Work Package 7 – Subgroup 3:

Methodological guideline “Therapeutic medical devices”

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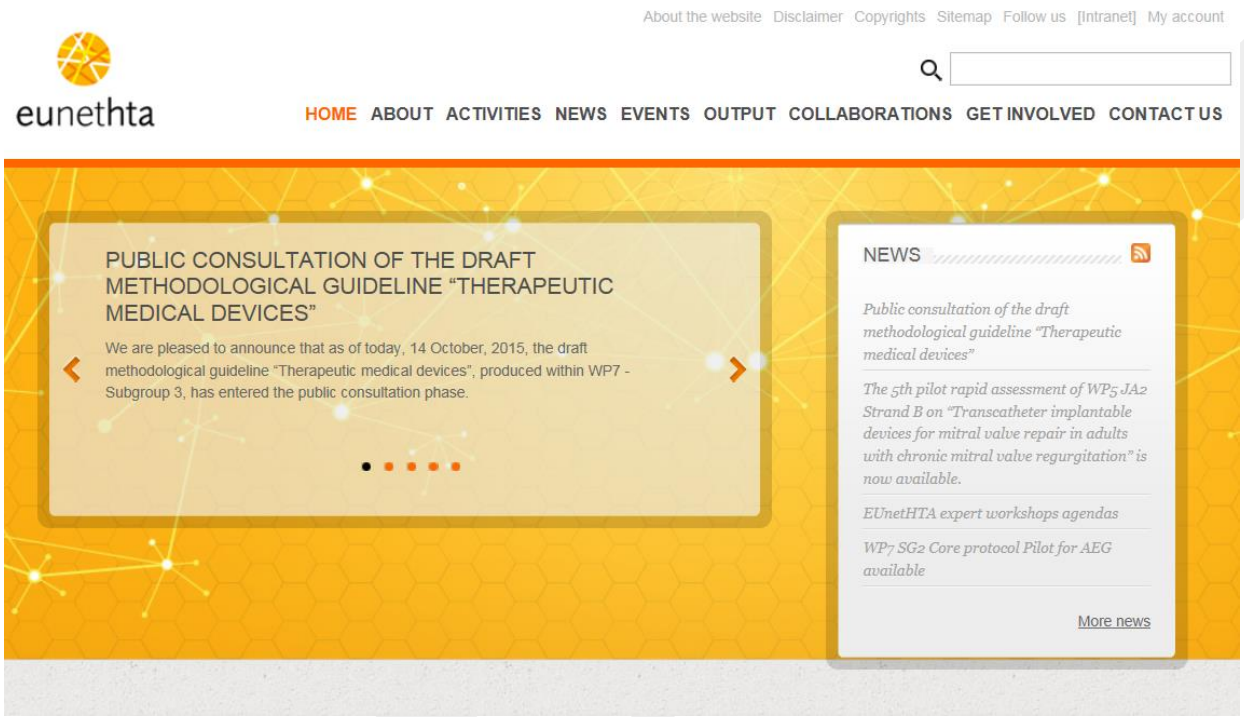
Agenda

Introduction

Guideline “Therapeutic medical devices”



Background

- Guideline work in Joint Action 1 to support the joint production of rapid relative effectiveness assessments (REAs) of pharmaceuticals
- Extension of scope and purpose in JA2: General methodological guidelines for (rapid) REA and full Core HTAs
- Objective: Alignment of HTA methodology for joint work in the network via consensus on recommendations, not new development of HTA methods
- Guidelines have no strictly binding character, especially not for national HTA work of the partners

http://www.eunethta.eu/eunethta-guidelines

EUnetHTA Guidelines

The development of the methodological guidelines was included in the work plan of the EUnetHTA JA in years 2009-2012, and is one of the objectives of the EUnetHTA JA2. The primary aim of the guidelines is to help the assessors of evidence to process, analyse and interpret the data.

The links to all published EUnetHTA methodological guidelines can be found below:

Methodological guidelines for rapid relative effectiveness assessment (REA) of Pharmaceuticals developed in WP5 of EUnetHTA JA

1. Clinical endpoints
2. Composite endpoints
3. Surrogate endpoints
4. Safety
5. Health-related quality of life
6. Criteria for the choice of the most appropriate comparator(s)
7. Direct and indirect comparison
8. Internal validity
9. Applicability of evidence in the context of a relative effectiveness assessment

Methodological guidelines developed in WP7 SG3 of EUnetHTA JA2

10. Meta-analysis of diagnostic test accuracy studies
11. Methods for health economic evaluations - A guideline based on current practices in Europe
12. Internal validity of non-randomised studies (NRS) on interventions
13. Process of information retrieval for systematic reviews and health technology assessments on clinical effectiveness

Further methodological guidelines (to be continuously published until the end of JA2)

14. Therapeutic medical devices

OUTPUT

- GUIDELINES
- TOOLS
- JOINT ASSESSMENTS
- DOCUMENTS AND MEDIA

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EUnetHTA general guidelines + reflection paper (JA2)

TOPICS
1. Internal validity of non-randomised studies (NRS) on interventions
2. Meta-analysis of diagnostic test accuracy studies
3. Methods of health economic evaluations
4. Process of information retrieval for systematic reviews and HTAs on clinical effectiveness
5. Therapeutic medical devices (under public consultation)
6. Personalised Medicine and co-dependent technologies (Reflection paper after internal consultation)

published

Guideline „ Therapeutic medical devices“

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Guideline

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Scope of the guideline

- Focus on therapeutic medical devices with high safety risks (class IIb and III)
- Addresses MD-specific issues in relative effectiveness assessment
- Focus on
  - Incremental development
  - Greater importance of context and user dependency
- We did not consider
  - Cost-effectiveness
  - Non-clinical benefits and harms (e. g. system/organisation, environment etc.)

Recommendation 1

Specifics of HTA of MD

HTA of medical device interventions **should be done without unnecessary modification of currently established methods** for finding, selecting, analysing, synthesizing and interpreting evidence on clinical effectiveness. A **need for specific methods** mainly derives from the **incremental development** of MDs and their **user and context dependency**, and some implications of the physical mode of action.

Recommendation 2

Framing the research question

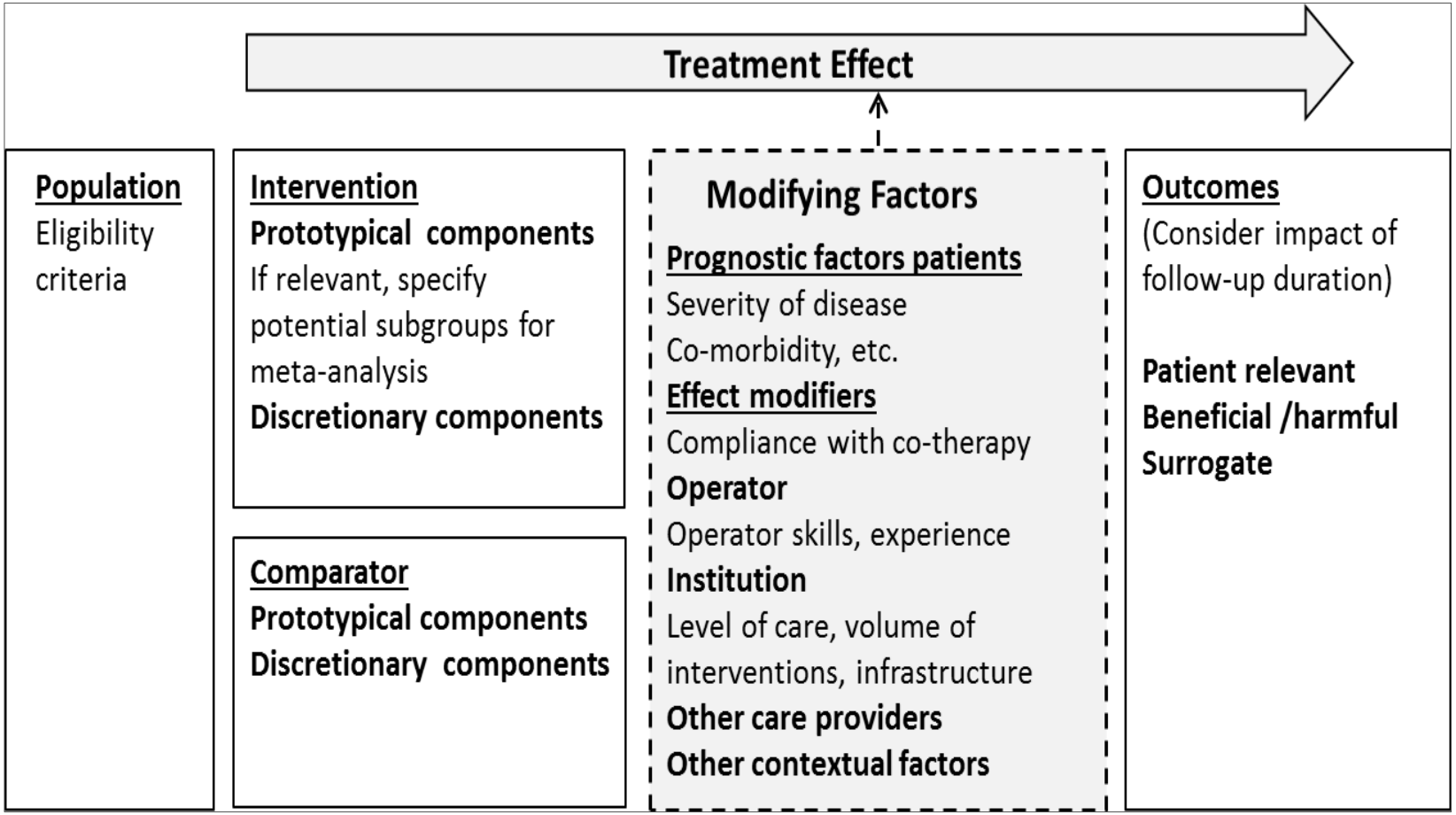
The **more complex nature of MD interventions** need a more elaborated development of the research question.

A logic model (e. g. analytical framework) may help in describing the components of the intervention and comparators, outcomes and effect-modifying factors such as individual and institutional learning.

Try to **use clinical prior information** about properties of the intervention that might influence treatment effects.

Provide the sources / evidence for this information.

Template for a logic model to clarify the research question for therapeutic MD



Prototypical components need to be present for the intervention to meet the working definition; discretionary components may be present but are not compulsory to meet the working definition (33)

Recommendation 3

Defining the intervention

Explicitly state whether the focus of the HTA report is the evaluation of one particular MD product (**single technology assessment, STA**) or of all MDs that can be used for a certain treatment method **(multi technology assessment, MTA)**.

If the aim is to perform a MTA, the review should take a broad scope for the definition of the intervention.

Try to identify

- all MD interventions,
- which technologies are used in combination or alternatively,
- potentially important differences.

Redefinition of the intervention may become necessary during the course of the assessment.

Recommendation 4

Information retrieval

For information retrieval search strategies may include both general search terms such as the generic name of the device type as well as specific devices (proprietary or brand names).

If randomized controlled trial (RCT) data are not available or for developing the research question, literature search can be broadened to include all types of study design, including case series and even case reports.

In addition to the search in bibliographical databases, information about the MD may also be retrieved from device registries, incident reporting databases and administrative databases.

Recommendation 5

Information requirements for clinical effectiveness

Although **RCT are to be preferred in the assessment of effectiveness**, HTA assessors should **anticipate that such evidence is frequently lacking for MD** interventions. Thus, no definite conclusions should be expected, especially when assessing the effectiveness of very new MD interventions.

HTA assessors should also **be familiar with special RCT designs that take into account the specifics of MD** (e.g. expertise-based trials, tracker designs).

Experimental designs addressing challenges prominent in MD

modified and adapted from Bernard 2014

Technological changes	Provider preferences	Patient preferences	Design	Principle	Advantages	Disadvantages
		x	Zelen's design	Randomizing before requesting consent	• Facilitates inclusion	• Selection bias possible • Loss of statistical power if many patients refuse treatment • Ethical problems
		x	Wennberg's Design (67)	Randomizing to preference group (people can choose their treatment) or randomization group	• Facilitates participation	• Blinding not possible • Statistical power low, when a high proportion of participants chooses the same treatment
	x		Expertise-based randomized trial	Randomizing patients to a specialized physician	• Better acceptability • Reduces execution bias and protocol deviations	• Difficulty of knowing whether the observed difference is related to the expertise of the therapist
x			Tracker trial design	Allowing changes in the study protocol during the trial	• Early assessment of technological developments	• Practical organization is complex • Higher budget
	x		Cluster randomized trials	Randomizing clusters of individuals (hospital, department)	• Easy to implement	• Lack of power • Selection bias possible
x			Sequential trials	Interim analysis (the results from patients already included are analysed before randomization of new patients)	• Reduces the number of patients needed	• Lack of power for secondary endpoints or adverse effects • The time between the inclusion of patients and endpoint must be short • Independent data monitoring committee is necessary
x			Adaptive randomization trials	• Interim analysis • Adjustments are possible, related to the ratio of randomization or the re-evaluation of the number of patients required or interim analysis	• Reduces the number of patients needed • Greater flexibility	• Logistical constraints • Independent data monitoring committee • Internal validity has also been called into question
x			Bayesian methods	• Combining prior information with information from the ongoing trial • A priori information is supplied by the literature or expert opinions	• Greater flexibility • Reduces the number of patients needed	• Risk of taking into account arbitrary and erroneous prior information

Recommendation 6

Information requirements for long-term effects

In case of an assessment of **long-term safety**, it is useful to **include disease-specific or MD-specific registries** of high quality and incident reporting databases.

Registry analyses **should be considered to assess long-term outcomes** but should **not be routinely used for the assessment of treatment effects due to their susceptibility to bias**.

Recommendation 7

User dependency and context factors

If it is likely that there is an **influence of institutional expertise, learning and infrastructure** (e. g. level of care, volume of interventions, case mix) and **individual proficiency or learning** (e. g. physician, patient, caregiver) on treatment effects, take this into account in the assessment.

User proficiency and healthcare setting may affect both, intervention and comparator.

Recommendation 8

Applicability of findings

When interpreting the review's findings **consider the influence of health care settings, user proficiency,** and **incremental treatment modification**.

In addition, **systematically check the applicability** by an applicability checklist (see EUnetHTA's guideline "Applicability of evidence in the context of a relative effectiveness assessment").

Limitations

Only clinical effectiveness was considered.There are specific issues in other domains (cost-effectiveness, organisational) as well.

The targeted literature review did not consider specific issues more in depth, such as

- patient‘s perspective on usability,
- MD user‘s preferences for device properties and handling,
- information retrieval, → using experience of the institutions of the GL draft group
- on sources for describing the technology

Thank you