PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	The impact of the communication and patient hand-off tool SBAR on patient safety – a systematic review
AUTHORS	Müller, Martin; Jürgens, Jonas; Redaelli, Marcus; Klingberg, Karsten; Hautz, Wolf; Stock, Stephanie

VERSION 1 – REVIEW

REVIEWER	Michael C. McCrory MD, MS Wake Forest University, Winston-Salem North Carolina, USA
REVIEW RETURNED	02-Mar-2018

GENERAL COMMENTS	In the manuscript “The impact of the communication and patient hand-off tool SBAR on patient safety – a systematic review”, the authors have performed a systematic review to address the important question of whether the most commonly used hand-off tool “SBAR” has any demonstrable effect on patient safety. The authors focus on adverse events and actual patient-related metrics rather than just provider satisfaction or other perceived benefits, and show that in several heterogenous studies there are some data to support use of SBAR as having a direct benefit for patients. The objectives and design of the study are excellent. However, the manuscript requires substantial revisions to the writing in the results and discussion sections to make it more clear to the reader as to what those benefits are and how convincing the data are to make any conclusions. The outcomes and reporting of the studies are heterogenous, and the authors need to more clearly summarize the results for the reader to have “take-away points” of understanding. Further specific comments are listed by section. Abstract: 1) First sentence of Results should read “were identified that met inclusion criteria” 2) There should be a comma after “hand-off” in second sentence of results 3) The results are too general and do not really give the reader enough substantive information. Need to better summarize what types of studies (e.g. trials, before/after), how many showed benefit, in what type of setting/use, and what type of benefit. This should overall be much better described in the actual results of the paper as well. 4) Sentence “no study found a significant increase” should be deleted from the abstract in favor of more relevant information as listed above. Introduction 5) “AIDS” should be spelled out 6) “commission” should be capitalized after “Joint” Results

	7) Overall the results are scattered, contain too many generalities and negative statements, and not enough clear positive summary statements that make the results understandable to the reader. For example, “in all studies except the RCT by Field . . “ sentence – what was controlled for in this study? 8) “Patients were largely blinded” – I don’t think this statement is necessary, but if you want to include it again it is too general. How many and what % of the studies had patients blinded? 9) “We further found study reporting to be incomplete mostly” – again very general and uninformative 10) “Most studies used a before-after design” – again too general. One summary sentence could concisely say “X studies used before/after design (y%), Z studies were trials . . etc” 11) There are several places in the document I received where it says “Error! Reference source not found!” 12) Did any of the studies include process measures? E.g. measuring whether communication was demonstrably improved to establish that SBAR may have contributed to the actual patient outcome measures? 13) Tables 2 and 3 are both cumbersome and confusing. Would consider combining elements of each in a more succinct form as your main outcome table, or at least streamlining them. The most important elements are study design, how SBAR was used (e.g. nurse-physician phone communication), what was the outcome measure, and whether there was a difference shown. The details of the setting are given yet it is still unclear whether it was inpatient or outpatient, was SBAR mainly used for nurse/physician or other communication? In table 3 there is no column heading for the up/down arrows and the column for “outcome measure” seems to actually mean “duration of follow-up”, and there is no indication of what type of study they are. 14) There is too much text about the Haig study under interventions, while generally not enough summary in the results of how many studies showed improved outcomes and what outcomes. 15) Under “Patient hand-off” section on page 19, should start the sentence “The critical incidence reporting system” with “In a controlled clinical trial in x setting, the critical incidence reporting system . .”. Similarly the sentence “Further a reduction. . “ should also start with the study type and setting. Later at the end of the results you could more effectively summarize these and other studies by category. 16) ($p>0.05$) at the bottom of page 19 is unhelpful and should be deleted. Discussion 17) By my count, 9 of the 11 studies included show at least some positive effect on outcome (counting studies with at least one up arrow in table 3). In the discussion, we need a more broad acknowledgement of this and explanation as to why the authors believe that this represents real results from SBAR or just heterogeneity and coincidence. The authors claim that “the results of our review indeed question the wide spread adoption of SBAR” despite 82% of their included studies having at least one improved outcome. Does it seem more likely that just more attention was paid to safety in general as SBAR was being implemented? Need to better explain. 18) The authors claim that “no study in our review found a significant increase in the occurrence of adverse events” yet in Table 3 it would appear that Andreoli et al showed a trend towards increased falls? Perhaps not statistically significant but if you would like to make this

	statement, should acknowledge this. 19) The paragraph “a number of studies …” on p 22 is not particularly relevant in the discussion and seems to fit more in the introduction. If any of these outcomes were assessed in your included studies, would be important to mention in the discussion as process measures as you consider causality.

REVIEWER	Guy Haller Geneva University Hospitals-University of Geneva
REVIEW RETURNED	19-Mar-2018

GENERAL COMMENTS	General Comments: This is an interesting systematic review which assesses the impact on patient related safety outcomes of the use of a standardised SBAR tool for handover. Due to a large between study heterogeneity, no meta-analysis could be performed. Study results shows a trend towards improved patient safety through the use of SBAR and emphasizes that there is a lack of high quality research on this hand-off tool. Although several studies have previously assessed the benefits of SBAR , only a few of them looked at patient-related outcomes rather than effectiveness of communication or staff satisfaction with the use of this communication standardisation tool. This is, with a rigorous methodology used throughout the study, the strength of this study. There are however some limitations, mainly in the manuscript itself rather than in the original study which deserve some attention. First, the introduction is a bit vague and some of the references are more than 20 years old. I would strongly suggest adding more up-to-date references on communication issues and their impact on patient outcomes. There is a wide body of literature in this area particularly in the perioperative care area including in french (annales françaises anesthésie réanimation). It should also be better explained in what sense SBAR can improve communication and being more accurate on issues related to communication breakdowns. The SBAR is a communication standardisation tool but not a magic bullet that will solve any communication issues in a complex organisation such as a hospital. This should be detailed. The second aspect relates to the result section itself. It is not aligned with the abstract section. While the first is encouraging and relates number of benefits on patient outcomes of the SBAR technique, the abstract mentions a “slight trend” towards improved patient outcome. Finally the discussion section should be reorganised into this study findings, other study findings, limitations, impact of this study on patient safety improvement. As is stands, it is mainly vague and polemic on the benefits of this technique without strong arguments fo or against supported by this study or others. A limitation section should be included as well and not only one limitation mentioned in the strength and limitation section. Authors should be able to demonstrate and discuss the impact of their study findings on the overall use of the SBAR tool and beyond.

REVIEWER	Jørgen T. Lauridsen University of Southern Denmark
REVIEW RETURNED	09-Apr-2018

GENERAL COMMENTS	The study is a review of literature on the effect of SBAR on preventing adverse events. It is performed in accordance with state of the art standards, and the presentation is professionally

	performed. Statistics is not directly applied, but referred to; I have checked that these refeneces are correct.

REVIEWER	Maria Kompoti Thriassio General Hospital of Eleusis, Athens, Greece
REVIEW RETURNED	15-Apr-2018

GENERAL COMMENTS	In this systematic review the authors summarized the available evidence and evaluated in the clinical setting the impact of the implementation of the communication tool SBAR on patient safety. The study was performed in accordance with Cochrane Collaboration standards. This is a well conducted review. However, the authors could not progress to meta-analysis, since the quality of the existing studies was inadequate. Minor points 1. Some references have not been correctly cited (page 15). 2. On page 19, line 30 «focused" should be "focused".

VERSION 1 – AUTHOR RESPONSE

Reviewer comments

Reviewer 1:

Comment R1.1: In the manuscript "The impact of the communication and patient hand-off tool SBAR on patient safety – a systematic review", the authors have performed a systematic review to address the important question of whether the most commonly used hand-off tool "SBAR" has any demonstrable effect on patient safety. The authors focus on adverse events and actual patient-related metrics rather than just provider satisfaction or other perceived benefits, and show that in several heterogenous studies there are some data to support use of SBAR as having a direct benefit for patients.

The objectives and design of the study are excellent.

Answer to comment #R1.1: Thank you for the positive overall evaluation.

Comment R1.2: However, the manuscript requires substantial revisions to the writing in the results and discussion sections to make it more clear to the reader as to what those benefits are and how convincing the data are to make any conclusions.

Answer to comment #R1.2: We appreciate your comments below and we revised the results and discussion section accordingly. We are confident that the manuscript sufficiently gained from these revisions.

Comment R1.3: The outcomes and reporting of the studies are heterogeneous, and the authors need to more clearly summarize the results for the reader to have “take-away points” of understanding.

Answer to comment #R1.3: We thank the reviewer for this critique. We have now clarified the result section, removing overly generalist statements and added detailed elaborations. In addition, a paragraph at the beginning of the new section (effect of SBAR on patient outcomes) and of each of the following section with take-away points was written in the revised version of the manuscript. Finally, we revised the tables and present a concise summary table with a one look-summary of the outcomes.

Comment R1.4: Abstract: First sentence of Results should read “were identified that met inclusion criteria”.

Answer to comment #R1.4: We added this information to the abstract.

Comment R1.5: Abstract: There should be a comma after “hand-off” in second sentence of results

Answer to comment #R1.5: Thank you for pointing out this typo. A comma was added.

Comment R1.6: Abstract: The results are too general and do not really give the reader enough substantive information. Need to better summarize what types of studies (e.g. trials, before/after), how many showed benefit, in what type of setting/use, and what type of benefit. This should overall be much better described in the actual results of the paper as well.

Answer to comment #R1.6: Thank you for the detailed suggestions. We revised the abstract and the results section to give the reader enough substantive information. Especially, table 2 was revised, a concise summary of the results and main characteristics for the reader.

Comment R1.7: Abstract: Sentence “no study found a significant increase” should be deleted from the abstract in favor of more relevant information as listed above.

Answer to comment #R1.7: The sentence was deleted and a concise summary of the found results was added.

Comment R1.8: Introduction: “AIDS” should be spelled out

Answer to comment #R1.8: We spelled out the word “AIDS” in the revised version of the manuscript.

Comment R1.9: Introduction: “commission” should be capitalized after “Joint”

Answer to comment #R1.9: We capitalized “Joint Commission”.

Comment R1.10: Results: Overall the results are scattered, contain too many generalities and negative statements, and not enough clear positive summary statements that make the results understandable to the reader. For example, “in all studies except the RCT by Field“ sentence – what was controlled for in this study?

Answer to comment #R1.10: We revised the result section and removed generalities and provide more detailed elaborations now. The study by Field et al. used a randomized controlled design with facility as randomization unit. Thus, by study design the results were controlled for potential (known and unknown) confounders such as infrastructure, patient safety culture, and management. These facts were added to the revised version of the manuscript.

Comment R1.11: Results: “Patients were largely blinded” – I don’t think this statement is necessary, but if you want to include it again it is too general. How many and what % of the studies had patients blinded?

Answer to comment #R1.11: We agree to this comment. The sentence was deleted. The percentage of studies that described blinding was added to the manuscript.

Comment R1.12: Results: “We further found study reporting to be incomplete mostly” – again very general and uninformative

Answer to comment #R1.12: Thank you. We replaced this sentence with an exact statement on incomplete study reporting.

Comment R1.13: Results: “Most studies used a before-after design” – again too general. One summary sentence could concisely say “X studies used before/after design (y%), Z studies were trials etc.

Answer to comment #R1.13: Thank you for this suggestion for improvement. We modified our summary statements accordingly.

Comment R1.14: Results: There are several places in the document I received where it says “Error! Reference source not found!”

Answer to comment #R1.14: We apologize for this problem with our citation software. Thank you for pointing out this issue. We corrected the citations.

Comment R1.15: Results: Did any of the studies include process measures? E.g. measuring whether communication was demonstrably improved to establish that SBAR may have contributed to the actual patient outcome measures?

Answer to comment #R1.15: Thank you for pointing out this important issue. Three of the included

studies controlled the use of SBAR by e.g. staff survey or review of medical records and identified high use rates within daily routine. Parameters of communication were not measured in the included studies although several (not included) studies suggested an improvement of communication quality by the implementation of SBAR. The lack of process measures within the included studies reduces internal validity and impedes the interpretation of the present results in regard to causation. We added all available information about process measurements to the result section and amended the discussion with a paragraph about process measurements.

Comment R1.16: Results: Tables 2 and 3 are both cumbersome and confusing. Would consider combining elements of each in a more succinct form as your main outcome table, or at least streamlining them. The most important elements are study design, how SBAR was used (e.g. nurse-physician phone communication), what was the outcome measure, and whether there was a difference shown. The details of the setting are given yet it is still unclear whether it was inpatient or outpatient, was SBAR mainly used for nurse/physician or other communication? In table 3 there is no column heading for the up/down arrows and the column for "outcome measure" seems to actually mean "duration of follow-up", and there is no indication of what type of study they are.

Answer to comment #R1.16: Thank you for pointing that out. We combined elements of Tables 3 and 4 as suggested and presented it as our main outcome table.

The original tables were streamlined and are now provided for detailed information as supplementary material. We added the column heading and information on the settings.

Comment R1.17: Results: There is too much text about the Haig study under interventions, while generally not enough summary in the results of how many studies showed improved outcomes and what outcomes.

Answer to comment #R1.17: We removed the passage about the Haig study and added detailed information about the number of improved outcomes and stated explicitly which outcomes showed improvement (see revised Table 2).

Comment R1.18: Results: Under “Patient hand-off” section on page 19, should start the sentence “The critical incidence reporting system” with “In a controlled clinical trial in x setting, the critical incidence reporting system . .”. Similarly the sentence “Further a reduction…“ should also start with the study type and setting. Later at the end of the results you could more effectively summarize these and other studies by category.

Answer to comment #R1.18: Thank you for that comment. We changed the beginning of the sentences and modified the end of the result section to get a more effective summary.

Comment R1.19: Results: (p>0.05) at the bottom of page 19 is unhelpful and should be deleted.

Answer to comment #R1.19: We agree with the reviewer and deleted it.

Comment R1.20: Discussion: By my count, 9 of the 11 studies included show at least some positive effect on outcome (counting studies with at least one up arrow in table 3). In the discussion, we need a more broad acknowledgement of this and explanation as to why the authors believe that this represents real results from SBAR or just heterogeneity and coincidence. The authors claim that “the results of our review indeed question the wide spread adoption of SBAR” despite 82% of their included studies having at least one improved outcome. Does it seem more likely that just more attention was paid to safety in general as SBAR was being implemented? Need to better explain.

Answer to comment #R1.20: Thank you. We elaborate on the general findings you refer to (i.e. some positive effect on study outcome) in the discussion section. However, regarding patient safety, evidence from our review is limited. We agree that SBAR implementation might indeed more generally affect a safety culture, which in turn might lead to better patient outcome – but evidence on such an effect is sparse. Thus, one potential implication of our review’s finding is the need to research this potential chain of effects (SBAR implementation -> increased awareness -> patient outcome) in more detail.

Comment R1.21: The authors claim that “no study in our review found a significant increase in the occurrence of adverse events” yet in Table 3 it would appear that Andreoli et al. showed a trend towards increased falls? Perhaps not statistically significant but if you would like to make this statement, should acknowledge this.

Answer to comment #R1.21: Thank you. We specified and discussed the trend towards increased falls in the discussion section.

Comment R1.22: Discussion: The paragraph “a number of studies …” on p 22 is not particularly relevant in the discussion and seems to fit more in the introduction. If any of these outcomes were assessed in your included studies, would be important to mention in the discussion as process measures as you consider causality.

Answer to comment #R1.22: We agree with the reviewer. Thank you. We shortened that section, rearranged the discussion and used the information at a relevant point. Furthermore, we added essential information about process measures in the results and discussion section (see answer to comment #R1.15).

Reviewer 2:

Comment R2.1: This is an interesting systematic review which assesses the impact on patient related safety outcomes of the use of a standardised SBAR tool for handover. Due to a large between study heterogeneity, no meta-analysis could be performed. Study results shows a trend towards improved patient safety through the use of SBAR and emphasizes that there is a lack of high quality research on this hand-off tool.

Although several studies have previously assessed the benefits of SBAR, only a few of them looked at patient-related outcomes rather than effectiveness of communication or staff satisfaction with the

use of this communication standardisation tool. This is, with a rigorous methodology used throughout the study, the strength of this study.

Answer to comment #R2.1: Thank you for this encouraging overall evaluation.

Comment R2.2: There are however some limitations, mainly in the manuscript itself rather than in the original study which deserve some attention. First, the introduction is a bit vague and some of the references are more than 20 years old. I would strongly suggest adding more up-to-date references on communication issues and their impact on patient outcomes. There is a wide body of literature in this area particularly in the perioperative care area including in french (annales françaises anesthésie réanimation).

Answer to comment #R2.2: Thank you for the thorough reading of the introduction. We updated our references wherever possible and a section on how SBAR can improve communication was added to the introduction. Furthermore, a reference from the perioperative care area is cited (annales françaises anesthésie réanimation).

There are however two references in the introduction where the articles are older than 15 years: The report "To err is human" from Donaldson et al. and the study of Brennan et al. published in the New England Journal of Medicine. Both of the studies are milestones in the young field of patient safety and thus deserve citation in our view.

Comment R2.3: It should also be better explained in what sense SBAR can improve communication and being more accurate on issues related to communication breakdowns. The SBAR is a communication standardisation tool but not a magic bullet that will solve any communication issues in a complex organisation such as a hospital. This should be detailed.

Answer to comment #R2.3: We thank the reviewer for this constructive critique. We added a subsection to the introduction to clarify this issue. We further address this concern together with comment R1.20 in the discussion.

Comment R2.4: The second aspect relates to the result section itself. It is not aligned with the abstract section. While the first is encouraging and relates number of benefits on patient outcomes of the SBAR technique, the abstract mentions a “slight trend” towards improved patient outcome.

Answer to comment #R2.4: Thank you for pointing that out. We revised our result section and abstract and aligned both.

Comment R2.5: Finally the discussion section should be reorganised into this study findings, other study findings, limitations, impact of this study on patient safety improvement. As is stands, it is mainly vague and polemic on the benefits of this technique without strong arguments for or against supported by this study or others. A limitation section should be included as well and not only one limitation mentioned in the strength and limitation section.
Authors should be able to demonstrate and discuss the impact of their study findings on the overall use of the SBAR tool and beyond.

Answer to comment #R2.5: We thank the reviewer for this constructive critique. We restructured the discussion in the following subsection: i) Summary of main results and ii) Quality of the evidence (in accordance with the recommendation of the Cochrane handbook of systematic reviews, 4.2.6), and added iii) Limitations, as well as iv) Implications for practice and research.

Reviewer 3:

Comment R3.1 The study is a review of literature on the effect of SBAR on preventing adverse events. It is performed in accordance with state of the art standards, and the presentation is professionally performed. Statistics is not directly applied, but referred to; I have checked that these references are correct.

Answer to comment #R3.1: Thank you for your very positive overall evaluation.

Reviewer 4:

Comment R4.1: In this systematic review the authors summarized the available evidence and evaluated in the clinical setting the impact of the implementation of the communication tool SBAR on patient safety. The study was performed in accordance with Cochrane Collaboration standards. This is a well-conducted review.

Answer to comment #R4.1: Thank you for the very positive evaluation of our manuscript.

Comment R4.2: However, the authors could not progress to meta-analysis, since the quality of the existing studies was inadequate.

Answer to comment #R4.2: The quality and heterogeneity of the trials forbid a meta-analysis. Instead, we provide a comprehensive summary of the studies' key findings to maximize reader's benefit.

Comment R4.3: Some references have not been correctly cited (page 15).

Answer to comment #R4.3: Thank you for pointing out this issue. We corrected the problem we had with our citation software (please also refer to comment R 1.14).

Comment R4.4: On page 19, line 30 «focussed" should be "focused".

Answer to comment #R4.4: Thank you for pointing out this typo. It was corrected in the revised manuscript.

VERSION 2 – REVIEW

REVIEWER	Michael C. McCrory MD, MS Associate Professor, Anesthesiology and Pediatrics, Wake Forest University School of Medicine
REVIEW RETURNED	31-May-2018

GENERAL COMMENTS	Thank you for the opportunity to review the revised manuscript "The impact of the communication and patient hand-off tool SBAR on patient safety – a systematic review". The authors have greatly strengthened the manuscript with their revisions. Minor comments

	by section are below: Abstract: 1) For participants, probably more relavant than “a wide range of sociodemographic groups” would be to indicate that both nurses and physicians were involved, whether adults and children patient populations were involved, or some such. Introduction: 2) Reads a little long – would consider shortening and getting to the point faster. Results: 3) The text becomes a bit confusing at times when trying to cross-reference with Table 2. Would consider using the author’s name a bit more in the text to make it easier to understand and cross-reference when you are discussing a single study in more detail, such as at the bottom of page 16 “In one before-after study” or at the top of page 17 “Another before-after trial”, etc. Discussion: 4) Would consider making it a little more clear in the beginning summary paragraph that there were 5 studies that showed improvement and recap what the outcomes were (INR in goal range, etc).

REVIEWER	Dr Guy Haller Geneva University Hospitals-Switzerland
REVIEW RETURNED	12-Jun-2018

GENERAL COMMENTS	Authors have correctly answered to all points raised. The introduction section provides now a broader perspective on patient safety and explains better why SBAR is important. The only improvement to be made could be integrating the following sentence “Patient safety is crucial for the delivery of effective, high-quality healthcare22 and is defined by the World Alliance for Patient Safety of the World Health Organisation (WHO) as “the reduction of risk of unnecessary harm associated with healthcare to an acceptable minimum“.23 To illustrate the impact of patient safety on healthcare quality, the incidence of adverse events is commonly cited. Following the definition of Brennan, et al.24, adverse events are injuries that are caused by medical conduct resulting in prolonged hospitalisation and/or disability at the time of discharge.” at the beginning of the manuscript, as it is redundant with the sentence at the beginning of the introduction. The methods and result section are clear and no additional modification is needed. In the discussion section, all benefits and limitations are clearly described now. The references should be all formatted according to the BMJ-open requirements.

VERSION 2 – AUTHOR RESPONSE

Reviewer comments

Reviewer 1:

Comment R1.1: The authors have greatly strengthened the manuscript with their revisions.

Answer to comment #R1.1: Thank you for this positive overall evaluation.

Comment R1.2: Abstract: For participants, probably more relavant than “a wide range of sociodemographic groups” would be to indicate that both nurses and physicians were involved, whether adults and children patient populations were involved, or some such.

Answer to comment #R1.2: Thank you for pointing that out. We changed the ‘Abstract - Participants’ subsection to “*A variety of heath professionals including nurses and physicians*”.

Comment R1.3: Introduction: Reads a little long – would consider shortening and getting to the point faster.

Answer to comment #R1.3: The introduction was restructured and shortened.

Comment R1.4: Results: The text becomes a bit confusing at times when trying to cross-reference with Table 2. Would consider using the author’s name a bit more in the text to make it easier to understand and cross-reference when you are discussing a single study in more detail, such as at the bottom of page 16 “In one before-after study” or at the top of page 17 “Another before-after trial”, etc.

Answer to comment #R1.4: Thank you for this suggestion. We changed the manuscript accordingly and use the author’s name a bit more in the text to make it easier to understand.

Comment R1.5: Discussion: Would consider making it a little more clear in the beginning summary paragraph that there were 5 studies that showed improvement and recap what the outcomes were (INR in goal range, etc).

Answer to comment #R1.5: Thank you for this constructive critique. We added the following lines to the beginning of the ‘Discussion - Summary of main results’ section: *“Study outcomes with statistically evidence for improvement included INR values within the target range[51] and unplanned transfers to hospitals[59] in nursing homes, as well as CIRS events due to communication errors[37], patient falls[56], unexpected death and ICU admissions[57] in hospitals.”*.

Reviewer 2:

Comment R2.1: Authors have correctly answered to all points raised. The introduction section provides now a broader perspective on patient safety and explains better why SBAR is important. The only improvement to be made could be integrating the following sentence "*Patient safety is crucial for the delivery of effective, high-quality healthcare*[22] *and is defined by the World Alliance for Patient Safety of the World Health Organisation (WHO) as 'the reduction of risk of unnecessary harm associated with healthcare to an acceptable minimum'.*[23] *To illustrate the impact of patient safety on healthcare quality, the incidence of adverse events is commonly cited. Following the definition of Brennan, et al.*[24]*, adverse events are injuries that are caused by medical conduct resulting in prolonged hospitalisation and/or disability at the time of discharge*." at the beginning of the manuscript, as it is redundant with the sentence at the beginning of the introduction.

Answer to comment #R2.1: The abovementioned sentence was moved to the beginning of the introduction and former beginning was removed to avoid redundancy.

Comment R2.2: The methods and result section are clear and no additional modification is needed. In the discussion section, all benefits and limitations are clearly described now.

Answer to comment #R2.2: Thank you.

Comment R2.3: The references should be all formatted according to the BMJ-open requirements.

Answer to comment #R2.3: Thank you. The references are now all formatted according to the BMJ-open requirements (https://authors.bmj.com/writing-and-formatting/formatting-your-paper/).