

This is a repository copy of *Cochrane Qualitative and Implementation Methods Group Guidance Paper 4 : Methods for integrating qualitative and implementation evidence within intervention effectiveness reviews*.

White Rose Research Online URL for this paper:

<https://eprints.whiterose.ac.uk/126119/>

Version: Accepted Version

Article:

Harden, Angela, Thomas, James, Cargo, M et al. (7 more authors) (2017) Cochrane Qualitative and Implementation Methods Group Guidance Paper 4 : Methods for integrating qualitative and implementation evidence within intervention effectiveness reviews. *Journal of Clinical Epidemiology*. ISSN 0895-4356

<https://doi.org/10.1016/j.jclinepi.2017.11.029>

Reuse

This article is distributed under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs (CC BY-NC-ND) licence. This licence only allows you to download this work and share it with others as long as you credit the authors, but you can't change the article in any way or use it commercially. More information and the full terms of the licence here: <https://creativecommons.org/licenses/>

Takedown

If you consider content in White Rose Research Online to be in breach of UK law, please notify us by emailing eprints@whiterose.ac.uk including the URL of the record and the reason for the withdrawal request.

Accepted Manuscript

Cochrane Qualitative and Implementation Methods Group Guidance Paper 4:
Methods for integrating qualitative and implementation evidence within intervention
effectiveness reviews

Prof Angela Harden, Prof James Thomas, Assoc Prof Margaret Cargo, Dr Janet
Harris, Prof Tomas Pantoja, Dr Kate Flemming, Dr Andrew Booth, Dr Ruth Garside,
Assoc Prof Karin Hannes, Prof Jane Noyes

PII: S0895-4356(17)31354-9

DOI: [10.1016/j.jclinepi.2017.11.029](https://doi.org/10.1016/j.jclinepi.2017.11.029)

Reference: JCE 9548

To appear in: *Journal of Clinical Epidemiology*

Received Date: 13 May 2016

Revised Date: 4 November 2017

Accepted Date: 10 November 2017

Please cite this article as: Harden A, Thomas J, Cargo M, Harris J, Pantoja T, Flemming K, Booth
A, Garside R, Hannes K, Noyes J, Cochrane Qualitative and Implementation Methods Group
Guidance Paper 4: Methods for integrating qualitative and implementation evidence within intervention
effectiveness reviews, *Journal of Clinical Epidemiology* (2018), doi: 10.1016/j.jclinepi.2017.11.029.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to
our customers we are providing this early version of the manuscript. The manuscript will undergo
copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please
note that during the production process errors may be discovered which could affect the content, and all
legal disclaimers that apply to the journal pertain.



Cochrane Qualitative and Implementation Methods Group Guidance Paper 4: Methods for
integrating qualitative and implementation evidence within intervention effectiveness
reviews

Author names and affiliations

Prof Angela Harden (*Corresponding author*)^a, Prof James Thomas^b, Assoc Prof
Margaret Cargo^c, Dr Janet Harris^d, Prof Tomas Pantoja^e, Dr Kate Flemming^f, Dr
Andrew Booth^g, Dr Ruth Garside^h, Assoc Prof Karin Hannesⁱ, Prof Jane Noyes^j

^a Institute for Health and Human Development

The University of East London

Stratford Campus

Water Lane

London, UK

E15 4LZ

Email: a.harden@uel.ac.uk

Tel: +44 7961482404

^b UCL Institute of Education

University College London

20 Bedford Way

London, UK

Email: james.thomas@ucl.ac.uk

^c Spatial Epidemiology & Evaluation Research Group

Centre for Population Health University of South Australia

8th Floor Office 310, SAHMRI Building (North Terrace)

Adelaide, Australia

Email: margaret.cargo@unisa.edu.au

^d School of Health and Related Research (SchARR)

University of Sheffield

Regent Court, 30 Regent Street

Sheffield, UK

Email: janet.harris@sheffield.ac.uk

^e Department of Family Medicine, Faculty of Medicine

Pontificia Universidad Católica de Chile

Centro Médico San Joaquín, Av. Vicuna Mackenna 4686, Macul

Santiago, Chile

Email: tpantoja@med.puc.cl

^f Department of Health Sciences,

Faculty of Science, University of York

Seebohm Rowntree Building

Heslington

York, UK

Email: kate.flemming@york.ac.uk

^g School of Health and Related Research (SchARR)

University of Sheffield

Regent Court, 30 Regent Street

Sheffield, UK

Email a.booth@sheffield.ac.uk

^h European Centre for Environment & Human Health

University of Exeter Medical School

Knowledge Spa, Royal Cornwall Hospital

Truro, Cornwall, UK

Email: r.garside@exeter.ac.uk

ⁱ Social Research Methodology Group, Centre for Sociological Research

Faculty of Social Sciences

KU Leuven

Leuven, Belgium

Email: karin.hannes@kuleuven.be

^j School of Social Sciences

Bangor University

Bangor

Gwynedd, UK

Email: jane.noyes@bangor.ac.uk

Abstract

The Cochrane Qualitative and Implementation Methods Group (CQIMG) develops and publishes guidance on the synthesis of qualitative and mixed-method evidence from process evaluations. Despite a proliferation of methods for the synthesis of qualitative research, less attention has focused on how to integrate these syntheses within intervention effectiveness reviews. In this paper we report updated guidance from the group on approaches, methods and tools which can be used to integrate the findings from quantitative studies evaluating intervention effectiveness with those from qualitative studies and process evaluations. We draw on conceptual analyses of mixed methods systematic review designs and the range of methods and tools that have been used in published reviews that have successfully integrated different types of evidence. We outline five key methods and tools as devices for integration which vary in terms of the levels at which integration takes place; the specialist skills and expertise required within the review team; and their appropriateness in the context of limited evidence. In situations where the requirement is the integration of qualitative and process evidence within intervention effectiveness reviews, we recommend the use of a sequential approach. Here evidence from each tradition is synthesised separately using methods consistent with each tradition before integration takes place using a common framework. Reviews which integrate qualitative and process evaluation evidence alongside quantitative evidence on intervention effectiveness in a systematic way are rare. This guidance aims to support review teams to achieve integration and we encourage further development through reflection and formal testing.

Keywords: Systematic reviews, mixed methods research, qualitative research, implementation research, process evaluations, Cochrane Collaboration, qualitative evidence synthesis.

Running title: 'Integrating qualitative and implementation evidence within intervention effectiveness reviews'

What's new?

- Systematic reviews which integrate qualitative and process evaluation evidence alongside quantitative evidence on intervention effectiveness are rare.
- We offer guidance on the range of approaches, methods and tools which can be specifically applied to the stage within a review at which the findings from each type of research are integrated.
- We identify, outline and compare and contrast the characteristics of five key methods and tools as devices for integration which have been tested within reviews.
- Review teams can use this guidance to help them choose the most appropriate method for their context.

Introduction

Qualitative evidence syntheses have become firmly established as a distinct type of systematic review [1-3]. Many systematic review organisations and collaborations around the world now conduct systematic reviews of qualitative research and these are often commissioned alongside systematic reviews of quantitative studies assessing intervention effectiveness (i.e. the balance of benefit and harm of interventions) to underpin clinical guidance. The publication of the first qualitative evidence synthesis in the Cochrane Library signalled growing recognition of both the rigour and utility of this type of review [4-5].

Whilst qualitative evidence syntheses can make an important contribution in their own right, much of the impetus for the development of methods for synthesising qualitative evidence acknowledges their potential to add value to reviews of quantitative studies assessing intervention effectiveness. Questions of context, meaning and process, which qualitative evidence address, are of great importance for understanding why or how interventions work across and within different settings and populations [6-8]. Further drivers for integration include the complex interventions agenda where qualitative evidence can help to unpack the mechanisms through which interventions work [9-10]; the extension of evidence-based healthcare to policy areas which have traditionally valued qualitative approaches [11]; a frustration with 'empty reviews' [12]; and interest in mixed methods in primary research [13].

Our remit in this paper includes qualitative evidence from a range of sources: qualitative studies conducted alongside quantitative studies such as randomised controlled trials; stand-alone qualitative studies; and mixed methods process evaluations. Process evaluations are designed to assess a variety of questions including assessing intervention fidelity and reach, barriers to implementation and participant and provider experiences of the intervention [14]. The findings of qualitative research and process evaluations can be used to build programme theory [14-15]. A common approach conceptualises programme theory as comprised of a theory of action and a theory of change, both of which are shaped by broader

contextual factors, and feedback mechanisms [16-20]. The action component articulates what the programme will do to bring about the change(s) including what is required to support programme delivery. This component features program implementation, the heterogeneity of which is captured quantitatively or qualitatively through process evaluation. The theory of change specifies how programme strategies and program implementation generates the primary outcome through a set of intermediate impacts (i.e. mechanisms). This approach recognises that the same theory of action can generate similar or differential primary outcomes and that broader political, economic, social and cultural contextual factors are powerful shapers of program implementation and outcomes.

The aim of this paper is to provide guidance on the approaches, methods and tools that can be used to integrate the findings from quantitative studies evaluating intervention effectiveness with those from qualitative studies and process evaluations. By 'integrate' we mean combining the findings from different types of studies to produce a more comprehensive synthesis of the evidence on 'what works'?. . This paper does not focus on the steps required before the integration of different types of research evidence is carried out; for example, it does not provide guidance on formulating the research question, searching or protocol development for reviews of qualitative studies and process evaluations, and it does not address issues of quality assessment, data extraction, and synthesis of study findings (analysis and summary) or how to report the findings of a review of qualitative studies or process evaluations. These topics are covered by papers 1, 2, 3 and 5 in this series. This paper focuses on issues relating to integrating the findings of diverse types of evidence and not on methods for reviewing single types of evidence.

Methods for integration are less well developed than methods for synthesising qualitative research per se. The latter has seen the rapid emergence of methods over the last ten to fifteen years [1, 21]. However, methods papers focusing on integration are plentiful [22-27-23] and there are small but growing numbers of reviews aiming to integrate [28]. Further, the rapidly evolving methodology of realist review seeks to integrate different types of research evidence in order to understand

intervention context, mechanisms and outcomes [29-30]; and, within reviews, Qualitative Comparative Analysis aims to transcend the traditional qualitative / quantitative divide entirely [31-32]. Multiple challenges for integration persist such as the lack of worked examples and guidance, the additional expertise needed within review teams and an increase in the costs of conducting the review [33-34]. Tricco and colleagues identified seven emerging synthesis methods for integrating qualitative and quantitative data but found that more work was needed to provide fuller guidance on how to implement the methods.

Previous guidance from the Cochrane Qualitative and Implementation Methods Group was published in 2011 and covered question formulation, protocol development, searching, data extraction and synthesis of qualitative research [35]. In this paper we report an update on this guidance to cover the new topic of integration. We focus, firstly, on the opportunities for integration within Cochrane reviews and the potential of different approaches to integration. We then offer guidance on the methods and tools that can be used to achieve integration before discussing emerging methodological developments.

Opportunities for integration of qualitative and process evaluation evidence with quantitative studies within Cochrane reviews

There are two main opportunities for integration within Cochrane: i) conducting a 'post-hoc' qualitative or process evaluation evidence synthesis linked to a completed Cochrane review; and ii) conducting a new Cochrane review which plans to include a synthesis (analysis or summary) of qualitative and/or process evaluation evidence with quantitative studies assessing the intervention effectiveness from its beginning. In the first scenario, the qualitative or process evaluation evidence synthesis may be conducted by the same review team if team members have the necessary skills and expertise required; a different review team or a team combining new and original review team members. In the case of a totally different review team, the extent to which the findings of the new post hoc review can be integrated with the existing review depends on the level of collaboration with the original team.

A possible advantage of a new team would be bringing a fresh or more open perspective less likely to be sensitised to the issues raised by the trial evidence. Scenario two is more likely to feature a single review team, possibly comprising sub-teams for the synthesis of qualitative and process evaluation evidence and for the synthesis of quantitative studies assessing intervention effectiveness. The challenge in both scenarios is how to get the different types of research evidence within, or across, the reviews to 'speak' to each other.

Approaches to integration of qualitative and process evaluation evidence with quantitative studies in effectiveness reviews

Review methodologists working within a mixed methods framework— i.e. research that aims to combine qualitative and quantitative methods and findings - have applied mixed methods research designs for primary research to classify mixed methods review designs. These highlight dimensions of difference in review designs such as paradigm stance (e.g. positivist, interpretivist), sequencing of the qualitative and quantitative elements (e.g. qualitative studies are synthesised together first followed by a synthesis of quantitative studies) and the extent of integration (e.g. qualitative research used to inform design of quantitative synthesis or explain quantitative findings) [28, 36-37]. Pluye and Hong [28] consolidate these configurations and identify two main approaches to integrating qualitative and quantitative research evidence in 'mixed studies' reviews: sequential and convergent. We recommend this classification as a first step to navigate the options available for integration (table 1).

- Insert table 1 about here -

As the name suggests, the sequential approach is characterised by the sequence in which different types of evidence are synthesised and then linked. Within a Cochrane context both scenarios for integrating qualitative and process evaluation

evidence with quantitative studies assessing intervention effectiveness described above conform to a sequential approach.

In contrast to a sequential approach, which involves a degree of independence between the different syntheses before they are integrated, a convergent design uses a common framework to synthesise all types of research evidence from the start. Opportunities for taking a convergent approach within a Cochrane context are limited by the absence of exemplar reviews within the Cochrane Library. However, numerous exemplar reviews using a convergent approach have been published outside of the Cochrane Library (Table 1).

Although some review methodologies have been associated with either sequential or convergent approaches, we argue that the sequential and convergent distinction should be separate from the review methodology. The same review methodology can be used in both sequential and convergent designs. For example, critical interpretive synthesis has been used in a convergent design [38] as well as a sequential design [39].

Integration can take place at various levels within a review. The sequential and convergent distinction addresses integration at the review level. Integration can also take place at a theoretical level whereby different types of evidence within the review contribute to building and testing theory; at the level of themes and type of outcomes (i.e. the product of each of the syntheses conducted within a review); at the level of a particular cluster of studies within a review; and at the level of the individual findings of studies within a review.

Methods and tools for achieving integration of qualitative and process evaluation evidence with quantitative studies in effectiveness reviews

We outline the following methods and tools for integration: a) juxtaposing findings in a matrix; b) analysing programme theory; c) using logic models or other types of conceptual framework as a scaffold for integration; d) testing hypotheses derived

from syntheses of qualitative and process evaluation evidence that can be contextualised with evidence on implementation in trial reports using sub-group analysis; and e) qualitative comparative analysis (QCA) (table 2) (see also supplementary web only table 1). The use of qualitative comparative analysis for integration is a promising new methodological development; unlike the other methods and tools discussed here it does not yet have sufficient methodological guidance available. However, an exemplar review using QCA is forthcoming within the Cochrane Library [40]. These methods and tools were derived from an analysis of those used within reviews which have been conducted to date to integrate qualitative and quantitative studies to better understand intervention effectiveness. They were identified through the collective expertise of the Cochrane Qualitative and Implementation Methods Group supported by its methodological register of 8,000 titles. We restricted inclusion to those methods and tools which have been used within the context of a Cochrane review.

It should be noted that i) these methods represent specific techniques for integration and should be used in the context of the overarching methodological approach of the review(s) in which the integration occurs; and ii) some methods can be used in combination (e.g. patterns observed through juxtaposing findings within a matrix can be tested using sub-group analysis).

-Insert table 2 about here -

All these methods and tools can be used in a sequential review approach, but only analysing programme theory and using logic models and other types of conceptual frameworks can be used in a convergent approach. However, the methods vary in terms of the levels at which integration takes place; whether or not additional specialist skills and expertise are required within the review team; and the extent to which they are appropriate for situations in which there is limited evidence (Table 3).

- Insert Table 3 about here -

The methods and tools for integration also depend on the quantity of studies and extracted evidence available. The depth of what can be achieved is also dependent on the quality of description within included studies on factors such as intervention content, context and study findings.

a) Juxtaposing findings in a matrix

Integrating syntheses of qualitative and process evaluation evidence with reviews of quantitative studies assessing intervention effectiveness can be achieved by using a matrix to compare and contrast the findings across the different syntheses in a review. The matrix can be a product of the integration in its own right or it can be used as an adjunct to other methods.

A classic illustration of the use of a matrix for integration is offered by Thomas and colleagues [27] in a review to address how to promote healthy eating amongst children. This review included a thematic synthesis of qualitative evidence as well as a statistical meta-analysis of randomised and non-randomised trials. The qualitative evidence mostly came from studies unrelated to the trials. The thematic synthesis produced themes which captured children's beliefs and experiences of eating healthily (e.g. children prioritise taste over health). To prepare for integration, the review team translated the findings from the thematic synthesis into recommendations for interventions. They then listed these recommendations along one side of a matrix (e.g. promote fruit and vegetables as tasty rather than healthy). The interventions evaluated by the trials within the effectiveness synthesis were plotted against the recommendations for interventions as either a 'match' (when the intervention or an intervention component matched a recommendation) or a 'mismatch' (when the intervention or an intervention component was the opposite of a recommendation). Gaps were identified when a particular recommendation for an intervention did not match with any of the interventions evaluated within the trials. In the healthy eating example, a recommendation from the qualitative synthesis was

not to promote fruit and vegetables in the same way as fruit and vegetables were conceptualised very differently by children. None of the tested interventions followed this recommendation and this was identified as a research gap.

The use of a matrix allows review teams to explore heterogeneity in the findings of the quantitative studies and explain why some interventions are effective (or more effective) and some are not. Candy and colleagues [41] took this approach and demonstrated that interventions that significantly improved adherence to medication by people living with HIV contained more components considered important by patients than interventions where no statistically significant effect was found. Review teams can also use a matrix to illustrate how contextual factors can influence the implementation of effective interventions [39].

b) Using logic models and other types of conceptual frameworks

Logic models can play a role in articulating programme theory by “representing the underlying processes by which an intervention effects a change on individuals, communities and organisations” [15]. Logic models can be expressed visually, usually in the form of a diagram showing the links between intervention inputs and outputs. Logic models have been recommended as a tool to capture intervention complexity in systematic reviews [42-43] and are recommended in this paper as one variant of a conceptual framework to support the integration of different types of evidence.

Glenton and colleagues [44] used a logic model as the device for integrating the findings of their ‘post hoc’ qualitative evidence synthesis - on the barriers and facilitators to the implementation of lay health worker programmes to facilitate access to maternal and child health services – with the findings from the pre-existing Cochrane intervention effectiveness review on the same topic. The studies within the qualitative evidence synthesis were mostly unrelated to the trials. The findings of the synthesis revealed many factors affecting success which were presented thematically. Identified factors included those related to ‘lay health worker training, supervision and working conditions’ and ‘lay health worker-recipient relationship’.

Informed by the interventions and outcomes measured by the trials in the intervention effectiveness review, the review team further organised the findings from the QES into proposed 'chains of events' which specified how the outcomes that lay health worker programmes are expected to bring about could be achieved. They further identified potential threats to each chain of events. For example, one 'chain of events' was triggered by the selection criteria for lay health workers. Lay health workers were selected because they display personal qualities such as empathy and kindness are able to develop good relationships with service users. This relationship is hypothesised to lead to greater uptake of services and improved health outcomes. However, threats to these effects include the inability to maintain professional boundaries on the part of lay health workers, and service user preferences not to discuss sensitive issues with lay health workers from local neighbourhoods.

Using a logic model facilitates integration by providing a common framework or 'scaffold' within which both effectiveness research and syntheses of qualitative and process evaluation evidence can each contribute [43]. The initial logic model is developed and/or refined from the reports of completed studies. However, published studies (and the logic models built on them) may not capture the non-linearity of complex interventions [45-46]. Several authors have noted that it is difficult to derive adequate descriptions of programme theory or the operation of programmes in practice from published research [47-49]. One potential solution for this lack of contextual detail is greater involvement of practitioners, researchers and patients/members of the public within the review [50-51]. This can increase intersubjective and contextual validity [52].

As noted earlier a logic model is one variant of framework approach to integration. The same underpinning principle may equally translate from logic models to other types of model such as conceptual models or policy frameworks and requires further testing [53-54]. The framework may pre-exist, as in 'best fit' framework synthesis [53], or the framework for integration may be generated within the review process itself. In the latter case a user-focused framework could be generated through the

involvement of review stakeholders or through the synthesis of qualitative and process evaluation evidence.

c) Analysing programme theory

Using a programme theory approach to facilitate integration involves analysing the theories underlying how interventions are expected to work and then using the findings from trials, trial reports of implementation factors and those from syntheses of qualitative and process evaluation evidence to examine how the theory works in practice. This process may involve adjudicating on the value of different theories and recommending a new or refined theory of change for further testing in new research. Although grounded theory, critical interpretive synthesis, concept analysis, meta-ethnography, meta-interpretation and realist review can all be used to generate, explore and/or test theory in qualitative or mixed method evidence synthesis, the latter is the most explicitly focused on testing and refining program theory [33].

In a realist review, the initial programme theory is comprised of a series of context-mechanism-outcome (CMO) configurations that represent hypotheses or propositions concerning which outcomes are generated through which mechanisms in which context. Some reviews may advance more than one programme theory and these initial theories are prioritised to guide the review. Candidate theories are iteratively tested and refined on the basis of integrating evidence of effectiveness (i.e., what works) with evidence derived from qualitative studies and implementation research (i.e. how and why it works). The effectiveness evidence usually contributes to the outcome and mechanism components of a CMO whilst the qualitative and implementation evidence often contributes to the mechanism and context components of a CMO. A recent Cochrane protocol has outlined an exemplar review design that incorporates a realist component.

Working within the above realist review tradition, Greenhalgh and colleagues [54] re-analysed the trials included in a Cochrane review of the effectiveness of school feeding programmes (e.g. providing a nutritional supplement) for disadvantaged children. The review team sought out additional process information; either in the form of formal process evaluations or information about the process of implementing the intervention contained within trial reports. The team then integrated their analysis of the underlying theories of how the feeding interventions were expected to bring about change in trial reports (e.g. through short-term hunger relief, children feeling valued and looked after) and the findings of the trials and the process evaluations of how the theory worked or did not work in practice. As a consequence, the review team identified factors that enhanced or reduced the effectiveness of feeding programmes (e.g. putting measures in place to supervise children taking the supplement).

d) Testing hypotheses derived from QES using sub-group analysis

Methods and tools for integration outlined so far in this paper involve using the qualitative and process evaluation evidence to generate programme theory or hypotheses in relation to the trials evaluating intervention effectiveness. This can involve explaining why some interventions showed no effect. Equally, it might explain why the findings of the individual trials differed from one another. In situations where a substantial number of trials are included in the intervention effectiveness synthesis, and where there has been sufficient qualitative and process evaluation evidence uncovered to achieve a robust synthesis, exploration of differences can be supported by sub-group analysis.

In sub-group analysis studies are grouped together on the basis of shared characteristics in, for example, intervention type, population or findings. Hypotheses generated by syntheses of qualitative and process evaluation evidence can be tested by grouping studies according to the presence or absence of the proposition specified by the hypotheses to be tested. In the healthy eating review described above [27], the implications - or hypotheses - for interventions to promote healthy eating, derived from qualitative research on children's perspectives and experiences,

were used to group trials. So for example, to explore the hypothesis that interventions are more likely to be effective in promoting healthy eating if they emphasise taste rather than health, the effect sizes from trials testing interventions which emphasized health were compared to those from trials testing interventions which emphasised taste.

Using qualitative and process evaluation evidence to set the parameters for subgroup analysis can help review teams to better understand and communicate the reasons why findings on the effects of interventions can vary between individual quantitative studies. However, the extent to which subgroup analysis can successfully handle the complexity inherent in many interventions remains limited.

e) Qualitative comparative analysis

In situations where many sources of variation exist between interventions and the contexts in which they are evaluated, meta-analysis, subgroup analysis and meta-regression may identify that different interventions result in different outcomes, but are unable to explain why. For example, in a review about the effectiveness of long-term weight management schemes for adults, these schemes showed a statistically significant effect in terms of weight reduction [55]. However, the variation between the contents of the schemes, the contexts they were conducted in, and the results that they obtained, meant that they were unable to explain why some schemes were more effective than others. In order to better understand the sources of variation – and to try to identify the components which were associated with more effective interventions – Sutcliffe and colleagues conducted a mixed methods review, which combined a qualitative evidence synthesis with a ‘Qualitative Comparative Analysis’ (QCA) [56].

The team used thematic synthesis to examine participants’ and providers’ experiences of attending (and providing) weight management schemes to identify the range of *features* that they considered important for successful weight loss, and the *mechanisms* through which these features operated. The team then undertook a qualitative comparative analysis to test whether or not the aforementioned

features *were* associated with greater weight loss by examining the ten most effective and ten least effective programmes from the meta-analysis conducted by Hartmann-Boyce and colleagues. The use of qualitative comparative analysis facilitated a theoretically-driven exploration of 'necessary' and 'sufficient' conditions which were associated with effectiveness. Qualitative comparative analysis also overcame the limitations of the statistical approach in unpicking multiple potential pathways to effectiveness (i.e. the same intervention feature might be associated *both* with effective and less effective interventions, depending on context), and a lack of replicated evaluations (see [57] for further detail). The mixed methods approach enabled the team to provide fine-grained evidence on the features of successful weight management programmes, grounded in the experiences – and expertise – of users and providers of those programmes.

Conclusions

This paper offers new guidance – in the form of a coherent set of tried and tested approaches, methods and tools which are systematically compared and contrasted – to support the stage at which findings from qualitative and process evaluation evidence are integrated with the findings from quantitative studies assessing intervention effectiveness, particularly in the context of systematic reviews produced within the Cochrane Collaboration. The five methods and tools highlighted are also more broadly applicable for reviews conducted within other organisations including for example the Campbell Collaboration, the Agency For Health Care and Quality, 3iie and the EPPI-Centre.

Systematic reviews which include qualitative and process evaluation evidence as well as quantitative studies assessing intervention effectiveness remain rare, as is the use of systematic methods for integration. This guidance is therefore intended to raise awareness of the methods and tools that are available, to stimulate a change in reviewing practice towards the judicious use of systematic methods and tools, and to encourage further development through reflection and formal testing.

The methods and tools highlighted have undergone actual testing ‘in the field’ and do not include methods and tools with potential application to integration of qualitative and quantitative evidence within the context of Cochrane intervention effectiveness reviews. Methods and tools are still emerging (e.g. Bayesian synthesis [61-62], extensions to the matrix approach[65]) and it is important to generate more worked examples with published reflections on the key choices made and the challenges experienced. In a Cochrane context, reviews that fulfil this function are currently classified as ‘exemplar’ reviews in the Cochrane library.

Acknowledgements

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Angela Harden is supported by the National Institute for Health Research (NIHR) Collaboration for Leadership in Applied Health Research and Care (CLAHRC) North Thames at Bart’s Health NHS Trust. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health

References

- [1] Barnett-Page E, Thomas J. (2009) Methods for the synthesis of qualitative research: a critical review. *BMC Med Res Methodol.* 9: 59
- [2] Hannes K and Lockwood C. *Synthesizing Qualitative Research: Choosing the Right Approach* John Wiley & Sons, Ltd, Chichester, UK.
- [3] Sandelowski M, Barroso J (2007) *Handbook for Synthesizing Qualitative Research*. New York: Springer.
- [4] Glenton C, Colvin CJ, Carlsen B, Swartz A, Lewin S, Noyes J, Rashidian A. Barriers and facilitators to the implementation of lay health worker programmes to improve access to maternal and child health: qualitative evidence synthesis. *Cochrane Database of Systematic Reviews* 2013, Issue 10. Art. No.: CD010414. DOI: 10.1002/14651858.CD010414.pub2
- [5] Hannes K, Booth A, Harris J, Noyes J (2013) Celebrating methodological challenges and changes: reflecting on the emergence and importance of the role of qualitative evidence in Cochrane reviews. *Systematic Reviews* 2:84
<http://www.systematicreviewsjournal.com/content/2/1/84>
- [6] Cargo M, Harris J, Pantoja T, Booth A, Harden A, Hannes K, Thomas J, Flemming K, Garside R, Noyes J (submitted manuscript) Methods for question formulation, identifying and processing evidence on intervention implementation: Guidance from the Cochrane Qualitative and Implementation Methods Group. *Journal of Clinical Epidemiology*
- [7] Harris et al., (submitted manuscript) Methods for question formulation, searching and protocol development for qualitative evidence synthesis: Guidance from the Cochrane Qualitative and Implementation Methods Group. *Journal of Clinical Epidemiology*
- [8] Noyes et al. (submitted manuscript) Methods for assessing methodological limitations, data extraction and synthesis, and confidence in synthesized qualitative findings: Cochrane Qualitative and Implementation Methods Group Guidance. *Journal of Clinical Epidemiology*
- [9] Petticrew M, Rehfuess E, Noyes J, Higgins J, Mayhew A, Panjota T, Shemilt I, Sowden A (2013) Synthesizing evidence on complex interventions: how meta-analytical, qualitative, and mixed-method approaches can contribute. *Journal of Clinical Epidemiology*, 66: 1230–1243.
- [10] Sutcliffe K, Thomas J, Stokes G, Hinds K, Bangpan M (2015) Intervention Component Analysis (ICA): a pragmatic approach for identifying the critical features of complex interventions. *Systematic Reviews*, 4:140
- [11] Saini, M. & Shlonsky, A (2012). *Systematic synthesis of qualitative research: A pocket guide for social work research methods*. Oxford University Press.
- [12] Yaffe J, Montgomery P, Hopewell S, Shepard LD. Empty reviews: a description and consideration of Cochrane systematic reviews with no included studies. *PLoS One*. 2012 May 4;7(5):e36626

- [13] Johnson R, Onwuegbuzie A (2004) Mixed methods research: a research paradigm whose time has come? *Educational Researcher* **33**: 14-26.
- [14] Moore G, Audrey S, Barker M, Bond L, Bonell C, Hardeman W et al. (2015) Process evaluation of complex interventions: Medical Research Council guidance *BMJ*; 350 :h1258
- [15] Kneale D, Thomas J, Harris K (2015) Developing and Optimising the Use of Logic Models in Systematic Reviews: Exploring Practice and Good Practice in the Use of Programme Theory in Reviews. *PLoS One*, 10: 11.
- [16] Funnell SC, and Rogers, P.J (2011) *Purposeful Program Theory: Effective Use of Theories of Change and Logic Models*: John Wiley/Jossey-Bass.
- [17] Rossi PH, Lipsey MW, Freeman HE (2004) *Evaluation. A systematic approach*. 7th ed. Thousand Oaks: Sage Publications.
- [18] Suchman E. *Evaluative research* (1967) New York: Russell Sage Foundation.
- [19] Weiss CH (1972) *Evaluation research. Methods of assessing program effectiveness*. Englewood Cliffs, NJ: Prentice-Hall.
- [20] Chen H-T (2005) *Practical program evaluation. Assessing and improving planning, implementation and effectiveness*. Thousand Oaks, CA: Sage Publications; 2005
- [21] Booth, A., Noyes J, Flemming K, Gerhardus, A., Wahlster, P., Van Der Wilt, G.J., Mozygemba, K., Refolo, P., Sacchini, D., Tummers, M., Rehfues, E. (2016) Guidance on choosing qualitative evidence synthesis methods for use in health technology assessments of complex interventions [Online]. Available from: <http://www.integrate-hta.eu/downloads/>
- [22] Dixon-Woods M, Agarwal S, Jones D, Young B, Sutton A. (2005b) Synthesising qualitative and quantitative evidence: a review of possible methods. *J Health Serv Res Policy*. 10: 45-53.
- [23] Harden A, Thomas J (2010) Mixed methods and systematic reviews: examples and emerging issues. In A Tashakkori, C Teddlie (Eds) *Mixed Methods Handbook* (Second Edition). New York: Sage Publications
- [24] Heyvaert M, Hannes K, Onghena P (2016) *Using Mixed Methods Research Synthesis for Literature Reviews*. New York: Sage Publications.
- [25] Pluye P, Hong QN (2014) Combining the power of stories and numbers: Mixed methods research and mixed methods reviews. *Annu. Rev. Public Health* 35:29–45.
- [26] Sandelowski M, Voils C, Barroso J (2006) Defining and designing mixed research synthesis studies. *Research in the Schools*, 13:29-40
- [27] Thomas J, Harden A, Oakley A, Oliver S, Sutcliffe K, Rees R, Brunton G, Kavanagh F. (2004) Integrating Qualitative Research with trials in systematic reviews: an example review from public health shows how integration is possible and some potential benefits. *BMJ* 328: 1010-12

- [28] Pluye P, Hong QN (2014) Combining the power of stories and numbers: Mixed methods research and mixed methods reviews. *Annu. Rev. Public Health* 35:29–45.
- [29] Pawson R (2006) *Evidence-based policy: A realist perspective*. London: Sage
- [30] Wong G., Greenhalgh T., Westhorp G., Buckingham J. & Pawson R. (2013a) RAMESES publication standards: realist syntheses. *Journal of Advanced Nursing* 69 (5), 1005–1022. doi: 10.1111/jan.12095
- [31] Ragin C (2008) *Redesigning Social Inquiry: Fuzzy Sets And Beyond*. London: University of Chicago Press.
- [32] Thomas, J, O'Mara-Eves, A & Brunton, G (2014) 'Using Qualitative Comparative Analysis (QCA) in systematic reviews of complex interventions: a worked example. *Systematic Reviews*, 3: 67 [10.1186/2046-4053-3-67](https://doi.org/10.1186/2046-4053-3-67)
- [33] Booth, A., Noyes J, Flemming K, Gerhardus, A., Wahlster, P., Van Der Wilt, G.J., Mozygemba, K., Refolo, P., Sacchini, D., Tummers, M., Rehfues, E. (2016) Guidance on choosing qualitative evidence synthesis methods for use in health technology assessments of complex interventions [Online]. Available from: <http://www.integrate-hta.eu/downloads/>
- [34] Tricco AC, Antony J, Soobiah C, Kastner M, MacDonald H, Cogo E, Lillie E, Tran J, Straus SE, Knowledge synthesis methods for integrating qualitative and quantitative data: A scoping review reveals poor operationalisation of the methodological steps, *Journal of Clinical Epidemiology* (2016), doi: 10.1016/j.jclinepi.2015.12.011.
- [35] Noyes J & Lewin S. Chapter 6: Supplemental Guidance on Selecting a Method of Qualitative Evidence Synthesis, and Integrating Qualitative Evidence with Cochrane Intervention Reviews. In: Noyes J, Booth A, Hannes K, Harden A, Harris J, Lewin S, Lockwood C (editors), *Supplementary Guidance for Inclusion of Qualitative Research in Cochrane Systematic Reviews of Interventions*. Version 1 (updated August 2011). Cochrane Collaboration Qualitative Methods Group, 2011. Available from URL <http://cqrmg.cochrane.org/supplemental-handbook-guidance>
- [36] Harden A, Thomas J (2010) Mixed methods and systematic reviews: examples and emerging issues. In A Tashakkori, C Teddlie (Eds) *Mixed Methods Handbook* (Second Edition). New York: Sage Publications
- [37] Heyvaert M, Maes B, Onghena P. 2013. Mixed methods research synthesis: definition, framework, and potential. *Qual. Quant.* 47:659–76.
- [38] Dixon-Woods M, Agarwal S, Jones D, Young B, Sutton A. (2005) Synthesising qualitative and quantitative evidence: a review of possible methods. *J Health Serv Res Policy.* 10: 45-53.
- [39] Flemming K. (2010) Synthesis of quantitative and qualitative research: an example using Critical Interpretive Synthesis. *J Adv Nurs.* 66(1): 201-17.
- [40] Harris KM, Kneale D, Lasserson TJ, McDonald VM, Grigg J, Thomas J. School-based self management interventions for asthma in children and adolescents: a mixed methods

systematic review (Protocol). Cochrane Database of Systematic Reviews 2015, Issue 4. Art. No.: CD011651. DOI: 10.1002/14651858.CD011651.

[41] Candy, B., King, M., Jones, L., & Oliver, S. (2011). Using qualitative synthesis to explore heterogeneity of complex interventions. *BMC Medical Research Methodology*, *11*, 124. doi:[10.1186/1471-2288-11-124](https://doi.org/10.1186/1471-2288-11-124)

[42] Anderson LM, Petticrew M, Rehfues E, Armstrong R, Ueffing E, Baker P, Francis D, Tugwell P. Using logic models to capture complexity in systematic reviews. *Research synthesis methods*. 2011 Mar 1;2(1):33-42.

[43] Rohwer A, Booth A, Pfadenhauer L, Brereton L, Gerhardus A, Mozygemba K, Oortwijn W, Tummers M, van der Wilt GJ, Rehfues E. (2016) *Guidance on the use of logic models in health technology assessments of complex interventions*. <http://www.integrate-hta.eu/wp-content/uploads/2016/02/Guidance-on-the-use-of-logic-models-in-health-technology-assessments-of-complex-interventions.pdf>

[44] Glenton C, Colvin CJ, Carlsen B, Swartz A, Lewin S, Noyes J, Rashidian A. Barriers and facilitators to the implementation of lay health worker programmes to improve access to maternal and child health: qualitative evidence synthesis. *Cochrane Database of Systematic Reviews* 2013, Issue 10. Art. No.: CD010414. DOI: 10.1002/14651858.CD010414.pub2

[45] Allmark, P., Baxter, S., Goyder, E., Guillaume, L., & Crofton-Martin, G. (2013). Assessing the health benefits of advice services: using research evidence and logic model methods to explore complex pathways. *Health & social care in the community*, *21*(1), 59-68

[46] Baxter SK, Blank L, Woods HB, Payne N, Rimmer M, Goyder E. Using logic model methods in systematic review synthesis: describing complex pathways in referral management interventions. *BMC Medical Research Methodology*. 2014 May 10;14(1):1.

[47] Leeuw FL. Reconstructing programme theories: methods available and problems to be solved. *Am J Eval* 2003;24:5–20. <http://dx.doi.org/10.1177/109821400302400102>

[48] Pearson, M., Hunt, H., Cooper, C., Shepperd, S., Pawson, R., & Anderson, R. (2015). Providing effective and preferred care closer to home: a realist review of intermediate care. *Health & social care in the community*, *23*(6), 577-593.

[49] Weiss, C. (1998) *Evaluation: Methods for Studying Programs and Policies*. Englewood Cliffs, NJ: Prentice Hall.

[50] Anderson LM, Oliver SR, Michie S, Rehfues E, Noyes J, Shemilt I. Investigating complexity in systematic reviews of interventions by using a spectrum of methods. *J Clin Epidemiol* 2013; 66:1223–9.

[51] Oliver, K., Rees, R., Brady, L. M., Kavanagh, J., Oliver, S., & Thomas, J. (2015). Broadening public participation in systematic reviews: a case example involving young people in two configurative reviews. *Research synthesis methods*, *6*(2), 206-217.

[52] Harris J, Springett J, Croot L, Booth A, Campbell F, Thompson J, Goyder E, Van Cleemput P, Wilkins E, Yang Y (2015) Can community-based peer support promote health literacy and reduce inequalities? A realist review. *Public Health Research* 3: <http://dx.doi.org/10.3310/phr03030>

[53] Booth, A., & Carroll, C. (2015). How to build up the actionable knowledge base: the role of 'best fit' framework synthesis for studies of improvement in healthcare. *BMJ quality & safety*, bmjqs-2014.

[54] Greenhalgh T, Kristjansson E, Robinson V. (2007) Realist review to understand the efficacy of school feeding programmes. *BMJ*. 335: 858-861.

[55] Hartmann-Boyce J, Johns D, Aveyard P, Onakpoya I, Jebb S, Phillips D, Ogden J, Summerbell C (2013) The clinical effectiveness of long-term weight management schemes for adults (Review 1a) National Institute for Health & Care Excellence.

[56] Sutcliffe K, Richardson M, Rees R, Melendez-Torres GJ, Stansfield C, Thomas J (2016) What are the critical features of successful Tier 2 weight management programmes?: A systematic review to identify the programme characteristics, and combinations of characteristics, that are associated with successful weight loss. London: EPPI-Centre, Social Science Research Unit, UCL Institute of Education, University College London.

[57] Thomas, J, O'Mara-Eves, A & Brunton, G 2014, 'Using Qualitative Comparative Analysis (QCA) in systematic reviews of complex interventions: a worked example' *Systematic Reviews*, vol 3, no. 67., [10.1186/2046-4053-3-67](https://doi.org/10.1186/2046-4053-3-67)

[58] Harden A, Brunton G, Fletcher A, Oakley A (2009) Teenage pregnancy and social disadvantage: a systematic review integrating trials and qualitative studies. *British Medical Journal* 339:b4254v <http://www.bmj.com/cgi/content/full/bmj.b4254>

[59] Shepherd J, Harden A, Barnett-Page E, Kavanagh J, Picot J, Frampton G, Cooper K, Hartwell D, Clegg A. Using process data to understand outcomes in sexual health promotion: an example from a review of school-based programmes to prevent sexually transmitted infections. *Health Education Research*, 2014: Advance Access published Feb 1st: doi:10.1093/her/cyt155

[60] Candy, B., King, M., Jones, L., & Oliver, S. (2013). Using qualitative evidence on patients' views to help understand variation in effectiveness of complex interventions: a qualitative comparative analysis. *Trials*, 14(179). doi:[10.1186/1745-6215-14-179](https://doi.org/10.1186/1745-6215-14-179)

[61] Roberts K, Dixon-Woods M, Fitzpatrick R, Abrams K, Jones D. (2002) Factors affecting uptake of childhood immunisation: a Bayesian synthesis of qualitative and quantitative evidence. *The Lancet*, 360:1596-1599

[62] Voils C, Hasselblad V, Crandell J, Chang Y, Lee E, Sandelowski M. (2009) A Bayesian method for the synthesis of evidence from qualitative and quantitative reports: the example of antiretroviral medication adherence. *Journal of Health Service Research and Policy*. 14: 226-233.

[63] Wong G., Greenhalgh T., Westhorp G., Buckingham J. & Pawson R. (2013b) RAMESES publication standards: meta-narrative reviews. *Journal of Advanced Nursing* 69(5),987–1004. doi: 10.1111/jan.12092

[64] Aslam RW, Hendry M, Carter B, Noyes J, Rycroft Malone J, Booth A, Pasterfield D, Charles JM, Craine N, Tudor Edwards R, Ntambwe LI, Williams N, Whitaker R. Interventions for preventing unintended repeat pregnancies among adolescents (Protocol). *Cochrane Database of Systematic Reviews* 2015, Issue 1. Art. No.: CD011477. DOI: [10.1002/14651858.CD011477](https://doi.org/10.1002/14651858.CD011477)

[65] van Grootel L, van Wesel F, O'Mara-Eves A, Thomas J, Hox J, Boeije H (2017) Using the realist perspective to link theory from qualitative evidence synthesis to quantitative studies: Broadening the matrix approach. *Res Synth Methods*. doi: 10.1002/jrsm.1241. [Epub ahead of print] PMID: 28429447

Table 1: Sequential and convergent approaches to integrating qualitative and quantitative research¹

	Sequential	Convergent
Description	Research from each tradition synthesised separately using methods from that tradition. Findings across syntheses are then integrated using common frameworks or rubrics	Research from different traditions are integrated from the start using common frameworks or rubrics
Key examples and named methods	<p>Qualitative research on experiences integrated with quantitative studies assessing intervention effectiveness [27] [41] [58]</p> <p>Qualitative or mixed methods implementation research integrated with quantitative studies assessing intervention effectiveness [44] [59]</p> <p>Qualitative comparative analysis [56] [60]</p> <p>Critical interpretive synthesis^a [39]</p> <p>Realist synthesis^a [54]</p>	<p>Critical interpretive synthesis^a [38]</p> <p>Bayesian synthesis [61] [62]</p> <p>Realist synthesis^a [29]</p> <p>Meta-narrative review [63]</p>

¹ Includes some methods (e.g critical interpretive synthesis, Bayesian synthesis) not yet applicable in Cochrane as they do not fit with the current Cochrane model

^a Review or protocol published in the Cochrane Library

Table 2: Methods and tools to integrate qualitative and process evaluation evidence within intervention effectiveness reviews

Methods and tools	Examples of contexts in which applied	Strengths and limitations
Juxtaposing findings in a matrix	Promoting positive health behaviours [27] Adherence to medication [41] Cancer related pain management [39]	Matrix relatively simple; does not require specialist skills or software Can aid explorations of heterogeneity in trials and identify research gaps. Features/factors influencing implementation are examined one by one
Using logic models/conceptual framework	Factors influencing implementation of lay health worker programmes[44] ^a School-based behavioural interventions to prevent sexually transmitted infections [59]	Contextual features from qualitative research are integrated holistically with findings on effectiveness to develop or refine the logic model Development of framework is flexible and can incorporate stakeholder input when description in published studies is poor
Analysing programme theory	School feeding programmes for disadvantaged children [54] Interventions to prevent repeat teenage pregnancy [64] ^a	Contextual features from qualitative research are integrated holistically with effectiveness findings to develop and refine programme theory Expertise in programme theory required (e.g.realist evaluation)
Testing hypotheses derived using sub-group analysis	Promoting positive health behaviours [27]	Hypotheses from qualitative synthesis can be tested statistically Requires sufficient numbers of trials to conduct sub-group analysis Features/factors influencing implementation are examined one by one
Qualitative comparative analysis.	Self-management of chronic conditions [60]) Weight loss and weight management interventions [56] School-based programmes to manage asthma [40] ^a	Able to examine multiple features across multiple contexts Requires a relatively large number of trials,

^a Review or protocol published in the Cochrane Library

Table 3: Comparison of methods and tools available for integrating qualitative and process evaluation evidence within intervention effectiveness reviews

Integrating device	Examples	Sequential or convergent approach?	Level(s) at which integration takes place?	Specialist skills and expertise required?^a	Substantial evidence required?
Juxtaposing findings in a matrix	Thomas et al. [27] Candy et al. [41] Flemming [39]	Sequential	Themes and outcomes	No	No
Using logic models/ conceptual frameworks	Glenton et al. [44] ^b Shepherd et al. [59]	Sequential or convergent	Theory Themes and outcomes	Yes	No
Analysing programme theory	Greenhalgh et al. [54] Aslam et al. [64] ^b	Sequential or convergent	Theory Individual findings	Yes	No
Testing hypotheses from qualitative syntheses with sub-group analysis	Thomas et al. [27]	Sequential	Cluster of studies within a review	No	Yes
Qualitative comparative analysis.	Candy et al. [60] Sutcliffe et al. [56] Harris et al. [40] ^b	Sequential	Themes and outcomes	Yes	Yes

^a Beyond the level expected for conducting either an intervention effectiveness review or a qualitative evidence synthesis

^b Review or protocol published in the Cochrane Library