



# When to replicate systematic reviews of interventions: consensus checklist

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Replication is an essential part of the scientific method, yet replication of systematic reviews is too often overlooked, and done unnecessarily or poorly. Excessive replication (doing the same study repeatedly) is unethical and a cause of research wastage. This article provides consensus based guidance on when to replicate and not replicate systematic reviews.

The inability to replicate research findings in various scientific disciplines has been a concern.<sup>1,2</sup> Systematic

reviews are increasingly used as the basis for informing health policy and clinical practice decisions.<sup>3</sup> However, reliance on systematic reviews for decision making assumes that review findings would not change if the review was replicated (eg, methods for the review are repeated by an independent team of reviewers). Given insufficient capacity to replicate all systematic reviews, researchers should determine which reviews warrant replication.

The need for replication of systematic reviews arises from concerns or lack of clarity about the technical or statistical methods or the judgments made, such as the subjective decisions related to defining criteria for inclusion of the population, intervention or exposure, and outcomes of interest; and data collection, synthesis, and interpretation.<sup>4</sup>

The compelling scientific case for replicating systematic reviews is complicated by research waste concerns (eg, multiple reviews of the same question outnumbering the original studies).<sup>5,6</sup> The term “duplication” has been used to refer to needless, frequently unwitting or unacknowledged repetition without a clearly defined purpose for the repetition.<sup>7,8</sup> With finite research resources available and the risk of potentially misleading results being introduced due to unrecognised bias, the issues surrounding replication are intensified.<sup>9-11</sup>

In this article, we discuss criteria for applying replication appropriately. Recognising that the terminology and conceptual framework for replication is not standardised across the sciences, we define replication of systematic reviews of interventions as either:

- Direct replication by purposeful repetition to verify the findings of the original research question; or
- Conceptual replication by purposeful broadening or narrowing of the research question in existing systematic reviews (eg, across broader or more focused populations, intervention types, settings, outcomes, or study designs).

## SUMMARY POINTS

For systematic reviews of interventions, replication is defined as the reproduction of findings of previous systematic reviews looking at the same effectiveness question either by: purposefully repeating the same methods to verify one or more empirical findings; or purposefully extending or narrowing the systematic review to a broader or more focused question (eg, across broader or more focused populations, intervention types, settings, outcomes, or study designs)

Although systematic reviews are often used as the basis for informing policy and practice decisions, little evidence has been published so far on whether replication of systematic reviews is worthwhile

Replication of existing systematic reviews cannot be done for all topics; any unnecessary or poorly conducted replication contributes to research waste

The decision to replicate a systematic review should be based on the priority of the research question; the likelihood that a replication will resolve uncertainties, controversies, or the need for additional evidence; the magnitude of the benefit or harm of implementing findings of a replication; and the opportunity cost of the replication

Systematic review authors, commissioners, funders, and other users (including clinicians, patients, and representatives from policy making organisations) can use the guidance and checklist proposed here to assess the need for a replication

Both types of replication could include differences in systematic review methods (appendix box 1), which include, for example, whether to use traditional comprehensive reviews versus rapid reviews or living systematic reviews. They can involve either independently conducting an entire review or simply repeating a selected part, such as a reanalysis or subgroup analysis.

Systematic review updates and replications are overlapping, but not mutually inclusive.<sup>12</sup> The decision to conduct an update of a systematic review is largely driven by the availability of new data to answer the question of interest, and could occasionally be driven by the availability of new systematic review methods. An update including more data will usually increase the statistical precision of effect estimates. The update could, however, fail to resolve important differences related to previous reviews' technical procedures or subjective decisions, which is best protected against by independent replication.

Although criteria for when to update systematic reviews have been proposed,<sup>13 14</sup> systematic review organisations and research funders or commissioners lack tools to judge the need for replicating previous systematic reviews, and thus have no way of knowing whether replication should be prioritised or when such replications would be a poor use of resources or even waste.

We have developed a checklist and guidance to help decide when to replicate or not replicate systematic reviews of studies looking at the effects of interventions to improve health and wellbeing. The checklist can be used by systematic review authors and organisations, funders, commissioners, and groups developing guidelines, consumer decision aids, and policy briefs.

## Methods

Our methods are adapted from guidance for developing research reporting guidelines.<sup>15</sup> We formed an executive group (SK, LM, JP, JPP, PT, VAW) to gather opinions of stakeholders, review the literature, hold a face-to-face consensus meeting of key stakeholders, and draft the checklist and article (fig 1).

We used an integrated approach for knowledge translation (as previously described<sup>16</sup>), with an international multidisciplinary team of methodologists and knowledge users at every stage of this research. The methodologists were experts in clinical epidemiology, consensus methods, guideline development, health economics, information management, information science, knowledge translation, preclinical research, qualitative methods, and statistics. The knowledge users included commissioners, funders, and other users of systematic reviews, including clinicians, patients, and representatives from organisations involved with policy making. This team was involved in the planning of this project and contributed to the interviews, online survey, consensus meeting, this guidance, as well as the dissemination of the output.

Following empirical and opinion gathering steps (appendices 2-5), the executive group collected data

and developed a 12 item list of criteria for replication (appendix 6), for deliberation at a consensus meeting (6-8 February, 2019) in Wakefield, Canada. During the meeting, each candidate criterion was presented, along with relevant data from the key informant interviews, literature review, and online survey. One designated meeting participant provided a brief commentary on the criterion and two others facilitated an interactive discussion on its value in determining when to replicate systematic reviews. At the end of a 30 minute discussion for each criterion, participants were asked whether they supported the usefulness of an item when deciding when to replicate systematic reviews. Comments were transcribed and considered in subsequent iterations of the checklist.

Following the meeting, the executive group formed the writing group. They summarised the meeting discussions, revised the checklist, and drafted this guidance document. They sought feedback on the checklist and guidance document from all team members through phone meetings and two rounds of manuscript revision. The final checklist was agreed on by all participants through email.

## Patient and public involvement

Seventeen members of the Cochrane consumer group (that is, patients, their families and carers, and members of the public) were recruited as research participants to complete the online survey. Our core research team included two patient partners who are included as authors. They provided input on the grant application, participated in the key informant interviews, online survey and consensus meeting, reflected the voices of consumers who responded to the survey, and revised and approved the manuscript.

## Results

The consensus meeting was attended in person by 36 of the 54 research team members who were invited. They represented a range of disciplines and stakeholder groups. Extensive discussion and debate was conducted in relation to the overall definitions and approaches to replication, the potential use of the checklist, and each of its proposed items. At the end of the meeting, the executive group summarised the main points and provided an opportunity for participants to comment before preliminary agreement on the direction of the checklist was reached.

Participants at the consensus meeting agreed that every systematic review of a policy or practice relevant question should be seriously considered for replication. However, given limited resources, before deciding whether to replicate a systematic review, all existing systematic reviews and overviews of systematic reviews on the same question should be identified, and the added value of conducting a replication assessed. Given the absence of a robust evidence base to justify systematic review replication, the group agreed that a checklist would encourage its users to give due consideration to the pragmatic use

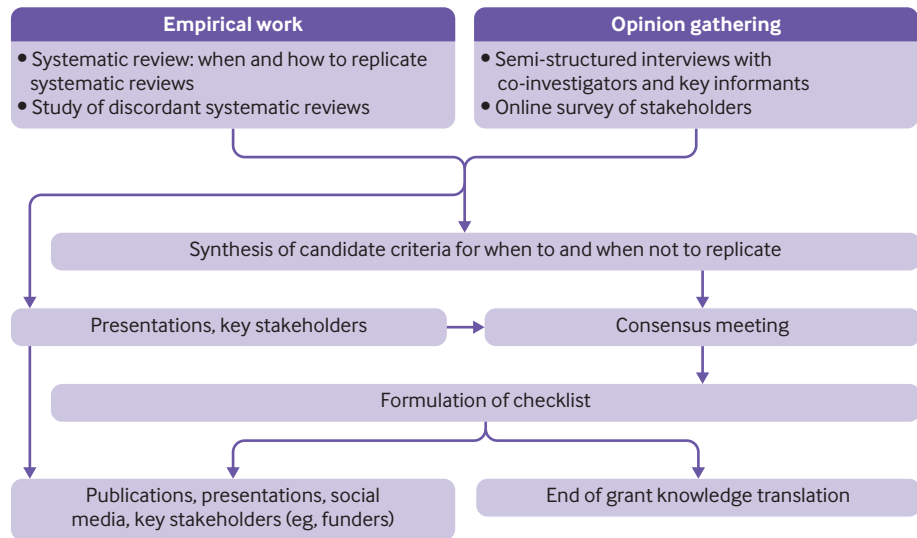


Fig 1 | Overall research plan: checklist development and dissemination

(clinical/policy/fiscal value) of conducting a project of this nature.

Since many of the discussions before the meeting focused on the implicit trade-offs between the benefits and costs of systematic review replication, participants agreed that the value of information (VOI) framework<sup>17 18</sup> could be helpful in developing criteria for when to replicate and when not to replicate prior systematic reviews. VOI is a quantitative approach that calculates the return on investment of conducting additional research (in this case, a replication of a systematic review) to generate clearer evidence to inform a clinical or policy decision, where decision uncertainty currently exists. Most VOI studies use cost effectiveness models to quantify the value of additional research. Based on the consensus meeting, the checklist adopted a conceptual VOI framework<sup>18</sup> and defined the value of systematic review replication as priority (question 1), potential implications (question 2), and potential impacts (question 3). Question 4 reflects the cost of a systematic review replication.

Participants at the consensus meeting decided collectively that the checklist needed to be a high level, simple tool that linked to available detailed tools for each step. For example, participants endorsed a general item on the methodological quality of previous systematic reviews; some quality assessment tools were suggested, such as AMSTAR-2,<sup>19</sup> which provide detailed guidance for users.

Participants also agreed that it would be important to consider the checklist items as examples of reasons for replicating rather than defining an exhaustive list, because some nuances in reasons for replication might be difficult to predict (eg, regarding concerns about conflicts of interest). Finally, participants concurred that replication methods would be driven by uncertainties expressed by users of the reviews (eg, patients and public, practitioners, press, professionals, policy makers). The specific uncertainty

would drive the selection of type of replication—direct replication by purposeful repetition or conceptual replication by purposeful broadening or narrowing, using permutations of previous review methods, data, or assumptions.

### Checklist

After the consensus meeting, the executive group formed the writing group. Members met regularly to revise the checklist on the basis of recommendations emerging from the meeting. The 12 item checklist was concentrated into four items. Some of the 12 items were subsumed under the four broader items. Other items were removed because they appear in the accompanying tools. For example, although the research team generally agreed that the durability of information produced through the replication was worth mentioning, this would generally be part of the item assessing the priority of a systematic review replication, and is included in priority setting tools such as the SPARK tool.<sup>20</sup>

Table 1 presents the final checklist for when a systematic review should be replicated. Checklist items are presented as questions to guide users. The checklist is aimed at systematic review authors and organisations, funders, commissioners, and groups developing guidelines, decision aids, and policy briefs; or anyone using systematic reviews of interventions as the basis of decision making. The extension statement (appendix 7) provides an explanation and example for each item.

### Application of the systematic review replication checklist: example

The checklist was applied to two systematic reviews that were considered under the Campbell International Development Coordinating Group (table 2). The first review was a replication of a 2015 Cochrane review on deworming to improve developmental health and

**Table 1 | Systematic review replication checklist**

Checklist items	Supporting methods and tools	Response options
Question 1. Has the priority for replication been assessed as high? For example, is it likely that a replication will remain relevant to policy and practice for a useful length of time? Is it likely for replication results to lead to implementation by practitioners and policy makers?	Priority setting tool (eg, SPARK tool, <sup>20</sup> James Lind Alliance, <sup>21</sup> CINARI <sup>22</sup> )	Yes / No
Question 2. Is it likely that direct replication by repetition or conceptual replication by broadening or narrowing of the scope will address uncertainties, controversies, or the need for additional evidence related to:		
2.1. The framing of the question in previous reviews?	Stakeholder engagement: James Lind	Yes / No
2.2. The conduct and reporting of previous reviews?	Alliance Priority Setting Partnerships <sup>21</sup> ;	Yes / No
2.3. Author influence or conflicts of interest in previous reviews?	conduct and reporting: AMSTAR-2, <sup>19</sup>	Yes / No
2.4. Discordant findings in previous reviews?	ROBIS <sup>23</sup>	Yes / No
Question 3. Would the implementation of the findings of a replication be likely to have a potentially important sizeable individual benefit or harm or affect a sizeable population?	—	Yes / No
Question 4. Are resources (time, money) best spent on replication rather than on alternative systematic reviews (considering opportunity cost)?	Stakeholder engagement priority setting	Yes / No

wellbeing,<sup>27</sup> and the second was an update of a 2012 Cochrane review on strategies to increase ownership of bednets to prevent malaria.<sup>28</sup> Both reviews involved simple, discrete, low cost interventions implemented by non-governmental organisations to manage a public health issue, with claims of a wide range of benefits. Responses to the checklist provided a strong justification for a replication of the first systematic review on deworming. A replication of the second review would be of much less value, because no substantive discordance was found and therefore would be less controversial.

#### Systematic review replication worksheet

Table 3 presents a replication comparative worksheet for appraising the body of evidence that can include multiple systematic reviews. The worksheet was developed by team members with expertise in guideline development, and it provides an example of

how the checklist can be adapted for use by decision makers. It delineates the decision making process of replication and proposes tools and instruments for each step, although some of these tools remain to be developed. The starting point is a specific question (known as the index PICO (population/intervention/comparison/outcome)) raised by a key stakeholder (eg, guideline panel). The PICOs of existing systematic reviews are then compared to the index PICO to assess their relevance. Other sources of uncertainty related to the conduct or reporting of existing reviews or conflicts of interest are also identified before determining whether a replication could reduce uncertainty related to the index PICO. The final decision to replicate a systematic review or not is based explicit consideration of benefits, harms, cost, feasibility, and acceptability of a given replication against other alternatives. We have plans for validating this worksheet in pilot studies with Cochrane and the Campbell Collaboration.

**Table 2 | Application of systematic review replication checklist on two example reviews**

Checklist items	Review 1: effects of mass deworming	Review 2: strategies to increase ownership and use of bednets
Question 1. Has the priority for replication been assessed as high using appropriate tools for setting research priorities?		
Is it likely for replication results to lead to implementation by practitioners and policy makers?	Yes	No
Is it likely that a replication will remain relevant to policy and practice for a useful length of time?	Relevant to Canadian Red Cross, WHO (update to deworming guidelines planned)	Not ranked as high priority as not being currently debated
Question 2. Is it likely that direct replication by repetition or conceptual replication by broadening or narrowing of the scope will address uncertainties, controversies, or the need for additional evidence related to:	Published critiques of the original review currently exist (long term studies excluded, data cut up, discrepancies with review by Hall et al <sup>24</sup> ), political controversy related to a replication of primary study by Miguel et al (impact of errors) <sup>25 26</sup>	No uncertainties or controversies had been raised
2.1. The framing of the question in previous reviews?	Yes	No
2.2. The conduct and reporting of previous reviews?	Yes	No
2.3. Author influence or conflicts of interest in previous reviews?	No	No
2.4. Discordant findings in previous reviews?	Yes	No
Question 3. Would the implementation of the findings of a replication be likely to have a potentially important sizeable benefit or harm or affect a sizeable population?	Yes, replication would have an important benefit for children in soil transmitted helminth endemic areas. Deworming is part of the implementation programmes for non-governmental organisations, with interest from WHO in updating its guidelines in 2016. Savings from ending deworming programmes could be transferred to education	No, because no change in findings or practice is expected; so no strong case for a sizeable benefit or harm
Question 4. Are resources (time, money) best spent on replication rather than on alternative systematic reviews (opportunity cost)?*	Resources are justified by the potential benefits of resolving the uncertainties around deworming	Although the cost of this update is much less than the deworming replication, the additional knowledge gained (that is, benefits) is also negligible

\*Costs of the exercise should be considered if difference in benefits are marginal.



Table 3 | Comparative worksheet for systematic review replication\*

2. Is it likely that replication will address uncertainties, controversies, or the need for additional evidence?							Trade-offs of replication assessed: 3. Would the implementation of the findings of a replication be likely to have a potentially important sizeable benefit or harm or affect a sizeable population? 4. Are resources (time, money) best spent on replication rather than alternative high priority SRs?	Decision whether to replicate
Step	1. Has the priority for replication been assessed as high?	2.1. Is the framing of the SR PICO not relevant enough to the PICO?	2.2. Is there poor conduct or reporting of the SR?	2.3. Are there concerns about the author influences or conflicts of interests?	2.4. Are there discordant findings across systematic reviews addressing the same question?	Overall assessment: Is it likely that replication will address uncertainties, controversies or the need for additional evidence?	Value of information framework	Judgment of SR team and decision makers based on previous steps
Sample tools and resources	Priority setting tools (eg. SPARK tool <sup>(26)</sup> )	GRADE relevance tool (under development), PICO mapping	AMSTAR-2, <sup>19</sup> ROBIS <sup>23</sup>	Conflict of interest funding verification	Jadad algorithm, <sup>29</sup> Moja et al methods, <sup>30</sup> discordance checklist	Based on answers to 2.1-2.4 (if “yes” to any of the questions)		
Evaluation of existing SRs and value of SR replication	Index PICO	Yes / No	Yes / No	Yes / No		Yes / No	Option 1: do not replicate, and use an existing SR.	
	SR1 (PICO1)	Yes / No	Yes / No	Yes / No		Yes / No	Option 2: partial replication (use existing SR after some fixing) or full replication (direct replication by purposeful repetition; conceptual replication by purposeful broadening or narrowing of the scope)	
	SR2 (PICO2)	Yes / No	Yes / No	Yes / No		Yes / No		
	SR3 (PICO3)	Yes / No	Yes / No	Yes / No		Yes / No		
	SR4 (PICO4)	Yes / No	Yes / No	Yes / No		Yes / No		
	SR5 (PICO5)	Yes / No	Yes / No	Yes / No		Yes / No		
	SR6 (PICO6)	Yes / No	Yes / No	Yes / No		Yes / No		
	SR ... (PICO ...)	Yes / No	Yes / No	Yes / No		Yes / No		
SR: systematic review; PICO=population/intervention/comparison/outcome.								

SR: systematic review; PICO=population/intervention/comparison/outcome.

## Discussion

Replication is a cornerstone of the scientific method, and critical to best practices; transparency; and accuracy of health, healthcare, and policy decisions. Although the need for purposeful replication of systematic reviews has been noted previously,<sup>31 32</sup> we provide here a structured approach to support this. Our systematic review replication checklist aims to provide guidance to authors, commissioners, funders, and other users of systematic reviews, including clinicians, patients, and representatives from organisations involved with policy making. Systematic reviews can often be subject to errors and ambiguity or uncertainty, owing to inaccurate data collection or analysis, as well as judgments and bias in how data are collected, analysed, and interpreted (eg, breadth of the question, criteria for inclusion, variables for adjustment, decisions about how data are combined). Replication should be optimised for appropriate selection of systematic reviews to replicate, while eliminating excessive waste of resources by unnecessary duplication.<sup>6 9</sup>

Because the checklist contains guidance considerations rather than formal mandatory items with only one correct approach, users must consider the relevance of each item, from the perspective of appropriate stakeholder. Use of the checklist might also stimulate additional questions that look at the unique characteristics related to replication in the substantive domain of interest. Users' increased familiarity with other supporting tools (eg, for prioritisation or quality assessment) will also facilitate use of this checklist. Most importantly, making a decision on whether to replicate requires a good understanding of the underlying body of evidence—that is, the extent, quantity, and quality of existing review (and primary study) results. This approach could require preliminary work, such as a scoping review.

The purpose of replication is to reduce but not necessarily to eliminate decisional uncertainty for translation of results into policy or practice. Identifying the specific sources of uncertainty to be resolved by the replication is therefore a key component of the checklist and will drive the design of the replication. Depending on the specific uncertainty or controversy, repeating only part of the review might be warranted. For example, when critics raised concerns about a systematic review on vaccines for human papillomavirus owing to the exclusion of unpublished reports,<sup>33</sup> the authors conducted a replication that focused mainly on a reanalysis after adding previously omitted data.<sup>34</sup> When author influence is a source of uncertainty, it is imperative to have an independent team conduct the replication. In other instances, author overlap between the original and replication reviews might be acceptable. All these associations should be declared in the published review. When considering each checklist item, users need to articulate what concerns or uncertainties of the previous reviews should be assessed and how a replication would resolve these concerns. Designing

replications to resolve specific sources of uncertainty in this way will limit the waste of research resources while contributing directly to the advancement of knowledge.

Recent guidance on when to consider updating systematic reviews<sup>13</sup> is relevant for assessing when replication of previous systematic reviews is likely to have value, for example, when new evidence has become available. However, such guidance does not ensure that uncertainties around the many judgments or choice of technical methods are addressed.

### Strengths

This checklist can help researchers decide whether scarce research resources should be dedicated to purposefully replicating previous systematic reviews to resolve uncertainties in the existing body of knowledge. The checklist was based on the input from multiple stakeholders including methodological experts, following a literature review, interviews, a structured survey, and a consensus meeting. A rigorous process was followed in consultation with representatives from key related disciplines and perspectives.

A varied set of examples of useful replication and wasteful duplication were used to ensure that the checklist is pragmatic. The Campbell Collaboration, Cochrane, and others represented at the meeting are now proposing to use the checklist to guide their decisions on when replication is warranted.

### Limitations

The usability, acceptability, and usefulness of the checklist will need to be assessed and tailored to different users. For example, we have proposed supporting tools, but others could be more suitable for specific review questions or users. Use of the checklist for other types of review questions beyond interventions needs to be evaluated. Furthermore, valid responses to the items depend on input from experts in both systematic review methods, as well as in the content area of the review question; both sources of information could be biased.

Application of the four item checklist requires time and human resources. However, our large team of stakeholders thought that the investment of resources for completing the checklist would be well justified given the potential value of replicating systematic reviews that inform policy and practice as well as the opportunity to limit waste related to unnecessary duplication.

Finally, the use of this checklist depends on stakeholders recognising the value of systematic review replication. Promoting the value of systematic review replication will be an important element in the dissemination and implementation of the checklist.

### Conclusions and next steps

This work emphasises the importance of systematic review replication as a necessary and useful element in the advancement of knowledge, along with the use of updates, living systematic reviews, and open evidence

synthesis. In view of the role of systematic reviews in policy making and guideline development, the validity and reliability of these updated findings should be tested. The checklist serves as an explicit prompt to carefully consider the value of replication alongside other options such as updating, new reviews, and overviews of reviews.

We will test and tailor the usability, acceptability, or usefulness of the tool with specific user groups as needed. A more detailed framework for identifying uncertainties and designing the replication response<sup>35</sup> is also being proposed as part of the guidance on how to replicate systematic reviews. Since this work focused on systematic reviews of interventions, its application to other types of review questions and involving other types of systematic reviews (eg, qualitative, scoping, diagnosis, and prognosis) should be explored.

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**Data sharing:** Background material for the consensus meeting are available on request from the corresponding author.

PT affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

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**Web appendix:** Supplementary appendix