Author's response to reviews

Title: Patient organization involvement and the challenge of securing access to treatments for rare diseases: report of a policy engagement workshop

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Author’s response to reviews:

We would like to thank the three reviewers and the editors for giving us an opportunity to revise and resubmit our commentary piece. Here we detail how we have responded to the comments provided by the reviewers.

Reviewer #1:

This reviewer comments that the report is “interesting and useful”, particularly in “documenting clearly and concisely issues which do not often get aired”; while “The challenges facing small patient advocacy groups and support organisations trying to work in this space, or being drawn into this space, were generally well and clearly articulated”. However, s/he also points to what s/he sees as a number of significant omissions from the workshop and report, as follows:

- S/he notes in particular the absence of representation of cancer patient groups, which s/he suspects may be due to “voices from the non-cancer community influencing that unbalancing decision”. In fact, we decided not to invite cancer organisations to take part on the basis of our own research into the development of the field of rare diseases and orphan drugs. Historically, rare cancer organisations have developed rather differently from other rare disease organisations, and they currently occupy a somewhat different medical, scientific, political and institutional space, with access to different (sometimes better, sometimes worse) resources. There is undoubtedly much to be gained by bringing the two kinds of organisations into closer engagement with one another, but we felt that attempting to do so in this particular workshop would risk confusing rather than clarifying the issues at stake. We appreciate that this meant giving voice to one community but not to the other, and our choice of community simply reflected the fact that we have studied the history of rare genetic disease organisations in some detail, and paid far less attention to the much more recent emergence of the rare cancer community. We have inserted a short explanation of our exclusion of rare cancers into our discussion of the planning of the workshop.

- The reviewer comments that “The workshop chose to divorce the ‘social’ context from the ‘scientific’ context” by failing to consider “the ‘scientific’ issues, and how these overlap with
and influence the ‘social’ issues”. S/he directs us to a paper on the design of clinical trials for rare cancers as an example of such “influence”. In fact, that paper shows how scientific methodology might be adjusted to meet the peculiar problems of assessing efficacy in rare disease populations, so if anything is more plausibly read as an example of the influence of social over scientific issues – though we would incline to a model of “co-production” rather than unidirectional influence. Whatever, the issue of how best to evaluate the efficacy of new medicines, and the need to adopt appropriately patient-centred criteria of clinical evaluation, is an important one, and was actually touched on a number of times in the workshop. It is mentioned in our report in Results section 2, on the need for more appropriate regulatory and assessment processes. We have amended and slightly expanded this section to make clearer that the workshop was aware that such issues are important for making new medicines available to patients, and that patients have special experience-based expertise that is invaluable for addressing them. It would take another, rather different workshop to consider the technical questions of how best to reorient clinical research to accommodate such expertise, however; while the workshop reported here was only able to point to the need for, and value of, such accommodation.

- The reviewer suggests that there was insufficient discussion of the politics of regulatory decision making and the regulatory environment. We agree that this is an important factor in determining the conditions of possibility of access to medicines. It is also enormously complex, varying across sectors and jurisdictions, while as we note in the report, advocacy and support organisations vary widely in their capacity to engage with those politics. We suspect that it was this granularity of experience, and the difficulty in generalising, rather than any lack of opportunity, that led to the issue not becoming a focus of sustained discussion in the workshop. We note in the report that the participants recognised the importance but also the challenges and risks of engaging with the politics of regulation. We have also added a sentence to the Results section 2, on regulatory and assessment processes, pointing to the political complexities they entail. But again, it would take a rather different kind of meeting, focused specifically on this topic and ideally informed by systematic comparative research, to really get to grips with this issue.

- Finally, this reviewer suggests that the problems arising from the diversity of small advocacy groups, and the diverse understanding of “partnership” among these different groups, should be given more prominence, as these issues are rarely addressed in academic studies of patient involvement. We agree, and have added a couple of sentences about the diversity of rare disease organisations, and the problems this poses for involving them in policy and other activities, in our Method section.

Reviewer #2:

This reviewer raises a number of quite specific issues, to which we respond as follows:

- The reviewer raises the issue of independent evaluation of efficacy and the need for greater involvement of critical scientists in drug development, approval and marketing. We agree that this is an important issue, needing much more analysis and discussion in its own right.
However, it is tangential to and analytically separable from the issue being explored in this workshop, which focused on the problems of securing access to rare disease treatments that have been judged effective (however adequate or otherwise the evaluation process might be).

- S/he points out that others besides rare disease patients are denied access to effective treatments, for instance in poor countries. We agree, but again we think that the problems of securing access to treatments for rare diseases in resource-rich settings raise questions that may be treated separately, even if they are members of a larger family of socio-economic problems.

- The reviewer questions what we meant by a “sustainable” solution. We have removed the word “sustainable” and replaced it with a short description of the key problems we think any longer-term solution will need to address.

- S/he asks for examples of “entrenched positions and animosities”. We replaced this with a reference to the need to avoid individuals “known to be dogmatic or confrontational in their behaviour”, which perhaps better captures our method. We have also added as sentence to the effect that policy engagement workshops “work best in exploring issues that have not yet attracted much notice from policy makers or other concerned groups – as for instance the workshop reported here – and are far less effective as a means of resolving established matters of disagreement.

- S/he asks for a definition of the Chatham House rule. This has been added.

Reviewer #3:

This reviewer seems to have read our paper as if it were intended to be a research article rather than a commentary piece; for instance, s/he refers repeatedly to “this research” and “this study”, asks for more information about how we collected and analysed our data, and observes that our discussion “read[s] more like a discussion rather than an analysis”. As s/he quite correctly proposes, more work would be needed to turn this into a piece of systematic research, and s/he concludes with a recommendation that we develop our work further using a more rigorous methodology. Since we are not in a position to undertake such research, and since reviewers #1 and #2 both consider the paper interesting and useful (subject to their specified revisions and clarifications) in its present commentary form, we have therefore discounted referee #3’s suggestions for further work. We have however inserted a short statement emphasising that the paper is a report of workshop discussions that we hope readers of this journal will find interesting, informative and helpful in taking forward their own research, rather than a piece of systematic research in its own right. We have also taken heed of referee #3’s questions and, where possible and appropriate, added clarifications that we hope go some way to address those questions, as follows:

- How were participants selected and why? As noted above, we have added a little more information about the challenges of dealing with a very diverse field of organisations, and made clear that while we strove to include a range of different kinds of organisations, we did not aim to be representative, which I assume is what motivates this reviewer’s question.
- How did these key headings / themes emerge and how did they represent the viewpoints of participants? Again, I think this is a question about methodological rigour and representativeness, which is not directly pertinent to this kind of workshop and report. We already discuss, at the end of the Method section, the process of drafting and correcting the report in light of feedback from the participants. We have now added a further sentence noting that “All participants agreed that the results section of this paper is a satisfactory representation of the main substance of the workshop conversations.”