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)	Development of a meta-algorithm for guiding primary care encounters for patients with multimorbidity using evidence-based and case-based guideline development methodology
AUTHORS	Muche-Borowski, Cathleen; Lühmann, Dagmar; Schäfer, Ingmar; Mundt, Rebekka; Wagner, Hans-Otto; Scherer, Martin

VERSION 1 - REVIEW

REVIEWER	Harm van Marwijk University of Manchester, UK
REVIEW RETURNED	22-Jan-2017

GENERAL COMMENTS	Hi, I have written my comments but then the text disappeared, very unsatisfactory! I had to write this again!! The aim of their study was to develop an overarching algorithm to structure primary care encounters of patients with multimorbidity. I was not entirely sure what they meant by this. What decisions does it support? What structure? GPs seldom use any structure, in my mind. The patient comes in and asks for a Zimmer frame and then what? They used a novel case-based and evidence-ased procedure to overcome methodological difficulties in guideline development for patients with complex care needs. The paper describes the development and does not present data of the testing of the tool in practice. They used systematic guideline development methodology including systematic evidence retrieval (guideline synopses), expert judgment and informal and formal consensus procedures. How does the tool link to existing tools such as ICPC? I do not like the concept of multimorbidity so much for general practice, patients never bring it in as the reason for their encounter. The resulting meta-algorithm may reflect the logic of a GP encounter of a patient with multimorbidity making explicit decision situations, communication needs and priorities. It is difficult to assess the reality of such claims. It can be filled with the complex problems of individual patients and hereby offer guidance to the practitioner. Nice, but does it work in the short space of time that GPs have? Is it a learning system? Contrary to simple, symptom-oriented algorithms the meta-algorithm seems to illustrate a superordinate process which permanently keeps the entire patient in view. Are GPs comfortable with that? How does that work exactly? This could work and is certainly innovative. I have worked with similar tools in practice (NHG.doc) and they did not work, however. The key thing is user involvement, not so much experts but usual GPs. The paper mostly focuses on itself it seems and seems to miss other tools such as the electronic Frailty Index

	(Clegg, 2016). More reflection on the literature could strengthen it.

REVIEWER	Susan Smith RCSI, Ireland
REVIEW RETURNED	03-Feb-2017

GENERAL COMMENTS	Thanks you for asking me to review this interesting paper that presents a novel approach to the difficult task of developing clinical guidance for patients with multimorbidity in primary care settings. It presents a substantial piece of work and makes a very valuable and important contribution to the literature on multmorbidity. As a result of the scope of the project, some of the elements of the study have not been reported clearly. I would recommend the following essential minor revisions: • It is a limitation that the Guideline group and the expert GP panel were relatively small and I think this should be acknowledged. I also think that the numbers involved at each stage should be included in Fig 1 which outlines the steps taken • It is a strength that the authors conducted both a synthesis of the quantitative and qualitative literature on patient perspectives on multimorbidity but these two pieces of work are not described clearly in the methods. I think the methods for each should be reported separately and then also the approach taken to synthesise them. The search strategy for the systematic review should be included as an appendix, as well as the usual flow chart of results etc • The authors state that the search only used the term multmorbidity – this would be a serious limitation given that it is not an actual mesh term but depends on what repositories were searched as there are some very comprehensive multmorbidity repositories such as the IRCMO in Canada • The same applies to the results of this part of the paper. Perhaps the authors are planning a separate publication outlining the qualitative study with patients but that should be stated explicitly and this paper should still outline the themes that arose and contributed to the development of the meta-algorithm. Likewise – the results of the mixed methods systematic review itself are not clear – how were the patient surveys and qualitative studies combined – would be usual to have a Table of included studies here – again perhaps as an appendix • The authors understandably used German Clinical Guidelines to build their algorithm and mentioned that they excluded some base don being out of date but no further information provided – an appendix could provide this. Were there guidelines for every scenario • Only one example is given of the n=1 guideline based on a case vignette. Presumably there are 9 others – these could be included as an appendix to illustrate how the meta-algorithm was developed. • The example case vignette chosen seemed like a very unusual clinical presentation- it implies the patient had become completely mute which I have never seen in that age group in 25 years of general practice apart from psychiatric inpatients with catatonic depression. I wonder is this a translation issue • The general text and particularly the text in the tables would benefit from being copy edited by a native English speaker • The discussion would benefit from more consideration of how the proposed algorithm compares to the existing literature – the AGS guideline is referenced but no real comparison. There was also an evidence based Clinical Review published in the BMJ that could be

	considered • The discussion should also consider the generalizability of the algorithm to systems outside Germany – the focus is on the GP-patient encounter but other literature in this areas stresses the value for the patient in engaging with other primary care team professional such as physio, OTs, psychologists etc • It is not clear why just one RCT is highlighted for comparison in the discussion though it is an important one. There is a systematic review of interventions that is referenced (but not the updated version, published last year in the Cochrane library) but not discussed. The Cochrane review also mentions other important studies such as the CarePlus study • Comment in the discussion on how the guidance could be evaluated from a research perspective would be useful, given that this is a research publication

VERSION 1 – AUTHOR RESPONSE

Reviewer: Harm van Marwijk
Institution and Country: University of Manchester, UK

Quote from paper: “The aim of their study was to develop an overarching algorithm to structure primary care encounters of patients with multimorbidity.”
I was not entirely sure what they meant by this.
What decisions does it support? What structure?
GPs seldom use any structure, in my mind.
The patient comes in and asks for a Zimmer frame and then what?
Abstract modified – “for” instead of “to structure”
Clarified in “Objective” – p. 6

They - quote from paper “used a novel case-based and evidence-based procedure to overcome methodological difficulties in guideline development for patients with complex care needs”.
The paper describes the development and does not present data of the testing of the tool in practice.
Yes - explanation added to conclusions in abstract (see also comments by the editors).
Conclusions in the full-text already contains a similar statement. (p. 17)

They - quote from paper: “... used systematic guideline development methodology including systematic evidence retrieval (guideline synopses), expert judgment and informal and formal consensus procedures.”
How does the tool link to existing tools such as ICPC?
Added in discussion, p. 17

I do not like the concept of multimorbidity so much for general practice, patients never bring it in as the reason for their encounter.
In our article multimorbidity is not the reason for encounter – the article refers to multimorbid patients presenting with a
specific reason for encounter.
Since this is pointed out in the algorithm we did not add any further explanation to the text.

Quote from paper: “The resulting meta-algorithm may reflect the logic of a GP encounter of a patient with multimorbidity making explicit decision situations, communication needs and priorities.”
It is difficult to assess the reality of such claims.
Quote from paper: “It can be filled with the complex problems of individual patients and hereby offer guidance to the practitioner.j”

Nice, but does it work in the short space of time that GPs have? Is it a learning system?
The next phase will be implementing and evaluation of the usefulness (acceptance and practicability) of the
meta-algorithm in general practice.
Explanation added p. 17

Quote from paper: “Contrary to simple, symptom-oriented algorithms the meta-algorithm seems to illustrate a superordinate process which permanently keeps the entire patient in view.”
Are GPs comfortable with that? How does that work exactly? This could work and is certainly innovative.
I have worked with similar tools in practice (NHG.doc) and they did not work, however. The key thing is user involvement, not so much experts but usual GPs.
GPs participated in the process of the development of the algorithm (s. fig. 1). These were experts but also “normal” GPs
without affiliation to university. To avoid misunderstanding renamed the “GP expert panel” into “GP panel”.

The paper mostly focuses on itself it seems and seems to miss other tools such as the electronic Frailty Index (Clegg, 2016). More reflection on the literature could strengthen it.
We have the impression that the reviewer thinks our meta-algorithm is some form of electronic tool. This is not the case – it is a graphical display of possible management pathways that may be sensible to apply in a
primary care encounter of patients with multimorbidity. Therefore we did not reflect the literature reporting on electronic
tools.

Reviewer: Susan Smith
Institution and Country: RCSI, Ireland

It is a limitation that the Guideline group and the expert GP panel were relatively small and I think this should be acknowledged. I also think that the numbers involved at each stage should be included in Fig 1 which outlines the steps taken
Size of the guideline group is set by the German College of General Practice and Family Medicine. Size of the GP panel
commented in discussion (p. 15),
Fig. 1 modified according to suggestions by the reviewer.

It is a strength that the authors conducted both a synthesis of the quantitative and qualitative literature on patient perspectives on multimorbidity but these two pieces of work are not described clearly in the methods. I think the methods for each should be reported separately and then also the approach taken to synthesise them. The search strategy for the systematic review should be included as an appendix, as well as the usual flow chart of results etc.
The analysis of qualitative and quantitative studies of health care preferences of patients with multimorbidity was
conducted in one review, not in two distinct approaches. The work was part of a dissertation project which will be
published separately. An explanatory sentence was added to the methods part (p. 9). Furthermore a web appendix was
added containing the main methodological steps and results.

Web appendix 2: Search strategy, flow chart, in-/exclusion criteria, [see also comment to results

section: table of included
studies, approach to synthesis: categories of patients' preferences deducted from the literature] added.

The authors state that the search only used the term multmorbidity – this would be a serious limitation given that it is not an actual mesh term but depends on what repositories were searched as there are some very comprehensive multmorbidity repositories such as the IRCMO in Canada
Search strategy presented in web appendix – multimorbidity was not the only search term. It was the search concept –
clarified on p. 15
Since our search covered the main two medical databases and we had no intention to include unpublished work or grey
literature we did not search any repositories or databases for grey literature.

The same applies to the results of this part of the paper. Perhaps the authors are planning a separate publication outlining the qualitative study with patients but that should be stated explicitly and this paper should still outline the themes that arose and contributed to the development of the meta-algorithm. Likewise – the results of the mixed methods systematic review itself are not clear – how were the patient surveys and qualitative studies combined – would be usual to have a Table of included studies here – again perhaps as an appendix
The fact, that a separate publication of patient's perspective is planned, was added to the methods section.
Categories outlined in the results part (p. 12)

Main results of the qualitative interviews were presented as a poster at the GIN-conference in 2015. Reference was
added to the text.

Web appendix 2: [See also comment to methods section: Search strategy, flow chart, in-/exclusion criteria,] table of
included studies, approach to synthesis: categories of patients' preferences deducted from the literature.

The authors understandably used German Clinical Guidelines to build their algorithm and mentioned that they excluded some based on being out of date but no further information provided – an appendix could provide this. Were there guidelines for every scenario
Inclusion criteria for guidelines specified (p.8). List of included guidelines added to web appendix 1.

Only one example is given of the n=1 guideline based on a case vignette. Presumably there are 9 others – these could be included as an appendix to illustrate how the meta-algorithm was developed.
Added to web appendix 3

The example case vignette chosen seemed like a very unusual clinical presentation- it implies the patient had become completely mute which I have never seen in that age group in 25 years of general practice apart from psychiatric inpatients with catatonic depression. I wonder is this a translation issue
It is indeed a translation issue – we mean he ceased to talk, fell silent.

The general text and particularly the text in the tables would benefit from being copy edited by a native English speaker
Text was checked by a native English speaker.

The discussion would benefit from more consideration of how the proposed algorithm compares to the

existing literature – the AGS guideline is referenced but no real comparison. There was also an evidence based Clinical Review published in the BMJ that could be considered
We added a discussion of the latest Cochrane Review (Smith et. al. 2016) to the discussion. (p. 16)

The discussion should also consider the generalizability of the algorithm to systems outside Germany – the focus is on the GP-patient encounter but other literature in this areas stresses the value for the patient in engaging with other primary care team professional such as physio, OTs, psychologists etc
The meta-algorithm itself is not limited to the use in the German context. Explanatory sentence added to discussion (p.
15)

The cooperation with other professions is addressed in the guideline but not in the meta-algorithm since this refers to
structuring the encounter with the primary care physician. No modification of the text.

It is not clear why just one RCT is highlighted for comparison in the discussion though it is an important one. There is a systematic review of interventions that is referenced (but not the updated version, published last year in the Cochrane library) but not discussed. The Cochrane review also mentions other important studies such as the CarePlus study
We added the discussion of the Cochrane Review (p.16)
Our intention was to refer to studies, using approaches similar to the meta-algorithm. That was the reason, that the 3D
study was cited here.

We thank the reviewer for referring to the CarePlus study – that approach indeed has some similarities to the
meta-algorithm. We included it in the discussion

Comment in the discussion on how the guidance could be evaluated from a research perspective would be useful, given that this is a research publication
Explanation added p. 18

VERSION 2 – REVIEW

REVIEWER	Harm van Marwijk University of Manchester. UK
REVIEW RETURNED	15-Mar-2017

GENERAL COMMENTS	Reasonably good rebuttal letter and interesting project, although it seems so complex I am not sure it will ever work. I did not think it was simple to make sense of their paper but I am happy to give them the benefit of the doubt.

REVIEWER	Susan Smith RCSI, Ireland
REVIEW RETURNED	16-Mar-2017

GENERAL COMMENTS	Thank you for addressing my comments. One last very minor edit needed - the English in the title Needs to be corrected: should be 'Development of a meta-algorithm etc' or 'Developing a meta-algorithm etc'

VERSION 2 – AUTHOR RESPONSE

Reviewer Name: Susan Smith
the English in the title Needs to be corrected: should be 'Development of a meta-algorithm etc' or 'Developing a meta-algorithm etc'
corrected: Development of a meta-algorithm

VERSION 3 – REVIEW

REVIEWER	Susan Smith RCSI Ireland
REVIEW RETURNED	21-Mar-2017

GENERAL COMMENTS	Thank you for correcting the title