European Reference Networks | ERN GUIDELINES

D-B.2

TENDER Nº
SANTE/2018/B3/030

European Reference Network: Clinical Practice Guidelines And Clinical Decision Support Tools

July 12th 2020

(D-B.2)

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

Introductory document

Prepared by WP-B leader:
Aragon Health Sciences Institute (IACS)

Disclaimer:

The information and views set out in this report are those of the author(s) and do not necessarily reflect the official opinion of the Commission. The Commission does not guarantee the accuracy of the data included in this study. Neither the Commission nor any person acting on the Commission's behalf may be held responsible for the use, which may be made of the information contained therein.

Document history:

Issue Date	Versions	Changes Made/Reason for this issue
September 28th 2020	V3.0	Final report delivered to Commission Services
September 3rd 2020	V2.1	Revised report delivered to Fundación Pública Andaluza Progreso y Salud
July 12th 2020	V2.0	Final report delivered to Commission Services
June 29th 2020	V1.3	Final version delivered to Fundación Pública Andaluza Progreso y Salud
June 29th 2020	V1.2	Last references added and formatting
June 24th 2020	V1.1	Draft version for initial review

Dissemination level:

PU	Public	
IN	Internal use only	
CO	Confidential, only for members of the consortium, expert panel participating in the consultation (including Commission Services)	X

Document information:

D-B.2 Methodological Toolkit for Clinical Practice Guidelines and Clinical Decision Support Tools for Rare Diseases - Introductory document

Authors: coordination team (in alphabetical order)

María Bono Vega, BSc in Biochemistry
Aragon Health Sciences Institute (IACS, Spain)

Patricia Gavín Benavent, MD, PhD
Aragon Health Sciences Institute (IACS, Spain)

María Soledad Isern de Val, BSc in Biochemistry, PhD
Aragon Health Sciences Institute (IACS, Spain)

Celia Muñoz Fernández, BA in Economics
Aragon Health Sciences Institute (IACS, Spain)

Lucía Prieto Remón, BA in Business and Marketing
Aragon Health Sciences Institute (IACS, Spain)

Authors: Information Specialist

María Pilar Blas Diez, Information Specialist
Aragon Health Sciences Institute (IACS, Spain)

Authors: internal reviewers (in alphabetical order)

María Pilar Calvo Pérez, MD
Aragon Health Sciences Institute (IACS, Spain)

Sandra García Armesto, MD, PhD
Aragon Health Sciences Institute (IACS, Spain)

Authors: collaborators (in alphabetical order)

Juan Ignacio Martín Sánchez, MD
Aragon Health Sciences Institute (IACS, Spain)

Silvia Vázquez Fernández del Pozo, MD, PhD
Aragon Health Sciences Institute (IACS, Spain)

María José Vicente Edo, BSc in Nursing
Aragon Health Sciences Institute (IACS, Spain)

Authors: Administrative assistance

María Esther García Pomar, Administrative officer
Aragon Health Sciences Institute (IACS, Spain)

Short Description:

Introduction to the D-B.2 Methodological handbook and toolkit for the prioritisation, appraisal, adaptation, development and implementation of CPGs and CDSTs for rare diseases.

TABLE OF CONTENTS

ABBREVIATIONS

AETSA	Andalusian Health Technology Assessment Department
AGREE II	Appraisal of Guidelines for Research & Evaluation II
CDSTs	Clinical Decision Support Tools
CPGs	Clinical Practice Guidelines
ERN	European Reference Network
EU	European Union
FPS	Fundación Pública Andaluza Progreso y Salud
G-I-N	Guidelines International Network
GRADE	Grading of Recommendations Assessment, Development and Evaluation
WP	Work package

01.

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 barrier is the lack of high-quality evidence, in which the foremost methodological frameworks like GRADE rely on 1.

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.

02.

SCOPE

2.1 | Aim of the Toolkit

This toolkit aims at providing methodological guidance and foster skill development for the prioritisation, appraisal, adaptation, adoption, development and implementation of CPGs and CDSTs for rare diseases in the context of ERNs.

2.1.1 / What this Toolkit is

This toolkit is a practical set of methodological handbooks and tools for the prioritisation, appraisal, adaptation, development and implementation of CPGs and CDSTs for rare diseases developed for the ERNs and based on existing methodologies relevant and applicable for rare diseases, as well as general methodological approaches with a wide international consensus.

2.1.2 / What this Toolkit is not

This toolkit is not a methodological approach developed de novo for the prioritisation, appraisal, adaptation, development and implementation of CPGs and CDSTs for rare diseases

2.2 | Who is the Toolkit for

The target audience of this toolkit are the ERNs, but it could also be useful for any professional working within the scope of rare diseases who would like to develop new or use existing evidence-based CPGs or CDSTs.

2.3 | Clinical Practice Guidelines (CPGs) and Clinical Decision Support Tools (CDSTs) covered in this Toolkit

This toolkit provides methodology for the appraisal, adaptation, adoption, development and implementation of the CPGs and CDSTs defined in a previous TENDER *Taxonomy and templates for the European Reference Networks documents* (SANTE/2017/B3/083), as per the specifications of the TENDER NºSANTE/2018/B3/030, under which this Toolkit has been developed. These CPGs and CDSTs are the following:

Clinical Practice Guidelines

Clinical practice guidelines (CPGs) are systematically developed statements that include recommendations, intended to optimise patient care, that are informed by a systematic review of evidence and an assessment of the benefit and harms of alternative care options [2]. The level of evidence needs to be stated.

Clinical Consensus Statements

Clinical consensus statements reflect opinions drafted by subject matter experts for which consensus is sought using explicit methodology to identify areas of agreement and disagreement. In contrast to clinical practice guidelines, which are based primarily on high-level evidence, clinical consensus statements are more applicable to situations where evidence is limited or lacking, yet there are still opportunities to reduce uncertainty and improve quality of care [3, 4]. It offers specific recommendations on a topic. It does not give specific algorithms.

Evidence Reports

Evidence reports are systematic reviews that summarises the best available evidence on a topic. Evidence reports are generally used by clinical professional organisations to support the development of clinical practice guidelines or by policy makers to inform their programme planning and research priorities [5].

Diagnostic, Monitoring and Therapy Pathways

Diagnostic, monitoring and therapy pathways are multidisciplinary management tools which describe the procedure for the care and treatment of a disease, condition or complex procedure. Their aim is to improve the care and management of patients, while enhancing the coordination of healthcare around the patient. They include the “red flags” that may lead to suspicion on the disease, condition or complex procedure, how to reach a definite diagnosis and the management and follow-up recommendations, establishing the sequences for each action and defining the responsibilities of the different professionals who will intervene in the diagnostic, monitoring and therapy pathway [6].

Evidence-based Protocols

Evidence-based protocols are an agreed detailed framework outlining in chronological order the care procedures that will be performed in a designated area of practice. Evidence-based protocols state what should be done, and how it should be done. It is adapted to the health care environment and the available resources [7]. In order to facilitate its use, evidence-based protocols usually include a flowchart in which the steps to be taken and the agents involved in the evidence-based protocols' workflow are clearly depicted.

Do’s and Don’ts Factsheets for Diseases

Do’s and Don’ts Factsheets are tools that provide advice that needs to be considered when assisting patients with specific rare diseases, conditions or in need of complex procedures. These documents aim to assist patients, caregivers 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) [8]. Do’s and don’ts factsheets can be based on existing CPGs or CDSTs recommendations (i.e., one or more documents), or they may consist of a stand-alone product developed from scratch by a panel of experts making recommendations by consensus (e.g., specialists on rare diseases who collect established and well-known clinical practice information about patient management, as a guide to other specialists involved in the treatment of people living with a rare disease).

Quality Measures

Quality measures are tools that quantify healthcare processes, outcomes, patient perceptions, and organizational structure and/or systems. These instruments provide healthcare professionals and policy makers with information associated with healthcare performance and the extent to which high quality health care is being provided. There are three types of quality measures/indicators (structure, process, and outcome), as framed in the Donabedian model [9, 10].

There are different frameworks for classifying quality measures. The main models structure measurements based on six aims for healthcare systems [11], which are effective, safe, efficient, patient-centered, equitable, and timely care according to the Institute of Medicine [12] approach.

Patient Information Booklets

Document that provides condition-specific information in lay language, to inform patients on best medical practice in an informative and accessible way [13, 14]. Patient information booklets can be based on a CPG, a CDST or consist of a stand-alone product that provides general information for the patient.

03.

OVERVIEW OF THE METHODS OF THE HANDBOOKS AND TOOLS

Work Package B work has been developed during the first six months of the TENDER NºSANTE/2018/B3/030, i.e., from January to June 2020. It started with an exhaustive analysis of the state of the art on methodologies for CPGs and CDSTs for rare diseases, which was reviewed by experts from the ERNs and institutions with methodological expertise. This was conducted from January to March 2020 and summarised in deliverable B.1 *Report on the Literature Review and Expert Consultation* (D-B.1). D-B.1 findings were incorporated in the development of this Methodological Handbooks and Toolkit, which is the second and last deliverable of WP-B (D-B.2) and has been developed from March 2020-June 2020.

In addition to the methodologies specific for rare diseases retrieved in D-B.1, other methodological approaches with a wide international consensus have been considered and used for the development of these Methodological Handbooks and for the Toolkit. These include, for example, the Guidelines International Network (G-I-N) standards for guideline development [15], the Appraisal of Guidelines for Research & Evaluation II (AGREE II) [16], Grading of Recommendations Assessment, Development and Evaluation (GRADE) [1] and the ADAPTE methodology for guideline adaptation [17, 18]

Furthermore, the ERNs and institutions with methodological expertise have participated in a consultation made by means of online surveys about the prioritisation of conditions that require CPGs and CDSTs the appraisal of CPGs and CDSTs for rare diseases.

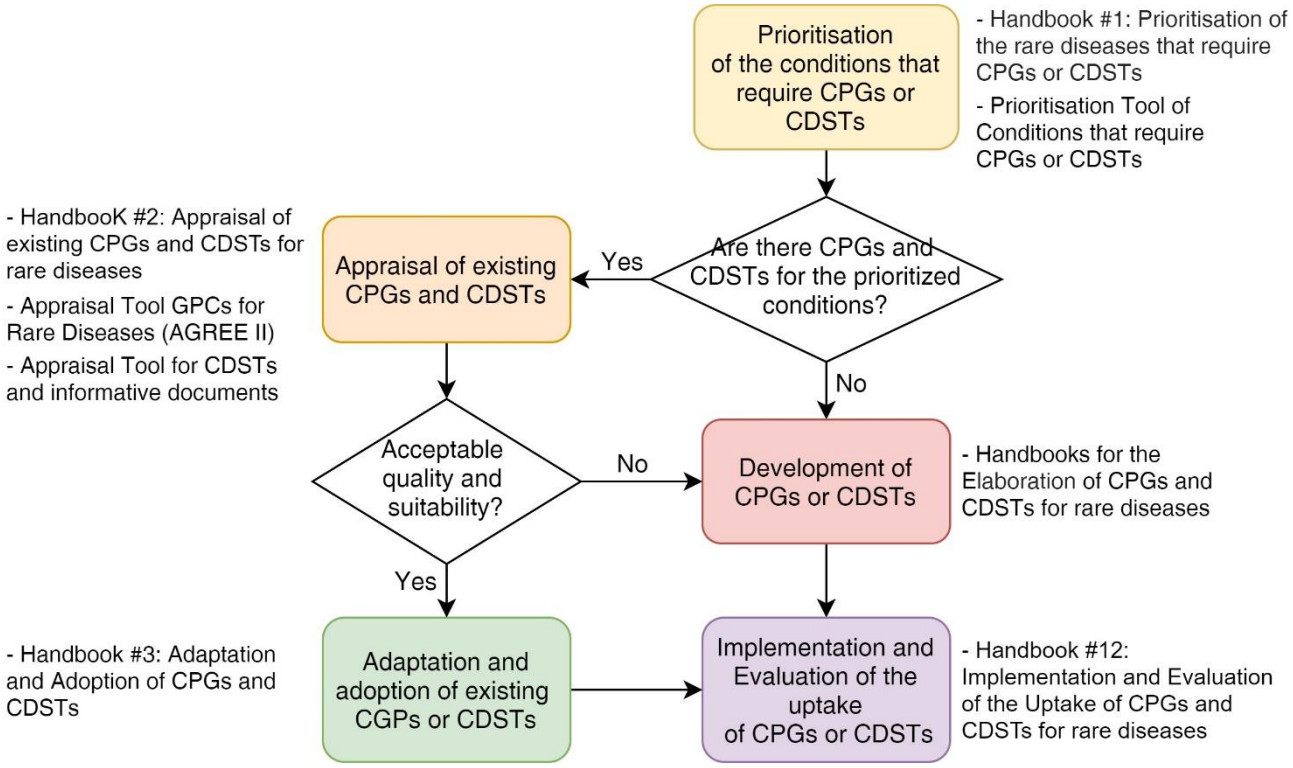
More detailed information on the development of each handbook and tool can be found in the respective documents.

04.

STRUCTURE OF THE TOOLKIT

The structure of the toolkit follows the subsequent milestones for the use of CPGs and CDSTs, from the prioritisation of conditions that require CPGs or CDSTs to the implementation of the CPGs or CDSTs. Figure 1 shows the main milestones of this process.

Figure 1. Milestones for the use of CPGs and CDSTs.



05.

CONTENT OF THE TOOLKIT: HANDBOOKS, TOOLS AND OTHER RESOURCES

5.1 | Prioritisation

Handbook #1: Prioritisation of the rare diseases that require CPGs or CDSTs

This handbook includes a detailed explanation of the prioritisation criteria and of the prioritisation process, including the use of the prioritisation tool.

Tool #1: Prioritisation Tool of Conditions that Require CPGs or CDSTs

This tool provides a prioritised list of conditions and a heat map, as a result of the assessment of the relevance of a pre-defined list of conditions for the development of CPGs or CDSTs.

5.2 | Appraisal

Handbook #2: Appraisal of existing CPGs and CDSTs for rare diseases

This handbook includes a pragmatic assessment process of the methodological quality of CPGs, CDSTs and informative documents for rare diseases, including the use of the CPG and CDSTs appraisal tools.

Tool #2.1: Appraisal Tool for CPGs (AGREE II)

The tool for the quality assessment of CPG has been developed based on AGREE II instrument. It includes a set of templates aimed at facilitating the quality appraisal of CPGs and the subsequent discussion within the working group.

Tool #2.2: Appraisal Tool for CDSTs and informative documents

This tool presents the appraisal criteria for CDST and informative documents in a template to be completed, which helps to assess whether they meet the minimum quality requirements for their use.

5.3 | Adoption and Adaptation

Handbook #3: Adaptation and Adoption of CPGs and CDSTs

This handbook describes the elements that should be addressed in order to decide on whether a CPG or a CDST for rare diseases can be adopted or adapted and indicates the actions that must be followed to adopt and adapt a CPG and a CDST for rare diseases.

5.4 | Development

Handbooks #4 – 11: Handbooks for the Elaboration of CPGs and CDSTs for Rare Diseases

These handbooks explain the steps to develop a CPG or CDST for rare diseases, including the definition of the scope and purpose, the formulation of clinical questions and the search, selection, appraisal and synthesis of the scientific evidence, among others. There is a development handbook for CPGs and each CDSTs covered in this toolkit.

- ✓ Handbook #4: Methodology for the elaboration of CPGs for rare diseases
- ✓ Handbook #5: Methodology for the elaboration of Clinical Consensus Statements for rare diseases
- ✓ Handbook #6: Methodology for the elaboration of Evidence Reports for rare diseases
- ✓ Handbook #7: Methodology for the elaboration of Diagnostic, Monitoring and Therapy Pathways for rare diseases
- ✓ Handbook #8: Methodology for the elaboration of Evidence-based Protocols for rare diseases
- ✓ Handbook #9: Methodology for the elaboration of Do's and Don't's Factsheets for Diseases for rare diseases
- ✓ Handbook #10: Methodology for the elaboration of Quality Measures for rare diseases
- ✓ Handbook #11: Methodology for the elaboration of Patient Information Booklets for rare diseases

5.5 | Implementation

Handbook #12: Implementation and Evaluation of the Uptake of CPGs and CDSTs for rare diseases

This handbook provides the steps that have to be taken in order to implement a CPG or a CDST for rare diseases, including the selection of the CPG or CDST to implement, the planning of the implementation, analysis of the context, design if the interventions and methods to carry out their evaluation of the implementation and of the uptake of the CPG or CDST, development of the implementation roadmap and design of the continuous improvement mechanism.

06.

BIBLIOGRAPHY

1. Guyatt G, Oxman AD, Akl EA, Kunz R, Vist G, Brozek J, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. J Clin Epidemiol. 2011;64(4):383-94.

2. Institute of Medicine (US) Committee on Standards for Developing Trustworthy Clinical Practice Guidelines. Clinical practice guidelines we can trust [Internet]. Washington (DC): National Academies Press (US); 2011 [cited 15/06/2020]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK209539/.

3. Rosenfeld RM, Nnacheta LC, Corrigan MD. Clinical Consensus Statement Development Manual. Otolaryngology--head and neck surgery: official journal of American Academy of Otolaryngology-Head and Neck Surgery. 2015;153(2 Suppl):S1-s14.

4. Beighton D. Consensus Statements. Caries Res. 2017;51(5):I-II.

5. EPC Evidence-Based Reports. 2013 [cited 19/03/2020]. Available from: https://www.ahrq.gov/research/findings/evidence-based-reports/index.html.

6. GuíaSalud: Biblioteca de Guías de Práctica Clínica del Sistema Nacional de Salud [Internet]. 2019 [cited 23/06/2020]. Definiciones y tipología OPBES: Vías Clínicas. Available from: https://portal.guiasalud.es/definiciones-tipologia-opbe/#1537695268615-b7f631b8-7a14.

7. GuíaSalud: Biblioteca de Guías de Práctica Clínica del Sistema Nacional de Salud [Internet]. 2019 [cited 23/06/2020]. Definiciones y tipología OPBES: Protocolos. Available from: https://portal.guiasalud.es/definiciones-tipologia-opbe/#1537695224514-45ead613-5807.

8. VASCERN [Internet]. European Reference Network on Rare Multisystemic Vascular Diseases (VASCERN); [2019] [cited 19/03/2020]. VASCERN Do's and Don'ts factsheets for rare vascular disease patients facing frequent situations. Available from: https://vascern.eu/what-we-do/dos-donts-factsheets-for-rare-vascular-disease-patients/.

9. Donabedian A. The definition of quality and approaches to its assessment. Ann. Arbor, Mich.: Health Administation Press; 1980.

10. Agency for Healthcare Research and Quality [Internet]. Rockville, MD: AHRQ; 2015 [cited 23/06/2020]. Select Health Care Quality Measures for a Consumer Report. Available from: https://www.ahrq.gov/talkingquality/measures/index.html.

11. Centers for Medicare & Medicaid Services [Internet]. CMS; [cited 23/06/2020]. Quality Measures. Available from: https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-

Instruments/QualityMeasures#:~:text=Quality%20measures%20are%20tools%20that,quality%20goals%20for%20health%20care.

12. Institute of Medicine Committee on Quality of Health Care in America. Crossing the Quality Chasm: A New Health System for the 21st Century. Washington (DC): National Academies Press (US). 2001.

13. European CHS Network. Central Hypoventilation Syndrome: Patient and Carer Information Booklet [Internet]. 2012 [cited 23/06/2020]. Available from: http://www.ichsnetwork.eu/upload/gaslini_ondine/gestionedocumentale/EU-CHS%20Patient%20Information%20Booklet_784_2550.pdf.

14. Keinki C, Zowalla R, Wiesner M, Koester MJ, Huebner J. Understandability of Patient Information Booklets for Patients with Cancer. J Cancer Educ. 2018;33(3):517-27.

15. Qaseem A, Forland F, Macbeth F, Ollenschlager G, Phillips S, van der Wees P, et al. Guidelines International Network: toward international standards for clinical practice guidelines. Ann Intern Med. 2012;156(7):525-31.

16. AGREE Next Steps Consortium. The Appraisal of Guidelines for Research and Evaluation (AGREE) II Instrument [Internet]. 2017 [cited 15/06/2020]. Available from: https://www.agreetrust.org/. .

17. The ADAPTE Collaboration. The ADAPTE Process: Resource Toolkit for Guideline Adaptation.[Internet]. 2009 [cited 23/06/2020]. Available from: http://www.g-i-n.net.

18. Abdul-Khalek RA, Darzi AJ, Godah MW, Kilzar L, Lakis C, Agarwal A, et al. Methods used in adaptation of health-related guidelines: A systematic survey. J Glob Health. 2017;7(2):020412.

European Reference Networks

European Reference Networks | ERN GUIDELINES

Contact info:

FPS-AETSA
jantonio.blasco@juntadeandalucia.es
Fundación Pública Andaluza Progreso y Salud (FPS)

Avd. Américo Vespucio 15, Edificio S-2
C.P. 41092 Seville, Spain

+34 955 006636

European Commission