PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Underlying mechanisms of complex interventions addressing the care of older adults with multimorbidity: A realist review
AUTHORS	Kastner, Monika); Hayden, Leigh; Wong, Geoff; Lai, Yonda; Makarski, Julie; Treister, Victoria; Chan, Joyce; Lee, Julianne; Ivers, N; Holroyd-Leduc, Jayna; Straus, Sharon

VERSION 1 – REVIEW

REVIEWER	Peter O'Halloran School of Nursing and Midwifery, Queen's University Belfast
REVIEW RETURNED	27-Jul-2018

GENERAL COMMENTS	Thank you for an interesting review on an important topic. I think this contains valuable material which has been rigorously analysed and should be published. However, the paper needs to be re-organised to bring out the significance of the findings. Here are my major and minor recommendations. MAJOR The clarity and usefulness of the paper as a realist review would be greatly helped by a focus on the context-mechanism-outcome configurations as such in the results and discussion. These are quite well presented in Appendices 3-5 but are not presented as CMOs in the body of the text. You might consider bringing the 'General CMO configurations' material into the body of the text under programme theories and leaving the 'Details of CMO configurations to explain Program Theory' in the appendices. Related to this are your frameworks for disease prioritization and multi morbidity determinants. These are interesting but it is not clear how they articulate with your CMOs, so you may want to reconfigure these to reflect the CMOs. A focus on the CMOs would also help you to provide more detailed discussion, conclusions and recommendations. Your Discussion section does not discuss context, mechanism (see your title) or outcomes, which are the focus of a realist review. This would also help you to show that you have met your objectives (how and why effective multi-chronic disease management interventions influence health outcomes). One of the advantages of a realist review is that it can generate practical recommendations and allow service providers to take a diagnostic approach to their organisation - drawing on the review to help them consider their context, resources, and goals and what can feasibly be attempted. For example, in relation to achieving the outcomes of program theory 1, you could recommend that organisations recruit highly skilled individuals and provide additional training on teamwork

	(designed to promote mutual respect and role understanding), with robust communication systems - and so on. This focus on CMOs should then be reflected in your abstract. In the section 'Programme theory development' you describe two programme theories to be tested and refined. These do not seem to be programme theories to me but rather templates for programme theories. For example, 'Complex multi-CDM interventions in different settings [context(s)] may improve patient outcomes such as [outcome(s)] for older adults because of [mechanism(s)].' This is simply a very broad description of the CMO structure. So, I am not sure what you are driving at here. Perhaps this corresponds to Item 7 in the RAMESES list, 'Scoping the literature,' which may allow reviewers ' to identify provisional program theories.' If so, I suggest you report along these lines (showing how you arrived at provisional theories) and leave out your two 'programme theories'. The description of the studies lacks detail. Item 13 of RAMESES suggests 'possibly relevant characteristics of documents that may be worth reporting include, where applicable: full citation, country of origin, study design, summary of key main findings.' This is largely absent. Perhaps this will be in your other review when published but it could be provided as supplementary material here and summarised in the text to allow the reader to grasp the shape of the literature. MINOR Provide aims/objectives at the end of the introduction. Under 'Strengths and limitations' you bring in a Cochrane review and NICE guidelines. Consider bringing these into the introduction to help set the scene for your review. Figures are not labelled Figure 1, 2 etc. Figure 1 - some of the text in boxes is partially obscured. Avoid contractions (e.g. don't) Standardise spelling of programme.

REVIEWER	Marjan van den Akker Maastricht University, School CAPHRI, dept of Family Medicine, the Netherlands
REVIEW RETURNED	10-Sep-2018

GENERAL COMMENTS	Thanks for giving me the opportunity to comment in the interesting realist review. The realist review has an important role in bridging the gap between study results and the actual implementation of interventions in clinical practice The application of realist review is rather new, which also shows off in Pubmed (only 147 hits with 'realist review' in title). Probably, many readers will not be familiar with this methodology. It might therefore be helpful to elaborate a bit more on the how and why of realist review. How does the realist review (or do the authors) handle ambiguous results? All results are now presented as rather firm findings, but I can easily imagine some of the mechanisms described not to be confirmed by all studies. Relation to the systematic review not completely clear to me. Did the results of the systematic review serve as selection criteria for

	the realist review? Or was a separate search performed for this realist review? Why not add a RAMESES checklist? Instead of filling out the only partly appropriate PRISMA checklist? References in appendices are more than included in the reference list. It is unclear to me where the numbers higher than 74 refer to. Authors might want to include this recent realist review, which overlaps partly with the manuscript currently under review. Brown S, Lhussier M, Dalkin SM, Eaton S. Care Planning: What Works, for Whom, and in What Circumstances? A Rapid Realist Review. Qual Health Res. 2018:1049732318768807. Epub 2018/04/21. doi: 10.1177/1049732318768807. PubMed PMID: 29676217.

VERSION 1 – AUTHOR RESPONSE

Comments/Questions	**Response**	**Corresponding Manuscript Section:** Page #
1. Please revise the 2nd and 3rd bullet points of the "strengths and limitations" section after the abstract. Each point should relate to the design or methods of the study. What are the study's methodological strengths?	• We revised the 2nd and 3rd bullets: o *Our search strategy was in part informed by a Systematic Review investigating the effectiveness of multimorbidity interventions for older adults that we conducted alongside this Realist Review* o *We created a 3-step synthesis process drawn from meta-ethnography to separate units of data from articles, and to derive explanatory statements across them.*	**Strengths and limitations of this study:** 3
2. Can you please revise the "authors' contributions" section so that it is in line with the ICMJE criteria for authorship? See: http://www.icmje.org/recommendations/browse/roles-and-responsibilities/defining-	• We have made this edit in the manuscript	**Author contributions:**15

the-roleof-authors-and-contributors.html		
Introduction		
3. The application of realist review is rather new, which also shows off in Pubmed (only 147 hits with 'realist review' in title). Probably, many readers will not be familiar with this methodology. It might therefore be helpful to elaborate a bit more on the how and why of realist review.	• We elaborated a bit more on the Realist Review method: *Realist review is particularly relevant for making sense of complex interventions (such as those focusing on CDM) that have context-sensitive outcomes. It can add important contextual and mechanistic detail to existing knowledge on this topic16. Such detail is likely to contribute to the limited existing clinical practice guidelines on multi-morbidity management such as those developed by NICE17, by explaining the contexts in which intended and unintended outcomes are likely to occur. Additional resources about realist reviews can be found the RAMESES Project website [REF]. Our overall objective of this review is to: understand how and why effective CDM interventions influence health outcomes in older adults 65 years of age or older.*	**Background:** 4-5
4. How does the realist review (or do the authors) handle ambiguous results? All results are now presented as rather firm findings, but I can easily imagine some of the mechanisms described not to be confirmed by all studies	• We elaborated a bit more on this in the limitations section of the Discussion section: *Finally, it is important to note that since this analysis was interpretive and inductive, it is possible that another team of researchers would have arrived at a different set of programme theories that incorporate mechanisms*	13

	and contextual of multi-CDM interventions for older adults. Thus, these findings should only be used as potential mid-range theories to explore and interrogate.	

	• We also added how we addressed ambiguous results in the methods section: *When the consolidated statements seemed to disagree, we unpacked the concepts and further examined them, consulting our literature and content experts as necessary for additional data and insights.*	**Methods *(Analysis and synthesis process):*** 7
5. Relation to the systematic review not completely clear to me. Did the results of the systematic review serve as selection criteria for the realist review? Or was a separate search performed for this realist review?	• We added a sentence to clarify in the "Search Strategy" section: *Since we performed our realist review alongside our systematic review of multimorbidity interventions[13], the search strategy was done simultaneously for both reviews. As such, we identified potentially relevant articles for our realist review (i.e., to provide data to test our programme theories) through our systematic review search strategy (inception to December 2017)[13] and performed additional iterative, targeted searches as needed for the realist review[19]. An experienced information specialist performed these additional searches in Medline and Embase (Appendix 1).*	**Methods *(Search strategy):*** 5-6
CMO configurations		

6. The clarity and usefulness of the paper as a realist review would be greatly helped by a focus on the context-mechanism-outcome configurations as such in the results and discussion. These are quite well presented in Appendices 3-5 but are not presented as CMOs in the body of the text. You might consider bringing the 'General CMO configurations' material into the body of the text under programme theories and leaving the 'Details of CMO configurations to explain Program Theory' in the appendices.	• Although the results contain C-M-O configurations, we removed their labels from the manuscript to minimize reading complexity. However, we added a paragraph in the Results to provide a bit more explanation for this: *To make our findings more succint, in the following paragraphs, we have provided narratives that summarise the most important aspects of our programme theories. This approach obscures the detailed CMO configurations that underpin these narratives and may make our manuscript less useful for those interested in realist review methodology. To address this issue, we have provided indications of the CMO configurations that our narratives are based on. For those interested in seeing the links between our data and CMO configurations, please see Appendices 3-6 that explains the outcomes that may be achieved by the different intervention strategies used in care coordination under different contexts.*	**Methods (*Program theories):*** 8
	• Additionally, we updated both Figure 2 and Figure 3 to highlight the CMO configurations of our program theories	**Figure 2** **Figure 3**
7. Related to this are your frameworks for disease prioritization and multi morbidity determinants. These are interesting but it is not clear how they articulate with your CMOs, so you may want to reconfigure these to reflect the CMOs.	• Thank you for this comment. We have revised our frameworks (Figures 2 and 3) to better reflect the CMOs	**Figure 2** **Figure 3**

8. A focus on the CMOs would also help you to provide more detailed discussion, conclusions and recommendations. Your Discussion section does not discuss context, mechanism (see your title) or outcomes, which are the focus of a realist review. This would also help	• These are great suggestions and we agree that this is one of the benefits of doing a realist review. We added a "Recommendations" section in the Discussion to summarize our bottom-line messages: *Findings from programme theory 1 (i.e., care coordination interventions for multimorbidity management) suggests that health care providers may wish to use 1) Team-based or collaborative approaches that involve highly*	**Discussion *(Recommendations):*** 12-13

you to show that you have met your objectives (how and why effective multi-chronic disease management interventions influence health outcomes).	*trained clinicians providing holistic and coordinated care through effective interdisciplinary communication and collaboration, and the providsion of education and counseling to patients to address their disease(s), medications, and lifestyle; 2) Disease management programs via care protocols or plans, checklists, follow-up timetables, and treatment targets; and 3) Case management strategies for situations when there may be multiple and diverse*	
9. One of the advantages of a realist review is that it can generate practical recommendations and allow service providers to take a diagnostic approach to their 3rganization – drawing on the review to help them consider their context, resources, and goals and what can feasibly be attempted. For example, in relation to achieving the outcomes of program theory 1, you could recommend that organisations recruit highly skilled individuals and provide additional training on teamwork (designed to promote mutual respect and role understanding), with robust communication systems – and so on. This focus on CMOs should		

then be reflected in your abstract.		*providers involved in a patient's care. For programme theory 2 (i.e., disease prioritization in multimorbidity management) the specific types of disease prioritization approaches that health care providers may wish to consider is to work with patients to identify what symptoms are bothering them and why, and exploring options that are acceptable to both clinicians and patients for addressing their symptoms. For programme theory 3 (patient self-management in multimorbidity), the specific types of self management approaches that health care providers may wish to consider include not assuming that all patients are capable of self care, identifying who is capable of self care and to what extent and, and establishing with the patient what*	

		they need (eg. informtion, support etc.) to enable self care.	
10. In the section 'Programme theory development' you describe two programme theories to be tested and refined. These do not seem to be programme theories to me but rather templates for programme theories. For example, 'Complex multi-CDM interventions in different settings [context(s)] may improve patient outcomes such as [outcome(s)] for older adults because of [mechanism(s)].' This is simply a very broad description of the CMO structure. So, I am not sure what you are driving at here. Perhaps this corresponds to Item 7 in the RAMESES list, 'Scoping the literature,' which may allow reviewers ' to identify provisional program theories.' If so, I suggest you report along these lines (showing how you arrived at provisional theories) and leave out your two 'programme theories'	•	Thanks so much for this suggestion. We removed the rough programme theory templates, and re-wrote this paragraph to better reflect how we arrived at these theories: *Duplicate screening of 97 reports by two reviewers identified 18 documents that contained data that helped us to understand CDM interventions. Through team discussion and a Delphi survey amongst our team, we indentified that our initial programme theory would have to incorporate the following concepts: 1) CDM interventions are complex interventions that do provide different*	**Methods *(Program theory development):*** 5

		outcomes in different settings; 2) health prioritization is an important aspect of multimorbidity and; 3) interventions that consider patient values and circumstances, the evidence and the clinician's expertise were more likely to produce desired outcomes. We then used the data from our included studies to gradually refine our understanding of these concepts and how(if at all) they fit into our more refined programme theory developed from this review.	
11. The description of the studies lacks detail. Item 13 of RAMESES suggests 'possibly	•	We didn't provide a study characteristics table because we have a large number of included studies (n = 106). However, if this is needed, we can generate this.	**Not applicable**

relevant characteristics of documents that may be worth reporting include, where applicable: full citation, country of origin, study design, summary of key main findings.' This is largely absent. Perhaps this will be in your other review when published but it could be provided as supplementary material here and summarised in the text to allow the reader to grasp the shape of the literature.	We have summarized the study characteristics in the Results section (i.e., publication date, country of conduct, multimorbidity topic) as per the RAMESES criteria. If you do decide that a table is preferred, please let us know what other specific details you would like to have included in such a table.	
12. Provide aims/objectives at the end of the introduction.	• We have added an objectives sentence at the end of the Introduction: *Our overall objective of this review is to: understand how and why effective CDM interventions influence health outcomes in older adults 65 years of age or older.*	**Background:** 4-5
13. Under 'Strengths and limitations' you bring in a Cochrane review and NICE guidelines. Consider bringing these into the introduction to help set the scene for your review.	• Thank you for this suggestion. We have incorporated these into the introduction: *Realist review is particularly relevant for making sense of complex interventions (such as those focusing on CDM) that have context-sensitive outcomes. It can add important contextual and mechanistic detail to existing knowledge on this topic16. Such detail is likely to contribute to the limited existing clinical practice guidelines on multi-morbidity management such as those developed by NICE17, by explaining the contexts in which intended and unintended outcomes are likely to occur. Additional resources about realist reviews can*	**Background:** 4

	be found the RAMESES Project website..	
Figures and Appendices		
14. Figures are not labelled Figure 1, 2 etc.	We have labelled both figures	**Figure 1** **Figure 2**
15. Figure 1 - some of the text in boxes is partially obscured.	We have updated both figures to make sure all elements are clear	
16. Why not add a RAMESES checklist? Instead of filling out the only partly appropriate PRISMA checklist?	We have added the RAMESES checklist	**Appendix**
17. Kindly re-upload each figure under 'Image' file designation with at least 300 dpi resolution and at least 90mm x 90mm of width in either TIFF or JPG format.	We have uploaded higher resolution versions of the figures	**Figure 1** **Figure 2**
18. Please include Figure legends at the end of your main manuscript	We included Figure legends at the end of our manuscript	**16**
19. Kindly re-upload Appendices in PDF format.	We have uploaded a PDF version of the Appendices	**Apendices**
References		
20. References in appendices are more than included in the reference list. It is unclear to me where the numbers higher than 74 refer to.	We have re-organized and cleaned up the references so that they match throughout the manuscript and Appendices.	**Throughout document and Appendices**
21. Authors might want to include this recent realist review, which overlaps partly with the manuscript currently under review. Brown S, Lhussier M, Dalkin SM, Eaton S. Care Planning: What Works, for Whom, and in What Circumstances? A Rapid Realist Review. Qual Health Res. 2018:1049732318768807. Epub 2018/04/21. doi:	Thank you for alerting us to this article. We incorporated some of the findings into our Discussion: *A rapid realist review investigating the underlying mechanisms of care planning strategies found that the mechanisms driving positive outcomes for people with long-term conditions are those that motivate them and promote an understanding of their role in self-management and how their lifestyle affects their*	**Discussion *(Strengths and limitations):*** 13

10.1177/1049732318768807. PubMed PMID: 29676217.	*conditions [ref]. Our findings build on these studies by providing explanations for why multimorbidity interventions may be effective for older adults. Additionally, we focused exclusively on older adults because they represent a relatively unstudied population, and given their projected population growth, they urgently need our attention to optimize their care.*	
Spelling and grammar		
22. Avoid contractions	We have edited throughout the manuscript to avoid contractions	**Througout**
23. Standardize spelling of programme	We have standardized the spelling of programme	**Throughout**

VERSION 2 – REVIEW

REVIEWER	Peter O'Halloran Queen's University Belfast, United Kingdom.
REVIEW RETURNED	05-Dec-2018

GENERAL COMMENTS	Thank you for the opportunity to review this resubmitted paper. I asked you to consider bringing the 'General CMO configurations' material from Appendices 3-5 into the body of the text under programme theories, leaving the 'Details of CMO configurations to explain Program Theory' in the appendices. You have chosen not to do this but rather to draw the readers' attention to the appendices. I still think the CMOs in the appendices are clearer than the presentation in the body of the text. However, this is a matter of judgement about presentation of results rather than an issue that undermines the paper, so I leave that to you! The inserted CMO labelling of the Figures is good but I think you have mislabelled some of your constructs. So, in Figure 2, almost everything is labelled as a mechanism when in a number of cases there are better alternatives. For example, 'Reassurance that there are treatments that work; being closely monitored' These are facets of the program/interventions (things that service providers do) rather than mechanisms. Disease factors (on the provider side) - difficult to treat, uncomplicated etc. These are part of the context (they are pre-existing in the situation when the intervention is introduced) not mechanisms. Similar things happen in Figure 3. It is helpful to think of these constructs in the following ways: The intervention is the set of behaviours that are introduced into the clinical situation that are intended to produce the desired outcomes. Context is the spatial or geographical or institutional

	location into which programs are embedded where there are prior social rules, norms, values and interrelationships which limit the efficacy of program mechanisms. Mechanisms are the reasoning, beliefs, feelings, motivations, and choices of individuals and groups, which lead to patterns of behaviour that we recognize as outcomes. When an intervention is introduced, it changes the context (by providing further reasoning, opportunities, permissions, legitimations, authorizations, and limitations), so presenting people with a different set of circumstances in which to exercise agency, leading to different outcomes. See RAMESES II for details. I think you should review the constructs in your figures and label accordingly. The figures also need rubric. Study characteristics table: I understand the concern about the large number of papers - I guess that could be a decision for the editors. You asked for specific details on what to include in such a table. Of course that is up to you but headings might include 1. First Author, Country, and Objectives, 2. Population and Setting, 3. Design, Methods of Data Collection, and Methodological Rigor, 4. Key Results, 5. Explanation of the results (this is where you can bring in some realist analysis), 6. Contextual Features Thought to Influence Implementation.

REVIEWER	Marjan van den Akker Dept of Family Medicine, School Caphri, Maastricht University, Maastricht, The Netherlands
REVIEW RETURNED	17-Dec-2018

GENERAL COMMENTS	The authors have done a good job in revising their manuscript!

VERSION 2 – AUTHOR RESPONSE

Comments/Questions	**Response**	**Corresponding Manuscript Section:** Page #
The reviewer(s) have recommended publication, but also suggest some minor revisions to your manuscript. Therefore, I invite you to respond to the reviewer(s)' comments and revise your manuscript.		
CMO configurations		
1. I asked you to consider bringing the 'General CMO configurations' material from Appendices 3-5 into the body of the text under programme theories, leaving the 'Details of CMO configurations to explain Program Theory' in the appendices. You have chosen not to do this but rather to draw the readers' attention to the appendices. I still think the CMOs in the appendices are	• Thank you for your comments. It is a lot of complex information and we are hoping that putting the greater details in the appendix will make it easier for the reader.	**N/A**

clearer than the presentation in the body of the text. However, this is a matter of judgement about presentation of results rather than an issue that undermines the paper, so I leave that to you!		
2. Study characteristics table: I understand the concern about the large number of papers - I guess that could be a decision for the editors. You asked for specific details on what to include in such a table. Of course that is up to you but headings might include 1. First Author, Country, and Objectives, 2. Population and Setting, 3. Design, Methods of Data Collection, and Methodological Rigor, 4. Key Results, 5. Explanation of the results (this is where you can bring in some realist analysis), 6. Contextual Features Thought to Influence Implementation.	• Thank you for supplying the details for a potential study characteristics table. We are happy to provide this – should the editors desire it, but only sections 1-3 would be relevant for such a table for a realist review for the following reasons: ○ Section 4 is redundant because the units of data extracted from each study are synthesized across studies so there is little relevance (or space) to show results for individual articles ○ For sections 5 and 6 of your suggested column headings, we feel that these would cover only some aspects of our analyses and therefore some readers might wonder why we provide only details on context and not on mechanisms or even information on which CMOCs each article/document contributed data to. These are the main reasons why we don't think it's necessary to include a study characteristics table. ○ Also, a note about including "Methological rigor" within section 3. In a Realist review, typically, no formal quality appraisal is done using any specific checklist/tool. Usually the judgment of rigor is done at the	**Not applicable**

	level of the coherence of the programme theory *[Data gathering for realist reviews: Looking for needles in haystacks. Wong G. In: Emmel N, Greenhalgh J, Manzano A, Monaghan M, Dalkin S, editors. Doing Realist Research. London: Sage, 2018.]*	
Figures and Appendices		
3. The inserted CMO labelling of the Figures is good but I think you have mislabelled some of your constructs. So, in Figure 2, almost everything is labelled as a mechanism when in a number of cases there are better alternatives. For example, 'Reassurance that there are treatments that work; being closely monitored' These are facets of the program/interventions (things that service providers do) rather than mechanisms. Disease factors (on the provider side) - difficult to treat, uncomplicated etc. These are part of the context (they are pre-existing in the situation when the intervention is introduced) not mechanisms. Similar things happen in Figure 3. It is helpful to think of these constructs in the following ways: • The intervention is the set of behaviours that are introduced into the clinical situation that are intended to produce the desired outcomes. • Context is the spatial or geographical or institutional location into which programs are embedded where there are prior social rules, norms, values	We thank the reviewer for these helpful comments and have taken them into consideration in making our revisions. We have discussed these comments and addressed them in the following ways: **FIGURE 2** a) We have removed the labels to C's, M's and O's in this Figure. This is because on discussion and reflection prompted by the comments we believe that this figure better represents a simplefied overall programme theory that has the purpose of providing our findings in a way that is more familiar and accessible to providers and patients that may wish to optimize disease prioritisation (rather than as a summary representation of our CMOCs). b) To drive home our point above, we have revised the text in page 11 of our manuscript to the following: To clarify what Figure 2 represents; we have changed a section of text on page 10 of our manuscript to: • *"For this simplefied overall programme theory, we have analysed and interpreted our findings in such a way as to provide a programme theory that presents out findings in a more familiar format using the concepts of 'barriers' and 'facilitators'. The prpgramme theory sets*	**Results:** Page 10

and interrelationships which limit the efficacy of program mechanisms. Mechanisms are the reasoning, beliefs, feelings, motivations, and choices of individuals and groups, which lead to patterns of behaviour that we recognize as outcomes. When an intervention is introduced, it changes the context (by providing further reasoning, opportunities, permissions, legitimations, authorizations, and limitations), so presenting people with a different set of circumstances in which to exercise agency, leading to different outcomes. See RAMESES II for details. • I think you should review the constructs in your figures and label accordingly. The figures also need rubric.	*out the factors that need to bbe taken into account if providers and patients wish to optimize disease prioritzation. In particular we provide an overview of factors that health care providers may need to address to help patients to: 1) identify what symptoms are bothering them; 2) why they bother them and; 3) exploring options that are acceptable to them for addressing their symptoms."* c) We have provided a rubric / title for Figure 2 as follows: *"A simplified overarching programme theory identifying factors (conceptualized in the form of barriers and facilitators) that need to be considered when trying to optimize disease priotisation."* **FIGURE 3** We have taken a similar approach to Figure 3 as for Figure 2 for the very same reasons as set out above in a). We have revised the in the following ways to address the reviewers comments: i) We have removed the [C], [M] and [O] labels ii) We have provided a rubric / title for Figure 3 as follows: *"A simplified overarching programme theory of identifying factors (conceptualized in the form of barriers and facilitators) that need to be considered when tyring to provide optimize multimorbidity mangament."*	

VERSION 3 – REVIEW

REVIEWER	Peter O'Halloran Queen's University Belfast, United Kingdom

REVIEW RETURNED	28-Jan-2019

GENERAL COMMENTS	An ambitious and interesting paper.