Chapter 14. Integrating qualitative and quantitative review evidence.

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Key points

- Integrating the findings of a qualitative evidence synthesis (QES) with the findings of a review of intervention effects can offer many insights. One key benefit of integration is that it allows review teams to explore the reasons for variation in intervention outcomes.
- QESs often generate theories and explanations for why and how interventions may work from the perspectives of those delivering or using them; by integrating these theories with evidence on intervention effects, review teams can offer vital information to support implementation of review findings in practice settings.
- Integration may involve systematically *comparing* the QES and effectiveness syntheses; the findings from each synthesis are juxtaposed, for example in a matrix, to illustrate where they are concordant or discordant. Comparing synthesis findings can reveal whether and how the evaluated interventions match QES findings about the needs and values of people who might receive such interventions.
- Integration may also involve the *connection* of syntheses; the synthesis of one type of evidence (qualitative or quantitative) is used to inform the focus and conduct of the synthesis of the other type, for example the QES findings are used to structure a sub-group analysis of the effects data. Connecting synthesis findings can reveal whether interventions that match people's needs and values are more effective than interventions which do not.

- Approaches for comparing and connecting QES and effectiveness syntheses vary, and are still evolving, but the robustness and utility of the integrated evidence, like for all systematic reviews, depends on the application of a systematic and transparent approach.

14.1 Introduction

A primary purpose of systematic reviews is to provide decision-makers with the best available evidence so that they can direct resources to the most effective and beneficial policies and practices and avoid harm or resource waste. Previous chapters of this book have demonstrated both the value of, and approaches for, synthesising qualitative research to understand the nature of a problem or to generate theories about how and why interventions work (or do not work). This chapter focuses on how to integrate the findings of a qualitative evidence synthesis (QES) with results from an effectiveness synthesis to understand such issues as variation in intervention effects and the factors that create barriers and facilitators to successful implementation (see also chapter 17 on implementation reviews).

There have been several drivers for integrating qualitative and quantitative evidence, such as to understand whether outcomes or harms that are important to patients are measured in trials, a frustration with 'empty reviews' when only quantitative evidence is sought but none is found, and a focus on the complementary role of qualitative research to better help understand 'complex' interventions (Flemming and Noyes 2021; Sutcliffe et al 2018). Perhaps the most important argument from the point of view of this chapter is the need to provide evidence to inform real world decisions. When introducing a new policy or deciding which treatment or intervention to implement, decision-makers need to consider not only whether the policy, treatment or intervention can produce the desired change in outcome, but also what factors or conditions need to be in place to achieve those desired changes. Questions of context, meaning and process, which qualitative evidence can address, are of great importance for understanding these factors or conditions and can shed light on why or how interventions work across and within different settings and populations.

In a guideline context, it is common for the guideline producer to commission different review types that address a range of questions related to the intervention and its effectiveness, cost-effectiveness, acceptability, feasibility, patient and provider experiences of the intervention, values and preferences, and the factors that create the barriers and facilitators to implementation. Quantitative results and qualitative findings from the different review types are then integrated in an evidence-to-decision framework in order to make recommendations. Noyes and colleagues (Noyes et al 2019) provide

examples of when this has been done but this type of integration as part of guideline production is not addressed further in this chapter.

Including different types of evidence in the same review or conducting a series of reviews to fully address policy questions has become commonplace recently. Variation in approaches for including different types of evidence in a single or linked reviews is widely acknowledged and well described (Heyvaert et al 2013; Hong et al 2017; Sandelowski et al 2006). However guidance on the 'difficult task' of integrating the different evidence types is limited (Ferguson et al 2020) and there are few worked examples of methods for integration (Harden et al 2018; Noyes et al 2019). Reviews which integrate qualitative and quantitative evidence are not always explicit about the methods that have been used making it difficult to assess quality of conduct and trustworthiness of output (Hong et al 2017). The guidance in this chapter therefore aims to support review teams to plan and carry out integration in a systematic way.

The next section of this chapter introduces the concept of 'mixed-methods systematic reviews' (MMSR) and offers a consideration of why integrating QES and effectiveness evidence (which can be conceptualised as a subset of MMSR) can be valuable (Noyes et al 2019). It then provides an overview of different approaches for integrating the findings of a QES with the findings of an effectiveness synthesis. The overview is followed by a series of case examples to illustrate some opportunities for integrating QES and effectiveness syntheses and the different ways that review teams have conducted the integration. The approaches used in the case examples are illustrative, as integration methods are still evolving. Guidance is also offered on how to determine which integration approach to use and the practicalities of how review teams can work together to conduct the integration. The benefits of involving and engaging stakeholders in conducting the integration and the opportunities for exploring equity, diversity and inclusion issues via integration are also considered. The chapter ends by considering the need for rigour, relevance and reflexivity in the approach to integration.

14.2 Overview of mixed-methods systematic reviews and approaches for integrating qualitative and quantitative evidence

In this chapter, we use the term mixed-methods systematic review (MMSR) as a collective term for systematic reviews which combine qualitative and quantitative research. As noted above, the chapter is focused on a particular sub-set of MMSRs: those which integrate qualitative evidence in the form of a QES with quantitative evidence in the form of an effectiveness synthesis. Many different terms including integrative review, mixed-methods research synthesis, mixed-research synthesis and mixed-studies review have been used to describe MMSR (Hong et al 2017). Designs for bringing qualitative and quantitative evidence

together are also varied. Some reviewers have sought to characterise broad MMSR types (Heyvaert et al 2013; Hong et al 2017; Sandelowski et al 2006; Stern et al 2020). Based on designs observed in their 2017 review of 459 reviews combining quantitative and qualitative evidence, Hong et al (2017) identified two broad categories of 'sequential' and 'convergent' MMSR. In sequential MMSR, a two-phase approach is employed; the collection and analysis of one type of evidence (qualitative or quantitative) occurs first, and the findings of this synthesis inform a subsequent synthesis of the other type of evidence. In convergent MMSR, quantitative and qualitative evidence is collected and analysed during the same phase of the research. There are similarities across the different typologies, for example the sequential design broadly maps on to what Sandelowski et al (2006) describe as the 'contingent' design, and sub-types of convergent MMSR described by Hong et al (2017) broadly map on to what Sandelowski et al (2006) describe as 'segregated' and 'integrated' designs.

One common feature of these typologies is that they focus on the synthesis design – essentially illustrating 'when' the integration of qualitative and quantitative evidence occurs; with some reviewers expressing frustration that they provide little guidance about 'how' to do the integration (Ferguson et al 2020). For example, the label 'sequential MMSR' foregrounds the fact that one synthesis occurs before the other, but perhaps obscures the fact that the first synthesis should inform the conduct of the subsequent one. A more recent typology by Hong et al (2020) focuses on how the different types of evidence are integrated. The authors outline three types of integration: assimilation, comparison and connection. The three types discussed below and summarised in Table 14.1.

MMSRs which integrate via assimilation transform one type of evidence (either qualitative or quantitative) into the other type so that both sets can be merged together. For example, qualitative evidence may be extracted from studies typically defined as 'quantitative' or numerical data from quantitative studies (e.g., effect sizes, percentages) are transformed into words and / or themes so that they can be merged with data from qualitative studies to develop theory (Guillaume et al 2020; Guillaume et al 2022; Popay et al 2006; van Grootel et al 2020). Methods work on the transformation of one type of evidence in to another has most often focused on quantitative into qualitative although there is a small body of work on calculating 'qualitative effect sizes' which aim to quantify the strength of relationships found within qualitative research (e.g. van Grootel et al 2020) However, it should be noted that calculating such qualitative effect sizes is not recommended currently for Cochrane and Campbell reviews as there are unresolved methodological concerns about this approach and quantifying qualitative evidence remains highly controversial and contested by qualitative researchers and reviewers. There are similar concerns regarding examples in the literature that attempt the assimilation of quanitative and qualitative research through qualitising quantiative research. These typically lack methodological explaination as to

why both types of evidence are needed to answer their review questions. Additionally, these examples do not detail how the quanitative evidence is qualitised and then intergrated with the qualitative. Reviews which integrate via assimilation are typically designed to answer a single question and aim, for example to identify barriers and facilitators of healthy behaviours. As such, assimilation as an integration strategy is not suited to reviews which seek to examine both intervention effects and how interventions work. Hence, assimilation methods are not recommended in this chapter or further discussed; instead this chapter focuses on approaches that are purposeful and methodologically driven which preserve the unique value of different types of methods.

This chapter focuses on MMSR comparison and connection integration strategies. Comparison and connection strategies are designed to examine varied facets of the same complex phenomenon (Greene 2007) and so are therefore ideal for integrating QES and effectiveness syntheses to explore reasons for variation in intervention outcomes. In MMSRs that integrate by comparing, the different types of evidence are initially synthesised separately, such that a QES and an effectiveness synthesis are undertaken independently to answer separate questions. For example, a QES would be aiming to answer a question such as 'What are the needs and experiences of people with condition X?' and an effectiveness review would be aiming to answer a question 'Is intervention Y effective for outcome Z among people with condition X?'. The findings of each synthesis are then systematically compared to identify synergies, contrasts and gaps. In MMSRs that integrate by connection, the results of the synthesis of one type of evidence are used to inform the synthesis of the other. For example, the findings of a QES may be used to structure a sub-group analysis of the effectiveness data.

Table 14.1: Different approaches and levels of integration in MMSR

Integration strategy, purpose and assumptions	**Example reviews**
Strategy: Assimilation of data* **Purpose:** To increase the pool of available data for synthesis by transforming one type of evidence (either qualitative or quantitative) into the other type so that both sets can be merged together. **Assumptions:** Qualitative and quantitative evidence on a similar topic can address the same research question(s) and so that they can be synthesised together. The synthesis involves transforming the findings so that they can be merged.	Guillaume et al. (2020), Guillaume et al. (2022) van Grootel et al. (2020)
Strategy: Comparison of results **Purpose:** To compare findings from standalone QES and quantitative / effectiveness synthesis to offer insight about how findings may be interpreted. **Assumptions:** That the distinct methods and worldviews underpinning qualitative and quantitative evidence mean that they must be synthesized separately – but that the findings of one type of evidence can help to explain the findings of the other.	See case examples 1-4 below

Strategy: Connection of phases **Purpose:** Findings from one synthesis used to *inform* the focus and conduct of another – for example QES derived theories are then tested using effectiveness evidence. **Assumptions:** That the distinct methods and worldviews underpinning qualitative and quantitative evidence mean that they must be synthesized separately – but that the synthesis of one type of evidence can inform the synthesis of the other.	See case examples 5-7 below

*Not currently recommended due to unresolved methodological concerns (see above)

MMSR which integrate QES and effectiveness evidence may take a number of forms:

(1) A new review which incorporates both a QES and an effectiveness synthesis and where the plan is to integrate from the outset.
(2) A "post hoc" QES linked to a completed effectiveness synthesis.
(3) A "post hoc" effectiveness synthesis linked to a completed QES.
(4) Integration of existing QES and effectiveness syntheses.

The form of the MMSR will inevitably shape the possibilities for integration. For example, an integration of existing QES and effectiveness syntheses (form 4) would most likely involve comparison only; where both syntheses have already been conducted there is limited opportunity for a connection integration in which one synthesis informs the conduct of another. However, whilst the MMSR by Melendez-Torres et al (2019) (see Box 6 below) drew on an existing meta-analysis, the work involved reanalysing the effectiveness studies such that the QES was able to inform the QCA (see also chapter 18). Similarly, a new or existing QES could be used to inform new sub-group analyses based on an existing meta-analyses.

The next sections of this chapter focus in detail on the particular ways that the different syntheses may interact or 'have a conversation' with one another (Greene 2007), and on the strengths and limitations of different approaches. A series of Case Examples illustrate how comparison and connection can be achieved in MMSR. Table 14.2 below provides an overview of the Case Examples. Methods for MMSR are still evolving, so whilst these examples illustrate the rich variety of comparison approaches, they are intended for illustrative purposes and should not be considered an exhaustive list. A key strength of mixed-methods research and MMSRs is that they encourage creativity in exploring and communicating complex issues (Johnson and Onwuegbuzie 2004). The Case Examples are followed by guidance on key decisions about which approach to use and practical advice about when and how to apply the approaches.

Table 14.2: Overview of approaches to integration in case examples

Example	Type (method)	Integration details	Purpose
1. Houghton et al *Recruitment to trials (Box 1)*	Comparison (Matrix)	QES themes *compared with* Effectiveness synthesis	To understand weight of effectiveness evidence supporting QES themes and gaps in evidence.
2. Borhen et al *Labour companions (Box 2)*	Comparison (Matrix)	QES themes *compared with* Components of individual interventions	To understand extent to which interventions reflect needs / preferences identified in QES.
3. Murray et al *Care farms (Box 3)*	Comparison (annotated logic model)	QES theory *compared with* Effectiveness synthesis	To understand whether effectiveness evidence supports overarching QES theory.
4. Lester et al *Adverse Childhood Experiences (Box 4)*	Comparison (Line-of-argument)	QES themes *compared with* Effectiveness synthesis	To illustrate how results of QES and effectiveness synthesis are discordant.
5.Foley et al *Inequities in travel behaviour in Africa (Box 5)*	Connection (sub-group analysis)	QES themes *Inform* Effectiveness synthesis	To derive hypotheses from QES that can then be tested using effectiveness / quantitative data.
6. Sutcliffe et al *Weight management programmes (Box 6)*	Connection (Qualitative comparative analysis (QCA))	QES themes *Inform* Analysis of intervention complexity	To identify key intervention, contextual or implementation factors that may influence outcomes from a QES. Combinations of interrelated factors are then tested via QCA (chapter 18).
7. Flemming *Pain management (Box 7)*	Connection (Framework)	Effectiveness synthesis *Informs* QES	The findings of the effectiveness research are used as a framework to guide the extraction and synthesis of qualitative data for the QES using Critical Interpretive Synthesis (chapter 19).

14.3 Approaches for integrating QES and effectiveness evidence by 'comparing'

The four Case Examples below illustrate how reviewers have used matrices, logic models and line-of-argument approaches to compare the QES and effectiveness synthesis findings. Comparisons of trial findings with qualitative evidence often require examination of more than the trial results, for example, examination of intervention components or the nature of outcomes measured may be needed.

Case example 1: Houghton et al 2020 – A matrix to compare QES themes with synthesised effectiveness findings

As illustrated in Box 1, Houghton and colleagues explored whether findings from existing effectiveness syntheses on recruitment to trials corresponded with the findings of their QES using a matrix (Houghton et al 2020). The matrix presents each finding from the QES (see column 1 in the matrix presented in Box 1), implications / questions that trialists can ask when designing a recruitment strategy to ensure it is patient centred (column 2), and any synthesis findings in the effectiveness review that relate to these implications for trial recruitment (columns 3 and 4). For example, as illustrated in the first row of the matrix, finding 1 of the QES was that participants reported that trial information delivered verbally during face-to-face contact was less confusing than written information. This implied that trialists should consider whether trial information will be delivered verbally during face-to-face contact. When examining the trials, the reviewers found that one effectiveness review (Treweek et al 2018) reported evidence of very low certainty (based on a GRADE assessment (Guyatt et al 2011)) that a researcher reading out consent details positively affects recruitment. The other effectiveness review (Gardner et al. 2020) found no evidence in support of this finding and so the relevant matrix cell is blank. As such, it is clear that there is very limited effectiveness evidence to support the QES finding; indicating that more trials, or perhaps more robust trials, are needed to evaluate the effect of a researcher reading out consent details. Other QES findings (not shown in the matrix excerpt in Box 1) were supported by more substantial effectiveness evidence, whilst some were entirely unsupported by effectiveness evidence. The matrix in this review illustrates the relative weight of effectiveness evidence supporting the QES findings and where there are gaps in the effectiveness evidence.

Box 1: Example review which integrates QES and effectiveness evidence

Review: Houghton et al (2020) Factors that impact on recruitment to randomised trials in health care: a qualitative evidence synthesis

Review objectives: To explore potential trial participants' views and experiences of the recruitment process for participation […] and to explore to what extent barriers and facilitators identified are addressed by strategies to improve recruitment evaluated in previous reviews of the effectiveness of interventions including a Cochrane Methodology Review.

Integration methods: QES findings were integrated with two previous intervention effects reviews (Gardner et al 2020; Treweek et al 2018) by juxtaposing the quantitative and qualitative findings in a matrix.

Value of integration: QES enabled development of key questions that trialists can ask when developing recruitment strategies to ensure participant centred approaches. Matching these to the identified gaps in effectiveness evidence (i.e. as indicated in the table below, there was no evidence from the Gardner review matching QES findings 1-3) and recommendations for future research.

Example findings from integration: (Note: only the first few rows of the matrix are presented)

Juxtaposing the findings in a matrix

Summary of qualitative findings	Implications for trialists	Treweek effectiveness Review	Gardner effectiveness Review
TRIAL INFLUENCES ON THE DECISION TO PARTICIPATE			
Communication of trial information			
Finding 1: Trial information delivered verbally during face-to-face contact can be less confusing than written trial information.	*Will trial information be delivered verbally with face-to-face contact?*	[D2] Researcher reading out the consent details (GRADE: very low).	
Finding 2: Written trial information may be beneficial as an adjunct to verbal information and facilitates time and space for reflection without the added influence of recruiters' presence.	*Will written information be offered as a supplement to / in addition to verbal information?*	[C3] Giving quotes from previous participants in SMS messages (GRADE: moderate). [D3] Easy to read consent form (no GRADE*).	
Finding 3: The person delivering trial information should have good communication skills, be approachable, trustworthy, person-centred and knowledgeable with a good ability to address potential participants' queries. Consideration needs to be given to whether a clinician or a researcher is the most appropriate person to provide the trial information.	*Is the person delivering the trial information approachable, trustworthy, participant-centred and knowledgeable with a good ability to address queries? Has the recruitment strategy identified whether a clinician or a researcher is the most appropriate person to provide the trial information?*	E18] Trained recruiters from a similar ethnic background to study population already taking part in a trial as lay advocates (no GRADE*).	

*Findings marked 'no GRADE' were not included in the summary of findings tables in Treweek et al. 2018 and have no GRADE assessment

Case example 2: Bohren et al (2019) – A matrix to compare QES themes with individual interventions

In contrast to Houghton et al (2020)'s approach, this review - on perceptions and experiences of labour companionship (Bohren et al 2019) - explored whether features of labour companionship interventions identified as important in the QES were addressed by individual interventions included in the intervention review. As illustrated in Box 2, Bohren et al. juxtaposed QES findings against characteristics of individual interventions, rather than with the overall synthesis findings, to show the extent to which each intervention included in the synthesis is aligned with the QES findings. The matrix is also valuable for highlighting the heterogeneity and complexity of the multi-component interventions in the effectiveness synthesis and for indicating the totality of evidence supporting each QES theme. By highlighting which interventions address few or no issues identified as important in the QES and which address more issues, review users can identify interventions that appear to be more appropriate and / or acceptable for service users. Like the Houghton et al (2020) review, this review involved a QES conducted to help interpret evidence in an existing effectiveness synthesis, although both were led by the same author.

Box 2: Case example 2: Comparison of QES themes and individual interventions in a matrix

Review: Bohren et al (2019) Perceptions and experiences of labour companionship: a qualitative evidence synthesis
Review objectives: To describe and explore the perceptions and experiences of women, partners, community members, healthcare providers and administrators, and other key stakeholders regarding labour companionship; to identify factors affecting successful implementation and sustainability of labour companionship; and to explore how the findings of this review can enhance understanding of the related Cochrane systematic review of interventions.
Integration methods: A matrix was produced to compare features of labour companionship identified as important in the qualitative evidence synthesis with the interventions included in the intervention review.
Value of integration: Provides a useful summary of how the synthesised qualitative findings are reflected in the content of the interventions in the studies included in the related Cochrane systematic review of interventions (Bohren et al 2017). The matrix shows that most interventions included in the Bohren et al (2017) review did not include the key features of labour companionship that were identified in the qualitative evidence synthesis.
Example findings from integration:

Matrix model applying key findings from the qualitative synthesis to studies included in the Cochrane intervention review (Bohren 2017)

Studies included in the relevant Cochrane intervention review	Was the intervention designed to address the following factors?**						
	1	2	3	4	5	6	7
Akbarzadeh 2014	?	?	?	?	?	N/A	N
Bréart - Belgium 1992	?	N	?	?	?	N/A	N
Bréart - France 1992	?	N	?	?	?	N/A	N
Bréart - Greece 1992	?	N	?	?	?	N/A	N
Bruggemann 2007	?	?	?	N	?	N	Y
Campbell 2006	?	Y	?	?	?	Y	Y
Cogan 1998	?	N	?	?	?	N/A	N
Dickinson 2002	Y	?	?	N/A	Y	N/A	Y
Gagnon 1997	Y	N	?	N/A	Y	N/A	N
Hans 2013	Y	Y	?	Y	Y	N/A	Y
Hemminki 1990a	?	N	?	?	?	N	N
Hemminki 1990b	?	N	?	?	?	N/A	N
Hodnett 1989	?	Y	?	?	?	N/A	N
Hodnett 2002	Y	N	?	?	?	N/A	N
Hofmeyer 1991	?	N	?	?	?	N	N
Isbir 2015	?	N	?	?	?	N/A	N
Kashanian 2010	?	N	*	N/A	?	N/A	N
Kennell 1991	?	N	N	?	?	N/A	N
Klaus 1986	?	N	N	?	?	N/A	N
Langer 1998	?	N	Y	?	?	N/A	N
Madi 1999	?	N	N	?	?	N	Y
McGrath 2008	?	Y	?	?	?	N/A	N
Morhason-Bello 2009	Y	Y	?	?	Y	N	Y
Safarzadeh 2012	?	?	Y	?	?	?	Y
Thomassen 2003	?	?	?	?	?	N/A	N
Torres 1999	?	Y	Y	?	Y	Y	Y
Yuenyong 2012	Y	Y	?	?	?	Y	Y

Y=Yes, N=No, N/A=Not applicable, ?=Not reported
*Women in the intervention group were in a private room. Women in the control group were in a labour ward with 5-7 women in labour in the same room.
**Factors identified from the QES:

1. Were providers trained on the benefits of labour companionship prior to implementation?
2. Were women educated about the benefits of labour companionship prior to implementation?

3. Was the labour ward structured or restructured in a way to ensure that privacy can be maintained for all women?
4. Were providers trained on how to integrate companions into the care team?
5. Were clear roles and expectations set for companions and providers?
6. For trials with lay companions, was training for companions on how to support women integrated into antenatal care?
7. Did the woman choose her own companion?

Case example 3: Murray et al (2019) – An annotated logic model to juxtapose effectiveness findings against overall QES derived theory

Murray et al (2019) sought to understand the mechanisms of change achieved by care farming interventions, i.e. the therapeutic use of agricultural and farming practices, for different population groups. In this review the same team conducted both the QES and effectiveness synthesis and integration was planned from the outset. The integrated findings of this Campbell review, described in Box 3, differ from the three previous examples in that rather than juxtaposing the effectiveness synthesis evidence against individual QES findings, the effectiveness synthesis findings are juxtaposed against the overarching QES theory. Additionally, rather than using a matrix, Murray et al (2019) employed an innovative method to juxtapose the effectiveness synthesis findings against a logic model based on QES evidence (see Chapter 4 on Logic Models). The logic model depicted care farming components, mechanisms and proximal outcomes such as self-efficacy and coping skills identified as important in the QES, with the ultimate goal of depicting the ways that care farms were experienced as working to improve quality of life. The quantitative evidence was then mapped onto both the proximal outcomes and the endpoint health outcomes (such as anxiety, depression and health-related quality of life) to identify whether outcomes in the logic model were supported by the effectiveness evidence base. Symbols were added to the logic model to illustrate the extent and direction of evidence of care farms for particular outcomes, for example for reducing anxiety. The value of this approach is in juxtaposing an account of how the intervention is experienced as working, against evidence of whether it works. Other examples of an annotated logic model approach have been published recently (Aventin et al 2023; Orr et al 2023).

Box 3: Case example 3: Comparison of QES theory with effectiveness findings using an annotated logic model

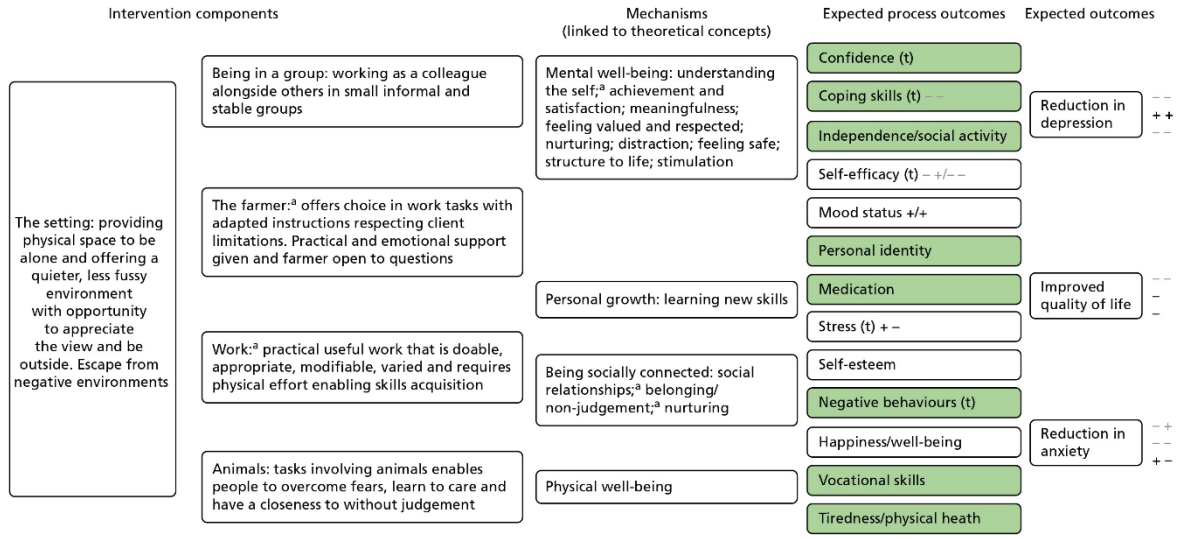
Review: Murray et al (2019) The impact of care farms on quality of life, depression and anxiety among different population groups: A systematic review

Review objectives: To systematically review the available evidence of the effects of care farms on quality of life, health and social well-being on service users […] to understand the mechanisms of change for different population groups.

Integration methods: Logic models depicting care farming components, mechanisms and proximal outcomes were developed using qualitative evidence. The effectiveness evidence was then mapped onto both the proximal and endpoint health outcomes (anxiety, depression and health-related quality of life) to identify whether outcomes in the logic models were supported by the evidence base.

Value of integration: Communicates the complexity of the intervention theory juxtaposed against the nature, extent and direction of effectiveness evidence.

Example findings from integration:



Logic model for combined mental ill health and substance misuse group. a, Mechanisms that were most frequently found and with greatest spread across studies. Grey and black symbols show quantitative evidence for which – means no significant difference and + means significant difference; grey represents RCT evidence; two symbols beside each other show different time points within the same study; and shaded process outcomes equate to evidence from qualitative literature. t, theory based.

Case example 4: Lester et al (2019) - Discussion of QES and effectiveness evidence in relation to each other

The MMSR on Adverse Childhood Experiences (ACEs) (Lester et al 2019) used a 'line-of-argument' approach to compare the QES and effectiveness synthesis findings. Lines of argument syntheses bring together 'dissimilar but related studies' in a narrative detailing and explaining the discordance between them. The findings of an overview of systematic reviews examining the effectiveness of interventions were compared to a QES on the experiences and service needs of young people affected by ACEs. The respective syntheses were conducted concurrently, but independently of each other, but with the lead author involved in both reviews. When comparing the evidence on people's experiences and needs with the evidence about interventions, the two sets of evidence were found to be highly discordant. As such, visual tools to juxtapose the evidence as used in Case Examples 1-3 were inappropriate and a line-of-argument approach illustrating the areas of discord was employed (see Box 4 for details).

Box 4: Case example 4: Comparison of QES and effectiveness findings using line-of-argument

Review: Lester et al (2019) What helps to support people affected by Adverse Childhood Experiences (ACEs)? A review of evidence.

Review objectives: To gather, assess and present evidence on what helps to mitigate the harmful impacts of ACEs through a review of reviews on the effectiveness of interventions for people affected by ACEs, a QES on the experiences and service needs of people in the UK affected by ACEs, and a stakeholder consultation with young people with lived experiences of ACEs in the UK.

Integration methods: A narrative line-of-argument was used to illustrate key areas of discord between the types of interventions examined in systematic reviews and the findings of the QES and stakeholder consultation.

Value of integration: The integration exposed the fundamental disconnect between the types of interventions examined in systematic reviews and people's needs as revealed in the QES and consultation findings.

Key findings from integration:

When comparing the evidence on people's experiences and needs with the evidence about the effectiveness of available interventions three areas of discordance were identified:

First, the importance of day-to-day practical and emotional support underpinned by relationships with a trusted adult (or mentor/ peer(s)) was consistently highlighted in the qualitative evidence. By contrast, the evidence relating to interventions focused on individualised 'crisis point' approaches. In the short term, these psychological interventions did improve mental health but failed to address the multifaceted and ongoing needs identified by young people in the QES and the stakeholder work.

Second, whilst the QES highlighted that young people valued consistency and stability, many of the interventions evaluated in systematic reviews were short-term in nature and so were unable to address this need.

Third, whilst the qualitative evidence revealed that children and young people felt the attributes of supportive adults were more important for providing effective support than their professional role, the interventions evaluated in the systematic reviews tended to be delivered by staff otherwise unknown to the young person in community or clinical settings.

14.4 Approaches for integrating QES and effectiveness evidence by 'connection'

Comparison approaches such as those described above use the QES findings to offer insight as to how the effectiveness findings *may* be interpreted. Connecting the evidence – i.e. using one set of evidence to inform the synthesis of the other - offers the opportunity for more concrete insights. For example, effectiveness evidence may be used to test hypotheses or theories derived from the QES or the effectiveness evidence may be used to structure a QES. Reviews which connect often use comparison as a precursor to the connection analysis. This may be one reason why examples of MMSR which integrate by connection are much less common than those which only compare (Hong et al 2017). Case Examples 5 and 6 illustrate ways that quantitative evidence can be used to test QES derived hypotheses or theories. Case example 7 illustrates how an effectiveness synthesis may be used to inform a QES.

Case example 5: QES generates hypotheses for testing with quantitative evidence

As illustrated in Box 5, this Case Example focused on inequities in travel behaviour in Africa using a QES to generate hypotheses about the impacts of socio-economic status (SES) and gender on travel behaviours that were then tested using quantitative evidence. Because the pool of connection MMSRs is small, this Case Example is a MMSR in which the quantitative synthesis is not an intervention effects synthesis. However, the principles could easily be applied to effectiveness evidence. The QES identified that compared to higher SES individuals, lower SES individuals would have higher prevalence of 'zero travel days' (i.e. days when no travel is undertaken) and live further from the central business district. These hypotheses were then tested using quantitative evidence on behaviours. The output (see Box 5) is similar to many of the tools used in comparative reviews to juxtapose the qualitative and quantitative evidence; but where Case Examples 1-4 sought to identify matches and gaps between the two independently synthesised sets of evidence, the difference here is that the QES determined the focus of the quantitative synthesis (i.e. which behaviours were examined). A similar approach could be used for connecting a QES with an effectiveness synthesis. For example, since the QES in Case Example 5 identified that cost influenced travel behaviour for low SES groups, this highlights a need to understand whether interventions that reduce travel costs help to reduce barriers to travel for low SES groups. By contrast, the factors affecting travel for women were personal safety and household responsibilities, indicating the types of intervention that an effectiveness synthesis should focus on for this group.

Box 5: Case example 5: QES generates hypotheses for testing with quantitative evidence

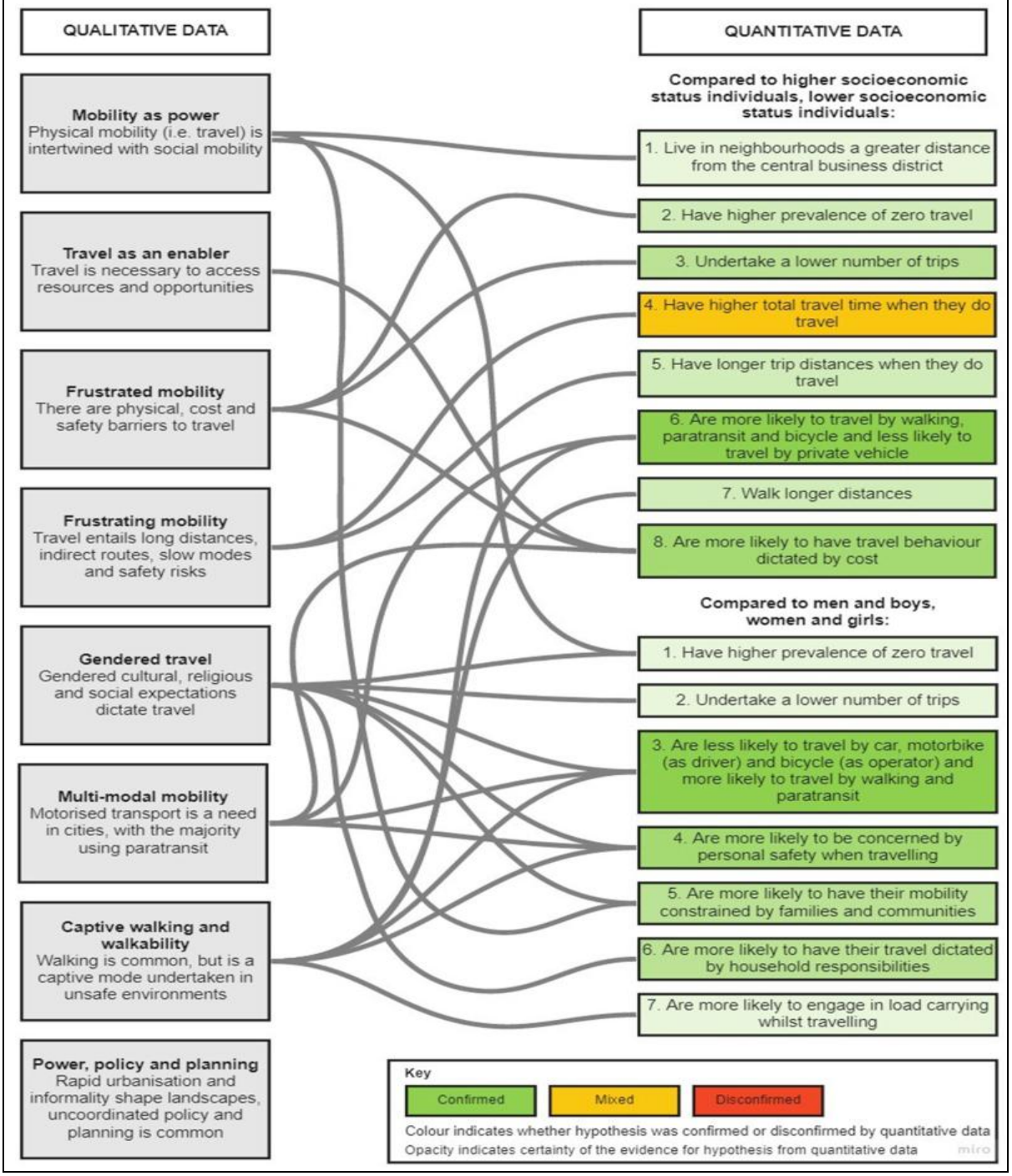
Review: Foley et al (2022) Socioeconomic and gendered inequities in travel behaviour in Africa: Mixed-method systematic review and meta-ethnography

Review objectives: To explore socioeconomic and gendered differences in travel behaviour in Africa, to develop an understanding of travel-related inequity.

Integration methods: Insights from the QES were used to generate hypothesised patterns of predictions. The quantitative evidence was then examined to see whether these patterns could be observed.

Value of integration: The qualitative data gave rich information on the production and experience of travel inequity; the quantitative data enabled the identification of differences in travel behaviour at scale across multiple countries.

Example findings from integration:



Case example 6: QES informs partitioning in analysis of effectiveness evidence

Melendez-Torres et al (2019) conducted a qualitative comparative analysis (QCA) to identify the critical ingredients of weight management programmes for adults (Melendez-Torres et al 2019). Systematic reviews using QCA aim to identify combinations of intervention, contextual and implementation factors associated with intervention success or failure (see Chapter 18 for more information on QCA). A key feature of QCA is that the analysis should be informed or underpinned by existing theory (Wagemann and Schneider 2010). In the review by Melendez-Torres et al (2019), a QES was undertaken to inform, structure and interpret the QCA; as such the theory underpinning the QCA was derived from the QES. The QES addressed the question "What do weight management programme users and providers feel are critical programme features and how are these features perceived to impact on weight loss?" The QCA then examined the features of interventions tested in randomized controlled trials (RCTs) to assess whether the interventions containing the programme features perceived to be important were associated with greater weight loss. As illustrated in Box 6, the QES-informed QCA was able to identify critical ingredients of successful weight management programmes. The review team found that the QES was vital for identifying critical but unanticipated or overlooked intervention factors (Sutcliffe et al 2018).

Similarly, QES findings have also been used to inform and structure statistical sub-group analyses. A review on healthy eating in children found that interventions aiming to increase children's fruit and vegetable consumption that matched intervention recommendations derived from a QES of children's views were more effective than those not matching the QES derived recommendations (Thomas et al 2004). Like Case Example 6, this review found that the QES was vital for identifying critical intervention factors that it would have been difficult to imagine in advance.

Reviews which connect a QES and effectiveness synthesis may also involve comparison as a precursor to the connection analysis. A preliminary analysis tool in QCA, known as the data table, is a matrix very similar to the one used in the Bohren et al (2019) review. In a QCA data table, each row represents an individual intervention in the analysis, and each column represents a specific intervention feature, allowing the review team to indicate in each cell the presence or absence of features in each intervention. That comparative matrix is then used to produce the main analysis in which combinations of features are systematically tested for their association with intervention outcomes. Matrices were also employed in the Thomas et al (2004) review to identify whether the evidence was amenable to sub-group analyses.

Box 6: Case example 6: QES informs QCA

Review: Melendez-Torres et al (2019) Developing and testing intervention theory by incorporating a QES into a qualitative comparative analysis of intervention effects
Review objectives: To identify the critical features of successful weight management programmes (WMPs) for adults.
Integration methods: QES provided working theory to structure a QCA, specifically by suggesting specific intervention features to be examined.
Value of integration: The QES helped to sharpen the focus on the most salient features to be examined, supported interpretation of findings, and ensured that we avoided data dredging.
Example findings from integration:

Critical feature	Example view	Most effective interventions (n=10)	Least effective interventions (n=10)
Good quality provider relation-ships	'You feel that some-body's batting for you'	**All 10** most effective interventions had: Provider-user relationships emphasised AND Characteristics perceived to foster self-regulation.	**All 10** least effective interventions had: **NO** emphasis on provider relationships. OR An emphasis on provider relationships BUT **NO** self-regulation characteristics.
Provider direction and support	'I need someone to take my hand and take me over'	**All 10** most effective interventions had: Provider-set energy-intake goals AND Provider-set exercise goals AND EITHER direct provision of exercise OR provider-set weight goals.	**All 10** least effective interventions had: **NO** provider-set energy-intake goals AND **NO** provider-set exercise goal AND **NO** direct provision of exercise. OR Direct provision of exercise AND provider-set exercise goals BUT **NO** provider-set energy-intake goals AND **NO** provider-set weight goals.
Oppor-tunities for peer relation-ships	'You wanted to come back and hear how the guys were getting on'	All interventions with both of the following characteristics (n=5) were in the most effective group*: Group work AND Targeted at a specific population group.	All interventions with both of the following characteristics **(n=5)** were in the least effective group*: **NO** group work AND **NO** population targeting

* Some WMPs with *either* group work *or* targeting (n=5) were most effective, but the presence of both conditions appears to ensure greater effectiveness.

Case example 7: Flemming (2010) – A matrix to compare effectiveness synthesis themes with individual QES findings

Each of the previous case examples are of MMSR in which the QES findings have been used to locate and interpret findings of an existing effectiveness synthesis. Whilst less common, there are examples of MMSR which take the opposite approach; that is, they use the findings of an existing effectiveness review to inform and structure the QES. Flemming (2010) used this approach in her Critical Interpretive Synthesis (see chapter 19) to examine the use of morphine to treat cancer-related pain. Flemming (2010) employed the findings of two existing syntheses of the effectiveness of morphine (a Cochrane Review and European

Association of Palliative Care (EAPC) guidelines) to develop a coding framework to drive the QES. As such, the integration involves connection, as the findings of each review were not undertaken independently and then compared, the effectiveness synthesis findings were used to develop a tool to extract and analyse qualitative evidence as well as to structure a matrix which was populated with the QES findings. The columns of the matrix (see Box 7) reflect key findings from the effectiveness syntheses, and the rows are populated with relevant data from each individual study in the QES. The author concludes that the strength of this approach was that it enabled the valuable aspects of the effectiveness literature – the notion of 'what works and when to use it'– to be protected and ensured that none of the key aspects of either the quantitative or qualitative research was lost at the point of interface (Flemming 2010).

Box 7: Case example 7: Effectiveness synthesis findings inform framework to drive QES

Review: Flemming (2010) Synthesis of quantitative and qualitative research: an example using Critical Interpretive Synthesis

Review objectives: To synthesize quantitative research, in the form of an effectiveness review and a guideline, with qualitative research, in the form of a QES, to examine the use of morphine to treat cancer-related pain.

Integration methods: The findings from the effectiveness review interface with and drive the synthesis of qualitative research. An integrative grid in which columns were organised around the effectiveness findings (indicated in the top row of the table below) and each was populated by relevant findings from individual qualitative studies (indicated in the subsequent rows of the table below).

Value of integration: The interface between quantitative and qualitative research demonstrated how the practical enactment of effective interventions can alter in relation to other elements, for example threats to health, interaction with healthcare professionals and perceived meaning of the intervention.

Example findings from integration:

	Opioid of first choice is morphine	If pain returns on a regular basis, regular dose should be increased and rescue medication taken	For patients on normal release medication a double dose should be taken at bedtime	Successful pain management requires adequate analgesia without adverse effects
Coyle 2004	Morphine is viewed as positive to relieve pain Good analgesia leads to a sense of control	Poorly controlled pain is interpreted as worsening disease Unlimited analgesia is required for a comfortable death		Adverse effects are a burden Cognitive side effects lead to 'loss of self' Opioids are a burden because of side effects
Ersek *et al.* 1999	Need to prove pain to get analgesia Patients took opioids regularly to improve functioning Side effects are tolerated		Patients wake at night in pain as they can't afford sustained release preparations	Functionality more important than pain relief Adverse effects are a deterrent Analgesic use altered because of side effects Side effects seen as a sign of addiction
Johnston-Taylor *et al.* 1993	Morphine works so it gets taken despite side effects	Patients had conflict over management of opioids, what, when how to take?	Fear that pain will increase towards death	Negative connotations associated with morphine use because of side effects Carers have concerns over side effects and addiction Nurses concerns over side effects

14.5 Determining which integration approach to use

The review's purpose and questions should drive the decision to conduct an MMSR (Cerigo and Quesnel-Vallée 2020); they should also drive the choice of integration approach. However, review teams also need to consider which approach is best suited to understanding the evidence at hand. Choice of method may also be driven by team expertise and preference. Decisions about which integration approaches are possible and / or preferable, may need to be determined once the nature and content of the separate reviews is known (Thompson Coon et al 2020). In line with recommendations for designing QES, the review team may therefore want to include some flexibility concerning the integration method in the protocol (See Chapter 1). Some potential considerations surrounding integration decisions are outlined below.

14.5.1. Limitations of the different approaches and appropriate contexts for their use

Whilst the value of each approach is considered above, there are also limitations for each approach. A limitation of the approach used for the ACEs MMSR (Case example 4) is that the application of high level line-of-argument lacks detail and so provides limited information for instrumental decision-making; instead the findings are suited to more diffuse and incremental impacts by shaping policy through conceptual enlightenment (Boswell and Smith 2017). The line-of-argument approach though, is useful to enable further understanding when the QES and effectiveness synthesis findings do not really "speak to each other" such that the evidence does not lend itself to detailed comparisons or juxtaposition. For example, if the QES and effectiveness synthesis findings are strongly discordant, or if it is difficult to determine whether and how interventions meet people's needs. The recruitment to trials MMSR (Case example 1) draws on evidence of effectiveness at the synthesis level, rather than the individual study level, and as such may obscure synergies between the QES findings and individual interventions. However, this approach may be particularly useful when a QES is conducted to understand the findings of an existing effectiveness synthesis (from which the features of individual interventions may not be known) and / or where the intention is to understand the weight of effectiveness evidence supporting QES themes. In the labour companionship MMSR (Case example 2), the juxtaposition of the QES themes against individual trials offers finer grained detail about whether and how interventions match the QES findings than the recruitment to trials example (Case example 1). However, this approach is very much dependent on the availability of detailed descriptions of the interventions but interventions are often poorly described in trial reports (Hoffmann et al 2014). Where intervention descriptions are sufficiently detailed in trial reports, related protocols or process evaluations, review teams may consider using the QES to inform sub-group analysis or QCA. However, this connection approach is only viable where there is a sufficient number of trials and substantial variation

in intervention effects. The authors of the travel behaviour in Africa review (Case example 5) acknowledge a potential limitation of reviews which integrate by connection, in that if the QES is targeted towards the objective of informing the quantitative synthesis, some insights could be missed (Foley et al 2022). Review teams should weigh up what is desirable against what is feasible given the extent and nature of the available evidence. The approaches listed above are not an exhaustive list, their diversity is testament to the need for creativity and for tailoring the approach to the evidence at hand.

14.5.2. Other factors that will shape the selection of integration approach

Inclusion of trial sibling and / or non-trial sibling studies

One decision-point relating to opportunities for integration, is whether to include trial sibling studies (i.e. qualitative studies of the experiences of participants in a trial included in the effectiveness synthesis) and / or non-sibling studies (i.e. qualitative studies unconnected to a trial) (Noyes et al 2016). Whilst trial sibling studies provide the most directly applicable evidence to help interpret or inform the effectiveness synthesis, such studies are often rare and restricting to sibling studies alone may limit the richness or insights gained from QES. Many of the Case Example MMSRs included non-trial sibling studies and still achieved important insights. For example, the MMSR on weight management programmes (Box 6) relied exclusively on non-trial sibling studies because the effectiveness synthesis included evaluations from across the globe, whilst the QES was restricted to UK studies in order to inform UK policy. Notably, a trial sibling qualitative study was available for only one of the included trials and was not eligible for inclusion in the QES as it was a non-UK study (Sutcliffe et al 2018).

Practicalities of working across different evidence bases

If review teams are integrating a post-hoc synthesis with an existing synthesis, another consideration is whether it may be useful or possible to involve authors of the original review in the work. Typically, these types of MMSR have been those in which a post-hoc QES is linked to a completed effectiveness review, which has meant that the QES team has been responsible for the integration. In the Houghton et al (2020) MMSR (Box 1), the QES was undertaken by a team with expertise in QES who were independent of the original effectiveness review. However, the lead author of the effectiveness review (Treweek et al 2018) joined the team as they conducted the integration of findings. Cochrane reviews have typically involved a post-hoc QES and the integration has been undertaken by the QES team. This may be one reason for the current lack of MMSR which integrate via connection, because the QES team responsible for integration may not have the skills required to undertake statistical sub-group analyses.

Where review teams are responsible for undertaking both the QES and the effectiveness synthesis, it is recommended that the team develop mechanisms to support the efficient sharing of emergent understandings across the different syntheses (Thompson Coon et al 2020). Thompson-Coon et al (2020) describe detailed case studies of conducting MMSR across large teams. They recommend employing an 'interweave synthesis' approach which involves intense debate and discussion between reviewers working on the QES and those working on an effectiveness synthesis, and relies heavily on teams working together across the evidence bases. In particular the team recommend:

- The use of intersubjective questions to understand the findings of the individual reviews through different lenses (e.g. members of teams conducting the QES and effectiveness syntheses question each other about emerging findings to identify connections).
- Immersion of key reviewers in the entirety of the evidence base (e.g. involvement in both the QES and effectiveness syntheses).
- Starting the integration during the final stages of the synthesis of individual reviews, when reviewers are developing an understanding of initial findings.

The extent of the work

Naturally, the approach to integration will affect the extent of the work required. A full report of the QES findings (themes, lines of argument and theories etc) is needed for integration (chapter 20). The GRADE-CERQual summary of findings tables are insufficient by themselves (chapter 13). Review authors will need to be familiar with and have a depth understanding of the findings and their meanings in order to preserve the context when integrating with an effectiveness synthesis. It can be helpful if there is an overlap of authors across the two reviews to support integration from both a qualitative and quantitative perspective, but this is not always possible if one of the reviews is already published. Where a QES is conducted to understand the findings of an existing effectiveness synthesis, if juxtaposition of themes against individual interventions is deemed appropriate, the review team may need to return to the original trial reports to extract that information, and even to seek out sibling studies or project websites if trial reports have scant information, thereby increasing the amount of work required. For example, the weight management MMSR conducted by Melendez-Torres et al (2019) (Box 6), reanalysed evidence from an existing effectiveness synthesis, but the detailed work to understand the features of successful interventions required that the review team engaged with the trial reports of individual interventions rather than the overall results of the effectiveness synthesis alone. As such, the time and resources available to review teams may also shape the type of integration possible.

14.6 Stakeholder engagement and involvement

Whilst the integration of a QES with an effectiveness synthesis provides valuable interpretation and insight about effectiveness evidence, involving stakeholders in the production of an MMSR may offer particularly valuable additional insights to support implementation in a particular practice setting. For example, the review team that conducted the MMSR on weight management programmes (Case Example 6) engaged with policy-makers and practitioners in Local Authorities in England (i.e. local government agencies responsible for providing public health and other services for a particular geographical area in England), to explore current weight management provision and consider how the review findings could be incorporated into future provision of services (Sutcliffe et al 2016) (Sutcliffe et al 2016). Similarly, engagement with seven young people affected by ACEs for the MMSR in Case Example 4, enabled the review team to understand how relevant the qualitative and effectiveness evidence was to current experiences in the UK (Lester et al 2019).

These examples illustrate the value of stakeholders input into interpreting findings from the integration. Stakeholders could also be involved at the point of integration. For example, patient experts by experience could help review teams to interpret whether an intervention addresses a particular need or perspective and how; by helping to identify particularly pertinent themes and findings to take forward for integrating with the effectiveness evidence; or by helping review teams to understand and interpret intervention descriptions. Alternatively, stakeholders' perspectives may be used as a source of evidence in an MMSR and directly integrated to some degree with other types of evidence (Hong et al 2020).

14.7 Equity, diversity and inclusion

Integrating QES with effectiveness evidence offers several opportunities to address equity, diversity and inclusion issues. QES offers opportunities to harness the voices and experiences of marginalised groups within evidence synthesis; integration of QES and effectiveness syntheses can ensure that the voices of marginalised groups are considered in effectiveness syntheses and flagged for attention when these voices are absent. For example, if there are diverse perspectives in the QES, there may be an opportunity to examine the extent to which the interventions address the needs of particular marginalised groups, or whether barriers to access identified by marginalised groups suggest that intervention impacts may not be realised. If the interventions have variable outcomes and there are associations with population characteristics, the QES can help explain variation in outcomes by different population groups. Case Example 5 illustrates the potential for MMSR to address equity issues.

14.8 Relevance, rigour and reflexivity

The opening sections of this chapter highlight that a key driver of MMSR is the need to ensure systematic reviews offer findings that can be used in policy and practice decision-making. The case examples illustrate how the integration of the QES and effectiveness synthesis findings offer review users insights about: how interventions may work (or not) in real world settings; the extent to which interventions meet the identified needs of services users; and the intervention, implementation and contextual factors that enhance or inhibit the success of interventions.

Additionally, robustness is important especially if MMSR evidence is to be used to support decision-making. As such, the principles that underpin systematic reviews should underpin the approach to integration, that is the integration should aim to answer a specific research question, and be undertaken meticulously and systematically to minimise bias (Chandler et al 2022). The Case Examples illustrate a variety of creative ways in which QES findings can be systematically compared to the effectiveness evidence, or indeed, how the findings of one type of evidence can inform the systematic synthesis of the other. Another key principle of systematic reviews and MMSR is that they should aim to offer synthetic evidence, that is the results of the integration should offer something new that goes beyond the separate elements (Gough et al 2017).

Another key feature that underpins the robustness of systematic reviews is transparency (See Chapter 20 on reporting a QES). As the case examples illustrate the methods for integrating a QES with effectiveness evidence vary and often feature iteration and innovation, this makes transparency in reporting integration methods particularly vital. Similarly, the non-standardised methods and high levels of interpretation and creativity required mean that reviewer reflexivity is vital in MMSR. For example, given that the endeavour involves making comparisons and connections between research studies that are not only conducted by different researchers, but are embedded in different research traditions, authors may not be using the same language or frame of reference when describing phenomena or interventions. As such, creating comparative matrices or determining how QES themes can inform sub-group analyses is unlikely to be simple. Thus, reflexive accountability from the review team about the way that their perspectives and personal biases shaped these judgements will be important.

Box 8 below offers some guiding questions that review authors can use to consider the conduct and communication of their own MMSR or to examine an existing MMSR.

Box 8: Guiding questions for the conduct and reporting of MMSR

Integration approach: Which approach is appropriate to integrate the findings of the QES and effectiveness syntheses - comparison or connection?

Method / tool: What method or tool is appropriate for integrating the QES and effectiveness evidence? For example, is a matrix, annotated logic model or line-of-argument most appropriate? Is a new method or tool appropriate / desirable?

Execution / reporting: How explicit / systematic is the procedure for integrating the QES and effectiveness syntheses? How transparently is the process of integration reported?

Diversity of perspective: In what ways has integrating different types of evidence in the review increased the diversity of perspectives included?

Findings: How informative / illuminating are the findings of the integrated evidence? How might this 'mixed' evidence support improved decision-making?

14.9 Chapter information

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