EUnetHTA Joint Action 3 WP4

**EUnetHTA Core HTA of other technologies using the HTA Core Model® / Rapid assessment of other technologies using the HTA Core Model®**

**for Rapid Relative Effectiveness Assessment**

[XXX] For the [INTERVENTION] of [XXXXX]

***Project ID: OTCA[XX]/OTJA [XX]***

Version [x], [day] [month] [year]

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# Document history and contributors

[Please adapt the text so it matches the actual processes.]

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| **Version** | **Date** | **Description** |
| **V0.1** | **dd/mm/yy** | First draft |
| **V0.2** | **dd/mm/yy** | Input from co-author has been processed |
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| **V0.5** | **dd/mm/yy** | Input from medical editor has been processed |
| **V1.0** | **dd/mm/yy** | Final assessment report |

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|  |
| --- |
| **ASSESSMENT TEAM** |
|  | Organisation listed | Individual names listed |
| **Authoring Team** | Author(s) | Expert from [organisation] ([country]) | [individual name] ([organisation], [country]) |
| Co-Author(s) | Expert from [organisation] ([country]) | [individual name] ([organisation], [country]) |
| Dedicated Reviewer(s) | Expert from [organisation] ([country]) | [individual name] ([organisation], [country]) |
| Observer(s) | Expert from [organisation] ([country]) | [individual name] ([organisation], [country]) |
| Project Manager(s) | Member of [organisation] ([country]) | [individual name] ([organisation], [country]) |

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| External Expert(s) | [Function] from [organisation] ([country]) | [individual name] [Function name] ([organisation], [country]) | [e.g.: clinical advisory activity, review of text sections with clinically relevant content, etc.] |
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All authors, co-authors, dedicated reviewers, observers, external experts (health care professionals, patients or patient representatives) involved in the production of this assessment have declared they have no conflicts of interest in relation to the technology and comparator(s) assessed according to the EUnetHTA declaration of interest (DOI) form, which was evaluated following the EUnetHTA Procedure Guidance for handling DOI form (https://eunethta.eu/doi).

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Contact the EUnetHTA Secretariat EUnetHTA@zinl.nl with inquiries about this assessment.

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# List of abbreviations

|  |  |
| --- | --- |
| AE  | Adverse Event  |
| CSR | Clinical Study Report |
| CUR | Health Problem and Current Use of the Technology |
| DOI  | Declaration of interest |
| GMDN | Global Medical Device Nomenclature |
| GRADE  | Grading of Recommendations, Assessment, Development and Evaluation  |
| HR | Hazard Ratio |
| HRQOL  | Health-related Quality of Life  |
| ICD | International Classification of Diseases  |
| ITT | Intention to treat |
| MAH  | Marketing Authorization Holder  |
| MD  | Mean Difference  |
| MeSH | Medical Subject Headings |
| OR | Odds Ratio |
| PP | Per protocol |
| RCT | Randomised Controlled Trial |
| RR | Relative Risk |
| SAE  | Serious Adverse Event  |
| SHI | Social Health Insurance |
| SD  | Standard Deviation  |
| SMD | Standardized mean difference |
| SOP  | Standard Operating Procedure  |
| TEC | Description and Technical Characteristics of the Technology |

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# EXECUTIVE Summary OF THE ASSESSMENT OF [INTERVENTION]

[In general, the executive summary should present a comprehensive and independently readable overview of the assessment. No “new information” (i.e. information that is not mentioned somewhere else in the assessment report) should be added here. The summary should be no longer than 2500 words.]

## Introduction

[Summarise information on the disease, target population and intervention and the current standard of care.]

## Objectives and scope

[Copy the PICO and include the objective and research questions of the assessment here.]

## Methods

[Describe briefly the methods used for compiling the assessment, including]

* [general information on searches, sources used and search date]
* [tools and methods chosen for quality assessments and data analyses]
* [study types included for the assessment of clinical effectiveness and safety, for the assessment of costs and economic evaluation as well as for the assessment of ethical, organisational, patients and social as well as legal aspects]
* [patient involvement (if applicable)]

## Results

[Report the number of included studies. Summarise. Furthermore, describe the risk of bias, certainty of evidence and the outcomes. Relevant (elements of) tables from the results section may be duplicated or the table “summary of findings” (see below) can be used. Results for each domain can be summarised in separate paragraphs. Also ongoing trials of technology for current indication can be noted which are in principle likely to provide evidence in the near future.]

Table 0‑1: Summary of findings table of [name of technology]

[The summary of findings table is optional and can be used in case the certainty of the evidence has been assessed with GRADE. Regenerate the table using an applicable online tool (e.g. GRADEpro). Also consider the recommendations by the EUnetHTA Task Group on Common Phrases and GRADE (these recommendations will need to be transferred into guidelines and SOPs after EUnetHTA JA3 prior to their implementation). For more information on this table, please refer to the Cochrane handbook.]

| **Outcome** | **Anticipated absolute effects (95% CI)** | **Relative effect (95% CI)** | **Number of participants (studies)** | **Quality** | **Comments** |
| --- | --- | --- | --- | --- | --- |
| **Risk with [comparison]** | **Risk with [intervention]** |
| [Outcome X1] | [X] per 1000 | [x] per 1000 | RR/OR/HR/SMD [XX] (XX to XX) |  | High/ moderate/ low/ very low |  |
| [Outcome X2] | [X] per 1000 | [x] per 1000 | RR RR/OR/HR/SMD [XX] (XX to XX) |  | High/ moderate/ low/ very low |  |
| RR: Relative risk; OR: Odds ratio; HR: Hazard ratio; SMD: Standardized mean difference |

[Summarise the most important issues presented in the Discussion sections, e.g., on the quality of the available evidence (internal validity), the applicability of the available evidence (external validity) or the societal consequences of implementing a health technology.]

## Concluding summary

[The concluding summary includes the brief response to the research questions of the report. For this purpose, give a brief benefit statement and a statement on the results of the economical, ethical, organisational, patient and social as well as legal domain.]

# BACKGROUND

[The background should be copied from the Project Plan. In case there is a need to deviate from the background proposed in the Project Plan in substantial points of content this should be justified in section 3.7 of this template.]

[This chapter presents a limited summary on the target population and intervention. It is based upon the HTA Core Model domains CUR and TEC. It aims at providing a pragmatic and practical set of background information and serves as a rationale for the research questions. The content presented here should be limited to only such information that are needed for an understanding of the report and should not exceed 4 pages.]

## Overview of the disease, health condition and target population

HTA CORE MODEL DOMAIN: CUR[[1]](#footnote-2)

[This subchapter presents information on the target population, indication, and the health condition. The following information can be added to the Assessment Report if it has not already been included in “Chapter 1 Background” of the Project Plan:]

* [Description of health condition and definition of target population (incl. ICD-10 code and possible limitations for instance in age, sex, severity, stage or risk)]
* [Information on numbers of people belonging to the target population (including for example information on prevalence and incidence of the target condition)]
* [Description of relevant symptoms, severity and burden of the disease, stages of the disease, effects on level of functioning]
* [Description of disease aetiology]
* [Information on natural course and prognosis of an untreated disease]
* [Description of risk factors]

## Current clinical practice

HTA CORE MODEL DOMAIN: CUR[[2]](#footnote-3)

[This subchapter presents information on disease management, standard care, and current treatment plans. The following information can be added to the Assessment Report if it has not already been included in “Chapter 1 Background” of the Project Plan:]

* [Information on patient flow, e.g. on how patients get to therapy]
* [Information on diagnosis and identification of eligible patients in standard care and according to guidelines]
* [Description of standard care, general treatment concepts and the current status of care and technology]
* [Information on utilisation of standard care]
* [Information on who decides on the application of a technology]

## Features of the intervention

HTA CORE MODEL DOMAIN: TEC[[3]](#footnote-4)

[This subchapter presents information on the target intervention. The following information can be added to the Assessment Report if it has not already been included in “Chapter 1 Background” of the Project Plan:]

* [Description of the new technology, including its core characteristics, required usage of (further) medical devices, information on pharmacology (e.g. dose range), mode of operation (on a theoretical and physiological level, etc.), context of care (outpatient treatment, hospital treatment etc.), information on the intended use of the technology (e.g., treatment or prevention, first line/second line treatment)]
* [Information on market authorisation of the technology (e.g., CE marking, EMA approval, FDA approval), detailed information on the regulatory and reimbursement status can be included in Appendix 6]
* [Information on the claimed benefit of the new technology (e.g. non-invasiveness) without anticipating results of the actual assessment, presentation on the basis of patient-relevant endpoints (differentiated from non patient-relevant endpoints and surrogate endpoints)]
* [Description of the basic requirements for patients, users, personnel (and other persons) regarding the necessary expertise, required tools, and material equipment for the application and quality assurance of the new technology]
* [Information on differentiation of the new method from previous ones (e.g., is it an add-on or a replacement of an existing method)]
* [Estimation for future utilisation of technology under assessment]
* [The following table can be modified by adding/removing/adapting columns.]

Table 1‑1: Features of the intervention and comparators

|  | **Intervention/ Technology** | **Comparator x** | **Comparator y** |
| --- | --- | --- | --- |
| Name |  |  |  |
| Proprietary name |  |  |  |
| Manufacturer |  |  |  |
| Names in other countries |  |  |  |
| Reference codes |  |  |  |
| Class/GMDN code |  |  |  |

# OBJECTIVES AND Scope

[The scope and PICO should be copied from the Project Plan. In case there was a need to deviate from the scope and PICO proposed in the Project Plan this should be justified in section 3.8 of this template. The scope should be in alignment with current EUnetHTA Methodological Guidelines and should consider recommendations of the . If further criteria are considered relevant for study inclusion, please provide details in this section. Additional PICOs may be added if there is more than one research question (for example, based on requirements of EUnetHTA partners) or for each of the HTA Core Model domains.]

[This chapter serves as a precise definition of the objective for this assessment. It specifies the PICO of the assessment, that is the type of population, type of intervention (and comparisons), the types of outcomes and the types of study design that are considered in the assessment. As an additional information, information can be given on the contracting body and the addresses of the HTA report.]

The aim of this EUnetHTA Assessment is to provide a reliable synthesis of the available evidence on [Intervention]. It comprises an assessment of the clinical benefit and safety of [name of technology] in the target patients with [health problem] in comparison with [comparators]. It further comprises an economic evaluation as well as an assessment of ethical, organisational, patients and social as well as legal aspects. The target patient populations and relevant comparators (based on the requirements of EUnetHTA Partners) for the assessment of [add domain here]] are defined in the project scope below.

Table 2‑1: Scope of the assessment

| **Description** | **Project scope** |
| --- | --- |
| **Population**  | * [Define the target population]
 |
| **Intervention**  | * [Define the intervention]
 |
| **Comparison** | * [Define the comparators for this assessment]
* [Please refer to the EUnetHTA guidelines “[Comparators and comparisons – Criteria for the choice of the most appropriate comparator(s](http://eunethta.eu/outputs/comparators-comparisons-criteria-choice-most-appropriate-comparators-amended-ja1-guideline-2))” and “Comparators & Comparisons: Direct and indirect comparisons“ for a description of possible comparators and for recommendations for the choice of comparators]
 |
| **Outcomes** | * [Define the most important outcomes for this assessment]
* [See the following guidelines for a description of relevant outcomes (i.e. outcomes covering the relevant endpoint categories of mortality, morbidity [symptoms of the disease, clinical events, function], health-related quality of life, and adverse events) and for recommendations for the choice of outcomes:]
	+ [Endpoints used for relative effectiveness assessment: Clinical endpoints]
	+ [Endpoints used for relative effectiveness assessment: Composite endpoints]
	+ [Endpoints used for relative effectiveness assessment: Health related quality of life and utility measures]
	+ [Endpoints used for relative effectiveness assessment: Safety]
	+ [Endpoints used for relative effectiveness assessment: Surrogate endpoints]
 |
| **Study design** | * [Define study designs for this assessment. Distinguish between different study designs for each Core Model domain if necessary]
* [Please refer to EUnetHTA guideline “Internal validity of non-randomised studies (NRS) on interventions” for a description on non-RCTs and a discussion on their internal validity]
 |

# METHODS

[In case there was a need to deviate from the methods proposed in the Project Plan this should be justified in section 3.8].

The assessment methods and processes adhere to the EUnetHTA Methodological Guidelines and EUnetHTA SOPs.

## Clinical effectiveness and safety

### Information retrieval

[In this section, please provide a summary on the search(es) performed. Indicate whether you made any restrictions to your search (e.g., restrictions in language or study design etc.). Include information on the name of information sources (databases, study registries, websites, other sources. Detailed tables on search strategy for each database and study registry separately should be included in Appendix 1.]

[Detailed information on the process of information retrieval as well as recommendations on information sources and search techniques are given in the EUnetHTA Methodological Guideline “Process of information retrieval for systematic reviews and health technology assessments on clinical effectiveness” as well as the SOP on “Information retrieval”.]

[If applicable, include a statement saying that “The PRESS (Peer Review of Electronic Search Strategies) checklist was used for the quality check of search strategies in bibliographic databases.”]

A systematic information retrieval for relevant studies or documents was carried out to obtain comprehensive information. The following sources of information as well as search techniques were considered:

Main information sources

* Bibliographic databases
	+ MEDLINE
	+ Embase
	+ Cochrane Central Register of Controlled Trials
	+ Regional or subject-specific databases (optional)
* Study registries
	+ U.S. National Institutes of Health. ClinicalTrials.gov
	+ World Health Organization. International Clinical Trials Registry Platform Search Portal
	+ European Medicines Agency. EU Clinical Trials Register (optional)

Possible further study registries (optional)

* Unpublished company documents (optional)

[For the assessment of procedures largely based on a medical device, the manufacturers of the technologies to be assessed are usually asked to provide previously unpublished information. Authors should refer to the SOP on “Identification of Stakeholders” for further information.]

Further information sources and search techniques

To identify further relevant studies or documents, depending on the research question, further information sources are used and further search techniques are applied.

* Regulatory documents (optional)
	+ European Medicines Agency
	+ Food and Drug Administration
	+ NICE list of interventional procedures
* Application of further search techniques
	+ Screening of reference lists of included SR / HTA
	+ Use of the “Cited Reference“ function in Web of Science (optional)

Use of the “similar articles” function in Pubmed (optional)

* Queries to authors (optional)

[Authors should refer to the SOP “Queries to Authors” for information and conditions on how and when to contact authors of study publications. Such queries to study authors are documented in Appendix 8.]

### Selection of relevant studies and documents

[Describe briefly how relevant studies and documents are selected. Information and recommendations on the selection of references is described in the EUnetHTA Methodological Guideline “Process of information retrieval for systematic reviews and health technology assessments on clinical effectiveness” as well as the SOP on “Information retrieval”.]

[Reference management software] is used for citation management. Study selection is performed in [study selection tool].

All selection steps are performed by 2 persons independently of each other. Discrepancies are resolved by discussion. In the first selection step, if doubts exist as to the relevance of a study, the corresponding full text is obtained and assessed.

### Data extraction

[Describe briefly how data is extracted. Further information and recommendations on the extraction of data from included studies is given in the SOP “Data Extraction”.]

All necessary information for the assessment is extracted from the documents on the included studies into standardised tables. If discrepancies arise in the comparison of the information from different documents on a study (but also from multiple data on an aspect within a document itself) which could have a considerable influence on the interpretation of the results, this is shown in the corresponding places in the results section of the report.

### Quality rating / Risk of bias assessment

[Please refer to the EUnetHTA Methodological Guidelines “Levels of Evidence - Internal validity of randomised controlled trials”, “Therapeutic medical devices” and “Internal validity of non-randomised studies (NRS) on interventions” for further information and recommendation on quality appraisal of included data. Furthermore, authors should refer to the SOP “Risk of Bias Assessment of Clinical Studies” and consider the recommendations by the EUnetHTA Task Group on Common Phrases and GRADE (these recommendations will need to be transferred into guidelines and SOPs after EUnetHTA JA3 prior to their implementation).]

[In this section, please briefly summarise which quality rating tools were used e.g., risk of bias assessment (on study level), GRADE (assessing quality of evidence), quality rating tool for guidelines etc.]

The assessment of risk of bias follows the criteria described in the two EUnetHTA guidelines on the internal validity of RCTs and non-randomised studies on interventions. Risk of bias is assessed at the study level as well as at the outcome level. Two independent assessors judge the risk of bias (‘low risk’, ‘high risk’ or ‘unclear’) on the basis of the information retrieved from the selected documents.

### Data analyses and synthesis

[Adapt the generic text to reflect the methods used. Delete the subparagraphs in case they are not relevant for the assessment.]

The information in the included documents on study design, study methods, populations, endpoints (patient relevance, validity, and operationalization) and study results are evaluated. The results of this evaluation is presented and is used for identification of relevant analyses and considered for the conclusions of the assessment report.

#### Meta-analyses

[Authors should refer to the EUnetHTA Methodological guideline “Comparators and comparisons – direct and indirect comparisons” for further information and recommendation on the topic of meta-analysis.]

If several studies are available for the same PICO, they are quantitatively pooled in a meta-analysis. For this, studies have to be sufficiently comparable from a clinical (e.g. patient groups) and methodological (e.g. study design) point of view.

#### Sensitivity analyses

To evaluate the robustness of results, the assessment may include sensitivity analyses with regard to methodological factors. These factors arise from decisions made within the framework of the retrieval and assessment of information, for example, the specification of cut-offs for the time point of data collection or the choice of effect measure. The sensitivity analysis should in particular consider the classification of the risk of bias of study results. The result of the sensitivity analysis can affect the assessment of the certainty of results.

#### Subgroup characteristics and other effect modifiers

The results are examined with regard to potential effect modifiers, i.e. clinical factors influencing the effects. The aim is to uncover possible differences in effects between patient groups and treatment characteristics. Statistical significance based on a heterogeneity or interaction test is a prerequisite for the detection of different effects. If potential effect modifiers are identified, the statements derived from the observed effects may be specified. For example, the conclusions inferred from the effects observed in the complete patient group can possibly be formulated more precisely.

#### Certainty of the evidence (if applicable)

[Authors should refer to the recommendations by the EUnetHTA Task Group on common Phrases and GRADE ([“GRADE Framework Paper”, “Common Phrases” and “Negative Phrases”](https://companionguide.eunethta.be/doku.php?id=ot:guidance#process-related_guidance_for_rapid_rea_other_technologies), ; these recommendations will need to be transferred into guidelines and SOPs after EUnetHTA JA3 prior to their implementation).]

For rating the quality of the evidence, the Grading of Recommendations Assessment, Development and Evaluation (GRADE)-method is applied.

### Patient involvement [if applicable]

[Authors should refer to the recommendations on “[Patient Input in Relative Effectiveness Assessments](https://eunethta.eu/wp-content/uploads/2019/06/Final_290519_Patient-Input-in-REAs.pdf)” developed by the EUnetHTA Patients & Consumer / Health Care Provider Task Group.]

### External expert involvement [if applicable]

[Authors should refer to the recommendations on “[Health Care Professional Involvement in Relative Effectiveness Assessments](https://eunethta.eu/hcp-involvement-in-rea/)” developed by the EUnetHTA Patients & Consumer / Health Care Provider Task Group].

## Costs and economic evaluation

[There are two approaches[[4]](#footnote-5) that are typically used in answering the research questions in this domain:

* review of published economic evidence or
* de novo economic evaluation.

Use at least one of these approaches (section 3.2.1 or section 3.2.2) for the economic evaluation. When providing a review of published economic evidence, an additional estimation of the intervention costs is optional, which include directly related costs to the intervention and its comparator.]

### Systematic review of health economic evaluations

[For this section, please consider national guidelines and the EUnetHTA guidelines “Methods for health economic evaluations” and “Practical considerations when critically assessing economic evaluations”.]

[Depending on the research question, adjustments and further additions to the template can be useful.]

#### Information retrieval

[In this section, please provide a short summary on the search(es) performed. Include information on names of databases. Indicate whether you restricted your search (e.g., restrictions in language or study design etc.). Consider national guidelines when choosing the study type(s) in this context.]

Health care system and national context

[Specify the inclusion criteria and whether there are any restrictions regarding the health care system or the national context of the publications included. Name concrete criteria for inclusion / exclusion (i.e. countries with a high per capita income, countries with a similar health care system) and specific countries whose studies are included and justify the restriction.]

[In the case of including a limitation to studies from specific countries, an evaluation of the transferability of results of all included studies to the respective health care system must take place.]

Summary of inclusion criteria

[Summarise the criteria necessary for the inclusion of studies in the economic evaluation. These inclusion criteria can be fulfilled in addition to the inclusion criteria of the assessment of clinical effectiveness and safety (see section 2).]

[The search for health-economic studies is performed by a regular, systematic search.]

The evaluation of health-economic aspects is performed by a regular, systematic search in the form of a focused information retrieval. The following primary and further information sources, as well as search techniques, were considered.

Main information sources

* Bibliographic databases
	+ MEDLINE
	+ Embase
	+ [further databases XXX for studies]
	+ HTA Database
	+ [further databases XXX for SR/HTA]

[Please add further project-specific data, if necessary.]

Further information sources and search techniques

[Choose optional project specific titles:]

* Application of further search techniques

Screening of reference lists of included SR / HTA

* Queries to authors (optional)

#### Selection of relevant publications

[Information and recommendations on the selection of references is described in the EUnetHTA Methodological Guideline “Process of information retrieval for systematic reviews and health technology assessments on clinical effectiveness” as well as the SOP on “Information retrieval”. Usually the titles and abstracts of the references are first screened against the inclusion and exclusion criteria, followed by the screening of the full texts of potentially relevant publications identified in the first step.]

[Reference management software] is used for citation management. Study selection is performed in [study selection tool].

All selection steps are performed by 2 persons independently of each other. Discrepancies are resolved by discussion. If doubts regarding the relevance of a study exist/arise in the first selection step, the corresponding full text is obtained and assessed.

#### Information evaluation

Dataextraction

[Regarding the extraction of quantitative data authors can refer to national recommendations (if applicable) or tables in the section 5.1.3 for information and recommendations.]

All information necessary for the assessment is extracted from the included publications and transferred to the standardized tables (see section 5.1.3).

Assessment of reporting quality

The assessment of reporting quality of included studies is performed according to the criteria of [e.g. the Consolidated Health Economic Evaluation Reporting Standards (CHEERS-Statement[[5]](#footnote-6))].

Assessment of transferability

The assessment of transferability of results is performed according to the criteria of [e.g. Drummond et al.[[6]](#footnote-7), Welte et al.[[7]](#footnote-8)].

#### Intervention costs

[Intervention costs include those costs, which directly relate to the intervention and its comparator. A focussed information retrieval is not necessary for the resource identification and quantity determination. In addition to a systematic review, the presentation of intervention costs as a separate aspect can be helpful to show national costs of the intervention and its comparator(s). This section is optional.]

To calculate intervention costs, average resource consumptions are determined which respectively are necessary during the application of the intervention and its comparator intervention.

#### Information analysis and synthesis

Results (from the studies) regarding cost-effectiveness and / or costs and the respective conclusions reached by the authors are comparatively described in the HTA report. Particularly the aspects of quality of the described studies as well as their transferability to the respective health care system should be discussed. Impacts of the use of outcomes, which diverge from those used in the benefit assessment, are to be discussed.

### De novo health economic evaluation

[The template does not include any information on the information retrieval e.g. for the model structure or specific input parameters. Please consider national guidelines and the EUnetHTA Methodological guidelines “Methods for health economic evaluations” und “Practical considerations when critically assessing economic evaluations".]

[Depending on the type of economic evaluation and the modelling approach, adjustments and further additions to the template can be useful.]

#### Population

[Choose the target population to represent the characteristics of the patient population(s) in the jurisdiction(s) or the healthcare setting for which the economic evaluation is intended.]

[Define clearly all possible subgroup analyses and provide a clinically justification.]

#### Intervention and comparator

The intervention to be assessed is the treatment with [intervention].

[…] is / are defined as comparator intervention.

#### Outcomes of economic evaluation

[The relevant outcomes from the ECO domain should generally reflect the context in which the evaluation is likely to be used, as well as the research question(s) posed. Please consider the respective national guidelines and the EUnetHTA guidelines “Methods for health economic evaluations” and “Practical considerations when critically assessing economic evaluations”.]

[The outcomes of a health economic evaluation are associated with the type of economic evaluation used, i.e., cost-effectiveness analysis (CEA), cost-utility analysis (CUA), cost-consequences analysis (CCA), cost-benefit analysis (CBA) or a combination of several types.]

#### Perspective

[Describe the choice of the perspective. The choice depends on national guidelines and should at minimum be conducted from a health care perspective (see EUnetHTA Guideline “Methods for health economic evaluations”). Regardless of perspective taken, it is recommended that the use of resources be presented in a manner as detailed as possible. For example, if a societal perspective is used, indirect costs should be presented separately.]

#### Model structure

To summarise the consequences of the different interventions regarding their clinical outcomes and costs incurred, decision-analytic modelling is applied.

[Describe the choice of model approach and justify the use of modelling, e.g., by the research question, the insufficient available data and national guidelines.]

[Add figures of the model structure.]

[In order to facilitate assessments of validity, also describe model assumptions, the process of validation and the types of validation addressed in the model.]

#### Time horizon

[In order to reflect all important and relevant differences in costs or outcomes between the technologies being compared, please choose a sufficiently long time horizon for the base case analysis.]

#### Clinical input parameters

Results of assessment of clinical effectiveness (section 4.7) provide the basis of health economic evaluation. The present model considers the following input parameter:

* [parameter]
* …

[Please indicate how clinical data are incorporated into the model. Furthermore, provide details on methods of extrapolation, estimation and application of transitional probabilities (if relevant), possible validation of the clinical parameters and respective references. A tabular presentation is recommended.]

#### Utility values for health economic evaluation

[Use this chapter only if QALYs were determined in the health economic evaluation.]

[Please describe methods used to obtain utilities, including method of elicitation, method of valuation, population, instrument, underlying survey or clinical trial. Please provide further details on how adverse events are incorporated in the utilities. If applicable, also describe how and why utilities used in the models have been adjusted.]

[Summarise utilities chosen for the model, including uncertainty (e.g. confidence interval), in a tabular form. Justify your choice and referencing the source of the utilities or the relating section in the HTA Report.]

#### Resource use and cost parameters

[Costing processes can usefully be divided into three phases: First, the relevant resources used have to be identified, secondly, the volume or number of units of the resource used has to be measured and, finally, these volumes need to be valued.]

*Resource identification*

[Describe how relevant cost and health care resource data were identified. The respective approach or a combination of several approaches depends on the research question and the availability of data.]

[In the course of resource identification, determine the relevant types of resource use, which arise within the treatment of the target population.]

[The inclusion or exclusion of cost items depends upon the chosen perspective or analytical approach and may vary between jurisdictions or health systems.]

*Resource quantification*

To determine a quantity structure, the frequency of consumption, the proportion of the relevant patient population and duration of the resource utilization are collected.

*Resource valuation*

[Valuate the resource unit according to the requirements of national guidelines. Include co-payments and private payments for medical services separately.]

The table below reports the total costs per unit for each intervention and comparator intervention.

Table 3‑1: Unit costs of intervention and comparators

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Items** | **Intervention** | **Reference** | **Comparator 1** | **Reference** | **[…]** |
| [Item x] |  |  |  |  |  |
| [Item y] |  |  |  |  |  |
| […] |  |  |  |  |  |
| Adverse event 1 |  |  |  |  |  |
| […] |  |  |  |  |  |
| Total |  |  |  |  |  |

Table 3‑2: Unit costs of health states and adverse events

|  |  |  |  |
| --- | --- | --- | --- |
| **Health states / adverse events** | **Items** | **Value** | **Reference** |
| Health state 1 |  |  |  |
| […] |  |  |
| Total |  |  |
| […] |  |  |  |

#### Discounting

[Report the decisions regarding discounting with clear reasoning or justification and, where relevant, according to available, e.g., country-specific guidelines.]

#### Summary of base-case analysis inputs

[Tabulate all variables applied in the base-case analysis of the economic model, including the values used, range (e.g. confidence interval, distribution) and source.]

Table 3‑3: Summary of variables applied in the health economic evaluation.

|  |  |  |  |
| --- | --- | --- | --- |
| **Variable** | **Value** | **Uncertainty and distribution**  | **Reference or section in HTA-report** |
| [Cohort starting age] | [xy years] | [CI (normal)] | [section x] |
| [Effectiveness on overall survival] | [HR: xy] | [CI (lognormal)] |  |
| [Transition probability 1] | [xy %] | [CI (Beta)] |  |
| [Proportion of patients suffering a specific adverse event] | [xy %] | [CI (Beta)] |  |
| […] |  |  |  |
| CI: confidence interval |

[Provide a list of all model assumptions in the health economic evaluation and justify each assumption.]

#### Metrics of health economic evaluation

One or more of the following outcomes or approaches should be used and described when reporting the results of health-economic evaluations:

* Listing of costs and outcomes of each technology in tabular and graphical form. Cost parameters were combined as cost-offsets.
* An incremental cost-effectiveness ratio (ICER) for CEA and CUA
* An incremental cost-effectiveness plane or efficiency frontier for CEA and CUA
* The net health benefit (NHB) for CEA and CUA and / or net monetary benefit (NMB)]

*Willingness-to-Pay threshold*

[Whether a technology can be referred to as ‘cost-effective’ depends on its relation to any extant “decision-makers’ willingness-to-pay” or “societal willingness-to-pay” for an additional unit of health outcome (so-called ‘ICER threshold’). Please consider the information of national guidelines as well as, whether and to what amount a threshold is to be used and justify the threshold amount if applicable.]

#### Sensitivity analyses

[Describe the performed sensitivity analyses in a transparent and comprehensible way. Specifically, define and justify the parameters and parameter values used in the analyses and their underlying distributions.]

In order to examine the sensitivity of results, the following analyses were determined for different aspects of the health economic evaluation:

* deterministic univariate/multivariate sensitivity analyses for the parameters [XXX]
* probabilistic sensitivity analyses for the parameters [XXX]
* […]

[Please justify the parameters included in the specific sensitivity analysis.]

## Ethical aspects

[The identification of ethical aspects is less pre-determined and more variable than for example clinical effectiveness analyses. In addition, the findings are normally more context-depended and less transferable. Detailed information and recommendations are provided in the chapter “Ethical analysis” (ETH) of the HTA Core Model Version 3.0. The HTA Core Model Version 3.0 has been developed in EUnetHTA JA 2 (2012-2015) and has not been updated since. Please always check first whether there is a more recent methodological paper on the respective topic available.]

[The level of detail with which ethical aspects should be addressed is related to the ethical relevance of the technology under assessment. The more the technology presents new, severe or fundamental value conflicts, or challenges to everyday norms or beliefs, the more emphasis should be placed on the ethical analysis.]

### Information retrieval

[General information on the process of information retrieval is given in the EUnetHTA Methodological Guideline “Process of information retrieval for systematic reviews and health technology assessments on clinical effectiveness”. Furthermore, it is recommended to use the Summarised Research in Information Retrieval for HTA ([SuRe Info](http://vortal.htai.org/)) providing recommendations on information retrieval (e.g., search strategies).]

[For the analysis of ethical aspects, authors may choose from a wider range of information sources to cover the scope of this domain (such as bibliographical databases or moderated discussion with stakeholders). As such, the relevant search and information sources are selected project specific. The following list is to be understood as a proposal and therefore only exemplary. Please adapt and customize the following information sources to match the current assessment.]

The following information sources as well as search techniques could be considered to identify relevant studies or documents:

Main information sources [optional]

[Please include information on the name of databases or other of sources searches (e.g., registries, websites) and indicate whether any restrictions to your search are made (e.g., restrictions in language or study design etc.)]

* Bibliographic databases
* Data from national and regional registers
* Statements from laws, regulations or guidelines
* Information from stakeholders (e.g. websites)
* Additionally, identified studies for the assessment of clinical effectiveness and safety as well as for the assessment of costs and economic evaluation were examined for ethical aspects.

Moderated discussion with stakeholders [optional]

[For moderated discussions with stakeholders (e.g. affected persons or their representatives, healthcare professionals, industry) please include information on the interviewees and how (which method including rationale) they are involved in the identification of ethical aspects. Also explain how interviewees are identified and selected, how the discussion is recorded and transcribed, etc. Please provide any further details in the appendix (e.g. interview questions, questionnaire, compliance with requirements etc.)]

[Authors should refer to the recommendations on “[Patient Input in Relative Effectiveness Assessments](https://eunethta.eu/wp-content/uploads/2019/06/Final_290519_Patient-Input-in-REAs.pdf)” developed by the EUnetHTA Patients & Consumer / Health Care Provider Task Group.]

Further relevant information were retrieved by a moderated discussion / interviews with relevant stakeholders.

Own primary study [optional]

[If no relevant information can be identified through this aforementioned procedures and sufficient resources are available, a separate survey can also be carried out. For own primary research, please provide a short study protocol comprising information on the study type, study participants and research question, etc. Different kind of research techniques can be applied here including e.g., surveys, observation, or participant observation.]

### Selection of references

[Describe how the selection is performed, e.g. by how many persons, by means of a study selection tool etc.]

Identified documents were checked for statements on ethical arguments and aspects. The selection was performed by 2 persons independently of each other [Alternative: The selection was performed by one person and controlled by another person]. Discrepancies were resolved by discussion.

### Data extraction

[Describe briefly how data are extracted. Further information and recommendations on the extraction of data from included studies is given in the chapter “Ethical Aspects” (ETH) of the HTA Core Model Version 3.0. Regarding the extraction of quantitative data authors should refer to the SOP “Data Extraction” for information and recommendations. When extracting data from qualitative research, authors can use the table template for data extraction in . If deemed necessary, different templates can be used here provided they ensure a complete, correct, and transparent data extraction. If moderated discussions with stakeholders are conducted, please describe how data is extracted from transcripts.]

All relevant information was extracted from the documents into tables.

### Data analysis and synthesis

[Please describe how relevant data is analysed, identified and synthesized. Authors are encouraged to refer to the chapter “Ethnical aspects” (ETH) of the HTA Core Model Version 3.0 for recommendations and guidance for identifying ethical aspects. Adapt the generic text to reflect the methods that are both used and relevant for the identification of ethical aspects, such as casuistry, coherence analysis, principalism, social shaping of technology, wide reflective equilibrium, axiological (socratic) approach or interactive, participatory HTA approach.]

The information in the included documents were evaluated and synthesized by means of [method for identifying ethical aspects].

## Organisational aspects

[The identification of organisational aspects is less pre-determined and more variable than for example clinical effectiveness analyses. In addition, the findings are normally more context-depended and less transferable. Detailed information and recommendations are provided in the chapter “Organisational Aspects” (ORG) of the HTA Core Model Version 3.0. The HTA Core Model Version 3.0 has been developed in EUnetHTA JA 2 (2012-2015) and has not been updated since. Please always check first whether there is a more recent methodological paper on the respective topic available.]

[The level of detail with which organisational aspects should be assessed is dependent on the resources available. Ideally, a systematic review of organisational aspects of a technology is conducted.]

### Information retrieval

[General information on the process of information retrieval is given in the EUnetHTA Methodological Guideline “Process of information retrieval for systematic reviews and health technology assessments on clinical effectiveness”. Furthermore, it is recommended to use the Summarised Research in Information Retrieval for HTA ([SuRe Info](http://vortal.htai.org/)) providing recommendations on information retrieval (e.g., search strategies).]

[For the analysis of organisational aspects, authors may choose from a wider range of information sources to cover the scope of this domain (such as bibliographical databases or moderated discussion with stakeholders). As such, the relevant search and information sources are selected project specific. The following list is to be understood as a proposal and therefore only exemplary. Please adapt and customize the following information sources to match the current assessment.]

[The following information sources as well as search techniques could be considered to identify relevant studies or documents:]

Main information sources [optional]

[Please include information on the name of databases or other of sources searches (e.g., registries, websites) and indicate whether any restrictions to your search are made (e.g., restrictions in language or study design etc.)]

* Bibliographic databases
* Data from national and regional registers
* Statements from laws, regulations or guidelines
* Information from stakeholders (e.g. websites)
* Additionally, identified studies for the assessment of clinical effectiveness and safety as well as for the assessment of costs and economic evaluation were examined for organisational aspects.

Further information sources and search techniques [optional]

[For moderated discussions with stakeholders (e.g. affected persons or their representatives, healthcare professionals, industry) please include information on the interviewees and how (which method including rationale) they are involved in the identification of ethical aspects. Also explain how interviewees are identified and selected, how the discussion is recorded and transcribed, etc. Please provide any further details in the appendix (e.g. interview questions, questionnaire, compliance with requirements etc.)]

[Authors should refer to the recommendations on “[Patient Input in Relative Effectiveness Assessments](https://eunethta.eu/wp-content/uploads/2019/06/Final_290519_Patient-Input-in-REAs.pdf)” developed by the EUnetHTA Patients & Consumer / Health Care Provider Task Group.]

Further relevant information were retrieved by a moderated discussion with relevant stakeholders.

Own primary study [optional]

[If no relevant information can be identified through this aforementioned procedures and sufficient resources are available, a separate survey can also be carried out. For own primary research, please provide a short study protocol comprising information on the study type, study participants and research question, etc. Different kind of research techniques can be applied here including e.g., surveys, observation, or participant observation.]

### Selection of references

[Describe how the selection is performed, e.g. by how many persons, by means of a study selection tool etc. Please adapt the following section accordingly.]

Identified documents were checked for statements on organisational arguments and aspects. The selection was performed by 2 persons independently of each other [Alternative: The selection was performed by one person and controlled by another person]. Discrepancies were resolved by discussion.

### Data extraction

[Describe briefly how data is extracted. Further information and recommendations on the extraction of data from included studies is given in the chapter “Organisational Aspects” (ORG) of the HTA Core Model Version 3.0. Regarding the extraction of quantitative data authors should refer to the SOP “Data Extraction” for information and recommendations. When performing a systematic review of qualitative research, authors can use the table template for data extraction in Appendix . If deemed necessary, different templates can be used here provided they ensure a complete, correct, and transparent data extraction. If moderated discussions with stakeholders are conducted, please describe how data is extracted from transcripts.]

All relevant information was extracted from the documents into tables.

### Quality rating [optional]

[Whether a quality rating of the included studies is carried out and which instruments are used depends on the research question pursued in the domain and the information and study types considered. If a quality rating of the information is made, please briefly summarise in this section, which tools were used. If no quality rating is planned, please delete the current subchapter.]

[Assessment of quality of quantitative studies should follow the EUnetHTA Methodological Guidelines “Critical evaluation of clinical evaluations”, “Levels of Evidence - Internal validity of randomised controlled trials”, and “Internal validity of non-randomised studies (NRS) on interventions”. Furthermore, authors can refer to the SOP “Risk of Bias Assessment of Clinical Studies”. Additional information and recommendation on the quality assessment of evidence is provided in the chapter “Organisational Aspects” of the EUnetHTA Core Model.]

[For data collected through moderated discussions, quality of data collection and analysis should be assessed. A recommended tool for the assessment of quality of qualitative data can be CASP, Guidance recommended by the Cochrane Qualitative Research Methods Group[[8]](#footnote-9).]

[The following section can be used and modified to reflect the sources of information retrieval and data used for the assessment.]

The assessment of risk of bias for quantitative studies followed the criteria described in the two EUnetHTA guidelines on the internal validity of RCTs and non-randomised studies on interventions. The quality of qualitative studies was critically appraised by means of the tool [name of Quality tool] and followed the following guideline on qualitative research [name of guideline on qualitative research].

### Data analysis and synthesis

[Please describe how relevant data are analysed, identified and synthesized. Authors are encouraged to refer to the chapter “Organisational Aspects” (ORG) of the HTA Core Model Version 3.0 for recommendations and guidance on identifying organisational aspects. Adapt the generic text to reflect the methods that are used and relevant for the identification of organisational aspects, such as grounded theory or content analysis.]

The information in the included documents were evaluated and synthesized by means of [method for identifying organisational aspects.]

## Patients and social aspects

[The identification of patients and social aspects is less pre-determined and more variable than for example clinical effectiveness analyses. In addition, the findings are normally more context-depended and less transferable. Detailed information and recommendations are provided in the chapter “Patients and Social Aspects” (SOC) of the HTA Core Model Version 3.0. The HTA Core Model Version 3.0 has been developed in EUnetHTA JA 2 (2012-2015) and has not been updated since. Please always check first whether there is a more recent methodological paper on the respective topic available.]

[The level of detail with which patients and social aspects should be assessed is dependent on the resources available. Ideally, a systematic review of patients and social aspects of a technology is conducted.]

### Information retrieval

[General information on the process of information retrieval is given in the EUnetHTA Methodological Guideline “Process of information retrieval for systematic reviews and health technology assessments on clinical effectiveness”. Furthermore, it is recommended to use the Summarised Research in Information Retrieval for HTA ([SuRe Info](http://vortal.htai.org/)) providing recommendations on information retrieval (e.g., search strategies).]

[For the analysis of patients and social aspects, authors may choose from a wider range of information sources to cover the scope of this domain (such as bibliographical databases or moderated discussion with stakeholders). As such, the relevant search and information sources are selected project specific. The following list is to be understood as a proposal and therefore only exemplary. Please adapt and customize the following information sources to match the current assessment.]

The following information sources as well as search techniques could be considered to identify relevant studies or documents:

Main information sources

[Please include information on the name of databases or other of sources searches (e.g., registries, websites) and indicate whether any restrictions to your search are made (e.g., restrictions in language or study design etc.)]

* Bibliographic databases
* Data from national and regional registers
* Statements from laws, regulations or guidelines
* Information from stakeholders (e.g. websites)
* Additionally, identified studies for the assessment of clinical effectiveness and safety as well as for the assessment of costs and economic evaluation were examined for patient and social aspects.

Further information sources and search techniques [optional]

[For moderated discussions with patients, individuals and caregivers please include information on the interviewees and how (which method including rationale) they are involved in the identification of ethical aspects. Also, explain how interviewees are identified and selected, how the discussion is recorded and transcribed, etc. Please provide any further details in the appendix (e.g. interview questions, questionnaire, compliance with requirements etc.)]

[Authors should refer to the recommendations on “[Patient Input in Relative Effectiveness Assessments](https://eunethta.eu/wp-content/uploads/2019/06/Final_290519_Patient-Input-in-REAs.pdf)” developed by the EUnetHTA Patients & Consumer / Health Care Provider Task Group.]

Further relevant information were retrieved by a moderated discussion / interviews with patients, individuals and / or caregivers.

Own primary study [optional]

[If no relevant information can be identified through this aforementioned procedures and sufficient resources are available, a separate survey can also be carried out. For own primary research, please provide a short study protocol comprising information on the study type, study participants and research question, etc. Different kind of research techniques can be applied here including e.g., surveys, observation, or participant observation.]

### Selection of references

[Describe how the selection is performed, e.g. by how many persons, by means of a study selection tool etc. Please adapt the following section accordingly.]

Identified documents were checked for statements on patient and social aspects. The selection was performed by 2 persons independently of each other. [Alternative: The selection was performed by one person and controlled by another person]. Discrepancies were resolved by discussion.

### Data extraction

[Describe briefly how data is extracted. Regarding the extraction of quantitative data authors should refer to the SOP “Data Extraction” for information and recommendations. When performing a systematic review of qualitative research, authors can use the table template for data extraction in Appendix . If deemed necessary, different templates can be used here provided they ensure a complete, correct, and transparent data extraction. If moderated discussions with stakeholders are conducted, please describe how data is extracted from transcripts.]

All relevant information was extracted from the documents into tables.

### Quality rating [optional]

[Whether a quality rating of the included studies is carried out and which instruments are used depends on the research question pursued in the domain and the information and study types considered. If a quality rating of the information is made, please briefly summarise in this section, which tools were used. If no quality rating is planned, please delete the current subchapter.]

[Assessment of quality of quantitative studies should follow the EUnetHTA Methodological Guidelines “Critical evaluation of clinical evaluations”, “Levels of Evidence - Internal validity of randomised controlled trials”, and “Internal validity of non-randomised studies (NRS) on interventions”. Furthermore, authors can refer to the SOP “Risk of Bias Assessment of Clinical Studies”.]

[For data collected through moderated discussions, quality of data collection and analysis should be assessed. A recommended tool for the assessment of quality of qualitative data can be CASP, Guidance recommended by the Cochrane Qualitative Research Methods Group[[9]](#footnote-10).]

[The following section can be used and modified to reflect the sources of information retrieval and data used for the assessment.]

The assessment of risk of bias for quantitative studies followed the criteria described in the two EUnetHTA guidelines on the internal validity of RCTs and non-randomised studies on interventions. The assessment of risk of bias for qualitative studies was critically appraised by means of the tool [name of Quality tool] and followed the following guideline on qualitative research [name of guideline on qualitative research].

### Data analyses and synthesis

[Please describe how relevant data is analysed, identified and synthesized. Authors are encouraged to refer to the chapter “Patients and Social aspects” (SOC) of the HTA Core Model Version 3.0 for recommendations and guidance on identifying patient and social aspects. Adapt the generic text to reflect the methods that are used and relevant for the identification of patients and social aspects, such as the [system of the Joanna Briggs Institute](https://wiki.joannabriggs.org/display/MANUAL%29) or framework approach[[10]](#footnote-11).]

The information in the included documents were evaluated and synthesized by means of [method for identifying patient and social aspects].

## Legal aspects

### Information retrieval

[General information on the process of information retrieval is given in the EUnetHTA Methodological Guideline “Process of information retrieval for systematic reviews and health technology assessments on clinical effectiveness”. Furthermore, it is recommended to use the Summarised Research in Information Retrieval for HTA ([SuRe Info](http://vortal.htai.org/)) providing recommendations on information retrieval (e.g., search strategies).]

[The relevant search and information sources are selected project specific. The following list is to be understood as a proposal and therefore only exemplary. Please adapt and customize the following information sources to match the current assessment.]

The following information sources as well as search techniques could be considered to identify relevant studies or documents:

Information sources

[Please include information on the name of databases or other of sources searches (e.g., regulations) and indicate whether any restrictions to your search are made (e.g., restrictions in language or study design etc.)]

* Bibliographic databases
* Laws, regulations, judgements of courts or guidelines

### Selection of references

[Describe how the selection is performed, e.g. by how many persons, by means of a study se-lection tool etc. Please adapt the following section accordingly.]

Identified documents were checked for statements on legal arguments and aspects. The selection was performed by 2 persons independently of each other [Alternative: The selection was performed by one person and controlled by another person]. Discrepancies were resolved by discussion.

### Data extraction

[Describe briefly how data are extracted. Regarding the extraction of quantitative data authors should refer to the SOP “Data Extraction” for information and recommendations. When performing a systematic review of qualitative research, authors can use the table template for data extraction in Appendix . If deemed necessary, different templates can be used here provided they ensure a complete, correct, and transparent data extraction.]

All necessary information is extracted from the documents into a table.

### Data analyses and synthesis

[Please describe how relevant data are analysed and synthesized. Authors are encouraged to refer to the chapter “Legal aspects” (LEG) of the HTA Core Model Version 3.0 for recommendations and guidance on identifying legal aspects. The HTA Core Model Version 3.0 has been developed in EUnetHTA JA 2 (2012-2015) and has not been updated since. Please always check first whether there is a more recent methodological paper on the respective topic available. Adapt the generic text to reflect the methods that are used and relevant for the identification of legal aspects.]

The information in the included documents were evaluated and synthesized by means of [method of synthesizing information].

## Division of work within the project

[Please describe how the contributors to the assessment (members to the assessment team and external contributors) shared the work. Authors should refer to the SOP “Identification of Stakeholders” for guidance on the involvement of external parties].

## Deviations from project plan

[Indicate in this section whether deviations from the project plan have occurred during the assessment. Give a rationale for any deviations that have occurred.]

# Results: Clinical Effectiveness AND SAFETy

[This section should limit itself to the results (facts). Interpretation of the data should be included in the discussion section.]

[For all included studies, detailed information is compiled in tables. This includes for example information on study design, interventions, participants, outcomes, and results.]

## Information retrieval

[Distinguish between effectiveness and safety if necessary. It is mandatory to indicate the reasons for the exclusion of full-text articles with corresponding numbers of studies excluded.]

Figure 1 shows the result of the information retrieval in the main and further information sources based on the predefined inclusion criteria. References of the documents that have been checked in full-texts but were excluded are presented in Appendix with the respective reason for exclusion.

Records identified through database searching
(n = ##)

***Screening***

***Included***

***Eligibility***

***Identification***

Additional records identified through other sources
(n = ##)

Records after duplicates removed
(n = ##)

Records screened
(n = ##)

Records excluded
(n = ##)

Full-text articles assessed for eligibility
(n = ##)

Full-text articles excluded, with reasons
(n = ##)

**Exclusion criteria are e.g.:**

Background literature (n= ))##))

Other population (n = ##)

Not available (n = ##)

Not English / German / French / etc. (n = ##)

Etc.

Studies included in qualitative synthesis
(n = ##)

**E.g.,**

RCTs (n = ##)

Controlled clinical trials (n = ##)

Studies included in quantitative synthesis (meta-analysis)
(n = ##)

Figure 1: Flow chart of information retrieval for clinical effectiveness and safety

[Please adapt the following section to reflect the methods on information retrieval used.]

Information retrieval identified XX randomised trials (YY documents) as relevant for the research question. XX ongoing studies were identified. In addition, xx planned, ongoing, withdrawn and completed studies without results were identified. The last search took place at DD.MM.YYYY.

## Studies included in the assessment

[Give an overview of the included studies for the assessment. Under available documentation, list all references to published literature for the study and whether CSRs are available for assessment. Also provide a table with a list of ongoing or planned studies on the intervention.]

The studies listed in the following Table 4‑1 were included in the assessment.

Table 4‑1: Study pool– list of relevant studies used for the assessment

|  |  |  |
| --- | --- | --- |
| **Study reference / ID** | **Available** **documentsa** | **Study registry entries [Reference] / Result report from study registries** |
| Study reference / ID | [Insert citation(s)] | [Insert study registry numbers and citation] |
| Study reference / ID |  |  |
| AbbreviationsFootnotes: a: publications, reports, clinical study reports etc. |

The following Table 4‑2 lists all planned, ongoing, withdrawn and completed studies without results on the intervention.

Table 4‑2: List of planned, ongoing, withdrawn and completed studies without results on [name of technology]

| **Study reference/ID** | **Estimated completion date** | **Study type** | **Number of patients** | **Intervention** | **Comparator** | **Patient population** | **Endpoints** |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Study reference / ID |  |  |  |  |  |  |  |
| AbbreviationsFootnotes: |

## Description of the evidence used

[Use the table templates provided in the SOP on data extraction and follow the process of data extraction as described in the SOP. Columns in the tables can be added or removed to account for the trial design (e.g. number of comparators). Delete tables that are not needed.]

[Provide a description of the included studies (consider e.g. design, inclusion and exclusion criteria, prior therapy, relevant subpopulations (if applicable), stratification, countries conducted, details on interventions (dosing) including subsequent therapies, primary and secondary outcomes, data cut offs). Refer to the tables for details. Describe how the studies were used to answer the research question (e.g. as direct comparison or indirect evidence). Use the headers within the table of characteristics of the studies included to indicate for which comparison the studies were used.]

The following tables Table 4‑3, Table 4‑4, Table 4‑5, Table 4‑6, and Table 4‑7 describe the studies used for the assessment.

Table 4‑3: Characteristics of the studies included

| **Study reference/ID** | **Sites or regions, countries, time of study** | **Study type** | **Intervention [number of (randomised / enrolled) patients]** | **Comparator(s) [number of (randomised / enrolled) patients]** | **Patient population** | **Primary endpoint; patient-relevant secondary endpointsa** |
| --- | --- | --- | --- | --- | --- | --- |
| Study reference / ID | XX XXX 20XX | e.g. RCT, pros-pective cohort study  | Group 1 (N = XX)Relevant subpopulation:Group 1 (n = XX) | Group 2 (N = XX)Relevant subpopulation:Group 2 (n = XX) | relevant characteristics, e.g. degree of severity | Primary: Secondary: |
| N: number of randomised (included) patients; n: relevant subpopulation; RCT: randomised controlled triala: Primary endpoints contain information without consideration of its relevance for this assessment. Secondary endpoints contain exclusively information on the relevant available outcomes for this assessment |

Table 4‑4: Characteristics of the included diagnostic accuracy studies

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Study reference / ID** | **Study type** | **Number of patients** | **Evidence level** | **Sites, countries, time of study** | **Diagnostic accuracy measures** |
| Study reference / ID |  |  |  |  | sensitivity, specificity, false-negative, false-positive rate |
| AbbreviationsFootnotes: |

Table 4‑5: Inclusion and exclusion criteria

|  |  |  |
| --- | --- | --- |
| **Study reference/ID** | Inclusion criteria | Exclusion criteria |
| Study reference / ID |  |  |
| AbbreviationsFootnotes: |

Table 4‑6: Characterisation of the interventions

|  |  |  |  |
| --- | --- | --- | --- |
| Study reference / ID | Intervention | Comparator | Possible additional column with treatment characteristicse.g. pre-treatment, treatment , prohibited medications |
| Study reference / ID |  |  |  |
| AbbreviationsFootnotes |

Table 4‑7: Characteristic of index test and reference standard

|  |  |  |
| --- | --- | --- |
| Study reference / ID | Index test | Reference standard |
| Study reference / ID |  |  |
| AbbreviationsFootnotes |

[Provide here a brief description of characteristics of the study populations. Use the table templates provided in the SOP “Data Extraction” and follow the process of data extraction as described in the SOP. In the text, describe also data on treatment and study discontinuation (e.g. lost to follow up). Add or delete columns if necessary.]

The following Table 4‑8 shows the characteristics of the patients in the studies included.

Table 4‑8: Baseline characteristics of the study population

| Study reference / IDCharacteristicsCategory | Intervention | Comparator |
| --- | --- | --- |
| Study reference / ID | Na = | Na = |
| Age [years], mean (SD) |  |  |
| Gender [f / m], % |  |  |
| ethnicity |  |  |
| more characteristics, n (%) |  |  |
| e.g. disease duration |  |  |
| e.g. stage |  |  |
| e.g. comorbidities |  |  |
| Treatment discontinuation, n (%) |  |  |
| Study discontinuation, n (%) |  |  |
| f: female; m: male; n: number of patients in the category; N: number of patients; ND: no data; RCT: randomised controlled trial; SD: standard deviation; vs.: versusa: Number of randomised patients. Values that are based on other patient numbers are marked in the corresponding line if the deviation is relevant |

## Outcomes included

[This section can be used to illustrate which outcomes (according to the project plan) from each study have been included in the analysis. When there is no great complexity in studies and outcomes, it can be considered not to include this section.]

[Use the table „matrix of outcomes“ provided in the SOP “Data Extraction”.]

The following Table 4‑9 shows for which of the outcomes to be included in the assessment data were available in the studies included.

Table 4‑9: Matrix of outcomes in the included studies to be assessed

|  |  |
| --- | --- |
| Study reference / ID | Outcomes |
|  | **Mortality** | **Morbidity outcomes**  | **Symptoms ()** | **Health-related quality of life (EQ-5D)** | **Pain (VAS)** | **Treatment discontinuation due to AE**  | **Serious AE** | **Specific AE** |
| Study reference / ID | Y / N | Y / N | Y / N | Y / N | Y / N | Y / N | Y / N | Y / N |
| AE: adverse event; EQ-5D: European Quality of Life-5 Dimensions; VAS: visual analogue scaleFootnotes: Yes / No |

## Risk of bias assessment

[Add here the results of any assessment of risk of bias of the studies included at the study level and for the relevant outcomes. Use tables provided in the SOP “Risk of Bias Assessment of Clinical Studies” (for RCT or non-RCT). See also the EUnetHTA guidelines: “Level of evidence: Internal validity of randomised controlled trials”, “Internal validity of non-randomised studies” and “Meta-Analysis of Diagnostic Test Accuracy Studies” for further information and recommendation on quality appraisal of RCTs, non-randomised and observational studies as well as diagnostic test accuracy studies.]

[Differentiate between outcomes if necessary (e.g. if for different outcomes different approaches were used/different judgement is made on blinding, ITT/PP analysis or incomplete outcome data). In that case, additional columns can be added to the RoB table (the template table provides an example on this regarding blinding). Provide a clear explanation for judgements. Make sure to summarise the risk of bias per outcome per study and across studies (in case of pooling of results). When, for non-randomised trials, the ROBINS-I tool was included, add the checklist as an appendix to the assessment.]

[For the evaluation of other study types (including case-series or modelling studies), please refer to the EUnetHTA Methodological Guideline “Therapeutic medical devices” for further information.]

The following tables Table 4‑10, Table 4‑11, Table 4‑12 and Table 4‑13 describe the risk of bias at the study level and for the relevant outcomes.

Table 4‑10: Risk of bias in randomised studies at the study level

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Study reference / ID | **Adequate generation of randomisation sequence** | **Adequate allocation concealment** | **Blinding** | **Selective outcome reporting unlikely** | **No other aspects increasing risk of bias** | **Risk of bias – study level** |
| Patient | Treating person |
| Study reference / ID | Y / N / U | Y / N / U | Y / N / U | Y / N / U | Y / N / U | Y / N / U | L / H |
| Study reference / ID |  |  |  |  |  |  |  |
| Footnotes: Yes / No / UnclearLow Risk / High RiskIf unclear or high, give reasons for the classification |

Table 4‑11: Risk of bias in randomised studies for relevant outcomes

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **Endpoint**Study reference / ID  | **Risk of bias – study level** | **Blinding – outcome assessors** | **ITT principle adequately realized**  | **Selective outcome reporting unlikely** | **No other aspects increasing risk of bias** | **Risk of bias – outcome level** |
| **Overall mortality** |
| Study reference / ID | L / H | Y / N / U | Y / N / U | Y / N / U | Y / N / U | L / H |
| Study reference / ID |  |  |  |  |  |  |
| **Health-related quality of life** |
| Study reference / ID |  |  |  |  |  |  |
| Study reference / ID |  |  |  |  |  |  |
| **Outcome X** |
| Study reference / ID |  |  |  |  |  |  |
| Study reference / ID |  |  |  |  |  |  |
| Footnotes: Yes / No / UnclearLow Risk / High Risk[If unclear or high, give reasons for the classification (mandatory)] |

Table 4‑12: Risk of bias in non-randomised / observational studies for relevant outcomes

| **Endpoint**Study reference / ID | **Bias due to confounding**  | **Bias in selection of participants into the study** | **Bias in classification of interventions** | **Bias due to deviations from intended interventions** | **Bias due to missing data** | **Bias in measurement of outcomes** | **Bias in selection of the reported result**  | **Overall bias** |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Overall survival** |
| Study reference / ID | L / M / S / C / NI | L / M / S / C / NI | L / M / S / C / NI | L / M / S / C / NI | L / M / S / C / NI | L / M / S / C / NI | L / M / S / C / NI | L / M / S / C / NI |
| **Health-related quality of life** |
| Study reference / ID |  |  |  |  |  |  |  |  |
| **Outcome X** |
| Study reference / ID |  |  |  |  |  |  |  |  |
| Footnotes: Low / Moderate / Serious / Critical / No information[if Serious or critical risk, give reasons for the classification (mandatory)] |

Table 4‑13: Risk of bias in diagnostic accuracy studies

|  |  |  |
| --- | --- | --- |
| **Study reference / ID** | **Risk of Bias** | **Applicability concerns** |
| **Patient selection(Domain 1)** | **Index test(Domain 2)** | **Reference standard (Domain 3)** | **Flow and timing (Domain 4)** | **Patient selection(Domain 1)** | **Index test(Domain 2)** | **Reference standard (Domain 3)** |
| Study reference / ID | L / H / U | L / H / U | L / H / U | L / H / U | L / H / U | L / H / U | L / H / U |
| Footnotes: Low / High / Unclear[if Unclear or High risk, give reasons for the classification (mandatory)] |

## External validity

[Explain the relation to the PICO (external validity). Add a justification for each judgement made. Recommendations on how to assess external validity are provided in the EUnetHTA Methodological guidelines “Levels of Evidence - Applicability of evidence for the context of a relative effectiveness assessment”. If a GRADE assessment is applied, the authors should consider that an assessment of both risk of bias and applicability (called “indirectness” in the GRADE terminology) are part of the GRADE assessment. Authors should consider the recommendations by the EUnetHTA Task Group on Common Phrases and GRADE (these recommendations will need to be transferred into guidelines and SOPs after EUnetHTA JA3 prior to their implementation). It is recommended to provide a summary characterising the applicability of studies in the following Table 4‑14.]

Table 4‑14: Summary table characterising the applicability of a body of studies

| **Domain** | **Description of applicability of evidence** |
| --- | --- |
| Population | Describe general characteristics of enrolled populations, how this might differ from target population, and effects on baseline risk for benefits or harms. Where possible, describe the proportion with characteristics potentially affecting applicability (e.g. % over age 65) rather than the range or average. |
| Intervention | Describe general characteristics, range of interventions and how they compare to those in routine use and how this might affect benefits or harms from the intervention. |
| Comparators | Describe comparators used. Describe whether they reflect best alternative treatment and how this may influence treatment effect size. |
| Outcomes | Describe what outcomes are most frequently reported and over what time period. Describe whether the measured outcomes and time of measurement reflect the most important clinical benefits and harms. |
| Setting | Describe geographic and clinical setting of studies. Describe whether or not they reflect the settings in which the intervention will be typically used and how this may influence the assessment of intervention effect. |

## Results on clinical effectiveness and safety

HTA CORE MODEL DOMAIN: EFF & SAF[[11]](#footnote-12)

[Use the table templates provided below for dichotomous, continuous or time to event outcomes (if applicable) and follow the process of data extraction as described in the SOP “Data Extraction”. Please adjust the tables to reflect the study type by adding/removing/adapting columns.]

[Describe the effects of the interventions in comparison with the comparators for each outcome per study and pooled estimates of meta-analysis if appropriate. In case of meta-analysis, justify the choice of the model used and assess any heterogeneity and provide the I2 and associated p-value. Include results on mortality, morbidity, HrQoL, and adverse events (or state when missing). Also include results on test accuracy (if appropriate), body functions, activities of daily living, and patient satisfaction. Use single subchapters for each outcome.]

[Use the text for a description of the results and findings but refer to the tables where possible. Add figures (e.g. forest plots, Kaplan-Meier curves) if applicable. If necessary, tables can be added for relevant subgroups (provide clear header explicitly stating that it concerns a subgroup analysis) or sensitivity analyses.]

[If GRADE is used, insert GRADE evidence profile table and provide judgements in the footnotes. Alternatively, a summary of findings table can be presented here with the GRADE evidence profile table in an appendix (see Appendix ).]

Table 4‑15 [and Table 4‑16, Table 4‑17, Table 4‑18, and Table 4‑19] summarise the results of the comparison of [intervention] with [comparator] in [indication].

Table 4‑15: Results for outcome (dichotomous)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Study reference / ID | Operationalization | Intervention | Comparator | Intervention vs. Comparator |
| **N** | **n (%)** | **N** | **n (%)** | **RR/OR [95% -CI]; (p-value)** |
| Study reference / ID |  |  |  |  |  |  |
| CI: confidence interval; N: number of analysed patients; n: number of patients with (at least one) event; ND: no data; OR: odds ratio; RR: relative risk; vs.: versusFootnotes: |

Table 4‑16: Results for outcome (continuous)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Study reference / ID | Operationalization | Intervention | Comparator | Intervention vs. Comparator  |
| N | Values at start of study Mean/Median (SD) | Change at end of treatment Mean/Median (SD) | N | Values at start of studyMean/Median (SD) | Change at end of treatment Mean/Median (SD) | MD/SMD [95%-CI];(p-value) |
| Study reference / ID |  |  |  |  |  |  |  |  |
| CI: confidence interval; MD: mean difference; N: number of analysed patients; ND: no data; RCT: randomised controlled trial; SD: standard deviation; SMD: squared mean difference; vs.: versusFootnotes: |

Table 4‑17: Results for outcome (time to event)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Study reference / ID | Operationalization | Intervention | Comparator | Intervention vs. Comparator  |
| N | Median time to event in months/weeks [95%-CI] Patients with event n (%) | N | Median time to event in months/weeks [95%-CI]Patients with event n (%) | HR [95%-CI]; (p-value) |
| Study reference / ID |  |  |  |  |  |  |
| CI: confidence interval; HR: hazard ratio; N: number of analysed patients; n: number of patients with (at least one) event; NA: not achieved; NC: not calculable; vs.: versusFootnotes: |

Table 4‑18: Results summary for diagnostic accuracy studies

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Study reference / ID | N | n | Index test | Cut-off | Reference standard | Cut- off | TP | FN | FP | TN | Sensitivity in %[95 %-CI] | Specificity in % [95 %-CI] |
| Study reference / ID |  |  |  |  |  |  |  |  |  |  |  |  |
| FN: false negative; FP: false positive; CI: confidence interval; N: number of included participants; n: number of evaluated participants; NIPT: non-invasive prenatal testing; TN: true negative; TP: true positiveFootnotes: |

Table 4‑19: Frequency and severity of adverse events

| Study [X] |
| --- |
| System organ/class/adverse events | Frequency (very common, common, uncommon, rare, very rare, not known | All grades | Grades ≥ 3 |
| Intervention (n = x)n (%) | Comparator (n = x)n (%) | RR (95% CI)  | RD (95% CI) | Intervention (n = x)n (%) | Comparator (n = x)n (%) | RR (95% CI)  | RD (95% CI) |
| Class 1 (for example, nervous system disorders) |
| Adverse event 1 |  |  |  |  |  |  |  |  |  |
| Adverse event 2 |  |  |  |  |  |  |  |  |  |
| Class 2 (for example, vascular disorders) |
| Adverse event 3 |  |  |  |  |  |  |  |  |  |
| Adverse event 4 |  |  |  |  |  |  |  |  |  |
| Total serious adverse eventsn (%) |  | - | - | - |  |  |  |  |  |
| Total deathsn (%) |  | - | - | - |  |  |  |  |  |
| CI: confidence interval; RR: Relative Risk; RD: Risk Difference Footnotes: Presentation of adverse events follows the Common Terminology Criteria of Adverse Events (CTCAE) |

### Subgroup analyses

HTA CORE MODEL DOMAIN: EFF & SAF[[12]](#footnote-13)

[Describe the results for subgroups relevant for the assessment. Add forest plots or Kaplan-Meier curves if applicable/available. For result presentation use the table provided in the SOP “Data Extraction”.]

## Patient involvement

[Summarise the main results and conclusion of the patient involvement.]

## Summary

[In this section, the evidence on clinical effectiveness and safety of the technology should be summarised and put in context with regard to the research question. For that end, the findings across endpoints should be evaluated (incl. an interpretation of the quality of the evidence) and summarised so that a concluding statement on the benefit and harms profile of the intervention can be given.]

# Results: costs and economic evaluation

[Two approaches[[13]](#footnote-14) are typically used in answering the research questions in this domain:]

* [review of published economic evidence]
* [de novo economic evaluation]

[Use at least one of these approaches (see section 5.1 or 5.2) for the economic evaluation. When providing a review of published economic evidence, determine the intervention costs, which include directly related costs to the intervention and its comparator, additionally.]

## Systematic review of health economic evaluations

### Information retrieval

Figure 2 shows the results of a focussed literature search in bibliographic databases and selection of relevant studies as required by the study inclusion criteria. The last search took place on TT.MM.20JJ.

References of reviewed full texts, which were excluded, as well as the reason for exclusion, can be found in Appendix .

Records identified through database searching
(n = ##)

***Screening***

***Included***

***Eligibility***

***Identification***

Additional records identified through other sources
(n = ##)

Records after duplicates removed
(n = ##)

Records screened
(n = ##)

Records excluded
(n = ##)

Full-text articles assessed for eligibility
(n = ##)

Full-text articles excluded, with reasons
(n = ##)

**Exclusion criteria are e.g.:**

Background literature (n= )

Other population (n = ##)

Not available (n = ##)

Not English / German / French / etc. (n = ##)

Etc.

Studies included
(n = ##)

Figure 2: Flow chart of information retrieval for health economic evaluation

### Resulting study pool

Overall, XX relevant studies were identified through various research steps (see Table 5‑1)

Table 5‑1: Overview of resulting study pool

|  |  |  |
| --- | --- | --- |
| **Study reference / ID** | **Available** **documentsa** | **Study registry entries [Reference] / Result report from study registries** |
| Study reference / ID | [Insert citation(s)] | [Insert study registry numbers and citation] |
| Study reference / ID |  |  |
| AbbreviationsFootnotes: a: publications, reports, clinical study reports etc. |

### Characteristics of studies included in the evaluation

Tables found in this section present characteristics of included studies, study data and relevant assumptions.

[Summarise the most relevant criteria for the assessment. If applicable, describe differences between studies. Information on the study pool provides an answer to the question of significant differences between studies. A possible non-compliance of the considered study pool with the overall study population has to be stated. To avoid redundancies, information provided in a table should not be described in a running text.]

**Study design**

[Use the following tables to characterise included studies. Tables, which are not applicable for the included study pool, can be omitted (i.e. Table 5‑6).]

Table 5‑2 shows study characteristics of included health economic evaluations.

Table 5‑2: Study characteristics

| Study | Study design and approach | Relevant characteristics of study population | Strategies | Country, health care context and perspective | OutcomeCost effectiveness | Discount rate | Time horizon | Study financing |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Intervention | Comparator |  |
| [Study] | [i.e. cost-effectiveness analysis/ decision-analytic model] |  |  |  | [i.e. incremental cost-effectiveness ratio (cost per QALY)] | [i.e. Sweden,Inpatient] |  |  |  |
|  | [cost effectiveness analysis/ health economic evaluation alongside a clinical trial] |  |  |  | [i.e. incremental cost effectiveness ratio(cost per avoided myocardial infarctions)] |  |  |  |  |
|  | [cost-consequences analysis] |  |  |  | not applicable |  |  |  |  |

[This table should additionally be used if the study is based on a health economic evaluation alongside a clinical trial]

Table 5‑3 shows study characteristics of concomitant health economic evaluations.

Table 5‑3: Study characteristics of the concomitant health economic evaluation

| Study | Study Type  | Inclusion criteria | Randomisation procedure | Study duration | Dealing with uncertainty |
| --- | --- | --- | --- | --- | --- |
| [Study] | i.e. RCT |  |  |  | [i.e. deterministic / probabilistic sensitivity analyses] [considered parameter types (i.e. effect measure)] |

Table 5‑4 shows the parameters of the underlying model.

Table 5‑4: Model parameters

| Study | Modelling approaches  / model type | Number and Type of health conditions / events | Cycle length (when using markov models) /timeline | Assumptions | Handling of uncertainty / statements / assertions regarding model validation |
| --- | --- | --- | --- | --- | --- |
| [StudyXxx] | [i.e. Markov model] |  | [Lifetime (until age 80) / cycle i.e. 1 year] |  | [i.e. deterministic / probabilistic sensitivity analyses, considered parameter types (i.e. effect measure)] |

**Input parameters**

HTA CORE MODEL DOMAIN: ECO[[14]](#footnote-15)

Table 5‑5 shows data on clinical effectiveness incorporated into the model.

Table 5‑5: Clinical input parameters

| Study | Primary clinical outcome parameter | Effectiveness parameter inmodel | Reference |
| --- | --- | --- | --- |
| [Study xxx] |  |  | [i.e. calculations in model, systematic overview [Reference]] |

Table 5‑6 shows data on utilities, which was included in the studies.

Table 5‑6: Utility parameters

| Study | Utility parameter | Methods to elicit utilities | Discount rate | Reference |
| --- | --- | --- | --- | --- |
| [Study xxx] |  |  |  | i.e. secondary literature, own assessment |

Table 5‑7 shows data on costs, which was included/used in the studies.

Table 5‑7: Cost parameters

| Study | Currency(Index year) | Type of costs | Cost parameters [References](quantity and price) |
| --- | --- | --- | --- |
| [Study xxx] |  | [i.e. direct medical, direct non-medical, indirect] |  |

### Results of included health economic studies

HTA CORE MODEL DOMAIN: ECO[[15]](#footnote-16)

Results of included studies are shown in Table 5‑8. Calculated costs per patient and / or the incremental cost-effectiveness ratio are shown in the currency suitable and the index year as stated in the study. To enable a comparison of results of included studies, costs are (if necessary) converted into [national currency]. These costs are then inflated according to current national requirements, i.e. Harmonised Index of Consumer Prices (HICP).

[State the costs of the intervention per patient as well as the incremental cost-effectiveness ratios as described in the studies. In addition, in brackets, present the costs converted into [national currency] and inflated. Present only data regarding the intervention and comparator relating to the present research question, regardless of further interventions, which might have been explored in the study. Notice: If reported, present absolute costs and clinical effectiveness per patient. If only incremental costs and effectiveness are presented in the study, state them.]

Table 5‑8: Results of included health economic studies

| Study | Absolute costs of the interventions per patient (extent of uncertainty if given) | Incremental costs of intervention per patient (extent of uncertainty if given) | Absolute health outcome per patient (extent of uncertainty if given) | Incremental health outcome per patient (extent of uncertainty if given) | Incremental cost-effectiveness ratio per patient | Threshold used  | Conclusions of the authors |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Study xxx |  |  |  |  |  |  |

[Summarise the results of the sensitivity analyses.]

### Assessment of the reporting quality and transferability

HTA CORE MODEL DOMAIN: ECO[[16]](#footnote-17)

**Reporting quality**

[Please summarize the results of the assessment of the reporting quality in the included studies. Therefore, you can use the tabular presentation in the appendix (xxx). The purpose of this catalogue of criteria is to identify differences between the included studies for example regarding the methodological approach and its underlying references, also whether they had an impact on results. Not every criteria has to be justified. Greyed out sections can largely be omitted.]

**Transferability**

[Please summarise the assessment of transferability of included studies.]

### Intervention Costs

HTA CORE MODEL DOMAIN: ECO[[17]](#footnote-18)

[When providing a review of published economic evidence, an additional determination of the intervention costs, which include directly related costs to the intervention and its comparator can be helpful to capture national costs of the intervention and its comparator(s). In addition, take all accompanying services of the utilization into account and describe all components of services for the intervention and comparator. Should a therapy last longer than a year, specify the average costs per patient per year. Furthermore, separately list the refundable and non-refundable costs as well as co-payments as far as possible.]

Table 5‑9 shows the costs of the intervention and the comparator(s) per application including additional health care services.

Table 5‑9: Costs of the intervention and comparator(s)

|  |  |
| --- | --- |
|  | [Patient Group] |
| [Technology] | cost item according to relevant reimbursement catalogue | Costs per application in [national currency] | Number of applications per year | Source / Reference year | Reimbursability |
| Intervention | [i.e. DRG-code] |  |  |  | [yes/no] |
|  | […] |  |  |  |  |
| Total Cost |  |  |  |  |  |
| Comparator [1] |  |  |  |  |  |
|  | […] |  |  |  |  |
| Total Cost |  |  |  |  |  |
| Comparator [2] |  |  |  |  |  |
|  | […] |  |  |  |  |
| Total Cost |  |  |  |  |  |

Table 5‑10 shows co-payments associated with the application of the intervention and comparators as well as additionally necessary services.

Table 5‑10: Co-Payments

|  |  |
| --- | --- |
|  | [Patient Group] |
| [Description of co-payment] | Unit | Co-payment per unit in [national currency] | Units per year  | Source /Reference year |
| [Type of co-payment] |  |  |  |  |

## Results of de novo Health Economic Evaluations

### Base-case results

HTA CORE MODEL DOMAIN: ECO[[18]](#footnote-19)

[Summarise the absolute clinical effectiveness and costs per patient and the incremental costs-effectiveness ratio per patient in the table below. Add figures depending on the defined outcome of the health economic evaluation.]

Results of the health economic evaluation are shown in Table 5‑11.

Table 5‑11: Results of the health economic evaluation

| Technologies | Costs per patient | Incremental costs of intervention per patient | Health outcome per patient | Incremental health outcome per patient  | Incremental cost-effectiveness ratio per patient  |
| --- | --- | --- | --- | --- | --- |
| [Intervention] |  |  |  |  |  |
| [Comparator A] |  |  |  |  |  |
| […] |  |  |  |  |  |

##

### Results of the sensitivity analysis

HTA CORE MODEL DOMAIN: ECO[[19]](#footnote-20)

[Describe the results of all transparently conducted sensitivity analyses and show the results also graphically. Please consider national guidelines and the EUnetHTA guidelines “Methods for health economic evaluations” and “Practical considerations when critically assessing economic evaluations”.]

## Summary and discussion

HTA CORE MODEL DOMAIN: ECO[[20]](#footnote-21)

[In this section, the evidence on health economics of the technology should be summarised und put in context with regard to the research question. For that end, the findings be evaluated and summarised. Discuss the results of the systematic review or the de novo health economic evaluation and make the limitations of the modelling undertaken as clear as possible. Consider aspects of uncertainty, heterogeneity and transferability of this domain.]

# Results: Ethical aspects

## Information retrieval

[The results of information retrieval should provide information on all search sources mentioned in Section 3.3.1. Please use and adapt the following subchapters accordingly].

### Main information sources [optional]

[If a systematic search in bibliographical databases was performed, please insert the following section. A flow chart on information retrieval can be given if deemed helpful, but is not mandatory.]

Figure 3 shows the result of the information retrieval in the main information sources based on the predefined inclusion criteria (see section 2). The last search took place at DD.MM.YYYY. References of the documents that have been checked in full-texts but were excluded are presented in Appendix with the respective reason for exclusion.

Records identified through database searching
(n = ##)

***Screening***

***Included***

***Eligibility***

***Identification***

Records after duplicates removed
(n = ##)

Records screened
(n = ##)

Records excluded
(n = ##)

Full-text articles assessed for eligibility
(n = ##)

Full-text articles excluded, with reasons
(n = ##)

**Exclusion criteria are e.g.:**

Other population (n = ##)

Other intervention (n = ##)

No ethical aspects (n= ##)

Not available (n = ##)

Not English / German / French / etc. (n = ##)

Etc.

Documents included
(n = ##)

Additional records identified through other sources
(n = ##)

Figure 3: Flow chart of information retrieval for ethical aspects

### Moderated discussion with stakeholders [optional]

[If stakeholders (e.g., affected persons or their representatives, healthcare professionals, industry) were consulted, please insert the following section.]

In addition, stakeholders were consulted on their perspectives. Table 6‑1 lists all stakeholders that were identified for the intervention under assessment.

[Please present function/role of the stakeholder and his/her personal relation to the technology under assessment. There is no naming of persons.]

Table 6‑1: List of stakeholders

|  |  |
| --- | --- |
| Stakeholder | Relation to intervention under assessment |
| [e.g. legal guardian] | [e.g., legal representative of person directly affected]  |
|  |  |

[Please provide information on the moderated discussion: Which stakeholders participated? What were the key data of the moderated discussion or interviews (place, date and duration)? In-depth information (e.g. interview questions, questionnaire, compliance with requirements etc.) should be provided in Appendix .]

The moderated discussion was held on DD.MM.YYYY. The following stakeholders participated in the moderated discussion: [name stakeholders incl. function/role]. [Alternatively: In the period from DD.MM.YYYY to DD.MM.YYYY moderated discussions were conducted with the following stakeholders [name stakeholders here.] The duration of the moderated discussion was [X] hours. Relevant passages from the moderated discussion were written down and entered in an extraction table (see Appendix ).

### Own primary study [optional]

[If own primary research was performed, please provide short information on the period the study was conducted and the investigators. Further characteristics of the study is given in chapter 6.2.1.]

## Included documents / references

[Give an overview of the documents / references used for the identification of ethical aspects by providing a table with a list of identified documents.]

Information retrieval identified XX references as relevant for the identification of ethical aspects. The identified references are listed in the following Table 6‑2.

Table 6‑2: Document pool– list of relevant documents used for the identification of ethical aspects

|  |  |  |
| --- | --- | --- |
| **Document name**  | **Source** | **[Reference]** |
|  |  | [Insert citation(s)] |
|  |  |  |
| AbbreviationsFootnotes: |

### Description of the evidence used [optional]

[In the following section, the document pool is roughly characterised in continuous text. Thereby the included documents are characterised (e.g. "The documents included patients with the indication xx"). The document type can also be characterised. Each document can be described in a short continuous or in a tabular presentation.]

## Identified aspects

HTA CORE MODEL DOMAIN: ETH[[21]](#footnote-22)

[Give a brief overview of the identified aspects based on the bibliographic research and other information searches. The compilation and presentation of the identified aspects should follow the procedure described in section 3.3.4.]

[The identified ethical aspects can be presented in a short continuous text. In this case, a separate heading should be chosen for each identified ethical aspect.]

### Ethical aspect 1: [name ethical aspect here]

[Describe the ethical aspect and which documents provide information. The results for each aspect can also be presented in tabular form and summarised in a short continuous text. For example: “The documents [name documents here] provide information and results on the ethical aspect “XYZ”. First document [name of the document] shows that […].]]

### Ethical aspect 2: [name ethical aspect here]

Describe the ethical aspect and which documents provide information. The results for each aspect can also be presented in tabular form and summarised in a short continuous text. For ex-ample: “The documents [name documents here] provide information and results on the ethical aspect “XYZ”. First document [name of the document] shows that […].]]

[Alternatively, the identified aspects can be presented in tabular form. Two examples of tabular presentation are given below. The form of the presentation is the responsibility of the authors.]

Table 6‑3: Table of identified ethical arguments and aspects [optional]

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Stakeholder** | **Benefits when proceeding with implementation** | **Harms when proceeding** | **Benefits when refraining from implementation** | **Harms when refraining** |
| Patient | [citation(s)] | [citation(s)] | [citation(s)] | [citation(s)] |
| Family and important others |  |  |  |  |
| Healthcare professionals and providers |  |  |  |  |
| Society |  |  |  |  |
| Others |  |  |  |  |
| Abbreviations Footnotes: |

Table 6‑4: Table of identified ethical arguments and aspects [optional]

|  |  |
| --- | --- |
| **Identified aspect** | **References including explanation** |
|  |  |
|  |  |
| Abbreviations Footnotes: |

## Summary

[In this section, the evidence on ethical aspects should be briefly summarised and put in context with regard to the research question so that a concluding statement can be given.]

# Results: Organisational aspects

## Information retrieval

[The results of information retrieval should provide information on all search sources mentioned in Section 3.4.1. Please use and adapt the following subchapters accordingly].

### Main information sources [optional]

[If a systematic search in bibliographical databases was performed, please insert the following section. A flow chart on information retrieval can be given if deemed helpful, but is not mandatory.] ]

Figure 4 shows the result of the information retrieval in the main information sources based on the predefined inclusion criteria (see chapter 2). The last search took place at DD.MM.YYYY. References of the documents that have been checked in full-texts but were excluded are presented in Appendix with the respective reason for exclusion.

Records identified through database searching
(n = ##)

***Screening***

***Included***

***Eligibility***

***Identification***

Records after duplicates removed
(n = ##)

Records screened
(n = ##)

Records excluded
(n = ##)

Full-text articles assessed for eligibility
(n = ##)

Full-text articles excluded, with reasons
(n = ##)

**Exclusion criteria are e.g.:**

Other population (n = ##)

Other intervention (n = ##)

No organisational aspects (n= ##)

Not available (n = ##)

Not English / German / French / etc. (n = ##)

Etc.

Documents included
(n = ##)

Additional records identified through other sources
(n = ##)

Figure 4: Flow chart of information retrieval for organisational aspects

### Moderated discussion with stakeholders [optional]

[If stakeholders (e.g., affected persons or their representatives, healthcare professionals, industry) were consulted, please insert the following section.]

In addition, stakeholders were consulted on their perspectives. Table 7‑1 lists all stakeholders that were identified for the intervention under assessment.

[Please present function/role of the stakeholder and his/her personal relation to the technology under assessment. There is no naming of persons.]

Table 7‑1: List of stakeholders

|  |  |
| --- | --- |
| Stakeholder | Relation to intervention under assessment |
| [e.g. legal guardian] | [e.g., legal representative of person directly affected]  |
|  |  |

[Please provide information on the moderated discussion: Which stakeholders participated? What were the key data of the moderated discussion or interviews (place, date and duration)? In-depth information (e.g. interview questions, questionnaire, compliance with requirements etc.) should be provided in Appendix .]

The moderated discussion was held on DD.MM.YYYY. The following stakeholders participated in the moderated discussion: [name stakeholders]. [Alternatively: In the period from DD.MM.YYYY to DD.MM.YYYY moderated discussions were conducted with the following stakeholders [name stakeholders here.] The duration of the moderated discussion was [X] hours. Relevant passages from the moderated discussion were written down and entered in an extraction table (see Appendix ).

### Own primary study [optional]

[If own primary research was performed, please provide short information on the period the study was conducted and the investigators. Further characteristics of the study is given in chapter 7.2.1.]

### Search in further information sources [optional]

[If a search was carried out in further information sources (see section 3.4.1), please provide date or period of the search and the number of references found.]

## Included documents / references

[Give an overview of the documents / references used for the identification of organisational aspects by providing a table with a list of identified documents.]

Information retrieval identified XX references as relevant for the identification of organisational aspects. The identified references are listed in the following table

Table 7‑2.

Table 7‑2: Document pool– list of relevant documents used for the identification of organisational aspects

|  |  |  |
| --- | --- | --- |
| **Document name**  | **Source** | **[Reference]** |
|  |  | [Insert citation(s)] |
|  |  |  |
| AbbreviationsFootnotes: |

### Description of the evidence used [optional]

[In the following section, the document pool is roughly characterised in continuous text. Thereby the included documents are characterised (e.g. "The documents included patients with the indication xx"). The assessment of the document type and the study’s risk of bias is roughly characterised (e.g. "Study x was a case-control study; the risk of bias for the study was rated as low”). Each document can be described in a short continuous or in a tabular presentation.]

## Identified aspects

HTA CORE MODEL DOMAIN: ORG[[22]](#footnote-23)

[Give a brief overview of the aspects identified in the bibliographic research and other information searches. The compilation and presentation of the identified aspects should follow the procedure described in section 3.4.5 and should take into account an evaluation of identified aspects.]

[The identified organisational aspects can be presented in a short continuous text. In this case, a separate heading should be chosen for each identified ethical aspect.]

### Organisational aspect 1: [name organisational aspect here]

[Describe the organisational aspect and which document provides information. The results for each aspect can also be presented in tabular form and summarised in a short continuous text. For example: “The documents [name documents here] provide information and results on the organisational aspect “XYZ”. First document [name of the document] shows that […].]

### Organisational aspect 2: [name organisational aspect here]

[Describe the organisational aspect and which documents provide information. The results for each aspect can also be presented in tabular form and summarised in a short continuous text. For example: “The documents [name documents here] provide information and results on the organisational “XYZ”. First document [name of the document] shows that […].]

[Alternatively, the identified aspects can be presented in tabular form. An example of a tabular presentation is given below. The form of the presentation is the responsibility of the authors.]

Table 7‑3: Table of identified organisational aspects and key questions)

|  |  |
| --- | --- |
| **Key question** | **Example (incl. references)** |
| Influence on requirements for the provision of services | Change in the place of medical care | * outpatient versus inpatient service (insert citation)
 |
|  | Change in qualification requirements for service providers / additional or reduced personnel | * Need for training in the correct and safe use of new technology (insert citation)
 |
|  | Changes in the requirements for personnel, material, organization of service provision (structural quality) | * Need for special equipment to provide certain services (insert citation)
 |
| Influence on processes | Alternative technologies | * Drug vs. non-drug intervention (insert citation)
 |
|  | Use of health services / resources | * Change in the length of hospital stay (insert citation)
 |
|  | Types of communication and cooperation | * Changes in forms of communication (e.g. telemedicine) (insert citation)
 |
| Further aspects  | Stakeholders | * Who benefits from the introduction of a technology, who loses,etc. (insert citation)
 |
|  | Acceptance | * Resistance to the introduction by personnel (insert citation)
 |
|  | Planning of investments | * Clarification, who is responsible for investing in the establishment of a new technology (insert citation)
 |
| Abbreviations Footnotes: Table translated and adapted from Perleth[[23]](#footnote-24)  |

## Summary

[In this section, the evidence on organisational aspects should be briefly summarised and put in context with regard to the research question so that a concluding statement can be given.]

# Results: Patients and Social aspects

## Information retrieval

[The results of information retrieval should provide information on all search sources mentioned in Section 3.5.1. Please use and adapt the following subchapters accordingly].

### Main information sources [optional]

[If a systematic search in bibliographical databases was performed, please insert the following section. A flow chart on information retrieval can be given if deemed helpful, but is not mandatory.]

Figure 5 shows the result of the information retrieval in the main information sources based on the predefined inclusion criteria (see section 2). The last search took place at DD.MM.YYYY. References of the documents that have been checked in full-texts but were excluded are presented in Appendix with the respective reason for exclusion.

Records identified through database searching
(n = ##)

***Screening***

***Included***

***Eligibility***

***Identification***

Records after duplicates removed
(n = ##)

Records screened
(n = ##)

Records excluded
(n = ##)

Full-text articles assessed for eligibility
(n = ##)

Full-text articles excluded, with reasons
(n = ##)

**Exclusion criteria are e.g.:**

Other population (n = ##)

Other intervention (n = ##)

No patient and social aspects (n= ##)

Not available (n = ##)

Not English / German / French / etc. (n = ##)

Etc.

Documents included
(n = ##)

Additional records identified through other sources
(n = ##)

Figure 5: Flow chart of information retrieval for patients and social aspects

### Moderated discussion with patients, individuals and caregivers [optional]

[If patients, individuals and caregivers were consulted, please insert the following section.]

In addition, stakeholders were consulted on their perspectives. Table 8‑1 lists all stakeholders that were identified for the intervention under assessment.

[Please present function/role of the stakeholder and his/her personal relation to the intervention under assessment. There is no naming of persons.]

Table 8‑1: List of stakeholders

|  |  |
| --- | --- |
| Stakeholder | Relation to intervention under assessment |
| [e.g. legal guardian] | [e.g., legal representative of persons directly affected]  |
|  |  |

[Please provide information on the moderated discussion: Which stakeholders participated? What were the key data of the moderated discussion or interviews (place, date and duration)? In-depth information (e.g. interview questions, questionnaire, compliance with requirements etc.) should be provided in Appendix .]

The moderated discussion was held on DD.MM.YYYY. The following stakeholders participated in the moderated discussion: [name stakeholders]. [Alternatively: In the period from DD.MM.YYYY to DD.MM.YYYY moderated discussions were conducted with the following stakeholders [name stakeholders here.] The duration of the moderated discussion was [X] hours. Relevant passages from the moderated discussion were written down and entered in an extraction table (see Appendix ).

###  Own primary study [optional]

[If own primary research was performed, please provide short information on the period the study was conducted and the investigators. Further characteristics of the study is given in chapter 0.]

## Included documents / references

[Give an overview of the documents / references used for the identification of patients and social aspects by providing a table with a list of identified documents.]

Information retrieval identified XX references as relevant for the identification of patients and social aspects. The identified references are listed in the following Table 8‑2.

Table 8‑2: Document pool– list of relevant documents used for the identification of patients and social aspects

|  |  |  |
| --- | --- | --- |
| **Document name**  | **Source** | **[Reference]** |
|  |  | [Insert citation(s)] |
|  |  |  |
| AbbreviationsFootnotes: |

### Description of the evidence used

[In the following section, the document pool is roughly characterised in continuous text. Thereby the included documents are characterised (e.g. "The documents included patients with the indication xx"). The assessment of the document type and the study’s risk of bias is roughly characterised (e.g. "Study x was a case-control study; the risk of bias for the study was rated as low”). Each document can be described in a short continuous or in a tabular presentation.]

## Identified aspects

HTA CORE MODEL DOMAIN: SOC[[24]](#footnote-25)

[Give a brief overview of the aspects identified in the bibliographic research and other information searches. The compilation and presentation of the identified aspects should be based on the proposed aspects in section 3.5.5 and should take into account an evaluation of the included aspects.]

[The identified aspects can be presented in a short continuous text. In this case, a separate heading should be chosen for each identified aspect.]

### Patient and social aspect 1: [name patient and social aspect here]

[Describe the patient and social aspect and which documents provide information. The results for each aspect can also be presented in tabular form and summarised in a short continuous text. For example: “The documents [name documents here] provide information and results on the patients and social aspect “XYZ”. First document [name of the document] shows that […].]

### Patient and social aspect 2: [name patient and social aspect here]

[Describe the patient and social aspect and which documents provide information. The results for each aspect can also be presented in tabular form and summarised in a short continuous text. For example: “The documents [name documents here] provide information and results on the patients and social aspect “XYZ”. First document [name of the document] shows that […].]

## Summary

[In this section, the evidence on patients and social aspects should be briefly summarised and put in context with regard to the research question so that a concluding statement can be given.]

# Results: Legal aspects

## Information retrieval

[The results of information retrieval should provide information on all search sources mentioned in section 3.6.1. Please use and adapt the following subchapters accordingly].

### Main information sources

[If a systematic search in bibliographical databases was performed, please insert the following section. A flow chart on information retrieval can be given if deemed helpful, but is not mandatory. ]

Figure 6 shows the result of the information retrieval in the main information sources based on the predefined inclusion criteria (see section 2). The last search took place at DD.MM.YYYY. References of the documents that have been checked in full-texts but were excluded are presented in Appendix with the respective reason for exclusion.

Records identified through database searching
(n = ##)

***Screening***

***Included***

***Eligibility***

***Identification***

Records after duplicates removed
(n = ##)

Records screened
(n = ##)

Records excluded
(n = ##)

Full-text articles assessed for eligibility
(n = ##)

Full-text articles excluded, with reasons
(n = ##)

**Exclusion criteria are e.g.:**

Other population (n = ##)

Other intervention (n = ##)

No legal aspects (n= ##)

Not available (n = ##)

Not English / German / French / etc. (n = ##)

Etc.

Documents included
(n = ##)

Additional records identified through other sources
(n = ##)

Figure 6: Flow chart of information retrieval for legal aspects

## Included documents / references

[Give an overview of the documents / references used for the identification of legal aspects by providing a table with a list of identified documents.]

Information retrieval identified XX references as relevant for the identification of legal aspects. The identified references are listed in the following Table 9‑1.

Table 9‑1: Document pool– list of relevant documents used for the identification of legal aspects

|  |  |  |
| --- | --- | --- |
| **Document name**  | **Source** | **[Reference]** |
|  |  | [Insert citation(s)] |
|  |  |  |
| AbbreviationsFootnotes: |

### Description of the evidence used [optional]

[In the following section, the document pool is roughly characterised in continuous text. Thereby the included documents und document type are characterised (e.g. "[Reference X] is a patent describing […]"). Each document can be described in a short continuous or in a tabular presentation.]

## Identified aspects

HTA CORE MODEL DOMAIN: LEG[[25]](#footnote-26)

[Give a brief overview of the identified aspects based on the bibliographic research and further searches. The compilation and presentation of the identified aspects should follow the procedure described in section 3.6.4 taken into account the different levels of legislation, that is national, European and international legislation.]

[The identified legal aspects can be presented in a short continuous text. In this case, a separate heading should be chosen for each identified legal aspect.]

### Legal aspect 1: [name legal aspect here]

[Describe the legal aspect and which reference provides information. The results for each aspect can also be presented in tabular form and summarised in a short continuous text.]

### Legal aspect 2: [name legal aspect here]

[Describe the legal aspect and which reference provide information. The results for each aspect can also be presented in tabular form and summarised in a short continuous text.]

## Summary

[In this section, the evidence on legal aspects should be briefly summarised and put in context with regard to the research question so that a concluding statement can be given.]

# Discussion

[In this section, the domain-specific results are combined to form an overall result in the form of a continuous text. For this purpose, the following points should be considered and discussed: quality of evidence (including internal and external validity), relevance of evidence, interpretation of the outcomes and validity of the outcomes, and interpretation of the statistics. Furthermore, name evidence gaps (if found, also use and refer to the Appendix 5 on evidence gaps) and discuss strengths and limitations of the evidence (for example on methodological issues). Discuss patient involvement.]

# CONCLUDING SUMMARY

[The concluding summary comprises a brief answer to the research questions, a summary of the benefit assessment and a summary of the results of the economic, ethical, organisational, patient and social as well as legal domain.]

[State the factual conclusions on all domains and the quality/certainty of the evidence (e.g. internal and external validity).]

[Conclude on further research required.]

# REFERENCES

[The references must be displayed according to Vancouver style [<http://monash.edu/library/skills/resources/tutorials/citing/index.html>]. Citations within the text of the report are identified with a number in square brackets (e.g., [1]).]

[Use of a reference managing software is mandatory from the beginning (1st draft version for internal review by dedicated reviewers)! The team needs to agree on which common software they will use for the task.]

# Appendix 1: DOCUMENTATION OF THE SEARCH STRATEGIES

[Include detailed tables on searches conducted in databases, study registries and other sources. Complete search strategies should be presented for each source separately. The SOP “Information Retrieval” in the Companion Guide shall be consulted for further guidance.]

# Appendix 2: GUIDELINES FOR DIAGNOSIS AND MANAGEMENT

Table A1: Overview of guidelines

| Name of society / organisation issuing guidance | Date of issue | Country/ies to which applicable | Summary of recommendation | Level of evidence (A,B,C)/ class of recommendation (I, IIa, IIb, III) |
| --- | --- | --- | --- | --- |
|  |  |  |  |  |
| AbbreviationsFootnotes |

# Appendix 3: GRADE EVIDENCE PROFILE

Table A2: Template for GRADE assessment

(e.g., using GRADEproGDT)

| **Quality assessment** | **Summary of findings** | **Importance** |
| --- | --- | --- |
| **Number of patients** | **Effect**  | **Quality** |
| **Number of studies**  | **Study design** | **Risk of bias** | **Incon-sistency** | **Indirect-ness** | **Impres-sion** | **Other considera-tions** | **[inter-vention]** | **[compa-rison]** | **Relative (95% CI)** | **Absolute (95% CI)** |
| **Overall survival** |
|  | Randomised trial/ observational study | Not serious/ serious/ very seriousa | Not serious/ serious/ very serious a | Not serious/ serious/ very serious a | Not serious/ serious/ very serious a | Publication bias (undetected/ strongly suspected)Large effect (no/ large/ very large)Plausible confounding (no/ would reduce demonstrated effect/ would suggest spurious effect)Dose response gradient (no/ yes) |  |  |  |  | high/moderate/lowvery low | critical/important/not important |
| **[Outcome X]** |
|  |  | Not serious/ serious/ very serious | Not serious/ serious/ very serious | Not serious/ serious/ very serious | Not serious/ serious/ very serious |  |  |  |  |  | high/moderate/lowvery low | critical/important/ not important |
| AbbreviationsFootnotes: a: [If serious or very serious, please give reasons for the classification (mandatory)] |

# Appendix 4: LIST OF EXCLUDED STUDIES

Table A3: List of excluded studies (full text level) with reasons for exclusion)

Clinical effectiveness and safety

|  |  |
| --- | --- |
| **Reference** | **Main reason for exclusion (full text level)** |
| *[Insert reference]* | *[e.g. conference abstract, wrong population, wrong intervention etc.]* |

Health economics

|  |  |
| --- | --- |
| **Reference** | **Main reason for exclusion (full text level)** |
| *[Insert reference]* | *[e.g. conference abstract, wrong population, wrong intervention etc.]* |

Ethical aspects

|  |  |
| --- | --- |
| **Reference** | **Main reason for exclusion (full text level)** |
| *[Insert reference]* | *[e.g. conference abstract, wrong population, wrong intervention etc.]* |

Organisational aspects

|  |  |
| --- | --- |
| **Reference** | **Main reason for exclusion (full text level)** |
| *[Insert reference]* | *[e.g. conference abstract, wrong population, wrong intervention etc.]* |

Patients and social aspects

|  |  |
| --- | --- |
| **Reference** | **Main reason for exclusion (full text level)** |
| *[Insert reference]* | *[e.g. conference abstract, wrong population, wrong intervention etc.]* |

Legal aspects

|  |  |
| --- | --- |
| **Reference** | **Main reason for exclusion (full text level)** |
| *[Insert reference]* | *[e.g. conference abstract, wrong population, wrong intervention etc.]* |

# Appendix 5: EVIDENCE GAPS

Table A4: Table on evidence gaps

|  |
| --- |
| **Additional Evidence Generation Needs** |
| **Research question 1:** [Structured research question] |
| **Evidence** | [Current state of the evidence available / reasons for uncertainty] |
| **Population** | [Population and any sub-population(s)of interest] |
| **Intervention** | [The technology/ intervention and setting of use] |
| **Comparator** | [Relevant comparator and setting of use] |
| **Outcome(s)** | [Outcome(s) of interest] |
| **Time stamp** | [Date of recommendation] |
| **Study design** | [Appropriate study design] |
| **Ongoing studies** | [Study registry numbers of relevant ongoing studies, with the date when the search for ongoing studies was performedPlease delete the row if no ongoing studies have been identified] |
| **Research question 2:** [Structured research question] |
| **Evidence** | [Current state of the evidence available / reasons for uncertainty] |
| **Population** | [Population and any sub-population(s)of interest] |
| **Intervention** | [The technology/ intervention and setting of use] |
| **Comparator** | [Relevant comparator and setting of use] |
| **Outcome(s)** | [Outcome(s) of interest] |
| **Time stamp** | [Date of recommendation] |
| **Study design** | [Appropriate study design] |
| **Ongoing studies** | [Study registry numbers of relevant ongoing studies, with the date when the search for ongoing studies was performedPlease delete the row if no ongoing studies have been identified] |
| **Research question 3:** [Structured research question] [Make copies of the lines above, if needed] |
| AbbreviationsFootnotes |

# Appendix 6: REGULATORY AND REIMBURSEMENT STATUS

Table A5: Regulatory status

| **Country** | **Institution issuing approval** | **Authorisation status yes/no/ ongoing** | **Verbatim wording of the (anticipated) indication(s)** | **Specified contra-indications** | **Date of approval (include expiry date for country of assessment)** | **Launched yes/no****If no include date of launch** | **Approval number (if available)** |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
|  |  |  |  |  |  |  |  |
| AbbreviationsFootnotes |

Table A6: Summary of (reimbursement) recommendations in European countries for the technology

[For countries with indication specific reimbursement include only the recommendations for the indication under assessment. Include a reference to any publically available guidance document.]

| **Country and issuing organisation e.g. G-BA, NICE** | **Summary of (reimbursement) recommendations and restrictions** | **Summary of reasons for recommendations, rejections and restrictions** |
| --- | --- | --- |
|  |  |  |
| AbbreviationsFootnotes |

# Appendix 7: INFORMATION ON MODERATED DISCUSSION

[Please provide in-depth information on moderated discussions with stakeholders here (including interview questions, questionnaire, compliance with requirements etc.)]

Table A7: Relevant passages of moderated discussion with stakeholders

|  |  |  |
| --- | --- | --- |
| Relevant content / aspect | Stakeholder | Passage from moderated discussion / interview |
|  |  |  |
|  |  |  |

# Appendix 8: MISCELLANEOUS

Table A8: Documentation of queries to study authors in the assessment report

|  |  |  |  |
| --- | --- | --- | --- |
| **Study reference / ID** | **Content of query** | **Reply received y / n**  | **Content of reply** |
| Study reference / ID |  |  |  |
| AbbreviationsFootnotes: Yes / No  |

**For the purpose of transparency, a separate document with comments on the 2nd draft assessment from external experts and the manufacturer(s) (fact check), as well as responses from the author, is available on the EUnetHTA website.**

# Appendix 9: REPORTING OF QUALITY OF HEALTH ECONOMIC STUDIES

Table A9: Assessment of the reporting quality (e.g. with CHEERS checklist)

|  |  |  |  |
| --- | --- | --- | --- |
| **Section / item** | **Item No** | **Recommendation** | **Reported on page No / line No** |
| Title and abstract |
| Title | 1 | [Identify the study as an economic evaluation or use more specific terms such as ‘cost-effectiveness analysis’, and describe the interventions compared.] |  |
| Abstract | 2 | [Provide a structured summary of objectives, perspective, setting, methods (including study design and inputs), results (including base case and uncertainty analyses), and conclusions.] |  |
| Introduction |
| Background and objectives | 3 | [Provide an explicit statement of the broader context for the study. Present the study question and its relevance for health policy or practice decisions.] |  |
| Methods |
| Target population and subgroups | 4 | [Describe characteristics of the base case population and subgroups analysed, including why they were chosen.] |  |
| Setting and location | 5 | [State relevant aspects of the system(s) in which the decision(s) need(s) to be made.] |  |
| Study perspective | 6 | [Describe the perspective of the study and relate this to the costs being evaluated.] |  |
| Comparators | 7 | [Describe the interventions or strategies being compared and state why they were chosen.] |  |
| Time horizon | 8 | [State the time horizon(s) over which costs and consequences are being evaluated and say why appropriate] |  |
| Discount rate | 9 | [Report the choice of discount rate(s) used for costs and outcomes and say why appropriate.] |  |
| Choice of health outcomes | 10 | [Describe what outcomes were used as the measure(s) of benefit in the evaluation and their relevance for the type of analysis performed.] |  |
| Measurement of effectiveness | 11a | [Single study-based estimates: Describe fully the design features of the single effectiveness study and why the single study was a sufficient source of clinical effectiveness data.] |  |
| 11b | [Synthesis-based estimates: Describe fully the methods used for identification of included studies and synthesis of clinical effectiveness data.] |  |
| **Section / item** | **Item No** | **Recommendation** | **Reported on page No / line No** |
| Measurement and valuation of preference based outcomes | 12 | [If applicable, describe the population and methods used to elicit preferences for outcomes.] |  |
| Estimating resources and costs | 13a | [Single study-based economic evaluation: Describe approaches used to estimate resource use associated with the alternative interventions. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.] |  |
| 13b | [Model-based economic evaluation: Describe approaches and data sources used to estimate resource use associated with model health states. Describe primary or secondary research methods for valuing each resource item in terms of its unit cost. Describe any adjustments made to approximate to opportunity costs.] |  |
| Currency, price date, and conversion | 14 | [Report the dates of the estimated resource quantities and unit costs. Describe methods for adjusting estimated unit costs to the year of reported costs if necessary. Describe methods for converting costs into a common currency base and the exchange rate.] |  |
| Choice of model | 15 | [Describe and give reasons for the specific type of decision-analytical model used. Providing a figure to show model structure is strongly recommended.] |  |
| Assumptions | 16 | Describe all structural or other assumptions underpinning the decision-analytical model. |  |
| Analytical methods | 17 | [Describe all analytical methods supporting the evaluation. This could include methods for dealing with skewed, missing, or censored data; extrapolation methods; methods for pooling data; approaches to validate or make adjustments (such as half cycle corrections) to a model; and methods for handling population heterogeneity and uncertainty.] |  |
| Results |
| Study parameters | 18 | [Report the values, ranges, references, and, if used, probability distributions for all parameters. Report reasons or sources for distributions used to represent uncertainty where appropriate. Providing a table to show the input values is strongly recommended.] |  |
| Incremental costs andoutcomes | 19 | [For each intervention, report mean values for the main categories of estimated costs and outcomes of interest, as well as mean differences between the comparator groups. If applicable, report incremental cost-effectiveness ratios.] |  |
| Characterising uncertainty | 20a | [Single study-based economic evaluation: Describe the effects of sampling uncertainty for the estimated incremental cost and incremental effectiveness parameters, together with the impact of methodological assumptions (such as discount rate, study perspective).] |  |
| 20b | [Model-based economic evaluation: Describe the effects on the results of uncertainty for all input parameters, and uncertainty related to the structure of the model and assumptions.] |  |
| **Section / item** | **Item No** | **Recommendation** | **Reported on page No / line No** |
| Characterising heterogeneity | 21 | [If applicable, report differences in costs, outcomes, or cost-effectiveness that can be explained by variations between subgroups of patients with different baseline characteristics or other observed variability in effects that are not reducible by more information.] |  |
| Discussion |
| Study findings, limitations, generalisability, and current knowledge | 22 | [Summarise key study findings and describe how they support the conclusions reached. Discuss limitations and the generalisability of the findings and how the findings fit with current knowledge.] |  |
| Other |
| Source of funding | 23 | [Describe how the study was funded and the role of the funder in the identification, design, conduct, and reporting of the analysis. Describe other non-monetary sources of support.] |  |
| Conflicts of interest | 24 | [Describe any potential for conflict of interest of study contributors in accordance with journal policy. In the absence of a journal policy, we recommend authors comply with International Committee of Medical Journal Editors recommendations.] |  |
|  |

1. This section addresses the following assessment elements: [Name relevant addressed assessment elements here] [↑](#footnote-ref-2)
2. This section addresses the following assessment elements: [Name relevant addressed assessment elements here] [↑](#footnote-ref-3)
3. This section addresses the following assessment elements: [Name relevant addressed assessment elements here] [↑](#footnote-ref-4)
4. A critical review of an existing economic evaluation submitted by, e.g., a marketing authorisation holder (MAH), is not part of this template. Please consider information given in the chapter “Costs and economic evaluations” of the HTA Core Model and the Methodological guideline “Methods for health economic evaluations””. [↑](#footnote-ref-5)
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6. Drummond M, Barbieri M, Cook J, et al. Transferability of economic evaluations across jurisdictions: ISPOR good research practices task force report. Value Health. 2009;12(4):409‐418. [↑](#footnote-ref-7)
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11. This section addresses the following assessment elements: [Name relevant addressed assessment elements here] [↑](#footnote-ref-12)
12. This section addresses the following assessment elements: [Name relevant addressed assessment elements here] [↑](#footnote-ref-13)
13. A critical review of an existing economic evaluation submitted by, e.g., a marketing authorisation holder, is not part of this template. Please consider information given in the chapter “Costs and economic evaluations” of the HTA Core Model Version 3.0 and the Methodological guideline “Methods for health economic evaluations” and “Practical considerations when critically assessing economic evaluations”. [↑](#footnote-ref-14)
14. This section addresses the following assessment element: E0001, E0002, E0005, E0009, D0023, G0007. [↑](#footnote-ref-15)
15. This section addresses the following assessment element: E0006. [↑](#footnote-ref-16)
16. This section addresses the following assessment element: E00010, E0012, E0013 [↑](#footnote-ref-17)
17. This section addresses the following assessment element: E0001, E0002, E0009, D0023, G0007. [↑](#footnote-ref-18)
18. This section addresses the following assessment element: E0006. [↑](#footnote-ref-19)
19. This section addresses the following assessment element: E00010, E0011, E0013. [↑](#footnote-ref-20)
20. This section addresses the following assessment element: E00010, E0011, E0012, E0013. [↑](#footnote-ref-21)
21. This section addresses the following assessment elements:[Name relevant addressed assessment elements here] [↑](#footnote-ref-22)
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24. This section addresses the following assessment elements:[Name relevant addressed assessment elements here] [↑](#footnote-ref-25)
25. This section addresses the following assessment elements:[Name relevant addressed assessment elements here] [↑](#footnote-ref-26)