

A METHODOLOGICAL UPDATE ON THE USE OF QUALITATIVE EVIDENCE IN HEALTH TECHNOLOGY ASSESSMENT

Report by the Decision Support Unit

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The Decision Support Unit (DSU) External Assessment Centre is based at the University of Sheffield with members at York, Bristol, Leicester and the London School of Hygiene and Tropical Medicine. The DSU is commissioned by The National Institute for Health and Care Excellence (NICE) to provide a research and training resource to support the Institute's Centre for Health Technology Evaluation Programmes. Please see our website for further information www.nicedsu.org.uk.

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EXECUTIVE SUMMARY

The last five years have seen unparalleled methodological developments in qualitative evidence synthesis. Some developments have accompanied increased recognition of the value of incorporating qualitative evidence within the evidence to decision-making process. Others have refined different stages of the systematic review process such as focusing the question, searching, quality assessment, and reporting. Finally, yet others have advanced an existing methodology for qualitative synthesis such as framework synthesis, meta-aggregation or meta-ethnography, or specifically, some technique or procedure within that methodology (e.g. reciprocal translation). Health technology assessment (HTA) agencies and guideline producing agencies, either separately or as unitary organisations as in the case of NICE, have proved particularly active within methodological developments, along with international collaborative networks and increasing numbers of academic researchers.

This report summarises methodological developments occurring over the period 2012 through to 2020, updating and overlapping with the literature that informed the previous edition of the NICE *Guide to the Methods of Technology Appraisal* (PMG 9). It begins by examining and critiquing existing mentions of qualitative evidence, in PMG9 and other relevant NICE Methods Guides. Relevant literature has then been identified through the specialist register of the Cochrane Qualitative and Implementation Methods Group, through citation searches of key methodology items, grey literature searches of health technology assessment agency and guideline production organisation websites and review of current awareness updates.

The report identifies four meta-themes that have shaped developments over the last eight years:

1. Increased interest in complex interventions;
2. Greater appreciation for the integration of diverse quantitative and qualitative evidence;
3. Recognition of the role of theory in understanding how interventions work;
4. Awareness of the differential effects of context.

After summarising data extracted in fulfilment of the following review questions:

- 1) What are the positions of key stakeholders, leading research initiatives, and international HTA bodies in using qualitative evidence to inform decision making in HTA? What are the rationales?
- 2) What elements of the decision problem could be informed by qualitative evidence or qualitative evidence synthesis in the HTA process?
- 3) With respect to each of those elements/aspects above, whose perspectives/views should be involved, collected, analysed and considered in the HTA process?
- 4) in what circumstance/scenarios or topic areas should special or greater attention given to the use of qualitative evidence/synthesis in informing decision making?
- 5) In a standard HTA process where evidence from multiple sources are considered, how should qualitative evidence be analysed, presented, evaluated, and considered in the deliberation process?

Recommendations are made for current and future NICE practice.

Recommended Changes:

It is recommended that:

1. NICE explore methods for integration of quantitative and qualitative evidence, through all its activities perhaps through use of, or development of, an appropriate evidence to decision-making framework, to be accommodated within existing organisational timescales, for guidelines and technology appraisal.
2. that NICE examine the feasibility of conducting rapid qualitative evidence syntheses as explored by Health Improvement Scotland, the World Health Organization and the Canadian Agency for Drugs and Technologies in Health (CADTH), proportionate to both timescale and qualitative input.

Suggested changes:

1. NICE explore systematic and extensive use of other purpose-specific frameworks, to accelerate analysis and to ensure standardisation of approaches (e.g. TIDieR, ICAT-SR, CICI, PROGRESS-Plus etcetera);
2. NICE examine the potential role of other contributions from qualitative evidence to the decision-making process, e.g. feasibility and implementation considerations and the values, preferences and attitudes of health providers and planners and identify “triggers” that flag the potential value of such approaches;
3. NICE explore the potential value of wider use of qualitative evidence in enhancing interpretation of the quantitative evidence.
4. NICE employ an integrated approach to evidence to decision-making that identifies circumstances where both quantitative and qualitative evidence might populate a specific decision-making domain, rather than separate the domains to either one type of evidence or the other.

Developments for ongoing monitoring:

1. Development of integrated approaches for combining quantitative and qualitative assessments culminating in approaches for handling mixed methods findings¹;
2. Further advances in methods for aggregation, synthesis and integration for qualitative data, primary qualitative research and qualitative evidence synthesis to include use of conceptual models and diagrammatic approaches.

¹ The NICE Centre for Guidelines is working on this with a view to introducing guidance for the next Guideline Manual update (to supplement PMG 20).

1. GLOSSARY

CASP	Critical Appraisal Skills Programme
EPPI-Centre Centre	Evidence for Policy and Practice Information and Co-ordinating Centre
FAME	Feasibility Acceptability Meaningfulness Effectiveness - JBI model for Evidence Based Healthcare
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
GRADE-CERQual	GRADE Confidence in the Evidence from Reviews of Qualitative Research rating system for qualitative findings
iCAT-SR Reviews	Intervention Complexity Assessment Tool for Systematic Reviews
JBI	Joanna Briggs Institute
NHMRC	(Australian) National Health and Medical Research Council
NICE	National Institute of Health and Care Excellence
PerSPECTiF	Perspective Setting Phenomenon of Interest Environment Comparator (if present) Timing Findings alternative question structure for complex interventions
PICO	Population Intervention Comparison Outcome question structure
PROGRESS-Plus	Cochrane Equity Group schema for equity considerations
QES	Qualitative Evidence Synthesis
RETREAT	Research question Epistemology Time/Timing Resources Audience & purpose and Type of Data – framework for choosing appropriate methods for qualitative synthesis

SIGN	Scottish Intercollegiate Guidelines Network
TIDieR	Template for intervention description and replication checklist and guide for describing intervention components
WHO	World Health Organization

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3. INTRODUCTION

3.1. BACKGROUND

Increasingly, health technology assessment (HTA) agencies and guideline producing organisations recognise that their methodologies should not only be evidence based but also that the resulting recommendations are relevant and implementable(1). Multiple criteria inform an eventual decision, in addition to evidence for the effectiveness of an intervention. Other criteria include values and preferences, acceptability, feasibility and equity implications. In order to populate such criteria qualitative evidence is required, both to supplement and complement evidence from rigorous quantitative studies. Transparency requires that qualitative evidence extends beyond the expert opinion of guideline stakeholders, and any research that they have serendipitously identified and brought to bear on a particular issue. In some cases it may require ad hoc or opportunistic collection of qualitative data, systematic identification of primary qualitative research studies or a formal process of systematic review of relevant qualitative research.

Evidence from qualitative research examining patients' experiences of a disease or condition, their experience of the treatment and how it affects the lives of patients, family and carers adds important context to findings from clinical and health services research. In stopping short of the claims of causation made by the clinical effectiveness data, qualitative evidence from patient experience "cannot prove effectiveness, but it can give context and inform feasibility and acceptability of clinical research"(2). Patients' experience of a treatment may work alongside the value of clinical effectiveness evidence to strengthen the case in favour of an intervention. Conversely, where patients' experience is negative this may undermine or even negate the perceived value of a demonstrated clinical effect.

At an aggregative level a systematic review of qualitative studies, or a qualitative evidence synthesis (QES) as labelled by the international Cochrane Collaboration, is "an approach for synthesising the findings from multiple primary qualitative studies"(1). Findings from QES may be considered more robust and potentially more useful than those from individual primary qualitative studies as they "bring together evidence from multiple studies, thus providing richer data than a single study can"(1). QES can also

“identify patterns in the data, explore similarities and differences across settings, lead to a new interpretive model or framework, and contribute broadly to a field of research”(1)..

Although evidence from QES has most commonly been factored into the latter stages of the guideline or health technology assessment process, as a moderating lens on the effectiveness evidence, it holds the potential to inform all stages of guidance production. Qualitative evidence may help from the very beginning in identifying what interventions are acceptable and which outcomes are desirable. It may help to understand differences in the contexts within which an intervention may or may not work. It can also help in developing implementation considerations. QES reviews may confirm that interventions indicated by the effectiveness evidence are acceptable, feasible and equitable. Conversely, they may act as a counterpoint to the prevailing direction indicated by the effectiveness evidence in flagging undesirable outcomes and unintended consequences. Furthermore, they may help to isolate specific contextual circumstances under which an intervention that works on average is likely to work better or worse than expected. Thus, they can help to indicate a specific population for whom an intervention works under specific circumstances, resulting in targeting of that population for benefit and cost-effective deployment of resources.

This review examines some of the claims made for qualitative evidence in contemporary methodological guidance authored by national and international organisations and agencies. It then explores some of the developments in methodology that hold the potential to inform future NICE Methods guidance. It critiques potential directions of travel against the tight constraints of the NICE evidence production process, assessing what is both feasible and potentially useful.

4. QUESTIONS TO BE ADDRESSED BY THE METHODOLOGICAL UPDATE

In commissioning this methodological update the National Institute for Health and Clinical Excellence team held certain key questions at the forefront of their minds. They articulated these in the form of five questions to be addressed, leading ultimately to a series of staged recommendations:

1. What are the positions of key stakeholders, leading research initiatives (eg. Integrate HTA), and international HTA bodies in using qualitative evidence to inform decision making in HTA? What are the rationales?
2. What elements of the decision problem could be informed by qualitative evidence or qualitative evidence synthesis in the HTA process? For example, according to Integrate HTA, those elements could include:
 - social, legal and ethical considerations in connection to the effectiveness of the technology;
 - views and opinions of patients, clinicians, families and carers;
 - patient moderations (characteristics that have a modifying impact on the treatment effect) and;
 - patients' preference and quality of the lives of people with the condition or being treated with the technology?
3. With respect to each of those elements/aspects above, whose perspectives/views should be involved, collected, analysed and considered in the HTA process? For example, patients, clinicians, families/carers, health care professionals in the community, service delivery providers, or the public? And how?
4. In what circumstance/scenarios or topic areas should special or greater attention be given to the use of qualitative evidence/synthesis in informing decision making? For example, in rare or ultra-rare diseases where there is often a lack of evidence on both clinical- and cost-effectiveness? Or in HTA of complex interventions? What are the positions/recommendations/suggestions of main stakeholders and leading research initiatives regarding using qualitative evidence/qualitative evidence synthesis to inform the decision making in these circumstances above and why?
5. In a standard HTA process where evidence from multiple sources are considered, how should qualitative evidence be analysed, presented, evaluated, and considered in the deliberation process?

These questions led to a final requirement:

- Based on the above findings, what are the recommendations/suggestions for NICE CHTE 2020 Methods Update with regards to using qualitative evidence/synthesis to inform decision making?

5. INTERPRETATION OF SCOPE

The INTEGRATE-HTA Project highlights the importance of assessing ethical aspects, socio-cultural aspects and legal aspects alongside a more typical focus on effectiveness and economic aspects(3). The INTEGRATE-HTA project paper cites Gerhardus and Stich (2014) in summarizing four methodological approaches for assessing social aspects of health technologies(4), namely checklists, literature reviews, participatory approaches, and primary empirical research. These correspond closely to the scope as identified for this report. Subsequently the same team has conducted a comprehensive systematic review accompanied by a query sent to all member agencies of the International Network of Agencies for Health Technology Assessment (INAHTA) to ask which methods they use to assess social and cultural aspects(5). They grouped 125 publications within the same four categories; checklists for experts, literature reviews, stakeholder participatory approaches, primary data collection methods, together with a category for combined methodological approaches.

We similarly consider that qualitative evidence for incorporation within health technology assessment processes may derive from several sources:

1. Ad hoc surveys or primary qualitative research commissioned by the agency or by representative groups
2. Qualitative data collected alongside the evaluation, perhaps collected by the manufacturer/pharmaceutical company
3. Qualitative evidence synthesis of published qualitative research
4. Opportunistic qualitative data (e.g. collected from patient bulletin boards, Twitter feeds or other social media)

Each of these approaches holds advantages and limitations as briefly rehearsed below.

To supplement the main analysis on health technology assessment activities and main methodological developments a brief desk-based review was undertaken exploring “health technology assessment” and “qualitative research”. A search was conducted on PubMed MEDLINE (150 hits), supplemented by Google Scholar searches (981 results), citation searches, use of Related Articles features and use of Co-Citations.

Included items covered the period 2012 to 2020 in order to complement coverage of the existing Centre methods manual.

5.1. AD HOC SURVEYS OR PRIMARY QUALITATIVE RESEARCH COMMISSIONED BY THE AGENCY OR BY REPRESENTATIVE GROUPS

Primary research offers one approach to gathering patient, family and carer perspectives as well as those of health care providers. Exemplar methods include those that can elicit mixed quantitative and qualitative data such as surveys, interview studies and those that employ genuinely mixed methods approaches. Face-to-face interviews, interviews by phone and postal questionnaires can be used. Qualitative methods are useful for exploring attitudes, acceptability and the values and preferences of stakeholders. However, primary research is characterised as high-cost, in both design and conduct and its timescales may be prohibitive. Therefore, primary research should only be used judiciously. Where primary research is conducted, then it is helpful to use an underpinning framework both in developing such tools as questionnaires, interview guidelines or observation protocols and in ensuring that all data items required are sufficiently targeted.

5.2. QUALITATIVE DATA COLLECTED ALONGSIDE THE EVALUATION, PERHAPS COLLECTED BY THE MANUFACTURER/PHARMACEUTICAL COMPANY

Typically, qualitative data collected alongside the evaluation may be specified via checklists, frameworks or templates. Aspects to be covered may be specified as checklists for experts or as specification templates for use by HTA agencies or by pharmaceutical companies and manufacturers. A series of questions and sub-questions are outlined with a view to structuring expert consultations or specifying literature. The INTEGRATE-HTA report(3) identifies the HTA Core Model(6) as an example of such a framework. It concludes that “the effort involved in the completion of such a checklist is manageable”. Checklists offer a structured agenda but for their utility depend upon their level of detail and “their degree of cultural sensitivity”. The INTEGRATE-HTA report further recommends that open questions are added to allow for additional information as well as to enable connections to be made across each component of the checklist.

5.3. QUALITATIVE EVIDENCE SYNTHESIS OF PUBLISHED QUALITATIVE RESEARCH

Systematic reviews seek to identify and synthesize research studies across multiple studies that address a predefined question, whether this relates to a specific condition, a particular technology or the intersect between the two. Specifically, qualitative evidence syntheses (QES) summarise qualitative research studies that relate to the experience of a particular condition or a specific treatment. They are typically used to underpin a guideline production process, to complement the clinical effectiveness and cost effectiveness data and are therefore familiar in agencies such as NICE where both technology assessments and guidelines are produced. Notwithstanding their resource intensity, they feature prominently within a health technology assessment context(7). Where different types of evidence are synthesized narrative approaches are considered more appropriate, such as content analysis and thematic summaries. Where qualitative evidence is more similar in form more interpretative approaches are used, namely framework or thematic synthesis, realist synthesis or meta-ethnography can be used. The strengths and weaknesses of these methods are presented in a specific INTEGRATE-HTA report(8) and accompanying article(9).

Inclusion of grey literature can be advantageous when seeking multiple perspectives. However, this may also challenge otherwise accepted processes of quality assessment by amplifying both “signal” and “noise”. Frameworks mentioned above (EUNetHA Core Model) and subsequently (the Evidence to Decision Making Frameworks) may offer a structure by which to target literature searches and populate a template for a systematic review.

5.4. OPPORTUNISTIC QUALITATIVE DATA (E.G. COLLECTED FROM PATIENT BULLETIN BOARDS, TWITTER FEEDS OR OTHER SOCIAL MEDIA)

Under certain circumstances, and notwithstanding concerns about their scientific quality, “websites, newspapers, or documents from different stakeholder groups such as professional umbrella organizations can be of interest to reconstruct different perspectives regarding a technology and its acceptance”(3). The Internet and the growth of social media have made harvesting of such data much easier. However, this

should not be allowed to mask the fact that assessment of the validity of such data becomes correspondingly more challenging.

The Internet also offers a practical vehicle for participatory approaches, as highlighted by Gerhardus and Stich(4) Participatory approaches, stakeholder involvement or the involvement of the public offer different approaches to including the “perspectives of different stakeholders and their priorities in HTA”. These can help in aligning the assessment with user values and therefore improve acceptance by different groups of stakeholders. Participatory approaches extend beyond the unstructured involvement of stakeholders and the public in HTA by prioritising formal mechanisms. Models of involvement typically need to be agency specific as different constitutions of “stakeholders with different experiences in HTA, different interests as well as with different levels of influence on decision making processes (e.g. representatives of industry, of national health care agencies, local government representatives, clinicians, patient associations)” are variously involved.

Participatory approaches can include Delphi methods and the Nominal group technique, as applied by the NICE’s Citizen Council. On the positive side participatory approaches can capture the heterogeneous perspectives of professionals, patients, relatives etc. with their varying expertise. At the same time selection bias in the recruitment of participants may result in bias and in undesirable power dynamics. As the INTEGRATE-HTA summary cautions “Group dynamics and socio-cultural differences can...cause misunderstandings, social desirability, and scepticism against research” while “differences in the understanding of the technology itself could also cause misunderstandings”(3). A particular challenge for HTA agencies relates to how to manage perceived “unscientific evidence” given that participatory approaches gravitate to the more value-laden territories of the HTA process.

It is important to acknowledge that although qualitative evidence may overlap with patient and public representation, and in some cases the mechanisms for both are the same, the two should not be considered synonymous(2). Patient and public representation serves multiple purposes of which only a limited few relate to the perceptions or experience of a condition or of a technology. Furthermore,

representation from stakeholders, whether patients, the public or those with other types of expertise, does not necessarily observe the checks and balances that qualitative evidence, particularly qualitative research, puts in place. A health technology agency may maintain good procedures for stakeholder engagement but may not necessarily possess satisfactory mechanisms for incorporating qualitative evidence within the decision-making process.

6. REVIEW OF EXISTING NICE METHODS MANUALS

The following NICE Methods Guides and Manuals were reviewed in the course of this update:

1. Guide to the Methods of Technology Appraisal (2013)
2. Interim Process and Methods of the Highly Specialised Technologies Programme
3. Diagnostic Assessment Programme Manual
4. Medical Technologies Evaluation Programme Methods Guide
5. Developing NICE Guidelines: the Manual (PMG 20)
6. Developing NICE Guidelines (Appendix H)

Other NICE Methods Manuals currently available on the Website include:

The Public Health Guidance (PMG4)(10), Guidelines Manual (PMG6)(11) [superseded by PMG 20] and the Social Care Manual (PMG10)(12)

6.1. GUIDE TO THE METHODS OF TECHNOLOGY APPRAISAL (PMG 9; 2013)

The Guide to the methods of technology appraisal (PMG 9) is the forerunner document for this update.

6.1.1. Summary of Contents

According to PMG 9:

“[In the context of technology appraisals] the main purpose of qualitative research is to explore areas such as patients' experiences of having a disease or condition, their experiences of having treatment and their views on the acceptability of different types of treatment (Section 3.3.8, p. 23).

This represents a circumscribed and functional interpretation of qualitative evidence, not extending beyond the disease/condition and its treatment. It would be interesting to explore whether this is interpreted, by patients and/or analysts, as including the wider service context within which treatment is delivered and whether this impacts upon the evaluation frame within which decision-making takes place.

PMG 9 acknowledges the perspectives of both patients and carers as experiential sources (4.3.1), to be elicited in the form of written submissions, on:

- the experience of having the condition, or in the case of carers, the experience of caring for someone with the condition
- the experience of receiving care for the condition in the healthcare system
- the experience of having specific treatments for the condition
- the outcomes of treatment that are important to patients or carers (which may differ from the outcomes measured in the relevant clinical studies and the aspects of health included in generic measures of health-related quality of life)
- the acceptability of different treatments and modes of treatment
- their preferences for different treatments and modes of treatment
- their expectations about the risks and benefits of the technology.

The written submission process allows for “written accounts of [patient, family or carer] experiences and points of view” and acknowledges that “narrative summaries, preferably with illustrative quotes...are acceptable”. Specifically, no provision is made for existing qualitative evidence syntheses, where available. Although it is appreciated that the innovative nature of the intervention or the rarity of the condition may preclude the availability of such syntheses these would, where available, offer a more systematic and wide-ranging coverage of issues than individual patient/family/carer responses. Indeed, the technical content recognises the value of primary qualitative techniques, such as thematic analysis, in facilitating synthesis but does not acknowledge the corresponding value of their secondary equivalents (e.g. thematic synthesis). Instead the implication is of primary data collection using a template (as in the first approach identified in Section 4).

The Methods Guide (PMG 9) does explicitly seek a diversity of opinion and this attention to the “disconfirming case” is to be welcomed. However, it is unclear how

current methods of consultation perform with regard to the equity of the response. Potentially, existing published accounts of the condition or intervention (whether as individual studies or syntheses) could serve a complementary function, alongside primary patient, family and carer data in ensuring a broader representation of patient voices.

6.1.2. Critique of Contents

PMG 9 does indicate an “open door” with regard to the importance of patient, family and carer voices, the elicitation of written qualitative evidence and the need to be cognizant of the minority voice. Detail on the methods for achieving this are sparse and favour the opportunistic collection of individual representation over a collective body of published experience and of primary data analysis over techniques of qualitative synthesis. While the underlying assumptions for these approaches may remain valid there is an attendant risk that such evidence is being overlooked even when available.

6.2. INTERIM PROCESS AND METHODS OF THE HIGHLY SPECIALISED TECHNOLOGIES PROGRAMME

6.2.1. Summary of Contents

The experiences of those with very rare conditions are particularly suited to exploration by qualitative evidence as well as posing particular challenges for patient recruitment and data collection. Evaluation of highly specialised technologies (HST) largely follows the methods of NICE’s Guide to the Process and Methods of Technology Appraisal (PMG 9; 2013) with variations specific to technologies for very rare conditions. Qualitative experience from patients can contribute to the decision-making of the Programme:

“When making decisions about new treatments, committees use criteria such as the nature of the condition, the impact of the new treatment, the cost and cost-effectiveness of the treatment, and the treatment’s impact beyond direct health benefits”.

The Evaluation Committee (p. 8) emphasises a remit that takes account a full range of categories of evidence, specifically including “any qualitative evidence related to the experiences of patients, carers and clinical experts who have used the technology being evaluated or are familiar with the relevant condition”. This additional mention of “experiences of clinical experts” in connection with qualitative evidence is not signalled by PMG 9.

6.2.2. Critique of Contents

While acknowledging a role for the contribution of qualitative experience, not just from patients but also from clinical experts, the highly specialised technologies methods manual extends the scope of qualitative evidence beyond that of its ‘parent’ methods manual of PMG 9. However, the manual does not acknowledge a particular role in relation to very rare conditions nor does it offer acknowledgement of the particular challenges associated with eliciting the views and experiences of those with very rare conditions using qualitative research methods.

6.3. DIAGNOSTIC ASSESSMENT PROGRAMME MANUAL

6.3.1. Summary of Contents

As with the highly specialised technologies Evaluation Committee, the diagnostic assessment programme committee (p. 105) acknowledges a remit that specifically includes “any qualitative evidence related to the experiences of patients, carers and clinical experts who have used the technology being evaluated or are familiar with the relevant conditions and patient groups”. It identifies a role for indirect evidence and models of the care pathway stating that its consideration includes “various kinds of evidence”, according to the type of question. How such evidence is handled “depends on both the overall balance and quality of the evidence from different sources, and the suitability of a particular type of evidence to address the issues under consideration”.

6.3.2. Critique of Contents

The Diagnostic Assessment Programme Manual acknowledges a role for qualitative evidence but does not provide detail on how such evidence is to be handled. In

particular its reference to the minimisation of bias in high quality sources of evidence appears to be predicated on quantitative conceptualisations of research quality.

6.4. MEDICAL TECHNOLOGIES EVALUATION PROGRAMME METHODS GUIDE (PMG 33)

6.4.1. Summary of Contents

In addition to the sponsor's submission and evidence presented by an independent external the Programme solicits the following evidence (p. 14) that might include qualitative evidence:

- evidence from the programme team or other relevant organisations or working groups;
- contributions from expert advisers;
- contributions from patient and carer organisations
- information about ongoing or future research.

The contribution of expert advisers does not explicitly engage with published qualitative evidence, either from single studies or from syntheses but is recognised as “providing additional knowledge, opinion and experience to the committee. They provide opinions on the published evidence and supplement it with information on anecdotal or theoretical outcomes, and other information relevant to the evaluation of the technology, its comparators and the conditions for which it is used”. However, in terms of coverage this expert contribution extends to the same domains that are covered by qualitative evidence relating to implementation factors, namely including “the technical specification of the technology if this might affect its capability in delivering the claimed benefits; to the training and experience needed to use the technology; and to organisational factors that might influence the technology's technical performance or use in clinical practice” . In this connection it is noteworthy that issues of feasibility and acceptability, to health practitioners not just patients, are included as the legitimate focus of qualitative evidence by organisations such as Cochrane and the Joanna Briggs Institute. The Manual specifically states that “expert advice can also be used as part of evidence synthesis” but does not give any detail on how this might be achieved.

In connection with contributions from patient and carer organisations (p 17) the Programme recognises the unique insights that are offered by the experience of

patients and carers and implements this recognition by approaching “patient and carer organisations to obtain their views on the technology”. It is noticeable that patients and carers are identified not only as a source of individual insights such as “information about living with the condition to which the technology relates”, “outcomes”, ease of use, discomfort, how the technology affects daily activities, and other aspects of quality of life” but are also charged with more synthetic population-level or comparative insights e.g. “about any subgroups of patients who may need special consideration in relation to the technology” and “about using the technology and/or comparator technologies”.

6.4.2. *Critique of Contents*

Again the publication demonstrates a volition to factor in views and experiences from patients and from clinical experts and to value evidence that extends beyond clinical and cost effectiveness. A place is acknowledged for evidence synthesis, with regard to expert input, not that from patients and carer organisations but no detail is given on how this is to be achieved. The Manual acknowledges that the patient and carer contribution extends beyond individual insights and indeed can be most helpful in exploring differences across subgroups or comparisons between technologies. However, these synthetic insights require a level of analysis and interpretation that may not be possessed by individuals and may be effected by aggregation, if not formal synthesis, of collective experiences.

6.5. DEVELOPING NICE GUIDELINES: THE MANUAL (PMG 20)

Developing NICE guidelines: the manual (PMG 20) is the Methods Manual for the NICE Clinical Guidelines programme. It focuses on formal methods of synthesis for inclusion of qualitative research within the programme. As such it differs from the processes available to the NICE Centre for Health Technology Evaluation (CHTE) and can only offer an internal yardstick to this Methods Update. The underlying assumptions for the NICE Guidelines programme are that it can accommodate a qualitative evidence synthesis (approach 3 from those identified in Section 4) alongside a review of clinical effectiveness. However, the tight timescales preclude formal integration of quantitative and qualitative evidence within the synthesis process.

Integration (more correctly, assimilation) of qualitative evidence with quantitative evidence takes place during the committee process.

6.5.1. *Summary of Contents*

Developing NICE Guidelines: the manual (PMG 20)(13) acknowledges use of diverse types of evidence:

“other non-randomised evidence, such as... experimental and qualitative evidence, may also be used to inform assessments of effectiveness, or aspects of effectiveness. This evidence may include ways of delivering services, or the experience of people using services and how this contributes to outcomes”(13).

This includes a broader interpretation of the role of qualitative research than is present in PMG9 as it goes beyond the immediate purview of a disease/condition and its treatment to the wider context in which services are delivered and experienced.

In particular, qualitative evidence may make a specific contribution when juxtaposed with complementary types of evidence:

“additional types of evidence reviews may be needed to answer different aspects of the question. For example, additional evidence reviews might address the views of people using services or the communities where services are based, or barriers to use as reported by practitioners or providers. Sometimes, a review may use different sources of evidence or types of data (for example, a review may combine current practice or map quantitative information with qualitative data [that is, a mixed methods review]”(13).

PMG20(13) identifies three main roles for qualitative evidence (Table 1). Qualitative studies may form the primary source of evidence (column 1), qualitative evidence may be synthesised to address specific review questions (column 2) and it may serve a supplementary role in interpreting quantitative evidence (column 3)

Table 1 - Roles identified for Qualitative Evidence

Qualitative studies as the primary source of evidence to address review questions on:	Examples of the types of review questions that could be addressed using qualitative evidence include:	Examples of questions for which qualitative evidence might supplement quantitative evidence include:
the experiences of people using services, family members or carers or practitioners (including information on what works, for whom and under which circumstances)	How do different groups of practitioners, people using services or stakeholders perceive the issue (for example, does this vary according to profession, age, gender or family origin)?	How acceptable is the intervention to people using services or practitioners?
the views of people using services, family members or carers, the public or practitioners opportunities for and factors hindering improvement of services (including issues of access or acceptability for people using services or providers)	What social and cultural beliefs, attitudes or practices might affect this issue?	How accessible is the intervention or service to different groups of people using services? What factors affect its accessibility?
variations in delivery and implementation for different groups, populations or settings factors that may help or hinder implementation	How do different groups perceive the intervention or available options? What are their preferences?	Does the mode or organisation of delivery (including the type of relevant practitioner, the setting and language) affect user perceptions?
Social context and the social construction and representation of health and illness	What approaches are used in practice? How effective are they in the views of different groups of practitioners, people	

	using services or stakeholders?	
Background on context, from the point of view of users, stakeholders, practitioners, commissioners or the public	What is a desired, appropriate or acceptable outcome for people using services? What outcomes are important to them? What do practitioner, service user or stakeholder groups perceive to be the factors that may help or hinder change in this area?	
theories of, or reasons for, associations between interventions and outcomes.	What do people affected by the guideline think about current or proposed practice?	
	Why do people make the choices they do or behave in the way that they do?	
	How is a public health issue represented in the media and popular culture?	

PMG20 references, and is discernibly influenced by, the Cochrane Qualitative and Implementation Methods Guidance (2017/2018), published as a series in *Journal of Clinical Epidemiology* and summarised in the most recent version of the Cochrane Handbook (2020). As a consequence it engages well with current debates being enacted within qualitative evidence synthesis. Box 1 illustrates this in relation to alternatives to comprehensive sampling.

Box 1 - NICE recognition of alternatives to comprehensive sampling

“For some types of review question, for example, questions for which qualitative research is more appropriate, it may not be necessary to identify all the literature on a topic. The objective may be to reach theoretical saturation, where any additional studies identified merely support the existing line of argument, rather than identify all relevant studies”(13).

“In this context, it may be possible to undertake searches which are more precise. The search approaches for this type of evidence have been reviewed and summarised by Booth (2016) and can be used to guide practice”(13).

PMG20(13) also references specific aspects of the qualitative evidence synthesis process. So, for quality assessment it recommends that “Critical appraisal of qualitative evidence should be based on the criteria from the Critical Appraisal Skills Programme”(14). *NB. No justification is given for preference for this specific instrument, although it remains the most widely used critical appraisal tool for qualitative research. However, by implication part of its attraction is seen in its clarity as evidenced by the juxtaposition of this sentence with a sentence on clarity of methods.*

PMG20(13) makes some useful distinctions between different types of evidence. For example, it acknowledges the importance of what it describes as “Context-sensitive scientific evidence” (p. 78-79). It relates this to “information on attitudes, implementation, organisational capacity, forecasting, economics and ethics...mainly derived using social science and behavioural research methods, including quantitative and qualitative research studies, surveys, theories, cost-effectiveness analyses and mapping reviews”. The Guidelines Manual comprehensively describes a complementary role for context sensitive evidence, in helping to interpret “context-free evidence” and to “provide the basis for more specific and practical recommendations”. This Guidelines Manual (PMG20) then offers the most broad-sweeping coverage of the many functions of qualitative evidence to be currently found in NICE Methods Manuals, matching most of the functions identified from other agencies (see below). Furthermore, PMG20 engages with the contemporary trend to engage with

programme theory, particularly in the form of logic models. These have featured in recent methodological work from INTEGRATE HTA, the AHCPR Methods work and the outputs of the World Health Organization on complex interventions.

Finally, the Manual identifies a role for 'Colloquial evidence' which can “complement scientific evidence or provide missing information on context”. Such evidence can derive from expert testimony, committee members, service users and registered stakeholders. Acknowledging that colloquial evidence can include “evidence about values (including political judgement), practical considerations (such as resources, professional experience or expertise and habits or traditions, the experience of people using services) and the interests of specific groups (views of lobbyists and pressure groups)” the guidance does not, however, suggest how this values-based material be reconciled with the filtered and quality assured evidence sources that draw upon formal qualitative research. Instead primary filtering, for example in expert testimony, engages with the markers of relevance, not rigour:

“Inclusion criteria for oral or written evidence specify the population and interventions for each review question, to allow filtering and selection of oral and written evidence submitted to the committee”.

The Guidelines Manual (PMG 20) acknowledges that “qualitative evidence occurs in many forms and formats and so different methods may be used for synthesis and presentation (such as those described by Cochrane)”. Where qualitative evidence is “extensive” (as undefined), then the Guidelines Manual states that “a recognised method of synthesis is preferable. If the evidence is more disparate and sparse, a narrative summary may be appropriate” (p 106-107). The Guidelines Manual identifies most of the major methods for qualitative synthesis e.g. thematic synthesis, 'conceptual mapping', a grounded approach, meta-ethnography and meta-synthesis.

In its Methods Manual (PMG 20) NICE articulates its commitment to tackling health inequalities, particularly in relation to factoring socioeconomic status with in its equality considerations. A key feature of qualitative evidence is its role in relation to identifying equity implications. This is briefly covered in the Section “Ensuring inclusivity of the evidence review criteria”. This refers to the use of

“PROGRESS-Plus criteria (including age, sex, sexual orientation, disability, ethnicity, religion, place of residence, occupation, education, socioeconomic position and social capital; Gough et al. 2012) and any other relevant protected characteristics, and record these where reported, as specified in the review protocol”

The NICE Guidelines Methods Manual (p. 108 – 113) demonstrates good consideration of the use of qualitative evidence in the generation of evidence statements, drawing on up-to-date thinking from the GRADE-CERQual initiative (See Box 6.3). GRADE-CERQual is well-conceived in relation to the four considerations of methodological limitations, adequacy, coherence and relevance. This structured approach to the attributes of qualitative synthesis is not mirrored in relation to defining attributes of primary qualitative evidence:

“Statements should summarise the evidence, its context and quality, and the consistency of key findings and themes across studies (meta-themes). Areas where there is little (or no) coherence should also be summarised”.

In Section 9.1 on Availability of evidence to support implementation (including evidence from practice) (p.169) the use of qualitative evidence is presented very much as an afterthought. The Methods Manual states that:

“The committee should also judge to what extent it will be feasible to put the recommendations into practice. They can use expert oral or written testimony, the experience of committee members or results from other approaches (see chapter 10 and appendix B) if these have been used”.

Before adding that:

“They may also be able to draw on qualitative studies or other forms of evidence relating to organisational and political processes where appropriate”.

Considerations of feasibility, recognised by the Joanna Briggs Institute and by Cochrane as the legitimate domain of qualitative evidence, are mentioned briefly without further details of methods for their inclusion:

“The committee should consider the extent of change in practice that will be needed to implement a recommendation, staff training needs, policy levers and funding streams, and the possible need for carefully controlled implementation with, for example, training programmes” (p. 169)

Finally the Glossary includes the following entry for “Qualitative research” (p 226)

“Qualitative research explores people's beliefs, experiences, attitudes, behaviour and interactions. It asks questions about how and why, rather than how much. It generates non-numerical data, such as a person's description of their pain rather than a measure of pain. Qualitative research techniques include focus groups and in-depth interviews.”

6.5.2. Critique of Contents

The Guidelines Manual demonstrates a good level of awareness of current methods of qualitative evidence synthesis, its main approach to use of qualitative evidence. However, it does not narrow the choice of methods down to the limited options now being preferred by Cochrane{Harden, 2018 #620} and the World Health Organization{Flemming, 2019 #485}, namely thematic synthesis, framework synthesis and meta-ethnography. Framework Synthesis based approaches are gaining increased popularity, partly because the output may already be in an easily assimilable form for audiences of policy makers. In contrast, thematic synthesis and meta-aggregation(72-76) have received sustained critiques, largely because of their reductionist approach to analysis and interpretation. Meta-ethnography, by way of contrast, is enjoying a considerable renaissance, largely because of research on its application(77, 78), work on developing reporting standards(79) and the potential utility of the method in the context of review updates(80) and reviews of reviews (so-called *mega-ethnography*(81)). The Guidelines Manual remains current with contemporary thinking with regard to the GRADE-CERQual approach and, indeed, is looking forward to potentially extending the synergies with the GRADE approach through methods for handling mixed methods evidence.

Qualitative research occupies a subordinate position along with other types of supplementary evidence to be potentially included in the committee's deliberations.

Little or no detail is given on how this type of evidence is to be included. This is particularly seen with regard to implementation, where qualitative evidence can yield important insights, for example in the acceptability and feasibility of training programmes. No detail is given on how this type of evidence is to be identified or presented.

Implicitly, the definition of qualitative research provided in the Glossary is not exclusive of the beliefs and experiences of patients, families, their carers, clinical experts and those delivering services. However, the way that this is explicitly framed, together with the example given, suggests that qualitative research is solely related to the experience of patients. Furthermore, the Glossary does not define “qualitative evidence” more generally, in terms of other types of data, that may not be included within “research”.

6.6. DEVELOPING NICE GUIDELINES (APPENDIX H)

6.6.1. Summary of Contents

Appendix H lists resources to be used in the technical process of rating and quality assessing evidence for inclusion in NICE Guidelines. Specifically, page 8 lists the following tools for use with a Qualitative review question:

1. GRADE-CERQual (for qualitative evidence synthesis and presentation after quality assessment of individual studies has been conducted).
2. (Preferred) CASP qualitative checklist
3. Cochrane qualitative checklist
4. JBI checklist for qualitative research
5. Quality Framework: Cabinet Office checklist for social research (if study is specific for qualitative 'evaluation' concerned with the development and implementation of social policy, programmes and practice)

6.6.2. Critique of Contents

The list of tools as given in Appendix H offers a reasonably contemporaneous spread of instruments for assessment. At the moment it is unclear why a review team would either want or need to extend beyond use of the “preferred” CASP qualitative checklist. A possible exception is the indication for the specific use of the Cabinet Office

instrument although this has been criticised for its lengthy impracticality within a review context.

Although the *CASP Checklist: 10 questions to help you make sense of a Qualitative research*(16) remains the most commonly used, and easiest to use, quality assessment instrument for qualitative research there is widespread recognition within the qualitative synthesis community that it cannot truly be considered “fit for purpose”. Its origins lie in critical appraisal of single qualitative papers; it was never intended for use in synthesis as seen in the latter questions about applicability:

“They are largely designed to familiarise users with study designs and help them evaluate the relevance of the paper to their practice as they contain several subjective elements which may not lend themselves to incorporation in a formal quality assessment” (15)

NICE does not favour a particular source for all its quality assessment tools but pursues a “best of class” approach. So, the Cochrane Risk of Bias Tool, used for assessment of randomised controlled trials is commonly regarded as the most valid instrument for this type of studies. The Cochrane sponsored CAMELOT project sought to identify candidate domains for a GRADE-CERQual compatible Risk to Rigour tool(15). Work is currently underway, as follow up to the CAMELOT project, to develop a checklist that is particularly amenable to use in conjunction with GRADE-CERQual assessments:

“Research is underway to examine which elements of critical appraisal are key for assessing the quality of research in the context of qualitative evidence synthesis and for use in the CERQual approach”(16).

This projected tool may well be “one to watch” given NICE endorsement of the GRADE-CERQual approach.

7. RESULTS AND ANALYSIS

Four meta-themes form a backdrop to this assessment of how wider developments in the use of qualitative evidence might inform production of NICE guidance. All are acknowledged to some extent in existing NICE methods manuals, particularly where these are recent (e.g. PMG 20). However, methodological developments constitute a shifting landscape and so the potential to become out of step is an important consideration. These four meta-themes are:

- Increased interest in **complex interventions**, requiring more sophisticated analytical techniques, evidenced by the recent WHO-sponsored mini-series in *BMJ Global Health*(17-25);
- Greater appreciation for the added value of **integration of quantitative, qualitative and other forms of evidence**, exemplified by papers from Cochrane and for the WHO;
- Realisation of the potential value of **theory-informed approaches(26-29)**, particularly those targeted at a programme theory or theory of change level illustrated by, but not confined to, the growth in popularity of realist approaches;
- Increased awareness of the **differential effects of context(19)** particularly in relation to disadvantaged groups, equity and wider transferability.

Many of these themes impact both at a conceptual level, informing the overall aims of the synthesis process, and instrumentally, in shaping how specific steps of the process are best undertaken.

7.1. OVERVIEW OF FINDINGS

Current NICE Methods Manuals already identify and acknowledge the importance of qualitative evidence in the deliberation process. They lack detail on the different forms such evidence might take and how exactly this evidence is to be integrated. In the most recently updated Manual (PMG 20) contemporary issues in Qualitative Evidence Synthesis are also acknowledged. Other Methods Manuals hint at a role for qualitative evidence but do not identify how this might best be managed. In particular, the documents fail to distinguish between rigorous sources of qualitative evidence and those that are less-filtered and which may be characterised as being value-laden. Use of evidence in decision-making frameworks may help to identify the respective contributions of available qualitative data, primary qualitative research and qualitative

evidence synthesis, of input from patients, families, carers and clinical experts, and of formal research versus opportunistic data collection and analysis.

The biggest limitation of current QES approaches within NICE, and more generally, is in not harnessing the integrative potential of bringing together quantitative and qualitative evidence in a way that adds value from complementarity and synergy. Current approaches juxtapose quantitative and qualitative evidence at committee meetings as the only way to identify relationships present in the data. How quantitative and qualitative might best be integrated within the tight time constraints of the production of NICE guidance is a challenge. Potential methods include an integrative commentary, an evidence-to-decision-making framework, and a more explicit presentation dynamic involving separate quantitative and qualitative discussions followed by an integrative facilitator.

6.2 LESSONS FROM CURRENT HTA PROGRAMMES AND INITIATIVES

The potential contribution of qualitative evidence is recognised throughout the Methods Manuals that support the technical processes that underpin NICE's decision-making. However, with the exception of the highly-developed approach to qualitative evidence synthesis outlined within the Guidelines Manual (PMG20), all the Manuals are short on the specific detail. In particular the Manuals lack detail on how qualitative evidence is to be handled technically, how qualitative evidence is to distinguish between evidence-based sources and those that are more value-laden and how qualitative evidence is to be integrated with clinical and cost effectiveness data. Typically, aggregation, synthesis or integration of qualitative evidence takes place within the deliberative processes of the various Committees. An assessment of NICE's methodological priorities(30), conducted in 2010, highlighted a need for assessment of qualitative research and its synthesis.

Health Improvement Scotland uses a two phased approach to the literature; first by identifying key qualitative studies to inform the user consultation and then by conducting rapid qualitative evidence syntheses. The latter are facilitated by using a patient experience template derived from multiple sources as a standardised approach to summarising data from qualitative research studies.

IQWiG (Germany) recognises the role of primary qualitative research and of qualitative evidence synthesis. Its most recent Methods Manual (Version 6.0) states that:

“research results from qualitative primary studies and from overviews of qualitative studies are used to determine (potential) information needs and to determine experiences with a specific clinical picture or with an intervention as well as for dealing with a disease”.

IQWiG (Germany) refers to its use of results from their own “qualitative surveys and analyses (individual or focus group interviews) as well as from qualitative studies and overviews” and these “form the basis for working on the domains of ethics, social issues and organizational matters”. As with NICE, IQWiG uses CASP quality assessment checklists within QES to determine study quality and it is currently observing a watching brief in relation to future use of GRADE-CERQual.

SBU (Sweden) has developed its own manual on using qualitative methods of analysis. The manual is divided into two sections; the first on primary methods of collection and analysis and the second on conducting qualitative synthesis. However, this manual in English focuses more on generic methods for qualitative analysis rather than specifically how they are used within the Agency.

The World Health Organization includes qualitative evidence syntheses within its guidelines process, to complement activity in relation to clinical effectiveness. An Evidence to Decision Making framework is used to martial the different types of evidence. GRADE-CERQual is then used to produce objective statements on the confidence associated with qualitative findings. It does not typically commission qualitative research to accompany its guidelines activities.

NICE timescales pose considerable challenges to the effective use of qualitative evidence whether as primary qualitative research, participatory approaches, qualitative synthesis or the integration of quantitative and qualitative evidence. Opportunistic input currently appears more feasible than structured and systematic approaches. Currently NICE methods do not capitalise on added-value features of mixed methods studies, most noticeably their shared context and the integration and

complementarity of their different approaches(22). Opportunistic approaches also raise potential equity concerns with certain populations being easier to mobilise whether through patient group representation or individual-based participatory approaches. The absence of Evidence to Decision Frameworks or of use of the PROGRESS-Plus Equity framework(19, 31-35) within NICE processes means that opportunities to identify equity considerations may be constrained. Recent guidance has been produced on how to use PROGRESS-Plus elements in the reporting of systematic reviews(36).

6.3 STAKEHOLDER POSITIONS AND RATIONALES (Q1)

Stakeholder positions were explored through use of the *CADTH Grey Matters* list of health technology agencies and guideline producing organizations and through a list of specific HTA agencies shared by the NICE analytical team (Appendix B). Health technology assessment agencies/guideline producing organisations across thirteen countries were reviewed (Australia, Austria, Belgium, Canada, Denmark, France, Germany, Ireland, Netherlands, Norway, Spain, Sweden, United States) plus seven international agencies or networks (Cochrane, EuNetHTA, HTA-I, INAHTA, Joanna Briggs Institute, WHO). A total of 73 entities (i.e. Web sites/ guidance documents/ separate initiatives) were reviewed.

Stakeholder recognition of the contribution of qualitative evidence synthesis has expanded over increasing domains and purposes. Early documents focused on the introduction of a patient or service user perspective alongside the well-established effectiveness worldview. Cumulatively, over thirty justifications for systematic assessment and synthesis of qualitative research can be identified in the stakeholder documents analysed for this report. Table 2 summarises these justifications and attributes these to one or more stakeholders. Fuller textual extracts articulating these positions and rationales are found in Appendix D.

Table 2 – Summary of Stakeholder positions and rationales

For the patient/service user	For the intervention	For other affected parties
How patients and the public relate to a given method/intervention (SBU/JBI)	Why and how interventions function (SBU/JBI/Cochrane)	Ethical dilemmas (SBU)
How individuals and communities perceive health (JBI)	Why interventions are not effective (JBI/Cochrane)	What actions need to be taken to achieve health outcomes and improve health and social systems (Cochrane)
How individuals and communities manage their own health (JBI)	Demands imposed by intervention in terms of knowledge and skills of professionals and organisations (SBU)	Demands imposed by intervention in terms of knowledge and skills of professionals and organisations (SBU)
How individuals and communities make decisions related to health service usage (JBI)	Understanding culture of communities in relation to implementing changes and overcoming barriers (JBI)	Inform planners and policy makers about how service users experience health as well as illness (JBI)
How individuals conceptualise good care (Cochrane)	How the implementation process produces (or fails to produce) improvements in health (Cochrane)	Not applicable
How patient/clients perceive different aspects of care (e.g. undergoing treatment or diagnosis, receiving different interventions, or living with different conditions) (SBU)	Evaluating activities of health services such as health promotion and community development (JBI)	How patient/clients' relatives perceive different aspects of care, (e.g. undergoing treatment or diagnosis, receiving different interventions, or living with different conditions) (SBU)

For the patient/service user	For the intervention	For other affected parties
Potential patient (mis)understandings of treatment and illness (GIN)	Improved potential for transferability (SBU)	Potential provider (mis)understandings of treatment and illness (GIN)
Utilisation of relevant data from lived experience of a health condition/illness experience (HIS/JBI)	Focus on context and similarities of context (SBU; Knowledge Synthesis Project)	Legal, financial and organisational health system factors (GIN)
Attitudes, beliefs, and perspectives of patients (JBI)	Additional (to patient representatives) transparent and systematic way of acknowledging contextual factors (GIN; SIGN; WHO; Carroll) (23)	Attitudes, beliefs, and perspectives of clinicians (JBI)
Recontextualising effectiveness with evidence on values and preferences, acceptability/appropriateness, feasibility and equity implications (Cochrane; JBI; WHO)	Recontextualising effectiveness with evidence on values and preferences, acceptability/appropriateness, feasibility and equity implications (Cochrane; JBI; WHO)	Increasing understanding of the values and attitudes toward, and experiences of, health conditions and interventions by those who implement or receive them
Impact of human suffering (JBI)	Wider understanding of factors that co-determine safety and cost-effectiveness (GIN)	Interpersonal nature of caregiver/patient relationships (JBI)
Develop a theory of why and how an intervention (complex or simple) works (WHO)	Examine factors affecting implementation, including context.	Explore experiences of providers of healthcare.
Explore experiences of living with a condition, which can impact on the feasibility and acceptability of an intervention.	Determine how components of complex interventions work to produce effects (WHO)	Not applicable

For the patient/service user	For the intervention	For other affected parties
Explore experiences of recipients of healthcare.	<p>Establish how and why implementation of interventions varies across contexts (WHO)</p> <p>Examine how a system changes when a complex intervention is introduced (WHO)</p> <p>What explains changes in the system over time (WHO)</p>	Not applicable
Unpack influence of individual characteristics, and attitudes toward health conditions and interventions (Cochrane)	Identify associations between broader environment within which people live and interventions are implemented (Cochrane)	Not applicable
Develop personalised/person-centred approaches (Cochrane/JBI)	Utilisation of relevant data from analogous technologies (HIS)	Not applicable
Improved patient satisfaction and willingness to follow treatment (Carroll) (23)	<p>Understand whether an intervention is likely to be useful and to be applicable to the local population (Cochrane)</p> <p>Why interventions are not adopted (JBI)</p> <p>Improved levels of adherence and clinical outcomes (Carroll) (37)</p> <p>Better understanding of complexity (Cochrane; Knowledge Synthesis Project)</p>	Understand political and operational factors associated with implementation of health policy, health systems, behavioral, environmental, or clinical interventions. (Cochrane)

For the patient/service user	For the intervention	For other affected parties
	Use of diverse sources of evidence (Cochrane; SIGN) Understand political and operational factors associated with implementation of health policy, health systems, behavioral, environmental, or clinical interventions. (Cochrane)	
Detailed understanding of complexity of interventions and implementation, and their impacts and effects on different subgroups of people and the influence of individual and contextual characteristics within different contexts (Cochrane)	Detailed understanding of complexity of interventions and implementation, and their impacts and effects on different subgroups of people and the influence of individual and contextual characteristics within different contexts (Cochrane)	Not applicable

NB - Where text is replicated across two or more adjacent cells this indicates that a rationale relates to multiple stakeholder positions.
 Cochrane = Cochrane Collaboration, GIN = Guidelines International Network; HIS = Health Improvement Scotland; JBI = Joanna Briggs Institute, SIGN = Scottish Intercollegiate Guidelines Network; SBU = Swedish Agency for Health Technology Assessment and Assessment of Social Services; WHO = World Health Organization.

Certain justifications have received particular emphasis over recent years, typically via multiple stakeholder agencies. These include:

1. The complementarity of qualitative evidence synthesis alongside the contribution of stakeholder groups and patient representatives, particularly in offering a wider range of perspectives and a systematic and explicit basis for decision making;
2. Factoring in of multiple evidence-to-decision criteria into decision-making, most notably feasibility, acceptability and equity, requiring the use of multiple data sources;

3. Increasing focus on intervention transferability and implementation context, together with the wider environment of social, cultural and legislative factors;
4. Privileging of other important perspectives beyond the patient/service user, most notably carers/relatives and the health service staff viewpoint
5. Use of theory in explaining why interventions may or may not work or why benefits may not be as great as anticipated either within the target population as a whole or differentially among certain target subgroups.

Finally, a minor thread can be detected that recognises that even domains conventionally assigned to be addressed by quantitative evidence e.g. effectiveness, safety and cost-effectiveness can be further informed by “recontextualising evidence” from qualitative research.

6.4 DECISION ELEMENTS TO BE INFORMED BY QUALITATIVE EVIDENCE (Q2)

Recent years have witnessed a growth in the use of decision-making frameworks and models which specify the decision elements to be informed by evidence, qualitative and/or quantitative. These frameworks can serve an overall conceptual (mapping) role in depicting the diversity of domains to be addressed by evidence within the decision-making process. Alternatively, they may perform an instrumental (data extraction) function as a lens by which to categorise and organise qualitative (and sometimes quantitative) data prior to analysis and interpretation. Frameworks that are particularly gaining traction, together with the function that they serve are identified in Table 3. Thereafter follows brief observations captured on the challenges and advantages of using framework-based approaches.

As an example, the Joanna Briggs Institute has revised its overall model (from 2005)(38) in an attempt to “to clarify the conceptual integration of evidence generation, synthesis, transfer and implementation, linking how these occur with the necessarily challenging dynamics that contribute to whether translation of evidence into policy and practice is successful”. In doing so the 2019 version demonstrates greater acknowledgement of “the role of different types of evidence, both research and text and opinion, and how evidence contributes to achieving improved health outcomes globally”(39). While the model targets evidence-based practice, and not simply evidence synthesis, it does resonate with diverse NICE-associated activities.

Specifically, a wedge that relates to “evidence synthesis” itemizes three main pragmatic components as “systematic reviews, evidence summaries and guidelines”.

Table 3 – Domain-based Frameworks - Frameworks used by other Synthesis Organisations and their possible application

Framework name	Description	Potential use within Health Technology Assessment
GRADE Evidence to Decision Framework(40)	<p>EtD frameworks help groups of people (panels) making healthcare recommendations or decisions move from evidence to decisions. Frameworks can:</p> <ul style="list-style-type: none"> • Inform panel members' judgements about pros and cons of each intervention • Ensure important factors that determine a decision are considered • Provide concise summary of best available research evidence to inform judgements about each criterion • Help structure discussion and identify reasons for disagreements • Make the basis for decisions transparent to guideline users or those affected by a policy decision <p>Framework adaptable to clinical recommendations, coverage-decisions, or health system and public health recommendations and decisions.</p>	<p>As structure to ensure that evidence covering all aspects of a decision is identified and examined and no individual aspect is overlooked.</p>
Health Improvement Scotland Rapid QES Framework(41)	<p>Coding framework based on thematic analysis of four frameworks</p> <ul style="list-style-type: none"> • The NHS Patient Experience Framework, • The EUnetha coreModel, • The Warwick Patient Experience Framework, and • Analytical patient experiences model published in Danish Centre for Health Technology Assessment HTA (DACHENTA) Handbook. <p>– and two qualitative evidence syntheses exploring patients' experiences of a health technology.</p>	<p>To ensure that the specific contribution of qualitative evidence in understanding the patient experience is recognised.</p>
INTEGRATE-HTA	<p>A framework for HTA that covers:</p>	<p>To provide concepts and methods that enable a patient-</p>

	<ul style="list-style-type: none"> • effectiveness, • economic aspects, • ethical aspects, • socio-cultural aspects • and legal aspects <p>in complex technologies</p>	centered, comprehensive, and integrated assessment of complex health technologies.
<p>JBI Feasibility Appropriateness Meaningfulness Effectiveness (FAME) Framework(38)</p>	<p>When making clinical decisions, health professionals consider whether their approach is Feasible, Appropriate, Meaningful and Effective (the FAME Framework):</p> <ul style="list-style-type: none"> • Feasibility (extent to which an activity or intervention is practical or viable in a context/situation – including cost-effectiveness). • Appropriateness (extent to which intervention/activity fits with a context/situation). • Meaningfulness (refers to how intervention/activity is experienced by an individual/group and meanings they ascribe to that experience). • Effectiveness (extent to which intervention achieves intended result or outcome). 	To articulate and consider the main streams of evidence involved in a clinical decision, including not just effectiveness but also social and individual concerns.
<p>SURE Framework(42)</p>	<p>Framework focusing on barriers to implementing health systems changes including: (a) knowledge and skills; attitudes regarding programme acceptability, appropriateness and credibility; and motivation to change or adopt new behaviours among recipients of care, providers of care, and other stakeholders;</p> <p>(b) health system constraints (including accessibility of care, financial resources, human resources, educational system, clinical supervision, internal communication, external communication, allocation of authority, accountability, management or leadership (or both), information systems,</p>	Focus on barriers and implementation factors may be compatible with factors identified via QES

	<p>facilities, patient flow processes, procurement and distribution systems, incentives, bureaucracy, and relationship with norms and standards); and (c) social and political constraints (including ideology, short-term thinking, contracts, legislation or regulations, donor policies, influential people, corruption, and political stability).</p>	
<p>WHO- INTEGRATE Evidence to Decision Framework(24)</p>	<p>Framework with six substantive criteria—balance of health benefits and harms, human rights and sociocultural acceptability, health equity, equality and non-discrimination, societal implications, financial and economic considerations, and feasibility and health system considerations—and the meta-criterion quality of evidence. Designed to facilitate structured reflection and discussion in a problem-specific and context-specific manner from start of guideline development or other health decision-making process.</p>	<p>Updated evidence-to-decision making criteria to address issues of concern to be addressed through WHO guidance process.</p>

Table 4 - Frameworks used by other Synthesis Organisations and their possible application

Purpose-Specific Frameworks

Framework name	Description	Potential use within Health Technology Assessment
CICI Framework(43)	Framework with three dimensions—context, implementation and setting—which interact with one another and with the intervention dimension. Context comprises seven domains (i.e., geographical, epidemiological, socio-cultural, socio-economic, ethical, legal, political); implementation consists of five domains (i.e., implementation theory, process, strategies, agents and outcomes); setting refers to specific physical location, in which intervention is put into practice.	Framework devised for the INTEGRATE-HTA project to specifically identify components associated with the Context and with Implementation. May provide complementary contextual framework alongside tools describing intervention (as below).
Intervention Complexity Assessment Tool for Systematic Reviews (iCAT-SR)	Six dimensions to help reviewers to describe and categorise levels of intervention complexity and think about how complexity might be incorporated into each stage of the review process.	For data extraction: developed within Cochrane to ensure that all aspects of intervention complexity are addressed during the review process.
Template for Intervention Description and Replication (TIDieR)	Checklist and guide to improve completeness of reporting, and replicability, of interventions. 12 item checklist (brief name, why, what (materials), what (procedure), who provided, how, where, when and how much, tailoring, modifications, how well (planned), how well (actual)) is extension of CONSORT 2010 statement and SPIRIT 2013 statement.	For data extraction: to ensure completeness of reporting detail when describing intervention components

Frameworks are recognised as a way of including conceptualising and theorising at an early stage of the review process(29). They may also be used to structure data extraction(19). Any relative advantage is contingent on identifying an appropriate framework from an early stage in the review(44). False starts or frameworks that can only accommodate a small proportion of the data can be costly in terms of time taken. More recently, Brunton and colleagues have demonstrated that approaches to framework synthesis depend on the “extent to which theory is tentative, emergent, refined, or established”(44). Furthermore, the authors observe that “stakeholder involvement may help to understand the topic's complexity where theory is more nascent”(44). These considerations may, by extension, help in managing the balance of effort between secondary synthesis and primary data collection through stakeholder involvement. Ultimately, the choice of approach is found to depend on the degree of “fit” of existing theories and “the scale and heterogeneity of the literature to be managed”(44).

6.5 PERSPECTIVES ELICITED BY QUALITATIVE EVIDENCE (Q3)

As illustrated by Table 1 above the primary concern of qualitative evidence with the views of the patient/service user, evidenced in early methodological writings, has been substantively augmented by considerations relating to the intervention, specifically on implementation issues, and with the perspectives of health providers. The first of these reflects a widespread concern with evidence for implementation as evidenced in the growth of the Implementation Science journal, the development of conceptual models such as the Consolidated Framework for Implementation Research and the rebranding of the Cochrane Qualitative Methods Group as the Cochrane Qualitative and Implementation Methods Group(45). This repurposing of the Cochrane mission has translated into guidance specifically looking at appraisal and reporting of implementation studies(46). Decision-makers are also interested in practical concerns relating to feasibility and these pose a particular challenge to systematic review methods. Feasibility concerns are not typically unearthed in rigorous study designs and may be located in process evaluations(47) and non-research sources such as professional journals, websites and newsletters. For example, NIHR review work on the feasibility of community diagnostic services populated a feasibility framework

under the mnemonic STEP-UP (Skills, Training, Equipment, Premises, User perspective and Primary–secondary interface)(48) with considerations for each component derived from diverse sources.

Related to this concern with feasibility and implementation comes a greater preoccupation with using qualitative evidence to document the attitudes and perspectives of healthcare providers; this partly stems from recognition that complex interventions are very often human-mediated and therefore require the support of providers to achieve their success and partly from identifying that comparison of qualitative evidence derived from both patients and providers can help in identifying, explaining and addressing gaps between both groups in communication, expectation or understanding.

6.6 SPECIAL CIRCUMSTANCES/TOPIC AREAS (Q4)

Historically, qualitative evidence has focused attention on the voices of those who are typically viewed as unempowered or disenfranchised(49, 50). This emphasis has been reaffirmed in recent years(51). Few, if any health technology assessment agencies, espoused this as an explicit rationale for qualitative synthesis. Increasingly, justifications for qualitative synthesis centre on the complementarity of quantitative and qualitative methods of inquiry and the need to populate multiple domains of evidence to decision-making frameworks.

However recent attention has turned to considerations of equity and this has re-stimulated the empowerment argument. Organisations such as NICE, SIGN(52), the Australian NHMRC(53) and the WHO are leading in their attempts to ensure that considerations of equity are included in their review processes. Cochrane has its own methodology group focusing on Equity meaning that such considerations are not being advanced exclusively via the qualitative paradigm(36, 54, 55). As a consequence, the evidence reviewed for this methodological update includes only a fraction of that relating to Equity methodological developments(56, 57). We suggest that further methodological review work be undertaken to explore the implications of equity more widely within NICE processes, rather than exclusively within the context of qualitative

evidence synthesis(53). Formal approaches to handling equity, as identified in this update, currently fall within four types:

1. Incorporation of equity within evidence to decision frameworks as a prompt for assembling such evidence at a meta-level;
2. Use of frameworks such as PROGRESS-Plus at a more instrumental level to determine extraction of data;
3. Analysis of specific subgroups to identify differences from main population results(52, 53);
4. Separate recommendations for subgroups taking differences into account(52, 53).

In addition, the methodological literature suggests a need to maintain constant awareness of implications for equity while engaging with the evidence(35). However, this approach risks the possibility of factoring in equity spasmodically and unsystematically.

Data extraction identified four specific “cases” for the use of qualitative methods. The first of these involves the disenfranchised groups referred to above(52, 53). Further to this an argument is made that very sick patients may not be able to participate in formal processes of primary qualitative data collection(41, 58). Eliciting the views of this particular subgroup through the published literature therefore offers a pragmatic alternative. By extension this “non-availability” argument extends to other difficult to access research groups such as children and young people. Within a relatively constrained time window an additional argument may relate to the extended requirements for ethical study design and consent procedures that more complex groups may present to primary researchers. Finally, there may be particular types of data that may be very difficult to capture from primary data sources, such as process evaluation data, for example. Capturing this data from available grey literature may avoid the need to put in place extensive longitudinal collection of routine data.

6.7 INCLUDING QUALITATIVE EVIDENCE IN THE HTA PROCESS (Q5)

A key recent development has been exploration of rapid methods of qualitative evidence synthesis. While current examples remain few(59), not least because rapid syntheses more typically require a rapid mixed-methods review of both quantitative and qualitative evidence, sufficient development has taken place to result in a Health

Improvement Scotland Methods Manual(41). Furthermore, WHO recognises that, alongside the principal QES that they commission, for example on the values and preferences of patient or service users, there is additional value in conducting specific rapid (or mini-)QES(60) (e.g. on provider attitudes or implementation issues). Methods for producing critically appraised topics for qualitative synthesis (so-called qual-CATs)(61, 62) may hold potential value for the NICE team; although their final output is not currently compatible with NICE guidance their techniques and presentational methods might help to streamline and expedite the QES process. Procedures for integrating quantitative and qualitative data have been articulated and summarised in recent methodological works from Cochrane(63) and WHO(22) and these include:

- Narrative synthesis or summary(22)
- Quantitising approach, (eg, frequency analysis)(22)
- Qualitising approach, (eg, thematic synthesis) (22)
- Tabulation(22)
- Logic model(22, 63, 64)
- Conceptual model/framework(22, 63)
- Matrix(22, 63, 65)
- Graphical approach(22)
- Analyzing program theory(63)
- Testing hypotheses using subgroup analysis(63)
- Qualitative comparative analysis(63)

Or a combination of approaches(22)

Work on the particular requirements to document and explore complexity has led commentators to propose alternatives to the flat PICO question formulation strategy. This has included an alternative question structure (PerSPE©TiF)(20, 66) specifically for complex interventions and the use of logic models(67). The PerSPE©TiF structure remains experimental and requires extensive further testing. Logic Models are well established within both public health evaluation and in systematic reviews(18, 68) but need to balance the flexibility to modify, and revise as new data is added, with version control and fixed systematic review project milestones(64).

A key issue in defining the way forward for QES within the NICE evidence ecosystem is whether expectations of comprehensive searches from the quantitative paradigm should persist within qualitative syntheses. Commentators such as Booth(51, 67) have

challenged this assumption for over two decades reasoning that the interpretative (configurative) intent of qualitative syntheses removes a requirement to identify additional evidence once a point of theoretical saturation has been reached(69, 70). The emphasis, informed by qualitative models of sampling, thus switches to the richness and diversity of the sample(71). Such reasoning is starting to gain considerable traction, particularly as resource use on study identification for quantitative reviews receives increased scrutiny. The challenge to comprehensive sampling comes from three directions:

- (1) An appeal to a different, qualitative-informed paradigm(72);
- (2) The growth of popularity of rapid qualitative evidence syntheses(41, 59);
- (3) Incorporation of concepts such as adequacy of data(71), coherence(73) and relevance(31) within the GRADE-CERQual approach allowing limitations of the sample to be identified and acknowledged.

Empirical work is starting to explore the strengths and limitations of purposive sampling approaches(74, 75).

Booth (2016)(51) has produced a methodological review as a technical document to support Cochrane guidance on searching. He identifies particular priorities for study identification and these may shape NICE’s own methodological research agenda.

Table 5 - Towards a research agenda (from: Booth(51))

Component	Research priorities
Sampling	Comparison of yields from exhaustive versus comprehensive sampling. Informed matching of sampling to search methods to synthesis approaches
Sources	Audits of relative yield(76, 77)
Structured questions	Exploration of techniques for automated document clustering to provide initial overview of available evidence across a broad range of topic areas

Component	Research priorities
Search procedures	More empirical testing of different approaches to searching. Exploration of iterative and theory-based approaches(78, 79)
Search strategies and filters	Ongoing rigorous development of methodological filters comparing parsimonious and exhaustive lists. Filters for different qualitative study types, process evaluations and mixed methods studies. Search strategies by discipline (e.g. social work), by application(77) (e.g. patient satisfaction) or for theories(80)
Supplementary strategies	Audits and evaluations of relative yield(81, 82)
Standards	Development of consensual reporting standards for QES iterative search approaches; audits of reporting standards generally and for specific methods

Ongoing information retrieval research continues to address such priorities(76, 81-83).

A quality assessment approach, as currently envisaged, that is compatible with the GRADE-CERQual approach for methodological limitations (<http://thecameloplot.pbworks.com/w/page/136970796/ClearFindings>), already holds relative advantages for NICE QES processes. It remains too early to predict whether GRADE-CERQual will gain the same widespread acceptance within the synthesis community as evidenced by GRADE. However, it is likely that the shared four- (then five-) component compatibility of GRADE with GRADE-CERQual will facilitate integrated Tables of Findings and presentation, including incorporation of genuinely mixed-methods forms of evidence.

Further issues related to quality assessment pertain to the utility of Qualitative Sensitivity Analysis(75, 84) in testing the robustness of the overall interpretation and the particular challenges posed by quality assessment of process evaluations(47, 85, 86).

8. RECOMMENDATIONS FOR NICE CHTE 2020 METHODS UPDATE (Q6)

The INTEGRATE-HTA project has identified four main ways of eliciting socio-cultural data and these broadly map to the wider role of qualitative evidence: checklists, literature reviews, participatory approaches, and primary empirical research. Within NICE the framework based (checklist) approach has not gained the type of ascendancy currently being enjoyed within the World Health Organization and the Joanna Briggs Institute. As a consequence, the frequent mentions of the importance of qualitative evidence alongside clinical and cost effectiveness are not accompanied by an integrated approach to health technology assessment as espoused by the INTEGRATE-HTA project. Use of such a framework appears feasible in all types of technology appraisal activity – in specifying content of manufacturer submissions, in specifying a template to be populated by analysts in assessing submissions and in directing the contents of syntheses and literature searches.

In contrast, NICE has demonstrated, through its most recent Methods Manual, the Guidelines Manual (e.g. PMG20(13), last updated October 2018) that it has kept good pace with methodological developments in qualitative evidence synthesis. However, the practical challenges faced in seeking to incorporate quantitative and qualitative evidence into the guidance development process are compounded within the timescales faced by the technology appraisal programme. Although the Guideline Programme recognises the distinctive contribution of both *individual strands* it fails to capitalise on the added value offered by *integration* of quantitative and qualitative strands. In practical terms, the prospect of adding a further step of integration to the already tight deadlines for review may seem unfeasible. Organisations such as the WHO (with its Evidence to Decision Frameworks(24, 87)) and the Joanna Briggs Institute (with its FAME framework(38)) offer a skeletal integration approach. Framework approaches are thought to accelerate the review process(44, 88-90) and this assumption is evidenced by the framework developed by Health Improvement Scotland (HIS). Although the HIS framework is designed to facilitate the speedy synthesis of qualitative evidence there is little reason to believe that an integration framework for both quantitative and qualitative research will not prove equally effective. Where integration is not achieved technically through aggregation or

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synthesis process then this necessary task is passed on down the line as an extra cognitive load for the committees, whether ratifying guidelines or technology appraisals. Within the wider context of the Guidelines programme technical integration is further facilitated by juxtaposing quantitative and qualitative outcomes/findings within a shared conceptual framework through the GRADE/GRADE CERQual process, to be facilitated by the development of a mixed methods methodology for GRADE. Clearly, within the technology appraisals programme, the challenge of integration of quantitative and qualitative evidence remains a major hurdle. Use of a common Evidence to Decision making framework as a scaffold for decision-making, if not a vehicle for data extraction, would seem to offer a proportionate response to this wider methodological need.

8.1. RECOMMENDED CHANGES

The following changes are recommended on the basis of this methodological update, the expert opinion of the analyst (as confirmed by methodological contributions from 2013 onwards) and observations from training sessions (face to face and webinars) delivered to both NICE clinical guidelines staff. It is recommended that:

1. NICE explore methods for integration of quantitative and qualitative evidence, through all its activities perhaps through use of, or development of, an appropriate evidence to decision-making framework, that can be accommodated within existing organisational timescales, for guidelines and technology appraisal.
2. In furtherance of point 1, that NICE examine the feasibility of rapid qualitative evidence syntheses as explored by Health Improvement Scotland, the World Health Organization and the Canadian Agency for Drugs and Technologies in Health (CADTH), proportionate to both timescale and qualitative input.

The idea is that a single decision-making framework would operate across both programmes but that activities would be commensurate and proportionate to current activity levels. So a common conceptual evidence to decision-making framework might be applied with different levels of detail and granularity.

8.2. SUGGESTED CHANGES

Furthermore, it is suggested that:

1. NICE explore systematic and extensive use of other purpose-specific frameworks, to accelerate analysis and to ensure standardisation of approaches (e.g. TIDieR, ICAT-SR, CICI, PROGRESS-Plus etcetera);
2. NICE examine the potential role of other contributions from qualitative evidence to decision-making process, e.g. feasibility and implementation considerations and the values, preferences and attitudes of health providers and planners and identify “triggers” that flag the potential value of such approaches;
3. NICE explore the potential value of wider use of qualitative evidence in enhancing interpretation of the quantitative evidence.
4. NICE employ an integrated approach to evidence to decision-making that identifies circumstances where both quantitative and qualitative evidence might populate a specific decision-making domain, rather than separate the domains to either one type of evidence or the other.

8.3. ISSUES REQUIRING ONGOING MONITORING/ANY IMPLICATIONS TO CONSIDER IN TERMS OF RECOMMENDED CHANGES

The following developments are anticipated over the foreseeable future and should be monitored on a regular basis:

1. Development of integrated approaches for combining quantitative and qualitative assessments culminating in approaches for handling mixed methods findings;
2. Further advances in methods for aggregation, synthesis and integration for qualitative data, primary qualitative research and qualitative evidence synthesis to include use of conceptual models and diagrammatic approaches.

Furthermore, an ongoing need exists to improve the systematicity of approaches to handling equity. In addition to the use of an evidence-to-decision framework that includes equity (see above) and explicit use of frameworks such as PROGRESS-Plus within technology appraisal or qualitative synthesis it may be helpful to identify and/or maintain information that relates to known inequalities. This could be particularly useful given that issues may be common across multiple types of intervention but the extent to which specific inequalities are documented for each intervention may differ widely e.g. written information and those with low literacy levels, appointments and those with no fixed address, access to services and those confined to their homes, screening interventions and those for whom English is not a first language etcetera.

APPENDIX A – METHODS FOR UPDATE

OVERALL METHODS BRIEF

The brief is to update previous NICE guidance on systematic reviews of qualitative research/qualitative evidence syntheses, from 2013 onwards by identifying and extracting:

- Relevant methodology content from other HTA agencies (e.g. CADTH, SBU, AHRQ) and other methodology producing organizations (e.g. Campbell, Cochrane, Joanna Briggs etc);
- Key methodology content of specific application to NICE activities (systematic reviews, technology appraisals, health technology assessments and health system and clinical guidelines).

LITERATURE SEARCH

Dates covered: January 2013 – January 2020

Sources Used: Cochrane Qualitative and Implementation Methods Methodology Register, Google Scholar, Web searches, Hand searching of NICE Methodology Current Awareness Bulletins.

OVERALL SEARCH STRATEGY

A five-part strategy will be used to identify relevant materials:

1. Searches of the Cochrane Qualitative and Implementation Methods Group Qualitative Evidence Syntheses and Methodology Register (INQUEST). This resource is populated by weekly PubMed searches using a sensitive search strategy and currently contains 11, 825 records (See Appendix 1). Records are currently categorized into 1 or more categories (See Appendix 2 – Screenshot)
2. A broad supplementary PubMed search on: "Review Literature as Topic"[mh] AND "Qualitative Research"[mh] – 256 Results (2013-2020)

(NB. This includes all 115 items retrieved by "Systematic Reviews as Topic"[mh] AND "Qualitative Research"[mh])

3. Web search of INAHTA and HTA-I Technology Assessment Agency sites combining domain/name with each of the following search terms: "qualitative systematic reviews"; "qualitative evidence synthesis" and "qualitative research"
4. Google Scholar Citation Searches for Ten key qualitative synthesis texts (See Appendix 3)

5. Hand search through NICE Monthly Updates in Research Methodology and Information Science (from February 2013 to January 2020)

Appendices

SEARCH APPENDIX 1 – SEARCH TERMS USED TO POPULATE CQIMG METHODOLOGY REGISTER

((("Qualitative systematic review" OR "qualitative systematic reviews") OR ("qualitative evidence synthesis" OR "qualitative evidence syntheses") OR ("qualitative research synthesis" OR "qualitative research syntheses") OR ("Qualitative synthesis" OR "qualitative syntheses")) OR (((("integrative synthesis" OR "integrative syntheses") AND qualitative) OR ("integrative review" OR "integrative reviews") AND qualitative) OR ("interpretive synthesis" OR "interpretive syntheses")) OR ((Mega-ethnograph* OR megaethnograph* OR "mega ethnograph*") OR (meta-ethnograph* OR metaethnograph* OR "meta ethnograph*")) OR ("meta interpretation"[All Fields] OR "meta interpretive"[All Fields]) OR (meta interpretation) OR (meta interpretive) OR (Meta-method* OR "meta method*" OR metamethod*) OR ("meta narrative" OR "meta narratives" OR "narrative synthesis" OR "narrative syntheses") OR (meta-study OR metastudy OR "meta study") OR (meta synthesise[All Fields] OR meta syntheses[All Fields] OR meta synthesis[All Fields] OR meta synthesise[All Fields] OR meta synthesised[All Fields] OR meta synthesist[All Fields] OR meta synthesized[All Fields] OR meta synthesizing[All Fields]) OR (meta-triangulation OR "meta triangulation" OR meta triangulation) OR ("realist review" OR "realist reviews" OR "realist synthesis" OR "realist syntheses") OR ("thematic synthesis" OR "thematic syntheses") OR ((synthesis OR syntheses) AND "Thematic analysis") OR (("systematic review" OR "systematic reviews") AND "Thematic analysis")) OR (((("literature search" OR "literature searching" OR "literature searches") AND ("qualitative literature" OR "qualitative research" OR "qualitative paper" OR "qualitative papers" OR "qualitative studies" OR realist)) OR (("quality assessment" OR "critical appraisal" OR checklist*) AND ("qualitative literature" OR "qualitative research" OR "qualitative paper" OR "qualitative papers" OR "qualitative studies" OR realist)) OR (Noblit AND Hare) OR (CERQUAL OR CONQUAL) OR (JBI-QARI OR QualSys) OR (("systematic review"

OR "systematic reviews") AND ("mixed method" OR "mixed methods" OR "mixed studies" OR "mixed study" OR "mixed research")) OR ((synthesis OR syntheses) AND ("mixed method" OR "mixed methods" OR "mixed studies" OR "mixed study" OR "mixed research")) OR (("literature search" OR "literature searching" OR "literature searches") AND ("mixed method" OR "mixed methods" OR "mixed studies" OR "mixed study" OR "mixed research")) OR (("quality assessment" OR "critical appraisal" OR checklist*) AND ("mixed method" OR Mixed Methods" OR "Mixed Studies" OR "Mixed Study" OR "Mixed Research")) OR ("Mixed Methods Appraisal Tool" OR MMAT))

SEARCH APPENDIX 3 – TEN KEY STUDIES USED FOR CITATION SEARCHING

1. Atkins S, Lewin S, Smith H, Engel M, Fretheim A, Volmink J. Conducting a meta-ethnography of qualitative literature: lessons learnt. *BMC medical research methodology*. 2008 Dec;8(1):21. [635 cites]
2. Barnett-Page E, Thomas J. Methods for the synthesis of qualitative research: a critical review. *BMC medical research methodology*. 2009 Dec;9(1):59. [1234 cites]
3. Carroll C, Booth A, Cooper K. A worked example of "best fit" framework synthesis: a systematic review of views concerning the taking of some potential chemopreventive agents. *BMC medical research methodology*. 2011 Dec;11(1):29. [194 cites]
4. Carroll C, Booth A, Leaviss J, Rick J. "Best fit" framework synthesis: refining the method. *BMC medical research methodology*. 2013 Dec;13(1):37. [163 cites]
5. Lockwood C, Munn Z, Porritt K. Qualitative research synthesis: methodological guidance for systematic reviewers utilizing meta-aggregation. *International journal of evidence-based healthcare*. 2015 Sep 1;13(3):179-87. [171 cites]
6. Noyes, J., Popay, J., Pearson, A., Hannes, K., & Booth, A. (2008). Chapter 20 - Qualitative Research and Cochrane Reviews. In: Higgins J & Green S. *Cochrane Handbook*. Chichester: Wiley. [272 cites]
7. Ring, N.A., Ritchie, K., Mandava, L. and Jepson, R., 2011. A guide to synthesising qualitative research for researchers undertaking health technology assessments and systematic reviews. NHS Quality Improvement Scotland
8. Sandelowski M, Barroso J. *Handbook for synthesizing qualitative research*. Springer Publishing Company; 2006 Jul 24. [1317 cites]
9. Thomas J, Harden A. Methods for the thematic synthesis of qualitative research in systematic reviews. *BMC Medical Research Methodology*. 2008 Dec;8(1):45. [2881 cites]
10. Walsh D, Downe S. Meta-synthesis method for qualitative research: a literature review. *Journal of advanced nursing*. 2005 Apr;50(2):204-11.[895 cites]

NB. No. of Citations given represents full number of citations since publication, Update searches will be limited to citations from 2013 onwards.

ACKNOWLEDGEMENT OF CONSTRAINTS

Currently no search strategy can distinguish between methodology work on qualitative evidence and published examples of qualitative evidence. As the ratio of irrelevant (examples) to relevant (methodology) references is greater than 20 to 1 and yield, taking into account false hits, makes this figure closer to 50 to 1 it is not cost- or time-effective to sift results from a conventional database search. Fortunately, the Cochrane Qualitative and Implementation Methods Group Methodology Register is an unparalleled reference collection of QES references. Supplementing this resource with citation searching, reference checking, Internet searches and hand searching offers a high level of reassurance that relevant items, beyond the expert knowledge of the review team, will be identified. Comments and feedback will be collated and addressed in the respective sections of the guide.

APPENDIX B – ORGANISATIONS REVIEWED

Based on *Grey Matters* (CADTH Research Information Services, Updated: April 2019), a systematic search was conducted of national and international guideline production and health technology assessment (HTA) agencies. Supplemental keyword searches on search engines such as Google were also undertaken, as recommended in the *Grey Matters* guide.

HEALTH TECHNOLOGY ASSESSMENT (HTA) AGENCIES

CANADA
The Alberta College of Family Physicians (ACFP). Tools for Practice http://www.acfp.ca/ No Methods Guidance
Alberta Health and Wellness. http://www.health.alberta.ca/ No Relevant Documents
Canadian Agency for Drugs and Technologies in Health (CADTH). https://www.cadth.ca/ Many examples and presentations but no Methods Guidance. Main guidelines: https://www.cadth.ca/about-cadth/how-we-do-it/methods-and-guidelines/guidelines-for-the-economic-evaluation-of-health-technologies-canada
Canadian Institutes of Health Research http://www.cihr-irsc.gc.ca No Methods Guidance

Health Quality Council of Alberta (HQCA). Completed Reviews

<http://hqca.ca/>

No Methods Guidance

Health Quality Ontario (HQO). Health Technology Assessment

<http://www.hqontario.ca/>

No Methods Guidance

The Hospital for Sick Children (SickKids).

<http://lab.research.sickkids.ca/>

No Methods Guidance

Institut national d'excellence en santé et en services sociaux (INESSS) [formerly AETMIS].

<http://www.inesss.qc.ca/>

No Methods Guidance

Institute of Health Economics (IHE).

<http://www.ihe.ca/>

No Methods Guidance

Manitoba Centre for Health Policy (MCHP).

<http://mchp-appserv.cpe.umanitoba.ca/>

No Methods Guidance

McGill University Health Centre (MUHC).

<https://muhc.ca/>

No Methods Guidance

NLCAHR : Newfoundland and Labrador Centre for Applied Health Research.
Contextualized Health Research Synthesis Program (CHRSP)

<http://www.nlcahr.mun.ca/>

No Methods Guidance

Ottawa Hospital Research Institute (OHRI). Knowledge Synthesis Group

<http://www.ohri.ca/>

No Methods Guidance

Programs for Assessment of Technology in Health (Canada).

<https://www.path-hta.ca/>

No relevant documents

University of British Columbia. Centre for Health Services and Policy Research

<http://chspr.ubc.ca/>

No Methods Guidance

INTERNATIONAL

EUnetHTA

<https://eunetha.eu/methods-and-procedures/>

HTA-I

<http://Htai.org>

Summarized Research in Information Retrieval for HTA (SURE-Info): Qualitative research | HTAi vortal (Chapter on how to search for qualitative reserch (updated October 2018) <http://vortal.htai.org/index.php?q=node/1235>

Hosts link to Health Improvement Scotland document on Rapid QES (see below) <https://htai.org/wp-content/uploads/2019/11/Rapid-qualitative-evidence-synthesis-guide.pdf>

INAHTA Secretariat. International Network of Agencies for Health Technology Assessment (INAHTA)

<http://www.inahta.org/>

No Methods Guidance

World Health Organization Regional Office for Europe. Health Evidence Network (WHO HEN)

<http://www.euro.who.int/>

Karlsson, L. E., & Takahashi, R. (2017). A resource for developing an evidence synthesis report for policy-making (Vol. 50). World Health Organization.

http://www.euro.who.int/_data/assets/pdf_file/0008/347930/HEN50-Web.pdf?ua=1 [Includes qualitative throughout]. *NB. Specific Qualitative Synthesis Guidance Currently at Proof stage (March 2020)*

AUSTRALIA

Australian Government. Department of Health and Ageing.

<http://www.health.gov.au>

No Methods Guidance

Australian Government Department of Health and Ageing. Medical Services Advisory Committee (MSAC).

<http://www.msac.gov.au/>

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<https://reviewersmanual.joannabriggs.org/>

Monash Health. Centre for Clinical Effectiveness (CCE). Centre for Clinical Effectiveness

<http://monashhealth.org/>

No Methods Guidance

Pharmaceutical Benefits Advisory Committee (PBAC)

Main guidelines: <https://pbac.pbs.gov.au/information/about-the-guidelines.html>

Queensland Government (Australia). Health Technology Reference Group.

<https://www.coaghealthcouncil.gov.au/>

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<http://www.oeaw.ac.at/ita/en/projects>

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BELGIUM

Kenniscentrum voor de Gezondheidszorg / Le Centre d'expertise des soins de santé. Belgian Health Care Knowledge Centre (KCE)

<https://kce.fgov.be/en/all-reports>

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<http://sundhedsstyrelsen.dk/>

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FRANCE

Comité d'Evaluation de Diffusion des Innovations Technologiques (CEDIT).

CEDIT Recommendations and Reports

<http://cedit.aphp.fr/>

No Methods Guidance

Haute Autorité de santé/ French National Authority for Health (HAS).

Haute Autorité de santé

<http://www.has-sante.fr/>

Only workshop presentation: <https://www.has-sante.fr/upload/docs/application/pdf/2019-11/colloque-has-j.noyes.pdf>

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GERMANY

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German Institute of Medical Documentation and Information

<https://www.dimdi.de/>

No Methods Guidance

IQWiG

https://www.iqwig.de/download/Allgemeine-Methoden_Entwurf-fuer-Version-6-0.pdf [download General Methods 6.0]

IRELAND

Health Information and Quality Authority.

<https://www.hiqa.ie/>

No Methods Guidance

<https://www.hiqa.ie/sites/default/files/2019-07/HTA-Economic-Guidelines-2019.pdf>

<p>Health Service Executive. Irish Health Repository (Lenus)</p> <p>http://www.lenus.ie/hse/</p> <p>No Methods Guidance</p>
<p>THE NETHERLANDS</p>
<p>De Gezondheidsraad (GR). Health Council of the Netherlands</p> <p>http://www.gezondheidsraad.nl/en/publications</p> <p>No Methods Guidance</p>
<p>Zorginstituut Nederland. National Health Care Institute Netherlands</p> <p>https://english.zorginstituutnederland.nl/publications</p> <p>No Methods Guidance</p> <p>https://english.zorginstituutnederland.nl/binaries/zinl-eng/documents/reports/2016/06/16/guideline-for-economic-evaluations-in-healthcare/Guideline+for+economic+evaluations+in+healthcare.pdf</p>
<p>NORWAY</p>
<p>Folkehelseinstituttet. Norwegian Institute of Public Health. Publications</p> <p>https://www.fhi.no/</p> <p>Only briefing materials on GRADE-CERQual</p>
<p>SPAIN</p>
<p>Agencia de Evaluación de Tecnologías Sanitarias, Instituto de Salud “Carlos III”. Institute of Health Carlos III</p> <p>http://publicaciones.isciii.es/</p>

No Methods Guidance
<p>Agència de Qualitat i Avaluació Sanitàries de Catalunya (AQuAS). Agency for Health Quality and Assessment of Catalonia</p> <p>http://aquas.gencat.cat/ca/publicacions/</p> <p>No relevant results</p>
SWEDEN
<p>Sahlgrenska Universitetssjukhuset. Sahlgrenska University Hospital. Regional activity-based HTA</p> <p>https://www.sahlgrenska.se/</p> <p>No relevant results</p>
<p>Swedish Council on Health Technology Assessment (SBU).</p> <p>https://www.sbu.se/</p>
<p>Report: SBU. Evaluation and synthesis of studies using qualitative methods of analysis. Stockholm: Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU); 2016.</p> <p>https://www.sbu.se/globalassets/ebm/metodbok/sbuhandbook_qualitativemethodsofanalysis.pdf</p> <p>Checklist: Tool to assess methodological limitations of qualitative evidence synthesis</p> <p>https://www.sbu.se/contentassets/14570b8112c5464cbb2c256c11674025/methodological_limitations_qualitative_evidence_synthesis.pdf</p> <p>https://www.sbu.se/contentassets/76adf07e270c48efaf67e3b560b7c59c/eng_metodboken.pdf</p>
UK

Healthcare Improvement Scotland.

<http://www.healthcareimprovementscotland.org>

A guide to conducting rapid qualitative evidence synthesis for health technology assessment. <https://htai.org/wp-content/uploads/2019/11/Rapid-qualitative-evidence-synthesis-guide.pdf>

National Institute for Health Research

<http://www.nihr.ac.uk/>

Report(91)Papers(92-97)

UK Department of Health (NHS). International Resource for Infection Control (iNRIC)

<http://www.nric.org.uk/>

No relevant results

National Health Service UK (NHS).

<http://www.england.nhs.uk/>

No Methods Guidance

United States

Agency for Healthcare Research and Quality (AHRQ).

<http://www.ahrq.gov/>

No Methods Guidance

Centers for Medicare & Medicaid Services (CMS).

<http://www.cms.gov/>

No relevant results

Institute for Clinical and Economic Review (ICER).

<https://icer-review.org/>

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HTA guide: http://icer-review.org/wp-content/uploads/2018/08/ICER-HTA-Guide_082018.pdf

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Washington State Health Care Authority (HCA).

<https://www.hca.wa.gov/>

No relevant results

CLINICAL PRACTICE GUIDELINES

CANADA

Alberta Medical Association.

<http://www.topalbertadoctors.org/>

No relevant results

British Columbia Ministry of Health.

<http://www2.gov.bc.ca/>

No relevant results

Canadian Medical Association (CMA).

<https://www.cma.ca/>

No relevant results

The College of Physicians and Surgeons of Ontario (CPSO)

<http://www.cpso.on.ca/>

No relevant results

Ontario Association of Medical Laboratories (OAML)

<https://oaml.com/>

No relevant results

Public Health Agency of Canada (PHAC). Disease Prevention and Control Guidelines

<http://www.phac-aspc.gc.ca/>

No relevant results

Registered Nurses' Association of Ontario (RNAO).

<http://rnao.ca/>

No Methods Guidance

University of Ottawa. School of Rehabilitation Science. Evidence-based Practice

<http://www.health.uottawa.ca/>

No relevant results

Winnipeg Regional Health Authority (WRHA).

<http://www.wrha.mb.ca/>

No relevant results

INTERNATIONAL

Academy of Medicine of Malaysia. Clinical Practice Guidelines

<http://www.acadmed.org.my/>

No relevant results

American Association for Clinical Chemistry (AACC). Practice Guidelines

<https://www.aacc.org/>

No Methods Guidance

Best Practice Advocacy Centre New Zealand (bpacNZ)

<http://www.bpac.org.nz/>

No relevant results

Centers for Disease Control and Prevention (CDC).

<http://cdc.gov>

Example of Qualitative Evidence Syntheses but no Methods Guidance

The Regulation and Quality Improvement Authority (RQIA). Guidelines

<https://rqia.org.uk/>

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Institute for Clinical Systems Improvement (ICSI).

<https://www.icsi.org/>

No synthesis.

ECRI Institute.

<https://www.ecri.org/>

No synthesis. ECRI Institute User Experience Network (UEN) surveys are designed to collect qualitative opinions from individuals

National Health and Medical Research Council (NHMRC).

Guidelines for Guidelines(53)

<https://www.nhmrc.gov.au/guidelinesforguidelines/>

National Institute for Health and Care Excellence (NICE). NICE Guidelines

<http://www.nice.org.uk/guidance>

PMG4(98), PMG10(12), PMG20(13) See Paper(37)

Scottish Intercollegiate Guidelines Network (SIGN)

<http://www.sign.ac.uk/our-guidelines.html>

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APPENDIX C – BIBLIOGRAPHY OF ITEMS REVIEWED

CORE ITEMS

Introductory Works

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https://www.sbu.se/contentassets/14570b8112c5464cbb2c256c11674025/methodological_limitations_qualitative_evidence_synthesis.pdf

Integrate-HTA Project

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AHRQ

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APPENDIX D – DATA EXTRactions OF ITEMS INCLUDED

QUESTION 1: POSITIONS AND RATIONALES OF KEY STAKEHOLDERS

Table 6 - Extracted Data relating to Question 1 (Positions & Rationales)

Issue (Stakeholder)	Source	Data Extract	Implications	Notes
Wider interpretation of Health Technology Assessment (International HTA organisations)	SBU(58)	“Among the international organisations in health technology assessment (HTA), interest in evaluating qualitative research increased once it was recognised that HTA is not always concerned solely with effect. HTA also examines such issues as why and how methods/interventions function, ethical dilemmas, how patients and the public relate to a given method/intervention, and the demands imposed by it, in terms of knowledge and skills of both professionals and organisations”.	Health Technology Assessment cannot afford to ignore the patient/client perspective	
Wider contribution to evidence base (International HTA organisations)	SBU(58)	“When a method/intervention is to be introduced, synthesis of qualitative studies in conjunction with HTA provides decision-makers with the best possible evidence-based foundation on which – for example – to assess patient- or client-related aspects. This foundation can also provide	Inclusion of QES results in more informed evidence-based decision making	

		support for different priority groups at local, regional and national levels”.		
QES offers improved transferability (SBU)	SBU(58)	“It is ...possible to improve the potential for transferability. This can be done by including as great a variety as possible of cases, of the same phenomenon, in the study. The argument for maximising variation is that the transfer is made not from a specific case or category, but from a number of such cases. The variation in the study is expected then to exist in other relevant situations to which one wishes to transfer the results”.	QES elicits natural variation through synthesising multiple cases	
QES can explore multiple contexts and contextual variation (SBU)	SBU(58)	“Another argument focuses on context and similarities of context. The focus must then be on empirical knowledge rather than on theoretical assumptions. Because the similarity between contexts has to be assessed empirically after the study, the researcher must determine whether or not there is in fact similarity with other contexts. This also presupposes that it is the context which determines a phenomenon or pattern”	QES offers opportunity to judge transferability after the fact	
Transferability of QES results relies on assumptions about homogeneity and	SBU(58)	“Recognition of a pattern may be considered to be a variant of transferability, insofar as the pattern which emerges is recognised in new cases. The argument here is that transferability can be achieved when someone can	QES relies on reviewer assessments of similarities and differences in context	

heterogeneity of context (SBU)		understand different situations, processes or phenomena with the aid of the interpretations within the research. The problem with this argument is that it is based on the individual researcher's interpretation of a context and an underlying assumption about homogeneity within a specific context"		
Multiple factors which co-determine how effective, safe or cost-effective interventions are	GIN Public Toolkit(105)	"In considering whether (and how) the results from RCTs will be reproducible in everyday practice, guideline developers must consider a wide range of additional factors which co-determine how effective, safe or cost-effective interventions ultimately are. For treatments - even those with solid quantitative evidence of effectiveness - to work in the complexity of the 'real world', we need to address the potential patient or provider (mis)understandings of the treatment and illness, and a range of legal, financial and organisational factors of distinct health care systems".		
Empirical research provides additional, transparent and systematic way of considering context	GIN Public Toolkit(105)	"Currently, such considerations are usually incorporated implicitly, by relying on the personal experience and expertise of those developing guidelines, including those of wider 'stakeholders' such as patient representatives included in the guideline development group. The incorporation of empirical research on these issues is an additional, and often more transparent and systematic, way of ensuring		

		these contextual factors are included in the guideline development process”.		
Informing policy and practice (NHS Quality Improvement Scotland)	Health Improvement Scotland (2019)(41)	“The basic rationale behind the synthesis of qualitative studies is to use the evidence for the purposes of informing policy and practice”.	Qualitative data within HTA should be filtered for policy and practical implications	In context of rapid QES
Value of evidence from analogy or patients’ experience of condition	Health Improvement Scotland (2019)(41)	“In qualitative research, very few primary studies are likely to have exactly the same research question or focus as the planned synthesis... a large number of primary research studies [may contain] relevant data to inform the decision (whether it be on an analogous technology or patients’ experiences of living with a health condition).” (p. 7)	“Indirect” qualitative evidence may inform decision making	In context of rapid QES
Qualitative research offers multiple approaches to explaining the phenomenon of interest	JBI Reviewers; Manual(106)	In the healthcare or medical context, qualitative research: “...seeks to understand and interpret personal experiences, behaviors, interactions, and social contexts to explain the phenomena of interest, such as the attitudes, beliefs, and perspectives of patients and clinicians; the interpersonal nature of caregiver and patient relationships; the illness experience; or the impact of human suffering”.		
QES offers person-centred perspective	JBI Reviewers; Manual(106)	“Qualitative evidence has a particular role in exploring and explaining why interventions are or are not effective from a person centered perspective, and address questions related		

		to the usability, meaningfulness, feasibility and appropriateness of interventions. Similarly, qualitative evidence is able to explain and explore why an intervention is not adopted in spite of evidence of its effectiveness. The strength of qualitative research lies in its credibility (i.e. close proximity to the truth), using selected data collection strategies that “touch the core of what is going on rather than just skimming the surface”.		
Explanatory power of QES facilitates personalised treatment approaches	CQIMG Paper 3(107)	“Good examples of questions...best answered by synthesizing findings from primary qualitative studies, building on the idea that an in-depth analysis and synthesis of qualitative findings across studies creates potential to develop a better understanding, or more comprehensive models or theories, of the phenomena of interest [that] can inform the design of interventions, strategies, and health systems and their implementation to develop more personalized approaches that benefit patients and improve outcomes”.	Need to incorporate theorising in creation of QES	
Contributes to shared decision making	Carroll (2017) (37)	“Failure to take account of a patient’s needs and views contributes to lower levels of adherence to treatments and poorer clinical outcomes, whereas well conducted shared decision making improves patient satisfaction and willingness to follow treatment plans. These are key	Principle of “nothing about me without me” requires that clinical decisions be consistent with the elicited	Complementary role with patient representation

		outcomes for any policy maker who wants to see research having its intended effect in practice”.	preferences and values of the patient.	
QES can supplement patient representative experience with specific issues for consideration.	Carroll (2017) (37)	“Although NICE has a quality standard and clinical guideline on involving patients and, where appropriate, their family or other representatives in treatment decisions, this guidance is quite generic. By contrast, a qualitative evidence synthesis of relevant studies can provide specific information about the many issues that need to be taken into account during shared decision making with particular groups of patients. This type of synthesis can therefore potentially offer a valuable supplement to the experiences of patient representatives on guideline panels, as the recent update of NICE guidelines for stroke rehabilitation show”.	QES performs supplementary role to patient representation.	Complementary role with patient representation
Complementarity to effectiveness reviews (Cochrane)	CQIMG Paper 1(45)	“From the beginning, Cochrane guidance on qualitative evidence synthesis has been based on the tenet that qualitative evidence can inform understanding of effectiveness, by increasing understanding of a phenomenon, identifying associations between the broader environment within which people live and interventions are	Wider role for QES	

		implemented, and unpacking the influence of individual characteristics, and attitudes toward health conditions and interventions.”		
Role of QES in examining complexity (Cochrane)	CQIMG Paper 1(45)	“The role of and methods for qualitative and mixed-method evidence synthesis in achieving a better understanding of complexity was outlined in a seminal series on considering complexity in systematic reviews of interventions published in 2013. The first series ...took a methodological lens that largely drew on Cochrane guidance on quantitative and qualitative evidence synthesis methods. It has been highly influential in getting guideline developers, reviewers and other key stakeholders to consider how to make best use of diverse sources of evidence to address questions about the complexity of complex interventions”.	Need to link QES to complexity perspective	
Broad role for qualitative research within health services research	Joanna Briggs Institute Reviewers' Manual(106)	“Qualitative research plays a significant role in understanding how individuals and communities perceive health, manage their own health and make decisions related to health service usage. It can assist to understand the culture of communities, in relation to implementing changes and overcoming barriers. It can also inform planners and policy makers about the manner in which service users experience health as well as illness, and can be used to		

		evaluate activities of health services such as health promotion and community development”.		
Models for QES within Cochrane context	CQIMG Paper 1(45)	<p>“An additional [QES] can be undertaken within a Cochrane context if the phenomenon of interest is likely to be best addressed by qualitative evidence and (i) the questions broadly align with one or more effect reviews of the same or a linked intervention, (ii) the Cochrane Review Group agrees to register the title, and (iii) the Cochrane Qualitative and Implementation Methods Group is able to provide methodological guidance and support as required.</p> <p>Reviewers undertaking a [QES] may conduct a stand-alone synthesis to integrate with an already completed, or published, Cochrane intervention effect review. Alternatively, reviewers may undertake the synthesis and subsequent integration in parallel with conducting a Cochrane intervention effect review”.</p>	Models for linkage with effectiveness reviews	
QES involves recontextualising effectiveness evidence [Cochrane]	CQIMG Paper 2(67)	[QES] recognises the need for new approaches to question formulations and development of... review protocols that allow us to ‘recontextualise’ effectiveness. Recontextualising requires considering effectiveness research in relation to issues in society to enable a decision-maker to make an informed decision about whether an intervention is likely to be useful and whether that intervention is applicable to their	Process must allow for re-introduction of context from extracted studies.	

		local population. Qualitative research produces contingent and experiential knowledge on why interventions work the way that they do (or fail to work).		
Role of QES in implementation	CQIMG Paper 2(67)	“Implementation questions provide information on how the implementation process produces (or fails to produce) improvements in health... The ultimate aim of any review team, ...is to produce pragmatic evidence on what actions need to be taken to achieve health outcomes and improve health and social systems”	Emphasis on pragmatic evidence for implementation	
Contribution of QES is more than simply barriers and facilitators and attitudes towards a health technology (Cochrane)	Cochrane Handbook(66)	A [QES] can inform understanding of how interventions work by: <ul style="list-style-type: none"> * increasing understanding of a phenomenon of interest (e.g. women’s conceptualization of what good antenatal care looks like); * identifying associations between the broader environment within which people live and the interventions that are implemented; * increasing understanding of the values and attitudes toward, and experiences of, health conditions and interventions by those who implement or receive them; and 	Potential role of QES in implementation issues	

		* providing a detailed understanding of the complexity of interventions and implementation, and their impacts and effects on different subgroups of people and the influence of individual and contextual characteristics within different contexts.		
Contribution of patient/relative perspectives to holistic assessment	SBU(58)	“SBU evaluates methods/interventions applied in health, medical and social care. Included in this evaluation is scrutiny of how the patient/client or their relatives perceive different aspects of care, such as experiences of undergoing treatment or diagnosis, experiences of receiving different interventions, or of living with different conditions....the focus here is on qualitative research, with special reference to perceptions of patient/clients”.	QES contributes at health service, health technology and health level of evaluations	
Contribution of QES to Implementation	CQIMG Paper 4(46)	“it is increasingly common that qualitative “sibling” studies and mixed-method process evaluations are undertaken alongside a trial, which can be synthesized to better understand the political and operational factors associated with the implementation of health policy, health systems, behavioral, environmental, or clinical interventions”.		
	CQIMG Paper 6(108)	“it is increasingly common that some studies include qualitative research alongside a trial, which can be synthesized to better understand implementation. A		

		synthesis of qualitative studies that are unrelated to trials can also be helpful in understanding the factors that affect intervention implementation”		
Strengths and weaknesses of integrating qualitative with quantitative data	Knowledge Synthesis Project(109)	“Strengths reported by the authors of the included articles...: provide rich contextual detail, can be used to generate or refine theory, have high methodological rigor, can be used to identify gaps in the literature, can be used to address complex questions, and increasing uptake of results by making qualitative evidence accessible. In contrast, the weaknesses reported by the authors...: include interpretive processes derived from processes for qualitative data analysis, lack guidance on conducting all steps of the knowledge synthesis method, bias or sampling error present, and labor intense”.	Requires precautions to each of these weaknesses	
SIGN advocates for enhanced guideline development process	Cooper et al(99)	“Inclusion of a range of evidence sources has enhanced the guideline development process discussed here. Without this evidence it would be difficult to make recommendations for clinical practice...; with this evidence the perspectives of patients, family members and healthcare professionals have informed the guideline (in addition to the perspectives of lay members of the guideline development group).		

SIGN acknowledges outstanding methodological challenges	Cooper et al(99)	"Limitations [still] to overcome to fully integrate this range of evidence in guideline development methodology, and of course, the extent to which the recommendations will be easily interpreted and implemented by the clinical community is as yet unknown".		
	Downe et al(1)Lewin et al(60) Glenton et al(110)	"WHO has recognised the need to improve its guideline methodology to ensure that guideline decision-making processes are transparent and evidence based, and that the resulting recommendations are relevant and applicable. Hence, the WHO Handbook for Guideline Development was produced....Evidence of several criteria is required to inform a WHO guideline recommendation in addition to evidence of the effectiveness of an intervention]. These other criteria include values and preferences, acceptability, feasibility and equity implications. Qualitative evidence can help inform these criteria.		
	Downe et al(1)	"there is increasing interest in the use of qualitative evidence to inform decisions in...health and social care, prison care, and education....until recently, the decisions made by guideline panels about these criteria have been largely based on the expert opinion of guideline development groups at WHO and/or on evidence that they happen to		

		know about or that has been collected ad hoc, rather than on a systematic review of relevant research”		
Synergies of use by decision-makers and methods development	WHO (Lewin)(111)	“The growing use of qualitative evidence to support decisions, and the availability of methods that can help us use this type of evidence in knowledge-to-action cycles, suggest that we are entering a new era for qualitative research”.		

QUESTION 2: ELEMENTS TO BE INFORMED BY QUALITATIVE EVIDENCE OR QUALITATIVE EVIDENCE SYNTHESIS

Table 7 - Extracted Data relating to Question 2 (Elements for Inclusion)

Issue	Source	Data Extract	Implications	Notes
Source of Framework	Health Improvement Scotland (2019)(41)	“Coding framework... based on the thematic analysis of four frameworks - the NHS Patient Experience Framework, the EUnetha core Model, the Warwick Patient Experience Framework, and an analytical patient experiences model published in the Danish Centre for Health Technology Assessment HTA (DACHENTA) Handbook – and two qualitative evidence syntheses exploring patients’ experiences of a health technology. Cites 6 source documents (Refs 59-64)	Generic framework informed by patient experience frameworks and previous QESs	In context of rapid QES

Structure of Framework	Health Improvement Scotland (2019)(41)	<p>“Five overarching themes... adopted from the DACHENTA handbook cover from a patients’ perspective what influence a particular health technology might have on various different aspects of patients’ lives (for example, in relation to them as individuals, the influence it has on their independence or on their family relations):</p> <p>Individual aspects, Social aspects, Communication aspects, Economic aspects, Ethical Aspects (p.17)</p>	Generic framework covering five main aspects of patient experience	In context of rapid QES
Contribution to organisational research	SBU(58)	<p>“One topic of research which has evolved in recent years is the question of how care services are organised, i.e. organisational research. This question has become increasingly important as it has been recognised that the ways in which care is organised, supervised and delivered can influence how successfully a method/intervention can be introduced and</p>	QES for examining how services can be delivered effectively	

		applied in the health and social care services”.		
Multiple lines of inquiry pursued by a QES (meaningfulness, appropriateness, feasibility, equity, affordability, and implementation)	CQIMG Paper 2(67)	“Lines of inquiry include questions about meaningfulness, appropriateness, feasibility, equity, affordability, and implementation. Questions may include one or more lines of enquiry as illustrated by the sample questions from Cochrane qualitative and mixed method reviews and protocols”	Need to articulate and prioritise potential lines of inquiry.	
	GIN Public Toolkit(69)	“The beliefs, experiences, values and practices of patients are amongst those factors that co-determine the ‘real world’ effectiveness of intervention. The inclusion of research that examines these domains is one of several possible methods to include the patient’s perspective into guidelines. By examining what problems patients face in their daily lives, research on patients’ views and experiences can be used to establish		

		<p>research questions for a guideline. It may inform a specific sub question, such as what information and support to offer patients, their family and carers. Patient views and experiences may also help policymakers and practitioners to interpret (and implement) evidence of effectiveness, for example by better understanding the barriers and facilitators for patients following a recommended treatment”</p>		
	GIN Public Toolkit(69)	<p>“Specific questions concerning patients’ perspectives may include patient views on a disease or treatment broadly speaking; or the factors that influence a patient’s treatment decisions, adherence and expectations. Qualitative research also examines behaviours and beliefs of medical professionals and can explore the economic, cultural and practical aspects of a treatment that will determine how successful it ultimately is in practice”.</p>		

	GIN Public Toolkit(69)	<p>“Depending on the question, a qualitative evidence review can be used to prepare the guideline development process (establishing priorities and determining the guideline’s questions). It can also be used throughout the guideline development process, its findings providing evidence of effectiveness in its own right, or helping explain and interpret quantitative evidence. Or, it can be mobilised after a guideline has been produced, helping to transform general recommendations into specific actions for local practices”</p>		
	Lewin et al(60)	<p>“the WHO Handbook for Guideline Development now stipulates that evidence on a number of questions is required to inform a WHO guideline recommendation. These questions include how people affected by the intervention value different outcomes, the effectiveness, acceptability and feasibility of the intervention, and equity implications. Along with other organisations, WHO increasingly uses the GRADE evidence-to-decision (EtD) framework for this purpose. The EtD framework helps to ensure that key questions or criteria are considered in decisions, and also supports people in assessing and using evidence in a more systematic, structured and</p>		

		transparent way. Evidence is compiled from systematic reviews and other sources to address each of the framework's criteria"		
<p> JBI Feasibility Appropriateness Meaningfulness Effectiveness (FAME) Framework </p>	<p> JBI Model Paper(112) </p>	<p>The center of the new Model [encompasses]:</p> <ul style="list-style-type: none"> • Feasibility (the extent to which an activity or intervention is practical or viable in a context or situation – including cost-effectiveness). • Appropriateness (the extent to which an intervention or activity fits with a context or situation). • Meaningfulness (refers to how an intervention or activity is experienced by an individual or group and the meanings they ascribe to that experience). • Effectiveness (the extent to which an intervention achieves the intended result or outcome). 		
<p> JBI Framework as elements of evidence-based healthcare </p>	<p> JBI Model Paper(112) </p>	<p> "...we define evidence-based healthcare as clinical decision-making that considers the feasibility, appropriateness, meaningfulness and effectiveness of healthcare practices...informed by the best available evidence, the context in which the care is delivered, the individual patient, and the professional judgment and expertise of the health professional". </p>		

Types of studies typically included in “patient views” studies	SIGN 50(52) SIGN 100(100)	Types of studies identified generally include patients’ views on: <ul style="list-style-type: none"> • positive and negative experiences of the condition, including diagnosis, medication and other treatments, follow-up care and quality of life • unfulfilled needs • information needs and preferences • participation in making decisions about treatment • overall satisfaction with the care received. A copy of the Medline version of the patient search strategy (https://www.sign.ac.uk/assets/search-filters-patient-issues.docx) is available on the SIGN website.		
	WHO Complex Interventions Mini-series(21)	Ways in which a qualitative evidence synthesis (QES) may help address elements of complexity <ul style="list-style-type: none"> • Develop a theory of why and how an intervention (complex or simple) works. • Explore the experiences of recipients or providers of healthcare. • Explore the experiences of living with a condition, which can impact on the feasibility and acceptability of an intervention. • Examine the factors affecting implementation, including context. • Determine how components of complex interventions work to produce effects. 		

		<ul style="list-style-type: none"> • Establish how and why the implementation of interventions varies across contexts. • Examine how a system changes when a complex intervention is introduced. • What explains changes in the system over time. 		
	WHO Complex Interventions Mini-series(21)	<p>Criteria from WHO-INTEGRATE evidence to decision framework to be informed by QES:</p> <ul style="list-style-type: none"> • Balance of health benefits and harms. • Human rights and sociocultural acceptability. • Health equity, equality and non-discrimination. • Societal implications. • Financial and economic considerations. • Feasibility and health system considerations. 		
SIGN includes JBI domains in its own qualitative evidence	YouTube Video (SIGN) (101)	Acceptability, Feasibility, Perspectives of service users and carers, Processes and Implementation		
Potential role of mini QES	Lewin et al(60)	A technical team may need to commission both broad QES that cover multiple guideline interventions as well as 'mini-QES' that focus on one specific intervention. It can sometimes be useful to use rapidly conducted 'mini-QES' to address important gaps in the evidence available for a guideline		

QUESTION 3: PERSPECTIVES AND VIEWS TO BE INCLUDED

Table 8 - Extracted Data relating to Question 3 (Perspectives and Views)

Issue	Source	Data Extract	Implications	Notes
Illness experience, Intervention programme theory and Barriers/facilitators to access	Health Improvement Scotland (2019)(41)	“In HTA, a synthesis of qualitative evidence can take as a starting point questions such as how do people experience illness; why does an intervention work (or not), for whom and in what circumstances; and what are the barriers and facilitators to accessing health care” (p.5)	Multiple options on where to target the synthesis – may require a single synthesis or multiple syntheses	In context of rapid QES
QES as a source of contradictory viewpoints	Carroll (2017) (37)	“The synthesis of several relevant qualitative studies can offer multiple perspectives as well as providing evidence of contradictory viewpoints that might otherwise be missed when considering a single study alone”.	Sampling for QES must prioritise diversity of sources/disciplines/ perspectives. Requires different approach to database selection.	Contrasts with comprehensive sampling
Quality of Life can be explored in a deeper way than through quantitative instruments	SBU(58)	“When the aim of a study is to achieve a deeper understanding of a person’s subjective perception of – for example – quality of life, a person’s individual perceptions, experiences, impressions and actions, then qualitative research methods may be more	Complementarity to Quality of Life data	

		relevant. Such methods offer an understanding of associations from the individual's perspective".		
Multiple perspectives are addressed by QES	CQIMG Paper 2(67)	Patients, policy makers, providers, purchasers, payors, and the public are end users of systematic reviews.	Six perspectives to be addressed (7Ps of stakeholder engagement, minus the principal investigators [who conduct the reviews])(113))	

Role of QES in intervention design and programme theory	Tricco(114)	Patients' expectations, adherence, preferences, knowledge, and values are factors that can influence the effectiveness of an intervention... Perspectives of various stakeholders, such as patients, researchers, clinicians, and policy makers, can shape the creation of different types of interventions. These factors provide rich contextual details that can be used to establish theories as to why certain		
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		interventions work (or fail) in particular settings and contexts		
Synthesis of theory	Pound & Campbell(115)	“increasing evidence of a more systematic approach to theory synthesis. The current impetus ...has its roots in an evidence-based approach to intervention design within public health (Craig et al., 2008, National Institute of Health and Clinical Effectiveness, 2007) and in a concern with the role that theory plays in the effectiveness of interventions”.		

QUESTION 4: CIRCUMSTANCES OR TOPIC AREAS REQUIRING PARTICULAR ATTENTION

Table 9 - Extracted Data relating to Question 4 (Particular Attention)

Issue	Source	Data Extract	Implications	Notes
Use of QES as alternative approach for very ill patients	Health Improvement Scotland (2019)(41)	“use of synthesis of qualitative studies makes it possible to avoid disturbing very ill patients with unnecessary interviews, conversations, participant observations, etc.” (p.5)	QES offers access to otherwise unavailable or unfeasible viewpoints	In context of rapid QES
	SBU(58)	“the launch of new, expensive and unnecessary studies can be avoided, i.e. further primary studies become redundant because the evidence is already available. This can – for example – avoid intruding on gravely ill patients with interviews, observations or questionnaires”.		For QES more generally
Use of “patient search” to identify disadvantaged groups	SIGN 50(52)	“Whereas other literature searches carried out for the guideline attempt to answer focused key questions by filtering out the volume of irrelevant evidence, the patient search is deliberately as broad and inclusive as possible. It focuses entirely on the health condition that is being considered,		

		and makes no attempt to concentrate on any social group or class. As the reviewer develops themes from the literature, they will pay particular attention to anything that suggests there are population groups that are disadvantaged and ensure their interests are specifically considered by the guideline development group”.		
Identifying equity considerations	SIGN 50(52)	“Guideline groups are required by law, as well as good practice, to consider whether any recommendations they make will have a differential impact on any of these ‘equality’ groups (age, disability, gender reassignment, marriage and civil partnership, race, religion or belief, sex, sexual orientation). Some aspects of equality issues have been addressed earlier in this manual. At this later stage in the process, it may be necessary to analyse the evidence for specific subgroups of the population to see if and how it differs from the main results. If there are substantial differences it will be necessary to make separate recommendations for these subgroups taking these differences into account”.		

	NHMRC Standards for Guidelines (53)	D.11.1 (desirable) Where evidence is identified showing that sociocultural factors (including ethnicity, gender, age, disability, socioeconomic status and location) affect treatment or prevention outcomes (see Requirement C.3.1), this evidence is clearly identified and considered in the formulation of the recommendations.		
	Lewin et al(60)	The guidance on populating an EtD framework notes that technical teams “should evaluate potential impacts on equity in relation to specific characteristics that are likely to be associated with disadvantage in relation to the question they are addressing”.		
	Lewin et al(60)	“Two ways in which we, as guideline technical teams, have used qualitative evidence to populate the gender, health equity and human rights impacts section within the EtD framework; firstly, issues may be identified directly from the findings of a QES. In these cases, we simply summarise these data for this criterion of the framework”.		

	Lewin et al(60)	“where a QES undertaken for a guideline does not identify gender, health equity or human rights issues explicitly, it may be possible to infer these from the findings through discussion within the technical team or experts in the field. A narrative summary of the issues can then be created. Where this is done, it is important to indicate to those making recommendations that these issues were hypothesised from the evidence rather than being described there explicitly and the technical team should consider including these issues under ‘Additional considerations’ in the EtD framework”.	Consider role of indirect/implicit equity evidence	
Exploring differences in observed effects for Equity reasons	NHMRC Guidelines on Guidelines(53)	One of the key objectives for evidence synthesis is to explore the reasons for different observed effects and to identify any populations or intervention/exposure categories that are associated with these differences. This can be a critical area of investigation used to inform the guideline’s recommendations to support specific actions, for different populations. It is especially relevant to considerations of equity	Consider differential needs of subgroups	

Clinical needs of specific groups	SIGN 50(52)	“Apart from issues of social equity, subgroups may need to be considered for clinical reasons such as specific comorbidities, or issues around polypharmacy where separate recommendations may be required for these groups”.	Consider specific needs of subgroups	
Use of QES for views of children and young people	Cooper et al(99)	“Without this evidence it would be difficult to make recommendations for clinical practice on two important aspects of epilepsy in children and young people; with this evidence the perspectives of patients, family members and healthcare professionals have informed the guideline (in addition to the perspectives of lay members of the guideline development group)”.	Consider special needs for QES evidence	
Under-researched areas require more persistent search strategies	CQIMG Paper 2(67)	“Unpublished studies, and grey literature reports, websites for interventions and programs may yield an additional pool of evidence, especially in critically under-researched areas. Exploration is currently underway to determine how publication bias may operate within qualitative research but it is likely, at least, that unpublished studies and reports may offer a more-extensive, but less-filtered, representation of the phenomenon of	Initial scoping should identify need for supplementary searching and evidence sources.	

		interest... No precise formula exists for deciding whether there is 'enough' research on a topic..., it depends rather on the combination of how much relevant information exists alongside its richness (and "thickness") of detail".		
	JBI Reviewers' Manual(106)	"A systematic review should consider papers published by both commercial and academic publishers as well as grey literature. Rather than compete with the published literature, grey literature has the potential to complement and communicate findings to a wider audience. Grey or Gray literature is also known as Deep or Hidden Web material may include: Theses and Dissertations, Reports, blogs, technical notes, non-independent research or other documents produced and published by government agencies, academic institutions and other groups that are not distributed or indexed by commercial publishers".	Consider role of grey literature	
QES in absence of process evaluation data on implementation	CQIMG Paper 4(46)	"When process evaluations in quantitative reviews are lacking or results do not adequately address decision-makers concerns and qualitative perspectives on implementation are sought, we	Need to consider potential contribution of process evaluations and implications for study identification	

		recommend review authors to collaborate with qualitative review teams to meet these minimum requirements”.		
	Lewin et al(60)	Our experience...highlighted that qualitative studies often do not include in-depth data on intervention feasibility.... These studies often focus on the views of service users or providers regarding a health issue, and do not include the views of healthcare managers or explore factors affecting the governance or financing of interventions or programme.	Consider deficiencies of existing evidence base	
	Lewin et al(60)	This evidence gap...led us to carry out multi-country case studies for several guidelines. These included a broader set of information sources, including programme descriptions and mixed method programme evaluations, that might provide evidence on factors influencing the feasibility and implementation of an intervention”.	Consider role of supplementary data	
	Lewin et al(60)	“These wider sources provided less data than anticipated as, firstly, we found fewer programme descriptions and evaluations than we expected and, secondly, those that we found generally		

		included only very thin data. ...it may be more useful to collect additional data on the feasibility of guideline interventions through qualitative key informant interviews with programme managers and decision-makers”.		

QUESTION 5: HOW SHOULD QUALITATIVE EVIDENCE BE ANALYSED, PRESENTED, EVALUATED, AND CONSIDERED

Table 10 - Extracted Data relating to Question 5 (Methods) - Question Formulation

Issue	Source	Data Extract	Implications	Notes
Wider context for question formulation process	CQIMG Paper 2(67)	“We describe question formulation and protocol development as a process of problem framing, constructing a preliminary framework or logic model to illustrate relationships, and developing an understanding of context. These activities lead to identifying potential lines of enquiry and searching to identify available evidence. Questions are then formulated and focused, followed by protocol development”.	Question formulation(20) must include exploration of relationships and an understanding of context(19)	
PerSPE(c)TiF offers alternative structure to SPICE for complex Intervention questions	Cochrane Handbook(66) WHO Complex Intervention guidance(20)	“Extended question framework (PerSPEcTiF) to describe both wider context and immediate setting that is particularly suited to QES and complex intervention reviews. Detailed attention to the question and specification of context at an early stage is critical to many aspects of qualitative synthesis”.	PerSPE(c)TiF structure may be suitable for QES or amenable to use in mixed methods reviews.	

Need to factor in Context into qualitative questions especially for complex interventions	Cochrane Handbook(66) WHO Complex Intervention guidance(20)	“By specifying the context a review team is able to identify opportunities for integration with the intervention review, or opportunities for maximizing use and interpretation of evidence as a mixed-method review progresses, and informs both the interpretation of the observed effects and assessment of the strength of the evidence available in addressing the review question”.	Question structures that include context may be more useful for qualitative/mixed methods synthesis	
SIGN Guidelines process modified question formulation	Cooper et al(99)	Following initial review of the literature, the guideline development group modified PICO to a qualitative PICO format (population, phenomenon of interest, context)(106) and conducted a second search of the literature to be comprehensive.		
Need to establish situational context	CQIMG Paper 2(67)	“Consultation with stakeholders, together with preliminary scoping of the literature, will help to establish ‘What situational circumstances surround the problem?’ Many relevant contextual factors are identifiable at an early stage of protocol development and will inform such decisions as the ultimate scope of the search, the inclusion and exclusion criteria and later considerations of transferability. A decision needs to be made at the outset as to whether the review will address a single context or multiple contexts”.		

Table 11 - Extracted Data relating to Question 5 (Methods) - Searching

Issue	Source	Data Extract	Implications	Notes
Scoping searches serve additional function in determining viability of different synthesis methods	Cochrane Handbook(66)	“Developing a clear picture of the type and conceptual richness of available qualitative evidence strongly influences the choice of methodology and subsequent methods. We recommend that authors undertake scoping searches to determining the type and richness of available qualitative evidence before selecting their methodology and methods. ”	Requires “spot-checking” of data availability before finalising protocol	
Search Filter for Patient experiences and preferences	SIGN 50(52)	“SIGN has developed a literature search strategy to identify both qualitative and quantitative studies that reflect patients’ experiences and preferences in relation to the clinical topic (see section 4.1). This search is performed at least three months prior to the first group meeting to ensure adequate time to obtain relevant articles and summarise their findings for presentation at the first guideline group meeting”.		
		“This search is designed to cover both quantitative and qualitative evidence, and is not limited to specific study designs. It is carried out over the same range of databases and sources as the main literature review, but		

		will normally include both nursing and psychological literature. The results of this search are presented to the guideline development group to inform the setting of key questions...The use of this literature search is discussed in more detail in SIGN 100(100).”		
Literature search for patient views	SIGN 100(100)	“The literature search will identify around 500 papers, some of which may not be directly relevant to the guideline. We then choose the papers that are relevant to the guideline topic and group the abstracts (brief summaries of the aims, methods, results and conclusions of a research study) from this search into themes to highlight patients’, service users’ and carers’ main concerns. Our Public Involvement Advisor presents these themes to the members of the guideline development group, who then take the themes into account”.		
Qualitative evidence synthesis requires diverse search strategies and sources	Booth(51)	“Reference or citation searching was used in more than half the QES in their sample. Other popular search strategies included hand-searching journals, contacting experts or authors or web searching. Reviewers...mentioned personal correspondence, related paper options in existing databases, email discussion lists, footnote chasing, or searching conference abstracts, etc.	Search strategies for qualitative evidence may need to include a more diverse selection of search sources than their quantitative equivalents.	

		Other approaches include scanning conference proceedings, contacting professional bodies, searching for grey literature and looking at included studies of earlier reviews, personal correspondence, related paper options in existing databases, email discussion lists, footnote chasing or searching conference abstracts”		
Selective choice of sources may be more effective than thorough searching across multiple databases	Booth(4)	“Empirical research is required to examine suggestions [...] that thorough searching of a small number of databases, supplemented by other searching methods, may be more efficient than searching across a wider range of databases.	Thorough searching may be more effective than broad searching	
Few methodological keywords may be required in qualitative filters	Booth(4)	“We are beginning to learn the merits of different sampling approaches and their alignment to named qualitative synthesis methodologies. Limited but important evidence exists to suggest that a few qualitative methodology keywords may perform equally well to more extensive filter terms”.	Select filter terms may be sufficiently effective, when compared with extensive filters	
Justification for initial scoping search	Downe(1)	Ideally, an initial scoping search should be conducted prior to the framing of the guideline parameters to identify potential concepts, e.g. values and associated outcomes that may be important to the population under investigation. Where this has been done, the findings from		

		the scoping review may guide the subsequent QES search criteria		
Decisions on use of filters should be informed by the specific review context.	Cochrane Handbook(66)	“[a] key decision is whether to use study filters or simply to conduct a topic-based search where qualitative studies are identified at the study selection stage. Search filters for qualitative studies lack the specificity of their quantitative counterparts [but] may facilitate efficient retrieval by study type (e.g. qualitative or mixed methods or by perspective (e.g. patient preferences) particularly where the quantitative literature is overwhelmingly large and thus increases the number needed to retrieve”.	The decision on use of filters may depend upon whether quantitative and qualitative search limits are co-terminous and how many sub-questions may be involved.	
Decisions on context will determine search methods and source selection	CQIMG Paper 2(67)	If preliminary searches indicate that individual study reports may lack details of context, review authors may seek to identify “clusters” of related study reports in order to reconstruct the study context. Search procedures, characterized by the CLUSTER mnemonic, have been developed to identify such clusters. Specification of a particular context in the review question e.g. geographical limits will typically exert an important influence on the selection of appropriate sources.	Need to decide how to characterise context to inform search construction.	

	JBI Reviewers' Manual(106)	<p>In a qualitative review, context will vary depending on the objective and question(s) of the review. Context may include but is not limited to consideration of:</p> <ul style="list-style-type: none"> • cultural or sub-cultural factors, • geographic location, • specific racial or gender based interests, or • detail about the specific setting (such as acute care, primary health care, or the community). 		
Preparatory work classifying intervention types and/or identifying heterogeneity may be required to inform analysis	<p>Cochrane Handbook(66)</p> <p>CQIMG Paper 4(46)</p>	<p>“An a priori scoping review, concept analysis, critical review or textual narrative synthesis can be undertaken to classify interventions and/or to identify the programme theory, logic model or implementation measures and processes. The intervention Complexity Assessment Tool for Systematic Reviews iCAT_SR may be helpful in classifying complexity in interventions and developing associated questions”.</p>	A priori identification of intervention types may help in subsequent grouping and analysis.	
Potential role for iCAT-SR in implementation reviews	CQIMG Paper 4(46)	<p>For [QES], the iCAT-SR may facilitate comparisons of staff experiences with implementation or the construction of implementation chains for different types of programs, enhancing the theoretical and interpretive validity of the review.</p>		

Sources of implementation data	CQIMG Paper 4(46)	Information on program operations (“implementation”) is often descriptive (i.e., textual) and not empirical and can appear in the background and methods section of a primary outcome evaluation paper or in a nonempirical “sibling” study. In addition, authors often provide reflections on implementation in the discussion section. To counteract some of these limitations..., we recommend that descriptive information and author reflections on the experience of implementing the intervention are used from trial and “sibling” reports and further that corresponding authors be contacted for specific information on implementation. Such information strengthens the descriptive validity of qualitative and quantitative reviews.		
Stakeholder involvement offers potential mechanism for identifying programme theory.	Cochrane Handbook(66)	“...these additional activities are very resource-intensive and are only recommended when the review team has sufficient resources to supplement the planned qualitative evidence syntheses with an additional explanatory review. Where resources are less plentiful a review team could engage with key stakeholders to articulate and develop programme theory”.	In a NICE context, engagement with stakeholders may help with conceptualisation and pre-protocol identification of meaningful groupings	

	CQIMG Paper 2(67)	“For some types of review, stakeholders may be involved in construction of the programme theory for the preliminary model”		
Need to factor in patient’s perspective from the beginning	SIGN 50(52)	“Incorporating the patient’s perspective from the beginning of the development process is essential if it is to influence the coverage of the final guideline. One of the methods used to achieve this is to conduct a specific search on patient issues in advance of the first meeting of the guideline development group”.		
Building blocks of review process	JBI Reviewers’ Manual(106)	<p>Core [JBI] assumptions...include:</p> <ul style="list-style-type: none"> • The requirement for an a priori protocol that describes all steps in the review, decisions on how they will be undertaken and appends all templates that will be used during the review; • Comprehensive and exhaustive searching, independent critical appraisal and standardised data extraction; • Synthesis of findings that authentically represents the aggregation of data from primary studies; • Presentation of a meta-aggregative schematic that represents the findings and their aggregation in to categories, and the aggregation of categories in to synthesized findings; and • The development of recommendations for policy or practice with assigned grades of recommendation. 		

<p>Purposive sampling may be appropriate to interpretative type of inquiry</p>	<p>Cochrane Handbook(66)</p>	<p>A key decision, aligned to the purpose of the qualitative evidence synthesis is whether to use the comprehensive, exhaustive approaches that characterize quantitative searches or whether to use purposive sampling that is more sensitive to the qualitative paradigm (Suri 2011). The latter, which is used when the intent is to generate an interpretative understanding, for example, when generating theory, draws upon a versatile toolkit that includes theoretical sampling, maximum variation sampling and intensity sampling.</p>	<p>In a resource constrained environment, NICE could consider the value and risks of alternatives to comprehensive sampling.</p>	
	<p>Booth(51)</p>	<p>“The interpretive nature of QES suggests the value of methods derived from primary qualitative research, such as the use of theoretical sampling until data saturation is reached. Whereas in quantitative meta-analysis, omission of a key paper is critical to statistically drawn conclusions; this is not true of a QES which aims to make a conceptual and interpretative contribution. Campbell et al. affirm that “omission of some papers is unlikely to have a dramatic effect on the results”.”</p>	<p>Theoretical sampling and saturation may be appropriate</p>	
	<p>Booth(51)</p>	<p>“the intention of QES is not to identify all literature on a particular topic, the aim being identification of papers with</p>		

		characteristics relevant to the phenomenon being studied, not statistical representativeness”.		
	CQIMG Paper 2(67)	Syntheses [lie] between summative/aggregative syntheses on the one hand and “knowledge building” and “theory generating” syntheses on the other(26). Summative/aggregative syntheses require identification of as comprehensive a sample of studies as possible with a prevailing acknowledgement that “every study counts” in contributing to understanding of a phenomenon. In contrast, knowledge building and theory generating reviews are predicated on a view that “every meaning matters”,	Need to decide whether NICE QES are to be summative/aggregative or knowledge building/theory generating	
	Downe(1)	“Unlike...quantitative studies for systematic reviews or meta-analyses, it is not essential to identify and include every available relevant study. The purpose of QES is interpretive rather than predictive. Important, transferable concepts (or themes) are unlikely to change substantially in subsequent studies once they are consistently found in a body of papers from a wide range of participants and contexts. The number of studies included in any specific QES will...depend on the variety of concepts identified, the range of sociocultural contexts of interest to the		

		guideline, and the degree of agreement between studies on the emerging concepts and themes”.		
	JBI Reviewers Manual(106)	“Approaches to qualitative synthesis that are more aligned with primary qualitative methodologies may not require reviewers to undertake comprehensive searching, appraisal to establish quality is not considered important, and data extraction and synthesis may be iterative and based upon the re-interpretation of published data”. [Acknowledges alternative views to JBI assumptions]		
	GIN Public Toolkit(69)	“Search strategies for qualitative research on people’s views or experiences differ from search strategies for quantitative research on effectiveness. When the research question is specific and narrow, an exhaustive search strategy is used to locate all findings...When the aim is to examine and map diverse perspectives on (or experiences of) a disease, as in a qualitative review, a purposive search can be a more useful and pragmatic strategy....Whether the aim is an exhaustive search or a purposive sampling, to locate the relevant qualitative research requires both automated searches of multiple electronic databases and the hand-searching of other sources”.		

Role of conceptual/ theoretic saturation	GIN Public Toolkit(69)	“A search for a purposive sample is completed not when all studies are found, but when additional studies do not add significant new approaches or results, indicating the search has reached “theoretic saturation” or “conceptual robustness”. To assess if theoretical saturation has been reached, an iterative approach to literature searching, screening and initial analysis of studies, is required”.		
	Skalidou & Oya(70)	“It is debatable whether a systematic qualitative synthesis should include all relevant studies...‘the sample is purposive rather than exhaustive because the purpose is interpretive explanation and not prediction’, as it is the case in meta-analysis....Aiming for ‘conceptual saturation’ may be more appropriate as a search strategy for qualitative research”.		
	Downe(1)	“Reviewers should seek to ensure that no one sampling system affects the overall quality of the review by introducing reviewer bias...[With] a number of sampling methods as well as a variety of approaches,...reviewers should be aware of the different techniques before deciding which to use”.		

<p>Role of linked studies (effectiveness plus) reviews.</p>	<p>Skalidou & Oya(70)</p>	<p>“Adopting an ‘effectiveness plus’ approach and drawing only on additional information from studies included in the effectiveness review, or evidence from different studies but on the same interventions or settings as the quantitative evidence, was not an option that could address the process question in a satisfactory way. Instead, we set out to search and synthesise relevant qualitative evidence on CS, regardless of whether this evidence was in any way linked to the specific programmes reviewed in our meta-analysis. This approach is not new...it seems to be more scarce,..we are aware only of few other reviews that have followed that path so far. On the contrary, mixed-methods reviews narrowing the inclusion of qualitative evidence only to the evidence that is linked to the interventions (or countries) included in the effectiveness review appear to be more common”.</p>		
<p>Role of unrelated studies in studying implementation</p>	<p>Skalidou & Oya(70)</p>	<p>Despite the high cost involved, however, our experience shows that broader but highly relevant qualitative evidence can be very valuable in illuminating implementation patterns across different contexts as well as in contributing to our understanding of why the same</p>		

		type of intervention can be effective in one context but not in another.		
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Table 12 - Extracted Data relating to Question 5 (Methods) - Quality Assessment

Issue	Source	Data Extract	Implications	Notes
SIGN used JBI methods for appraisal and certainty	Cooper et al(99)	“Studies were critically appraised using JBI tools and the first step of the JBI ConQual approach was used to establish dependability and credibility of these individual studies.”		
SIGN highlights potential value of GRADE-CERQual	Cooper et al(99)	“During development of this guideline,...the GRADE CERQual (Confidence in the Evidence from Reviews of Qualitative Research) approach was published, and CERQual is increasingly being used by guideline developers such as the WHO. GRADE CERQual will be applied in our ongoing qualitative synthesis...”		
Use of qualitative sensitivity analysis to check impact of bias	NHMRC Guidelines for Guidelines(53)	Conduct sensitivity analysis to consider the potential impact of studies at high risk of bias on your overall conclusions. This can be done quantitatively using meta-		NHMRC uses NICE case studies to illustrate

		analysis, or qualitatively if you are using narrative or qualitative synthesis.		qualitative risk of bias assessments
SIGN identifies gaps in existing methodologies	Cooper et al(99)	“we were unable to apply a structured approach to critical appraisal or determining confidence in the findings of some other types of evidence (scoping reviews, mixed methods reviews)”		

Table 13 - Extracted Data relating to Question 5 (Methods) - Synthesis and Analysis

Issue	Source	Data Extract	Implications	Notes
Iterative process of data extraction and synthesis	CQIMG Paper 3(107)	“a key principle of qualitative data extraction, analysis, and synthesis is that the process is not sequential and linear. It typically involves moving backward and forward between these review stages. Completing the iterative review stages will benefit from regular team meetings to discuss and further interrogate the evidence to achieve a shared understanding”		
Exploring heterogeneity(53)	NHMRC Guidelines on Guidelines	If you are using alternative synthesis methods or non-statistical methods — including qualitative synthesis — heterogeneity can still be assessed through a careful and planned comparison of effects between studies. This can		

		be based on the similar categorisation of populations, settings or interventions as those used in subgroup analysis or meta-regression. Further guidance on approaching this kind of investigation is available elsewhere		
Meta-aggregation as potential method for generating recommendations	JBI Reviewers' Manual(106)	“A strong feature of the meta-aggregative approach is that it seeks to enable generalizable statements in the form of recommendations to guide practitioners and policy makers. In this regard, meta aggregation contrasts with meta-ethnography or the critical interpretive approach to qualitative evidence synthesis, which have a focus on re-interpretation and theory generation rather than aggregation”.		
		JBI considers, however, that [Meta-ethnography, Narrative Synthesis and Thematic synthesis] do not seek to provide guidance for action and aim only to ‘anticipate’ what might be involved in analogous situations and to understand how things connect and interact. Meta-aggregation is the preferred JBI approach for developing recommendations for action.		

Four methods of synthesis considered more rapid	Health Improvement Scotland (2019)(41)	“some methodologies for synthesising qualitative evidence... are considered as more rapid than others and, therefore, are more likely to be suitable for using within rapid review timescales. Review methods which require shorter timeframes... are: textual narrative synthesis, thematic synthesis, framework synthesis, ‘best fit’ framework synthesis.” (p. 14)	In context of HTA, limited variation in synthesis methods may be appropriate	In context of rapid QES
Three methods of synthesis considered more suitable to integration	Cochrane Handbook(66)	[Key issues for consideration when selecting a method that is particularly suited to a Cochrane Review and decision making context(21, 22).... Three QES methods (thematic synthesis, framework synthesis and meta-ethnography) are recommended to produce syntheses that can subsequently be integrated with an intervention review or analysis.	In context of HTA, limited variation in synthesis methods may be appropriate	In context of Cochrane Reviews
	GIN Public Toolkit(69)	The challenge of synthesis is...to “combine the findings of multiple qualitative studies while preserving and respecting their complexity” Such a process combines the ‘distilling down’ of individual studies (into summaries and evidence tables) to reduce diversity, with the creation of ‘remainders’ where the differences, details and contexts of the original studies is preserved (in appendices and footnotes).		

Usefulness of methods in integrating quantitative and qualitative findings should be considered when selecting methods.	Carroll (2017) (37)	“Framework, narrative, and thematic synthesis are particularly useful for answering questions about the uptake of interventions and for integrating quantitative and qualitative findings. These methods are therefore potentially the most appropriate for use in developing clinical guidelines. In the UK, NICE public health guidance...uses a form of thematic synthesis and integrates quantitative and qualitative evidence using a narrative approach”.	Synthesis methods need to look beyond requirements for included study materials to look at potential for subsequent integration.	Needs comparable Mixed Methods methodological guidance.
Integrating qualitative findings is outstanding challenge	GIN Public Toolkit(69)	“The final phase of integrating qualitative research within guideline development is perhaps the most difficult to capture by simple rules or steps. Many agree both qualitative research and patient perspectives are valuable contributions, but no methods exist to include such ‘other knowledge’ in Evidence-Based guidelines....The integration of different kinds of knowledge largely remains a pragmatic and informal process, often invisible in the final product”.		
Framework for analysing qualitative data	Health Improvement Scotland (2019)(41)	“Framework... designed for use in the analysis of qualitative studies which look at patient and social aspects related to the use of a health technology. The framework	Generic framework may target (and speed up) extraction of relevant data	In context of rapid QES

		provides pre-existing themes against which data extracted from the primary qualitative studies can be coded.” (p. 16)		
Frameworks may alter or evolve through the course of the QES	CQIMG Paper 2(67)	“In qualitative and implementation protocols, preliminary models are considered a starting point, acknowledging that what emerges during the review process may alter or refine the original model. Although qualitative and implementation protocols may be exploratory and allow for iterative searching and subsequent question reformulation and refocusing, the protocol should aim for transparency, by including a statement that deviations from the expected process will be documented and justified”	Deviations or amendments to the model should be documented.	
SURE framework may hold specific utility for QES of policy	CQIMG Paper 2(67)	“Qualitative reviews that are commissioned to enable policy making could use the SURE framework for implementing policy, which enables teams to identify where further information is needed before deciding to pursue a particular policy option”	SURE framework should be considered alongside other frameworks.	
RETREAT Framework used in deciding on methods of synthesis	Cochrane Handbook(66)	“The RETREAT framework outlines seven key considerations that review authors should systematically work through when planning a review. Flemming and colleagues further explain how to factor in such considerations when undertaking a [QES] within a	RETREAT outlines a <i>priori</i> questions when planning for review methods	

		complex intervention and decision making context when complexity is an important consideration”.		
	CQIMG Paper 3(107)	“The CQIMG endorses the INTEGRATE-Health Technology Assessment guidance on selecting methodology and methods for qualitative evidence synthesis in a health technology assessment context as the starting point for selecting an appropriate methodology and methods such as data extraction”.		
Mechanisms for linking QES to effectiveness review	Cochrane Handbook(66)	“It is increasingly common for sequential and convergent reviews to be conducted by some or all of the same authors; if not, it is critical that authors working on the qualitative evidence synthesis and intervention review work closely together to identify and create sufficient points of integration to enable a third synthesis that integrates the two reviews, or the conduct of a mixed-method review.”	Joint working can facilitate integration across effectiveness and QES reviews.	
	Cochrane Handbook(66)	Harden and colleagues(63) and Noyes and colleagues(22) outline [five] methods and tools for integration with an intervention review: <ul style="list-style-type: none"> • Juxtaposing findings in a matrix • Analysing programme theory 	Need to evaluate which methods are compatible with NICE preferred practices.	

		<ul style="list-style-type: none"> Using logic models or other types of conceptual framework Testing hypotheses derived from QES Qualitative comparative analysis (QCA) 		
	Cochrane Handbook(66)	<p>“This consideration (for joint working) also applies where an intervention review has already been published and there is no prior relationship with the qualitative evidence synthesis authors. We recommend that at least one joint author works across both reviews to facilitate development of the [QES] protocol, conduct of the synthesis, and subsequent integration of the qualitative evidence synthesis with the intervention review within a mixed-methods review”.</p>	Joint working can facilitate integration across effectiveness and QES reviews.	
Process evaluations as source of intervention and implementation data	CQIMG Paper 1(45) CQIMG Paper 4(46)	<p>“We anticipate that publication of the UK Medical Research Council Guidance on designing complex intervention process evaluations will increase the need to synthesise process evaluation evidence, and this will lead to further methodological innovation in methods of synthesis and assessing the confidence in synthesised findings”.</p>	Need to accommodate process evaluations in future guidance	Future agenda

Contribution of Dissertations and Theses	Skalidou & Oya(70)	“...despite representing a rather small percentage of the total of the included studies, searches for theses and dissertations rewarded us with...exceptionally rich sources of trustworthy and insightful primary qualitative evidence.... Having the space (and obligation) to provide detailed methodological and analytical chapters, these studies commonly met all the methodological criteria for inclusion and...ticked most of the boxes in the quality appraisal process and provided evidence that could convincingly unpack the “black box””.		
Need to develop practical methods to integrate quantitative and qualitative data	Carroll (2017)(37)	“Despite the availability of methods for integrating quantitative and qualitative evidence, there is no ready-made toolkit for doing so. The NICE stroke guideline and public health programme...offer relevant templates, but future work should seek to identify the most appropriate approach for clinical guidelines”. (p.2)	Practical methods for integration of quantitative and qualitative data are a priority	Need for toolkit
Method for incorporating diverse evidence, including qualitative, in development of recommendations for	Cooper et al(99)	“Our approach to critical appraisal and grading the evidence was informed by JBI systematic review methodology; we are confident that this brought rigour to the guideline development process. However, our approach is not without limitations. Inclusion of qualitative evidence, in the absence of existing qualitative systematic		

key SIGN Guidelines questions.		reviews, is a substantial undertaking for a guideline development group. Adequate time, resources and expertise needs to be allocated for the conduct of novel qualitative syntheses alongside the guideline development process”.		
Inclusion of a thickness /richness marker as extra quality filter	Skalidou & Oya(70)	“We...decided to only include studies which contained ‘relevant and substantive’ evidence on the specific thematic areas of interest,...and other contextual factors shaping the causal pathways to impact. This allowed us to exclude a large number of studies which passed the basic methodological criteria and contained relevant evidence, but whose analysis was rather thin and descriptive, findings were not clearly linked to data and overall lacked the ability to explain how, for whom and under what circumstances CS could or could not work.		
Need to seek rich, diverse and disconfirming cases	Booth(51)	“Innovative techniques might be “borrowed” from primary qualitative research such as deliberately seeking studies to act as negative cases, aiming for maximum variability and designing results set to be heterogeneous, as an alternative to “the homogeneity that is often the aim in statistical meta-analyses”“.	Innovative techniques for study identification might include deliberately seeking negative cases, maximum variability	

			and seeking heterogeneous results	
Findings may be located throughout a qualitative paper	CQIMG Paper 3(107)	“useful findings in qualitative studies may be found outside of the section labeled “results or findings”...a discussion of the theoretical framework used to interpret data may be discussed in the background or methods section....Some journals prefer the authors’ interpretations of their data to be in the discussion section, not in the results, and it is not uncommon to find more interpretative theoretical findings discussed here. Increasingly, findings and additional explanations can be located in supplemental online only files”.	Informs guidance on data extraction	
Evidence to Decision Making (EtD) Frameworks may reveal overlaps	Lewin et al(60)	“Because qualitative evidence is often broad in nature, it may be relevant to more than one of the frameworks included in a guideline...Findings from several QES may be relevant to one or more frameworks...Such findings can either be repeated in each relevant framework or included in an overarching text linked to multiple frameworks”.	Consider redundancy of domains or concepts when developing a framework	

Crosscutting approaches may be required across EtD frameworks	Lewin et al(60)	“[One] reason to use an overarching or cross-cutting approach is that it can be challenging to summarise qualitative evidence succinctly without losing meaning and data on context. Where an overarching narrative is developed, the technical team need to ensure that it is clear to the guideline panel that the qualitative evidence for several frameworks is presented in an overarching document, and each EtD needs to link to this document. Importantly, whilst the qualitative evidence might be the same for different guideline questions, the guideline panel’s judgements for each criterion might differ, depending on the intervention evaluated in each question”.	Use of overarching document complements use of frameworks	
Use of generic findings across review topics	Lewin et al(60)	“Wider, less specific findings may need to be used in relation to an intervention where more specific findings are not available”.	Consider classes or types of mechanisms or interventions	
Use of directly and indirectly relevant evidence	Lewin et al(60)	“Qualitative evidence may have direct relevance to a guideline question or may be indirectly relevant. Indirect evidence, for example, qualitative evidence regarding a related intervention or context to the one of interest, can be included in the ‘Research evidence’ section of the EtD framework. ...it may be helpful to indicate clearly to users,	Develop procedures for handling indirect evidence	See Noyes(31)

		for instance, through the CERQual assessment of confidence, that the evidence is indirectly relevant.		
Need to accommodate evidence from non-NHS settings	Carroll (2017)(37)	“The qualitative evidence might also come from settings that are not directly applicable to the NHS, so this needs to be taken into account, though the same problem can apply to quantitative evidence”. (p.2)	Signals a need for potential work to extend current thinking on context, relevance and transferability.	See GRADE-CERQual (Relevance)(116), BMJ Global Health (Context)(117) and FITAR(118)/TRANSFER(119, 120) (transferability)

Table 14 - Extracted Data relating to Question 5 (Methods) - Presentation

Issue	Source	Data Extract	Implications	Notes
Avoid synthesis in the Introduction	JBIR Reviewers' Handbook(106)	“The introduction should avoid synthesizing findings from multiple authors given this is exactly what your review will aim to achieve, it should however, provide some indication	Distinguish background studies from included studies	

		that there is evidence available that will be included in your review and inform your question”.		
Utility of a reflexivity statement	Downe et al(1)	“The reflexivity statement expresses the a priori views, values and beliefs of the review authors about the subject of interest. It is intended to provide some transparency and give readers an insight into the lens through which the authors have viewed their data”.	Requirement for reflexivity	Also see Paper (121)
Reporting synthesis methods (based on meta-aggregation).	JBI Reviewers' Handbook(106)	Reporting the methods of data synthesis requires reviewers to describe: <ul style="list-style-type: none"> • what data was considered ‘findings’ in their review (i.e. was it limited to themes and metaphors, or did it include other analytic data from the papers that might have been an author observation rather than a thematic analysis); • the process by which findings were identified (i.e. repeated reading of text, or selection of themes from the results section only; • how findings were grouped in order to develop categories (i.e. was it based on similarity in wording, or concepts; • how category descriptions were created (i.e. by single reviewer, or by consensus process between reviewers/review group members); 	May complement current reporting standards particularly to enhance ENTREQ statement(122)	

		how synthesized findings and their accompanying descriptions were created and finalized.		
Use of mapping (framework synthesis)	Health Improvement Scotland(41)	“Mapping and interpretation: using the charts to define concepts, map the range and nature of phenomena, create typologies and find associations between themes with a view to providing explanation for the findings”. (p.15)	Mapping may offer accessible presentation of QES findings	In context of rapid QES
Characteristics of Included Studies Tables are useful for presentation	Cochrane Handbook(66)	“Irrespective of the review type and choice of synthesis method, we consider it best practice to extract detailed contextual and methodological information on each study and to report this information in a table of ‘Characteristics of included studies’”	Characteristics of included studies Tables should include contextual and methodological detail.	
	CQIMG Paper 3(107)	“Irrespective of the review type and selection of synthesis method, it is considered best practice to extract contextual and methodological information on each study and to report this information in an included studies table. The length and type of detail varies according to the report type.”		

The TIDieR checklist and ICAT_SR tool may help in exploring intervention characteristics	Cochrane Handbook(66)	“The template for intervention description and replication TIDieR checklist (Hoffmann et al 2014) and ICAT_SR tool may help with specifying key information for extraction (Lewin et al 2017). Review authors must ensure that they preserve the context of the primary study data during the extraction and synthesis process to prevent misinterpretation of primary studies (Noyes et al 2019)”.	Detail of data extraction should be determined by planned subsequent level of analysis and interpretation	
NICE data extraction templates offer alternative to framework synthesis approaches or to line-by-line coding in software	Cochrane Handbook(66)	“ Using a bespoke universal, standardized or adapted data extraction template. Review authors can develop their own review-specific data extraction template, or select a generic data extraction template by study type (e.g. templates developed by the National Institute for Health and Clinical Excellence”.	Within three data extraction options NICE processes may already determine a preferred approach.	
Use of tables and maps (all methods)	Health Improvement Scotland (2019)	“Results can be presented in different ways including topical tables and concept maps. Concept maps provide a graphic representation of concepts or categories of interest to the review question. Concept maps highlight the key concepts relevant to the review question and display a relationship among the identified concepts”.	Tables and maps can complement textual presentation	In context of rapid QES

Use of tables to display relationships between studies (all methods)	Health Improvement Scotland (2019)	“Key insights from the primary studies can also be displayed in table format so that broad conceptual comparisons can be made across studies. Depending on the complexity of these comparisons, these matrices can increase in complexity to demonstrate the various connections among primary studies and to highlight the differences between them”.	Tables/matrices can demonstrate connections and differences	In context of rapid QES
Need for explicit labels for implementation aspects	CQIMG Paper 6(108)	“Process evaluation” or “implementation assessment” subheadings in systematic reviews may be useful for highlighting the procedures and/or measures used to extract and synthesize evidence on implementation. Use of such headings may facilitate data interpretation and knowledge translation by end users.	Possible implications for QES reporting templates	
Need to optimise reporting guidelines for standardisation <u>and</u> creativity	CQIMG Paper 6(108)	“Many authors choose to deviate from or to adapt [reporting] guidelines [which]...suggests that review authors either “require” some methodological flexibility in approaching their review topic or “request”...freedom to adapt methods to better fit their purpose. Review authors may “require” methodological flexibility because it allows them to bring together different perspectives and strategies. The act of “requesting” the freedom to develop a style of reporting that fits the review project is probably	Reporting guidelines must be a framework not a scaffold	

		linked to the idea that reporting guidelines risk becoming too rigid or too narrow restricts creativity and prevents review authors from borrowing emerging or innovative approaches when analyzing or disseminating their findings”		
	CQIMG Paper 6(108)	<p>“Although CQIMG recommends that reporting guidelines should be embraced for increasing the level of transparency</p> <p>and clarity in reporting styles... perversely they may introduce insufficient reporting. In novice reviewers, in particular, adherence to reporting guidelines may initiate a rather mechanistic approach to synthesizing evidence, moving the focus away from the content and toward the procedural aspects of the review. This may create a false sense of security in reviewers”.</p>	Be aware that reporting guidelines may have unintended consequences	
	CQIMG Paper 6(108)	<p>“The development of reporting guidelines may be construed as an attempt to standardize practice. Standardization contributes to the establishment of a language that facilitates communication between different stakeholders, offering a basis for comparison of reviews and review proposals. Such comparison is particularly</p>	Be aware that reporting guidelines are not universally welcomed	

		useful for peer reviewers, funders, and end users....the idea that reporting guidelines are useful in stimulating debates on what constitutes “good” practice is opposed by many stakeholders in the qualitative research community”		
Crafting of findings statements	Downe(1)	“Each finding statement should be clear and concise and accurately capture the meaning of the underlying data that contribute to it. Each one should include an assessment of confidence in the contributing evidence. A finding statement should be developed iteratively so that key concepts can be clarified and explored, but it should be no more than a few sentences in length”.	Need to develop findings statements iteratively which may require GRADE-CERQual assessments need to be revisited	
	Downe(1)	“Reviewers need to strike a balance between splitting issues emerging from the synthesis into multiple review findings, resulting in findings that are no longer useful to end users and do not fully represent the phenomenon of interest, and generating a smaller number of broad findings that oversimplify or fail to adequately capture variations across different contexts”.	Requires guidance on lumping versus splitting of findings	

Optimal characteristics of Evidence to Decision frameworks	Lewin et al(60)	We do not have evidence on the optimal length of the narrative text for framework criteria and this is influenced by the nature of the findings and the number of frameworks that a guideline panel has to consider as part of a guideline process.	Frameworks may result in artificial expansion of material for consideration	
	Lewin et al(60)	<p>The narrative should include the key points from the findings that are relevant to the decision that the framework will inform.</p> <p>The narrative should include enough information on the context of the findings... to reduce ambiguity and allow interpretation, including of the relevance of the evidence as assessed using CERQual.</p>	Need to include context in findings	
	Lewin et al(60)	A graded entry or layered approach to presenting information may be helpful, with the most summarised information presented in the EtD framework. In a graded entry format, users can then navigate from this summary to more detailed information, for example, the full summary of qualitative findings table, and from there to the full synthesis report.	Graded entry approach may be useful	

	Lewin et al(60)	Users should be able to trace back from the narrative to the individual findings that informed the narrative. Traceability can be enhanced by giving a unique code to each QES finding and including these codes in the narrative.	Need for auditability and transferability	
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Table 15 - Extracted Data relating to Question 5 (Methods) - Evaluation

Issue	Source	Data Extract	Implications	Notes
Characteristics of quality assessment tools	CQIMG Paper 3(107)	“Assessment of methodological strengths and limitations of included studies are considered essential to the Cochrane review process. In our initial guidance..., we ...suggested that any “verified” quality appraisal tool...could be used to assess the quality of qualitative studies that met the review inclusion criteria. We have subsequently observed that quality appraisal practice, the choice and application of tools, and the use of appraisal information have varied widely in both Cochrane and non-Cochrane reviews...We are now able to provide guidance	Some minimum criteria for quality assessment tools need to be met to recommend their use.	

		on the selection of a more narrowly defined set of tools that focus on assessing methodological strengths and limitations and provide additional guidance on how to interpret and use information gained from assessments when developing review findings”.		
Focus of quality assessment tools	CQIMG Paper 3(107)	“We now recommend selection of published and commonly used tools that privilege and focus on the assessment of the methodological strengths and limitations of qualitative studies”... ”Tools that would not meet the criteria of focusing on assessment of methodological strengths and limitations include those that integrate assessment of the quality of reporting (such as scoring of the title and abstract etc.) into an overall assessment of methodological strengths and limitations. Nor are reporting guidelines recommended for assessing methodological strengths and limitations because their primary purpose is to ensure that critical information is included in the study report”.	Reporting tools should not be used for quality assessment	
	CQIMG Paper 3(107)	“Whichever tool is selected for whatever qualitative study design or method, an important guiding principle is that it	Primary purpose of quality assessment is to explore study	

		should be used as a way of engaging with and better understanding the methodological strengths and limitations of primary studies... “	characteristics in a systematic way	
	CQIMG Paper 3(107)	“The preferred convention is for review authors to discuss the studies and the assessment outcome for each paper and determine how study methodological limitations play out at the level of review findings”.	Quality assessment should be applied at a review findings level	
Scoring for quality should not be used	Cochrane Handbook(66)	“As with other risk of bias assessment tools, we strongly recommend against the application of scores to domains or calculation of total quality scores. We encourage review authors to discuss the studies and their assessments of ‘risk to rigour’ for each paper and how the study’s methodological limitations may affect review findings”.	Qualitative assessment of risks to rigour can be used to evaluate the evidence base. Scores should <u>not</u> be used.	
	CQIMG Paper 3(107)	Applying scores to domains and calculating total quality scores should not be used because not all domains of quality are equal, and therefore scores are not useful and may give a false sense of precision. Many review teams also use total quality scores as a cutoff point to determine inclusion or exclusion of studies; we do not advocate or support this practice because these cutoffs are arbitrary and therefore not methodologically defensible”.		

Multiple assessors should be used to assess study quality	CQIMG Paper 3(107)	<p>“In completing the quality assessment process, it is considered best practice for more than one person to assess study quality and to agree concerns about study strengths and limitations by consensus. For transparency, it is helpful to report the assessment of methodological strengths and limitations for each study and each domain of quality in the appendices or additional online file of the qualitative evidence synthesis report”.</p>	Implications for teams and resources	
Transparency of quality assessment decisions is critical	CQIMG Paper 3(107)	<p>“Decisions on whether to include all studies or to include a sample of studies depend on...general and review-specific criteria (see Box 4). The guiding principle is transparency in the reporting of all decisions and their rationale. This should include a clear audit trail of evidence included or excluded from the review. Clarifying these considerations to the reader is an important step in</p>	Requires explicit guidance on how quality assessment is to be used	

		producing methodological transparent qualitative and mixed-method syntheses”.		
Qualitative sensitivity analysis is to be preferred to exclusion of studies on the basis of quality	Cochrane Handbook(66)	We further advise that qualitative ‘sensitivity analysis’, exploring the robustness of the synthesis and its vulnerability to methodologically limited studies, be routinely applied regardless of the review authors’ overall confidence in synthesized findings. Evidence suggests that qualitative sensitivity analysis is equally advisable for mixed methods studies from which the qualitative component is extracted.	Qualitative sensitivity analysis should be used to explore confidence in findings.	
Use of GRADE-CERQual	CQIMG Paper 3(107)	We recommend the use of the Grades of Recommendation, Assessment, Development, and Evaluation Confidence in the Evidence from Qualitative Reviews (CERQual) approach to assess confidence in synthesized qualitative findings.	Role of GRADE-CERQual	

Table 16 - Extracted Data relating to Question 5 (Methods) - Consideration within Deliberation Process

Issue	Source	Data Extract	Implications	Notes
Timing and extent of QES reviews	Downe et al(1)	<p>“the process of undertaking qualitative reviews (particularly scoping reviews) identified factors that were important to stakeholders but that had not been considered in the prior guideline group agreements about which effectiveness reviews to include...undertaking the qualitative reviews earlier might have improved the scope of the final guidelines. For other guidelines, it became clear that some sub-questions could have benefited from more focused qualitative reviews earlier in the process”.</p>	Need to consider timing, frequency and purpose of interactions between stakeholders and qualitative evidence	
Stakeholders may be involved at different points of the review	CQIMG Paper 2(67)	<p>“Approaches to involving stakeholders in the review process may be broadly characterised as before-after involvement, iterative involvement and synchronous involvement”</p> <p>“1) Before-After involvement: Stakeholders are included during the problem framing stage, and then comment on the results of the review towards the end of the process.</p> <p>2) Iterative involvement: Stakeholders are consulted at agreed milestones during the review which may entail a number of milestones with the aim of promoting higher</p>	Three different models for involvement in the synthesis.	

		<p>levels of engagement, ownership and active dissemination of findings.</p> <p>3) Synchronous involvement: is 'real time' two-way involvement representing an active exchange and comparison of review findings with practitioner and service user experience, where involvement is used to collectively interpret and co-produce the review.</p> <p>Before-after involvement requires skills in promoting dialogue about the meaning of evidence and reflexivity, and in eliciting multiple views. When dealing with complexity, and when aiming to ensure that review findings are mobilized, iterative and synchronous involvement can help to create shared ownership of the review process.</p>		
Stakeholder role in preparation	CQIMG Paper 4(46)	...we recommend that reviewers engage stakeholders in the preparatory stage to ensure that the review scope is appropriate and the resulting products address the implementation inquiry questions and concerns of decision-makers. These review activities will increase the internal validity of constructs, measures, and methods used in a quantitative review.	Need to consider early involvement of stakeholders	

Stakeholder role in interpretation and formulation of findings	CQIMG Paper 3(107)	“it may be helpful to draw on a key stakeholder group to support interpretation of evidence and formulation of key findings. Additional approaches (such as subgroup analyses) can be used within the synthesis to further explore the evidence pertaining to specific contexts”.	Implications for QES resources and timescales	
Championing the qualitative evidence	GIN Public Toolkit(69)	“To encourage the uptake of qualitative evidence in the guideline, development group members might need to be reminded when the synthesis provides relevant knowledge. While any group member may be expected to read, mobilise, integrate and value its findings, this championing role might more easily be taken up by the producer of the synthesis, the methodologist or patient representatives”.	Need to consider who will be the “voice” for qualitative findings (e.g. analyst, discussant etc)	
Use of QES to identify parameters for subgroup analysis	CQIMG Paper 5(63)	“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”.	Need to identify subgroups	
Review Author Reflexivity and Conflicts of Interest	CQIMG Paper 3(107)	“a key marker of methodological quality in primary qualitative studies is the reflexivity of the researchers, including how they make transparent their potential and actual impacts on the research context, participants, and	Procedures for managing Conflict of	

		interpretation of findings. Similarly, review authors should make transparent their conflicts of interests, prior beliefs, and potential/actual prejudices with potential to impact on data interpretation”.	Interest and documenting reflexivity	
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Table 17 - Key Stakeholders as represented by key documents

Item	Influencing Stakeholders
BMJ Paper(37)	NICE
Cochrane Handbook (2020)(66)	Cochrane CQIMG
CQIMG Paper on Searching (2016)(51)	Cochrane CQIMG
Cochrane CQIMG Supplementary Guidance(45, 46, 63, 67, 107, 108)	Cochrane CQIMG
GIN Public Toolkit	GIN Network
GRADE-CERQual Guidance(71, 73, 116, 123-126)	Alliance for Health Policy and Systems Research, Cochrane CQIMG, WHO
Identifying the Need for Good Practices in Health Technology Assessment: Summary of the ISPOR HTA Council Working Group Report on Good Practices in HTA.(127)	ISPOR
International Journal of Evidence-Based Healthcare paper	SIGN
Knowledge Synthesis Series(109, 114)	Knowledge Synthesis Project
Rapid Qualitative Evidence Synthesis(59)	CADTH
A guide to conducting rapid qualitative evidence synthesis for health technology assessment(41)	Health Improvement Scotland
Evaluation and synthesis of studies using qualitative methods of analysis(58)	SBU
WHO Mini-Series on Qualitative Evidence and Guidelines(1, 60, 110)	WHO
WHO Guidance on Complex Interventions(19-22)	WHO

In addition, the Campbell Collaboration and Collaboration for Environmental Evidence are currently (March 2020) working on guidance and the World Health Organization Health Evidence Network are producing guidance currently at the final draft stage (March 2020).

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