NEPHIRD

NEtwork of **P**ublic **H**ealth **I**nstitutions on **R**are **D**iseases

Project of the DG Sanco Rare Diseases Programme

FINAL ACTIVITY REPORT

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SUMMARY

NEPHIRD (Network of Public Health Institutions on Rare Diseases) is a project supported by the European Commission for a 4-year period (starting November 2002). Fifteen European and EU associated countries participated in the project: Armenia, Belgium, Croatia, Denmark, Finland, France, Germany, Italy, Lithuania, Malta, Netherlands, Portugal, Spain, Sweden and UK. Moreover, EUROCAT give an important contribution to NEPHIRD activities.
NEPHIRD aimed at discussing and analysing the epidemiological data collection for rare diseases (RDs) in participating countries in order to identify and suggest possible approaches for estimating epidemiological indices (incidence and prevalence). It aimed also at analysing the state of the art with regard to RDs focusing on health care services accessibility and quality for RDs patients and undertaking a specific assessment of the quality of life of RDs patients.

To achieve these objectives, the following research activities were undertaken:

- Assessment of the situation of RDs in participating countries including information on the surveillance system for RDs and the data sources available for the epidemiological data collection of RDs
- Estimation of epidemiological indices
- Evaluation of the quality of and accessibility to health and social care for patients (and families) with RDs
- Assessment of the quality of life of patients (and families) with RDs
- Approach in assessing health indicators on RDs

1. Assessment of the situation of RDs

The assessment on RDs showed that the posture on RDs at the European level is very heterogenous:

- Different policy attitudes with regards to RDs
- Few countries have publicly funded structures dedicated to RDs
- Few countries have national plans
- Few countries have a system to collect data on RDs

In this context it will be important to advocate for keeping RDs a priority in the political agenda by promoting a comprehensive approach for addressing RDs.
Strengthening the collaboration among EU countries is another key action to promote. In addition to the collaboration at the European level, the development of national plans at the country level will be essential to ensure the comprehensive approach for addressing RDs.
The development of a surveillance system for RDs remains a priority action to promote and support. Major obstacles to overcome follow: lack of awareness of the Ministries of Health (MOH) on the importance of accurate diagnosis, continuous surveillance, treatment and data collection on RDs; lack of funds; lack of networks and referral systems for the diagnosis and treatment of RDs.

2. Estimation of epidemiological indices

Focusing on 2 diseases (Myasthenia Gravis and Cornelia de Lange syndrome), two different approaches (a review of relevant scientific literature and a population-based register) were used to estimate the prevalence of these rare conditions. Accordingly to our analysis, a review of the literature is useful when dealing with diseases for which a data collection system is not yet in place. Taking into account the limitations, due to the different characteristics of the studies available and

therefore used on the analysis, it is a rapid way to have an idea of the prevalence of a specific condition but it provides a crude estimation of the prevalence thus data have to be carefully interpreted. The prevalence based on registers is more reliable. It is a common understanding that registers are the ideal sources of data that give valid and reliable epidemiological information. Only a "population-based register" could ensure a comprehensive view of RDs however, running a register is a cumbersome and costly activity that is not always effective and efficient.
EUROCAT is a large European network of birth defects registers with multiple sources of active case ascertainment; thus, following the EUROCAT example, it seems possible and therefore urgent to promote and support the development of a European network of registers for collecting epidemiological data on RDs. This would ensure the availability of reliable and comprehensive information on RDs.

3. Evaluation of the quality of and accessibility to health and social care for patients (and families) with RDs

To assess accessibility to and quality of health care and social services a pilot survey involving patients' Associations was carried out in several EU Countries in patients with Myasthenia Gravis, Neurofibromatosis type 1, Prader Willi Syndrome and Rett Syndrome. The pilot study was undertaken in the following NEPHIRD countries: Italy, Spain, France, UK, Romania and Turkey. The assessment encompassing clinical, rehabilitative, social and legal dimensions identified and confirmed the multidimensional needs of RDs patients.
The overall rate of negative and positive experiences were relatively similar for the four diseases, suggesting that rare conditions have major common problems: 1) poor social services (educational and work); 2) lack of health information and 3) inadequate provision of legal support. The study confirmed the two-fold advantage of carrying out surveys engaging patients and/or their families: 1) it helps healthcare providers to improve the quality of and accessibility to their services and 2) it empowers patients.

4. Assessment of the quality of life of patients with RDs

To assess the health-related quality of life (HRQoL) Myasthenia Gravis, Neurofibromatosis type 1 and Prader Willi syndrome were selected as case-study. The study protocol was a multiperspective protocol including clinical assessment and patient-oriented measures of Quality of life (QoL). The objective was to link clinical evaluation with HRQoL measurements in order to identify the clinical aspects that mainly impair QoL. To assess the QoL the most validated generic (SF-36, CHQ-PF50) and specific QoL questionnaires (MGQ and Skindex) were administered.
The studies confirmed the heavy impact that RDs have on both mental and physical aspects of patients' life. Physical and mental aspects of QoL were impaired in all the diseases studied.
In addition, our data demonstrated also that clinical variables are related to the HRQoL.

5. Approach in assessing health indicators on RDs

NEPHIRD contributed to the assessment of health indicators on RDs and provided recommendations on the identification of indicators for RDs. Discussing different indicators it seems important to:

- work on mortality data derived from death certificate and morbidity data derived from hospital discharge. These specific indicators are available in all countries of the EU although, comparability between countries is a major issue;
- continue the discussion to identify a list of health indicators for RDs including indicators to assess social support for RDs patients and policy actions undertaken with regards to RDs,
- engage patients when defining specific indicators on the quality and accessibility of care.

Conclusions

The results of NEPHIRD activities highlighted major challenges in defining RDs prevalence and in identifying RDs indicators. The project described also major problems related to the provision of care for patients with RDs including: poor quality of care, lack of information on RDs, limited access to and quality of social care. Finally it confirmed the heavy impact of RDs on QoL of patients with RDs.

Based on the experience derived from NEPHIRD activities, we suggest to give priority attention to the following:

- Improving the collection and the exchange of epidemiological data at national and at the European level
- Promote patient involvement and empowerment
- Promote a multidisciplinary/multi-faceted approach in order to tackle RDs
- Develop information for patients and health professionals concerning RDs
- Support research on RDs.

OBJECTIVES OF THE PROJECT

NEPHIRD aimed at analysing and discussing possible approaches for collecting epidemiological data (prevalence, incidence and mortality) for RDs and at identifying unmet needs and challenges for patients with RDs.

Focusing on selected RDs, the **specific objectives** follow:

1. to undertake an assessment of the state of the art of RDs at the European level;
2. to estimate epidemiological indices (incidence and prevalence);
3. to assess the access to and quality of health and social care services for selected RDs;
4. to assess the quality of life of patients affected by the selected RDs;
5. to identify public health indicators for RDs.

The RDs identified follow:

- Prader-Willi syndrome
- Neurofibromatosis type-I
- Rett syndrome
- Myasthenia Gravis
- Cornelia de Lange syndrome
- Limb Reduction Defects

The selection criteria used to identify the diseases follow:

- the representation of a group of RDs with major physical involvement (Myasthenia Gravis, Limb reduction defects), mental impairment (Rett Syndrome), physical-mental impairment (Prader Willi syndrome), or the impairment of different apparatus and/or organs (Neurofibromatosis, Cornelia de Lange syndrome).
- age group (paediatric or adult).

ACTIVITIES

In this session we describe all the activities undertaken in the frame of the project. In collaboration with NEPHIRD partners, a website (http://www.iss.it/cnmr/neph/index.php?lang=2) dedicated to the project, was developed, implemented and it is still active. The website was used to provide information about the ongoing activities and meetings of the project, to share tools and results.

1. ASSESSMENT OF THE SITUATION OF RDs IN THE PARTICIPATING COUNTRIES

In 2001, in the framework of the project "NEPHIRD 1 – feasibility phase" a questionnaire was sent to all NEPHIRD partners to collect information about RDs within their countries.
Following the 2001 experience, in 2005 the NEPHIRD project, in collaboration with the Rare Diseases Task Force (RDTF), decided to undertake another assessment of the state of the art of RDs to update the information considering the increased efforts of EU Member States with regard to RDs.

In this report, we describe the results of both assessments: the one performed in 2001 and the more recent one of 2005 in order to facilitate the comparison of results and to obtain a comprehensive overview of how the situation has changed between 2001 and 2005.

Assessment of the situation of RDs - 2001

In 2001, a questionnaire was sent to all NEPHIRD partners.
The questionnaire aimed at collecting the following information:

- policy and major public health measures taken by the Government of each Country adhering to the project (articulated in terms of legislative actions, creation of an organ or a unit that deals specifically with RDs, and efforts made to (re)organise health institutions to deliver services to patients affected by RDs);
- existing surveillance or data collection systems for RDs;
- availability of centres able to diagnose the selected diseases and
- availability of a systematic data collection process within the centre.

The summary of the results of 2001 assessment follow:

- Legal basis (Denmark, Italy, Luxembourg, Netherlands)
- National public health units (Denmark, Italy)
- Network of service delivery institutes (Denmark, Italy, Luxembourg)
- Data collection with registers, including birth defects registers (Croatia, Italy, Lithuania)
- Current major public health initiatives (Croatia, Italy, Denmark)

Assessment on the situation of RDs - 2005

In 2005, in collaboration with the Rare Diseases Task Force, a new questionnaire was sent to NEPHIRD partners. The new questionnaire explored additional topics regarding RDs at the European level as follows:

- Availability of National Plans and/or National Centres for RDs treatment;
- Availability of National Networks for data collection;

- Availability of National Registers on RDs.

Accordingly to the assessment, the situation is non homogeneous: many Countries have public funded structures for RDs however, MS have different policy attitudes for RDs; epidemiological data at EU level are scarce; there is poor collaboration among MS in the research field and limited attention is given to the role of patients organisations.

The summary of the situation in several MS follow:

- National plans (France);
- National centres (Denmark, Italy, France, Spain);
- National network /registers (France, Germany, Italy, Spain);
- Public funded structures (Belgium, Denmark, Estonia, France, Germany, Italy, Netherlands, Spain, Sweden and United Kingdom);
- Steering Committee on RDs (France, Italy);
- Steering committee on Orphan Drugs (Denmark, France, Italy, Netherlands);
- Databases on RDs (Estonia, France, Italy, Netherlands, Spain);
- Databases on RDs on Orphan Drugs (Denmark, France, Italy, Netherlands, Spain);
- Research: specific schemes (Belgium, France, Germany, Italy, Netherlands);
- Public support to patients' organisations (Denmark, Estonia, France, Italy, Netherlands, Spain, Sweden);

The details per Country are available on the NEPHIRD website

http://www.iss.it/cnmr/neph/atti/cont.php?id=142&lang=2&tipo=19

In conclusion, it seems that the posture on RDs at the European level is still very heterogeneous thus immediate actions are required:

- Advocate for keeping RDs a priority in the political agenda;
- Promote a comprehensive approach for addressing RDs;
- Strengthen collaboration among EU countries;
- Promote and support the development of national plans at country level;
- Promote and support the establishment of surveillance systems for RDs.

The "Rare Diseases Task Force" (RDTF) represents the most appropriate forum to promote such actions, support and ensure a co-ordinated and comprehensive strategy for RDs at EU level.
The RDTF was set up in January 2004 by the European Commission's Public Health Directorate to assist the European Commission Public Health Directorate in addressing RDs and to promote the optimal prevention, treatment and diagnosis of RDs through collaboration among European countries. The RDTF currently has 37 members including leaders of current or former European research projects relevant to RDs, member state experts, and representatives of other relevant European programmes or organisations. The NEPHIRD co-ordinator has been a member of the RDTF since 2004 and will continue to actively contribute to the RDTF activities.

2. Estimation of epidemiological indices (i.e. incidence, prevalence) at the European level

The NEPHIRD project provided two important contributions for the estimation of epidemiological indices at the European level:

- focusing on 2 selected diseases, analysed and identified pros and cons of two different methods for estimating prevalence and incidence of RDs
- developed recommendations for establishing network for data collection among EU countries.

The following paragraphs present the above-mentioned contributions.

Evaluation of epidemiological indices

In order to estimate prevalence and incidence of RDs, two possible methods/data source were considered: literature review and register-based data collection and analysis.
The literature review was undertaken to estimate prevalence and incidence of the Myasthenia Gravis (MG), the register data were used to estimate prevalence and incidence of the Cornelia de Lange syndrome (CdLS).

Epidemiology of Myasthenia Gravis

A review of the relevant scientific literature was undertaken to serve as an example of how to estimate the prevalence of RDs that don't have a routine epidemiological data collection system. Searches were conducted in several data sources: Pubmed, Geneclinics, OMIM, Orphanet and e-medicine, selecting all articles with the objectives of estimating epidemiological indices of prevalence and/or incidence during the last twenty years only in european countries. The information collected and summarised for each of the studies follow:

- Design of the study (case reports, cross-sectional surveys);
- Target (total population; specific group population; unknown);
- Availability of case definition;
- Date of diagnosis;
- Date of manifestation of first symptoms;
- Prevalence and incidence estimate;
- Data source (medical record; special survey; multiple source).

Thirteen available studies on the epidemiology of MG during the last twenty years in the European countries were found and a summary of the results follow:

- The overall prevalence was 1.2/10,000.
- The point prevalence rate ranged from 0.7 (Greece) to 1.5 (England) per 10,000.
- The highest prevalence was in England and Sweden.
- The annual incidence was reported to range from 0.04 (Norway) to 0.21 (Italy) per 10,000.
- Age-standardized rate to European population were reported only in Norway and Denmark.

The report of this study is available on the NEPHIRD website

http://www.iss.it/cnmr/neph/atti/cont.php?id=147&lang=2&tipo=19

The review of epidemiology of MG suggests that it's difficult to have a reliable estimation of prevalence (or incidence) at the European level, however a literature review can provide rapid, cheap and crude values.
Two useful tools for conducting a systematic review were developed:

- Steps in conducting a systematic review on how to assess the prevalence in Europe of each RDs and
- Data extraction form on how to collect the data of each scientific article.

The tools are available on the NEPHIRD website

http://www.iss.it/cnmr/neph/atti/cont.php?id=147&lang=2&tipo=19

Epidemiology of Cornelia de Lange Syndrome

The data provided by Registers were used to serve as an example of how to estimate the prevalence from routine data collection system.
This study has been performed through a formal collaboration between NEPHIRD and EUROCAT, a large European network of birth defects registers with multiple sources. This collaboration has made it possible to conduct a population-based study of the epidemiologic and clinical aspects of the classical form of CdLS. The data were provided by 33 registers from 16 European countries that register congenital malformations in live births, stillbirths and terminations of pregnancy covering approximately 25% of annual births in the countries included in the EUROCAT network.
In particular, this study was elaborated by the EUROCAT Working Group: Barisic, V. Tokic, M. Loane, F. Bianchi, E. Calzolari, E. Garne, D. Wellesley, H. Dolk.

Based on the 20-year epidemiologic monitoring of birth defects in Europe it was found that:

- the prevalence of classical CdLS is 1.23/ 100,000 births;
- the overall prevalence for classical and mild cases is estimated to be 1.6 – 2.2 /100,000 births;
- the most frequent major congenital malformations associated with CdLS are limb defects (73.1%), congenital heart defects (45.6%), central nervous system malformations (40.2%) and cleft palate (21.7%);
- prenatal diagnosis by ultrasound examination accounts for almost a quarter of diagnosed cases;
- infants with CdLS have a high first week survival rate;
- in the majority of cases the karyotype is normal. Identified abnormal karyotypes may be responsible for the Cornelia de Lange syndrome by disruption of the gene/genes responsible for the CdLS phenotype;
- maternal age and paternal age do not seem to be a risk factors for CdLS;
- almost 80% of cases, born after the 37^{th} week of gestation, weighed less than 2,500 g; low birth weight correlates with a more severe phenotype, including severe limb anomalies.

The report of this study is available on the NEPHIRD website

http://www.iss.it/cnmr/neph/atti/cont.php?id=147&lang=2&tipo=19

The prevalence based on registers is more reliable. It is a common understanding that registers are the ideal sources of data that give valid and reliable epidemiological information.
However, running a register is a cumbersome and costly activity that is not always effective and efficient. It is also technically difficult to ensure its quality. EUROCAT is a good example of a network of registers: EUROCAT network surveys more than 1 million births per year in 19 countries, providing essential epidemiological information on congenital anomalies. Such registers are quite uniformly distributed throughout Europe, they are good sources of reliable information for several RDs, fulfilling almost all needs, from serving as a tool for surveillance to providing epidemiological estimates.

Accordingly to NEPHIRD studies, immediate actions are needed to promote, support and implement registers for RDs. It is essential to develop registers able to collect information on different groups of RDs and not only one.
The model of EUROCAT, could be used to establish a network for collecting epidemiological data on RDs among different countries. This would ensure the availability of reliable and comprehensive information on RDs.

Recommendations for establishing a network for data collection among EU countries

NEPHIRD experts held different meetings to discuss and agree on the most important issues to consider for establishing a network for data collection among EU countries. Experts discussed and addressed the following major issues: disease selection, type of information to be collected, identification of centre for data collection, data management, data quality and coding system.

Disease selection

For the purpose of data collection, diseases could be selected on the basis of several factors such as:

- possibility for preventive action;
- presence of national or regional databases;
- interest of specific stakeholder such as scientists;
- technical feasibility e.g. presence of clear case definition;
- presence of other factors, e.g. on-going clinical or therapeutic research;
- availability of patient's associations;
- political visibility;
- representative of other groups of pathologies (metabolic disorders, congenital malformations, rare tumours, neurological disorders, auto-immune diseases, etc.)

Type of information to be collected

The type of information to be collected depends on the objectives desired. Estimates of frequency of occurrence and surveillance may need relatively limited information, however the quality of this information (completeness and reliability) will be fundamental in establishing a surveillance system thus great expertise will be needed to ensure it.
In principle, the minimum data-set to be collected for all diseases should include the following information:

Patient related

- Identification code
- Date of birth
- Age
- Sex
- Place of birth
- Locality of residence
- Educational level
- Occupation
- Personal data of parents: education and occupation

Institution related

- The diagnosing/treating centre: name, address
- Date of compilation
- Institution that sends data (name and address)

Disease related

- Name of the disease
- Date of onset
- Date of diagnosis

- Modality of diagnosis
- Other possible features: severity

Information on the course of illness
- Treatment given
- Patient outcome (dead, alive…)

Information on possible risk/protective factors
- Environmental exposure: residence, work place
- Lifestyle and behaviour: alcohol, smoking, drugs, etc.
- Familiarity

Additional variables can be included according to specific problems related to the condition.

In addition to the identification of the variable, a standardised data collection processes is essential for collecting reliable and homogeneous data.
A standardised data collection process should include: computerized data collection system; standard definition of the variable to collect, data management security. In addition, the elaboration of technical standards and their implementation improve the quality of information collected.

Data management and mechanisms to ensure quality

It is important to introduce mechanisms which could contribute to guarantee the quality of the data collected. This can be done through both a managerial and a statistical approach.
The elements to ensure the quality of data collection process include:
- the presence of clearly established objectives for data collection;
- the availability of a standardised case definition;
- the ability of each centre to make appropriate diagnosis of the diseases of interest;
- the correlation of the objectives with the data set,
- the identification of a team responsible for data management. The team should minimise the errors at all stages of the programme by:
    - supervising the data entry, data collection, data validation;
    - organising the flow of data;
    - ensuring data quality and security (backups, confidentially), including paper forms;
    - installing and maintaining the hardware and software;
    - producing summary of the data.

Experts suggest that data must be: Timely; Accurate; Complete; Oriented; Measurable and Applicable. The acronym TACOMA is well known and used to recall these characteristic (Guidelines for conducting Birth Defects Surveillance, 2004).

The Coding system

An important aspect for data collection is the Coding Process.
Codes for RDs are necessary for case storage and retrieval. Problems with coding have a major impact on RDs. Only few inappropriately coded cases can greatly influence the epidemiological rate.
During the coding process (the translation of medical terminology into a code) the information is lost or distorted as the patient is viewed, described by the physician and abstracted and recoded by the programme.

The goal should be to minimize this distortion as much as possible, while realizing that a certain amount of distortion is inevitable. Although verbal descriptions are helpful, consistent terminology is often not used.
Codes need to be specific. Coding the diseases as specifically as possible is advantageous to prevent additional work at time of analysis. However, this goal for specificity needs to be balanced against producing a coding system that becomes cumbersome; codes that will be used only rarely are not beneficial.
An effort should be made to:

- minimize the number of diseases that will be coded under non-specific code categories, such as “other specified” diseases of a particular system.
- avoid code redundancy, since it can occur when several non specific codes are used to describe a specific code (ex. Tetralogy of Fallot). Redundant codes are inefficient and can lead to confusion. A redundant coding can result in counting an infant in multiple diseases categories.

The selection of a coding system is a critical decision for a surveillance programme.
A clinical modification of the ICD-9 (the ICD-9-CM), consists of five-digit system used in hospital discharge diagnosis. This system is still not sufficiently precise for many birth defects register uses. For example in ICD-9-CM 756.79 code for “other congenital anomalies of abdominal codes” includes both omphalocele and gastroschisis, defect that are etiologically and epidemiologically heterogeneous. In particular the coding of syndromes has presented some challenge.
A tenth revision of the clinical modification of ICD-10 (with alphanumeric codes) allows for additional expansion of the codes, without codes becoming unwieldy.
An important function of surveillance programme is to follow trends in rates and geographical distribution therefore, a coding system need to be relatively static and uniform. However advances in medical technology do necessitate changes in the coding system.
Because of the importance of coding, a process to evaluate coding quality should be included to a surveillance programme. The system of ICD-9 (ICD-9-CM) and ICD-10 are still not sufficiently precise for many RDs.
In fact, the RDTF is collaborating closely with WHO on the ICD-10 international classification of diseases, (considering all other existing classifications) in order to provide the RDs community with a unified system.

3. Evaluation of the quality of and accessibility to health and social care for patients with rare diseases

A pilot study was carried out to assess the quality of and accessibility to health and social care services. The study focused on 4 of the diseases studied by NEPHIRD: Myasthenia Gravis, Neurofibromatosis, Prader Willi syndrome and Rett Syndrome. These diseases were selected because of their major physical involvement (Myasthenia Gravis), mental impairment (Rett Syndrome), physical-mental impairment (Prader Willi syndrome) or because of the impairment of different systems and/or organs (Neurofibromatosis). The pilot study was undertaken in 4 Countries: Italy, Spain, France and UK. It is worth mentioning that because of the increasing interest on RDs and the better networking at the EU and not EU level, additional countries such as Romania and Turkey expressed their interest in being involved in the study and they were welcomed to participate.
For each of the 4 diseases, patients' associations were identified among the different countries as follows:

Prader Willi Syndrome

- La Federazione delle Associazioni Italiane per l'aiuto ai soggetti con sindrome Prader Willi (Federation of Italian Prader Willi Associations), Italy;
- Romanian Prader Willi Association, Romania.

Neurofibromatosis

- Associazione Neurofibromatosi (Neurofibromatosis Association), Italy;
- Francaise contre les Myopathies (France Myopathies Association), France;
- Associazione Linfa (Lymph Association), Italy.

Myasthenia Gravis

- A.I.M. Toscana Onlus and A.I.M. Veneto Onlus (Italian Myasthenia Gravis Association), Italy;
- Asociacion Espanola de Nerofibromatosis (Spanish Myasthenia Gravis Association), Spain.

Rett Syndrome Syndrome

- Association of Rett Syndrome families, Turkey;
- Associazione Italiana Rett Sindrome, (Italian Rett Syndrome Association) Italy.

A self-filled questionnaire was elaborated and validated by the health service research experts in collaboration with the clinical experts of the selected diseases.

The questionnaire is available on the NEPHIRD website

http://www.iss.it/cnmr/neph/atti/cont.php?id=148&lang=2&tipo=19

In total 302 questionnaires were filled in: 66 for Prader Willi Syndrome, 89 for Myasthenia Gravis, 99 for Neurofibromatosis, 48 for Rett Syndrome.

For Prader Willi and Rett syndromes, almost all questionnaires were filled in by caregivers due to patients' mental retardation.

The most negative experiences were reported on coordination of health services (58%), quality of information (44%) and social care (27%).
Eighteen percent of respondents reported a negative opinion on financial support and only 16% on the relational quality including lack of kindness and empathy of professionals.

More details follow:

- the most frequent negative opinions on health care were reported on quality of and accessibility to psychological support (31%);
- the most frequent negative opinions on social care are related to the quality of and accessibility to work (29%);

Other negative opinions were reported on the following:

- health information on the diseases provided by professional (41%);
- quality and quantity of information on laws and rights (48%) and
- quality of vocational training (44%).

The assessment encompassing clinical, rehabilitative, social, educational and legal dimensions identified and confirmed the multidimensional aspect of the needs of RDs patients.

Although the study presents some technical limitation due mainly to the small numbers of the samples, the results appear to be of great interest:

- The overall rate of negative and positive experiences are relatively similar for the four diseases, suggesting that rare conditions have major common problems: 1) social services (educational and work); 2) lack of health information and 3) inadequate provision of legal support.
- More social then medical problems were reported, however it could be due to the different availability of social and health care services within each country thus the results have to be carefully interpreted.
- This study clearly stresses the importance of considering the different needs of RDs patients, needs that go clearly beyond the clinical side of the disease.
- It also points out interesting differences between countries with a different socio-economic situation. Further studies should be conducted to better explore such differences.
- The study confirmed the two fold advantage of carrying out surveys engaging patients and/or their families: 1) it helps healthcare providers to improve the quality of and accessibility to their services and 2) it empowers patients.

The report of this study is available on the NEPHIRD website

http://www.iss.it/cnmr/neph/atti/cont.php?id=148&lang=2&tipo=19

This study has produced the two following peer-reviewed publications:

1. Kodra Y, Morosini PR, Petrigliano R, Agazio E, Salerno P, Taruscio D. Access and Quality of health and social care on rare diseases: patients' and caregivers' experiences. Ann Ig. 2007 Mar-Apr;19(2):153-60.

2. Kodra Y, Salerno P, Agazio E, Mirabella F, Taruscio D. Accessibility and quality of Italian health and social services: the experiences of patients with Neurofibromatosis type 1 and of their relatives. Ann Ig. 2007 Sett-Oct 19 (5) (in press).

4. ASSESSMENT OF THE QUALITY OF LIFE OF PATIENTS (AND FAMILIES) WITH RARE DISEASES

The Health Related Quality of Life (HRQoL) is a concept of Quality of Life (QoL) that relates specifically to a person's health and refers to the measure of the patients' functioning, well-being and general health perception in each of the three domains: physical, psychological and social.
Over the last two decades, clinical researchers emphasized the need for a thorough evaluation of patient's quality of life (QoL) in order to study the impact of chronic illnesses and their treatments on patient's life.

To assess the impact of a disease on the QoL, it is necessary to link conventional clinical variables with HRQoL measures.
HRQoL measure can be obtained through general and specific standardized tools. The need for standardized tools stimulated an extensive and rigorous process leading to the development of validated patient-oriented instruments.

The availability of such tools is very important to increase the understanding of RDs. Because RDs have an impact on the physical, emotional, psychological, cognitive and social aspects of the lives of patients, within the NEPHIRD framework it was agreed to undertake different QoL studies aimed at assessing the relationship between the severity of the diseases and the QoL of the patients.

Three diseases were selected because of their major physical-mental impairment (Prader Willi syndrome), physical involvement (Myasthenia Gravis) or because of the impairment of different systems and/or organs (Neurofibromatosis). The study protocol was a multiperspective protocol including clinical assessment and patient-oriented measures of QoL.
The most validated generic and specific QoL questionnaires were used:

- the Short Form-36 (SF-36);
- the Child Health Questionnaire-Parent Form 50 (CHQ-PF50);
- Myasthenia Gravis Questionnaire (MGQ);
- Skindex designed to assess the QoL in NF1.

SF36 and CHQ-PF50 questionnaires are available

on the NEPHIRD website

http://www.iss.it/cnmr/neph/atti/cont.php?id=149&lang=2&tipo=19

The studies confirmed the heavy impact that RDs have on both the mental and physical aspects of a patients' life. Physical and mental aspects of QoL were impaired in all the diseases studied.
For diseases with more disfigurement such as PWS (presence of characteristics facial features) and NF1 (presence of neurofibromas), mental aspects of quality of life were compromised. For MG, physical aspects of the quality of life was more impaired.
Our data demonstrated also that clinical variables are related to the HRQoL.
The studies support the idea of promoting QoL assessment to guide clinical decision and to identify specific patient needs to be considered in the everyday management of the disease.

In patients with NF1 the impact of the cosmetic features due to the presence of neurofibromas represent a major concerns for patients as reported in the QoL assessment (emotional aspect showed the greatest impact).
In Prader Willi patients body weight is the clinical finding which mainly and negatively influences the physical aspects of quality of life.

Promoting the assessment of QoL, it is important to discuss the different tools available. So far two different kinds of instruments exist: the generic and the specific.
The generic instruments evaluate QoL as a whole. They are applicable to a wide range of individuals of different cultures, different type and severity of diseases. These instruments are more appropriate to compare different diseases and interventions and to support decision-making process.
The specific tools are those developed for specific diseases. They focus on the phenomenon of interest, are more sensitive and more acceptable however they do not allow comparisons. Specific tools are less common and available, thus more specific instruments need to be developed and validated in order to further study RDs.

The report of the assessment of QoL for NF1, Prader Willi syndrome and Rett syndrome are available on the NEPHIRD website

http://www.iss.it/cnmr/neph/atti/cont.php?id=149&lang=2&tipo=19

This study has produced the two following peer-reviewed publications:

1. Yllka Kodra, Sandra Giustini, Luigina Divona, Roberto Porciello, Stefano Calvieri, Pierre Wolkenstein, Domenica Taruscio. Health related Quality of Life in patients with Neurofibromatosis type 1: A survey of 129 Italian patients. (submitted).

2. Pietro Caliandro, Graziano Grugni, Luca Padua, Yllka Kodra, Pietro Tonali, Luigi Gargantini, Letizia Ragusa, Antonino Crinò, Domenica Taruscio. Quality of life assessment in a sample of patients affected by Prader-Willi Syndrome. J Paediatr Child Health (in press).

5. APPROACH IN ASSESSING HEALTH INDICATORS ON RDs

Most of the actions supported by the Programme of Community Action in the Field of Public Health (2003-2008) have been related to the development of indicators.
In this context the NEPHIRD project has used its network of experts to provide recommendations on the identification of indicators for RDs.
Subsequently, when the Rare Diseases Task Force (RDTF) was established, the NEPHIRD coordinator was invited to join the RDTF; since then the NEPHIRD coordinator and NEPHIRD experts have been working with the RDTF working group.
In the following paragraphs we summarise the initial discussion and recommendations of NEPHIRD experts on indicators for RDs. They focused mainly on 2 categories:

- Health status;
- Health care system.

Health status indicators

Mortality

The source of information is death certificates; the reliability of mortality data depends on accuracy of the vital registration system in each country. Causes of death are coded according to the International Classification of Diseases and Causes of Death (ICD). Problems of temporal and geographic comparison derive from different versions of the ICD adopted over time. Specific indicators are:

- crude death rate: total number of deaths divided by estimated mid-year population per 100,000;
- cause-specific crude death rate: number of cause-specific deaths divided by estimated mid-year population per 100,000;
- age-standardized death rate: death rate estimated after age-standardization has been performed;
- age-specific death rate: total number of deaths divided by mid-year population per 100,000 for specific age groups.

Mortality data are routinely collected in all countries and are of fairly good quality. In order to use mortality data for studying RDs, particular attention should be paid to multiple cause-of-death data (including underlying and non-underlying causes) which can allow researchers to maximize the use of the diagnostic information on the death certificate and provide ways of looking at mortality data that go well beyond the typical examination of the underlying cause of death.
In addition, it will be important to consider how to link mortality data with other data sources (such as registers, hospital discharges), in order to evaluate the completeness of mortality data and how to combine them with the high quality of data coming from the other data sources.
Moreover, fatal diseases are more likely to be reported on the death certificate. Thus mortality data are more accurate for these diseases and attention should be paid in interpreting data related to non-fatal diseases.

Further discussion is available on the NEPHIRD website

http://www.iss.it/cnmr/neph/atti/cont.php?id=150&lang=2&tipo=19

Morbidity data

Morbidity rates are the number of cases of a disease within a given time in a defined population. Morbidity can be described using the following frequency measurements: incidence rate, prevalence.

The definitions of specific morbidity indicators follow:

- *incidence rate:* the number of first events divided by the population at risk per 10,000 or 100,000 person/years at risk. Person/years at risk consists of the sum of periods of time (years) at risk contributed by each of the person included in the study. Incidence may be estimated through the follow-up of a population enrolled in a cohort or the identification of new events in a dynamic population. It can be obtained using longitudinal studies or disease registers.

- *prevalence:* the proportion of persons with the disease in a population per 10,000 or 100,000 at a particular time. It is assessed by surveys, or by indirect methods on the basis of incidence and survival data. Prevalence is the most important indicator in the surveillance of elderly people since patients with chronic diseases have a greater impact on public health system; these data are useful for hospital and primary health care planning.

The importance of these measures differs according to the disease and the age group. In younger age groups the most important indicator is the incidence rate; in older people, prevalence are more important since patients with chronic diseases require more continuous therapy and rehabilitation, and have a greater impact on the public health system. For acute events, incidence rates are in general target measures, while for chronic conditions incidence as well as prevalence may be of interest. Incidence is used mostly for etiological research objectives; prevalence is useful for hospital and primary care planning.
Standardised rates are important to make cross-group comparisons and to investigate time trends, although absolute numbers are often necessary to evaluate the burden of the disease.

Generic health status

The most important indicator of generic health status is Quality of Life. This includes measures of perceived health and of health-related quality of life, often expressed in functional terms. Measurement instruments may address each of these health dimension separately. Examples of general ‘health-related quality of life’ instruments are the SF-36 and Euroqol-5D questionnaires.
The importance of QoL measurement in patients with RDs and issues of the different tools available for QoL assessment have already been discussed in section: “Assessment of QoL”, thus in here we can only reinforce our message of the importance of data collection on QoL.

Composite health status

These indicators are constructed as combinations of mortality data, on one hand, and data on morbidity or generic health status measures, on the other. We propose to consider disability as a composite measure of health status according to ECHI definitions. RDs are the leading cause of disabilities. The indicator of Disability is Disability-Adjusted Life Year-DALY: years lost due to premature mortality and years lived with disability. It is equal to the sum of the number of years lost due to RDs in a population (YLL) and to the number of years lived with disability of known

severity and duration for a RDs in a population (YLD). Routinely data collection and indicators on these indicators are still not available.

Health care system indicators

Possible indicators for health care systems are those related to the quality of the service provided. Because the quality of care is mainly assessed through the assessment of patient's and caregivers opinions, an *ad hoc* questionnaire needs to be developed.
Other important indicators with regard to the health care system are those of utilisation.
A few examples of utilisation indicators follow:

Hospital multi-stay rate:	is the observed average number of hospitalizations for patients with one or more hospital stays
Hospital's standardised multi-stay ratio:	is the ratio of the geometric mean of the observed number of hospitalizations per patient to the geometric mean of the expected number of hospitalizations per patient, conditional on the types of patients admitted to that hospital
Global readmission rate:	
Related adverse readmission:	readmissions that indicate potentially sub-optimal care during initial hospitalization, identified from administrative data using readmission diagnoses and intervening time periods designated by physician panels
Early readmission rate:	unscheduled readmission within 31 days after discharge

Data on these indicators should be based on hospital discharge.
Moreover, indicators should be identified and defined for the following areas: neonatal screening; access to care, health operator training; reference centres or reference networks; highly specialized technologies, transplantation, access to innovative drugs, therapeutic trial participation, insurance coverage for costly drugs, expenditures for specific diseases, equity of access, genetic laboratories, prenatal diagnosis, public health surveillance programs, public policies for rare diseases, clinical research support and fundamental research.

The following challenges have to be considered in selecting indicators on health care system:

- the long process for field testing the indicators. It is a time consuming exercise, however it is essential to ensure validity and reliability (Table 5.1).

Table 5.1 Development and field testing of indicators

Stage	Notes
1	a literature review together with interviews with college fellows in clinical practice to collect views and suggestions for appropriate indicators
2	formation of an expert working party (delphi group) to consider the literature and interview report (field review report) and to draft prospective indicators
3	field testing in hospitals with an emphasis on whether the relevant data can be extracted easily
4	further review by the college working party with indicator adjustments made where necessary
5	pilot studies in hospitals with an emphasis on whether the indicator is useful in a quality assurance program
6	final approval of the indicators by the college
7	introduction of the indicator in accreditation assessments

The differences existing among EU MS in terms of health system. The responsibility for patient care implies collaboration between different health care providers and also with non-health care providers. The health care systems and the interface with the social network of support differ among the EU Member States and this influence the selection of indicators. In addition, there are some differences also in clinical practice between different countries and these also have an impact on the relevance of particular health care indicators.
Defining health care system indicators, it is important to find a balance between the need of a large number of indicators that allow a comprehensive assessment of the different dimensions of quality of health care services and the feasibility/practicability of collecting all the indicators. Greater effort is needed to collect, analyse and interpret many indicators. In addition, the interpretation of many indicators may be difficult and challenging for the organisations trying to improve the quality of their services.

Indicators may be inappropriate for assessing health care if:

- they represent low frequency events;
- there are no available/accessible data to measure them;
- they represent subjective issues;
- they require a complex risk adjustment.

General Conclusions

In the previous chapters of this report we described the results of the NEPHIRD activities highlighting major challenges in defining RDs prevalence and in identifying RDs indicators. We have also described major problems related to the provision of care for patients with RDs: limited access to and quality of social and health care, lack of information on RDs, etc.
Finally we confirmed the heavy impact of RDs on QoL of patients with RDs.
Results of the project activities have been presented during a 4-day-conference organised by the Italian National Institute of Public Health (Istituto Superiore di Sanità, Rome) in order to discuss with experts and stakeholders strategies and actions required to address RDs. The meeting was also an opportunity to increase awareness on RDs and to advocate for immediate actions to tackle RDs.

The results of the conference are available on the NEPHIRD website

http://www.iss.it/cnmr/neph/rice/cont.php?id=135&lang=2&tipo=20

Accordingly to our findings, we think that attention should be given to the following:

Strengthen the exchange of epidemiological data

More cooperation is required among EU MS for addressing epidemiological gaps.
The collaboration of EU countries should aim at implementing European networks for epidemiological data collection.
Many European registers for single, specific RDs exist. It is urgent to develop networks to collect data on groups of RDs at European level.
Moreover, cooperation with ORPHANET should be strengthened for estimating prevalence and incidence of RDs in Europe on the basis of available data sources.

Recommendations

- Development of networks for epidemiological data collection on the basis of the lessons learnt from the already well established and functioning registers network such as EUROCAT.
- Support the discussion on the Centre of reference exploring the idea of developing the network for data collection using the centres of reference as data sources. One of the criteria that these centres should fulfil is the involvement in epidemiological surveillance. In case, promote the idea of including expert epidemiologists in these centres to guide and supervise the data collection process.
- Support the implementation of a European pilot project for the development of a European network for data collection.

Promote engagement of patients

A growing body of evidence shows that patient engagement in treatment decisions and in managing their own healthcare can improve patients' experience and often results in better health outcomes and more appropriate and cost-effective utilisation of health services. In addition to the potential for

achieving greater efficiencies in resource use, encouraging patients to take more control when they are ill may also prove to be an effective tool for improving public health, as well as personal health. The key to greater patient engagement lies in promoting involvement; empowerment, and a sense of ownership of their healthcare.

As much as we advocate for patients' engagement we should also provide them with the skills and knowledge necessary to fulfil the important role we are asking them to play.
Patient literacy and capacity building are fundamental to patient engagement.

Initiatives aiming at building the capacity of patients are scarce. The EURORDIS (European Organisation for Rare Diseases) is actively implementing training for patients and the EMEA (European Agency for the Evaluation of Medicinal Products) is now planning some training programmes. These initiatives should be better supported and the collaboration with EURORDIS should be strengthened to ensure a meaningful engagement of patients with RDs.

Recommendations

- Promote and support further studies on patients' experiences and needs;
- Promote engagement of patients in research and disease management to explore unmet needs and to plan new strategies and more effective interventions on RDs;
- Promote the development of new methods to collect information on patients' needs. In particular, Narrative Medicine is an approach to gather relevant information on diseases from patients through "Illness stories" and it could be used to improve clinical knowledge;
- Support patients literacy and patients empowerment.

Promote a multidisciplinary/multifaceted approach to tackle RDs

People suffering from a RD often experience the same problems: failure or delay in diagnosis, scarcity of health information, lack or delay of referral to specialised professionals, poor co-ordination of in- and out-patient care, scarce social welfare support, and lack of support towards integration into work, social and family environments.
These multi-dimensional problems of patients with RDs can not be treated with a single intervention thus a multiperspective approach is needed to study, manage and treat RDs.
The large number, low prevalence and heterogeneity of RDs, need a multidisciplinary approach bringing together teams working in clinical, social science and research fields. In this context, particular attention should be given to the ethical emerging issues such as those related to privacy and confidentiality in data collection from individual records, to clinical research or to the use of techniques derived from human genetics or biotechnologies.

Recommendations

- Strengthen the collaboration at the European level to develop lessons learned and identify models for a comprehensive approach to tackle RDs
- Promote the development of comprehensive national plans for RDs in each MS
- Promote the provision of social support for RDs patients
- Explore the need for an Advisory Ethical Committee for RDs at the European level

Develop information for patients and health professionals involved with RDs

Patients and their families have difficulties in getting information on their disease and in finding their way within the healthcare system. This leads to diagnostic errors, which alter the quality of their care, and increases their feelings of isolation.

In addition, the information aimed at professionals is dispersed and difficult to access in a context where knowledge is evolving rapidly. Health care workers need to have real-time access to validated and updated recommendations for clinical practice, and should be able to identify the specialised services to which they can send patients.
The availability of validated information, which is pertinent and easy to access, is therefore essential to the improvement of patient care.

Recommendations

- Promote and support the development and dissemination of clinical guidelines;
- Support the development of information materials for patients;
- Support training of healthcare workers;
- Promote the availability and share of information through web-base systems.

Support research on RDs, in particular

- in epidemiology (networks of data collection considering the involvement of centres of reference)
- descriptive and analytical epidemiology in the domain of the natural history and clinical nosology of a disease;
- social impact of RDs;
- social care needs and differences among EU countries. Validated tools to assess quality of care on the basis of patients' opinions/health care users are needed. The questionnaire used in this study was only a pilot tool and it would be very important to improve it. Rigorous methods should be used to elicit the patients' experiences; responses are subjective and difficult to interpret since they depend also on expectations that vary greatly among patients. The best way to collect patient's opinions should be further discussed (general evaluation categories versus detailed description of the experience);
- access to healthcare and treatment for patients with RDs.

APPENDIX 1

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APPENDIX 2

NEPHIRD PROJECT MANAGEMENT ORGANISATION

Appendix 2 NEPHIRD Project Management Organisation

The project was comprised of the Project Managememnt Group (PMG) and three Expert Working Groups (EWGs).

PMG

- coordinate, monitor progress and provide directions to the overall implementation of the project

Members

Domenica Taruscio	Centro Nazionale Malattie Rare, Istituto Superiore di Sanità, Italy
Fabrizio Bianchi	Fisiologia Clinica, Unità di Epidemiologia, Istituto CNR, Italy
Helen Dolk	Epidemiology and Health Services Research, School of Health Sciences University of Ulster at Jordanstown, UK
Elizabeth Ettorre	Department of Sociology, University of Plymouth, UK
Pier Luigi Morosini	Centro Epidemiologia e Biostatistica, Istituto Superiore di Sanità, Italy
Luca Padua	Facoltà di Medicina, Università Cattolica, Italy
Manuel Posada	Ministerio de Sanidad y Consumo, Istituto de Salud Carlo III, Spain
Benedetto Terracini	Dipartimento di Scienze Biomediche e Oncologia Umana, Università di Torino, Italy

EWGs 1: Assessment of the situation of Rare Diseases in the participating countries and estimation of epidemiological indices

- identify the ongoing national activities on RDs in the participating Countries
- assess the prevalence of selected RDs
- develop a minimum and standard data set for RDs data collection across EU countries
- design, build and run the NEPHIRD Website

Members

Barisic Ingeborg, Croatia	Pelz Joerg, Germania
Bianchi Fabrizio, Italy	PoortmaN Ysbrand, Netherlands
Calzolari Elisa, Italy	Posada De La Plaz Manuel, Spain
Dallapiccola Bruno, Italy	Queisser-Luft Annette, Germany
De Almeida Salomé, Portugal	Salerno Paolo, Italy
Di Stefano Sandra, Malta	Sänger Annette, Denmark
Kucinskas Vaidutis Lithuania	Seyoum Ido Moges, Italy
Mastroiacovo Pierpaolo, Italy	Stoll Claude, France
Tarsitani Gianfranco, Italy	Taruscio Domenica, Italy
Tenconi Romano, Italy	Terracini Benedetto, Italy
Jean-Pierre Fryns, Belgium	

EWGs 2: Evaluation of the quality of health care for patients with Rare Diseases

- evaluating the quality of health care
- developing tools to measure and assess the quality of health care
- defining the domain of health care to be assessed
- defining common methodology for rare diseases structure and process of care evaluation
- patients and care givers satisfaction assessment

Members

Elizabeth Ettorre, UK
Mastroiacovo Pierpaolo, Italy
Donatella Sessa, Italy
Maria Antonietta Ricci, Italy
Michele Lipucci, Italy
PierLuigi Morosini, Italy
Gaia Marsico, Italy

EWGs 3: Assessment of the Quality of Life of patients with Rare Diseases

- approach to assessing Quality of Life (Health related Quality of Life)
- designing the methodology of instrument application
- identifying the appropriate instrument to measure and assess the Quality of Life
- defining the determinants of health to be assessed

Members

Amedeo Spagnolo, Italy
Luca Padua, Italy
Elisa Calzolari, Italy
Alison Kerr, UK
Angelo Selicorni, Italy
Alberto Burlina, Italy
Giuseppe Hayek, Italy

APPENDIX 3

MEETINGS AND CONFERENCES

Appendix 3 Meetings and Conferences

1. Project Management Group (PMG) and Expert Working Group (EWG) Meetings

- July 2, 2001: "Approaches for epidemiological data collection" – Rome, Istituto Superiore di Sanità (ISS);
- December 16-17, 2002: "The role and contribution of patient's organisations" – Rome, Istituto Superiore di Sanità (ISS);
- December 9-10, 2002: "Sociological aspects of Rare Diseases and Quality of Life"– Rome, Istituto Superiore di Sanità (ISS);
- February 10, 2003 PMG and the EWG had a project management meeting to agree together on the next steps of the project;
- In 2004-2005, several meetings were organised by the EWG. These meetings were aimed at discussing how to undertake the activities agreed upon during the project management meeting:
  - survey of assessment on quality of and accessibility to health and social care;
  - identification and selection of public health indicators for RDs;
  - assessment of the QoL.

2. September 2006, the final meeting with all participants of the project was held in Rome (Italy) (see Appendix 4).

3. Abstract and oral presentations during the European Conference Rare Diseases 2005-ECRD2005.

Oral presentations:

- Summary comparison of national plans and practices
  Speaker: Domenica Taruscio
- Data collection and management
  Discussant: Yllka Kodra

Abstracts:

- Access and quality of health care on rare diseases performed in NEPHIRD network
  Authors: Kodra Y, Agazio E, Salerno P, Morosini P, Taruscio D.
- Epidemiology of Myasthenia Gravis in European region
  Authors: Kodra Y, Agazio E, Salerno P, Taruscio D.
- From difficulties to solutions for the rare diseases community: lesson to be learned from a socio-ethical approach performed in the frame of the NEPHIRD project.
  Authors: Elizabeth Ettorre, Gaia Marsico, Domenica Taruscio
- Network of Public Health Institutions on Rare Diseases (NEPHIRD)
  Authors: P. Salerno, Y. Kodra, A. Agazio, P. Morosini, G. Marsico, E. Ettorre, D. Taruscio, and all partners of NEPHIRD.

APPENDIX 4

FINAL MEETING OF THE NEPHIRD PROJECT: PROGRAMME AND PARTICIPANTS

Appendix 4 Final meeting of NEPHIRD project Programme and participants

The Italian National Institute of Public Health (Istituto Superiore di Sanità) organised a 4-day-conference to discuss the results of the NEPHIRD project and to continue the discussion on strategies and actions required to address RDs.
The conference was organized in Plenary section in the morning and Discussion Working Group in the afternoon on the topics addressed in the morning.
Plenary sessions focused on the following: prevention and epidemiology; diagnosis and treatment; social aspects and quality of life.
Each Discussion Working Group was composed of about 10 participants with a discussion leader and a rapporteur; the latter was in charge of reporting the outcomes of the group work in the plenary; The summary of all contributions during the Discussion Working Group are reported in the project website.
Moreover, a full day was dedicated to seminars on each of the Rare Diseases studied in NEPHIRD in order to increase the knowledge about these diseases (Neurofibromatosis, Cornelia de Lange syndrome, Rett Syndrome, Prader Willi syndrome, Myasthenia Gravis).

International Conference

Conferenza Internazionale

NETWORK OF PUBLIC HEALTH INSTITUTIONS ON RARE DISEASES (NEPHIRD)

NEPHIRD CONFERENCE

September 20thy – 23rd 2006
20 – 23 Settembre 2006

Aula Marotta
Viale Regina Elena, 299

Rome, Italy

Organized by/*Organizzato da*
NATIONAL INSTITUTE OF HEALTH
ISTITUTO SUPERIORE DI SANITÀ

September 20thy, 20 Settembre 2006

09.00 Welcome address / *Saluto di benvenuto*
D. Taruscio

Session I / I *Sessione*
Prevention and Epidemiology/*Prevenzione ed Epidemiologia*

Chairpersons / *Moderatori*
G. Tarsitani, B. Terracini

09.30 Primary prevention: the model of folic acid / *Prevenzione primaria: il modello dell'acido folico*
D. Taruscio

09.50 Screening for rare metabolic diseases in the newborn: experiences in Finland / *Screening neonatale per malattie metaboliche rare:esperienze in Finlandia*
I. Autti-Ramo

10.10 Epidemiological registration and epidemiological surveillance of rare malformations: the model of EUROCAT / *Registrazione e sorveglianza epidemiologica delle malformazioni rare: il modello di EUROCAT*
F. Bianchi

10.30 Coffee break / *Intervallo*

10.50 Exploiting available databases: mortality and hospital discharge / *Utilizzo di database disponibili: mortalità e dimissione ospedaliera*
S. Conti

11.10 Collection and evaluation of epidemiological data on rare diseases in Europe: experiences of NEPHIRD-EUROCAT collaboration / *Raccolta e valutazione dati epidemiologici sulle malattie rare in Europa: esperienze collaborative NEPHIRD-EUROCAT*
I. Barisic

11.30 National and Regional registries: italian experiences / *Registri regionali e nazionale: esperienze italiane*
E. Daina, D. Roccatello, D. Taruscio

12.30 Discussion / *Discussione*

13.00 Lunch / *Pausa pranzo*

Discussion Groups:
*Prevention and Epidemiology/*Prevenzione ed Epidemiologia

14.00 Focus Group 1: Prevention / *Prevenzione*
Discussion Leader: **I. Barisic**
Rapporteurs: **B. Doray, R. Stefanov**

Focus Group 2: Epidemiological data collection / *Raccolta dati epidemiologici*
Discussion Leader: **B. Terracini**
Rapporteurs: **Y. Kodra, E. Petrela**

Focus Group 3: Epidemiological indicators / *Indicatori epidemiologici*
Discussion Leader: **S. Conti**
Rapporteur: **J. Sandor**

Focus Group 4: Case study / *Studio dei casi*
Discussion Leader: **F. Bianchi**
Rapporteur: **R. Scarinci**

16.00 Coffee break / *Intervallo*

16.30 Presentation of the outcomes of focus groups by Rapporteurs / *Presentazione dei risultati dei focus groups a cura dei* Rapporteurs

17.30 Conclusion / *Conclusione*

September 21st, 21 Settembre 2006

Session II / II *Sessione*
Diagnosis and treatment / *Diagnosi e trattamento*

Chairperson / *Moderatore*
S. Bernasconi

09.30 Diagnostic tests: principles of validation and quality / *Test diagnostici: principi di validazione e qualità*
A. Menditto, M. Patriarca

09.50 Genetic tests/ *Test genetici*
B. Dallapiccola

10.10 Quality assurance of genetic tests: the Italian national project / *Controllo di qualità dei test genetici: il progetto nazionale italiano*
V. Falbo, G. Floridia, D. Taruscio

10.30 Coffee break / *Intervallo*

10.50 Counselling and risk communication / *Consulenza e comunicazione del rischio*
E. Calzolari, O. Calabrese

11.10 Informed Consent / *Consenso informato*
M. Siouti

11.30 Pharmacogenomics and pharmacogenetics / *Farmacogenetica e Farmacogenomica*
G. Novelli

11.50 Innovative therapies on rare cancers / *Terapie innovative nei tumori rari*
K. Kubáčková

12.10 Rare diseases: the role of the media / *Malattie rare: il ruolo dei media*
L. Carra

12.30 Discussion / *Discussione*

13.00 Lunch / *Pausa pranzo*

Discussion Groups:
Diagnosis and treatment / *Diagnosi e trattamento*

14.00 Focus Group 1: Diagnostic Test / *Test diagnostici*
Discussion Leaders: **A. Utkus, F. Torricelli**
Rapporteur: **M. Salvatore**

Focus Group 2: Counselling and risk Communication / *Consulenza e comunicazione del rischio*
Discussion Leaders: **I. Blanco, A. Matevosyan**
Rapporteur: **P. Zinzi**

Focus Group 3: Therapies and rehabilitation /*Terapie e riabilitazione*
Discussion Leader: **J. Peltonen**
Rapporteurs: **I. Sipila, A. Loizzo**

Focus Group 4: Case study / *Studio dei casi*
Discussion Leader: **M. Morfini**
Rapporteurs: **E. Daina, S. Baldovino**

16.00 Coffee break / *Intervallo*

16.30 Presentation of the outcomes of focus groups by Rapporteurs
Presentazione dei risultati dei focus groups a cura dei Rapporteurs

17.30 Conclusion / *Conclusione*

September 22nd, 22 Settembre 2006

Session III / III *Sessione*
Social aspects and Quality of Life / *Aspetti sociali e qualità della vita*

Chairpersons / *Moderatori*
G. Sabetta

09.30 Psychosocial impact of rare diseases / *L'impatto psicosociale delle malattie rare*
E. Ettorre

09.50 Narrative medicine / *Medicina narrativa*
G. Marsico

10.10 Coping with social needs: experience from intervention studies / *Affrontare i bisogni sociali: l'esperienza da studi di intervento*
A. Olauson

10.30 Coffee break / *Intervallo*

10.50 The contribution of Patients' Groups on of epidemiological – health data / *Il contributo delle Associazioni dei Pazienti alla raccolta dei dati epidemiologico – sanitari*
Interventi preordinati:
P. Moore,. F. Guerra, C. Buttarelli and other Associations

11.50 Criteria for quality of life assessment / *Criteri per la valutazione della qualità della vita*
L. Padua

12.10 Assessment on Patients' needs: results of NEPHIRD survey / *Valutazione dei bisogni dei Pazienti: risultati dell'indagine NEPHIRD*
Y. Kodra

12.30 Discussion / *Discussione*

13.00 Lunch / *Pausa pranzo*

Discussion Groups:
Social aspects and Quality of Life / *Aspetti sociali e qualità della vita*

14.00 Focus Group 1: Social aspects / *Aspetti sociali*
Discussion Leaders: **A. Knight**
Rapporteur: **S.A. Peltonen**

Focus Group 2: Quality of life / *Qualità della vita*
Discussion Leaders: **L. Padua, P. Caliandro**
Rapporteur: **L. Ege**

Focus Group 3: Communication and Narrative Medicine
Comunicazione e Medicina Narrativa
Discussion Leader: **D. Zarri**
Rapporteur: **S. Pulciani**

Focus Group 4: Case study/ *Studio dei casi*
Discussion Leader: **A. Crinò, M. Dentamaro**
Rapporteurs: **G. Evans**

16.00 Coffee break / *Intervallo*

16.30 Presentation of the outcomes of focus groups by Rapporteurs / *Presentazione dei risultati dei focus groups a cura dei* Rapporteurs

September 23rd, 23 Settembre 2006

Session IV / IV *Sessione*
Rare diseases studied in NEPHIRD / *Malattie rare studiate in NEPHIRD*

Chairpersons / *Moderatori*
S. Bombardieri, D. Taruscio

09.30 Neurofibromatosis type 1/ *Neurofibromatosi tipo 1*
M. Upadhaya

09.50 Prader Willi syndrome / *Sindrome Prader Willi*
G. Grugni

10.10 Myasthenia Gravis / *Myasthenia Gravis*
A. Melms

10.30 Coffee break / *Intervallo*

10.50 Cornelia de Lange syndrome / *Sindrome di Cornelia de Lange*
A. Selicorni

11.10 Rett syndrome / *Sindrome di Rett*
G. Hayek

11.30 Metabolic rare diseases / *Malattie rare metaboliche*
A. Burlina

11.50 Future programmes / *Programmi futuri*
D. Taruscio

12.10 Rare diseases: the USA experience / Malattie rare: l'esperienza USA
S. Groft

12.30 Discussion / *Discussione*

13.30 Conclusion / *Conclusione*

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