PEER REVIEW HISTORY

This paper was submitted to a another journal from BMJ but declined for publication following peer review. The authors addressed the reviewers' comments and submitted the revised paper to BMJ Open. The paper was subsequently accepted for publication at BMJ Open.

(This paper received three reviews from its previous journal but only two reviewers agreed to published their review.)

ARTICLE DETAILS

TITLE (PROVISIONAL)	Utilizing the Extended Self-Regulatory Model to Characterize Diabetes Medication Adherence: A Cross-Sectional Study
AUTHORS	Shiyanbola, Olayinka O; Unni, Elizabeth; Huang, Yen-ming; Lanier, Cameron

VERSION 1 – REVIEW

REVIEWER	Navin Kumar Devaraj Department of family Medicine, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Serdang, Selangor, MALAYSIA.
REVIEW RETURNED	16-Apr-2018

GENERAL COMMENTS	An excellent research using a very difficult adherent theory (Extended Self-Regulatory Model).A research of this quality deserves to be published.Full salutations to the recommendations suggested to improve this research. I am happy that necessary approval have been obtained from the copyright owners of MMAS-8. I am happy to recommend this paper for publication. The authors have done their homework well.

REVIEWER	Nurainul Hana Shamsuddin Department of Family Medicine, Faculty of Medicine & Health Sciences, Universiti Putra Malaysia, Malaysia
REVIEW RETURNED	19-Apr-2018

GENERAL COMMENTS	1. The hypothesis did not include the 2nd objective. 2. The sample size determination & calculation were not described. 3. On page 14, it's interesting that the skeptical group has "less understanding of their illness" but their health literacy was contradicting and rated high. Part of the definition of health literacy is the capability of understanding the disease. Your team may want to look into the information sources the group subscribes to. Furthermore, this group has low self-efficacy, which previously has been associated with low health literacy. Why are the findings different in your study population? Perhaps a qualitative study in this particular group would give a better understanding. Overall, this study is academically interesting and significant, but whether it is practical in clinical practices to apply ie identifying the patient's cluster to tailor diabetic management. Despite their cluster, the mainstay of diabetic management is always individualized care.

	The reviewer provided a marked copy with additional comments. Please contact the publisher for full details.

REVIEWER	Anna Serlachius The University of Auckland, New Zealand
REVIEW RETURNED	26-Jun-2018

GENERAL COMMENTS	My main concern with this paper was the lack of a significant contribution to the literature. The paper was very similar to what they reported for asthma (Unni & Shiyanbola, 2015), and although I understand the need to examine different patient groups I did not see that this study found anything particularly novel. My other concerns had to do with the rationale behind using the four clusters, design issues, and the numerous typos and grammatical errors. I did not feel the rationale was strong enough, e.g. "However, the sparse studies on patients with diabetes has generated inconsistent results and does not indicate which factors mainly affect medication adherence" (pg 5). I don't think one can argue that the literature on adherence in diabetes is sparse. Even the literature looking at illness beliefs and diabetes could not be argued to be sparse. Although there are some mixed findings, I don't feel these were clearly identified in the introduction. I also struggled to see how clustering adherence behaviours of patients with T2D based on their medication beliefs and illness beliefs into four clusters would be beneficial for developing tailored interventions. Wouldn't the same goal be achieved by simply assessing medication beliefs/illness beliefs without the need for clustering into four groups? The rationale for this approach was too vague. I also thought the sample size was quite small for such an approach, compared to Horne and colleagues who had a sample of nearly 2000 patients. I also wonder whether growth curve modelling would have been a better approach to use to examine adherence trends/behaviours and beliefs in T2D. There were several sentences that were rather unclear. For example on page 3 in the strengths/limitations: "This study highlighted the importance of content and theory-driven components to enable replication of successful adherence interventions". I'm not sure how this cross-sectional study achieved this? Lastly, the paper needs to be proof-read as there were many typographical and grammatical errors as well as many long sentences which were hard to follow. Also I was confused by the sentence "No patients were involved in the study design...recruitment or implementation" (pg 10). How can you have recruitment with no patients? In summary I think the paper needs to be revised to emphasise the contribution to the literature and provide a better rationale for using the cluster analysis.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Navin Kumar Devaraj

Institution and Country: Department of family Medicine, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Serdang, Selangor, MALAYSIA.

Competing Interests: None declared

An excellent research using a very difficult adherent theory (Extended Self-Regulatory Model). A research of this quality deserves to be published. Full salutations to the recommendations suggested to improve this research. I am happy that necessary approval has been obtained from the copyright owners of MMAS-8. I am happy to recommend this paper for publication.

Thank you for your recommendation to have the paper published.

Reviewer: 2

Reviewer Name: Nurainul Hana Shamsuddin

Institution and Country: Department of Family Medicine, Faculty of Medicine & Health Sciences, Universiti Putra Malaysia, Malaysia Competing Interests: None declared

1. The hypothesis did not include the 2nd objective.

Thank you for your comment. We have included the hypothesis related to the 2nd objective.

2. The sample size determination & calculation were not described.

Thank you for your comment. We have addressed this issue and added more information in the data analysis section.

*Prior researchers suggested that the adequate sample size for cluster analysis should be at least 2^{m} cases, preferably 5*2^{m} cases, where m is the number of clustering variables. Since we used 3 variables for the clustering analysis, a minimal sample size to include no less than 8 cases, preferably more than 40 cases is sufficient to perform a cluster analysis. Additionally, based on an analysis of cluster studies, Dolnicar reports that the median sample size is 293. (http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.475.2288&rep=rep1&type=pdf)*

3. On page 14, it's interesting that the skeptical group has "less understanding of their illness" but their health literacy was contradicting and rated high. Part of the definition of health literacy is the capability of understanding the disease. Your team may want to look into the information sources the group subscribes to. Furthermore, this group has low self-efficacy, which previously has been associated with low health literacy. Why are the findings different in your study population? Perhaps a qualitative study in this particular group would give a better understanding.

We have reviewed our sentence that indicated that the skeptical group perceived that they did not understand their diabetes but their health literacy was somewhat higher. By further examining the mean illness coherence of the group, we see that the skeptical groups' understanding of their illness was higher (mean is 3.15) than the mean 'understanding of illness' of the entire group (2.75). We have modified our sentence to reflect that their understanding the illness was not low. Thank you for bringing this to our notice.

The reviewer is right that the group of 'skeptical' patients in our study had low self-efficacy, known in the literature to be associated with low health literacy. It is possible that though patients had the ability to understand and process health information, this ability enhanced their self-efficacy for other aspects of diabetes management, not for self-efficacy for medication use (specifically measured in our study). This low self-efficacy for medication use is also reflected in the study sample's perception that they also did not think their medications were necessary, had high concerns about their medicines, and had less perceptions of treatment control.

This shows that patients with high health literacy might have self-efficacy in specific areas of diabetes management. Providers need to pay attention to the fact that self-efficacy in managing areas of diabetes management, such as exercise, might not translate to self-efficacy in managing medicines.

We agree that a follow-up qualitative study to further explore the understanding of the clusters would be great. We will explore this possibility in the future.

Overall, this study is academically interesting and significant, but whether it is practical in clinical practices to apply i.e. identifying the patient's cluster to tailor diabetic management. Despite their cluster, the mainstay of diabetic management is always individualized care.

It might seem impractical in clinical practice to identify patient clusters and tailor medication adherence counseling and development of unique self-management interventions for patients with diabetes. However, clustering patients' adherence behavior based on their beliefs may provide a mechanism for providers to focus on the specific belief needs of the patients in the context of their psychosocial characteristics, a more tailored approach than the general 'size fits all' approach to addressing adherence. Clustering may be done in a single visit with the provider, included in a patient's records, and available to providers via electronic patient portals, similar to reviewing a patient's medical history.

By clustering patients prospectively before clinic visits or after patients' intake, the short time available to providers can be used more effectively for a tailored counseling approach. One possibility is for healthcare providers to explore patient attitudes and beliefs during consultations and use these responses to judge which cluster a patient corresponds to. Patient-centered techniques, such as those drawing on motivational interviewing principles developed for adherence counseling, can help providers ascertain the views, beliefs, and concerns a patient may have about diabetes and the medications used in treatment. A short validated questionnaire or online profiling tool that patients complete in advance of a consultation could also be developed, which automatically calculates which cluster a patient belongs to.

Reviewer: 3

Reviewer Name: Anna Serlachius

Institution and Country: The University of Auckland, New Zealand Competing Interests: None declared

My main concern with this paper was the lack of a significant contribution to the literature. The paper was very similar to what they reported for asthma (Unni & Shiyanbola, 2015), and although I understand the need to examine different patient groups I did not see that this study found anything particularly novel. My other concerns had to do with the rationale behind using the four clusters, design issues, and the numerous typos and grammatical errors.

Thank you for your comments.

The novelty of the paper has been further highlighted.

We have addressed the rationale for the clustering, the reviewer's advice to use a different data analysis approach, and the grammatical errors.

I did not feel the rationale was strong enough, e.g. "However, the sparse studies on patients with diabetes has generated inconsistent results and does not indicate which factors mainly affect medication adherence" (pg 5). I don't think one can argue that the literature on adherence in diabetes is sparse. Even the literature looking at illness beliefs and diabetes could not be argued to be sparse. Although there are some mixed findings, I don't feel these were clearly identified in the introduction.

This sentence has been deleted to avoid confusion.

I also struggled to see how clustering adherence behaviours of patients with T2D based on their medication beliefs and illness beliefs into four clusters would be beneficial for developing tailored interventions. Wouldn't the same goal be achieved by simply assessing medication beliefs/illness beliefs without the need for clustering into four groups? The rationale for this approach was too vague.

We do not think the same goal for possible development of tailored interventions would be similar to simply assessing beliefs. The next steps in simplifying the information received from assessing beliefs (i.e., clustering) is needed for better efficient clinic visits. Providers do not have time to go over patient surveys of medication and illness beliefs each time. An automatic calculation of a patient's cluster allows for the accessibility of a provider to this individualized information without poring over surveys during clinic visits.

We have added more details regarding this in the introduction section.

I also thought the sample size was quite small for such an approach, compared to Horne and colleagues who had a sample of nearly 2000 patients. I also wonder whether growth curve modelling would have been a better approach to use to examine adherence trends/behaviours and beliefs in T2D.

Thank you for your comment. We have addressed this issue and added more information in the data analysis section. Due to the nature of the study design, we collected data at one-time point in this cross-sectional study. It is inappropriate to use growth curve modeling to examine adherence trends/behaviors and beliefs in T2DM for this type of study design.

Prior researchers suggested that the adequate sample size for cluster analysis should be at least 2^m cases, preferably $5*2^m$ cases, where m is the number of clustering variables. Since we used 3 variables for clustering analysis, a minimal sample size to include no less than 8 cases, preferably more than 40 cases is sufficient to perform a cluster analysis. Additionally, based on an analysis of cluster studies, Dolnicar reports that the median sample size is 293. (*http://citeseerx.ist.psu.edu/viewdoc/download?doi=10.1.1.475.2288&rep=rep1&type=pdf*)

There were several sentences that were rather unclear. For example on page 3 in the strengths/limitations: "This study highlighted the importance of content and theory-driven components to enable replication of successful adherence interventions". I'm not sure how this cross-sectional study achieved this?

We have corrected this sentence to not reflect that the study results are useful for the replication of adherence intervention.

Lastly, the paper needs to be proof-read as there were many typographical and grammatical errors as well as many long sentences which were hard to follow. Also I was confused by the sentence "No patients were involved in the study design...recruitment or implementation" (pg 10). How can you have recruitment with no patients?

We have proofread the paper for errors. We have corrected the confusing sentence to indicate that patients did not have direct involvement in developing the study design and research questions.

In summary I think the paper needs to be revised to emphasise the contribution to the literature and provide a better rationale for using the cluster analysis.

We agree with you. We have added more details to provide a better rationale for using the cluster analysis in T2D patients in the Introduction section.

VERSION 2 – REVIEW

REVIEWER	Nurainul Hana Shamsuddin Department of Family Medicine, Faculty of Medicine & Health Sciences Universiti Putra Malaysia Malaysia
REVIEW RETURNED	19-Aug-2018

GENERAL COMMENTS	The queries were addressed appropriately. However, this study is not generalisable to the population as it is not representative.