PEER REVIEW HISTORY

ARTICLE DETAILS

TITLE (PROVISIONAL)	Clinicians' opinions on recommending aspirin to prevent colorectal cancer to Australians aged 50 to 70 years: a qualitative study
AUTHORS	Milton, Shakira; McIntosh, Jennifer; Yogaparan, Thivagar; Alphonse, Pavithran; Saya, Sibel; Karnchanachari, Napin; Nguyen, Peter; Lau, Phyllis; Macrae, Finlay; Emery, Jon

VERSION 1 – REVIEW

REVIEWER	Jennifer Weiss University of Wisconsin School of Medicine and Public Health
REVIEW RETURNED	23-Aug-2020

GENERAL COMMENTS	The authors conducted a qualitative study using semi-structured interviews with a multi-disciplinary group of providers examining their knowledge, attitudes, practices, and barriers and facilitators to the implementation of new guidelines on use of low-dose aspirin to reduce CRC risk. The variety of providers and healthcare settings was appropriate, as well as the use of the CFIR framework to guide the interview questions and analysis. I have the following suggestions to make this manuscript even more impactful: 1. in both the abstract and the introduction, the authors state that they aimed to explore clinicians' "attitudes, practices, knowledge, opinions, and barriers and facilitators". The words "attitudes" and "opinions" are synonyms - I recommend choosing one of them. 2. Introduction, line 86 - Add the abbreviation "CVD" after cardiovascular disease since this abbreviation is used later in the introduction in line 92. 3. Methods - I appreciate that the authors describe that interview questions were adapted from the online CFIR guide and supply the reference. If it is felt to be appropriate by the authors and the editors, it might be helpful to include a copy of the actual interview questions as supplemental material with the manuscript. 4. Results, lines 143 and 145-146 - These sentences can be combined to the following, "Interviews ranged from 20-50 minutes and were face-to-face in the participants place of work (clinic, pharmacy or hospital consulting or meeting room), except for four GPs who were interviewed on the phone." 5. Table 1 - Include the total number of participants in the title of the table - this will help as a reference point if someone is quickly looking at the table.

	6. Add a second table that maps themes using the CFIR framework to quotes from the interviews and subsequent interventions that can be used to address the issues identified by the study participants. All of this information is within the text of the manuscript, but a table would provide an overall take home message at a glance. Including the potential interventions (e.g., pharmacists on the front lines to assist with discussions about aspirin, decision-aid to help with patient-provider conversations, stronger wording in guidelines) would be a nice lead into the discussion section.

REVIEWER	Gladys Honein-AbouHaidar American University of Beirut, Lebanon
REVIEW RETURNED	23-Oct-2020

GENERAL COMMENTS	The manuscript is a very welcome contribution to the literature. The research question and the study design are appropriately reported and adequately addressed. I have some major and other minor comments that I thought are important to be addressed to improve the quality of reporting the study. I. Abstract Line 46. 'Coding was inductive and themes were developed through consensus between the authors'. The interview questions were based on a theoretical framework (CFIR) and the themes were mapped according to the constructs of this framework. I think the approach was rather hypothetico-deductive rather than purely inductive. II. Introduction The Cancer Council Australia updated guidelines were issued in 2017. Three years after, are there any studies showing the level of recommendation of Aspirin by providers and compliance by patients. Understanding the current implementation status is an important factor motivating the study. III. Method Line 96: It is important to specify the type of qualitative research approach adopted e.g. descriptive, grounded theory etc… Line 99-102. "A constructivist paradigm was used to generate new ideas from participants, using interviews to explore current practice, knowledge and opinions toward recommending aspirin to people at average risk of CRC and potential barriers and facilitators to implementing the guidelines". It is unclear what is meant by constructivist? Is it interpretivist or simply exploratory? As the philosophical underpinning of the approach dictates the data analysis. Line 103-106: Sampling approach was purposive. Then on line 105, the recruitment was done through personal networks.. as well as snowball sampling. The latter two approaches cannot be slated as purposive. They are known as convenience sampling and snowball sampling. Also emailing and cold calling approaches were not clear. Was there an email/ phone number lists? Line 108-109: 'General practitioners, as private practitioners, were reimbursed $100 for their time as this group was the most difficult to recruit'. I am not totally convinced that this is ethically appropriate. I understand that the reason may be because those are private physicians and this is considered compensation for their time, but still it is an incentive that is used disproportionately. Often, it is recommended that researchers who opt to use

	incentives need to provide explanation for why an incentive is necessary for their study: Is it to avoid additional financial burden on individuals or is it to attract individuals to participate? If the main motive is to attract more individuals to participate, then ethical considerations may arise about potential financial motivation as risk factor in participation (Ref: Ayoub et al. The interaction of personal, contextual, and study characteristics and their effect on recruitment and participation of pregnant women in research: a qualitative study in Lebanon). Line 112-113: I think a brief paragraph describing CFIR's constructs is necessary for the reader. As a reviewer, I also had to debate whether the results were adequately categorized per construct. Lines 130-137: The data analysis approach is poorly described. First, there is a need to describe the data analysis approach. Was it thematic analysis (Braun and Clarke approach) or Framework analysis (here is an interesting reference: Hackett A, Strickland K (2018) Using the framework approach to analyse qualitative data: a worked example. Nurse Researcher. doi: 10.7748/nr.2018.e1580). Second, the data analysis steps are not adequately addressed. IV. Results Line 145: 'The interviews were conducted in participants' place of work' is repeated twice. Lines 152- 161: Just for consideration, the "confusion regarding the dose of aspirin to be used. While some participants were comfortable deciding on a dose within the 100 – 300mg range recommended in the guideline, others felt this range created uncertainty". This statement may be interpreted that there was confusion during the execution of the guideline under implementation process. Line 182-190: "Guidelines on the use of aspirin for disease prevention have changed over time, generating confusion among participants. Historically, aspirin was recommended for primary prevention of cardiovascular disease in certain at-risk patients, but guidelines were later altered, recommending it only for secondary prevention. Participants stated that it is hard to keep up with the latest recommendations, and that this ongoing change in advice caused reluctance to recommend them. (Quotation 1f). My understanding this statement is referring to changing evidence on using Aspirin for primary prevention of cardiovascular disease and not bowel cancer. If that is the case, then it should be slated under outer setting. Line 214-215: 'Cancer Council Australia was perceived as a trustworthy organisation and this gave greater weight and trust in the guidelines'. I considered this result as part of the "Characteristics of the intervention, evidence source" rather than 'outer setting". Line 252- 256: "The FCC staff were more knowledgeable of the guidelines, specifically as they work with populations at increased risk of CRC, and awareness of recommendations about aspirin use in people with Lynch syndrome. Whereas GPs, pharmacists and gastroenterologists were either unaware or had limited knowledge of the guidelines. (Figure 4. 256 quotations 4e and 4f)". This statement needs to be extensively discussed as a major barrier for implementation and explicitly addressed in the implementation strategy in the discussion. Lines 315-316, the authors re-iterate this finding but do not propose a strategy.

	V. Discussion The authors indicated in the purpose that they are ultimately interested in “developing implementation methods to increase the uptake of aspirin for CVD and CRC prevention, and reduce development of colorectal cancer in the Australian population”. In the discussion, the authors discussed the major factors influencing implementation but fell short of developing implementation methods to increase uptake of aspirin. For example, using the results of the CFIR framework, what suggestions to improve the characteristics of the intervention, inner and outer setting etc.. are necessary to increase uptake. Lines 328-339: Implications are very brief. What is the next step for this study? Any lessons learned for disseminating guidelines? Etc…

VERSION 1 – AUTHOR RESPONSE

Reviewer: 1
Reviewer Name: Jennifer Weiss

Reviewer: 2
Reviewer Name: Gladys Honein-AbouHaidar

Reviewer: 1
Institution and Country: University of Wisconsin School of Medicine and Public Health

Reviewer: 2
Institution and Country: American University of Beirut, Lebanon

Reviewer: 1

Comments to the Author
The authors conducted a qualitative study using semi-structured interviews with a multi-disciplinary group of providers examining their knowledge, attitudes, practices, and barriers and facilitators to the implementation of new guidelines on use of low-dose aspirin to reduce CRC risk. The variety of providers and healthcare settings was appropriate, as well as the use of the CFIR framework to guide the interview questions and analysis. I have the following suggestions to make this manuscript even more impactful:

1. in both the abstract and the introduction, the authors state that they aimed to explore clinicians' "attitudes, practices, knowledge, opinions, and barriers and facilitators". The words "attitudes" and "opinions" are synonyms - I recommend choosing one of them.
Thank you, we have omitted the word “attitude” from both the abstract and introduction

2. Introduction, line 86 - Add the abbreviation "CVD" after cardiovascular disease since this abbreviation is used later in the introduction in line 92.
Agreed and abbreviation added.

3. Methods - I appreciate that the authors describe that interview questions were adapted from the online CFIR guide and supply the reference. If it is felt to be appropriate by the authors and the editors, it might be helpful to include a copy of the actual interview questions as supplemental material with the manuscript.
We have added in the interview questions to the supplementary material section.

4. Results, lines 143 and 145-146 - These sentences can be combined to the following, "Interviews ranged from 20-50 minutes and were face-to-face in the participants place of work (clinic, pharmacy or hospital consulting or meeting room), except for four GPs who were interviewed on the phone." As this sentence is more concise, we have replaced the two sentences with this one.
5. Table 1 - Include the total number of participants in the title of the table - this will help as a reference point if someone is quickly looking at the table.
The total number of participants have been added to the caption of the table.

6. Add a second table that maps themes using the CFIR framework to quotes from the interviews and subsequent interventions that can be used to address the issues identified by the study participants. All of this information is within the text of the manuscript, but a table would provide an overall take home message at a glance. Including the potential interventions (e.g., pharmacists on the front lines to assist with discussions about aspirin, decision-aid to help with patient-provider conversations, stronger wording in guidelines) would be a nice lead into the discussion section.
A second table has been added that maps the themes from the research onto the five CFIR constructs.

Reviewer: 2

Comments to the Author
The manuscript is a very welcome contribution to the literature. The research question and the study design are appropriately reported and adequately addressed. I have some major and other minor comments that I thought are important to be addressed to improve the quality of reporting the study.

I. Abstract

Line 46. 'Coding was inductive and themes were developed through consensus between the authors'. The interview questions were based on a theoretical framework (CFIR) and the themes were mapped according to the constructs of this framework. I think the approach was rather hypothetico-deductive rather than purely inductive.
Thank you for your thorough feedback of our manuscript. We can see your point of view here, but we believe the coding itself was still inductive because it was done independently of the CFIR framework. Although our questions were informed by the CFIR framework, the participants were able to answer openly. We mapped the themes that emerged onto CFIR as a last step, therefore the coding is still inductive.

II. Introduction
The Cancer Council Australia updated guidelines were issued in 2017. Three years after, are there any studies showing the level of recommendation of Aspirin by providers and compliance by patients. Understanding the current implementation status is an important factor motivating the study.
With the publication of the guidelines, there was no implementation strategy and upon reviewing the literature there have not been any studies done of the implementation or rate of uptake for clinicians or compliance by patients.

III. Method
Line 96: It is important to specify the type of qualitative research approach adopted e.g. descriptive, grounded theory etc…
We've specified this type of qualitative research approach as a case study because the participants are reviewing the guidelines which provides new insights and opens new ideas for how to implement the guidelines into clinical care.

Line 99-102. "A constructivist paradigm was used to generate new ideas from participants, using interviews to explore current practice, knowledge and opinions toward recommending aspirin to people at average risk of CRC and potential barriers and facilitators to implementing the guidelines". It is unclear what is meant by constructivist? Is it interpretivist or simply exploratory? As the philosophical underpinning of the approach dictates the data analysis.
A constructivist paradigm was selected because the participants, although were presented with specific guidelines they were answered the interview questions from their own understanding and had different perspectives on what the guidelines meant for them and their patients. As a result of using a constructivist paradigm, new ideas about the guidelines and implementation were generated.

Line 103-106: Sampling approach was purposive. Then on line 105, the recruitment was done through personal networks.. as well as snowball sampling. The latter two approaches cannot be slated as purposive. They are known as convenience sampling and snowball sampling.
Also, emailing and cold calling approaches were not clear. Was there an email/ phone number lists?
Thank you, we have now updated the setting and sampling strategy section of the methods to address your above comments. We have also explicitly named the email staff list and clarified our cold calling methods.

Line 108-109: 'General practitioners, as private practitioners, were reimbursed $100 for their time as this group was the most difficult to recruit'. I am not totally convinced that this is ethically appropriate. I understand that the reason may be because those are private physicians and this is considered compensation for their time, but still it is an incentive that is used disproportionately. Often, it is recommended that researchers who opt to use incentives need to provide explanation for why an incentive is necessary for their study: Is it to avoid additional financial burden on individuals or is it to attract individuals to participate? If the main motive is to attract more individuals to participate, then ethical considerations may arise about potential financial motivation as risk factor in participation (Ref: Ayoub et al. The interaction of personal, contextual, and study characteristics and their effect on recruitment and participation of pregnant women in research: a qualitative study in Lebanon).
To address your concerns about us only reimbursing the GPs I've included what we submitted to our ethics committee at the University of Melbourne which was approved.

> *The general practitioner recruitment has been challenging as we are asking for 20-50 minutes of their time for a one on one interview during their working hours. We would like to reimburse them with a $100 Coles Myer group gift voucher. This will only be for the GPs who will be interviewed. General practitioners, unlike the other clinicians being interviewed in the project, regularly receive reimbursement for their time and expect it. The other clinicians in the project have also already been recruited without as much difficulty and do not regularly get reimbursed for participating in research so we have decided that it is not needed.*

Line 112-113: I think a brief paragraph describing CFIR's constructs is necessary for the reader. As a reviewer, I also had to debate whether the results were adequately categorized per construct.
We've added in a short description of the five CFIR domains. Figure 1 does list all 39 constructs which are quite easy to understand and expands on what the paragraph briefly covers.

Lines 130-137: The data analysis approach is poorly described. First, there is a need to describe the data analysis approach. Was it thematic analysis (Braun and Clarke approach) or Framework analysis (here is an interesting reference: Hackett A, Strickland K (2018) Using the framework approach to analyse qualitative data: a worked example. Nurse Researcher. doi: 10.7748/nr.2018.e1580).
Second, the data analysis steps are not adequately addressed.
We have expanded on the analysis section of the paper. Thematic analysis was employed here as after the first-level coding was completed and the themes were organically identified. We have expanded on this in the manuscript.

IV. Results
Line 145: 'The interviews were conducted in participants' place of work' is repeated twice.
We have revised this now.

Lines 152- 161: Just for consideration, the "confusion regarding the dose of aspirin to be used. While some participants were comfortable deciding on a dose within the 100 – 300mg range recommended in the guideline, others felt this range created uncertainty". This statement may be interpreted that there was confusion during the execution of the guideline under implementation process.
Although it could impact on the process during implementation, we believe the dose accurately fits within the characteristic of the Intervention.

Line 182-190: "Guidelines on the use of aspirin for disease prevention have changed over time, generating confusion among participants. Historically, aspirin was recommended for primary prevention of cardiovascular disease in certain at-risk patients, but guidelines were later altered, recommending it only for secondary prevention. Participants stated that it is hard to keep up with the latest recommendations, and that this ongoing change in advice caused reluctance to recommend them. (Quotation 1f). My understanding this statement is referring to changing evidence on using

Aspirin for primary prevention of cardiovascular disease and not bowel cancer. If that is the case, then it should be slated under outer setting.
Yes, this great observation. We have moved this section to the out setting.

Line 214-215: 'Cancer Council Australia was perceived as a trustworthy organisation and this gave greater weight and trust in the guidelines'. I considered this result as part of the "Characteristics of the intervention, evidence source" rather than 'outer setting".
Although the organisation is an aspect of the guidelines, we believe that the reputation of the organisation itself better reflects the outer setting so we have left this section as is in the manuscript.

Line 252- 256: "The FCC staff were more knowledgeable of the guidelines, specifically as they work with populations at increased risk of CRC, and awareness of recommendations about aspirin use in people with Lynch syndrome. Whereas GPs, pharmacists and gastroenterologists were either unaware or had limited knowledge of the guidelines. (Figure 4. 256 quotations 4e and 4f)". This statement needs to be extensively discussed as a major barrier for implementation and explicitly addressed in the implementation strategy in the discussion. Lines 315-316, the authors re-iterate this finding but do not propose a strategy.
We agree with your above comment and have now updated the discussion to explicitly address the barrier. The change can now be found in lines 353-356.

V. Discussion
The authors indicated in the purpose that they are ultimately interested in "developing implementation methods to increase the uptake of aspirin for CVD and CRC prevention, and reduce development of colorectal cancer in the Australian population". In the discussion, the authors discussed the major factors influencing implementation but fell short of developing implementation methods to increase uptake of aspirin. For example, using the results of the CFIR framework, what suggestions to improve the characteristics of the intervention, inner and outer setting etc.. are necessary to increase uptake.
Lines 328-339: Implications are very brief. What is the next step for this study? Any lessons learned for disseminating guidelines? We have updated our implications and limitations section to address your comments above.

VERSION 2 – REVIEW

REVIEWER	Jennifer Weiss University of Wisconsin School of Medicine and Public Health, Madison, WI, USA
REVIEW RETURNED	14-Dec-2020

GENERAL COMMENTS	Overall, the authors adequately addressed the reviewer concerns. I have only the following minor comments: 1. Introduction, second paragraph, second to last sentence - there is a period missing at the end of the sentence. 2. Introduction, last paragraph, first sentence - the comma between the words clinicians' and practices should be removed. 3. Methods - The authors talk about recruitment through snowball sampling. Snowball sampling is where research participants recruit other participants for a test or study. I don't see how social media posts and cold calling a list of providers fits the definition of snowball sampling. 4. Methods, fifth paragraph, fourth sentence - there is an extra period that should be removed at the end of this sentence 5. Methods, seventh paragraph - The following sentence is a little awkward and needs to be reworded, "Themes from each

	professional group type were discussed between the researchers brought together if they could be." I suspect that a word or two are missing from the sentence. 6. Results, Table 2 - In the response to reviewers, the authors state that the final number of participants have been added to the caption of the table, but I do not see it in the document. I suggest changing the caption to "Table 2. Characteristics of participants (N=64)" 7. Results, Table 3 - I really like the addition of this table to the paper, but I think the number 64 can be removed from the caption of this table.

REVIEWER	Gladys Honein-AbouHaidar American University of Beirut- Lebanon
REVIEW RETURNED	07-Dec-2020

GENERAL COMMENTS	None

VERSION 2 – AUTHOR RESPONSE

Reviewer: 1

Comments to the Author
Overall, the authors adequately addressed the reviewer concerns. I have only the following minor comments:

1. Introduction, second paragraph, second to last sentence - there is a period missing at the end of the sentence.
Thank you, Jennifer, for your comments on our manuscript. I've added on the period.

2. Introduction, last paragraph, first sentence - the comma between the words clinicians' and practices should be removed.
I've removed the comma.

3. Methods - The authors talk about recruitment through snowball sampling. Snowball sampling is where research participants recruit other participants for a test or study. I don't see how social media posts and cold calling a list of providers fits the definition of snowball sampling.
I have removed snowball sampling, as we attempted to recruit participants through others but didn't in the end.

4. Methods, fifth paragraph, fourth sentence - there is an extra period that should be removed at the end of this sentence
I have removed the extra period.

5. Methods, seventh paragraph - The following sentence is a little awkward and needs to be reworded, "Themes from each professional group type were discussed between the researchers brought together if they could be." I suspect that a word or two are missing from the sentence.
Great pick up, I've added in the missing word.

6. Results, Table 2 - In the response to reviewers, the authors state that the final number of participants have been added to the caption of the table, but I do not see it in the document. I suggest

changing the caption to "Table 2. Characteristics of participants (N=64)"
I've added in the (N=64) to table 2 as suggested.

7. Results, Table 3 - I really like the addition of this table to the paper, but I think the number 64 can be removed from the caption of this table.
I've removed 64 from this table as suggested.

Reviewer: 2
Competing interests 1: No competing interests