

Patient Involvement in Centres of Expertise for Rare Diseases

Teilbericht

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Erstellt im Auftrag des Bundesamtes für Gesundheit (16.020498 / 500.0000 / -542)

Bericht von ProRaris, Allianz Seltene Krankheiten - Schweiz

Bern, September 2016

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Acronyms

EC - European Commission

ECRD - European Conference on Rare Diseases

ERN - European Reference Network

EU - European Union

EUCERD - European Union Committee of Experts on Rare Diseases

EUROPLAN - European Project for Rare Diseases National Plans Development

EURORDIS - European Organisation for Rare Diseases

FOPH - Federal Office of Public Health

MS - Member State

NHS - National Health System

ORPHANET - The web portal for rare diseases and orphan drugs

SAMS - Swiss Academy of Medical Sciences

1. Introduction

1.1 Background

A rare disease is an often chronic, progressive, and life-threatening disease that affects 1 person or fewer in 2000 citizens. On the whole, rare diseases may affect 30 million citizens in Europe. In Switzerland, estimated 580'000 citizens suffer from rare diseases. In the past years, rare diseases and the impact they have on health care systems have become increasingly prominent in policy development. In 2009, a Recommendation of the Council of the European Union called for each EU State to have in place a rare diseases plan or strategy by the end of 2013 (1). Today, twenty of the twenty-eight countries in the EU have adopted such a plan or strategy to date and the others are in the process of adopting their plan or strategy (2).

The identification, and creation, of Centres of Expertise (or Centres of Reference¹) is a key element of national plans and strategies for rare diseases and a step towards European networks. The goal of national centres and European networks of these national centres is to gather the expertise concerning these rare diseases in order to ensure coordination of high quality care, appropriate and timely diagnosis and early intervention for rare disease patients.

In order to provide guidance to countries wishing to elaborate Centres of Expertise within the scope of their national plans for rare diseases, recommendations and criteria have been elaborated (3). Among these key publications and multi-stakeholder consultations, there is a strong agreement that patient representatives and patient organisations should be involved in the planning and functioning of national Centres of Expertise.

For example EURORDIS, the European organization for Rare Diseases, has published the declaration of Common Principles on Centres of Expertise and European Reference Networks for Rare Diseases (4) (see ANNEX 1). The declaration was officially launched on February 28th Rare Disease Day 2009 as an advocacy tool for all rare disease patient groups, national alliances, European federations on rare diseases and medical experts working in the field of rare diseases. The principles stress the critical role of patient representatives and organisations in the functioning of Centres of Expertise for Rare Diseases, specifically:

- “Centres of Expertise and European Reference Networks shall actively involve patients and their representatives in the establishment and

¹ The Rare Diseases Task Force (RDTF) recommends that the wording "Centre of Reference" is not used anymore, but the preferred wording is "centre of expertise" (Centres of Reference for rare diseases in Europe: State-of-the-art in 2006 and recommendations of the Rare Diseases Task Force, December 2006).

performance, management and evaluation of the centre. These evaluations should be made publicly available” (Recommendation 9)

- “Centres of Expertise and European Reference Networks shall provide guidelines on the most appropriate care management for patients, closely integrating both medical and social aspects. They should involve patients and give them an active role as recognised partners at all stages” (Recommendation 13)

The EUCERD (European Union Committee of Experts on Rare Diseases) Recommendations on Quality criteria for Centres of Expertise for Rare Diseases in Member States (5) (see ANNEX 2) also promote the role of rare disease patients and their representatives in the functioning of Centres of Expertise, recommending:

- “Centres of Expertise collaborate with patient organisations to bring in the patient perspective” (Recommendation 7)
- “Link and collaboration with patient organisations where they exist” (Recommendation 29)

Even though the criteria for Centres of Expertise are delineated, currently the organisation of Centres of Expertise and the extent to which patients are involved varies greatly from country to country. Some countries have specialised centres by disease or group of diseases, some countries have generalist centres for all rare diseases and some have both types of centres. Some national centres are uniquely clinical whilst others undertake clinical research, whereas others have a focus on technology and/or expert intervention. Some national Centres of Expertise focus on the management of patients whereas others focus more on expert advice and the production of guidelines. Many centres do both.

In Switzerland, the Federal Council of Switzerland has approved the “National Concept Rare Diseases” in September 2014 (6). The plan proposes 19 measures, including the establishment of Centres of Expertise. The process of designating reference centers has turned out to be very challenging, to some extent because responsibility for the provision of healthcare lies with the cantons, also in fields that are regulated by the federal government. In February 2015, the Federal Office of Public Health (FOPH) asked the Swiss Academy of Medical Sciences (SAMS) to realise measure 1 “A process for the establishment of reference centers is defined”. A concept for the designation was presented by the SAMS to the public at a Rare Disease Day event on 27 February 2016. After further consultations with representatives of ProRaris, the SAMS has produced a new concept which will be submitted to the FOPH in June 2016 (7). This latest concept proposes that patient-centred care of patients with rare diseases will be implemented on two levels: A care provision network consisting of specialized care providers and Reference Centres (disease-specific), and platforms for rare diseases (disease-spanning). The establishment of the first level, care provision networks and Reference Centres, is to be carried out in collaboration with patient organisations and specialised care providers. In addition, the concept suggests criteria that should be fulfilled for the accreditation of Reference Centres. One criterion defines that “a structured contact

with the relevant patient organisations” must be established. But how is this structured contact set up? And how is collaboration with patients and patient organisations organised in the planning, establishing and functioning of Centres of Expertise in Switzerland?

The present report aims to contribute to answer this question by providing an informative and descriptive overview of patient involvement in national Centres of Expertise in Europe.

1.2 Aim

The aim of the present report is to answer the following questions:

- How are patient organisations and patient representatives involved in national Centres of Expertise in Europe?
- How can the experience of patient representatives and patients’ organisations best be used in the development and management of Centres of Expertise?
- In which fields of work can patient representatives and patients’ organisations be involved in Centres of Expertise?
- What role and responsibilities could patient representatives and patients’ organisations take in Centres of Expertise?

It is anticipated this report will be used to support the elaboration and designation of Centres of Expertise in Switzerland. The recommendations in this report are intended to facilitate partnership between Centres of Expertise and patients organisations and to illustrate possible fields of collaboration.

1.3 Search Strategy

All information and documentation used in order to establish this report was obtained by a computerised search. Since the topic of the present report is not a scientific focus and the development of Centres of Expertise is still in the fledgling stages in most European countries, only very few journal articles were found on the topic. Other search sources had to be reverted to such as Google, Google Scholar, official Websites of various institutions and committees (EUCERD, EURORDIS, Orphanet, OrphaNews, national alliances of patient organization) and the European Commission websites. References from relevant articles were also examined in order to identify key texts and other potentially relevant articles. The author of this report has compiled information which is accurate to the best of knowledge. However, readers should take note that the contents of this report are illustrative and not exhaustive. The main documents chosen for inclusion in the present report include EUCERD and EURORDIS publications such as reports on the State of the Art of Rare Disease Activities in Europe and reports from workshops and meetings of

the EUCERD. A further source of information concerned national plans or strategies for rare diseases in Europe.

Initially, key words searched were: Reference Centre, empowerment, patient involvement, and patient participation. These search terms did not yield many results, so the search strategy was continuously enlarged. The following key words and combinations of these words were finally used for the present review in order to obtain a sufficiently large number of publications:

Patient Empowerment	Reference network	Relationship
Patient involvement	Reference Centre	Relation
Patient participation	Centre (of) expertise	Involvement
Patient engagement	Good/ best practices	Involve
Patient organisation	Establishment	Involving
Patient	Management	Rare disease

1.4 Structure

The structure of this review is largely based on the principles of the Good practices report for the Collaboration between Centres of Expertise and Patients' Organisations (8) that has been developed within the frame of the POLKA² project. These principles or good practices have been developed to improve the collaboration between patients, their representatives and Centres of Expertise and to encourage transparent and effective dialogue between interested parties. The principles are supplemented with recommendations from different key publications and examples from different European countries.

2. Fields of Patient involvement

2.1 Designation

Despite the official criteria for the designation of Centres of Expertise by EUCERD (5), the current processes to identify, select and designate Centres of Expertise for rare diseases vary greatly from country to country. Few countries currently even have a designation process in place. The designation process at country level can follow one of the following models: through a call for proposals (bottom/up), or a public health plan (top/down). The bottom/up method is more pragmatic whereas a top/down approach is more ambitious (9). EURORDIS and its Members recommend that patient organisations should be consulted at each stage of the designation of Centres of Expertise (10). National conferences for rare diseases

² Patients „Consensus on Preferred Policy Scenarii for Rare Diseases, a project project by EURORDIS and its partners: Rare Disorders Denmark, National Commissioning Group NCG-NHS, Fundacio Doctor Robert, and supported by the European Commission DG SANCO. 2008-2011.

recognise the value of patients and patient organisation's involvement in the accreditation process of Centres of Expertise (9). It is suggested that patient organisations have a key role in advising on needs, prioritisation and where expert centres should be developed depending on the geography of their country. Patient organisations should continue to advocate the value of a more formal role in accreditation and operational delivery of Centre of Expertise. But in practice, not all countries have a designation or accreditation process in place (11). And there are significant variations in approach and the extent of patient involvement between countries (12). In addition, it proved difficult to find evidence for patient involvement in the designation process. For those countries where examples of patient involvement were published, almost all of them had a patient organisations or representative of patient organisations involved in only one stage of the designation process:

France (13): The applications of candidate centres are reviewed by an advisory committee (Comité National Consultatif de Labellisation des centres de reference de maladies rares (CNCL)) comprised of patient representatives, experts, and members of relevant societies and administrations.

Denmark (13): The final selection is done by the National Board of Health after consultation of the learned societies, the administration and the patients organisations.

Spain (9): A Designation Committee has been established which is charged with studying identified needs and proposing pathologies or diagnostic/therapeutic techniques, technologies and procedures for which a Centre of Expertise needs to be designated. Patient representatives have participated in the National Strategy working groups to define needs and identify the Centres of Expertise that are reported to the Designation Committee.

Finland (14): When designating Centres of Expertise on the basis of invitation, the representatives of all hospital districts, special fields and relevant patient organisations will be consulted. The designation of the Centres of Expertise is prepared by the coordinating centre for rare diseases, whose executive board includes representatives of both university hospitals and patient organisations.

But there's one example of an approach of patient involvement in the designation of Centres of Expertise that stands out: the dutch example. In the Netherlands, patient organisations participated formally in every step of the designation of Centres of Expertise, making sure patient perspective was included in addition to the medical/scientific perspective. The dutch approach will be described in more detail as a positive role model.

Netherlands (15,16,17): To begin with, the Dutch Ministry of Health, Welfare and Sport appointed the NFU (Netherlands Federation of University Medical Centres) as lead in the development and implementation of a procedure for the designation of rare disease Centres of Expertise. In close collaboration with Orphanet NL and the VSOP (Dutch National Alliance for Rare and Genetic Diseases representing patient organisations), a NFU project team developed a system to evaluate candidate Centres of Expertise and officially designate those fulfilling a defined set

of criteria. The set of criteria used to evaluate candidate Centres of Expertise consists of the EUCERD criteria in combination with specific criteria from the Dutch Rare Disease Plan (see Annex 3). Questionnaires had to be filled out by the candidate Centre of Expertise itself, by VSOP, and by the patient organisations representing the rare disease(s) declared by the Centres of Expertise. The questionnaires for patient organisations included specifying the 5 most relevant criteria out of the 16 criteria that will be assessed and answering the SMART questions covering each of the 16 criteria, per cluster and per disease. The patient organisations were then asked to conclude if the Centre of Expertise should be given accreditation for 5 years, conditional accreditation for 1 year, or no accreditation at all. Finally, they had to give suggestions for improvements and examples of strong points. The role of VSOP included the search for matching Patient organisations and convincing them to participate, even if Centre of Expertise was unknown to them. They supported the participating patient organisations through instructional meetings, a telephone and e-mail helpline for assistance in filling out the questionnaire and forming an opinion, Q&A and other information on www.vsop.nl, and a basic questionnaire for membership consultation. In addition, a patient representative from the VSOP took part in the assessment committee consisting of an independent chair, the NFU project leader, a secretary and a medical specialist from the Orphanet NL Scientific Advisory Board. Furthermore, VSOP prepared interim and final evaluation. In 2015, of 417 candidate centres 302 centres were designated, either completely or partially. 85 unique patient organisations participated. 298 questionnaires were filled out by patient organisations in total, with 1 to 19 questionnaires filled out per patient organization. 196 centres were designated for 5 years, 83 centres were designated for 1 year, 23 centres were partly designated for 5 years and partly for 1 year. The Centres of Expertise are published on the Orphanet website www.orpha.net, the Erfocentrum website www.erfelijkheid.nl and the VSOP website www.zichtopzeldzaam.nl. Accredited CE can participate in call for ERNs

The unique aspect of the Dutch designation process is the combination of the medical/scientific evaluation of centres by medical specialists and the concomitant evaluation by patient organisations, adding the patients perspective. The collaboration of medical specialists and patient organisations in this Dutch designation procedure resulted in a joint decision process and forms the basis for future collaborations between all relevant stakeholders in the Dutch rare disease field. The assessment of candidate Centres of Expertise from the patients' perspective was of great added value in the process of designation. Patient organisations gave their own unique perspective based on their experiences with the Centres of Expertise and the patients (and/or their parents) experience with these elements of healthcare. It also became clear-from patient perspective-which candidate Centres of Expertise were already performing good on criteria like (international) collaboration and which candidate Centre of Expertise's could improve. As a result, the collaboration between the Centres of Expertise and patient organisations improved and resulted in a better mutual understanding and cooperation, to work together and improve the quality of healthcare and research.

2.2 Planning

Patient organisations should already participate in the planning process during the setting up of new Centres of Expertise. Involving patients and their families in service planning must be promoted. The Centres of Expertise must collaborate with patient organisations in such a manner that the patients' perspectives are taken into account in the measures proposed. Patients organisations can advise on day-to-day organisation and medical practices adapted to patient special needs within the centre: for example waiting times, consultation days and hours compatible with attendance at school and work, blood tests and other examinations, food adapted to special dietary needs, physical infrastructure of the centre, and adequate care pathways.

Centres and patients' organisations are encouraged to structure their collaboration at the beginning by a written agreement between the two parties (18). According to Christel Nourissier, the EURORDIS Secretary General (19), a written agreement between Centres of Expertise and patient organisations is for the mutual benefit of patients and coordinators of centres. It should be based on the declaration of Common Principles on Centres of Expertise and adapted to each centre. Fields are to be defined where cooperation exists, where it needs to be improved, and where it is not expected. Christel Nourissier recommends to list all necessary pluridisciplinary competences and infrastructures for the disease or group of diseases (Health professionals, Social workers, Equipments) and to list all missing competences and infrastructures, with up to date contact details on where to find them outside the centre. The agreement describes what is included or excluded from the collaboration, the Patient Organisations commitments, confidentiality issues, clauses in case of restrictions to data access (e.g. registries, surveys, databases, scientific communication). The agreement is to be written out in adequate language and formats according to age, skills, language, and culture. It is then signed by both centres and patient groups, and finally disseminated to the users and made public on the websites.

Belgium (20): At the planning stage of a new Centre of Expertise, the specific needs of the patients with a specific rare disease or a specific group of rare diseases should be mapped and documented based on a consultation of patients and their relevant organisation (if it exists). The type of staffing of the Centre of Expertise on that specific disease or group of diseases, and the organisation of the multidisciplinary patient management must meet those needs.

Scotland (21): The Neurological Alliance of Scotland involves patient representatives in a 'Neurological Voices Programme'. This Programme prepares people with different neurological conditions (eg, Ataxia, Dystonia, Epilepsy, Huntington's Disease, ME, Multiple Sclerosis, Parkinson's disease, Neuropathies and more) and their informal carers to get involved in planning neurological health services. The aim of Neurological Voices is to provide a robust and sustainable patient and carer involvement training package to empower those in Scotland affected by neurological conditions to contribute to the development of local neurological services.

2.3 Involvement in decision-making structures

Representatives of the patients should be formally included in relevant decision-making structures in every Centre of Expertise. Their contribution must be taken into account in the policy and functioning of the centre. Examples of internal structures aimed at officially involving patients are the Board of the centre, the Steering Committee, and the Medical Advisory Panel. Involvement of patient representatives in the decision-making structures of the Centre of Expertise has to be discussed and negotiated from the beginning in order not to bring in the patient's perspective too late (18).

Belgium (20): Patient participation and involvement in the current centres is often minimised by denying access to patient representatives in Boards or Advisory Boards. In some centres, patients have a seat in these commissions, but patients have the feeling that their remarks and comments are often ignored and disregarded.

Scotland (22): In diabetes services, the chair of an active patient subgroup is also on the national Diabetes Managed Clinical Networks (MCN) steering group.

2.4 Provide support to fellow patients

Patient representatives could offer counselling, especially for new patients or patients with special needs. Or they could take part in self-help groups or manage discussion groups for patients and families, with teachers, fellow students, and employers. It is especially important that patients and families have the opportunity to get support and information from other patients right before and after they receive diagnosis. Of course, counselling by patients can't replace professional work by psychologists and social workers, but fellow patients are in the position to provide unique inside information about living with the condition, share experiences, and suggest a number of support tools and strategies. Receiving information and experiences from fellow patients on medication, usefulness and/or side effects of certain treatments, aspects of quality of life, etc. are valuable for many patients. In addition, companion contact has shown to improve adherence to therapy (20). And a study assessing the experiences at existing UK and Danish Centres of Expertise (23), stressed that patients and their families should be regularly provided with information about their condition using appropriate channels and formats, such as advice and information from other patients. As a patient explained: "As a patient who has been here for many years, I would gladly be in a phonebook to help any new patients get accustomed".

Belgium (20): Each Centre of Expertise should create the possibility that a representative from a patients' organisation can be consulted by (new) patients. It is important that patients can meet each other and exchange experiences. Therefore it is useful for Centres of Expertise to organise a patient information point in their consultation rooms, allow access to representatives from patients' organisations during consultation hours, and/or organise a yearly patient day in collaboration with the relevant patients' organisation(s). By involving patient

representatives in the working of the Centres of Expertise, the quality of patient centred care will improve since enforceable patient participation in the Centres of Expertise ensures a focus on real patient needs.

2.5 Creating information

According to the Recommendations to support the integration of rare diseases into social services and social policies (3), Centres of Expertise have a key role in contributing to and provide accessible information adapted to the specific needs of patients and their families, of health and social professionals. Centres of Expertise should collaborate with patient organisations to collect information and experiences on the disease and its treatments in order to produce information sheets for patients, families and professionals. These information documents may include information on

- available services and how to access them
- medical treatment options
- financial support
- social care / social work
- useful contacts (i.e., helplines)
- good practice advice on pain alleviation, swallowing, nutrition and diets, cleaning medical devices, emergency situations, dealing with unexpected events, learning disabilities, behaviour problems, etc.
- on how to travel with the disease, including cross-border care

The information documents should be written in a patient-friendly information way and disseminated efficiently in and outside of the Centres of Expertise.

Belgium (20): Patients who might feel uncertain, timid or sometimes confused during consultations, will be offered instruments and tools to help them in their communication with professionals. These instruments can take the form of checklists, diaries, etc. They serve as guidance instruments during the consultation to ensure that patients do not forget to express the questions and remarks they have during the stressful moments of the consultation. The information documents will be jointly developed by the Centres of Expertise and the relevant patients' organisations. As a result, patients who are insecure during consultations will be more comfortable with the proper auxiliary tools and will address the questions they consider themselves as being important.

Finland (14): Individual rare disease patients and their families must receive adequate information about care, rehabilitation, social welfare and support services. Both the Centres of Expertise and rare disease units must operate as readily accessible, "low threshold" information centres. There must be comprehensive collection of information in cooperation with patient organisations and the entire healthcare service, social welfare service and rehabilitation service network. The information in question will be available through computerised access to the coordination centre's databank, as well as via help-lines.

2.6 Training and Education

The Common Principles on Centres of Expertise (4), and the Recommendations to support the integration of rare diseases into social services and social policies (3) clearly state that Centres of Expertise are expected to be instrumental in providing training and education to all stakeholders involved. This includes training activities for patients and their representatives, non-healthcare professionals (such as school teachers, personal/homecare facilitators) and health care professionals (general practitioners, allied specialists, etc.) in order to improve referrals and follow up.

The role of Centres of Expertise in education at several levels was emphasized during a round table discussion on how to implement EUCERD recommendations for Centres of Expertise at a EUCERD workshop in Madrid (24). Regarding specialized university training, it was mentioned that a curriculum design could include sessions taught by medical professors and patients, offering the students different perspectives on rare diseases. Education of healthcare professionals outside the field of rare diseases was also mentioned and identified as a priority.

Finland (14): Experts from the Centres of Expertise should visit rare disease peer support groups in person, to give and receive information. Reciprocity is important, so that rare disease patients and their families can contribute effectively to the development of care, rehabilitation, and other services. Rare disease patients and their families are necessary sources of empirical knowledge. The knowledge they contribute will be used in rare disease training modules for healthcare professionals.

Norway (25): Frambu is one of 10 national centres for rare disorders in Norway. It is a private foundation funded by the Norwegian state, which provides services for over 120 rare diagnoses. It offers both courses and visits to the local environment in order to train the professionals. The centre offers different types of courses: specialised courses, brief courses and local guidance, and development of expertise. The target audience are health professionals, local health services, professionals in the education system and other professionals working on behalf of individuals with one of Frambu's focal RDs. Frambu's courses revolve around RDs and the home environment, information on diagnosis, medical information, special education/work places and facilitation. Frambu works closely with patient organisations, local communities and expert professionals to develop the training programmes. Patients/families and patient organisations are often consulted during the process of conception of the training contents and can also be involved directly in the training programmes by giving their testimonial. Frambu has produced videos for the trainings, for example for a training for Neurofibromatosis Type 1 (26). Three young adults share their needs, experiences, reflections about life with the diagnose NF 1 with the trainees. This is an innovative and safe way to involve patients in the training without invading their privacy. In addition, trainings might be accompanied by patients and/ or relatives.

Sweden (25): Ågrenska is a National Competence Centre For Rare Diseases. The centre designs and arranges seminars, courses, and conferences for professionals

e.g. habilitation personnel, educational staff, health care professionals, social workers, who meet children and adults with rare diseases. The training and education programmes at Ågrenska include trainings for professionals during family stays, trainings for medical students and tailor-made trainings. For the training of professionals during family stays, parents invite the staff working with their child in the local community for a 2 day training and experience. The parents are mostly responsible for coordinating this training. Target groups are teachers, preschool teachers, support staff, habilitation staff, personal assistants, student health team, respite care personnel, etc. The training aims at increasing knowledge, understanding and collaboration. Contents of the training are lectures and discussions with the parents about medical issues, education aspects, etc. The training presents a unique opportunity for the participants to get updated knowledge, meet colleagues in the same situation and share experiences, take note of the differences and similarities of up to 10 children with the same diagnosis, understand the situation of the family, and define a common platform for further work.

Germany (27): The national plan of action for people with rare diseases (2013) plans for Centres of Expertise to provide courses in continuing education approved by the state medical associations at regular intervals and in association with the respective patient organizations (inasmuch as present). The goal of these courses is to provide physicians with information on rare diseases and to inform them of existing information sources as well as how to deal with a lack of information.

Hungary (28): In the Hungarian national plan for rare diseases patient organisations play an important role in layman education. Patient organisations can recruit the participants of trainings, they themselves can take part in them and become an information base of qualified professionals playing a role in the coordination between patients and qualified professionals. The knowledge of experienced helpers shall be increased by training, where the patients may also participate as experts from the side of experience. Such training and preparation facilitates the solution of problems related to rare diseases (e.g. by training helpdesk workers, representatives of patient rights and patient organisations as well as social workers). The inclusion of patient organisations in the development, maintenance and operation of a telephone helpdesk, using the expert staff and tools of patient organisations and, if possible, by providing employment to employees with rare diseases.

Italy: In Italy, there is an example of parent involvement in a training program for parents of a child affected by Prader-Willi syndrome (30). The Italian national plan for rare diseases states that there must be specific training programmes for patients and their Associations, ordered by groups of pathologies, treatment needs and practices and involving decision-making processes (29). Training programmes can be self-help groups, parent trainings, parent to parent trainings, etc., developed and conducted by the Centres of Expertise and the local services. The Italian National Centre for Rare Diseases (CNMR) organizes and carries out the “Parent Training on Prader-Willi syndrome”. Objectives of the programme are to engage

the parents of children with Prader-Willi syndrome in order to improve their relationship with the children and children's behaviour, to increase the knowledge on PWS and to empower parents in managing their children affected by PWS. The training programme is conducted by two moderators, a psychologist and an expert parent. The selected expert parent is both, experienced in parent training methods and experienced in the daily difficulties of managing a child with PWS. The parent's task is to facilitate communication between the participants of the course (parent-parent and parent-lecturer) and to focus on the well-being of the group.

Belgium (20): The Belgium plan of rare diseases outlines that education and teaching on rare diseases should be integrated in the curricula of health care professionals and in the continuous medical education of health care professionals (i.e. medical doctors, paramedical professionals, nurses, pharmacists ...). In view of their first-hand expertise, patients and patient organizations should be actively involved in education on rare diseases. Already, these organisations play an important role in the guidance and accompaniment of master and doctoral students during their research and the writing of their theses. In addition, professional organizations should prioritize rare diseases in their activities (annual meetings, publications, research and clinical projects...). They should develop interaction with rare disease Patients Organizations and train their members in the application of Orphanet. Collaboration between patient and professional organizations needs to be actively pursued in order to optimize the visibility of rare diseases: interactive workshops during annual meeting could be a good opportunity to follow and to develop these links.

2.7 Monitoring and evaluation

Patients must participate in the evaluation and quality assurance of the Centres of Expertise. The management and treatment of rare disease patients forms the 'core business' of these centres. Visiting patients as clients therefore know the strengths and weaknesses of each centre and know best what can be improved or what is missing. Patient organisations could for example conduct surveys on patient needs and satisfaction. Or they may list missing competences and infrastructures, when needed, with up-to-date contact details on where to find them outside the centre.

Scotland (22): In designated national specialist services patients are involved in annual performance reviews of specialist services and in the regular 3-5 year planning reviews. Another example is the Patient Opinion website www.patientopinion.org.uk where patients, their carers or family members can tell other people about their experiences of the NHS, completely independent of government and the NHS. NHS Boards are alerted to stories posted about services in their area and are encouraged by the Scottish Government to post responses saying what they have done in light of what patients have said. It aims to make it easier for people to give feedback and for NHS Boards to get those opinions to the people who need to see them and ultimately, to make services better.

Belgium (20): The Belgium plan for rare diseases proposes a procedure where patient representatives have the right to notify a monitoring official body if the

Centre of Expertise does not function according to the agreements stipulated in the convention and the criteria list for recognition. Furthermore, it is suggested that patients and patients' organisations should be involved during the periodic evaluation of the Centres of Expertise.

Finland (14): According to the national action plan, each Centre of Expertise will set up a customer panel in cooperation with patient organisations. The panel will raise questions for discussion, evaluate operation, provide supportive advice on the Centre of Expertise's general policies and make development proposals. In addition, patient organisations will participate in the regular evaluation of the activities of the Centres of Expertise.

2.8 Patient registration

Under the terms of EUCERD's Core Recommendations on Rare Disease Patient Registration and Data Collection (31), Centres of Expertise should contribute to registries. The creation of a registry can be a powerful tool to create and structure networks of experts, whether they being European Reference Networks of Centres of Expertise or national expert networks for RD. In either case, the experts and Centres of Expertise involved are a primary source of data for registries (32). Furthermore, according to the 10 Key Principles for Rare Disease Patient Registries submitted by EURORDIS, NORD, and CORD (33), patients should be equally involved with other stakeholders in the governance of Rare Disease Patient Registries. Involvement of patients in the design, analysis and governance of registries is important to address the complexity and scarcity of knowledge on Rare Diseases (31). Patient representatives should be invited to provide best possible expert support through an advisory board or committee to ensure appropriate exchange of information and knowledge into and from the registry (34). Patients should be involved at all levels of development, management and maintenance in order to best represent patient needs, increase awareness among all stakeholders of the existence of the registry and, ultimately, improving the quality and quantity of data collected through a patient-centred approach. Patient groups are willing and able to be involved in the following tasks which should be reflected in the governance of the registry as the essential role of patients (34):

- initiating the establishment of registries;
- defining content and purposes of the registries;
- resolving ethical and legal issues;
- authorising access and utilisation of data;
- creating partnerships with health professionals and industry representatives;
- contributing to the selection of data items collected (in particular on the impact of the disease on their daily life);
- helping to recruit patients for participation into the registry;
- preparing specific information for patients to be registered prior to their consent;
- motivating health professionals to input data, and directly entering data.

Bulgaria (35): In Bulgaria, a number of rare disease registries were created as a result of joint activities between scientific societies, clinical centers, patient organizations and Non-Governmental Organizations (NGOs). The involvement of all stakeholders proved to be key to the success and to the long-term duration of RD registries. This is especially recommended as it offers diversification of funding sources (government, academia, industry, patient organisations,...).

Belgium (36): Patient involvement in the field of registries is particularly important because of their roles in monitoring and recruitment. “Patients will be more likely to agree to being registered if they are contacted by other patients and if they are assured that the data they provide will be used properly and that the monitoring system includes patient representatives,” argues Lut de Baere, Chair of RaDiOrg.be, the Belgian national alliance for rare disease patients.

2.9 Research

Involvement with research is an important way to empower patients. And input from patients and their families can improve both the quality and effectiveness of research. Their involvement should be encouraged at all stages of the research process. The Good practices for the collaboration between Centres of Expertise and patients’ organization (8) recommend that patients’ organisations are involved in working groups, and disseminate information about research. They should understand studies and trials and be a partner in designing, executing, translating (international) trials. Experts who examined the experience of national Centres of Expertise at a workshop in Luxembourg (9) agreed that research and clinical care should both be missions of Centres of Expertise. It was highlighted that clinical researchers usually have European contacts whereas clinical practitioners sometimes do not, which are crucial for networking. A recent study by Syed et al. (23) assessed experiences of healthcare professionals and rare diseases patients at existing UK and Danish Centres of Expertise, to develop policy recommendations in order to improve care for rare disease patients. The results suggest that Centres of Expertise establish themselves as research facilities, and include patient organisations in the design and execution of studies. In addition, Centres of Expertise should ensure appropriate dissemination of research results to all stakeholders.

Eurordis has outlined the main guiding principles for conducting rare disease research at the national and EU level for the decade ahead (37). According to this position paper, empowering patients in research means recognising that patients are full and equal partners, developers, and funders of research in rare diseases. Patient associations should have a more proactive role as research partners. In particular, patients should be partners in research not only as subjects, but also as advocates for fundraising and key stakeholders in the drafting of guidelines and policies. In practice this should translate into fostering:

- the participation of patient groups to EC-funded research projects, by simplifying the procedure for obtaining support during the application preparatory phase. Patient organisations collaborating with research

groups by writing proposals to be included in the main project should be supported.

- capacity-building of patient representatives on specific research topics, such as patient registries and databases, clinical trials, basic research, etc. In particular, patient organisations should be provided with the appropriate tools to create greater awareness on research and drug development among patients. Patient representatives should be trained and provided with the financial support to contribute as fully-fledged partners in the definition of research priorities in the fields of their concern at the European and national levels.
- the development of research tools and infrastructures that include patient-driven governance and the sharing of results with patients.
- patient involvement in each step of the clinical trial protocol development to ensure literacy of patient information notices, informed consent forms, case record forms or self-administered questionnaires, report summary for patients, etc.
- patient involvement in steering and evaluation committees on research, HTA committees, ethics committees, research on clinical ethics. A sustainability plan should exist in order to support the participation of the patient.
- communication amongst involved scientists and patient organisations by setting up special sessions to report and discuss recently obtained scientific results in a non-specialised language should be promoted. Projects related to science communication (scientific reports in a non-specialised language, information booklets, sheets, etc.) would be welcome in order to establish closer links between researchers, policy and decision-makers, media, private sector, NGOs, citizens, etc.

Wales (38): In Wales, rare disease patients are involved, with the support of Genetic Alliance UK, throughout the research pipeline – from setting research priorities and study design through to input into health and social policy.

Scotland (38): The Implementation Plan for Rare Diseases in Scotland aims to encourage staff involved in the care of people with rare diseases to signpost them to appropriate sources of information about research, clinical trials and opportunities to participate. To support those with rare diseases in participating in research, Scotland is currently exploring the development of an online application process and related patient registers.

UK (38): Actively involving and engaging patients are core to the work of the NIHR Rare Diseases Translational Research Collaboration (NIHR RD-TRC). Over almost a decade, patients have contributed to the work of NIHR by helping it to decide what research to fund and how it should do this. They help to review and shape research projects and proposals and actively collaborate with researchers, clinicians and other health professionals to deliver and disseminate research results. Their knowledge and insight play a vital role in helping the UK to recruit hundreds of thousands of volunteers to clinical studies every year. The overall activity of the

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programme is directed by the Strategic Oversight Group. This group includes two lay members, as well as patient representatives. The role of the group is to oversee the fundamental values and ethical principles of the NIHR RD-TRC. The involvement of lay members and outpatients helps the group to champion patient and public views regarding topics for research and makes sure that the most relevant research gets funded. Researchers applying for funding must specify how patients have been involved in the research proposals and their plans for future patient and public involvement in the proposed work. Monitoring this activity is part of the regular reporting that researchers need to submit.

3. Summary

The identification and creation of Centres of Expertise is a key element of national plans and strategies for rare diseases and a step towards European networks. In all national plans, there is a strong agreement that patient representatives and patient organisations should play an integral role in the planning and functioning of national Centres of Expertise. In Switzerland, the National Concept for Rare Diseases suggests that the establishment of Centres of Expertise is to be carried out in collaboration with patient organisations and a structured contact with the relevant patient organisations must be established. This report aimed at providing an informative and descriptive overview of patient involvement in national Centres of Expertise in Europe. By examining key documents deriving from a thorough computerized search, this report has identified fields of collaboration and recommendations that are intended to facilitate partnership between Centres of Expertise and patients organisations. It is recommended that Centres of Expertise demonstrate meaningful patient involvement, patient-centeredness and empowerment in the following areas within Centres of Expertise:

- **Designation:** Patient representatives or patient organisations participate formally in every step of the designation process of Centres of Expertise. They can be part of committees and boards to define needs, identify, assess, evaluate and finally select the Centres. As such, patient organisations may give their own unique perspective based on their experiences with the Centres of Expertise.
- **Planning:** Patient representatives or patient organisations already participate in the planning process during the setting up of new Centres of Expertise (day-to-day organisation and medical practices adapted to patient special needs within the Centre). A written agreement between Centres and patients' organisations is developed to facilitate their collaboration.
- **Decision-making structures:** Representatives of patients are formally included in relevant decision-making structures in every Centre of Expertise (e.g. Board of the Centre, the Steering Committee, the Medical Advisory Panel).
- **Support to fellow patients:** Patient representatives offer counselling to fellow patients, and they take part in self-help groups or manage discussion groups for patients and families, with teachers, fellow students, and employers. Centres of Expertise organise a patient information point in their consultation rooms, allow access to representatives from patients' organisations during consultation hours, and organise a yearly patient day in collaboration with the relevant patients' organisations.
- **Create information:** Centres of Expertise collaborate with patient organisations to collect information and experiences on the disease and its treatments in order to produce information sheets for patients, families and professionals.
- **Training and education:** Centres of Expertise provide training and education to patients and their representatives, non-healthcare

professionals (such as school teachers, personal/homecare facilitators) and health care professionals (general practitioners, allied specialists, etc.). Patients/families and patient organisations can be consulted during the process of conception of the training contents and can also be involved directly in the training programmes (e.g. by giving their testimonial, as experts).

- **Monitoring and Evaluation:** Patients participate in the evaluation and quality assurance of the Centres of Expertise. For example, patient organisations conduct surveys on patient needs and satisfaction. And they are involved during the periodic evaluation of the Centres of Expertise.
- **Patient registration:** Patients are involved at all levels of development, design, analysis, management and governance of registries.
- **Research:** Centres of Expertise establish themselves as research facilities, and include patient organisations in the design and execution of studies. Patients' organisations are involved in working groups, and disseminate information about research, advocate for fundraising and are key stakeholders in the drafting of guidelines and policies in research.

It has already been emphasized that only very few journal articles were found on the topic and thus, other search sources had to be reverted to. The main types of documents included in this report were EUCERD and EURORDIS publications, and national plans or strategies for rare diseases in Europe. But even with the extension of sources of information, it remained difficult to obtain useful and detailed information on patient involvement in national Centres of Expertise, especially in the area of service provision. It is therefore recommended to further investigate this topic in a second step in more detail by conducting interviews with key informants of relevant Centres of Expertise in Europe. As suggested by Lenja Wiehe, Patient Advocacy Group Manager at EURORDIS, the clinical steering committees of ERN applications may be contacted as they are coordinating the most important Centres of Expertise in Europe. The results of this report can be used as basis for developing targeted interview questions to ensure receiving purposeful information that will promote patient involvement in the elaboration of Centres of Expertise in Switzerland.

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ANNEX 1: Declaration of Common Principles on Centres of Expertise and European Reference Networks for Rare Diseases

Rare diseases are often complex diseases

1. Centres of Expertise shall aim at providing a multi-disciplinary approach
2. Centres of Expertise shall aim at providing patient centred-care. Multidisciplinarity shall be managed in a coordinated manner, and shall not result in disconnected medical services
3. Centres of Expertise shall represent a reliable source of accurate diagnosis, and shall include genetic testing and genetic counselling
4. Centres of Expertise shall share their competences at both national and European levels and shall endeavour to constantly increase and update their level of expertise
5. Centres of Expertise should join in European Reference Networks for Rare Diseases.

Rare disease patients are too often excluded from health systems and socially marginalised, in spite of their tenacious personal commitment

6. Centres of Expertise shall be places where patients feel welcome and safe and where patients are received by knowledgeable and understanding professionals
7. Centres of Expertise shall facilitate and improve the autonomy of the patient
8. Centres of Expertise shall provide access to social assistance, which respond to the special needs of the disease

Centres of Expertise shall not only be “care giving structures”, but shall also engage in the following activities:

9. Centres of Expertise and European Reference Networks shall actively involve patients and their representatives in the establishment and performance, management and evaluation of the centre (11). These evaluations should be made publicly available
10. Centres of Expertise shall exchange information with local professionals, including general practitioners
11. Centres of Expertise and European Reference Networks shall disseminate information on the diseases to social and other relevant stakeholders involved
12. Centres of Expertise shall provide training to all stakeholders involved, including health care professionals, patients and their representatives
13. Centres of Expertise and European Reference Networks shall provide guidelines on the most appropriate care management for patients, closely integrating both

medical and social aspects. They should involve patients and give them an active role as recognised partners at all stages.

14. Centres of Expertise and European Reference Networks shall facilitate the coordination of both basic and clinical research activities and infrastructures, including clinical trials, registries, biobanks, exploration of innovative techniques, etc. They should also be required to publish and disseminate research results, irrespective of whether the results are positive or negative

15. Access to Centres of Expertise must be ensured to all patients, regardless of their country or region of origin

ANNEX 2: EUCERD Recommendations on Quality Criteria for Centres of Expertise for Rare Diseases in Member States

RECOMMENDATIONS:

Mission and scope of Centres of Expertise (CEs) for rare diseases (RD) in Member States (MS)

1. CEs tackle diseases or conditions requiring specific care due to the difficulty in establishing a diagnosis, to prevent complications and/or to set up treatments.
2. CEs are expert structures for the management and care of RD patients in a defined catchment area, preferably national, and at international level if necessary.
3. The combined scope of all CEs within a MS covers all RD patients' needs, even if they cannot provide a full range of services with the same level of expertise for each RD.
4. CEs bring together, or coordinate, within the specialised healthcare sector multidisciplinary competences/skills, including paramedical skills and social services, in order to serve the specific medical, rehabilitation and palliative needs of rare diseases patients.
5. CEs contribute to building healthcare pathways from primary care.
6. CEs have links with specialised laboratories and other facilities.
7. CEs collaborate with patient organisations to bring in the patients' perspective.
8. CEs contribute to the elaboration of good practice guidelines and to their dissemination.
9. CEs provide education and training to healthcare professionals from all disciplines, including paramedical specialists and non-healthcare professionals (such as school teachers, personal/homecare facilitators) whenever possible.
10. CEs contribute to and provide accessible information adapted to the specific needs of patients and their families, of health and social professionals, in collaboration with patient organisations and with Orphanet.
11. CEs respond to the needs of patients from different cultures and ethnic groups (i.e. have cultural sensitivity).
12. According to national/international ethical and legal frameworks, CEs should ensure respect of non-discrimination and non-stigmatisation of RD patients across Europe, within their sphere of competencies.

13. CEs contribute to research, to improve the understanding of the disease and to optimise diagnosis, care and treatment, including the clinical evaluation of long-term effects of new treatments.

14. The scope of diseases covered by each CE, or by a CE at national level, will vary depending on the size of the country and the structure of the national health care system.

15. CEs liaise with other CEs at National and European level when relevant.

16. A national directory of formally designated CEs is compiled and made publicly available, including on the Orphanet portal.

Criteria for designation of CEs for RD in MS

17. Capacity to produce and adhere to good practice guidelines for diagnosis and care.

18. Quality management in place to assure quality of care, including National and European legal provisions, and participation in internal and external quality schemes when applicable.

19. Capacity to propose quality of care indicators in their area and implement outcome measures including patient satisfaction.

20. High level of expertise and experience documented, for instance, by the annual volume of referrals and second opinions, and through peer-reviewed publications, grants, positions, teaching and training activities.

21. Appropriate capacity to manage RD patients and provide expert advice.

22. Contribution to state-of-the-art research.

23. Capacity to participate in data collection for clinical research and public health purposes.

24. Capacity to participate in clinical trials, if applicable.

25. Demonstration of a multi-disciplinary approach, when appropriate, integrating medical, paramedical, psychological and social needs (e.g. RD board).

26. Organisation of collaborations to assure the continuity of care between childhood, adolescence and adulthood, if relevant.

27. Organisation of collaborations to assure the continuity of care between all stages of the disease.

28. Links and collaboration with other CE at national, European and international level.

29. Links and collaboration with patient organisations where they exist.

30. Appropriate arrangements for referrals within individual Member States and from/to other EU countries if applicable.

31. Appropriate arrangements to improve the delivery of care and especially to shorten the time taken to reach a diagnosis.

32. Consideration of E-Health solutions (e.g. shared case management systems, expert systems for tele-expertise and shared repository of cases).

Process for designating and evaluating CEs for RD in MS

33. MS take action concerning the establishment and designation and evaluation of CEs and facilitate access to these centres.

34. MS establish a procedure to define and approve designation criteria and a transparent designation and evaluation process.

35. The designation criteria defined by MS are adapted to the characteristics of the disease or group of diseases covered by the CE.

36. CEs may not fulfill some of the designation criteria defined by the MS as long as the absence of fulfillment of those criteria does not impact on the quality of care and as long as CEs have a strategy in place to attain designation criteria in a defined time period.

37. The designation process at MS level ensures that the designated CEs have the capacity, and the resources to fulfill the obligations of designation.

38. The designation of a CE is valid for a defined period of time.

39. CE are re-evaluated on a regular basis through a process incorporated into the designation process at MS level.

40. The designating authority at MS level may decide to withdraw the designation of a Centre of Expertise if one or more of the conditions that formed the basis for designation is no longer satisfied, or if there is no longer a need to maintain the national service.

The European dimension of CEs

41. MS with established CEs share their experience and quality indicators with other MS and coordinate their efforts to identify CEs for all RD patients at EU level.

42. Networking of CEs is a key element of their contribution to patient diagnosis and care, to ensure that expertise travels rather than patients themselves when appropriate; exchange of data, biological samples, radiological images, other diagnostic materials, and e-tools for tele-expertise are promoted.

43. Cross-border healthcare is organised, where appropriate, with designated CEs in neighbouring or other countries, where patients or biological samples can be referred to.

44. Member States should provide adequate information to professionals, citizens and patients organisations concerning the possibilities and conditions of access to health care at national and international levels in the field of rare diseases.

45. Designated CEs at MS level are the key elements of the future ERNs.

ANNEX 3: Set of criteria used to evaluate candidate Centres of Expertise

	Theme	Criteria	
1	Quality of care	CE is able to provide highly specialized complex patient care	Number of patients in The Netherland Number of patients that are a member of your PO Number of patients visiting the CE For first doctor's appointment For second opinion
2		CE is responsible for contributing to the development of Standards of Care and guidelines, incl. patient versions.	CE should contribute to the distribution of these professional standards, in collaboration with representatives of patient organisations. Is there an Standard of Care for the disease(s) you represent? Was PO involved in the development? Patient version available? VSOP develops Standards of Care
3		System for safeguarding quality of care	CE has formulated procedures to guarantee the quality of care. Criteria and/or indicators for Quality of Care present? Patient organisation involved in development? CE involved in development? Patient organisation structurally informed?

4		CE provides healthcare with a permanent multidisciplinary team	<p>Specify the multidisciplinary team</p> <p>Are you informed about the different roles within the team? How? When?</p> <p>Are you informed on: How to reach the team in acute situations?</p>
5		Care provision within the entire chain	<p>CE coordinates integrated care.</p> <p>Is it clear who coordinates the different stages of the care process, provided by different care professionals?</p> <p>Is 'shared, integrated care' applied?</p>
6		Scientific developments	<p>CE has been informed about recent scientific developments regarding diagnostics, causal & symptomatic treatments, preventive procedures. Furthermore, CE meets social and psychological needs.</p> <p>Does the CE inform the PO about these developments?</p>
7	Transition of care	Transition from childhood into adulthood	<p>CE guarantees the continuity of care between childhood, adolescence and during adulthood.</p> <p>Does the CE guarantee continuity of care and if so, how?</p> <p>What is the quality of this transition care (performance, timing)?</p> <p>Are you involved in the development of quality</p>

			indicators or quality assessment?
8	Continuity	Transfer of knowledge within the centre	<p>CE is responsible for education and for sharing knowledge and competences with (new) experts within the multidisciplinary team.</p> <p>The continuity of care is guaranteed within the CE? How?</p>
9		Accredited by the hospital Board of Directors	
10		Open to auditing	<p>CE is willing to be audited for quality control.</p> <p>Can you confirm if this is the case?</p> <p>Would you like to participate in audits?</p>
11	Cooperation	With patients and patient organisations	<p>CE collaborates with patient organisations to improve the quality of care.</p> <p>Are you willing to sign a Letter of Agreement?</p> <p>What is the frequency of contact?</p> <p>How does the CE include patients' perspective? (questionnaires, meetings etc.)</p>
12		Other (inter)national centers of expertise	<p>CE collaborates with other national and international CE's regarding research and care.</p> <p>(Inter)national collaboration? Care? Research? How?</p>
13	Information and communication	Point of information	CE provides information to healthcare professionals, patients and their families.

			<p>Via National Genetic Information Centre, Orphanet or otherwise?</p> <p>CE refers individual patients to reliable resources of medical, psychological, social and cultural information?</p> <p>CE also functions as an information resource centre for PO?</p> <p>Information available and accessible?</p>
1 4		Education/ raising Awareness	<p>CE provides information and enhances knowledge and competences to healthcare and non-healthcare professionals</p> <p>Is CE willing to work with PO in order to contribute to more awareness?</p>
1 5	Research	Scientific research	<p>CE contributes to scientific research and publishes about the outcome.</p> <p>Does the CE consult the PO regarding the research agenda?</p> <p>Have you been invited to participate in research?</p> <p>How does the CE communicate about the relevance of the outcomes of the research for individual patients? (via PO, meetings, website, etc.)</p>
1 6		Patient registration/Biobank	<p>CE is responsible for storage of medical data and tissue samples.</p>

			<p>Does the CE inform the PO on development, existence, goal of the bio bank?</p> <p>Does CE work together with the PO on development/governance of the bio bank?</p> <p>Was the PO involved in the development of information materials / informed consent for participants?</p>
1 7	Cross-border healthcare	Participation in cross-border healthcare	<p>CE coordinates and advises on cross border healthcare in designated CE's in other EU-countries for referral of patients/ tissue samples.</p> <p>What is the role of the CE concerning cross-border health care (advising or organising)?</p> <p>Why could cross-border health care be relevant for your disease: diagnosis, treatment, second opinion?</p>