Challenges for guidelines in rare diseases

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Rare Diseases (RDs)

- Diseases that affect < 1/2000 people (EU)
- Frequently life-threatening or seriously debilitating
- > 7000 RDs

=> > 30 Mio EU habitants affected
Treatment of RDs

• Limited therapeutic options
  – Low availability / accessibility

• Many affect already children
  – Lack of appropriate formulations/dosing forms
  – Lack of formal drug approval

• Lack of expertise
  – Diagnosis
Trustworthy guidelines
Trustworthy guidelines in rare diseases
Challenges in guideline development (in RDs)

- Lack of
  - methodological expertise
  - resources
- Selection of experts
- Few treatment alternatives
- Little or lack of evidence
- Dissemination of guidelines
Lack of methodological expertise / resources

• Content expertise required for state-of the art guideline development
• Few experts have required methodological expertise
• Regional / National guidelines not feasible due to very small number of experts
• Limited resources available for RD guideline development
Selection of experts

• Few experts, distributed over many countries

• Meetings challenging:
  – Timing
  – Resources

• Conflicts of Interests likely
IT LOOKS LIKE A PERFECTLY BALANCED SYSTEM TO ME.
Col Management

• A priori decision on criteria to be used

• Transparent documentation of Cols

• Appropriate management of residual Cols during guideline development
Few treatment alternatives

• RDs less attractive for industry to develop treatments

• Often drugs not approved for RD (or not approved in given country)
Little or lack of evidence

• RCTs sparse

• Well-done, large observational studies also sparse

• Often case series and case reports

• Registry data
Involve information specialist !!
Dissemination of guidelines

- Difficult to reach experts
- Difficult to reach patients
- Lack of resources
RARE Bestpractices

- **Objectives WP 3**
  - agree on methodological quality standards for the development of guidelines on clinical management of RD
  - to delineate the current state of existing institutional programmes, as well as processes and tools for developing, updating, adapting guidelines in the field of RD
  - **to define methodological quality standards for BP guidelines on RD**
  - to develop one new BP guideline for a specific rare condition implementing the methodological quality standards
  - to develop a methodology to implement through Business Processes Modelling Notation (BPMN) implicit processes subtended by the guideline activities
RARE Bestpractices

- **Deliverables**
  - D3.1 – Report on the Ethical regulations applicable at the Survey (M02)
  - D3.2 - State of the art of BP guidelines (M10)
  - **D3.3 - Methodology for BP guidelines on RD (M20)**
  - D3.4 - Method of representation of BP guideline through BPMN (M36)
  - D3.5 - Pilot BP guideline (M36)
  - D3.6 - Patient version of the pilot BP guideline (M42)
Developing methodology for the creation of clinical practice guidelines for rare diseases: A report from RARE-Bestpractices

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Rare diseases are a global public health priority; they can cause significant morbidity and mortality, can gravely affect quality of life, and can confer a social and economic burden on families and communities. These conditions are, by their nature, encountered very infrequently by clinicians. Thus, clinical practice guidelines are potentially very helpful for diseases. This paper summarizes key results of the first workshop, and explores how the current GRADE approach might (or might not) work for rare diseases. Avenues for future research are also identified.
GRADE: 80+ organizations
Evidence synthesis (SR, HTA)

Recommendation/Decision

Grade recommendations (Evidence to Decision)
- For or against (direction) ↓↑
- Strong or conditional/weak (strength)

By considering balance of consequences (evidence to recommendations):
- Quality of evidence
- Balance benefits/harms
- Values and preferences
- Feasibility, equity and acceptability
- Resource use (if applicable)

Guideline/Decision

Formulate Recommendations/Decision
"The panel recommends that ….should..."
"The panel suggests that ….should..."
"The panel suggests to not ...
"The panel recommends to not..."

Transparency, clear, actionable Research?
Key findings
Freiburg workshop

• Draft EtD frameworks are particularly helpful to increase transparency in the face of little evidence about effects
  – Nothing missing, COI to be made transparent also in EtD
• Transparent dealing with conflict of interest perhaps more important in rare disease
• Expert-based evidence requires careful description
**Question/Problem**
- Question: Should ACP recommend any dietary intervention for preventing kidney stone recurrence?

**Benefits and harms**
- Benefits: No specific benefits are listed.
- Harms: No specific harms are listed.

**Quality of evidence**
- Evidence: The evidence is not provided in the table.

**Values**
- Values: Not specified in the image.

**Resources**
- Resources: Not specified in the image.

**Equity**
- Equity: Not specified in the image.

**Acceptability**
- Acceptability: Not specified in the image.

**Feasibility**
- Feasibility: Not specified in the image.

**Recommendation**
- Recommendation: Not specified in the image.