

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form ([see an example](#)) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below. Some articles will have been accepted based in part or entirely on reviews undertaken for other BMJ Group journals. These will be reproduced where possible.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Does contact with a podiatrist prevent the occurrence of a lower extremity amputation in people with diabetes? A systematic review and meta-analysis
AUTHORS	Buckley, Claire; Perry, Ivan; Bradley, Colin; Kearney, Patricia

VERSION 1 - REVIEW

REVIEWER	William Jeffcoate Nottingham University Hospitals Trust, UK
REVIEW RETURNED	26-Nov-2012

GENERAL COMMENTS	<p>The authors have undertaken what they believe is the first systematic review designed to provide evidence of the effectiveness of podiatry in the management of the foot in diabetes. The work seems to be methodologically sound (although they have failed to detect one very relevant RCT – see below). Even so, I doubt the value of this exercise. The whole field is too complex (in terms of professional roles, confounders, population definition and outcome selection) and it is for this reason that it is impossible to draw useful conclusions from reviewing the literature in the way that they have. The small number of relevant papers makes it impossible. I will group my criticisms as below:</p> <ol style="list-style-type: none">1. The first problem is that the role of podiatrist is multifactorial, covering screening for risk, management of increased risk, regular surveillance and treatment of active disease, rapid referral to other experts, as well as education of both users and professionals. Most of the published work (including a lot that is reviewed here) relates to patient education and hence the only conclusions that can be drawn from this work relate to the educational activity. In this respect this review adds nothing to the Cochrane reviews by Dorresteijn (apart from including studies that aren't RCTs). On the other hand, it excludes some papers on education because podiatrists were not specifically involved). To search only for interventions performed by a single professional group reveals limited insight into the importance of team working in this clinical area.2. The second problem is the fact that the training and clinical responsibilities of podiatrists are enormously different in different countries (unrelated to whether they are called podiatrists or chiropodists). Most diabetic foot care in the US is, for example, led by podiatrists who are medically and surgically trained and will undertake many of the operations that are required below the knee, including BKA, and they are also prescribers. In UK and many other countries, the majority of podiatrists are not so highly qualified and they have different roles and more often work in MDTs. Team-working may be to the patient's advantage because it is known that the incidence of major amputation in UK is currently about half that
-------------------------	--

	<p>in the USA: about 1 per 1000 ppy, versus 2+ (probably). Because there are different types of podiatrist, it is illogical to lump both together.</p> <p>3. The third problem is that this analysis is – as, indeed, is much of the US literature – based on the use of the term LEA (lower extremity amputation: minor and major amputations combined). LEA is a poor marker of effectiveness of care, and this has been extensively debated in the published literature. The first reason is that amputation is a treatment and not necessarily a robust marker of disease severity or progression. It makes as much sense to count amputations as it does to count operations in the management of malignancies, colectomies or mastectomies for example. The second problem is that the incidence of amputation for foot disease is dependent on many different stages of clinical care, taking place over many years: glycaemic control, smoking cessation, screening, education and appropriate early management of new ulceration by all the many health care professionals who may be involved. In such circumstances it can be difficult to demonstrate the benefit of one particular professional group. The third reason is the fact that minor and major amputations are done for different reasons (either to save a leg or to remove one that cannot be saved, and in different patient groups: those with better and worse circulation, respectively; those with differing survival expectations in some cases). It is for these reasons that it makes no sense to combine them as a single outcome measure for diabetic foot disease.</p> <p>4. The fourth problem is that the involvement of a podiatrist may actually reflect the fact that their input is required: ie they see the people who are at greater risk. This will confound cohort studies. The involvement of podiatrists may also sometimes lead to an increase in the number of minor amputations. This is seen in the US, in particular, because of the still widely-held belief that bone infection should properly be treated by bone excision – and this does not reflect usual practice in other countries, including the UK.</p> <p>5. There is one important reference missing: RCT reported by McMurray SD (in 2002 or 2003) on the introduction of podiatry into dialysis units – probably the best evidence that there is a chance that this professional group may have a beneficial effect on outcome.</p>
--	--

REVIEWER	David J Margolis University of Pennsylvania School of Medicine
REVIEW RETURNED	28-Nov-2012

GENERAL COMMENTS	<p>This is a nice meta-analysis. It should be published. It is a nice example of how committees make decisions about methods of care not based on evidence. While it makes sense that comprehensive care including podiatrist care should be beneficial the proper studies have not been done. There are likely many reasons that your study is negative and may be related to the heterogeneity you describe as well as issue of selection bias this does not diminish the need to publish your study.</p> <p>Your manuscript needs to be edited for style and grammar. You also need to be careful with some of your terms. For example randomization does not assure the elimination of bias and confounding. It is certainly a gold standard technique to minimize these biases. It is also important to remember that heterogeneity is not always bad and may be informative with respect to generalizability</p>
-------------------------	--

	a topic often overlooked in homogeneous meta-analyses.
--	--

REVIEWER	John Steinberg, DPM Georgetown University I am a podiatrist.
REVIEW RETURNED	12-Dec-2012

THE STUDY	<p>Very difficult question to answer and I appreciate the attempt. It seems that the source data is very weak and inconclusive. Difficult to perform study. Should include reference to this paper:</p> <p>Display Settings:AbstractFormatSummarySummary (text)AbstractAbstract (text)MEDLINEXMLPMID ListApply Send to:Choose DestinationFileClipboardCollectionsE-mailOrderMy BibliographyCitation manager FormatSummary (text)Abstract (text)MEDLINEXMLPMID ListCSVCreate File Search: driver podiatry diabetic foot FormatSummarySummary (text)AbstractAbstract (text)MEDLINEXMLPMID ListMeSH and Other DataE-mailSubjectAdditional textE-mail"SPAM" filtering software notice Add to Clipboard Add to CollectionsOrder articles Add to My BibliographyGenerate a file for use with external citation management software.</p> <p>Create File</p> <p>J Am Podiatr Med Assoc. 2011 Mar-Apr;101(2):93-115. The economic value of specialized lower-extremity medical care by podiatric physicians in the treatment of diabetic foot ulcers. Carls GS, Gibson TB, Driver VR, Wrobel JS, Garoufalis MG, Defrancis RR, Wang S, Bagalman JE, Christina JR. SourceHealth Outcomes, Thomson Reuters, Ann Arbor, MI 48108, USA.</p> <p>Abstract BACKGROUND: We sought to examine the economic value of specialized lower-extremity medical care by podiatric physicians in the treatment of diabetic foot ulcers by evaluating cost outcomes for patients with diabetic foot ulcer who did and did not receive care from a podiatric physician in the year before the onset of a foot ulcer.</p> <p>METHODS: We analyzed the economic value among commercially insured patients and Medicare-eligible patients with employer-sponsored supplemental medical benefits using the MarketScan Databases. The analysis consisted of two parts. In part I, we examined cost or savings per patient associated with care by podiatric physicians using propensity score matching and regression techniques; in part II, we extrapolated cost or savings to populations.</p> <p>RESULTS: Matched and regression-adjusted results indicated that patients who visited a podiatric physician had \$13,474 lower costs in commercial plans and \$3,624 lower costs in Medicare plans during 2-year follow-up (P < .01 for both). A positive net present value of increasing the share of patients at risk for diabetic foot ulcer by 1% was found, with a range of \$1.2 to \$17.7 million for employer-</p>
------------------	--

	sponsored plans and \$1.0 to \$12.7 million for Medicare plans. CONCLUSIONS: These findings suggest that podiatric medical care can reduce the disease and economic
RESULTS & CONCLUSIONS	Very subjective question. Insufficient data.

REVIEWER	Tim Pickles, Statistician South East Wales Trials Unit, Cardiff University
REVIEW RETURNED	20-Dec-2012

GENERAL COMMENTS	<p>Quick summary:</p> <p>This systematic review and meta-analysis provides an interesting look into lower extremity amputation in diabetics, and with contract with a podiatrist has any effect on this. This paper is very well written, though I have a few questions surrounding the analysis done here, and also one of the papers included.</p> <p>I have a few other comments, corrections and questions I would like to highlight here. Some of them may be personal preference but I hope none are trivial. I am going to refer to decimal places (dps) in the following as they are a particular bugbear of mine ...</p> <p>Abstract:</p> <ul style="list-style-type: none"> Define LEA, RR, 95% CI and RCT before using the acronym <p>Article Summary:</p> <ul style="list-style-type: none"> Reverse 'LEA' and 'Lower Extremity Amputation' <p>Introduction:</p> <ul style="list-style-type: none"> Space between 'unfolding' and '[1]', i.e. 'unfolding [1]' Split references 3 and 4 by adding brackets, i.e. '[3] [4]' Single quotes around chiropodist Add full stop after 'et al', i.e. 'Dorresteijn et al.' Split references 16 and 17 by adding brackets, i.e. '[16] [17]' <p>Methods:</p> <ul style="list-style-type: none"> Reverse 'RR' and 'relative risk' 'P-values', not 'P values' Space between 'studies' and '[19]', i.e. 'studies) [19]' <p>Results:</p> <ul style="list-style-type: none"> Delete 'PRISMA flow chart' Did you choose a fixed effects model for the RCTs because of low Q? It is not stated in the paper, though the attached protocol does mention this. They are definitely not similar on paper, regardless of the value of Q. Did you try a random effects model to see if there is any difference? Did you consider not doing a meta-analysis? After all, there are only 2 studies here. The selection of a random effects model probably I sensible here (as you have a variety of different characteristics within the studies available) but it should not be decided on the basis of Q. Did you try a fixed effects model to see if there was any difference? Did you try combining RCTs and Cohorts? There is no
-------------------------	---

	<p>specified reason behind doing them separately, either in the protocol or the paper. If nothing else, the investigation of heterogeneity existing in this combination, and then the (potential) lessening of it after splitting would be a good piece of analysis.</p> <ul style="list-style-type: none"> • Consistency with spaces around '=' signs. Gaps in 'Q = 32.698' but none elsewhere <p>Discussion:</p> <ul style="list-style-type: none"> • You note that the two RCTs are different but still you choose a fixed effects model • Were 'a priori sensitivity analyses' planned? There is no mention in the protocol • There is no mention of a 7 year follow-up in the Ronnema et al. paper, so I don't know where that result comes from. Is this result in a separate paper? • Split references 16 and 17 by adding brackets, i.e. '[16] [17]' <p>References:</p> <ul style="list-style-type: none"> • Nothing <p>Tables and Figures:</p> <ul style="list-style-type: none"> • Table 4: <ul style="list-style-type: none"> ○ Ronnema – there is nothing on a 7 year follow-up in this paper. Is this result in a separate paper? ○ Plank – you have calculated this result from the numbers of amputations, so why not give it to 2dps like most of the rest of this table ○ Lipscombe – you have calculated this result from the numbers of amputations, so why not give it to 2dps like most of the rest of this table ○ Sloan – the result for Stage 1 is 2.20, not 2.2. <p>PRISMA Checklist:</p> <ul style="list-style-type: none"> • You state your objectives are on page 4 but I can't see any • You state that you indicate the existence of a protocol and where it can be accessed. Whilst you have provided me with a protocol, it is not mentioned in the text, and I don't know how anyone could actually access it. • You state that you describe the methods of additional analyses. Calculating Q is not an additional analysis. • You state you give the results of additional analyses. Without any stated, you can't give any
--	--

VERSION 1 – AUTHOR RESPONSE

Reviewer #1: William Jeffcoate

1. We share the opinion of this reviewer that the role of a podiatrist is multifactorial. In addition to providing formal education, the majority of podiatrists will informally deliver education as part of their treatment of clinical conditions. Thus, we decided 'attending a podiatrist for treatment alone or for treatment and education' is an intervention worthy of review.

We consider this review to build on the two previous Cochrane reviews on this topic by highlighting an area where further research is needed [1, 2]. To the best of our knowledge, research is underway to evaluate the effectiveness of podiatry services as part of the 'Putting Feet First' Campaign in the National Health Service (NHS), UK. We agree however, that this review has limited implication to current clinical practice. We state in the discussion that 'this review cannot make any

recommendations about practice’.

We recognise the importance of the role of the multidisciplinary team in the clinical setting. In the discussion, we mention that ‘looking at one service in isolation could be flawed as services are seldom delivered in isolation’. However, ideally evidence should exist that all members of a multidisciplinary team are effective and that together, the overall effectiveness is improved. It would be preferable for policy-makers to base decisions and fund investment in podiatry services on sound evidence. Thus, we consider this review looking at contact with one member of the team, the podiatrist, valid but we do suggest in the discussion that ‘a systematic review of the literature looking at the effectiveness of multidisciplinary teams which include contact with a podiatrist would be useful’.

2. We acknowledge that the varying training and clinical responsibilities of podiatrists in different countries is a concern. However, notwithstanding these differences, podiatrists treat foot disease in all countries. Thus, we consider the intervention in this review valid.

3. The use of the term Lower Extremity Amputation (LEA) has indeed been extensively debated in the published literature. It is becoming more widely recognised that an early minor amputation can be prevent a later major amputation [3]. Thus, minor amputations may reflect improved quality of care with earlier intervention; consequently preventing the progression from minor to major amputation [4]. As clinical practice changes, the distinction between major and minor LEAs are more commonly being described in the literature [5] [6]. This is preferable [7]. However, as we did not impose time limits on our search, it would be unwise to limit the search to major LEAs only. Furthermore, two previous Cochrane reviews by Dorresteijn et al studied the outcome of LEA in patients with diabetes and included papers with partial or total amputation rates [1] [2].

4. We acknowledge that involvement of a podiatrist may actually reflect the fact their input is required. Recent guidelines from Scotland outline a diabetic risk stratification and triage tool, highlighting which people need podiatry referral [8]. 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. For each study included in this review, risk of foot disease at baseline was assessed using this Diabetic foot risk stratification and triage system. As mentioned in the discussion section of the manuscript, ‘‘A priori’’ sensitivity analyses were planned for different levels of baseline risk but there were insufficient data’.

5. Many thanks for your suggestion that we should include the RCT by McMurray SD et al. [9]. In our protocol, we outlined that the intervention under review was ‘attending a podiatrist for treatment alone or for treatment and education’. In the RCT by McMurray SD et al., the intervention was attending a multidisciplinary team, of which a podiatrist was one member. Dorresteijn et al. included this RCT in the Cochrane review evaluating the effectiveness of complex interventions. However, the RCT by McMurray SD et al. does not comply with the inclusion criteria of this review.

Reviewer #2: David J Margolis

Many thanks for the positive feedback. As this reviewer correctly highlighted, randomisation is the gold standard technique to minimize bias but it does not eliminate bias and confounding. The manuscript has been amended to clarify this point and has been edited for style and grammar.

Reviewer #3: John Steinberg

We agree that the source data is weak and inconclusive and we hope that this review will encourage further research in this area. We thank the reviewer for the suggestion of a potential paper for inclusion [10]. This paper looks at the outcome of diabetic foot ulcers and thus, does not comply with the inclusion criteria in the protocol where an outcome of lower extremity amputation was specified.

Reviewer #4: Tim Pickles

Results:

As the reviewer correctly assumed, we chose the fixed effects model for RCTs because of the low Q value ($Q=0.328$, $p=0.567$). Both fixed and random effects models produced the same result; RR of 1.41 (95% CI 0.20-9.78). As the reviewer suggested, we did consider not doing a meta-analysis for RCTs as only two suitable studies exist. However, for the sake of consistency, we decided to present both meta-analyses for randomised and non-randomised studies.

In relation to the non-randomised studies, the criterion to use the fixed model was not met so the random effects model was the more appropriate choice.

There is much debate on the appropriateness of combining the results of randomised and non-randomised studies in a single meta-analysis. Initially, we performed meta-analyses of the RCTs and cohort studies both in combination and separately. However, we excluded the combined analysis from this paper based on expert statistical advice received after presenting those findings at a Cochrane Collaboration Conference in Dublin City University, Ireland (January 2012). Also, expert guidelines on the reporting of meta-analysis of RCTs and observational studies exist individually but not in combination [11] [12]. We have used the PRISMA Checklist here to report the results of both meta-analyses.

Discussion:

'A priori' sensitivity analyses as per study design and as per baseline foot risk were planned. As mentioned in the protocol, 'The search will include case-control studies, cohort studies, retrospective and prospective studies, articles, clinical trials and RCTs' and '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'. Apologies for not outlining in the protocol that we planned to perform analyses as per study design and as per baseline foot risk.

The 7 year follow-up data from Ronnema et al. was extracted from results of data (published and unpublished) presented by Dorresteijn et al. in the Cochrane review on complex interventions for preventing diabetic foot ulceration [1]. We have now included as data sources both the original paper by Ronnema et al. outlining the RCT and results after 1 year of follow-up and the Cochrane review describing results after 7 years of follow-up. We are most grateful for your accurate observation.

Tables and Figures:

Data on 7 year follow-up from RCT by Ronnema et al. described in Cochrane review by Dorresteijn et al. on complex interventions for preventing diabetic foot ulceration [1].

Decimal places corrected.

PRISMA Checklist:

The reviewer correctly pointed out that objectives were not explicitly outlined on page 4. We have amended the manuscript to include in the introduction an explicit statement of the question being addressed with reference to participants, intervention and outcome.

We mention in the methods that '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)'. Our understanding is that the supplementary file containing the protocol would be accessible online to the reader.

The additional analysis that we refer to in the PRISMA Checklist is the sensitivity analysis as per baseline foot risk we had planned. As the reviewer correctly pointed out, results of the additional analysis was not presented as insufficient data existed to facilitate performance of the sensitivity analysis. We have now amended the PRISMA Checklist accordingly.

References

1. Dorresteijn Johannes AN, Kriegsman Didi MW, Valk Gerlof D: Complex interventions for preventing diabetic foot ulceration. In: Cochrane Database of Systematic Reviews. Chichester, UK: John Wiley & Sons, Ltd; 2010.
2. Dorresteijn Johannes AN KDM, Assendelft Willem JJ, Valk Gerlof D: Patient education for preventing diabetic foot ulceration. In: Cochrane Database of Systematic Reviews. vol. John Wiley & Sons, Ltd; Updated.
3. Jeffcoate W, Van Houtum W: Amputation as a marker of the quality of foot care in diabetes. *Diabetologia* 2004, 47(12):2051-2058.
4. Buckley CM, O'Farrell A, Canavan RJ, Lynch AD, De La Harpe DV, Bradley CP, Perry IJ: Trends in the Incidence of Lower Extremity Amputations in People with and without Diabetes over a Five-Year Period in the Republic of Ireland. *PLoS ONE* 2012, 7(7):e41492.
5. Holman N, Young R, Jeffcoate W: Variation in the recorded incidence of amputation of the lower limb in England. *Diabetologia*:1-7.
6. Vamos EP, Bottle A, Edmonds ME, Valabhji J, Majeed A, Millett C: Changes in the Incidence of Lower Extremity Amputations in Individuals With and Without Diabetes in England Between 2004 and 2008. *Diabetes Care* 2010, 33(12):2592-2597.
7. Jeffcoate WJ: The incidence of amputation in diabetes. *Acta Chir Belg* 2005, 105(2):140-144.
8. SIGN: Management of diabetes. A national clinical guideline In.; March 2010.
9. McMurray SD, Johnson G, Davis S, McDougall K: Diabetes education and care management significantly improve patient outcomes in the dialysis unit. *American Journal of Kidney Diseases* 2002, 40(3):566-575.
10. Carls GS, Gibson TB, Driver VR, Wrobel JS, Garoufalis MG, DeFrancis RR, Wang S, Bagalman JE, Christina JR: The Economic Value of Specialized Lower-Extremity Medical Care by Podiatric Physicians in the Treatment of Diabetic Foot Ulcers. *Journal of the American Podiatric Medical Association* 2011, 101(2):93-115.
11. Moher D, Liberati A, Tetzlaff J, Altman DG: Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *BMJ* 2009, 339.
12. Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, Moher D, Becker BJ, Sipe TA, Thacker SB et al: Meta-analysis of Observational Studies in Epidemiology. *JAMA: The Journal of the American Medical Association* 2000, 283(15):2008-2012.