RBP Newsletter
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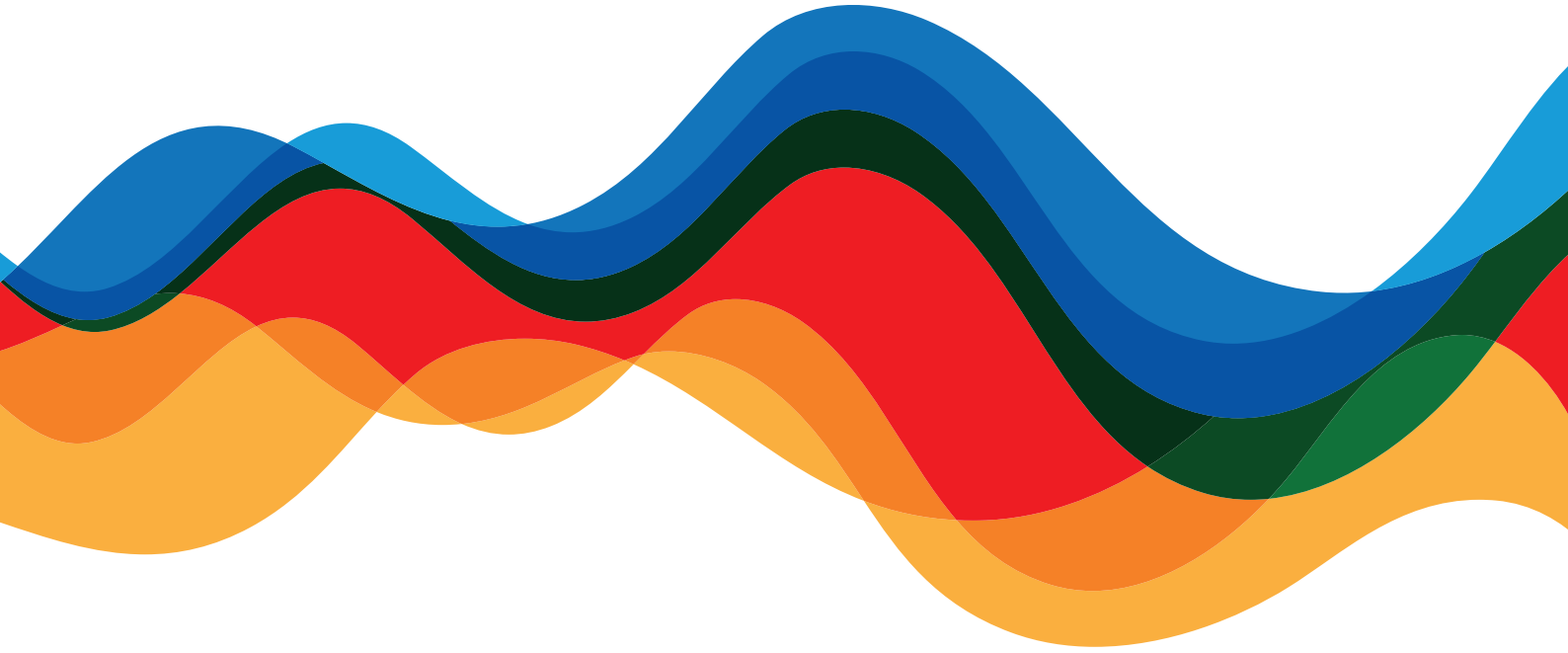
RARE-Bestpractices

A platform for sharing best practices for the management of rare diseases



www.rarebestpractices.eu

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MESSAGE FROM THE PROJECT LEADER

RARE-Bestpractices project stems from the international requirement of increasing and sharing knowledge on rare diseases. The project is developing a comprehensive and updated platform to facilitate cooperation among scientists, experts and institutions in the field of guidelines, health technology assessments and horizon scanning to improve the healthcare management of patients. There are critical challenges that have to be addressed, including the efficient translation of research into public health actions and benefits for rare disease patients, the provision of high quality information to health professionals, to patients and their families, the ways how high-level, multidisciplinary expertise can be exploited to support consistent health interventions, as well as the way how stakeholder's inputs can help coping with these challenges.

RARE-Bestpractices aims at meeting some major needs on guidelines identified by the European Union and rare disease community: their development and collection in a publicly-accessible database, the assessment of priority research needs, the implementation into best practice of cost-effectiveness analyses for pharmaceuticals, dissemination and training.

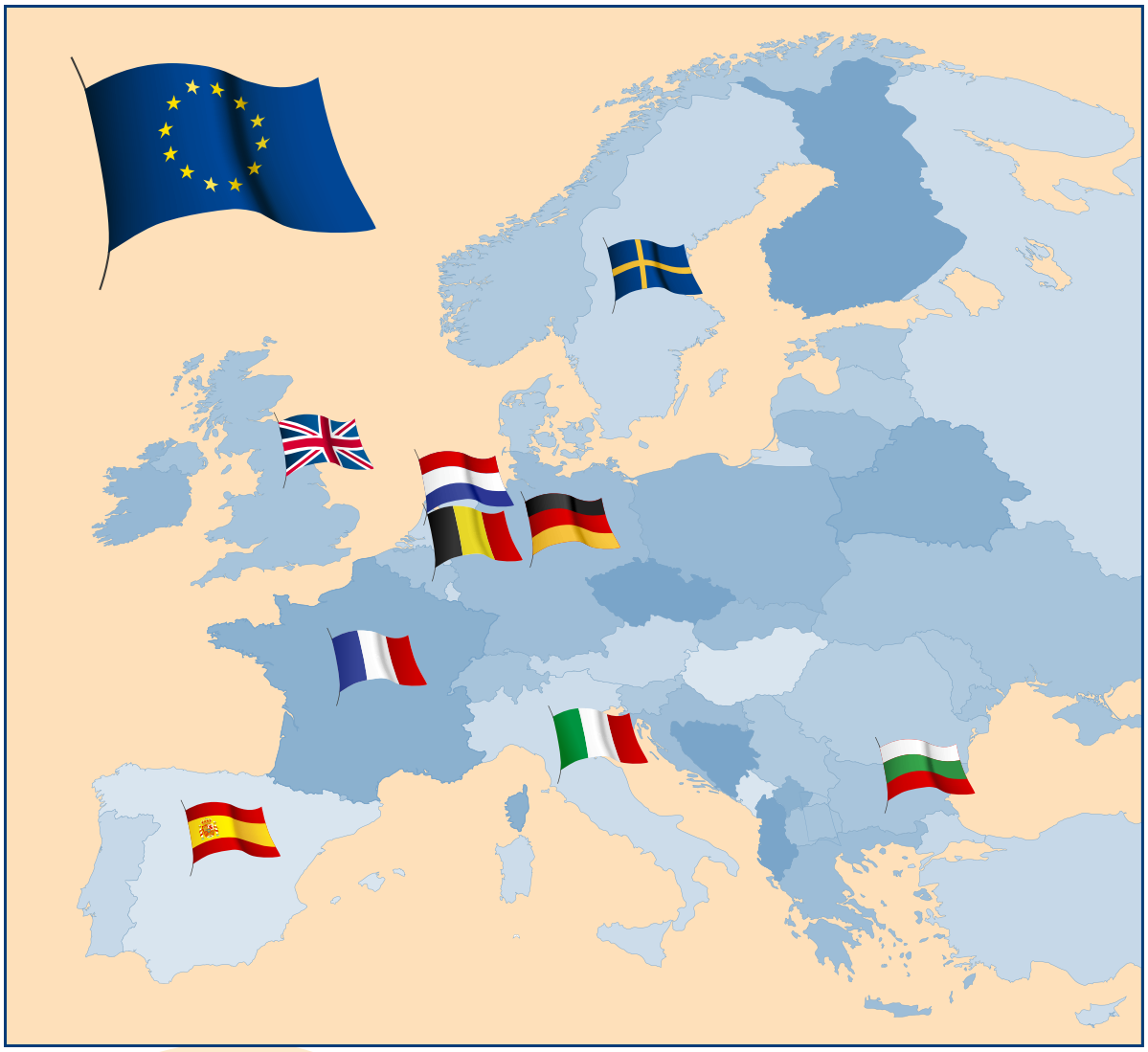
RARE-Bestpractices consortium is very well aware that a best practice is, eventually, of no avail if not interconnected with scientific advances. Therefore, a further main project focus is to proceed side-to-side with the international and interdisciplinary scientific community, such as the International Rare Diseases Research Consortium (IRDiRC, www.irdirc.eu) in order to facilitate the translation of research into a better level of health care for rare disease patients.

Domenica Taruscio
Project leader

Istituto Superiore di Sanità

THE RARE-BESTPRACTICES PROJECT

RARE-Bestpractices is a four-year project (January 2013-December 2016) funded by the Seventh Framework Programme of the European Union (FP7/2007-2013).
The National Centre for Rare Diseases (CNMR) of the Istituto Superiore di Sanità acts a a coordinator, bringing together a team of highly qualified experts in the area of guidelines, systematic reviews, health technology assessments, health policy, rare disease epidemiology, public health coming from 9 countries across Europe. The project aims to improve the management of rare diseases and it is shaped by advisors who bring a broad range of perspectives from across world.
Please go to the project participants chapter at page 15 to see the full list of institutions, organisations and people involved.



Improving the care of rare disease patients

First, making an informed readership

High quality and up to date information on rare diseases is not easy to be found and feeling disoriented in the currently existing landscape of databases and websites can be more confusing than enlightening. This is the consideration leading to the idea of developing, within RARE-Bestpractices, a collection of guidelines which describes the best approach to manage rare diseases while providing an explicit judgment about quality and updating of the guidelines included.

Second, setting guideline quality standards

Guidelines developed in a transparent and rigorous manner and following a precise and reproducible development methodology have potential benefits in health care. A part of the work of RARE-Bestpractices is dedicated to explore if one of the most used worldwide standards for developing recommendations, the GRADE approach, might work for rare diseases. In fact rare diseases have specific features for which methodology standards currently available for common conditions are not proven to be applicable.

Third, orienting research

RARE-Bestpractices will make available an important tool for rare disease research: the research recommendation database. Research recommendations should be included in guidelines to underline aspects not supported by studies and for which further research would be necessary. Highlighting shortcomings in research, such database will be another important and very informative resource in rare diseases.

Fourth, investigating medicine access inequality

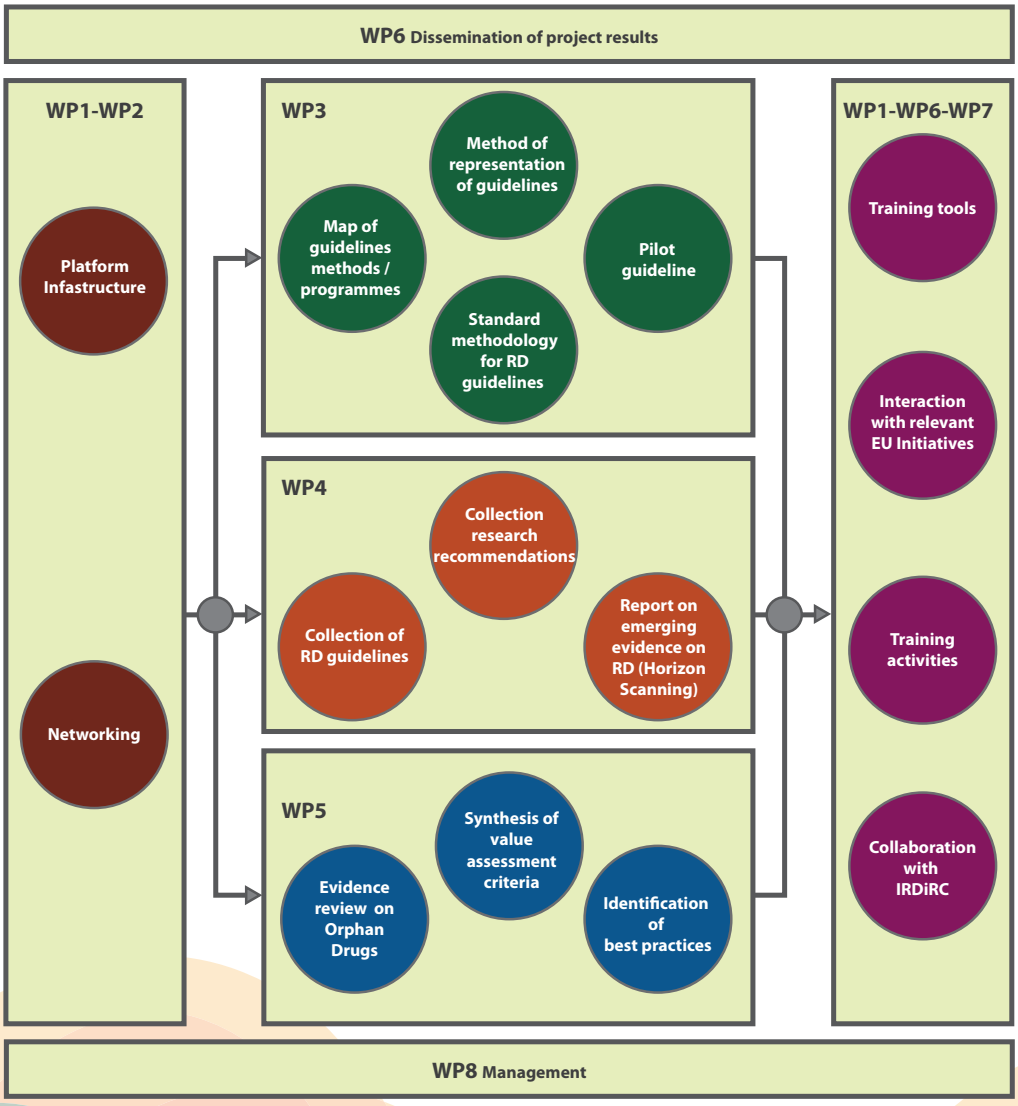
Equal access to treatment should be guaranteed worldwide. Actually what happens for rare diseases is that the high cost of medicines leads to disparities across countries in public spending. A study will be conducted within RARE-Bestpractices to understand the criteria for funding decisions, why there are disparities and how medicine assessments are conducted.

Fifth, organizing training activities

How to get started with a guideline development project? RARE-Bestpractices will provide whoever is interested in guideline development with the necessary support and training to promote the development of high-quality guidelines and their use across European countries.

The RARE-Bestpractices Work plan

The project activities have been broken down into eight work packages (WP) to facilitate the coordination of the RARE-Bestpractices research. WP3, WP4 and WP5 include the core research activities. WP6 aims at building awareness of project goals and achievements in scientific and patients community, as well as decision makers and general public (see also work packages chapter at page 9). Main responsibility of WP2 is to support WP3, WP4, WP5 and WP6 activities and outputs by developing technical web solution (web site, databases, web community etc). WP7 is responsible for establishing collaboration with the International Rare Diseases Research Consortium (IRDiRC). WP1 is dedicated to provide the overall scientific strategy and to maintain and encourage interaction between research groups within and outside the project network; WP1 is also responsible for the organization of training courses which intend to provide participants with the opportunity to learn about the basics of the rare diseases guideline development process defined in WP3.
WP8 is responsible for managing the work plan and for administrative and intellectual property right issues.



WHAT GUIDELINES ARE AND THEIR IMPORTANCE

WHAT ARE GUIDELINES?

Guidelines are documents including recommendations on health care interventions. Health care interventions may include any kind of treatment, test or preventive measure as well as public health activities or government policies. Recommendations may be defined as brief statements which provide detail of the recommended actions, and description of the target people as well as of the specific health professionals should carry out the intervention.
There are various organizations and groups which develop guidelines (government agencies, speciality societies, academia institutions, patient advocacy groups, commercial companies) as well as various are the names and formats of the documents in that it is possible to find recommendations about health care interventions (consensus statements, consensus conferences, best practices, protocols).
Regardless their name and their format, it is important that guidelines are "good guidelines", since "bad guidelines" that are also defined "biased guidelines" can cause harm to patients. Over the last years there was an intensive debate about the recommended attribute of a good guideline. In essence guidelines are "good guidelines" when they are based on the systematic search and analysis of biomedical or health related research studies in human beings (referred to as the best available evidence) with an assessment of the benefit and harms in the light of the health care professionals practical knowledge and of the patient values. Guidelines have also to include a clear description of the people who develop the recommendations and the methodology behind their elaboration.

THE IMPORTANCE OF GUIDELINES

Guidelines developed in a transparent and rigorous manner can improve health care decisions and ultimately health care quality. Guidelines together with patient booklets that explain recommendations, ensure that patients are given all the information necessary for informed decision-making and enhance the doctor-patient relationship. They can also inform research priorities by highlighting areas where uncertainty or no evidence exists. Guidelines have also been demonstrated to be effective means for accelerating translation of scientific discovery into health care practices.

WHAT HTAs ARE AND THEIR IMPORTANCE

What are HTAs?

Health Technology Assessment (HTA) is the term generally used to describe the systematic process of evaluating benefits, and most often the costs, of a new intervention in relation to a comparator, usually the standard of care. In other words, for example, what are the incremental benefits of a new medicine for patients and society? And how much does it cost? These two key considerations are used to determine whether a new medicine can be considered "good value for money". Often medicines for rare conditions are more expensive than other medicines, and therefore it may be more difficult to prove that they are good value for money. In such cases, individual countries may have special rules for allowing such medicines to be covered.

The importance of HTAs

The idea behind the HTA process is to ensure value for money in health spending. If a new medicine receives a negative HTA appraisal, suggesting that its benefits do not justify its costs, this means the health system and the population are better off spending that money on something else. Since most health systems have limited budgets, there will always be certain medicines or other treatments that are unaffordable. It is the role of HTA to ensure that the money invested in the health system is only spent on medicines and treatments that are clinically cost effective and provide as much public benefit as possible.

WORK PACKAGE 3

What are the activities of Work Package 3?

A major goal for the RARE-Bestpractices project is to inform about presently available guidelines for rare diseases, and to recommend processes for how best to develop future guidelines for rare diseases. These topics are in main focus in our work package. The way we address these questions is first by means of surveys sent to all EU countries to gather information on what guidelines for rare diseases are presently in use in EU member states, and also information on methods used to produce them. Next, we address the question on how best to produce future guidelines for rare diseases. Presently, we are faced with two major difficulties here. One is the lack of guidelines for rare diseases, and a second problem is the lack of agreement on how such guidelines should best be produced in order to be reliable. Therefore, our aim is now to reach agreement on proper methodologies to develop new guidelines for health care interventions. Once this has been agreed upon, we intend to make use of these methods to develop guidelines for one rare disease, in order to investigate the feasibility and value of agreed protocols.

How will this work make a difference to patients?

There are several reasons why guidelines for rare diseases are important. One is to facilitate for individuals with rare diseases to get informed on recommendations for diagnosis, treatments and long-term care. Another is to help health providers with the same information. A third often forgotten reason is the importance in clinical trials of new therapies to have a common basis of care in order best to distinguish the effect of the new therapy in question. Our work aims to improve this by collecting available rare disease guidelines, and to agree on methods for future development of guidelines for rare diseases.

Thomas Sejersen
Leader of Work Package 3

Karolinska Institute

WORK PACKAGE 4

What are the activities of Work Package 4?

Healthcare Improvement Scotland is leading Work Package 4 of the RARE-Bestpractices project. This Work Package will find and create a collection of guidelines describing the best approaches to diagnosing and treating people with rare diseases. Guidelines for rare diseases are developed and published by many different groups making them difficult to find when they are needed, particularly by clinicians who are not experts in the particular disease. We will make a collection of guidelines available through a publically accessible website with search facilities that should make it easy to find the right information. The website will provide information on how up to date the guidelines are. We will also develop a way for users of guidelines to tell how well they have been developed and therefore how likely the health and wellbeing of people with the rare condition is to improve if the guideline is followed. In addition to the collection of guidelines, an associated collection of research recommendations will be made to help clinicians and researchers to identify the aspects of rare disease management that would benefit most from new research.

How will this work make a difference to patients?

At present, clinicians with expertise in a particular rare disease may be scattered across countries and geographical regions and not have the opportunity to share their knowledge to identify best practice in managing patients with these conditions. This work package will benefit patients by making available to clinicians across Europe (and the world) the best, most up-to-date guidelines on the treatment of rare diseases irrespective of where they live. This will help make sure that wherever a patient lives in Europe their doctor will know about the best diagnosis and treatments for them.

Karen Ritchie
Leader of Work Package 4

Healthcare Improvement Scotland

WORK PACKAGE 5

What are the activities of Work Package 5?

Health Technology Assessment (HTA) is becoming increasingly prominent across Europe along with the realization that public budgets for health care are bounded just like any other budget. To ensure the sustainability of health care systems in the future, governments must ensure value for money in their health spending, while balancing a number of other objectives, one of which is equal access to care. The price tag of developing a new medication is high, and since rare diseases necessarily mean only small quantities will be sold, these medicines are often very expensive compared with other medicines. As a consequence, they may often be considered "poor value for money" if governments did not make explicit allowances for the fact that they are for rare conditions.The EU directive on Cross Border Care means that patients should have access to the same level and standard of care, regardless of their country of residence. This should be true for rare diseases as well, but is not always the case. In fact it is known that the availability of certain medicines for rare conditions varies significantly across member states. Our contribution to the RARE-Bestpractices project will help policy makers and national governments understand how medicines for rare diseases are assessed in other countries, allowing them to develop best practices on how this should be approached from an comparative perspective.

How will this work make a difference to patients?

Since medicines for rare diseases are often more expensive than other medicines, some countries may find they are too expensive to purchase with public money. Other countries may apply special criteria, for example, they may accept higher value for money thresholds up to a point and depending on the value these medicines bring to patients because only small amounts of the medicine needs to be purchased, or they may have an explicit policy of ensuring all of the population has equal access to treatment. The first steps towards ensuring that patients across different countries have equal access to care are to understand why some countries decide to cover certain medicines for rare diseases while others do not, what the criteria for coverage decisions are, as well as understand the value orphan drugs bring from a patient perspective.

Panos Kanavos
Leader of the Work Package 5

London School of Economics and Political Science

WORK PACKAGE 6

What are the activities of Work Package 6?

The RARE-Bestpractices project will make a major effort in disseminating the project results and achievements to the scientific community, to the policy makers and to the general public.
A website has already been developed, www.rare-bestpractices.eu, which now provides information about the project aims, work plan and network. The website will be continuously updated with news about the project and about relevant work by other researchers and networks.
This site will be linked to the database of guidelines and to the database of research recommendations on rare diseases which will be created during the course of the project. These two databases will be made both freely accessible and suitable for use by the scientific and patient rare diseases community.
We will make an effort for an intensive use of the web and of the online facilities to communicate our results and support data sharing in the field of best practice. We will provide free access to educational material and tutorials suitable for people interested in developing or using guidelines and research recommendations for rare diseases.
An important goal is to encourage discussion and debate that goes beyond the precise limits of the project itself. As a contribution to this goal and as one of the project deliverable a new science journal has been created. This journal is entitled *Rare Diseases and Orphan Drugs,* an International Journal of Public Health and will provide an advanced forum on important aspects of public health.

How will this work make a difference to patients?

This Work Package intends to increase awareness of health care professionals, patients and policy makers across Europe about the importance of developing health care guidelines on rare diseases that are "performed rigorously" through the identification and the dissemination of the most scientifically sound healthcare practices.

Our work will also pursue interaction with EURORDIS, EUCERD and EUCERD joint action to provoke social and governmental response for the integration of the project results into sustainable health policies.

Cristina Morciano
Leader of Work Package 6

Istituto Superiore di Sanità

ENGAGING WITH PATIENTS

What are the needs and expectations of patients regarding the subjects covered by the RARE-Bestpractices project?

Patient needs regarding these subjects include an access to early and accurate diagnosis and the reduction of misdiagnosis, as well as ensuring that the correct treatment is administered in the proper healthcare context. The implementation of "strategies of care" is a necessity for people living with rare diseases. Patients also express the need of raising awareness of healthcare professionals regarding the complexity and the peculiarities of rare diseases.
The development of guidelines is of high relevance in this context. To better address patients' needs, healthcare recommendations should be informed by the best available evidence, and should be broad, comprehensive, including paramedical treatments, use of medical devices, physiotherapy, nutrition, surgery and complementary treatments.
Guidelines should promote a multidisciplinary approach for the care of rare disease patients, as well as provide reliable information to guide and orientate treatment.

What will be the outcomes of the project for patients?

The project aims at improving clinical management of rare disease patients and narrowing the existing gap in quality of health care among EU member states as well as in other countries. This will be achieved by collecting, evaluating and disseminating best practices as well as sharing knowledge. The ultimate impact of the RARE-Bestpractices project should be an improvement of health outcomes and quality of life for rare diseases patients, through a reduction of inequalities in health care and an increased equity of access to better diagnostics and therapeutics at EU level.

How are patient representatives going to be involved in the course of the project?

EURORDIS, the European Organisation for Rare Diseases, will act as a transversal partner in the different work packages, ensuring the involvement and the capacity-building of patient organisations across Europe - This way, patient representatives will have many occasions to participate in the course of the project. EURORDIS will build capacities of rare diseases patient organisations and of people living with rare diseases on the importance, use and benefits of guidelines and HTA (Health Technology Assessment), through the dissemination of information as well as through training activities targeted at patient advocates, among others. EURORDIS will also be involved in the development and in the implementation of the methodology for guidelines for rare diseases, ensuring that this methodology places patients' need foremost. As part of the project EURORDIS will produce a patient version of the pilot guideline and will ensure the involvement of patients and their families in the development process. Patient representatives will be asked to give their input. This patient version will provide a summary of recommendations made for health professionals, in a language adapted for patients and their families.

Juliette Senecat
EURORDIS

PROJECT EVENTS

Past events

RARE-Bestpractices kick-off meeting (Istituto Superiore di Sanità, Rome, 11-12 February 2013). Organized by the project coordinator Istituto Superiore di Sanità

First workshop to identify challenges in developing guidelines on rare diseases. (Istituto Superiore di Sanità, Rome, 12 February 2013).
Organized by the Freiburg University partner in the framework of the Work Package 3, the workshop was the first of a series of two on exploring how the GRADE approach (http://www.gradeworkinggroup.org/) might work for creating guideline for rare diseases.

RARE-Bestpractices meeting. (London School of Economics and Political Science, London, 28-29 May 2013).
A project meeting to revise project plans and strengthen collaboration among beneficiaries, organized by the Istituto Superiore di Sanità and the London School of Economics and Political Science partners.

Launch of the project website www.rarebestpractice.eu. (30 June 2013)

Call for Papers of the RARE-Bestpractices Journal "Rare Diseases and Orphan Drugs. An International Journal of Public Health". August 2013, http://rarejournal.org

Second workshop to finalize methodology for developing guidelines on rare diseases. (University of Freiburg, Germany 11-12 October 2013).
Organized by the University of Freiburg partner in collaboration with the Istituto Superiore di Sanità and representatives of the American Society of Hematology and with the participation of relevant stakeholders it was focused on simulating guideline recommendations development following GRADE approach (http://www.gradeworkinggroup.org/).

Forthcoming events

Publication of the first issue of the RARE-Bestpractices Journal "Rare Diseases and Orphan Drugs. An International Journal of Public Health. (December 2013 - January 2014)

RARE-Bestpractices annual meeting (Istituto Superiore di Sanità Rome, 20-21 March 2014). Organized by the Istituto Superiore di Sanità

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