## PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

## ARTICLE DETAILS

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| **TITLE (PROVISIONAL)** | ESPACOMP Medication Adherence Reporting Guidelines (EMERGE): A Reactive-Delphi Study Protocol |
| **AUTHORS** | Helmy, Remon; Zullig, Leah; Dunbar-Jacob, Jacqueline; Hughes, Dyfrig; Vrijens, Bernard; Wilson, Ira; De Geest, Sabina |

## VERSION 1 - REVIEW

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| **REVIEWER** | Parisa Aslani<br>University of Sydney, Australia |
| **REVIEW RETURNED** | 17-Aug-2016 |

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| **GENERAL COMMENTS** | Title: ESPACOMP Medication Adherence Reporting Guidelines (EMERGE): A Reactive-Delphi Study Protocol<br>Manuscript ID – bmjopen-2016-013496<br>General Comments:<br>Thank you for the opportunity to review this manuscript. This is a very interesting study describing the approach to the development of guidelines for the reporting of adherence research. These guidelines are long overdue and it is great to see that ESPACOMP has taken the initiative. Whilst it is very useful to know about the protocol and the approach to be used, it is imperative that this manuscript describes the actual guidelines. Therefore, I would strongly recommend the inclusion of the “results” ie the guidelines themselves. Furthermore, as the Delphi process has not commenced, it is not possible to assess the methods described, nor changes made as the process gets underway.<br>Specific Comments:<br>There is a need for a stronger justification for the guidelines, compared to existing guidelines. This probably would be easier to do, and clearer to the leader if the guidelines could be seen and directly compared with existing ones.<br>In the Introduction, please ensure that the pros and cons of the Delphi process described, are indeed those of the modified or reactive Delphi process.<br>Why will two rules be applied for item-level decision making for “relevance” and only one (with different cut off) for “clarity”? |

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| **REVIEWER** | Jocelyne Moisan, Ph.D. professor<br>Chaire sur l'adhésion aux traitements et Faculté de pharmacie, Université Laval<br>Axe Santé des populations et pratiques optimales en santé, Centre de recherche du CHU de Québec, Université Laval, Québec, Province de Québec, Canada<br><br>I am one of the experts participating in this Delphi study. However, I had no information on the study protocol before I was asked to |

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| | review it. |
| **REVIEW RETURNED** | 13-Sep-2016 |

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| **GENERAL COMMENTS** | This is a very interesting manuscript, well written and easy to read. It adresses an important issue. I believe it will of interest to the BMJ Open readers. |

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| **REVIEWER** | Shah, KC<br>UCLA USA |
| **REVIEW RETURNED** | 07-Nov-2016 |

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| **GENERAL COMMENTS** | Thank you for your detailed manuscript.<br>May I suggest revision of the Figure to allow the reader to follow it easily? |

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| **REVIEWER** | Kathy J. Wheeler, PhD, RN, APRN, NP-C, FNAP, FAANP<br>University of Kentucky College of Nursing<br>United States of America |
| **REVIEW RETURNED** | 26-Nov-2016 |

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| **GENERAL COMMENTS** | Initially I was puzzled over the premise of this article. But, on reading, it becomes clear it is a description of a process to build consensus for a guideline, specifically a guideline on reporting of medication adherence. Having studied and published on medication adherence I fully appreciate the need for a guideline on reporting. Indeed, poor medication adherence is a significant, troublesome problem and cuts across all healthcare delivery disciplines. Data on medication adherence suffers because of poor reporting and poor consensus on the process.<br><br>I also think discussing the plan in an open journal before the effort is attempted is intriguing, a true opportunity uniquely available through an open journal. It has the potential to open the study to consideration before it is fully planned or undertaken.<br><br>Nonetheless, the process as described seems appropriate and well thought out. The provided diagram is helpful and seems representative of the described process, essentially going through three review rounds, and allowing items to be added along the way. I do wonder if the process can produce a list or guideline that addresses medication initiation, implementation and persistence, and can do so in all the settings where initiation, implementation and persistence take place (hospitals, clinics, schools, home, acute problems, chronic problems, etc).<br><br>Guideline development is complex and can be costly and time intensive. If this process successfully produces a list useful to guideline development it will be an interesting illustration of a process that could be duplicated reasonably.<br><br>While I appreciate one of the advantages of the process is to eliminate face-to-face dialogue, reduce individual dominance and reduce dialogue noise, one has to wonder what might also be lost by limiting the iterative process. At the same time it may be refreshing |

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| | to see if historically non-dominant professions contribute more, producing a better product in the end. I hope future articles will provide some analysis of this.<br><br>At the same time I would also be concerned about the possibility the core group could dominate the process, and make decisions without group review or input. I am not sure how this could be controlled and nothing in the article seemed to acknowledge that or address that in any way. |

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| **REVIEWER** | Jimmy Jose MPharm, PhD<br>Associate Professor (Pharmacy Practice)<br>School of Pharmacy<br>University of Nizwa<br>Sultanate of Oman |
| **REVIEW RETURNED** | 04-Dec-2016 |

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| **GENERAL COMMENTS** | This manuscript on protocol design for development of EMERGE guidelines is comprehensive and well written.<br>It would be better if redundancy is reconfirmed to have avoided in the section on generation of the initial item list, decision rules .....and study procedure. |

**VERSION 1 – AUTHOR RESPONSE**

Reviewer 1

Thank you for the opportunity to review this manuscript. This is a very interesting study describing the approach to the development of guidelines for the reporting of adherence research. These guidelines are long overdue and it is great to see that ESPACOMP has taken the initiative. Whilst it is very useful to know about the protocol and the approach to be used, it is imperative that this manuscript describes the actual guidelines. Therefore, I would strongly recommend the inclusion of the “results” ie the guidelines themselves. Furthermore, as the Delphi process has not commenced, it is not possible to assess the methods described, nor changes made as the process gets underway.

** Response: We thank the reviewer for their enthusiasm to see the final product of our work (the guidelines). However, this manuscript is submitted as a protocol for our Delphi study. Hence, we do not intend to include the results as the final guidelines are planned to be published in a separate article where all details before and after the Delphi process will be described.

Specific Comments: There is a need for a stronger justification for the guidelines, compared to existing guidelines. This probably would be easier to do, and clearer to the reader if the guidelines could be seen and directly compared with existing ones.

** Response: Since this manuscript is meant to be only a protocol for the Delphi part of the guidelines development process, the guidelines are planned to be published separately later when it will be finalized. However, we adapted the introduction section to provide a stronger justification for the guidelines and a brief explanation of their novelty.

In the Introduction, please ensure that the pros and cons of the Delphi process described are indeed those of the modified or reactive Delphi process.

** Response: The reactive-Delphi process is almost the same as the original process. Therefore, the

same pros and cons apply to both processes. The reactive process has one advantage over the original one in that it provides the participants with an initial list of items. This leads to relative reduction of effort needed from the experts and faster arrival at consensus. This extra advantage is explained in the methods section, under the “Overview of the study design” paragraph.

Why will two rules be applied for item-level decision making for “relevance” and only one (with different cut off) for “clarity”?

** Response: Relevance of items is more critical to the item list than clarity because it leads to keeping or deleting items which impact the structure and content of the item list more than clarity scoring that just leads to modifying the items. So, to be more sure about the included or deleted items, we wanted to decrease the scoring range for relevance and create a third category “no consensus” to allow items in this category to enter into further rounds until they are confirmed as either relevant or irrelevant. To clarify more, considering the scoring scale (1 to 4), the decision rule for clarity states that if an item is given by 30% or less of the experts a score of 3 or 4, then it needs to be clarified more, otherwise it is clear. For relevance, if an item is given by 30% or less of the experts a score of 3 or 4, then it is irrelevant, if between 30 – 70% then there is no consensus on its status, and if more than 70%, then it is relevant and should be kept on the list. The figure attached (for editor only) illustrates this idea.

Reviewer 2

This is a very interesting manuscript, well written and easy to read. It addresses an important issue. I believe it will of interest to the BMJ Open readers.

** Response: We thank the reviewer for the positive feedback.

Reviewer 3

Thank you for your detailed manuscript.
May I suggest revision of the Figure to allow the reader to follow it easily?

** Response: We thank the reviewer for the positive feedback. Although it couldn’t be simplified to keep it informative, the figure was revised to a more neat and enhanced appearance.

Reviewer 4

Initially I was puzzled over the premise of this article. But, on reading, it becomes clear it is a description of a process to build consensus for a guideline, specifically a guideline on reporting of medication adherence. Having studied and published on medication adherence I fully appreciate the need for a guideline on reporting. Indeed, poor medication adherence is a significant, troublesome problem and cuts across all healthcare delivery disciplines. Data on medication adherence suffers because of poor reporting and poor consensus on the process.

I also think discussing the plan in an open journal before the effort is attempted is intriguing, a true opportunity uniquely available through an open journal. It has the potential to open the study to consideration before it is fully planned or undertaken.

Nonetheless, the process as described seems appropriate and well thought out. The provided diagram is helpful and seems representative of the described process, essentially going through three

review rounds, and allowing items to be added along the way. I do wonder if the process can produce a list or guideline that addresses medication initiation, implementation and persistence, and can do so in all the settings where initiation, implementation and persistence take place (hospitals, clinics, schools, home, acute problems, chronic problems, etc).

Guideline development is complex and can be costly and time intensive. If this process successfully produces a list useful to guideline development it will be an interesting illustration of a process that could be duplicated reasonably.

While I appreciate one of the advantages of the process is to eliminate face-to-face dialogue, reduce individual dominance and reduce dialogue noise, one has to wonder what might also be lost by limiting the iterative process. At the same time it may be refreshing to see if historically non-dominant professions contribute more, producing a better product in the end. I hope future articles will provide some analysis of this.

At the same time I would also be concerned about the possibility the core group could dominate the process, and make decisions without group review or input. I am not sure how this could be controlled and nothing in the article seemed to acknowledge that or address that in any way.

** Response: We thank the reviewer for the positive feedback. Indeed, as they indicated, guideline development is complex and time intensive. Therefore, the benefit of implementing Delphi methodology in this process is to use pre-defined decision rules that indicate when consensus is reached. Although, as the reviewer refers, this might be limiting for further feedback to be included, it provides a practical and efficient way of incorporating feedback, especially that a variety of experts from various disciplines and countries will be included from the beginning. Additionally, the same experts will continue on the following survey rounds and no new experts can respond to the survey from the 2nd round onwards. Hence, there is low probability that major feedback can arise at later stages as the opinions converge towards consensus (as defined by the rules).
Considering the concern regarding the domination of core group, it is avoided by using the decision rules. Although modifying the items based on received comments is qualitative work, modified items will enter in each survey round and only decision rules, which are quantitative in nature, will determine when consensus is reached. Beyond experts' consensus, the core group will not modify the items on their own.

Reviewer 5

This manuscript on protocol design for development of EMERGE guidelines is comprehensive and well written.
It would be better if redundancy is reconfirmed to have avoided in the section on generation of the initial item list, decision rules and study procedure.

** Response: We thank the reviewer for the positive feedback. We checked these 3 sections and made sure there was no redundancy. The section "Generation of the initial item list" discusses exclusively how the item list, to be used for the survey, was generated. The section "Decision rules and definition of consensus on relevance and clarity of items" is concerned with the definitions of consensus on item's relevance and clarity. The section "Study procedures" explains only how the item list will be used through the survey rounds to reach consensus using the decision rules.

## VERSION 2 – REVIEW

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| **REVIEWER** | Parisa Aslani<br>The University of Sydney, Australia |
| **REVIEW RETURNED** | 17-Jan-2017 |

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| **GENERAL COMMENTS** | The authors have addressed the reviewers' comments |