Roundtable IV
ERN and better outcomes: good clinical practices

Evidence based practices and rare / low prevalence diseases

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ERNs and evidence-based practices (1/2)

- **Directive 2011/24/EU** on the application of patients'rights in cross - border healthcare

Article 12 (4)(A) point (iii)

ERNs "**offer a high level of expertise and have the capacity to produce good practice guidelines and to implement outcome measures and quality control**"

- Commission Delegated Decision (OIEU 2014, L147/71)
- Commission Implementing Decision (OIEU 2014, L147/79)

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ERNs and evidence-based practices (2/2)

- **Commission Delegated Decision** (OIEU 2014, L147/71)

  Annex 1: *Criteria and conditions to be fulfilled by the networks*

  (4) To fulfil the requirement set out in point (iii) of Article 12(4)(a) of Directive 2011/24/EU **the networks must**:

  c) develop and implement clinical guidelines and cross-border patient pathways;

  d) design and implement outcome and performance indicators;

  (5) a) identify and fill research gaps

  (6) a) identify and fill training gaps

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Challenges, facilitators and opportunities

for the production and use of guidelines in rare diseases

Challenges

Guideline production and implementation is far from satisfactory in the EU

Few Countries have well-established systems in place sustained by regulations that provide mechanisms for quality assurance, implementation and use of clinical guidelines

Many countries still rely on sporadic initiatives, others lack the capacity for evidence-based guideline development

Legido-Quigley et al. 2012

Facilitators

Directive 2011/24/EU supports ERNs, which must have the capacity to produce good practices guidelines

Public funds available for methodological research in guidelines

i. **GRADE working group'** EU-funded DECIDE project

ii. **RARE-Bestpractices** EU - funded project

iii. **COMET initiative**

IV. **DECIDE**

Morciano et al. 2015; Menaka et al. for the RARE-BestPractices Consortium, 2015

Opportunities

MS are at a decisive point in establishing the criteria to ensure the transparent and effective functioning of ERNs

MS should consider the **importance** and **devote resources** to build efficient systems and capacities for the production of trustworthy guidelines, according to international standards

Ms could adopt a **cooperative approach** to optimize guideline production and implementation across countries

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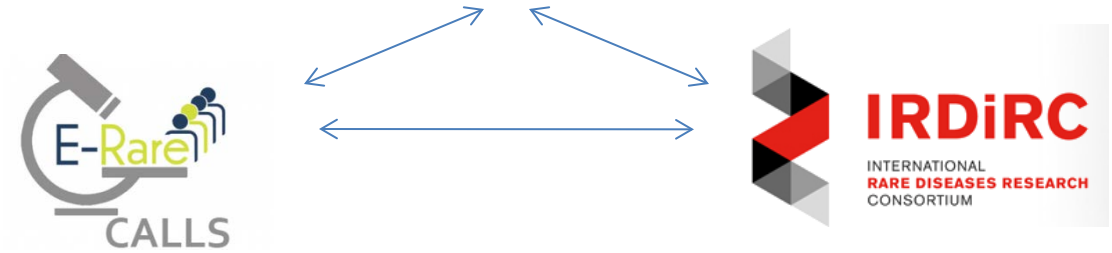
Challenges, facilitators and opportunities
to the production and use of guidelines in rare diseases

Opportunities

ERNs can be **a concrete opportunity** for initiating **processes of cooperation among MS** in producing trustworthy guidelines, according to international standards

Potential results of this cooperation

- **shared** health care guidelines
- identifying **research gaps**
- **formulate, prioritize** and comunicate **research recommendations** to researchers and **research funders**



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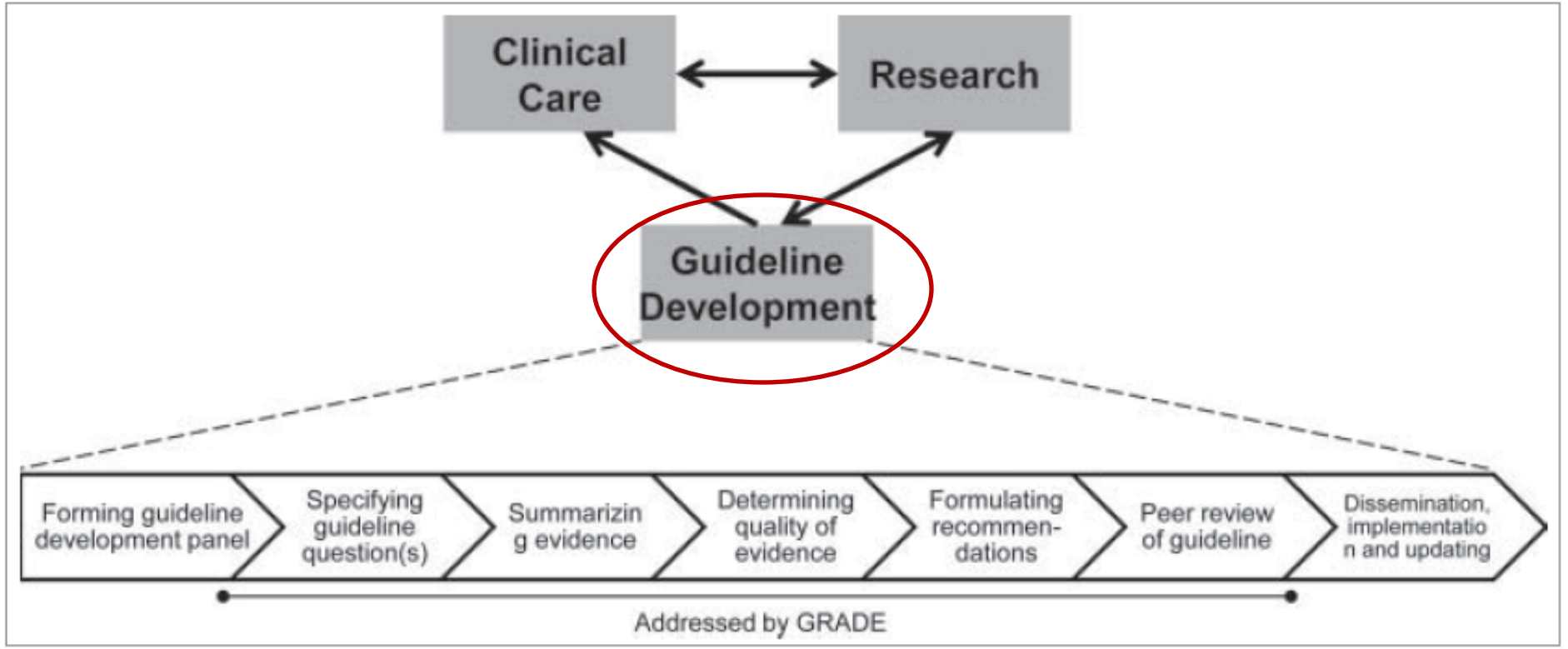
The relationship between clinical care, research and guidelines



Menaka Pai et al. for the RARE-BestPractices Consortium, 2015

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Standards for Developing Trustworthy Clinical Practice Guidelines

1. Establishing **transparency**
2. Management of **conflict of interest**; **independency**
3. **Group composition: multidisciplinary and balanced**, comprising a variety of methodological experts and clinicians, and key affected groups. Patient preferences
4. **Systematic review of the existing evidence**
5. **Provide ratings of both the quality of evidence** and **the strength** of the recommendations

6 Recommendations should be articulated in a **standardized form**

7. **External reviewers** should comprise a full spectrum of relevant stakeholders, including scientific and clinical experts, organizations (e.g., health care, specialty societies), agencies (e.g., federal government), patients, and representatives of the public.
8. **Updating**

(IOM 2011)

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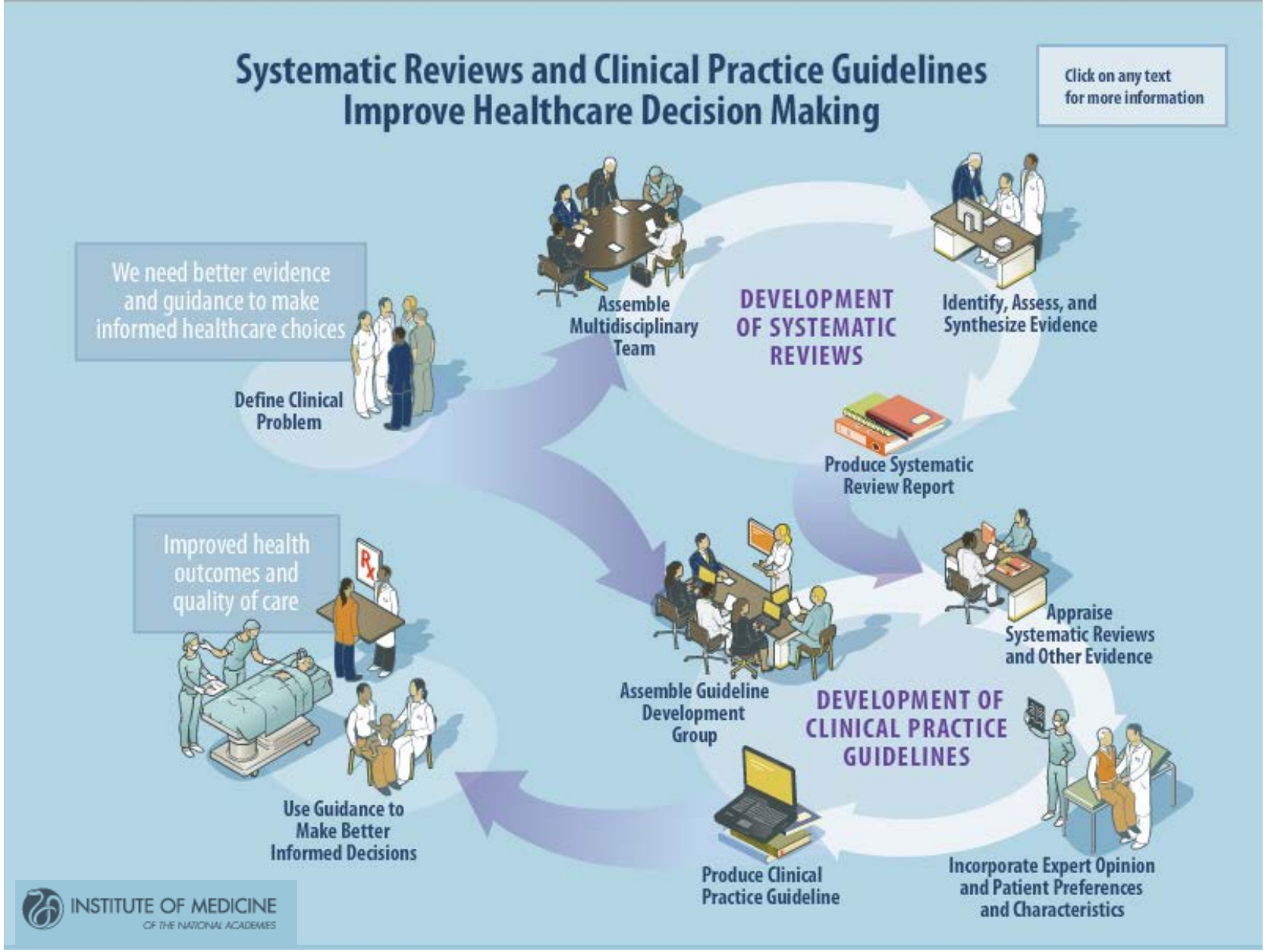

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Specific challenges for guideline production in rare diseases: the PICO question

- **P - Population:** defining the population of interest is a major challenge (small numbers of patients, diagnostic uncertainty, etc.)

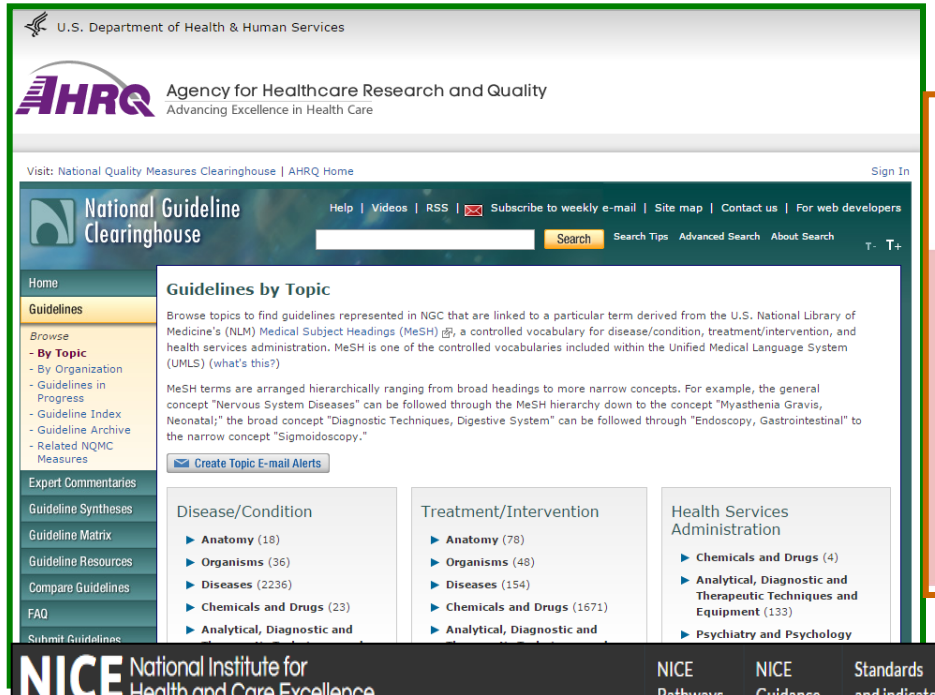
- **I- C - Intervention and comparator :** there is often only one treatment for any given RD.

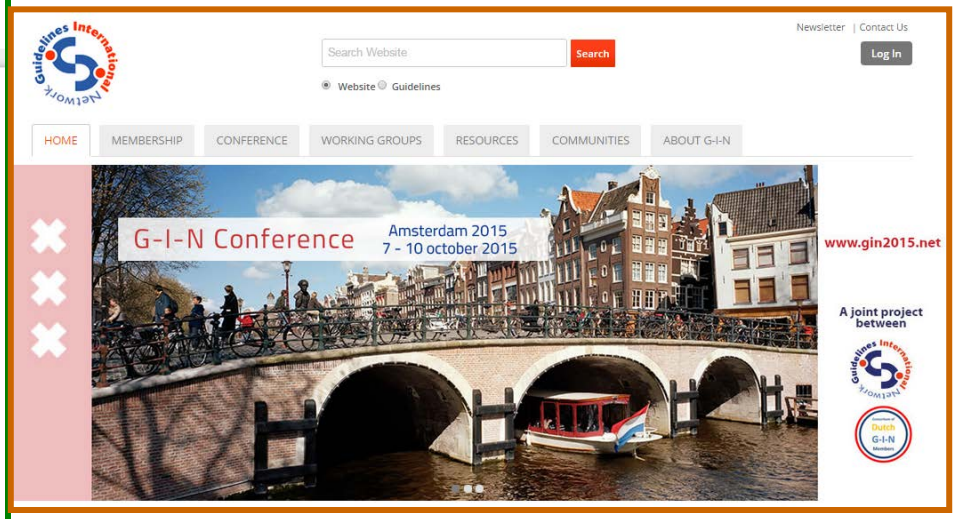
  In many cases, use of placebo is not an option due to the severe course on the untreated disease.

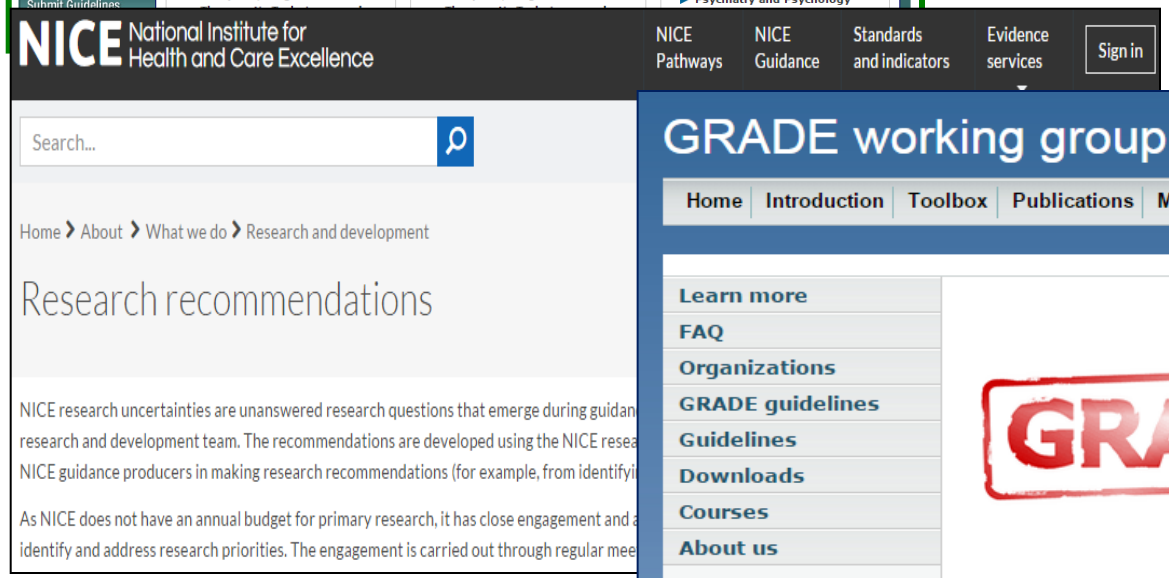
- **Outcomes:** a key step in creating evidence-based guidelines is determing critical disease outcomes, factors important for patients, providers and health care systems. There are several challenges in defining relevant outcomes in RD (case reports, surrogate outcomes, patient reported outcomes).

  The most reliable outcomes only be those related to morbidity and mortality

Menaka Pai et al. for the RARE-BestPractices Consortium, 2015







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Rare Best Practices

Platform for sharing best practices for the management of rare diseases

Project funded EU funded (7FP)
Coordination: National Centre for Rare Diseases-Istituto Superiore di Sanità, Rome
Duration: 2013-2016

The mandate of the RARE-Bestpractices is **knowledge management** to support evidence-informed decision-making of the rare disease community & also to support ERNs

We do this by **creating a platform with resources and tools** to facilitate access and interpretation of the rare diseases synthesis of evidence

- 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

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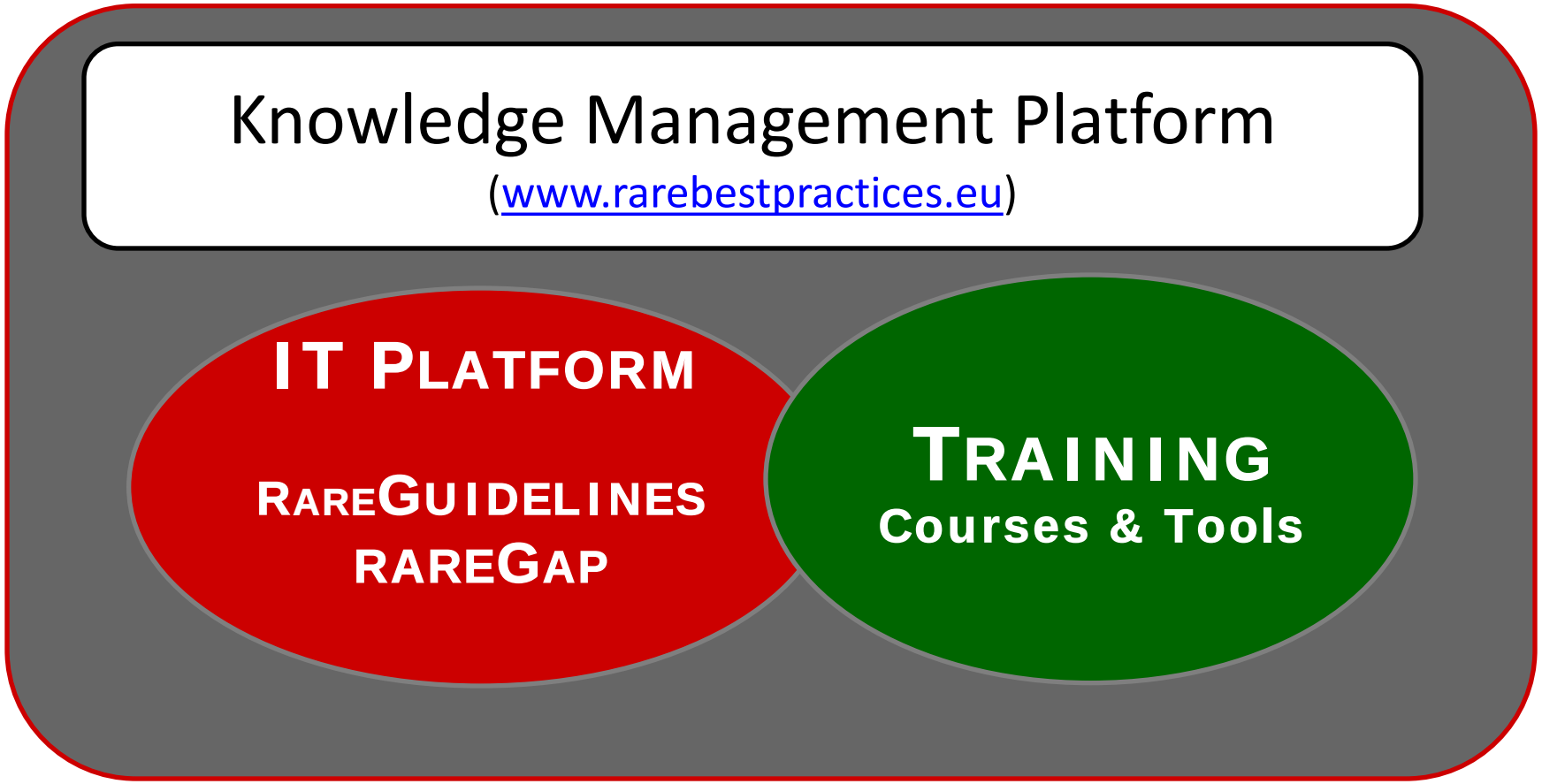
The RARE-Bestpractices Platform



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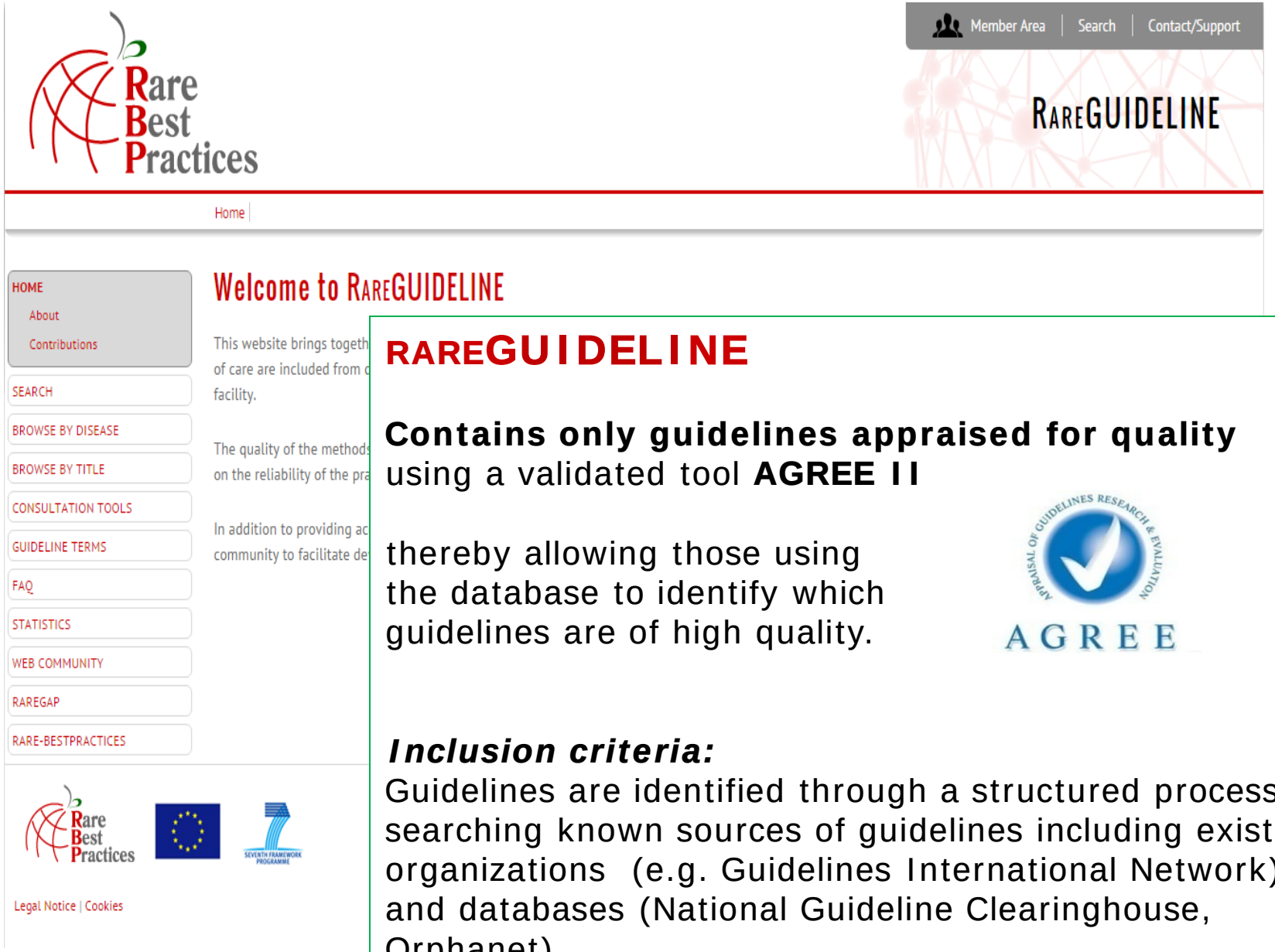

RAREGUIDELINE

Contains only guidelines appraised for quality using a validated tool **AGREE II**

thereby allowing those using the database to identify which guidelines are of high quality.

Inclusion criteria:

Guidelines are identified through a structured process of searching known sources of guidelines including existing organizations (e.g. Guidelines International Network) and databases (National Guideline Clearinghouse, Orphanet).

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RAREGUIDELINE as a resource

Guideline users

Retrieve information to help ensure best possible care
Inform decision making
Select the best quality guidelines for their context
Provide feedback/input to guidelines

Guideline developers

Identify existing guidelines and their quality & identify gaps
Collaborate – e.g. invite/collate comment on draft guidelines
Disseminate their new guidelines
Avoid duplication of effort in producing guideline

Information specialists

Responsible for developing search strategies
Use as search resource
Generate bibliographies

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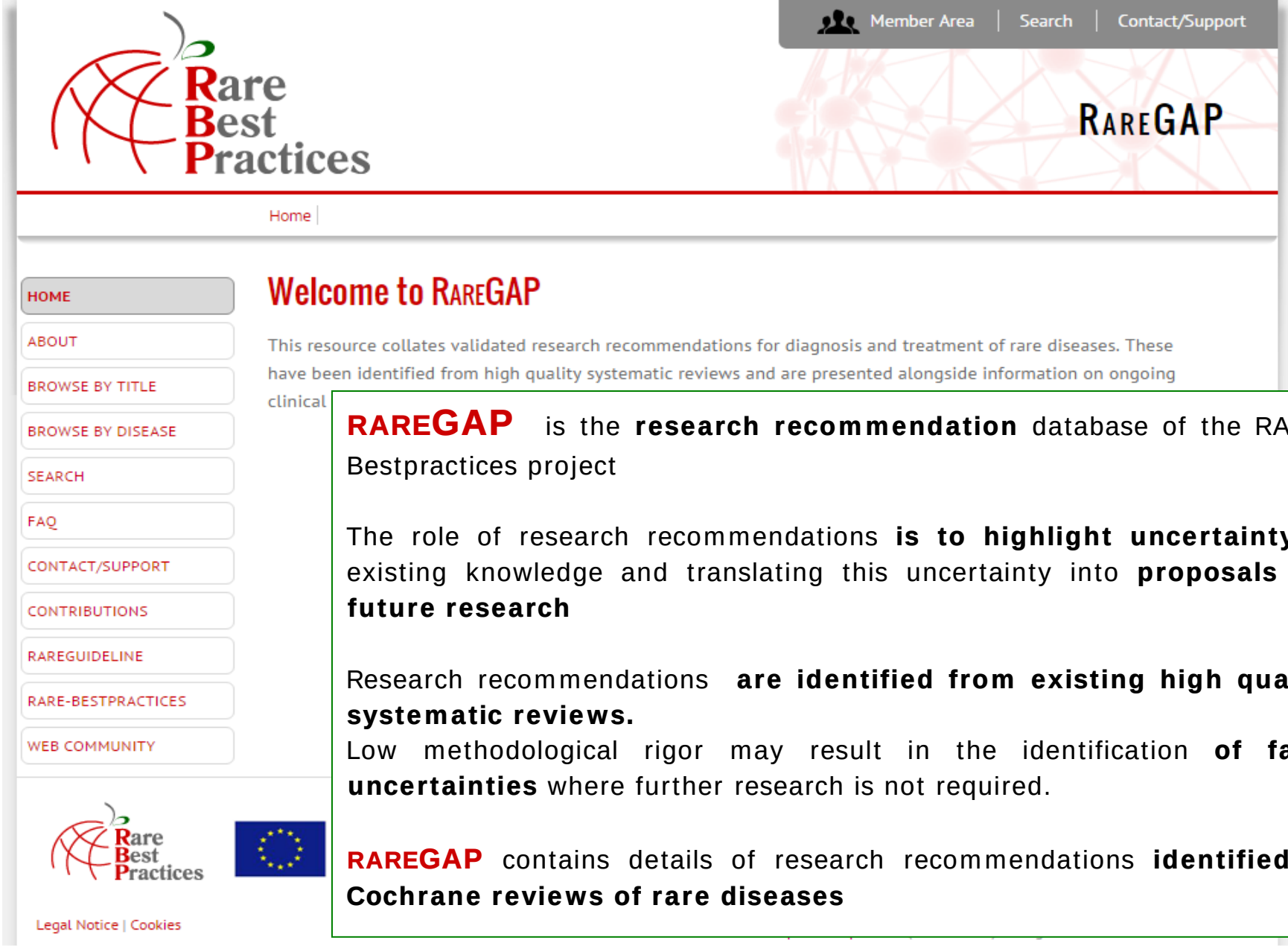

RAREGAP is the **research recommendation** database of the RARE-Bestpractices project

The role of research recommendations **is to highlight uncertainty** in existing knowledge and translating this uncertainty into **proposals for future research**

Research recommendations **are identified from existing high quality systematic reviews.**
Low methodological rigor may result in the identification **of false uncertainties** where further research is not required.

RAREGAP contains details of research recommendations **identified in Cochrane reviews of rare diseases**

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Training courses and tools

based on the RARE-Bestpractices work
to promote the development of trustworthy health care guidelines for rare diseases
and their use across Europe and to support the establishment of European Reference Networks

Rare Best Practices

International Course

Health care guidelines on rare diseases: Quality assessment

February 23-24, 2015

Istituto Superiore di Sanità
Rome (Italy)

AGREE

Rare Best Practices

2nd International Course

Health care guidelines on rare diseases: Quality assessment

December 3-4, 2015

Istituto Superiore di Sanità
Rome (Italy)

Rare Best Practices

2 Courses for

guideline developers

Development of
treatment guidelines
10-11-12 February 2016
Milan

Development of
diagnostic guidelines
September 2016
Milan

Cochrane Italy

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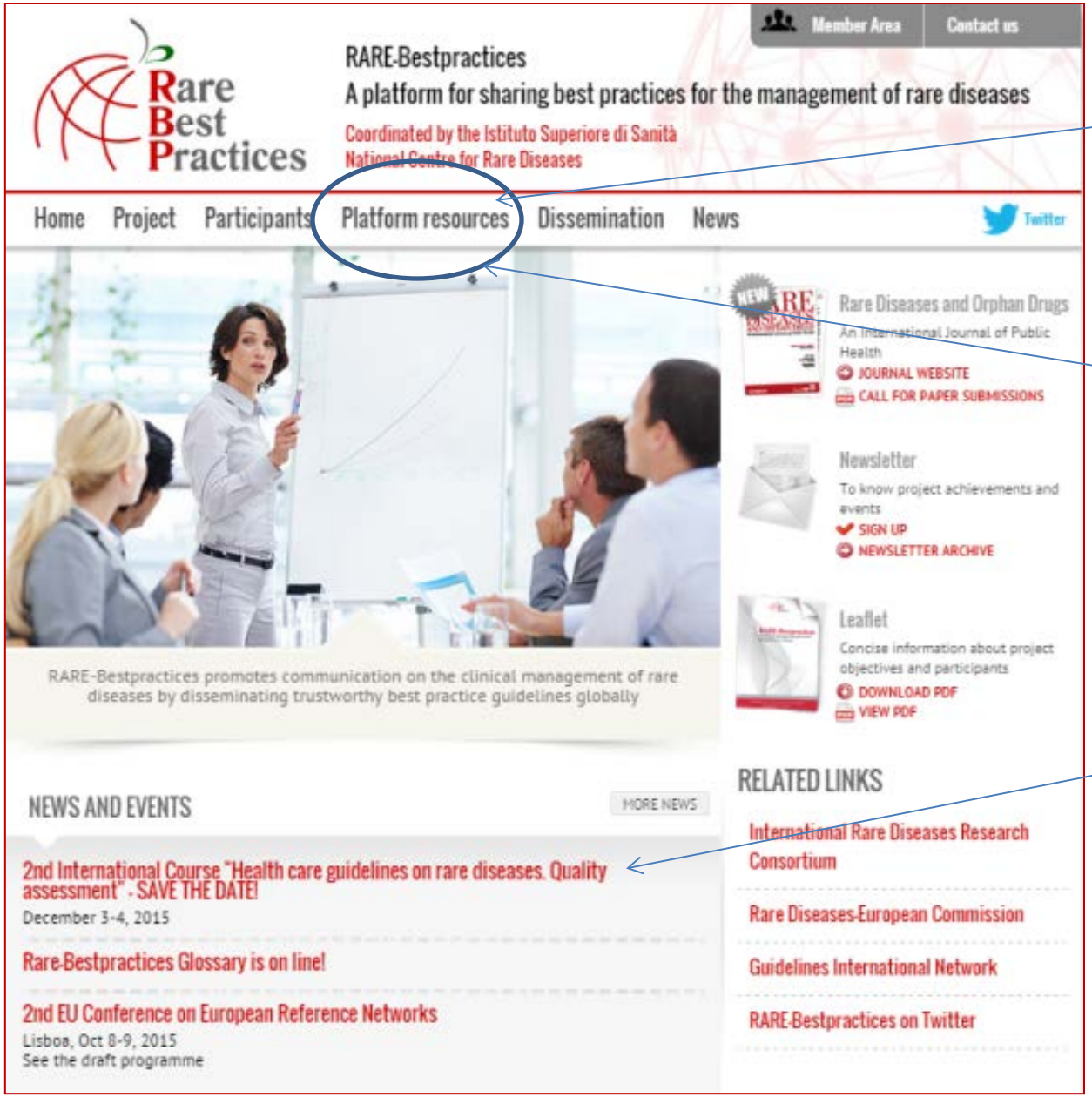

RAREGUIDELINE
a collection of appraised guidelines
& development tools

RAREGAP
a collection of research recommendations

Training courses and training tools
for guideline users and developers

www.rarebestpractices.eu

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RARE DISEASES AND ORPHAN DRUGS *An International Journal of Public Health*

February 2014, Volume 1, Number 1

Improving the retrieval and dissemination of rare disease guidelines and research recommendations: a RARE-Bestpractices initiative

Michele Hilton Boon[1], Karen Ritchie[1], Jan Manson[1] for the RARE-Bestpractices Consortium[2]

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Public Health Genomics

Policy Statement

Public Health Genomics
DOI: 10.1159/000435852

European Reference Networks and Guideline Development and Use: Challenges and Opportunities

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MEETING REPORT

Rare Diseases 3:1, e1058463; June 1, 2015; Published with license by Taylor & Francis Group, LLC

Developing methodology for the creation of clinical practice guidelines for rare diseases: A report from RARE-Bestpractices

Menaka Pai[1,2,*], Alfonso Iorio[1], Joerg Meerpohl[3], Domenica Taruscio[4], Paola Laricchiuta[4], Pierpaolo Mincarone[5], Cristina Morciano[4], Carlo Giacomo Leo[6,7], Saverio Sabina[8], Elie Akl[8], Shaun Treweek[9], Benjamin Djulbegovic[10], and Holger Schunemann[1,3] for the RARE-Bestpractices Consortium[†]

[1]McMaster University; Hamilton, Canada; [2]Hamilton Regional Laboratory Medicine Program; Hamilton, Canada; [3]Universitaetsklinikum; Freiburg, Germany; [4]National Center for Rare Diseases; Istituto Superiore di Sanità; Rome, Italy; [5]National Research Council; Institute for Research Institute of Clinical Physiology; Lecce, Italy; [7]Tufts Medical Center; Boston, MA USA; [8]American Univ [10]University of Florida; Gainesville,

Conflicts of interest policies and health care guidelines: what (whom) can we trust?

Morciano , C.M., Istituto Superiore di Sanità, Rome, Italy (Presenting author)

Basevi , V.B.
Faralli , C.F.
Tonon , S.T.
Taruscio , D.T.

G-I-N Conference Amsterdam 2015 7 - 10 october 2015

4.1 Management of conflicts of interest

Conclusions (1/2)

The **Directive** 2011/24/EU is intended to **provide a legal framework** within the European Union **to facilitate cross-border care**

Art 12 (Directive 2011/24/EU) **supports ERNs,**
which **must have the capacity to produce good practices guidelines**

Good quality guidelines, produced according to international standards, do **improve health care**

MS have a great opportunity, through the establisment of ERNs,

to foster **a cooperative and coordinate approach**

to share exiting expertise and resources

for the production and implementation of care guidelines

across countries

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Conclusions (2 / 2)

ERNs are paramount to foster

a cooperative and coordinate approach among MS to :
- optimize guideline production and ameliorate quality assurance practices

- identify and fill knowledge gaps

- formulate, prioritize and comunicate recommendations to researchers and research funders

ERNs can be an opportunity to devise a new research governance

Thank you !

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