EURORDIS
Rare Diseases Europe

RARE-Bestpractices: how to retrieve, appraise and disseminate rare disease guidelines

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Council of European Federations, 28 October 2015

Best practice guidelines and European policy

Best practice guidelines:

a definition

- In health care, **guidelines** are **systematically developed statements** which assist providers, patients and stakeholders to make **informed decisions** about appropriate health care for specific circumstances (…)." (*RARE-Bestpractices project, Glossary*)
- Guidelines include **recommendations intended to optimize patient care** that are informed by a **systematic review of evidence** and an assessment of the **benefits and harms** of alternative care options. (*Institute of Medicine, 2011*)
- Guidelines can accelerate **translation of scientific evidence into health care practice** and **reduce uncertainty in clinical practice.**

The European context:

European Reference Networks

- The **Directive 2011/24/EU** on cross-border healthcare [OJEU 2011, L88/45] and the recent **Commission Delegated Decision** [OJEU 2014, L147/71] as well as **the Implementing Decision** [OJEU 2014, L147/79] **require ERNs and health care providers wishing to join ERNs to have the capacity of developing good practices guidelines**.

RARE-Bestpractices project

- **A platform for sharing best practices for the management of rare diseases**
- The project facilitates the exchange of knowledge on RD guidelines through the development of an online platform for sharing and appraising best practice guidelines, common methodological standards specific to RD guidelines, and the organisation of trainings for stakeholders.

- **A 4 years project : 2013-2016**
- **A European project Funded by DG Research under FP7-HEALTH-2012 INNOVATION-1**
- **15 partners across Europe**
- **Coordinated by the National Centre for Rare Diseases-Italian National Institute of Health.**
- http://www.rarebestpractices.eu

RARE-Bestpractices project

Project aims:

- The **collection, evaluation and dissemination** of existing best practices;
- An **agreed methodology** suitable to develop and update best practice guidelines;
- A **forum for exchanging information**, sharing lessons learnt and facilitating collaborations.

Objectives :

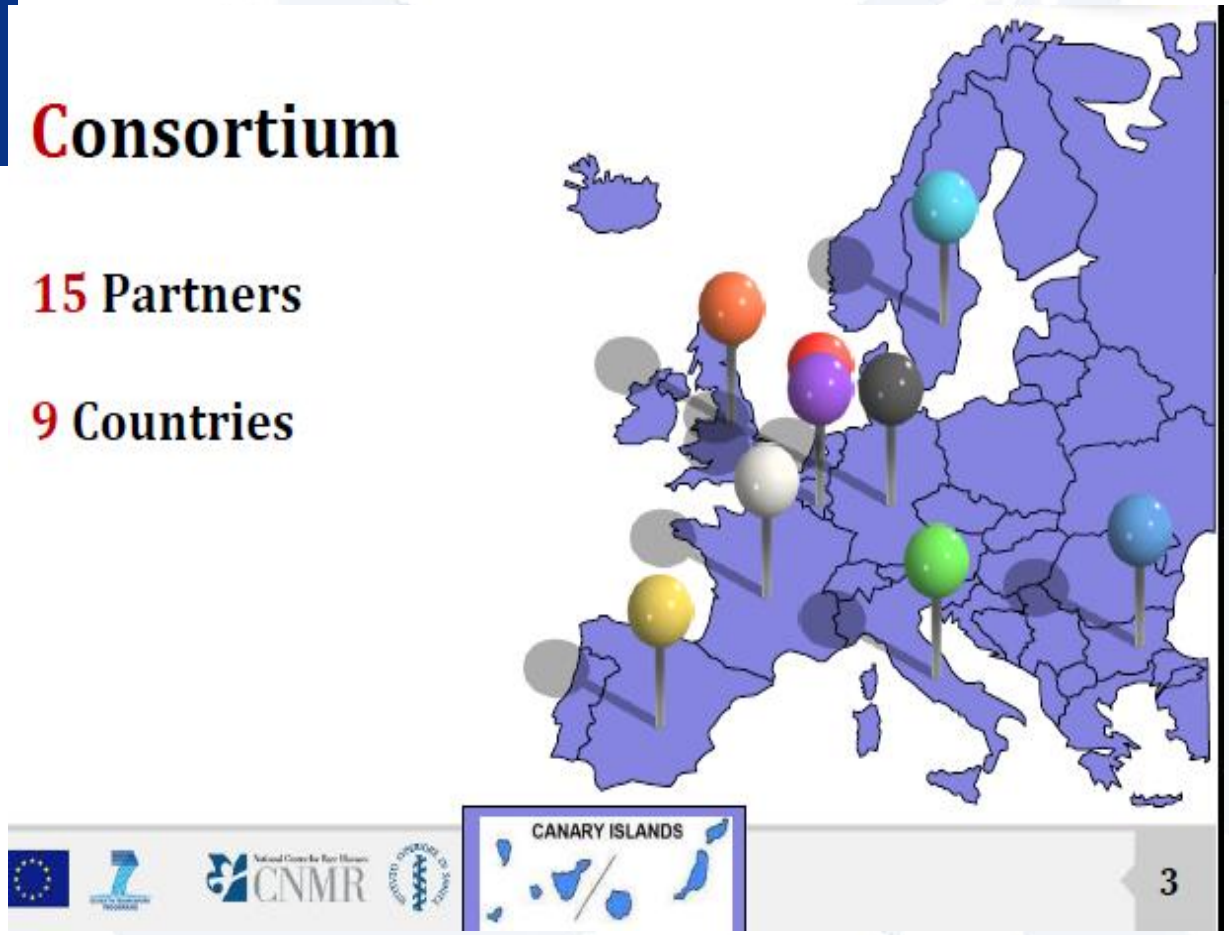
1. To capitalize on existing best practices documents
2. To develop an international, innovative, efficient framework to build consensus on the methodology suitable for the development and implementation of best practice guidelines for rare diseases
3. To provide training activities targeted to different stakeholders to share expertise and knowledge
4. To systematically identify gaps in scientific knowledge as well as related research needs, and recommend relevant research initiatives
5. To foster synergistic collaborations among agencies, institutions, networks and organizations experienced in best practices guideline development.

RARE-Bestpractices project: Partners

Consortium

15 Partners

9 Countries



Partners

Click on the institution's name for names and a profile of collaborators

- Istituto Superiore di Sanità - National Centre for Rare Diseases
- Jamarau
- Karolinska Institutet
- Healthcare Improvement Scotland
- London School of Economics and Political Science
- National Research Council
- EURORDIS, European Organisation for Rare Diseases
- Associazione per la Ricerca sull'Efficacia dell'Assistenza Sanitaria Centro Cochrane Italiano
- Universitaetsklinikum Freiburg
- Bulgarian Association for Promotion of Education and Science
- Fundación Canaria de Investigación y Salud
- Universiteit Maastricht - Institute for Public Health Genomics (IPHG)
- Newcastle University Upon Tyne
- The European Academy of Paediatrics
- Instituto de Salud Carlos III

EURORDIS Rare Diseases Europe

How can European Federations benefit from this project?

Identify and access guidelines developped in different EU countries and **languages**

Share guidelines internationally with patients and other stakeholders

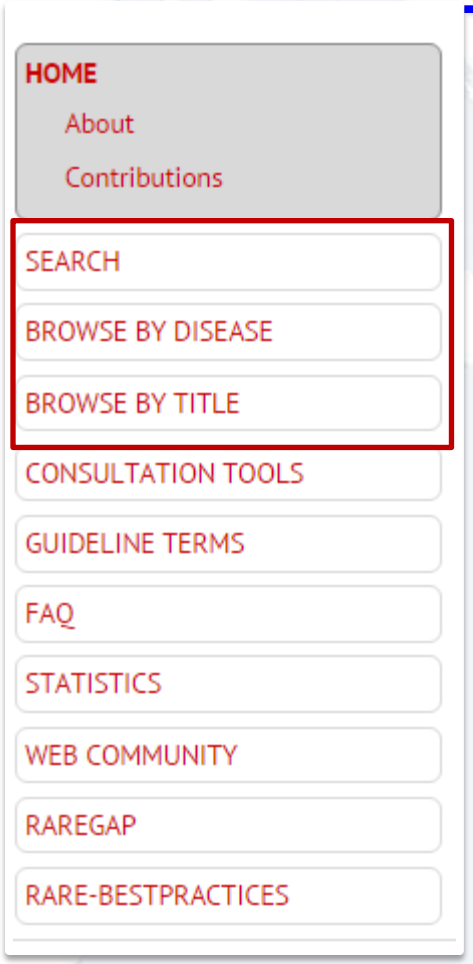
Access information about the **quality of guidelines** developped for your disease of interest

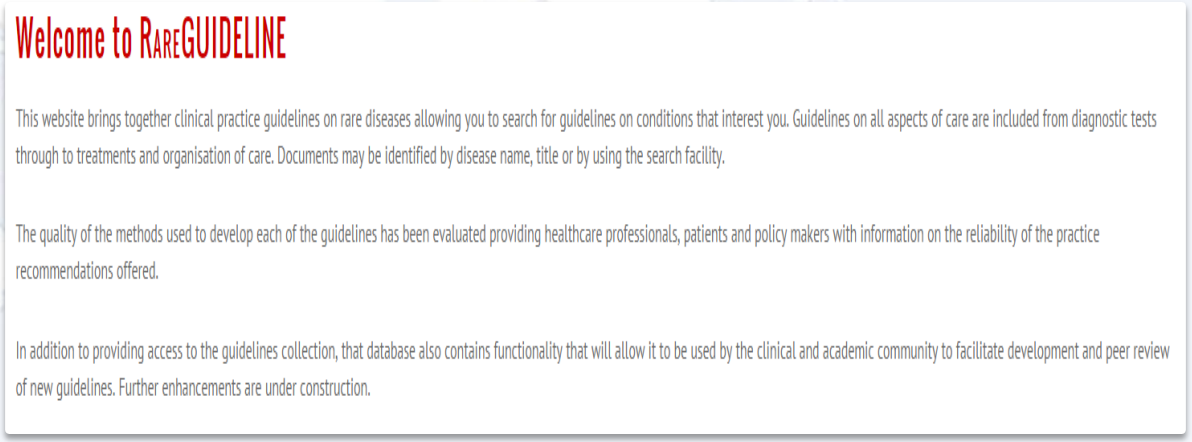
Access **training resources** on guidelines development and on quality assessment

Access **methodological support by the project consortium** to develop guidelines or to assess their quality.

A rare disease guideline database

http://rbpguidelines.eu/

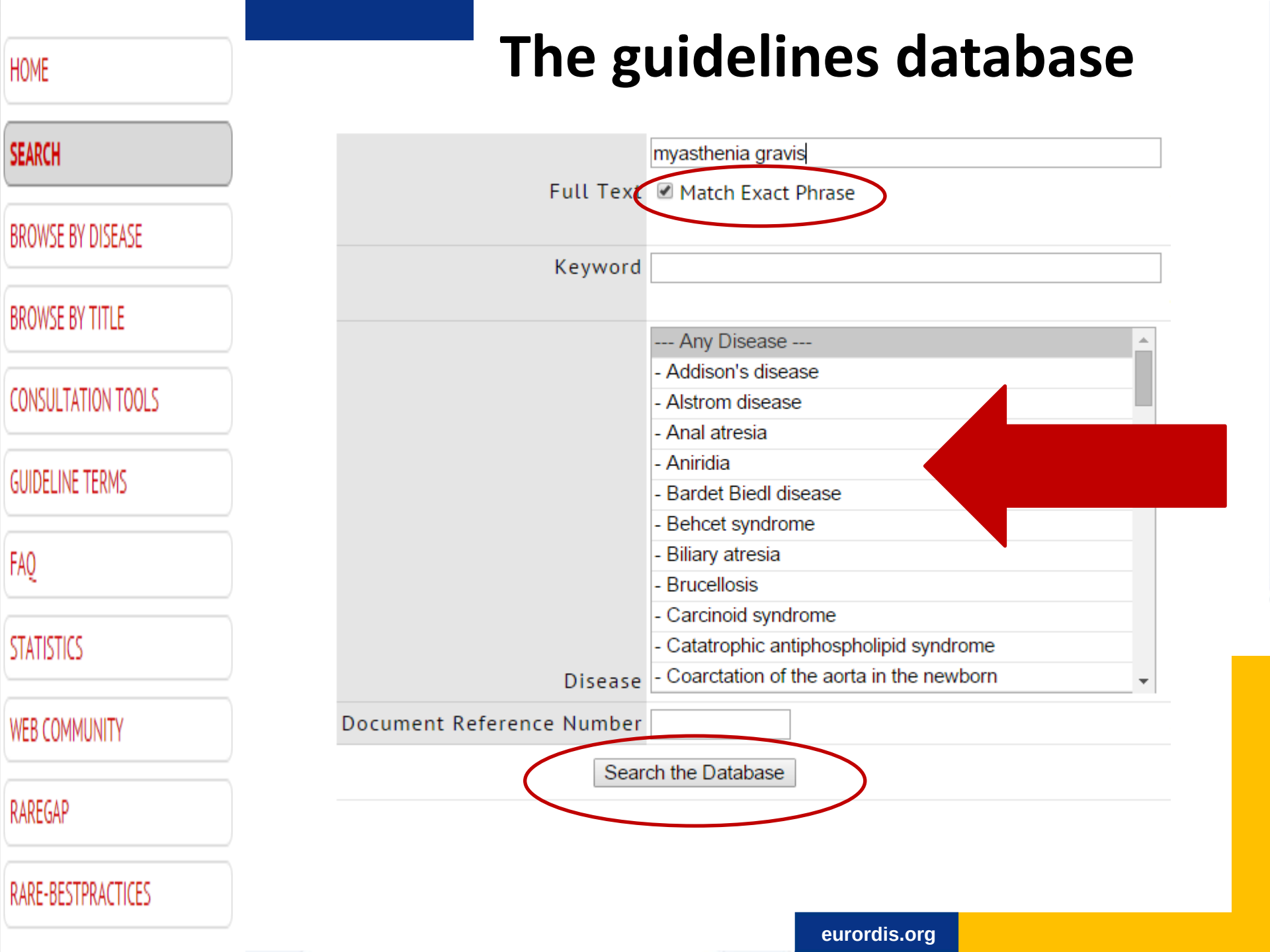




The collection of guidelines has started for an initial list of 44 RD drafted based on:

- Test conditions from search protocol development
- Project partners areas of interest
- Consultation of EURORDIS CEF (Spring 2014)
- NICE CKS topic suggestions
- European Academy of Paediatrics

The guidelines database



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The results of your search are provided below. Where your search has been successful results will be liste
Information, these will be displayed further down the page. A brief summary description for each docume
If your search has been unsuccessful (i.e. too many matches) you may need to broaden or tighten your sea
search parameters. To perform a new search click the 'search again' link below.

(VIEW SUMMARY DESCRIPTIONS) **(SEARCH AGAIN)**

(00009) Anaesthesia recommendations for patients suffering from myasthenia gravis
(00006) Guidelines for treatment of autoimmune neuromuscular transmission disorders
(00005) Intravenous immunoglobulin in the treatment of neuromuscular disorders
(00003) Myasthenia in pregnancy: best practice guidelines from a U.K. multispecialty working group

1

ASSOCIATED INFORMATION

Anesthesia recommendations for patients suffering from myasthenia gravis
EFNS/ENS guidelines for the treatment of ocular myasthenia
Guidelines for treatment of autoimmune neuromuscular transmission disorders
Intravenous immunoglobulin in the treatment of neuromuscular disorders
Myasthenia in pregnancy - best practice guidelines from a UK multispecialty working group

2

Exploring a guideline record

Bone cancer

Current Version | Status and Details | Guideline Evaluation | Guideline Development | Associated Information | Historic Versions | Print

This guideline has been subjected to an evaluation conducted applying the AGREE II methodology. The details of the evaluation are shown below, including the number of evaluators and their i responses to each review question.

Note that the response range is: Strongly Disagree (1) (2) (3) (4) (5) (6) (7) Strongly Agree.

Question	Evaluators: 2	
Scope and Purpose	Response	Comments
1. The overall objective(s) of the guideline is (are) specifically described.	2	Can be inferred but not clear at all to a naive reader
	4	Statement on pMS-2 describes which types of bone cancers are covered. Also table of contents is helpful in identifying what is covered. Also, general statement in the guideline development info 'The NCCN Guidelines are intended to assist all individuals who impact the decision making in cancer care including physicians, nurses, pharmacists, payers, patients and their families, and many others.'
2. The health question(s) covered by the guideline is (are) specifically described.	2	Can be inferred but not described
	3	No specifically described but can be identified from table of contents.
3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	2	Can be inferred but not specifically described.
	4	Yes via statement of which tumours encompassed in the guidance.
Stakeholder Involvement	Response	Comments
4. The guideline development group includes individuals from all relevant professional groups.	5	Many relevant specialists but it appears that not all appropriate ones included. Online AGREE Advancing the science of practice guidelines. 2 information however indicates that panel makeup is designed to be inclusive: http://www.nccn.org/professionals/transparency.asp

Bone cancer

Current Version | Status and Details | Guideline Evaluation | Guideline Development | Associated Information | Historic Versions | Print

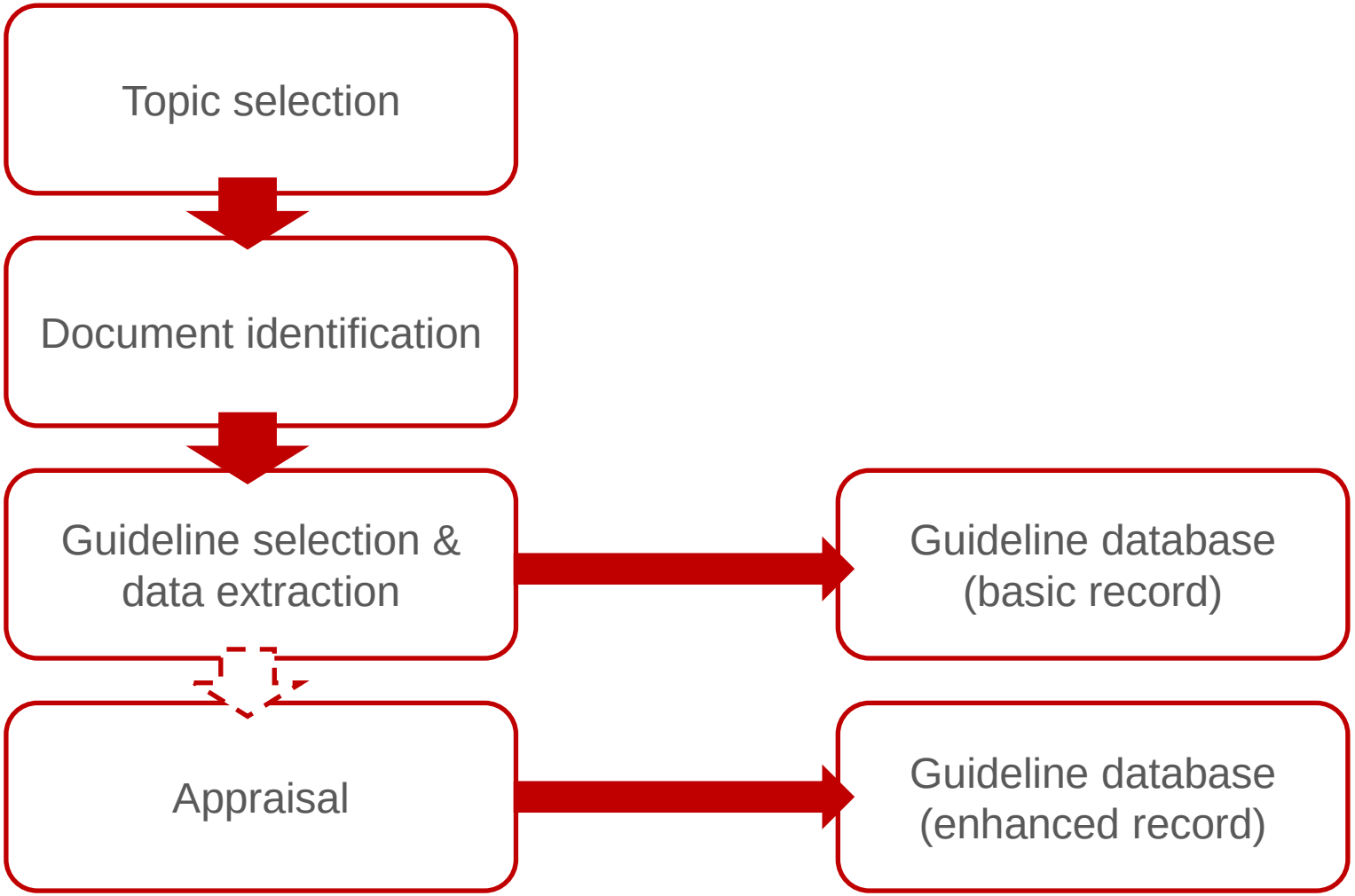
Associated Information (View Historic Versions)

This page contains links to full text versions of Guidelines where they are published in another database. It may also contain links to abstracts and other related information. You may have to purchase a subscription or pay a fee to access the full text of a guideline depending on the copyright and licensing provisions. Such fees have nothing to do with Rare-Bestpractices and you should contact the licenced distributor if you have any questions or concerns in regard to such fees.

Guidelines

Bone cancer

Guideline collection and appraisal: Process outline



Sources for collection of existing guidelines

Resource	URL
Orphanet	http://www.orpha.net/consor/cgi-bin/Disease.php?lng=EN
G-I-N (Guidelines Internat. Network)	http://www.g-i-n.net/
National Guidelines Clearinghouse	http://www.guideline.gov/
EuroGentest Molecular Testing	http://www.eurogentest.org/index.php?id=700
EuroGentest Clinical Utility Gene Cards	http://www.eurogentest.org/index.php?id=668
NICE Evidence Search*	http://www.evidence.nhs.uk/
Google (first 100 PDFs)	www.google.com
PubMed	http://www.ncbi.nlm.nih.gov/pubmed/

Inclusion/Exclusions in the database

	Inclusion	Exclusion
Document type	Any document produced by a stakeholder group which is described as a guideline, consensus statement, or best practice statement **AND** contains recommendations* for practice.	Patient information documents. Local (e.g. hospital) care protocols or pathways. Single author publications i.e. documents not produced by a stakeholder group.
Year	Published within 10 years	
Language	English, French, Spanish, Dutch, Swedish, Italian, German	
Topic	Directly relates to the named condition. Guidelines on single interventions for the named condition.	Generic symptom management e.g. dementia management. Reviews of single interventions which do not contain recommendations .
Format	PDF, web document, print document, journal article	Textbook or E-book

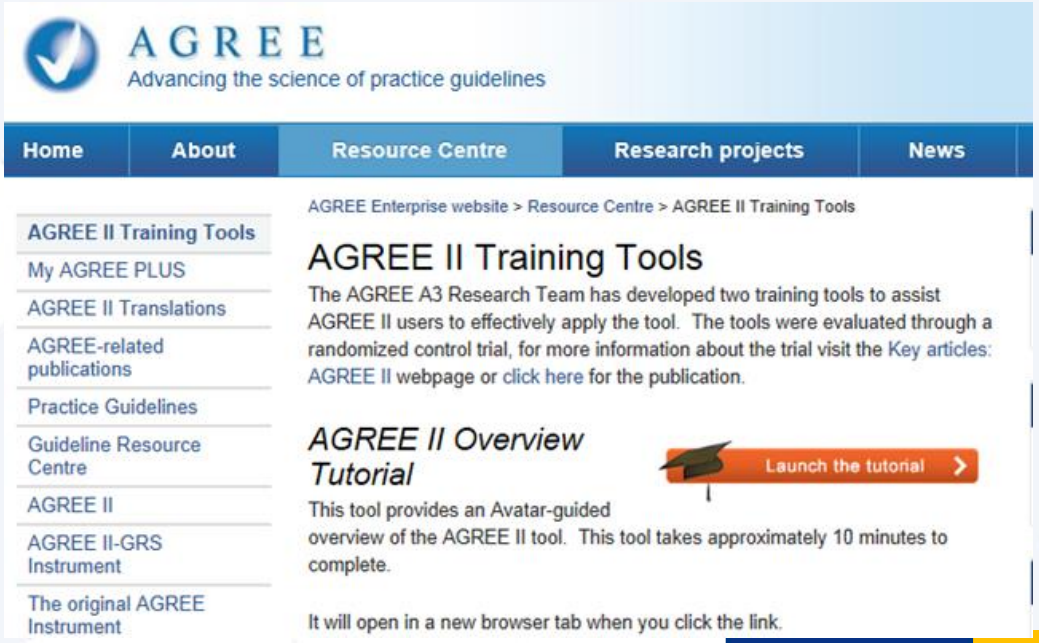
Initial list of 44 rare diseases for guidelines collection

1	Addison's disease	12	Congenital cataract	23	Herpes simplex encephalitis	34	Noonan syndrome
2	Alstom disease	13	Congenital myasthenias	24	Klinfelter's syndrome	35	Osteosarcoma
3	Anal atresia	14	Costello syndrome	25	Joint hypermobility syndrome	36	Paroxysmal haemoglobinuria
4	Aniridia	15	Cushing's syndrome	26	Huntington's disease	37	Phaeochromocytoma
5	Bardet Biedl disease	16	Cushing's disease	27	Long QT syndrome	38	Phenylketonuria
6	Biliary atresia	17	Cystic fibrosis	28	Lichen sclerosis	39	Porphyrias
7	Brucellosis (human)	18	Duchenne muscular dystrophy	29	Hirschsprung's disease	40	Progressive subnuclear palsy
8	Carcinoid syndrome	19	Epidermolysis bullosa	30	Lyme disease	41	Turner syndrome
9	Catatrophic antiphospholipi d syndrome	20	Gaucher's disease	31	Mitochondrial disease (multiple disorder)	42	Spinal muscular atrophy
10	Coarctation of the aorta in the newborn	21	Giant cell arteritis	32	Multiple myeloma	43	Phaeochromocytoma
11	Congenital anaemias	22	Hereditary spastic paraplegia (Strumpell-Lorrain disease)	33	Myasthenia gravis	44	Wolfram disease

Methodology for appraising guidelines

The project is using AGREE II, a tool to assess the quality of guidelines.

- An instrument developed by a group of international guideline developers and researchers, the AGREE Collaboration.
- Comprehensive tool for guideline appraisal
- Free resources: online tutorials, a guidelines assessment manual, etc. available on **AGREE II** website.



List of domains included in the AGREE II tool

The AGREE II tool includes 23 items for the evaluation of guidelines, organised into 6 domains:

- Domain 1: Scope and purpose
- Domain 2: Stakeholder involvement
- Domain 3: Rigour of Development
- Domain 4: Clarity of presentation
- Domain 5: Applicability
- Domain 6: Independence

Domain 1: Scope and purpose

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.

Domain 2: Stakeholder involvement

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.

Domain 3: Rigour of Development

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.

Domain 4: Clarity of presentation

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

Domain 5: Applicability

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.

Domain 6: Independence

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.

Guidance to adapt the AGREE II tool to RDs

Key issues:

- **Rigour of development:** **even if there is a low quantity of published evidence** for many RDs, the evaluator should assess the **rigour of the systematic methods** used to identify, select and synthetise evidence as well as the **transparency** in the presentation of the process used.
- **External review by experts**: these should absolutely **include patients, carers and/or patient groups. Comprehensive stakeholder involvement** (professionals/patients) is cricitcal for RDs even more as for common conditions because of the scarcity of experts.
- **Editorial independence:** for many RDs, there are likely to be only a **small number of experts worldwide, limiting the potential for editorial independence.**
- **Overall guideline assessment:** the **existence of only a few / or one guideline** on a topic should not prevent a judgment of « **no** » to the question: **would you recommend this guideline for use?** This would indicate that **better quality guidelines are needed (recommendation for researchers and for guidelines developers).**

How to be involved in the project:

- Contribute to the search and collection of guidelines
- Contribute to the appraisals of these guidelines
- Disseminate project tools
- Attend project trainings
- Engage in the project Patient Advisory Council

Your contribution to the collection / appraisal of guidelines

Topics still needing searches:

- Addison's disease
- Anal atresia
- Biliary atresia
- Brucellosis (human only)
- Carcinoid syndrome
- Congenital cataract
- Cushing's disease
- Cushing's syndrome
- Giant cell arteritis
- Herpes simplex encephalitis
- Hirschsprung's disease
- Huntington's disease
- Joint hypermobility syndrome
- Lichen sclerosis
- Long QT syndrome
- Multiple myeloma
- Noonan syndrome
- Paroxysmal nocturnal haemoglobinuria
- Phaeochromocytoma
- Progressive subnuclear palsy

Topics still needing appraisals:

- Cystic fibrosis
- Epidermolysis Bullosa
- Duchenne Muscular Dystrophy,
- Spinal Muscular Atrophy.

This list of topics is indicative and not limitative:

it will be extended as the project continues.

Your suggestions and contributions are most welcome.

Next trainings on guidelines: GET INVOLVED!

2nd International Course "Health care guidelines on rare diseases: Quality assessment" - Dec 3-4, 2015 - The application is now open!

Rome

The course will take place on **December 3-4, 2015** at Istituto Superiore di Sanità, Aula Rossi, via Giano della Bella, 34, 00162 Rome (Italy).

The application is now open!

Please refer to this link for the course programme and for further information.

http://www.iss.it/binary/cnmr4/cont/Programme_GL_assessment_2015_10_12.pdf

Rare Best Practices

Course for health care guidelines developers on treatments of rare diseases

February 10-12, 2016

Milan

EURORDIS Rare Diseases Europe

More information on project website

www.rarebestpractices.eu

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RARE-Bestpractices
A platform for sharing best practices for the management of rare diseases
Coordinated by the Istituto Superiore di Sanità
National Centre for Rare Diseases

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Dissemination

RARE-Bestpractices in peer-reviewed Journals

Menaka Pai, Alfonso Iorio, Joerg Meerpohl, Domenica Taruscio, Paola Laricchiuta, Pierpaolo Mincarone, **Cristina Morciano,** Carlo Giacomo Leo, Saverio Sabina, Elie Akl, Shaun Treweek, Benjamin Djulbegovic, Holger Schunemann & Consortium for the RAREBestpractices (2015) Developing methodology for the creation of clinical practice guidelines for rare diseases: A report from RARE-Bestpractices, Rare Diseases, 3:1, e1058463, DOI: 10.1080/21675511.2015.1058463

Taruscio D, Morciano C, Laricchiuta P, et al. RARE-Bestpractices: a platform for sharing best practices for the management of rare diseases. *Rare Diseases and Orphan Drugs. An International Journal of Public Health* 2014; 1(1):5-8 (EN)

Sejersen T, Del Giovane C, Filippini G, Leo CG, Meerpohl JJ, Mincarone P, Minozzi S, Saverio S, Schünemann H, Senecat J, Taruscio D, and the RARE-Bestpractices Consortium. Methodology for production of best practice guidelines for rare diseases. *Rare Diseases and Orphan Drugs. An International Journal of Public Health* 2014; 1(1):10-19 (EN)

Hilton Boon M, Ritchie K, Manson J for the RARE-Bestpractices Consortium. Improving the retrieval and dissemination of rare disease guidelines and research recommendations: a RARE-bestpractices initiative. *Rare Diseases and Orphan Drugs. An International Journal of Public Health* 2014; 1(1):20-29 (EN)

RARE DISEASES AND ORPHAN DRUGS
An International Journal of Public Health

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Vol 1: December 2014, Supplement 4	Abstracts presented to the EPIRARE International Workshop 24-25 November 2014 *Luciano Vittozzi, Marco Salvatore, Domenica Taruscio*	ABSTRACT PDF
Vol 1: April 2014, Supplement 2	Abstracts presented to the Second International EPIRARE workshop *Domenica Taruscio*	ABSTRACT PDF
Vol 1, No 2 (2014)	Audiological profile of a patient with MPS type IVA *Saransh Jain, Vikas Mysore Dwarakanath, Suman Suresh*	ABSTRACT PDF
Vol 1, No 2 (2014)	Bone marrow transplant for a boy with alpha-mannosidosis illustrates a family's decision-making in rare diseases *Clara van Karnebeek, Mary Dunbar, Jeff Davis, Kristin Bowden, Kevin Chaplin, Robin Chaplin, Dina McConnell, Paul Moxham, Millan S. Patel, Paul Steinbok, Hilary Vallance, Sylvia Stockler*	ABSTRACT PDF
Vol 1, No 1 (2014)	Editorial *Domenica Taruscio, Holger Schünemann*	ABSTRACT PDF
Vol 1, No 1 (2014)	Improving the retrieval and dissemination of rare disease guidelines and research recommendations: a RARE-Bestpractices initiative	ABSTRACT PDF

ANY QUESTIONS?

For more information:

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Juliette.senecat@eurordis.org

Many thanks to the team of **Healthcare Improvement Scotland**

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