Author’s response to reviews

Title: Addressing the affordability of cancer drugs: using deliberative public engagement to inform health policy

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Author’s response to reviews:

Rosanna Gonzalez-Mcquire
Editorial Office
Health Research Policy and Systems

December 19, 2018

Dear Rosanna Gonzalez-Mcquire,

RE: Manuscript HRPS-D-18-00184: "Addressing the affordability of cancer drugs: using deliberative public engagement to inform health policy”

We would like to thank you and the reviewers for considering our manuscript and welcome the opportunity to revise it for potential publication Health Research Policy and Systems.

We have revised the manuscript, and our point-by-point response to the reviewers’ comments appears, below. Unfortunately, the formatting does not allow us to clearly present a recruitment
table in response to Reviewer 2's Comment 1, below. For this reason, we have uploaded a Personal Cover letter as an attached file to better view our point-by-point responses. We feel our manuscript has been improved by incorporating these comments, and thank the reviewers for their feedback.

Changes have been entered in red text in the manuscript; page references have been provided in our responses, below, to indicate where in the manuscript the changes were made. The revised manuscript has been uploaded, along with the figures, tables, and supplementary files. All files were uploaded and submitted online as of December 19, 2018.

Response to reviewers

Reviewer #1: 'Addressing the affordable of cancer drugs: using the deliberative public engagement to inform health policy': Review and Comments

The paper, 'Addressing the affordable of cancer drugs: using the deliberative public engagement to inform health policy', provides important information input from the public deliberations on the issues of affordability, fairness and equity impinging on the cancer patients and their caregivers. The skyrocketing prices are having negative and profound financial impact on patients and family members. These burning issues (known as financial toxicity, Rimer 2018), require immediate redressal measures from the public health authorities. Another serious issue is the lack of association between the cost of new drugs and their therapeutically benefits. Patients, as a consequence, are facing a painful dilemma of paying high prices for drugs that have uncertain value(Cohen 2016). Limited and shrinking public health funding is precipitating the shift of health financing burden on to the patients in the form of high out-of-pocket expenses.

The authors of the study have shed evidence on the problems of affordability and fairness through public deliberations, organized around selected provinces of Canada. Information is gathered through well planned and random-based selection of participants on a range of problems faced by the affected public. The deliberations center on the value-based and cost-effective pricing strategy of cancer medicines. The study places the onus on public funding to achieve the goal of affordable, equitable, and of uniform quality of therapeutic treatment across all provinces of Canada.

It is suggested here that the project can make more valuable and practical contributions if the following points are incorporated in the study.

(i) The heavy reliance on public funding, though highly warranted from equity and affordability angle, is not a financially sustainable and viable proposition, given the continuing trend of the restrictive budgetary policy of fiscal consolidation in many developed countries, including Canada. Poor and sluggish economic growth performance in Canada has constrained the availability of public funding in the health sector in the past two decades.

(ii) In addition to the limited availability of government funding, insurance companies, which are among the largest payer for health services, offer limited options for reimbursement plans that
are further subject to onerous qualifying conditions. Lack of competition and lack of regulations on their functioning have led these dominant players to resort to restrictive practices such as selective cream skimming policies, long waiting period clauses, heavy co-payments, and deductibles conditions. These provisions act as major barriers to affordable and equitable treatment. Such issues need to be addressed and settled from time to time in joint forums comprising of public bodies, insurers, and pharmaceutical companies.

(iii) The high cost of generic cancer drugs and the government's inaction to use its negotiating power are another set of barriers to cost control. It has been found that even if there are acceptable generic alternatives with equal efficacy, the prices of many such drugs are set at quite a high level compared with those for non-malignant diseases (Siddiqui and Rajkumar 2012). Another reported hurdle is that governments in many countries generally do not realize the bargaining power they have to place more emphasis on price-volume negotiations (WHO 2017).

(iv) The practice of linking prices of new cancer drugs with the R&D cost is considered as a root cause of escalating prices of new drugs. The key issue is the exclusive marketing right -- the monopoly -- rather than the patent system itself for escalating prices (Love 2007). A suggested strategy is to de-link the price from the R&D costs by instituting prize scheme within the patent system. A growing number of public health, economics, and innovation experts are now focusing attention on the use of prizes as a potential alternative to marketing monopolies. However, the introduction of new prize mechanisms to stimulate R&D will require effort, ingenuity and political leadership (Love 2007). Prize funds can also be used for promoting R&D in neglected rare cancer diseases.

(v) A long-term issue related to drug cost is the of lack public sponsored, public funded research and research in public labs to generate useful research knowledge for developing commercial applications of biomedical advances, in most countries excepting in USA and UK. The USA has a long tradition of conducting basic research in the public domain that has helped pharmaceutical companies to make innovative breakthroughs in this knowledge-intensive field. Government's involvement in promoting and funding basic research and joint public-private partnership initiatives are worth exploring by countries to retain influence on pricing decisions (WHO 2017). All relevant stakeholders (government, academia, and industry) need to be engaged in tackling the issue of affordability and fairness while supporting public investments in basic and developmental research for driving future innovations.

It is hoped that the hard and elaborate work done by the authors in the above project would incorporate ideas of innovative financing alternatives, address joint public-private partnership in R&D and coordinate information from all stakeholders in their subsequent project.

Authors' response: Thank you for these important suggestions on the topic of affordability and fairness in cancer drug funding decisions in Canada. As your suggestions make clear, the topic is complex and intersects with a wide range of policy considerations, like the commercialization of biomedical research, the government's role in driving scientific discovery, Canada's regulatory frameworks for patents and reimbursement, and its fiscal policy. We agree that these are worthwhile considerations for policy; however, their inclusion is beyond the scope and
activities of this study, and thus of this manuscript. They are, as is suggested, suitable topics for subsequent studies.

Reviewer #2: General comments:

Thank you for the opportunity to review this paper, which describes a set of public engagement activities conducted across Canada to elicit the views of the general public on decision-making around the funding of cancer drugs in Canada. I fully support the need to consider public values during these processes and recognize the lack of solid empirical research done to date in this area. While I found this paper extremely interesting, I'm afraid I would need more information on a few elements before being able to make a fair judgement on the robustness of the results. Also, I would recommended that the manuscript be structured to comply with currently accepted published guidelines for presenting qualitative research (e.g., COREQ).

Authors’ response: Thank you for this comment. Two appendices have been added to the manuscript containing the recommendations from the provincial panels (Appendix 2) and the pan-Canadian panel (Appendix 3). Also see our response to Comment 6, below. We hope this additional information will provide useful context for the study findings.

The research team is sympathetic to the need for transparency in reporting the results of qualitative research. COREQ is a check-list approach to making results reporting more transparent in qualitative studies. Checklists can be useful reporting guidelines; however, we feel that several of COREQ’s items are not relevant to this study (for example, items 4, 13, 18, 23, and 28), and others are covered throughout the manuscript. Moreover, we believe that the analysts’ holistic sense of the data and expertise in interpretive practice were key to producing robust analyses of the transcripts. For these reasons, we did not use COREQ and elected instead for an explanatory account of our approach to data analysis for this study, stating in the Methods section that we used constant comparison and thematic analysis to interpret the transcripts (see pages 10-11). However, we agree we need to be more transparent about the coding and interpretation process, and so have added the following text to the manuscript’s Methods section:

Two qualitative researchers (CB, ODP) who also attended multiple panels analyzed the transcripts, which were entered into NVivo 11 software. Weekly sessions were held to review the concepts and terms within each deliberative context. The study team also met weekly to discuss the interpretation of findings across panels and provide feedback on them. (Page 11)

Specific comments:

Comment 1: Page 7 (participant recruitment): This section is clearly written, but it would be helpful to know how many letters of invitation were sent out, whether the final decision on selection of panelists was made by the market research firm or the investigative team, and how that selection was made. Also, I would like to see some information that would help me to know whether the market research panel from which these individuals were picked was representative of the population at large.
Authors’ response: Asking Canadians’ panels provide their clients with access to over one million Canadians, with regional representation across Canada. They have been successful in matching their panel data with Statistics Canada data for statistical representation across many variables. Their 2017 Panel Book provides information on the robustness of their panels. See http://www.delvinia.com/wp-content/uploads/2018/12/2017_AC_panel_book_ENG-FINAL.pdf

The market research firm provided access to its members by distributing a recruitment/eligibility survey to randomly selected members of the panel and then providing the research team with a list of panel members who were eligible to participate in the study based on the survey results. The research team then made final decisions regarding which panellists would be invited to participate in the study. For the five local panels, the research team selected the specific criteria that were used to determine eligibility. The market research firm allocated potential participants to panels as survey responses came in, being sure to provide coverage across all criteria and not using other criteria or subjective factors in their allocations. The research team then sent formal letters of invitation to these individuals. For the pan-Canadian panel, the study team selected panelists from among those participating in previous panels and then sent formal letters of invitation to these individuals.

The following table shows the number of invitations sent and the number of participants per event:

<table>
<thead>
<tr>
<th></th>
<th>Overall Total (provincial)</th>
<th>Hamilton</th>
<th>Halifax</th>
<th>Montreal (English)</th>
<th>Saskatoon</th>
<th>Montreal (French)</th>
<th>Pan-Canadian</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invited</td>
<td>163</td>
<td>34</td>
<td>28</td>
<td>38</td>
<td>30</td>
<td>33</td>
<td>44</td>
</tr>
<tr>
<td>Participants</td>
<td>115</td>
<td>25</td>
<td>24</td>
<td>20</td>
<td>21</td>
<td>25</td>
<td>24</td>
</tr>
</tbody>
</table>

Comment 2: Page 8: Who comprised the "steering and advisory committees", and what roles did they play?

Authors’ response: The project’s steering committee was comprised of three senior decision makers in cancer control, two of whom were from pan-Canadian organizations and one was in charge of a provincial drugs budget. In keeping with an ‘integrated knowledge translation’ or ‘co-production’ model, they provided guidance and oversight on the project’s direction, as is appropriate for members of a steering committee. The project’s advisory committee was comprised of research personnel from the McMaster Health Forum and the Canadian Centre for Applied Research in Cancer Control with expertise in deliberative public engagement methods, recruitment methods, research ethics, and institutional oversight. They provided advice to ensure that the project was in compliance with relevant regulations (e.g., informed consent processes, financial reporting, etc).

We have added the following text to page 8 the manuscript:
In keeping with an ‘integrated knowledge translation’ or ‘co-production’ model, the steering committee provided guidance and oversight on the project’s direction. It was comprised of three senior decision makers in cancer control, two of whom were from pan-Canadian organizations and one was in charge of a provincial drugs budget. The advisory committee included members of the research team with expertise in deliberative public engagement and recruitment methods, research ethics, and institutional oversight. They provided advice to ensure that the project was in compliance with relevant regulations (e.g., informed consent processes, financial reporting, etc).

Comment 3: Page 9: It is stated that a cancer patient representative and an oncologist participated in the sessions. While both of these perspectives are critical, I’m not sure they adequately cover the "local decision-making context". Neither are administrators or budget holders responsible for allocating scarce resources. Also, the perspective of the innovator was not included. Previous juries have demonstrated the value that the public places on innovation. Therefore, some rationale for the decision to include some stakeholders’ perspectives and not others on the expert witness panels is needed.

Authors’ response: Thank you for this comment. Each oncologist participating at each event was also a senior administrator with expert knowledge of the cancer drug funding processes in his/her own province. In addition, the oncologists were either responsible for cancer drugs budgets and/or were members of advisory committees tasked with making cancer drug funding recommendations at local or pan-Canadian levels. To make this clearer in the manuscript, we have added the following sentence on page 9:

The oncologists also had expert knowledge of cancer drug funding process and budgets locally and/or at the pan-Canadian level.

Every effort was made by the research team to provide participants with a range of perspectives on the topic of how to make decisions about cancer drug funding fair and sustainable. These efforts are detailed on page 9 of the manuscript. It is important to support participants in their deliberations by providing information based on evidence and experience, and to do this without overwhelming members of the public who themselves are not experts in the complex topic of cancer drug funding. In deliberative public engagement events, a balance must be struck between providing participants with sufficient and relevant information so they feel supported in their discussions, and also to allow time across a 2-day agenda for participants to listen and learn from one another, to understand and respect the differences in their values and perspectives, and ultimately come together as a civic body to deliberate on a challenging topic and formulate recommendations for policy. The research team discussed at length how to strike this balance across the 6 events, and our conclusion is outlined on page 9 of the manuscript. We did not include more perspectives—such as the perspective of the innovator—because we felt participants had the appropriate amount of information to inform their deliberations without turning them into experts. Moreover, we wanted to give members of the public ample time to deliberate about cancer drug funding; adding another perspective would have reduced their time to deliberate.
Comment 4: Page 9 (reference to Appendix 1): I don't see how this Appendix includes "relevant research evidence on the topic of cancer drug funding decisions in Canada".

Authors’ response: Appendix 1 is the 34-page Citizen Brief for Making Fair and Sustainable Decisions about Funding for Cancer Drugs in Canada (the “Brief”). The purpose of the Brief is to stimulate participants’ discussions on the topic of cancer drug funding in Canada under the condition of limited resources. As such, it provides information on cancer drug approval and funding processes, government cancer drug coverage in the 5 provinces in which the deliberative events were held, the burden of cancer and the cost of cancer drugs, and outlines how decisions about cancer-drug funding affect some patient groups more than others. This information is drawn from the academic literature and outlines what the available evidence says about the challenges of cancer drug funding—including possible approaches to address the challenges and opportunities to address them—as it evident from the 33 references cited in the Brief. The Brief is intended to support and stimulate participants’ discussions by providing evidence-based information so as not to steer participants’ views in any one direction. Thus the purpose of the Brief is to inform but not overwhelm non-expert participants.

Comment 5: Page 9 (structure of deliberation): More details on "collective deliberation and making recommendations" would be helpful. This section doesn't clearly explain the structure of the process. How did the deliberations begin? And was it identical in all panels?

Authors’ response: All deliberations followed the same format. We have included the following description on page 10 of the manuscript of how the panels were structured:

All panels followed the same format. On Day 1, participants heard from expert speakers and asked them questions, viewed the video, and deliberated and made recommendations on Topic 1. On Day 2, participants deliberated on Topics 2 and 3 and made recommendations on them. (pg 10)

Comment 6: Pages 11 to 16 (Results): No information provided on the 86 recommendations is provided, making it difficult to see how the 6 themes emerged. A description of how they came to be (e.g., if the recommendations, themselves, were seen as sub-themes, etc.) would be helpful. Although "voting" is mentioned in the prior section, there is no mention of whether this happened and what it means for the general agreement on the recommendations or the themes.

Authors’ response: Thank you for this comment. To provide the 86 recommendations, two appendices have been added to the manuscript. They are:

Appendix 2: List of Recommendations by Province and Deliberative Topic

Appendix 3: List of Recommendations from the pan-Canadian Panel
All recommendations were voted upon. Voting was done to gauge the degree of support or disagreement for the recommendation. Participants who abstained or voted against a recommendation were asked to explain their views. This was done so that other participants could hear arguments against a recommendation and so that the research team could capture via audio recording—and thus through transcript analysis—the particular reasons why a recommendation was not supported by some participants. Because the public deliberation is a policy informing event, capturing the nuances in public support or disagreement on a particular policy question or initiative is useful information for policy makers.

Pages 10-11 of the manuscript describes our approach to analysing the recommendations within their deliberative context (i.e., their embeddedness in the context of deliberation via transcript analysis) and through a comparative lens. Using the method of constant comparison across recommendations and deliberative contexts, we were able to identify thematic categories that aligned with the deliberative topics and questions presented to participants. Because participants discussed the recommendation and reasons for or against it before they voted on each recommendation, and then were asked to explain the reasons why they voted as they did, we were able to capture and then explore through transcript analysis the range of reasons why participants agreed with—or abstained from or disagreed with—each recommendation. We could thus assess the degree of agreement and divergence within and across recommendations and contexts, thereby allowing us to characterize the themes more fully.

Page 11 (Theme 1): Does "strong support for clear criteria" mean unanimous agreement? Did the Quebec panels not have a view on this theme?

Authors’ response: The two appendices added to the manuscript (see Authors’ Response to Comment 6, above) contain notes that explain the terms used to indicate the degree of support for each recommendations. The terms are: “All support” indicates that all participants agreed with the recommendation; “Support” indicates that a majority of participants agreed with the recommendation; and “Persistent disagreement” indicates that participants were deeply divided about the recommendation. “Strong support for clear criteria” does not mean unanimous agreement.

It was not possible to include and comment upon all 86 recommendations in the manuscript. The Quebec panels recommended incorporating patient input to support drug evaluations, with the Quebec-French panel suggesting a “useable database” that specified patient experiences to support drug funding decisions (see added Appendix 2).

Page 12 (reference to Figure 1): The 3 choice scenarios provided in this figure are fairly limited. Choice options of the "all else being equal" kind ask the participants to focus on one dimension only (e.g., length of life). In reality, decision-makers rarely, if ever, face that kind of scenario. They have to make decisions between options that vary on multiple dimensions, and it has been shown that such decisions are usually contingent upon something (i.e., option A may be picked...
over option B if all else is equal but if there are other factors (values) that are seen to be relevant, the choice may be reversed). This needs to be addressed in the discussion and reflected in the conclusions.

Authors’ response: Decision scenarios of this type are commonly used to elicit preferences in health economics literature (see for instance Ryan M and Gerard K (2003) PMID: 14619274 and de Bekker-Grob EW et al (2012) DOI: 10.1002/hec.1697). We agree decision scenarios have limitations. We identify and explain these limitations in the Discussion section of the manuscript (see page 19). To be more explicit about the limitations of choice scenarios, we have added the phrase “The scenarios were intentionally limited to force the specific trade-offs” to the manuscript where the scenarios are first introduced (page 13). A similar phrase was added to the Discussion section on page 19 to make our acknowledgement of the limitations as explicit as possible.

The scenarios also provide a specific context where abstract principles like fairness, equity, access and inclusiveness must be considered as part of the trade-offs, although using the term ‘principles’ to describe the recommendations may introduce ambiguity about the recommendations and these higher level principles. Our approach to deliberation moves beyond merely supporting abstract principles that do not fully determine a funding decision to having participants consider specific decisions and articulate how these abstract principles are operationalized.

Page 13 (para. 2): 12 months is identified here as a sort of "threshold" for additional survival before a "significant" cost is paid. What was the rationale for selecting 12 months and what does "significant" means with regards to cost?

Authors’ response: Participants themselves considered a new drug that costs twice as much as the current drug to be a significant cost, and most settled on 12 months’ increase in the duration of life to be appropriate health benefit for that cost (i.e., other time frames were considered). To make this explicit in the manuscript, the sentence on page 13 was modified and now reads as follow:

With respect to funding drugs that extend life, the majority of participants considered doubling the cost—i.e., going from $15,000 per patient to $30,000 per patient—to be significant cost increase and was a worthwhile expenditure only if life was extended by at least 12 months.

Page 14 (Fairness and equity): The panels were not asked about what they would give up in order to achieve better fairness and equity. "Opportunity cost" was mentioned earlier in the paper, and what panels were prepared to give up in order to help specific populations would have made the findings all that more relevant and useful to decision-makers. Some discussion around how decision-makers could use the findings in their current form would be helpful.

Authors’ response: Participants were not asked to trade-off the values of fairness and equity against other values or against costs (e.g., raising taxes, privatized or diminished health care, etc). Deliberative public engagements bring together members of the public to provide policy advice on complex topics like health care, where some of society’s most ethically, financially,
and politically inflected decisions are made. Decision makers themselves cannot agree on the best approach to these decisions, which inevitably involve values trade-offs, among other trade-offs. The limitations of a 2-day deliberation, as well as guidance from our advisory committee, encouraged us to focus on the criteria for funding, not funding and disinvestment. The notions of fairness and equity were woven throughout the discussions, and when recommendations were made, they reflected how fairness and equity were considered in the specific scenarios or decisions. So the participants did in fact consider what they would give up to achieve fairness and equity, for example in whether to recommend national consistency of what is funded, and equity, or when considering when an improvement in outcome was too small to justify additional costs, with the implied opportunity costs.

How decision makers could use the findings of this deliberation are presented in the Discussion section of the manuscript on page 18, where we discuss new policy options be considered in light of our findings. These options include developing and implementing new mechanisms in Canada that allow for the reassessment and disinvestment of under-performing drugs and technologies, and the use of real-world cost-effectiveness data as part of reassessment and disinvestment in order to achieve better value for money. Participants’ recommendations also provide decision makers with support for funding cancer drugs that improve survival and help patients be more independent, improve their general well-being and mental health, and that create cost savings, if the new drug is comparable in effectiveness to the existing drug. These are specific ways in which decision makers can be guided by the findings from this study to make cancer drug funding decisions.

We hope that these revisions have addressed the reviewers’ concerns sufficiently for the revised manuscript to be accepted for publication in Health Research Policy and Systems. Clean versions of the manuscript, tables, figures, and appendices have been uploaded and submitted for your consideration.

If you have any further questions or concerns, please do not hesitate to contact us. We look forward to hearing from you at your earliest convenience.

Yours sincerely,

The Authors