

# Guidance on choosing qualitative evidence synthesis methods for use in health technology assessments of complex interventions

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**INTEGRATE-HTA**



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# About this guidance



## ***Who would find this guidance useful?***

This guidance is intended for individuals and institutions that develop guidelines, perform or commission health technology assessments (HTAs) and systematic reviews (SRs) and that have an interest in the use of qualitative evidence synthesis (QES)/ qualitative systematic review within the framework of an integrated HTA or SR.

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## ***Purpose and scope of this guidance***

This guidance summarises current thinking and practice in the choice of QES methods for HTAs and SRs. It offers a seven-domain framework (RETREAT) to assess the principal considerations when choosing between different methods and methodologies for QES, and provides additional examples of other important considerations that have impacted upon choice of QES methods.

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## ***Added value for an integrated assessment of complex technologies***

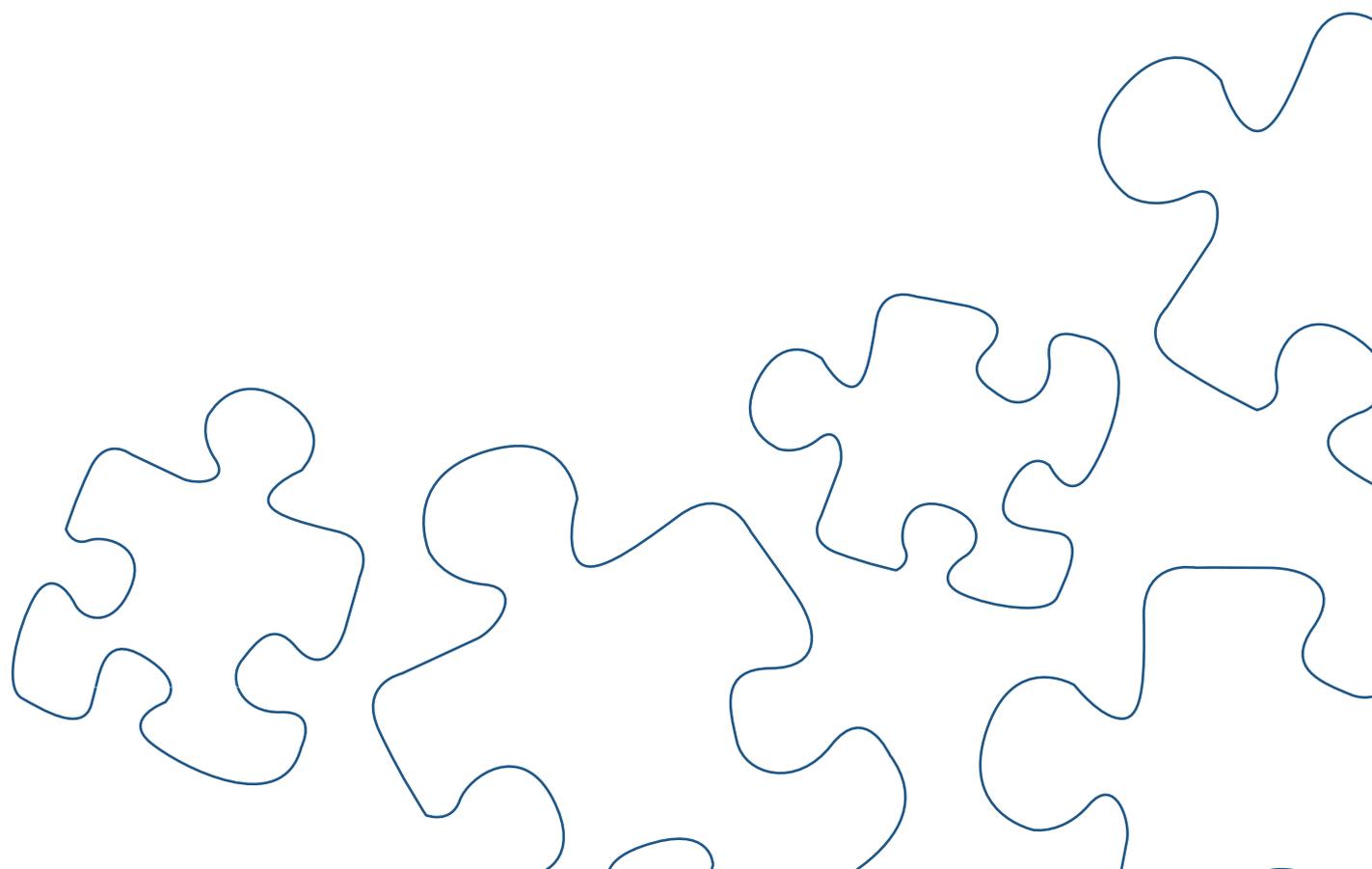
A qualitative evidence synthesis can be used to explore important qualitative aspects of any HTA or SR decision-problem including whether a complex technology is acceptable, the lived experience of those with the target condition and issues relating to the implementation of the complex technology in context. This guidance facilitates use of QES methods alongside other data sources including when quantitative and qualitative data are to be juxtaposed for synthesis and interpretation.

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## ***INTEGRATE-HTA***

INTEGRATE-HTA is an innovative project that has been co-funded by the European Union under the Seventh Framework Programme from 2013 until 2015. Using palliative care as a case study, this project has developed concepts and methods that enable a patient-centred, comprehensive, and integrated assessment of complex health technologies.

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# Executive Summary

## **Challenges in assessments of health technologies**

In recent years there have been major advances in the development of health technology assessment (HTA). However, HTA still has certain limitations when assessing technologies which

- ▶ are complex, i.e. consist of several interacting components, target different groups or organizational levels, have multiple and variable outcomes, and/or permit a certain degree of flexibility or tailoring (Craig et al., 2008),
- ▶ are context-dependent - current HTA usually focusses on the technology, not on the system within which it is used,
- ▶ perform differently depending on the way they are implemented,
- ▶ have different effects on different individuals.

Furthermore, HTA usually assesses and appraises aspects side-by-side, while decision-making needs an integrated perspective on the value of a technology. In the EU-funded INTEGRATE-HTA project, we developed concepts and methods to deal with these challenges, which are described in six guidance documents. An integrated assessment requires that a variety of effectiveness, cost effectiveness, socio-cultural and ethical questions are simultaneously addressed. Many questions will require reference to qualitative research data. Qualitative evidence syntheses (qualitative systematic reviews) offer one possible way in which findings from qualitative research might be systematically integrated within an HTA. They attempt to identify transferable findings from a body of evidence with a view to addressing a specific contextual problem. Multiple methods of qualitative evidence synthesis currently exist. Even though increasing numbers of available published examples are facilitating the consolidation of lessons learnt very little guidance exists on how to select an appropriate method of synthesis.

## **Purpose and scope of the guidance**

▶ The aim of the INTEGRATE-HTA project is to provide concepts and methods that enable a patient-centred, comprehensive, and integrated assessment of complex health technologies. This guidance on choosing appropriate methods of qualitative evidence synthesis (QES) is to be used when a review team has genuine uncertainty about which type of QES to undertake to meet the needs of a particular question or purpose. It may also be used when a review team seeks to make an informed judgement between two or more competing methods or methodologies. This guidance is not intended to be used prescriptively; additional considerations may inform the final selection of an appropriate synthesis method. It simply seeks to help a review team to navigate an otherwise bewildering array of methodological choices. Pointers to detailed

specification of the characteristics of each methodology, together with published examples, are provided for further clarification and exemplification.

### ***Development of the guidance***

This guidance represents further development of principles first explored at a variety of HTA and systematic review conferences, workshops and forums. For the first time we have systematically explored the published literature in relation to the choice or selection of qualitative synthesis methodologies. We analysed 26 separate items published between 2001 and 2014 and identified those elements thought to be important when selecting a synthesis method. We used an embryonic five item framework to organise these considerations. Subsequently we expanded the framework to seven items covered by the RETREAT mnemonic (Review question – Epistemology – Time/Timescale – Resources – Expertise – Audience and purpose – Type of Data). We then compiled a list of specific considerations when selecting a synthesis method according to the published literature and the expertise of members of the Cochrane Qualitative and Implementation Methods Group. The final guidance, revised after internal and external peer-review includes approaches suitable for stand-alone methodologies and those used when integrating quantitative and qualitative data.

### ***Application of this guidance***

The INTEGRATE-HTA process seeks to facilitate production of a comprehensive integrated assessment of a complex technology to inform a complex decision problem. Within this context it is important to be able to select appropriate review methodologies – selection of a quantitative review methodology is comparatively straightforward with a limited number of available alternatives, usually determined by the nature of the data and its heterogeneity. In contrast selection of a method for qualitative synthesis is more complex, not least when it is required to integrate with the quantitative elements of a larger review.

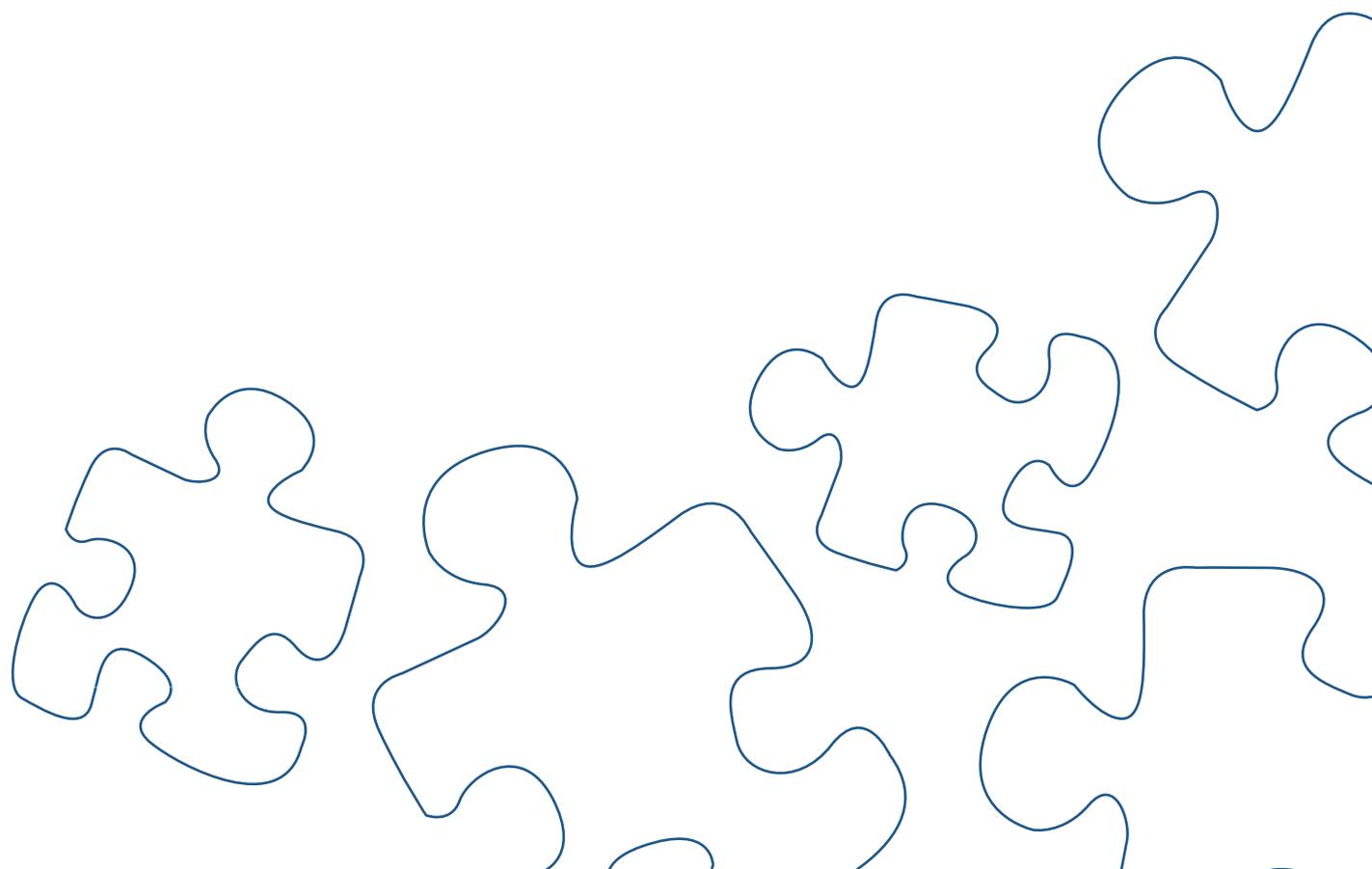
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- ▶ **Step 1:** To use this guidance you first take stock of what is already known about the topic; the nature of the Review question, the characteristics of the evidence base, the quantity and quality of included study designs, the Type of Data required to satisfactorily address the overall review question and all its associated sub-questions.
- 
- ▶ **Step 2:** Next you consider the available Resources for the review; the Time, and the requisite Expertise.
- 
- ▶ **Step 3:** Then you examine the intended Audience and Purpose and any implications that these might have for the Epistemology behind the review. Having broadly characterised these factors you will have limited the number of available options in terms of synthesis methodology.
- 
- ▶ **Step 4:** Finally you turn your consideration to more specific features of the methodology to inform the final selection of the method.

### ***Conclusions***

In current HTA, different aspects are usually assessed and presented independent of each other. Context, implementation issues and patient characteristics are rarely considered. The INTEGRATE-HTA Model enables a coordinated assessment of all these aspects and addresses their interdependencies. The perspective of stakeholders such as patients and professionals with their values and preferences is integrated in the INTEGRATE-HTA Model to obtain HTA results that are meaningful for all relevant stakeholders. Finally, health policy makers obtain an

integrated perspective of the assessment results to achieve fair and legitimate conclusions at the end of the HTA process. This guidance document is directed at specific challenges relating to the assessment of complex technologies, such as the need to integrate qualitative research studies within a qualitative evidence synthesis and then with the results from a review of the effectiveness and cost-effectiveness studies. It offers a way to navigate challenges posed by a variety of methodological choices that determine the nature of the final HTA in incorporating data to inform effectiveness, economic, ethical, socio-cultural, and legal aspects of HTA. The application of the model will usually require more time and resources than traditional HTA. An initial assessment of the degree and the character of complexity of a technology might be helpful to decide whether or not the whole process or only specific elements will be applied.

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## List of abbreviations

| Abbreviation  | Long form  |
|---------------|--|
| BMC           | BioMed Central   |
| BMJ           | British Medical Journal  |
| CHIP          | A structure for formulating a review question, the mnemonic relates to the Context of the particular study, How the study was conducted, the Issues examined, and the People involved in the study (Shaw, 2010).                       |
| CIS           | Critical Interpretive Synthesis  |
| CRD           | Centre for Reviews & Dissemination, University of York   |
| ENTREQ        | Enhancing transparency in reporting the synthesis of qualitative research: tentative reporting standard for documenting qualitative evidence syntheses.  |
| EPPI-Centre   | A specialist centre at University College London for: (i) developing methods for systematic reviewing and synthesis of research evidence; and (ii) developing methods for the study of the use research.                               |
| HTA           | Health Technology Assessment   |
| INAHTA        | International Network of Agencies for Health Technology Assessment   |
| INTEGRATE-HTA | Integrated health technology assessment for the evaluation of complex technologies – Innovative, three-year European Union Framework (FP7) methodological project (January 2013 – December 2015) using palliative care as a case study |
| INTERUPT      | Intervention Now To Eliminate Repeat Unintended Pregnancy in Teenagers (INTERUPT) – a United Kingdom based HTA project combining multiple components each with a corresponding review type.  |
| PICO          | Population – Intervention – Comparison – Outcome: The original mnemonic for a focused question developed by Richardson et al (1995)  |
| PICOC         | Population – Intervention – Comparison – Outcome – Context : an expanded mnemonic for a focused question developed by Petticrew & Roberts (2006)   |
| QARI          | Qualitative Assessment and Review Instrument – Software and corresponding critical appraisal instrument from Joanna Briggs Institute for performing quality assessment of qualitative research studies and subsequent synthesis.       |
| QES           | Qualitative Evidence Synthesis   |
| RAMESES       | Realist synthesis and Meta-narrative reviews : project developing training resources and reporting standards for realist syntheses and meta-narrative reviews. By extension the reporting standards for these two types of reviews.    |
| RETREAT       | Review Question – Epistemology – Time/Timeframe – Resources – Expertise – Audience – Type of Data : a revised mnemonic outlining considerations when planning a qualitative synthesis  |
| SBU           | Swedish Council on Technology Assessment in Health Care  |
| SPICE         | Setting - Perspective- Interest, Phenomenon of – Comparison – Evaluation : a variant of the PICO mnemonic designed for social science questions by Booth (2006)  |
| SPIDER        | Sample - Phenomenon of Interest – Design – Evaluation - Research type: a variant of the SPICE mnemonic designed for mixed methods questions by Cooke et al (2014).   |
| TREAD         | Time/Timeframe – Resources – Expertise – Audience – Data: an initial mnemonic outlining considerations when planning a qualitative synthesis   |

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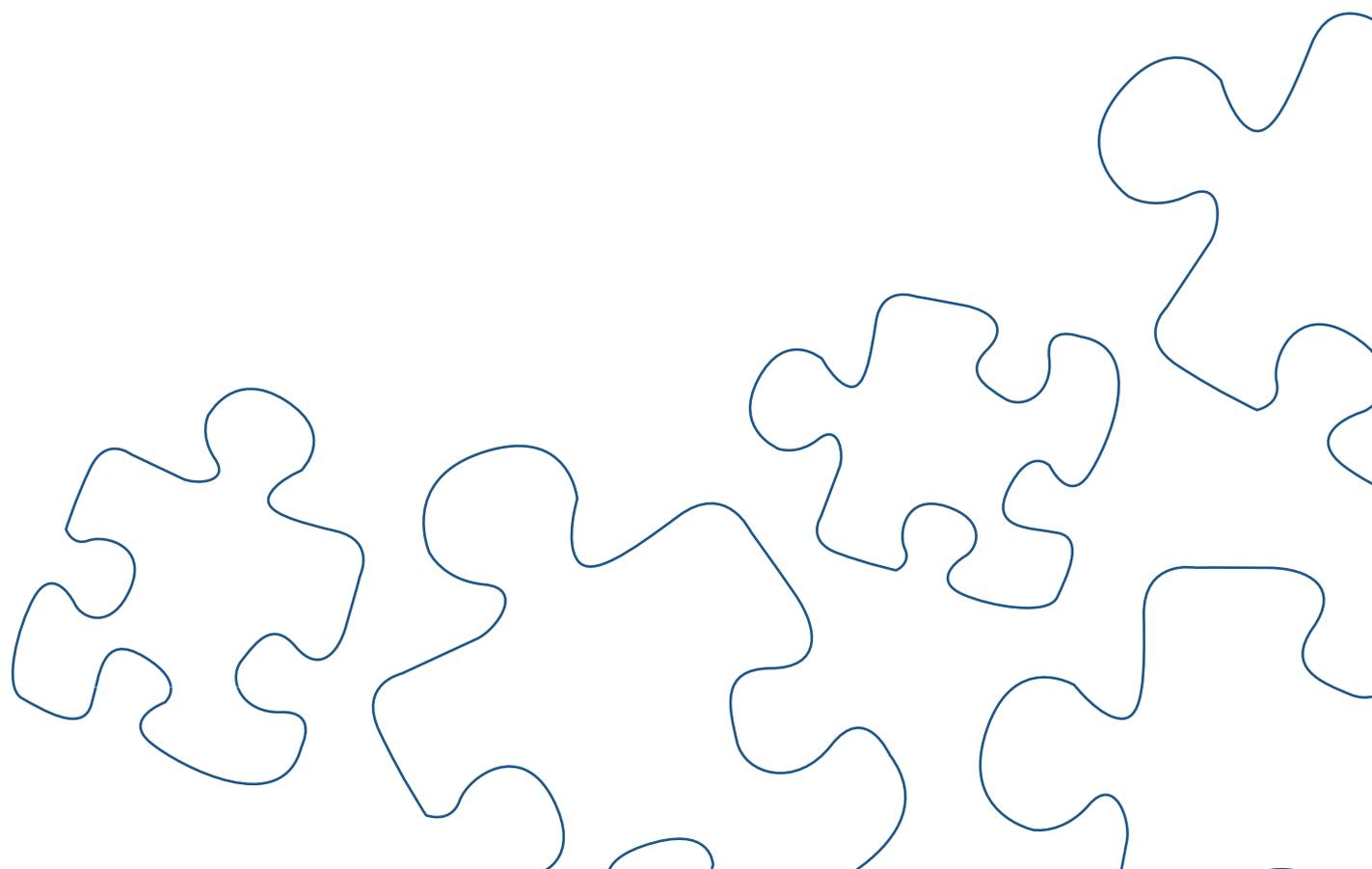
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# 1 PURPOSE AND SCOPE OF THE GUIDANCE

## 1.1 AIM OF THIS GUIDANCE

This guidance focuses on the main considerations to be taken into account when selecting an appropriate method of qualitative evidence synthesis. By focusing on the choice of methods and methodologies it does not seek to replicate the extensive guidance available on using qualitative synthesis in health technology assessments (HTAs) or systematic reviews nor the method-specific texts that explore each of the many synthesis methodologies in more detail. The guidance synthesises and interprets findings from those texts that offer an overview of methodological choices and the rationale underpinning them.

## 1.2 TARGET AUDIENCE FOR THIS GUIDANCE

This guidance is aimed primarily at those conducting and those commissioning the qualitative systematic review component of an HTA, whether as a stand-alone product or, more typically, within an integrated approach to technology assessment. The guidance offers a framework for deciding on the most appropriate method for a specific purpose and, as such, may prove valuable to research teams and review commissioners in conducting negotiations. It may have wider applicability to researchers or research students when facing methodological choices in conducting systematic reviews or when seeking to offer an integrated approach to multiple associated review questions.

## 1.3 THE ADDED VALUE OF THIS GUIDANCE IN RELATION TO EXISTING GUIDANCE

Currently there is limited guidance on how to select methods for qualitative evidence synthesis. The Cochrane Qualitative and Implementation Methods Group (CQIMG) has produced an algorithm to assist selection (Noyes and Lewin, 2011). However the CQIMG guidance dates from a time (2008) when there was little empirical evidence on the advantages of different methods. The CQIMG guidance was also limited by a remit of informing only qualitative synthesis alongside Cochrane systematic reviews of effects. Some methodology texts speculate on the usefulness of different synthesis methods but are typically located within the perspective of individual review-producing organisations such as the EPPI-Centre and the Joanna Briggs Institute. This guidance represents an attempt to expand coverage of the types of qualitative synthesis involved when selecting an appropriate method. Rather than prescribing detailed

methodological guidance on individual methods it seeks to help navigate through an otherwise bewildering variety of methodology choices. The guidance also points to appropriate reporting standards such as ENTREQ (Tong et al, 2012) and RAMESES (Wong, 2013a, 2013b) where available.

## 1.4 LOCATING THE GUIDANCE IN THE INTEGRATE-HTA PROJECT

Any integrated approach to HTA should seek to maximize the value of different types of data in addressing different types of technology assessment question. The INTEGRATE-HTA project necessarily includes those questions for which qualitative data may be considered important (Figure 1). For example, the INTEGRATE-HTA project examined social, legal and ethical aspects (Lysdahl et al, 2016a). It also examined modifying factors relating to Patient Characteristics (van Hoorn et al., 2016a) and Context and Implementation issues (Pfadenhauer et al, 2016). Qualitative questions also arise in connection with the effectiveness of a health technology (Burns et al, 2016), such as its feasibility and acceptability to patients, informal caregivers, families and health and social care professionals. Finally economic aspects relating to patient choice and valuation of health outcomes (Chilcott et al, 2016) are also informed by qualitative data. This guidance is intended to support the choice of method of qualitative synthesis by teams involved in addressing all qualitative aspects of an HTA. QES can thus contribute at multiple points of the integrated HTA process (primarily in Steps 3 and 4) depending upon the type of question and the type of data being synthesised.

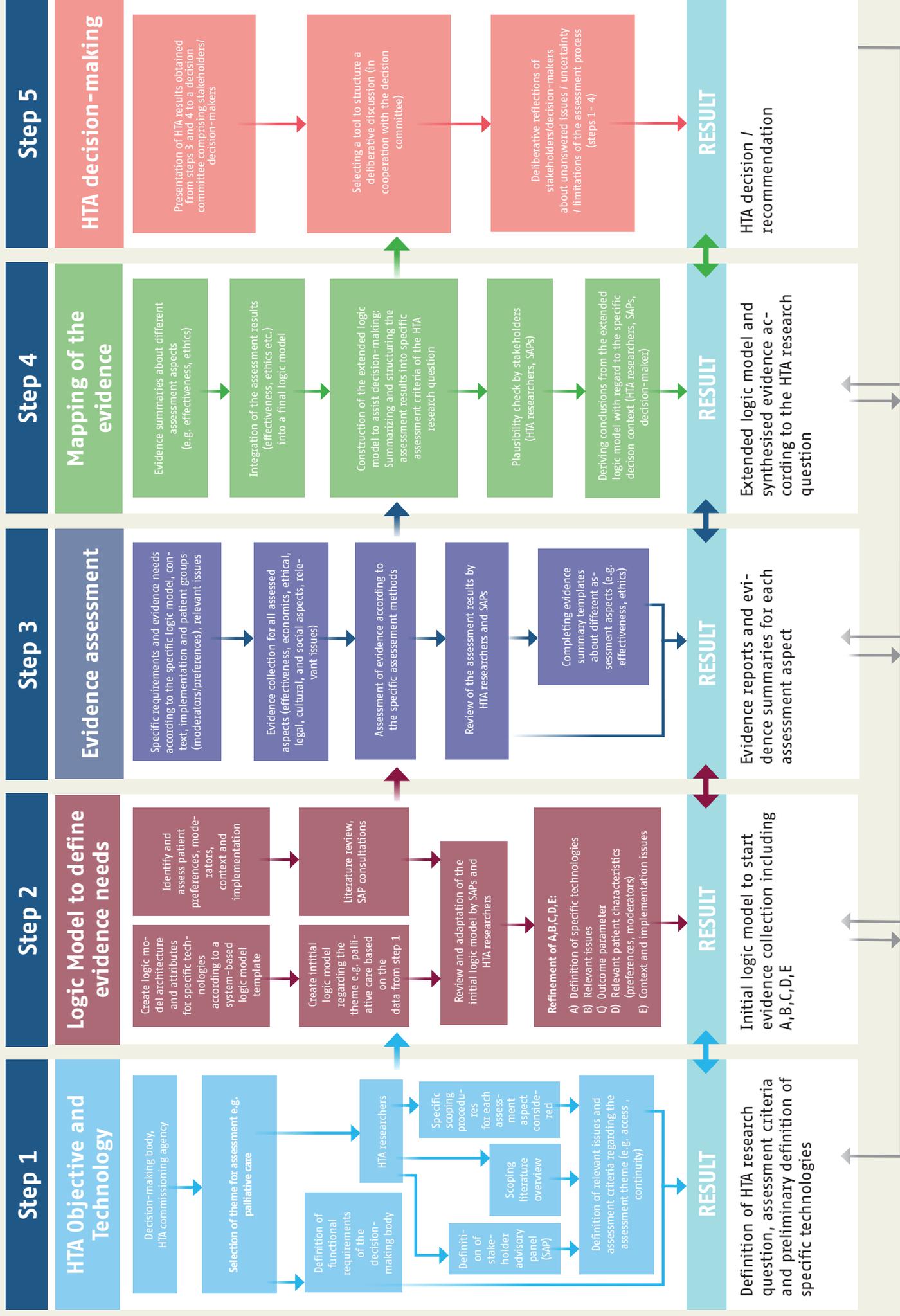
# 2 BACKGROUND

## 2.1 PROBLEM DEFINITION

Recent years have seen increased recognition that decision problems faced by HTA agencies cannot be informed only by evidence on effectiveness and cost effectiveness. For example, the effectiveness of a pharmaceutical in a real world setting depends upon adherence, both individually and collectively as a target population. If patients find an intervention unacceptable, for whatever reason, this will have a profound impact in limiting the positive effects that might otherwise be achieved (Mozygemba et al, 2016). Successful implementation of complex human-mediated interventions, such as those delivered in health and social care, depends upon the attitudes, perceptions and beliefs of all those involved in delivering that intervention (Michie et al, 2009). Programme developers need an understanding of perceptions of the disease and its immediate and long-term consequences when targeting interventions and programmes.

An integrated HTA needs to engage with the beliefs, perceptions and attitudes of patients, their family members and

Figure 1: Locating this guidance within the INTEGRATE-HTA process.



their informal and formal caregivers as well as all those involved in delivering a service. In many cases collection of primary qualitative research data from the actual target population, although preferable, is prohibited by constraints of time, money and other resources such as staffing. Qualitative evidence synthesis therefore offers one possible route by which the views of stakeholders might be factored into an overall HTA. While an agency may not be able to identify qualitative research studies derived from the exact constituency within which they are planning to implement an intervention or programme they may be able to derive valuable insights that are transferable from other settings. A well-conducted QES offers several useful functions for health technology agency decision-makers. For example it can explore questions such as “how do people experience illness, why does an intervention work (or not), for whom and in what circumstances?” (Noyes et al, 2015). Where reviews seek to address healthcare delivery, it may be useful to explore barriers and facilitators to accessing healthcare, or the impact of specific barriers and facilitators on people, their experiences and behaviours. In relation to context and implementation (Pfadenhauer et al, 2016) qualitative evidence can offer insight into “factors that are external to an intervention including, for example, the impact of other policy developments, factors which facilitate or hinder successful implementation of a programme, service or treatment and how a particular intervention may need to be adapted for large-scale roll-out” (Noyes et al, 2015).

## 2.2 DEFINITIONS

**Qualitative Systematic Review** – a systematic review of qualitative research – not to be confused with the same term historically misappropriated to analgesia and pain control studies which refers to a systematic review where meta-analysis is not technically possible.

**Qualitative Evidence Synthesis** – the preferred umbrella term of the Cochrane Qualitative and Implementation Methods Group for over twenty different methods of qualitative synthesis (See Table 1). This term is preferred because (i) it offers the flexibility to incorporate other types of qualitative evidence not considered formal qualitative research studies (such as postings to a patient support bulletin board or policy documents) and (ii) it acknowledges that qualitative research may require its own methods of synthesis, sensitive to the qualitative paradigm, rather than simply translating the standards of the systematic review of quantitative research.

**Qualitative Research** – seeks to understand and interpret personal experiences, behaviours, 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. (Wong et al, 2004)

**Methods** – typically the techniques that researchers use for practising the craft of research (Bryman, 2008). Within the context of research synthesis “methods” might be instruments for data collection, such as data collection forms; they might refer to the tools used for performing quality assessment or for extracting themes from study data; or the term might refer to aspects of the research process like sampling.

**Methodology** – the study of the methods that are employed by researchers (Bryman, 2008). Methodology is concerned with uncovering the practices and assumptions of those who use different types of methods. In this guidance methodology is used to refer to the overall strategies used by which a researcher or reviewer addresses their chosen research question. Thus a methodology may draw upon several methods. For example meta-ethnography uses a method labelled reciprocal translation – this method has recently been identified as an unnamed element within most methods of qualitative synthesis.

**Mixed methods reviews** – synthesis products that bridge quantitative and qualitative research paradigms (Harden, 2010). More specifically, mixed methods reviews are defined as reviews that integrate (i) qualitative and quantitative review questions, (ii) studies using qualitative and quantitative research designs, (iii) studies using qualitative and quantitative techniques for collecting and analyzing data, and (iv) qualitative and quantitative review findings. In doing so, a mixed methods review allows the review team to harness flexible combinations of one or several qualitative (e.g. semi-structured interviews, focus groups, observation, ethnography) and quantitative (e.g. randomized controlled trial, cohort study, cross-sectional study, case series) research components within one or several syntheses. Through integration, the insights gained from the synthesis go beyond an additive combination of results obtained through quantitative and qualitative components to foster a more holistic and in-depth understanding. (Adapted from Gerhardus et al, 2016)

## 2.3 DESCRIPTION OF THEORETICAL BACKGROUND AND AVAILABLE APPROACHES

Increasing recognition of the complexity of technology assessment questions (Anderson et al, 2013a; Squire et al, 2013; Petticrew et al, 2013a), and the consequent demands for more sophisticated and flexible review methods (Petticrew et al, 2013b), have led to renewed interest in the incorporation of a wider range of study designs and types of data (Anderson et al, 2013b) in the decision-making process (Burford et al, 2013). Qualitative evidence synthesis (QES), the preferred label of the Cochrane Qualitative and Implementation Methods Group, has to date primarily focused on the synthesis of

Table 1: Identified terminology relating to methods of qualitative synthesis.

| Methodologies for Qualitative Synthesis   |  |                              |
|---|--|------------------------------|
| UMBRELLA TERMS  |  |                              |
| <ul style="list-style-type: none"> <li>▶ Qualitative Systematic Review</li> <li>▶ Qualitative Evidence Synthesis<sup>1</sup></li> <li>▶ Qualitative Meta-synthesis</li> <li>▶ Qualitative Research Synthesis</li> </ul> |  |                              |
| SPECIFIC TERMS  |  |                              |
| Methodologies for Qualitative Synthesis   | Methods for Qualitative Synthesis  | Sub-categories               |
| Concept Analysis  |  |                              |
| Ecological Triangulation  | Triangulation<br>Ecological sentences  |                              |
| Framework Synthesis   | Framework analysis<br>Indexing<br>Charting<br>Thematic analysis  | Best Fit Framework Synthesis |
| Grounded Formal Theory  | Coding<br>Constant Comparison Method   |                              |
| Meta-Aggregation  | Thematic analysis  |                              |
| Meta-Ethnography  | Thematic analysis<br>Reciprocal Translation<br>Line-of Argument Synthesis<br>Refutational Synthesis                                |                              |
| Meta-Interpretation   | Thematic Analysis<br>Context Analysis  |                              |
| Miles and Huberman's data analysis techniques   | Coding<br>Case Summary   |                              |
| Narrative Summary   | Narrative juxtaposition  |                              |
| Qualitative Interpretive Meta-Synthesis   | Theme extraction<br>Reciprocal Translation<br>Theme synthesis<br>Triangulation<br>Credibility Reporting                            |                              |
| Thematic synthesis  | Line by Line Coding<br>Thematic Analysis (Descriptive and Analytic Themes)<br>Reciprocal Translation<br>Constant Comparison Method |                              |
| EPPI-Centre Methods   | Thematic Analysis  |                              |
| Critical Interpretive Synthesis   | Line-of Argument Synthesis<br>Thematic Analysis<br>Constant Comparison Method<br>Charting<br>Matrices                              |                              |
| Meta-Narrative Review   | Storylines<br>Meta-Narrative Maps  |                              |
| Meta-Study  | Meta-theory<br>Meta-method<br>Meta-data analysis   |                              |
| Meta-Summary  | Topical Summary<br>Thematic Summary  |                              |
| Narrative Synthesis   | Narrative Synthesis<br>Thematic Analysis<br>Structured Summary   | Textual narrative synthesis  |
| Realist Synthesis   |  | Rapid Realist Synthesis      |

<sup>1</sup> Preferred term within Cochrane Qualitative and Implementation Methods Group (CQIMG)

qualitative research studies. However the term QES is deliberately broad in order to accommodate a wide range of types of qualitative data such as case studies, policy analysis, process evaluations, contents of web sites, discussion sections of quantitative studies etcetera. While more empirical testing of individual approaches is required (Noyes et al, 2013) it is likely that many current methods of synthesis have applicability to qualitative data other than that yielded by studies that use formal methods of qualitative data collection and analysis.

With a confusing variety of methods of qualitative synthesis, each supported by a wealth of available guidance, the challenge for HTA agencies is not so much how to implement guidance for a particular method but more how to identify the most appropriate candidate method in the first place. Several authors have attempted to help researchers to navigate the available choices. Indeed one book is entitled: *Synthesizing Qualitative Research: Choosing the Best Approach* (Hannes & Lockwood, 2011a). Other authors have attempted to depict the available choices as an algorithm or decision chart (Noyes & Lewin, 2011). However the range of methods from which to choose is prodigious and all attempts at comprehensive coverage remain incomplete.

The focus of this guidance is on review types that utilise qualitative approaches to synthesis. It includes methods that are predominantly qualitative (**Thematic synthesis, Meta-Ethnography**), mixed methods approaches with a qualitative orientation (qualitatising) (**Critical Interpretive Synthesis, Meta-Narrative**) and mixed methods approaches that handle quantitative and qualitative data equally (**Meta-Study, Meta-Summary, Realist Synthesis, Rapid Realist Synthesis**). A broader consideration of methods that incorporate qualitative aspects within an overall quantitative approach (quantitatising) would include **Bayesian Meta-analysis/Synthesis, Case Survey, Content Analysis, Cross Case Analysis and Qualitative Comparative Analysis** (Dixon-Woods et al, 2004, 2005). However these are excluded from this guidance. These methods are covered in the overview, Integrative approaches to qualitative and quantitative evidence, by Dixon-Woods and colleagues (2004).

### 3 GUIDANCE DEVELOPMENT

The Cochrane Qualitative and Implementation Methods Group Methodological Register was searched for references relating to method choice or articles reviewing two or more synthesis methods. This register is populated monthly from keyword searches

of PubMed and Web of Science and from Citation Alerts from Google Scholar for 12 key methodological texts. Presentation materials used in Cochrane Qualitative and Implementation Methods Group workshops in Sheffield (Booth, 2011-2015), Leuven (Booth, 2012) and the HTAi Conference in Bilbao (Booth, 2012a) and Cochrane Colloquium in Auckland (Booth, 2012b) were also used to inform the guidance.

Search terms included those listed in Table 2.

Table 2: Search terms used in the Guidance Development.

| Qualitative | Method(s)           |
|-------------|---------------------|
| Choice      | Synthesis           |
| Choose      | synthesis method(s) |
| Choosing    | Type of synthesis   |
| Selection   | Synthesis type      |
| Select      |                     |
| Selecting   |                     |

Very few titles and abstracts indicated a focus on choice or selection of method. In most cases this level of detail was only present in the full-text of included articles. Supplementary strategies using full-text searches of Google Scholar employing variants of the terms listed above were therefore essential. In addition references from identified works were followed up, citation searches were performed on all included works and contact was made with members of the Cochrane Qualitative and Implementation Methods Group.

Twenty-six items were identified from the search process (Table 3). Each included paper was examined to identify considerations considered important when determining the choice of synthesis methods. The TREAD (Time/Timeframe, Resources, Expertise, Audience & Purpose, Data) framework, originally developed to facilitate teaching on selection of qualitative review methods for the annual international ESQUIRE courses (Booth, 2011-2015), was used as a starting point for synthesising these considerations. Mapping of these considerations against the five subdomains of TREAD revealed a need to add two further considerations: the nature of the Research question and issues relating to Epistemology, leading to the new RETREAT (Research question, Epistemology, Time/Timeframe, Resources, Expertise, Audience & Purpose, Type of Data) framework.

Table 3: Considerations when choosing a synthesis method from identified literature.

|  | Review Question | Epistemology | Time/ Timeframe | Resources | Expertise | Audience & Purpose | Type of Data |
|--|-----------------|--------------|-----------------|-----------|-----------|--------------------|--------------|
| Paterson et al (2001)                        |                 |              |                 |           |           | ✓                  |              |
| Sandelowski & Barroso (2003)                 |                 |              |                 |           |           | ✓                  | ✓            |
| McDermott et al (2004)                       |                 |              |                 |           |           | ✓                  |              |
| Dixon-Woods et al (2004; 2005)               | ✓               |              |                 |           | ✓         |                    |              |
| Mays et al (2005)                            | ✓               |              |                 |           |           |                    |              |
| Lucas et al (2007)                           |                 |              |                 |           |           | ✓                  |              |
| Pope et al (2007)                            | ✓               | ✓            |                 |           | ✓         |                    | ✓            |
| CRD (2008)                                   | ✓               |              |                 |           | ✓         |                    | ✓            |
| Garside (2008)                               |                 |              |                 |           | ✓         |                    | ✓            |
| Barnett-Page & Thomas (2009)                 |                 | ✓            |                 |           | ✓         | ✓                  |              |
| Ring et al (2010)                            | ✓               | ✓            |                 |           |           | ✓                  |              |
| Manning (2011) [In Hannes & Lockwood, 2011]  | ✓               |              |                 |           | ✓         | ✓                  |              |
| Noyes & Lewin (2011)                         | ✓               |              |                 | ✓         | ✓         |                    | ✓            |
| Paterson (2011) [In Hannes & Lockwood, 2011] |                 | ✓            | ✓               | ✓         | ✓         | ✓                  | ✓            |
| Urquhart (2011)                              | ✓               |              |                 |           |           | ✓                  | ✓            |
| Booth (2012)                                 |                 |              | ✓               | ✓         | ✓         | ✓                  | ✓            |
| Gough et al (2012)                           | ✓               | ✓            | ✓               | ✓         | ✓         | ✓                  |              |
| Saini (2012); Saini & Shlonsky (2012)        | ✓               | ✓            |                 |           |           |                    |              |
| Shaw (2012)                                  | ✓               |              |                 |           |           | ✓                  |              |
| Snilstveit et al (2012)                      | ✓               |              | ✓               | ✓         |           | ✓                  | ✓            |
| Tong et al (2012)                            | ✓               | ✓            |                 |           |           | ✓                  | ✓            |
| Greenhalgh & Wong (2014)                     | ✓               | ✓            | ✓               | ✓         | ✓         | ✓                  |              |
| Toye et al (2014)                            |                 | ✓            |                 | ✓         | ✓         |                    | ✓            |
| Whitaker et al (2014)                        | ✓               |              |                 |           |           |                    | ✓            |

The seven sub-domains of the RETREAT framework were mapped against 19 specific methodologies of qualitative synthesis previously identified (See Table 4). The identified documents were used to map whether each review method was appropriate for each consideration. This was supplemented by experiential insights from experienced reviewers from

the Cochrane Qualitative and Implementation Methods Group. Where the authors/reviewers considered the issue to be positively addressed by the methodology items were rated as Green (Appropriate). Where the issue is not specifically mentioned but is compatible with existing knowledge on the methodology items were rated Yellow (Potentially Appropriate).

Table 4: Subdomains representing more detailed considerations for choice of qualitative synthesis method.

| Review Question             | Epistemology          | Time/ Timeframe       | Resources | Expertise  | Audience & Purpose          | Type of Data                      |
|-----------------------------|-----------------------|-----------------------|-----------|--|-----------------------------|-----------------------------------|
| Fixed                       | Generation of Theory  | Degree of Iteration   | Personnel | In Qualitative Research                          | Academics                   | Thin/Thick                        |
| Emerging                    | Exploration of Theory | Degree of Integration | Funding   | In Systematic Reviewing                          | Policymakers                | Rich/Poor                         |
|                             | Testing of Theory     | Points of Integration | Effort    | In Topic Area                                    | Practitioners               | Individual Article                |
|                             | Idealist              |                       |           | In Theory  | Developers of Interventions | Body of Literature                |
|                             | Realist               |                       |           | In Literature searching                          |                             | Theory                            |
|                             | Aggregative           |                       |           | Disciplinary, Methodological and Perspective Mix |                             | Likely number of relevant studies |
| Interpretive/ Configurative |                       |                       |           |  | Unit of Analysis            |                                   |

priate). Finally where authors/reviewers comment on the unsuitability of a methodology for a particular consideration items were flagged with Red (Not Appropriate) (Table 5). Other more qualitative considerations are indicated by additional, non-indicative colour shading.

## 4 APPLICATION OF THE GUIDANCE

To apply this guidance a reader compares the characteristics of their planned review with the requirements and functions of the respective types of synthesis. So, for example, they start by defining whether their intention is to conduct a stand alone qualitative synthesis (Table 7) or a review that integrates quantitative and qualitative data (Table 8). Having tracked their decision to the appropriate Table the reader then compares the options contained in each criteria (row) with the available methodological options (columns). Optimally the reader will reach a point at which the range of available options has been reduced to a limited number, preferably a single choice.

### 4.1 REVIEW QUESTION

The review question is consistently identified as an important factor when determining the methodology

of synthesis. The review question carries several considerations. Unlike effectiveness questions, where the starting point for a synthesis is a fixed PICO (Population-Intervention-Comparison-Outcome) question framework (Richardson et al, 1995), methods of qualitative synthesis may utilise either a fixed question or a more negotiable, emerging question. Where there is an accompanying effectiveness question review teams often use a corresponding PICO or SPICE (Setting-Perspective- Interest, Phenomenon of – Comparison – Evaluation) pre-defined question (Booth, 2006). In essence the question structure within this type of qualitative synthesis is used as an “anchor” (Eakin & Mykhalovskiy, 2003) to ensure that the effectiveness and qualitative aspects remain co-terminous. Other methods, usually with an interpretive intent (e.g. **grounded formal theory** or **meta-ethnography**), treat the review question in a way that is more analogous to primary qualitative research. The question is seen as negotiable and thus to be explored as a result of the initial review process. In short the question itself becomes clearer as the review team examines their data in a manner analogous to **grounded theory** approaches in primary research. This may pose particular challenges with regard to determination of the review protocol which may consequently need to be delayed or produced in a more iterative manner. The review question can be conceived as a “compass” (Eakin & Mykhalovskiy, 2003) offering a general direction of travel without predetermining its limits.

Table 5: Choosing the Review Method – What are the Critical Requirements?

| Considerations for Review Methodology | Review Question              |                  |                                 |                          |                     |                        |                  |                  |                     |                            |                |                |                   |                     |   |                         |                       |                             |                    |       |
|---------------------------------------|------------------------------|------------------|---------------------------------|--------------------------|---------------------|------------------------|------------------|------------------|---------------------|----------------------------|----------------|----------------|-------------------|---------------------|---|-------------------------|-----------------------|-----------------------------|--------------------|-------|
|                                       | Best Fit Framework Synthesis | Concept Analysis | Critical Interpretive Synthesis | Ecological Triangulation | Framework Synthesis | Grounded Formal Theory | Meta-Aggregation | Meta-Ethnography | Meta-Interpretation | Meta-Narrative             | Meta-Study     | Meta-Summary   | Narrative Summary | Narrative Synthesis | Qualitative Interpretive Meta-Synthesis | Rapid Realist Synthesis | Realist Synthesis     | Textual narrative synthesis | Thematic synthesis |       |
| Question Type                         | Multiple-Qual <sup>2</sup>   | Multiple-Qual    | Multiple-Qual <sup>3</sup>      | Qual                     | Multiple-Qual       | Qual                   | Qual             | Qual             | Qual                | Multiple-Qual <sup>4</sup> | Multiple       | Multiple       | Multiple          | Multiple            | Qual                                    | Multiple                | Multiple <sup>5</sup> | Multiple                    | Multiple-Qual      |       |
| Fixed/ Emerging                       |                              |                  |                                 |                          |                     |                        |                  |                  |                     |                            |                |                |                   |                     |   |                         |                       |                             |                    |       |
| Dixon-Woods et al (2004; 2005)        | FIXED                        | FIXED            | FIXED                           | FIXED                    | FIXED               | EMERG-ING              | FIXED            | EMERG-ING        | EMERG-ING           | FIXED                      | EMERG-ING      | FIXED          | Unclear           | FIXED               | FIXED                                   | FIXED                   | FIXED                 | FIXED                       | FIXED              | FIXED |
| Epistemology                          |                              |                  |                                 |                          |                     |                        |                  |                  |                     |                            |                |                |                   |                     |   |                         |                       |                             |                    |       |
| Epistemology Dependence               | LOW                          | MOD              | HIGH                            | HIGH                     | LOW                 | HIGH                   | MOD              | HIGH             | HIGH                | HIGH                       | MOD            | MOD            | LOW               | LOW                 | MOD                                     | HIGH                    | HIGH                  | LOW                         | LOW                |       |
| Idealist/ Realist                     | Realist?                     | Unclear          | Idealist                        | Realist/Idealist         | Realist             | Idealist               | Realist?         | Idealist         | Idealist?           | Idealist                   | Idealist       | Realist?       | Unclear           | Realist?            | Idealist?                               | Realist                 | Realist               | Realist                     | Realist            |       |
| Time/Timeframe                        |                              |                  |                                 |                          |                     |                        |                  |                  |                     |                            |                |                |                   |                     |   |                         |                       |                             |                    |       |
| Time Required                         | LOW                          | MOD              | MOD                             | MOD                      | LOW                 | HIGH                   | MOD              | HIGH             | HIGH                | HIGH                       | HIGH           | MOD            | MOD               | MOD                 | MOD                                     | LOW                     | HIGH                  | LOW                         | LOW                |       |
| Resources                             |                              |                  |                                 |                          |                     |                        |                  |                  |                     |                            |                |                |                   |                     |   |                         |                       |                             |                    |       |
| Comprehensive/ Purposive Sampling     | COMPRE-HENSIVE               | PURPO-SIVE       | PURPO-SIVE                      | COMPRE-HENSIVE           | COMPRE-HENSIVE      | PURPO-SIVE             | COMPRE-HENSIVE   | PURPO-SIVE       | PURPO-SIVE          | PURPO-SIVE                 | COMPRE-HENSIVE | COMPRE-HENSIVE | UNCLEAR           | COMPRE-HENSIVE      | PURPO-SIVE                              | PURPO-SIVE              | PURPO-SIVE            | COMPRE-HENSIVE              | BOTH               |       |
| Interlibrary loans & photocopies      | HIGH                         | MOD              | LOW                             | HIGH                     | HIGH                | MOD                    | HIGH             | MOD              | HIGH                | HIGH                       | HIGH           | HIGH           | MOD               | MOD                 | MOD                                     | LOW                     | MOD                   | HIGH                        | MOD                |       |
| Expertise                             |                              |                  |                                 |                          |                     |                        |                  |                  |                     |                            |                |                |                   |                     |   |                         |                       |                             |                    |       |
| Qualitative Researcher                | LOW                          | LOW              | HIGH                            | MOD                      | LOW                 | HIGH                   | MOD              | HIGH             |                     | HIGH                       | HIGH           | MOD            | LOW               | LOW                 | MOD                                     | HIGH                    | HIGH                  | LOW                         | LOW                |       |
| Info Specialist                       | HIGH                         | LOW              | HIGH                            | MOD                      | MOD                 | LOW                    | MOD              | LOW              |                     | HIGH                       | MOD            | MOD            | MOD               | MOD                 | MOD                                     | MOD                     | HIGH                  | MOD                         | MOD                |       |

2 Best Fit Framework synthesis has not been used to integrate quantitative and qualitative data but in principle it meets the requirements of a framework-based mixed methods approach.  
 3 It is unlikely that a critical interpretive synthesis would only review qualitative literature as it seeks to purposively and theoretically sample independent of study quality and study design.  
 4 It is unlikely that a meta-narrative approach would only review qualitative literature as the objective is to identify different research paradigms which might be split across quantitative and qualitative methodologies  
 5 Although realist synthesis is conceived as an integrative approach published examples exist of realist synthesis of qualitative research only.

**Considerations for Review Methodology**

|                               | Best Fit Framework Synthesis | Concept Analysis | Critical Interpretive Synthesis | Ecological Triangulation | Framework Synthesis | Grounded Formal Theory | Meta-Aggregation | Meta-Ethnography | Meta-Interpretation | Meta-Narrative | Meta-Study | Meta-Summary | Narrative Summary | Narrative Synthesis | Qualitative Interpretive Meta-Synthesis | Rapid Realist Synthesis | Realist Synthesis | Textual narrative synthesis | Thematic synthesis |
|-------------------------------|------------------------------|------------------|---------------------------------|--------------------------|---------------------|------------------------|------------------|------------------|---------------------|----------------|------------|--------------|-------------------|---------------------|---|-------------------------|-------------------|-----------------------------|--------------------|
| <b>Audience &amp; Purpose</b> |                              |                  |                                 |                          |                     |                        |                  |                  |                     |                |            |              |                   |                     |   |                         |                   |                             |                    |
| Academics                     | MAYBE                        | YES              | YES                             | MAYBE                    | MAYBE               | YES                    | MAYBE            | YES              | YES                 | YES            | YES        | YES          | YES               | YES                 | YES                                     | NO                      | YES               | MAYBE                       | MAYBE              |
| Designers of Interventions    | YES                          | NO               | MAYBE                           | YES                      | YES                 | NO                     | MAYBE            | NO               | NO                  | NO             | NO         | NO           | NO                | MAYBE               | MAYBE                                   | YES                     | YES               | MAYBE                       | MAYBE              |
| Policymakers                  | YES                          | NO               | MAYBE                           | YES                      | YES                 | NO                     | YES              | NO               | NO                  | NO             | NO         | NO           | NO                | YES                 | YES                                     | YES                     | YES               | YES                         | YES                |
| Practitioners                 | YES                          | NO               | MAYBE                           | YES                      | YES                 | NO                     | YES              | NO               | NO                  | NO             | NO         | NO           | NO                | YES                 | YES                                     | YES                     | YES               | YES                         | YES                |
| Commissioners of Research     | MAYBE                        | NO               | YES                             | MAYBE                    | MAYBE               | MAYBE                  | MAYBE            | MAYBE            | MAYBE               | YES            | YES        | YES          | MAYBE             | YES                 | MAYBE                                   | MAYBE                   | MAYBE             | YES                         | MAYBE              |
| <b>Type of Data</b>           |                              |                  |                                 |                          |                     |                        |                  |                  |                     |                |            |              |                   |                     |   |                         |                   |                             |                    |
| Conceptually Rich Data        | NO                           | YES              | YES                             | NO                       | NO                  | YES                    | NO               | YES              | YES                 | YES            | MAYBE      | NO           | NO                | NO                  | MAYBE                                   | YES                     | YES               | NO                          | NO                 |
| Contextually Thick Data       | NO                           | MAYBE            | MAYBE                           | NO                       | NO                  | NO                     | NO               | MAYBE            | YES                 | NO             | MAYBE      | NO           | NO                | NO                  | MAYBE                                   | YES                     | YES               | NO                          | NO                 |
| Large number of studies       | YES                          | MAYBE            | YES                             | MAYBE                    | YES                 | NO                     | YES              | NO               | NO                  | YES            | YES        | YES          | YES               | YES                 | MAYBE                                   | NO                      | MAYBE             | YES                         | YES                |
| <b>Other Considerations</b>   |                              |                  |                                 |                          |                     |                        |                  |                  |                     |                |            |              |                   |                     |   |                         |                   |                             |                    |
| Reporting Standards           | ENTREQ?                      | NONE             | ENTREQ                          | ENTREQ                   | ENTREQ              | ENTREQ                 | NONE             | ENTREQ, eMERGE   | NONE                | RAMESES        | ENTREQ     | NONE         | NONE              | NONE                | NONE                                    | NONE                    | RAMESES           | ENTREQ                      | ENTREQ             |

■ Method is appropriate     
 ■ Method may be appropriate     
 ■ Method is not appropriate

Table 6: Common formats for Question Formulation for Qualitative Synthesis.

| SPICE                   | SPIDER                 | PICOC        | CHIP       |
|-------------------------|------------------------|--------------|------------|
| Setting                 | Sample                 | Population   | Context    |
| Perspective             | Phenomenon of Interest | Intervention | How        |
| Interest, Phenomenon of | Design                 | Comparison   | Issues     |
| Comparison (if any)     | Evaluation             | Outcome      | Population |
| Evaluation              | Research Type          | Context      |            |

Recently researchers have revisited whether a qualitative review question, carried out to support an HTA effectiveness question, should actually be co-terminous with the effectiveness question (Lorenz et al, 2012). They note that qualitative research relating to a new technology may necessarily be limited. As a consequence the review team may need to broaden the scope of the qualitative systematic review to include exploration of the phenomenon of the untreated/pre-treated condition and the lived experience of patients with the target condition.

Other question formulations proposed for systematic reviews of qualitative research include SPIDER (Cooke et al, 2012), PICOC (Petticrew & Roberts, 2006) and CHIP (Shaw, 2010; 2012) (Table 6).

## 4.2 EPISTEMOLOGY

Commentators tend to agree that the reviewer should be mindful of the need to not violate the philosophical foundations or the integrity of the qualitative primary studies (Sandelowski & Barroso, 2007). For some types of synthesis considerations of epistemology are particularly important i.e. that the method of synthesis should be compatible with the epistemology of the included studies. For example **meta-ethnography** and **grounded formal theory** make frequent recourse to epistemological considerations at each stage of the review process. In contrast other methods may be regarded as more epistemology-neutral – for example best fit **framework synthesis**, **narrative synthesis** and **thematic synthesis**. Within the discipline of education Major and Savin-Baden (2010) take the extreme position in their **qualitative research synthesis** methodology that only studies with the same epistemological underpinnings should be handled within the same synthesis. In contrast

health services research and technology assessment pursues a more pragmatic orientation with it being common practice to integrate qualitative studies of different types within a single synthesis. Even meta-ethnography, which implies the systematic analysis of ethnographies, typically exhibits inclusion of a wide range of study types.

Barnett-Paige and Thomas (2009) seek to characterise types of qualitative synthesis on an idealist – realist continuum. They note that the developers of **meta-narrative synthesis**, **critical interpretive synthesis** and **meta-study** "all articulate what might be termed a "subjective idealist" approach to knowledge". However some methodologies, notably ecological triangulation can be both idealist and realist.

According to Toye et al (2014) synthesis approaches can be divided into "(a) those that aim to describe or 'aggregate' findings and (b) those that aim to interpret these findings and develop conceptual understandings or 'theory'". Several types of qualitative synthesis have been characterised as being aggregative in intent. These start from the meta-analytic principle that "every study counts". Other types of qualitative synthesis are variously characterised as interpretive or, more recently, as configurative. However synthesis types do not necessarily cluster around this often cited distinction between aggregative and interpretive (or configurative) reviews with regard to epistemology. For example meta-aggregation (Hannes & Lockwood, 2011b) carries a strong philosophical component. The critical appraisal instrument used within meta-aggregation to make an assessment of study quality, QARI, requires the reviewer not only to explore the epistemologies, methodologies and methods of each included primary qualitative research article but also a sophisticated assessment of the degree of congruence (or "fit") between them.

A common application for qualitative synthesis is in exploring barriers or facilitators to a particular intervention or programme. Where the purpose is simply to map such barriers and facilitators a thematic approach may be considered appropriate (e.g. **Meta-Aggregation, Thematic Synthesis** etc). In some cases barriers and facilitators may have already been mapped generically and so a review team can use the resultant framework to incorporate data specific to a particular intervention (**Framework synthesis** or **Best fit framework synthesis**). However where a more explanatory purpose is required to understand how such barriers or facilitators operate interpretive approaches (e.g. **grounded theory, meta-ethnography**) will be more appropriate.

A final type of synthesis approach, where quantitative and qualitative methods are used synergistically, can be characterised as integrative. **Realist synthesis, critical interpretive synthesis** and **meta-narrative review** were conceived as genuinely integrative methods (See section 3.9) while **narrative synthesis** seeks to best exploit its inherent strengths within a mixed-method context.

Recent years have witnessed increasing interest in the synthesis of theory (Pound & Campbell, 2015) and in the use of theory to explain review findings (Gough et al, 2012). Reviews of theory may aid our attempts to navigate a diverse literature and potentially lead to insights into how factors relate to one another (Pound & Campbell, 2015). HTA, with its very pragmatic focus, does not need to access the complete range of applications of theory synthesis. Instead it focuses on circumstances where theory can be used instrumentally to explain or explore how an intervention or programme achieves its intended effect. Potentially those components that are underpinned by an explanatory theory may help us to understand how to achieve more of an effect or how to minimise loss of effectiveness through lack of fidelity.

Gough and colleagues (2012) usefully characterise the three activities of Generating, Exploring and Testing Theory and the G-E-T mnemonic is a further useful way of characterizing the epistemological intent of different types of qualitative synthesis. In HTA particular attention focuses on “studies which include theories about cause and effect; such studies may test these theories in a ‘black box’ way or attempt to generate, explore, and test more clearly articulated causal-pathway frameworks, such as those presented in logic models”. Different methods of synthesis may

contribute to these different theory-associated activities. Foremost among approaches that seek to develop conceptual understanding, rather than to aggregate findings, is the method known as “**meta-ethnography**”.

Generation of theory may require a temporary “suspension of disbelief” i.e. a stage of theory generation unconstrained by concerns relating to the quality of the included studies). Quality assessment, and the use of the resultant quality judgements, would thus take place at a subsequent stage in the review. Contribution to the interpretation is privileged, albeit only temporarily, over rigour – as is the case in brainstorming approaches where item generation precedes item evaluation. Such approaches as **grounded theory** and **meta-ethnography** may therefore hold particular value in this process.

Synthesis may also be used to explore a potential role for theory. In this case the primary function of the synthesis is to construct patterns which the review team subsequently seek to explain by drawing upon theory-linked resources. For example a specific programme may include a patient education component. Where patients are given the opportunity to engage, interact and ask their own questions the programme may be more effective than more passive methods of delivery. The review team could explore whether statements related to better perceived self-efficacy are associated with more interactive approaches. Identification of patterns may be facilitated by fairly linear and modular methods of synthesis such as **Narrative Synthesis, Thematic Synthesis** or **Meta-Aggregation**.

Finally, once a candidate theory is identified synthesis may be used to “test” that theory to establish the extent to which the theory is supported by empirical evidence. For example **Framework Synthesis** (including **Best Fit Framework Synthesis**) can be used in this theory testing role. Under these circumstances quality assessment becomes important in establishing whether particular aspects of the theory are underpinned by good quality empirical evidence. Current interest is focused on whether the quality of the theory itself can be formally assessed.

### 4.3 TIME/ TIMEFRAME

It is challenging to seek to characterise review methods by the time taken to conduct a review. Many variables are involved such as the complexity of the methodology, the number of review processes to be

conducted, the number of studies to be included and the richness and thickness of the data. Richness and thickness are often used interchangeably, however previously we have attempted to differentiate between use of the two concepts (Booth et al, 2013b). By richness we refer to the conceptual detail of the included studies, that is the degree to which the studies sustain theoretical development and explanation. On the other hand, by thickness we refer to the extent to which included studies allow the identification of important features of the Context and Implementation. Further considerations may relate both to the degree of iteration and the extent to which, and at which points, the final HTA seeks to integrate the products of different workstreams. The multiple variables involved explain why some commentators e.g. Toye et al (2014) characterise **meta-ethnography** as less time intensive (because of limited number of studies) while Booth and others characterise the same methodology as lengthy (because of the complexity of the methods and the ambition of the interpretation).

#### 4.4 RESOURCES

The availability of resources introduces pragmatic considerations into the selection of a method of synthesis. In the broad sense resources include time, people, and funding although these are split within the RETREAT taxonomy. A useful distinction can be drawn between people in the sense of skills (as captured in the domain Expertise below) and people in the sense of the input of effort into a synthesis project (as part of the Resources). Optimally a review project will access the right level of expertise for each task for the right amount of input; failure to manage this may result in tasks not being completed, tasks being executed poorly through lack of expertise or experience or, alternatively, in more experienced team members having to substitute for tasks that could be accomplished by a less experienced member of staff. Synthesis studies may “range from small scale projects aimed to inform clinical practice at a local level, to funded projects with a practice and policy focus” (Toye et al 2014). The “dose” of input may be important – where a synthesis method follows the norms and expectations of the systematic review method then two reviewers are required on a regular basis to conduct activities as independent observers. It has been noted, however, that even when following this pattern the role of the second reviewer in qualitative evidence synthesis may lie more in identifying alternate vie-

wpoints (Booth et al, 2013a) rather than in verifying and validating data. For interpretive activities it may be beneficial to include a wider research team, possibly with even broader advisory group input, in order to maximise interpretive insights. Critical information points when determining resources will include the number of abstracts to be sifted and screened (where considerations of comprehensive versus purposive sampling are important) and the number of studies to be included (where the extent of data extraction, quality assessment and analysis per article will also be important). Overall, as Toye et al (2014) observe, “an important consideration for research stakeholders is the impact of available resources (or lack of) on the integrity of knowledge synthesis, and where, how and who to draw these lines”.

#### 4.5 EXPERTISE

Certain methods of qualitative synthesis place heavier requirements for expertise in Qualitative Research Methods (drawing on such primary techniques as **Grounded Theory, Framework Analysis, Thematic Analysis**). All synthesis methods share a requirement for expertise in Synthesis Methods (including Searching, Data Extraction, Quality Assessment, Interpretation). Where approaches are interpretive, and therefore heavily reliant on theory and/or context, a review team needs to secure the active ongoing involvement of topic experts. For aggregative approaches it may be less necessary to interact regularly with topic experts and input may be secured on a planned basis at the question formulation stage, when examining the preliminary findings and in testing the findings from the final report.

Expertise in literature searching has long been recognised as a prerequisite for quantitative systematic reviews (McGowan & Sampson, 2005) and is increasingly being viewed as equally important in the context of qualitative evidence synthesis. Although the proportion of qualitative references in MEDLINE is considerably smaller than the proportion of quantitative studies, conceivably resulting in smaller sets of bibliographic references for sifting, qualitative literature searches are frequently iterative and require intensive interaction with the review team. Supplementary searches may be required to identify articles containing theory (Booth & Carroll, 2015; Pound et al, 2015b) or to build up clusters of related (sibling or kinship) studies in order to supply greater contextual detail (Booth et al, 2013b). On many occasions conducting a QES will

involve searching for, appraising and synthesising a wide range of types of qualitative data such as case studies, policy analyses, theses, book chapters, self-help bulletin boards etcetera. Sections of quantitative studies, such as the Results or Discussion sections of randomized controlled trials may also yield data to be incorporated qualitatively. As a consequence, syntheses of multiple qualitative data types can become large and time-consuming.

Sometimes particular qualitative synthesis methods may be selected because of perceived similarity to the conventional systematic review process. For example the highly-structured protocol-driven methods prescribed by **meta-aggregation**, supported by the Joanna Briggs Institute QARI software, were considered sufficiently similar to those with a quantitative reviewing background and familiarity with the Cochrane Collaboration's REVMAN software, to facilitate transfer between methodologies (Briggs & Flemming, 2007). However privileging methods on technical grounds may be achieved at the expense of the more in-depth illuminative insights that may be yielded by more interpretive approaches.

A review team should not fall into the mistake of simply equating expertise with requisite technical skills such as being able to use a particular type of software (e.g. QARI or Atlas.ti). Expertise requires more than simply 'does our review team possess the technical expertise to carry out the review'. It also involves the epistemological, methodological, and in health, clinical, backgrounds that individuals in the team bring to the review. Subsequently this "**disciplinary, methodological and perspective mix**", will shape how the review team collectively approach the review. Even the same reviewer may contribute different types of expertise to different reviews; in some cases the expertise may derive from general systematic reviewer experience, in others it may be clinical experience and in yet others it will involve a particular disciplinary background (e.g. psychology or sociology). The focus of a particular review may shape these varied requirements; a review of implementation will be strengthened by clinical experience whereas a theory-oriented review may be configured in relation to theories from contributing disciplines.

## 4.6 AUDIENCE & PURPOSE

All systematic review findings, quantitative or qualitative, can be broadly characterised on a continuum between **Description** and **Interpretation**. A descrip-

tive review finding might state "Based on studies in Norway and Germany patients receiving palliative care experienced difficulties in verbalising their anticipation of future consequences of their illness". For the same data an interpretive finding might read; "Patients receiving palliative care exhibit behaviours indicating the presence of denial, as a defence mechanism (according to psychoanalytic theory), when required to verbalise the anticipated future consequences of their illness". Different review methods vary in their respective balance with regard to descriptive and interpretive findings. Essentially description asks the question "What does the data say?" Factual reporting of the data represents what might characterise as the "epidemiology" of studies, themes etc. Under such circumstances the reviewer passes the burden of interpretation on to the reader who essentially seeks patterns in the data and findings. Such a purpose requires clear and transparent methods of presentation. In contrast interpretation seeks to address the more subjective question "What does the data mean?". If description is the "epidemiology" of studies then interpretation corresponds to the "diagnosis". The reviewer presents their own subjective interpretation of what might be characterised as "signs and symptoms" from data and themes etcetera. Because the reviewer does the work of interpretation these interpretive insights may, in fact, be contested. The requirement for transparency is usurped by a requirement for plausibility. If the intention is description then accessible methods such as **framework synthesis, thematic synthesis** or **meta-aggregation** may be required. On the other hand an interpretive approach may be acknowledged in the choice of **critical interpretive synthesis, meta-ethnography** or **grounded formal theory**. If integration of both quantitative and qualitative data is required then an approach like **realist synthesis** may be justified.

A further consideration related to purpose centres on a detailed reviewer knowledge of the population being targeted within the review. For example Flemming (2015) describes how, for a review on smoking in pregnancy, the review team sought to develop a deep understanding of the circumstances surrounding why a particular health behaviour (smoking in pregnancy) occurs, despite almost universal knowledge, among the populations reviewed, of the harms it causes. In a suite of reviews, as part of a UK National Institute for Health Research HTA project, the review team explored behaviours around smoking in pregnancy from the perspective of pregnant women, their partners or other family members, and health professionals. The

methodology was kept the same for all three reviews for consistency. Subsequently, however, the team discovered that, whilst the overarching question for all three reviews was similar, it was the nature of the population that should have influenced the methodology. The reviews of women and of their partners were highly suited to **meta-ethnography**, despite a focus on barriers and facilitators which might otherwise have indicated a more straightforward **thematic synthesis** approach. The review team reached this conclusion because of a real need to understand the context in which the health behaviour was occurring. In hindsight the review examining health professionals would have been better suited to a more fundamental thematic analysis, as predominantly this particular review involved understanding the descriptions that health professionals gave about their smoking cessation work and the systems in which this work occurred. In this particular example we can identify a further potential tension in that integrating the three reviews may be considered more straightforward when they share a common methodology and thus a common format for findings. However the ramifications of this choice may have been minimised by the fact that a form of **thematic synthesis** is commonly seen as a prelude to the meta-ethnography process. Of course limitations in the availability of the data may pose a further constraint which may prevent selection of the method of choice.

With regard to Audience Barnett-Page & Thomas (2009) affirm that “the output of some methods of synthesis (**Thematic Synthesis, textual Narrative Synthesis, Framework Synthesis, and ecological triangulation**) is more directly relevant to policymakers and designers of interventions than the outputs of methods with a more constructivist orientation (**Meta-Study, Meta-Narrative, Meta-Ethnography, Grounded Theory, critical interpretive synthesis (CIS)**) which are generally more complex and conceptual” (Barnett-Page & Thomas, 2009). In a further observation Thomas & Harden (2008) state that **Thematic Synthesis** (including **Meta-Aggregation**) and **Framework Synthesis** produce findings that directly inform practitioners (Thomas & Harden, 2008). In contrast interpretive approaches (e.g. **CIS, Meta-Ethnography**) produce a model that requires practitioners to interpret relevance and applicability to their own context. Where the intention is to integrate quantitative and qualitative data then **Narrative Synthesis** or **EP-PI-Centre (matrix) methods** (Candy et al, 2011) may prove useful.

## 4.7 TYPE OF DATA

### 4.7.1 Quality/Quantity

Commentators are understandably reluctant to specify numbers of studies when selecting methods of synthesis. Nevertheless some useful empirically-based rules of thumb have been suggested. Paterson (2011) describes how the “available primary research may be too few or too many, too homogenous or too heterogeneous, to enact the procedures of a particular synthesis method in the way the developers prescribe”. She cites Wilson and Amir (2008) who rejected the possibility of **meta-ethnography** when they discovered six heterogeneous primary research reports were so different as to prevent reciprocal translation. In essence they settled for a form of thematic synthesis.

When data from studies are rich and/or thick there are limitations in the number of studies that the review team can assess in a coherent manner. In contrast more descriptive approaches, such as **Meta-Aggregation and Thematic Synthesis** can handle large numbers of studies. Meta-study (Paterson et al, 2001) makes a particular virtue of using large numbers of studies in yielding insights from the collective evidence base. At the other extreme metasynthesis has been undertaken with only three studies (Russell et al, 1997). However, Paterson et al (2001 p 38) suggest that at least a dozen discrete studies are needed to make meta-study meaningful.

In connection with **meta-ethnography** Noblit and Hare took the line that ‘few studies are sufficient’ (Noblit and Hare, 1988), but did not define ‘few’. Interestingly none of the examples they present involve more than six studies. In an HTA methodological review Campbell et al (2011) argue that **meta-ethnography** is more suited to synthesising a limited ( $n=40$ ) number of studies. However Toye and colleagues report that, through methodological innovation they were able to produce a meta-ethnographic synthesis that included 77 studies (Toye et al (2013).

The number of included studies can be actively managed by the review team, either by limiting the scope of a review question following a rigorous scoping process or by using purposive sampling. Non-comprehensive sampling approaches should be considered experimental, particularly within the context of HTAs where the typical expectation is that the entire relevant literature has been identified. It may in fact be difficult

to manage the number of included studies when the parameters of the literature search for qualitative research are expected to be co-terminous with those of the effectiveness and/or cost-effectiveness search process. Where studies are less plentiful, or where the review is intended to engage more widely with theory, the scope of the literature search may be expanded to incorporate experience of the untreated condition or to accommodate indirect evidence that contributes by analogy (e.g. seat belt legislation targeted at parents of young children to inform an understanding of attitudes to passive smoking in a vehicle, aimed at the same target group).

#### 4.7.2 *Thin/Thick data (on Context)*

When reviewing the qualitative literature a review team needs to identify “thick” data to enable them to explain not simply “what works” but ‘what works for whom, in what contexts, and why’ (Booth et al, 2013b). “Thin” data, from brief case reports or textual responses to surveys, will not sustain contextual interpretation. Where data is considered to be thin the choice of synthesis methods may be limited to **Meta-Aggregation, Thematic Synthesis, Framework Synthesis, Narrative Synthesis** – type approaches.

Flemming (2015) describes how, in work undertaken in palliative care looking at the experience of individuals living with a life-limiting condition or caring for someone with that condition, the context in which these individuals are living drives the method of synthesis. She concludes that, in this instance, the context of the situation cannot be extracted from the population who is experiencing it. For example, in work exploring carers’ perceptions of their educational and support needs when providing care, the review team had to do more than simply identify what these needs are. In contrast the team needed to achieve a deeper understanding of the context in which the education was required (caring for a dying relative) and the meaning associated with this. Of course such an observation is linked to the availability of primary qualitative studies and the chosen approach that these utilise. Where the phenomenon is contextually sensitive not only will the review hold a more interpretive intent but it will more likely be populated with thick primary studies that contain such contextually rich data.

#### 4.7.3 *Rich/Poor data (on Theory)*

When reviewing the qualitative literature a review team requires “rich” data to enable them to generate potential explanations that may contribute to

theory. Where generation of theory is an objective of the review interpretive approaches such as **meta-ethnography** and grounded theory may be appropriate. Such approaches may allow application of qualitative techniques such as purposive sampling (involving selective inclusion of studies) and theoretical saturation. Consequently, as interpretive approaches make fuller use of the available rich data they are likely to require a smaller number of included studies.

#### 4.7.4 *Unit of Analysis*

Not all synthesis methods are designed to handle data from findings from individual qualitative research studies. Some common approaches do analyse and aggregate findings from individual studies (e.g. **Meta-Aggregation, Thematic Synthesis**) or construct new synthetic constructs at above the level of individual studies (e.g. **Meta-ethnography** or **Grounded theory approaches**). However other approaches operate from a “Body of Evidence” (e.g. **Meta-Narrative Review**, or **Critical Interpretive Synthesis**) or seek to interpret individual study characteristics (e.g. **Meta-Study**).

### 4.8 OTHER CONSIDERATIONS

Review of the methodological literature revealed some considerations that should not be afforded importance when choosing the synthesis method. These include:

- ▶ **Frequency with which a method is used.** Although some commentators couch this in terms of the availability of methodological guidance and exemplars (McDermott et al, 2004; Booth, 2011-2015) this should not be allowed to override more important considerations of appropriateness. For example, **meta-ethnography** has frequently figured as one of the most popular methods of synthesis (Dixon Woods et al, 2005; Hannes & Macaitis, 2012). However **meta-ethnography** is demanding in terms of skills, time and amount of analytical and interpretive input.
- ▶ **Popularity of the method.** Methods of synthesis tend to enjoy periods of time when they experience a surge in popularity. Whereas the frequency of use of a method can be considered the overall prevalence of that method, popularity equates to the prevalence of a method at a particular point in time. For example, at the time of writing (2016) realist synthesis is experiencing a particularly high

profile, signalled by a proliferation of conferences and workshops. However **realist synthesis** is a demanding methodology with a specialist terminology.

- ▶ **Referral from a friend/colleague/mentor.** At a time when there is limited experience of many types of qualitative synthesis, especially for methodologies that are less developed, it may be tempting to follow the recommendation of a colleague or mentor. However considerations such as the nature of the question, the type of the data and the intended purpose/audience will vary from review to review. These variables should be given precedence over limited familiarity with a specific method. Those with experience across a wide range of question types and methodologies may offer useful pointers. Hopefully their advice will be compatible with, and indeed based upon, the guidance outlined above.
- ▶ **Warning experiences of others.** For similar reasons to the previous point it is not a sound decision to base choice of synthesis exclusively upon the cautionary experience of others. While advice and cautions may be valuable the prospective reviewer should seek to establish similarities and differences

between the proposed review and the cautionary exemplar. It may be that the exemplar review method was chosen inappropriately and that the failure of a particular method of synthesis could have been predicted by this guidance.

- ▶ A review of a decade of qualitative synthesis research in the health sciences (Bondas & Hall, 2007), found that it is common for reviewers to make modifications of qualitative synthesis methods without explanation and to provide little information about the procedures used. Table 10 identifies one core methodological text for each of the types of synthesis. Often researchers blur the boundaries of the methods by adopting languages across methods to describe concepts and data synthesis strategies. Technically they may also be too quick to aggregate findings instead of interpreting findings across studies, regardless of their chosen method for qualitative synthesis. All these tendencies make it difficult to examine individual methods of synthesis and any distinctions between them. This guidance is intended as a protection against inappropriate selection of choice of synthesis method.

Table 7: Conducting a Qualitative Evidence Synthesis – Which Review Processes Are Required?

| Component of Review Process  | Best Fit Framework Synthesis | Concept Analysis | Ecological Triangulation | Framework Synthesis | Grounded Formal Theory | Meta-Aggregation | Meta-Ethnography | Meta-Interpretation | Meta-Study | Meta-Summary | Narrative Synthesis | Qualitative Interpretive Meta-Synthesis | Textual narrative synthesis | Thematic synthesis |
|------------------------------|------------------------------|------------------|--------------------------|---------------------|------------------------|------------------|------------------|---------------------|------------|--------------|---------------------|---|-----------------------------|--------------------|
| Generating Theory            | ⊕                            | ⊕                | ⊗                        | ●                   | ⊕                      | ⊗                | ⊕                | ⊕                   | ⊗          | ⊗            | ●                   | ●                                       | ⊗                           | ⊗                  |
| Exploring Theory             | ●                            | ⊕                | ⊕                        | ●                   | ⊕                      | ⊗                | ⊕                | ⊕                   | ⊗          | ⊗            | ⊕                   | ●                                       | ⊗                           | ⊕                  |
| Testing Theory               | ⊕                            | ⊕                | ⊕                        | ⊕                   | ⊕                      | ⊗                | ⊕                | ⊕                   | ⊗          | ⊗            | ●                   | ●                                       | ⊗                           | ⊗                  |
| Use of Logic Models          | ●                            | ⊗                | ●                        | ●                   | ⊗                      | ●                | ⊗                | ⊗                   | ⊗          | ⊗            | ●                   | ●                                       | ⊗                           | ⊗                  |
| Comprehensive Search         | ⊕                            | ⊗                | ⊕                        | ⊕                   | ●                      | ⊕                | ●                | ⊗                   | ⊕          | ⊕            | ⊕                   | ⊗                                       | ⊕                           | ⊕                  |
| Purposive Search             | ●                            | ⊕                | ●                        | ●                   | ⊕                      | ⊗                | ●                | ⊕                   | ⊗          | ⊗            | ⊗                   | ⊕                                       | ⊗                           | ⊗                  |
| Rich Conceptual Data         | ⊗                            | ⊕                | ⊕                        | ⊗                   | ⊕                      | ⊗                | ⊕                | ⊕                   | ⊗          | ⊗            | ⊗                   | ●                                       | ⊗                           | ⊗                  |
| Thick Contextual Data        | ⊗                            | ⊗                | ⊕                        | ⊗                   | ●                      | ⊗                | ●                | ⊕                   | ⊗          | ⊗            | ⊗                   | ●                                       | ⊗                           | ⊗                  |
| Quality Assessment           | ⊕                            | ⊗                | ⊕                        | ⊕                   | ●                      | ⊕                | ●                | ⊕                   | ●          | ●            | ⊕                   | ⊕                                       | ⊕                           | ⊕                  |
| Interpretive level of Themes | ●                            | ⊕                | ⊗                        | ●                   | ⊕                      | ⊕                | ⊕                | ⊕                   | ⊗          | ⊗            | ⊗                   | ●                                       | ⊗                           | ●                  |
| Model as Output              | ⊕                            | ●                | ⊗                        | ●                   | ⊗                      | ⊗                | ●                | ⊗                   | ●          | ●            | ●                   | ●                                       | ⊗                           | ⊗                  |
| Graphical Presentation       | ⊕                            | ●                | ⊕                        | ●                   | ⊗                      | ⊗                | ●                | ⊗                   | ●          | ●            | ●                   | ●                                       | ⊗                           | ⊗                  |

⊗ = Not Required ● = Uncertain ⊕ = Essential

## 4.9 INTEGRATING QUALITATIVE AND QUANTITATIVE DATA

While many considerations in the guidance relate to the selection of the method of qualitative synthesis in isolation a key point for discussion is whether the overall objective includes integrating quantitative and qualitative data within an integrated health technology assessment. While the choice of methods for integrating qualitative and quantitative evidence within a review is necessarily less extensive than for qualitative evidence synthesis the decision on the most appropriate method is no less complex. A key consideration at the early stages of an HTA relates to whether, and if so how, quantitative and qualitative evidence is to be integrated. Answering complex questions by bringing together quantitative and qualitative data may require an additional stage at which to integrate the qualitative and quantitative synthesised findings; essentially a third review uses narrative synthesis techniques to bring both types of data in juxtaposition – either narratively via text, graphically, or in tabular form. Alternatively it may utilise a common framework (e.g. logic model, matrix or theoretical framework, using framework synthesis) for bringing the data together. A further method would be to use some method for the translation of data into a common format (such as a truth table). Finally an additional option is to use a methodology that accommodates both types of data, for example realist synthesis.

In response to the challenges of conducting two, or in the case of the EPPI-Centre method, three (Thomas et al, 2004), separate reviews certain methods have been developed that seek to handle quantitative and qualitative evidence simultaneously within a common method. Foremost amongst current examples is **realist synthesis** (or **realist review**). However, notwithstanding its flexibility, realist synthesis has as a primary objective the purpose of identifying programme theory (i.e. how a programme is perceived to work for whom under what circumstances). As such it may be perceived to be an overly elaborate solution to an HTA decision problem. Partly as a consequence an accelerated method, more suited to informing policy within a tight window of opportunity, has been developed known as **rapid realist review** (Saul et al, 2013).

The above guidance focuses on methodologies, and specific methods, for conducting a self-contained qualitative evidence synthesis. The implication in the literature is often that integration takes place upon completion of the systematic reviews of effectiveness and of qualitative research. Such an approach simplifies the review process but may miss opportunities to

be gained from a fully integrated approach. In contrast certain methods explicitly seek to accommodate both quantitative and qualitative data, integrating the two in addressing a specific type of review question. For example **realist synthesis** seeks to address the question “what works for whom under what circumstances” while critical interpretive synthesis seeks to critique how a particular concept, for example access to health care, has been conceptualised in both the quantitative and qualitative literature.

With regard to when data are integrated three alternatives exist; first, **sequential** refers to when either the quantitative or the qualitative component precedes and thus informs the second and subsequent component. So, for example, a review of effectiveness might precede a qualitative evidence synthesis that seeks to capture the acceptability of a pre-defined treatment choice or, alternatively, patient preferences for a particular type of intervention might be used to narrow the focus of available interventions to be explored quantitatively in terms of effect. Second, **parallel non-integrated** refers to where each component is performed contemporaneously but with no effort at integration across the quantitative and qualitative streams. The decision-maker reads each review bringing to bear overall impressions from each into the decision-making process. The full evidence is available once whichever of the two reviews that takes longest is completed. However a decision-maker may find it challenging to make mental linkages across the very different types of evidence. Finally **parallel integrated** refers to a review in which the two component streams are conducted separately and, in effect, a third review is used to join the streams. This is the method popularised by the EPPI-Centre (Thomas et al, 2004). However such an approach might prove challenging within the tight time constraints required for many HTAs.

### Mechanisms for Integrating Quantitative and Qualitative Data

As mentioned above the options are to conduct separate reviews and then to bridge with a “third review” (the EPPI Centre method), to use some common structure – model, framework or matrix – upon which to hang both sets of data, to convert the data into a transferable format (e.g. to transfer quantitative data into themes or qualitative data into numerical categories or variables), or to use a genuinely integrative method of synthesis (e.g. **realist synthesis**). While choice of methods for qualitative synthesis and for integration is determined primarily by the review question and the nature of the data it is helpful to think of a choice of two basic “strategies”:

Table 8: Integrating Quantitative and Qualitative Data within a Mixed-Method Synthesis – Which Review Processes Are Required?

| Component of Review Process  | Best Fit Framework Synthesis | Concept Analysis | Critical Interpretive Synthesis | Ecological Triangulation | Framework Synthesis | Meta-Narrative | Meta-Study | Meta-Summary | Narrative Synthesis | Rapid Realist Synthesis | Realist Synthesis | Textual narrative synthesis | Thematic synthesis |
|------------------------------|------------------------------|------------------|---------------------------------|--------------------------|---------------------|----------------|------------|--------------|---------------------|-------------------------|-------------------|-----------------------------|--------------------|
| Generating Theory            | ⊕                            | ⊕                | ⊕                               | ⊗                        | ●                   | ⊗              | ⊕          | ⊗            | ●                   | ⊕                       | ⊕                 | ⊗                           | ⊗                  |
| Exploring Theory             | ●                            | ⊕                | ⊕                               | ⊕                        | ●                   | ⊕              | ⊗          | ⊗            | ⊕                   | ⊕                       | ⊕                 | ⊗                           | ⊕                  |
| Testing Theory               | ⊕                            | ⊕                | ⊕                               | ⊕                        | ⊕                   | ⊕              | ⊗          | ⊕            | ●                   | ●                       | ⊕                 | ⊗                           | ⊗                  |
| Use of Logic Models          | ●                            | ⊗                | ⊗                               | ●                        | ●                   | ⊗              | ⊗          | ⊗            | ●                   | ⊕                       | ⊕                 | ⊗                           | ⊗                  |
| Comprehensive Search         | ⊕                            | ⊗                | ●                               | ⊕                        | ⊕                   | ⊕ <sup>6</sup> | ⊕          | ⊕            | ⊕                   | ⊗                       | ⊗                 | ⊕                           | ⊕                  |
| Purposive Search             | ●                            | ⊕                | ●                               | ●                        | ●                   | ⊕ <sup>7</sup> | ⊗          | ⊗            | ⊗                   | ⊕                       | ⊕                 | ⊗                           | ⊗                  |
| Rich Conceptual Data         | ⊗                            | ⊕                | ⊕                               | ⊕                        | ⊗                   | ⊗              | ⊗          | ⊗            | ⊗                   | ⊕                       | ⊕                 | ⊗                           | ⊗                  |
| Thick Contextual Data        | ⊗                            | ⊗                | ●                               | ⊕                        | ⊗                   | ⊗              | ⊗          | ⊗            | ⊗                   | ⊕                       | ⊕                 | ⊗                           | ⊗                  |
| Quality Assessment           | ⊕                            | ⊗                | ●                               | ⊕                        | ⊕                   | ●              | ●          | ●            | ⊕                   | ⊗                       | ⊗                 | ⊕                           | ⊕                  |
| Interpretive level of Themes | ●                            | ⊕                | ⊕                               | ⊗                        | ●                   | ⊗              | ⊗          | ⊗            | ⊗                   | ⊕                       | ⊕                 | ⊗                           | ●                  |
| Model as Output              | ⊕                            | ●                | ●                               | ⊗                        | ●                   | ●              | ●          | ●            | ●                   | ●                       | ●                 | ⊗                           | ⊗                  |
| Graphical Presentation       | ⊕                            | ●                | ⊗                               | ⊕                        | ●                   | ●              | ●          | ●            | ●                   | ●                       | ●                 | ⊗                           | ⊗                  |

⊗ = Not Required ● = Uncertain ⊕ = Essential

- 1) To choose a more aggregative method of synthesis to keep the qualitative data “simple” and therefore facilitate integration (e.g. **meta-aggregation, thematic synthesis or narrative synthesis**) perhaps through a matrix or table. Thus the EPPI-Centre method integrates data from view studies elicited via thematic synthesis.
- 2) To use methods of synthesis where the review output is a model or framework which can be used as a structure for integration e.g. **framework synthesis, best fit framework synthesis**, and some forms of **meta-ethnography**.

Currently we have identified a limited number of mechanisms for integrating quantitative and qualitative data. Broadly speaking you can translate quantitative evidence into qualitative evidence (e.g. by looking for the occurrence of themes in the quantitative studies) or translate qualitative evidence into quantitative evidence (e.g. by creating numerical categories and assessing their frequency in the qualitative literature).

A third approach is to integrate qualitative and quantitative data using a shared framework or structure. This may be:

- A theoretical or policy framework (Booth & Carroll, 2015)
- A programme theory or context-mechanism-outcome configurations
- A logic model (Rohwer et al, 2016; Pfadenhauer et al, 2016)
- A conceptual model (Carroll et al, 2011)
- A structured summary or narrative (Popay et al, 2006)
- A table (Popay et al, 2006)
- A graphic (e.g. mind map etcetera) (Popay et al, 2006)
- A matrix (Candy et al, 2011)

These methods are not necessarily methodology-specific and potential applications are identified in Table 9.

<sup>6</sup> Characterised as Systematic Meta-narrative review  
<sup>7</sup> Characterised as Rapid Meta-narrative review

## 5 CONCLUSIONS

Choice of synthesis method can be seen to be a complex multifactorial decision which requires consideration of multiple variables. Such is this complexity that it has not been possible to embody methodological advice in a single algorithm. While such an algorithm has been attempted by some commentators this approach has tended to give primacy to one or more guiding variables (e.g. the role of theory). It is not yet clear which considerations should be prioritised and so, as an alternative approach we present a matrix of considerations that can be examined for each individual planned review.

This guidance seeks to capture the complexity present in the source texts. Nevertheless it has been possible

to identify a relatively risk averse strategy when faced with numerous unknown variables. The most accessible method of synthesis is thematic synthesis – this can be selected in the absence of other positive indications. It carries the added utility of being convertible to meta-ethnography should the source data prove sufficiently rich.

Experimentation and empirical testing of methods of synthesis remains in its infancy and we anticipate that, while the overall guiding principles will continue to stand the test of time, the detail of considerations will become progressively more granular and specific. We welcome the opportunity for continued debate within the methodological community on the determinants of choice of synthesis for a qualitative evidence synthesis.

Table 9: Mechanisms for Integration and their Point of Integration.

| Mechanism                                      | Method              | Point of Integration               | Example  |
|--|---------------------|------------------------------------|--|
| Textual Summary                                | Narrative synthesis | Synthesis stage                    | Iwelunmor, J., Plange-Rhule, J., Airhihenbuwa, C. O., Ezepue, C., & Ogedegbe, O. (2015). A narrative synthesis of the health systems factors influencing optimal hypertension control in Sub-Saharan Africa. <i>PLoS one</i> , 10(7), e0130193.  |
| Tables   | Tabulation          | Synthesis stage                    | Leamy, M., Bird, V., Le Boutillier, C., Williams, J., & Slade, M. (2011). Conceptual framework for personal recovery in mental health: systematic review and narrative synthesis. <i>The British Journal of Psychiatry</i> , 199 (6), 445-452.   |
| Matrices                                       | Tabulation          | Synthesis stage                    | Nowak, P. (2011). Synthesis of qualitative linguistic research – A pilot review integrating and generalizing findings on doctor-patient interaction. <i>Patient education and counseling</i> , 82(3), 429-441.   |
| Themes   | Thematic            | Synthesis stage                    | Robinson, L., Hutchings, D., Cozner, L., Finch, T., Hughes, J., Brittain, K., & Bond, J. (2007). Balancing rights and risks: Conflicting perspectives in the management of wandering in dementia. <i>Health, Risk &amp; Society</i> , 9(4), 389-406.   |
| Conceptual Model or Framework                  | Framework           | A priori and/or at synthesis stage | Hulland K, Martin N, Dreibelbis R, DeBruicker Valliant J, Winch P (2015) What factors affect sustained adoption of safe water, hygiene and sanitation technologies? A systematic review of literature. London: EPPI-Centre, Social Science Research Unit, UCL Institute of Education, University College London. |
| Logic Model                                    | Framework           | A priori and/or at synthesis stage | Turley, R., Saith, R., Bhan, N., Doyle, J., Jones, K., & Waters, E. (2013). Slum upgrading review: methodological challenges that arise in systematic reviews of complex interventions. <i>Journal of public health</i> , 35(1), 171-175.  |
| Context-Mechanism-Outcome (CMO) Configurations | Framework           | Data Extraction                    | de Goeij, M. C., Suhrcke, M., Toffolutti, V., van de Mheen, D., Schoenmakers, T. M., & Kunst, A. E. (2015). How economic crises affect alcohol consumption and alcohol-related health problems: A realist systematic review. <i>Social Science &amp; Medicine</i> , 131, 131-146.                                |
| Graphic  | Narrative synthesis | Synthesis stage                    | Belanger, E., Rodriguez, C., & Groleau, D. Shared decision-making in palliative care: A systematic mixed studies review using narrative synthesis. <i>Palliative Medicine</i> , 25(3), 242-261.  |

Table 10: Core Methodological Texts by Methodology.

| Methodology Label                 | Core Methodological Text  | Published Worked Example   |
|-----------------------------------|---|--|
| 1 Qualitative Systematic Review   | POPAY J, ROGERS A, WILLIAMS G. (1998) Rationale and Standards for the Systematic Review of Qualitative Literature in Health Services Research. <i>Qual Health Res</i> , 8:341-351.  | NOYES, J., & POPAY, J. (2007). Directly observed therapy and tuberculosis: how can a systematic review of qualitative research contribute to improving services? A qualitative meta synthesis. <i>Journal of Advanced Nursing</i> , 57: 227-243.                             |
| 2 Concept Analysis                | WALKER, L.O.; AVANT, K. C. (2005). <i>Strategies for Theory Construction in Nursing</i> , 4th ed. Pearson Prentice Hall, Upper Saddle River, NJ.  | BRUSH BL, KIRK K, GULTEKIN I, et al. (2011) Overcoming: a concept analysis. <i>Nursing Forum</i> , 46:160-8.   |
| 3 Qualitative Evidence Synthesis  | NOYES J, POPAY J, PEARSON A, et al. (2011) Chapter 20: Qualitative research and Cochrane reviews. In: Higgins J,PT, Green S (editors), <i>Cochrane Handbook for Systematic Reviews of Interventions</i> Version 5.1.0 (updated March 2011). The Cochrane Collaboration. Available from <a href="http://www.cochrane-handbook.org">www.cochrane-handbook.org</a> . | GLENTON C, COLVIN CJ, CARLSEN B, et al (2013). Barriers and facilitators to the implementation of lay health worker programmes to improve access to maternal and child health: qualitative evidence synthesis. <i>Cochrane Database of Systematic Reviews</i> , 10:CD010414. |
| 4 Critical Interpretive Synthesis | DIXON-WOODS M, CAVERS D, AGARWAL S, et al (2006) Conducting a critical interpretive synthesis of the literature on access to healthcare by vulnerable groups. <i>BMC Medical Research Methodology</i> 6(35).  | REYNOLDS, J., EGAN, M., RENEDO, A. et al. (2015). Conceptualising the 'community' as a recipient of money-A critical literature review, and implications for health and inequalities. <i>Social Science &amp; Medicine</i> , 143, 88-97.                                     |
| 5 Qualitative Meta-synthesis      | ZIMMER, L. (2006). Qualitative meta-synthesis: a question of dialoguing with texts. <i>Journal of Advanced Nursing</i> , 53(3), 311-318.  | CHEER, K. (2015). Asia-Pacific women's experiences of stillbirth: A metasynthesis of qualitative literature. <i>Health care for women international</i> , 1-17.  |
| 6 Ecological Triangulation        | BANNING, J. H. (2013). Ecological triangulation: an approach for qualitative meta-synthesis. <i>What Works for Youth with Disabilities Project: US Department of Education</i> .  | GEDŽ NE, G., GEŽ NE, I. (2013). Action Research for Education for Sustainable Development in Teacher Education: Research and Learning Environment at Daugavpils University. In <i>School and Community Interactions</i> (pp. 127-156). Springer Fachmedien Wiesbaden.        |
| 7 Qualitative Research Synthesis  | MAJOR, C. H., SAVIN-BADEN, M. (2010). An introduction to qualitative research synthesis: Managing the information explosion in social science research. London: Routledge.  | WIMPENNY, K., SAVIN-BADEN, M., COOK, C. (2014). A qualitative research synthesis examining the effectiveness of interventions used by occupational therapists in mental health. <i>The British Journal of Occupational Therapy</i> , 77(6), 276-288.                         |
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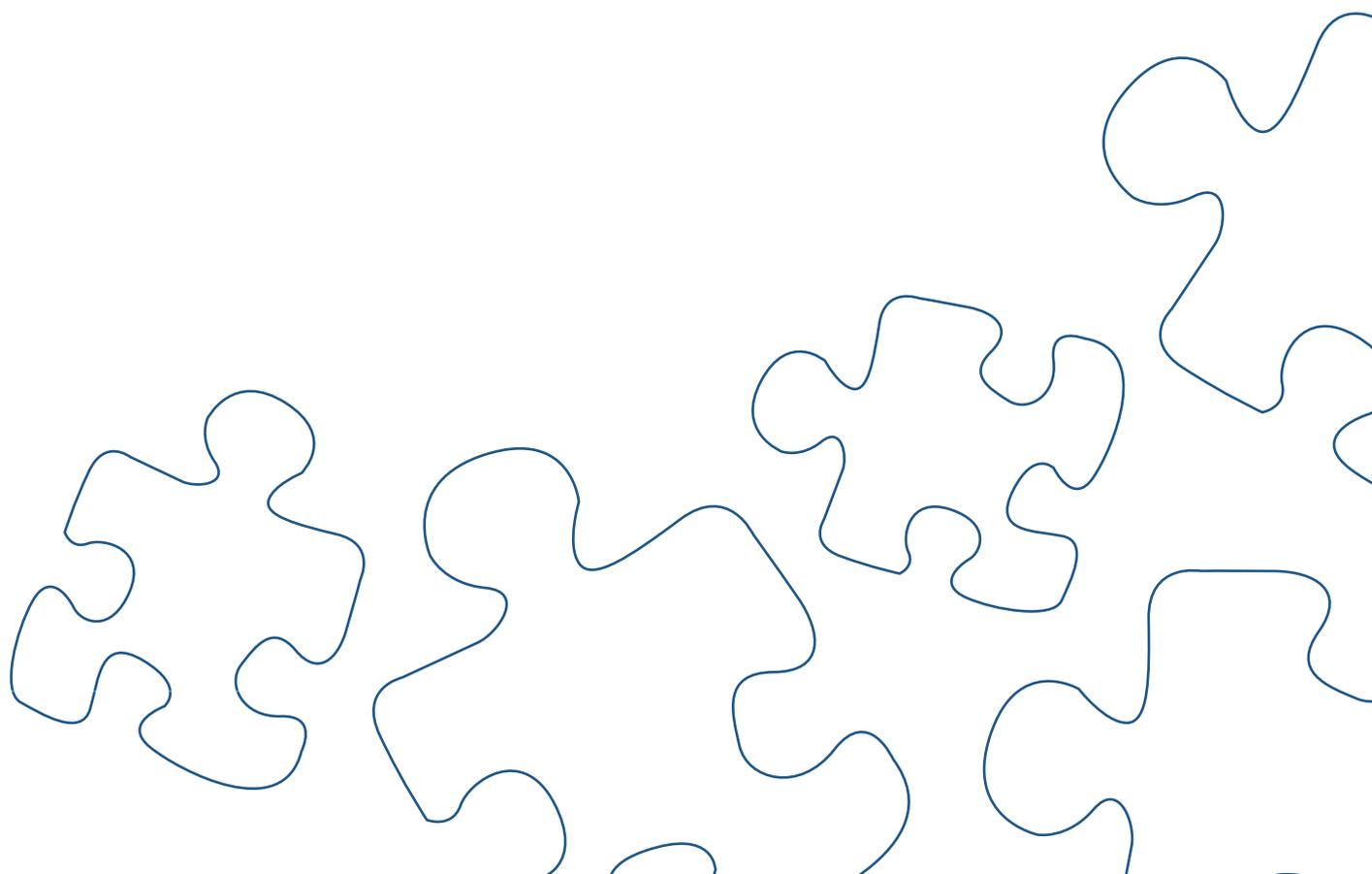
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*Guidance on choosing qualitative evidence  
synthesis methods for use in health technology assessments  
of complex interventions*



- 1 Integrated health technology assessment for evaluating complex technologies (INTEGRATE-HTA): An introduction to the guidances
- 2 Guidance on the integrated assessment of complex health technologies – The INTEGRATE-HTA Model
- 3 Guidance for assessing effectiveness, economic aspects, ethical aspects, socio-cultural aspects and legal aspects in complex technologies
- 4 Guidance for the assessment of treatment moderation and patients' preferences
- 5 Guidance for the Assessment of Context and Implementation in Health Technology Assessments (HTA) and Systematic Reviews of Complex Interventions: The Context and Implementation of Complex Interventions (CICI) Framework
- 6 Guidance on the use of logic models in health technology assessments of complex interventions
- 8 Integrated assessment of home based palliative care with and without reinforced caregiver support: A demonstration of INTEGRATE-HTA methodological guidances – Executive Summary



**INTEGRATE-HTA**



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