Author's response to reviews

Title: Effect of telemedicine follow-up care of leg and foot ulcers: a systematic review

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Author's response to reviews: see over
Re: 1356054838103360 /"Effect of telemedicine follow-up care of leg and foot ulcers: a systematic review”.

Thank you for considering our manuscript for publication in *BMC Health Services Research*. We appreciate your interest and the reviewers' considerations. Their comments were very helpful and constructive, and were taken into account when revising the manuscript.

Our responses to the reviewers, and changes made in the manuscript, can be found in the "Responses to the Editor and Reviewers" section below and in the uploaded revised manuscript.

Please do not hesitate to contact us if further clarification or adjustment is required.

On behalf of the authors,

Yours sincerely

Marjolein M. Iversen, PhD
Response to Reviewer 1.'s report

Reviewer: Sascha SK Köpke

Reviewer's report:

Re: Introduction: The introduction should be extended. I agree with the authors that there is a need for a systematic review, but in my view an important aspect is missing to provide a meaningful rationale for a systematic review i.e. the potential specific role of telemedicine in foot and leg ulcer patients.

• Therefore, the authors should state how usual care (referred to as “traditional follow-up”) looks like in Norway and other health systems and why telemedicine might be an appropriate way to improve this or may be of importance in regions with special challenges (e.g. patients in remote areas, lack of health professional etc.).

• Also it would be interesting to learn something about different health professionals potentially involved in the application of telemedicine.

RE: This is now included and discussed in the introduction.

Re: Literature search

• The search was done more than 2 years ago which is definitely not appropriate and the authors should perform an update search.

RE: We have updated the literature research in all databases. Unfortunately, the final strategy for the previous search in CINAHL was not saved electronically. Accordingly, we had to reconstruct the search based on a draft strategy (Word file) from September 2011. MTH performed the previous CINAHL search in Ebsco CINAHL with Fulltext. We have used the same version in the updated search; this is specified in the Methods section. Efforts were made to construct a strategy that retrieved all citations identified in the previous search. The new and updated search yielded substantially more hits than the previous search (approx. three times the number of hits). As we don’t have the previous CINAHL search available we are not able to make comparisons between the two strategies and provide specific explanations for these results. However, the new search is clearly more comprehensive than
the previous one. Thus, we believe the reconstructed search does not impose any flaws to results of the review.

Final searches in the databases were performed on May 16th, 2014. No further relevant studies were identified. A search for ongoing studies was performed on June 10th and potentially relevant studies are described in a separate table (Table 4).

- It is stated that there was “no limit for publication date”, but the MEDLINE search was limited to studies since 1996. I can see that there might be a “natural” limit for studies on telemedicine, but this should be clarified.
  RE: The limitations from 1996 and onwards in the Medline search were a flaw in the initial search. We have now searched Medline from 1980 and onwards. The date restriction is applied because relevant telemedical equipment was not available before 1980.

- I think that the implications for further research should be a central result of this review. I suggest presenting this using the EPICOT format possibly using a table (see e.g. Brown et al. How to formulate research recommendations. BMJ 2006;333:804-6).
  RE: Research recommendations are presented using the EPICOT format in Table 7 and are given more priority in the discussion section.

- There are two aspects that should at least be briefly added to the discussion section: First the authors might want to discuss (within the context of telemedicine) the problems of developing, evaluating and synthesizing “complex interventions” as described in the MRC framework. Second, as there is definitely more evidence on telemedicine in other disease fields, there should be a short discussion whether this could be used to assess the potential use of telemedicine in foot and leg ulcer.
  RE: We discussed the MRC framework within the context of telemedicine and highlighted the potential use of telemedicine in foot and leg ulcer in the discussion. We also added a separate discussion on the transfer of evidence from other disease fields to telemedicine in foot and leg ulcer.

Some further aspects:
• Methods: What is meant by “HBA1C related to healing time”? I would not have considered HBA1C an important “clinical outcome”.

RE: As high HbA1c will increase healing time of a diabetes-related foot ulcer, this is more a confounding factor. Therefore, we agree and have removed it as an outcome.

• In the search strategy section it should be mentioned that experts were contacted.

RE: We have added this information.

• The term “controlled before-after study” is not adequate and should be changed to either “controlled trial” or “non-randomised controlled trial”.

RE: We checked the Cochrane EPOC criteria for inclusion of study designs (http://epoc.cochrane.org/epoc-author-resources). They recommend to separate between non-randomized trials (which is used instead of controlled clinical trials and quasi-randomized trials) and controlled before-after studies. We prefer to use their terminology.

• Synthesis of the results: In my view one reference to GRADE methodology is sufficient.

RE: We agree and only one reference is used.

• Quality assessment: I am not sure if ulcer assessment can really be rated as “objective assessment”.

RE: We understand your concern and have problematized this in the text.

• The Norwegian titles in the reference list should also be given in English.

RE: We have adjusted the reference list.

• In the flow chart: what is the difference between “Irrelevant study design” and “Study design” (Bottom right box)?

The two study design categories in the flow chart are merged into one category, named “irrelevant study design”.

We have also compiled and included a ‘Characteristics of excluded studies’ table (Table 3) in line with recommendations from EPOC (http://epocoslo.cochrane.org/epoc-specific-resources-review-authors). During this process it became apparent that many of the
studies/articles that were initially screened in full-text should have been excluded already when screening at title/abstract level. This applied to 31 of the 45 studies/articles assessed in full-text. By re-examining the titles and/or abstracts of these articles (as provided in the databases) it was clear that these studies were testing the feasibility of telemedicine equipment for assessing ulcers (feasibility studies, n=16); their study design were otherwise irrelevant (n=7); or the population (n=2), intervention (n=2), or topic (n=4) was irrelevant. Accordingly, only 14 of the 45 excluded studies/articles should have been assessed in full-text in the first place. From the updated search we screened an additional 5 articles in full-text, they were all excluded. This left us with a total of 19 excluded studies that were potentially relevant to describe in a ‘Characteristics of excluded studies’ table. Reasons for exclusion are specified in the text and in the flow chart (Fig 1). We have described all excluded studies besides those categorized as “not a study” (n=8), leaving us with a total of 11 studies relevant for the excluded studies table.

**RE: Reviewer 2**

**Reviewer:** Louise Forsetlund

Major revisions

1. The search is from October 2011 and should be updated.

**RE:** We have updated the literature research. (see comment Reviewer 1).

2. Databases for ongoing studies should be searched.

**RE:** We have searched databases for ongoing studies and the final searches were performed on June 10th 2014. A search for ongoing studies was performed on June 10th and potentially relevant studies are described in a separate table (Table 4).

3. P. 2-3, Abstract: “The patients receiving telemedicine and traditional follow-up did not significantly differ in outcomes.” Could you consider this sentence? I suppose that you mean that there were no statistically significant differences in results of the different outcomes.

**RE:** We have re-formulated the sentence.

4. P.7: Data collection chapter: “We only identified one eligible study (25)”. This is reported twice (also in the Result chapter, where it to my preference rightly belong). Likewise, the two next chapters should not anticipate the fact that only
one study was found – this belongs in the Result chapter. However, I do see that there may be a challenge in expressing what was done when only one study was found, but you might consider if it is possible to rephrase it!

RE: We agree and this is now only mentioned in the result section. Accordingly the text in the subsections “data collection” and “Assessment of risk of bias” are re-written.

5. P7: Chapter title “Quality assessment” – I would rename this chapter to ‘Assessment of risk of bias’. The RoB table emphasizes that risk of assessment pertains to each outcome (because this may vary between outcomes). We do not assess the quality of the study.

RE: We agree and have re-named this chapter.

6. P. 7: Chapter title “Synthesis of the results” – You present GRADE here so perhaps you should call the chapter ‘Synthesis of the results and quality assessment’

RE: We agree and have re-named this chapter.

7. P.9: Chapter title “Quality assessment” - I would rename this to ‘Risk of bias’

RE: We agree and have re-named this chapter.

8. P. 9: “Because the study design was a controlled before-and-after study, it does not meet the Cochrane criteria related to randomization and allocation sequence.” Could you try to rephrase this – it’s not the Cochrane criteria which is interesting in this connection, but the fact that this design does not use randomization and that this is a threat to the validity of the findings per se. The Cochrane checklist just reminds us to check up on this when we assess studies.

RE: We have re-phrased the paragraph.

9. P.9: “The researchers only made minor corrections for confounders, for example …”

The small sample size may have limited the possibility of including all potentially confounding factors in the analysis. A more relevant question is perhaps whether they included the most important potentially confounding factors. Of those mentioned in the method chapter – two of them seems to be identical to those
that actually were used in the analysis: ulcer duration and the extent of the ulcer (which sounds like either severity or size).

RE: We have re-phrased the paragraph.

10. P. 9: “The sample size was small, especially in the intervention group, limitations in study design and high risk of bias were the main reasons why the study achieved a very low GRADE score.” Could you reconsider this sentence – it is not grammatically correct (the first part does not connect to the last part). Apart from that, limitations in study design was one of the reasons why the results were assessed as having high risk of bias, so high risk of bias was in that case the main reason for the assessment of the quality of the evidence for each outcome as very low.

RE: We have re-phrased the sentence and adjusted Table 5: Assessment of risk of bias in the included study.

11. P. 10: “To our knowledge this is the first systematic review that summarized studies measuring the effectiveness of telemedicine follow-up care of patients with leg and foot ulcers.” I would rephrase this to: “To our knowledge this is the first systematic review with the purpose of summarizing studies measuring the effectiveness of telemedicine follow-up care of patients with leg and foot ulcers.”

RE: We have re-phrased the sentence.

12. P 10: “The included study [25] indicated that telemedicine management of people with diabetes related foot ulcers may be an equivalent alternative to traditional follow-up concerning the healing time of the ulcers.” I do not agree. If you calculate the confidence interval around the mean difference you will see that the uncertainty around the effect estimate opens up for both positive as well as negative differences in healing time. So, basically, the result is inconclusive.

RE: We have re-written the paragraph.

13. P. 10, Discussion chapter: “The strength of the evidence, assessed using GRADE, is very low and limited by the study design.” I think that ‘assessed using GRADE’ may be omitted here, being mentioned several times elsewhere.

RE: We agree and deleted these words.
14. P 10, Discussion chapter: “Methodological aspects need to be standardized to produce evidence about the effectiveness of the telemedicine services assessed using predefined outcome measures [7].” Sorry, I do not quite understand what you mean by this.

**RE:** We have re-formulated the sentence.

15. P. 10, Discussion: “The combination of these two challenges may explain why few studies evaluate the effectiveness of telemedicine follow-up of patients with leg and foot ulcers on the other specified outcomes – HbA1c, quality of life, self-care, change in interaction and cooperation between the patient and health care personnel – or within health care personnel and organizational outcomes.”

Which few studies? You only found one? Could you be referring to references 19, 20, 21 and 22? Please make this more clear.

**RE:** We have clarified this paragraph and re-organized the discussion section.

16. P 11, Discussion: Thus, the time frame employed by W and other researchers (but you only found one study or are you thinking of references 19, 20, 21 and 22??) may have been too short and so on. Do you mean that the intervention may have been inadequately implemented? And do you mean that the time frame of the W study was too short for telemedicine to be evaluated in a rct? It is unclear to me how this make sense.

**RE:** We clarified the sentence and referred to a previous systematic review.

17. P. 11, Discussion: “Randomized controlled trials have several inherent design disadvantages, because the study procedures in follow-up care may be difficult to achieve in clinical practice.” Comment: Is this really an inherent design disadvantage?

**RE:** We agree and deleted this sentence.

“Randomizing individual patients can threaten the internal validity, because nurses and other health care personnel in the municipalities treat patients in both the intervention and control groups, which might be a rationale for choosing a cluster randomized trial.” Well, is it the randomization that threatens the validity
or is it letting the same health care personnel take care of patients in both groups? Could you rephrase it?

**RE:** We have rephrased the sentence and integrated it in a previous paragraph.

I suppose you wanted to say something about the desired direction of future research by raising the issue of rcts. However, it should be better linked to the context. The sentences on rcts seem a little detached from the rest!

**RE:** See comment above.

Some comments on the purpose of comparing telemedicine to traditional follow-up: In the Conclusion chapter in the abstract you state that: “There is insufficient evidence available to unambiguously determine whether telemedicine consultation about leg and foot ulcers is more effective than traditional follow-up.” Does it have to be better? Wouldn’t it suffice if it were just as good? And would not equivalence or non-inferiority trials be a more suitable design for establishing this?

**RE:** We have changed the wording in the abstract. We have integrated the point about the use of equivalence or non-inferiority trials in the discussion section.
Reviewer 3:

Reviewer: Mark Hawley

Major compulsory revisions

1. The rationale for carrying out the review needs to be strengthened
   a. There is no convincing explanation of why telemedicine is or may be a clinically sound approach to the follow-up of leg or foot ulcers. Is it widely used clinically but not evaluated? Why is it important to do this review at this time? This needs to be justified from a clinical and research perspective.
   
   **RE:** We agree and we have added further justifications for the review in the introduction section.

   b. Is this simply relevant to Norway, because of its sparse population? Some international background should be given here.
   
   **RE:** We agree and the relevance of telemedicine is described in an international perspective in the introduction.

2. The search was carried out almost 2.5 years ago. In a fast-developing field like telemedicine, other studies have probably been reported by now. The search should be updated. Given that only one paper was found which met the inclusion criteria, it is surprising that the authors did not hand-search key journals. This should be done, or the reasons for not doing so should be justified.
   
   **RE:** See comment Reviewer 1.

   Hand searching requires a focus, usually the specialist literature, which may not exist for newly developed fields such as telemedicine in wound care. Given the resources and time provided for this systematic review a hand search for studies was not justifiable and hence not performed.

3. There is insufficient explanation of why studies were excluded from review. Given the fact that only one study was included in the review, the reasons for exclusion are important. In particular, in Figure 1, five studies were excluded for 'irrelevant study design' and 7 more were excluded for 'study design'. What is the difference between these two categories?
   
   **RE** See comment Reviewer 1.
Minor essential revisions

4. Page (P)4: In the introduction the author’s state ‘Several review indicate that telemedicine improves health care…’ but only references one review [17] for that statement.
   RE: We have adjusted this in the text.

5. P.8 ‘foot screening of the feet’ could do with re-phrasing
   RE: We have re-phrased this sentence.

6. P10: ‘…its effects has been limited…’ should read 'have'.
   RE: We have changed the wording.

7. References: The authors use a variety of reference styles; I suggest the authors write all references in same format.
   RE: We have re-written the style of the references.

8. Table 2: The authors have provided an incorrect reference number for Wilbright et al. – should be (25) not (41).
   RE: We have changed the reference number. The table is now numbered as Table 5, and not Table 2.

9. Table 3: The authors need a heading in the first column to say (25) is the study number.
   RE: We have put the reference number immediately after the author/year. The table is now numbered as Table 2, and not Table 3.