

## 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

<b>TITLE (PROVISIONAL)</b>	Pathways to a Cancer-Free Future: a protocol for modelled evaluations to minimise the future burden of colorectal cancer in Australia.
<b>AUTHORS</b>	Feletto, E; Lew, Jie Bin; Worthington, Joachim; He, Emily; Caruana, Michael; Butler, Katherine; Hui, Harriet; Taylor, Natalie; Banks, Emily; Barclay, Karen; Broun, Kate; Butt, Alison; Carter, Rob; Cuff, Jeff; Dessaix, Anita; Ee, Hooi; Emery, Jon; Frayling, Ian; Grogan, Paul; Holden, Carol; Horn, Christopher; Jenkins, Mark; Kench, James; Laaksonen, Maarit; Leggett, Barbara; Mitchell, Gillian; Morris, Susan; Parkinson, B; St John, D James; Taoube, Linda; Tucker, Katherine; Wakefield, Melanie; Ward, Robyn; Win, Aung; Worthley, Dan; Armstrong, Bruce; Macrae, Finlay; Canfell, Karen

### VERSION 1 – REVIEW

<b>REVIEWER</b>	Mandi Pratt-Chapman, PhD GW Cancer Center, The George Washington University, Washington, DC, USA
<b>REVIEW RETURNED</b>	03-Jan-2020

<b>GENERAL COMMENTS</b>	While the coalition-approach to Pathways is laudable, it is not clear what the specific research question is for the present study. There is a mix of past, present, and aspirational work described. Therefore, it is not clear what the present question examines or what the results to that question are. I would suggest narrowing the scope to describe one model answering a specific research question.
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<b>REVIEWER</b>	Belinda Goodwin Cancer Council Queensland, Australia
<b>REVIEW RETURNED</b>	24-Jan-2020

<b>GENERAL COMMENTS</b>	<p>The manuscript details a program of work aimed to inform improvements to CRC control in Australia; a key component being the current and proposed use of established micro-simulation modelling program (Policy 1 - bowel) to assess the economic and health impacts of various interventions. The research program described is well-designed and is likely to provide valuable, evidence-based recommendations to policymakers and public health professionals in Australia and other comparable nations.. My suggestions relate to improving the clarity and accessibility of the manuscript.</p> <p>Some concepts should be better explained for readers who are unfamiliar with these methodology/terms:</p>
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	<p>Line 47, page 6. It is not clear what the term “Pathways” is at this point - an initiative, a program of research, a model? Please provide brief explanation.</p> <p>End of page 7 - first mention of Policy-1 and micro-simulation. It's fine to refer readers to other sources for technical details, but the manuscript would benefit from a short plain English description of this key method. Please add a short paragraph summarizing the general method and purpose of micro-simulation modelling, ideally with an example in the context of this study.</p> <p>The rationale for selecting each intervention to evaluate is clear. The methods involved in collecting data to enter into the micro-simulation is less well-explained and should be expanded. It is touched on very briefly on page 8 - line 33 when the authors write "Pathways-Bowel will synthesize the existing evidence to determine the likely impact on CRC outcomes in the future". Please include a summary of the sources of data that are/will be used to inform the evaluations in this study towards the beginning of the methods section.</p> <p>Please provide more detail in the aims/objectives at the end of the introduction to summarize the program of work (i.e., evaluations of interventions, research, modelling expert consultation etc). Although this is laid out in the following sections, a concise summary in the intro would be helpful.</p> <p>Other minor comments:</p> <p>Page 6, Line 32: Suggest using "best investment or value" here as "best buy" is defined after this.</p> <p>Page 6, Line 33: Please provide a citation for the statement "On current evidence, the best buy in CRC control is increasing participation in Australia's National Bowel Cancer Screening Program (NBCSP)"</p> <p>Page 7, Lines 27 - 40: Check the use of past and present tense here.</p> <p>Page 7 to 8. It appears that the reader is referred to Figure 1 for a depiction of model components/versions described in a-d, however, it is not clear from this image how b-d fit into the model - is something missing?</p>
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## VERSION 1 – AUTHOR RESPONSE

### Reviewer(s)' Comments to Author:

#### Reviewer: 1

1. *While the coalition-approach to Pathways is laudable, it is not clear what the specific research question is for the present study. There is a mix of past, present, and aspirational work described. Therefore, it is not clear what the present question examines or what the results to that question are. I would suggest narrowing the scope to describe one model answering a specific research question.*

We thank the reviewer for their comment and acknowledgement of our comprehensive research program. We have chosen to present the broader scope of our work as it sets the context for how we can guide and underpin future research investment and policy implementation. As a result, our research question is stated in the paper and is “how can we use modelled evaluations of CRC interventions to guide and underpin future research investment and policy implementation?” (see Introduction). We use one model, Policy1-Bowel, informed by expert and end-user engagement and relevant evidence from published literature and/or planned statistical projections and epidemiological analyses. The current text, which has been greatly improved in response to the reviewers’ comments, now clearly explains the question, scope and model used.

**Reviewer: 2**

2. *The manuscript details a program of work aimed to inform improvements to CRC control in Australia; a key component being the current and proposed use of established micro-simulation modelling program (Policy 1 - bowel) to assess the economic and health impacts of various interventions. The research program described is well-designed and is likely to provide valuable, evidence-based recommendations to policymakers and public health professionals in Australia and other comparable nations. My suggestions relate to improving the clarity and accessibility of the manuscript.*

**We thank the reviewer for this comment and note that it contrasts with Reviewer 1 comment 3 (above). We address Reviewer 2’s detailed comments below, including clarifying the research questions and results.**

3. *Some concepts should be better explained for readers who are unfamiliar with these methodology/terms:*
  - a. *Line 47, page 6. It is not clear what the term “Pathways” is at this point - an initiative, a program of research, a model? Please provide brief explanation.*

*Thank you for the comment. We have clarified this wording by including ‘is a program of research’ and moving an explanatory sentence earlier in the text:*

**In view of the changing landscape of CRC control, “Pathways to a cancer-free future” (‘Pathways’) is a program of research that was developed to focus investment where the biggest impact can be made at a population level. It aims to identify the best-value investments, or “best buys”, in cancer control to inform future decision making.**

- b. *End of page 7 - first mention of Policy-1 and micro-simulation. It’s fine to refer readers to other sources for technical details, but the manuscript would benefit from a short plain English description of this key method. Please add a short paragraph summarizing the general method and purpose of micro-simulation modelling, ideally with an example in the context of this study.*

**Thank you for the comment. We have added the text below to replace the sentence that was previously in the paper (the strikethrough sentence below).**

**Policy1-Bowel is a comprehensive microsimulation platform that synthesises clinical, epidemiological, demographic, behavioural and economic data and has been used to simulate the impact of CRC screening in Australia (15). Existing Policy1-Bowel evaluations have assessed a range of screening scenarios and provided estimates of CRC outcomes, resource utilisation and costs. They have, for example, analysed the use of various CRC screening test technologies and target age ranges for the NBCSP to inform Australian guidelines (19,20). ~~The platform has, thus far, been developed to evaluate the NBCSP (15,19,20).~~**

4. *The rationale for selecting each intervention to evaluate is clear. The methods involved in collecting data to enter into the micro-simulation is less well-explained and should be expanded. It is touched on very briefly on page 8 - line 33 when the authors write "Pathways-Bowel will synthesize the existing evidence to determine the likely impact on CRC outcomes in the future". Please include a summary of the sources of data that are/will be used to inform the evaluations in this study towards the beginning of the methods section.*

**Thank you for this comment. We agree that the data sources are not clear, and we have added information to remedy this throughout the paper. As outlined in response to point 5b. We have included that "Policy1-Bowel is a comprehensive platform that synthesised clinical, epidemiological, demographic, behavioural and economic data and has been used to simulate the impact of CRC screening in Australia (15)."**

**We have also added the following clarification to the end of the Modelling platform: Policy1-Bowel section. "For modelled evaluations of CRC interventions, data are sourced from national surveys and data collection agencies (e.g. Australian Institute of Health and Welfare: AIHW) and the published literature including meta-analyses, systematic reviews, randomised controlled trials, cohort studies and other relevant publications. Where empirical data are not available, the SAC and other experts are consulted to guide the assumptions used." We have also clarified the sentence mentioned in the comment and it now reads "Pathways-Bowel will synthesise the available evidence from national and international data sources and published evidence to estimate the likely impact on CRC outcomes in the future for modelled evaluations."**

5. *Please provide more detail in the aims/objectives at the end of the introduction to summarize the program of work (i.e., evaluations of interventions, research, modelling expert consultation etc). Although this is laid out in the following sections, a concise summary in the intro would be helpful.*

**Thank you for the suggestion. We have revised the aim to read "The aim of the current article is to outline the design and objectives of Pathways-Bowel. Pathways-Bowel will inform ongoing and planned modelled evaluations of CRC interventions by integrating: expert and end-user engagement; relevant evidence; modelled interventions to guide future research investment; and policy-driven implementation of interventions using evidence-based methods." This is concise and we have chosen to be brief in order to respect the word count without repeating the details that are more comprehensively explained later, as acknowledged by the reviewer.**

6. *Page 6, Line 32: Suggest using "best investment or value" here as "best buy" is defined after this.*

**Thank you for this suggestion. We have changed the text to read "Pathways-Bowel (and all Pathways) uses a common framework so the best value investment, or "best buys", can be compared within and between groups"**

7. *Page 6, Line 33: Please provide a citation for the statement "On current evidence, the best buy in CRC control is increasing participation in Australia's National Bowel Cancer Screening Program (NBCSP)"*

**Reference #15 has been added here.**

8. *Page 7, Lines 27 - 40: Check the use of past and present tense here.*

**This has been reviewed and modified.**

9. Page 7 to 8. It appears that the reader is referred to Figure 1 for a depiction of model components/versions described in a-d, however, it is not clear from this image how b-d fit into the model - is something missing?

Thank you for this comment. Figure 1 is relevant for point a, Figure 2 is relevant for point b and points c and d provide more detail on the process used for evaluation. To aid the reader's understanding, we have revised the text for clarity and it now reads:

“It incorporates the development of CRC from adenoma (via the adenoma-carcinoma pathway) and sessile serrated lesions (via the serrated pathways) and survival from CRC (see Figure 1). Policy1-Bowel then incorporates screening for average-risk people, including post-screening diagnosis, treatment, and surveillance (Figure 2 summarises the current NBCSP screening delivery pathways included). As evaluations are conducted, single- or multiple-cohort approaches are used to simulate the development of polyps and CRC, screening, diagnosis and other downstream NBCSP processes in the target population over a time period of interest. The resulting evaluation is informed by Australian-specific demographic data and economic and health utilities data obtained from national and international literature (including cost and quality-adjusted life-years) to produce cross-sectional results for the population.”

#### VERSION 2 – REVIEW

<b>REVIEWER</b>	Belinda Goodwin Cancer Council Queensland
<b>REVIEW RETURNED</b>	23-Mar-2020
<b>GENERAL COMMENTS</b>	The authors have addressed my comments well.