Webinar #9 - WG Guidelines

Guidelines from Start to Finish: An overview of the methodology.

Chaired by Dr. Agnies van Eeghen,

Amsterdam University Medical Centre, Netherlands

Tuesday 7 November

from 5pm to 6.30 pm French time

Co-funded by the Health Programme of the European Union

Amsterdam UMC
Universitair Medische Centra

European Reference Networks

ITHACA

Welcome – Technical points

- *We are please to be numerous **(100)***
- *Webinar is being recorded*
- *Thank you for*
  - *Turn off your microphone and disconnect your camera*
  - *Raise your hand at the time of the questions and discussions*
  - *We will answer the questions sent in the registration form*
  - *A satisfaction survey will be sent to you*

- *Webinars # will be available on ITHACA's Website*

https://ern-ithaca.eu/documentation/educational-resources/

Anne Hugon Project Manager ERN ITHACA - anne.hugon@aphp.fr

Survey registration feed back

- 100 registrations
- 45% ITHACA's members , Welcome to all 25% new comers
- 26 Countries : Netherlands, France, Italy, Belgium, Norway, Poland, Sweden, Romania, Latvia, Lithuania, Slovenia, Serbia, Croatia, Ireland, Spain, Germany, Denmark, Portugal, Greece, Georgia, Cyprus, Egypt, UK, Australia, USA, Brazil
- 38 Patients representatives, PO, ePAGS
- Involved in 11 Guidelines : Kleefstra syndrome, Fragile X Syndrome , Williams Beuren syndrome , Phelan McDermid syndrome, RASopathy, Cornelia de Lange syndrome , KBG syndrome, SATB2 syndrome, Transition of Care guidelines , Transdiagnostic guidelines , Polyhandicap PIMD

Fields of interest

Agenda

- Welcome and Introduction
  - Speaker: Dr. Agnies van Eeghen (intellectual disability physician), Chair of WG Guideline; From: Amsterdam University Medical Centre, The Netherlands
- Guideline methodology: how to start and finish an ERN-ITHACA clinical practice guideline, and how to take all roles into account
  - Speakers: Dr. Charlotte Gaasterland (guideline methodologist) & Mirthe Klein Haneveld (PhD candidate); From: Amsterdam University Medical Centre, The Netherlands
- ERN-ITHACA procedure for endorsement of existing clinical practice guidelines
  - Speaker: Dr. Katalin Szakszon (clinical geneticist & paediatrician), Co Chair of WG Guideline; From: University of Debrecen, Clinical Center, Paediatrics Clinic, Hungary
- Discussion time

Welcome and Introduction

- Dr. Agnies van Eeghen
  - In this webinar, we present the ERN-ITHACA view on clinical practice guideline methodology. What does the guideline development process entail and how do we ensure that our guidelines are methodologically sound? What does the endorsement procedure for existing guidelines look like? How will we include the experiences of our patient community and clinical experts? If you are involved in one of our guideline projects, or would like to get involved in the future, participation in this webinar is highly recommended!
  - We strongly recommend this Webinar to all HCP Teams wishing to develop EU Guidelines for the ITHACA ERN.
  - ITHACA's Guideline TEAMS

ITHACA Guideline projects (WP4)

- Chair: Agnies van Eeghen (Amsterdam UMC, NL) and Vice Chair: Katalin Szakszon (Medical University of Debrecen, HU)
- Methodological support and research: Charlotte Gaasterland (postdoc), Mirthe Klein Haneveld (PhD-candidate)
- Project management: Anne Hugon, Klea Vyshka

Agnies van Eeghen, Katalin Szakszon, Charlotte Gaasterland, Mirthe Klein Haneveld, Anne Hugon, Klea Vyshka

ITHACA Guideline projects (WP4)

- Specific (genetic) conditions
  - Phelan-McDermid syndrome ✓!
  - Rubinstein-Taybi syndrome;
  - Kabuki syndrome;
  - Noonan syndrome;
  - Kleefstra syndrome;
  - Williams syndrome;
  - Fragile X syndrome;
  - Spina bifida.
- Shared health problems
  - Transition to adult healthcare;
  - Polyhandicap/PMID;
  - Challenging behaviour.

ITHACA Guideline methodology:

how to start and finish an ERN-ITHACA clinical practice guideline, and how to take all roles into account

Dr. Charlotte Gaasterland
Mirthe Klein Haneveld

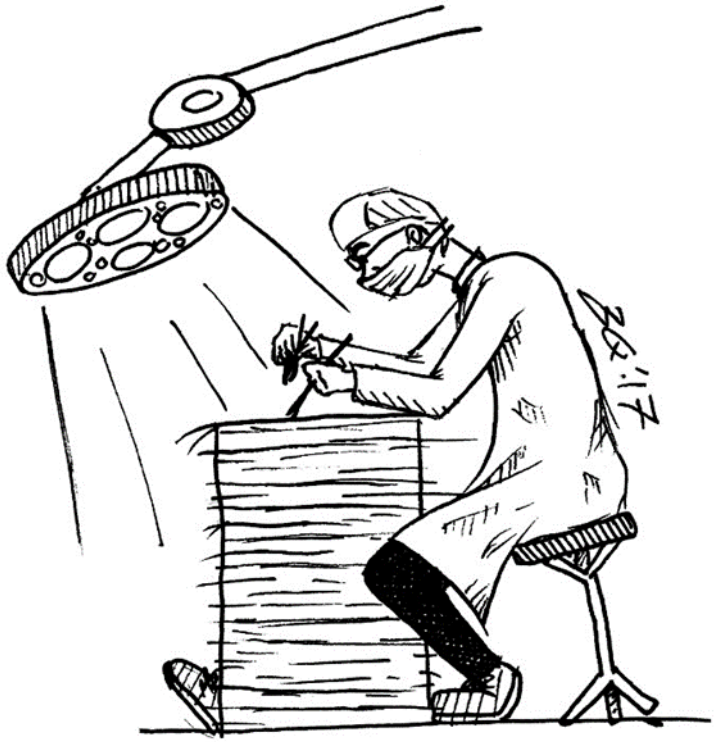
European Commission

Amsterdam UMC
Universitair Medische Centra

European Reference Network
for rare or low prevalence complex diseases

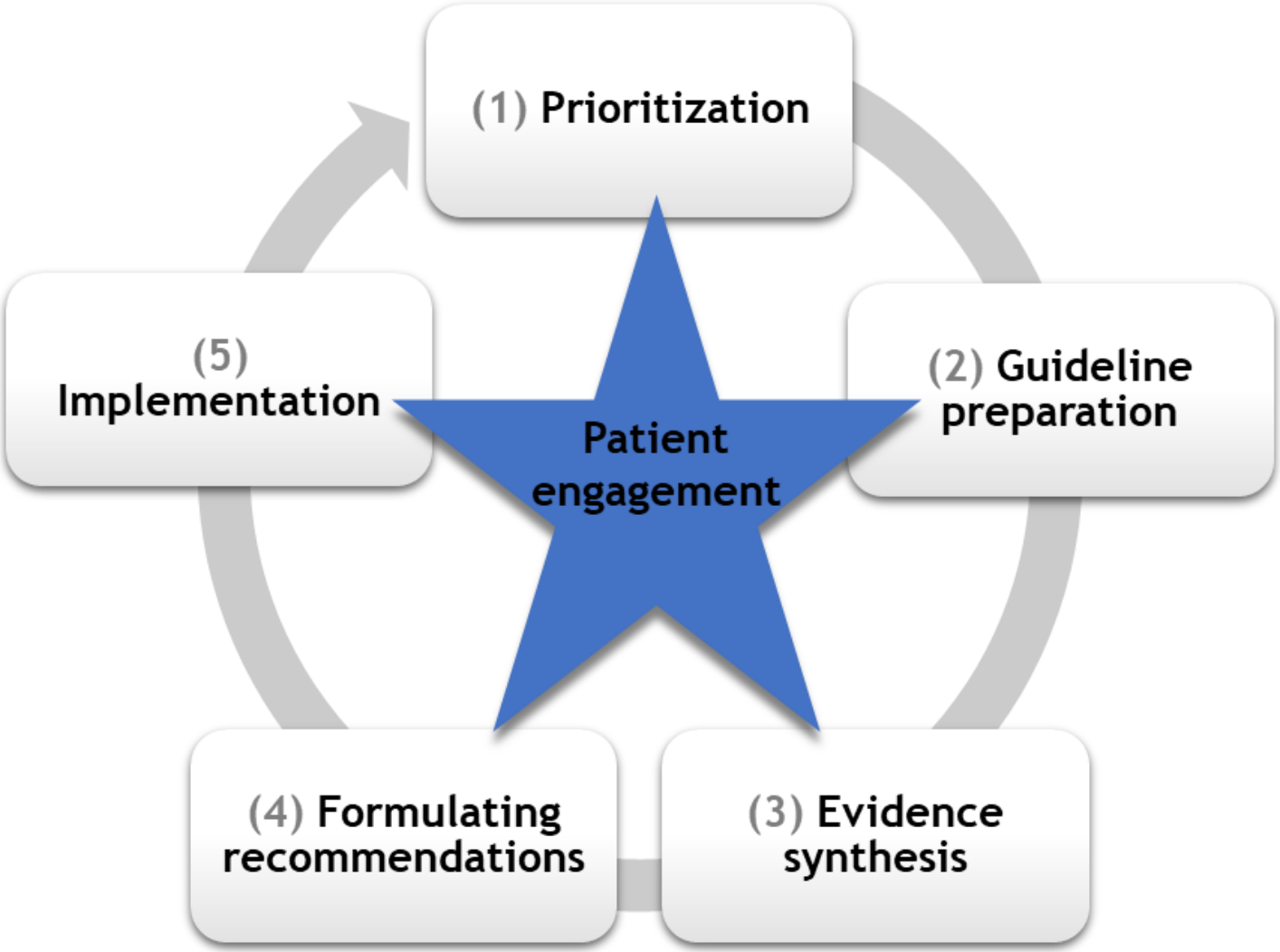
Network Intellectual Disability and Congenital Malformations (ERN ITHACA)

Why guidelines?



- Improve quality of health
- Evidence based medicine
- Less unwanted clinical variance between hospitals/countries
- Make sense of the growing pile of research output
- Make care more transparent
- Identify knowledge gaps and shape research agendas

Our vision on guideline methodology



History of guidelines

Development of guidelines is relatively new:

Introduction in the US and Europe in the ‘80s,

Development from *consensus statements* to *evidence-based guidelines*

- 2002: GIN working group
- 2003: Introduction of GRADE

Good Old Boys Sat Around a Table

Good Old Boys Sat Around a Table

AGREE II

GRADE

AGREE II

- Set of criteria to evaluate quality of guidelines
  - Scope and purpose
  - Stakeholder involvement
  - Rigour of development
  - Clarity of presentation
  - Applicability
  - Editorial independence

ITHACA website: methodology (extended)

Guidelines & consensus statements produced by ITHACA members and endorsed by ERN-ITHACA

Guidelines & Consensus Statements available in Member States and endorsed by ERN-ITHACA

Websites with Guidelines & Consensus Statements available on the Web

ERN Guidelines Methodological Handbook

ERN Guidelines Methodological Handbook

The ERN GUIDELINES Methodological Handbook of the programme of ERN Clinical Practice Guidelines (CPG) and other Clinical Decision Support Tools (CDST) is now available.

This handbook is the outcome of the extensive literature review and consultation process carried out by the Consortium in charge of the implementation of the Programme. The presented methodology is based on the current international "gold standards" that have been developed along the years and used by key international and national bodies and organisations specialised in the development of Clinical Practice Guidelines and other Clinical Decision Support Tools.

This material is an important step forward of the ERN CPG programme and a key element and tool for the work of the ERNs in the production, adaptation, adoption and appraisal of the different guidelines and technical sub-products to be used for now on by all the ERNs. The methodology will ensure the quality and standardisation of the CPG and CDST produced and used by the ERNs, the backbone of the process of the diagnosis and treatment of patients suffering of rare or low prevalence and complex diseases.

The handbook includes 12 separated guidelines addressing the following conceptual and methodological aspects of the programme:

- 1# Prioritisation
- 2# Appraisal
- 3# Adaptation & Adoption
- 4# Elaboration of CPG
- 5# Elaboration of Clinical Consensus Statements
- 6# Elaboration of Evidence Reports
- 7# Elaboration of Pathways
- 8# Elaboration of Evidence Based Protocols
- 9# Elaboration of Do's & Don'ts Factsheets
- 10# Elaboration of Quality Measures
- 11# Elaboration of Patient Information Booklets
- 12# Evaluation of Uptake of CPGs and CDST

Methodology: process

FORMING THE WORKING GROUP

FRAMEWORK, ANALYSIS OF CLINICAL ISSUES

PRIORITIZATION OF CLINICAL ISSUES

LITERATURE SEARCH AND SELECTION

LITERATURE SUMMARY, GRADE ANALYSIS

RECOMMENDATIONS

CONSENSUS MEETING, ROUND OF COMMENTS

PUBLICATION

Forming the working group

Chair (has to be from Europe)

Steering group/core group

Working groups per chapter/organ system/clinical topic

Clinical topics

- Not the same as research questions
- How can we be of help for the clinical practice?

- Research agenda – may be a separate deliverable

Prioritization

- A guideline is probably not complete
- Prioritization of topics is essential, based on:
  - Prevalence
  - Burden
  - Clinical variance in Europe
  - Potential improvement in quality of care

Methodology

- GRADE-system:

1. Systematic literature search
2. Summarize and grade existing literature
3. Weigh level of evidence
4. Recommendation based on both level of evidence and expert-input

Systematic search

- Preferably done by a literature specialist
- Based on PICO format questions, such as:
  - P: children with Dravet syndrome
  - I: medication A
  - C: medication B
  - O: number of attacs, quality of life, complications

Methodology: GRADE

- Levels of evidence (usually graded per outcome):
  - High
  - Moderate
  - Low
  - Very low

Methodology: GRADE

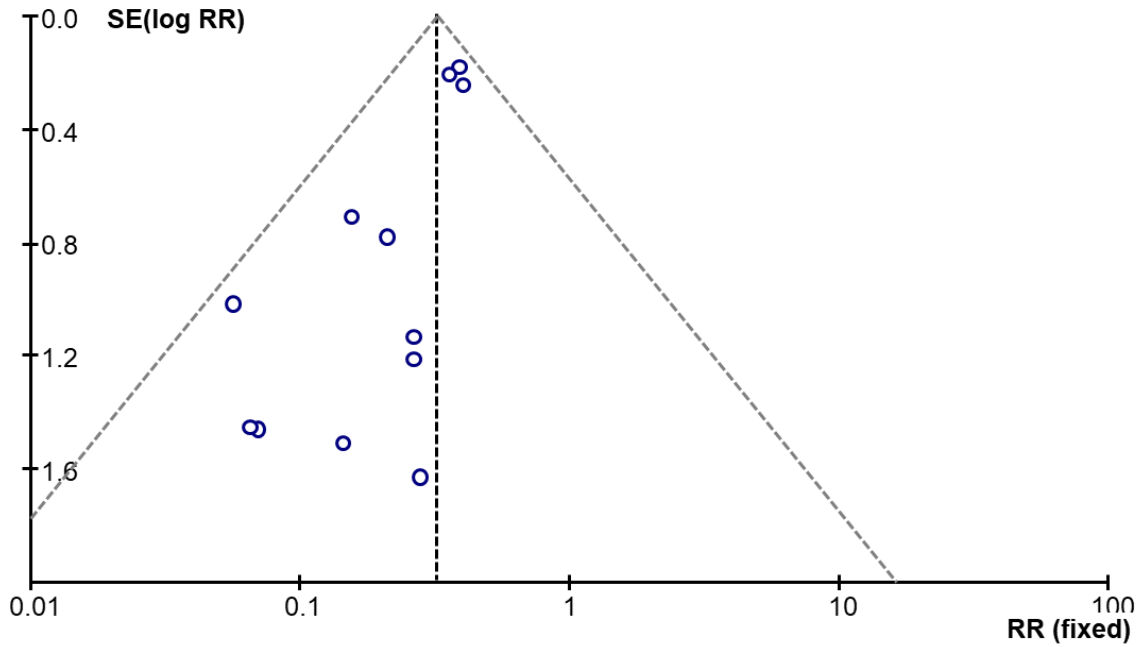
5 factors may downgrade level of evidence

1. Risk of bias
2. Inconsistency
3. Indirectness
4. Imprecision
5. Publication bias

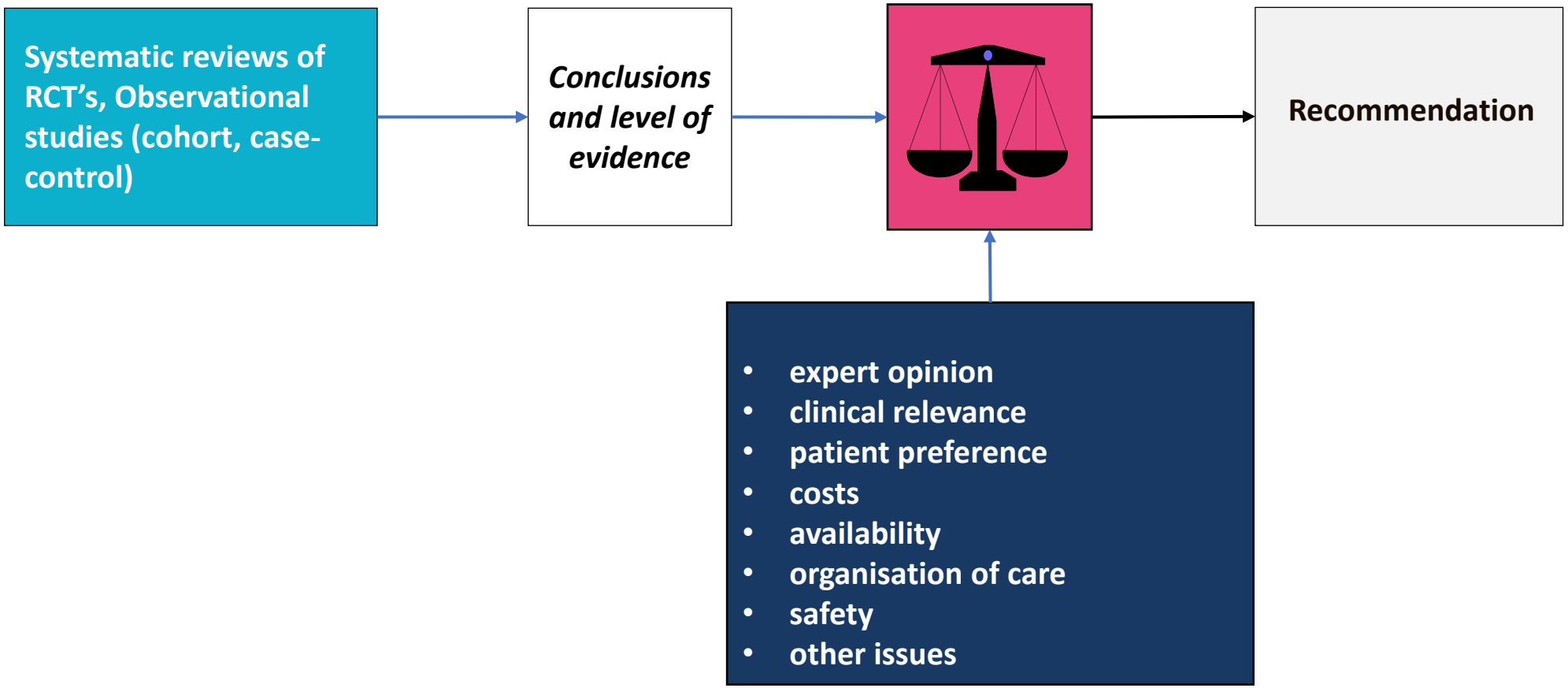
DOWN

Examples

- Studies on Dravet syndrome are scarce, but some interventions on epilepsia may work for this population: *downgrade for indirectness*
- Wide heterogeneity in quality of life outcome for pharmacotherapeutical interventions in Fragile X individuals: *downgrade for inconsistency*
- Publication bias found in funnel plot: *downgrade for publication bias*



Methodology



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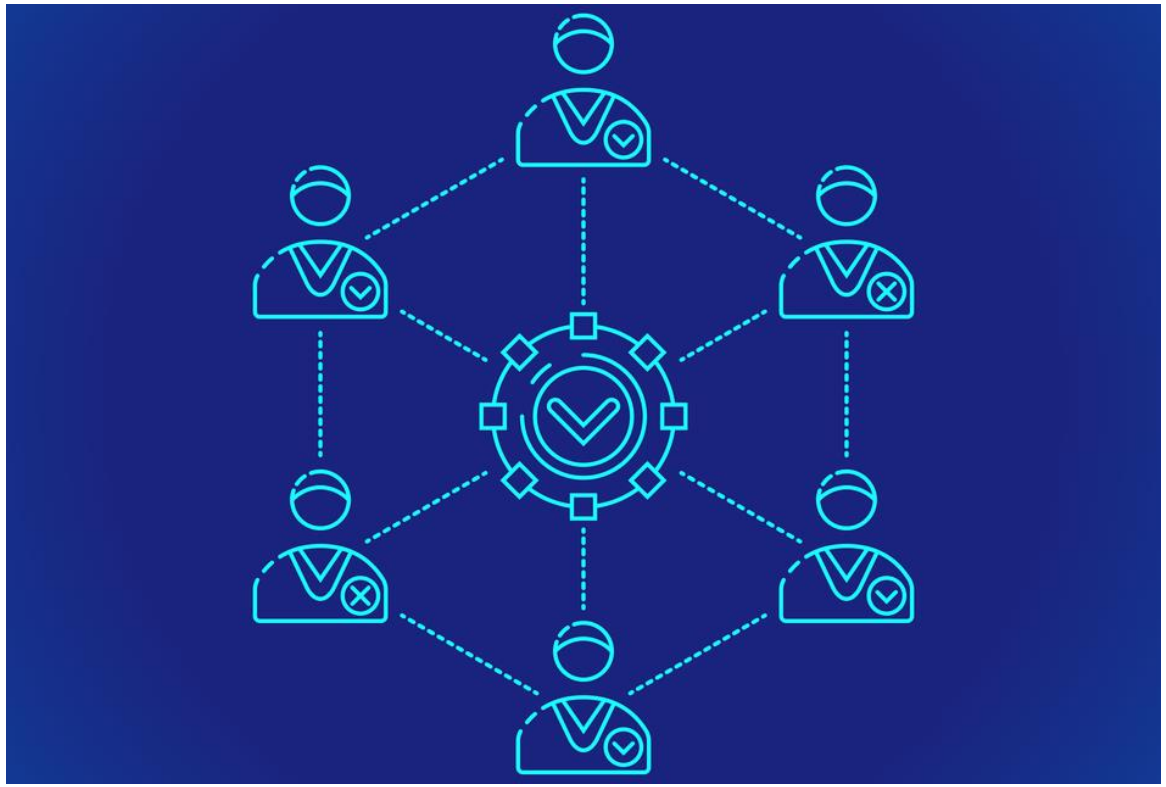
Methodology

- Patient perspective is key
- More than one type of methodology can be used:
  - Patient experts part of the core group
  - Surveys or Focus groups
  - Input in finding clinical topics and prioritization (Delphi)
  - Co-authors for the recommendations
  - Evaluation of the recommendation in focus groups/surveys

Consensus meeting



- Face-to-face (minimum of two days)
- Discussion of all the recommendations
- Voting

Declaration of interests

- Important to know for the credibility of the guideline
- Commonly asked by journals

End products

- Peer-reviewed article in international journal
- Full document available on ITHACA website
- Health care provider summary (incl. surveillance scheme)
- Patient/lay summary (incl. surveillance scheme)
- Webinar
- Research agenda (optional)

Methodology: process

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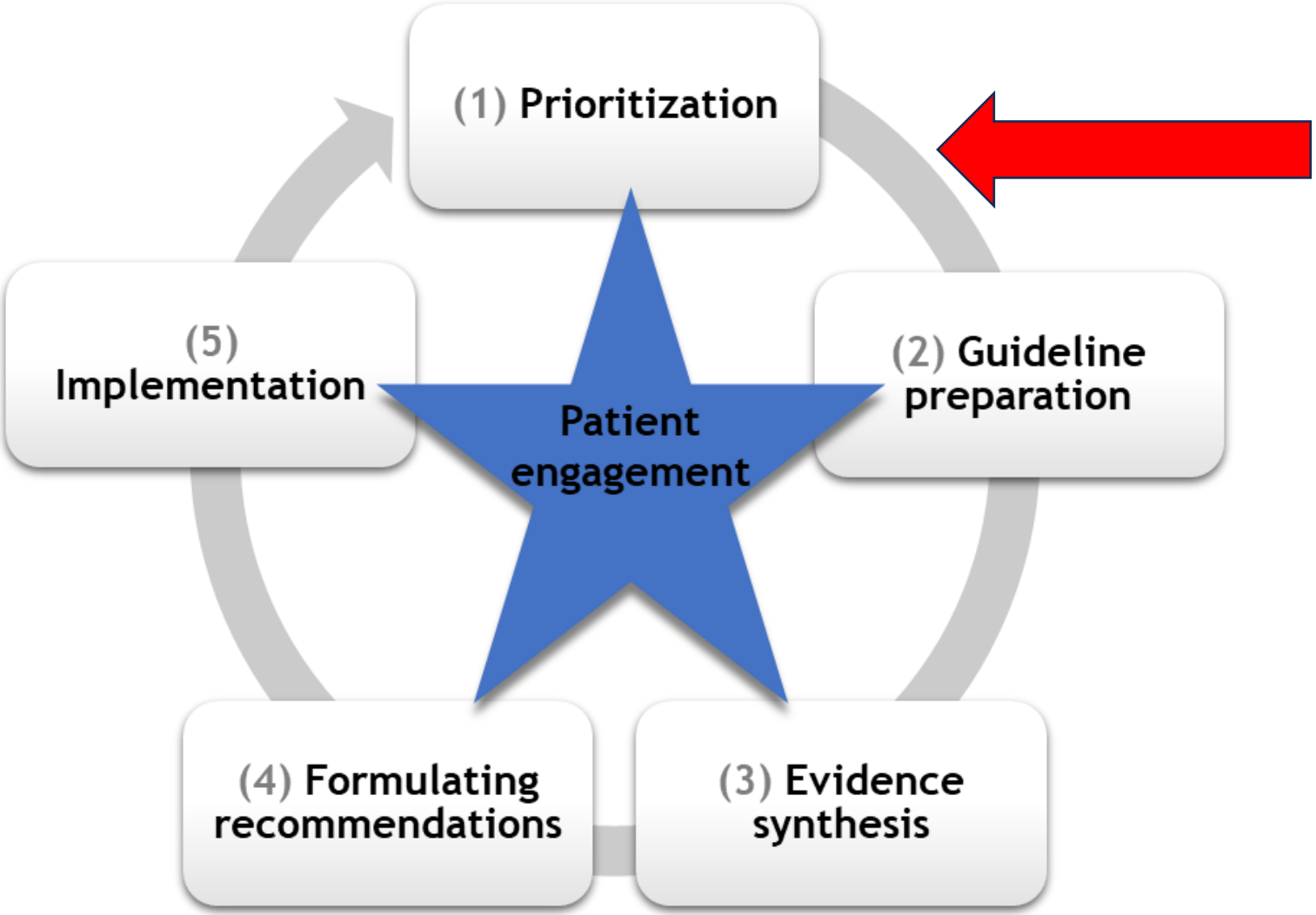
Our vision on guideline methodology



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Prioritization of new guideline topics

- Guideline topics
  - Specific (genetic) conditions (*e.g. Phelan-McDermid syndrome*)
  - Shared health problems (*e.g. transition to adult healthcare; challenging behaviour*)
- Why prioritization?
  - Large number of conditions + health problems relevant to ERN-ITHACA
  - Significant efforts and resources required for guideline development
- Next steps
  - → Survey on prioritization criteria (*e.g. prevalence, multisystemic nature & complexity of care, availability of scientific evidence, stakeholder interest, diversity*, etc.)
  - → Future ERN-ITHACA guidelines will follow this procedure

ITHACA guideline endorsement

Procedure for endorsement of existing clinical practice guidelines

Dr. Katalin Szakszon

European Commission

European Reference Network
for rare or low prevalence complex diseases

Network Intellectual Disability and Congenital Malformations (ERN ITHACA)

Endorsement of existing guidelines

- In addition to developing consensus statements, ERN-ITHACA are also looking at those already in existence in Member States, how we can endorse their content and translate them, and how we can ensure they reach the widest possible audience.

- Fit ERN-ITHACA's target population and goals (patients with rare/multiple malformation syndromes and rare intellectual and other neurodevelopmental disorders)
- Fit the prioritization criteria summarized previously
- Published in a high quality, English language journal (external review AND peer review of professional content)
- Its process of development is in accordance with ERN-ITHACAs recommended guideline methodology – see Leaflet on how to develop guidelines on ITHACA's website appear soon)
- Covers all relevant health care topics of the condition

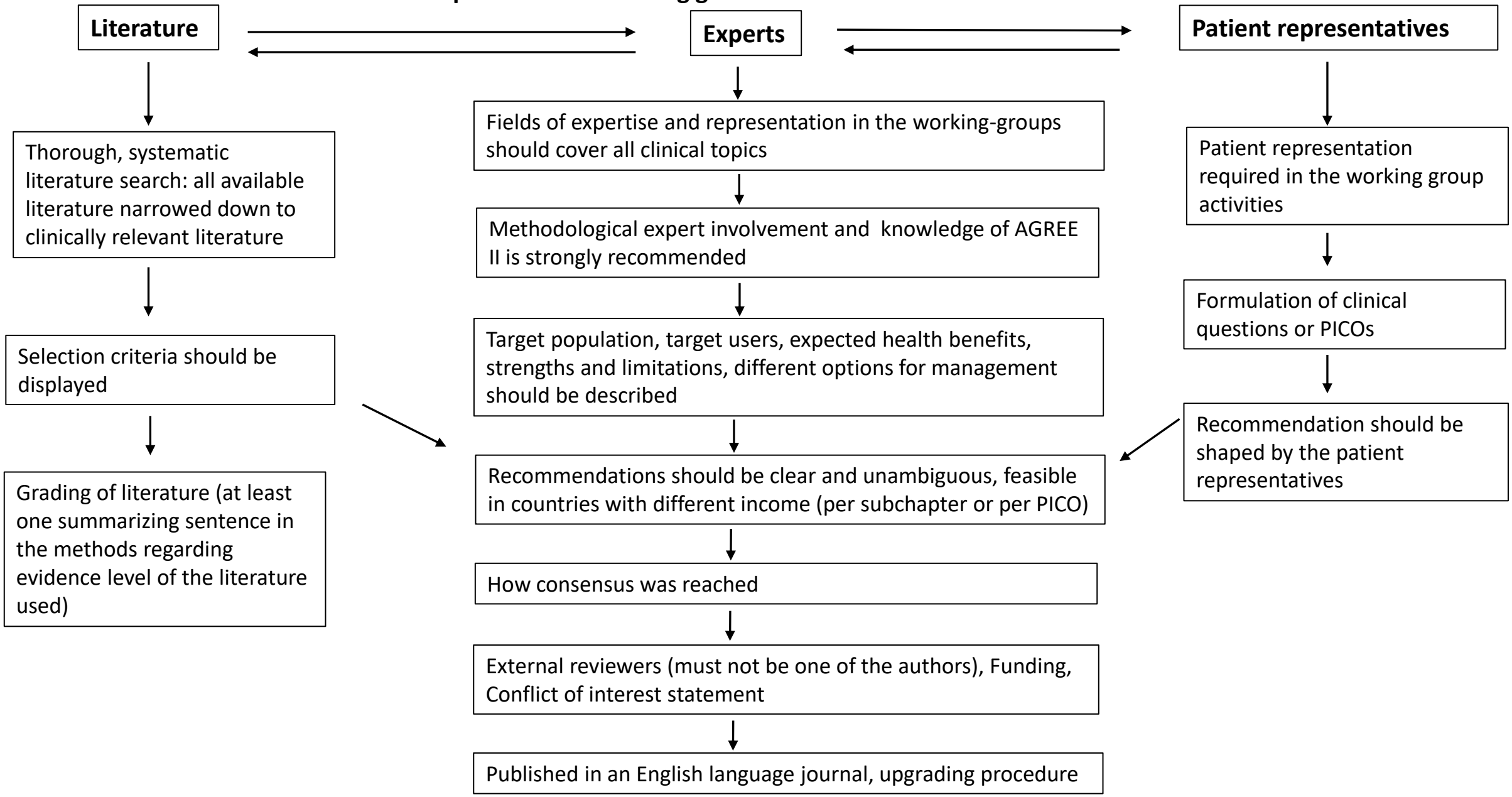
Endorsement of existing guidelines

- Recommendations are based on 3 three major pillars and formulated in a democratic fashion (consensus meeting, voting):

1. available scientific literature,
2. involvement of Patient expertise affiliated with recognised or officially declared patient organizations, represented by endorsed representatives,
3. involvement of experts in multiple fields of expertise in the condition,

- Can be put in use by multiple levels of (health) care providers

Expectations to existing guidelines for ERN-ITHACA endorsement



Evaluation and decision on ERN-ITHACA endorsement/adolopement will be based on the AGREE II evaluation tool

Professional aspects – peer reviewed

Methodological aspects: AGREE II (Appraisal of Guideline for Research and Evaluation II; https://www.agreetrust.org/wp-content/uploads/2013/10/AGREE-II-Users-Manual-and-23-item-Instrument_2009_UPDATE_2013.pdf

APPRAISAL OF GUIDELINES FOR RESEARCH & EVALUATION II

AGREE II

INSTRUMENT

I. Domain 1. Scope and Purpose .....
II. Domain 2. Stakeholder Involvement .....
III. Domain 3. Rigour of Development .....
IV. Domain 4. Clarity of Presentation.....
V. Domain 5. Applicability.....
VI. Domain 6. Editorial Independence .....
VII. Overall Guideline Assessment.....

1 Strongly Disagree	2	3	4	5	6	7 Strongly Agree

1. The overall objective(s) of the guideline is (are) specifically described.
2. The health question(s) covered by the guideline is (are) specifically described.
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.
4. The guideline development group includes individuals from all relevant professional groups.
5. The views and preferences of the target population (patients, public, etc.) have been sought.
6. The target users of the guideline are clearly defined.
7. Systematic methods were used to search for evidence.
8. The criteria for selecting the evidence are clearly described.
9. The strengths and limitations of the body of evidence are clearly described.
10. The methods for formulating the recommendations are clearly described.
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.
12. There is an explicit link between the recommendations and the supporting evidence.
13. The guideline has been externally reviewed by experts prior to its publication.
14. A procedure for updating the guideline is provided.
15. The recommendations are specific and unambiguous.
16. The different options for management of the condition or health issue are clearly presented.
17. Key recommendations are easily identifiable.
18. The guideline describes facilitators and barriers to its application.
19. The guideline provides advice and/or tools on how the recommendations can be put into practice.
20. The potential resource implications of applying the recommendations have been considered.
21. The guideline presents monitoring and/or auditing criteria.
22. The views of the funding body have not influenced the content of the guideline.
23. Competing interests of guideline development group members have been recorded and addressed.

		1	2	3	4	5	6	7	Rating
Domain 1	Item1							X	7
	Item2							X	7
	Item3							X	7
Domain 2	Item4				X				4
	Item5				X				4
	Item6		X						2
Domain 3	Item7						X		6
	Item8							X	7
	Item9							X	7
	Item10							X	7
	Item11				X				4
	Item12							X	7
	Item13				X				4
	Item14			X	X				3
Domain 4	Item15							X	7
	Item16					X			5
	Item17							X	7
Domain 5	Item18						X		5
	Item19	X							1
	Item20					X			5
	Item21					X			4
Domain 6	Item22	X							1
	Item23			X					3

The scaled domain score will be:

$$\frac{\text{Obtained score} - \text{Minimum possible score}}{\text{Maximum possible score} - \text{Minimum possible score}}$$

- After we have evaluated the guideline, we propose a voting process at work-meetings and ExCom meetings before we fully endorse the guideline
- Endorsement procedure takes time, and we have to prioritize which ones to select and evaluate
- High standard for guideline development – high standards for endorsement

- We must ensure that only knowledge that is the right knowledge reaches the target population

Thank for answering our satisfaction survey

https://forms.office.com/e/tW2Rhtnf4x

Thank you for your participation