Does contact with a podiatrist prevent the occurrence of a lower extremity amputation in people with diabetes? A systematic review and meta-analysis

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DOES CONTACT WITH A PODIATRIST PREVENT THE OCCURRENCE OF A LOWER EXTREMITY AMPUTATION IN PEOPLE WITH DIABETES? A SYSTEMATIC REVIEW AND META-ANALYSIS

Short title

Contact with podiatry and lower extremity amputation in people with diabetes

CM BUCKLEY (CMB)[1,2], IJ PERRY (IJP)[2], CP BRADLEY (CPB)[1], PM KEARNEY (PMK)[2]

1. Dept of General Practice, UCC, Western Gateway Building, Cork, Ireland
2. Dept of Epidemiology and Public Health, UCC, Western Gateway Building, Cork, Ireland,

Corresponding author

Claire Buckley, Department of General Practice, Room 2.57, Western Gateway Building, University College Cork, Ireland
Tel No: 00353 86 6020313, Fax No: 00353 21 4205469,
Email: Claire.buckley@ucc.ie

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ABSTRACT

Objective

To determine the effect of contact with a podiatrist on the occurrence of lower extremity amputation in people with diabetes.

Design & data sources

We conducted a systematic review of available literature on the effect of contact with a podiatrist on the risk of lower extremity amputation in people with diabetes. Eligible studies, published in the English language, were identified through searches of PUBMED, CINAHL, EMBASE, and Cochrane databases. The key terms, 'podiatry', 'amputation' and 'diabetes', were searched as MeSH (Medical Subject Heading) terms. Reference lists of selected papers were hand-searched for additional eligible articles. No date restrictions were imposed.

Study Selection

Published randomised and analytical observational studies of the effect of contact with a podiatrist on the risk of LEA in people with diabetes were included. Cross-sectional studies, review articles, chart reviews and case series were excluded. Two reviewers independently assessed titles, abstracts, and full articles to identify eligible studies and extracted data related to study design, characteristics of participants, interventions and outcomes, control for potential confounding factors and risk estimates.

Analysis

Meta-analysis was performed separately for randomised and non-randomised studies. Relative risks with 95% confidence intervals were estimated with fixed and random effects models as appropriate.

Results

Six studies met the inclusion criteria and five provided data included in meta-analysis. The identified studies were heterogenous in design and included people with diabetes at both low and high risk of amputation. Contact with a podiatrist did not significantly affect the RR of LEA in a meta-analysis of available data from RCTs; (1.4, 95% CI 0.2-9.8, 2 RCTs) or from cohort studies; (0.7, 95% CI 0.4-1.3, 3 Cohort studies with 4 substudies in one cohort).

Conclusions

There is very limited data available on the effect of contact with a podiatrist on the risk of LEA in people with diabetes.

ARTICLE SUMMARY

Article Focus

- People with diabetes are at increased risk of LEA (Lower Extremity Amputation). As the prevalence of diabetes escalates worldwide, it is anticipated that there will be an increase in the number of LEAs.
- It is assumed that contact with a podiatrist prevents the occurrence of a LEA.
- This systematic review aims to determine from available literature the documented effect of contact with a podiatrist on the occurrence of a LEA in people with diabetes.

Key Messages

- Very limited data is available and the authors conclude that there is insufficient evidence to determine whether contact with a podiatrist has an effect on the risk of LEA in people with diabetes.
- Some existing studies suggest that contact with a podiatrist has a positive effect on shorter term outcomes including patient knowledge of foot care and ulcer recurrence.
- Further research on the long-term outcome of LEA is warranted.

Strengths and Limitations

- This is the first systematic review which investigates if contact with a podiatrist prevents the occurrence of a LEA in people with diabetes.
- Failure to demonstrate an effect on this long-term outcome is most likely due to limitations of available studies.
- Limitations include that studies in this systematic review looked at different sample populations ranging from patients with low baseline risk to patients with active disease. Also, included RCTs were underpowered to detect a significant difference for the outcome of LEA.

INTRODUCTION

A worldwide diabetes epidemic is unfolding[1]. Diabetes is associated with a significantly increased risk of LEA (Lower Extremity Amputation). LEA rates vary between populations with estimates ranging from 46 to 9,600 per 10^5 people with diabetes [2]. A number of factors influence the occurrence of a LEA in people with diabetes; including hypertension, obesity and hyperglycaemia [3 4]. In the foot, previous ulceration, infection and ischaemia are proven risk factors [5]. Nearly 85% of amputations begin as foot ulcers among persons with diabetes [6]. Protective factors include control of clinical parameters and screening to identify those people at high risk and many LEAs are preventable [7] [8]. The effects of clinical and socio-demographic risk factors on the occurrence of a LEA have been well documented in people with diabetes [9] [10] [11] [12].

In 2008, a task force report by the Foot Care Interest Group of the American Diabetes Association, which included podiatrists, stated that all people with diabetes should be assigned to a foot risk category [13]. These categories were designed to direct referral to and subsequent therapy by a speciality clinician or team but did not refer specifically to the role of podiatry. Recent guidelines from Scotland outline a diabetic risk stratification and triage tool, highlighting which people need podiatry referral. According to these guidelines, all patients classified as moderate risk (i.e. at least one risk factor present), severe risk or with active disease require podiatry review [14] . Podiatry is practiced as a specialty in many countries and in many English-speaking countries, the older term of "chiropodist" may still be used. According to the National Health Service in the UK , there is no difference between a chiropodist and a podiatrist [15]. It is assumed that podiatrists prevent LEAs by treating existing disease and educating people with diabetes on proper foot care. However, the effect of patient contact with a podiatrist on the risk of LEA in people with diabetes is unproven.

Two previous Cochrane reviews by Dorresteijn et al have looked at firstly the effect of an integrated care approach and secondly the effect of patient education on the outcome of LEA in people with diabetes [16 17]. The first of these reviews found no high quality evidence evaluating an integrated care approach and insufficient evidence of benefit in preventing diabetic foot ulceration [16]. The second review, updated in 2012, concluded that there is insufficient robust evidence that limited patient education alone is effective in achieving clinically relevant reductions in ulcer and LEA incidence [17]. Individual patient contact with a podiatrist was not examined as an intervention in either review. The present systematic review of published literature examines the effect of contact with a podiatrist on risk of LEA in people with diabetes.

METHODS

The research question, inclusion and exclusion criteria and proposed methods of analysis were specified in advance and documented in a protocol (attached as supplementary file).

Search Strategy

Pubmed, CINAHL, EMBASE (Excerpta Medica), and Cochrane databases were searched to identify relevant studies published up to and including September 25th 2011. The key terms, 'podiatry', 'amputation' and 'diabetes', were searched as MeSH (Medical Subject Heading) terms. Randomised and observational studies, published in English, which reported the effect of contact with a

podiatrist on risk of LEA in people with diabetes (type 1 or 2), were included. No date restrictions were imposed. Cross-sectional studies, review articles, non-systematic reviews, chart reviews and case series were excluded. A manual search of references cited in relevant articles was performed. All potentially eligible studies were independently reviewed by two authors (CMB and PMK).

Data abstraction and quality assessment:

Using a standardised data collection form, two reviewers (CMB, PMK) independently abstracted information on study design, year of study, characteristics of participants, interventions and outcomes, control for potential confounding factors and risk estimates. A modified version of a checklist developed by Downs and Black for assessing the methodological quality of both randomised and non-randomised studies of health care interventions was used to critically appraise the studies in this review [18]. Inconsistencies between reviewers were discussed and resolved through consensus.

Statistical Analysis

Review Manager Software Version 5 (Revman 5.0; the Cochrane Collaboration, Oxford, England) and STATA Version 12IC were used for statistical analysis. The RR (relative risk) with 95% CI was recorded for included studies. One study presented individual results for four various stages of disease so this study was analysed as 4 substudies. Meta-analysis was performed separately for randomised and non-randomised studies, using either the fixed or random effects model as appropriate. Statistical heterogeneity was assessed with Cochran's *Q* statistic. Cochran's *Q* is computed by summing the squared deviations of each study's estimate from the overall meta-analytic estimate, weighting each study's contribution in the same manner as in the meta-analysis. P values were obtained by comparing the statistic with a χ^2 distribution with $k-1$ degrees of freedom (where k is the number of studies)[19]. To assess publication bias, a funnel plot of the overall estimate and its standard error (SE) was derived.

RESULTS

Four hundred and ninety-nine titles were retrieved from searches of electronic databases. Duplicates (138) were removed and 361 titles/abstracts were reviewed. Eighteen papers were considered for review after initial screening of titles and abstracts. Three further studies were identified as potentially eligible from reference checking. After reviewing the full text articles, 6 studies met the inclusion criteria; 2 RCTS and 4 cohort studies (PRISMA flow-chart-figure 1)[20]. Studies were excluded because of study design e.g. chart review/audit; intervention e.g. contact with a multidisciplinary team instead of contact with a podiatrist; or in one case, the study was described in another article already included in this systematic review.

Table 1 describes the included studies according to study design, participants, interventions and outcomes. Quality of included studies was assessed and all studies were deemed of suitable quality for inclusion (tables 2 & 3). Risk of foot disease at baseline was assessed using the Diabetic foot risk stratification and triage system from the SIGN (Scottish Intercollegiate Guidelines Network) guidelines (Appendix 1) [14]. Results of included studies are presented in table 4.

Results from available studies were pooled together in separate meta-analyses for RCTs and observational studies. Five of these studies provided sufficient data to allow meta-analysis. For

RCTs, the fixed effects model was applied (Q=0.328, p=0.567) and for cohort studies, the random effects model is reported as there was evidence of significant heterogeneity between the cohort studies (Q = 32.698, p=0.000). Meta-analysis of the two RCTs yielded an insignificant pooled RR of 1.4 (0.2-9.8) while meta-analysis of the cohort studies also yielded an insignificant pooled RR of 0.7 (0.4-1.3) (figure 2).

Data required for inclusion in the meta-analysis was unavailable for 1 eligible study. Lavery et al compared people with diabetes on dialysis and people with diabetes with a history of a healed ulcer. During a 30-month evaluation period, only 30% of patients from both groups combined were seen for preventative care prior to ulceration. The amputation incidence density was high in both groups (dialysis group 58.7 and ulcer group 13.1 per 1,000 person-years) [21]. However, it was not possible to extract the LEA event rate in those who did or did not have contact with a podiatrist.

Visual inspection of the funnel plot produced for the included studies shows no strong evidence of publication bias (figure 3).

DISCUSSION

In this systematic review, we conclude that there is insufficient evidence to determine whether contact with a podiatrist has an effect on LEA in people with diabetes.

Strengths and limitations of this review

This is the first systematic review that the authors are aware of that investigates if contact with a podiatrist prevents the occurrence of a lower extremity amputation in patients with diabetes. A thorough literature search examining multiple databases was undertaken and 6 studies with 2 different study designs were included. While individual study design meta-analysis was performed in an effort to pool the available data, we acknowledge that heterogeneity exists between studies included in the meta-analysis in terms of baseline diabetic foot risk and type of intervention.

Included studies looked at different sample populations ranging from patients with low baseline risk to patients with active disease. For example, Ronnemaa et al recruited patients with diabetes from the national drug imbursement register in Finland which is representative of the total population with diabetes [22]. However, Plank et al recruited patients with diabetes from a tertiary referral centre which represents a population of patients with diabetes that have developed complications requiring referral to a tertiary centre [23]. In 5 of the 6 included studies, the population at risk were patients with diabetes. However, Sowell et al examined a population mix of patients with diabetes, PVD and gangrene [24]. It was decided to include this study due to the dearth of research in this area. This difference in populations studied between the Sowell paper and the other 5 studies needs to be highlighted as a limitation in this review.

The diabetic foot risk of the participants at baseline (low-active) reflects the different treatment settings at recruitment and highlights heterogeneity amongst the studies (table 1). Cochran's Q statistic was used to assess heterogeneity. For RCTs, the fixed effects model was appropriate but this meta-analysis is limited as there are only 2 included studies. For cohort studies, the Q statistic of 32.698 (p=0.000) indicated that strong heterogeneity existed so the random effects model was applied to account for both random variability and the variability in effects among the studies. However, use of the random effects model limits the conclusions that can be drawn from the meta-

analysis [25]. 'A priori' sensitivity analyses were planned for different levels of baseline risk but there were insufficient data.

Sources of potential bias should be considered in relation to the observational studies. Although information was collected on potential confounders in many of the included observational studies, the analyses were not adjusted for potential confounders and sources of bias. Clinical practices may vary per individual and per location. Guidelines have been recently developed to standardise referral of patients with diabetes to podiatry [14]. Healthcare-seeking behaviours are complex and multifactorial and ethnicity and socio-economic position can influence attendance at podiatry [26] [27]. Level of disease may also influence a patient's decision to attend the podiatrist and create a self-selection bias in the patients with diabetes that attend the podiatrist. Patients that attend healthcare services in early stages of disease may be more likely to engage in other healthy lifestyle behaviours e.g. healthy diet, not smoking and this phenomenon of 'healthy user bias' has been previously documented [28]. In their retrospective cohort study, Sowell et al reported 20 LEAs in the intervention group and 130 in the control group (noting that the population at risk in this study is patients with diabetes and/or gangrene and/or PVD) [24]. This study described the majority of included participants with the outcome of LEA. However, their analysis did not adjust for important potential confounders which limit the conclusions that can be drawn from this study.

The issues of bias and confounding are eliminated by randomisation in RCTs. However, there is a lack of RCTs in this area. The 2 available RCTs have a lack of power as few participants had the outcome of LEA. The most likely cause of the low numbers of outcomes in the included studies is length of follow-up. LEA takes years to develop, especially from the time-point when a patient is classified as low risk. In the 1st included RCT, Plank et al described 2 LEAs in the intervention group and 1 in the control group [23]. In the 2nd RCT, Ronnemaa et al noted no LEA after 1 year of follow-up and 1 LEA in the intervention group after 7 years of follow-up [22]. Neither RCT was designed to assess LEA as a primary outcome and thus, had insufficient power to detect a significant difference for the outcome of LEA.

Conclusions and Implications

Two Cochrane reviews have looked at the outcome of LEA in patients with diabetes [16 17]. These reviews concluded that there is insufficient evidence that brief educational interventions or complex interventions reduce the risk of LEA. This systematic review concludes that there is insufficient evidence that contact with a podiatrist reduces the risk of LEA in patients with diabetes. Thus, this review cannot make any recommendations about practice. To detect the true effect, adequately powered RCTs and longer follow-up studies are needed to examine the effect of contact with a podiatrist on LEA in patients with diabetes. Perhaps, podiatry programmes could be rolled out in a manner designed to answer the question of effect on outcomes such as LEA. Such studies could also assess the impact of the timing and intensity of the podiatry intervention on outcomes. Perhaps studies focusing on high-risk participants are too close in timing to the LEA event and studies of lower-risk participants would be better to detect an effect in LEA prevention.

International standards recommend a multidisciplinary team should manage the footcare of a patient with diabetes [14]. Many studies have looked at the effects of a multidisciplinary team of which podiatry serves as a member of the team and found positive effects on various outcomes [29-36]. This may be a more realistic reflection of how patients with diabetes are managed; looking at

one service in isolation could be flawed as services are seldom delivered in isolation. According to the SIGN (Scottish Intercollegiate Guidelines Network) guidelines a multidisciplinary foot team should include a podiatrist, diabetes physician, orthotist, diabetes nurse specialist, vascular surgeon, orthopaedic surgeon and radiologist [14]. A systematic review of the literature looking at the effectiveness of multidisciplinary teams which include contact with a podiatrist would be useful.

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Declaration of Competing Interests

Nothing to declare.

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Contributor statement

Claire M Buckley (CMB) conceived and designed the study, extracted the data and wrote the paper. Ivan J Perry (IJP) revised the paper. Colin P Bradley (CPB) approved the final version to be published. Patricia M Kearney (PMK) designed the study, extracted the data and wrote the paper. CMB will act as guarantor for the paper.

Ethical Approval

None required.

Data Sharing Statement

There is no additional data available.

Abbreviations

CINAHL, Cumulative Index to Nursing and Allied Health Literature, LEA, Lower Extremity Amputation, MeSH, Medical Subject Headings, NHS, National Health Service, PVD, Peripheral Vascular Disease, RCT, Randomised Controlled Trial, SIGN, Scottish Intercollegiate Guidelines Network, UCC, University College Cork, UK, United Kingdom

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Table legends

Table 1 Characteristics of Included Studies

Table 2 Quality Assessment of Included RCTs

Table 3 Quality Assessment of Included Cohort Studies

Table 4 Results of Included Studies

Appendices legends

Appendix 1 Diabetic foot risk stratification and triage

Appendix 2 Search Strategy for PUBMED (1966 – Sept 25th 2011)

Appendix 3 Search Strategy for CINAHL (1981 – Sept 25th 2011)

Appendix 4 Search Strategy for EMBASE (1974 – Sept 25th 2011)

Appendix 5 Search Strategy for Cochrane (1993 – Sept 25th 2011)

Appendix 6 Table of Excluded Studies

TABLES

Table 1 Characteristics of Included Studies

Study (Author, Country, Year)	Type of study	Participants	Interventions	Source of data used in study	Length of follow-up	Baseline risk as per diabetic foot risk stratification [14]	Outcomes
Ronnemaa, Finland, 1997[22]	RCT	530 patients with diabetes randomised Intervention: 267 Control: 263	Intervention: 45 minutes individual patient education Podiatric care visits as necessary Control: Written information	Clinical report forms	1 year and 7 years	Low	Primary: Patient Knowledge about foot care Secondary: Ulcer incidence Amputation rate
Plank, Austria, 2003[23]	RCT	91 patients with diabetes randomised Intervention: 47 Control: 44	Intervention: Chiropodist visit at least once a month Control: chiropodist treatment not specifically recommended	Clinical report forms	386 days (368-424, 25^{th}-75^{th} percentile)	High (healed foot ulcers)	Primary: recurrence rate of ulcers Secondary: Amputation rate Death
Sowell, USA, 1999[24]	Cohort	255,256 with diabetes or PVD or gangrene followed over time	Intervention: Podiatric Medical care – receipt of any M0101 services Comparison: Did not receive podiatry (M0101) services	Medicare claims database	1 year	Unknown	Number of Amputations
Lipscombe, Canada, 2003 [37]	Cohort	132 patients with diabetes on PD (Peritoneal Dialysis)	Intervention: Assessment, education and footcare by chiropody	Medical charts	3 years	High	Amputation

Lavery, USA, 2010[21]	Cohort	300 high-risk patients with diabetes 150 with an ulcer history 150 on dialysis followed over time	Intervention: Podiatry services - number of visits to podiatrist for prevention, ulcer treatment of other pathology	Claims data & Electronic Medical Records	30 months	High (history of foot ulcer)	Amputation rate Ulcer incidence
Sloan, UK, 2010[38]	Cohort	189,598 patients with diabetes followed over time Participants grouped into different stages (1-4) of disease depending on severity of symptoms & signs	Intervention: Care provided by podiatrist Comparison: Care provided by 'other health professional' – GP/Internist/Endocrinologist/Nurse/Physician Assistant	Medicare claims database	6 years	Stage 1: Moderate Stage 2: High Stage 3: Active Stage 4: Active	Amputation rate

Table 2 Quality Assessment of Included RCTs

Study (Author, Country, Year)	Type of study	Base Population	Randomisation	Blinding	Confounding	Losses to follow-up	Analysis
Ronnemaa, Finland, 1997[22]	RCT	Community based care in Finland, receiving anti-diabetic drug treatment from the national drug reimbursement register	Randomisation performed separately for men/women and patients </> 20 years. Method of randomisation not described	Outcome assessor blinded to baseline characteristics but no further information on blinding provided	Baseline Characteristics not described	Follow-up completed by 63% of patients in intervention group and 62% patients in control group at seven years	No intention to treat analysis undertaken
Plank, Austria, 2003[23]	RCT	All in routine outpatient care at hospital diabetic foot clinic in Austria	Subjects were assigned a patient number in ascending order and randomly allocated to the intervention or control group	Allocation concealment ensured	Similar Baseline Characteristics	All patients followed up	Intention to treat & per protocol analysis

Table 3 Quality Assessment of Included Cohort Studies

Study (Author, Country, Year)	Type of study	Base Population	Confounding	Losses to follow-up	Analysis
Sowell, USA, 1999[24]	Cohort	All Medicare population at risk for lower extremity amputation in 1993-1994	Not addressed – only looked at 1 variable – acknowledged as a limitation	No losses to follow-up	Amputation incidence rates with & without exposure to podiatry
Lipscombe, Canada, 2003 [37]	Cohort	Patients in Peritoneal Dialysis program at University Health Network, between January 1997 and December 1999	Data on confounding variables collected	No losses to follow-up	Descriptive Stats
Lavery, USA, 2010[21]	Cohort	Patients with diabetes attending Scott and White Health Plan, Texas, USA	Data on confounding variables collected	150 consecutive patients with at least 30 months follow-up from the time of diagnosis recruited so no losses to follow-up	Descriptive Stats
Sloan, UK, 2010[38]	Cohort	All individuals with a DM-related LEC diagnosis between 1994 and 2001	Data on confounding variables collected	No losses to follow-up	Hazard Ratios adjusted for Medicare expenditures from care received from non-study health professionals

Table 4 Results of Included Studies

Study (Author, Country, Year)	Type of study	Primary Outcome	Baseline risk as per diabetic foot risk stratification [14]	Relative risk of amputation with contact with a podiatrist compared to no contact with a podiatrist
Ronnemaa, Finland, 1997 [22]	RCT	*Diabetes-related Amputation:* One year follow-up: Intervention: 0 Control: 0 Seven years follow-up: Intervention: 1 Control: 0	Low	2.96
Plank, Austria, 2003[23]	RCT	*Diabetes-related Amputation:* One year follow-up: Intervention: 2 Control: 1	High (healed foot ulcers)	0.9
Sowell, USA, 1999[24]	Cohort	*Amputation related to diabetes/gangrene/PVD* One year follow-up: Intervention: 20 Control: 130	Unknown	0.25
Lipscombe, Canada, 2003 [37]	Cohort	*Diabetes-related Amputation:* Amputation during any of the 3 years of the study: Intervention: 11 Control: 4	High	2.1
Lavery, USA, 2010[21]	Cohort	*Diabetes-related Amputation:* Actual number of amputations not outlined *Amputation Incidence Density:* 58.7 in Dialysis Group per 1,000 person years 13.1 in Ulcer Group per 1,000 person years	High (history of foot ulcer)	Unknown
Sloan, UK, 2010[38]	Cohort	*Diabetes-related Amputation:* Six year follow-up: actual number of amputations not outlined	Stage 1: Moderate Stage 2: High Stage 3: Active Stage 4: Active	Stage 1 disease : 2.2 Stage 2 disease : 0.85 Stage 3 disease : 0.44 Stage 4 disease : 0.36

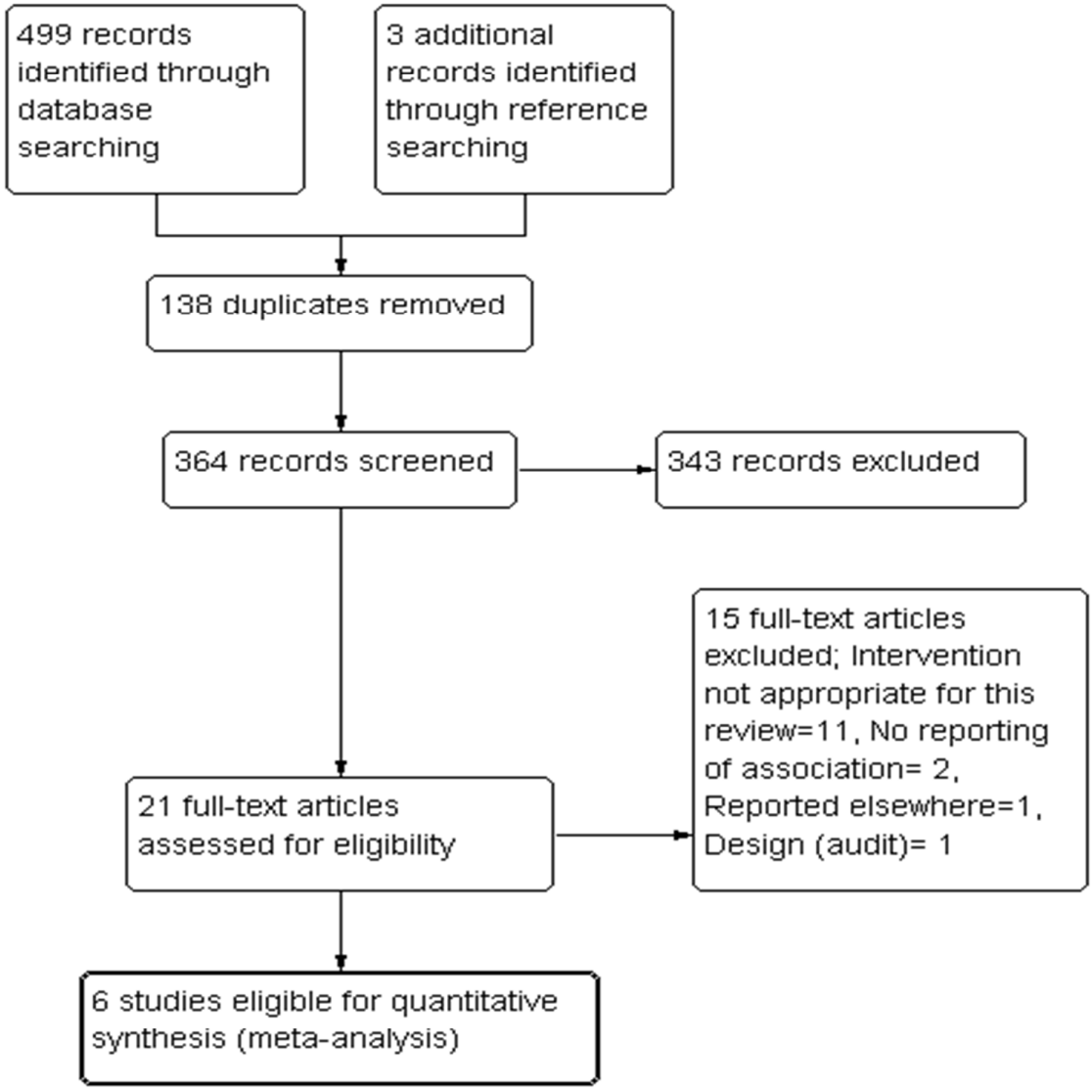

Figure 1 Selection of studies for inclusion in review

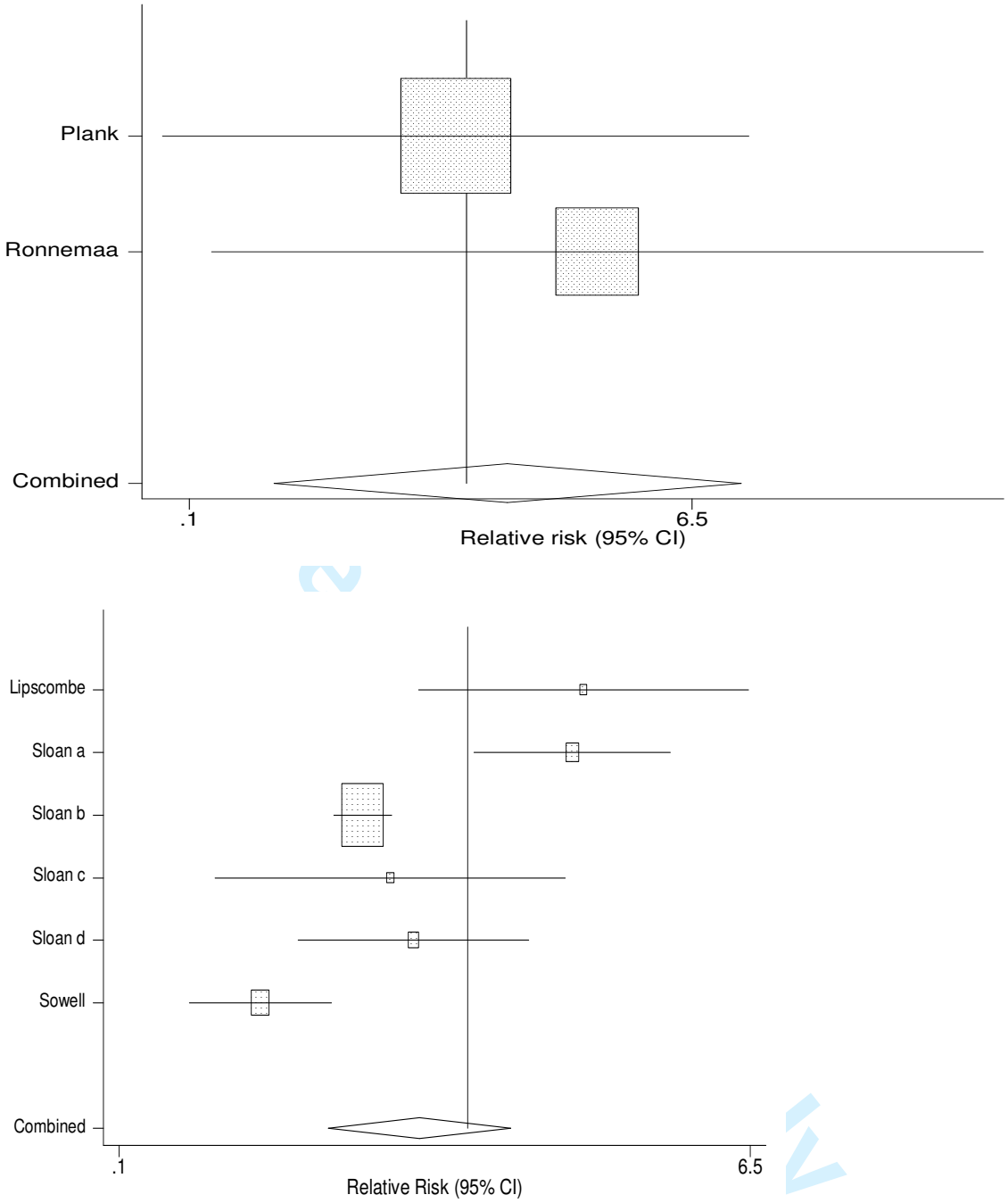

Figure 2 Forest plots of meta- analysis of RCTs (top) and Cohort studies (bottom) with the intervention of contact with a podiatrist on left side of plot

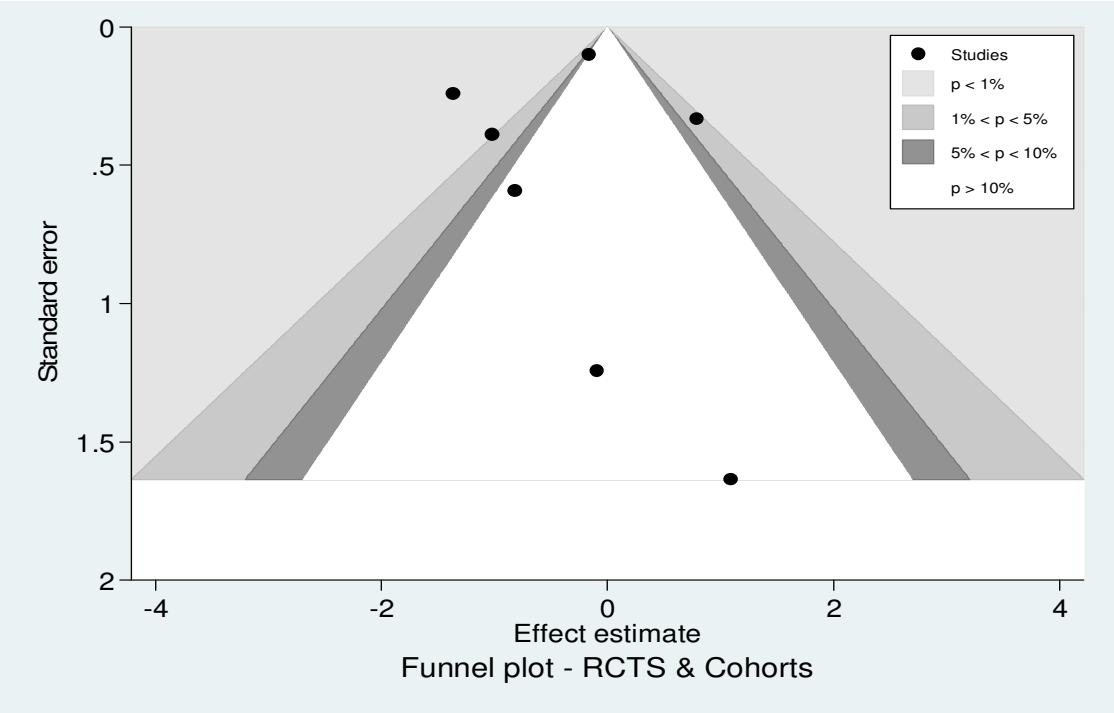

Figure 3 Funnel plot of included studies (RCTs and Cohort studies)

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4-5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	19-22
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	5

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	5
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5 Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	13-14
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	15-16
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	17 Figure 2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	6
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	6 Figure 3
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	7
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	6
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	6
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	7-8
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	8

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

PROTOCOL FOR SYSTEMATIC REVIEW

DOES CONTACT WITH A PODIATRIST PREVENT THE OCCURRENCE OF A LOWER EXTREMITY AMPUTATION IN PEOPLE WITH DIABETES? A SYSTEMATIC REVIEW AND META-ANALYSIS

Authors:
Dr Claire M. Buckley
Professor Ivan J. Perry
Professor Colin P. Bradley
Dr Patricia M. Kearney

BACKGROUND

Diabetes is associated with a significant risk of LEA (lower extremity amputation)[1]. LEA rates vary between communities, 46-9,600 per 10^5 people with diabetes, for many reasons [2]. A number of factors influence the occurrence of a LEA in patients with diabetes; including hypertension, obesity and hyperglycaemia [3-7]. In the foot, previous ulceration, infection and ischaemia are proven risk factors [8]. Nearly 85% of amputations begin as foot ulcers among persons with diabetes [9]. Protective factors include control of clinical parameters and screening to identify those patients at high risk [10]. Many LEAs are preventable [11]. Thus, the effects of clinical and socio-demographic risk factors on the occurrence of a lower extremity amputation have been well documented in patients with diabetes in previous studies [12] [13] [14]. However, the effect of patient contact with a podiatrist on the occurrence of LEA in patients with diabetes is less well explored.

In 1998, the ADA (American Diabetes Association) published a technical review and position statement on preventive foot care in people with diabetes, highlighting the importance of foot care in people with diabetes to prevent adverse outcomes [15 16]. An updated position statement by the ADA in 2003 stated that early recognition and management of independent risk factors for ulcers and amputations can prevent or delay the onset of adverse outcomes [17]. However, these statements did not specify the role of podiatry. In 2005, the Standards of Medical Care of Diabetes issued by the ADA advised that problems involving the feet, especially ulcers and wound care, may require care by a podiatrist [18]. And in 2008, a task force report by the Foot Care Interest Group of the ADA stated that all patients with diabetes should be assigned to a foot risk category. These categories were designed to direct referral and subsequent therapy by the speciality clinician or team [19]. This report did not outline the role of podiatry but panel members included podiatric medicine representatives, suggesting that podiatry does have a place in footcare of patients with diabetes. It is now being recognised across the globe that podiatry has a role in the management of the diabetic foot. Guidelines from Scotland, Europe outline a diabetic risk stratification and triage tool, highlighting which patients need podiatry referral [20] (Appendix 1).

The management of diabetes is a complex process involving many healthcare professionals, including podiatrists. Two previous Cochrane reviews by Dorrestiejn et al have looked at lower extremity amputation in patients with diabetes as an outcome [21 22]. In 2009, Dorrestiejn et al concluded that there is no high quality evidence evaluating complex interventions (complex intervention defined as an integrated care approach) and insufficient evidence of benefit in preventing diabetic foot ulceration [21]. The second Cochrane review in 2010 concluded that there is insufficient robust evidence that limited patient education alone is effective in achieving clinically relevant reductions in ulcer and amputation incidence [22]. Individual patient contact with a podiatrist was not examined as an intervention in either review. To the best of our knowledge, the effect of contact with a podiatrist on the occurrence of a LEA in patients with diabetes has not been previously examined in any systematic review.

This review will look at contact with a podiatrist as an intervention to prevent LEA in patients with diabetes. Randomised and non-randomised studies will be included.

Objectives

To conduct a systematic review of international literature to determine if contact with a podiatrist has an effect on the occurrence of LEA in patients with diabetes.

METHODS

Criteria for considering studies for review

Types of study design

Randomised and non-randomised studies that allow analysis of the effect of patient contact with a podiatrist in preventing LEAs will be included.

Types of participants

People with type 1 or type 2 diabetes mellitus in any health care setting.

Types of interventions

Studies of patients with diabetes attending a podiatrist for treatment alone or for treatment and education to prevent the occurrence of LEA will be included. Comparison groups will be those that were not in contact with podiatrists or received written instructions only.

Types of outcome measures

Primary: LEA (first or repeat)

Secondary: N/A

Table 1 Inclusion & Exclusion Criteria

Inclusion Criteria:	Exclusion Criteria:
• Any time	• Cross-sectional studies
• English language	• Review articles
• Any Country	• Non-systematic reviews
• Any age	• Chart reviews /Case series
• Patients with a diagnosis of diabetes – either type 1 or type 2	

Search strategy for identification of studies

Published studies will be identified through searches of PUBMED, CINAHL, EMBASE (Excerpta Medica), and Cochrane databases. No time-limits will be implemented. Where a study is reported in more than one article, data will be extracted from the most relevant report. The key search terms will be 'podiatry', 'amputation' and 'diabetes'. (Figure 1)

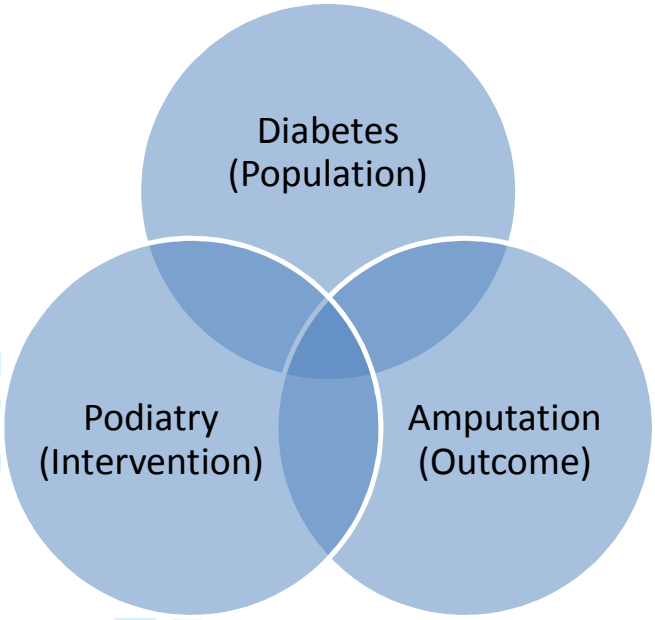

Figure 1 Venn diagram of key terms for search strategy

A comprehensive search strategy will be devised with the advice of the librarian. Key terms will be searched as MeSH (Medical Subject Heading) terms e.g. 'diabetes - MeSH term' and as free text with/without truncation as appropriate e.g. 'Diabet*(this symbol is used for identifying all words starting with Diabet, e.g. diabetes, diabetic etc.). The search will include case-control studies, cohort studies, retrospective and prospective studies, articles, clinical trials and RCTs. The strategy will be adapted as per database requirements.
In addition, hand searches will be conducted of the reference lists of all articles retrieved to identify other potentially eligible articles.

Methods - data collection and analysis

Selection of studies

Full copies of potentially eligible studies will be obtained and two review authors (CMB and PK) will decide independently on inclusion or exclusion (table 1). In the case of disagreement, consensus will be reached by discussion between four review authors (CMB, PK, CB and IJ).

Data extraction and management

Data on eligible studies will be extracted and summarised using a pre-agreed data extraction summary form. This form will include study design, baseline characteristics of participants including number of participants, age, gender, ethnicity, type of diabetes, information on exposure, outcome measure (lower extremity amputation) and other relevant data. Risk of foot disease at baseline will be assessed using the Diabetic foot risk stratification and triage system from the SIGN (Scottish Intercollegiate Guidelines Network) guidelines (Appendix 1). If the data required for the review is missing from the published article, the authors will be contacted.

Assessment of quality in included studies

A modified version of a checklist developed by Downs and Black for assessing the methodological quality of both randomised and non-randomised studies of health care interventions will be used to critically appraise the studies in this review [23].

Assessment of heterogeneity

All eligible studies will be included in the data analysis. If data are too scarce or the quality of the studies is inadequate or results are too varied to present in numerical form, the authors will perform a narrative qualitative summary. If appropriate, meta-analysis will be attempted to pool outcome data. Either a fixed or random effects model will be used depending on the heterogeneity between studies. The most suitable model will be chosen after assessing the I^2 statistic for heterogeneity.

Pilot Results

Preliminary searches of the electronic databases have yielded approximately 500 titles & abstracts for initial screening.

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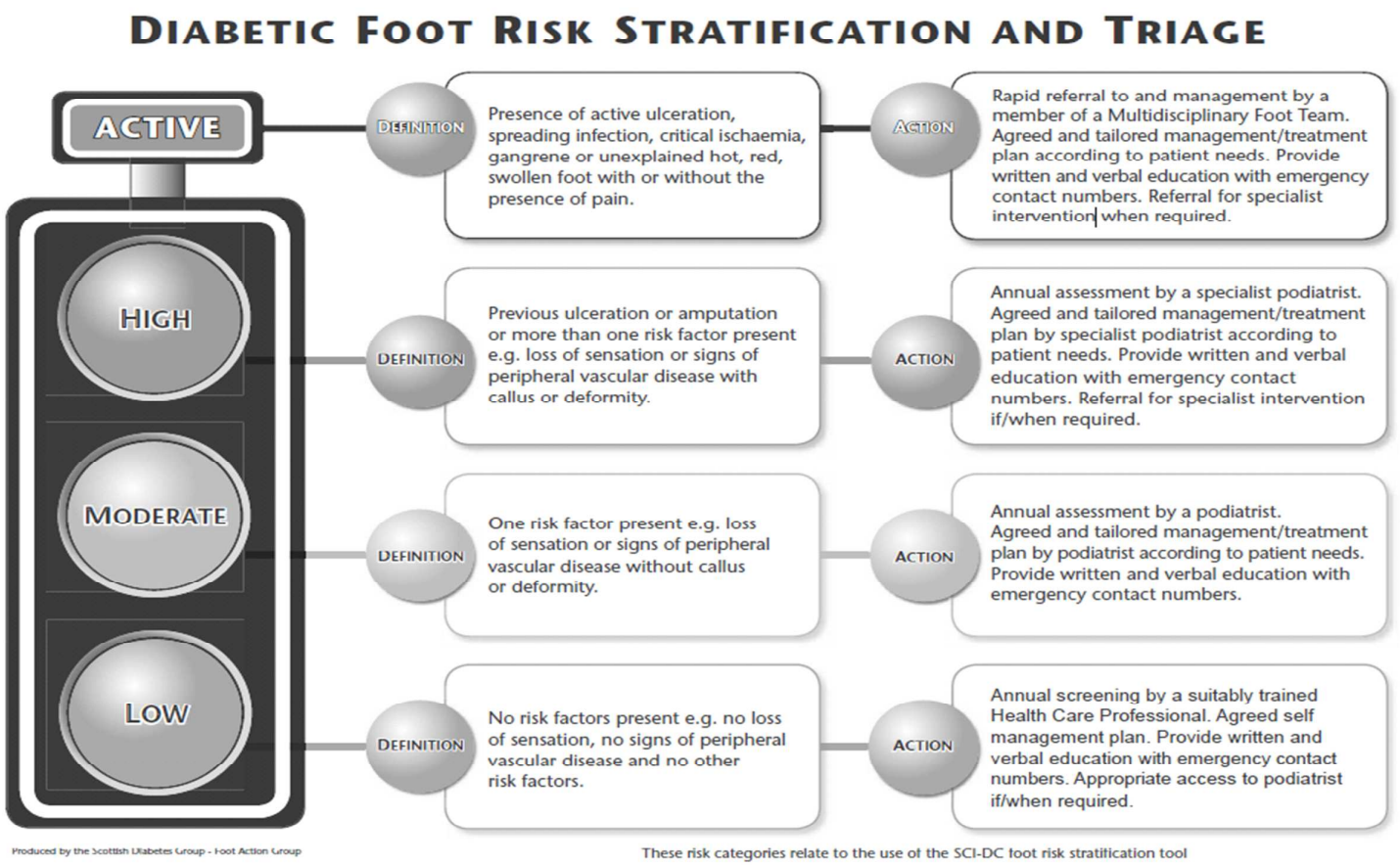
Appendices

Appendix 1 Diabetic foot risk stratification and triage



Appendix 2 Search Strategy for PUBMED (1966 – Sept 25th 2011)

1. Diabetes mellitus (MeSH)
2. Diabet*
3. 1 or 2
4. Amputation (MeSH)
5. Amput*
6. 4 or 5
7. Podiatry (MeSH)
8. Podiatr*
9. 7 or 8
10. Case-control study (MeSH)
11. Case-control* (free text)
12. Cohort studies (MeSH)
13. Cohort* (free text)
14. Retrospective Studies (MeSH)
15. Prospective Studies (MeSH)
16. Journal Article (Publication type)
17. Clinical Trial (Publication Type)
18. Randomized Controlled Trial (Publication Type)
19. 10 or 11 or 12 or 13 or 14 or 14 or 16 or 17 or 18
20. 3 and 6 and 9 and 19

Results: 184

Appendix 3 Search Strategy for CINAHL (1981 – Sept 25th 2011)

1. (MH "Diabetes Mellitus+") OR (MH "Diabetes Mellitus, Insulin-Dependent") OR (MH "Diabetes Mellitus, Non-Insulin-Dependent")
2. Diabet*
3. 1 or 2
4. (MH "Amputation+") OR (MH "Above-Knee Amputation") OR (MH "Amputation Stumps") OR (MH "Amputation Care (Iowa NIC)")
5. Amput*
6. 4 or 5
7. Podiatric Assessment") OR (MH "Education, Podiatry") OR (MH "Surgery, Podiatric+") OR (MH "Podiatric Care")
8. Podiatr*
9. 7 or 8
10. (MH "Case Control Studies+")
11. Case-control* (free text)
12. Cohort studies (MeSH)
13. Cohort* (free text)
14. (MH "Retrospective Panel Studies") OR (MH "Retrospective Design")
15. (MH "Prospective Studies") OR (MH "Concurrent Prospective Studies") OR (MH "Nonconcurrent Prospective Studies")
16. (MH "Electronic Publications+") OR (MH "Electronic Journals") OR (MH "Publication Formats+")
17. Article (free text)
18. (MH "Clinical Trials+")
19. (MH "Randomized Controlled Trials")
20. 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
21. 3 and 6 and 9 and 20

Results: 43

Appendix 4 Search Strategy for EMBASE (1974 – Sept 25th 2011)

1. 'diabetes mellitus'/exp
2. diabet*
3. 1 or 2
4. 'amputation'/exp
5. amput*
6. 4 or 5
7. 'podiatry'/exp
8. podiatr*
9. 7 or 8
10. 'case control study'/exp – (mesh/emtree)
11. 'case control study'/exp OR 'case control study' – (case control*)
12. 'cohort study'/exp – (mesh/emtree)
13. Cohort*
14. 'retrospective study'/exp
15. 'prospective study'/exp
16. 'article'/exp
17. 'clinical trial'/exp
18. 'randomized controlled trial'/exp
19. 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18
20. 3 and 6 and 9 and 19

Results: 246

Appendix 5 Search Strategy for Cochrane (1993 – Sept 25th 2011)

1. MeSH descriptor Diabetes Mellitus explode all trees in all MeSH products
2. Diabet*
3. 1 or 2
4. MeSH descriptor Amputation explode all trees
5. Amput*
6. 4 or 5
7. MeSH descriptor Podiatry explode all trees
8. Podiatr*
9. 7 or 8
10. MeSH descriptor Case-Control Studies explode all trees in all MeSH products
11. Case control stud*
12. MeSH descriptor Cohort Studies explode all trees in all MeSH products
13. Cohort stud*
14. MeSH descriptor Retrospective Studies explode all trees in all MeSH products
15. MeSH descriptor Prospective Studies explode all trees in all MeSH products
16. Article
17. Clinical Trial
18. Randomised Control Trial
19. 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18
20. 3 and 6 and 9 and 19

Results: 25
13 Cochrane Reviews
2 Other Reviews
6 Clinical Trials
2 Technology Assessments
2 Economic Evaluations
1 Cochrane Group

Appendix 6 Table of Excluded Studies

Study (Author, Country, Year)	Exclusion criteria	Details
Driver, 2010[39]	Intervention	Podiatric lead limb preservation team - No data on contact with a podiatrist as the intervention available
Ellis, 2010[40]	Design / Outcome	Audit / Diabetic Foot Complication
Zayed, 2009[41]	Intervention	Podiatry as part of Multidisciplinary team - No data on contact with a podiatrist as the intervention available
Snyder, 2006[42]	Design No reporting of association	Chart review/case series, Intervention on subset of patients, comparison group not available for this subset
Robbins, 2006[43]	Intervention	Podiatry as part of Multidisciplinary team - No data on contact with a podiatrist as the intervention available
El Sakka 2006[30]	Intervention	Podiatry as part of Multidisciplinary team - No data on contact with a podiatrist as the intervention available
Schraer, 2004[44]	Intervention	Program
Dargis, 1999[31]	Intervention	Podiatry as part of Multidisciplinary team - No data on contact with a podiatrist as the intervention available
Van Gils, 1999[32]	Intervention	Podiatry as part of Multidisciplinary team - No data on contact with a podiatrist as the intervention available
Del Aguila, 1994[45]	No report of association	Number of podiatry visits in 12 months described - Unable to determine whom were not exposed to podiatry
Malone, 1989[46]	Intervention	Intervention involved education by podiatrists, not treatment
Crane, USA, 1999[47]	Intervention	Podiatry-established critical pathway
Carrington, UK, 2001[48]	Intervention	Program including podiatry

Hamalainen, Finland, 1998 [49]	Study described in another paper	
McCabe, UK, 1998 [50]	Intervention	Clinical foot screening programme, only subset of population seen by podiatrist, no comparison group involved

BMJ open

Does contact with a podiatrist prevent the occurrence of a lower extremity amputation in people with diabetes? A systematic review and meta-analysis

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2012-002331.R1
Article Type:	Research
Date Submitted by the Author:	19-Feb-2013
Complete List of Authors:	Buckley, Claire; UCC, Perry, Ivan; University College Cork, Department of Epidemiology and Public Health Bradley, Colin; University College Cork, Dept of General Practice Kearney, Patricia; University College Cork, Department of Epidemiology and Public Health
Primary Subject Heading:	Diabetes and endocrinology
Secondary Subject Heading:	Health services research, Evidence based practice, Surgery
Keywords:	Diabetic foot < DIABETES & ENDOCRINOLOGY, VASCULAR SURGERY, Organisation of health services < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

DOES CONTACT WITH A PODIATRIST PREVENT THE OCCURRENCE OF A LOWER EXTREMITY AMPUTATION IN PEOPLE WITH DIABETES? A SYSTEMATIC REVIEW AND META-ANALYSIS

Short title

Contact with podiatry and lower extremity amputation in people with diabetes

CM BUCKLEY (CMB)[1,2], IJ PERRY (IJP)[2], CP BRADLEY (CPB)[1], PM KEARNEY (PMK)[2]

1. Dept of General Practice, UCC, Western Gateway Building, Cork, Ireland
2. Dept of Epidemiology and Public Health, UCC, Western Gateway Building, Cork, Ireland,

Corresponding author

Claire Buckley, Department of General Practice, Room 2.57, Western Gateway Building, University College Cork, Ireland
Tel No: 00353 86 6020313, Fax No: 00353 21 4205469,
Email: Claire.buckley@ucc.ie

Keywords

Podiatry, Amputation, Diabetes Mellitus, Systematic Review, Meta-analysis

Word Count

Abstract: 300 words
Main text: 2,696 words (excluding title page, abstract, references, figures, tables and appendices)

ABSTRACT

Objective

To determine the effect of contact with a podiatrist on the occurrence of Lower Extremity Amputation (LEA) in people with diabetes.

Design & data sources

We conducted a systematic review of available literature on the effect of contact with a podiatrist on the risk of LEA in people with diabetes. Eligible studies, published in English, were identified through searches of PUBMED, CINAHL, EMBASE, and Cochrane databases. The key terms, 'podiatry', 'amputation' and 'diabetes', were searched as Medical Subject Heading (MeSH) terms. Reference lists of selected papers were hand-searched for additional articles. No date restrictions were imposed.

Study Selection

Published randomised and analytical observational studies of the effect of contact with a podiatrist on the risk of LEA in people with diabetes were included. Cross-sectional studies, review articles, chart reviews and case series were excluded. Two reviewers independently assessed titles, abstracts, and full articles to identify eligible studies and extracted data related to study design, characteristics of participants, interventions, outcomes, control for confounding factors and risk estimates.

Analysis

Meta-analysis was performed separately for randomised and non-randomised studies. Relative risks (RRs) with 95% confidence intervals (CIs) were estimated with fixed and random effects models as appropriate.

Results

Six studies met the inclusion criteria and five provided data included in meta-analysis. The identified studies were heterogenous in design and included people with diabetes at both low and high risk of amputation. Contact with a podiatrist did not significantly affect the RR of LEA in a meta-analysis of available data from Randomised Controlled Trials (RCTs); (1.41, 95% CI 0.20-9.78, 2 RCTs) or from cohort studies; (0.73, 95% CI 0.39-1.33, 3 Cohort studies with 4 substudies in one cohort).

Conclusions

There is very limited data available on the effect of contact with a podiatrist on the risk of LEA in people with diabetes.

ARTICLE SUMMARY

Article Focus

- People with diabetes are at increased risk of Lower Extremity Amputation (LEA). As the prevalence of diabetes escalates worldwide, it is anticipated that there will be an increase in the number of LEAs.
- It is assumed that contact with a podiatrist prevents the occurrence of a LEA.
- This systematic review aims to determine from available literature the documented effect of contact with a podiatrist on the occurrence of a LEA in people with diabetes.

Key Messages

- Very limited data is available and the authors conclude that there is insufficient evidence to determine whether contact with a podiatrist has an effect on the risk of LEA in people with diabetes.
- Some existing studies suggest that contact with a podiatrist has a positive effect on shorter term outcomes including patient knowledge of foot care and ulcer recurrence.
- Further research on the long-term outcome of LEA is warranted.

Strengths and Limitations

- This is the first systematic review which investigates if contact with a podiatrist prevents the occurrence of a LEA in people with diabetes.
- Failure to demonstrate an effect on this long-term outcome is most likely due to limitations of available studies.
- Limitations include that studies in this systematic review looked at different sample populations ranging from patients with low baseline risk to patients with active disease. Also, included RCTs were underpowered to detect a significant difference for the outcome of LEA.

INTRODUCTION

A worldwide diabetes epidemic is unfolding[1]. Diabetes is associated with a significantly increased risk of LEA (Lower Extremity Amputation). LEA rates vary between populations with estimates ranging from 46 to 9,600 per 10^5 people with diabetes [2]. A number of factors influence the occurrence of a LEA in people with diabetes; including hypertension, obesity and hyperglycaemia [3] [4]. In the foot, previous ulceration, infection and ischaemia are proven risk factors [5]. Nearly 85% of amputations begin as foot ulcers among persons with diabetes [6]. Protective factors include control of clinical parameters and screening to identify those people at high risk and many LEAs are preventable [7] [8]. The effects of clinical and socio-demographic risk factors on the occurrence of a LEA have been well documented in people with diabetes [9] [10] [11] [12].

In 2008, a task force report by the Foot Care Interest Group of the American Diabetes Association, which included podiatrists, stated that all people with diabetes should be assigned to a foot risk category [13]. These categories were designed to direct referral to and subsequent therapy by a speciality clinician or team but did not refer specifically to the role of podiatry. Recent guidelines from Scotland outline a diabetic risk stratification and triage tool, highlighting which people need podiatry referral. According to these guidelines, all patients classified as moderate risk (i.e. at least one risk factor present), severe risk or with active disease require podiatry review [14] . Podiatry is practiced as a specialty in many countries and in many English-speaking countries, the older term of 'chiropodist' may still be used. According to the National Health Service in the UK , there is no difference between a chiropodist and a podiatrist [15]. It is assumed that podiatrists prevent LEAs by treating existing disease and educating people with diabetes on proper foot care. However, the effect of patient contact with a podiatrist on the risk of LEA in people with diabetes is unproven.

Two previous Cochrane reviews by Dorresteijn et al. have looked at firstly the effect of an integrated care approach and secondly the effect of patient education on the outcome of LEA in people with diabetes [16] [17]. The first of these reviews found no high quality evidence evaluating an integrated care approach and insufficient evidence of benefit in preventing diabetic foot ulceration [16]. The second review, updated in 2012, concluded that there is insufficient robust evidence that limited patient education alone is effective in achieving clinically relevant reductions in ulcer and LEA incidence [17]. Individual patient contact with a podiatrist was not examined as an intervention in either review. Thus, the objective of the present systematic review of published literature is to examine the effect of contact with a podiatrist on risk of LEA in people with diabetes.

METHODS

The research question, inclusion and exclusion criteria and proposed methods of analysis were specified in advance and documented in a protocol (attached as supplementary file).

Search Strategy

Pubmed, CINAHL, EMBASE (Excerpta Medica), and Cochrane databases were searched to identify relevant studies published up to and including September 25th 2011. The key terms, 'podiatry', 'amputation' and 'diabetes', were searched as Medical Subject Heading (MeSH) terms. Randomised and observational studies, published in English, which reported the effect of contact with a

podiatrist on risk of LEA in people with diabetes (type 1 or 2), were included. No date restrictions were imposed. Cross-sectional studies, review articles, non-systematic reviews, chart reviews and case series were excluded. A manual search of references cited in relevant articles was performed. All potentially eligible studies were independently reviewed by two authors (CMB and PMK).

Data abstraction and quality assessment:

Using a standardised data collection form, two reviewers (CMB, PMK) independently abstracted information on study design, year of study, characteristics of participants, interventions and outcomes, control for potential confounding factors and risk estimates. A modified version of a checklist developed by Downs and Black for assessing the methodological quality of both randomised and non-randomised studies of health care interventions was used to critically appraise the studies in this review [18]. Inconsistencies between reviewers were discussed and resolved through consensus.

Statistical Analysis

Review Manager Software Version 5 (Revman 5.0; the Cochrane Collaboration, Oxford, England) and STATA Version 12IC were used for statistical analysis. The relative risk (RR) with 95% CI was recorded for included studies. One study presented individual results for four various stages of disease so this study was analysed as 4 substudies. Meta-analysis was performed separately for randomised and non-randomised studies, using either the fixed or random effects model as appropriate. Statistical heterogeneity was assessed with Cochran's *Q* statistic. Cochran's *Q* is computed by summing the squared deviations of each study's estimate from the overall meta-analytic estimate, weighting each study's contribution in the same manner as in the meta-analysis. P-values were obtained by comparing the statistic with a χ^2 distribution with $k-1$ degrees of freedom (where k is the number of studies) [19]. To assess publication bias, a funnel plot of the overall estimate and its standard error (SE) was derived.

RESULTS

Four hundred and ninety-nine titles were retrieved from searches of electronic databases. Duplicates (138) were removed and 361 titles/abstracts were reviewed. Eighteen papers were considered for review after initial screening of titles and abstracts. Three further studies were identified as potentially eligible from reference checking. After reviewing the full text articles, 6 studies met the inclusion criteria; 2 RCTS and 4 cohort studies (figure 1)[20]. Studies were excluded because of study design e.g. chart review/audit; intervention e.g. contact with a multidisciplinary team instead of contact with a podiatrist; or in one case, the study was described in another article already included in this systematic review.

Table 1 describes the included studies according to study design, participants, interventions and outcomes. Quality of included studies was assessed and all studies were deemed of suitable quality for inclusion (tables 2 & 3). Risk of foot disease at baseline was assessed using the Diabetic foot risk stratification and triage system from the SIGN (Scottish Intercollegiate Guidelines Network) guidelines (Appendix 1) [14]. Results of included studies are presented in table 4.

Results from available studies were pooled together in separate meta-analyses for RCTs and observational studies. Five of these studies provided sufficient data to allow meta-analysis. For

RCTs, the fixed effects model was applied (Q=0.328, p=0.567) and for cohort studies, the random effects model is reported as there was evidence of significant heterogeneity between the cohort studies (Q=32.698, p=0.000). Meta-analysis of the two RCTs yielded an insignificant pooled RR of 1.41 (95% CI 0.20-9.78) while meta-analysis of the cohort studies also yielded an insignificant pooled RR of 0.73 (95% CI 0.39-1.33) (figure 2).

Data required for inclusion in the meta-analysis was unavailable for 1 eligible study. Lavery et al. compared people with diabetes on dialysis and people with diabetes with a history of a healed ulcer. During a 30-month evaluation period, only 30% of patients from both groups combined were seen for preventative care prior to ulceration. The amputation incidence density was high in both groups (dialysis group 58.7 and ulcer group 13.1 per 1,000 person-years) [21]. However, it was not possible to extract the LEA event rate in those who did or did not have contact with a podiatrist.

Visual inspection of the funnel plot produced for the included studies shows no strong evidence of publication bias (figure 3).

DISCUSSION

In this systematic review, we conclude that there is insufficient evidence to determine whether contact with a podiatrist has an effect on LEA in people with diabetes.

Strengths and limitations of this review

This is the first systematic review that the authors are aware of that investigates if contact with a podiatrist prevents the occurrence of a lower extremity amputation in patients with diabetes. A thorough literature search examining multiple databases was undertaken and 6 studies with 2 different study designs were included. While individual study design meta-analysis was performed in an effort to pool the available data, we acknowledge that heterogeneity exists between studies included in the meta-analysis in terms of baseline diabetic foot risk and type of intervention.

Included studies looked at different sample populations ranging from patients with low baseline risk to patients with active disease. For example, Ronnemaa et al. recruited patients with diabetes from the national drug imbursement register in Finland which is representative of the total population with diabetes [22]. However, Plank et al. recruited patients with diabetes from a tertiary referral centre which represents a population of patients with diabetes that have developed complications requiring referral to a tertiary centre [23]. In 5 of the 6 included studies, the population at risk were patients with diabetes. However, Sowell et al. examined a population mix of patients with diabetes, PVD and gangrene [24]. It was decided to include this study due to the dearth of research in this area. This difference in populations studied between the Sowell paper and the other 5 studies needs to be highlighted as a limitation in this review.

The diabetic foot risk of the participants at baseline (low-active) reflects the different treatment settings at recruitment and highlights heterogeneity amongst the studies (table 1). Cochran's Q statistic was used to assess heterogeneity. For RCTs, the fixed effects model was appropriate but this meta-analysis is limited as there are only 2 included studies. For cohort studies, the Q statistic of 32.698 (p=0.000) indicated that strong heterogeneity existed so the random effects model was applied to account for both random variability and the variability in effects among the studies. However, use of the random effects model limits the conclusions that can be drawn from the meta-

analysis [25]. 'A priori' sensitivity analyses were planned for different levels of baseline risk but there were insufficient data.

Sources of potential bias should be considered in relation to the observational studies. Although information was collected on potential confounders in many of the included observational studies, the analyses were not adjusted for potential confounders and sources of bias. Clinical practices may vary per individual and per location. Guidelines have been recently developed to standardise referral of patients with diabetes to podiatry [14]. Healthcare-seeking behaviours are complex and multifactorial and ethnicity and socio-economic position can influence attendance at podiatry [26] [27]. Level of disease may also influence a patient's decision to attend the podiatrist and create a self-selection bias in the patients with diabetes that attend the podiatrist. Patients that attend healthcare services in early stages of disease may be more likely to engage in other healthy lifestyle behaviours e.g. healthy diet, not smoking and this phenomenon of 'healthy user bias' has been previously documented [28]. In their retrospective cohort study, Sowell et al. reported 20 LEAs in the intervention group and 130 in the control group (noting that the population at risk in this study is patients with diabetes and/or gangrene and/or PVD) [24]. This study described the majority of included participants with the outcome of LEA. However, their analysis did not adjust for important potential confounders which limit the conclusions that can be drawn from this study.

The issues of bias and confounding are minimised by the gold standard technique of randomisation in RCTs. However, there is a lack of RCTs in this area. The 2 available RCTs have a lack of power as few participants had the outcome of LEA. The most likely cause of the low numbers of outcomes in the included studies is length of follow-up. LEA takes years to develop, especially from the time-point when a patient is classified as low risk. In the 1st included RCT, Plank et al. described 2 LEAs in the intervention group and 1 in the control group [23]. In the 2nd RCT, Ronnemaa et al. noted no LEA after 1 year of follow-up and 1 LEA in the intervention group after 7 years of follow-up [22] [16]. Neither RCT was designed to assess LEA as a primary outcome and thus, had insufficient power to detect a significant difference for the outcome of LEA.

Conclusions and Implications

Two Cochrane reviews have looked at the outcome of LEA in patients with diabetes [16] [17]. These reviews concluded that there is insufficient evidence that brief educational interventions or complex interventions reduce the risk of LEA. This systematic review concludes that there is insufficient evidence that contact with a podiatrist reduces the risk of LEA in patients with diabetes. Thus, this review cannot make any recommendations about practice. To detect the true effect, adequately powered RCTs and longer follow-up studies are needed to examine the effect of contact with a podiatrist on LEA in patients with diabetes. Perhaps, podiatry programmes could be rolled out in a manner designed to answer the question of effect on outcomes such as LEA. Such studies could also assess the impact of the timing and intensity of the podiatry intervention on outcomes. Perhaps studies focusing on high-risk participants are too close in timing to the LEA event and studies of lower-risk participants would be better to detect an effect in LEA prevention.

International standards recommend a multidisciplinary team should manage the footcare of a patient with diabetes [14]. Many studies have looked at the effects of a multidisciplinary team of which podiatry serves as a member of the team and found positive effects on various outcomes [29-36]. This may be a more realistic reflection of how patients with diabetes are managed; looking at

one service in isolation could be flawed as services are seldom delivered in isolation. According to the SIGN (Scottish Intercollegiate Guidelines Network) guidelines a multidisciplinary foot team should include a podiatrist, diabetes physician, orthotist, diabetes nurse specialist, vascular surgeon, orthopaedic surgeon and radiologist [14]. A systematic review of the literature looking at the effectiveness of multidisciplinary teams which include contact with a podiatrist would be useful.

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Declaration of Competing Interests

Nothing to declare.

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Contributor statement

Claire M Buckley (CMB) conceived and designed the study, extracted the data and wrote the paper. Ivan J Perry (IJP) revised the paper. Colin P Bradley (CPB) approved the final version to be published. Patricia M Kearney (PMK) designed the study, extracted the data and wrote the paper. CMB will act as guarantor for the paper.

Ethical Approval

None required.

Data Sharing Statement

no additional data available.

Abbreviations

CINAHL, Cumulative Index to Nursing and Allied Health Literature, LEA, Lower Extremity Amputation, MeSH, Medical Subject Headings, NHS, National Health Service, PVD, Peripheral Vascular Disease, RCT, Randomised Controlled Trial, SIGN, Scottish Intercollegiate Guidelines Network, UCC, University College Cork, UK, United Kingdom

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Figure legends

Figure 1 PRISMA flow chart: selection of studies for inclusion in review

Figure 2 Forest plots of meta- analysis of RCTs (top) and Cohort studies (bottom) with the intervention of contact with a podiatrist on left side of plot

Figure 3 Funnel plot of included studies (RCTs and Cohort studies)

Table legends

Table 1 Characteristics of Included Studies
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Appendices legends

Appendix 1 Diabetic foot risk stratification and triage
Appendix 2 Search Strategy for PUBMED (1966 – Sept 25th 2011)
Appendix 3 Search Strategy for CINAHL (1981 – Sept 25th 2011)
Appendix 4 Search Strategy for EMBASE (1974 – Sept 25th 2011)
Appendix 5 Search Strategy for Cochrane (1993 – Sept 25th 2011)
Appendix 6 Table of Excluded Studies

TABLES

Table 1 Characteristics of Included Studies

Study (Author, Country, Year)	Type of study	Participants	Interventions	Source of data used in study	Length of follow-up	Baseline risk as per diabetic foot risk stratification [14]	Outcomes
Ronnemaa, Finland, 1997[22] [16]	RCT	530 patients with diabetes randomised Intervention: 267 Control: 263	Intervention: 45 minutes individual patient education Podiatric care visits as necessary Control: Written information	Clinical report forms	1 year and 7 years	Low	Primary: Patient Knowledge about foot care Secondary: Ulcer incidence Amputation rate
Plank, Austria, 2003[23]	RCT	91 patients with diabetes randomised Intervention: 47 Control: 44	Intervention: Chiropodist visit at least once a month Control: chiropodist treatment not specifically recommended	Clinical report forms	386 days (368-424, 25^{th}-75^{th} percentile)	High (healed foot ulcers)	Primary: recurrence rate of ulcers Secondary: Amputation rate Death
Sowell, USA, 1999[24]	Cohort	255,256 with diabetes or PVD or gangrene followed over time	Intervention: Podiatric Medical care – receipt of any M0101 services Comparison: Did not receive podiatry (M0101) services	Medicare claims database	1 year	Unknown	Number of Amputations

Lipscombe, Canada, 2003 [37]	Cohort	132 patients with diabetes on PD (Peritoneal Dialysis)	Intervention: Assessment, education and footcare by chiropody	Medical charts	3 years	High	Number of Amputations
Lavery, USA, 2010[21]	Cohort	300 high-risk patients with diabetes 150 with an ulcer history 150 on dialysis followed over time	Intervention: Podiatry services - number of visits to podiatrist for prevention, ulcer treatment of other pathology	Claims data & Electronic Medical Records	30 months	High (history of foot ulcer)	Amputation rate Ulcer incidence
Sloan, UK, 2010[38]	Cohort	189,598 patients with diabetes followed over time Participants grouped into different stages (1-4) of disease depending on severity of symptoms & signs	Intervention: Care provided by podiatrist Comparison: Care provided by 'other health professional' – GP/Internist/Endocrinologist/Nurse /Physician Assistant	Medicare claims database	6 years	Stage 1: Moderate Stage 2: High Stage 3: Active Stage 4: Active	Amputation rate

Table 2 Quality Assessment of Included RCTs

Study (Author, Country, Year)	Type of study	Base Population	Randomisation	Blinding	Confounding	Losses to follow-up	Analysis
Ronnemaa, Finland, 1997 [22]	RCT	Community based care in Finland, receiving anti-diabetic drug treatment from the national drug reimbursement register	Randomisation performed separately for men/women and patients </> 20 years. Method of randomisation not described	Outcome assessor blinded to baseline characteristics but no further information on blinding provided	Baseline Characteristics not described	Follow-up completed by 63% of patients in intervention group and 62% patients in control group at seven years	No intention to treat analysis undertaken
Plank, Austria, 2003 [23]	RCT	All in routine outpatient care at hospital diabetic foot clinic in Austria	Subjects were assigned a patient number in ascending order and randomly allocated to the intervention or control group	Allocation concealment ensured	Similar Baseline Characteristics	All patients followed up	Intention to treat & per protocol analysis

Table 3 Quality Assessment of Included Cohort Studies

Study (Author, Country, Year)	Type of study	Base Population	Confounding	Losses to follow-up	Analysis
Sowell, USA, 1999 [24]	Cohort	All Medicare population at risk for lower extremity amputation in 1993-1994	Not addressed – only looked at 1 variable – acknowledged as a limitation	No losses to follow-up	Amputation incidence rates with & without exposure to podiatry
Lipscombe, Canada, 2003 [37]	Cohort	Patients in Peritoneal Dialysis program at University Health Network, between January 1997 and December 1999	Data on confounding variables collected	No losses to follow-up	Descriptive Stats
Lavery, USA, 2010 [21]	Cohort	Patients with diabetes attending Scott and White Health Plan, Texas, USA	Data on confounding variables collected	150 consecutive patients with at least 30 months follow-up from the time of diagnosis recruited so no losses to follow-up	Descriptive Stats
Sloan, UK, 2010 [38]	Cohort	All individuals with a DM-related LEC diagnosis between 1994 and 2001	Data on confounding variables collected	No losses to follow-up	Hazard Ratios adjusted for Medicare expenditures from care received from non-study health professionals

Table 4 Results of Included Studies

Study (Author, Country, Year)	Type of study	Primary Outcome	Baseline risk as per diabetic foot risk stratification [14]	Relative risk of amputation with contact with a podiatrist compared to no contact with a podiatrist
Ronnemaa, Finland, 1997 [22] [16]	RCT	*Diabetes-related Amputation:* One year follow-up: Intervention: 0 Control: 0 Seven years follow-up: Intervention: 1 Control: 0	Low	2.96
Plank, Austria, 2003 [23]	RCT	*Diabetes-related Amputation:* One year follow-up: Intervention: 2 Control: 1	High (healed foot ulcers)	0.92
Sowell, USA, 1999 [24]	Cohort	*Amputation related to diabetes/gangrene/PVD* One year follow-up: Intervention: 20 Control: 130	Unknown	0.25
Lipscombe, Canada, 2003 [37]	Cohort	*Diabetes-related Amputation:* Amputation during any of the 3 years of the study: Intervention: 11 Control: 4	High	2.16
Lavery, USA, 2010 [21]	Cohort	*Diabetes-related Amputation:* Actual number of amputations not outlined *Amputation Incidence Density:* 58.7 in Dialysis Group per 1,000 person years 13.1 in Ulcer Group per 1,000 person years	High (history of foot ulcer)	Unknown
Sloan, UK, 2010 [38]	Cohort	*Diabetes-related Amputation:* Six year follow-up: actual number of amputations not outlined	Stage 1: Moderate Stage 2: High Stage 3: Active Stage 4: Active	Stage 1 disease : 2.20 Stage 2 disease : 0.85 Stage 3 disease : 0.44 Stage 4 disease : 0.36

DOES CONTACT WITH A PODIATRIST PREVENT THE OCCURRENCE OF A LOWER EXTREMITY AMPUTATION IN PEOPLE WITH DIABETES? A SYSTEMATIC REVIEW AND META-ANALYSIS

Short title

Contact with podiatry and lower extremity amputation in people with diabetes

CM BUCKLEY (CMB)[1,2], IJ PERRY (IJP)[2], CP BRADLEY (CPB)[1], PM KEARNEY (PMK)[2]

1. Dept of General Practice, UCC, Western Gateway Building, Cork, Ireland
2. Dept of Epidemiology and Public Health, UCC, Western Gateway Building, Cork, Ireland,

Corresponding author

Claire Buckley, Department of General Practice, Room 2.57, Western Gateway Building, University College Cork, Ireland
Tel No: 00353 86 6020313, Fax No: 00353 21 4205469,
Email: Claire.buckley@ucc.ie

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ABSTRACT

Objective

To determine the effect of contact with a podiatrist on the occurrence of Lower Extremity Amputation (LEA) in people with diabetes.

Design & data sources

We conducted a systematic review of available literature on the effect of contact with a podiatrist on the risk of LEA in people with diabetes. Eligible studies, published in English, were identified through searches of PUBMED, CINAHL, EMBASE, and Cochrane databases. The key terms, 'podiatry', 'amputation' and 'diabetes', were searched as (Medical Subject Heading (MeSH) terms. Reference lists of selected papers were hand-searched for additional articles. No date restrictions were imposed.

Study Selection

Published randomised and analytical observational studies of the effect of contact with a podiatrist on the risk of LEA in people with diabetes were included. Cross-sectional studies, review articles, chart reviews and case series were excluded. Two reviewers independently assessed titles, abstracts, and full articles to identify eligible studies and extracted data related to study design, characteristics of participants, interventions, and outcomes, control for confounding factors and risk estimates.

Analysis

Meta-analysis was performed separately for randomised and non-randomised studies. Relative risks (RRs) with 95% confidence intervals (CIs) were estimated with fixed and random effects models as appropriate.

Results

Six studies met the inclusion criteria and five provided data included in meta-analysis. The identified studies were heterogenous in design and included people with diabetes at both low and high risk of amputation. Contact with a podiatrist did not significantly affect the RR of LEA in a meta-analysis of available data from Randomised Controlled Trials (RCTs); (1.41, 95% CI 0.20-9.78, 2 RCTs) or from cohort studies; (0.73, 95% CI 0.394-1.33, 3 Cohort studies with 4 substudies in one cohort).

Conclusions

There is very limited data available on the effect of contact with a podiatrist on the risk of LEA in people with diabetes.

ARTICLE SUMMARY

Article Focus

- People with diabetes are at increased risk of ~~LEA (~~Lower Extremity Amputation (LEA). As the prevalence of diabetes escalates worldwide, it is anticipated that there will be an increase in the number of LEAs.
- It is assumed that contact with a podiatrist prevents the occurrence of a LEA.
- This systematic review aims to determine from available literature the documented effect of contact with a podiatrist on the occurrence of a LEA in people with diabetes.

Key Messages

- Very limited data is available and the authors conclude that there is insufficient evidence to determine whether contact with a podiatrist has an effect on the risk of LEA in people with diabetes.
- Some existing studies suggest that contact with a podiatrist has a positive effect on shorter term outcomes including patient knowledge of foot care and ulcer recurrence.
- Further research on the long-term outcome of LEA is warranted.

Strengths and Limitations

- This is the first systematic review which investigates if contact with a podiatrist prevents the occurrence of a LEA in people with diabetes.
- Failure to demonstrate an effect on this long-term outcome is most likely due to limitations of available studies.
- Limitations include that studies in this systematic review looked at different sample populations ranging from patients with low baseline risk to patients with active disease. Also, included RCTs were underpowered to detect a significant difference for the outcome of LEA.

INTRODUCTION

A worldwide diabetes epidemic is unfolding[1]. Diabetes is associated with a significantly increased risk of LEA (Lower Extremity Amputation). LEA rates vary between populations with estimates ranging from 46 to 9,600 per 10^5 people with diabetes [2]. A number of factors influence the occurrence of a LEA in people with diabetes; including hypertension, obesity and hyperglycaemia [3] [4]. ~~[3 4].~~ In the foot, previous ulceration, infection and ischaemia are proven risk factors [5]. Nearly 85% of amputations begin as foot ulcers among persons with diabetes [6]. Protective factors include control of clinical parameters and screening to identify those people at high risk and many LEAs are preventable [7] [8]. The effects of clinical and socio-demographic risk factors on the occurrence of a LEA have been well documented in people with diabetes [9] [10] [11] [12].

In 2008, a task force report by the Foot Care Interest Group of the American Diabetes Association, which included podiatrists, stated that all people with diabetes should be assigned to a foot risk category [13]. These categories were designed to direct referral to and subsequent therapy by a speciality clinician or team but did not refer specifically to the role of podiatry. Recent guidelines from Scotland outline a diabetic risk stratification and triage tool, highlighting which people need podiatry referral. According to these guidelines, all patients classified as moderate risk (i.e. at least one risk factor present), severe risk or with active disease require podiatry review [14] . Podiatry is practiced as a specialty in many countries and in many English-speaking countries, the older term of '~~"~~chiropodist'~~"~~ may still be used. According to the National Health Service in the UK , there is no difference between a chiropodist and a podiatrist [15]. It is assumed that podiatrists prevent LEAs by treating existing disease and educating people with diabetes on proper foot care. However, the effect of patient contact with a podiatrist on the risk of LEA in people with diabetes is unproven.

Two previous Cochrane reviews by Dorresteijn et al. have looked at firstly the effect of an integrated care approach and secondly the effect of patient education on the outcome of LEA in people with diabetes [16] [17] ~~[16 17]~~. The first of these reviews found no high quality evidence evaluating an integrated care approach and insufficient evidence of benefit in preventing diabetic foot ulceration [16]. The second review, updated in 2012, concluded that there is insufficient robust evidence that limited patient education alone is effective in achieving clinically relevant reductions in ulcer and LEA incidence [17]. Individual patient contact with a podiatrist was not examined as an intervention in either review. Thus, the objective of t~~T~~he present systematic review of published literature is to examine~~s~~ the effect of contact with a podiatrist on risk of LEA in people with diabetes.

METHODS

The research question, inclusion and exclusion criteria and proposed methods of analysis were specified in advance and documented in a protocol (attached as supplementary file).

Search Strategy

Pubmed, CINAHL, EMBASE (Excerpta Medica), and Cochrane databases were searched to identify relevant studies published up to and including September 25th 2011. The key terms, 'podiatry', 'amputation' and 'diabetes', were searched as ~~MeSH (~~Medical Subject Heading (MeSH) terms. Randomised and observational studies, published in English, which reported the effect of contact

with a podiatrist on risk of LEA in people with diabetes (type 1 or 2), were included. No date restrictions were imposed. Cross-sectional studies, review articles, non-systematic reviews, chart reviews and case series were excluded. A manual search of references cited in relevant articles was performed. All potentially eligible studies were independently reviewed by two authors (CMB and PMK).

Data abstraction and quality assessment:

Using a standardised data collection form, two reviewers (CMB, PMK) independently abstracted information on study design, year of study, characteristics of participants, interventions and outcomes, control for potential confounding factors and risk estimates. A modified version of a checklist developed by Downs and Black for assessing the methodological quality of both randomised and non-randomised studies of health care interventions was used to critically appraise the studies in this review [18]. Inconsistencies between reviewers were discussed and resolved through consensus.

Statistical Analysis

Review Manager Software Version 5 (Revman 5.0; the Cochrane Collaboration, Oxford, England) and STATA Version 12IC were used for statistical analysis. The ~~RR (~~relative risk (RR) with 95% CI was recorded for included studies. One study presented individual results for four various stages of disease so this study was analysed as 4 substudies. Meta-analysis was performed separately for randomised and non-randomised studies, using either the fixed or random effects model as appropriate. Statistical heterogeneity was assessed with Cochran's *Q* statistic. Cochran's *Q* is computed by summing the squared deviations of each study's estimate from the overall meta-analytic estimate, weighting each study's contribution in the same manner as in the meta-analysis. P-values were obtained by comparing the statistic with a χ^2 distribution with $k-1$ degrees of freedom (where k is the number of studies) [19]. To assess publication bias, a funnel plot of the overall estimate and its standard error (SE) was derived.

RESULTS

Four hundred and ninety-nine titles were retrieved from searches of electronic databases. Duplicates (138) were removed and 361 titles/abstracts were reviewed. Eighteen papers were considered for review after initial screening of titles and abstracts. Three further studies were identified as potentially eligible from reference checking. After reviewing the full text articles, 6 studies met the inclusion criteria; 2 RCTS and 4 cohort studies (~~PRISMA flow chart -~~figure 1)[20]. Studies were excluded because of study design e.g. chart review/audit; intervention e.g. contact with a multidisciplinary team instead of contact with a podiatrist; or in one case, the study was described in another article already included in this systematic review.

Table 1 describes the included studies according to study design, participants, interventions and outcomes. Quality of included studies was assessed and all studies were deemed of suitable quality for inclusion (tables 2 & 3). Risk of foot disease at baseline was assessed using the Diabetic foot risk stratification and triage system from the SIGN (Scottish Intercollegiate Guidelines Network) guidelines (Appendix 1) [14]. Results of included studies are presented in table 4.

Results from available studies were pooled together in separate meta-analyses for RCTs and observational studies. Five of these studies provided sufficient data to allow meta-analysis. For RCTs, the fixed effects model was applied (Q=0.328, p=0.567) and for cohort studies, the random effects model is reported as there was evidence of significant heterogeneity between the cohort studies (Q-=-32.698, p=0.000). Meta-analysis of the two RCTs yielded an insignificant pooled RR of 1.41 (95% CI 0.20-9.78) while meta-analysis of the cohort studies also yielded an insignificant pooled RR of 0.73 (95% CI 0.394-1.33) (figure 2).

Data required for inclusion in the meta-analysis was unavailable for 1 eligible study. Lavery et al. compared people with diabetes on dialysis and people with diabetes with a history of a healed ulcer. During a 30-month evaluation period, only 30% of patients from both groups combined were seen for preventative care prior to ulceration. The amputation incidence density was high in both groups (dialysis group 58.7 and ulcer group 13.1 per 1,000 person-years) [21]. However, it was not possible to extract the LEA event rate in those who did or did not have contact with a podiatrist.

Visual inspection of the funnel plot produced for the included studies shows no strong evidence of publication bias (figure 3).

DISCUSSION

In this systematic review, we conclude that there is insufficient evidence to determine whether contact with a podiatrist has an effect on LEA in people with diabetes.

Strengths and limitations of this review

This is the first systematic review that the authors are aware of that investigates if contact with a podiatrist prevents the occurrence of a lower extremity amputation in patients with diabetes. A thorough literature search examining multiple databases was undertaken and 6 studies with 2 different study designs were included. While individual study design meta-analysis was performed in an effort to pool the available data, we acknowledge that heterogeneity exists between studies included in the meta-analysis in terms of baseline diabetic foot risk and type of intervention.

Included studies looked at different sample populations ranging from patients with low baseline risk to patients with active disease. For example, Ronnemaa et al. recruited patients with diabetes from the national drug imbursement register in Finland which is representative of the total population with diabetes [22]. However, Plank et al. recruited patients with diabetes from a tertiary referral centre which represents a population of patients with diabetes that have developed complications requiring referral to a tertiary centre [23]. In 5 of the 6 included studies, the population at risk were patients with diabetes. However, Sowell et al. examined a population mix of patients with diabetes, PVD and gangrene [24]. It was decided to include this study due to the dearth of research in this area. This difference in populations studied between the Sowell paper and the other 5 studies needs to be highlighted as a limitation in this review.

The diabetic foot risk of the participants at baseline (low-active) reflects the different treatment settings at recruitment and highlights heterogeneity amongst the studies (table 1). Cochran's Q statistic was used to assess heterogeneity. For RCTs, the fixed effects model was appropriate but this meta-analysis is limited as there are only 2 included studies. For cohort studies, the Q statistic of 32.698 (p=0.000) indicated that strong heterogeneity existed so the random effects model was

applied to account for both random variability and the variability in effects among the studies. However, use of the random effects model limits the conclusions that can be drawn from the meta-analysis [25]. 'A priori' sensitivity analyses were planned for different levels of baseline risk but there were insufficient data.

Sources of potential bias should be considered in relation to the observational studies. Although information was collected on potential confounders in many of the included observational studies, the analyses were not adjusted for potential confounders and sources of bias. Clinical practices may vary per individual and per location. Guidelines have been recently developed to standardise referral of patients with diabetes to podiatry [14]. Healthcare-seeking behaviours are complex and multifactorial and ethnicity and socio-economic position can influence attendance at podiatry [26] [27]. Level of disease may also influence a patient's decision to attend the podiatrist and create a self-selection bias in the patients with diabetes that attend the podiatrist. Patients that attend healthcare services in early stages of disease may be more likely to engage in other healthy lifestyle behaviours e.g. healthy diet, not smoking and this phenomenon of 'healthy user bias' has been previously documented [28]. In their retrospective cohort study, Sowell et al. reported 20 LEAs in the intervention group and 130 in the control group (noting that the population at risk in this study is patients with diabetes and/or gangrene and/or PVD) [24]. This study described the majority of included participants with the outcome of LEA. However, their analysis did not adjust for important potential confounders which limit the conclusions that can be drawn from this study.

The issues of bias and confounding are minimis~~eliminat~~ed by the gold standard technique of randomisation in RCTs. However, there is a lack of RCTs in this area. The 2 available RCTs have a lack of power as few participants had the outcome of LEA. The most likely cause of the low numbers of outcomes in the included studies is length of follow-up. LEA takes years to develop, especially from the time-point when a patient is classified as low risk. In the 1st included RCT, Plank et al. described 2 LEAs in the intervention group and 1 in the control group [23]. In the 2nd RCT, Ronnemaa et al. noted no LEA after 1 year of follow-up and 1 LEA in the intervention group after 7 years of follow-up [22] [16]. Neither RCT was designed to assess LEA as a primary outcome and thus, had insufficient power to detect a significant difference for the outcome of LEA.

Conclusions and Implications

Two Cochrane reviews have looked at the outcome of LEA in patients with diabetes [16] [17]~~[16 17]~~. These reviews concluded that there is insufficient evidence that brief educational interventions or complex interventions reduce the risk of LEA. This systematic review concludes that there is insufficient evidence that contact with a podiatrist reduces the risk of LEA in patients with diabetes. Thus, this review cannot make any recommendations about practice. To detect the true effect, adequately powered RCTs and longer follow-up studies are needed to examine the effect of contact with a podiatrist on LEA in patients with diabetes. Perhaps, podiatry programmes could be rolled out in a manner designed to answer the question of effect on outcomes such as LEA. Such studies could also assess the impact of the timing and intensity of the podiatry intervention on outcomes. Perhaps studies focusing on high-risk participants are too close in timing to the LEA event and studies of lower-risk participants would be better to detect an effect in LEA prevention.

International standards recommend a multidisciplinary team should manage the footcare of a patient with diabetes [14]. Many studies have looked at the effects of a multidisciplinary team of

which podiatry serves as a member of the team and found positive effects on various outcomes [29-36]. This may be a more realistic reflection of how patients with diabetes are managed; looking at one service in isolation could be flawed as services are seldom delivered in isolation. According to the SIGN (Scottish Intercollegiate Guidelines Network) guidelines a multidisciplinary foot team should include a podiatrist, diabetes physician, orthotist, diabetes nurse specialist, vascular surgeon, orthopaedic surgeon and radiologist [14]. A systematic review of the literature looking at the effectiveness of multidisciplinary teams which include contact with a podiatrist would be useful.

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Declaration of Competing Interests

Nothing to declare.

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Contributor statement

Claire M Buckley (CMB) conceived and designed the study, extracted the data and wrote the paper. Ivan J Perry (IJP) revised the paper. Colin P Bradley (CPB) approved the final version to be published. Patricia M Kearney (PMK) designed the study, extracted the data and wrote the paper. CMB will act as guarantor for the paper.

Ethical Approval

None required.

Data Sharing Statement

There is no additional data available.

Abbreviations

CINAHL, Cumulative Index to Nursing and Allied Health Literature, LEA, Lower Extremity Amputation, MeSH, Medical Subject Headings, NHS, National Health Service, PVD, Peripheral Vascular Disease, RCT, Randomised Controlled Trial, SIGN, Scottish Intercollegiate Guidelines Network, UCC, University College Cork, UK, United Kingdom

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Table legends

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Appendix 1 Diabetic foot risk stratification and triage
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Appendix 3 Search Strategy for CINAHL (1981 – Sept 25th 2011)
Appendix 4 Search Strategy for EMBASE (1974 – Sept 25th 2011)
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Appendix 6 Table of Excluded Studies

TABLES

Table 1 Characteristics of Included Studies

Study (Author, Country, Year)	Type of study	Participants	Interventions	Source of data used in study	Length of follow-up	Baseline risk as per diabetic foot risk stratification [14]	Outcomes
Ronnemaa, Finland, 1997[22] [16]	RCT	530 patients with diabetes randomised Intervention: 267 Control: 263	Intervention: 45 minutes individual patient education Podiatric care visits as necessary Control: Written information	Clinical report forms	1 year and 7 years	Low	Primary: Patient Knowledge about foot care Secondary: Ulcer incidence Amputation rate
Plank, Austria, 2003[23]	RCT	91 patients with diabetes randomised Intervention: 47 Control: 44	Intervention: Chiropodist visit at least once a month Control: chiropodist treatment not specifically recommended	Clinical report forms	386 days (368-424, 25^{th}-75^{th} percentile)	High (healed foot ulcers)	Primary: recurrence rate of ulcers Secondary: Amputation rate Death
Sowell, USA, 1999[24]	Cohort	255,256 with diabetes or PVD or gangrene followed over time	Intervention: Podiatric Medical care – receipt of any M0101 services Comparison: Did not receive podiatry (M0101) services	Medicare claims database	1 year	Unknown	Number of Amputations

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Lipscombe, Canada, 2003 [37]	Cohort	132 patients with diabetes on PD (Peritoneal Dialysis)	Intervention: Assessment, education and footcare by chiropody	Medical charts	3 years	High	Number of Amputations
Lavery, USA, 2010[21]	Cohort	300 high-risk patients with diabetes 150 with an ulcer history 150 on dialysis followed over time	Intervention: Podiatry services - number of visits to podiatrist for prevention, ulcer treatment of other pathology	Claims data & Electronic Medical Records	30 months	High (history of foot ulcer)	Amputation rate Ulcer incidence
Sloan, UK, 2010[38]	Cohort	189,598 patients with diabetes followed over time Participants grouped into different stages (1-4) of disease depending on severity of symptoms & signs	Intervention: Care provided by podiatrist Comparison: Care provided by 'other health professional' – GP/Internist/Endocrinologist/Nurse /Physician Assistant	Medicare claims database	6 years	Stage 1: Moderate Stage 2: High Stage 3: Active Stage 4: Active	Amputation rate

Table 2 Quality Assessment of Included RCTs

Study (Author, Country, Year)	Type of study	Base Population	Randomisation	Blinding	Confounding	Losses to follow-up	Analysis
Ronnemaa, Finland, 1997 [22]	RCT	Community based care in Finland, receiving anti-diabetic drug treatment from the national drug reimbursement register	Randomisation performed separately for men/women and patients </> 20 years. Method of randomisation not described	Outcome assessor blinded to baseline characteristics but no further information on blinding provided	Baseline Characteristics not described	Follow-up completed by 63% of patients in intervention group and 62% patients in control group at seven years	No intention to treat analysis undertaken
Plank, Austria, 2003 [23]	RCT	All in routine outpatient care at hospital diabetic foot clinic in Austria	Subjects were assigned a patient number in ascending order and randomly allocated to the intervention or control group	Allocation concealment ensured	Similar Baseline Characteristics	All patients followed up	Intention to treat & per protocol analysis

Table 3 Quality Assessment of Included Cohort Studies

Study (Author, Country, Year)	Type of study	Base Population	Confounding	Losses to follow-up	Analysis
Sowell, USA, 1999 [24]	Cohort	All Medicare population at risk for lower extremity amputation in 1993-1994	Not addressed – only looked at 1 variable – acknowledged as a limitation	No losses to follow-up	Amputation incidence rates with & without exposure to podiatry
Lipscombe, Canada, 2003 [37]	Cohort	Patients in Peritoneal Dialysis program at University Health Network, between January 1997 and December 1999	Data on confounding variables collected	No losses to follow-up	Descriptive Stats
Lavery, USA, 2010 [21]	Cohort	Patients with diabetes attending Scott and White Health Plan, Texas, USA	Data on confounding variables collected	150 consecutive patients with at least 30 months follow-up from the time of diagnosis recruited so no losses to follow-up	Descriptive Stats
Sloan, UK, 2010 [38]	Cohort	All individuals with a DM-related LEC diagnosis between 1994 and 2001	Data on confounding variables collected	No losses to follow-up	Hazard Ratios adjusted for Medicare expenditures from care received from non-study health professionals

Table 4 Results of Included Studies

Study (Author, Country, Year)	Type of study	Primary Outcome	Baseline risk as per diabetic foot risk stratification [14]	Relative risk of amputation with contact with a podiatrist compared to no contact with a podiatrist
Ronnemaa, Finland, 1997 [22] [16]	RCT	*Diabetes-related Amputation:* One year follow-up: Intervention: 0 Control: 0 Seven years follow-up: Intervention: 1 Control: 0	Low	2.96
Plank, Austria, 2003 [23]	RCT	*Diabetes-related Amputation:* One year follow-up: Intervention: 2 Control: 1	High (healed foot ulcers)	0.92
Sowell, USA, 1999 [24]	Cohort	*Amputation related to diabetes/gangrene/PVD* One year follow-up: Intervention: 20 Control: 130	Unknown	0.25
Lipscombe, Canada, 2003 [37]	Cohort	*Diabetes-related Amputation:* Amputation during any of the 3 years of the study: Intervention: 11 Control: 4	High	2.16
Lavery, USA, 2010 [21]	Cohort	*Diabetes-related Amputation:* Actual number of amputations not outlined *Amputation Incidence Density:* 58.7 in Dialysis Group per 1,000 person years 13.1 in Ulcer Group per 1,000 person years	High (history of foot ulcer)	Unknown
Sloan, UK, 2010 [38]	Cohort	*Diabetes-related Amputation:* Six year follow-up: actual number of amputations not outlined	Stage 1: Moderate Stage 2: High Stage 3: Active Stage 4: Active	Stage 1 disease : 2.20 Stage 2 disease : 0.85 Stage 3 disease : 0.44 Stage 4 disease : 0.36

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2-3
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4, Supplementary File
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4-5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	Appendices 2-5
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	5
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	5
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	5

PRISMA 2009 Checklist

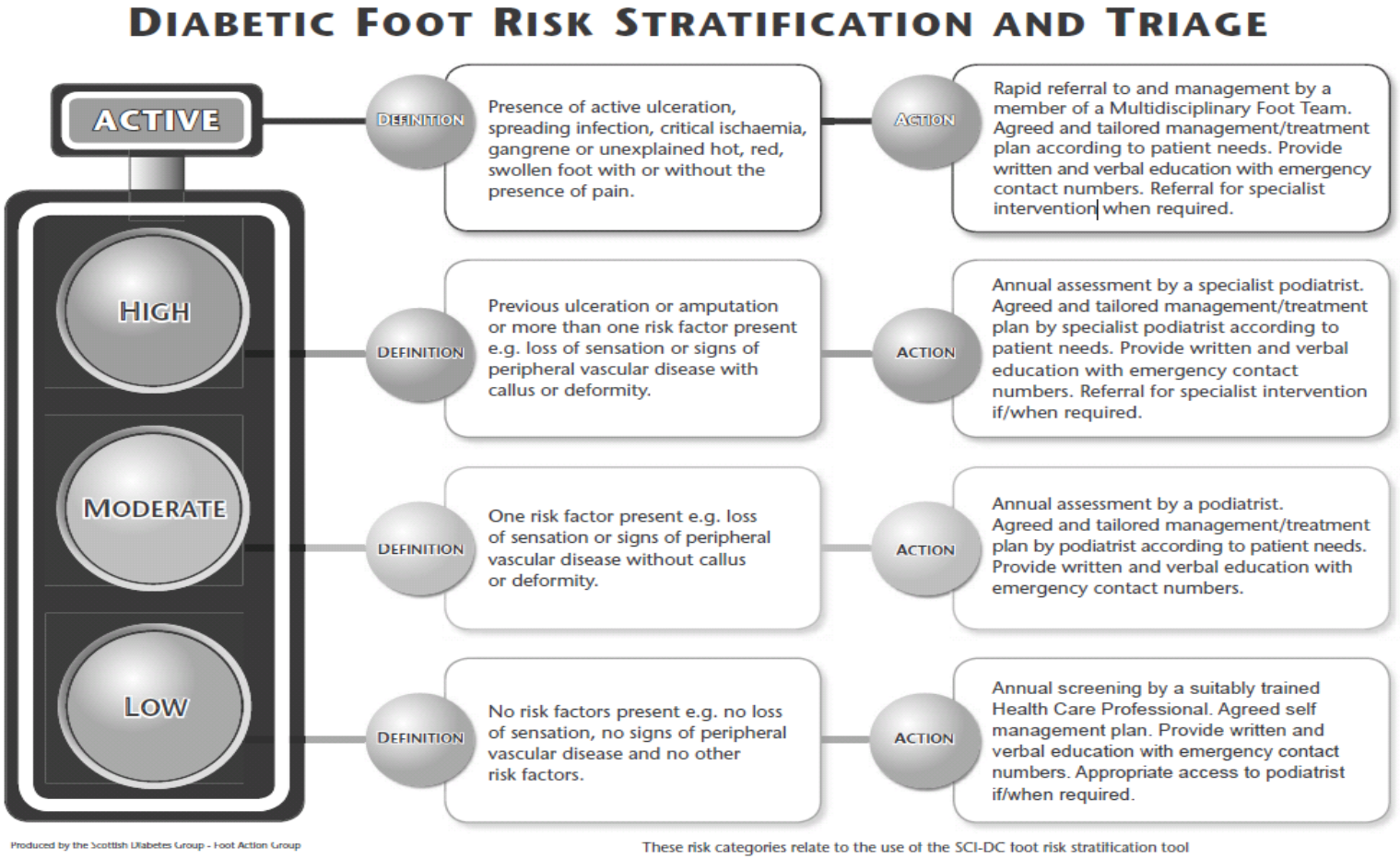
Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	5
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	7
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5 Figure 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	13-14
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	15-16
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	17 Figure 2
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	6
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	6 Figure 3
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	n/a
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	6
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	6
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	7-8
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	8

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: www.prisma-statement.org.

Appendices

Appendix 1 Diabetic foot risk stratification and triage



Appendix 2 Search Strategy for PUBMED (1966 – Sept 25th 2011)

1. Diabetes mellitus (MeSH)
2. Diabet*
3. 1 or 2
4. Amputation (MeSH)
5. Amput*
6. 4 or 5
7. Podiatry (MeSH)
8. Podiatr*
9. 7 or 8
10. Case-control study (MeSH)
11. Case-control* (free text)
12. Cohort studies (MeSH)
13. Cohort* (free text)
14. Retrospective Studies (MeSH)
15. Prospective Studies (MeSH)
16. Journal Article (Publication type)
17. Clinical Trial (Publication Type)
18. Randomized Controlled Trial (Publication Type)
19. 10 or 11 or 12 or 13 or 14 or 14 or 16 or 17 or 18
20. 3 and 6 and 9 and 19

Results: 184

Appendix 3 Search Strategy for CINAHL (1981 – Sept 25th 2011)

1. (MH "Diabetes Mellitus+") OR (MH "Diabetes Mellitus, Insulin-Dependent") OR (MH "Diabetes Mellitus, Non-Insulin-Dependent")
2. Diabet*
3. 1 or 2
4. (MH "Amputation+") OR (MH "Above-Knee Amputation") OR (MH "Amputation Stumps") OR (MH "Amputation Care (Iowa NIC)")
5. Amput*
6. 4 or 5
7. Podiatric Assessment") OR (MH "Education, Podiatry") OR (MH "Surgery, Podiatric+") OR (MH "Podiatric Care")
8. Podiatr*
9. 7 or 8
10. (MH "Case Control Studies+")
11. Case-control* (free text)
12. Cohort studies (MeSH)
13. Cohort* (free text)
14. (MH "Retrospective Panel Studies") OR (MH "Retrospective Design")
15. (MH "Prospective Studies") OR (MH "Concurrent Prospective Studies") OR (MH "Nonconcurrent Prospective Studies")
16. (MH "Electronic Publications+") OR (MH "Electronic Journals") OR (MH "Publication Formats+")
17. Article (free text)
18. (MH "Clinical Trials+")
19. (MH "Randomized Controlled Trials")
20. 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
21. 3 and 6 and 9 and 20

Results: 43

Appendix 4 Search Strategy for EMBASE (1974 – Sept 25th 2011)

1. 'diabetes mellitus'/exp
2. diabet*
3. 1 or 2
4. 'amputation'/exp
5. amput*
6. 4 or 5
7. 'podiatry'/exp
8. podiatr*
9. 7 or 8
10. 'case control study'/exp – (mesh/emtree)
11. 'case control study'/exp OR 'case control study' – (case control*)
12. 'cohort study'/exp – (mesh/emtree)
13. Cohort*
14. 'retrospective study'/exp
15. 'prospective study'/exp
16. 'article'/exp
17. 'clinical trial'/exp
18. 'randomized controlled trial'/exp
19. 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18
20. 3 and 6 and 9 and 19

Results: 246

Appendix 5 Search Strategy for Cochrane (1993 – Sept 25th 2011)

1. MeSH descriptor Diabetes Mellitus explode all trees in all MeSH products
2. Diabet*
3. 1 or 2
4. MeSH descriptor Amputation explode all trees
5. Amput*
6. 4 or 5
7. MeSH descriptor Podiatry explode all trees
8. Podiatr*
9. 7 or 8
10. MeSH descriptor Case-Control Studies explode all trees in all MeSH products
11. Case control stud*
12. MeSH descriptor Cohort Studies explode all trees in all MeSH products
13. Cohort stud*
14. MeSH descriptor Retrospective Studies explode all trees in all MeSH products
15. MeSH descriptor Prospective Studies explode all trees in all MeSH products
16. Article
17. Clinical Trial
18. Randomised Control Trial
19. 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18
20. 3 and 6 and 9 and 19

Results: 25
13 Cochrane Reviews
2 Other Reviews
6 Clinical Trials
2 Technology Assessments
2 Economic Evaluations
1 Cochrane Group

Appendix 6 Table of Excluded Studies

Study (Author, Country, Year)	Exclusion criteria	Details
Driver, 2010[39]	Intervention	Podiatric lead limb preservation team - No data on contact with a podiatrist as the intervention available
Ellis, 2010[40]	Design / Outcome	Audit / Diabetic Foot Complication
Zayed, 2009[41]	Intervention	Podiatry as part of Multidisciplinary team - No data on contact with a podiatrist as the intervention available
Snyder, 2006[42]	Design No reporting of association	Chart review/case series, Intervention on subset of patients, comparison group not available for this subset
Robbins, 2006[43]	Intervention	Podiatry as part of Multidisciplinary team - No data on contact with a podiatrist as the intervention available
El Sakka 2006[30]	Intervention	Podiatry as part of Multidisciplinary team - No data on contact with a podiatrist as the intervention available
Schraer, 2004[44]	Intervention	Program
Dargis, 1999[31]	Intervention	Podiatry as part of Multidisciplinary team - No data on contact with a podiatrist as the intervention available
Van Gils, 1999[32]	Intervention	Podiatry as part of Multidisciplinary team - No data on contact with a podiatrist as the intervention available
Del Aguila, 1994[45]	No report of association	Number of podiatry visits in 12 months described - Unable to determine whom were not exposed to podiatry
Malone, 1989[46]	Intervention	Intervention involved education by podiatrists, not treatment
Crane, USA, 1999[47]	Intervention	Podiatry-established critical pathway
Carrington, UK, 2001[48]	Intervention	Program including podiatry

Hamalainen, Finland, 1998 [49]	Study described in another paper	
McCabe, UK, 1998 [50]	Intervention	Clinical foot screening programme, only subset of population seen by podiatrist, no comparison group involved

PROTOCOL FOR SYSTEMATIC REVIEW

DOES CONTACT WITH A PODIATRIST PREVENT THE OCCURRENCE OF A LOWER EXTREMITY AMPUTATION IN PEOPLE WITH DIABETES? A SYSTEMATIC REVIEW AND META-ANALYSIS

Authors:
Dr Claire M. Buckley
Professor Ivan J. Perry
Professor Colin P. Bradley
Dr Patricia M. Kearney

BACKGROUND

Diabetes is associated with a significant risk of LEA (lower extremity amputation)[1]. LEA rates vary between communities, 46-9,600 per 10^5 people with diabetes, for many reasons [2]. A number of factors influence the occurrence of a LEA in patients with diabetes; including hypertension, obesity and hyperglycaemia [3-7]. In the foot, previous ulceration, infection and ischaemia are proven risk factors [8]. Nearly 85% of amputations begin as foot ulcers among persons with diabetes [9]. Protective factors include control of clinical parameters and screening to identify those patients at high risk [10]. Many LEAs are preventable [11]. Thus, the effects of clinical and socio-demographic risk factors on the occurrence of a lower extremity amputation have been well documented in patients with diabetes in previous studies [12] [13] [14]. However, the effect of patient contact with a podiatrist on the occurrence of LEA in patients with diabetes is less well explored.

In 1998, the ADA (American Diabetes Association) published a technical review and position statement on preventive foot care in people with diabetes, highlighting the importance of foot care in people with diabetes to prevent adverse outcomes [15 16]. An updated position statement by the ADA in 2003 stated that early recognition and management of independent risk factors for ulcers and amputations can prevent or delay the onset of adverse outcomes [17]. However, these statements did not specify the role of podiatry. In 2005, the Standards of Medical Care of Diabetes issued by the ADA advised that problems involving the feet, especially ulcers and wound care, may require care by a podiatrist [18]. And in 2008, a task force report by the Foot Care Interest Group of the ADA stated that all patients with diabetes should be assigned to a foot risk category. These categories were designed to direct referral and subsequent therapy by the speciality clinician or team [19]. This report did not outline the role of podiatry but panel members included podiatric medicine representatives, suggesting that podiatry does have a place in footcare of patients with diabetes. It is now being recognised across the globe that podiatry has a role in the management of the diabetic foot. Guidelines from Scotland, Europe outline a diabetic risk stratification and triage tool, highlighting which patients need podiatry referral [20] (Appendix 1).

The management of diabetes is a complex process involving many healthcare professionals, including podiatrists. Two previous Cochrane reviews by Dorrestiejn et al have looked at lower extremity amputation in patients with diabetes as an outcome [21 22]. In 2009, Dorrestiejn et al concluded that there is no high quality evidence evaluating complex interventions (complex intervention defined as an integrated care approach) and insufficient evidence of benefit in preventing diabetic foot ulceration [21]. The second Cochrane review in 2010 concluded that there is insufficient robust evidence that limited patient education alone is effective in achieving clinically relevant reductions in ulcer and amputation incidence [22]. Individual patient contact with a podiatrist was not examined as an intervention in either review. To the best of our knowledge, the effect of contact with a podiatrist on the occurrence of a LEA in patients with diabetes has not been previously examined in any systematic review.

This review will look at contact with a podiatrist as an intervention to prevent LEA in patients with diabetes. Randomised and non-randomised studies will be included.

Objectives

To conduct a systematic review of international literature to determine if contact with a podiatrist has an effect on the occurrence of LEA in patients with diabetes.

METHODS

Criteria for considering studies for review

Types of study design

Randomised and non-randomised studies that allow analysis of the effect of patient contact with a podiatrist in preventing LEAs will be included.

Types of participants

People with type 1 or type 2 diabetes mellitus in any health care setting.

Types of interventions

Studies of patients with diabetes attending a podiatrist for treatment alone or for treatment and education to prevent the occurrence of LEA will be included. Comparison groups will be those that were not in contact with podiatrists or received written instructions only.

Types of outcome measures

Primary: LEA (first or repeat)

Secondary: N/A

Table 1 Inclusion & Exclusion Criteria

Inclusion Criteria:	Exclusion Criteria:
• Any time	• Cross-sectional studies
• English language	• Review articles
• Any Country	• Non-systematic reviews
• Any age	• Chart reviews /Case series
• Patients with a diagnosis of diabetes – either type 1 or type 2	

Search strategy for identification of studies

Published studies will be identified through searches of PUBMED, CINAHL, EMBASE (Excerpta Medica), and Cochrane databases. No time-limits will be implemented. Where a study is reported in more than one article, data will be extracted from the most relevant report. The key search terms will be 'podiatry', 'amputation' and 'diabetes'. (Figure 1)

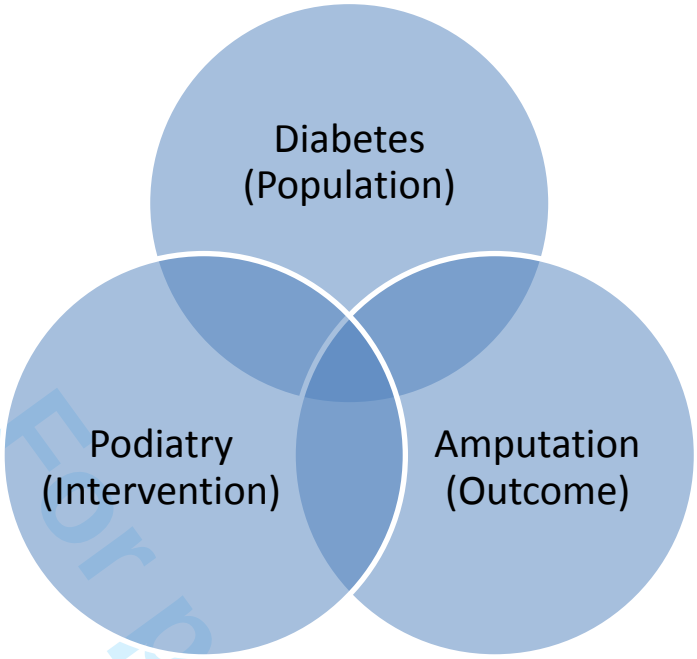


Figure 1 Venn diagram of key terms for search strategy

A comprehensive search strategy will be devised with the advice of the librarian. Key terms will be searched as MeSH (Medical Subject Heading) terms e.g. 'diabetes - MeSH term' and as free text with/without truncation as appropriate e.g. 'Diabet*(this symbol is used for identifying all words starting with Diabet, e.g. diabetes, diabetic etc.). The search will include case-control studies, cohort studies, retrospective and prospective studies, articles, clinical trials and RCTs. The strategy will be adapted as per database requirements.
In addition, hand searches will be conducted of the reference lists of all articles retrieved to identify other potentially eligible articles.

Methods - data collection and analysis

Selection of studies

Full copies of potentially eligible studies will be obtained and two review authors (CMB and PK) will decide independently on inclusion or exclusion (table 1). In the case of disagreement, consensus will be reached by discussion between four review authors (CMB, PK, CB and IJ).

Data extraction and management

Data on eligible studies will be extracted and summarised using a pre-agreed data extraction summary form. This form will include study design, baseline characteristics of participants including number of participants, age, gender, ethnicity, type of diabetes, information on exposure, outcome measure (lower extremity amputation) and other relevant data. Risk of foot disease at baseline will be assessed using the Diabetic foot risk stratification and triage system from the SIGN (Scottish Intercollegiate Guidelines Network) guidelines (Appendix 1). If the data required for the review is missing from the published article, the authors will be contacted.

Assessment of quality in included studies

A modified version of a checklist developed by Downs and Black for assessing the methodological quality of both randomised and non-randomised studies of health care interventions will be used to critically appraise the studies in this review [23].

Assessment of heterogeneity

All eligible studies will be included in the data analysis. If data are too scarce or the quality of the studies is inadequate or results are too varied to present in numerical form, the authors will perform a narrative qualitative summary. If appropriate, meta-analysis will be attempted to pool outcome data. Either a fixed or random effects model will be used depending on the heterogeneity between studies. The most suitable model will be chosen after assessing the I^2 statistic for heterogeneity.

Pilot Results

Preliminary searches of the electronic databases have yielded approximately 500 titles & abstracts for initial screening.

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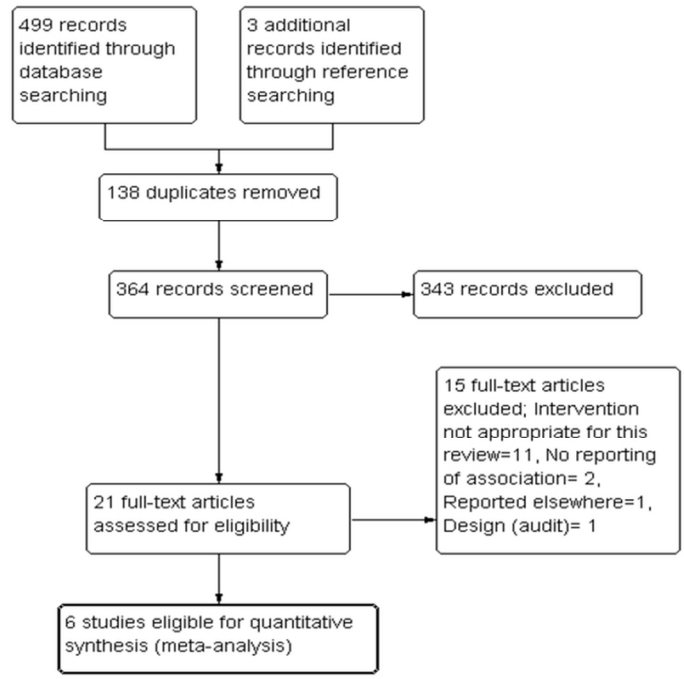

Figure 1 PRISMA flow chart: selection of studies for inclusion in review

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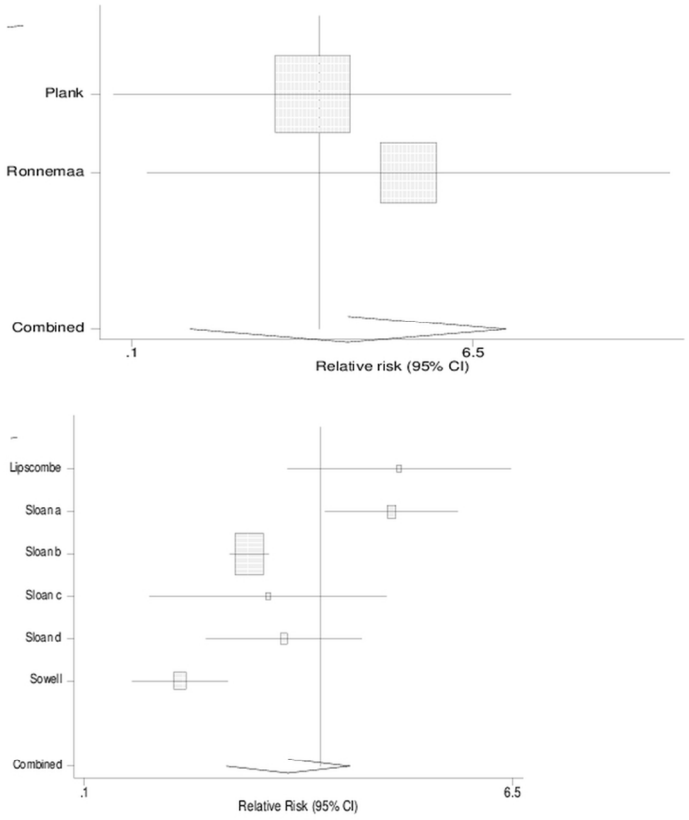

Figure 1 Forest plots of meta- analysis of RCTs (top) and Cohort studies (bottom) with the intervention of contact with a podiatrist on left side of plot

90x116mm (300 x 300 DPI)

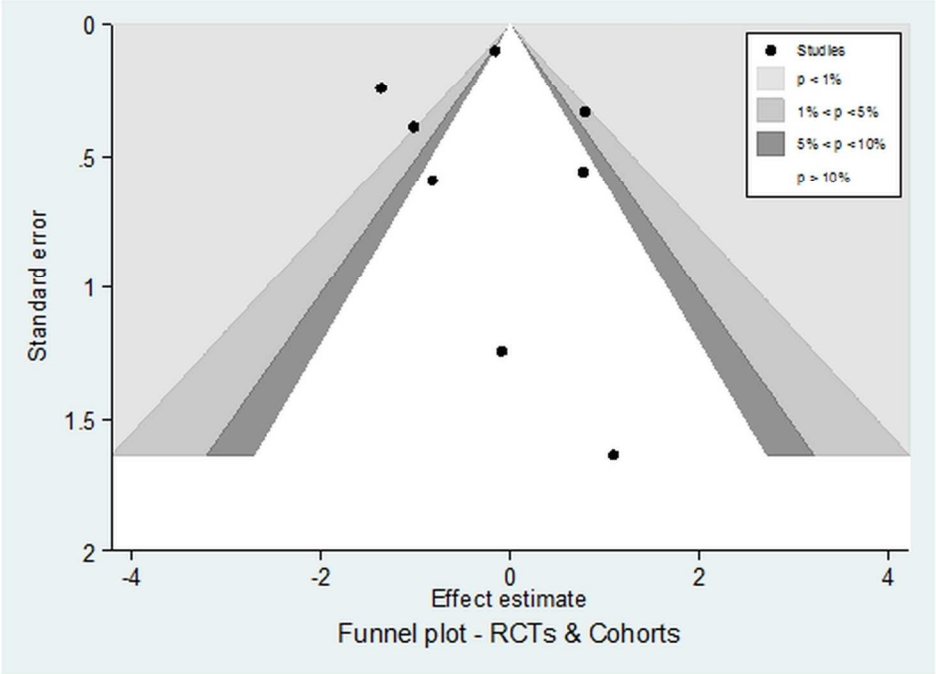

Figure 3 Funnel plot of included studies (RCTs and Cohort studies)

117x90mm (300 x 300 DPI)