

# Rare diseases, from European resolutions and recommendations to actual measures and strategies

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## I. INTRODUCTION

A rare disease is a disease affecting less than 5 in 10000 individuals (1-3). There are over 7000 rare diseases registered to date, of which 80% are genetic. New rare diseases are identified and defined on a weekly basis. Rare diseases affect around 1.3 million people in Romania and 25 million people in Europe. A large number of them are still called orphan diseases, because the people affected by them do not yet benefit from an adequate treatment.

Despite the absence of extended research for these diseases, it is estimated that 6 – 8% of the world population is affected by a rare disease. This is how the estimates of 1.3 million Romanians, 25 million Europeans and 27 million North American have been reached (2).

75% of the rare diseases may be present at birth or will manifest themselves before the age of 2. Other rare diseases, around 25% of them, have a set on at the age of 40. For 80% of those affected, the disease has an obvious impact on

life expectancy, and for 35% of them, the disease and/or its complications cause death before the age of 1. In over 65% of the cases, the diseases cause disabilities that affect the everyday life, while in 9% of the cases, autonomy is completely lost.

The most numerous rare diseases are caused by genetic mutations, either hereditary (even if the disease has a late onset in the patient's life), or they are caused by a new mutation (de novo).

These monogenetic diseases are transmitted according to Mendel's laws (mucoviscidosis, haemophilia, phenylketonuria, Marfan syndrome, osteogenesis imperfecta, etc). Mitochondrial and chromosomal diseases are included in this same category.

Mitochondrial diseases, caused by the alteration of the mitochondria genome, are transmitted exclusively by the mother (certain encephalomyopathies, Leber optical atrophy).

Chromosomal diseases are caused by numeric or structural chromosomal aberrations: the excessive presence of a chromosome or

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part of a chromosome (trisomy) or the absence of a chromosome or a fragment of a chromosome (monosomy).

Some rare diseases have a multi-factorial polygenic determinism: more than one gene is involved, causing genetic predisposition, and it is converted into a disease through environment intervention.

Although there is a large clinical and genetic heterogeneity, rare diseases present common characteristics. Very often, they are severe, chronic and progressive, affecting life prognosis. The physical and functional deficiencies often lead to loss of autonomy or to invalidity (disability levels), which alter the quality of life (3).

What is specific to these diseases – diagnosis difficulties, feelings of isolation, absence of treatment – these all generate an emotional pain to these patients and their families.

Being numerous and complex, these diseases are not very well known by doctors and by officials from the health system.

They concern all medical specialities, showing extremely variable degrees of severity, depending on the patient and the disease.

Rare diseases often encounter difficulties related to orientation and medical pathway to establish diagnosis and subsequently adequate follow-up, both medical and social.

Although there isn't always an effective cure for rare diseases (active research is ongoing, encouraged by a policy which promoted orphan medicines), early and adequate care may improve the survival rates and the patients' quality of life.

A disability is by definition a long-term limitation of activities or participation to social life, caused by the alteration of physical, sensory, mental or psychological functions, or by a combination of them. Rare diseases can generate all kinds of disabilities. Often, the disability caused by a rare disease is by itself a rare disability. It corresponds to rare combinations of associated deficiencies and difficulties, requiring specific care protocols, consisting of more than just simple additions of techniques and methods used to compensate each of the respective deficiencies. For example, if deafness and blindness are associated, specific education and communication methods are required, which cannot be those used by deaf people, or those used by blind people (3,4). □

## II. EUROPEAN POLICIES IN THE FIELD OF RARE DISEASES

For the European Union, rare diseases represent a major public health issue and a priority in health and research programmes (5, 6).

In 1995, the European Union Council adopted a resolution stating that rare diseases are a public health priority for Europe. A 4 years programme has been developed at European level (1999-2002), setting 8 public health priority objectives, among which rare diseases too. There were 23 projects funded under the Rare Diseases programme, and certain initiatives received a series of community funds, such as Orphanet or the Eurocat network.

On September 23, 2002, the European Parliament and the European Union Council adopted a decision regarding the new community action programme in the field of public health (2003-2008). On October 23, 2007, the second community action programme in the field of public health was adopted (2008-2013). Rare diseases are a priority in this programme, with the following priority areas:

- Information exchange through European information networks in the field of rare diseases (name of disease, prevalence, description of main symptoms, causes, treatment, prevention measures, specialised consults and ongoing research), widely accessible networks especially by internet.
- Development of strategies and solutions regarding the exchange and coordination of information between people affected by rare diseases and professionals – volunteers interested in this field, with the purpose to encourage the continuity of research and transnational cooperation.

In December 1999, the European Union adopted a regulation meant to facilitate the establishment of "orphan medicines" policies, for the benefit of rare disease patients. For this, EU committed to fund research and development projects in order to encourage pharmaceutical and biotech companies to develop orphan medicines.

By developing networks, sharing the expertise of more advanced health systems in the field of rare diseases (such as France) and by disseminating information, there is hope for an integrated approach, able to respond to this

major issue in a coordinated and uniform way, at the level of all EU states (6-8). □

### III. WHO AND RARE DISEASES

The World Health Organisation (WHO) is just as preoccupied by rare diseases, having this issue among its major priorities. In WHO vision, the fight against rare genetic diseases is more and more possible, thanks to all the knowledge gained in the past few years about the human genome.

The efforts of the medical world target classic genetic diseases caused by modifications of the genetic information, as well as diseases caused by variable contributions of gene modifications and environment factors that intervene in the disease onset.

Practical applications of genomic discoveries are showing great progress in this field as well, and it is expected that they will have a huge contribution in the field of public health.

The effectiveness of prevention methods in the field of rare diseases has been demonstrated in countries where a certain disease was more frequent and the identification of abnormal gene carriers is possible and is easy. For example, in Cyprus, Greece and Italy, the identification of Thalassaemia is a classical practice and there is a national database (National Registry of Thalassaemia). Couples at high risk are identified fast enough to receive prenatal diagnosis from the first pregnancy. Most of them request these services and have healthy children.

Health programmes may be applied through efforts to educate and sensitise the population, giving people the opportunity to take informed decisions (9,10). □

### IV. THE ROLE OF PATIENT ORGANISATION IN HEALTH POLICIES RELATED TO RARE DISEASES

Actions to support patient organisations are a priority in EU, taking into consideration the fact that these associations have a precious experience in caring for patients, representing a group ready to educate the population and prevent rare genetic diseases (1,5,9).

The development of partnerships between patient support groups, national and international associations, national alliances in different countries, specialised European structures, such as the European Organisation for Rare

Diseases (EURORDIS), will facilitate the exchange of information, access to European data bases, leading to greater possibilities for prevention, diagnosis and care for these patients.

On June 9, 2009, the Health Ministries from the European Union adopted a European Strategy for Rare Diseases. Through this strategy, member states are requested to implement national plans for rare diseases, by the end of 2013 (8). The Council recommendation is extremely important and appeals to a joint actions, focused at European and national level, with the following objectives:

- To ensure an adequate codification and classification of rare diseases;
- To intensify research in the field of rare diseases;
- To identify Centres of Reference and to include them in European Networks of Reference;
- To support bringing together European level expertise;
- To share evaluations on added clinical value of orphan medicines;
- To encourage patients' initiatives by involving them and their representatives in all stages of decision making;
- To ensure sustainability of rare disease infrastructure.

Adopting a European strategy is the peak of all documents and regulations facilitating the recognition of rare diseases as a public health priority and the concentration of European efforts in this field.

EURORDIS and national rare disease patients organisations are in the centre of this process, making known the patients' requests regarding the necessity to have a legal framework for rare diseases. It all started with the success of the public consultations regarding rare diseases in November 2007, followed by adopting the Commission Communicate on rare diseases in November 2008, then adopting the Council recommendations on European actions in the field of rare diseases. Each step demonstrated the vital importance of European actions and cooperation between member states.

The Council recommendation represents a milestone for rare disease patients all over Europe. Adopting it requires patient representatives to become more involved in developing the strategy in each member state, in implementing and monitoring it. The social side of

service provision and patient centred research will be supported.

Now, that there are political instruments, EURORDIS together with the other organisations interested, will follow the implementation of the Council recommendation both at European and at national level (8,9). □

## V. NATIONAL PLANS FOR APPROACHING RARE DISEASES

France is the country with the most concrete and coherent measures in the field of rare diseases. France had the first National Plan for Rare Diseases (2005-2008), tracing the main action lines, necessary to improve the quality of life for rare disease patients.

At European level, the EUROPLAN programme has been launched in April 2008, for three years. It is mainly aimed at issuing recommendations regarding ways to develop strategic plans to fight against rare diseases, providing information on different stages and priority intervention domains.

Funded by the European Commission (DG SANCO), this project plans to provide a series of instruments consisting of methodologies, best practices, case studies and indicators which would allow each member state to define its own national plan for rare diseases.

EUROPLAN includes 25 countries from European countries, and EURORDIS is one of the main partners in the project, representing rare disease patients (7, 9).

The Romanian National Alliance for rare Diseases (RoNARD) is member of European networks for rare diseases (especially EURORDIS) and has fruitful collaborations with similar bodies from EU countries (11).

In partnership with the Health Ministry and together with Romanian and European special-

ists, RoNARD has been organising since 2006 the process of developing the Romanian national Plan for rare Diseases.

This plan defines the institutional frame of approaching rare diseases, through reference and competence centres. The main objectives of the national plan for rare diseases are:

- To develop services for the diagnosis, treatment, rehabilitation and prophylaxis of these diseases;
- To improve access to a correct and fast diagnosis, to specialised social services;
- To intensify efforts regarding orphan medicines;
- To implement prenatal and neonatal screening programmes.

The national plan also aims at developing efficient laboratories for genetic investigations, as well as developing human resources, both with regards to specialists in genetics and to other specialists, through rare disease training programmes.

Improving access to information regarding rare diseases will increase the level of accessibility for families and will allow early diagnosis, an essential condition for the rehabilitation and improvement of life quality in certain diseases.

In conclusion, it is therefore essential that Romania adopts the coherent European approach regarding rare diseases, taking into account – on one hand – stimulating research in this field and – on the other hand – increasing the role of patient organisations.

The National Plan for Rare Diseases is certainly a difficult, long term challenge, but it will lead to improving the quality of medical and social services and the patients' and families' lives will become more bearable. □

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