Author’s response to reviews

Title: On the edges of medicine – a qualitative study on the function of complementary, alternative, and non-specific therapies in handling therapeutically indeterminate situations

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Author’s response to reviews:

Responses to the comments by editor and to peer reviewers

Editor Comments:
Thank you for the opportunity to consider your interesting paper. I have read this carefully with interest, as have 3 experts in the area. All the reviewers see considerable merit in the paper. I agree that the concept of 'therapeutically indeterminate consultations' extends our thinking around Medically Unexplained Symptoms and that the study has potential to make a novel contribution to this literature. However the reviewers agree that there is scope for a much more developed analysis that is more interpretive and considered. I would therefore like to invite a revised version of the manuscript that addresses the reviewers comments in particular relating to the analysis. In addition please provide more detailed methods relating to the analytical approach taken and steps taken to increase the trustworthiness of the analysis including background and positioning of the research team.

A general response to the editor and the peer reviewers

We sincerely thank the peer reviewers for their detailed, highly constructive, basically positive, but quite critical feedback! As requested, we now report our methods in much more detail. But as you will see, we made fundamental changes in the other sections which make the revision almost a new manuscript. When writing the original manuscript, we deliberately aimed to put the focus on the concept of therapeutically indeterminate situations. Although this construct indeed was an important part of the starting position of our study, it was probably not a good idea to develop
the original submission around it, as it resulted in an upside down representation. We fear that
the limited experience in qualitative research of three of us (KL, AO and AS) was the reason for
this, and we apologize. In our revised manuscript, we try to put the right side up again. The
revised version reflects much better the original analysis made for the first authors’ yet
unpublished thesis. While quotations and an important part of the wording did not change that
much, the overall changes are so fundamental that we do not submit a track change version.

In the revised background section, we describe our starting position in detail, and how we arrived
at this position. Based on previous, mostly quantitative studies on the use of CAM and non-
specific or placebo interventions lead by the senior author (KL), literature on prescribing, and
sociological work we primarily asked why (German) GPs use these strategies, and how GPs not
using these approaches manage the routine work. Indeterminateness was an important
background construct for allowing a joint view on a variety of phenomena.

Due to this change of perspective and based on your critical comments, the results section was
re-structured. We tried to find a better balance between description and interpretation, yet we
must admit that this remained a challenge for us (given the limited qualitative research
experience of three of us).

After frustrating attempts to revise the original discussion, this part was almost completely re-
written. We systematically tried to interpret our findings in relation to existing literature. We
hope that you will not be disappointed that also in the revised submission the discussion of the
MUS literature is relatively limited. While there are important relations with some of the MUS
literature, our perspective is quite different. We hope that the revision makes this
comprehensible.

Due to the added details in background and methods, our revised manuscript is considerably
longer than the original submission. Some shortening would be possible by moving parts of the
methods section into an appendix.

Below we try to respond to the single comments. However, due to the fundamental changes in
the revised version we often refer to this general response.

Reviewer reports:

Gareth Drake (Reviewer 1):

I found this to be an interesting and clinically pertinent paper, especially given current pushes to
reduce anti-biotic use, and the high prevalence of MUS consultations. It appeared that having an
extra set of interventions called CAM increased the options for GPs who still felt able to 'give
something’ to patients so that they weren’t left ‘empty handed’. This is really interesting and rich and maybe a good counterpoint to the more harmful use of pharmaco-active placebos like antibiotics. Also, interesting questions are raised that could be thought about further. Why is it so hard to leave patients empty handed? How could GPs be supported to move a step further, from the CAM that they know isn’t pharmacologically active to a more purely relational approach? But perhaps this is beyond the aims of the paper.

Response: Indeed our study raises more questions than answers. A number of these questions are not even discussed. We hope that our more humble and focused revised discussion is not too disappointing in this respect.

It might seem below that many of the comments are on readability and grammar. I hoped this wouldn’t take over, but I found the paper wasn’t very clearly written in certain sections. Overall it was possible to follow, but there are substantial difficulties with some passages that got in the way of being able to grasp in a coherent manner some of the very rich results that the authors drew from the data. Given that resonance with the reader, coherence, and a clear narrative are aspects of quality assurance in qualitative work (Elliot, 1999) a close look for readability and grammar would be advisable. It does make a big difference when something reads well. Though I selected 'Needs some language corrections before being published', I do think some of these need to be substantial - though 'Not suitable for publication unless extensively edited' was perhaps too harsh.

Response: We hope that our revised version is more easy to follow. As with the original submission, a native speaker with ample experience in science editing checked our revised manuscript (a few changes to the manuscript were made after the language check).

Background

Clear rationale given for the study, though slightly unexpected introduction of CAM at the end, although I see complementary therapies are mentioned higher up on line 29, though only in brackets - could the CAM acronym be used at line 29 to integrate it more in the narrative of the background? The second aim on page 3, makes clear the rationale for studying CAM, but only with the final three words on line 58, 'in this respect'. Perhaps another sentence in the background, making clear that CAM use by GPs is being studied by the authors as a way to further explore the broader finding that GPs prescribe non indicated drugs, placebos etc. The authors could have investigated all non-essential prescribing, and seem to end up doing that, but the focus on CAM is due to its use in Germany - I suppose I am suggesting just a small elaboration, justifying further the focus on CAM and linking it more explicitly to the general pattern of defensive prescribing mentioned earlier in the background.
Response: please see our general response above.

Some small grammatical suggestions:

Page 3 line 20/21, is 'correct' the appropriate word here - optimal maybe? Doesn't seem to be clear from current research what 'the correct' solution is. Gives an impression that the field is clearer than it is.

Response: “correct” substituted by “optimal”

Page 3 line 47 'One study investigated on…', doesn't need the word 'on'.

Response: Phrase no longer part of the introduction.

Methods

Page 4 - 'problem orientated interviews' - could a reference or further explanation be given?

Response: We apologize for a bad translation of a term used in German social science studies (problemzentriertes Interview – probably better problem centered interview; Witzel https://uk.sagepub.com/en-gb/eur/the-problem-centred-interview/book234106). As this term is rarely used in non-German studies, we skipped it. In the data collection section, we now describe the interviews in more details.

Data collection: Could interview schedule be included in supplementary material?

Response: Done

Recruitment

It was unclear why 'skeptics' 'pragmatists' and 'convinced CAM users' became a key dividing criteria in recruitment. I wasn't sure how much value this added, particularly when only 1 GP was deemed sceptical. It also felt quite jarring - it reads as if initially the focus was on exploring therapeutically indeterminate situations, with CAM being introduced as an interesting tool used by some GPs especially in Germany to manage indeterminacy. But by the recruitment section of
the article CAM seemed to have reified into the focus. Could a general nod to purposive sample be given: 'Given the prevalence of CAM in Germany, at the recruitment phase, attempts were made using purposive sampling to ensure a representative range of attitudes to CAM were gained'?? The criteria (skeptic, pragmatist, convinced…) also didn't seem to capture the richness with which CAM was used by GPs - often with clinicians approaching it as a relational tool rather than with belief in efficiency beyond placebo effect.

Response: We tried to describe the rational of our sampling strategy better now. Together with the changes in the introduction, we hope this clarifies our approach.

I wondered could the whole issue of 'Range in attitude in GP toward use of CAMs' be shifted to the results as an introductory theme? It did seem to be very rich as it arose in the results sections but the 3 dividing categories didn't really capture that.

Response: Following your recommendation, we added a new paragraph to the results.

Analysis: Could a reference be used to show how analysis was informed by grounded theory or thematic analysis literature?

Might it be helpful to include a note on quality assurance? E.g. Elliot 1999 Results Page 6, Line 53, 'general key issue' just key issue? - This sentence is difficult to follow e.g. 'was to what extent'. Next line 'sceptical' not 'sceptic'?

Response: We added two references (including the German book by Strübing which was our main reference). Our revised methods description should also make clear why we wrote “inspired by grounded theory”.

Reading on, the whole paragraph that begins with 'A key general issue…' is unclear and seems slightly crow-barred in. The opening of the theme on page 5, and the quotation above are rich and coherent and interesting. And then the section immediately afterwards starting with 'While the details of the accounts of our participants differed…' is again coherent and clear. Is it the attempt to link CAM use from the sampling criteria that doesn't seem to fit here?

Response: this part has been re-structured (see our general response above)
Line 58, at bottom of the page. Sentence beginning 'However, due to the deceptive element…' - wasn't clear whether the authors are saying that GPs did or didn't use these placebos, or that GPs didn't want to talk about it?

Response: This was rephrased (“However, pure placebos were used only rarely by a minority of participants. The main reason for rejecting or avoiding placebo use was the discomfort about actively deceiving patients.”)

Page 8

This seems to be one of the few times that explicit reference is made to the initial sampling division (into skeptic, pragmatist, etc…). 'Our most cam-sceptic participant characterised…' If the dividing criteria were ditched it could just read ' A GP sceptical in the use of CAM commented….'

Response: Throughout the results section, the approach to the classification is now reported in a different (and hopefully better) way.

Page 9, line 1, 'However, some participants…'- difficult sentence to follow Page 9 line 24, "Under the category, 'non-specific treatment'" - italics or quotation marks or comma to delineate it as theme….later in same sentence not clear what 'patient in front' means.

Response: Significant changes have been made throughout the paragraph.

Page 10

The quote on line 28 that begins 'Does the subject of the placebo play a role….' Is very interesting. The complex and intuitive way that the GP uses CAM is not clear from the recruitment information. This GP knows the therapy is a placebo but incorporates it relationally. This openness seems indicative of a relational flexibility in the face of indeterminate situations rather than a belief in homeopathy - again this is not clear from the recruitment information. Maybe I am being slow on the update but I thought 'convinced CAM user' meant you were recruiting people who believed in the pharmacological properties of homeopathy - but then there didn't seem to be any evidence of this in the results. Similar example on page 11.

Response: The section was revised.
Discussion

Page 12, line 32, delete 'older'?

Response: whole discussion re-written (see general response above)

Page 13, paragraph on line 6, starting 'the concept of therapeutically indeterminate….' This whole paragraph is unclear and difficult to follow.

Response: the paragraph was deleted.

Line 45 - 'Morphologically', I think this is the first time this is used, could it be explained. The sentence that begins, 'The spectrum of strategies described morphologically…' seems like a summary, could it be moved to start of discussion?

Response: the paragraph was deleted.

Page 14, line 1, 'Communication without giving a treatment is a different strategy…' - different to what? I assume it's to points 1 and 2 but this is not clear.

Response: the paragraph was deleted.

Rhetorical question on line 9. The answer 'lack of empathy and lack of time' is both unfair on GPs and not comprehensive. The authors go on to talk about human warmth and true interest in a slightly anecdotal manner but a manner that does approach the problems of a medical model. However, there is a huge literature on burn-out rates in front-line clinicians, the function of distancing from emotional involvement, the lack of supportive or emotional resources for clinicians, systemic separating of clinician from patient in a biomedical model, that could be included. The paragraph concludes by saying some GPs can come up with creative solutions - but it seems, from the results, that the GPs who used CAMS were doing so humanely and warmly within the context of a good relationship. Or is that the point the authors are making also? Not quite clear what the thrust of this paragraph is.

Response: We agree that our simplified and short discussion of this complex problem was insufficient. The paragraph was deleted (the subject is no longer discussed in this respect).
Limitations - sampling choice and representativeness might be a weakness?

Response: xxx

Conclusions - not clear what 'Reflecting therapeutic indeterminateness..' is/looks like?

Response: conclusions re-written

Peter Salmon (Reviewer 2):

The methods are described realistically, albeit briefly. It is hard to describe qualitative methods convincingly, and I would not want the authors to resort to listing 'techniques' that would not bring the process to life for the reader. However, they could say a little more. For instance, I wondered how they recognized when analysis was proceeding in a useful direction, i.e. how they judged its quality. Were they aiming at a purely descriptive account, or something more interpretative and inductive?

Response: the methods are now described in much more detail (see our general response above).

In practice, the Results suggest the analysis remained rather descriptive, structured under 'a priori' headings. However, it seemed to me that there were potentially exciting ideas bursting out of the constraint of the descriptive account. Taking the main sections of the Results in order:

Response: thank you for your critical, thoughtful comments. They were a major reason for re-structuring our results section completely. We hope that the flow of thoughts is now more clear, the link to citations more developed, the naming of themes more instructive, and the reporting (at least somewhat) less descriptive.

1. The heading 'perception of indeterminateness…' does nothing to evoke the tensions that this section indicates between valuing conventional medicine but also apparently valuing the ambiguity and indeterminacy of much general practice. One GP, at least, indicates, with some emotion, a personal transition here. Then the part of this section that addresses the potentially exciting issue of what GPs feel 'responsible for at the edges of medicine' falls rather flat in a confusing (to my mind) account of the heterogeneity between GPs. There is also phrasing here that confuses the writing: 'seemed almost specialised on patients, 'patient selection process', 'live up with the complaints'. Finally, the statement in text that GPs felt
they 'should have an answer to each medical problem' seems to me to contradict the
subsequent quote, which implies that the GP recognizes the folly of THINKING that one has
to have an answer. In sum, I left that section intrigued but confused by the tensions that GPs
were describing and the heterogeneity in endpoints of resolving them.

Response: the whole section was changed and split into two themes.

2. Communication, again, is an uninformative and unevocative heading. I think the authors are
getting at reassurance and empathy in this section.

Response: theme re-named (“The therapeutic encounter instead of a medical treatment”)

3. 'Stretching' the indication for symptomatic treatment is itself an interesting title - the word
'stretch' indicates some tension and discomfort. But the text does not do justice to this, merely
acknowledging that the one GP quoted thought he might prescribe diclofenac too much.
That's a serious thing for a GP to be thinking, and warrants more exploration. There is again
language here that is confusing: 'issue until which point', 'extension of the indication'.

Response: we changed the section and we point now to the fact that the material is somewhat
weak and indirect here. In the revised discussion we now refer in more detail to the “prescribing”
literature which gives some support to our interpretation.

4. In non-specific treatment I did not see that the first illustration of acquiescing to patient
pressure for antibiotics belonged here at all. The subsequent account of non-specific
treatments is potentially very interesting, but again I wanted to see more exploration. For
instance, GP06 refers to the 'ritual' surrounding homeopathy - how does s/he internalize this
within his/her practice given that s/he doesn't want to use the term placebo, but sees this as a
placebo?

Response: We understand your comment problem because unnecessary antibiotics are a very
specific case. However, they are the most prominent example of an impure placebo/a non-
specific intervention in the whole (placebo) literature. Also in the accounts of our participants
this was a major issue. We hope that the flow of thought in the revised revision makes it easier to
follow our interpretation.

5. Going on to the CAM section, it seemed that the 'non-specific' section was for treatments
seen as placebos, whereas the same treatments could appear in this section if the GPs using
them believed in them. So, again, there are more questions raised than answered here. Why do some GPs see these CAMs as genuine treatments, while others just see them as placebos? What are the implications of these different views for GPs' attempts to manage the tensions they describe in this area?

Response: For the revision, we split the CAM theme into sub-themes, and we address the problem of individual perspectives (regarding what is functionally specific and what not) both in the background and discussion section. We hope this clarifies this important issue.

In Discussion I was looking for the authors to show how their findings added to the literature, but they say little about this. Much of the discussion could, I think, have been written before this study was done. More engagement with the data, clarifying, and perhaps going beyond, the rather descriptive findings would give the authors much more to write about in Discussion.

Response: we hope the new discussion is better.

Christopher Burton, MD (Reviewer 3):

Overall this is an interesting approach to a topic which has been considered from some angles previously (e.g. Dowrick & Salmon on normalisation; various groups on antibiotic prescribing) but which probably could do with a generalisable framework for understanding / teaching. At the moment I don't think this paper is strong enough to outline such a framework (though maybe that is too ambitious) but I think it should at least show us one way forward and also look more carefully backwards at earlier work.

Response: we tried to make our manuscript less ambitious and more focused (see our general response above).

The introduction needs to be clearer about the exact scope of this work. It refers to situations where treatment is "not medically necessary or evidence based treatment not available". This needs to be unpacked more fully and I think this could be done before embarking on the analysis rather than depending on it. As part of re-thinking the starting point I think the authors need to be familiar with the work on normalisation etc (e.g. Dowrick / Salmon) and be explicit about how the current study relates to that. Some of what is included here might well be covered by normalisation.
The introduction (and a surprisingly prominent section of the results) relates to diagnostically (rather than therapeutically) indeterminate situations. It highlights that some of the indeterminacy is at the knowledge of what something is rather than just what to do about it. A willingness to accept conceptual or diagnostic indeterminacy is implicit in the way some GPs talk of "medically unexplained symptoms"; and doctors' failure to be able to explain disorders in this conceptual space is particularly relevant to what goes wrong in medical consultations (Johannsen & Risor).

Response: Thank you for these important comments. As described above, we intensively revised the introduction. Thank you for pointing us to two important papers in the area of MUS we were not aware of (particularly, the great Johannsen & Risor meta-synthesis)! We address these papers in the discussion now. Yet, as described in our general comment, we think that our perspective is quite different from the MUS literature. Therefore, we do not discuss it in greater detail. We hope this is acceptable.

Treatment in the context of this study does not seem to include self-management or even temporalisation (waiting for the body to recover itself), or where they do occur they are just seen as part of communication. We need to understand more about them.

Response: Indeed, we focused on treatments prescribed, applied or recommended by physicians. We shortly address temporalization and similar issues on page 12 (lower part).

The methods section reports how participants were thought of as supportive of / sceptical of CAM but we should also be informed of the researchers' positions. I would have liked to see whether participants' views influenced the way they described both CAM and non-CAM decisions. (In the interests of transparency, I'm CAM-sceptic in terms of its proposed mechanism of effect, but am happy to optimise the non-specific effects of consultation to maximise the effects of communication / weakly effective treatments)

Response: we added a short self-classification in the analysis section.

The analytical method is described as "inspired by grounded theory" - we need to hear something much clearer and more concrete than that.

Response: we hope that our expanded analysis section provides sufficient information now. The translated interview guide has been added as an appendix.
The reported data includes a number of "good stories" but with relatively little critical analysis. The "voice of experience" of the GP who has come to realise IBS can be as disruptive as IBD may be a salutary lesson about the difference between person-centred and technical medicine, but I think one could hear almost the same from an "enlightened" gastro-enterologist. This story tells us little about indeterminate-ness in general practice so much as about a shift from disease-centred to person-centred care. If that boundary is one aspect of indeterminacy (inclusion of "illegitimate" distress) then it should be the focus of the data and analysis.

Response: We hope we now succeed at least partly to present a more critical analysis. You are right, that the IBS story could come from an gastro-enterologists, too. We shortly take this issue up in the limitations section.

There is an interesting assertion in the abstract - about the relationship between perceived responsibility and preferred strategies - which doesn't really feature in the results. This is where the analysis would go deeper than the relatively straightforward reportage we see in the results section. There are hints at it but it really needs to be brought out in the analysis.

Response: In the new two sections at the end of the results, we try to explore the relationship now in more detail.

The quality of the written English is generally very good but there are just a few areas for clarification:

* I think purposive rather than purposeful sampling was used

* Methods / Data collection /2nd sentence would usually be something like "interviews were informed by a topic guide…." As written it implies that you had one but didn't use it!

Response: done (thank you!)

Overall I think this paper has potential merit, but needs better grounding in earlier work, more rigorous detail about the methods, and a more critical depth of analysis.

Response: hopefully done.

Finally while it's not mandatory, it might be helpful for the authors to complete a reporting checklist (such as COREQ) and submit it with any revisions.
Response: As clinical researchers AS and KL routinely use standard checklists like CONSORT or PRISMA. When revising our manuscript we used COREQ as tool for cross-checking that we include as many items as possible. However, COREQ is a long list and addressing all items in sufficient detail would have further lengthened our long manuscript. If the revised description of our methods is still considered insufficient, we could submit an appendix including COREQ items which were not addressed or addressed only very shortly with a second revision.