PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Adapting Health Interventions for Local Fit when Scaling-up: A Realist Review Protocol
AUTHORS	Power, Jessica; Gilmore, Brynne; Vallières, Frédérique; Toomey, Elaine; Mannan, Hasheem; McAuliffe, Eilish

VERSION 1 – REVIEW

REVIEWER	Steven Ariss University of Sheffield UK
REVIEW RETURNED	07-Mar-2018

GENERAL COMMENTS	Excellent proposal. This study will make a significant contribution to knowledge and application. There are a few suggestions below that might be useful in preparing the final manuscript. However, nothing significant enough to suggest compulsory revisions. 1) P5: Re: "...tendency for effectiveness to taper with ongoing implementation." Also see: Parry, G. J. Carson-Stevens, A. Luff, D. F. McPherson, M. E. Goldmann, D. A. (2013) “Recommendations for Evaluation of Health Care Improvement Initiatives”. Academic Pediatrics. Vol. 13, S23-S30. & Ioannidis JPA. Contradicted and initially stronger effects in highly cited clinical research. JAMA. 2005;294:218–228. Also Rossi's Iron Law of Evaluation. 2) P8: "Identify what contextual factors influence whether these actions work and whether mechanisms are elicited in different settings." -Should this be how these actions work, rather than whether they work; looking at outcome patterns rather than binary results. 3) P16, L24: There is a bit of a jump from CMO extraction to construction of CMOCs. Also see P.12 L.15. -It will be expected for each case to only provide fragments of CMOCs, and not necessarily provide causal links or relationships. Whilst I think the approach for CMOC development can be eventually understood, it would be useful for the reader to have this explicitly described in light of the expected fragmentary evidence from each case, perhaps on P16?

REVIEWER	Dr Nicola Willand RMIT University, Australia
REVIEW RETURNED	22-Mar-2018

GENERAL COMMENTS	Overall, a review of how and why health interventions are upscaled effectively is a useful addition to the literature. A better understanding of the mechanisms that make local adaptations

	effective will be relevant to policy and program designers and may improve the implementation, upscaling or adaptation of health initiatives in varied contexts. The publication of the protocol will help avoid duplication and rigour to the study. However, the clarity of the paper could be improved in some sections. The review idea is original. The outcomes will fill an important gap in the literature. The assessment of the validity of the proposed review is guided by the *Quality standards for realist syntheses and meta-narrative reviews* (Wong et. Al. 2014). The effectiveness of scaling-up health interventions depends on their successful adaptation to the local context. Hence, the topic is appropriate for a realist review which tried to answer questions on what works, when, how, for whom and for how long. However, the research questions need to be articulated clearly in the protocol. The objectives stated in the paper will guide the data extraction. There seems to more clarity in the logic surrounding adaptations, actions and mechanisms. E.g. on page 9 *In the current research, we view actions that were carried out to achieve adaptations when scaling-up […] as a mechanism in the form of a resource.* Hence, actions are different from adaptations. Actions result in adaptations. Actions are mechanisms. The next sentence, however, suggests that actions produce mechanisms: *These actions […] may trigger a mechanism in the form or reasoning or response […]* Hence, mechanisms may produce mechanism, which is confusing. Similarly, the third objective is unclear: *Discover by what mechanisms do these actions work to achieve adaptations when scaling-up health interventions for local fit.* To guide the non-expert reader it may also help, if the links between scaling-up, adaptation and fidelity were addressed in one or two sentences before the authors go into more detailed description. An appropriate place may be under the heading introducing these concepts (page 4). The scope of the review appears very broad. It does not seem to be restricted to a specific health intervention, e.g. vaccination programs, or disease, e.g. HIV. It may be useful to allow for a focussing of the review. Figure 1 illustrates the generic stages of a realist review. The diagram would add more value, though, if it reflected the process already used and proposed for the further stages of this study. In particular, the involvement of the stakeholders should be shown. The construction of the initial programme theory is described in detail the section Stage 1. This section is sometimes too wordy and repetitive without added clarity. Many different frameworks were considered. The decision to use the one by Willis and colleagues

	should be justified. The description of the search strategy is detailed, sound and in keeping with realist review guidelines. The definitions of scale-up, health interventions and adaptations should be moved from the Stage 3 section to the Introduction section. The use of tenses is inconsistent. Stage 3 uses future tense to express that this is a search guide for a study which will still be conducted. The supplementary file 3 is referenced. The first sentence there is written in past tense (… evidence needed tomeet…). The dates of when which part of the study is or will be conducted need to be clearly stated. Explain "positive and negative adaptations". Re Stage 6 Explain the relation of the Irish realist Researcher Group and "stakeholder". Reflection on the use of stakeholders should be included. The article is generally well written, correctly referenced and provides excellent supplementary files, e.g. the Codebook. Abstract: Care should be taken to differentiate parts of the study which have already been completed and those that will be conducted in the future. E.g. *This protocol will describe the first stage of developing an initial programme theory framework, identifying potential actions,* … is misleading as the theory framework has already been developed. In addition, the methodology description should be specific to the study which is presented here rather than referring to Pawson's five stages. It is suggested that the review be registered with PROPERO (https://www.crd.york.ac.uk/prospero/) Reference Wong, G, Greenhalgh, T, Westhrop, G & Pawson, R 2014, *Quality standards for realist syntheses and meta-narrative reviews*, London, <http://www.ramesesproject.org/media/Quality_standards_for_RS_and_MNR_v4final.pdf>.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1.	
Overview: Excellent proposal. This study will make a significant contribution to knowledge and application. There are a few suggestions below that might be useful in preparing the final manuscript. However, nothing significant	Thank you for the encouragement on the study and for the helpful feedback that we have incorporated as noted below.

enough to suggest compulsory revisions.	
1) P5: Re: "...tendency for effectiveness to taperwith ongoing implementation." Also see: Parry, G. J. Carson-Stevens, A. Luff, D. F. McPherson, M. E. Goldmann, D. A. (2013) "Recommendations for Evaluation of Health Care Improvement Initiatives". Academic Pediatrics. Vol. 13, S23-S30. & Ioannidis JPA. Contradicted and initially stronger effects in highly cited clinical research. JAMA. 2005;294:218– PubMed ;228. Also Rossi's Iron Law of Evaluation.	Thank you for these references. Parry and colleagues added. Others also noted for further papers on this review.
2) P8: "Identify what contextual factors influence whether these actions work and whether mechanisms are elicited in different settings." - Should this be how these actions work, rather than whether they work; looking at outcome patterns rather than binary results.	Thank you for bringing this to our attention. Language amended to reflect this, please see page 8, that has now been changed to: *"Discover how these actions work by uncovering what mechanisms are triggered, in what contexts, to achieve adaptations when scaling-up health interventions for local fit."*
3) P16, L24: There is a bit of a jump from CMO extraction to construction of CMOCs. Also see P.12 L.15. -It will be expected for each case to only provide fragments of CMOCs, and not necessarily provide causal links or relationships. Whilst I think the approach for CMOC development can be eventually understood, it would be useful for the reader to have this explicitly described in light of the expected fragmentary evidence from each case, perhaps on P16?	Thank you for identifying where further clarification was needed. For a CMOC elicitation this will initially be kept to one case example (however that may include more than one source i.e. a peer reviewed article and a national report may be used for the same case example and CMOC elicitation), as this ensures that the C-M-O occurs together displaying generative causation. Demi-regularities will then be sought between the CMOCs of the different case examples. Clarification added in section on data synthesis (please see pg. 17 & 18). We have also addedclarification that only a selection of CMOCs from cases will be identified from each case where we have noted (pg. 18): *"To explore how these actions achieved adaptations, the CMOCs identified from each case example will be coded in NVivo to look for demi-regularities occurring across the different case examples. Therefore some, but not all, of the CMOCs from each case example may be identified based on whether demi-regularities were seen and if they add value to theory building and refinement at this stage. These results will be synthesized to make further sense of the findings and refine the theory."*
Reviewer 2	
Overview:	Thank you for encouragement and the helpful review guided by the Wong and colleagues

Overall, a review of how and why health interventions are upscaled effectively is a useful addition to the literature. A better understanding of the mechanisms that make local adaptations effective will be relevant to policy and program designers and may improve the implementation, upscaling or adaptation of health initiatives in varied contexts. The publication of the protocol will help avoid duplication and rigour to the study. However, the clarity of the paper could be improved in some sections. The review idea is original. The outcomes will fill an important gap in the literature. The assessment of the validity of the proposed review is guided by the Quality standards for realist syntheses and meta-narrative reviews (Wong et. Al. 2014). The effectiveness of scaling-up health interventions depends on their successful adaptation to the local context. Hence, the topic is appropriate for a realist review which tried to answer questions on what works, when, how, for whom and for how long. … The article is generally well written, correctly referenced and provides excellentsupplementary files, e.g. the Codebook.	(2014) quality standards.
The research questions need to be articulated clearly in the protocol. The objectives stated in the paper will guide the data extraction.	Thank you for identifying where further statement of research questions and clarity of objectives needed. Research questions now stated in protocol. Language of objectives clarified. Please note, they now read (pg. 8): "*Research questions:* *What are the actions that can be used to guide adaptations when scaling-up healthcare interventions?* *How do these actions work (i.e. by what mechanisms, and in what contexts)?* *Aims and Objectives* *The aim of this research is to develop theory on*

	what and how actions can be used in different contexts to make adaptations to health interventions for local fit when scaling-up across diverse contextsthat has practical application for implementers involved in scaling-up. *Objectives:* Ø *Identify what adaptations are being made in practice when scaling-up health interventions for local fit.* Ø *Identify what actions are used to achieve adaptations when scaling-up health interventions for local fit.* Ø *Discover how these actions work by uncovering what mechanisms are triggered, in what contexts, to achieve adaptations when scaling-up health interventions for local fit.* Ø *To put forward theories on what actions can be used, and how these actions may work to achieve adaptations when scaling-up health interventions for local fit, by identifying demi-regularities within the uncovered contexts and mechanisms."*
There seems to more clarity in the logic surrounding adaptations, actions and mechanisms. E.g. on page 9 In the current research, we view actions that were carried out to achieve adaptations when scaling-up [...] as a mechanism in the form of a resource. Hence, actions are different from adaptations. Actions result in adaptations. Actions are mechanisms. The next sentence, however, suggests that actions produce mechanisms: These actions [...] may trigger a mechanism in the form or reasoning or response [...] Hence, mechanisms may produce mechanism, which is confusing. Similarly, the third objective is unclear: Discover by what mechanisms do these actions work to achieve adaptations when	Thank you for identifying where more clarity was needed. For this research actions are viewed as mechanisms in the form of a resource. In keeping with Dalkin and colleagues' (2015) conceptualisation of mechanisms we agree that mechanisms (in the form of a resource) can trigger other mechanisms (in the form of reasoning). Clarity was added to the explanation of mechanisms and outcomes (pg. 9). Please note it has been changed to: *"Dalkin and colleagues[46] conceptualised mechanisms as either resources or reasoning. They put forward that a mechanism can be a resource which can be introduced in a context, which can trigger a mechanism in the form of response or reasoning, resulting in an outcome."* More details on definitions are also available in the codebook (supplemental file 5) for the reader. Language of objectives clarified (please see pg. 8 or text in box above).

scaling-up health interventions for local fit.	
The definitions of scale-up, health interventions and adaptations should be moved from the Stage 3 section to the Introduction section. To guide the non-expert reader it may also help, if the links between scaling-up, adaptation and fidelity were addressed in one or two sentences before the authors go into more detailed description. An appropriate place may be under the heading introducing these concepts (page 4).	Thank you for identifying where we could introduce and provide more explanation to the reader. These definitions have been moved to be introduction section of the paper. Opening sentences on scale-up, adaptation and fidelity added in introduction section prior to more detailed description. Please see page 4, where we now note: "*When scaling-up it can be necessary to adapt for local contexts as needs and resources may differ between scale-up sites [7 12]. By addressing and adapting for local fit, it can assist in successful implementation and sustainability of an intervention [12]. However, with adaptations there is also a need to ensure fidelity to the intervention theory and essential components to ensure the effectiveness of an intervention is not reduced or lost [7]*."
The scope of the review appears very broad. It does not seem to be restricted to a specific health intervention, e.g. vaccination programs, or disease, e.g. HIV. It may be useful to allow for a focussing of the review.	Thank you for this comment. We agree the scope is very broad at this stage and may need to be focused further at a later stage. This is in keeping with the non-linear iterative nature of realist reviews. We have re-run the pilot search terms put forward in supplemental file 3 as a test following this and there is a higher volume of results returned than when previously pilot tested while completing stage one. The specific search terms for each database will be further refined in consultation with the subject librarian when stage two takes place from June 2018. The supplemental file 3 has been amended to reflect this and now contains the concept headings and proposed databases only. As the focus of this review is on how adaptations are carried out during the process of scale-up rather than a specific disease or programme, we felt focussing on a disease or programme may limit the findings. Depending on the scope and breadth of what is returned in stage two it may be more beneficial to focus the review on a specific action or group of actions for making adaptations (e.g. those that involved participatory community approaches, or those that involving the generation of local evidence). Should this occur the decision-making process will be transparently reported in the research logbook and the dissemination, and further searches may take

	place as needed. We have also added the broad scope and potential need for further refinement to the strengths and limitations section (pg. 3): *"The scope of this review is ambitious within the time-frame, however in keeping with realist reviews this may befurther refined throughout the stages in light of findings from the literature or by stakeholder consultation"*
Figure 1 illustrates the generic stages of a realist review. The diagram would add more value, though, if it reflected the process already used and proposed for the further stages of this study. In particular, the involvement of the stakeholders should be shown.	We definitely take this point on board, however we wanted to introduce the non-expert reader to the standard realist review stages, (Figure 1), and to help clearly demonstrate how this methodology is appropriate for this complex topic. Figure 4 then provides a more detailed overview of the specific processes proposed under each of these stages for this review, to which the reader could then refer back to Figure 1 to see how our detailed process fit within the typical cycle.
The use of tenses is inconsistent. Stage 3 uses future tense to express that this is a search guide for a study which will still be conducted. The supplementary file 3 is referenced. The first sentence there is written in past tense (... evidence needed to meet...). The dates of when which part of the study is or will be conducted need to be clearly stated.	Thank you for highlighting this. The tenses have been clarified throughout. It is now clearly stated that stage one is completed. More clarification has been provided in the text that stages 2-6 will be carried out from June 2018 to March 2019 (please note on pg. 14 and revised supplemental file 3).
The construction of the initial programme theory is described in detail the section Stage 1. This section is sometimes too wordy and repetitive without added clarity. Many different frameworks were considered. The decision to use the one by Willis and colleagues should be justified.	Thank you for this helpful comment. This section was reviewed and edited for clarity. The Willis and colleagues review guided the realist methodology (in how to develop an IPT framework for this realistreview). While the other frameworks only guided the content (i.e. what went into the IPT framework in terms of scale-up or adaptation content). The Willis and colleagues review did both as the methods they used and also the findings and content were also relevant. This was not clear in the initial paper and more clarity was added on pg. 11 & 12.: *"The methodology and format of the IPT framework to guide this review was informed by Willis and colleagues[39] realist review, which focused on the process of scale-up of complex*

	interventions, identifying in their initial IPT framework actions, contexts and outcomes. After analysis and synthesis of three case studies they further identified what mechanisms were triggered to achieve scale-up of complex interventions and what contexts influenced this. Therefore, the Willis and colleagues[39] realist review provided an appropriate guide to inform the methodology for the IPT development for this review. In light of this method, this study developed an IPT framework focusing on what potential actions, contexts, mechanisms, distal outcomes and proximal outcomes may be of relevance to scale-up and adaptation."
Explain "positive and negative adaptations".	Sentence added (pg. 6) for more clarity. It reads: "…*With positive adaptations supporting implementation and achieving desired clinical outcomes, while negative adaptions could potential hinder or reduce these."*
Re Stage 6 Explain the relation of the Irish realist Researcher Group and "stakeholder". Reflection on the use of stakeholders should be included.	More details on Irish realist researcher group added, (pg. 18) and reads: *"This is a group of 8-10 researchers with experience in realist methods."* As noted in the paper under stage 6, stakeholdersfrom both the fields of research and practice of scale-up and adaptation will be sought. As this stage has not yet been completed and stakeholders are yet to be identified, exact details of the make-up of the stakeholders are cannot be added. Reflection on potential benefits added to this section (pg. 19) reading: *"This involvement of stakeholders with experience in adaptation and scale-up through research and practice, may assist in ensuring the findings are useful in practice for implementers in the field. The involvement of stakeholders will allow for initial dissemination of the research findings."* Note the benefits of use of stakeholders is also present in justification of realist review methods (pg. 10).

Abstract: Care should be taken to differentiate parts of the study which have already been completed and those that will be conducted in the future. E.g. This protocol will describe the first stage of developing an initial programme theory framework, identifying potential actions, ... is misleading as the theory framework has already been developed. In addition, the methodology description should be specific to the study which is presented here rather than referring to Pawson's five stages.	Thank you for identifying that clarity of timelines needed. Language clarified to address what has taken place and what is still to occur in abstract. The methods specific to this study followed the methodology of Pawson's five stages for realist review therefore it felt appropriate to reference this in abstract. The additional stage of stakeholder involvement will be used in this review which is stated in the abstract. Further in-depth details of the methods for each of these six stages was beyond the word count for the abstract.
It is suggested that the review be registered with PROPERO (https://www.crd.york.ac.uk/prospero/)	PROSPERO had previously been approached for registration however this review does not fit their criteria as it is not focused on a direct to patient intervention.

VERSION 2 – REVIEW

REVIEWER	Steven Ariss ScHARR University of Sheffield UK
REVIEW RETURNED	28-May-2018

GENERAL COMMENTS	An interesting and worthwhile study. Whilst I consider this paper adequate for publication in its current form, the following suggestions could strengthen the paper or the study: There doesn't seem to be a full consideration of limitations. For instance, a key methodological limitation of this type of study is the extent to which evidence to support the development of theories is available in the literature, and whether this evidence is representative of common experiences. It is not clear how limitations will be imposed on theory development or how theories might be prioritised in terms of, for instance, importance, relevance or likely frequency of being useful in the field. It would be useful if this were a consideration of the protocol. It might be worth considering linking with the emerging evidence from the Health Foundation Scaling-up programme (now in third round).

REVIEWER	Nicola Willand RMIT University
REVIEW RETURNED	17-May-2018

GENERAL COMMENTS	The authors have addressed all the issues I have raised in the review, and I am happy to recommend publication.

VERSION 2 – AUTHOR RESPONSE

We have added some further consideration and clarification on theory development and focusing of the review based on these helpful comments from the reviewer. This can be seen on page 17 (on the marked copy of the manuscript). With further clarification on page 12 and 18.

"Numerous theories may emerge from the literature. Therefore, further focusing of the review in an iterative fashion may be required. Focusing on particular theories may be guided by demi-regularities occurring across examples. However, it is acknowledged that frequency of occurrence may not necessarily correlate to importance in practice. Therefore, if certain areas are highlighted as particularly critical for successful adaptation by the literature this may also assist focusing of the review. This will be further be guided by stakeholder involvement to give a "reality check"[41], aiming to ensure the review will focus on what is of relevance and importance to those in practice. Decision making for this process will be recorded in the research logbook for transparency."