Reviewer’s report

Title: The effectiveness of non-surgical interventions for common plantar digital compressive neuropathy (Morton's neuroma): a systematic review and meta-analysis

Version: 0 Date: 22 Jun 2018

Reviewer: Tom Walsh

Reviewer's report:

Thank you for the opportunity to review this manuscript, which investigates the efficacy of non-surgical interventions for Morton's neuroma. Morton's neuroma is a common foot complaint and understanding which non-surgical measures are supported by good evidence is important. I congratulate the authors on undertaking a large piece of work, but I have some reservations about the review in its current form.

I believe there are a number of items that should be reconsidered throughout the manuscript, but one of my major concerns is that this review proposes new or modifications to treatment 'algorithms' based on the results, without a considered criteria of how these decisions were made. Shifting treatments between first / second / third line interventions, as the authors have done, based on underpowered studies of largely low/moderate-quality (mostly case series) should be done so with caution. I would suggest that the results of this review be presented based on what is found, rather than to try and recommend an order by which treatments should be implemented.

Major items

i. Can you explain why surgical intervention wasn't assessed in this review? i.e. why didn't you review all treatment for Morton's neuroma? Surgical management may be more effective than non-surgical management - if indeed this was the case, surgery may indeed trump all non-surgical management. You allude to this in Line 97.

ii. Why have you selected size of neuroma as a secondary outcome measure? Patients will ordinary present with a painful forefoot and an asymptomatic neuroma wouldn't be treated to reduce its size. Has the reliability of US or MRI to measure neuroma size been established?

iii. Line 70-72 - Imaging and the diagnosis of Morton's neuroma can be problematic. There is a high prevalence of asymptomatic neuroma detected using ultrasound. I think it would be worth drawing the reader to this.

v. Line 210-212 - I would recommend updating your protocol after your initial searches, which you are able to do with PROSPERO, rather than accepting a level of evidence that does not align with your protocol. This can't be modified now, but for future reviews it may be worthwhile considering.

vi. Throughout the manuscript MD is used (for mean differences). In your Figures WMD is used (for weighted mean differences). In your protocol you planned to report standardised mean differences. Can you please clarify which mean differences you are reporting?

vii. The first paragraph in your discussion should provide a strong summary of what your review found and what were the main outcomes. Listing that meta-analysis found significant reductions for multiple treatments may be misleading, as these studies were of poor quality and largely had no control.

viii. The discussion is quite hard to follow. I would recommend 'batching' your findings into paragraphs which will make the flow and reading the review easier.

ix. Your data doesn't support the proposed algorithm in the conclusion. The best evidence is from the RCTs, which isn't mentioned in any detail here and it is unclear why surgery is recommended after all of the treatments that are listed. Surgery was not assessed with this systematic review, and without a review of these data, probably shouldn't be mentioned. Indeed, surgery may be more efficacious than all non-surgical treatment, but this review is unable to conclude this. I would also recommend tempering the recommendations on the order by which treatments should be considered.

Minor items

i. Line 20 - The first sentence doesn't read quite right. I would suggest 'Morton's neuroma (MN) is a compressive neuropathy of the common plantar digital nerve…..'

ii. Line 21 - You state that current treatment algorithms are based on low-quality studies, but given this is a systematic review, this seems presumptive. I appreciate that other reviews may have found this, but it may be better to present the why Morton's neuroma is a problem, rather than current treatment algorithms.

iii. Line 32 & 164- Should be Downs and Black Quality Index

iv. Line 32-33 & 40 - Randomised controlled trials?

v. Line 63 - See comment from abstract regarding this first sentence

vi. Line 65 - 'women' and 'men' may be more correct than 'females' and 'males'

vii. Line 66 - 'in terms of presentations to primary care…' could be improved

viii. Line 66 - Define UK.
ix. Line 67 - Suggest change 'patients' to 'people'

x. Line 74-81 - Whilst this is interesting, it reads a little out of place. I would suggest working some of it into the first paragraph, essentially describing when it was first described and the fact (which is something that you allude to) that it is a misnomer

xi. Line 99 & 101 - Suggest replace 'papers' with either studies or articles

xii. Line 106-107 - This is methods

xiii. Line 112 - You have already defined, and used, MN for Morton's neuroma

xiv. Line 113 & Line 143 - The acronym should come after the words you are defining

xv. Line 115 - Suggest 'adults aged…'

xvi. Line 118 - This reads a little vague. 'interventions aimed to improve outcomes…' Should this be interventions aimed to reduce pain?

xvii. Line 131 - 'Cochrane' should be 'Cochrane Central Register of Controlled Trials'

xviii. Line 139 - Is this correct? Three people performed a full-text review? As in Line 142 - it states that a third reviewer resolved disagreements. Can you please check this?

xix. Line 149 - Suggest 'data' rather than 'information'

xx. Line 151 - Suggest 'participants' rather than 'subjects'

xxi. Line 167 - Should '=' between r and numbers. Do you have a citation for these r values?

xxii. Line 173 - Should be 'score' not 'sore'

xxiii. Line 205-212 - I would recommend moving this to be either the first or second paragraph of the methods

xxiv. Line 216 - It may be worthwhile adding how many articles remained after removal of duplicates

xxv. Line 218 - Suggest 'following full-text review' rather than 'at the final stage'

xxvi. Line 218-219 - Why was a non-adult population a common reason for exclusion? Were there studies in paediatrics?

xxvii. Line 274 & 277 - Does the pooled MD and success rate referred to the pre/post reduction in pain? This could be made clearer, and should be before the follow-up time
xxviii. Line 300 - This paragraph lists the studies that have investigated wider footwear and metatarsal padding, but the pseudo RCT used footwear and padding as the control arm. Can you justify combining these data with that of a case series?

xxix. Line 313 - Avoid starting sentences with acronyms

xxx. Line 315-317 - What statistically significant treatment effect did ESWT have, as there was no statistically significant reduction in pain?

xxxi. Line 354 - I would recommend listing the methodological assessment before listing the results, as this allows the reader to think about the results in context of the quality of the studies.

xxxii. Line 432 - Should be 'Prefabricated' not 'Prefab'

xxxiii. Study heterogeneity is only mentioned in the discussion, this should have some presence in the results section.

xxxiv. Table 1 - This search strategy appears quite limited. I have some concerns about whether this is broad enough for this type of review.

xxxv. Table 2 - Should be 'MFPDI' not 'MFPDS'

xxxvi. Table 3 - You have listed the studies in under intervention headings (which is fine) but the studies are then listed by author alphabetical order. It would be easier to read these tables in they were listed by study type, rather than by author name

xxxvii. Figure 1 (Heading) - This heading could be improved. It is not a flow of information.

xxxviii. Figure 3, 4, 5 - It is unclear why there are interventions listed here with the results of one study. I do not think that this is required in these figures, this can be reported in-text

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An article whose findings are important to those with closely related research interests

Quality of written English
Please indicate the quality of language in the manuscript:

Needs some language corrections before being published

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