D-B.2

Methodological Handbooks & Toolkit for Clinical Practice Guidelines and Clinical Decision Support Tools for Rare Diseases

TENDER Nº SANTE/2018/B3/030 EUROPEAN REFERENCE NETWORK: CLINICAL PRACTICE GUIDELINES AND CLINICAL DECISION SUPPORT TOOLS

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Handbook #9: Methodology for the elaboration of Do's and Don'ts Facsheets for rare diseases

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Contents

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This handbook describes the elaboration method to develop Do's and Don'ts Factsheets for rare diseases. These documents have the aim to assist patients and their families, as well as the medical community in knowing the basic do's and don'ts of common and emergency situations (e.g., delivery, physical activity, anaesthesia, stroke, surgery)[1]. Hence, do's and don'ts factsheets are intended to provide useful and practical recommendations: what is recommended to be done and what shouldn't be done.

1. Background

With the launching of the first European Reference Network (ERN) in 2017, a care model based on the concentration of knowledge and resources in highly specialised care units for rare diseases became effective in Europe. As of today, 24 European Reference Network work co-ordinately and demand reliable and practical tools, like Clinical Practice Guidelines (CPG) and Clinical Decision Support Tools (CDST) to ensure the safest and most efficient care is provided to patients with rare diseases and carers through the EU.

Nonetheless, there are a number of challenges surrounding the development of CPG and CDST for rare diseases. One of the most relevant barriers is the lack of high-quality evidence, in which the foremost methodological frameworks like GRADE[2] rely on.

Therefore, there is a need for specific methodological approaches that can provide reliable and useful Clinical Practice Guidelines (CPGs) and Clinical Decision Support Tools (CDST) for rare diseases to be used by ERNs. The project also aims to provide a common methodology, in order to harmonise the elaboration process of CDST and CPGs in the ERNs.

1.1. Work Package B: Methodologies for CPGs and CDSTs for Rare Diseases

Work Package B of TENDER NºSANTE/2018/B3/030 pursues the development of methodologies for the prioritisation, appraisal, adaptation, development and implementation of CPGs and CDSTs for rare diseases.

The objective of WP-B of TENDER NºSANTE/2018/B3/030 entails two main steps: Firstly, an analysis of the state of the art on methodologies for CPGs and CDSTs for rare diseases, and secondly, the elaboration of methodological handbook and toolkit for the prioritisation, appraisal, adaptation, development and implementation of CPGs and CDSTs for rare diseases.

It is worth noting that within the scope of WP-B, "rare diseases" is the term used to refer to rare diseases as well as low prevalence complex diseases.

1.2. Context for Do's and Don'ts Factsheets for rare diseases development

Do's and Don'ts Factsheets for rare diseases are documents that provide advice to be considered when assisting patients with specific rare diseases, conditions or in need of complex procedures.

These documents have the aim to assist patients, carers and the medical community in knowing the basic do's and don'ts of common and emergency situations (e.g., delivery, physical activity, anaesthesia, stroke, surgery)[1].

Do's and don'ts factsheets for rare diseases aims to:

- Promote best clinical practices
- Provide information to patients and empower them
- Inform health professionals not familiar with the management of these patients
- Remove from clinical practice any action that has been shown to be ineffective, or to have poor or questionable effectiveness, or to be not cost-effective.

This section of the Elaboration Handbook describes the elaboration method to develop Do's and don'ts factsheets for rare diseases.

1.3. The development process of Do's and Don'ts Factsheets for Rare Diseases: Main Steps

TASK	DEFINITION
Composition of the Development Group	• The develoment group shall be multisiciplinary, consisting of patients and carers, health professionals and a technical team
Define the scope and purpose	•The objective of the document, the target audience and the condition/health problem addressed are described
Developing a Do's and Don'ts Facsheet for Rare Diseases	• Structure of the document • Selection of the conten, key recommendations from CPGs, CDSTs and good-practice points • The documents retrieves must be assessed •Key ideas must be selected
Edition of the final document	•Do's and Don'ts Facsheets for rare diseases should be easily accesible to end-users.
External review	• The draft should undergow an external review by experts, to ensure its relevance and appropriateness

2. Composition of the Development Group

The development group of do's and don'ts factsheets for rare diseases shall be multidisciplinary. Ideally representatives from different geographical locations are incorporated in the development group.

The following profiles should be represented on the working group:

- Health professionals from all relevant professional groups
    - Ideally, members of the ERN should come from different parts of Europe, but this will be influenced by the expertise available
    - General practitioners, and/or paediatricians, in the case of a paediatric disease. For diseases revealed at paediatric age, the group should involve specialists in childhood and adulthood management of the disease, to cover the transition from paediatric to adult healthcare services [3]
    - Specialists integrating the set of activities of all the professionals involved
    - It would be appropriate to include members of the development groups of retrieved CPGs and CDSTs, if possible
- Patients and/or carers and/or patient representatives

  When the term 'patients' and 'carers' is used in this handbook, it is intended to include people with specific rare disease conditions and disabilities and their family members and carers. It also includes members of organisations representing the interests of patients and carers.
- A technical team consisting of:
    - A methodologist with knowledge in critical appraisal
    - An information specialist with knowledge of databases and literature searching

It is desirable that the number of participants included in the working group is 7 to 15 members, apart from the technical team, in order to work effectively and be representative.

The following data for each author is included in the final document: name, discipline/content expertise, institution, geographical location, a description of the member's role and contact details.

Potential conflict of interests should be carefully identified and duly addressed, following the indications established in WP-A of the TENDER.

3. Developing a Do's and Don'ts Factsheets for Rare Diseases

3.1. Scope and purpose

It is essential to define the objective and the scope of the do's and don'ts factsheet for rare disease.

- The objective of the document
- The target audience could be:
    - Professionals not used to the management of patient with a rare disease
    - Patients and their families
- The condition/health problem addressed is reported
    - The population to whom the document is meant to apply is specifically described
    - The topic(s) addressed (e.g., surgery, pregnancy, physical activity, anesthesia, etc.)

3.2. Structure of Do's and Don'ts Factsheets for rare diseases

Common points that this type of documents should contain are the following:

- Condition or topic(s) addressed
- Objective
- Target audience
- Data on the people who have elaborated the document: name, discipline/content expertise, institution, geographical location, a description of the member's role and contact details. Specify whether they are professionals or patients.
- Declaration of interest of all members who have participated in the elaboration must be included
- Funding of the document
- Date of publication
- Methodology approach:
    - Either it is derived from evidence-based documents (CPGs or CDSTs) or good-practice points
    - Literature searches (key characteristics on how the search is conducted, e.g., information sources)
    - Method used for the quality appraisal of the evidence
- A brief introduction that contextualises the "do's" and "don'ts" recommendations. E.g., when and how recommendations would be considered and applied
- List of recommendations:
    - What is recommended to be done
    - What shouldn't be done
- Bibliography

3.3. Content of Do's and Don'ts Factsheets for rare diseases

A do's and don'ts factsheet for rare diseases can be based on CPGs, CDSTs (e.g., clinical consensus statements) recommendations and good-practice points based on the clinical experience of the development group.

- They must be based on the latest evidence-based practice and research on the topic

- "Do's" and "don'ts" recommendations will be agreed upon by the working group

3.3.1. Search and selection of the scientific evidence

The relevant information to be considered by the development group may come from the following sources:

- CPGs
- CDSTs (e.g., clinical consensus statements)

An information retrieval expert with knowledge of databases and literature searching must be incorporated to the technical team. Indications on how to conduct a literature search (identification and selection of information sources, development of search strategies, database navigation) can be found at chapter 5. Selection of sources of information of the Handbook #4: Methodology for the elaboration of CPGs for rare diseases.

In some cases, the development group may find it necessary to retrieve available original studies (clinical trials and observational studies) or systematic reviews and related research on the topic too.

3.3.2. Quality appraisal

A quality assessment of retrieved CPGs and CDSTs must be performed, as good quality "do's" and "don'ts" recommendations must be based on good quality original CPGs or CDSTs.

- It is not necessary to perform the quality appraisal of CPGs or CDSTs elaborated *de novo* by ERNs
- Existing CPGs must be evaluated with AGREE II instrument and rated as recommended or highly recommended [4] (see Handbook #2: Appraisal of existing CPGs and CDSTs for rare diseases and Assessment Phase on Handbook #3: Adaptation and Adoption of CPGs and CDSTs)
- Existing CDST (e.g., clinical consensus statements) must be critically evaluated. Please see Handbook #2: Appraisal of existing CPGs and CDSTs for rare diseases and Assessment Phase on Handbook #3: Adaptation and Adoption of CPGs and CDSTs

When performing the quality appraisal of an existing CPG or CDST, it must be assessed if bias has been minimised in the evidence review of the original CPG or CDST. The choice of methodology for analysing data should have been justified in the existing documents, as well as the quality appraisal of individual studies described (see Handbook #2: Appraisal of existing CPGs and CDSTs for rare diseases). Besides, how recommendations have been informed (from evidence to decision) should be assessed, since the original document must show consistency, as described in the Assessment Phase on Handbook #3: Adaptation and Adoption of CPGs and CDSTs.

- For original studies (clinical trials and observational studies) or systematic reviews, the evidence will be analysed and synthesised in evidence tables

For further information in the appraisal and synthesis of scientific evidence, please see chapter 6 of Handbook #4: Methodology for the elaboration of CPGs for rare diseases.

3.3.3. Key ideas to be transmitted must be selected

The "do's" and "don'ts" recommendations must be reliable and reflect what is in the original documents, when they are based on CPGs and CDSTs, and/or regular clinical care. When there is insufficient information available to make an evidence-based "do's" or "don't" recommendation, and the development working group reaches a consensus about an activity or procedure based only on their clinical experience, it must be identified and differentiated from those based on scientific evidence.

The experts must make recommendations by consensus, the development of which is detailed in the Handbook #5: Methodology for the elaboration of Clinical Consensus Statements for rare diseases.

4. Edition of the final document

The final document should be easily accessible to end-users. The information must be structured to facilitate its reading and understandability. Furthermore, some aspects concerning readability are very relevant (e.g., the use of the language and the format). More detailed information on editing and format is provided in the Handbook #11: Methodology for the elaboration of Patient Information Booklets for rare diseases"

The working group should select the most relevant information to be transmitted to the target audience (basic "do's" and "don'ts" recommendations). Another key aspect is the contextualisation of the information (e.g., common situations, emergency situations, etc.).

Recommendations must be clearly differentiated:

- What is recommended to be done ("do's" recommendations)
- What shouldn't be done ("don'ts" recommendations)

In addition, it should include a plan for a future updating, as it is appropriate to update these documents so that they do not include "don'ts" recommendations that are no longer followed in regular practice.

4.1. Do's and Don'ts Factsheets for rare diseases should be easy to find and use

It is important to define the media in which the factsheet will be displayed, which will be determined by the target population to which it is addressed (e.g., printable materials, social media, etc.).

4.2. Languages

In the ERN framework, do's and don'ts factsheets for rare diseases must be available in all languages in EU.

5. External review

After the development of the document, the draft must undergo an external review by experts, to ensure its relevance and appropriateness.

The document will be circulated to ERN members, other health professionals (e.g., general practitioners, paediatricians, physical therapists, surgical specialists, etc.), and patients and/or carers. A structured questionnaire/survey could be used to collect information.

The whole process should be well documented and transparent.

Key issues

- *The development group of do's and don'ts factsheets for rare diseases shall be multidisciplinary and geographically representative*
- *The first step is to define the scope and purpose of the Do's and Don'ts Factsheet for rare diseases*
- *Relevant information considered by the development group may come from CPGs, CDSTs (e.g., clinical consensus statements) and clinical experience*
- *A quality appraisal must be performed (see Handbook #2: Appraisal of existing CPGs and CDSTs for rare diseases and Assessment Phase on Handbook #3: Adaptation and Adoption of CPGs and CDSTs)*
- *"Do's" and "don'ts" recommendations must be made by consensus*
- *A list of recommendations must be provided, with a clear distinction between:*
    - *What is recommended to be done ("do's" recommendations)*
    - *What shouldn't be done ("don'ts" recommendations)*
- *Aspects regarding readability and contextualisation are very relevant*
- *In the ERN framework, do's and don'ts factsheets for rare diseases must be available in all languages in EU*
- *The draft of the do's and don'ts factsheet should be reviewed by experts, to ensure its relevance and appropriateness*

6. Abbreviations

CPG	Clinical Practice Guideline
CDST	Clinical Descision Support Tool
ERNs	European Reference Networks
EtD	Evidence to Decision
EU	European Union
IACS	Instituto Aragonés de Ciencias de la Salud (Aragon Health Sciences Institute)
SR	Systematic Reviews
WP	Work Package

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