those with Wagner grade 1,2 or 3 in the non-dialysis population: OR 3.80 (95% CI 1.25-11.56) P=0.019 after multivariate analysis. Risk of major lower limb amputation was found not to be significantly greater in those with Wagner grade 4 or 5 when compared to those with Wagner grade 1,2 or 3 in the dialysis population: OR 3.70 (95% CI 0.85-16.09) P=0.081.	Authors conclude that Wagner proved a significant risk factor for lower extremity amputation in non-dialysis groups however seemed to lose its predictive power in the dialysis group. This is likely due to the rapid increase in wound severity amongst dialysis patients.

Study	Participants	Characteristics	Tool	Follow up	Outcomes	Results	Comments
Won (2014) RERUN Retrospective cohort	173 patients with diabetic foot ulcers who visited or were referred from march 2003 to October 2012	Mean age 67.5 ± 11.4 years Male 74% Mean duration of diabetes: 18.9 ± 10.2 years	Wagner grade Major amputations were defined as above the ankle. Wagner grade was determined from clinical information.	Retrospective. Mean duration of follow up was 14.6 ± 15.9 months 1 year amputation survival rates were recorded	Major and minor amputation after hazards regressional model	Of all patients 12 experienced a major amputation and 47 experienced a minor amputation. Risk of all lower limb amputation was found to be significantly greater in those with higher Wagner grade: HR 7.99 (95% CI 3.12-20.47) P=<0.01 after regression analysis. Risk of major limb amputation was found to be significantly greater in those with higher Wagner grade: HR 8.02 (95% CI 0.97-66.33) P=0.05 after regression analysis. Risk of minor limb amputation was found to be significantly greater in those with higher Wagner grade: HR 9.36 (95% CI 3.25-26.92) <P=0.01 after regression analysis.	Authors conclude that severity of ulcer as defined by Wagner criteria was the strongest risk factor for amputation after multivariate analysis.
Wang (2014) RERUN Retrospective case control	194 patients with diabetic foot ulcers Hospitalised between	Mean age 67.00 ± 12.26 years Male 52.58% Mean duration of diabetes: 9.78 ± 6.75	Wagner grade Major amputation was defined as above the ankle amputation	1 year follow up	Patients were grouped into amputation group, a non-healing group and a cured	Of all patients 12 patients were classified in the amputation group, 20 patients in the non-healing group and 162 patients in the cured	Authors conclude that severity of ulcer as defined by Wagner criteria was negatively correlated to diabetic foot prognosis after multivariate analysis.

Study	Participants	Characteristics	Tool	Follow up	Outcomes	Results	Comments
	January 2009 and January 2010	years			group.	group Wagner grade was found to have an Odds ratio of 0.262 (95% CI 0.261-0.037) p=<0.01 after regression analysis. Wagner classification was found to negatively correlate to prognosis.	

Table 45: Evidence table - Diagnostic tests for soft tissue infection and osteomyelitis

Study	Participants	Characteristics	Index test	Reference test	Results	Comments
2013 Alvaro-Afonso (2013) **NEW** Prospecti ve cohort Spain Review ID 5226	123 patients with diabetic foot ulcers and clinical suspicion of osteomyelitis. Patients admitted to Diabetic Foot Unit. Oct 2009 to July 2011	Male 72% Mean age 65y +/- 13.3y Mean duration of diabetes 16y +/- 12.2y 89% type II Excluding people who had surgery in preceding 3m and people with Charcot.	Plain film radiography for the diagnosis of osteomyelitis.	2 groups of 3 professionals with different levels of skill interpreted imaging in isolation: Inexperienced Moderately experience Very experienced 2m re-examination for intra-observer variability	Inter reliability: Low concordance rates of agreement between clinicians with similar levels of experience (very experienced K=.35, mod experienced K=.39, inexperienced K=.40) Intra-observer agreement highest in experienced clinicians (K=.75), follow by mod experienced (K=.61) and lowest in inexperienced clinicians (K=.57)	Authors conclude that plain radiography for the diagnosis of osteomyelitis is operator dependent and shows low association strength, even among experienced clinicians.

Study	Participants	Characteristics	Index test	Reference test	Results	Comments
2013 Saeed (2013) **NEW** Prospecti ve cohort Pakistan Review ID 5205	65 patients with type 2 diabetes, foot ulcer and suspected osteomyelitis. Suspicion based on clinical examination. 10 lost to follow up, final analysis = 55 patients No dates given. Unclear setting.	Male 80% Mean age 53.42y +/- 8.8y Mean duration of diabetes 11.85y +/- 6.18y Exclusion: Patients with acute limb threatening infection. Patients with a negative three phase bone scan.	Diagnostic test for osteomyelitis: ^{99m}Tc-UBI 29-41 scintigraphy following three phase bone scan (^{99m}Tc-MDP) on average 2 days apart. Test considered to be positive for osteomyelitis if ^{99m}Tc-UBI 29-41 uptake concordant with ^{99m}Tc-MDP uptake.	Bone biopsy histopathology and culture (37 patients). Clinical decision and/or radiographic changes if biopsy not possible(3-12m, 18 patients).	Osteomyelitis confirmed by reference test in 37 of 55 patients (29 by histopathology/culture and 8 by clinical follow up). Pre-test probability 67%. ^{99m}Tc-UBI 29-41 scintigraphy positive in all 37 patients and negative for all 18 negative patients. Ref test: + / - / Total Index test +: 37 / 0 / 37 Index test -: 0 / 18 / 18 Total: 37 / 18 / 55 Se 100, Sp 100, PPV 100, NPV 100.	Authors conclude that ^{99m}Tc-UBI 29-41 appears to be a promising radiotracer for the evaluation of bone infection. However further studies are needed to compare with other radiotracers and radiography.
2012 Kagna (2012) **NEW** Prospecti ve cohort Israel Review ID 114	39 consecutive patients with diabetic foot ulcer (46 sites) referred to Nuclear Medicine with suspected infection. Suspicion based on clinical examination. Feb 2003 to May 2010	Male 74% Mean age 57y (range 28-71) Mean duration of diabetes 13y (range 4-25) At time of study, 29 were on antibiotic therapy.	Diagnostic test for osteomyelitis: FDG PET/CT interpreted in consensus by two nuclear medicine physicians and a skeletal radiologist.	Histological examination of bone biopsy, clinical examination of bone during surgery or clinical decision (4-12m follow up if not diagnosed by samples)	18/ 46 lesions diagnosed with osteomyelitis by reference test. Pre-test probability 39%. 13/39 patients diagnosed with osteomyelitis by reference test. Lesion-based analysis: Ref test + / - / Total Index test +: 18 / 2 / 20 Index test -: 0 / 26 / 26 Total: 18 / 28 / 46 Se 100, Sp 93, PPV 90, NPV 100 Patient based analysis: Ref test + / - / + Index test +: 13 / 2 / 15 Index test -: 0 / 24 / 24 Total: 13 / 26 / 39	Authors conclude that FDG PET/CT is of value in the diagnosis of osteomyelitis.

Study	Participants	Characteristics	Index test	Reference test	Results	Comments
					Se 100, Sp 92, PPV 87, NPV 100)	
2012 Mutluoglu (2012b) **NEW** Retrospective cohort Turkey. Review ID 244	Records of 54 patients seen with diabetic foot ulcer in a teaching hospital's Hyperbaric Medicine Centre (Military Medical Academy) who had both superficial swab and deep tissue biopsy. Jan 2008 to Dec 2009	Male 80% Mean age 62.5 (+/-10.3) Mean duration of diabetes 15.5y (+/- 7.1y) 28 patients were on antibiotics in the previous month. UT grade 3 in 35 (65%) of patients.	Cotton-tipped swab of base of ulcer to identify causative pathogen of tissue infection.	Deep tissue biopsy. A cube of viable tissue excised from the base of the ulcer following debridement.	Positive result in 69 samples with reference test (78% pre-test probability) 65/89 (73%) had identical isolates on swab (including 11 sterile pairs). Extra isolates on swab 10/89 (11%) Isolates missed on swab 8/89 (9%) Identical or more isolates on swab 75/89 (84%) Diagnostic accuracy: Index test: + / Ref test: + = 54; + / - = 10; + / Total = 64 Index test: - / Ref test: + = 14; - / - = 11; - / Total = 25 Total / Ref test: + = 68; - = 21; Total = 89 Se 79, Sp 52, PPV 84, NPV 44 Acc 73	Authors conclude that superficial swabs are not sufficiently accurate to identify causative organisms in patients with infected foot ulcer.
2012 Mutluoglu (2012a) **NEW** Cross-sectional Turkey. Review ID 94	65 in and outpatients with infected diabetic foot ulcer (as per IDSA guidelines) and clinical suspicion of osteomyelitis at a teaching hospital 's Hyperbaric Medicine Centre (Military medical Academy)	Male 78% Mean age 62y (+/- 11y) Mean duration of diabetes 18y (+/- 8 years)	Probe to bone test for diagnosis of osteomyelitis using sterile metal probe. Positive results when a blunt stiff sensation suggestive of bone was palpated	Culture from bone biopsy obtained during bedside debridement with a rongeur (17 patients). MRI used when biopsy not available (48 patients).	39/65 patients diagnosed with osteomyelitis on reference test (16/17 Bone biopsy and 23/48 MRI). Pre-test probability 60%. Probe to bone test: + / Ref test: + = 26; + / - = 4; + / Total = 30 Probe to bone test: - / Ref test: + = 13; - / - = 22; - / Total = 35 Total / Ref test: + = 39; - = 26; Total = 65 Se 66, Sp 84, PPV 87, NPV 62	Authors conclude that the probe to bone test provide some support for diagnosing osteomyelitis but it is not strong.

<table>
<tr><th>Study</th><th>Participants</th><th>Characteristics</th><th>Index test</th><th>Reference test</th><th>Results</th><th>Comments</th></tr>
<tr><td></td><td>Suspicion of osteomyelitis based on clinical examination

Jan 2007 to Dec 2008.</td><td></td><td></td><td></td><td></td><td></td></tr>
<tr><td>2011 Asli (2011)
NEW
Cross sectional
Iran

Review ID 528</td><td>18 patients (23 lesions) referred to a nuclear medicine department in a University hospital with a clinical suspicion of osteomyelitis.
Unclear selection criteria.
2006 to 2008</td><td>Male 83%
Age range 45-80y</td><td>Diagnostic tests for osteomyelitis.
^{99m}Tc-IgC scinitgraphy at 5h and 24h.
^{99m}Tc-MDP scintigraphy at 3-4d interval.
Interpreted by consensus between three nuclear medicine consultants (blinded to other clinical data).</td><td>Consensus of clinical opinion based on MRI, culture, histopathology and presentation.</td><td>10 lesions identified with osteomyelitis (pre-test probability 43%).
<table><tr><td colspan="2">5h-^{99m}Tc-IgC scintigraphy</td><td>Ref test</td><td></td></tr><tr><td colspan="2"></td><td>+</td><td>-</td><td>Total</td></tr><tr><td rowspan="3">Index test</td><td>+</td><td>10</td><td>4</td><td>14</td></tr><tr><td>-</td><td>0</td><td>9</td><td>9</td></tr><tr><td>Total</td><td>10</td><td>13</td><td>23</td></tr></table>Se 100, Sp 69, PPV 71, NPV 100.
<table><tr><td colspan="2">24h-^{99m}Tc-IgC scintigraphy</td><td>Ref test</td><td></td></tr><tr><td colspan="2"></td><td>+</td><td>-</td><td>Total</td></tr><tr><td rowspan="3">Index test</td><td>+</td><td>6</td><td>3</td><td>9</td></tr><tr><td>-</td><td>4</td><td>10</td><td>14</td></tr><tr><td>Total</td><td>10</td><td>13</td><td>23</td></tr></table>Se 60, Sp 77, PPV 67, NPV 71.
<table><tr><td colspan="2">^{99m}Tc-MDP scintigraphy</td><td>Ref test</td><td></td></tr><tr><td colspan="2"></td><td>+</td><td>-</td><td>Total</td></tr><tr><td rowspan="3">Index test</td><td>+</td><td>10</td><td>6</td><td>16</td></tr><tr><td>-</td><td>0</td><td>7</td><td>7</td></tr><tr><td>Total</td><td>10</td><td>1 3</td><td>23</td></tr></table>Se 100, Sp 54, PPV 63 NPV 100</td><td>Authors conclude that both tests can sensitively detect osteomyelitis however lack the specificity.
Early 5 hour images are adequate in ^{99m}Tc-IgC scintigraphy, there is no need for 24h images.</td></tr>
</table>

Study	Participants	Characteristics	Index test	Reference test	Results	Comments
2011 Garcia-Morales (2011) **NEW** Cross sectional study Spain Review ID 510	75 patients with diabetic foot ulcer and clinical suspicion of infection. Suspicion based on clinical examination. Diabetic foot unit of a podiatric clinic. Oct 2009 to Jun 2010	Male 61.3% Mean age 67y +/- 12y. 9.3% type I diabetes Mediation duration of diabetes 11y Median duration of ulcer 8w. Excluded if bone visible or if previous surgery in past 3 months	Probe to bone testing to diagnose osteomyelitis using metal forceps. Three different levels of experience. Observer 1: several years' experience in treating diabetic foot. Observer 2: 6 to 12m experience in treatment of diabetic foot Observer 3: no experience in treating diabetic foot or using the tool.	Not applicable.	Inter-observer reliability. Kappa concordance index relative: 1 to 2: 0.593 (0.407-0.778 CI95%) 1 to 3: 0.397 (0.188-0.604 CI95%) 2 to 3: 0.53 (0.335-0.725 CI95%)	Authors conclude that probe to bone testing demonstrates moderate to fair concordance with an experienced examiner although the degree of concordance is not significant between groups.
2011 Meyr (2011) **NEW** Cross sectional USA Review ID 472	39 consecutive patients retrospectively identified receiving bone biopsy for suspicion of osteomyelitis in a foot and ankle surgery service at a teaching hospital. Dec 2009 to Feb 2010	No details of patient characteristics given. Inclusion: patients who had a bone biopsy	Bone biopsy for histo-pathological analysis to diagnose osteomyelitis. Obtained from primarily amputated bone, apparently clean osseous margins after partial amputation and bone biopsy through full thickness chronic. 4 pathologists independently examined bone samples to assess presence of OM. wounds.	Not applicable.	Inter-observer reliability. Complete agreement of findings consistent with osteomyelitis 13 (33%), Kappa coefficient 0.31. Agreement between >=3 pathologists in 80% of cases. Clinically significant disagreement in 41% cases (at least one pathologist finding no evidence of osteomyelitis whilst at least one did find evidence) Agreement of findings consistent with acute or chronic osteomyelitis 5 (50%), Kappa coefficient 0.16.	Authors conclude that the reliability of bone biopsy could be far less than the level of reliability required for a "reference standard".

<table>
<tr><th>Study</th><th>Participants</th><th>Characteristics</th><th>Index test</th><th>Reference test</th><th>Results</th><th>Comments</th></tr>
<tr>
<td>2010 Bernard (2010)
NEW
Cross sectional
Switzerland

Review ID 732</td>
<td>68 patients with diabetic toe osteomyelitis with bone contact seen in an Orthopaedic Surgery Service.

3 year period, no dates given.

39 patients with prior antibiotic treatment</td>
<td>Median age 70y

57% already on antibiotic treatment for a median of 9d.

Exclusions: implant related infections and absence of surgery for cure.</td>
<td>Two consecutive bone contact swabbing to identify pathogen of underlying osteomyelitis. Samples obtained with sterile cotton swabs through ulcer less than 24h apart.
All samples obtained by same nurse.</td>
<td>Bone biopsy culture. Sample obtained during surgical through a clinically uninfected area outside the ulcer.
Bone swabbing and biopsies obtained less than 24h apart.
All samples obtained by same orthopaedic surgeon.</td>
<td>On reference test:
22 poly-microbial infections
26 mono-microbial infections
20 no growth (prior antibiotics)

56 concordant swab samples.
Un-weighted kappa statistic indicated 82.35% agreement.
<table>
<tr><td colspan="2">Either sample identified dominant pathogen</td><td>Ref test +</td><td>-</td><td>Total</td></tr>
<tr><td rowspan="3">Index test</td><td>+</td><td>46</td><td>4</td><td>50</td></tr>
<tr><td>-</td><td>2</td><td>16</td><td>18</td></tr>
<tr><td>Total</td><td>48</td><td>20</td><td>68</td></tr>
</table>
Se 96, Sp 79, PPV 92, NPV 88.

Where both samples were concordant in identification of dominant pathogen: Se 95, Sp 100, PPV 100, NPV 88

Where either sample identified main pathogen in patients with prior antibiotic treatment: Se 95, Sp 82, PPV 88, NPV 93

Where exact number and type of all pathogens are identified: Se 90, Sp 58, PPV 78, NPV 79.</td>
<td>Authors conclude that bone contact swabbing can accurately predict dominant pathogen of osteomyelitis in >90% of cases however bone biopsy should remain as gold standard.</td>
</tr>
<tr>
<td>2010 Elamurugan (2010)</td>
<td>144 consecutive patients with diabetic foot</td>
<td>Mean age 56.6y (+/- 4.2y)
Mean duration</td>
<td>Superficial ulcer swab to assess concordance in identifying presence of</td>
<td>Bone biopsy culture. Sample obtained</td>
<td>134/144 bone biopsy specimens showed positive culture. Pre-test probability 93%.
140 /144 swabs showed positive culture.</td>
<td>Authors conclude that ulcer swab culture has poor</td>
</tr>
</table>

<table>
<tr><th>Study</th><th>Participants</th><th>Characteristics</th><th>Index test</th><th>Reference test</th><th>Results</th><th>Comments</th></tr>
<tr><td>NEW
Cross sectional
India

Review ID 662</td><td>ulcer and suspicion of underlying osteomyelitis.
Suspicion based on clinical features.

Attending casualty or surgical outpatients department.

July 2008 to July 2010.</td><td>of foot ulcer 13.5d (+/- 3.5)
60% Wagner’s grade III.
57.2% had prior treatment for foot ulceration (antibiotics or debridement).</td><td>osteomyelitis and type of pathogen.

Swab was taken from base of ulcer.</td><td>percutaneously or by open biopsy using an 11-gauge bone biopsy needle (local anaesthetic)</td><td>Cultures strictly identical in 17 cases (11.8%), at least one organism similar in 38 cultures (26.4%) and different in 89 cultures (61.8%)
Overall concordance of 29.1% (swab and biopsy isolated same pathogens). Staphylococcus aureus had the highest concordance (46.5%) but this was not statistically significant.</td><td>reliability in isolating all the pathogens causing osteomyelitis.</td></tr>
<tr><td>2010 Heiba (2010)
NEW
Retrospective cohort.
USA

Review ID 806</td><td>272 consecutive patients with foot ulcer and high clinical suspicion of osteomyelitis referred to nuclear medicine for imaging.

Sept 2006 to Dec 2009</td><td>Mean age 59 +/- 15
Male 69%

35 lost to follow up
24 excluded because no uptake to In-111WBC
213 in final analysis.</td><td>Imaging tests to discriminate soft tissue infection and osteomyelitis
DI SPECT/CT
BS SPECT/CT
WBCS SPECT/CT
DI Planar
DI SPECT

Further analysis in 67 with DI SPECT/CT Step 2.

2 observers jointly reviewed images (consensus).</td><td>Bone and tissue sample (culture or histology) in 97 patients.
Clinical examination and other imaging (CT and MRI) in 116 patients.</td><td>104 patients with final diagnosis of OM or OM/STI (68 confirmed by pathology / microbiology). Pre-test probability 49%.

<table>
<tr><td colspan="2">BS SPECT/CT:</td><td>Ref test</td><td></td><td></td></tr>
<tr><td></td><td></td><td>+</td><td>-</td><td>Total</td></tr>
<tr><td rowspan="3">Index test</td><td>+</td><td>98</td><td>58</td><td>156</td></tr>
<tr><td>-</td><td>6</td><td>51</td><td>57</td></tr>
<tr><td></td><td>Total</td><td>104</td><td>109</td><td>213</td></tr>
</table>
Se 94, Sp 47, AUC 73, PPV 63, NPV 89.

<table>
<tr><td colspan="2">WBCS SPECT/CT</td><td>Ref Test</td><td></td><td></td></tr>
<tr><td></td><td></td><td>+</td><td>-</td><td>Total</td></tr>
<tr><td rowspan="3">Index test</td><td>+</td><td>90</td><td>35</td><td>125</td></tr>
<tr><td>-</td><td>14</td><td>74</td><td>88</td></tr>
<tr><td></td><td>Total</td><td>104</td><td>109</td><td>213</td></tr>
</table>
Se 87, Sp 68, AUC 79, PPV 63 NPV 89.</td><td>Authors conclude that DI SPECT/CT is a highly accurate imaging protocol for the evaluation of the diabetic foot than BS or WBCS alone. When needed, step 2 DI SPECT/CT can yield additional information.</td></tr>
</table>

Study	Participants	Characteristics	Index test	Reference test	Results	Comments
					DI SPECT/CT: / Ref test: + / - / Total Index test + : 99 / 7 / 105 Index test - : 5 / 102 / 108 Total: 104 / 109 / 213 Se 95, SP 94, AUC 95, PPV 93, NPV 95. DI Planar / Ref Test: + / - / Total Index test + : 97 / 37 / 134 Index test - : 7 / 72 / 79 Total: 104 / 109 / 213 Se 93, Sp 66, AUC 80, PPV 71, NPV 91. DI SPECT / Ref test: + / - / Total Index test + : 97 / 25 / 122 Index test - : 7 / 84 / 91 Total: 104 / 109 / 213 Se 93, Sp 77, AUC 87, PPV 80, NPV 92 DI SPECT/CT step1 / Ref test: + / - / Total Index test + : 34 / 13 / 47 Index test - : 2 / 18 / 20 Total: 36 / 31 / 67 Se 94, Sp 58, AUC 88, PPV 72, NPV 90.	

Study	Participants	Characteristics	Index test	Reference test	Results	Comments
					DI SPECT/CT step2 / Ref test: + / - / Total Index test: + 35 2 37; - 1 29 30; Total 36 31 67 Se 97, Sp 94, AUC 95, PPV 95, NPV 97.	
2010 Morales Lozano (2010) **NEW** Cross sectional study. Spain Review ID 834	200 diabetic patients with single foot lesion assessed for infection by clinical signs and soft tissue sample. Those diagnosed with infection given plain film radiography and PTB test for presumptive diagnosis of osteomyelitis. 132 patients with presumptive diagnosis received bone biopsy. Diabetic foot clinic	Mean duration of diabetes 15.6y (+/- 9.5y) Wagner grade III 93.9%, grade II 5.3% and grade IV 0.8% Inclusions: Patients with single ulcer. Patients who had undergone surgery for acute osteomyelitis or unsuccessful local or antibiotic treatment. Exclusions: Patients with critical ischemia or awaiting operation	Tests to diagnose osteomyelitis Clinical signs of infection (two or more signs and symptoms of local inflammation or systemic signs of infection of no other apparent cause, along with purulent exudate. Also specific signs such as necrosis, delayed wound healing, foul odour and bone exposure). Soft tissue culture. Exudate obtained with sterile cotton swab and deep tissue sample by scalpel. Probe to bone test using blunt, sterile metal instrument considered positive if hard substance assumed to be bone was	Histological examination of bone biopsy obtained during conservative surgery. Histological criteria considered diagnostic of osteomyelitis were inflammatory cell infiltrate mostly composed of lymphocyte cells, plasma cells, and neutrophils within spongy and cortical bone; bone necrosis; reactive bone neoformation possibly	105 of 132 patients diagnosed with osteomyelitis by bone biopsy (Pre-test probability 79.5%). Clinical signs and symptoms: / Ref test: + / - / Total Index test: + 71 20 91; - 34 7 41; Total 105 27 132 Se 68, Sp 26, PPV 78, NPV 17 Soft tissue culture: / Ref test: + / - / Total Index test: + 90 22 112; - 15 5 20; Total 105 27 132 Se 86, Sp 19, PPV 80, NPV 25 Radiography: / Ref test: + / - / Total Index: + 94 21 115	2x2 tables +/- figures reverse calculated by reviewer. Authors conclude that PTB was the best test for predicting biopsy results, particularly for neuropathic ulcers. Clinical signs and symptoms, soft tissue culture and plain radiography are of limited use in diagnosis of osteomyelitis because of poor specificity.

Study	Participants	Characteristics	Index test	Reference test	Results	Comments
	May 2006 to Nov 2008.	unrelated to osteomyelitis.	palpated. Plain film radiography considered positive if presence of periosteal elevation, cortical disruption, medullary involvement, osteolysis and sequestra	accompanied by prominent periosteal bone proliferation.	test - 11 6 17 Total 105 27 132 Se 90, Sp 22, PPV 82, NPV 35 PTB: Ref test + - Total Index test + 103 6 109 - 2 21 23 Total 105 27 132 Se 98, Sp 78, PPV 95, NPV 91.	
2010 Nawaz (2010) **NEW** Prospecti ve cohort USA Review ID 988	110 consecutive patients attending a University hospital medical centre. March 2003 to August 2007.	Mean age 59.3y (range 29-85) Male 69% Inclusions: people with diabetic foot disease and/or diabetes with suspected deep-seated infection of the lower extremity. Serum glucose levels less than 200mg/dl	Imaging tests to diagnose osteomyelitis FDG-PET (106 patients). Criteria for positive infection: focally increased FDG uptake with intensity clearly higher than physiological uptake in adjacent structures. PFR (99 patients). Criteria for positive infection were presence of osseous destruction or intra-osseous sinus tract. MRI (94 patients) Criteria for positive infection: focally decreased bone marrow signal intensity	Histological examination and microbiological culture of bone (37) Clinical examination [unknown content] (73).	27 patients confirmed by reference standard with osteomyelitis (pre-test probability 25%). 19 of the 27 patients (70%) diagnosed positive by the reference standard had all 3 tests and 9 had correct diagnosis on all 3 tests. None of these 19 was misdiagnosed by all 3 tests. FDG-PET Ref test + - Total Index test + 21 6 27 - 5 74 79 Total 26 80 106 Se 81, Sp 93, PPV 78, NPV 94, Acc 90. PFR Ref test + - Total Index test + 15 10 25 - 9 65 74 Total 24 75 99	Authors conclude that FDG-PET is a highly specific imaging modality that should be considered for complimenting MRI. Also, when MRI is contraindicated, high sensitivity and specificity justifies FDG-PET after negative or inconclusive PFR.

<table>
<tr><th>Study</th><th>Participants</th><th>Characteristics</th><th>Index test</th><th>Reference test</th><th>Results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td>(SI) on T1-W, focally increased SI of bone or bone marrow on fat-suppressed T2-W, focal enhancement of bone or bone marrow on contrast-enhanced images or presence of osseous destruction on either T1-W or T2-W images.

Test results interpreted nuclear medicine physician and diagnostic radiologists.</td><td></td><td>Se 63, Sp 87, PPV 60 NPV 88 Acc 81.

MRI | | Ref test | |
| | | + | - | Total
Index test | + | 20 | 16 | 36
| | - | 2 | 56 | 58
| | Total | 22 | 72 | 94

Se 91, Sp 78, PPV 56, NPV 97, Acc 81.</td><td></td></tr>
<tr><td>Ertugrul (2009)
Cohort
Turkey</td><td>46 inpatients with diabetic foot ulcer

September 2004 and June 2007</td><td>30 male and 16 female
Age (mean±SD) = 64±9.2 yrs. (range: 46–82 yrs.)
Duration of diabetes = 14±8.38 yrs (1–30 yrs)
ESR level = 65.87±28.08 mm/h</td><td>Erythrocyte sedimentation rate (ERS) levels (60, 65, 70, 75, 80 mm/h)</td><td>One of the following criteria as the diagnosis of osteomyelitis:
1. Histopathology based on the presence of osteonecrosis and infiltration with leukocytes or chronic inflammatory cells such as lymphocytes or plasma cells.
2. Microbiologic based on the presence of bacteria in bone-tissue culture.</td><td>ESR >=60 Se 92, Sp 68
ESR >=65 Se 88, Sp 73
ESR >=70 Se 83, Sp 77
ESR >=75 Se 79, Sp 82
ESR >=80 Se 71, Sp 91</td><td>Note: extracted from CG119</td></tr>
</table>

<table>
<tr><th>Study</th><th>Participants</th><th>Characteristics</th><th>Index test</th><th>Reference test</th><th>Results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td></td><td>3. MRI with conventional spin echo.</td><td></td><td></td></tr>
<tr><td>Rozzanigo (2009)
Cross sectional
Italy</td><td>16 patients with unilateral diabetic foot ulcer.

January 2006 and September 2007
Hospital setting</td><td>11 men and 5 women
Mean age (range) = 58 years (42–78)

The infected ulcer had been medicated, drained and treated with systemic antibiotics for at least 2 weeks, with little response</td><td>MRI
A primary sign of osteomyelitis on MRI is evidence of low-signal-intensity areas in the bone marrow on T1-weighted SE images, with higher signal intensity on STIR images and enhancement after contrast administration.
Secondary signs are identified close to the altered bone marrow signal and include oedema caused by septic inflammation (cellulitis or phlegmon), soft-tissue abscess, skin ulcer and fistula, with possible interruption of the cortical bone</td><td>Clinical and laboratory data by means of bacteriological and/or histological tests.</td><td>Osteomyelitis confirmed by reference test in 13 of 16 patients. Pre-test probability 81%.<table><tr><td colspan="2" rowspan="2">MRI</td><td colspan="2">Ref test</td><td></td></tr><tr><td>+</td><td>-</td><td>Total</td></tr><tr><td rowspan="3">Index test</td><td>+</td><td>13</td><td>1</td><td>14</td></tr><tr><td>-</td><td>0</td><td>2</td><td>2</td></tr><tr><td></td><td>Total</td><td>13</td><td>3</td><td></td></tr></table>Se 100, Sp 67, PPV 93, NPV 100</td><td>Note: extracted from CG119</td></tr>
<tr><td>Malabu (2007)
Cross sectional
Saudi Arabia</td><td>43 people with diabetic foot ulcer and osteomyelitis in a hospital setting.

Jan to Dec 2005</td><td>With osteomyelitis (22): 11 male and 11 female
Mean age (SD) = 56.3 (12.2)
Mean duration of diabetes (years, SD) = 19.9 (6.5)
With cellulitis (21):</td><td>ESR
Haematocrit
Haemoglobin
Platelet count
Red cell distribution width
White cell count</td><td>Pathological and histological determination, surgical observation and clinical resolution in diagnosing osteomyelitis

The diagnosis of cellulitis was</td><td>22 patients with osteomyelitis confirmed by reference test (pre-test probability 51%
ESR >70 Se 90%, Sp 94%
Hematocrit >36% Se 95%, Sp 84%
Hemoglobin < 12 g/dl Se 81%, Sp 90%
Platelet count > 400 x 109/L Se45% Sp 95%
RDW >14.5 Se 67%, Sp 63%
White cell count >400x109/L Se 52%, Sp 80%</td><td>Note: extracted from CG119</td></tr>
</table>

<table>
<tr><th>Study</th><th>Participants</th><th>Characteristics</th><th>Index test</th><th>Reference test</th><th>Results</th><th>Comments</th></tr>
<tr><td></td><td></td><td>12 male 9 female
Mean age (SD) = 56.3 (12.6)
Mean duration of diabetes (years, SD) = 15.3 (8.0)</td><td></td><td>confirmed by correlating clinical signs of infection with positive wound cultures</td><td></td><td></td></tr>
<tr><td>Al-Khawari (2007)
Cross sectional
Kuwait</td><td>29 people with suspected diabetic foot infection in a hospital setting
August 2000 to July 2002</td><td>17 male and 12 female
Mean age (range) = 61 (41–81)</td><td>MRI
Osteomyelitis was diagnosed when focally increased bone marrow signal on FST2WI and focally decreased marrow signal on T1WI with or without cortical destruction, and focal marrow enhancement on postcontrast T1WI was observed. Normal marrow signal on T1WI with high signal on FST2WI and marrow enhancement post contrast were also considered as osteomyelitis</td><td>Culture growth or characteristic histological findings including aggregates of inflammatory cells (neutrophils, lymphocytes, histocytes and plasma cells), erosion of trabecular bone, and bone marrow changes that ranged from loss of normal marrow fat with acute osteomyelitis to fibrosis and reactive bone formation with chronic disease</td><td>Osteomyelitis confirmed by reference standard in 11 people. Pre-test probability 38%.
<table><tr><td colspan="2" rowspan="2">MRI</td><td colspan="2">Ref test</td><td></td></tr><tr><td>+</td><td>-</td><td>Total</td></tr><tr><td rowspan="3">Index test</td><td>+</td><td>11</td><td>3</td><td>14</td></tr><tr><td>-</td><td>0</td><td>5</td><td>5</td></tr><tr><td>Total</td><td>11</td><td>8</td><td></td></tr></table>Se 100, Sp 63, PPV 79, NPV 100</td><td>Note: extracted from CG119</td></tr>
</table>

Study	Participants	Characteristics	Index test	Reference test	Results	Comments
Lavery (2007) **NEW** Prospective cohort USA Review ID 2088	247 patients with a single diabetic foot wound. Primary care diabetes management programme. No dates given	Data presented split by presence of osteomyelitis on bone biopsy. People with osteomyelitis: Male 59% Age >70y 51% Mean duration of diabetes 17y People without osteomyelitis: Male 52% Age >70y 53% Mean duration of diabetes 13y Excluded wounds characterised as blisters, minor lacerations or abrasions.	Probe to bone test for osteomyelitis. Performed by one of two podiatrists using sterile probe. Positive result defined as palpating hard or gritty substance presumed to be bone or joint space.	Bone biopsy culture for people with clinical and radiographic signs suggestive of bone infection. Positive culture defined as growth of any organism.	150 of 247 had infected foot wounds (by clinical signs) 30 patients had osteomyelitis on bone biopsy (pre-test probability 12%). In all 247 wounds^: Index test: + : 26 / 20 / 46 Index test: - : 4 / 197 / 201 Total: 30 / 217 / 247 Se 0.87, Sp 0.91, PPV 0.57, NPV 0.98 In 150 infected wounds†: Index test: + : 26 / 20 / 46 Index test: - : 4 / 100 / 104 Total: 30 / 120 / 150 Se 0.87, Sp 0.83, PPV 0.57, NPV 0.96	Authors conclude that probe to bone testing amongst this population (community setting) had a relatively low positive predictive value, but a negative test may exclude diagnosis. ^ As presented in paper. † As calculated by reviewer.
Ertugrul (2006) Cross sectional Turkey	31 Patients with >grade 3 diabetic foot lesion attending a hospital setting. No dates	23 male and 8 female Age (mean ± sd) = 62±8.8 years (range 40-77 years) Duration of diabetes =	MRI 99mTc-MDP-labelled leukocyte scan MRI - High signal intensity on TIRM, low signal intensity on T1	Histopathological findings in diagnosing osteomyelitis based on the presence of osteonecrosis and infiltration	Osteomyelitis confirmed by reference test in 26 patients. Pre-test probability 84% MRI / Ref test: + / - / Total Index test: + : 18 / 2 / 20 Index test: - : 5 / 3 / 8	Note: extracted from CG119

Study	Participants	Characteristics	Index test	Reference test	Results	Comments
	specified	16.8±8.9 years (range 1-35 years); Duration of foot infection = 3.6±3.1 months (range 0.5-12 months)	sequence and contrast enhancement as the definition of osteomyelitis Combined 4P-MDP and Tc99m WBC scans were considered positive for osteomyelitis when there was an abnormal accumulation of leucocytes in a zone concordant with the area of up-take on bone scintigraphy	with leucocytes or chronic inflammatory cells such as lymphocytes or plasma cells	Total 23 5 Se 78, Sp 60, PPV 90, NPV 38 99Tc-MDP / Ref test: + / - / Total Index test + 21 1 22 Index test - 2 2 4 Total 23 3 Se 91, SP 67, PPV 95, NPV 50	
Shone (2006) Cross sectional	104 foot ulcers seen in an outpatient clinic No dates specified	No details provided.	Probe to bone	Clinical signs of osteomyelitis, supported by MRI and microbiological analysis of deep tissue samples	Osteomyelitis confirmed by reference standard in 21 of 104 ulcers. Pre-test probability 20% PTB / Ref test: + / - / Total Index test + 8 7 15 Index test - 13 76 89 Total 21 83 Se 38, Sp 91, PPV 53, NPV 85	Note: extracted from CG119
Slater (2004) Cohort	56 people with 60 infected diabetic foot wounds attending a diabetic foot clinic. January to September 2000	People: 56 Sex(M/F): 36/20 Age (years): 62.4 ± 11.7 (Range- 35-85) Disease duration: 12.8 ± 9 years (range-1-42) Duration of the wound:	Swab culture Two cultures were taken from every wound. The first swab was held in contact with the wound for at least 5 s before any debridement was done. At the end of debridement, a deep tissue sample (second) was taken at the junction	Deep tissue biopsy	Swab and biopsy identical 62% Extra isolates on swab 20% Isolates missed on swab 18% Identical or extra isolates on swab 82%	Note: extracted from CG119

<table>
<tr><th>Study</th><th>Participants</th><th>Characteristics</th><th>Index test</th><th>Reference test</th><th>Results</th><th>Comments</th></tr>
<tr><td></td><td></td><td>30d or less: 30
30d+: 30
27 received antibiotic treatment at time of specimen collection

Wounds with gangrene, those with a dry, unbroken eschar and those in which surgical debridement was contraindicated (e.g. simple cellulitis, severe ischaemia, etc.) were excluded.</td><td>of non-viable and viable tissue by using a new set of sterile instruments</td><td></td><td></td><td></td></tr>
<tr><td>Rubello (2004)
Cross sectional</td><td>78 people with diabetic foot ulcer. No setting specified

Sept. 1999 to Jun. 2002</td><td>None mentioned</td><td>LeukoScan (4 h and 18–24h)</td><td>Microbiological findings or other laboratory and imaging techniques in detecting bone infection</td><td>Osteomyelitis confirmed by reference test in 62 of 78 people. Pre-test probability 79%.
<table>
<tr><td colspan="2" rowspan="2">4h</td><td colspan="2">Ref test</td><td></td></tr>
<tr><td>+</td><td>-</td><td>Total</td></tr>
<tr><td rowspan="3">Index test</td><td>+</td><td>57</td><td>4</td><td>61</td></tr>
<tr><td>-</td><td>5</td><td>12</td><td>17</td></tr>
<tr><td>Total</td><td>62</td><td>16</td><td></td></tr>
<tr><td colspan="5">Se 100, Sp 75, PPV 93, NPV 71</td></tr>
<tr><td colspan="2" rowspan="2">24h</td><td colspan="2">Ref test</td><td></td></tr>
<tr><td>+</td><td>-</td><td>Total</td></tr>
<tr><td>Index</td><td>+</td><td>57</td><td>2</td><td>59</td></tr>
</table></td><td>Note: extracted from CG119</td></tr>
</table>

Study	Participants	Characteristics	Index test	Reference test	Results					Comments
					test	-	5	14	16	
						Total	62	16		
					Se 100, Sp 88, PPV 97, NPV 74					
Palestro (2003) Cross sectional USA	25 people with diabetic foot ulcer in a hospital setting	17 men and 8 women 22 patients, the ulcer was in the forefoot, and in 3 it was in the mid-foot Diabetic patients older than 18 years of age with a peripheral leukocyte count of at least 2,500/mm3, who were suspected of having osteomyelitis underlying a pedal ulcer based on the presence of one or more of the following: localized pain, fever greater than 100°F for at least 3 days, elevated peripheral leukocyte count, elevated erythrocyte sedimentation	Leukocyte 24h 99mTc-labelled monoclonal antibody. Images were interpreted as positive for osteomyelitis when focal activity, felt to be bony, was increased relative to adjacent activity. In-WBC Images were classified as positive for osteomyelitis when focally increased activity, equally well seen on the dorsal and plantar views, was present 3-phase (99mTc-MDP-labelled bone scintigraphy). Focal hyperperfusion, focal hyperemia, and focally increased bony uptake on delayed images was interpreted as positive for osteomyelitis	Bone biopsy examination and culture (20) and clinical judgement (5)	Osteomyelitis confirmed by reference test in 10 of 25 patients. Pre-test probability 40%.					Note: extracted from CG119
					MOAB		Ref test			
							+	-	Total	
					Index test	+	9	5	14	
						-	1	10	11	
						Total	10	15		
					Se 90, Sp 67, PPV 64, NPV 91					
					In-WBC		Ref test			
							+	-	Total	
					Index test	+	8	5	13	
						-	2	10	12	
						Total	10	15		
					Se 80, Sp 67, PPV 62, NPV 83					
					99mTc-MDP		Ref test			
							+	-	Total	
					Index test	+	9	11	20	
						-	1	4	5	
						Total	10	15		

Study	Participants	Characteristics	Index test	Reference test	Results	Comments
		rate, radiographic findings suggestive of osteomyelitis, or positive blood or wound cultures. Patients with granulating surgical incisions or who had received 7 or more days of antibiotic therapy at the time of enrollment were excluded			Se 90, Sp 27, PPV 45, NPV 80 MOAB + 99mTc-MDP / Ref test: + / - / Total Index test +: 9 / 5 / 14 Index test -: 1 / 10 / 11 Total: 10 / 15 Se 90, Sp 67, PPV 64, NPV 91 In-WBC +99mTc-MDP / Ref test: + / - / Total Index test +: 8 / 3 / 11 Index test -: 2 / 12 / 14 Total: 10 / 15 Se 80, Sp 75, PPV 73, NPV 86	
Poirier (2002) Cross sectional France	75 people (101 feet) with diabetic foot ulcer and suspected osteomyelitis in a hospital setting. 83 feet in final analysis. November 1993 to March 2001	46 males, 29 females Median age = 61.3 years (range: 40-86) Median duration of diabetes = 12 years (range 5-35) HbAlc = 8.7% (range 6.9-12)	99mTc-MDP bone scintigraphy 99mTc-HMPAO-labelled leukocyte scan Each imaging study was independently evaluated by one experienced radiologist and one nuclear medicine physician who knew the site of interest but did not have any additional information	Osteomyelitis was diagnosed by radiological examination at inclusion or during follow-up: a needle bone biopsy for bacteriological and histological studies was performed only if accurate cultures could be obtained	Osteomyelitis confirmed by reference test in 41 of 101 feet. Pre-test probability 41%. 99mTc-MDP / Ref test: + / - / Total Index test +: 41 / 30 / 71 Index test -: 0 / 12 / 12 Total: 41 / 42 Se 100, Sp 28, PPV 58, NPV 100 99mTc-HMPAO / Ref test: + / - / Total Index +: 38 / 1 / 39	Note: extracted from CG119

Study	Participants	Characteristics	Index test	Reference test	Results					Comments
			The HMPAO-Leu/MDP scan was considered to be positive for osteomyelitis when there was an accumulation of leucocytes concordant in all the incidences with an abnormal uptake on bone scintigraphy	through uninvolved tissue and when the radiograph at inclusion was negative or doubtful contrasting with a positive bone scintigraphy. Histopathologic criteria for osteomyelitis include necrotic bone with inflammatory excudate adjacent to an extensive resorption	test	-	3	41	44	
						Total	41	42		
					Se 93, Sp 98, PPV97, NPV 93					
Kaleta (2001) Cross sectional USA	29 people with diabetic foot ulcer in a medical centre setting. Dec. 1998 to Dec. 1999	Number of with osteomyelitis-19 Male- 11 Female- 9 Age ± SD- 58.8 ± 11.0	ESR	Histological examination (pathological reports)	ESR >=60 Se 90, Sp 90 ESR >=65 Se 90, Sp 90 ESR >=70 Se 90, Sp 90 ESR >=75 Se 84, Sp 100 ESR >=80 Se 79, Sp 100					Authors conclude an erythrocyte sedimentation rate value equal to or greater than 70 mm/h was the optimal cut off, with the highest sensitivity (89.5%) and highest specificity (100%) for the presence of osteomyelitis. It also had the highest predictive value of 100% and negative predictive value of 83%.

Study	Participants	Characteristics	Index test	Reference test	Results	Comments
Harwood (1999) Cross sectional USA	150 patients with suspected infected diabetic foot ulcer in an outpatient hospital setting. 122 in final analysis (28 had unreadable images) No dates specified	123 men and 27 women Mean age = 58 years. (all ≥21 years) Diabetic patients, presence of a foot ulcer with characteristics suggestive of osteomyelitis, non-pregnant, able to return for follow-up visits, no known allergies to mouse proteins, no history of renal insufficiency, and not currently taking any investigational therapy were included	99m-Tc HMPAO In-WBC 99m-Tc MDP	Histology and/or microbiological cultures in detecting osteomyelitis	Osteomyelitis confirmed by reference test in 81 of 150 patients. Pre-test probability 54%. 99m-Tc HMPAO / Ref test: + / - / Total Index test: + 74 18 92; - 7 23 30; Total 81 41 Se 91, Sp 56, PPV 80, NPV 77 In-WBC / Ref test: + / - / Total Index test: + 59 12 71; - 16 24 40; Total 75 36 Se 79, Sp 67, PPV 83, NPV 60 99mTc-MDP / Ref test: + / - / Total Index test: + 31 11 42; - 2 3 5; Total 33 14 Se 94, Sp 21, PPV 74, NPV 60	Note: extracted from CG119
Remedios (1998) Cross sectional UK	9 people with diabetic foot ulcer in a hospital setting No dates specified	4 men and 5 women Mean age = 57 years Pedal ulcers were all on the plantar aspect, mostly related to the metatarsal	99m-Tc nanocolloid. Studies were considered to be positive for osteomyelitis if static images showed significantly more focal activity than corresponding blood pool images. Images were	Biopsy cores and surgical excision specimens were examined histologically and microbiologically. A positive	Osteomyelitis confirmed by reference standard in 4 of 9 patients. Pre-test probability 44%. 99mTc-NC / Ref test: + / - / Total Index test: + 4 2 6; - 0 3 3; Total 4 5	Note: extracted from CG119

Study	Participants	Characteristics	Index test	Reference test	Results	Comments
		heads and os-calcis	interpreted by two radiologists with a consensus opinion. MRI. Studies were considered to be positive for osteomyelitis if there was evidence of reduced marrow signal on T1 images and increased marrow signal on STIR or T2 images, particularly associated with adjacent deep ulceration. Images were interpreted by two radiologists with a consensus opinion.	diagnosis for osteomyelitis was taken as either microbiological and/or histological evidence of bone infection.	Se 100, Sp 60, PPV 67, NPV 100 MRI / Ref test: + / - / Total Index test +: 4 / 1 / 5 Index test -: 0 / 4 / 4 Total: 4 / 5 Se 100, Sp 80, PPV 80, NPV 100	
Harvey (1997) Cross sectional USA	52 patients with non-healing ulcer and suspected infection attending a veterans medical centre No dates specified	Not mentioned	99mTc-HMPAO-labelled leukocyte scintigraphy (52) 99mTc-MDP-labelled bone scintigraphy (31)	Histology, bone cultures and radiographic results	21/52 who had HMPAO were positive of reference standard 11/31 who had MDP were positive on reference standard HMPAO / Ref test: + / - / Total Index test +: 18 / 3 / 21 Index test -: 3 / 28 / 31 Total: 21 / 31 Se 86, Sp 90, PPV 86, NPV 90 MDP / Ref test: + / - Index test +: 10 / 12 / 22 Index test -: 1 / 8 / 9 Total: 11 / 20	Note: extracted from CG119

Study	Participants	Characteristics	Index test	Reference test	Results	Comments
					Se 91, Sp 40, PPV 45, NPV 89	
Croll (1996) Cross sectional Canada	27 Inpatients with diabetic foot infections. Hospital setting. November 1991 and December 1992	19 men and 8 women Mean age (range) = 66 years (34 to 82 years) Mean duration of diabetes = 20 years.	MRI 99mTc-MDP bone scan In-WBC Plain radiographs Interpretation of the studies was done by staff radiologists and nuclear medicine specialists and was reviewed by the clinicians. The physicians were not specifically blinded to the results of the other diagnostic studies, but none was aware of the pathologic end point of the presence or absence of osteomyelitis before submitting their reports.	Pathological specimen, or bone culture in diagnosing osteomyelitis based on: Histological findings of subpcriosteal new bone formation, lytic areas of bone loss, the presence of fibrosis, and infiltration of polymorphonuclear leukocytes and lymphocytes.	MRI / Ref test / + / - / Total Index test + / 8 / 0 / 8 Index test - / 1 / 18 / 19 Total / 9 / 18 Se 89, Sp 100, PPV 100, NPV 95 99mTc-MDP / Ref test / + / - / Total Index test + / 4 / 7 / 11 Index test - / 4 / 7 / 11 Total / 8 / 14 Se 50, Sp 5, PPV 36, NPV 63 In-WBC / Ref test / + / - / Total Index test + / 2 / 4 / 6 Index test - / 4 / 9 / 13 Total / 6 / 13 Se 33, SP 69, PPV 33, NPV 69 PFR / Ref test / + / - / Total Index test + / 2 / 1 / 3 Index test - / 7 / 17 / 24 Total / 9 / 18 Se 22, Sp 94, PPV 67, NPV 71	Note: extracted from CG119

Study	Participants	Characteristics	Index test	Reference test	Results	Comments
Grayson (1995) Cohort	76 diabetic foot ulcer with clinical suspicion of infection attending hospital. 2 year from Dec. 1988	Average age- 60± 12 years Male- 52 Female-23 Duration of diabetes- 19 ± 10 years. Patients without pedal ulceration, with nonhealed recent surgical wounds, or with pedal infection that had been debrided in a manner likely to expose the adjacent bone were excluded	Probe to bone testing Bone was considered palpable (positive probe test) when, on gentle probing, the evaluator detected a rock-hard, often gritty structure at the ulcer base without the apparent presence of any intervening soft tissue	Histology	Osteomyelitis confirmed by reference test in 50 of 76 ulcers. Pre-test probability 66%. PTB / Ref test: + / - / Total Index test +: 33 / 4 / 37 Index test -: 17 / 22 / 39 Total: 50 / 26 Se 66, Sp 85, PPV 85, NPV 56	Note: extracted from CG119
Morrison (1995) Cross sectional USA	59 people (62 feet) with suspected osteomyelitis in a hospital setting. 27 diabetic 35 non-diabetic Hospital setting No dates specified	39 male and 20 female Mean age (range) = 51 years (2-85).	MRI Diagnosis based on: Decreased signal intensity of marrow on T1-weighted images and increased signal intensity on T2-weighted images, with marrow enhancement after injection of gadopentetate dimeglumine. Also evaluated cortical interruption, rim-enhancing abscess within the marrow cavity, sequestrum formation,	Histologic analysis of biopsy specimens OR clinical and radiographic demonstration of progression despite conservative antibiotic therapy	Osteomyelitis confirmed by reference test in 17 of 62 feet. Pre-test probability 27%. MRI / Ref test: + / - / Total Index test +: 14 / 2 / 16 Index test -: 3 / 8 / 11 Total: 17 / 10 Se 82, Sp 94, PPV 88, NPV 73	Note: extracted from CG119 Differences in these values between study and control group were not statistically significant (sensitivity = p > 0.30; specificity = p > 0.20).

<table>
<tr><th>Study</th><th>Participants</th><th>Characteristics</th><th>Index test</th><th>Reference test</th><th>Results</th><th>Comments</th></tr>
<tr><td></td><td></td><td></td><td>extension of a sinus tract from the bone to the skin surface.

MR images were evaluated prospectively by 2 interpreters who had access to information on age, sex, and the clinical question of osteomyelitis in a particular region of the foot or ankle.</td><td></td><td></td><td></td></tr>
<tr><td>Newman (1992)
Cross sectional
USA</td><td>12 patients attending a medical centre with 16 diabetic foot ulcers

Sept. 1989 to Jun 1990</td><td>Duration- 52 weeks (range = 1-364)
Size- 0.5cm2 (range = 0.25 to 0.35)

Excluding myocardial infarction in the previous 6 months, severe peripheral vascular disease (ankle-brachial index <50%), ongoing antibiotic treatment for >7 previous days, or patient declining to participate</td><td>MRI
Leukocyte scanning (In-WBC)

Leukocyte imaging was classified as positive for osteomyelitis when focally increased activity was present on both dorsal and plantar images at 24h.

MRI was considered positive for osteomyelitis if signal intensity decreased on T1WI and increased on T2WI in the bone in the area of the foot ulcer.</td><td>Bone biopsy and culture in diagnosing osteomyelitis

Pathological diagnosis required the presence of all 3 criteria including: osteonecrosis (the absence of osteocytes in their lacunae in the presence of nuclear staining for other cells in the section), marrow fibrosis, and inflammatory cells</td><td>Osteomyelitis confirmed by reference test in 7 of 12 patients. Pre-test probability 58%.
<table>
<tr><td colspan="2" rowspan="2">In-WBC</td><td colspan="2">Ref test</td><td></td></tr>
<tr><td>+</td><td>-</td><td>Total</td></tr>
<tr><td rowspan="3">Index test</td><td>+</td><td>7</td><td>3</td><td>10</td></tr>
<tr><td>-</td><td>0</td><td>6</td><td>6</td></tr>
<tr><td>Total</td><td>7</td><td>9</td><td></td></tr>
<tr><td colspan="5">Se 100, Sp 67, PPV 70, NPV 100</td></tr>
<tr><td colspan="2" rowspan="2">MRI</td><td colspan="2">Ref Test</td><td></td></tr>
<tr><td>+</td><td>-</td><td>Total</td></tr>
<tr><td rowspan="3">Index test</td><td>+</td><td>2</td><td>2</td><td>4</td></tr>
<tr><td>-</td><td>5</td><td>7</td><td>12</td></tr>
<tr><td>Total</td><td>7</td><td>9</td><td></td></tr>
<tr><td colspan="5">Se 29, Sp 78, PPV 50, NPV58</td></tr>
</table></td><td>Note: extracted from CG119</td></tr>
</table>

Study	Participants	Characteristics	Index test	Reference test	Results	Comments
Newman (1991) Cross sectional USA	35 inpatients and outpatients at a medical centre. Dec. 1988 to April 1990	Mean age- 55 years (± 11 years-SD) Mean duration of diabetes- 21.5 years (range- 5 to 30 years) in those with osteomyelitis 12 years (range- 5 to 20 years) in those without osteomyelitis. 61% had prior amputations Median ulcer duration- 4 months (range- 3 days to 7 years) 19 exclusions because of antibiotic treatment, MI, inadequate biopsy, peripheral vascular disease, patient choice and lack of approval.	ESR Plain film radiograph Bone scan Leukocyte 4h Leukocyte 24h	Bone biopsy and culture	Osteomyelitis confirmed by reference test in 28 of 35 ulcers. Pre-test probability 80%. ESR >70 Ref test: + / - / Total Index test +: 5 / 0 / 5 Index test -: 13 / 10 / 23 Total: 18 / 10 Se 28, Sp,100, PPV 100, NPV 43 ESR >100 Ref test: + / - / Total Index test +: 6 / 0 / 6 Index test -: 20 / 13 / 33 Total: 26 / 13 Se 23, Sp 100, PPV 100, NPV 39 PFR Ref test: + / - / Total Index test +: 7 / 1 / 8 Index test -: 18 / 11 / 29 Total: 25 / 12 / 37 Se 28, Sp 92, PPV 88, NPV 38 Bone scan Ref test: + / - / Total Index test +: 18 / 7 / 25 Index test -: 8 / 5 / 13 Total: 26 / 13 Se 69, Sp 39, PPV 72, NPV 38 Leukocyte 4h Ref test: + / - / Total	Note: extracted from CG119

Study	Participants	Characteristics	Index test	Reference test	Results	Comments
					Index test: + 17 3 20 - 5 10 15 Total 22 13 Se 77, Sp 77, PPV 85, NPV 67 Leukocyte 24h: Ref test + - Total Index test: + 23 4 27 - 3 9 12 Total 26 13 Se 89, Sp 69, PPV 85, NPV 75	
Wang (1990) Cross sectional USA	50 people with suspected osteomyelitis in a medical centre setting (62 specimens) No dates specified	Male-35 Female-15 Age range- 23 to 81 years (mean- 49 years) 31 -Insulin Dependent 19 -oral agents and diet Onset of symptoms: <6 weeks- 20 >6 weeks- 30	MRI Plain radiographs For MRI, criteria for osteomyelitis included hypo- to isointensity in T1WI sequence and hyperintensity and homogeneous signals with either partial or entire involvement of the bone in STIR.	Histological examination in detecting osteomyelitis. Pathologic criteria for os-teomyelitis included proliferation of inflammatory cells (such as lymphocytes, plasma cells, macrophages), fibrosis, bone necrosis, and new bone formation	Osteomyelitis confirmed by reference test in 46 of 62 samples. Pre-test probability 74%. MRI: Ref test + - Total Index test: + 45 3 48 - 1 13 14 Total 46 16 Se 98, Sp 81, PPV 94, NPV 93 PFR: Ref test + - Total Index test: + 24 5 29 - 22 11 33 Total 46 16 Se 52, Sp 69, PPV 83, NPV 33	Note: extracted from CG119
Weinstein (1993)	47 patients (62 samples) with suspected	Male- 32 Female- 15	MRI (62) Plain radiographs (62)	Histological examination	Osteomyelitis confirmed by reference test in 46 of 62 samples. Pre-test probability 74%.	Note: extracted from CG119

Study	Participants	Characteristics	Index test	Reference test	Results	Comments
Cross sectional USA	osteomyelitis, nonhealing foot ulcer, or soft tissue infection of the foot attending a medical centre No dates specified	Mean age- 49 years (range- 23 to 81)	99mTc/Ga scan (22)		MRI / Ref test: + / - / Total Index test +: 46 / 3 / 49 Index test -: 0 / 13 / 13 Total: 46 / 16 Se 100, Sp 81, PPV 94, NPV 100 PFR / Ref test: + / - / Total Index test +: 24 / 3 / 27 Index test -: 22 / 13 / 35 Total: 46 / 13 Se 69, SP 83, PPV 89, NPV 37 Tc/GA scan / Ref test: + / - / Total Index test +: 11 / 1 / 12 Index test -: 5 / 5 / 10 Total: 16 / 6 Se 52, Sp 81, PPV 92, NPV 50	
Yuh (1989) Cross sectional	24 patients with clinical suspicion of osteomyelitis and/or non-healing foot ulcers No dates specified	Age range- 32-74 years (mean- 58.2 years)	Plain film radiography MRI 99mTc-MDP scintigraphy All bone scans and plain films were obtained within 48 hours of the MRI examinations	Pathological tests 29 bone specimens from 14 patients were obtained by either biopsy (6) or amputation (8). 15 bones (10 patients) had resolution of foot ulcers or	25 of 29 samples had osteomyelitis confirmed on reference test. Pre-test probability 86%. PFR / Ref test: + / - / Total Index test +: 18 / 1 / 19 Index test -: 6 / 3 / 9 Total: 24 / 4 Se 75, Sp 75, PPV 95, NPV 33 MRI / Ref test: + / - / Total	Note: extracted from CG119 When cases of non-osteomyelitis were included , there were increased false-positives in all three techniques, presumably caused by acute or recent trauma, soft-tissue

Study	Participants	Characteristics	Index test	Reference test	Results	Comments
				cellulitis with only local wound care and/or a short course of oral antibiotics. These were considered clinically not to have Osteomyelitis (nonosteomyelitis) because there was no pathologic proof of bone infection.	Index test: + / 25 / 0 / 25 Index test: - / 0 / 4 / 4 Index test: Total / 25 / 4 Se 100, Sp 100, PPV 100, NPV 100 99mTc-MDP: Ref test: + / - / Total Index test: + / 17 / 3 / 20 Index test: - / 1 / 0 / 1 Index test: Total / 18 / 3 Se 94, Sp 0, PPV 85, NPV 0	infection, and/or vascular insufficiency./or plain radio
Michail (2013) **NEW** Cross sectional	61 consecutive patients with diabetic foot infection. Diagnostic accuracy for osteomyelitis. A total of 34 patients had soft-tissue infection and 27 had osteomyelitis No dates specified	Age, years (mean) 63.1 ± 7.1 Male=45 Female=16 Type 1 diabetes= 7 Type 2 diabetes= 54	White blood cell count (WCC) Erythrocyte sedimentation rate (ESR) C-reactive protein (CRP) Procalcitonin (PCT)	The diagnosis of osteomyelitis was based on clinical examination (positive probe-to-bone test) and was confirmed by plain X-rays, nuclear scintigraphy, or MRI.	White cell count >14x10^9/L Sensitivity: 74 (57 to 91) Specificity: 82 (69 to 95) PPV: 65 (47 to 83) NPV: 81 (68 to 94) ESR >67 mm/h Sensitivity: 84 (70 to 98) Specificity: 75 (60 to 90) PPV: 73 (57 to 89) NPV: 86 (74 to 98) CRP >14 mg/L Sensitivity: 85 (72 to 98) Specificity: 83 (70 to 96) PPV: 71 (54 to 88) NPV: 77 (62 to 92) Procalcitonin >0.30 ng/mL	The authors found that the values of ESR remained high until month 3 only in patients with bone infection. Values as presented were the optimal values for distinguishing an osteomyelitis from a soft tissue infection both for sensitivity and specificity.

Study	Participants	Characteristics	Index test	Reference test	Results	Comments
					Sensitivity: 81 (66 to 96) Specificity: 71 (56 to 86) PPV: 65 (48 to 82) NPV: 81 (67 to 95)	

F.8 Review question 8 full evidence tables

Table 46: Warriner 2012

<table>
<tr><td>Reference</td><td>Warriner,R.A.,III; Wilcox,J.R.; Carter,M.J.; Stewart,D.G. (2012) More frequent visits to wound care clinics result in faster times to close diabetic foot and venous leg ulcers, Advances in Skin & Wound Care, 25 (11) 494-501</td></tr>
<tr><td>Study type & aim</td><td>A retrospective cohort study to determine whether the time to closure of ulcers of patients with Wagner grades 1 and 2 diabetic foot ulcers (DFUs) or venous leg ulcers (VLUs) differed depending on frequency of visit to wound care centres.</td></tr>
<tr><td>Number of participants & patient characteristics</td><td>Total number of participants:
Data from 206 patients was collected from 9 wound care centres
Inclusion criteria:
Eligibility criteria were closure of DFU. All DFUs had to be Wagner grade 1 or 2 or VLUs. Analysis looked at DFUs and VLUs separately (for the purpose of this review only the data on DFUs was looked at).
Each patient had to be seen every other week (more than 10 days) between visits or seen weekly (at least once a week) between visits for the first 4 weeks. After 4 weeks visit frequency restrictions were relaxed
Exclusion criteria:
Surgically closed wounds and amputations were excluded, also excluded was data with no visible entries for each DFU or VLU.
Patient characteristics:
Patient baseline characteristics are shown below. Mean age was significantly higher in the weekly group compared to the every other week whereas visit number was significantly higher for the every other week group.
<table>
<tr><td></td><td></td><td>Weekly visit group</td><td></td><td>Every other week visit group</td></tr>
</table>
</td></tr>
</table>

Reference	Warriner,R.A.,III; Wilcox,J.R.; Carter,M.J.; Stewart,D.G. (2012) More frequent visits to wound care clinics result in faster times to close diabetic foot and venous leg ulcers, Advances in Skin & Wound Care, 25 (11) 494-501

Characteristic	n (Available data)	n (%)	Mean	Median	SD	n (%)	Mean	Median	SD	P
Visit no	105/101			5				7		.00003
Patient age y	105/97		71.6	11.15			64.5		12.64	.00003
Age of DFU before treatment	83/101		13					13		.039
DFU area cm^2	105/101		1.20		2.75		3.72		17.68	.159
DFU area geometric mean cm^2	105/101						0.876			.00006
DFU volume area cm^3	105/101		0.280		1.16		0.760		3.56	.199
Exicisoral debridement count	47/51			2				4		.00003
Proportional time to 1st debridement	47/51			0.25				0.17		.011
Wagner Grade 1 **Wagner Grade 2**	105/101	70 (66.7) 35 (33.3)				55 (54.4) 46 (45.6)				.073
Prior DFU **Yes** **No**		 74 (70.5) 31 (29.5)				 76 (75.2) 25 (24.8)				.442
Physician speciality **Podiatrist** **Surgeon** **Family practitioner** **Other**	105/97	 36 (34.3) 14 (13.3) 27 (25.7) 28 (26.7)				 30 (31) 26 (27) 20 (20) 21 (22)				.118
Comorbidity **CVD** **COPD** **Hypertension**	76/23	 26 (34) 4 (5) 50 (66)	3.8		3.01	 11 (48) 2 (9) 2 (9)	3.1		2.26	.270 .237 .621 .000001

Reference	**Warriner,R.A.,III; Wilcox,J.R.; Carter,M.J.; Stewart,D.G. (2012) More frequent visits to wound care clinics result in faster times to close diabetic foot and venous leg ulcers, Advances in Skin & Wound Care, 25 (11) 494-501**

Obesity		26 (36)				6 (26)				.465
PVD		27 (36)				0 (0)				.0003
PAD		19 (25)				12 (52)				.02
RF		6 (8)				0 (0)				.195
Paraplegia		4 (5)				0 (0)				.341
Cancer		2 (3)				0 (0)				.588

Abbreviations: CVD= cardiovascular disease; COPD= chronic obstructive pulmonary disease; PVD-peripheral vascular disease; PAD= peripheral arterial disease; RF= renal failure

Monitoring information & definitions	**Monitoring:** Data at the point of care was collected from a clinical management database that collected data on clinical status, utilisation, surveillance and financial monitoring. Foot ulcers were treated by offloading and standard wound care. Offloading meant the wound received total contact casting or an offloading device or graft (if required) **Outcome measures:** The primary outcome measures were wound healing, (median time to close). Kaplan Meier graphs were used to plot time to closure. Hazard ratios were used to link DFU closure to area or depth, and number of visits
Intervention	In the first 4 weeks of treatment one group t were seen by a foot specialist once every week defined as at least one visit a week
Comparator:	In the first 4 weeks of treatment. One group were seen by a foot specialist once every other week defined as at least one visit every 10 days
Length of follow-up	Follow up unspecified (only first 4 weeks of treatment were restricted to visit frequency requirements)
Outcome measures & effect sizes	**Wound healing:** After 4 weeks 63.87% of the DFUs had closed in the weekly group compared with 2.0% in the every other week group. ($p=2.3 \times 10^{-14}$). Median time to close in the weekly group was 21 days; 95%CI=16.02-25.98 compared to 79 days (95%CI 69.15 -88.85, p8.0 x10 $^{-41}$ Visit numbers, initial depth, depth of DFU, Physician speciality were treated as confounding variables. A Cox regression was used to adjust for these factors. Outcomes are shown in the table below.

Variable	**HR**	**95% CI**	**P**
Visit number			
2-3	1.0[a]		
4-5	0.51	0.33-0.81	.004
6-8	0.16	0.09-0.29	2.9×10^{-10}
>8	.041	0.02-0.074	
Depth, cm			
0.1	1.0[a]		

Reference	**Warriner,R.A.,III; Wilcox,J.R.; Carter,M.J.; Stewart,D.G. (2012) More frequent visits to wound care clinics result in faster times to close diabetic foot and venous leg ulcers, Advances in Skin & Wound Care, 25 (11) 494-501**
	0.2 0.59 0.41-0.84 .003 **>0.2** 0.48 0.32-0.73 .001 **Physician speciality** **Podiatrist** 1.0[a] **Other** 1.20 0.80-1.79 .386 **Surgeon** 0.60 0.39-0.92 .018 **Family practitioner** 0.65 0.43-0.98 .038 **Visit frequency** **Weekly** 1.0[a] **Every other week** 0.048 0.029-0.079 8.01×10^{-32} **(Log) area** 0.63 0.48-0.83 .001 [a] Reference category
Study location	USA
Authors conclusion	More frequent visits may be beneficial to reducing DFU closure times
Source of funding	Not reported
Comments	

F.9 Review question 9 full evidence tables

Table 47: Malone 1989

Bibliographic reference	**Malone,J.M.; Snyder,M.; Anderson,G.; Bernhard,V.M.; Holloway,G.A.; Bunt,T.J.1989) Prevention of amputation by diabetic education, American Journal of Surgery, 158 (6) 520-23.**
Study type & aim	A single centre RCT to analyse the impact of a patient education programme on the incidence of limb amputation in patients with diabetes and foot infection, ulceration or prior amputation
Study quality	Low
Number of patients	Out of a total of 227 eligible participants 203 patients were randomised to receive a weekly or bi-monthly education class 182

<table>
<tr><th>Bibliographic reference</th><th>Malone,J.M.; Snyder,M.; Anderson,G.; Bernhard,V.M.; Holloway,G.A.; Bunt,T.J.1989) Prevention of amputation by diabetic education, American Journal of Surgery, 158 (6) 520-23.</th></tr>
<tr><td></td><td>patients completed the study (group 1; 90 patients; 177 limbs) or to receive standard care (group 2; 92 patients; 177 limbs)</td></tr>
<tr><td>Patient characteristics</td><td>Inclusion criteria: All patients who were referred to the podiatry or vascular surgery clinic were eligible. Stable patients with uninfected ulcers or prior amputation were included.
Exclusion criteria: Patients requiring wound debridement, formal incision and drainage of foot infections, amputation or vascular reconstruction were excluded.
Patient characteristics: There was no significant difference between groups in the incidence of foot deformities, neuropathy, gangrene, prior amputation, prior foot ulcer, hypertrophic nails, medical management of diabetes, prior diabetic foot education or level of distal pulses.
The incidence of foot callous was significantly higher in group 1 (p<0.005), and the incidence of below knee vascular reconstruction was higher in group 2 (but this was not statistically significant).</td></tr>
<tr><td>Monitoring information & definitions</td><td>Monitoring:
Prior to enrolment both groups received standard wound care including debridement, drainage of wound infection,
Education class given on a monthly or bi-monthly basis. Class included slides depicting infected diabetic feet and amputated diabetic limbs and a simple set of patient instructions on diabetic foot care.
Outcome measures:
The primary outcome measure was the incidence of limb amputation in the group receiving education, or in the group that did not receive education
Secondary outcomes included the number of successes (fully healed wounds) and failures (infections or ulcer)
Other outcomes included mortality rates during the study.</td></tr>
<tr><td>Intervention</td><td>Patients in group 1 attended a weekly or bi monthly 1 hour educational class. The class provided information about symptoms of foot infection and images of amputated diabetic limbs and provided patient instructions for care of an infected foot.</td></tr>
<tr><td>Comparison</td><td>Patients in group 2 did not attend the education class but did receive standard care</td></tr>
<tr><td>Length of follow up</td><td>All patients were followed up until satisfactory completion of class. Range of follow up for both groups was 1 to 26 months</td></tr>
<tr><td>Location</td><td>USA</td></tr>
<tr><td>Outcomes measures and effect size</td><td>Success and failure rate: The table below shows the success and failure results of the education program ~(based on limbs)
<table>
<tr><th></th><th></th><th colspan="3">Failure</th></tr>
<tr><th></th><th>Success</th><th>Infection</th><th>Ulcer</th><th>Amputation</th></tr>
<tr><td>Group 1: Education</td><td>160/177</td><td>2/177</td><td>8/177</td><td>7/177</td></tr>
<tr><td>Group 2: No education</td><td>128/177</td><td>2/177</td><td>26/177</td><td>21/177</td></tr>
<tr><td>Chi-square</td><td>17.89</td><td>-</td><td>9.4</td><td>6.55</td></tr>
</table></td></tr>
</table>

<table>
<tr><th>Bibliographic reference</th><th>Malone,J.M.; Snyder,M.; Anderson,G.; Bernhard,V.M.; Holloway,G.A.; Bunt,T.J.1989) Prevention of amputation by diabetic education, American Journal of Surgery, 158 (6) 520-23.</th></tr>
<tr><td></td><td>
<table>
<tr><td>P-value</td><td>≤).0005</td><td>-</td><td>≤0.005</td><td>≤0.025</td></tr>
</table>
Success rate in group 1 was significantly better than in group 2 with 90 percent success for group 1 versus 72 percent for group 2 (p≤0.0005).
There was no significant difference in the incidence of foot infection between groups 1 and group 2 but the differences in foot ulcer were highly significant: Ulceration was 3 times as likely in group 2 (15 percent) compared to group 1 (5 percent; p≤0.005).
Amputation was also significantly greater in group 2 (12 percent) compared to group 1 (4 percent;p≤0.025).

Level of amputation:
The table below shows the level of amputation. Percentages are shown in parentheses. The majority of amputations were below knee level.

<table>
<tr><th></th><th>Toe</th><th>Foot</th><th>Below knee</th><th>Above knee</th><th>Total</th></tr>
<tr><td>Group 1: education</td><td>1 (14)</td><td>1 (14)</td><td>5 (71)</td><td>0</td><td>7</td></tr>
<tr><td>Group 2: no education</td><td>1 (5)</td><td>2 (10)</td><td>14 (67)</td><td>4 (19)</td><td>21</td></tr>
</table>
Mortality:
There were no differences in the overall mortality rate between groups 1 (3 percent; 3 of 108 patients); and group 2 (4 percent; 4 of 100 patients).
</td></tr>
<tr><td>Authors conclusion</td><td>The study demonstrated that a simple education programme significantly reduced the incidence of ulcer or foot and limb amputation in patients with diabetes</td></tr>
<tr><td>Source of funding</td><td>Not reported</td></tr>
<tr><td>Comments</td><td></td></tr>
</table>

Table 48: Al-Wahbi 2010

<table>
<tr><th>Bibliographic reference</th><th>Al-Wahbi,A.M. (2010) Impact of a diabetic foot care education program on lower limb amputation rate, Vascular Health & Risk Management 6, 923-34.</th></tr>
<tr><td>Study type and aim</td><td>A retrospective before and after cohort chart review to assess the impact of a diabetic foot care programme upon the rate of lower extremity amputation due to diabetic foot complications</td></tr>
<tr><td>Study quality</td><td>Very low</td></tr>
<tr><td>Number of patients</td><td>41 patients attending a city hospital for diabetic foot complications. 20 patients presented with complications prior to implementation of the foot care programme (before group); 21 presented with complication after the programme was established (during the first 2 years of the programme)</td></tr>
<tr><td>Patient characteristics</td><td>Inclusion criteria: All patients had diabetic foot complications (classified by the International classification of diseases clinical modification; ICD-CM) presenting before (between 1983 - 2002) or in first 2 years after implementation of programme (2002 to 2004).
Exclusion criteria: Not reported
Patient characteristics:
There was no difference between the two groups regarding age, sex or comorbidities.
Patient demographics are shown in the table below.

<table>
<tr><th>Characteristics</th><th>After (2002-2004)</th><th>Before (1983-2002)</th><th>P value</th></tr>
<tr><td>n</td><td>21</td><td></td><td>n/a</td></tr>
<tr><td>Men</td><td>16</td><td></td><td>0.69</td></tr>
<tr><td>Age (years)</td><td>61.1 ± 13.7</td><td>58.6 ± 10.18</td><td>0.49</td></tr>
<tr><td>Type 2/ \Type 1 diabetes</td><td>17/3</td><td>15/1</td><td>0.61</td></tr>
<tr><td>Neuropathy (%)</td><td>23.8</td><td>0</td><td>0.027</td></tr>
<tr><td>Peripheral arterial disease (%)</td><td>4.8</td><td>0</td><td>0.512</td></tr>
</table></td></tr>
<tr><td>Monitoring information & definitions</td><td>Monitoring:
The foot care program included foot care education for health care staff and patients. Health care staff received lectures and workshops on diabetic foot care.
Patient education was provided by a diabetic educator who conducted a series of educational seminars and distributed educational pamphlets on diabetic foot care.
Outcome measures:
The primary outcome was the number of amputations recorded before and after implementation of the programme.
Secondary outcome measures included extent of amputation (major or minor) before and after implementation of the</td></tr>
</table>

<table>
<tr><th>Bibliographic reference</th><th>Al-Wahbi,A.M. (2010) Impact of a diabetic foot care education program on lower limb amputation rate, Vascular Health & Risk Management 6, 923-34.</th></tr>
<tr><td></td><td>programme.</td></tr>
<tr><td>Intervention</td><td>After implementation of a foot care education programme for both health care staff and patients. The programme was designed to improve skills and knowledge about diabetic foot care</td></tr>
<tr><td>Comparison</td><td>Prior to implementation of the foot care programme</td></tr>
<tr><td>Length of follow up</td><td>2 years</td></tr>
<tr><td>Location</td><td>Saudi Arabia</td></tr>
<tr><td>Outcomes measures and effect size</td><td>Presentation with ulcer:
The table below shows the number of presentations and investigations treated at the hospital before and after implementing the programme.
85 percent of patients who attended the hospital with an ulcer before the programme was implemented compared with all patients in the after group.

<table>
<tr><th>Presentation</th><th>After (2002-2004)</th><th>Before (1983-2002)</th><th>P value</th></tr>
<tr><td>n</td><td>21</td><td>20</td><td></td></tr>
<tr><td>Ulcers (%)</td><td>100</td><td>85</td><td>0.329</td></tr>
<tr><td>Gangrene (%)</td><td>63.3</td><td>36.4</td><td>0.272</td></tr>
<tr><td>Osteomyelitis of foot x-ray (%)</td><td>42.9</td><td>38.9</td><td>n/a</td></tr>
</table>

Amputation rate and extent
Amputation rate was higher in the before group (70%) compared to after (61.9%). Toe amputation was lower in the after group (28.6% and below-knee amputation was higher in the before group (33.3%)

The table below shows the amputation rates
<table>
<tr><th>Amputation level</th><th>After (2002- 2004)</th><th>Before (1983-2002)</th><th>P value</th></tr>
<tr><td></td><td>21</td><td>20</td><td></td></tr>
<tr><td>Overall amputation (%)</td><td>61.9</td><td>70</td><td>0.314</td></tr>
<tr><td>Toe level (%)</td><td>28.6</td><td>40*</td><td>n/s</td></tr>
<tr><td>Below knee level (%)</td><td>33.3</td><td>20*</td><td>n/s</td></tr>
<tr><td>Above knee level (%)</td><td>0</td><td>0.5*</td><td>n/s</td></tr>
</table>
*NB: total number of patients was unclear</td></tr>
</table>

Bibliographic reference	Al-Wahbi,A.M. (2010) Impact of a diabetic foot care education program on lower limb amputation rate, Vascular Health & Risk Management 6, 923-34.
Authors conclusion	The programme increased the awareness of both patients and health care staff about prevention and management of diabetic foot disease and decreased the rate of lower extremity amputation
Source of funding	Not reported
Comments	

Table 49: Rerkasem 2007

Bibliographic reference	Rerkasem,K.; Kosachunhanun,N.; Tongprasert,S.; Khwanngern,K.; Matanasarawoot,A.; Thongchai,C.; Chimplee,K.; Buranapin,S.; Chaisrisawadisuk,S.; Manklabruks,A. (2007) The development and application of diabetic foot protocol in Chiang Mai University Hospital with an aim to reduce lower extremity amputation in Thai population: a preliminary communication, International Journal of Lower Extremity Wounds 6 (1) 18-21.
Study type and aim	A retrospective cohort study to determine whether a structured diabetic foot protocol compared to earlier interventions of standard care affects the rate of lower extremity amputations
Study quality	Very low
Number of patients	Results for a total of 171 patients were evaluated (61 patients received the foot care protocol; 110 patients received standard care (prior to implementation of foot care protocol)
Patient characteristics	**Inclusion criteria:** All diabetes patients with a diagnosed foot ulcer attending the clinic between two time periods were included in the study. Patients in the earlier time period (2003 to 2005) received standard care; patients attending the clinic during the second time period (2005 to 2006) received a structured diabetic foot care programme. 110 patients received standard care; 61 patients received the foot care programme; **Exclusion criteria:** Not reported **Patient characteristics:** Table 1 shows the patient characteristics of patients in each group

Item	Foot care programme n=61	Standard programme n=110
Males (%)	20 (32.8)	37 (33.6)
Mean age (years)	57.8	60.6
Patients with hypertension (%)	42 (68.9)	49 (44.6)
Patients with history of smoking (%)	26 (42.6)	55 (50.0)

<table>
<tr><td>Bibliographic reference</td><td colspan="3">Rerkasem,K.; Kosachunhanun,N.; Tongprasert,S.; Khwanngern,K.; Matanasarawoot,A.; Thongchai,C.; Chimplee,K.; Buranapin,S.; Chaisrisawadisuk,S.; Manklabruks,A. (2007) The development and application of diabetic foot protocol in Chiang Mai University Hospital with an aim to reduce lower extremity amputation in Thai population: a preliminary communication, International Journal of Lower Extremity Wounds 6 (1) 18-21.</td></tr>
<tr><td></td><td>Patients with hyperlipidemia (%)</td><td>27 (44.3)</td><td>73 (66.4)</td></tr>
<tr><td>Monitoring information & definitions</td><td colspan="3">Monitoring:
Patients received either standard care (no education) including debridement or a foot care education programme. Foot care education was based on the patients risk factors, previous foot care knowledge and self-care behaviour. Each session took 10 to 20 minutes and included verbal and written instructions upon risk factors, washing & drying feet, toenail care, footwear , moisturising feet and when to report foot problems.
Outcome measures:
The primary outcome was the number of lower extremity amputations in each group. The secondary outcomes were the type of amputation ((below knee, above knee etc)</td></tr>
<tr><td>Intervention</td><td colspan="3">Patients in the intervention group received an integrated foot care programme consisting of standardised ulcer assessments, self-care education for patients, provision of routine palliative foot care and protective footwear based upon detailed guidelines and protocol procedures set out for an integrated foot care team</td></tr>
<tr><td>Comparison</td><td colspan="3">Patients in the comparison group received standard care such as debridement. Neuropathy and ischemia were treated by consultation. There were no detailed guidelines for specific services</td></tr>
<tr><td>Length of follow up</td><td colspan="3">Not reported</td></tr>
<tr><td>Location</td><td colspan="3">Thailand</td></tr>
<tr><td>Outcomes measures and effect size</td><td colspan="3">Incidence of major or minor amputations
The table below shows the number of lower extremity amputations in each group. Percentages are in parentheses
<table>
<tr><th>Type of amputation</th><th>Foot care programme (n=61)</th><th>Standard programme (n=110)</th></tr>
<tr><td>Toe</td><td>2 (3.4)</td><td>10 (10.5)</td></tr>
<tr><td>Transmetatarsal</td><td>0</td><td>4 (4.2)</td></tr>
<tr><td>Syme</td><td>0</td><td>1 (1.1)</td></tr>
<tr><td>Below knee</td><td>2 (3.3)</td><td>12 (10.9)</td></tr>
<tr><td>Above knee</td><td>0</td><td>3 (2.7)</td></tr>
</table>

The incidence of major amputations was significantly lower in the foot care programme group compared to the standard care group (3.3% and 13.6, p=.03)

The incidence of minor amputation was also significantly lower in the foot care programme group compared to the standard care group (3.4% and 15.8%, p=.02)</td></tr>
</table>

Bibliographic reference	**Rerkasem,K.; Kosachunhanun,N.; Tongprasert,S.; Khwanngern,K.; Matanasarawoot,A.; Thongchai,C.; Chimplee,K.; Buranapin,S.; Chaisrisawadisuk,S.; Manklabruks,A. (2007) The development and application of diabetic foot protocol in Chiang Mai University Hospital with an aim to reduce lower extremity amputation in Thai population: a preliminary communication, International Journal of Lower Extremity Wounds 6 (1) 18-21.**
Authors conclusion	Implementing an integrated foot care programme was associated with improved diabetic foot care outcomes
Source of funding	Not reported
Comments	

Table 50: Weck 2013

Bibliographic reference	**Weck,M.; Slesaczeck,T.; Paetzold,H.; Muench,D.; Nanning,T.; von,Gagern G.; Brechow,A.; Dietrich,U.; Holfert,M.; Bornstein,S.; Barthel,A.; Thomas,A.; Koehler,C.; Hanefeld,M. (2013) Structured health care for subjects with diabetic foot ulcers results in a reduction of major amputation rates, Cardiovascular Diabetology, 12 45.**
Study type and aim	A prospective non- randomised observational study to test the effects of a structured health care system for diabetic foot care
Study quality	Very low
Number of patients	Out of a total of 1475 patients hospitalised for diabetic foot ulceration 684 patients were enrolled in a structured health care programme. In a control hospital, where the structured programme was not implemented, 560 patients admitted with a diabetic foot ulcer were eligible. Data on 508 patients was included in the final analysis
Patient characteristics	**Patient characteristics:** The mean age of the population of the structured health care program was 66.9 ± 10.5 years. Controls were significantly older (71.4 ± 10.8 years; p<0,001). Diabetes duration (16.1 ± 10.2 vs. 15.8 ± 9.5 years), HbA1C (61.8 ± 14.2 vs. 61.8 ± 14.2 mmol/mol and 7.8 ± 1.8 vs. 7.8 ± 1.8%), BMI (29.7 ± 5.8 vs 29.2 ± 5.7 kg/m2) and blood pressure (139 ± 21/76 ±11 vs. 140 ± 25/76 ± 13 mmHg) were comparable between the structured health care program and controls. **Inclusion criteria:** All patients with diabetes and new foot ulcers admitted to a hospital were included **Exclusion criteria:** Exclusion criteria were patients having acute myocardial infarction or stroke within the last 6 months, terminal renal failure or any kind of cancer.

Bibliographic reference	**Weck,M.; Slesaczeck,T.; Paetzold,H.; Muench,D.; Nanning,T.; von,Gagern G.; Brechow,A.; Dietrich,U.; Holfert,M.; Bornstein,S.; Barthel,A.; Thomas,A.; Koehler,C.; Hanefeld,M. (2013) Structured health care for subjects with diabetic foot ulcers results in a reduction of major amputation rates, Cardiovascular Diabetology, 12 45.**
Monitoring information & definitions	**Monitoring:** Following referral to an interdisciplinary diabetic foot -ward for initial diagnostic procedures, patients were transferred to the rehabilitation clinic. After discharge, a diabetic foot outpatient department carried out semi-annual check-up's including all additional interventions for a 2 year period. Standard care comprised a foot inspection and ulcer grading using a modified UT system. Patients in both the intervention and control hospitals received identical standard ulcer wound care including use of proper footwear, non-weight bearing limb support, daily wound debridement and careful clinical monitoring. **Outcome measures:** The primary outcome was the ulcer healing rate. Secondary outcomes included rate and extent of amputation and mortality rates
Intervention	Patients in the intervention hospital received a structured care programme.
Comparison	Patients in the control hospital received standard care.
Length of follow up	2 years
Location	Germany
Outcomes measures and effect size	**Ulcer healing:** Patients receiving the structured programme: At discharge about 30% of all foot wounds were healed. 52% of foot wounds were improved to modified UT-Wagner grade 1. At the 2 year follow–up examination 74% of the ulcers were healed completely and another 17% were UT-Wagner grade 1. **Control group:** At discharge from the clinic 23.0% of all foot wounds of the controls were healed and 49.8% were a modified UT-Wagner grade 1. Patients in the structured programme had a significantly (p=0.001) lower level of ulcer severity at discharge compared to controls **Amputation:** 32 patients in the structured group underwent major amputation (above the ankle) during hospital treatment (major amputation rate 4.7%). At the 2-year follow up 22 patients underwent major amputation (major amputation rate during follow-up 3.2%). 215 patients (31.4%) experienced minor amputations (distal of the ankle); the rate of major/ minor amputations was about 1:7.

Bibliographic reference	**Weck,M.; Slesaczeck,T.; Paetzold,H.; Muench,D.; Nanning,T.; von,Gagern G.; Brechow,A.; Dietrich,U.; Holfert,M.; Bornstein,S.; Barthel,A.; Thomas,A.; Koehler,C.; Hanefeld,M. (2013) Structured health care for subjects with diabetic foot ulcers results in a reduction of major amputation rates, Cardiovascular Diabetology, 12 45.**
	Of the controls 110 patients (21.7%,) had a major amputation (p< 0.0001 compared to structured group). 179 control patients had minor amputations (35.2%); the ratio of major/ minor amputations was 1:1.6. **Mortality:** At discharge mortality in the group treated by the structured programme was 2.5% (n = 17) mortality for the controls had a significantly higher age adjusted mortality rate of 9.4% (n=48, p<0.001)
Authors conclusion	Implementation of the structured health care programme achieved a significant reduction of major amputation rates as compared to standard care.
Source of funding	Health insurance company AOK
Comments	

Table 51: Aragon-Sanchez 2011

Bibliographic reference	**Aragon-Sanchez,J.; Lazaro-Martinez,J.L. (2011) Impact of perioperative glycaemia and glycated haemoglobin on the outcomes of the surgical treatment of diabetic foot osteomyelitis, Diabetes Research & Clinical Practice, 94 (3) 83-85.**
Study type and aim	Prospective cohort study of patients with diabetes undergoing surgical treatment for osteomyelitis to establish whether perioperative glycaemic control influenced the outcomes of surgical treatment for diabetic foot osteomyelitis
Study quality	Very low
Number of patients	A total of 81 patients were included in the cohort (20 patients in group A; 61 in group B) (21 patients in group C; 60 patients in group D)
Patient characteristics	**Inclusion criteria** All included patients were hospitalised patients with diabetes and were due to undergo surgical treatment for osteomyelitis **Exclusion criteria** Not reported **Patient characteristics** Median age was 65 years (median duration of diabetes 20 years) 48 patients (59.3%) did not undergo amputation 32 patients (39.5%) had minor amputations 1 patient (1.2%) had a major amputation (above the knee)

<table>
<tr><th>Bibliographic reference</th><th>Aragon-Sanchez,J.; Lazaro-Martinez,J.L. (2011) Impact of perioperative glycaemia and glycated haemoglobin on the outcomes of the surgical treatment of diabetic foot osteomyelitis, Diabetes Research & Clinical Practice, 94 (3) 83-85.</th></tr>
<tr><td></td><td>Median capillary glucose value = 161.1 mg/dl; Median HBA1c = 8.2%</td></tr>
<tr><td>Monitoring information & definitions</td><td>Monitoring:
The distribution of HBA1c levels upon admission were divided into quartiles . Patients in quartile 1 were compared to patients in quartile 2-4 Pre meal bedside glucose monitoring using capillary blood was performed 3 times a day . Mean values were determined for each patient and converted into quartiles
Outcome measures:
Number of amputations, (major and minor), reoperations, exitus, hospital stay, time to healing</td></tr>
<tr><td>Comparison groups</td><td>Outcomes of patients with pre meal glucose levels were compared:
Capillary glucose levels: Patients with pre meal glucose levels102-140.8 mg/dl (group A) were compared to patients with pre-meal glucose levels 140.9 mg/dl – 274 mg/dl (group B)
HBA1c levels Patients with HBA1c levels 5.3%-7.3% (group C) were compared to patients with HBA1c levels 7.4%- 14% (group D)</td></tr>
<tr><td>Length of follow up</td><td>Not reported</td></tr>
<tr><td>Location</td><td>Spain</td></tr>
<tr><td>Outcomes measures and effect size</td><td>The table below shows the analysis of outcomes amongst groups
<table>
<tr><th></th><th>Group A
Pre-meal glucose (quartile 1)
n=20</th><th>Group B
n=61 (pre-meal glucose quartile 2-4)</th><th>p-value</th><th>Group C
n=21
HBA1c (quartile 1)</th><th>Group D
n=60
HBA1c ((quartile 2-4)</th><th>p-value</th></tr>
<tr><td>Amputation, n (%)</td><td>4 (20)</td><td>29 (47.5)</td><td>0.03</td><td>7 (33.3)</td><td>26 (43.3)</td><td>0.42</td></tr>
<tr><td>Reoperation, n (%)</td><td>7 (35)</td><td>13 (21.3)</td><td>0.24</td><td>6 (28.6)</td><td>14 (23.3)</td><td>0.63</td></tr>
<tr><td>Mortality, n (%)</td><td>2 (10)</td><td>3 (4.9)</td><td>0.59</td><td>3 (14.3)</td><td>2 (3.3)</td><td>0.1</td></tr>
<tr><td>Hospital stay in days, median (Q1, Q3)</td><td>44.5 (27.5, 58.5)</td><td>28 (13, 40)</td><td>0.005</td><td>40 (8, 45.5)</td><td>29 (16, 48)</td><td>0.66</td></tr>
<tr><td>Period of antibiotic treatment in days median (IQR)</td><td>36 (25.5, 46.5)</td><td>36 (27, 48)</td><td>0.66</td><td>40.5 (32, 50)</td><td>36 (27, 48)</td><td>0.53</td></tr>
<tr><td>Time to healing in days, median (IQR)</td><td>59.5 (43, 141)</td><td>66 (36, 124)</td><td>0.82</td><td>92 (52.5, 152)</td><td>60 (34, 120)</td><td>0.26</td></tr>
</table></td></tr>
<tr><td>Authors conclusion</td><td>Glycaemic control before admission did not have any influence on the outcomes.</td></tr>
<tr><td>Source of funding</td><td>Not reported</td></tr>
</table>

Bibliographic reference	Aragon-Sanchez,J.; Lazaro-Martinez,J.L. (2011) Impact of perioperative glycaemia and glycated haemoglobin on the outcomes of the surgical treatment of diabetic foot osteomyelitis, Diabetes Research & Clinical Practice, 94 (3) 83-85.
Comments	

Table 52: Markuson 2009

Bibliographic reference	Markuson,M.; Hanson,D.; Anderson,J.; Langemo,D.; Hunter,S.; Thompson,P.; Paulson,R.; Rustvang,D. (2009) The relationship between hemoglobin A(1c) values and healing time for lower extremity ulcers in individuals with diabetes, Advances in Skin & Wound Care 22 (8) 365-72.
Study type	A retrospective descriptive correlational study of patients with diabetic leg and foot ulcers to examine ulcer healing times in relation to HBA1c
Study quality	Very low
Number of patients	Data for 63 patients was included in the study
Patient characteristics	**Inclusion criteria:** All patients included were diabetes patients with a leg or foot ulcer being examined at the wound care centre **Exclusion criteria** Not reported **Patient characteristics** The patient demographic data is shown in the table below.

History	Male (n=41) n (%)	Female (n=22) n (%)
History of previous ulcer	24 (58.9)	16 (72.7)
History of tobacco	23 (56.1)	7 (31.8)
Current tobacco	6 (14.6)	3 (13.6)
Previous ulcer-related amputation	8 (19.5)	3 (13.6)
Location of ulcers	n	%
Toes	16	25.4

<table>
<tr><th>Bibliographic reference</th><td colspan="4">Markuson,M.; Hanson,D.; Anderson,J.; Langemo,D.; Hunter,S.; Thompson,P.; Paulson,R.; Rustvang,D. (2009) The relationship between hemoglobin A(1c) values and healing time for lower extremity ulcers in individuals with diabetes, Advances in Skin & Wound Care 22 (8) 365-72.</td></tr>
<tr><td></td><td colspan="4">
<table>
<tr><td>Plantar foot</td><td>15</td><td>23.8</td></tr>
<tr><td>Leg</td><td>11</td><td>17.4</td></tr>
<tr><td>Dorsal/medial foot</td><td>10</td><td>15.9</td></tr>
<tr><td>Heel</td><td>10</td><td>15.9</td></tr>
<tr><td>Residual limb</td><td>1</td><td>1.6</td></tr>
<tr><td>Total</td><td>63</td><td>100</td></tr>
<tr><td>Ulcer type</td><td>n</td><td>%</td></tr>
<tr><td>Diabetic</td><td>30</td><td>47.6</td></tr>
<tr><td>Vascular</td><td>11</td><td>17.5</td></tr>
<tr><td>Mixed</td><td>11</td><td>17.5</td></tr>
<tr><td>Pressure</td><td>8</td><td>12.7</td></tr>
<tr><td>Other</td><td>3</td><td>4.7</td></tr>
<tr><td>Total</td><td>63</td><td>100</td></tr>
</table>
</td></tr>
<tr><td>Monitoring information & definitions</td><td colspan="4">Monitoring:
HBA1c values closest to admission and closest to ulcer closure were collected. All diabetic ulcers were treated with off-loading, debridement and dressings (including silver dressings, non-adhesive foams, hydrocolloids, enzymatic dressings and growth factors)
Outcome measures:
The primary outcome was relationship between HBA1c and ulcer healing time Secondary outcome measures included ulcer reopening and area of ulcer</td></tr>
<tr><td>Comparisons</td><td colspan="4">Ulcer healing time and patients baseline HBA1C (4%-7%; 7.1-10%; > 10%)</td></tr>
<tr><td>Length of follow up</td><td colspan="4">3 years</td></tr>
<tr><td>Location</td><td colspan="4">USA</td></tr>
<tr><td>Outcomes measures and effect size</td><td colspan="4">Healing time
The table below shows mean healing time based on HBA1c level
<table>
<tr><th>HBA1c level</th><th>Mean ulcer healing time</th><th>SD</th><th>Significance difference</th></tr>
<tr><td>HBA1c 4%- 7%</td><td>85 days</td><td>80.34 days</td><td>-</td></tr>
<tr><td>HBA1c 7.1%-10</td><td>123.63 days</td><td>135.11 days</td><td>Non-significant</td></tr>
<tr><td>HBA1c >10%</td><td>147.1 days</td><td>173.1 days</td><td>Non-significant</td></tr>
</table>
</td></tr>
</table>

<table>
<tr><th>Bibliographic reference</th><th>Markuson,M.; Hanson,D.; Anderson,J.; Langemo,D.; Hunter,S.; Thompson,P.; Paulson,R.; Rustvang,D. (2009) The relationship between hemoglobin A(1c) values and healing time for lower extremity ulcers in individuals with diabetes, Advances in Skin & Wound Care 22 (8) 365-72.</th></tr>
<tr><td></td><td>Mean healing times were divided into 3 categories: 1 to 84 days 85 to168 days, and more than 168 days.
The table below shows the admission type HBA1c and days to heal ulcer for patients with type 1 and type 2 diabetes.
<table>
<tr><th>HBA1c level</th><th>1-84 days (12 weeks),</th><th>85-168 days 12 to 24 weeks,</th><th>>168 days > 24 weeks,</th></tr>
<tr><td>HBA1c 4%- 7%</td><td>6 (66%)</td><td>2 (22%)</td><td>1 (11%)</td></tr>
<tr><td>HBA1c 7.1%-10</td><td>8 (50%)</td><td>4 (25%)</td><td>4 (25%)</td></tr>
<tr><td>HBA1c >10%</td><td>1 (25%)</td><td>1 (25%)</td><td>2 (50%)</td></tr>
</table>

HBA1c and Ulcer reopening
39 ulcers healed during the study.
5 of 9 (55.6%) reopened with admission HBA1c 4%-7%
5 of 13 (38.5%) reopened with admission HBA1c 7.1% -10%
1 of 4 (25%) reopened with admission HBA1c > 10%

In patients closest to closure time
2 of 4 ulcers (50%) reopened in patients with admission HBA1c 4%-7% closest to time of closure
2 of 8 ulcers (25%) reopened in patients with admission HBA1c 4.1% -7 % closest to time of closure
0 of 2 ulcers reopened in patients with admission HBA1c > 10% closest to time of closure</td></tr>
<tr><td>Authors conclusion</td><td>Ulcers on patients with higher HBA1c levels took a significantly longer period to heal.</td></tr>
<tr><td>Source of funding</td><td>Not reported</td></tr>
<tr><td>Comments</td><td></td></tr>
</table>

Table 53: Young 2008

<table>
<tr><th>Bibliographic reference</th><th>Young,M.J.; McCardle,J.E.; Randall,L.E.; Barclay,J.I. (2008) Improved survival of diabetic foot ulcer patients 1995-2008: possible impact of aggressive cardiovascular risk management, Diabetes Care, 31 (11) 2143-47.</th></tr>
<tr><td>Study type and aim</td><td>Retrospective cohort to determine whether a strategy of cardiovascular risk management reduced mortality associated with diabetic foot ulceration</td></tr>
<tr><td>Study quality</td><td>Very low</td></tr>
<tr><td>Number of patients</td><td>355 foot ulceration patients (404 patients in cohort 1 – patients seen at the clinic prior to introduction of cardiovascular risk management programme (receiving standard care) and 251 patients in cohort 2- patients seen at the clinic after introduction of cardiovascular risk management programme)</td></tr>
<tr><td>Patient characteristics</td><td>Inclusion criteria
All patients attending a specialist foot clinic having been referred for a new foot ulceration
Exclusion criteria
Not reported
Patient characteristics
The table below shows patient demographics for patients included in the 2 cohorts
<table>
<tr><th></th><th>Cohort 1 (n=404)</th><th>Cohort 2 (n=251)</th></tr>
<tr><td>Sex (% male)</td><td>62</td><td>66</td></tr>
<tr><td>Type 2 diabetes (%)</td><td>70</td><td>77</td></tr>
<tr><td>Age at first ulcer (years)</td><td>63.2 ± 13.8</td><td>61.9 ± 14.9</td></tr>
<tr><td>Mean duration of diabetes (years)</td><td>13.4 ± 11.2</td><td>13.8 ± 10.8</td></tr>
<tr><td>Ischemic ulcers (%)</td><td>52</td><td>48</td></tr>
<tr><td>Previous cardiovascular disease (%)</td><td>39</td><td>36</td></tr>
<tr><td>Current smoker (%)</td><td>24</td><td>24</td></tr>
<tr><td>Systolic blood pressure (mmHg)</td><td>-</td><td>139.1 ± 23.7</td></tr>
<tr><td>Diastolic blood pressure (mmHg)</td><td>-</td><td>81.7 ± 13.6</td></tr>
<tr><td>A1C</td><td>8.6 ± 1.6</td><td>8.4 ± 1.8</td></tr>
<tr><td>Creatinine > 130 µmol/l (%)</td><td>22</td><td>19</td></tr>
<tr><td>Total cholesterol (mmol/l)</td><td>5.21 ± 1.01</td><td>4.77 ± 1.30*</td></tr>
<tr><td colspan="3">Data are means ± SD or % *P<0.05 cohort 1 versus cohort 2</td></tr>
</table></td></tr>
</table>

Bibliographic reference	Young,M.J.; McCardle,J.E.; Randall,L.E.; Barclay,J.I. (2008) Improved survival of diabetic foot ulcer patients 1995-2008: possible impact of aggressive cardiovascular risk management, Diabetes Care, 31 (11) 2143-47.
Monitoring information & definitions	**Monitoring:** Cohort 1 comprised patients presenting at the clinic with a new ulcer between 1995-199; Cohort 2 comprised patients presenting with an ulcer between 2001 & 2004. The identified notes were examined for initial therapy, history on attendance and clinic notes for antiplatelet therapies given to cohort 1. Care for cohort 2 was adapted to include screening for cardiovascular risk factors (blood pressure, serum cholesterolA1c, total cholesterol to obtain a cardiovascular risk score using the UKPDS risk engine on primary prevention) **Outcome measures:** Survival was measured from time of first ulcer to death;
Comparisons	Mortality associated with diabetic foot ulcerations in 2 cohorts of patients: before and after introducing a cardiovascular risk management programme
Length of follow up	13 years for cohort 1; 4 years for cohort 2
Location	UK
Outcomes measures and effect size	**Mortality:** Overall mortality at 4 years was 43.3% in cohort 1; 21.9% in cohort 2 . Survival for cohort 2 was compared with 5-year survival for cohort 1. Overall 5- year mortality was reduced from 48.0% in cohort 1 to 26.8% in cohort 2 ($p<0.001$) Patients who died in first 5 years after presentation (number of deaths to date) were 194 of 285 deaths to date for cohort 1 and 63 of 87 total deaths to date for cohort 2.
Source of funding	Sanofi-Aventis & Bristol-Myers Squibb
Authors conclusion	The adoption of an aggressive cardiovascular risk management policy in diabetic foot ulcer clinics is recommended.
Comments	

Table 54: Flahr 2010

<table>
<tr><th>Bibliographic reference</th><th>Flahr, D (2010) The effect of nonweight-bearing exercise and protocol adherence on diabetic foot ulcer healing: a pilot study, Ostomy Wound Management, 56 (10) 40-50.</th></tr>
<tr><td>Study type</td><td>A prospective randomised pilot study to assess the effects of non-weight bearing exercises on healing of diabetic foot ulcers</td></tr>
<tr><td>Study quality</td><td>Very low</td></tr>
<tr><td>Number of patients</td><td>Out of 19 patients included 18 patients completed the study (10 in the intervention group completed the ankle exercises;8 control patients received their standard care regimen</td></tr>
<tr><td>Patient characteristics</td><td>Inclusion criteria
All included patients were aged 18 years or over with a foot ulcer referred to the local podiatric service. Inclusion criteria included: diabetes, ulceration, sensory neuropathy and the ability to provide informed consent in English.
Exclusion criteria
Patients with cognitive impairment, infection and ischemia were excluded from participation in the study.
Patient characteristics
Patient demographics are shown in the table below:
<table>
<tr><th>Variable</th><th>Intervention group (n=10)</th><th>Control group (n=8)</th></tr>
<tr><td>Age
Range
Mean
Median
SD</td><td>
49-74
61.9
60
8.117</td><td>
54-94
74.25
74.5
16.255</td></tr>
<tr><td>Gender
Male
Female</td><td>
8 (80%)
2 (20%)</td><td>
4 (50%)
4 (50%)</td></tr>
<tr><td>Comorbidities
Yes
No</td><td>
6 (60%)[a]
4 (40%)</td><td>
3 (38%)[b]
5 (62%)</td></tr>
<tr><td>Alternative therapies
Yes
No</td><td>
2 (20%)[c]
8 (80%)</td><td>
0
8 (100%)</td></tr>
<tr><td>Dartmouth scores [d]
Range</td><td>
13-24</td><td>
12-24</td></tr>
</table></td></tr>
</table>

Bibliographic reference	Flahr, D (2010) The effect of nonweight-bearing exercise and protocol adherence on diabetic foot ulcer healing: a pilot study, Ostomy Wound Management, 56 (10) 40-50.

Mean	17.2	18.5
Median	16	19
LEAP scores		
20%	1 (10%)	
80%	1 (10%)	3 (37.5%)
90%	20 (20%)	1 (12.5%)
100%	6 (60%)	4 (50%)

[a] Comorbidities 30% had arthritis; 10% had history of cerebral vascular incident, 10% had back surgery
1% had history of herniated disc
[b] Comorbidities 38.5% had arthritis
[c] Alternative therapies 10% reported use of meditation techniques; 10% reported use of therapeutic sheepskin
[d] Dartmouth scores The scores are inversely related to individual function. A high score indicates increased functional limitation

Monitoring information & definitions	**Monitoring:** Patients in the intervention group received a sheet describing a selection of exercises with explanations. Patients were asked to complete 4 ankle exercises 10 times each twice a day. The study was home-based and no time frame was established for completion of the exercise regimen. Adherence was self supervised, although, patients were given an exercise journal and provided with information upon self-completion Patients in the control group were asked to continue their care as they had done before study involvement. Size of wounds were measured every 4 weeks for a maximum of 12 weeks **Outcome measures:** The primary outcome was percentage wound reduction at 12 weeks. Secondary outcomes included number of healed wounds; exercise frequency.
Intervention	The use of non-weight bearing exercise in a population of patients with diabetic foot ulceration
Comparison	A non-exercising population with the same diagnosis
Length of follow up	12 weeks
Location	Canada
Outcomes measures and effect size	**Reduction in wound size:** 9 patients included in the intervention group (90%) experienced a wound size reduction compared to 5 patients (62.5%) in the control group. The difference in percentage wound reduction was non significant (p=.696)

<table>
<tr><th>Bibliographic reference</th><th>Flahr, D (2010) The effect of nonweight-bearing exercise and protocol adherence on diabetic foot ulcer healing: a pilot study, Ostomy Wound Management, 56 (10) 40-50.</th></tr>
<tr><td></td><td>1 patient in the intervention group experienced a wound size increase compared to 3 patients (37.5%) in the control group
The table below shows the wound measurement data for patients in the study
<table>
<tr><th>Experimental group</th><th>Week 0</th><th>Week 4</th><th>Week 8</th><th>Week 12</th><th>Size increase (+) or decrease (-)</th></tr>
<tr><td>E1</td><td>1.84</td><td>1.26</td><td>0.38</td><td>0.22</td><td>-88%</td></tr>
<tr><td>E2</td><td>6.22</td><td>2.53</td><td>Withdrew</td><td></td><td>-59%</td></tr>
<tr><td>E3</td><td>0.27</td><td>0.33</td><td>0.24</td><td>0.09</td><td>-67%</td></tr>
<tr><td>E4</td><td>0.16</td><td>0.05</td><td>0.07</td><td>Closed</td><td>-100%</td></tr>
<tr><td>E5</td><td>0.16</td><td>0.22</td><td>0.27</td><td>0.12</td><td>-25%</td></tr>
<tr><td>E6</td><td>0.09</td><td>0.13</td><td>Closed</td><td></td><td>-100%</td></tr>
<tr><td>E7</td><td>0.16</td><td>0.06</td><td>1.32</td><td>0.05</td><td>-69%</td></tr>
<tr><td>E8</td><td>0.27</td><td>0.24</td><td>0.31</td><td>0.09</td><td>-67%</td></tr>
<tr><td>E9</td><td>0.31</td><td>0.25</td><td>Closed</td><td></td><td>-100%</td></tr>
<tr><td>E10</td><td>1.02</td><td>5.89</td><td>3.06</td><td>2.36</td><td>-131%</td></tr>
<tr><td>Control Group</td><td>Week 0</td><td>Week 4</td><td>Week 8</td><td>Week 12</td><td>Size increase (+) or decrease (-)</td></tr>
<tr><td>C1</td><td>0.63</td><td>0.79</td><td>0.38</td><td>0.79</td><td>+25%</td></tr>
<tr><td>C2</td><td>0.43</td><td>0.75</td><td>0.59</td><td>0.49</td><td>+14%</td></tr>
<tr><td>C3</td><td>1.26</td><td>0.39</td><td>0.16</td><td>0.14</td><td>-88%</td></tr>
<tr><td>C4</td><td>0.25</td><td>0.19</td><td>0.05</td><td>Closed</td><td>-100%</td></tr>
<tr><td>C5</td><td>6.03</td><td>5.42</td><td>8.1</td><td>9.18</td><td>+2%</td></tr>
<tr><td>C6</td><td>0.14</td><td>0.07</td><td>Closed</td><td></td><td>-100%</td></tr>
<tr><td>C7</td><td>0.16</td><td>Withdrew</td><td></td><td></td><td></td></tr>
<tr><td>C8</td><td>10.2</td><td>Not seen</td><td>0.42</td><td>Closed</td><td>-100%</td></tr>
<tr><td>C9</td><td>1.32</td><td>0.71</td><td>Not seen</td><td>0.06</td><td>-95%</td></tr>
<tr><td></td><td></td><td></td><td></td><td></td><td></td></tr>
</table></td></tr>
<tr><td>Source of funding</td><td>Not reported</td></tr>
<tr><td>Authors conclusion</td><td>The results of the pilot study comparing exercise interventions with standard care were inconclusive.</td></tr>
<tr><td>Comments</td><td></td></tr>
<tr><td></td><td></td></tr>
</table>

Bibliographic reference	Flahr, D (2010) The effect of nonweight-bearing exercise and protocol adherence on diabetic foot ulcer healing: a pilot study, Ostomy Wound Management, 56 (10) 40-50.

Table 55: Alzahrani 2013

Bibliographic reference	Alzahrani, H., Bedir, Y., & Al-Hayani, A. (2013). Efficacy of shellac, a natural product, for the prevention of wet gangrene. Journal of International Medical Research, 0300060513483391.
Study type	A prospective "randomised" study to assess the effects of shellac a natural product for the treatment of dry gangrene for the prevention of wet gangrene
Study quality	Very low
Number of patients	Out of 26 patients included 23 patients completed the study (13 in the intervention group completed the study; 10 control patients received their standard care regimen)
Patient characteristics	**Inclusion criteria** Patients with type 2 diabetes who presented with peripheral, dry, well-demarcated gangrene in their feet and who were offered the option to wait for non-surgical autoamputation; elderly, bed ridden patients with diabetes who refused amputation and/or were contraindicated for revascularisation or surgery; patients who had recently received initial antibiotic therapy could enter the study 1 week after cessation of such therapy. **Exclusion criteria** Patients who presented with any evidence of wet or infected gangrene, evidence of osteomyelitis or those currently on antibiotics were excluded from the study. **Patient characteristics** Patient demographics are shown in the table below:

Variable	Intervention group (n=10)	Control group (n=8)
Age	67.2 ± 12.8	64.8 ± 13.6
Gender **Male** **Female**	 10 3	 6 4
Evidence of prior infection	7	3

<table>
<tr><th>Bibliographic reference</th><td colspan="3">Alzahrani, H., Bedir, Y., & Al-Hayani, A. (2013). Efficacy of shellac, a natural product, for the prevention of wet gangrene. Journal of International Medical Research, 0300060513483391.</td></tr>
<tr><td></td><td colspan="3"><table>
<tr><td>Evidence of ischaemia</td><td>9</td><td>7</td></tr>
<tr><td>Evidence of trauma</td><td>4</td><td>4</td></tr>
</table></td></tr>
<tr><td>Monitoring information & definitions</td><td colspan="3">Monitoring:
All patients were asked to visit the clinic every month or when signs of inflammation or fever were observed
Outcome measures:
Amputation rates</td></tr>
<tr><td>Intervention</td><td colspan="3">Application of Shellac to dry gangrenous wounds</td></tr>
<tr><td>Comparison</td><td colspan="3">Application of 10% povidone-iodine (standard care)</td></tr>
<tr><td>Length of follow up</td><td colspan="3">12 months</td></tr>
<tr><td>Location</td><td colspan="3">Saudi Arabia</td></tr>
<tr><td>Outcomes measures and effect size</td><td colspan="3">Amputation rates:

<table>
<tr><td></td><td>Shellac group n=13</td><td>Conventional treatment group n=10</td></tr>
<tr><td>Toe amputations</td><td>3</td><td>3</td></tr>
<tr><td>Major amputation</td><td>3</td><td>3</td></tr>
<tr><td>Alive without amputations at 1 year</td><td>4</td><td>3</td></tr>
</table>
No significant differences were found for any of the above outcomes

Mortality rate:
<table>
<tr><td></td><td>Shellac group n=13</td><td>Conventional treatment group n=10</td></tr>
<tr><td>Diead during the trial</td><td>3</td><td>1</td></tr>
</table>
No significant differences were found for any of the above outcomes, no deaths were directly related to the patient’s lower extremity clinical condition</td></tr>
<tr><td>Source of funding</td><td colspan="3">The Chair for Diabetic Foot Research</td></tr>
<tr><td>Authors conclusion</td><td colspan="3">The results of the pilot study comparing shellac treatment with standard care were inconclusive and larger studies are needed.</td></tr>
</table>

Bibliographic reference	Alzahrani, H., Bedir, Y., & Al-Hayani, A. (2013). Efficacy of shellac, a natural product, for the prevention of wet gangrene. Journal of International Medical Research, 0300060513483391.
Comments	

F.10 Review question 10 evidence tables

F.10.1 New studies

Table 56: Tallis 2013

Bibliographic reference	Tallis,A. Motley,T.A. Wunderlich,R.P. Dickerson,J.E.,Jr. Waycaster,C. Slade,H.B.(2013) Clinical and economic assessment of diabetic foot ulcer debridement with collagenase: results of a randomized controlled study, Clinical Therapeutics, 35 (11) 1805-20.
Study type and aim	Multicentre, parallel group randomised controlled trial (RCT) to compare the clinical effectiveness of clostridial collagenase ointment (CCO) debridement to debridement using a saline moistened gauze (SMG) and selective sharp debridement for treatment of diabetic foot ulcers (DFUs).
Study quality	Very low
Patient characteristics	**Total number of participants:** A total of 48 participants were randomised to treatment with CCO or SMG **Inclusion criteria:** Patients aged 18 years or over with type 1 or type 2 diabetes and neuropathic foot ulcers of at least one months duration between 0.5 and 10cm in depth. Inclusion criteria was adults of any race and either sex who were willing and able to use offloading device, willing and able to

Bibliographic reference	Tallis,A. Motley,T.A. Wunderlich,R.P. Dickerson,J.E.,Jr. Waycaster,C. Slade,H.B.(2013) Clinical and economic assessment of diabetic foot ulcer debridement with collagenase: results of a randomized controlled study, Clinical Therapeutics, 35 (11) 1805-20.

change dressings at home, and with no target wound tunnelling and the target wound should not be on the heel or over a charcot deformity.

Adequate perfusion to target ulcer foot (transcutaneous oxygen pressure greater than 40mm Hg or toe pressure > 40mm Hg)

Adequate nutrition (albumin equal to or greater than 2.0g/dL and prealbumin equal to or greater than 15mg/ dL)

Exclusion criteria:

Not reported

Patient characteristics:

Demographic and baseline wound characteristics are shown in the table below

Characteristic	Treatment group			
	Total (n=48)	CCO (n=24)	SMG (n=24)	P (Anova or χ^2 test)
Age (y)				
Mean	61.0	58.5	63.5	0.1483
Median	61.0	59.0	63.5	
SD	11.8	13.3	9.8	
Range	38-86	38-86	47-85	
Age group, No (%)				
<65 years	28 (58)	15 (62)	13 (54)	
>65 years	20 (42)	9 (38)	11 (46)	
Sex, No (%)				>0.99
Female	16 (33)	8 (33)	8 (33)	
Male	32 (67)	16 (67)	16 (67)	
Race, ethnicity, No (%)				
Black/ African American	3 (6)	2 (8)	1 (4)	0.5510
White	45 (94)	22 992)	23 (96)	
Hispanic/ Latino	9 (19)	5 (21)	4 (17)	
Non Hispanic/ non Latino	39 (81)	19 (79)	20 (83)	
Wound area (cm^2)				0.3014
Mean	2.7	3.0	2.4	
Median	1.9	2.6	1.6	
SD	2.1	2.1	2.1	

Bibliographic reference	**Tallis,A. Motley,T.A. Wunderlich,R.P. Dickerson,J.E.,Jr. Waycaster,C. Slade,H.B.(2013) Clinical and economic assessment of diabetic foot ulcer debridement with collagenase: results of a randomized controlled study, Clinical Therapeutics, 35 (11) 1805-20.**

Range	0.5-9.0	0.5-9.0	0.5-7.6	
Wound location, No (%)				0.6003
Distal	3 (6)	2 (8)	1 (4)	
Dorsal	4 (8)	1 (4)	3 (12)	
Lateral	4 (8)	2 98)	2 98)	
Medial	2 (4)	2 (8)	--	
Plantar	29 (60)	15 (62)	14 (58)	
Plantar/ distal	5 (10)	2 (8)	3 (12)	
Plantar/ lateral	1 (2)	-	1 (4)	
Wound side , No (%)				0.7711
Left	21 (44)	10 (42)	11 (46)	
Right	27 (56)	14 (58)	13 (54)	
Wound shape, No (%)				0.3059
Bowl/ boat	2 (4)	2 (80	--	
Irregular	17 (35)	9 (38)	8 (33)	
Round/oval	29 (60)	13 (54)	16 (67)	

Monitoring & definitions	**Monitoring:** Randomisation to treatment group was centralised based on computer-generated randomisation sequence. Baseline wound bed assessment and measurement were performed for each eligible patient. **Outcome measures:** The primary outcome was a treatment group analysis of change from baseline in wound status. Other outcomes included the percentage of wound area change from baseline during the 4 week period and at end of follow-up. Tolerability was assessed through analysis of adverse events.
Intervention	CCO was applied once a day (thickness 2mm) to the DFUs of patients in the CCO group.
Comparator	Saline moistened cotton gauze was applied and changed daily for patients in the SMG group.
Length of follow up	Treatment was given for 4 weeks followed by an 8 week study follow-up period (or until complete wund closure was achieved)
Location	USA
Outcomes measures and effect size	**Percentage change in DFU area** DFUs in the CCO group had a mean percentage reduction from baseline in area of -44.9% (p=0.016) after 4 weeks and -53.8% (p=0.012) at the end of follow-up.

Bibliographic reference	**Tallis,A. Motley,T.A. Wunderlich,R.P. Dickerson,J.E.,Jr. Waycaster,C. Slade,H.B.(2013) Clinical and economic assessment of diabetic foot ulcer debridement with collagenase: results of a randomized controlled study, Clinical Therapeutics, 35 (11) 1805-20.**
	DFUs in the SMG group were +0.8% after 4 weeks and +8.1% at the end of follow-up (non significant) Mean number of surgical debridements performed during the study period was 1.0 for the CCO group and 6.9 for the SMG group **Tolerability** Of the 48 patients 23 experienced 61 treatment emergent adverse events (28 reported in CCO group; 33 in the SMG group)
Source of funding	Not reported
Authors conclusion	CCO is tolerable and clinically effective in achieving the removal of nonviable tissue in a healthy wound bed
Comments	

Table 57: Piaggesi 1998

Bibliographic reference	**Piaggesi,A. Schipani,E. Campi,F. Romanelli,M. Baccetti,F. Arvia,C. Navalesi,R. (1998) Conservative surgical approach versus non-surgical management for diabetic neuropathic foot ulcers: a randomized trial, Diabetic Medicine 15 (5) 412-17**
Study type and aim	A randomised controlled trial (RCT) to evaluate the effectiveness and safety of surgical treatment of diabetic foot ulcers compared to non-surgical management.
Study quality	Low
Patient characteristics	**Total number of participants:** Out of 53 eligible patients, 41 patients were randomised to treatment with non-operative treatment (group A, n= 20,) or outpatient surgery (n=21) **Inclusion criteria:** Inclusion criteria were type 1 or type 2 diabetes of at least 5 years duration; presence of one or more painless foot ulcers with clinical characteristics of neuropathy and vibration perception threshold (VPT) at malleolus and first toe **Exclusion criteria:** Exclusion criteria were presence of symptomatic claudication or absence of foot pulses; recent ketoacidosis; renal failure;

<table>
<tr><th>Bibliographic reference</th><th>Piaggesi,A. Schipani,E. Campi,F. Romanelli,M. Baccetti,F. Arvia,C. Navalesi,R. (1998) Conservative surgical approach versus non-surgical management for diabetic neuropathic foot ulcers: a randomized trial, Diabetic Medicine 15 (5) 412-17</th></tr>
<tr><td></td><td>presence of infection; patients with congenital foot deformities; diabetic neuroarthropathy; BMI greater than 30kg-m^2; clinical history of stroke; cardiac failure HIV positivity or cancer; history of mental illness.
Patient characteristics:
Baseline patient demographics are shown in the table below.
<table>
<tr><th></th><th>Group A</th><th>Group B</th><th>ANOVA</th></tr>
<tr><td>Number of patients (T1DM/T2DM)</td><td>20 (17/3)</td><td>21 (19/2)</td><td>ns</td></tr>
<tr><td>Age (yr)</td><td>63.24 ± 13.46</td><td>65.53 ± 9.87</td><td>ns</td></tr>
<tr><td>Duration of diabetes (yr)</td><td>18.20 ± 8.41</td><td>16.84 ± 10.61</td><td>ns</td></tr>
<tr><td>Body mass index</td><td>27.71 ± 9.43</td><td>28.12 ± 13.04</td><td>ns</td></tr>
<tr><td>Glycated haemoglobin (HBA1c%)</td><td>9.5 ± 3.8</td><td>8.9 ± 2.2</td><td>ns</td></tr>
<tr><td>VPT at first toe (V)</td><td>46.13 ± 18.24</td><td>48.42 ± 24.19</td><td>ns</td></tr>
<tr><td>VPT at malleolus (V)</td><td>40.08 ± 11.91</td><td>43.17 ± 15.22</td><td>ns</td></tr>
</table>
Characteristics of lesions treated are shown below.
<table>
<tr><th></th><th>Group A</th><th>Group B</th><th>ANOVA</th></tr>
<tr><td>Number of lesions (lesion/patient)</td><td>24 (1.2)</td><td>22 (1.05)</td><td>--</td></tr>
<tr><td>Maximum diameter (cm)</td><td>4.25 ± 2.35</td><td>4.32 ± 1.95</td><td>ns</td></tr>
<tr><td>Maximum depth (cm)</td><td>1.58 ± 2.20</td><td>1.98 ± 1.07</td><td>ns</td></tr>
<tr><td>Duration (days)</td><td>32.74 ± 19.25</td><td>39.43 ± 18.92</td><td>ns</td></tr>
</table>
The location of lesions is shown below
<table>
<tr><th></th><th>Group A</th><th>Group B</th></tr>
<tr><td>Plantar side n (%)</td><td>16 (67)</td><td>13 (59)</td></tr>
<tr><td>Medial first MTF joint n (%)</td><td>5 (21)</td><td>5 (23)</td></tr>
<tr><td>Lateral fifth MTF joint n (%)</td><td>2 (8)</td><td>4 (18)</td></tr>
<tr><td>Upper side of toes n (%)</td><td>1 (4</td><td>--</td></tr>
</table></td></tr>
<tr><td>Monitoring & definitions</td><td>Monitoring:
Patients were randomised to management groups based upon a table of randomisation.
Both treatments were performed on an outpatient basis. Following treatment, patients in group A were seen twice a week and</td></tr>
</table>

Bibliographic reference	**Piaggesi,A. Schipani,E. Campi,F. Romanelli,M. Baccetti,F. Arvia,C. Navalesi,R. (1998) Conservative surgical approach versus non-surgical management for diabetic neuropathic foot ulcers: a randomized trial, Diabetic Medicine 15 (5) 412-17**
	on these occasions lesions were irrigated with an antiseptic lotion and covered again with a saline moistened gauze Patients in Group B received surgical operations carried out with local or regional anaesthesia. They were observed for 3-4 hours after the intervention and then discharged home. The surgical wound was closed with stitches and removed after 48 hours. The wound was treated with a sterile gauze and the limb was positioned in an anti orthostatic position for 48 hours. The wound was treated with antiseptic solution twice a week and stitches were removed after 3 weeks. Patients in group B received systemic parenteral therapy with wide spectrum antibiotics 5 days after surgery. **Outcome measures:** The primary outcome was healing rate at follow-up (defined as complete re-epithilization of lesions in group A and formation of a continuous complete scar for group B); duration of healing time; prevalence of recurrence and number of infective complications.
Intervention	Patients in group B received outpatient surgery. Surgery consisted of removal of the ulcer through conic ulcerectomy (removing the walls and bottom of the ulcer). Bony segments which might interfere with wound closure were also debrided and removed with scalpels or a rong.
Comparison	After initial debridement, ulcers in group A were dressed with a saline moistened gauze (to be changed every 24 hours) and patients were given shoes with a custom-made orthosis.
Length of follow up	6 months
Location	Italy
Outcomes measures and effect size	**Healing rate:** All but one surgical wounds in group B closed by first intention (21/22; 95.5%) whereas 5 ulcers in group A failed to heal over the 6 months follow-up (19/24; 79.2%, p<0.05) but 4 of these did heal after 11 months **Healing time:** Ulcer healing time was significantly shorter in group B compared to group A (46.73 ± 38.94 days compared to 128.91 ± 86.60 days (p<0.001). Excluding the ulcers in group A that healed after 6 months also showed a significant difference (38.67 ± 9.56 days in group B compared to 98.11 ± 53.92 days in group A; p<0.001) **Ulcer recurrence:** During the 6 month follow-up recurrence of ulcer in group B was less frequent in group A (3/21, 14.3% versus 8/19; 41; 42.1%; p<0.01) In group A 5/8 recurrences occurred in the same site of previous ulceration whereas all recurrences for group B were in different sites to that of surgery.
Source of funding	**Number of infective complications:** Group A patients experienced significantly more complications than group B (3/24; 12.5%versus 1/22; 4.5%; p<0.05)
Authors conclusion	Surgical treatment proved to be an effective approach compared to conventional treatment, in terms of healing time,

Bibliographic reference	Piaggesi,A. Schipani,E. Campi,F. Romanelli,M. Baccetti,F. Arvia,C. Navalesi,R. (1998) Conservative surgical approach versus non-surgical management for diabetic neuropathic foot ulcers: a randomized trial, Diabetic Medicine 15 (5) 412-17
	complications and relapses for treatment of neuropathic foot ulcers in diabetes patients.

Table 58: Clever 1996

Bibliographic reference	Clever, H. U., & Dreyer, M. (1996). Comparing two wound dressings for the treatment of neuropathic diabetic foot ulcers. In Proceedings of the 5th European Conference on Advances in Wound Management (pp. 201-203).
Study type and aim	A randomised controlled trial (RCT) to evaluate the effectiveness of hydroactive versus hydrophilic dressing
Study quality	Very low
Patient characteristics	**Total number of participants:** 40 patients (20 received hydroactive dressing; 20 received hydrophilic dressing) **Inclusion criteria:** Patients aged 18-80 years with a pure neuropathic diabetic ulcer of 1-5 cm diameter **Exclusion criteria:** All patients with an ankle brachial pressure index <0.8 and with clinical or radiological signs of osteomyelitis. Large vessel disease. Allergies to the products. **Patient characteristics:** Baseline patient demographics are shown in the table below.

	hydroactive dressing	hydrophilic dressing
Number	20	20
Age (yr)	58.85 ± 11.64	53.15 ± 14.65
Duration of ulcer (days)	162.37 ± 325.55	165.00 ± 318.68
Male/female	15/5	17/3
Number of smokers	9	4
Mean size of ulcer	205.09	207.83
Ankle brachial pressure index	1.33 ± 0.24	1.27 ± 0.22
Systemic antibiotics yes/no	14/6	15/5

Bibliographic reference	**Clever, H. U., & Dreyer, M. (1996). Comparing two wound dressings for the treatment of neuropathic diabetic foot ulcers. In Proceedings of the 5th European Conference on Advances in Wound Management (pp. 201-203).**
	Vibration threshold **L** 1.50 ± 1.99 1.55 ± 1.90 **R** 1.35 ± 1.79 1.45 ± 1.73 **Recurrence of ulcer yes/no** 15/5 15/5
Monitoring & definitions	**Monitoring:** Standard treatment continued until healing occurred or for a maximum of 16 weeks. Dressing changes were performed as often as required, but at least once a week. **Outcome measures:** The primary outcome was healing time and wound reduction recorded by ulcer tracing and photographs.
Intervention	Hydroactive polyurethethane gel dressing Standard care consisted of pressure relief, infection control, wound cleansing and debridement as required.
Comparison	Hydrophilic dressing polyurethethane foam dressing Standard care consisted of pressure relief, infection control, wound cleansing and debridement as required.
Length of follow up	16 weeks
Location	Germany
Outcomes measures and effect size	**Wound reduction rate:** Mean reduction of ulcer Hydroactive = 172.72mm Hydrophilic = 174.37mm **Healing time:** Mean time to healing (SD) Hydroactive = 25.9 (23.52)days Hydrophilic = 20.43 (14.74) days Median time to healing

Bibliographic reference	Clever, H. U., & Dreyer, M. (1996). Comparing two wound dressings for the treatment of neuropathic diabetic foot ulcers. In Proceedings of the 5th European Conference on Advances in Wound Management (pp. 201-203).
	Hydroactive = 15.5 days (range = 4-76 days Hydrophilic = 16.5 days (range = 4-52 days)
Source of funding	Beiersdorg AG, Hamburg
Authors conclusion	Hydroactive dressing is as safe and effective as hydrophilic dressing in the management of diabetic foot ulcers

Table 59: Jensen 1997

Bibliographic reference	Jensen,J.L. Seeley,J. Gillin,B. (1997) Diabetic foot ulcerations. A controlled, randomized comparison of two moist wound healing protocols: Carrasyn Hydrogel Wound dressing and wet-to-moist saline gauze, Advances in Wound Care 11(7:Suppl):Suppl-4.
Study type and aim	A randomised controlled trial (RCT) to compare Carrasyn hydrogel wound dressings and a wet to moist saline gauze dressing in the management of diabetic foot ulcerations.
Study quality	Very low
Patient characteristics	**Total number of participants:** Thirty one patients with diabetic foot ulcers were randomised (14 received Carrasyn hydrogel wound dressings; CHWD; 17 received the control wet to moist saline gauze) **Inclusion criteria:** Inclusion criteria was approval of protocol and informed consent; diabetic foot ulcer of at least 1cm diameter; no evidence of infection in the ulcer or peri wound tissue; a Wagner grade II ulcer; documented blood supply with the ability to heal; **Exclusion criteria:** Not reported **Patient characteristics:** Baseline demographics were not reported. Baseline wound chronicity was not available for all patients, but where recorded, the data showed that average ulcer duration was longer in CHWD group versus saline gauze group (8.9 months versus 3.0 months

<table>
<tr><th>Bibliographic reference</th><th>Jensen,J.L. Seeley,J. Gillin,B. (1997) Diabetic foot ulcerations. A controlled, randomized comparison of two moist wound healing protocols: Carrasyn Hydrogel Wound dressing and wet-to-moist saline gauze, Advances in Wound Care 11(7:Suppl):Suppl-4.</th></tr>
<tr><td>Monitoring & definitions</td><td>Monitoring:
CHWD dressing or saline gauze changed daily. Patients were evaluated weekly for 16 weeks and followed for an additional 4 weeks. The ulcers were photographed, size documented and wound tracings recorded at each visit.
Outcome measures:
The primary outcome was complete wound closure (defined as complete re-epithilisation). Also considered were the average time to close; healing rate (reduction in wound area); complications and costs.</td></tr>
<tr><td>Intervention</td><td>Patients received dressing with CHWD applied over entire wound with a gauze pad, wrapped in a Kling bandage and secured with tape.</td></tr>
<tr><td>Comparison</td><td>Patients received a saline gauze dressing, cleansed with wound cleanser, dressed with gauze pad soaked in sterile saline, covered with Kling bandage and secured with tape. The dressing was re-moistened as needed.</td></tr>
<tr><td>Length of follow up</td><td>16 weeks treatment plus 4 weeks additional follow-up.</td></tr>
<tr><td>Location</td><td>USA</td></tr>
<tr><td>Outcomes measures and effect size</td><td>The table below shows the summary of findings
<table>
<tr><th></th><th>CHWD group</th><th>Saline gauze group</th></tr>
<tr><td>No of patients enrolled</td><td>14</td><td>17</td></tr>
<tr><td>Adverse events</td><td>2</td><td>4</td></tr>
<tr><td>No patients dropped</td><td>1</td><td>4</td></tr>
<tr><td>No patients completed</td><td>13</td><td>13</td></tr>
<tr><td>No ulcers healed</td><td>11 (84.6%)</td><td>6 (46.1%)</td></tr>
<tr><td>No failed to close</td><td>2 (15.4%)</td><td>11 (53.9%)</td></tr>
<tr><td>Average time to close (weeks)</td><td>10.30</td><td>11.69</td></tr>
<tr><td></td><td></td><td></td></tr>
</table>
Wound closure rate was greater in the CHWD group compared to the saline gauze group (84.6% vs 46.1%, p=0.05)
Average time to close was also shorter (CHWD= 10.30 weeks versus saline gauze = 11.69 weeks)

The following table shows comparative costs per day for the two groups.
<table>
<tr><th></th><th>CHWD group ($)</th><th>Saline gauze group($)</th></tr>
<tr><td>Nursing time</td><td>4.00</td><td>8.00</td></tr>
<tr><td>Wound gel</td><td>0.53</td><td>--</td></tr>
</table></td></tr>
</table>

Bibliographic reference	**Jensen,J.L. Seeley,J. Gillin,B. (1997) Diabetic foot ulcerations. A controlled, randomized comparison of two moist wound healing protocols: Carrasyn Hydrogel Wound dressing and wet-to-moist saline gauze, Advances in Wound Care 11(7:Suppl):Suppl-4.**
	Sterile saline -- 1.30 **Gauze** 0.50 1.00 **Ultraklenz** 0.38 0.38 **Kling** 1.50 1.50 **Tape** 0.10 0.10 **Total** 7.01 12.28
Source of funding	Grant from Carrington laboratories inc
Authors conclusion	Use of CHWD resulted in better patient outcomes than saline gauze but further controlled trials are needed to document or disprove these findings.

Table 60: Gottrup 2013

Bibliographic reference	**Gottrup,F. Cullen,B.M. Karlsmark,T. Bischoff-Mikkelsen,M. Nisbet,L. Gibson,M.C. (2013) Randomized controlled trial on collagen/oxidized regenerated cellulose/silver treatment, Wound Repair & Regeneration 21 (2) 216-25.**
Study type and aim	A two centre, randomised controlled trial (RCT) to compare the clinical outcomes of collagen/oxidised regenerated cellulose (ORC)/ silver therapy or control treatment
Study quality	Moderate
Patient characteristics	**Total number of participants:** A total of 39 patients were randomised to treatment (n=24 in collagen/ORC/silver therapy; n=15 received control therapy). **Inclusion criteria:** Eligible participants were patients with diabetes aged 35-80 years with diabetic foot ulcer of at least 30 days duration (Wagner grade 2 or 3; no local or systemic signs of infection, normal leukocyte and CRP levels **Exclusion criteria:** Exclusion criteria was known allergies to collagen/ORC/silver; peripheral arterial disease or toe pressure ≤ 45mm,concomitant

<table>
<tr><th>Bibliographic reference</th><th>Gottrup,F. Cullen,B.M. Karlsmark,T. Bischoff-Mikkelsen,M. Nisbet,L. Gibson,M.C. (2013) Randomized controlled trial on collagen/oxidized regenerated cellulose/silver treatment, Wound Repair & Regeneration 21 (2) 216-25.</th></tr>
<tr><td></td><td>conditions known to have interfered with the wound healing; pregnancy or lactating; history of drug misuse or excessive alcohol consumption; undergoing chemotherapy; inability to walk; patient suffers from hemolytic iron and/or anaemia deficiency; malnutrition, severe cardiac, hepatic, renal, pulmonary insufficiency, or chronic administration of cortisones for chronic inflammatory disease and/or autoimmune disease.
Patient characteristics:
Baseline patient characteristics are shown in the table below
<table>
<tr><th></th><th>Collagen/ORC/silver (n=24)</th><th>Control (n=15)</th><th>P-value</th></tr>
<tr><td>Female (%)</td><td>2 (8.3%)</td><td>2 (13.3%)</td><td>0.631</td></tr>
<tr><td>Age (years)</td><td>62.9 ± 13.5 (35-85)</td><td>57.6 ± 14.6 (29-92)</td><td>0.242</td></tr>
<tr><td>Diagnosed with lower extremity vascular disease</td><td>9 (37.5%)</td><td>5 (33.3%)</td><td>0.305</td></tr>
<tr><td>Ankle brachial index</td><td>0.94 ± 0.11</td><td>0.97 ± 0.15</td><td>0.532</td></tr>
<tr><td>Toe pressure (mm Hg)</td><td>95.62 ± 31.11</td><td>83 ± 30.8</td><td>0.176</td></tr>
<tr><td>Toe brachial index</td><td>0.71 ± 0.31</td><td>0.58 ± 0.21</td><td>0.273</td></tr>
<tr><td>HBA1c (%)</td><td>6.54 ± 3.73 (0.05-10.9)</td><td>5.19 ± 4.17 (0.05-11.8)</td><td>0.259</td></tr>
<tr><td>Duration of diabetes diagnosis (years)</td><td>17.2 ± 11.9 (2-50)</td><td>14.4 ± 10.7 (0.08-37)</td><td>0.466</td></tr>
<tr><td>Wound duration (months)</td><td>12.9 ± 13.0 (1-48)</td><td>16.9 ± 36.6 (1-144)</td><td>0.651</td></tr>
<tr><td>Wound area (cm^2)</td><td>2.1 ± 3.1 (0.5-15.9)</td><td>4.4 ± 6.3 (0.4-22.7)</td><td>0.334</td></tr>
<tr><td>Wound depth (cm)</td><td>0.35 ± 0.18 (0.1-0.7)</td><td>0.51 ± 0.54 (0.1-2.0)</td><td>0.791</td></tr>
</table></td></tr>
<tr><td>Monitoring & definitions</td><td>Monitoring:
Randomisation was performed independently of research team by random number table. Group assignment was kept in sealed envelopes.
Outcome measures:
The primary outcome was response to treatment. (≥ 50% reduction in wound area by week 4), healing (full epithelialisation).
The secondary outcome was withdrawals due to infection.,</td></tr>
<tr><td>Intervention</td><td>The collagen/ORC/silver dressing was applied directly to the wound bed</td></tr>
<tr><td>Comparisons</td><td>The control group received standard treatment (not detailed in the study) although the same type of foam dressing was used for both intervention & control groups.</td></tr>
<tr><td>Length of follow up</td><td>14 weeks</td></tr>
<tr><td>Location</td><td>Denmark</td></tr>
</table>

<table>
<tr><th>Bibliographic reference</th><th>Gottrup,F. Cullen,B.M. Karlsmark,T. Bischoff-Mikkelsen,M. Nisbet,L. Gibson,M.C. (2013) Randomized controlled trial on collagen/oxidized regenerated cellulose/silver treatment, Wound Repair & Regeneration 21 (2) 216-25.</th></tr>
<tr><td>Outcomes measures and effect size</td><td>The table below shows the clinical outcomes of the treatment groups.
<table>
<tr><td></td><td>≥ 50% reduction in wound area by week 4</td><td>Healed by week 14</td><td>Withdrew due to infection</td></tr>
<tr><td>Collagen/ORC/silver</td><td>19/24 (79%)</td><td>12/23 (52%)</td><td>0/23 (0%)</td></tr>
<tr><td>Control</td><td>6/14 (43%)</td><td>4/13 (31%)</td><td>4/13 (31%)</td></tr>
<tr><td>P-value</td><td>0.035</td><td>ns</td><td>0.012</td></tr>
<tr><td>Fishers exact test</td><td></td><td>p>0.05</td><td></td></tr>
</table>
Percentage reduction in wound area:
Significantly more wounds in the collagen/ORC/silver treatment reached 50% closure at 4 weeks follow-up (19/24 79%) compared to the control group 6/14 43%) p=0.035
At the end of the study 91% of wounds in the collagen/ORC/silver group had either healed or reduced to 50% closure compared to 69% in the control group

Withdrawals due to infection:
In the control group there were 4/13 (31%) of patients withdrawn compared to 0/23 (0%) in the collagen/ORC/silver group (p=0.012)

Adverse events:
There were no adverse events in the collagen/ORC/silver group compared to 5 reported in the control group</td></tr>
<tr><td>Source of funding</td><td>A financial grant from Systagenix</td></tr>
<tr><td>Authors conclusion</td><td>Collagen/ORC/silver treatment consistently increased healing compared with control treatment.</td></tr>
<tr><td></td><td></td></tr>
</table>

Table 61: Donaghue 1998

Bibliographic reference	Donaghue,V.M, Chrzan,J.S. Rosenblum,B.I. Giurini,J.M. Habershaw,G.M.; Veves,A. (1998) Evaluation of a collagen-alginate wound dressing in the management of diabetic foot ulcers, Advances in Wound Care 11(3) 114-19.
Study type and aim	An open label randomised controlled trial (RCT) to examine the effectiveness, safety and patient acceptability of a collagen-

<table>
<tr><th>Bibliographic reference</th><th>Donaghue,V.M, Chrzan,J.S. Rosenblum,B.I. Giurini,J.M. Habershaw,G.M.; Veves,A. (1998) Evaluation of a collagen-alginate wound dressing in the management of diabetic foot ulcers, Advances in Wound Care 11(3) 114-19.</th></tr>
<tr><td></td><td>alginate dressing compared to a saline moistened gauze</td></tr>
<tr><td>Study quality</td><td>Very low</td></tr>
<tr><td>Patient characteristics</td><td>Total number of participants:
A total of 75 patients were included in the trial
Inclusion criteria:
Inclusion criteria was patients aged at least 21 years, adequate nutritional update; adequate blood flow to the lower extremities; foot ulceration of at least 1cm2
Exclusion criteria:
Exclusion criteria were severe renal or liver impairment; any medical disorder; evidence of osteomyelitis; clinical signs of infection; a history of alcohol abuse.
Patient characteristics:
Patient demographics are shown in the table below:
<table>
<tr><th></th><th>Intervention group</th><th>Control group</th><th>Statistics</th></tr>
<tr><td>No of patients</td><td>50</td><td>25</td><td></td></tr>
<tr><td>Males/ females</td><td>33/17</td><td>21/4</td><td>p=0.171</td></tr>
<tr><td>Age, years (range)</td><td>59 (30-81)</td><td>60 (33-79)</td><td>T=0.3374
p=0.69961</td></tr>
<tr><td>Diabetes duration, years, (range)</td><td>19 (4-47)</td><td>17 (2-25)</td><td>T=0.9443
p=0.3481</td></tr>
<tr><td>Weight, pounds</td><td>195 ± 45</td><td>214 ± 49</td><td>p=0.1052</td></tr>
<tr><td>Retinopathy</td><td>28 (56%)</td><td>19 (76%)</td><td>p= 0.901</td></tr>
<tr><td>Creatinine (mg/dL)</td><td>1.2 ± 0.6</td><td>1.14 ± 0.06</td><td>p=0.5433</td></tr>
<tr><td>Serum albumin (grams/dL)</td><td>3.72 ± 0.07</td><td>3.79 ± 0.11</td><td>T=0.5582
p=0.5784</td></tr>
</table>
The following table shows baseline ulcer characteristics
<table>
<tr><th></th><th>Intervention group</th><th>Control group</th><th>Statistics</th></tr>
<tr><td>No of patients completing study</td><td>50</td><td>25</td><td></td></tr>
<tr><td>Ulcer duration (days)</td><td>148 ± 73</td><td>225 ±104</td><td>T=0.6204
p=0.5369</td></tr>
<tr><td>Range (days)</td><td>1-365</td><td>1-1,825</td><td></td></tr>
</table></td></tr>
</table>

Bibliographic reference	**Donaghue,V.M, Chrzan,J.S. Rosenblum,B.I. Giurini,J.M. Habershaw,G.M.; Veves,A. (1998) Evaluation of a collagen-alginate wound dressing in the management of diabetic foot ulcers, Advances in Wound Care 11(3) 114-19.**
	Ulcer size (cm^2) 2,6 ± 0.50 2.99 ± 0.62 T=0.49 p=0.6237 **Wagner stage** p=0.310 **I** 8 (16%) 1 (4%) **II** 36 (72%) 20 (80%) **III** 6 (12%) 4 (16%)
Monitoring & definitions	**Monitoring:** Patients were assigned in a 2:1 ratio to treatment groups. They received a physical examination and review of medical history, and evaluation of the ulcer at the initial patient visit. All patients and caregivers were given specific wound change instructions. Patients were seen on a weekly basis, where the dressing was observed for exudate. The ulcer was examined and treated at each visit. **Outcome measures:** The main outcomes were reduction in wound area; complete healing rate; time to healing. And adverse events.
Intervention	Patients received collagen-alginate dressing
Comparison	Patients received a conventional dressing of saline gauze
Length of follow up	8 weeks or until complete ulcer healing
Location	USA
Outcomes measures and effect size	**Mean percentage in wound reduction:** The mean percentage in wound reduction was 80.6% in the intervention group and 61.1% in the control group (p=0.4692) **Complete wound healing:** Complete healing was achieved in 24/50 (48%) of the intervention group versus 9/25 (36%) in the control group (p=0.3933) **Mean time to complete healing:** Mean time to complete healing was 6.2 ± 0.4 weeks for the intervention group versus 5.8 ± 0.4 weeks for the control group. **Adverse events:** There was no difference in the number or severity of adverse reactions between treatment groups (p=0.453)
Source of funding	Not reported
Authors conclusion	Collagen-alginate dressing is as effective and safe as the currently used treatment.

Bibliographic reference	Donaghue,V.M, Chrzan,J.S. Rosenblum,B.I. Giurini,J.M. Habershaw,G.M.; Veves,A. (1998) Evaluation of a collagen-alginate wound dressing in the management of diabetic foot ulcers, Advances in Wound Care 11(3) 114-19.

Table 62: Armstrong 2005

Bibliographic reference	Armstrong DG, Lavery LA, Wu S, Boulton AJ. (2005) Evaluation of removable and irremovable cast walkers in the healing of diabetic foot wounds: a randomized controlled trial. Diabetes Care 28 (3) 551-4
Study type and aim	A randomised controlled trial (RCT) to examine the effectiveness of an instant total contact cast (iTCC) a removable cast walker (RCW) for healing neuropathic diabetic foot ulcerations.
Study quality	Moderate
Patient characteristics	**Total number of participants:** A total of 50 participants were randomised to treatment with one of two different off-loading modalities. **Inclusion criteria:** All patients had a neuropathic diabetic plantar and foot ulcer corresponding to the University of Texas classification as grade 1A They had experienced the loss of protective sensation and had at least one palpable foot pulse. **Exclusion criteria:** Patients with active infection; unable to walk without a wheelchair; with wounds in location on the heel, rear-foot; or a location other than plantar; or patients with severe peripheral vascular disease were excluded. **Patient characteristics:** The table below shows baseline patient characteristics.

	N	Age (years)	BMI (kg/m^2)	Males	Wound size (cm^2)	Vibration perception threshold	HbA1C
Total	50	65.6 ± 9.9	33.4 ± 6.4	88.0 (44)	2.3 ± 1.2	37.1 ± 7.5	8.2 ± 1.4
iTCC	23	66.9 ± 10.1	33.3 ± 6.8	87.0 (20)	2.7 ± 1.3	37.0 ± 8.1	8.5 ± 1.5
RCW	27	64.6 ± 9.8	33.5 ± 6.2	88.9 (24)	2.0 ± 1.1	37.3 ± 7.0	8.0 ± 1.4

Monitoring & definitions	**Monitoring:** Patients were assigned to treatment groups using a computerised randomisation schedule. All patients were instructed to use

Bibliographic reference	**Armstrong DG, Lavery LA, Wu S, Boulton AJ. (2005) Evaluation of removable and irremovable cast walkers in the healing of diabetic foot wounds: a randomized controlled trial. Diabetes Care 28 (3) 551-4**
	their devices all times during ambulation and were followed up on a weekly basis to inspect wound, provide wound care and wound debridement. **Outcome measures:** The main outcome was wound healing; time to wound healing was assessed; and a Kaplan Meier was used to predict wound survival.
Intervention	Patients received treatment with an iTCC (a RCW wrapped in a cohesive bandage - to make it irremovable).
Comparison	Patients received treatment with an RCW.
Length of follow up	12 weeks
Location	UK
Outcomes measures and effect size	**Wound healing:** Significantly more patients in the iTCC group healed at 12 weeks compared to the RCW group (19 versus14 patients; 82.6% versus 51.9%; OR 1.8 [95%CI 1.1-2.9; p=0.02) **Time to wound healing:** Patients treated with the iTCC healed significantly sooner than the RCW group (41.6 ± 18.7 days versus 58.0 ± 15.2 days; p=0.02)
Source of funding	Not reported
Authors conclusion	Modifying an RCW to increase patient adherence to that jpressure off-loading may have an increase on the proportion of the ulcers that heal and the rate of healing in patients with diabetic neuropathic wounds.

Table 63: Faglia 2010

Bibliographic reference	**Faglia, E., Caravaggi, C., Clerici, G., Sganzaroli, A., Curci, V., Vailati, W., ... & Sommalvico, F. (2010). Effectiveness of Removable Walker Cast Versus Nonremovable Fiberglass Off-Bearing Cast in the Healing of Diabetic Plantar Foot Ulcer A randomized controlled trial. Diabetes care, 33(7), 1419-1423.**
Study type and aim	An open randomised controlled trial (RCT) to evaluate the efficacy of a removable cast walker (RCW) compared to a non-removable fiber glass off-bearing cast in the treatment of diabetic plantar foot ulcers.
Study quality	Low
Patient characteristics	**Total number of participants:** Out of 48 patients screened for participation, 45 took part in the trial.

<table>
<tr><th>Bibliographic reference</th><th>Faglia, E., Caravaggi, C., Clerici, G., Sganzaroli, A., Curci, V., Vailati, W., ... & Sommalvico, F. (2010). Effectiveness of Removable Walker Cast Versus Nonremovable Fiberglass Off-Bearing Cast in the Healing of Diabetic Plantar Foot Ulcer A randomized controlled trial. Diabetes care, 33(7), 1419-1423.</th></tr>
<tr><td></td><td>Inclusion criteria:
Patients with a neuropathic forefoot plantar ulcer classification were eligible for inclusion.
Exclusion criteria:
An ankle brachial index of less than 0.9 and/or transcutaneous oxygen tension less than 50mmHg and clinical signs of infection were excluded. Additional exclusion was use of steroids or antimitotic drugs; visual problems; ulcers on the contralateral limb; previous major amputation on contralateral limb; previous or calurrent deep vein thrombosis of the lrmental disorders.
Patient characteristics:
The table below shows baseline characteristics.
<table>
<tr><th></th><th>TCC group</th><th>Fiber glass cast group</th><th>P value</th></tr>
<tr><td>n</td><td>23</td><td>22</td><td>0.35</td></tr>
<tr><td>Age (years)</td><td>59.0 ± 8.5</td><td>61.7 ± 10.4</td><td>0.83</td></tr>
<tr><td>Sex (female/male)</td><td>8 (34.8)/15 (65.2)</td><td>7 (31.8)/15 (68.2)</td><td>0.21</td></tr>
<tr><td>Diet/insulin/oral therapy</td><td>4(17.4)/16(69.6)/3(13.0)</td><td>5(22.7)/10(45.5)/7(31.8)</td><td>0.88</td></tr>
<tr><td>Duration of diabetes (years)</td><td>17.7 ± 11.2</td><td>17.2 ± 10.7</td><td>0.16</td></tr>
<tr><td>BMI (kg/m^2)</td><td>32.3 ± 4.5</td><td>30.3 ± 1.1</td><td>0.18</td></tr>
<tr><td>A1c (% Hb)</td><td>9.1 ± 2.1</td><td>7.5 ± 1.1</td><td>0.82</td></tr>
<tr><td>Previous foot ulcer</td><td>15 (65.2)</td><td>15 (68.2)</td><td>0.85</td></tr>
<tr><td>Previous minor amputation</td><td>11 (47.8)</td><td>12 (54.5)</td><td>0.65</td></tr>
<tr><td>Mean area of lesion (cm^2)</td><td>1.4 ± 1.2</td><td>2.2 ± 2.2</td><td>0.47</td></tr>
</table></td></tr>
<tr><td>Monitoring & definitions</td><td>Monitoring:
Ulcers were debrided a initial visit, photographed and measured, dressed with paraffin gauze (covered in sterile gauze) before application of off-loading. At each follow-up off-loading devices were removed, dressings were changed, photographed and measured.
Outcome measures:
The primary outcome was decrease in ulcer size. The secondary outcome was rate of complete healing at end of study period.</td></tr>
<tr><td>Intervention</td><td>Patients received a TCC</td></tr>
<tr><td>Comparison</td><td>Patients received the Stabil-D device with a rigid boat shaped, fully rocker sole</td></tr>
</table>

Bibliographic reference	**Faglia, E., Caravaggi, C., Clerici, G., Sganzaroli, A., Curci, V., Vailati, W., ... & Sommalvico, F. (2010). Effectiveness of Removable Walker Cast Versus Nonremovable Fiberglass Off-Bearing Cast in the Healing of Diabetic Plantar Foot Ulcer A randomized controlled trial. Diabetes care, 33(7), 1419-1423.**
Length of follow up	12 weeks or until complete reepithelisation.
Location	Italy
Outcomes measures and effect size	**Wound healing:** In the TCC group 17 patients (73.9%) achieved complete wound healing compared to 16 patients (72.7%) in the fiberglass cast group (p=0.794). **Wound reduction:** Ulcer surfaces decreased from 1.41 to 0.21cm^2 in the TCC group (p=<0.001) compared to 2.18 to 0.45cm^2 in the fiberglass cast group (p=<0.001). The difference between groups was non significant (p=0.708). **Healing time:** The mean duration of healing in the TCC group was 35.3 ± 3.1 days compared to 39.7 ± 4.2 days in the fiberglass cast group (p=0.708)
Source of funding	Not reported
Authors conclusion	The fiberglass cast walker is equivalent to the TCC in terms of ulcer size reduction and healing rate.

Table 64: Caravaggi 2000

Bibliographic reference	**Caravaggi,C. Faglia,E. De,Giglio R. Mantero,M. Quarantiello,A. Sommariva,E. Gino,M. Pritelli,C. et al (2000) Effectiveness and safety of a nonremovable fiberglass off-bearing cast versus a therapeutic shoe in the treatment of neuropathic foot ulcers: a randomized study, Diabetes Care 23 (12) 1746-51**
Study type and aim	A randomised controlled trial (RCT) to examine the effectiveness of a non-removable fiberglass off-bearing cast compared to a cloth shoe with a rigid sole for patients with diabetes and neuropathic foot ulcers.
Study quality	Moderate
Patient characteristics	**Total number of participants:** Fifty patients were enrolled via telephone to one of two pre-randomised treatment groups. Twenty four received the therapeutic

<table>
<tr><th>Bibliographic reference</th><th>Caravaggi,C. Faglia,E. De,Giglio R. Mantero,M. Quarantiello,A. Sommariva,E. Gino,M. Pritelli,C. et al (2000) Effectiveness and safety of a nonremovable fiberglass off-bearing cast versus a therapeutic shoe in the treatment of neuropathic foot ulcers: a randomized study, Diabetes Care 23 (12) 1746-51</th></tr>
<tr><td></td><td>shoe; 26 received the fiberglass cast.
Inclusion criteria:
All patients were insensitive to a monofilament and had a vibration perception threshold of 25V.
Exclusion criteria:
Exclusion criteria included presence of deep or superficial tissue infection; underlying osteomyelitis; transcutaneous PO_2;severe problems in maintaining equilibrium; severe visual deficit; skin lesions of the foot; ; leg amputation; plantar bilateral ulcerations
Patient characteristics:
The table below shows baseline characteristics
<table>
<tr><th>Clinical characteristics</th><th>Shoe group</th><th>Cast group</th><th>P</th></tr>
<tr><td>Age (years)</td><td>59.2 ± 9.9</td><td>60.5 ± 10.7</td><td>0.70</td></tr>
<tr><td>Female/Male</td><td>8/16</td><td>8/18</td><td>0.94</td></tr>
<tr><td>Tablet treatment</td><td>12</td><td>13</td><td>---</td></tr>
<tr><td>Insulin treatment</td><td>12</td><td>13</td><td>---</td></tr>
<tr><td>Diabetes duration (years)</td><td>16.2 ± 9.1</td><td>17.3 ± 10.7</td><td>0.93</td></tr>
<tr><td>Prior lesion</td><td>9</td><td>10</td><td>0.24</td></tr>
<tr><td>BMI (kg/m^2)</td><td>27.3 ± 2.5</td><td>27.0 ± 1.6</td><td>0.34</td></tr>
<tr><td>Smoking</td><td>10</td><td>5</td><td>0.08</td></tr>
<tr><td>Hypertension</td><td>11</td><td>13</td><td>0.78</td></tr>
<tr><td>Retinopathy</td><td>13</td><td>14</td><td>0.98</td></tr>
<tr><td>Microalbuminuria</td><td>4</td><td>4</td><td></td></tr>
<tr><td>Proteinuria</td><td>3</td><td>5</td><td>0.56</td></tr>
<tr><td>Renal impairment</td><td>2</td><td>5</td><td></td></tr>
<tr><td>Ankle brachial index</td><td>1.03 ± 0.8</td><td>1.00 ± 0.7</td><td>0.18</td></tr>
<tr><td>Transcutaneous oxygen tension on dorsum of foot</td><td>52.6 ± 11.6</td><td>53.5 ± 12.6</td><td>0.80</td></tr>
</table></td></tr>
<tr><td>Monitoring & definitions</td><td>Monitoring:
Ulcer area was traced using a transparent dressing and the area was calculated using an image analysis. Tracings were performed on day of entry and after 30 days of treatment. All ulcers were medicated with a paraffin gauze throughout the study and surgically debrided if necessary. Dressings were changed by the patient every 2 days.
Outcome measures:</td></tr>
</table>

Bibliographic reference	Caravaggi,C. Faglia,E. De,Giglio R. Mantero,M. Quarantiello,A. Sommariva,E. Gino,M. Pritelli,C. et al (2000) Effectiveness and safety of a nonremovable fiberglass off-bearing cast versus a therapeutic shoe in the treatment of neuropathic foot ulcers: a randomized study, Diabetes Care 23 (12) 1746-51
	The primary outcome was rate of reduction in the surface area. Secondary outcomes were side effects and patient acceptance of treatment.
Intervention	Patients received a fiberglass off-bearing cast
Comparison	Patients received a cloth therapeutic shoe with a rocker-bottom sole
Length of follow up	30 days
Location	Italy
Outcomes measures and effect size	**Reduction in ulcer area:** At 30 days the ulcers had healed completely in5 patients treated with shoe compared to 13 patients treated with the cast (χ^2 =4.6079; p=0.032) At 30 days 2 patients in the foot group had an increase in ulcer size compared to 0 in the cast group. **Side effects:** There were no side effects in either group during the 30 day observation period.
Source of funding	Not reported
Authors conclusion	The study showed that the use of off-bearing casts is the elective treatment for neuropathic plantar ulcers.

Table 65: Gutekunst 2011

Bibliographic reference	Gutekunst,D.J. Hastings,M.K. Bohnert,K.L. Strube,M.J. Sinacore,D.R. (2011) Removable cast walker boots yield greater forefoot off-loading than total contact casts, Clinical Biomechanics 26 (6)649-54.
Study type and aim	A randomised controlled trial (RCT) to compare the off-loading capabilities of a total contact cast (TCC) and a removable cast walker (RCW) boot for plantar loading during barefoot walking
Study quality	Low
Patient characteristics	**Total number of participants:** A total of 23 patients took part in the study (11 received TCC; 12 received RCW) **Inclusion criteria:** Patients with diabetes and one or more plantar ulcer were eligible for inclusion. Patients had to have peripheral neuropathy

<table>
<tr><th>Bibliographic reference</th><th>Gutekunst,D.J. Hastings,M.K. Bohnert,K.L. Strube,M.J. Sinacore,D.R. (2011) Removable cast walker boots yield greater forefoot off-loading than total contact casts, Clinical Biomechanics 26 (6)649-54.</th></tr>
<tr><td></td><td>and ulcers classed as grade I or II according to the Wagner classification system.
Exclusion criteria:
Patients with infection, lower extremity ischemia or cellulitis were excluded.
Patient characteristics:
Baseline characteristics are shown in the table below.
<table>
<tr><td></td><td>TCC group</td><td>RCW group</td><td>P value</td></tr>
<tr><td>n</td><td>11</td><td>12</td><td></td></tr>
<tr><td>Sex (f/m)</td><td>2/9</td><td>2/10</td><td>1.00</td></tr>
<tr><td>Type of diabetes (T1/T2)</td><td>1/10</td><td>2/10</td><td>1.00</td></tr>
<tr><td>Ulcer location (forefoot/midfoot)</td><td>8/3</td><td>11/1</td><td>0.23</td></tr>
<tr><td>Age (years)</td><td>55 (13)
95%CI 48-63</td><td>53 (10)
95%CI 48-59</td><td>0.69</td></tr>
<tr><td>Height (cm)</td><td>183 (8)
95%CI 179-188</td><td>183 (10)
95%CI 177-188</td><td>0.83</td></tr>
<tr><td>Mass (kg)</td><td>31.4 (6.2)
95%CI 90-123</td><td>32.3 (4.5)
95%CI 29.7-34.8</td><td>0.92</td></tr>
<tr><td>BMI</td><td>31.4 (6.2)
95%CI 27.8-35.1</td><td>32.3 (4.5)
95%CI 29.7-34.8</td><td>0.71</td></tr>
<tr><td>HBA1c</td><td>8.5 (2.3) (6.2)
95%CI 7.1-9.8</td><td>8.9 (1.8)
95%CI 29.7-34.8)</td><td>0.64</td></tr>
<tr><td>Diabetes duration (years)</td><td>19 (14)
95%CI 8-26</td><td>17 (13)
95%CI 10-24</td><td>0.79</td></tr>
<tr><td>Walking speed (m/min)</td><td>53 (16)
95%CI 44-62</td><td>94 (64)
95%CI 48-62</td><td>0.70</td></tr>
</table></td></tr>
<tr><td>Monitoring & definitions</td><td>Monitoring:
Patients were randomised to treatment groups using a software randomisation programme in an open, unblended manner. For both off-loading modalities patients feet were cleaned and covered with an antimicrobial sock. Patients in the TCC group had a layer of low density foam padding to cover the toes. A Pedar insole was placed between he sock and inner layer of plaster.
For patients in the RCW group the Pedar insole was placed in the bottom of the pressure relief walker. Patients in both group wore their own footwear on the contralateral foot.
Outcome measures:</td></tr>
</table>

Bibliographic reference	Gutekunst,D.J. Hastings,M.K. Bohnert,K.L. Strube,M.J. Sinacore,D.R. (2011) Removable cast walker boots yield greater forefoot off-loading than total contact casts, Clinical Biomechanics 26 (6)649-54.
	The main outcome was force reduction, peak pressure and pressure reduction. Other outcomes included ulcer healing proportion and ulcer healing time.
Intervention	Patients received RCW
Comparison	Patients received TCC
Length of follow up	Not reported
Location	USA
Outcomes measures and effect size	**Ulcer healing:** In the TCC group 9/11 (82%) of patients had ulcers that healed compared to 5/12 (42%) of patients in the RCW group (p<0.05) **Ulcer healing time:** In the TCC the mean duration of healing was 95 days (SD=61) compared to 94 days (SD=64) in the RCW group (p=0.95) **Force reduction, peak pressure and pressure time** In the midfoot mask there was a significantly greater reduction in peak pressure in the RCW group (77%) compared to the TCC group (63%,p=0.036) In the forefoot there were significantly greater reductions in the RCW group compared to the TCC group (92% versus 84%), pressure time integral (94% versus 85%), maximum force (86% versus 75%) and force time integral (91% versus 79%)
Source of funding	Not reported
Authors conclusion	Cast walker boots provided greater off-loading reduction in the forefoot for patients with diabetes and plantar ulcers. However, a total contact cast or cast walker rendered irremovable does provide better healing outcomes.

Table 66: Zimny 2003

<table>
<tr><th>Bibliographic reference</th><th>Zimny,S. Schatz,H. Pfohl,U. (2003) The effects of applied felted foam on wound healing and healing times in the therapy of neuropathic diabetic foot ulcers, Diabetic Medicine 20 (8) 622-25.</th></tr>
<tr><td>Study type and aim</td><td>A randomised controlled trial (RCT) to evaluate the effects of felted foam on wound healing in diabetic foot ulcers compared to a standard method of plantar pressure relief.</td></tr>
<tr><td>Study quality</td><td>Low</td></tr>
<tr><td>Patient characteristics</td><td>Total number of participants:
A total of 54 patients were randomised to treatment (24 patients received felted foam; 30 patients received a conventional therapy).
Inclusion criteria:
Patients had type 1 or type 2 diabetes and plantar ulcers Wagner grade 1 or 2.
Exclusion criteria:
Patients with peripheral vascular occlusive disease were not included.
Patient characteristics:
The table below shows baseline characteristics
<table>
<tr><th></th><th>Felted foam group (n=24)</th><th>Conventional group (n=30)</th></tr>
<tr><td>Age (years)</td><td>62.1 ± 13.0</td><td>62.1 ± 10.8</td></tr>
<tr><td>BMI (kg/m^2)</td><td>27.4 ± 4.9</td><td>28.5 ± 4.3</td></tr>
<tr><td>Male/female</td><td>13/11</td><td>17/13</td></tr>
<tr><td>Type 1/2 diabetes</td><td>7/17</td><td>13/17</td></tr>
<tr><td>Diabetes duration (years)</td><td>18.2 ± 7.6</td><td>22.1 ± 11.8</td></tr>
<tr><td>HBA1c (%)</td><td>7.9 ± 0.6</td><td>7.5 ± 1.2</td></tr>
<tr><td>Transcutaneous partial Oxygen therapy (kPa)</td><td>8.9 ± 1.3</td><td>8.7 ± 1.0</td></tr>
<tr><td>Ankle brachial index</td><td>1.0 ± 0.1</td><td>1.0 ± 0.2</td></tr>
<tr><td>Ulcer localisation metatarsal head I-III/ IV-V</td><td>19/5</td><td>24/6</td></tr>
<tr><td>Wagner grade 1/2</td><td>6/18</td><td>7/23</td></tr>
</table></td></tr>
<tr><td>Monitoring & definitions</td><td>Monitoring:
All patients received identical wound care which included debridement and daily monitoring of wound. If there were signs of infection appropriate antibiotics were given.
The felted foam dressing was measured to fit exactly to fit the plantar of the foot and an aperture was cut at the exact location of the ulcer. The foot was wrapped in a gauze and wrapped around the foot. The wound was covered in a saline soaked</td></tr>
</table>

	sponge. The dressing was changed every 3 days. Wounds were traced at entry and at each follow up **Outcome measures:** The main outcomes were healing time and healing reduction.
Intervention	Patients received a felted foam dressing.
Comparison	Patients received a pressure relief half shoe.
Length of follow up	10 weeks
Location	Germany
Outcomes measures and effect size	**Wound reduction:** The mean wound radius reduction was 0.48 mm (95%CI 0.42-0.56) in the felted foam group compared to 0.39 mm (95%CI 0.35-0.42) in the conventional group (p=0.06) **Healing time:** The mean healing time was 75.2 days (95%CI 67-84 days) in the felted foam group compared to 85.2 days (95%CI 79-92 days) in the conventional group (p=0.03)
Source of funding	Not reported
Authors conclusion	Felted foam treatment appears to be as effective as conventional treatment for neuropathic foot ulcerations

Table 67: Zhang 2014

Bibliographic reference	**Zhang, Y., & Xing, S. Z. (2014). Treatment of Diabetic Foot Ulcers using Mepilex Lite Dressings: A Pilot Study. Experimental and Clinical Endocrinology & Diabetes, 122(04), 227-230.**
Study type	Randomised controlled trial
Study quality	Summary Population: China Intervention:.Standard care with Soft silicone dressing Comparison:.Standard care with vasline gauze dressing Outcomes: wound healing, healing time, wound pain, adverse events

<table>
<tr><th>Bibliographic reference</th><th>Zhang, Y., & Xing, S. Z. (2014). Treatment of Diabetic Foot Ulcers using Mepilex Lite Dressings: A Pilot Study. Experimental and Clinical Endocrinology & Diabetes, 122(04), 227-230.</th></tr>
<tr><td></td><td>1) Has an appropriate method of randomisation been used? - UNCLEAR – not reported
2) Was there adequate concealment of allocation? UNCLEAR – Not reported
3) Were the groups comparable at baseline for all major confounding/prognostic factors? - YES
4) Did the comparison groups receive the same care apart from interventions studied? - YES
5) Were participants receiving care kept blind to treatment allocation? – UNCLEAR – not reported
6) Were the individuals administering care kept blind to treatment allocation? - UNCLEAR – not reported
7) Were groups comparable with respect to availability of outcome data and for how many participants were no outcome data available? - UNCLEAR – not reported
8) Did the study have an appropriate length of follow up? - YES
9) Did the study use a precise definition of outcome? - YES
10) Was a valid and reliable method used to determine that outcome? - YES
11) Were investigators kept blind to participant’s exposure to the intervention? - UNCLEAR – not reported
12) Were investigators kept blind to other important confounding and prognostic factors? - UNCLEAR – not reported</td></tr>
<tr><td>Number of patients</td><td>Randomised=50
Silicone dressing = 24
Vaseline gauze = 26</td></tr>
<tr><td>Patient characteristics</td><td>Inclusion:
Patients 18 years of age ro older, with evidence of peripheral neuropathy, Wagner Grade I or II, ankle brachial pressure index of >0.5 and a diabetic foot ulcer of ≥ 4 weeks duration

Excluded:
Patients with acute ischaemia (ankle brachial pressure index < 0.5, rest pain and necrosis), grade 3 or 4 soft tissue infection, osteomyelitis or with a wound clinically ‘probing to bone’, with significant or end-stage renal disease or on haemodialysis

Baseline characteristics: No reported significant differences between groups. Many important variables missing. No P values reported.
<table>
<tr><td>Characteristics</td><td>Silicone dressing</td><td>Vaseline gauze</td></tr>
<tr><td>N</td><td>24</td><td>26</td></tr>
<tr><td>Age, y</td><td>61.5 ± 8.3</td><td>62.7 ± 5.9</td></tr>
<tr><td>Male/female</td><td>17/7</td><td>19/7</td></tr>
<tr><td>Weight, kg</td><td>Not reported</td><td>Not reported</td></tr>
<tr><td>Ethnicity</td><td>Not reported</td><td>Not reported</td></tr>
</table></td></tr>
</table>

Bibliographic reference	Zhang, Y., & Xing, S. Z. (2014). Treatment of Diabetic Foot Ulcers using Mepilex Lite Dressings: A Pilot Study. Experimental and Clinical Endocrinology & Diabetes, 122(04), 227-230.

(Caucasian/black/hispanic/other)		
Insulin therapy	Not reported	Not reported
Duration of diabetes, y	Not reported	Not reported
Type of diabetes type1/type2	Not reported	Not reported
Smokers	2	1
Ulcer size at baseline (cm^2)	4.3 ± 2.7	5.0 ± 1.9
Ulcer duration (years)	0.35 ± 0.17	0.41 ± 0.23
Ulcer location (plantar/other)	Not reported	Not reported
Neuropathy	Not reported	Not reported
Hypertension	Not reported	Not reported
Renal disorder	Not reported	Not reported
Ophthalmic disorder	Not reported	Not reported
Ankle Brachial Index Right Left	Not reported	Not reported
TCPO2, mmHg	Not reported	Not reported
Previous amputation Minor Major	Not reported	Not reported
Previous ulcers	Not reported	Not reported
HbA1c, mean	7.4 ± 1.2	7.5 ± 1.1
Mobility Walking with support Walking without support	Not reported	Not reported
Wagner Classification Grade I Grade II Grade III Grade IV	Not reported	Not reported
Total hospital stay	Not reported	Not reported

Intervention	Soft silicon dressing added to standard care of debridement and offloading
Comparison	Standard care of Vaseline gauze dressing, offloading and debridement
Length of follow up	Length of follow up 12 weeks
Location	China

Bibliographic reference	Zhang, Y., & Xing, S. Z. (2014). Treatment of Diabetic Foot Ulcers using Mepilex Lite Dressings: A Pilot Study. Experimental and Clinical Endocrinology & Diabetes, 122(04), 227-230.
Outcomes measures and effect size	Cure rates of foot ulcer resulting from diabetes: Soft silicone dressing = 18/24 ulcers Vaseline gauze = 16/26 ulcers Complete wound closure Not reported Rates and extent of amputation: Not reported Length of stay: Not reported Health related quality of life: Not reported Adverse events: Soft silicone dressing = 3/24 Vaseline gauze = 4/26
Source of funding	None reported
Comments	

Table 68: Lavery 2014

Bibliographic reference	Lavery, L. A., Higgins, K. R., La Fontaine, J., Zamorano, R. G., Constantinides, G. P., & Kim, P. J. (2014). Randomised clinical trial to compare total contact casts, healing sandals and a shear-reducing removable boot to heal diabetic foot ulcers. International wound journal.

Study type and aim	A randomised controlled trial (RCT) to evaluate the effects of total contact casting on wound healing in diabetic foot ulcers compared to healing sandles and shear reducing removable boot
Study quality	Low
Patient characteristics	**Total number of participants:** A total of 73 patients were randomised to treatment (23 patients received healing sandles; 23 patients received total contact casting and 27 patients received shear reducing removable walker). **Inclusion criteria:** Diabetic patients with grade 1A or 2A fore foot ulcers (University of Texas Classification System) on the sole of the foot were enrolled. **Exclusion criteria:** Inability to care for ulcer during study period; widespread malignancy; systematically immune-compromising disease, severe peripheral vascular disease; substance abuse within 6 months; untreated osteomyelitis; Charcot arthropathy with residual deformity too severe to allow proper fitting and patients with postural instability to prevent safe ambulation in the boot. **Patient characteristics:** The table below shows baseline characteristics

	Healing sandals (n=23)	**Total contact cast (n=23)**	**Shear Walker (n=27)**
Race **Hispanic** **Non-hispanic white** **African America** **Other**	 14 7 1 1	 12 10 1 0	 17 8 2 0
BMI (kg/m^2)	Not reported	Not reported	Not reported
Male %	52.20	60.90	55.60
Type 2 diabetes	22	20	25
Diabetes duration (years)	Not reported	Not reported	Not reported
HBA1c (%)	Not reported	Not reported	Not reported
Transcutaneous partial Oxygen therapy (kPa)	40.87 ± 13.83	37.39 ± 7.78	38.63 ± 9.24
Ankle brachial index **R** **L**	 1.11 ± 0.32 1.15 ± 0.27	 1.11 ± 0.19 1.16 ± 0.18	 1.13 ± 0.21 1.12 ± 0.23
Vibration perception T **R**	 56.2 ± 20.6	 56.9 ± 21.3	 40.6 ± 8.6

	L	50.6 ± 21.8	48.1 ± 18.4	39.0 8.0
	Ulcer history	13	15	23
	Amputation history	15	10	4
Monitoring & definitions	**Monitoring:** All patients were seen every 7-10 days for follow up **Outcome measures:** The main outcomes were healing time and complete healing			
Intervention	Patients received a total contact cast			
Comparison	Patients received a removable healing sandal Or Patients received a shear reducing removable walker			
Length of follow up	12 weeks			
Location	USA			
Outcomes measures and effect size	**Wound healing:** Completely healed by 12 weeks in the intent to treat population Defined as full reepithelialisation with no drainage Healing sandals group= 10 of 23 participants Total contact casting group= 16 of 23 participants Shear walker= 6 of 27 participants Total contact casting vs healing sandals = no significant difference (no P values provided) Total contact casting vs shear reducing walker = significant difference (no P values provided) **Healing time:** Mean time to healing (weeks) Defined as full reepithelialisation with no drainage Healing sandals group= 8.9 ± 3.5 weeks Total contact casting group= 5.4 ± 2.9 weeks Shear walker= 6.7 ± 4.3 weeks			

	Total contact casting vs healing sandals = P=<0.001 i.e. significant difference Total contact casting vs shear reducing walker = P= 0.22 i.e. no significant difference
Source of funding	Grant from the National Institute of Health, National Institute of Diabetes and Digestive and Kidney Diseases
Authors conclusion	The results of this study confirm the efficacy of total contact casting to heal diabetic foot ulcers. Uneven loss to follow up especially in the shear reducing walker group make it difficult to come to certain conclusions for this treatment group.

Table 69: Caravaggi 2014

Bibliographic reference	**Caravaggi, C., Sganzaroli, A., Fabbi, M., Cavaiani, P., Pogliaghi, I., Ferraresi, R., ... & Morabito, A. (2007). Nonwindowed Nonremovable Fiberglass Off-Loading Cast Versus Removable Pneumatic Cast (AircastXP Diabetic Walker) in the Treatment of Neuropathic Noninfected Plantar Ulcers A randomized prospective trial. Diabetes Care, 30(10), 2577-2578.**
Study type and aim	A randomised controlled trial (RCT) to evaluate the effects of a non-removable fiberglass off-loading cast on wound healing in diabetic foot ulcers compared to a removable pneumatic cast.
Study quality	Very low
Patient characteristics	**Total number of participants:** A total of 60 patients were randomised to treatment (29 patients received non-removable fiberglass off-loading cast; 29 patients received removable pneumatic cast). **Inclusion criteria:** All participants had peripheral neuropathy,as highlighted by insensitivity to 10 g monofilament and vibration perception threshold measured by biothesiometer at malleolus of at least 25 volts, and presented with a neuropathic ulcer on the whole part of the plantar surface of the foot, including ulcers correlated with Charcot neuroarthropathy deformities **Exclusion criteria:** patients with superficial tissue infection, osteomyelitis, TcPO2 (transcutaneous PO2) 30 mmHg, ankle brachial index 0.6, severe visual deficit, severe problems of equilibrium, amputation of the contralateral limb, and bilateral plantar ulcers. **Patient characteristics:** (age, sex, type of diabetes, and duration of diabetes) of both groups were reported comparable. The mean area of the ulcer was 3.4 +- 3.0 cm2 in group A and 3.9 +- 3.4 cm2 in group B (NS). No statistical difference was reported between groups in the positioning of the ulcer on the plantar surface of the foot. No further information was provided.
Monitoring & definitions	**Monitoring:**

	At the initial visit the ulcer area was traced using a transparent dressing and measured with an image analysis software device. Unclear if visits were similarly frequent in both groups. **Outcome measures:** The main outcomes were healing time and complete healing
Intervention	Patients received a Fibreglass offloading cast The dressing in both groups consisted of a mesh of hyaluronic acid.
Comparison	Patients received a removable pneumatic cast walker Surgical debridement was performed at each control visit (every 12 days), eliminating all nonviable tissue. The dressing in both groups consisted of a mesh of hyaluronic acid. At each visit, patients in this group were informed about the importance of wearing the offloading device as much as possible.
Length of follow up	90 days
Location	Italy
Outcomes measures and effect size	**Wound healing:** Completely healed by 90 days (12 weeks) Unclear definition Non-removable fibreglass cast= 24 of 29 participants Removable pneumatic cast walker= 23 of 29 participants **Healing time:** Average time to healing (kaplan meier) Unclear definition Non-removable fibreglass cast= 48 days Removable pneumatic cast walker= 71 days
Source of funding	Footnote: The costs of publication of this article were defrayed in part by the payment of page charges. This article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact
Authors conclusion	The results of the study show that in the 90-day follow-up period the healing rate in both groups was similar, while the healing time of the fiberglass off-loading cast group was significantly lower.

F.10.2 Included from CG119

Title: Wound Healing: Total contact cast vs. custom-made temporary footwear for patients with diabetic foot ulceration.

Level of Evidence	Patient Population/ Characteristics	Selection/ Inclusion criteria	Intervention	Comparison	Follow-up	Outcome and Results
ID: 11112 Level of evidence: () Study type: RCT Authors: Van de Weg et al. (2008)	<u>Total no. of patients:</u> Baseline = 226 158-do not meet inclusion criteria 68-eligible, of which- 14- no interest 5- no transport 6- co-morbidity 43-randomised Allocated TCC-23 Received TCC-20 Allocated and received CTF-20 Before the intervention, ulcers were debrided of necrotic tissue; hypertrophic edges were removed.	<u>Inclusion:</u> Confirmed diabetes, sensory neuropathy, and a plantar ulcer Grade 1 or 2 using the Wagner scale. <u>Exclusion:</u> People unable to walk indoors, with	Total-contact casts (TCC) A well moulded and minimally padded non-removable below-knee cast that maintains contact with entire plantar aspect of the foot was used.	*Custom-made temporary footwear (CTF)* It was custom-made and supplied with a rigid leather socket stiffened with Rhenoflex, a composite of rubber and plastic with thermoplastic	At 2,4,8 and 16 weeks	**Table 1: Decrease in wound surface (cm^2) after baseline (mean, SD) in patients with diabetic foot ulcers using a cast or footwear.** | | TCC | Shoe | Mean difference (95% CI) | Adjusted mean difference (95% CI)* | |---|---|---|---|---| | At 2 weeks, n= 41 | -0.98 (1.7) | -0.50 (1.5) | 0.48 (-0.55 to 1.51) p= 0.35 | 0.14 (-0.68 to 0.96) p= 0.73 | | At 4 weeks, n= 40 | -1.76 (1.8) | -0.92 (1.4) | 0.84 (-0.19 to 1.87) p= 0.11 | 0.51 (-0.25 to 1.26) p= 0.19 |

They received same educational guidelines on foot care.

Baseline characteristics:

	TCC (n=23)	Shoe (n= 20)
Age (years) Mean, (SD), n=43	64.8 (10.8)	58.1 (11.1)
Gender, n=42 n (% female)*	7 (32%)	2 (10%)
Duration of diabetes (years) Median (IQR)*	12 (6.20)	12 (7.17)
Duration of ulcer (weeks) Median (IQR)	4 (3-8)	5 (4-8)

dementia or life-threatening co-morbidity, ankle/brachial index <0.4 and/or osteomyelitis.

properties.

At 8 weeks, n= 38	-1.64 (2.3)	-0.94 (2.7)	0.70 (-0.98 to 2.38) p= 0.41	0.41 (-1.21 to 2.02) p= 0.61
At 16 weeks, n= 40	-2.88 (2.5)	-2.16 (3.4)	0.72 (-1.19 to 2.62) p= 0.45	0.10 (-0.92 to 0.72) p= 0.81

*-adjusted for differences in wound surface at baseline.

Reduction of wound surface area (WSA)

It was not significantly different between groups at any point during the follow up.

After adjustment for differences in baseline values, the difference between groups in reduction of wound surface was 0.10 cm^2 (95% CI -0.92 to 0.72)

Wound healing (days)

	<table><tr><td>Wound surface (cm^2) at baseline Median (IQR)</td><td>3.6 (1.7-6.1)</td><td>1.9 (1.0-4.2)</td></tr><tr><td>Wound surface (cm^2) at baseline Mean (SD)</td><td>4.2 (3.1)</td><td>3.0 (3.1)</td></tr><tr><td>Ulcer Grade 1 (n)</td><td>2</td><td>2</td></tr><tr><td>Forefoot location (n)</td><td>20</td><td>18</td></tr></table> *1 missing value SD-standard deviation, IQR-interquartile range <u>Setting:</u> Rehabilitation departments of 2 hospitals					6 people wearing shoes (mean baseline WSA 4.5) and 6 people using a cast (mean baseline WSA 4.7) had a completely healed ulcer. The mean time to healing was shorter for patients using a cast: 59 (SD-39) days for TCC vs. 90 (SD-12) days for CTF, but the difference in this small subgroup was not statistically significant (p= 0.11). <table><tr><td></td><td>Completely healed ulcer</td><td>Not completely healed</td><td>Total</td></tr><tr><td>TCC</td><td>6</td><td>17</td><td>23</td></tr><tr><td>CTF</td><td>6</td><td>14</td><td>20</td></tr><tr><td>Total</td><td>12</td><td>31</td><td>43</td></tr></table> **Relative Risk- 6/23 ÷ 6/20 = 0.866**
<u>Additional comments:</u> Allocation was concealed using opaque, sealed envelopes. Analysis of effectiveness was done according to the intention-to-treat principle. All							

analysis was adjusted for potential confounding. Accounted for people lost to follow up (n= 2) and discontinued (n= 3). Power calculation done.

Reference: Van De Weg, FB, Van Der Windt, DA, Vahl, AC Wound healing: total contact cast vs. custom-made temporary footwear for patients with diabetic foot ulceration. *Prosthetics & Orthotics International* 2008; **32:** 3-11.

Title: A randomised trial of two irremovable Off-Loading devices in the management of plantar neuropathic diabetic foot ulcers.						
Level of Evidence	Patient Population/ Characteristics	Selection/Inclusion criteria	Intervention	Comparison	Follow-up	Outcome and Results
ID: 5478 Level of evidence: () Study type: RCT Authors: Katz et al. (2005)	<u>Total no. of patients:</u> Baseline = 41 TCC-20 4 lost to follow up iTCC-21 2 lost to follow up 1 found to have osteomyelitis Before the intervention, wounds were evaluated, debrided, and dressed <u>Baseline characteristics:</u>	<u>Inclusion:</u> If they had chronic, non-ischemic, non-infected University of Texas stage Ia or IIA ulcers. They had moderate to severe neuropathy, with a loss of protective sensation. <u>Exclusion:</u> If they had clinical evidence of	Removable cast walker (RCW) rendered irremovable (iTCC) They were wrapped circumferentially with a single roll of fibreglass casting material thus rendering them 'irremovable.'	*Total contact cast (TCC)*.	Weekly until 12 weeks.	**Proportions of people with ulcers healed in ≤12 weeks:** TCC= 74 ± 45% iTCC= 80 ± 41%, p= 0.65 If patients lost to follow up are excluded in this analysis, these proportions change to 93±26%- TCC and 94±24%-iTCC (p= 0.97) Of the ulcers that healed in the 12-week period, the median (mean) healing times were: 5 weeks-TCC 4 weeks- iTCC

<table>
<tr>
<td></td>
<td>There were no statistically significant demographic differences between the two groups at study entry with respect to age, sex, race, type of diabetes, duration of diabetes, co morbid conditions, severity of neuropathy, or ulcer characteristics.

<u>Setting:</u>
Referral clinic</td>
<td>active infection at the ulcer site; active Charcot neuroarthropathy; significant peripheral arterial disease; inability to walk; or if they did not meet the entry criteria.</td>
<td></td>
<td></td>
<td></td>
<td>Complications (defined as any potential side effect from the treatment, no matter how minor) showed a relative risk reduction of 41% and absolute risk reduction of 27% (95% CI -4.3 to 58, p= 0.09) between the TCC and iTCC groups.

Table 1: Complication
<table>
<tr><th>Complication</th><th>Total</th><th>TCC</th><th>iTCC</th><th>p</th></tr>
<tr><td>N</td><td>41</td><td>20</td><td>21</td><td></td></tr>
<tr><td>Complications</td><td>21 (65)</td><td>13 (65)</td><td>8 (38)</td><td>0.09</td></tr>
<tr><td>Maceration</td><td>13 (32)</td><td>7 (35)</td><td>6 (29)</td><td>0.49</td></tr>
<tr><td>Broken cast</td><td>4 (10)</td><td>3 (15)</td><td>1 (5)</td><td>0.29</td></tr>
<tr><td>Second ulcer</td><td>3(7)</td><td>2 (10)</td><td>1 (5)</td><td>0.53</td></tr>
<tr><td>Abrasions</td><td>2 (5)</td><td>2 (10)</td><td>0 (0)</td><td>0.15</td></tr>
<tr><td>Toe amputations</td><td>2(5)</td><td>1 (5)</td><td>1 (5)</td><td>0.97</td></tr>
<tr><td>Oedema</td><td>1 (2)</td><td>1 (5)</td><td>0 (0)</td><td>0.3</td></tr>
</table>
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				3
Kissing ulcer	1(2)	1 (5)	0 (0)	0.33
Fall	1 (2)	0 (0)	1 (5)	0.33

Data are n(%)

65% of people that used TCC developed a complication

38% of people that used iTCC developed a complication.

Additional comments:

Randomisation was performed. Allocation concealment not mentioned. All parameters were analysed as intention to treat. Confounding not mentioned. Power calculation done.

Reference: Katz, IA, Harlan, A, Miranda-Palma, B, Prieto-Sanchez, L, Armstrong, DG, Bowker, JH, Mizel, MS, Boulton, AJ A randomized trial of two irremovable off-loading devices in the management of plantar neuropathic diabetic foot ulcers. *Diabetes Care* 2005; **28:** 555-59.

Title: Off-loading the diabetic foot wound. A randomised clinical trial.

Level of Evidence	Patient Population/ Characteristics	Selection/Inclusion criteria	Intervention	Comparison	Follow-up	Outcome and Results
ID: 951 Level of evidence: ()	Total no. of patients: Baseline = 75 12 failed to complete the study Total- 63	Inclusion: All people had clinically significant loss of protective sensation (>25 V), at least one	*Total contact cast (TCC)*. Were applied	Removable cast walker (RCW- the Aircast diabetic walker -	Weekly until 12 weeks.	The proportion of healing in people treated with TCC, RCW, and half-shoes was 89.5, 65.0, and 58.3% respectively.

Study type: RCT Authors: Armstrong et al. (2001)	TCC-19 RCW-20 Half-shoe-24 All people were followed on a weekly basis for device inspection, wound care, and wound debridement. All wounds were surgically debrided as required on each visit. <u>Baseline characteristics:</u> No significant differences were observed in any of the characteristics evaluated, including age, sex, duration of diabetes, size or location of wounds, or duration of plantar wounds <u>Setting:</u> Not mentioned	palpable foot pulse or a transcu-taneous oximetry ($TcPo_2$) measurement higher than 40 mmHg, and a neuropathic plantar diabetic foot ulcer corresponding to grade 1A using the University of Texas Diabetic Foot Wound Classification System. <u>Exclusion:</u> If they had active infection, were unable to walk without wheelchair assistance, had wounds in locations on the heel, rear foot, or area other than the plantar aspect of the foot, or had severe peripheral vascular disease.	using a modification of the technique described by Kominsky.	Aircast, Summit, NJ) and Half-shoes (.Darco, Hun-tington, WV) Both were applied using the directions dispensed with the original packaging.		At 12 weeks, the proportion of healing was significantly higher in the TCC group than in people treated with the 2 other modalities (89.5 vs. 61.4%, P = 0.026, odds ratio 5.4, 95% CI 1.1-26.1). a) There was also a significant difference in cumulative wound survival at 12 weeks between patients treated with a TCC and both the RCW (P = 0.033) and the half-shoe (P = 0.012). b) c) Among patients healing within the 12-week period, the meantime to healing was significantly shorter in patients treated with the TCC compared with those treated with the half-shoe (33.5 ± 5.9 vs. 61.0 ± 6.5 days, respectively; P = 0.005). d) e) But not the RCW (50.4 ± 7.2 days, P = 0.07), with the numbers available for study. f) g) No falls or device-related ulcerations were reported during the course of study.

h)

Patients treated with the TCC were significantly less active (600.1 ± 320.0 daily steps) than those treated with the half-shoe (1,461.8 ± 1,452.3 daily steps, P — 0.04).

There was not a significant difference in activity between patients treated with the TCC and with the RCW (767.6 ± 563.3 daily steps, P = 0.67) or between those treated wiih the RCW and with the half-shoe (P = 0.15).

TCC vs. RCW

	Complete wound healing	Not completely healed	Total
TCC	17	2	19
RCW	13	7	20
Total	30	9	39

RR= 0.894/0.65 = 1.37

TCC vs. Half-shoes

	Complete wound healing	Not completely healed	Total
TCC	17	2	19
Half-shoes	14	10	24
Total	31	12	43

RR= 0.894/0.583= 1.53

RCW vs. Half shoes

	Complete wound healing	Not completely healed	Total
RCW	13	7	20
Half-shoes	14	10	24
Total	27	17	44

RR= 0.65/0.583= 1.11

Additional comments:

i)	People were randomized through a computerized randomization schedule. Accounted for people lost to follow up or withdrawn. Concealment not mentioned. Confounding not mentioned. Power calculation done.

Reference: Armstrong, DG, Nguyen, HC, Lavery, LA, van Schie, CH, Boulton, AJ, Harkless, LB Off-loading the diabetic foot wound: a randomized clinical trial.[Erratum appears in Diabetes Care 2001 Aug;24(8):1509]. *Diabetes Care* 2001; **24:** 1019-22.

Title: Total contact casting in treatment of diabetic plantar ulcers. Controlled clinical trial.

Level of Evidence	Patient Population/ Characteristics	Selection/Inclusion criteria	Intervention	Comparison	Follow-up	Outcome and Results
ID: 951 Level of evidence: () Study type: RCT Authors: Mueller et al. (1989)	<u>Total no. of patients:</u> Baseline = 40 TCC-21 TDT-19 Standard protocol for patients referred to the diabetic foot center was followed for all people. <u>Baseline characteristics:</u> There was no significant difference in distribution of subject characteristics between the two	<u>Inclusion:</u> All people had been diagnosed with diabetes mellitus and currently had a plantar ulcer. <u>Exclusion:</u> Evidence of gross infection (no significant edema or drainage), osteomyelitis), or gangrene (visibly discolored or necrotic tissue).	*Total contact cast (TCC)*. A total contact plaster shell was moulded around the lower leg.	Traditional dressing treatment (TDT). Procedures, except for casting, were identical for the TDT group. The wound was covered with a wet-to-dry dressing	Weekly until 6 weeks.	a) In the TCC group, 19 of 21 (90%) ulcers healed in a mean time of 42 ± 29 days (range 8-91 days). b) In the TDT group, 6 of 19 (32%) ulcers healed in a mean time of 65 ± 29 days (range 12-92 days). c) None of the TCC group required hospitalization during this study. d) Five of 19 (26%) patients in the TDT group showed serious foot infection that required admission to a hospital. Two of these patients required a forefoot amputation. e) The $\chi 2$-value was statistically significant (P < .05), both for the

<table>
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<td>groups (P= 0.05).

Setting:
The diabetic foot center and physical therapy department at Washington University School of Medicine.</td>
<td>.</td>
<td></td>
<td>(sterile saline), and patients were instructed to change the dressing two to three times daily.</td>
<td></td>
<td>number of ulcers healed ($\chi 2$= 12.36) and incidence of infection ($\chi 2$= 4.1).

TCC vs. TDT

<table>
<tr><th></th><th>Complete ulcer healing</th><th>Not completely healed</th><th>Total</th></tr>
<tr><td>TCC</td><td>19</td><td>2</td><td>21</td></tr>
<tr><td>TDT</td><td>6</td><td>13</td><td>19</td></tr>
<tr><td>Total</td><td>25</td><td>15</td><td>40</td></tr>
</table>
RR= 0.904/0.315= 2.86</td>
</tr>
<tr>
<td colspan="7">Additional comments:

j) People were randomized. No power calculation mentioned. No intention to treat analysis done. Concealment and confounding not mentioned.</td>
</tr>
</table>

Reference: Mueller, MJ, Diamond, JE, Sinacore, DR, Delitto, A, Blair, VP, III, Drury, DA, Rose, SJ Total contact casting in treatment of diabetic plantar ulcers. Controlled clinical trial. *Diabetes Care* 1989; **12:** 384-88.

Title: The use of felt deflective padding in the management of plantar hallux and forefoot ulcers in patients with diabetes

Level of Evidence	Patient Population/ Characteristics	Selection/ Inclusion criteria	Intervention/ Comparison	Follow-up	Outcome/ Results
ID: 7910 Study type: RCT Authors: Nube et al. (2006)	Total no. of patients = 38 6 patients discontinued. Final analysis: Felt to the skin = 15; Felt within the shoe =17 All wounds were neuropathic in origin with the presence of peripheral neuropathy defined by a vibration perception threshold of over 30 V when tested with a biothesiomeler. <u>Skin group:</u> Median age (IQR) = 59 (50-70) Males = 14; females = 1 Type 2 diabetes = 14 Median duration of diabetes (years) (IQR) = 14 (10-19) Median HbAIc (%) (IQR) = 10.4 (6.8-11.4) Median duration of ulcer (months) = 11.5	Patients presenting with grade 1 ulcers according to the Texas Wound Grading system were recruited consecutively from our foot clinic. <u>Inclusion:</u> 'Type 1 or Type 2 diabetes, plantar neuropathic foot ulcer of the hallux or metatarsal area, grade 1A or IB. <u>Exclusion:</u> Impalpable pulses or AB1 <0.6; highly exudative ulcer; deep sinus.	Felt deflective padding to the skin vs. felt deflective padding within the shoe At the weekly appointment, wound debridement was performed and *infections* were monitored and treated.	4 weeks or until healing	<u>Wound size reduction at week 4 (percentage change):</u> Skin = 73%; Shoe = 74% [z = 0.02, p = 0.9] Overall, 24 patients included in the analysis healed by week 14 (not reported which group these 24 patients were from).

	Median size of ulcer (cm^2) = 0.5 <u>Shoe group:</u> Median age (IQR) = 56 (55-66) Males = 12; females = 5 Type 2 diabetes = 16 Median duration of diabetes (years) (IQR) = 12 (6-19) Median HbAIc (%) (IQR) = 8.5 (7.3-9.9) Median duration of ulcer (months) = 4.5 Median size of ulcer (cm^2) = 0.5				
<u>Additional comments:</u> All ulcers were randomly assigned by drawing lots to receive fell deflective padding adhered directly to the skin of the foot or adhered to the insole of the shoe. The randomisation was also stratified according to whether the ulcer was on the hallux or forefoot and whether it was greater or less than 1 cm2 in area. Setting not clear. No blinding, no allocation concealment, no ITT.					

Reference: NubÇ¸, VL, Molyneaux, L, Bolton, T, Clingan, T, Palmer, E, Yue, DK The use of felt deflective padding in the management of plantar hallux and forefoot ulcers in patients with diabetes. *Foot* 2006; **16:** 38-44.

Title: An off-the-shelf instant contact casting device for the management of diabetic foot ulcers

Level of Evidence	Patient Population/ Characteristics	Selection/ Inclusion criteria	Intervention/ Comparison	Follow-up	Outcome/ Results
ID: 8506 Study type: RCT Authors: Piaggesi et al. (2007)	Total no. of patients = 40 Group A = 20 Group B = 20 Group A: Mean age (SD) = 61.1 (6.4) Mean duration of diabetes (years) (SD) = 13.4 (7.5) Mean A1C (%) (SD) = 7.6 (0.9) Mean area of lesions (cm^2) (SD) = 3.9 (1.8) Group B: Mean age (SD) = 59.8 (8.2) Mean duration of diabetes (years) (SD) = 14.7 (11.1) Mean A1C (%) (SD) = 7.9 (1.1)	<u>Inclusion criteria:</u> Type 1 or type 2 diabetes for a period of at least 5 years, have peripheral neuropathy as highlighted by insensitivity to a 10-g monofilament and by a vibration perception threshold measured at malleolus of at least 25 volts, a forefoot plantar ulcer for a period of at least 3 weeks with an area wider than 1 cm^2 graded 1A or 2A according to Texas University classification. <u>Exclusion criteria:</u> Peripheral vascular disease with an antebrachial pressure index <0.9; the presence of clinical signs of infection, including edema, erithema, increased local skin temperature, secretion, fever, and leukocytosis, confirmed by culture exams; previous ulcer in the same site in the last 6 months; probing to bone and/or radiographic signs of osteomyelilis; Charcot foot; bilateral ulceration; serum creatinine >2 mg/dl; any systemic pathology or therapy possibly interfering with the healing process; severe visual or motor impairment that could expose	Optima Diab device (instant casting) (group A) vs. Standard Non-removable fiber-glass cast (TCC) (group B) Besides the off-loading treatment, patients received specific instructions on how to manage the off-loading devices and the standard therapy of neuropathic ulceration performed in our clinic according to the international consensus on the diabetic foot. Ulcers were surgically debrided, eliminating all the nonviable tissue, as well as any sinus or undermined zone, and exposing the entire area of the lesion.	Followed-up weekly for 12 weeks or up to complete reepithelialization of the lesions.	*<u>Complete healing at 12 weeks:</u>* Group A = 17/20 (85%) Group B = 19/20 (95%) RR = 0.89 (95%CI: 0.73 to 1.10) *<u>Mean duration of healing time:</u>* Group A = 6.7 ± 3.4 weeks (range 2-17); [P = 0.8745] Group B = 6.5 ± 4.4 weeks (range 2-14) *<u>Treatment complications:</u>* Group A = 5/20 Group B = 4/20 RR = 1.25 (95%CI: 0.39 to 3.99)

	Mean area of lesions (cm^2) (SD) = 3.7 (1.6) Setting: Diabetic foot clinic of the University of Pisa between April and October 2005	the patient to risk of accidents while participating in the study; and/or a life expectancy shorter than 1 year.			<u>*Patients' levels of satisfaction with the treatment (with VAS):*</u> Group A = 8.45 ± 1.79 Group B = 6.85 ± 2.39 (P < 0.05)
<u>Additional comments:</u> Computer-generated randomization list, with ITT. No blinding, no allocation concealment.					

Reference: Piaggesi, A, Macchiarini, S, Rizzo, L, Palumbo, F, Tedeschi, A, Nobili, LA, Leporati, E, Scire, V, Teobaldi, I, Del, PS An off-the-shelf instant contact casting device for the management of diabetic foot ulcers: a randomized prospective trial versus traditional fiberglass cast. *Diabetes Care* 2007; **30:** 586-90.

- **Dressings**

- **Title: Sodium carboxyl-methyl-cellulose dressings in the management of deep ulcerations of diabetic foot**.

Level of Evidence	Patient Population/ Characteristics	Selection/Inclusion criteria	Intervention	Comparison	Follow-up	Outcome and Results
ID: 8497	<u>Total no. of patients:</u> Baseline = 24	<u>Inclusion:</u> Age 18-75 years,	Group B (n=10)- Dressed	Group A (n= 10)-	Weekly until 8 weeks,	**<u>8 Weeks</u>**

<table>
<tr>
<td>Level of evidence: ()

Study type:
RCT

Authors:
Piagessi et al. (2001)</td>
<td>2-refused to give consent

1-considered unreliable

1-had neuroarthropathy

20-enrolled

People underwent a brief medical history and thorough local examination. The people with purely neuropathic lesions also underwent an aggressive surgical debridement with elimination of all non-viable tissue, before being included in the study.

<u>Baseline characteristics:</u>

There was no significant difference in distribution of subject characteristics between the two groups (P= 0.05).

<u>Setting:</u>
Foot clinic</td>
<td>type 1 or type 2 diabetes for over 5 years, foot ulcerations for more than 3 weeks, > 1 cm wide and! cm deep, good peripheral blood supply, with palpable peripheral pulses or an ankle-brachial pressure index (ABPI) > 0.9

<u>Exclusion:</u>

Active infection, recent episodes of ketoacidosis, malignancies, any chronic pathology or systemic therapy which could obstruct the healing process were other exclusion criteria. Candidates for a major amputation were also excluded.</td>
<td>with Carboxyl-methyl-cellulose dressing

(Aquacel™; ConvaTec, UK)</td>
<td>Dressed with saline-moistened gauze</td>
<td>then until complete re-epithelisation.</td>
<td>Table 1: Outcomes at week 8 of therapy (median[inter quartile range])

<table>
<tr><td>Variable</td><td>Group A</td><td>Group B</td><td></td></tr>
<tr><td>•</td><td>•</td><td>•</td><td>•</td></tr>
<tr><td>•</td><td>•</td><td>•</td><td>•</td></tr>
</table>

RLV-Reduction of lesional volume; GT-granulation tissue

At the 8-week control visit all the variables chosen to monitor the development of the lesion healing process scored better in Group B patients than in Group A.</td>
</tr>
</table>

Aquacel vs. Saline moistened gauze (RLV)

	RLV achieved	No RLV achieved	Total
Aquacel	3	7	10
Saline moistened gauze	2	8	10
Total	5	15	20

RR= 0.3/0.2 = 1.5

Aquacel vs. Saline moistened gauze (GT)

	GT achieved	No GT achieved	Total
Aquacel	4	6	10
Saline moistened gauze	1	9	10
Total	5	15	20

						RR= 0.4/0.1 = 4 ILTC (intralesional temperature) was significantly higher in Group B than in Group A patients (34.76 ± 2.06 vs. 30.65 ± 1.36"C; P<0.01) and ∆TC (difference in intralesional and perilesional temperature) was positive in Group B and negative in Group A patients (2.02 ± 1.67 vs.-2.71 ± 1.24; P < 0.01). **Adverse Events** Adverse events observed during treatment, apart from infections, which were considered as complications, included maceration of perilesional skin which was observed in 2 Group A and 1 Group B patients. All the cases of infective complications (3/10 in Group A and 1/10 in Group B; P - 0.582) were confined to the area of the lesion.

Aquacel vs. Saline moistened gauze

	Adverse events	No adverse events	Total
Aquacel	1	9	10
Saline moistened gauze	3	10	10
Total	4	19	20

RR= 0.1/0.3 = 0.33

Healing Time:

All patients in both groups healed during the observational period apart from one in Group A who underwent trans-metatarsal amputation due to infection.

Healing time of patients in Group B was shorter than that observed in Group A (127 ± 46 vs. 234 ± 61 days;

						p < 0.001)

Additional comments:

k) People were randomized. No intention to treat analysis mentioned. Power calculation not mentioned. Concealment and confounding not mentioned.

Reference: Piaggesi, A, Baccetti, F, Rizzo, L, Romanelli, M, Navalesi, R, Benzi, L Sodium carboxyl-methyl-cellulose dressings in the management of deep ulcerations of diabetic foot. *Diabetic Medicine* 2001; **18:** 320-324.

Title: A RCT of promogran (collagen/oxidized regenerated cellulose dressing) vs standard treatment in the management of diabetic foot ulcers					
Level of Evidence	Patient Population/ Characteristics	Selection/ Inclusion criteria	Intervention/ Comparison	Follow-up	Outcome/ Results
ID: 11260 Study type: RCT Authors: Veves et al. (2002)	Total no. of patients = 276 Promogan group = 138 Moistened gauze (control) = 138 <u>Promogan group:</u> Age, mean (range) = 58 (23-85) Male/female = 95/43 HbA_{tc} (range) (%) = 8.6 (5.3-14.0) Mean wound area (range) (cm^2) = 2.5 (0.2-27.4) Median wound duration (range) (mth) = 3 (1-84) <u>Control group:</u> Age, mean (range) = 59 (37-83) Male/female = 108/30	Inclusion criteria: 18 years or older with a diabetic foot ulcer of at least 30 days duration; Wagner grade 1 to 2; an area of at least 1 cm^2; had adequate circulation with an oscillometer reading of the limb that had the target wound of at least 1 U; a wound that was debrided of necrotic/nonviable tissue at enrolment. Exclusion criteria: Clinical signs of infection; a target wound that had exposed bone; a concurrent illness or a condition that may have interfered with wound healing (eg, carcinoma, vasculitis, connective tissue disease, or an immune system disorder); known current abuse of alcohol or other drugs or treatment with dialysis, corticosteroids, immunosuppressive agents, radiation therapy, or chemotherapy at a dose that might have interfered with wound	Promogan vs. moistened gauze (control) *[both with tape as the secondary dressing]* Surgical debridement of healthy tissue was per-formed in the studied ulcer during the initial and all follow-up visits when necessary. The debridement technique was standardized during an initial meeting of the investigators, at which all investigators were instructed to debride the wound until healthy granulating tissue or healthy bleeding tissue was reached.	12 weeks or sooner if the patient discontinued the study or the wound healed. Follow-up evaluations were completed on a weekly basis.	Only 188 patients completed the study (104 in the Promogran group and 84 in the control group). <u>Wound completely healed (at 12 weeks or shorter):</u> Promogan group = 51/104 Moistened gauze (control) = 39/84 RR = 1.06 (95%CI: 0.78 to 1.43) <u>Mean percentage of wound size reduction (12 weeks):</u> Promogran group = 64.5% Control group = 63.8% <u>Mean time to healing (SD):</u> Promogran = 7.0±0.4 weeks

	HbA_{tc} (range) (%) = 8.5 (4.9-13.1) Mean wound area (range) (cm^2) = 3.1 (0.1-42.4) Median wound duration (range) (mth) = 3 (1-144) <u>Setting:</u> US university teaching hospitals and primary care centres (11 centres in total)	healing within the last 30 days before study enrolment; known hypersensitivity to any of the dressing components; unwillingness or inability or an ambulatory patient to be fitted with appropriate shoe gear or an off-loading device; and multiple diabetic ulcers on the same foot.	Frequency of changing the dressings differed between the 2 groups.		Control = 5.8±0.4 weeks. <u>Nonserious adverse events:</u> Promogran = 37/104 (26.8%) Control = 34/84 (24.6%) RR = 0.88 (95%CI: 0.61 to 1.26) <u>Serious adverse events:</u> Promogran = 25/104 (18.1%) Control = 35/84 (25.4%) RR = 0.58 (95%CI: 0.38 to 0.88) *None of these events were described as related to the study dressings.*
<u>Additional comments:</u> A stratified randomization was used in assigning treatments to patients on the basis of their wound area. Eligible patients were stratified in 2 groups, ie, patients with a wound area of less than or of at least 10 cm^2. The same technique of off-loading was performed in each centre for both the controls and the Promogran-treated patients. However, the choice of the off-loading technique was left to the individual investigator. No ITT.					

Reference: Veves, A, Sheehan, P, Pham, HT A randomized, controlled trial of Promogran (a collagen/oxidized regenerated cellulose dressing) vs standard treatment in the management of diabetic foot ulcers. *Archives of Surgery* 2002; **137:** 822-27.

Title: Prospective randomised controlled study of Hydrofiber dressing containing ionic silver or calcium alginate dressings in non-ischaemic diabetic foot ulcers					
Level of Evidence	Patient Population/ Characteristics	Selection/ Inclusion criteria	Intervention/ Comparison	Follow-up	Outcome/ Results
ID: 5340 Study type: open-label-RCT Authors: Jude et al. (2007)	Stratification: 21 systemic antibiotics 113 no systemic antibiotics. AQAg = 67; CA = 67 AQAg group: Male/female = 46/21 Mean age (SD) = 58.9 (12.6) On antibiotics = 13 Ulcer duration (years) (SD) = 1.2 (2.1) Ulcer depth (cm) = 0.40 (0.45) Ulcer baseline area (cm^2) = 3.1 (4.1) AQAg group:	Inclusion criteria: Adults with Type 1 or 2 DM, with HbA1c < 12.0%, serum creatinine < 200 umol/l and with Wagner Grade 1 or 2 DFUs of non-ischaemic aetiology (neuropathic or neuro-ischaemic ulcers, none solely ischacmic) were included in the study. Adults with diabetic foot infections were not excluded. Exclusion criteria: Patients were excluded from participation if allergic to a component of the dressings studied; known or suspected malignancy local to the study ulcer; had been on systemic antibiotics > 7 days prior to enrolment; had inadequate arterial perfusion, as defined by the ankle-to-brachial index < 0.8; great toe systolic blood pressure < 40 mmHg or forefoot TcP02 < 30 mmHg	Hydrofiber (ionic silver dressing) [AQAg] vs. calcium alginate dressing [CA] Standardized surgical debridement was performed at all centres at baseline prior to stratification and at subsequent dressing changes to remove callus and ensure that there was no more than 5% slough or eschar on the ulcer.	8 weeks (evaluation every 7 days).	Wound completely healed at 8 weeks: AQAg = 21/67; CA = 15/67 RR = 1.40 (95%CI: 0.79 to 2.47) Discontinued due to adverse events: AQAg = 8/67; CA = 13/67 RR = 0.61 (95%CI: 0.27 to 1.39) Adverse events (complications): AQAg = 23/67; CA = 26/67 RR = (95%CI:

	Male/female = 53/14 Mean age (SD) = 61.1 (11.4) On antibiotics = 8 Ulcer duration (years) (SD) = 1.4 (2.6) Ulcer depth (cm) = 0.40 (0.39) Ulcer baseline area (cm^2) = 4.2 (7.8) Study period: Between December 2002 and February 2004 Setting: 18 European centres: 8 in the UK, 5 in France, 4 in Germany and 1 in Sweden.	(subject supine) or <40 mmHg (subject sitting). When TcP02 was measured the electrode temperature was set at 44^{o}C. All wounds were > 1 cm^2 in area, stratified according to current use or non-use of systemic antibiotics for that ulcer on enrolment in the study.	Each primary dressing was covered with a sterile, non-adherent foam dressing. Accommodative footwear for non-plantar ulcers and off-loading for plantar ulcers were provided as required for individual subjects; the products used were not specified		Study-related adverse events: AQAg = 11/67; CA = 9/67 RR = 1.22 (95%CI: 0.54 to 2.76) Mean time in days to 100% healing: AQAg = 52.6 (1.8); CA = 57.7 (1.7), p = 0.340 8-week % reduction in ulcer area: AQAg = 58.1 (53.1); CA = 60.5 (42.7), p = 0.948 Ulcer depth reduction during 8-week: AQAg = 0.25 ±0.49 cm CA = 0.13 ±0.37 cm, p = 0.04

Additional comments:

Patients stratified by antibiotic use on enrolment were randomly assigned to similar protocols including off-loading and secondary foam dressings for 8 weeks or until healing. Eligible individuals were randomly assigned to receive either AQAg or CA dressings according to instructions in a sealed envelope and stratified according to whether or not systemic antibiotics were being administered for treatment of the study ulcer.

ITT was conducted.

Reference: Jude, EB, Apelqvist, J, Spraul, M, Martini, J, Silver Dressing Study Group Prospective randomized controlled study of Hydrofiber dressing containing ionic silver or calcium alginate dressings in non-ischaemic diabetic foot ulcers. *Diabetic Medicine* 2007; **24:** 280-288.

- **Title: Comparing two dressings in the treatment of diabetic foot ulcers.**

Level of Evidence	Patient Population/ Characteristics	Selection/Inclusion criteria	Intervention	Comparison	Follow-up	Outcome and Results
ID: 3544 Level of evidence: () Study type: RCT Authors: Foster	Total no. of patients: Baseline = 58 Category A-29 with 39 ulcers Category B-29 3 lost to follow up 26 left with 33 foot ulcers Patients were prescribed appropriate antibiotics and debridement offered. Baseline characteristics:	Inclusion: Aged at least 18 years, had a clean diabetic foot ulcer and were willing and able to comply with the study protocol. Exclusion: If the ulcer was sloughy, necrotic, or infected.	Polyurethane foam dressing (n-15)	Alginate dressing (n-15)	Weekly until ulcer was fully healed or 8 weeks.	**Healing** Polyurethane group-9/15 Alginate group- 8/15 **Relative risk- 9/15 ÷ 8/15 = 1.12** **Time to healing** No statistically significant difference between treatments was found with respect to time to healing.

et al. (1994)	There was no significant difference in distribution of subject characteristics between the two groups Setting: Not mentioned					**Number of patients withdrawn from study** Polyurethane group-0/15 Alginate group- 4/15
Additional comments: l) People were randomized. Blinding not performed. No intention to treat analysis mentioned. Power calculation not mentioned. Concealment and confounding not mentioned.						

Reference: Foster, AVM, Greenhill, MT, Edmonds, ME Comparing two dressings in the treatment of diabetic foot ulcers. *Journal of Wound Care* 1994; **3:** 224-28.

Title: Randomised controlled trial of the use of three dressing preparations in the management of chronic ulceration of the foot in diabetes.

Level of Evidence	Patient Population/ Characteristics	Selection/Inclusion criteria	Intervention/ Comparison	Follow-up	Outcome and Results
ID: 5177 Level of evidence: ()	Total no. of patients: Baseline = 317 patients 88 withdrawals 229 evaluable	Inclusion: • Type 1 or 2 diabetes. • 18 years of age or more. • A foot ulcer which had	N-A (non adherent, knitted, viscose filament gauze product) vs. Inadine (iodine impregnated dressing) vs. Aquacel (newer hydrocolloid product)	2 weekly for 24 weeks	**Incidence of Healing** **Table 1: incidence of healing at 12 weeks analysed on the basis of ITT** Ongoing/withdrawn | Healed (%) | Total

Study type: RCT Authors: Jeffcoate et al. (2009)	patients N-A-106 Inadine-108 Aquacel-103 <u>Baseline characteristics:</u> The distribution of baseline demographics between the groups was very similar by intervention. There was no statistical difference between the groups in terms of distribution by ulcer size at baseline, <u>Setting:</u> Multidisciplinary clinics across the UK.	been present for at least 6 weeks and had a cross-sectional area of between 25 and 2500 mm^2. • Able and willing to give informed consent. • Reasonably accessible by car to the hospital base. • Under routine review by the multidisciplinary clinic. <u>Exclusion:</u> • Those with a known allergy to any of the trial preparations (including iodine). • Any ulcer on either foot extending to tendon, periosteum or bone. • Infection of bone. • Soft tissue infection requiring treatment with systemic antibiotics. • An ulcer on a limb being considered for revascularisation. • Those chosen for	All patients received standard care which included appropriate debridement and off-loading as and when necessary		<table><tr><td></td><td>(%)</td><td></td><td></td></tr><tr><td>Inadine</td><td>76 (70.4)</td><td>32 (29.6)</td><td>108</td></tr><tr><td>N-A</td><td>79 (74.5)</td><td>27 (25.5)</td><td>106</td></tr><tr><td>Aquacel</td><td>74 (71.8)</td><td>29 (28.2)</td><td>103</td></tr><tr><td>Total</td><td>229</td><td>88</td><td>317</td></tr></table> The incidences of healing by 12 weeks for the three dressings were Inadine 29.6%, Aquacel 28.2% and N-A 25.5%. The differences between groups were not statistically significant. **Relative risk (Inadine vs. N-A)- 1.16 (0.75-1.80)** **Relative risk (Inadine vs. Aquacel)- 1.05 (0.69-1.61)** **Relative risk (Aquacel vs. N-A)- 1.11 (0.71-1.73)** **Table 2: Incidence of healing: Week 12 (Per protocol basis)** <table><tr><td></td><td>Ongoing/withdrawn (%)</td><td>Healed (%)</td><td>Total</td></tr><tr><td>Inadine</td><td>64 (66.7)</td><td>32 (33.3)</td><td>96</td></tr><tr><td>N-A</td><td>53 (66.3)</td><td>27 (33.7)</td><td>80</td></tr><tr><td>Aquacel</td><td>52 (64.2)</td><td>29 (35.8)</td><td>81</td></tr></table>

		management with a non-removable cast without a dressing window. • Gangrene on the affected foot. • Eschar which was not removable by clinical debridement. Those with evidence of a sinus or deep track. • Those in whom the hallux had been amputated on the affected side (preventing the measurement of toe pressure). • Those with an ankle:brachial pressure index (ABPI) of less than 0.7 or toe systolic pressure less than 30 mmHg. • Ulceration judged to be caused primarily by disease other than diabetes. • Patients with any other serious disease likely to compromise the outcome of the trial. • Patients with critical renal disease (creatinine greater			

Total	169	88	257

Per protocol basis- including only those participants who remained in the study until week 12 (and withdrawals being excluded).

The data suggest an overall healing rate of approximately 34% with no statistical difference between the groups.

Relative risk (Inadine vs. N-A)- 0.99 (0.65-1.50)

Relative risk (Inadine vs. Aquacel)- 0.93 (0.62-1.61)

Relative risk (Aquacel vs. N-A)- 1.06 (0.69-1.62)

Table 3: Incidence of healing: Week 24 (ITT)

	Ongoing/withdrawn (%)	Healed (%)	Total
Inadine	60 (55.6)	48 (44.4)	108
N-A	65 (61.3)	41 (38.7)	106
Aquacel	57 (55.3)	46 (44.7)	103
Total	182	135	317

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<td>than 300 mmol/l), and those receiving

immunosuppressants, systemic corticosteroid therapy (other than by inhalation) or any other

preparation which could, in the opinion of the supervising clinician, have interfered with wound healing.

• Those living at such a distance (generally further than 10 miles) from the clinic as would have made frequent assessment visits

inappropriately expensive and/or impractical.

• Those who withheld consent.</td>
<td></td>
<td></td>
<td>The overall healing rates for the three dressings were: Inadine 44%, Aquacel 45% and N-A 39%. These differences were not statistically significant.

Relative risk (Inadine vs. N-A)- 1.15 (0.84-1.58)

Relative risk (Inadine vs. Aquacel)- 1.00 (0.74-1.34)

Relative risk (Aquacel vs. N-A)- 1.15 (0.84-1.59)

Table 4: withdrawal from study by dressing group at week 24
<table>
<tr><td></td><td>Frequency</td><td>Percentage</td></tr>
<tr><td>Inadine</td><td>21</td><td>19.4</td></tr>
<tr><td>N-A</td><td>30</td><td>29.1</td></tr>
<tr><td>Aquacel</td><td>37</td><td>34.9</td></tr>
<tr><td>Total</td><td>88</td><td>100</td></tr>
</table>
However, there was a trend in the data whereby N-A had the poorest healing and the highest withdrawal rate, and the withdrawal rates were statistically significant at week 24: Inadine 19%, Aquacel 29%, N-A 35% (p = 0.038

Relative risk (Inadine vs. N-A)- 0.69 (0.42-1.12)</td>
</tr>
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Relative risk (Inadine vs. Aquacel)- 0.54 (0.34-0.86)

Relative risk (Aquacel vs. N-A)- 1.27 (0.85-1.89)

Table 5: Incidence of healing: Week 24 (Per protocol basis)

	Ongoing/withdrawn (%)	Healed (%)	Total
Inadine	39 (44.8)	48 (55.2)	87
N-A	28 (40.6)	41 (59.4)	69
Aquacel	27 (37)	46 (63)	73
Total	94	135	229

Per protocol analysis at week 24 suggested an overall healing rate approaching 60% with no statistical difference between the groups.

Relative risk (Inadine vs. N-A)- 0.93 (0.71-1.22)

Relative risk (Inadine vs. Aquacel)- 0.88 (0.68-1.13)

Relative risk (Aquacel vs. N-A)- 1.06 (0.82-1.38)

Time to healing

Table 6: Time to Healing in days by week 12 (ITT)

	Mean	SD	95% CI
Inadine (n-108)	74.1	20.6	70.2-78.1
N-A (n-103)	72.4	20.6	68.4-76.5
Aquacel (n-106)	75.1	18.1	71.6-78.6

There were no significant differences (p-0.61) between groups in time to healing using ITT

Table 7: Time to Healing in days by week 12 (Per protocol basis)

	Mean	SD	95% CI
Inadine (n-96)	72.9	21.6	68.5-77.3
N-A	69.3	22.3	64.4-74.3

(n-81)			
Aquacel (n-80)	72.3	20.1	67.8-76.8

There remained no statistically significant differences (p-0.5) between the groups when the analysis was repeated on a per protocol basis

Table 8: Time to Healing in days by week 24 (ITT)

	Mean	SD	95% CI
Inadine (n-108)	127.8	54.2	117.5-138.2
N-A (n-103)	125.8	55.9	114.9-136.7
Aquacel (n-106)	130.7	52.4	120.6-140.8

There are no significant differences in time to healing using ITT. The calculated mean time to healing for all 317 participants using these criteria was 129 days.

Table 9: Time to Healing in days by week 24 (Per protocol basis)

	Mean	SD	95% CI
Inadine (n-87)	118.1	56.3	106.1-130.1
N-A (n-73)	108.5	58.2	94.9-122.1
Aquacel (n-69)	110.7	55.6	97.4-124.1

When the analysis was repeated on a per protocol basis, the descriptive statistics changed but there were still no statistically significant differences between the groups.

Recurrence of Ulcers

Table 10: Recurrence of ulceration at the same site within 3-month follow-up for those whose index ulcer healed during the intervention phase

	Inadine	Aquacel	N-A	Total

Ulcer remained healed	32	35	37	104
Ulcer recurred at same site	7	3	3	13
Total	39	38	40	117

Of the 135 patients who healed during the intervention phase, only 117 provided information on the clinical status of the ulcer during the 3-month follow-up review.

Twelve of those patients for whom data are available (10%) had a recurrence during the 3-month review, but the difference between groups was not statistically significant.

Relative risk (Inadine vs. N-A)- 2.39 (0.67-8.60)

Relative risk (Inadine vs. Aquacel)- 2.27 (0.63-8.15)

Relative risk (Aquacel vs. N-A)- 1.05 (0.23-4.90)

Episodes of secondary infection

Table 11: Number of cases of infection reported as serious adverse event (SAE)

	Inadine	Aquacel	N-A
Number of episodes of infection as SAEs	10	7	7
Number of episodes of infection listed as SAE but unrelated to the index ulcer.	2	2	0
Total	12	9	7

Twenty-eight such episodes were registered as SAEs but there was no significant difference in incidence of SAEs between dressing

Groups.

Major and Minor amputation

Table 12: list of amputations according to dressing allocation

	Inadine	Aquacel	N-A
Minor amputation	1	3	1
Major amputation	0	1	1
Total	1	4	2

RR for both major and minor amputation:

Relative risk (Inadine vs. N-A)- 0.49 (0.05-5.33)

Relative risk (Inadine vs. Aquacel)- 0.24 (0.03-2.10)

Relative risk (Aquacel vs. N-A)- 2.06 (0.39-11)

Adverse events and Withdrawals

Serious adverse events

Table 13: Total No. of SAEs by dressing allocation.

Dressing	No. of SAEs
Inadine	37
N-A	35
Aquacel	28
Total	100

Only 11 of the 100 SAEs recorded were considered to be 'slightly or possibly' related to the dressing; these events were spread evenly across the intervention groups.

Relative risk (Inadine vs. N-A)- 1.04 (0.71-1.51)

Relative risk (Inadine vs. Aquacel)- 1.26 (0.84-1.90)

Relative risk (Aquacel vs. N-A)- 0.82 (0.54-1.25)

Withdrawals

Table 14: Withdrawal from study by dressing group at week 24

	Frequency	Percentage
Inadine	21	19.4
N-A	30	29.1

Aquacel	37	34.9
Total	88	100

There were a total of 88 withdrawals (21 for those using Inadine, 30 for Aquacel and 37 for N-A).The difference between groups was significant (p-0.038)

Relative risk (Inadine vs. N-A)- 0.69 (0.42-1.12)

Relative risk (Inadine vs. Aquacel)- 0.54 (0.34-0.86)

Relative risk (Aquacel vs. N-A)- 1.27 (0.85-1.89)

Additional comments:

m) People were randomized. Observer Blinding performed. Intention to treat analysis performed. Power calculation. Concealment and confounding not mentioned.

Reference: Jeffcoate, WJ, Price, PE, Phillips, CJ, Game, FL, Mudge, E, Davies, S, Amery, CM, Edmonds, ME, Gibby, OM, Johnson, AB, Jones, GR, Masson, E, Patmore, JE, Price, D, Rayman, G, Harding, KG Randomised controlled trial of the use of the three dressing preparations in the management of chronic ulceration of the foot in diabetes. *Health Technology Assessment* 2009; **13(54):** 1-110.