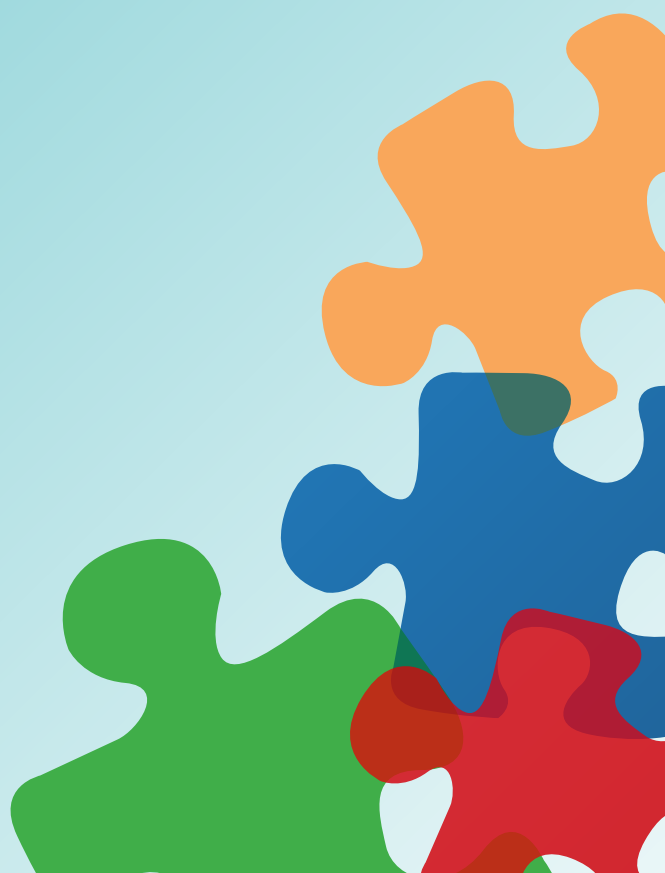


Integrated health technology assessment for evaluating complex technologies (INTEGRATE-HTA):

An introduction to the guidances

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INTEGRATE-HTA



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COMPLEX TECHNOLOGIES DEMAND INNOVATIVE CONCEPTS AND METHODS FOR ASSESSMENT

INTEGRATE-HTA was a research project involving interdisciplinary scientists from seven European countries. It ran from 1.1.2013 to 31.12.2015 and has been co-funded by the European Commission within the FP7 Cooperation Work Programme. INTEGRATE-HTA has developed six guidances to support an integrated assessment of complex health technologies. The guidances have been tested in a case study on palliative care. The main audiences for the guidances are producers and users of health technology assessments.

In the following we will give a brief overview of the rationale of the project, the overall process of the assessment and the individual guidances.

With changing disease patterns, complex health technologies have gained massive importance. Increasingly multifaceted strategies, such as disease-management programs (DMPs) or combined complex public-health-programmes are employed.

The UK Medical Research Council (MRC) defines complex interventions as being characterised by the number of interacting components within the experimental and control interventions, the number and difficulty of behaviours required by those delivering or receiving the intervention, the number of groups or organisational levels targeted by the intervention, the number and variability of outcomes, and the degree of flexibility or tailoring of the intervention permitted (MRC 2008).

To avoid misleading conclusions, health technology assessment (HTA) should take the complexity of a technology, its means of implementation, its environment, and its varying effects on different individuals into account. For example, when assessing an educational program to prevent the transmission of the human immunodeficiency virus (HIV) the success or failure might depend on the message itself (e.g. abstention or condoms or both), the messenger (a young celebrity or a respected religious leader), the target group (sexually active adolescents or elderly religious persons), the medium transmitting the message (internet spots or lectures), and the perceived prevalence of the disease

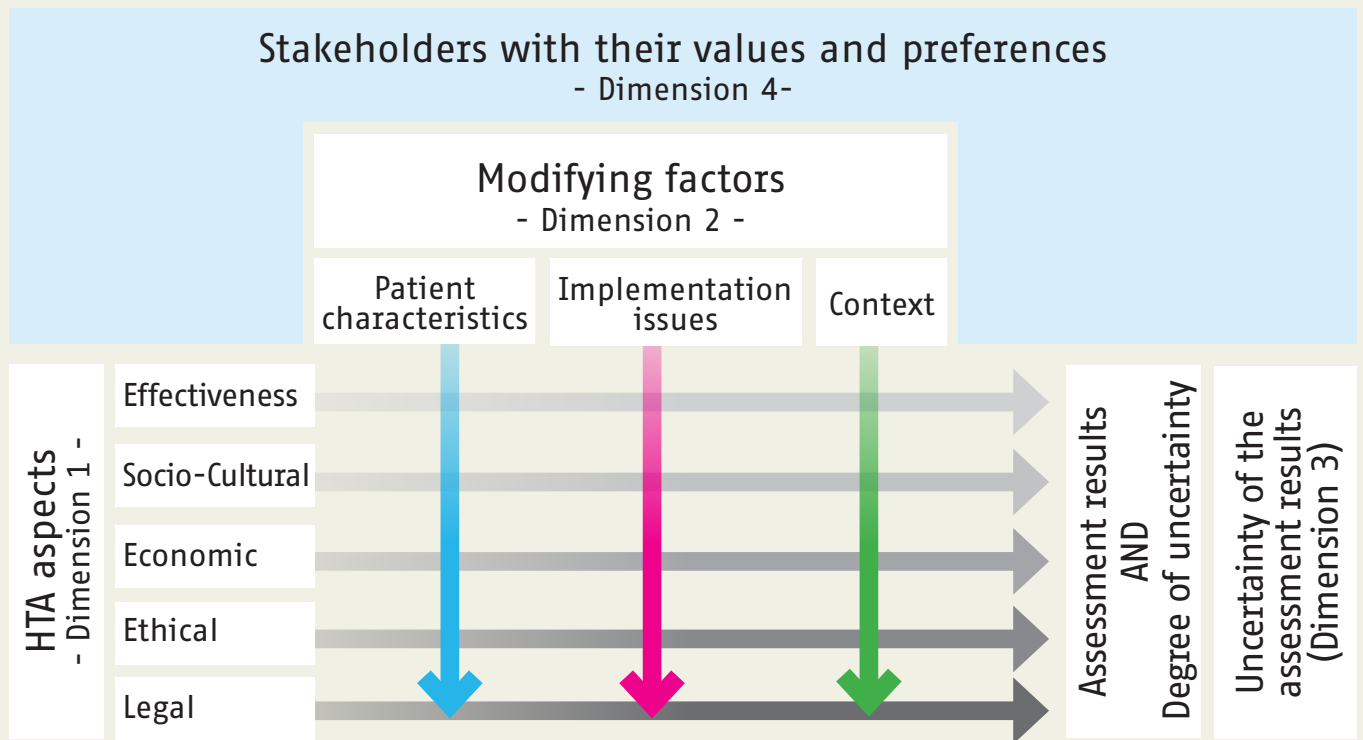
(omnipresent threat or unlikely event). To focus only on the content of the program without considering the other variables and the interactions may result in misleading conclusions.

All interventions could, therefore, be considered complex to a certain extent. This guidance, however, focuses on those health technologies where the presence of complexity has strong implications for the planning, conduct and interpretation of the HTA.

In recent years there have been major advances in the development of HTA-methods. However for the assessment of complex health technologies there are still major conceptual and methodological gaps. They are caused by

- conceptual and methodological insufficiencies for assessing social, cultural, ethical, and legal issues in complex health technologies.
- a lack of attention to the diversity of characteristics and preferences of the individuals who are supposed to use health technologies: Individuals differ from each other with regard to their biological, social or cultural characteristics and in their preferences.
- the limited consideration of context and implementation issues: "...lack of impact may reflect implementation failure" (MRC 2008). Complex technologies are especially prone to variations in context or implementations, whereas HTA so far has hardly been concerned with implementation and/or contextual influences.
- missing strategies to integrate all these aspects (see figure 1) into a comprehensive assessment: So far there have been no systematic strategies to integrate the findings on the different issues (effectiveness and economic, social, cultural, ethical, and legal issues; dimension 1 in figure 1); interactions related to patient characteristics, the context, and implementation issues (dimension 2); the degree of uncertainty in the assessment (dimension 3); and the values and preferences of the stakeholders (dimension 4) of a technology. Figure 1 illustrates the four different dimensions of integration:

Figure 1: The four dimensions of integration in HTA.



THE INTEGRATE-HTA PROJECT

In the project INTEGRATE-HTA we developed concepts and methods for HTA to enable a patient-centred, integrated assessment of the effectiveness, and the economic, social, cultural, legal, and ethical issues of complex technologies that takes context and implementation into account.

More specifically we developed guidances

- ▶ to assess the effectiveness and economic, social, cultural, legal, and ethical issues of complex health technologies (Guidance for assessing effectiveness, economic aspects, ethical aspects, socio-cultural aspects and legal aspects in complex technologies);
- ▶ to elicit patient preferences and patient-specific moderators of treatment (Guidance for the assessment of treatment moderation and patients' preferences);

- ▶ to include context, setting, and implementation in the assessment of complex health technologies (Guidance for the Assessment of Context and Implementation in Health Technology Assessments (HTA) and Systematic Reviews of Complex Interventions and Guidance on the use of logic models in health technology assessments of complex interventions);
- ▶ to choose adequate qualitative evidence synthesis methods (Guidance on choosing qualitative evidence synthesis methods for use in health technology assessments of complex interventions);
- ▶ how to integrate all these issues to a patient-centred, comprehensive assessment of complex technologies (Guidance on the integrated assessment of complex health technologies - The INTEGRATE-HTA Model);

The guidances were tested in a case study on palliative care (Case study: Integrated assessment of home based palliative care with and without reinforced caregiver support: 'A demonstration of INTEGRATE-HTA methodological guidances' – Executive Summary)

Figure 2: INTEGRATE-HTA Model for the process of an integrated HTA on complex health technologies.

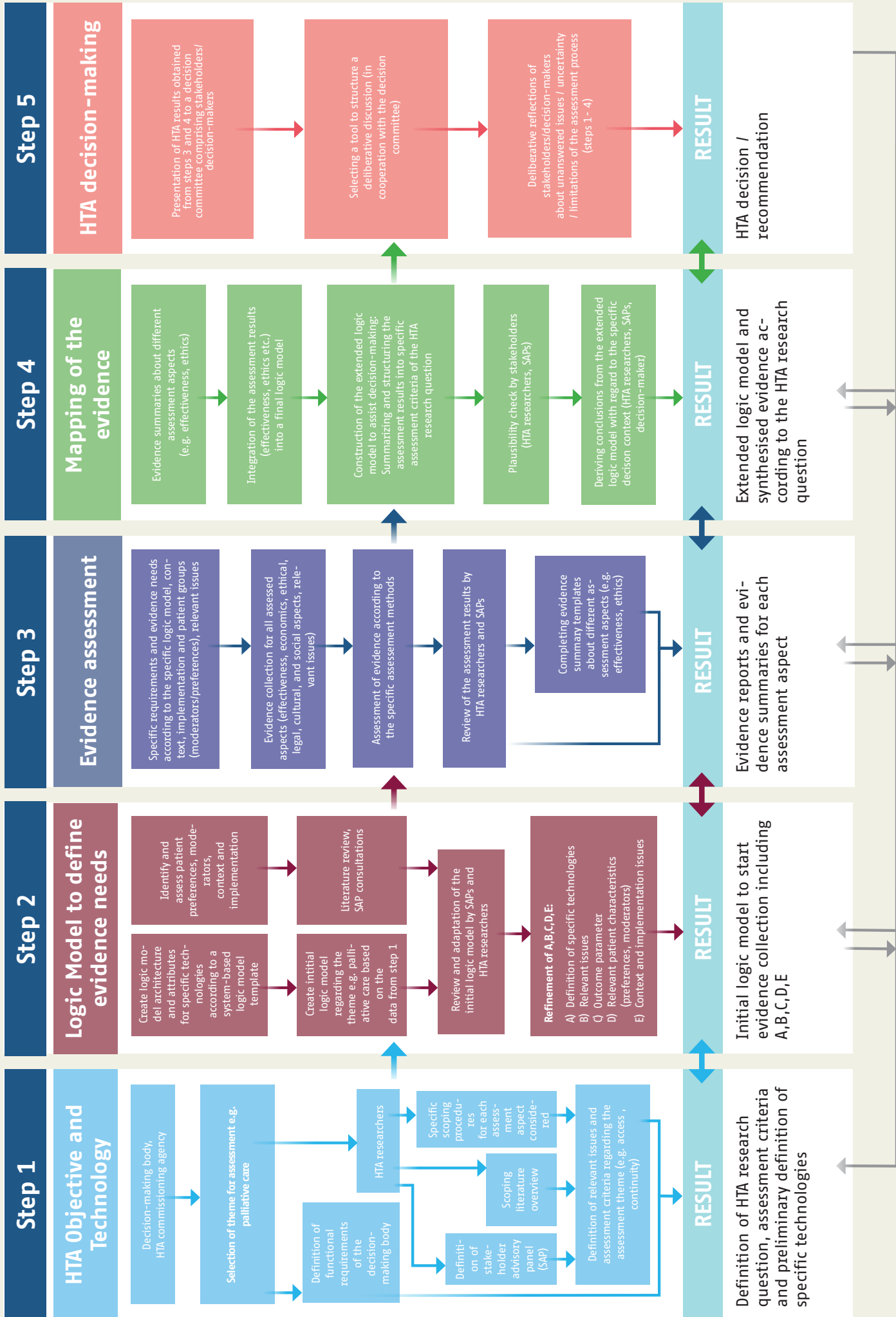


Figure 2, the INTEGRATE-HTA Model, illustrates the full process for an integrated HTA on complex health technologies. It covers the four dimensions of integration in HTA (see Figure 1) and structures the process of an integrated HTA into five steps.

In step 1 the technology under assessment and the objective of the HTA are defined. It is recommended to do this based on a tentative literature review and with the support of stakeholder advisory panels (SAPs).

In step 2 an initial logic model is developed (see Guidance on the use of logic models in health technology assessments of complex interventions). It provides a structured overview of participants, interventions, comparators, and outcomes. Groups of patients are identified that are distinguished by different preferences and treatment moderators (see Guidance for the assessment of treatment moderation and patients' preferences). Context and implementation issues are identified as part of the initial logic model (see Guidance for the Assessment of Context and Implementation in Health Technology Assessments (HTA) and Systematic Reviews of Complex Interventions). The product of this step is a graphical representation of all aspects and their interactions that are relevant for the assessment of the complex health technology.

In step 3 the logic model serves as a conceptual framework for the evidence assessment. Depending on the specific aspect (e.g. effectiveness, economic, ethical, socio-cultural, or legal aspects), different methods are available for the assessment (see Guidance for assessing effectiveness, economic aspects, ethical aspects, socio-cultural aspects and legal aspects in complex technologies). The outputs of step 3 are evidence reports and standardized evidence summaries for each assessment aspect.

In step 4 the assessment results of step 3 are structured by the extended logic model that has been developed. The model visualizes the results as well as the interactions between assessed aspects. It also allows consideration of different scenarios depending on the variation in context, implementation and patient characteristics.

Step 5 involves a structured decision-making process and is not an integral part of the HTA in a narrow sense. Based on the extended logic model decision-making can be supported by applying quantitative (e.g. MCDA- (Multi-criteria decision analysis) or qualitative decision support tools.

SUMMARY OF THE GUIDANCES

In the following we present short summaries of the six guidances and the executive summary of the case study on palliative care:

Guidance on the integrated assessment of complex health technologies – The INTEGRATE-HTA Model

In current HTA, different aspects (e.g. effectiveness, costs, ethics, etc.) are usually assessed and presented independently of each other. Context, implementation issues and patient characteristics are rarely considered. This guidance introduces the INTEGRATE-HTA Model which enables a coordinated assessment of all these aspects and addresses their interdependencies. It structures the HTA-process into five steps, all of which could involve stakeholders:

- **Step 1:** Definition of the technology under assessment and the objective of the HTA with the involvement of stakeholders.
- **Step 2:** Development of an initial logic model which structures participants, interventions, comparators, context, implementation issues and outcomes.
- **Step 3:** Based on the logic model, the evidence of the different aspects is assessed, taking variability of participants, context, implementation issues and interactions between these into account.
- **Step 4:** The assessment results of step 3 are structured and visualized by an extended logic model.
- **Step 5:** A structured decision-making process (not an integral part of the HTA in a narrow sense)

An initial assessment of the complexity of a technology (i.e. the degree of complexity through an assessment of complexity characteristics) might be helpful to decide whether all five steps or only some of them will be applied.

Guidance for assessing effectiveness, economic aspects, ethical aspects, socio-cultural aspects and legal aspects in complex technologies

The guidance comprises five interlinked aspects of HTA: effectiveness, economic, socio-cultural, ethical and legal aspects, which together provide concepts, methods, approaches and frameworks for handling the challenges of assessing complex health technologies. The guidance evaluates the appropriateness of existing methodological approaches and provides guidance for the selection and further development of these approaches. In addition new methodological tools are developed, particularly for the socio-cultural and the legal assessment aspects, where the methodological guidance available has so far been scarce.

1. The **effectiveness guidance** gives an overview of existing methods and provides guidance for dealing with heterogeneous study designs in effectiveness reviews of complex interventions. It also summarizes existing methods and provides guidance for evidence synthesis in effectiveness reviews of complex interventions. Which of the highlighted methods are appropriate depends on the effectiveness research question, the specific technology and the system within which it exists, the resulting complexity, and the available evidence base. This guidance highlights the aspects that should be considered when making these decisions and outlines the implications of such considerations in selecting methods. Choosing appropriate types of evidence and methods for evidence synthesis should ensure that decision makers are provided with the most suitable information to inform the decision making process.
2. The **economics guidance** aims to identify the potential impact of complexity for health economic evaluations within HTA. A review of health economics guidance relating to HTA was undertaken with a focus on its relevance and appropriateness for the evaluation of complex interventions acting in complex settings. Guidance recommendations were developed from the review, tested and further developed through implementation in a demonstration economics case study in reinforced caregiver support in home palliative care. Guidance includes

recommendations for practice, focusing on systems approaches to model based health economic evaluation for complex interventions in complex settings and recommendations for methodological research.

3. The **ethics guidance** provides a stepwise procedure for addressing ethical aspects in the assessment of HTA, with the following main content elements: A) Assessing the complexity of the technology, using the characteristics of complexity relevant for ethical analyses, such as Multiple and changing perspectives, Indeterminate phenomena, Uncertain causality, Unpredictable outcomes, and Ethical complexity. B) Identifying the best type of ethical approach to use for the type of complex technology (based on A), selecting this from existing available approaches for ethical assessment. Tools to aid decision making about the selection of the ethical approach are provided, which take into account contextual factors of the HTA in addition to the complexity profile of the technology. C) Guidance about how to adjust existing ethical methods for the assessment of complex interventions, based on information about the general features of the ethical approaches and on information about important ethical aspect of the specific technology. D) Guidance on how to apply the ethical approach, emphasizing integration perspectives. How the context of the health technology and the HTA influences the main steps in ethical analyses in the framework is outlined.
4. The **socio-cultural guidance** presents a framework for the identification and evaluation of socio-cultural aspects relevant in HTA as well as a stepwise assessment process. The socio-cultural framework contains three main categories: 1) the socio-cultural understanding of the health issue; 2) the understanding of the health technology and 3) socio-cultural aspects of the implementation of the technology. These three categories provide an over-arching framework for eight sub-categories. The framework can be applied in each step of the suggested assessment process, i.e. to identify and evaluate socio-cultural aspects of health technologies as well as to structure the results of the assessment. The guidance offers four methodological approaches, presented with their advantages and disadvantages. Furthermore, theoretical approaches are taken into account, which can help in structuring the whole HTA and/or in the understanding of specific aspects of the socio-cultural assess-

ment. We also refer to theoretical approaches as an option to capture the cultural heterogeneity of different social groups using Cultural Theory as an example.

5. The **legal guidance** provides a structured framework to allow HTA conductors without legal education to identify legal aspects relevant for the assessment of complex health technologies and, with that, to allow for a better integration of legal aspects in HTA of such technologies. The guidance focuses on nine core aspects, which are potentially relevant. The guidance assists HTA conductors to focus on legal aspects that are of major importance for the specific HTA by pointing out links between each core aspect and other (including non-legal) aspects of the HTA as well as the respective relevant level of decision-making. Determining these connections allows the user of this guidance to avoid unnecessary assessments of legal aspects of minor relevance for the specific HTA

Guidance for the assessment of treatment moderation and patients' preferences

The INTEGRATE-HTA guidance on the assessment of treatment moderation and patients' preferences adopts the perspective of HTA researchers who wish to make use of the best available evidence in order to develop recommendations as to how and for whom healthcare technologies may be optimally used. The guidance consists of three parts:

1. **Guidance on the retrieval and critical appraisal of literature on moderators and predictors of treatment effects.** This guidance draws the attention of HTA researchers to heterogeneity in treatment response: how widely do patients differ in their response to certain treatments, both beneficially and adversely, and what is known about patient characteristics that seem to be associated with this variability? For HTA researchers, it is important to know how such knowledge can be found efficiently and how it can be critically appraised for its validity and relevance. Specific search filters and an appraisal checklist were developed and tested.
2. **Guidance on the retrieval and critical appraisal of literature on patient preferences for treatment outcomes.** This guidance focuses on differences in patients in how they value specific outcomes of treat-

ment: what is important to them and how do patients vary in this respect? It shows how relevant information on this subject can be found and how it can be critically appraised. Specific search filters and an appraisal checklist were developed and tested.

3. **Guidance on the integration of moderators of and patient preferences for treatment outcomes.** This guidance aims to support HTA researchers in using information on moderators or predictors and preferences when developing recommendations regarding the use of healthcare technologies. Given what is known about differences in treatment response between patients, about associated patient characteristics and about differences in valuation of these outcomes, can a case be made for a personalised approach? The methods presented in this guidance describe how to synthesize this evidence in a model in order to determine the possible effects, but also the costs, of making treatment decisions more personalised.

Guidance for the Assessment of Context and Implementation in Health Technology Assessments and Systematic Reviews of Complex Interventions: The Context and Implementation of Complex Interventions (CICI) Framework

The purpose of this guidance is to provide a framework for commissioners, producers and users of systematic reviews and health technology assessments (HTA) that allows for the systematic conceptualisation, assessment and documentation of the setting, context and implementation of a complex intervention.

It presents an overarching framework (the Context and Implementation of Complex Interventions (CICI) Framework) comprising eight domains of context (i.e. setting, geographical, epidemiological, socio-cultural, socio-economic, ethical, legal and political issues) and four domains of implementation (i.e. provider, organisation and structure, funding and policy), including definitions and descriptions of each of these domains.

The CICI framework can be applied in HTAs and systematic reviews of effectiveness, as well as in qualitative systematic reviews. The guidance provides definitions

and descriptions of the domains of context and implementation and provides examples which may be of relevance for each domain. In addition, it proposes a list of questions to assess each domain: a) to retrieve quantitative information about the domain (which characteristics influence ...?) and b) to generate a more in-depth understanding of the domain's influence (how do the characteristics influence ...?). Moreover, the list encourages the researcher to assess relevant interactions between domains (e.g. ethical and socio-cultural domain). Additionally, it suggests a graphical representation of the domains contained in the CICI framework that supports researchers in systematically assessing domains of context and implementation.

The CICI framework can also be used to assess the applicability of a technology to a specific context. The domains serve as the basis for a semi-structured questionnaire that can be used with experts when exploring potential contextual barriers and facilitators to the implementation of a specific technology.

Guidance on the use of logic models in health technology assessments of complex interventions

Logic models are one important means of conceptualising and handling complexity in HTAs or systematic reviews (SRs) of complex technologies, as well as of integrating the findings of multi-component HTAs. When evaluating complex health technologies, logic models can serve an instrumental purpose at every stage of the HTA/SR process, from scoping the topic of the HTA/SR, including formulating the question and defining the intervention; conducting the HTA/SR; interpreting results and making the HTA/SR relevant for decision-makers to implement in policy and practice.

Three types of logic model are described: With a priori logic models the logic model is specified upfront and remains unchanged during the HTA/SR process. With iterative logic models the logic model is subject to continual modification throughout the course of an HTA/SR. The staged logic model harnesses the strengths of both a priori and iterative approaches by pre-specifying revision points at which major data inputs are anticipated. In addition, two subtypes of logic models are identified, namely those that seek to represent structure (system-based logic models) and those that focus on processes or activities (pro-

cess-orientated logic models). This guidance offers direction on how to choose between distinct types and sub-types of logic models, describes each logic model type and its application in detail, and provides templates for getting started with the development of an HTA/SR-specific logic model.

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

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 qualitative evidence synthesis (QES).

This guidance on choosing appropriate methods of QES should 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 research 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.

Case study: 'Integrated assessment of home based palliative care with and without reinforced caregiver support:

A demonstration of INTEGRATE-HTA methodological guidances' –

Executive Summary

This case study is a so-called 'Demonstration-HTA' as it is designed to demonstrate the application of a number of the key concepts and methods developed in the INTEGRATE-HTA project to the assessment of complex health technologies. The aim is to show the feasibility and value of the concepts and methods developed within the INTEGRATE-HTA project. The case study focuses

on models of home based palliative care with and without an additional element of caregiver support, known as reinforced and non-reinforced home based palliative care respectively.

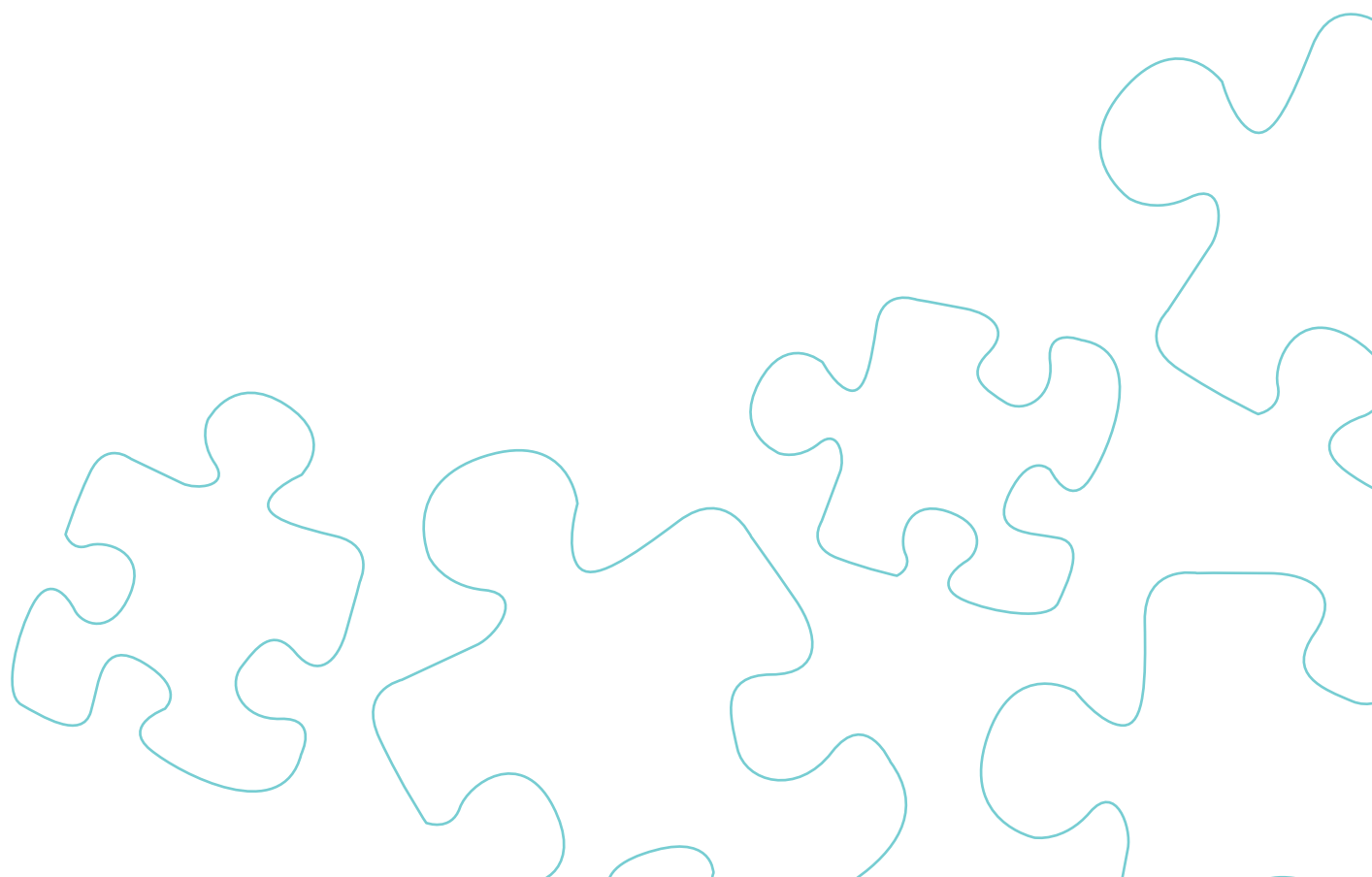
The case study provides a synthesis of a broad range of evidence to the assessment of reinforced and non-reinforced home based palliative care as one complex health technology. It may be of interest to those involved in Health Technology Assessment (HTA) as it demonstrates the application of some of the key concepts and methods developed in the INTEGRATE-HTA project and to the palliative care community (i.e. those commissioning, delivering and using palliative care services) as it draws together a range of heterogeneous evidence that may assist decision making in a complex area of health care.

REFERENCE

MEDICAL RESEARCH COUNCIL, UK (MRC) (2008). Developing and evaluating complex interventions: new guidance [Online] Available from: <http://www.mrc.ac.uk/documents/pdf/complex-interventions-guidance/> [Accessed: 25.01.2016].

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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

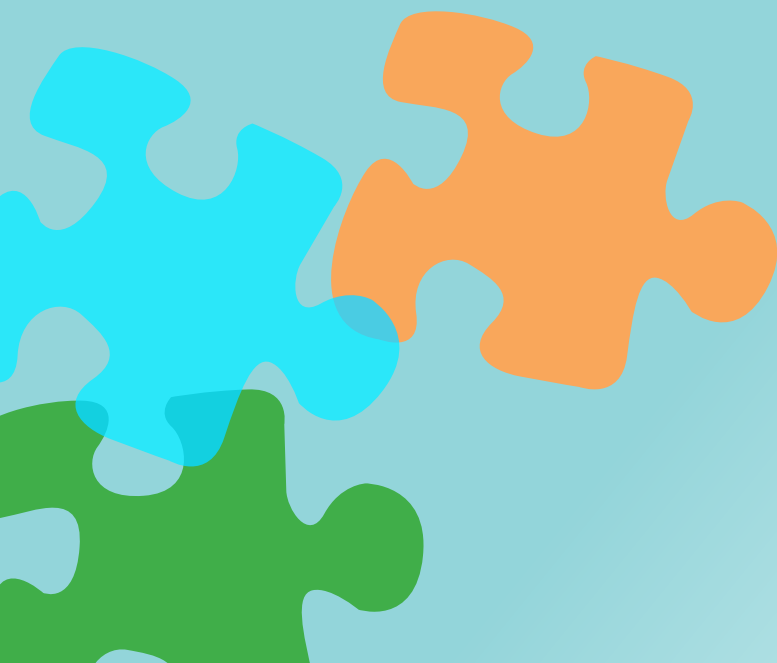
4 Guidance for the assessment of treatment moderation and patients' preferences

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

7 Guidance on choosing qualitative evidence synthesis methods for use in health technology assessments of complex intervention

8 Integrated assessment of home based palliative care with and without reinforced caregiver support: A demonstration of INTEGRATE-HTA methodological guidances – Executive Summary



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