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

TITLE (PROVISIONAL)	How GPs value guidelines applied to patients with multimorbidity – a qualitative study
AUTHORS	Luijks, Hilde; Lucassen, Peter; van Weel, Chris; Loeffen, Maartje; Lagro-Janssen, Antoine; Schermer, Tjard;

VERSION 1 - REVIEW

REVIEWER	Eirik Abildsnes University of Bergen Norway
REVIEW RETURNED	31-Mar-2015

GENERAL COMMENTS	This paper targets an interesting topic. A more detailed background description, a link to relevant theory, and a major revision of the discussion section is needed prior to publication. The reviewer also provided a marked copy with detailed comments. Please contact the publisher for full information about it.

REVIEWER	Carol Sinnott Research Fellow Dept of General Practice University College Cork Ireland
REVIEW RETURNED	03-Jun-2015

GENERAL COMMENTS	I have attached comments for the authors and the editor in two documents attached. The reviewer also provided a marked copy with detailed comments. Please contact the publisher for full information about it.

VERSION 1 – AUTHOR RESPONSE

Comments Reviewer 1

bmjopen-2015-007905
The topic of this paper is highly relevant. I have read the paper with interest, and have some suggestions to develop the paper furter.

C: Introduction
The introduction is very brief, and may be further developed. I miss information about the guidelines

the authors refer to. Are these national guidelines? (Some indication is given in the quotations). How many clinical guidelines are dutch GPs expected to follow? Did GPs take part in establishing the guidelines? I miss a link to relevant theory.

R: When discussing 'guidelines', participants in our focus groups indeed generally referred to the DCGP guidelines. We have inserted a text, before the final paragraph of the Introduction, to stress GPs' leading role in de development and critical appraisal of these guidelines.

C: Multimorbidity is usually not a stable situation, and GPs work with multimorbidity represents series of complex interventions. Theoretical input based on complexity theory is suggested.

R: We added a section on this in the Introduction (first paragraph) and in the Discussion (Subheading Comparison with existing literature, next to last paragraph).

C: I also suggest to have a look at the "silo" methaphor introduced by
Parekh et al: http://www.ncbi.nlm.nih.gov/pubmed/20371790 .

R: We added this reference (second paragraph of the Introduction).

C: The participants mention guideline- derived incentives. In the introduction I miss a statment concering the use of these incentives.

R: Thank you for reminding us – clarification is appropriate. We added some background information on the use of incentives in Dutch primary care. This was added before the final paragraph of the Introduction.

C: Objectives in manuscript:
Explore and describe the value GPs attribute to medical guidelines….and to describe which benefits GPs experience from guideline…
Also we aimed to identify limitations from guideline adherence in patients with multimorbidity,….

Abstract:
To explore how GPs value guidelines when applied to patients with multimorbidity, and which benefits and barriers they experience from adherence to guidelines in these patients.

The objectives given in the abstract and the manuscript are not the same. As a rule of thumb: Aims are what you want to achieve, objectives are what you will do to achieve them.

R: We have modified the text in the abstract to clarify the point raised by the Reviewer, by making sure the text in abstract and introduction are identical to specify the aims of the study. (In this revised version, we changed 'Objectives' in 'Aims' in the abstract.)
However, after submitting the revised manuscript, it was returned to us by the editorial office of BMJ Open. Some issues needed to be addressed by us before it could be assigned to the Editor. These issues included: 'Please remove the entire 'Aim' and re-construct your abstract (max. 300 words) including the following headings (…): Objectives: clear statement of main study aim and major hypothesis/research question.'
We modified the abstract once again and strived to meet both BMJ Open's authors instructions and the Reviewers point at the same time.

C: Method
I don't like the idea of referring to a previous published study (reference 16) instead of describing the methods used in sufficient detail. It should be possible to read the present paper separately. The

origin of the idea of the present study is well described. The reason for choosing focus groups to gain information, and choice of method in analysis, is not given. However, focus groups and constant comparative analysis is absolutely
relevant. In the previous published paper based on the same focus groups, the method description is much more detailed. You need to know the analysis method in some detail to understand the concepts used in the method description. I suppose most readers of BMJ Open are not familiar with the concepts axial and selective coding. A medical student transcribed the interviews. This should be mentioned. Did the researcher know some of the informants in advance? The location, and the setting of the interviews are not explained. How many participants in each focus group? Did the participants know each other? Did the authors use the observer's field notes in analysis?

R: We agree with this Reviewer and the other Reviewer that providing more detail regarding the methods applied in this study would be appropriate. In the revised version, we added information throughout the Methods section. We would like to mention that, in addition, some methodological choices are discussed in the Strengths and limitations paragraph of the Discussion section.

C: Results
I would prefer to present the participants in the method section.

R: We moved this paragraph to the Methods section.

C: The quotations are good illustrations of the results presentation. The results represent answers I would expect, and no surprises. I would have expected more information about how the GPs cooperated with hospitals and home-based care.

R: We can agree with the Reviewer, but in the focus group meetings the relation with specialists, hospitals, and home-based care appeared not to be a major topic in the discussions regarding GPs' evaluation of guidelines, the subject of interest of the current study - which makes it difficult to present. We have added this as a surprise finding in the discussion, where we also refer to our previous paper, where GPs had been describing views on cooperation with specialists.
Our previous paper, describing GPs' considerations and main objectives in multimorbidity management, included indeed some quotations representing GPs' views on cooperation with specialists, for example to illustrate their perceived importance of applying an integrated approach in the care for patients with multimorbidity.

C: Discussion
I believe that GPs in most countries struggle with complying with guidelines, and even if the study is focusing on national guidelines, the external validity of the major findings is beyond what the authors state when they describe the limitations of the study.

R: We agree with the Reviewer's comment that our findings may have more implications for healthcare professionals in other countries than what was stated in our initial version of the manuscript. We adapted this part of the Discussion section (second paragraph, subheading Strengths and limitations).

C: The authors state that to the best of their knowledge, no previous papers specifically explored guidelines' value for patients with multimorbidity as experienced by practitioners who use them in clinical practice. I believe the authors are wrong. A starting point may be professor of primary care Guthrie et al :
http://www.bmj.com/content/345/bmj.e6341 and the references listed in this article. A
number of efforts to target the complexity of multimorbidity in primary care:
http://www.bmj.com/content/345/bmj.e6341 . I will also mention several works of

Barbara Starfield, the focus on the chronic care model by WHO:
http://www.who.int/chp/knowledge/publications/icccreport/en/ and NICE guidelines
on clinical assessment and management of multimorbidity:
http://www.nice.org.uk/guidance/gid-cgwave0704/documents/multimorbidity-scopeconsultation

R: We are aware of the literature suggested by the Reviewer. Indeed extensive literature on multimorbidity and on chronic disease management exists. In their report, the WHO recommends actions to be taken in healthcare systems globally to improve the management of chronic diseases. NICE is preparing a guideline on the clinical assessment and management of multimorbidity, with anticipated publication in September 2016. On the NICE website, the scope of this anticipated guideline is presented. We added this reference in the second paragraph of the Introduction. Moreover, many papers in peer-reviewed journals describe multimorbidity and associated complexity. The 'Analysis' paper published in BMJ by professor Guthrie and colleagues raises attention for the limited applicability of clinical guidelines for patients with multimorbidity, and presents suggestions for improvement in this respect. However, it does not present results of original research, but it contains the ideas of experts in the field of multimorbidity. In fact this paper was already cited in our manuscript (ref. 14 in our initial submission). We still believe that doctors' experiences with, and values attributed to the use of (single disease) guidelines, applied to patients with multimorbidity, have not been studied and described thoroughly in the available literature – since we were unable to locate original research papers with this type of exploration as their main focus. We therefore believe that our current paper presents an important contribution to the empirical evidence in this field.

Comments Reviewer 2

Dear Authors/ BMJ Open,

Thank you for the opportunity to review this interesting paper on the value GPs place on guidelines in the management of patients with multimorbidity, and the benefits and barriers they experience from adherence to guidelines in these patients.

This paper uses data from focus groups which were conducted for a different purpose: to explore the broader issue of GPs' considerations and main objectives in the management of multimorbidity. The original study was published in the BJGP in July 2012, and made a substantial contribution to the literature on multimorbidity in primary care. I am familiar with the original study having included it in a qualitative synthesis on GPs' perspectives on the management of patients with multimorbidity. While the current study focuses on an area of importance in the field of multimorbidity, I think the manuscript could strengthened - many of my comments relate to the overlap between the findings of the two studies (BJGP and current).

C1. Introduction, page 4 line 42: the authors reference the qualitative synthesis here stating that included papers "focused merely on the challenges" experienced by GPs. While the synthesis did not look at empirical knowledge, many of the included papers did, so this reference is not entirely accurate.

R: We deliberately cited the qualitative synthesis by Sinnott and colleagues instead of referring to multiple original studies included in this meta-etnography, since we believed that if an overarching message can be drawn from a review paper this makes multiple citings to the original papers unnecessary (and reduces readability). However, we acknowledge that in the original phrase, confusion might be raised on the intended meaning. We rewrote this sentence and feel that it now better expresses what our current study adds to the existing literature.

C2. Methods, page 5 lines 3-31: the authors discuss the rationale for the original paper, and their subsequent awareness that the role of guidelines merited “deeper exploration on itself”. This is a good example of the iterative nature of qualitative research and shows that the team were in tune with emerging findings. However, they also discuss that that the topic guide was not altered to account for this deeper exploration. The original study achieved data saturation after five focus groups. I think it is important to establish how the authors were assured that data saturation was reached regarding the aim of this current study given this scenario. It is also important that they substantiate further that the “deeper exploration” of the issue of guidelines was possible within the predetermined structure/topic guide of the original study.

R: Please also see our response to comment 4. We attached a copy of the interview guide (English translation) for your information, and we will make this available for readers upon request.
As described in the methods, the idea of analysing the data for the current, separate research question, in addition to the original research question, arose during the iterative process of participant sampling, data collection, and analysis. We sought for data saturation not only regarding the initial research question but also regarding the current research question. After having conducted four focus groups, in all of which at least one GP with an academic affiliation (GP trainer or researcher) participated, we decided to organise a fifth focus group with only non-academic GPs, since we anticipated that an academic affiliation might influence their ideas regarding both research questions. Presence of data saturation was determined after close reading and re-reading of the transcripts, and evaluated both towards the research question of the current study and towards our previous research question (previous paper). Saturation was reached after having conducted five focus groups, a number not uncommon in focus group methodology for arriving at it.
We agree with the Reviewer that additional information regarding this issue improves the quality of the manuscript. It has been adapted accordingly throughout the Methods section.

C3. Methods, page 5, lines 32- 44: The authors reference the original study methods in lieu of providing this detail here. While I appreciate that this may be to limit the use of unnecessary words/prevent duplication, I think it is also important that the reader should be able to easily discern how GPs were contacted, what practices were contacted and why these were chosen, how many practices were contacted, and what incentives were provided to participants.

R: Please also see our response to the comments of the other Reviewer. We added these details in the Methods section (subheading Study design and participants). We did not meticulously track the number of practices that were contacted. Of the practices approached, approximately 70% agreed to participate. From some practices more than one GP was included in the study, but focus groups were composed to avoid that GPs from the same practice attended the same sessions.

C4. Methods, page 5, lines 50-56: There is little information given on the topic guide. The authors mention in the preceding section that there was one question on the role of guidelines. It would be useful to know what this question was to help determine what role the interview itself had on the expression of views.

R: Please also see our response to comment 2. The moderator used the interview guide as an aid to address all items of interest concerning the research questions, which fitted the explorative nature of this research. The order of questions and formulation could be adapted to fit the ‘natural flow’ of the group discussions.

C5. The focus of the original paper differs from the current one. What were participants told about the aims/ goal of the study? If they had been told that the study was to examine the value associated with guidelines, would the findings have been different? While it is not possible for the research team to change this now, I think it is important to address this issue within the text.

R: The goal of this study was presented similarly to all participants, so that they all had similar starting points for the focus group discussions. Fitting the explorative nature of this study, its aim was not formulated very narrowly and explained to the participants as 'gaining insight into GPs experiences with the care for patients with multimorbidity' (added in the Methods section, subheading Study design and participants). Right before the start of the focus groups, the moderator once again explained the goal of the study. It was the task of the moderator to guide discussions in such a way that all topics of interest for both research questions were discussed in sufficient detail.
In our revised manuscript, we added this point to the Discussion section (subheading Strengths and limitations).

C6. Results, page6, lines 28-32: The authors present the characteristics of participants in a table which is useful and easy to read. The original paper discussed that a high percentage of participants had an academic affiliation (page 28/33, line 28)- I think it is important that this is addressed within the results or discussion sections of the current paper, in particular how the academic nature of participating GPs may have influenced their familiarity with/ views on the use of guidelines in patients with multimorbidity. Were any of the other GP characteristics/ contexts reported associated with particular themes or findings?

R: Please also see our response to comment 2. We thank the Reviewer for reminding us of the importance of elaborating on this issue.
Most of the topics discussed in the Results section had equal contributions from GPs with and GPs without an academic involvement subheadings 'Value of guidelines applied to patients with multimorbidity', 'Limited usefulness of guideline adherence in multimorbidity' and 'Guideline adherence conflicts with a patient centred approach'). The discussions on the topics 'Concerns about the applicability of guidelines for multimorbidity' and 'Empirical solutions' however had more input provided by GPs with an academic affiliation. These GPs more frequently brought up discussions on these themes. GPs without an academic affiliation did not show to have opposing views: they accepted these beliefs and approved them in general. We commented upon this in the Discussion section. We did not find other GP characteristics that were associated with specific themes, for example no clear differences between GPs from different sexes, ages, or with different practice types.

C7. Results, page 7, line 5- 7: I think the line "…guidelines provided guidance to medical decision-making, for example prescription of medication" needs to be expanded on, as the same could be said for guidelines in any context.

R: We slightly changed the formulation of this sentence so that it better covers the statement we would like to make. It is true that this statement could be made in another context, but that is why it is important to evaluate it not on itself but in relation to the entire paragraph. It discusses in which particular cases with multimorbidity the GPs found the guidelines useful. This phrase relates to patients with multimorbidity 'who are relatively young and healthy', and especially if several diseases of the same patient require a similar approach (concordant comorbidity).

C8. Results, page 7, lines 9-11: "reduction of patients' perceived symptoms… was an important reason for GPs to adhere to guidelines" – was there any evidence in your transcripts that the guidelines helped GPs achieve this aim? If so, or if not, it would be useful and interesting to provide this information.

R: Yes, the transcripts do contain data demonstrating that GPs were supported by guideline recommendations for providing symptom relief to patients with multimorbidity. Because some of these fragments were not very concise, and therefore not the best ones to include in the manuscript as quotations, we gave very short examples of them between brackets ('pain, shortness of breath'). This

was derived from discussions where GPs articulated that for symptomatic diseases such as COPD or arthritis, guidelines were perceived as very useful, and were more closely adhered to than guidelines for non-symptomatic diseases, or than guidelines for risk factors. We feel that, in addition to these short examples between brackets, the selected corresponding citations (C and D, which were much shorter) do also illustrate this point. Since it is not always possible to find a suitable quote, the researchers / authors also need to summarise some points discussed. However, if the Reviewer or the Editor feels that these citations are insufficient, we are willing to search the transcript once again for the best additional quotation.

C9. Results, page 7, line15 and line29: the authors discuss the difficulties that GPs experience implementing guidelines in multimorbidity. Is there any empirical data within the transcripts to say what these difficulties actually are? For example, is there data on the actual conflicts that arose for the GPs or are the descriptions limited to generic discussion of the difficulties? If available, more detailed accounts of the difficulties experienced would be a substantial addition to this section.

R: Yes, the transcripts do contain concrete conflicts experienced by GPs. However, this paragraph details on the positive evaluation of guidelines. Limitations are described after this paragraph. The following discussion from the transcript gives an example of what type of problems GPs experience when they try to translate guidelines to patients with multimorbidity. It is a discussion that preceded the quoted text in citation E, which corresponds to this part of the results. Please note that this quotation has been translated by ourselves and not by our translator:

But the point is, we don't have enough knowledge, I think, about weighing. You see, all these indicators have been sorted out, for, for single problems, right? And much less in coherence. So when the renal function deteriorates, what is most important then, you know? Would that be the type of diuretic you give, or is [blood] pressure more important, ehh, or the glycaemic regulation of the diabetes? How should you weigh things against each other? What is supposed to get the most emphasis? I think we just don't have a clue, right? So we all just give it a go, I suppose. (GP 14, male, 63 years)
Moderator: Do you think the guidelines tell us too little about this?
Ehh, yes that's what I think, well, of course, the cardiovascular guideline has indeed tried to, to connect the risk factors for cardiovascular disease, right? With those risk tables. (GP 11: nods) Ehh, what has to be stressed, is not really illustrated yet. So someone, who has a risk of 12 per cent for a [cardiovascular] event, should you prioritise cholesterol, or [blood] pressure, or quit smoking? Ehh, that has not been defined. (GP 14)
-turns are interrupted-
Well I think, it can be questioned, whether it should be explained… (GP 13, male, 45 years)
I'm not sure if this is supposed to… (GP 14)
…exactly what the guidelines… (GP 13)
I don't know either… (GP 14)
Sometimes that should be left to the doctor's judgement. (GP 13)
Yes, but if you don't emphasise the importance or the statistics, then it's easy to stay in limbo… (GP 15) (continued in the manuscript)

In the manuscript, we added a sentence to make the original statement more concrete (final sentence, subheading Value of guidelines applied to patients with multimorbidity).

C10. Results, page 7, lines 48: when the authors say "limited therapeutic or preventative options" , I wonder if they mean limited therapeutic or preventative benefits??

R: This is a correct observation. Thank you. It has been changed.

C11. Results, page 8, line 13: " some GPs expressed this explicitly while many agreed with such comments" – is this a case that a few GPs dominated the focus groups? Looking through the quotes, GP 7 and GP 24 seem to dominate!

R: We can state with confidence that there was no domination of a few GPs in any focus group. Group sizes were small enough for all GPs to express their beliefs, and the experienced moderator ensured that all were provided sufficient opportunity to do so. Some GPs have been quoted more frequently than others indeed. This however does not represent possible domination in the group discussions but that some were more 'fluent' than others, i.e. that they formulated their ideas concisely / to the point, which made them 'quotable'.
The statement that some expressed this explicitly while many others agreed could have been made in different locations too. We felt it is important to show to readers that we were receptive both for explicitly and implicitly expressed beliefs.
Please also see our response to comment 8. The citations included there are from GP 7 and GP 24 and were selected because of their conciseness.

C12. Results, page 8, line 49-58: the section on GPs empirical solutions is novel, interesting and flows well.

R: Thank you.

C13. Discussion, page 10, line 15: " Recommendations from single disease guidelines are not generalizable to patients with multimorbidity" – is this an overstatement?

R: We intended to say that recommendations from single disease guidelines cannot be downright transferred to patients with multimorbidity. The formulation has been slightly changed.

C14. "when GPs apply guidelines in multimorbidity, they incorporate patients' specific circumstances." – do you think this is specific to multimorbidity? Perhaps, this could be elaborated on?

R: Applying patients' personal circumstances in clinical decisions around guideline recommended care is not specific to multimorbidity. GPs will often do this, based on their personal relation with their patients and continuity of care. In handling multimorbidity, GPs rely on the core values of primary care. From our findings we conclude that 'multimorbidity' is a good illustration of the use of core values of primary care. We added this observation in the manuscript (Discussion, subheading Summary).
Please note that the Results section (subheading 'Guideline adherence conflicts with a patient-centred approach') and the accompanying quotations give more details on this issue.

C15. Discussion, page 11, line 21: I think there is some other important literature that was not discussed here – for example a study by Schuling et al, BMC Fam Pract 2012 also discussed the role of guidelines in multimorbidity, especially with respect to preventative medicines, and the GPs sense of compulsion to "prescribe by present guidelines". Fried et al specifically examine the varying barriers, benefits and approaches to guideline use in multimorbidity in their study in the Arch Intern Med. 2011. I think it would be useful for the authors to situate their findings with respect to these two studies.

R: We agree that these references are appropriate in the Discussion of our paper. They have been added.

C16. Page 12, line 3: the authors state that they "specifically explored guidelines value for patients with multimorbidity". While this is true, in that their analysis was specifically orientated to this aim, the

data collection and focus groups were not specifically orientated to it.

R: We agree that a slight change in the formulation of this phrase would be more accurate. This has been adapted.

C17. Page 13, line 33: “consistent adherence to guidelines is undesirable in the care for patients with multimorbidity” - is this an overstatement??

R: This formulation has been adapted.

C18. Abstract: If the main manuscript is revised in line with the above, the abstract will need revisions accordingly.

R: The largest revisions took place in the methods section. We feel that adding many details to the abstract reduces its readability. We made some small changes in the abstract in the revised version and in the ‘Article summary’ section while at the same time we still meet the word limit that was set for the abstract by BMJ Open.

VERSION 2 - REVIEW

REVIEWER	Eirik Abildsnes University of Bergen, Norway
REVIEW RETURNED	03-Aug-2015

GENERAL COMMENTS	Thank you for letting me read the revised manuscript. I believe that the authors have responded to the suggestions made by the reviewers in a way that has improved the quality of the manuscript. I only have one single remark about a possible difference in the statements in the discussion section and the abstract: Discussion: GPs in countries with a healthcare system comparable to that in the Netherlands may experience similar problems from guideline application to patients with multimorbidity, and their practical answers to such puzzles might show similarities to the empirical solutions described in the current study. Abstract: Focus group discussions were held in the context of Dutch healthcare, not allowing generalisations to the primary care context in general, but the resemblance of the GP sample to the Dutch professional GP group does increase transferability of our findings.

REVIEWER	Carol Sinnott Dept of GP, University College Cork Ireland
REVIEW RETURNED	03-Aug-2015

GENERAL COMMENTS	The greater detail now provided in the methods and results section has substantially improved the quality of this manuscript. Thank you.

VERSION 2 – AUTHOR RESPONSE

In response to the final comment of Reviewer 1, we added a sentence to the Article summary section so that it better matches the Discussion.

We would like to remind the Reviewer that this passage falls outwith the abstract. BMJ Open's instruction to authors for the 'Article summary box' is as follows: 'Article summary section consisting of the heading: 'Strengths and limitations of this study', and containing up to five short bullet points, no longer than one sentence each, that relate specifically to the methods of the study reported. They should not include the results of the study and should be placed after the abstract.'