



EUCERD WORKSHOP REPORT



Centres of Expertise & European Reference Networks for Rare Diseases

Luxembourg, 8 - 9 December 2010

AGENDA

WEDNESDAY, 8th DECEMBER 2010, 14:00 – 18:00

Session 1: Centres of expertise in Europe: Where do we stand?

Chairs: Milan Macek and Christel Nourissier

- 14:00 Welcome address: *Antoni Montserrat*
- 14:15 Overview of the concepts and current situation: *Ségolène Aymé*
- 15:00 Application of the concepts in some Member States:
1. Norway : *Stein Are Aksnes (15 minutes)*
 2. France : *Ségolène Aymé (15 minutes)*
- 15:45 Coffee break
- 16:15
4. Italy: *Domenica Taruscio*
 5. Denmark: *Annette Haagerup*
 6. Germany: *Véronique Héon-Klin*
- 17:00 Discussion on steps to define guidelines
- 18:00 End of the workshop

THURSDAY, 9th DECEMBER 2010, 9:00 –12:30

Session 2: European Reference Networks: Where do we stand?

Chair: Yann Le Cam and Thomas Wagner (*excused*)

- 9:00 Overview of the concepts and current situation – *Ségolène Aymé*
- 9:30 Application of the concepts in different examples of European networks:
1. Care NMD – *Janbernd Kirschner*
 2. EPNET – *Jean-Charles Deybach*
 3. TAG – *Louis Dubertret*
- 11:00 Discussion on steps to define guidelines
- 12:30 End of the workshop

SUMMARY REPORT

General Introduction

One of the objectives of the European Union Committee of Experts on Rare Diseases is the surveillance of initiatives and incentives in the field of rare diseases at European level and at member state level. A report has been produced detailing initiatives and incentives in the field at EU and MS level prior to 2009 and during 2009: *2009 Report on Initiatives and Incentives in the Field of Rare Diseases of the European Union Committee of Experts on Rare Diseases*¹. The analysis this report led to the decision to explore in further depth the area concerning centres of expertise for rare diseases and European Reference Networks of Centres of Expertise (ERNs) for Rare Diseases. Centres of expertise and ERNs in the field of RD are mentioned in the High Level Group on Health Services and Medical Care Report of November 2005, the Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of Regions on Rare Diseases: Europe's challenges (11.11.08) and the Council Recommendation on an action in the field of rare diseases (08.06.09), as well as in the recommendations for National Plans and Strategies for Rare Diseases (Europlan) and in Point 15 of the draft directive for cross-border healthcare.

In order to build on previous work in the field of centres of expertise and ERNs, there was a need to examine the experience of national centres of expertise, to examine the experience and outcomes of the pilot ERNs financed by DG Sanco and to revise recommendations and guidelines in these areas in the light of these experiences. To launch this work, a workshop was organised on 8-9 December in Luxembourg which was attended by 32 experts (see list of participants in Annex).

The first session of the workshop concentrated on centres of expertise at national level in Europe with an overview of the concepts and current situation, followed by presentations on the application of the concepts in some Member States (France, Italy, Denmark, Germany and also Norway). For this first session, a draft Orphanet Report Series listing designated centres of expertise in Europe in the Orphanet database was provided to participants as supporting documentation. The second session was dedicated to European Reference Networks with an overview of the concepts and current situation, followed by examples of the application of the concepts in different European networks (Care NMD, EPNET, TAG). Prior to the workshop the participants received a draft preliminary analysis of the outcomes and experiences of pilot ERNs prepared by the Scientific Secretariat. Both sessions were followed by a general discussion on steps to define guidelines in these areas.

¹ <http://www.orpha.net/nestasso/EUCERD/upload/file/Reports/2009ReportInitiativesIncentives.pdf>

CENTRES OF EXPERTISE IN EUROPE: WHERE DO WE STAND?

1. Overview of the concepts and current situation (*Ségolène Aymé*)

Ségolène Aymé gave an overview of the concepts related to centres of expertise for rare diseases in Europe at national level and the current situation.

It was explained that centres of expertise for RD seem to be needed: patients are rare, and so are experts and there is a real need to identify this expertise. Expertise may only be found at international level, and it is impossible for most countries to offer appropriate services to all patients. In addition to this, clinical research for RD is needed and requires large enough cohorts, the systematic collection of data. One other necessity for RD is the production of clinical recommendations. Centres of expertise aim to provide healthcare services to patients with conditions requiring a particular concentration of resources or expertise. They also aim to provide high quality and cost-effective care, and to act as focal points for medical training and research, information dissemination and evaluation.

The European Commission's Rare Diseases Task Force has held two dedicated workshops on centres of expertise (2005 & 2006) and has produced two reports "*RDTF Report: Overview of Current Centres of Reference on rare diseases in the EU - September 2005*" and "*RDTF Report: Centres of Reference for Rare Diseases in Europe – State-of-the-art in 2006 and Recommendations of the Rare Diseases Task Force – September 2006*". These workshops and reports helped reach the following consensus:

- centres of expertise have a European added-value,
- there is a need to disseminate information on centres of expertise,
- networks of centres should be encouraged,
- there should be no hierarchy between European centres and national/regional centres.

A definition of what constitutes a centre of expertise was also established, including:

- an appropriate capacity to diagnose and manage patients/good outcomes,
- a multidisciplinary approach,
- a capacity to provide expert advice,
- a capacity to produce and adhere to good practice guidelines,
- documented expertise/experience/attractivity,
- a multidisciplinary approach/data collection/strong contribution to research
- close links with other expert centres/patient organisations.

Some countries have designated centres of expertise at country level either via a call for proposals (bottom up) or a public health plan (top down). Other countries have no process to designate centres of expertise. As there is no standard definition of a centre of expertise it is difficult to determine which centres are 'expert' when no official designation/identification programme exists in a country.

The new political context was then highlighted: centres of expertise for rare diseases have been mentioned as key instruments both in the Communication “Rare Diseases: Europe’s challenge” of 11 November 2008, and the Recommendation of the Council of 8 June 2009. There is thus a strong agreement that centres of expertise should be established in the framework of a national policy for RD. However, no analysis has yet been carried out of the experiences of MS with centres of expertise in place. MS that have not yet put in place a plan for RD need this information in order to establish official designation/identification processes. Without good centres of expertise at **national level**, sustainable ERNs cannot be created. Although MS are responsible for the organization, financing and delivery of healthcare, guidelines for centres of expertise can be of use. Guidelines should also take into account the diversity of health care systems and economies, and the differences between large, medium and small-sized countries.

Discussion after this presentation included comments on the over-simplification of previous guidelines established by the HLG and RDTF: MS are heterogenous and it is possible that different strategies are needed for different sizes and types of countries. In addition to this, more attention should be paid to healthcare pathways and networks of experts. The difference between centres of expertise and coordination centres (as exists in Belgium) should also be considered. Questions concerning the coverage of rare diseases by expert centres were also raised: should centres of expertise be organised by group of diseases so that no patient is without a centre of expertise for their specific disease?

2. Application of the concepts in Norway (*Stein Are Aksnes*)

Stein Are Aksnes (Senior Advisor, Norwegian Directorate of Health) gave a presentation of the system of centres of expertise in place in Norway. In Norway, 30’000 people have a rare disorder, and 17’000 of them are covered by a ‘national resource centre for rare conditions’. These centres have evolved over the past 25 years and are in place so as to ensure that the necessary support is provided for rare disease patients which would not be met by normal procedure, such as access to specialized information, consultations, medical and pedagogical studies, preventive and diagnostic treatments and the possibility to get in touch with other persons with the same/similar condition. Norwegian “Komptenansesentre” (centres of expertise) are financed by earmarked grants through the state budget and cover around 320 diseases, distributed as clusters. 16 centres exist, and 6 are dedicated to dual sensory impairment.

All centres are involved in research (mainly clinical). Some centres practice telemedicine. To obtain services from a centre, a condition must be congenital, complex/compound, and need multidisciplinary and coordinated services. The centres are heterogenous: there are bigger centres covering a number of diseases (such as Frambu Centre, 60-70 diagnoses) and smaller centres covering a group of diseases (NAPOS Porphyria Centre). However, currently 13,000 patients are not covered by a centre of expertise. Some

changes are foreseen from 2011: centres of expertise for RD will have to meet the same requirements as other national health services, and there is an ongoing process to create a new central unit under which the existing centres will act as units which should help improve synergy between the centres and increase efficiency. As a small country, Norway needs international cooperation as expertise is lacking in some areas, which can result in a delay in diagnosis for RD and delays in referral. The presentation also highlighted that there is a centre dedicated to Integrated Care and Telemedicine (www.telemmed.no) and individual plans for users of long-term, coordinated health and/or social centres, as well as coordinating units for habilitation and rehabilitation.

3. Application of the concepts in France (*Ségolène Aymé*)

Ségolène Aymé presented the experience of France in the area of centres of expertise for RD over the past six years. In France centres of expertise (called “centres de référence”) were a key measure of the 1st French National Plan for Rare Diseases (2004-2008). Their mission is to act as national centres in public teaching hospitals with the aim of organising health care pathways and ensuring a global and coordinated approach by improving care through liaison with local professionals. These centres have a budget for the coordination of these activities. The centres should also contribute to improving knowledge and professional practices, and contribute to providing data to health authorities to assess the impact of policies and network with other similar centres of reference in France and abroad. The process of ‘labelling’ the centres (led by a National Committee) was then explained, along with the assessment scheme. Over the 4 years of the first plan, 131 reference centres were established, approved and funded with a total of 4€ million over 4 years which has helped to create 200 MD positions and 200 non-MD positions. In 2009 ‘competence centres’ were established: these centres, at regional level, are selected by the reference centre and approved by the National Committee, and are nominated by the regional authority.

However the system has highlighted some problems: the coherence of the organisation in terms of regional coverage is disputable, as is the selection of centres on a first-come, first-served basis, and the lack of coherence in terms of disease coverage (i.e. only some fields, such as rare hepato-gastro-enterologic diseases, are well covered with complementary centres). There are also difficulties in communicating about centres’ missions and coverage. Funding is also distorted due to different numbers of patients in each centre.

Despite these problems, patient organizations are highly satisfied by the measures. Centres of reference have noted a 20% increase in referrals since the start of the system. Patient databases are in place in most of the centres of reference although there is no standard system.

The system faces specific challenges as there is no process in place to handle the life cycle of the centres (resignation/disputes/emergence of new teams), demotivation of

the teams outside the centres (i.e. jealousy), and it is impossible to have an impact on the budgetary decision at local level (some teams do not receive their budget).

Although the centres of reference are considered to be an excellent measure of the first plan (and a good decision of a highly centralized country like France), there is a lack of coherence in terms of disease coverage, a lack of coherence with the health care system in general (the concept is too specific), there is a difficulty in communicating about the centres of reference and the system needs to be redesigned through a dialogue with regional health authorities and learned societies.

Discussion following the presentation focussed on how to designate centres without creating animosity, and how to put the patient first above professional competition. It was highlighted that the concepts of centres of care and centres of expertise should not be confused and the relationship between expertise and care, and experts, patients and diseases should be explored.

4. Application of the concepts in Italy (*Domenica Taruscio*)

Domenica Taruscio (Istituto Superiore di Sanità) gave presentation on the concept of centres of expertise in Italy beginning with an overview of regulatory framework (Ministerial Decree 18 May 2001 n.279 – “Regulation for the institution of the National Network for the prevention, surveillance, diagnosis and therapy of rare diseases and the exemption from patients’ participation in the costs of the relevant healthcare”). This Decree created a list of exempted diseases and their ICD codes. The Decree also established the National Network for RD: each region has since identified its own centres of expertise to be part of the regional and national network for RD. Regional and interregional coordination centres have also been established. Regional centres must have documented experience in diagnostic and or therapeutic activity for single and/or groups of rare diseases, and possess adequate services and structures (emergency services and services for bio-chemical and genetic-molecular diagnosis). Regional centres have been identified in the entire national territory. In total, the Italian Regions have identified about 253 centres for the diagnosis and management of RD or groups of RD. Moreover, some Regions have identified integrated operational units, for specific rare diseases or groups of them, as components of the Centres. Finally, some Regions have established centers for the coordination of its own regional rare diseases network. The regional centres for rare diseases, delivering free services, are embedded within the already existing regional systems. As a consequence, the identification of regional centres for rare diseases does not respond to uniform criteria, but each Region has developed its own on the basis of the specific organization of the Region.

In Italy there are therefore several “scenarios”: some Centres are “Centres of Expertise” (which can be viewed as part of a Vertical Network) possessing great experience and cooperating at an international scientific level for a specific disease or group of diseases, and some Centres are for a more comprehensive care of patients (which can be viewed as part of a Horizontal Network), connecting health professionals and other peripheral

institutions (e.g. social services) present in the territory (where the patient and their family lives). These networks are functionally linked to each other. Some examples of regional networks (i.e. Emilia Romagna, Lombardia, Piemonte, Valle d'Aosta, Toscana, Area Vasta) were then given, and the role of the National Centre for Rare Diseases explained.

Discussion after the presentation included the practicalities of organising care for RD by region, especially concerning issues of prevalence (i.e. some regions may not have patients with a certain diseases). It was also explained that interregional registries exist and patients must be included in the register to be exempted from charges for their healthcare. There is no real selection of the 'best' centres for a certain disease/group of the diseases, the Italian model is based which centres see patients. The evaluation process is still ongoing, and potentially the movement of patients will be examined, as if a centre attracts patients it can be perhaps judged to be a good centre.

5. Application of the concepts in Denmark (*Annette Haagerup*)

Annette Haagerup from the Aarhus University Hospital Centre for Rare Diseases gave a presentation of the system of expert centres in Denmark. The political background was explained: in 2001 the Danish Board of Health released a statement establishing the basis for two rare disease centres to provide centralised expert health care, and determining 11 specific diseases for which healthcare pathways had to be set up. In 2010 a National Specialty Plan was launched identifying RD expertise in 87 different University Hospital Departments. The two centres were presented: the KSH Clinic for Rare Disabilities in Copenhagen, and the CSS Centre for Rare Diseases in Aarhus. The CSS treats primarily children and adults with NF, Marfan, Vascular EDS, PWS and Spielmeier-Vogt. The main activities of the centre are: specialised diagnostic and treatment, updating treatment protocols, counseling and guidance, planning and coordination (between the centre and local networks), collecting and promoting knowledge, research, development and education and international collaboration. The patient flow at the CSS was presented and the challenges faced by the team were outlined (i.e. increasing numbers of patients, the fact that adults are treated in a paediatric clinic, demands for increasing efficiency.) Patients can choose the centre they attend, but they have to cover travel costs.

An outline was then given of the Danish patient alliance Sjaeldne Diagnoser's vision for the centres set out at the Danish Europlan Conference: this include expanding the centres into child and adult centres with independent departments, attaching the 87 specialised functions to the centre, meeting all the recommendations at EU level for centres of expertise, and improving the national reimbursement of activities in the rare disease clinic.

Discussion following the presentation was based on whether a centre covering rare diseases in general can provide good care for all diseases, or rather they should play a role in organising health care. Annette Haagerup explained that the CSS refers patients

to hospital specialist departments for their care. It was suggested that there is a difference between centres of expertise for a rare disease, and coordinating centres for multidisciplinary networks, and that the Danish example in some ways corresponds to this model.

6. Application of the concepts in Germany (*Véronique Héon-Klin*)

Véronique Héon-Klin from the German Federal Ministry of Health then gave an overview of the work underway led by the National Action League for People with Rare Diseases (NAMSE) in implementing the Council recommendation on an action in the field of rare diseases in Germany, and in particular plans for centres of expertise. It was explained that the establishment of centres of expertise is discussed in the National Action League for People with Rare Diseases: at the moment no criteria or designation process are in place, although some centres have named themselves centres for rare diseases (Freiburg, Tübingen, Berlin). There are however 16 designated research networks for RD. One proposed model is to cross-link centres of expertise and European Reference Networks. In Germany it will have to be decided how to organise and how to determine the criteria of the calls. It also has to be determined how the abstract criteria previously agreed on by the RDTF can be transformed into indicators of quality.

General conclusions

The general discussion following these presentations was based on the criteria for centres of expertise as defined by the RDTF in the 2008 Report “European Reference Networks in the Field of Rare Diseases: State of the Art and Future Directions – Third Report”².

Amongst the main themes discussed were the different models for expert care for rare diseases: two models were identified:

- The health care pathway model
- The coordinating centre and centre of expertise model.

The first model (health care pathway) implies a step-wise approach where healthcare is organised in function of an individual’s health care needs (this model corresponds to the system in place in Denmark). The second model (a structured system of centres of expertise and coordinating centres) involves a network of centres of expertise acting as regional/local access points providing treatment and diagnosis which are linked to coordinating centres of which the vocation is not to treat patients outside their region but to coordinate healthcare and lead transversal actions such as the production of information and guidelines, participating in research and giving second expert opinions (this model corresponds to the system of ‘centres de compétence’ and ‘centres de référence’ in place in France).

² <http://www.eucerd.eu/upload/file/Publication/RDTFERN2008.pdf>

Apart from differing missions, the two models also imply a different method of financing: the first model (health care pathway) implies a budget per patient, whilst the second model (centres of expertise/coordinating centres) implies a global budget for their missions.

Also highlighted was the role of learned societies in the discussion concerning which type of centre and which model best fits the need of the community. It was agreed that they should be consulted as most rare diseases depend directly on a medical specialty.

It was also highlighted that the question concerning what defines a centre of expertise should be clarified in respects to individual expertise: i.e. is a centre of expertise a centre where an expert works, or is it a physical structure/team which provides expert services. When a centre of expertise is defined by the expertise of one person an element of instability is introduced into a system as this expert may change jobs, retire etc., and the centre would cease to exist.

Participants also discussed the contradiction between the preference for proximate health care for rare diseases and the rarity of expertise and therefore its inevitable concentration: the advantages and disadvantages of both sides of the coin have to be considered.

The question of the scope of centres of expertise was also discussed: more work should be done by the working group to identify a list of the types of centres which should be recommended. It was suggested that the scope should be by group of diseases: i.e. centres for neuromuscular diseases, bleeding disorders etc. It was also discussed whether there should be a prioritisation of the provision of centres of expertise for rare diseases according to whether or not something can be done for the patient.

This discussion was coupled with debate on the existing expertise at national level: it was argued that in each country expertise does not necessarily exist in all medical domains. One solution to be explored is to put into place centres by medical specialty in order to 'capture' all rare diseases. The working group will establish a proposal for a recommended list of centres needed in each country.

To better inform health professionals and patients about the possible centres for a given disease, it was decided that Orphanet should clearly present which centres are officially designated and the criteria applied to designate these centres. Due to the sensitivity of this information, it is necessary that any such information released in Orphanet is validated by health authorities. It was suggested that a colour coding system or logo in Orphanet could help maintain transparency by signaling whether a centre is officially designated by health authorities at national level or selected through another mechanism.

Workshop participants also discussed the usefulness of patient organisations' and patients' assessment of centres rather than self declaration when no official designation process is in place at MS level.

Another discussion centred on the dynamic of the systems of centres of expertise: it was highlighted that these systems should not be fixed and should allow for the development of health care needs and developments (i.e. E-Health). A periodic re-evaluation process should be incorporated into systems of designation of centers of expertise. A discussion also took place on the indicators that should be put into place to monitor implementation and outcomes in the field.

It was generally agreed that the concepts concerning this field must be defined and stabilised for further work to be carried out. It was also agreed that any recommendation must respect the sovereignty of each MS. The different models may be more or less adapted to the situation in different sized countries. **It was also agreed that expertise needs to be identified at a national level before networks of expertise at a European level can be built.**

EUROPEAN REFERENCE NETWORKS: WHERE DO WE STAND?

For this session, three supporting documents were provided: the draft Orphanet Report Series listing designated centres of expertise for RD at national level, the Orphanet Report Series listing European Reference Networks supported financially by the EC (by DG Research from 2000/DG Sanco from 2007) and the draft Preliminary Analysis of the Outcomes and Experiences of Pilot European Reference Networks for Rare Diseases.

1. Overview of the concepts and current situation (*Ségolène Aymé*)

Ségolène Aymé gave an overview of the work already carried out by the RDTF and the HLG in the area of ERNs for RD: this includes the report from the High Level Group on Health Services and Medical care (November 2007 - based on the report on centres of expertise published by the RDTF in 2006) as well as a RDTF workshop in 2008 followed by a RDTF report entitled “European Reference Networks in the field of rare diseases: state of the art and future directions – March 2008”.

The typology of European networks in the field of RD was explained: there exist both research networks (sharing data, repositories of biological samples and expertise for research purposes) and public health networks (sharing clinical experience to manage difficult cases, producing clinical guidelines and information and documenting the natural history of diseases). Examples of the networks funded by DG Research and DG Sanco were given.

The recommendations so far for ERNs were commented upon: the HLG set the same set of criteria as for centres of expertise. The RDTF recommended that DG Sanco continue funding current pilot networks until an evaluation is carried out, that DG Sanco fund a project to define a methodology to assess the benefit of such networks, that tools to develop telemedicine and teleexpertise be developed and that a multi-stakeholder consensus on the real added-value of ERN based on documented experiences be drawn up.

The preliminary analysis of the outcomes and experiences of the DG Sanco funded pilot ERNs showed: that ERNs’ activities extremely heterogenous, that there are different types of networks for different needs, that there are many networks with similar activities funded by DG Research, that geographical coverage is heterogenous (not all EU MS covered), that all networks face the challenge of durability of funding/sustainability, that ERNs strategies are globally in line with the recommendations of RDTF/EUCERD that expertise (or experts) should travel, rather than patients, and that there has been no analysis to date of the experience and outcomes of ERN.

An overview of the concepts in place was given. Networking is firstly and foremostly about collaboration and sharing, both of expertise and tools. Examples of the sharing of

expertise are: case management/ teleexpertise, the production of standards of care/information packages/ training/ education, and multidisciplinary research. Examples of sharing tools are: the use of ICT tools for sharing expertise, the use of ICT tools for disseminating information, and databases/ cohorts/ biobanks.

Some concepts have been modified since the last report:

- There is a clear distinction between the missions of centres of expertise and of European Reference Networks
- ERNs are not supra-centres
- Expert care and clinical research go together: both activities should be included in the same network
- ERNs contributes to derisking R&D
- Establishment of ERNs requires long term effort : it is a process
- It is a waste of money to establish ERNs if renewal of funding is not feasible

However some points are left to clarify:

- What are the prioritisation criteria?:
 - European added-value
 - Complex clinical management
 - Innovative clinical research
 - Costly management
 - Possibility to improve health outcome
- How should the networks be built?:
 - Should designated centres of expertise only be allowed to join?
 - What is the expansion process?
- What is the designation and evaluation process?:
 - Which body should be in charge of this?
 - What indicators should be put in place?
- Sustainability:
 - What type of funding mechanism?
 - Which funding body?
- Cross-border healthcare:
 - What are the implications of the directive?

Discussion following the presentation focused on the fact that the 'pilot networks' are all different and their experiences should be examined without paying too much attention to this label. Participants highlighted the fact that sustainability is a key issue when establishing ERNs, and whilst some networks will still have a purpose if they are discontinued, others will be useless without continued support and financing.

It was highlighted that in 2012 they are plans to finance more networks, but without a real evaluation of the networks funded up till now, this initiative is premature.

Participants agreed that a consensus on criteria for ERN (concerning their missions) should be reached before more networks are funded, therefore before the next call. It was also agreed that a new mechanism should be devised to ensure the sustainability of these networks, to avoid projects trying to source funding from either DG Sanco or DG Research alternately in order to sustain their activities (in DG Sanco projects the problem of finding co-funding was also raised). The most important aspect is to determine how to fund the infrastructure of the networks as no such instrument currently exists. Member States also have a role to play in ensuring the sustainability of such networks, as although the EC currently funds the setting up of networks, MS are expected to ensure the sustainability: the suitability of a Joint Action instrument was thus discussed, as was the interest of evaluating the current commitment and participation of MS in the existing networks.

It was agreed that the infrastructures needed at EU level should be considered (e.g. biobanking) and the resources that can be shared should be identified. This discussion is maturing at MS level as it is becoming a trend in countries with a national plan to establish national centres with mutualised tools (i.e. for data analysis and collection) for rare diseases.

2. Application of the concepts in the Care-NMD pilot ERN (*Janbernd Kirschner*)

Janbernd Kirschner gave a presentation of a recent pilot ERN funded by DG Sanco from May 2010 for a duration of 3 years. The project uses the existing framework of the Treat-NMD Network of Excellence (financed by DG Research in the 6th Framework Programme), mainly registries, in order to bring together leading care centres in a reference network for the care of patients with Duchenne Muscular Dystrophy, to evaluate current treatment practices across Europe, to implement newly agreed international consensus care recommendations, and to evaluate the impact of care on patients' quality of life.

Currently, guidelines exist but patients do not receive the recommended care and treatment due to lack of training, inability to access centres of expertise, and lack of resources for treatment. The Care-NMD project uses and extends the existing Treat-NMD database of Care and Trial Sites for Neuromuscular Disorders. The project will also define criteria for centres of expertise and care centres for DMD based on EU recommendations and disease specific treatment guidelines. Care-NMD also aims to assess the infrastructure and quality of care through questionnaires sent to care sites in participating countries, as well as using patient registries to address questionnaires for DMD patients to evaluate the care received and the quality of life.

Janbernd Kirschner then introduced the Treat-NMD Care and Trial Site Registry, an internet based database for self registration of centres originally developed for clinical trials which has now been extended for care aspects. The database contains information on patient cohorts, access to diagnostic techniques, personal and previous experience

with clinical trials and local infrastructure. A questionnaire concerning criteria for centres of expertise and care centres will be added.

As the centres are linked to a registry it is possible for quality of care indicators (both outcome and process indicators) to be built with available data: it was highlighted that it will be hard to show a change in indicators and the impact of the project after only 3 years (the duration of the project).

The challenges faced by the ERN were then outlined: for example, in some countries, there are existing networks of centres of expertise which perhaps have different criteria; care sites will self-report as there are insufficient resources for on-site monitoring; there is a selection bias of registries towards active patients seen at care centres and receiving better care; and finally there is no funding in the project for patient care or a care infrastructure.

Despite these challenges, it is hoped that the Care-NMD project will allow for care to be evaluated and improved for DMD patients and their families, and that the instruments developed can be used for other rare diseases (i.e. the Care and Trial Site Registry).

Discussion included the possibility of linking to the Orphanet database so as to not build a new database for the Care-NMD project. It was highlighted during discussions that this is a pilot project, which due to limited funding does not cover all of Europe, and which in the future could be used as a model for other neuromuscular diseases. The role of patient organisations in the sponsoring of translations was also highlighted.

Evaluation and selection of centres was discussed at length: it was explained that a national approach has been taken and partners have been asked to evaluate what services the sites offer and what can be put into place. Due to this, the partners are monitored, so that there is no conflict of interest in the selection of centres. Centres are selected foremostly because they see patients. Also discussed was the question of quality of care indicators: it was explained that location registries (due to lack of adequate coding for neuromuscular disorders in population registries) are the only sources for building indicators: in order to improve the registries' coverage the project aims to actively recruit patients to the registries. It was commented that if the project is not funded after the initial 3 years, it will be difficult to say that care has been improved as this is too short a period of time

3. Application of the concepts in the EPNET pilot ERN (*Jean-Charles Deybach*)

The experience of the EPNET (European Porphyrin Network) pilot ERN which was funded by DG Sanco from 1 April 2007 to 31 May 2010 was presented. The main objectives were: to draw up consensus-agreed information about all porphyrias and translate them into patients' languages, to standardise the evidence about drug use, to monitor the performance of specialist diagnostic services by external QA, and to collect epidemiological data for public health authorities (MS and EU levels).

The workpackages of the project were elaborated upon. Patient information on acute porphyria was reviewed and updated and patient information leaflets were produced for 3 conditions, which were translated into 10 languages and posted on the website. The drug safety workpackage was then described: this work has resulted in the evaluation of 5093 reports and the reclassification of 37 drugs and the classification of 49 new drugs. In addition, the review of diagnostic services was explained: this process has helped define minimum quality standards for specialised porphyria diagnostic and clinical advisory services and has helped establish external quality assessment schemes (for samples and clinical history). Finally, epidemiological data on acute attacks was collected and analysed for public health authorities (at MS and EU levels).

To continue the work started during the pilot phase, using a one year operating grant EPNET aims to extend the network to additional EU countries, to improve the diagnostic and analytical quality of specialist centres, to extend registry data collection to prevalence data and additional clinical detail on acute porphyrias, and to simplify the reporting procedure for the drug database.

The presentation concluded by highlighting the importance of collaboration and cooperation in networking as well as the need to avoid duplicating efforts as well as the importance of interaction with patient groups.

The ensuing discussion touched on the difficulty of identifying suitable partners due to the heterogeneity of national approaches to centres of expertise and their identification. When centres are not identified/designated, potential partners can be identified by reputation and publications. The involvement of patient organizations in ERNs was also discussed: it was highlighted that patient organisations cannot apply for co-funding in such projects and yet their role is sometimes important in the creation and dynamic of networks.

4. Application of the concepts in the TAG pilot ERN (*Louis Dubertret*)

Louis Dubertret presented an overview of the Together Against Genodermatoses pilot ERN. The general context was explained and the interest of networking between European centres of expertise for genodermatoses and countries in the South (i.e. Mediterranean countries) was exposed.

The background to the pilot phase financed by DG Sanco was given: 6 years before obtaining EC financing for a pilot ERN, the “Genodermatoses in the Mediterranean” project had initiated collaborations between the North and the South by: identifying dermatologists to develop a specific strategy for health care and social support of patients with severe genodermatoses, organising yearly meetings, encouraging the development of thematic outpatients’ clinics, and by involving some EU countries in order to share expertise and to network.

The TAG pilot project aims to build on this background by implicating more European and southern countries in the network so as to: better know the needs of patients, define best prevention strategies, develop solutions to improve access to drugs and medical devices, promote training of care givers, organise meetings of stakeholders, raise public awareness and to network specialists, paramedics, associations of patients. The TAG project's strategy is to structure working groups focused on patients' needs, to organise yearly working sessions, to organise training sessions and to build links with different stakeholders as well as supporting the activities of patients' associations and help the development of genodermatoses' networks in the countries joining the network.

Concerning centres of expertise, Louis Dubertret explained the concept of expert centres and competence centres. An expert centre in this case is devoted to a specific group of genodermatoses, associates clinical and biological research activities and training facilities, networks with competence centres and is a competence centre for other genodermatoses. Competence centres are open to all genodermatoses and have an outpatient clinic for genodermatoses patients; they also network with different centres of expertise for different groups of genodermatoses. These centres also follow regular training sessions.

The project aims to provide a directory of these centres with details of the services they offer as well as identifying the resources they need/lack. The procedure used to identify and evaluate a centre as either an expertise or competence centre was explained (this process relies on the reputation of centres, the experience of patient associations and the information provided by learned societies and Orphanet). It is overall a multistep process where centres declare themselves and these centres are verified. Competence centres are identified by their links with expertise centres and patient associations.

The TAG network is already fostering collaborations which render access to high quality skin care easier. The project leader hopes to launch a second phase of the project which will be focused on patient care including training, skin care evaluation, and clinical and genetic research.

At the end of the presentation, it was highlighted that the creation and organization of a network is a fulltime job for a non-medical expert in networking and should be paid for by the EU.

The discussion after the presentation revolved around the concept of centres of expertise and centres of competence and the relevance of this organisation for other networks and rare diseases.

General conclusions

To address the question of prioritisation, it was suggested that the calls for these ERN pilot projects be advertised more largely, and that a higher priority be given to diseases with complex clinical management and innovative clinical research, as there are a limited number of funding opportunities for networks.

Antoni Montserrat explained that in the work plan for 2008-2013 there is a category covering projects on information on RD and in 2012-2013: in this context, it was suggested that prioritization should be considered and it should be decided whether existing networks should receive continued funding, or to fund new networks. This matter will be decided by external experts. A new health programme will come into action in 2013 and the EUCERD should play an important role in proposing priorities in the field of RD.

The general discussion also revolved around the funding mechanisms that could be proposed for ERNs: for example 5 year projects (such as in FP7) or a new instrument entirely which could be a body/foundation/platform which receives EC funds to maintain networks and registries in the long run. Another option is the Joint Action, but this implicates the commitment of member states. The ERA-NET mechanism could also be explored as a possibility.

We currently observe a stepwise approach of self declaration, followed by acceptance by the network. Although the prioritisation criteria and the validity of this idea have been discussed, this issue needs to be worked on further by the working group. The networks currently in place concentrate on training, producing information and guidelines as well as sharing resources such as registries and tools for teleexpertise. Networks should also consider the use of outcome and process indicators.

It was highlighted that none of the pilot ERNs funded by DG Sanco are networks of expertise as defined by the previous criteria: they share data and expertise, but this takes place between experts, and not between centres. The work they have carried out/carry out is of great benefit to the RD community, but they do not equate with the concept of an ERN as defined by the HLG and RDTF. The main outcomes of these pilot ERNs are databases and guidelines. If the commitment of MS is to be sought, there is a real need to discuss the resources and infrastructures that can be shared instead of discussing networks of centres of expertise as it is too early to do so as many countries have no designation process in place.

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