PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	The use of Patient-Reported Outcome Measures (PROMs) in clinical diabetes consultations: study protocol for the DiaPROM randomized controlled trial pilot study.
AUTHORS	Haugstvedt, Anne; Hernar, Ingvild; Strandberg, Ragnhild; Richards, David; Nilsen, Roy; Tell, Grethe; Graue, Marit

VERSION 1 – REVIEW

REVIEWER	David T. Eton, Ph.D. Mayo Clinic Rochester, Minnesota, USA
REVIEW RETURNED	20-Jun-2018

GENERAL COMMENTS	The use of Patient-Reported Outcome Measures (PROMs) in clinical diabetes consultations: study protocol for the DiaPROM randomized controlled trial. This investigative team aims to develop, test, and evaluate the effectiveness of an empowerment-based intervention using patient-reported outcome measures (PROMs) of diabetes distress to support dialogue in clinical diabetes consultations between clinicians and their patients with type I diabetes. The evaluation phase will consist of a randomized-controlled trial of the PROM system to determine whether such a system can improve the quality of consultations and lead to better clinical outcomes in these patients (e.g., lower distress, better glycemic control, higher perceived competence in managing diabetes). INTRODUCTION What are the hypotheses on page 5 based on? What are the proposed mechanisms by which the intervention will lead to the outcomes? There needs to be some kind of theory or conceptual logic model to justify making these particular hypotheses, currently there is none put forth. PHASE I – DEVELOPMENT Only a single measure was revealed by the literature review (i.e., the PAID). What were the criteria for selecting an intervention measure? Were other measures considered (there are several in the diabetes literature)? Why were other measures dismissed as less appropriate? Greater justification for selecting the PAID is needed. In the development, the authors say that they consulted with “several groups of health service users.” How many? What is the make-up of these groups? Are the groups diverse and therefore

	representative of different types of people? More detail is essential here. Were the “health services users” allowed to judge the relevance of any other measures besides the PAID? If not, it is hard to envision them not arriving at the PAID as the appropriate measure. What were the measure evaluation criteria used by these individuals to arrive at the PAID? P.9. Study intervention. Will physicians be trained in how to discuss the PAID scores? If so, how will they be trained? P.9. Evaluation measures. The Diabetes Distress Scale shares content with the PAID. In fact, Dr. Polonsky was a developer of both measures. Priming of patient responses (the PAID [intervention measure] priming responses to the DDS [outcome measure]) could be a concern here given the content overlap. This could be resolved by selecting a different disease-specific measure for the evaluation. PHASE III – THE RCT P.14. What constitutes “severe co-morbidities?” Why would these conditions make people ineligible for the study? P.15. Will there be a way to determine whether any clinical attention to psychological/emotional distress is provided in the control condition, so that this can be taken into account during analysis? Such attention in the control arm could contaminate the findings. P.15. The control subjects will be asked to complete the PAID instrument before the consultation and then the responses will NOT be discussed with the physician. It is a little ethically dubious to ask patients to complete a measure about their distress and then not talk about it at all during the consultation. Might these patients become a little angered by this and therefore report worse outcomes at follow-up – especially if they are distressed? It could create an imbalance between the two study arms, and set up an expectation among patients in the control group that they are not receiving the best possible care. The study is not blinded so the control-group patients know that other patients in the study will be allowed to discuss their PROM responses with their physicians, even though they are not being allowed to do so.

REVIEWER	Dr Stanley Landau Centre for Diabetes and Endocrinology Johannesburg, South Africa
REVIEW RETURNED	08-Aug-2018

GENERAL COMMENTS	1.I note the inconsistency of the terms describing diabetes in the abstract as 'disease' and then as a 'condition' in the 1st line of the introduction. 2. What opportunity would a person with diabetes have open to them to see their nurse after a life event/ ER visit or admission?Would that upset the timetable for the next score assessment?

REVIEWER	Lisa Hynes

	West Virginia University Research Corporation, United States of America
REVIEW RETURNED	28-Aug-2018

GENERAL COMMENTS	This manuscript describes the protocol for a 3-phase study, aiming to identify relevant PROMs and pilot test their use among adult with type 1 diabetes, before implementing them to support dialogue during clinical consultations within an empowerment-based intervention. This manuscript reports on an important topic of research, however there are two major issues with the manuscript in my opinion. First, the abstract, aims and introduction sections are misleading by not giving adequate weight to the fact that this is an intervention study, rather than a study focusing on the identification of a PROM for use as a dialogue support tool alone. It's not until well into the Method section that the fact that an intervention was developed, as well as identifying a suitable PROM and pilot testing its use in a clinic setting, becomes clear. Second, I believe this manuscript is trying to do too much, without giving sufficient space to any one aspect of the program of research. I would suggest that the authors focus their attention, for the purposes of this manuscript, on the pilot testing phase of the intervention (including pilot testing the PROM), and just report the findings of the first phase by way of background, OR wait to write up the protocol for the full RCT, once it's fully developed on the basis of the findings of phase 1 & 2. Currently there is a lack of detail in relation to the methodological approaches being used, for example, guidance used for the Public and Patient Involvement aspect of the work, and for qualitative and quantitative approaches to analysis. Overall, referencing the role of the MRC framework more explicitly would also be helpful. Below are some specific pieces of feedback, however, addressing the two points I raised above are most Important, in my opinion, and if major revisions are made, the feedback below may not be particularly helpful. Abstract: - I suggest rephrasing the last sentence under the heading of introduction, as the aim is a little clunky. For example, is it necessary to say that you're planning to test and evaluate the intervention? It may be helpful to briefly introduce the planned intervention before this sentence too, and reduce the background information at the start of this section. It may also be helpful to refer to this manuscript as a protocol for an intervention at this stage. - The Methods and analysis section is unclear in terms of the aim of this manuscript specifically. - When referring to the use of PROMs in dialogue support, the authors might consider the way this phrase is used, e.g. referring to PROMs as a dialogue support tool, or similar. current use of the phrase doesn't read well. Introduction: This section is clear and does a nice job of providing a basis for the present study. However, there is a lack of detail in relation to the extent of the planned study, and the evidence-base for the components of the planned study. For example, in the last paragraph before 'Aim', more details would be helpful in describing existing use of PROMs in practice.

	Methods: - In the first paragraph of the Method section on page 5, consider clarifying why the MRC framework may be a useful tool in the development of a complex intervention, such as this. - I commend the integration of Public and Patient Involvement (PPI) within this work. Can the authors provide any information of frameworks that were utilized to guide the use of a PPI approach, whether the research team and PPI members took part in training, and some indication of decision-making regarding identifying and recruiting PPI team members. -Unless the findings of the literature review are published elsewhere, the decision-making process that resulted in the focus on the PAID scale is not sufficiently detailed in this manuscript. The reader may be better able to follow this decision-making process if some details are provided related to the other measures identified in the review and the number of studies using each, along with a critique of available measures, and justification for then choosing the PAID scale. Is there a justification for choosing only one PROM in this case? -The table outlining the phases of this program of research seems to focus on the PROMs aspect of the work, with insufficient attention to the significant intervention development component. Use of the MRC framework to inform this process is not adequately described throughout each part of the Method section. The description of the development of the intervention and plans for testing the components are insufficient. For example, do nurses delivering the intervention receive training, what is the evidence base for addressing concerns related to diabetes distress based on the proposed criteria in this study, etc.? -Some additional information on the chosen outcomes measures may be useful. For example, why add the Diabetes Distress Scale, rather than using the PAID scale as the primary outcome to assess change? Why is HbA1c or a behavioral measure of self-management not included? - In the feasibility study aims, on page 10, the authors refer to the evaluation of participants' perceived understanding. Is this perceived understanding of the PAID items? Discussion: - The authors might consider beginning this section with a summary of the proposed study before summarizing key factors and decisions. The authors might also elaborate on the value of utilizing the MRC framework, maybe eluding to its impact in existing research and value added so far as part of the present study.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: David T. Eton, Ph.D.

1. *INTRODUCTION*
   What are the hypotheses on page 5 based on? What are the proposed mechanisms by which the intervention will lead to the outcomes? There needs to be some kind of theory or conceptual logic model to justify making these particular hypotheses, currently there is none put forth.

Re: We have developed an empowerment-based intervention, and our proposition is that the intervention that include discussions of the reported diabetes distress and actions to reduce the distress actually will reduce diabetes distress (the emotional burden associated with managing diabetes in everyday life). Further, reduced diabetes distress and the discussions focusing among others autonomy support may improve overall well-being, competence for diabetes management and glycaemic control as indicated in the introduction section (p. 5). In addition, we believe that the improved focus on the psychological and emotional burden of the disease will improve satisfaction with diabetes follow-up. In the revised paper, we describe a pilot RCT with embedded qualitative study on participants' and health care personnel's views of the DiaPROM intervention initiative. We have deleted the text describing the fully powered RCT and hereby we do not include explicit hypotheses.

2. *PHASE I – DEVELOPMENT*
Only a single measure was revealed by the literature review (i.e., the PAID). What were the criteria for selecting an intervention measure? Were other measures considered (there are several in the diabetes literature)? Why were other measures dismissed as less appropriate? Greater justification for selecting the PAID is needed.

Re: In the revised paper, we have moved the literature review to the introduction. In addition, we have revised the text to clarify why we selected PAID as instrument for dialogue support in the intervention (p. 6-8).

3. *In the development, the authors say that they consulted with "several groups of health service users." How many? What is the make-up of these groups? Are the groups diverse and therefore representative of different types of people? More detail is essential here*.

Re: In accordance with reviewer's questions, we have added more details about the health service representatives in the "P*atient and public involvement*" section (p. 7-8).

4. *Were the "health services users" allowed to judge the relevance of any other measures besides the PAID? If not, it is hard to envision them not arriving at the PAID as the appropriate measure. What were the measure evaluation criteria used by these individuals to arrive at the PAID?*

Re: We have added text in the PPI section (p. 7-8). In the meeting with the health service users, we first allowed an open discussion to determine which topics they perceived as important and relevant to include in a set of PROMs. Thereafter, we asked the user representatives to review several generic and disease specific instruments as described in the revised manuscript. They considered the advantages and shortcomings of using PAID as dialogue support in the intervention, and they found it relevant and suitable to be used in the intervention.

5. *P.9. Study intervention. Will physicians be trained in how to discuss the PAID scores? If so, how will they be trained?*

Re: In the methods section of the revised manuscript, we have added a sub-section with the heading "Training of participating health care personnel" (p. 12-13) to explain the training of physicians and diabetes nurses.

6. *P.9. Evaluation measures. The Diabetes Distress Scale shares content with the PAID. In fact, Dr. Polonsky was a developer of both measures. Priming of patient responses (the PAID [intervention measure] priming responses to the DDS [outcome measure]) could be a concern here given the content overlap. This could be resolved by selecting a different disease-specific measure for the evaluation.*

Re: We consider the PAID and the DDS as the most appropriate instruments to measure diabetes distress as both of them measure a breadth of emotional responses related to life with diabetes. Other existing measures most often assess a specific part of possible emotional responses (e.g. "fear of hypoglycemia", "family conflict"). Further, previous publications have indicated that PAID seems to have some advantages for use in clinical diabetes consultations while DDS has some

advantages for use in research. Our choice of using PAID in the intervention and the DDS as the primary outcome measure is described on p. 8, 13-14 and 16-17 in the revised manuscript.

7. *PHASE III – THE RCT*
   P.14. What constitutes "severe co-morbidities?" Why would these conditions make people ineligible for the study?

   Re: Thank you for important questions. The third phase of the study has been removed from the revised paper. However, the exclusion criteria related to the pilot RCT is the same as previously described for the evaluation study. The explanation of the comorbidities has been revised in the new manuscript (p. 10).

8. *P.15. Will there be a way to determine whether any clinical attention to psychological/emotional distress is provided in the control condition, so that this can be taken into account during analysis? Such attention in the control arm could contaminate the findings.*

   Re: Please see our response to points 8 and 9 below.

9. *P.15. The control subjects will be asked to complete the PAID instrument before the consultation and then the responses will NOT be discussed with the physician. It is a little ethically dubious to ask patients to complete a measure about their distress and then not talk about it at all during the consultation. Might these patients become a little angered by this and therefore report worse outcomes at follow-up – especially if they are distressed? It could create an imbalance between the two study arms, and set up an expectation among patients in the control group that they are not receiving the best possible care. The study is not blinded so the control-group patients know that other patients in the study will be allowed to discuss their PROM responses with their physicians, even though they are not being allowed to do so.*

   Re: Comments 8 and 9 are important. We are aware of the possible contamination challenge in the study, and we have mentioned this as an important point in the "Strengths and limitations of the study" (p. 3) and in the discussion section (p. 17). Further, we have explained how we will evaluate to what extent psychological or emotional distress are discussed (and reported in the electronic patient records (EPR)) in the consultations with control participants (p. 12). We have also mentioned that we, for ethical reasons, cannot prevent physicians discussing psychological or emotional issues with the controls if some of them specifically raise such an issue. However, unlike participants in the intervention group, such discussions will not be structured with reference to PAID data (p. 12).

Reviewer: 2
Reviewer Name: Dr Stanley Landau

1. *I note the inconsistency of the terms describing diabetes in the abstract as 'disease' and then as a 'condition' in the 1st line of the introduction.*

   Re: We have changed "disease" to "condition" in the abstract.

2. *What opportunity would a person with diabetes have open to them to see their nurse after a life event/ ER visit or admission? Would that upset the timetable for the next score assessment?*

   Re: During the study, as is usual in clinical practice, participants in both the intervention and the control group will be able to contact the diabetes nurse if they experience a specific adverse event or if they for example need to discuss their technical devices. We have described how we will record this matter in the manuscript (p. 11-12).

Reviewer: 3
Reviewer Name: Lisa Hynes

1. *First, the abstract, aims and introduction sections are misleading by not giving adequate weight to the fact that this is an intervention study, rather than a study focusing on the identification of a PROM for use as a dialogue support tool alone. It's not until well into the Method section that the*

fact that an intervention was developed, as well as identifying a suitable PROM and pilot testing its use in a clinic setting, becomes clear.

Re: Thank you for this comment. We now mention in the abstract that this is an intervention study.

2. *Second, I believe this manuscript is trying to do too much, without giving sufficient space to any one aspect of the program of research. I would suggest that the authors focus their attention, for the purposes of this manuscript, on the pilot testing phase of the intervention (including pilot testing the PROM), and just report the findings of the first phase by way of background, OR wait to write up the protocol for the full RCT, once it's fully developed on the basis of the findings of phase 1 & 2.*

   Re: Thank you for a very important comment that makes us reconsider the structure of the manuscript. We have described how we have dealt with this issue in the beginning of this response letter.

3. *Currently there is a lack of detail in relation to the methodological approaches being used, for example, guidance used for the Public and Patient Involvement aspect of the work, and for qualitative and quantitative approaches to analysis.*

   Re: In accordance with the comment, we have added text in the "Patient and Public involvement" section (p. 7-8) and in the methods section under the sub heading "Data analysis" (p. 14-15).

4. *Overall, referencing the role of the MRC framework more explicitly would also be helpful.*

   Re: In the second point in the "Strengths and limitations of the study" (p. 3) we now describe the importance of utilizing the MRC framework. Under the heading "The development of the DiaPROM trial" (p. 5), we have revised the text to make the role of the framework more explicit.

   Below are some specific pieces of feedback, however, addressing the two points I raised above are most Important, in my opinion, and if major revisions are made, the feedback below may not be particularly helpful.

5. *Abstract: I suggest rephrasing the last sentence under the heading of introduction, as the aim is a little clunky. For example, is it necessary to say that you're planning to test and evaluate the intervention? It may be helpful to briefly introduce the planned intervention before this sentence too, and reduce the background information at the start of this section. It may also be helpful to refer to this manuscript as a protocol for an intervention at this stage.*

   Re: The restructuring of the manuscript has also led to a revision of the study aim.

6. *The Methods and analysis section is unclear in terms of the aim of this manuscript specifically.*

   Re: An important comment. We hope the methods and analysis section are clearer now as a result of the restructuring and revision of the manuscript.

7. *When referring to the use of PROMs in dialogue support, the authors might consider the way this phrase is used, e.g. referring to PROMs as a dialogue support tool, or similar. current use of the phrase doesn't read well.*

   Re: In the revised manuscript, we have tried to be more consistent and clear in how we describe the use of PAID in the clinical intervention consultations.

8. *Introduction: This section is clear and does a nice job of providing a basis for the present study. However, there is a lack of detail in relation to the extent of the planned study, and the evidence-base for the components of the planned study. For example, in the last paragraph before 'Aim', more details would be helpful in describing existing use of PROMs in practice.*

Re: In accordance with the comment, we have restructured the manuscript and the description of the development of the study in the introduction section make these issues more clear (p. 5-9).

9. *Methods: In the first paragraph of the Method section on page 5, consider clarifying why the MRC framework may be a useful tool in the development of a complex intervention, such as this.*

   Re: Please see our response to comment 4 (reviewer 3).

10. *I commend the integration of Public and Patient Involvement (PPI) within this work. Can the authors provide any information of frameworks that were utilized to guide the use of a PPI approach, whether the research team and PPI members took part in training, and some indication of decision-making regarding identifying and recruiting PPI team members.*

    Re: Under the heading "Patient and public involvement" (p. 7), we have included information on the use of the GRIPP2 short form as guidance for including and reporting patient and public involvement, and the recruitment of PPI team members.

11. *Unless the findings of the literature review are published elsewhere, the decision-making process that resulted in the focus on the PAID scale is not sufficiently detailed in this manuscript. The reader may be better able to follow this decision-making process if some details are provided related to the other measures identified in the review and the number of studies using each, along with a critique of available measures, and justification for then choosing the PAID scale. Is there a justification for choosing only one PROM in this case?*

    Re: After changing the manuscript to describe the protocol for the pilot RCT, the comment regarding the literature review is dealt with in the introduction section. We have revised the text under the heading "The development of the DiaPROM trial" (p. 5-8) to clarify the process regarding the development of the study so that the reader may be better able to follow the decision-making process and choice of measures.

12. *The table outlining the phases of this program of research seems to focus on the PROMs aspect of the work, with insufficient attention to the significant intervention development component.*

    Re: As result of the restructuring of the paper, the table has been removed.

13. *Use of the MRC framework to inform this process is not adequately described throughout each part of the Method section. The description of the development of the intervention and plans for testing the components are insufficient. For example, do nurses delivering the intervention receive training, what is the evidence base for addressing concerns related to diabetes distress based on the proposed criteria in this study, etc.?*

    Re: Thanks again for constructive and important comments. We have clarified the use of the MRC framework in the revised paper. When it comes to the description of the intervention in the methods section, we have revised and added text under the sub-headings "Trial intervention", "Control procedure" and the "Training of health care personnel" (p. 11-13) to meet the comments above. Moreover, addressing concerns related to diabetes distress, we have expanded the introduction section in the revised paper (p. 4-9).

14. *Some additional information on the chosen outcomes measures may be useful. For example, why add the Diabetes Distress Scale, rather than using the PAID scale as the primary outcome to assess change? Why is HbA1c or a behavioral measure of self-management not included?*

    Re: As described above (comment 6, reviewer 1), we have added text to clarify why PAID is our intervention instrument (p. 13 and 16). As described in the overarching aim of the DiaPROM trial (p. 5), HbA1c and the participants' perceived competence for self-management (measured by the Perceived Competence for Diabetes Scale) are included as secondary outcomes.

15. *In the feasibility study aims, on page 10, the authors refer to the evaluation of participants' perceived understanding. Is this perceived understanding of the PAID items?*

Re: We have added text under the subheading “Feasibility study” (p. 9) to clarify that we asked the participants about their understanding and relevance of all PROMs completed on the touchscreen computer. This includes both the items in PAID and the items in the outcome measures.

16. *Discussion: The authors might consider beginning this section with a summary of the proposed study before summarizing key factors and decisions. The authors might also elaborate on the value of utilizing the MRC framework, maybe eluding to its impact in existing research and value added so far as part of the present study.*

    Re: In accordance with the comment, we have added text in the beginning of the discussion section (p. 16). The strength of using the MRC framework is now mentioned in the discussion’s strengths and limitations section (p. 16-17).

VERSION 2 – REVIEW

REVIEWER	David T. Eton, Ph.D. Mayo Clinic, Rochester, MN USA
REVIEW RETURNED	09-Nov-2018

GENERAL COMMENTS	Nice revisions. Just a few comments remain that require address. INTRODUCTION: There is still not much of a conceptual basis for the intervention. How will talking about distress with the provider (identified through PROMs) lead to less distress? Potential answers may lie in the “empowerment theory” being referenced, but the mediating mechanisms of action remain un-articulated in the manuscript. For a pilot trial, it is critical to identify not only if the intervention works, but how it works as this will inform the design of the future (larger) clinical trial. At present, the intervention mechanism exists in a “black box.” OVERLAP OF INTERVENTION AND OUTCOME MEASURES: The issue regarding the use of the DDS as a principal outcome measure in this study is one of content overlap with the tool being employed in the intervention (the PAID). About one third of the items in the PAID also appear on the DDS. The intervention tool could prime patient responses to the outcome measure given the content overlap and/or lead to hypothesis guessing from participants. It is a threat to the validity of the study that needs to at least be recognized, if not addressed altogether. One way to address it is by using a completely different measure to assess outcome, for instance, a diabetes-specific quality of life measure (e.g., Diabetes-39, Diabetes Health Profile, Diabetes-specific Quality of Life Scale) or a measure of treatment/regimen-related impact (e.g., Treatment-Related Impact Measure-Diabetes, Survey of Treatment Burdens in Diabetes).

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

10. *INTRODUCTION: There is still not much of a conceptual basis for the intervention. How will talking about distress with the provider (identified through PROMs) lead to less distress? Potential answers may lie in the "empowerment theory" being referenced, but the mediating mechanisms of action remain un-articulated in the manuscript. For a pilot trial, it is critical to identify not only if the intervention works, but how it works as this will inform the design of the future (larger) clinical trial. At present, the intervention mechanism exists in a "black box."*

    Re: Thank you for this important comment. We have now included a new text in the introduction section as well as in the discussion section on the conceptual basis for the intervention. We have put emphasize on the discussions of PROMs with participants, and further elaborated the focus on empowerment theory as the basis for the communication between the providers and the patients.

11. *OVERLAP OF INTERVENTION AND OUTCOME MEASURES: The issue regarding the use of the DDS as a principal outcome measure in this study is one of content overlap with the tool being employed in the intervention (the PAID). About one third of the items in the PAID also appear on the DDS. The intervention tool could prime patient responses to the outcome measure given the content overlap and/or lead to hypothesis guessing from participants. It is a threat to the validity of the study that needs to at least be recognized, if not addressed altogether. One way to address it is by using a completely different measure to assess outcome, for instance, a diabetes-specific quality of life measure (e.g., Diabetes-39, Diabetes Health Profile, Diabetes-specific Quality of Life Scale) or a measure of treatment/regimen-related impact (e.g., Treatment-Related Impact Measure-Diabetes, Survey of Treatment Burdens in Diabetes).*

    Re: This is also an important comment to be addressed. In the discussion section of the revised manuscript, we have added text that further emphasize the overlap between PAID and DDS. We have also reflected on the inclusion of the WHO-5 wellbeing index (WHO-5) and the Perceived Competence for Diabetes Scale (PCCDS) as measures to make up for some of the overlap. We agree that using a completely different measure to assess outcome could have been an option, however such instruments might not map the actual intervention well enough. The primary aim of our study is to reduce diabetes distress.

VERSION 3 – REVIEW

REVIEWER	David Eton, PhD Mayo Clinic, Rochester MN USA
REVIEW RETURNED	29-Nov-2018

GENERAL COMMENTS	Revisions and responses are satisfactory.