PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	An informed shared decision making programme for patients with type 2 diabetes in primary care: cluster randomised controlled trial
AUTHORS	Buhse, Susanne; Kuniss, Nadine; Liethmann, Kathrin; Müller, Ulrich; Lehmann, Thomas; Mühlhauser, Ingrid

VERSION 1 – REVIEW

REVIEWER	Andrea Siebenhofer Professor of Chronic Care and Health Services Research, Institute of General Practice, Goethe University Frankfurt, Germany, and Institute of General Practice and Evidence based Health Services Research at the Medical University of Graz, Austria.
REVIEW RETURNED	25-May-2018

GENERAL COMMENTS	This interesting study is based on the UK MRC framework for complex interventions (Craig 2008) and was carried out by an experienced study group. I appreciated the inclusion of the results of the process evaluation and all the materials which make this work reproducible, in line with the recommendations of evidence-based medicine (Hoffmann T, JAMA internal medicine. 2017;177(9):1243-1244; Lehman R. Sharing as the Future of Medicine. JAMA internal medicine. 2017;177(9):1237-1238.) The paper describes a single-blind, cluster-randomised controlled trial that evaluates an informed shared decision-making programme (ISDM-P) for people with type 2 diabetes mellitus in 22 general practices. However, although well written, the abstract does not clearly describe the content of the study and should be re-formulated. It seems to me to be important to discuss whether this study was underpowered and if so why? We recently published a paper in the J of Clin. Epidemiology in 2017 (https://www.ncbi.nlm.nih.gov/pubmed/29111470), which may which may help to critically appraise the results obtained in this study. Title: Please complete the title so it conforms with the protocol publication in BMC Fam. Practice 2015. Abstract: The mentioned objective is not the objective of the study, as two secondary endpoints are missing. Introduction: The research question described in the manuscript should be in line with the abstract and the protocol publication.... it is best to be consistent and to use the definition in the protocol. Methods:

	Outcome measure: I would suggest deleting the sentence on line 24 of page 10, as it repeats the second sentence on the page and is not clearly formulated. Results: Please check the numbers on line 47 of page 12 (they are not the same as in table 2), please check that the numbers on line 22 of page 13 are correct (compared to Suppl. 6) Please note that the results on informed choices with regard to smoking were not mentioned in the text (for completeness' sake, I would find it useful to see them here) Discussion Page 16, line 20: please provide references for the RCTs. Please discuss potential reasons for a non-significant difference in your chosen primary outcome. Figures and Tables: - Table 2: see title: what's the endpoint: adherence to antihypertensive or statin therapy, or adherence to antihypertensive and statin therapy? Check the information in the main section of the paper as well. In addition, please check the numbers are the same as in the text of the paper (page 12, line 47). Add more information to your legends (also in other tables): MI; OR... - See table 3, Suppl. 4 and the text in the result sections of the main text and abstract... maybe it could be presented in a more structured way. Minor point Please be aware of your choice of words. Your RCT was a proof of concept study. I therefore wouldn't call it pilot study throughout the paper.

REVIEWER	France Légaré Department of Family Medicine and Emergency Medicine, Faculty of Medicine, Laval University (Québec), Canada I lead the update of the Cochrane review on Interventions for increasing the use of shared decision making by healthcare professionals. we just published its 2nd update on july 19th 2018
REVIEW RETURNED	22-Jul-2018

GENERAL COMMENTS	Title and Abstract In the title, it has been clarified that this is a randomized cluster trial. The abstract is presented with the recommended structure. 1. Objective Objective as presented in the abstract is unconvincing. Why target primary care? The justification is not clear. The objective worded as "To Translate an informed joint decision making program (ISDM-P) for patients with type 2 diabetes from a specialized diabetes center to the primary care setting" does not correspond to what has been developed. In the main text, the authors refer to the implementation of the ISDM-P in primary care. The goal is presented in different ways that may not refer to the same concepts. Overall, the goal is not clearly defined. We suggest that it be reworded and presented in such a way that the same understanding emerges in the manuscript.

	2. Abstract All items required in the abstract are present. It is therefore complete. However, the conclusion needs to be reviewed: This sentence "Informed shared decision making is absent in standard care" does not seem to us to be a conclusion of this study. This is a reminder that in our opinion is rather obvious and therefore not a conclusion of this study. We suggest replacing it with the observed outcome of the trial. Using a PICO format would be useful P=participants; I=intervention; C: comparator; O=outcome. Since the adhesion between the intervention and control groups is not significantly different, the presentation of a global adhesion is a good idea. Some of the presented results and outcomes that appear in the abstract and are not to be found in the manuscript (eg agreement on priority 88.5% vs 57% comparing Patients and Doctors). Overall, the abstract is not complete. 3. Study design Seems appropriate to answer the research question. 4. Reproducibility of the study The method has been well detailed and reproducible if one refers to the protocol. 5. Ethics Committee The informed consent of the participants was obtained. An ethics committee validated the protocol of the study. 6. Have the issues been clearly Primary and secondary outcome measures have been clearly defined (see protocol). However, please note that there are no outcome or measurements of the presence of shared decision making; primary outcome is a patient outcome; it is not about shared decision making being assessed during the consultation; thus one may wonder if this trial was about implementing SDM; please specify the PICO question; reviewing the Cochrane review on Interventions to implement SDM may be useful 7. Appropriate and complete statistical analyzes Intention to treat was used. There was 3.9% missing data (less than 5%), and the processing of this missing data by imputation prevents potential selection bias. The use of generalized mixed models is ok and takes into account the cluster effect. Deviations from the protocol were noted. Overall, the analyzes were well described and deemed appropriate. 8. Updated references We have reviewed the list of references. They seem fine; the Cochrane review by Legare and all has been updated on july 19th 2018. 9. The results related to the research question or objective? The results are in agreement with some of the research questions. As we mentioned, the goal is to be reformulated to be better in line with the PICO; as there were no assessment of SDM during the consultation, this need to be kept in mind. Tables 2,3 and 4 present the main issues of the study. 10. Presentation of the results The Flow chart is presented. The baseline characteristics are presented according to the randomization groups; which allows to appreciate the quality of the randomization which seems adequate (ie the groups are well balanced). The other tables highlight the results on the issues studied. In total appropriate presentation of the results 11. Discussion and conclusions related to the results The discussion was well developed. The results of the issues are summarized. Nevertheless, the discussion of primary issues should

	be before that of secondary issues. Lastly, there was no primary outcome of SDM being assessed; this should be kept in mind. in other words, this trial is not about implementing SDM but rather to assess the impact of a multicomponent intervention on the stated primary outcome, a patient outcome. thus the discussion should take this into account. 12. Adequate discussion of the limits of the study The limits have been well developed. The data collected by structured telephone interview are subject to social desirability bias, smoking status and drug adherence. The external validity (generalizability) of the results is not clearly discussed. In total, the discussion of boundaries is broadly adequate. We suggest exploring the presence of social desirability bias. 13. CONSORT Checklist The mechanism of the allocation sequence for randomization does not appear to have been presented. The methods section was not clearly identified in the abstract. The generalizability of the results not presented. 14. Paper free from concerns over publication ethics To the best of our knowledge, we have no knowledge of plagiarism, or conflict of interest. 15. Languages - Quality of English English is fine.

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1

Reviewer Name: Andrea Siebenhofer

Institution and Country: Professor of Chronic Care and Health Services Research, Institute of General Practice, Goethe University Frankfurt, Germany, and Institute of General Practice and Evidence based Health Services Research at the Medical University of Graz, Austria.

Please state any competing interests or state ‘None declared’: None declared

This interesting study is based on the UK MRC framework for complex interventions (Craig 2008) and was carried out by an experienced study group. I appreciated the inclusion of the results of the process evaluation and all the materials which make this work reproducible, in line with the recommendations of evidence-based medicine (Hoffmann T, JAMA internal medicine. 2017;177(9):1243-1244; Lehman R. Sharing as the Future of Medicine. JAMA internal medicine. 2017;177(9):1237-1238.)

We thank the reviewer for appreciation of our study. Please find our point by point response below.

The paper describes a single-blind, cluster-randomised controlled trial that evaluates an informed shared decision-making programme (ISDM-P) for people with type 2 diabetes mellitus in 22 general practices. However, although well written, the abstract does not clearly describe the content of the study and should be re-formulated.

It seems to me to be important to discuss whether this study was underpowered and if so why? We recently published a paper in the J of Clin. Epidemiology in 2017 (https://www.ncbi.nlm.nih.gov/pubmed/29111470), which may which may help to critically appraise the results obtained in this study.

Power calculations were based on literature searches (see protocol) and estimations based on the former proof of concept study. We do not think that our study is underpowered. Rather, the lack of effect on the primary endpoint is due to the overall unexpectedly high adherence rates (about 90%)

among our study participants. Also, clinical parameters indicated that patients were truly adherent to their medication.

Title: Please complete the title so it conforms with the protocol publication in BMC Fam. Practice 2015.

We slightly modified the title in order to adjust it to the intervention that we actually evaluated in our study. The decision aid and the group teaching session not only provided information about heart attack prevention but also about other diabetes related complications. We added the following sentences to the section “deviation from the protocol” which is included in the supplement material:

The title of this publication slightly differs from the title of the protocol (“An informed shared decision making programme on the prevention of myocardial infarction for patients with type 2 diabetes in primary care: protocol of a cluster randomised, controlled trial”). Our intervention is about more than just prevention of myocardial infarction. It also includes information about other diabetes related complications. Therefore, the current and correct title is “An informed shared decision making programme for patients with type 2 diabetes in primary care: cluster randomised controlled trial”.

Abstract: The mentioned objective is not the objective of the study, as two secondary endpoints are missing.

The objective of our study was to translate an informed shared decision making programme (ISDM-P) for patients with type 2 diabetes from a specialized diabetes centre to the primary care setting. We assessed the same parameters as we did in the proof of concept study. BMJ Open sets a limit of 300 words for the abstract. That is why we chose to report the three main secondary endpoints which also include the other two endpoints, goal achievement and realistic expectations. Risk knowledge (score 0 to 11) comprises realistic expectations whereas informed choice includes goal achievement. We think, we thereby fulfil the CONSORT criteria for abstracts.

Introduction:

The research question described in the manuscript should be in line with the abstract and the protocol publication.... it is best to be consistent and to use the definition in the protocol.

We reworded the objective in the main text to make it more clear and consistent with the abstract and protocol.

Protocol:

“The ISDM programme has been evaluated in a randomised, controlled trial (RCT) [34] under high fidelity conditions in an outpatient setting at the Department for Endocrinology and Metabolic Diseases of the University Hospital Jena, Germany.
…
The aim of the planned cluster randomised, controlled trial is to evaluate the efficacy of the ISDM programme in the primary care context.”

Abstract:

“To translate an informed shared decision making programme (ISDM-P) for patients with type 2 diabetes from a specialized diabetes centre to the primary care setting.”

Main text:

“In the present study, we investigated whether the results of the proof of concept RCT[21] could be repeated under routine care conditions for patients with type 2 diabetes. The aim was to translate the optimised ISDM-P to the primary healthcare setting.”

In the manuscript, the objective is operationalized in the outcome measures section, which is in line with the protocol.

Methods:

Outcome measure: I would suggest deleting the sentence on line 24 of page 10, as it repeats the second sentence on the page and is not clearly formulated.

The two sentences describe different aspects. The second sentence reports our hypothesis regarding SDM and the primary endpoint:

"Our hypothesis was that patients would be more adherent when they defined personal treatment goals."

In order to make it more clear, we added the following phrase on page 10:

Our hypothesis was that patients would be more adherent when they defined personal treatment goals *together with their healthcare professionals*.

The sentence on line 24 of page 10 is supposed to explain the operationalisation of patient adherence: "Patients were considered to have been adherent if their answers were consistent with the prescription documented in the patients' record."

Results:

Please check the numbers on line 47 of page 12 (they are not the same as in table 2),

The numbers are not the same because not all of the patients with prescriptions could be reached by telephone to answer the questions regarding medication intake. That is why we had a few more data on prescriptions rates than on self-reported medication intake (for antihypertensive agents, 10 patients were not reached and for statins, 4 patients could not be contacted). Table 2 additionally shows data using the method of multiple imputation which considers missing values.

please check that the numbers on line 22 of page 13 are correct (compared to Suppl. 6)

The numbers are correct. Within the text, we reported the adjusted difference.

Please note that the results on informed choices with regard to smoking were not mentioned in the text (for completeness' sake, I would find it useful to see them here)

We added the following sentences on page 13:

There were less than 20% smokers in both groups. We found no difference in informed choices regarding smoking cessation.

Discussion

Page 16, line 20: please provide references for the RCTs.

We changed the sentence as followed: *The proof of concept RCT*[21] showed that patients with standard care lack the necessary risk knowledge.

Please discuss potential reasons for a non-significant difference in your chosen primary outcome.

The reason for a non-significant difference in our primary endpoint is an overall unexpectedly high adherence rate. We explained this aspect on page 17:

However, in the present cluster RCT, adherence to antihypertensive medication and statins was very high already under standard care. No changes from baseline to follow up were observed for prescription rates or clinical parameters (such as levels of HbA1c, blood pressure and cholesterol). Thus, it is very likely that adherence was already high at baseline.

Figures and Tables:

- Table 2: see title: what's the endpoint: adherence to antihypertensive or statin therapy, or adherence to antihypertensive and statin therapy?

We changed the title to "Adherence to antihypertensive *or* statin therapy", so that it is in line with the main text.

Check the information in the main section of the paper as well. In addition, please check the numbers are the same as in the text of the paper (page 12, line 47).

Please see the first point of the results part within this point-by-point response.

Add more information to yourlegends (also in other tables): MI; OR...

- See table 3, Suppl. 4 and the text in the result sections of the main text and abstract... maybe it could be presented in a more structured way.

We added more explanations to the tables.

Minor point

Please be aware of your choice of words. Your RCT was a proof of concept study. I therefore wouldn't call it pilot study throughout the paper.

You are right. Thank you! We followed your advice.

Reviewer: 2

Reviewer Name: France Légaré

Institution and Country: Department of Family Medicine and Emergency Medicine, Faculty of Medicine, Laval University (Québec), Canada

Please state any competing interests or state ‘None declared’: I lead the update of the Cochrane review on Interventions for increasing the use of shared decision making by healthcare professionals. we just published its 2nd update on july 19th 2018.

We thank the reviewer for appreciation of our study. Please find our point by point response below:

Title and Abstract

In the title, it has been clarified that this is a randomized cluster trial. The abstract is presented with the recommended structure.

1. Objective

Objective as presented in the abstract is unconvincing. Why target primary care? The justification is not clear.

In Germany, care for patients with type 2 diabetes is usually provided by family physicians at the primary health care level, whereas persons with type 1 diabetes are referred to specialized diabetes centres. Diabetes care for persons with type 2 diabetes is based on the German Disease Management Programme (DMP) for type 2 diabetes. Most patients are inscribed in the DMP. They participate in patient education programmes which aim at enhancing self-management. Patients’ clinical parameters are assessed every six months. Documentation of the data by the general practitioners and quality assurance are prerequisite and the basis for physician reimbursement. Therefore, the transfer of our intervention to the primary care setting is very relevant. We explained the structure of diabetes care in Germany in more detail in the published study protocol.

We added the following sentence to the main text (contextand setting); page 8:
In Germany, care for patients with type 2 diabetes is usually provided by family physicians at the primary health care level.

The objective worded as "To Translate an informed joint decision making program (ISDM-P) for patients with type 2 diabetes from a specialized diabetes center to the primary care setting" does not correspond to what has been developed. In the main text, the authors refer to the implementation of the ISDM-P in primary care.

The goal is presented in different ways that may not refer to the same concepts.

Overall, the goal is not clearly defined. We suggest that it be reworded and presented in such a way that the same understanding emerges in the manuscript.

We did not implement the ISDM-P at a national level, rather, we developed a strategy to transfer the programme to the primary health care setting. We evaluated the effectiveness of the ISDM-P as implemented in the practices of family physicians. Additionally, we focussed on facilitators that may foster the implementation of the ISDM-P in routine care.

We reworded the objective in the main text to make it more clear and consistent with the abstract and protocol.

Page 7: “In the present study, we investigated whether the results of the proof of concept RCT[21] could be repeated under routine care conditions for patients with type 2 diabetes. The aim was to translate the optimised ISDM-P to the primary healthcare setting.”

Moreover, we changed some sentences in the methods section of the manuscript:

Page 12: Process *evaluation*

“Barriers and facilitators of *implementing the ISDM-P in routine care* were identified using the documentation from the MAs for the teaching sessions as well as interviews with MAs and GPs of each ISDM P practice.”

2. Abstract

All items required in the abstract are present. It is therefore complete. However, the conclusion needs to be reviewed: This sentence "Informed shared decision making is absent in standard care" does not seem to us to be a conclusion of this study. This is a reminder that in our opinion is rather obvious and therefore not a conclusion of this study. We suggest replacing it with the observed outcome of the trial. Using a PICO format would be useful P=participants; I=intervention; C: comparator; O=outcome. Since the adhesion between the intervention and control groups is not significantly different, the presentation of a globaladhesion is a good idea.

The absence of informed shared decision making might be obvious, but we provided evidence for these claims. Our study demonstrated that patients in the control group did not make informed choices. In addition, to a large extent, they prioritized other treatment goals than their general practitioners. We think that these are relevant indicators for the lack of informed shared decision making.

Considering the primary endpoint in our conclusion, we rephrased the conclusion as follows:

The ISDM-P was successfully implemented in general practices. Adherence to medication was very high making improvements hardly detectable.

Some of the presented results and outcomes that appear in the abstract and are not to be found in the manuscript (eg agreement on priority 88.5% vs 57% comparing Patients and Doctors).

The results regarding the matching of treatment goals between GPs and patients are shown in table 4 and summarized on page 14.

Overall, the abstract is not complete.

We assume, you mean “complete” because you stated before that the abstract is complete.

3. Study design

Seems appropriate to answer the research question.

4. Reproducibility of the study

The method has been well detailed and reproducible if one refers to the protocol.

5. Ethics Committee

The informed consent of the participants was obtained. An ethics committee validated the protocol of the study.

Thank you.

6. Have the issues been clearly

Primary and secondary outcome measures have been clearly defined (see protocol). However, please note that there are no outcome or measurements of the presence of shared decision making; primary outcome is a patient outcome; it is not about shared decision making being assessed during the consultation; thus one may wonder if this trial was about implementing SDM; please specify the PICO question; reviewing the Cochrane review on Interventions to implement SDM may be useful

We had intensive discussions about our primary endpoint and how to assess informed shared decision making. There is no gold standard to quantify patient involvement. SDM is a multidimensional construct. Assessing only patients' or physicians' perceived involvement is not sufficient and does not provide valid information. Objectively rated consultations often lead to different results. Observer-based evaluation of videotaping of teaching sessions and consultation would be a more valid assessment method of SDM but this is not feasible under routine care conditions within implementation studies.

We agree with France Légaré that we at least tried to use a patient outcome of informed shared decision making. It was our explicit intention to use a patient relevant endpoint for SDM. We consider the achievement of any treatment goal prioritized by the individual patient as a patient relevant endpoint. However, we found it most difficult to reliably assess this endpoint under routine care conditions. In our proof-of-concept study [1], patients in the control group mostly prioritized HbA1c goals, which were already low at baseline. Knowledge is a prerequisite for informed decisions and for setting rational and realistic treatment goals. The proof-of-concept study showed that patients of the control group had no adequate knowledge to make informed choices. We assessed knowledge as a secondary endpoint and as an indirect indicator for the transferability of our ISDM-P.
Our hypothesis was that patients would be more adherent to medication when this is prescribed based on informed shared decision making. That is the reason why adherence became the primary endpoint. Our derivation of the outcome measure is comprehensively described in the study protocol. In addition, we used the patient-held sheet for the documentation of treatment goals as an indicator for SDM. Patients who are involved in informed decision making are more likely to agree on treatment goals and strategies with their physicians than control patients. The patient-held documentation sheet ensures that patients and physicians pursue common treatment goals and therefore could be used as an indicator of SDM quality.

7. Appropriate and complete statistical analyzes

Intention to treat was used. There was 3.9% missing data (less than 5%), and the processing of this missing data by imputation prevents potential selection bias. The use of generalized mixed models is ok and takes into account the cluster effect. Deviations from the protocol were noted.

Overall, the analyzes were well described and deemed appropriate.

8. Updated references

We have reviewed the list of references. They seem fine; the Cochrane review by Legare and all has been updated on july 19th 2018.

Thank you, we updated the reference.

9. The results related to the research question or objective?

The results are in agreement with some of the research questions. As we mentioned, the goal is to be reformulated to be better in line with the PICO; as there were no assessment of SDM during the consultation, this need to be kept in mind. Tables 2,3 and 4 present the main issues of the study.

We refer to our explanations above.

10. Presentation of the results

The Flow chart is presented. The baseline characteristics are presented according to the randomization groups; which allows to appreciate the quality of the randomization which seems adequate (ie the groups are well balanced). The other tables highlight the results on the issues studied.

In total appropriate presentation of the results

Thank you.

11. Discussion and conclusions related to the results

The discussion was well developed. The results of the issues are summarized. Nevertheless, the discussion of primary issues should be before that of secondary issues. Lastly, there was no primary outcome of SDM being assessed; this should be kept in mind. in other words, this trial is not about implementing SDM but rather to assess the impact of a multicomponent intervention on the stated primary outcome, a patient outcome. thus the discussion should take this into account.

We added an explanation (according to point 6) to the discussion part of the manuscript; page 17:

The proof of concept RCT indicated lower adherence rates to statin prescriptions in the standard care group. Adherence is a patient relevant endpoint that may reflect successful ISDM when it is based on adequate knowledge and mutual agreement on treatment goals between patients and health professionals. We hypothesised that patients would be more adherent to medication when prescriptions were based on SDM principles.

We discussed the derivation of the primary endpoint on pages 16f.

12. Adequate discussion of the limits of the study

The limits have been well developed. The data collected by structured telephone interview are subject to social desirability bias, smoking status and drug adherence. The external validity (generalizability) of the results is not clearly discussed.

We added the following sentences on page 17:

Generalizability of our results to other health care systems remains speculative. Our study participants had unexpectedly high adherence rates to prescribed medications and overall good control of diabetes and hypertension. This might be a result of diabetes care within the disease management programme for patients with type 2 diabetes in Germany. In populations with lower adherence rates, the ISDM¬ P could presumably improve adherence to medication.

In total, the discussion of boundaries is broadly adequate. We suggest exploring the presence of social desirability bias.

We added the following sentences on page 17:

Patients' self-reported adherence to medication uptake was used to assess the primary endpoint. Telephone interviews were conducted independently from practices, but socially desirable answers cannot be completely ruled out. The interviewer asked patients to read out the substance that was labelled on the medication boxes. To do that, patients had to have the medication box at home.

13. CONSORT Checklist

The mechanism of the allocation sequence for randomization does not appear to have been presented. The methods section was not clearly identified in the abstract. The generalizability of the results not presented.

We added the Method used to generate the random allocation sequence on page 11:

"Concealed randomisation was performed in blocks of four practices *using a computer generated allocation sequence*, after patient recruitment and collection of baseline data, by the Centre for Clinical Studies at the Jena University Hospital."

We followed requirements of BMJ open for abstracts. It includes the relevant information on methods according to CONSORT.

We refer to point 12 for generalizability.

14. Paper free from concerns over publication ethics

To the best of our knowledge, we have no knowledge of plagiarism, or conflict of interest.

15. Languages - Quality of English

English is fine.

Thank you.

VERSION 2 – REVIEW

REVIEWER	Andrea Siebenhofer Professor of Chronic Care and Health Services Research, Institute of General Practice, Goethe University Frankfurt, Germany, and Institute of General Practice and Evidence based Health Services Research at the Medical University of Graz, Austria.
REVIEW RETURNED	08-Oct-2018

GENERAL COMMENTS	A nice revision and thank you for your valuable responses.