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**Title:** The top 10 research priorities for early-stage colorectal cancer: a Canadian patient-oriented priority setting partnership

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**Reviewer 1:** Dr. Rich Sobel

**Institution:** Port Moody, BC

General comments (author response in bold)

1. The Lay Abstract is not very well written. Just a quick edit from the main abstract. Sort of token "lay".

Response: this has been revised.

2. There is one grammatical error in the Methods paragraph that needs to be corrected. [Editor's note: the paper will be copyedited prior to publication.]

**Reviewer 2:** Dr. Madhusudana Girija Sanal

**Institution:** Institute of Liver and Biliary Sciences, Delhi, India

General comments (author response in bold)

Comments are marked on the manuscript file attached.

[Editor's note: Since this study has been completed, we are aware that the sample size cannot be increased. The implications of the sample size could be addressed in the Limitations]

**The small sample size is noted in the limitations section**

**Reviewer 3:** Dr. Clarence Wong

**Institution:** University of Alberta, Cross Cancer Institute

General comments (author response in bold)

Patient centred research has received increased awareness and importance in fields such as colorectal cancer. This study highlights a consensus based approach to identify research issues important to early colon cancer patients. Overall, this is a thorough study, with well described methodology of choosing the research priorities once questions were identified.

A few issues that require further comment are:

1-Further elucidation on how recruitment occurred. Convenience sampling through advocacy groups, posters and social media was used. However, only 99/185 provided any demographic data. There was also bias towards Caucasian respondents in all categories.

a. Were there any steps to address patients with different social determinants of health?

Response: We attempted to reach a diverse patient population by using multiple recruitment strategies including social media, poster advertisements, advocacy groups,

physical presence in clinical settings, patient support groups. This information has been included in the limitations section. Page 14-15

b. What about patients that did not belong to a mailing list from an advocacy group?  
Response: We attempted to reach a diverse patient population by using multiple recruitment strategies including social media, poster advertisements, advocacy groups, physical presence in clinical settings, patient support groups. This information has been included in the limitations section. Page 14-15

c. Was there any attempt to reach patients of different ethnicity or may not have had internet access?

Response: We attempted to reach a diverse patient population by using multiple recruitment strategies including social media, poster advertisements, advocacy groups, physical presence in clinical settings, patient support groups. This information has been included in the limitations section. We did not specifically reach out to different ethnic groups. Page 14-15

d. If demographics were not captured, how did you ensure that a respondent did not answer multiple times?

Response: The survey platform we used, Qualtrics, would only allow 1 response per IP address. This has been included in the methods section. Page 6

2-What was your definition of early colorectal cancer? Stage I-III?

a. What about patients with carcinoma in situ (malignant polyps)? There appears to be a bias towards patient that were assessed at a cancer centre. Many early colon cancer patients may not require medical or radiation oncology referrals. What about patients that were early stage that did not require adjuvant therapy (and thus, may never have been seen at a cancer centre)?

**Our definition of early stage disease was those with stage I-III disease as noted in the background section. In the methods section on recruitment, we detailed how we used multiple recruitment strategies including (but not limited to cancer centers). We did not collect information on where the respondents heard about the survey, therefore, we have no idea if they were only seen at a cancer center. We agree, most stage I and some stage II patients would not be referred to a cancer center which is why we used multiple recruitment strategies.**

3-How was this survey disseminated among health professionals?

a. Given that gastroenterology and general surgery account for 99% of colon cancer screening in Canada, there was only response from 1 surgeon.

**We have included a detailed list of all the health care professionals and their respective organizations that we contacted. We contacted multiple surgical groups including the Enhanced recovery after surgery National group, the Alberta health Services surgical strategic clinical network, and surgeons within our own collegial network. We are unsure why only 1 surgeon responded.**

b. As well, why was primary care not involved (or had meaning input)? The perspective of screening would have swayed had more endoscopists and primary care physicians been involved. This is a limitation of the study and should be addressed.

**We attempted to contact primary care physicians through the Canadian Association of General Practitioners in Oncology – they declined to disseminate our survey to their members. We did not try to contact any gastroenterology**

**groups or associations directly. Both of these points have been added to the limitations. Page 14-15**

Overall, the process once the question list was procured, was sound. However, the foundation of the questions come from the respondents - thus more explanation is required how this group was acquired, or there would a consideration of bias in any results.

**Reviewer 4:** Dr. Heinz Endres

**Institution:** Ruhr-University Bochum, Bochum, Germany

General comments (author response in bold)

Using the method pioneered by the James Lind Alliance (JLA) in 2003, the authors Cuthbert et al. bring together patients, caregivers, clinicians, and researchers in Priority Setting Partnerships (PSPs) with the goal of determining the 10 most important unanswered questions in the management of early stage (I - III) colorectal cancer, from the perspective of patients, their caregivers, and healthcare professionals. The focus of the survey was to improve health care for patients following a colorectal cancer diagnosis.

The authors were successful in engaging stakeholders (patients, patient caregivers, healthcare professionals) from across Canada in the collaborative partnership. Ultimately, 66 unique unanswered questions were first compiled from 370 submitted responses, and from these, after preliminary prioritization, a list of 30 most important questions. From this list, the top 10 priorities for future research on CRC, ranked from 1 (most important) to 10 (least important), were summarized in a final consensus meeting. The top research priority (1) was given to prevention of recurrence of CRC. Research to determine the most effective methods of preventing recurrence could improve quality of life by reducing fear of recurrence, according to the authors. The second most important research priority is how screening rates could be improved. The need for more research on implementing personalized medicine into CRC treatment also appears in the top 10.

Some Minor Revisions:

1.) The authors state in their manuscript that colorectal carcinoma is the third most diagnosed cancer in Canada. Isn't it now the second most common cancer in Canada?

**It has now changed to be the third most common**

2.) It would be important for the reader to know what qualifications the 14 members of the Steering Committee had.

a. For example, there is only a very general report of 4 investigators who had methodological expertise (which one?) or content expertise (which one?).

**initials have been included in the descriptions of the committee members. Page 5**

b. What is meant by the dual role that some members had? Was the lead author (CC) one of these 4 researchers?

**This has been amended. There were 3 members with research or methodological expertise. Two of these members (CC and WC) had dual roles as clinicians and researchers. initials have been included in the descriptions of the committee members. Page 5**

3.) Were the same 14 members always involved in all consensus meetings?

**Yes, this is consistent with the JLA process. This has been clarified in the steering committee section. Page 5**

a. Could the qualifications of the members have had an impact on the selection of the top 10 research priorities?

**The intention of the JLA process is to bring together those with lived experience of an illness (patient, caregiver, or clinicians) - in this case colorectal cancer. This lived experience is thought to bring a unique and important perspective about living with the disease and the research priorities that arise from that perspective. The qualification of having lived experience of colorectal cancer is meant to impact the selection of the research priorities.**

b. Were top 10 experts involved in setting the main research priorities?

**Consistent with the JLA process, those with lived experience of an illness are considered the experts. Thus, the top experts were involved in setting the priorities.**

4.) The authors should write something about how many of the people (in percent) who were contacted by email participated in the survey.

a. Were people who were contacted reminded to participate in the survey?

**We used convenience and snowball sampling and multiple recruitment strategies including social media, email, poster advertisement and word of mouth.**

**Organizations did not provide us with contact information, instead they sent out the survey information for us. We did not have the ability to track the number of contacts made through email. Some professional organizations agreed to send out reminder emails for us, while others did not.**

b. What percentage were recruited through posters and social media?

**We have no way to capture this information.**

c. In the Limitations, the authors write that although they invited people from across Canada to participate in the survey, few responded. How few is few? Can the authors give that as a percentage? [Editor's note: the response rate if calculable, should be included in the Results.]

**The response rate is not calculable**

d. Could the number of participants and the profession of the participants have influenced the Top 10 list?

**Yes, this is noted in the limitations section page 14-15**

5.) In the Limitations, the authors write that the survey participants may not be representative of the broader CRC community. What might this mean for prioritizing the top 10?

**As noted in the limitations section, our results are consistent with our priorities identified in different tumor types. This helps confirm that although our sample was small, the research priorities are in keeping with what is demonstrated in cancer survivor populations in general.**

6.) Who participated in the final consensus meeting? From the manuscript, we can see that this was a total of 24 people (page 10, lines 8 through 15).

**Information on the participants for the final consensus meeting has been clarified in the manuscript and updated in table 1. Page 8**

a. Were the 25 people involved who also participated in the Interim Prioritization, or were members of the Steering Committee involved?

**The consensus meeting included some people from the interim prioritization, some from the steering committee and 5 participants were completely new to the study. This is consistent with JLA methodology. Page 6**

b. How were the participants selected?

**The participants were selected in a similar manner to recruitment to all other phases of the study. This has been clarified in the manuscript. Page 8**

c. Could the selection have influenced the list of the top 10?

**Yes, this is noted in the limitations section. Page 14-15**

7.) In the Conclusions, the authors write that the top ten research priorities for early-stage CRC should be pursued by researchers and clinicians.

a. How do the authors plan to do this specifically?

**The authors have used the top 10 priorities to apply for 3 grants since this study has finished. In addition, Alberta Health Services has used the priorities in a recent grant competition. This has been included in the conclusion section. Page 15-16**

b. What plans exist for the necessary post-PSP process?

**This has been added to the conclusion section page 15-16**

c. How can the top 10 be translated into funded studies?

**This has been added to the conclusion section page 15-16**

8.) Already in 2018, a publication has been published in Gut by M. Lawler et al. dedicated to the same topic: "Critical research gaps and recommendations to inform research prioritization for more effective prevention and improved outcomes in colorectal cancer". In a more detailed discussion, the authors should compare their results (top 10 in Canada) with those of Lawler et al (15 critical research gaps in the UK). For the reader, this direct comparison would be important and of considerable value.

**This findings from this 2018 study identified some research gaps similar to our JLA process. This again is reassuring that our findings are in keeping with CRC research gaps and priorities more broadly. A reference to this study has been included in the limitations section. It is beyond the scope of this paper to provide a detailed comparison of the findings between these two studies. Page 14**

**Reviewer 4:** Dr. Carolyn Canfield

**Institution:** University of British Columbia

General comments (author response in bold)

Thank you for this opportunity to review your manuscript. I have used the CMAJ Guidelines (Jan 2021) for patient reviewers as a template reproduced below.

[Editor's note: Numbered comments below indicate those that require response in the decision letter and revisions in the text, as appropriate]

✓ Do the researchers provide a clear description of how they engaged patients in their research?

This manuscript exemplifies overall clear writing, including a commendable plain language summary.

- Were patients engaged in various phases of the project? (e.g., Were patients involved in identification of priorities for what should be studied, in how the research should be done, in analyzing or making sense of the data or in disseminating the findings?)

Patient partners participated on the steering committee throughout the project.

- Did patients contribute meaningfully to the research (rather than just as a participant, or as a token member of the research team)?

1. Patient and carer partners actively participated in each stage of the project in their roles, making up half of the steering committee. It is clear they were not "token" project members. However, there is no documentation of their specific contributions.

**We feel it is clearly explained in the steering committee section how the members contributed. Page 5**

2. Also, it is not clear how their participation was valued, as the only mention of compensation to these same patients and carers is a meal gift card associated with their attendance at the final priority setting meeting, not for participation on the steering committee. The significance of compensation is growing as an indicator of valuing patient partnership in co-produced research.

**We agree. Since starting the project in 2019 the process and philosophy for patient engagement has changed considerably. At the time of our study, it was not as common to compensate patients for their time. In our ongoing work with patient partners, beyond this study, we now compensate patients with an hourly rate.**

✓ Do the researchers describe how the engagement of patient partners added value (or did not add) to the results or outcomes of the study?

The entire project celebrates the value of patient and carer perspectives on research priorities. Those many participants are in effect the research subjects.

1. It would be helpful to document examples of how the contribution of patient and carer members of the steering committee added value. How did the direction of the research change as a result of these co-leaders?

**We feel this is explained in the lessons learned from patient engagement section. Page 15**

2. What did professional members on the steering committee learn from their experiences with patient and carer steering partners?

**We feel this is explained in the lessons learned from patient engagement section. Page 15**

3. What did patient and carer members take away from their participation in this co-led research project? What specific knowledge dissemination did they contribute?  
**We feel this is explained in the lessons learned from patient engagement section. Page 15**

✓ Do the researchers describe any challenges with engaging patients in the study?

1. No challenges are described. Learning what barriers were overcome or tolerated would assist other researchers keen to adopt the JLA protocol.  
**This has been included in the lessons learned from patient engagement section. Page 15**

2. Specific considerations for successful virtual-only meetings in JLA PSPs would be helpful, as an example.  
**This has been described elsewhere with a reference to the article. There is also reference to the satisfaction survey that occurred post virtual meeting with the results included as supplementary material.**

✓ Does the article include lessons learned from using a patient-oriented approach to research, so that others can learn from their experience?

This manuscript ably illustrates successful application of the JLA priority setting protocol to identify research topics with high priority in the views of patients, caregivers and clinicians.

1. I wonder if the patient and carer participants and members of the steering committee would have suggestions for improvement in the protocol or how it was carried out?  
**The patient partners were involved in the design of the protocol. This is described in the section on the steering committee. Page 5**

✓ In your opinion, are the outcomes of the research ones that will make a real difference to patients, their families and their providers?

The outcomes of this project are designed to have a high impact on patients, their families and providers. It will support patients as well as practitioners in advancing what matters to those experiencing care in the clinic and the community.