3 DIAGNOSING RARE DISEASES:
health care systems always challenged

3.1 EurordisCare2: patients loose confidence in health care systems

SPEAKER

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The rare disease dilemma: EU health care systems unable to diagnose what patients are suffering from.

EurordisCare2, a survey on delay in diagnosis in Europe for 8 rare diseases[5].
Late diagnosis of rare diseases: a remaining issue resulting in individual and familial consequences

Rare diseases are poorly taken into consideration the general public and also health care professionals. As a result, even their diagnosis is an issue.
This survey was launched to document, through patient experience, the extent, causes and consequences of late diagnosis in 8 rare diseases in Europe. 69 patient organisations from 17 countries sent questionnaires in 12 languages to 18 000 patients.Patients returned 5980 to Eurordis, (5300 analysed).
This study was the first approach on this matter

→ **METHODS**

Table below shows the main characteristics of the diseases:

	Genetic	Prevalence /10 000	Main clinical aspects
Crohn	No	2-15	digestive
Cystic fibrosis	inheritable	3	digestive, respiratory
Duchenne	inheritable	1,2	neuromuscular
Ehlers Danlos	inheritable	-	dermatologic, joints
Fragile X	inheritable	1,5	cognitive
Marfan	inheritable	2	cardiovascular, osteoart, OPH
Prader Willi	Sporadic	0,5	metabolic, cognitive
Tub, sclerosis	Sporadic Anher	1	neurologic, cognitive

For a given disease, the number of returned questionnaires varied from 485 (Ehlers Danlos Syndrome) to 1079 (cystic fibrosis) and the number of participating countries from 5 for Crohn's disease and Ehlers Danlos syndrome to 14 for Prader Willi syndrome.

5. [This article has been submitted to a peer-reviewed scientific magazine for publication. Therefore only a preliminary report can be published in this report]

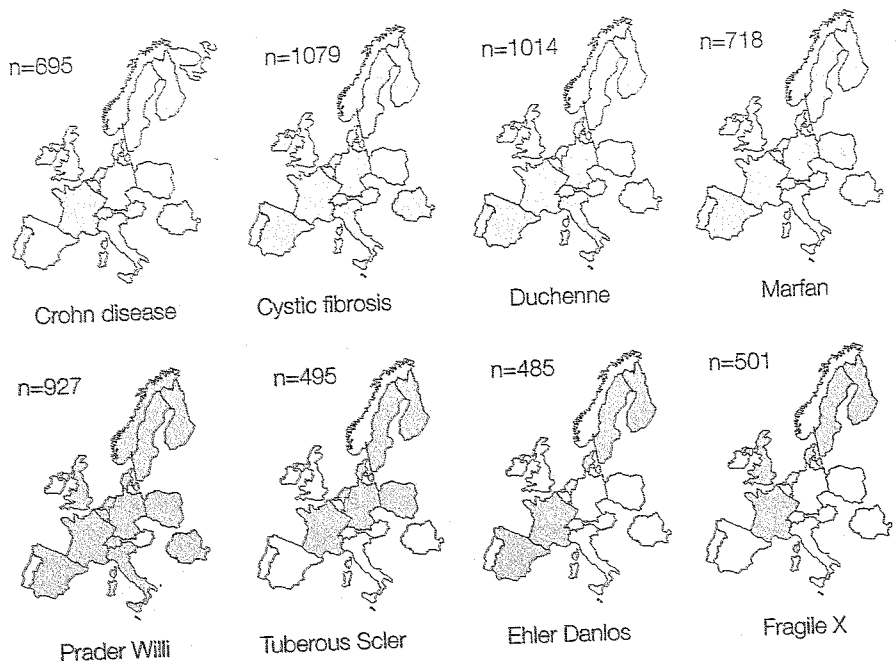

Figure 9 displays, by disease, the countries in which the questionnaire was sent to patients.

→ STUDY POPULATION

The study population (respondents) was well distributed geographically, a third living in a country village, a third in small and medium-size cities, and a third in larger cities.

Respondents were from all professional categories, with a slight over representation of the management and teacher sectors, and under representation of manual workers and retired persons.

→ RESULTS: DELAYS FROM FIRST SYMPTOMS TO CONFIRMATORY DIAGNOSIS

For a given disease, there was a wide variability in delays. For most diseases, a diagnostic was obtained without delay for one quarter or half of the patients. Unfortunately, a consistent number of patients had to wait for a long time before diagnosis.

The final 25% of diagnosis required at least 1.5 years in cystic fibrosis, 3 to 6 years in Duchenne muscular dystrophy, Prader Willi syndrome, Fragile X syndrome and Crohn's disease, 11 years in Marfan syndrome and 28 years in Ehlers Danlos syndrome!

Waiting for diagnosis was not a calm period but a continuous quest. Patients had to consult numerous doctors. One quarter of patients consulted at least 4 doctors in Fragile X syndrome, 6 doctors in Prader Willi syndrome and Marfan syndrome and 16 in Ehlers Danlos syndrome.

Before receiving a confirmatory diagnosis, 40% of patients received first an erroneous diagnosis, while 60% received none.
The trend to misdiagnosis depended both on the disease (1/4 in Marfan syndrome versus _ in Ehlers Danlos syndrome), and on the country (1/3 in Finland, Spain, United Kingdom and Ireland versus _ in Austria, Denmark, Germany, Romania, Sweden and Poland).
Frequently, misdiagnosis resulted in various medical interventions: medical treatments in 1 out of 3 patients, surgery in 1 out of 6 patients, and psychological care in 1 out of 10 patients.

The loss of confidence in medicine was observed in all diseases with frequencies varying from 11 to 17 % of patients.

Delay in diagnosis had personal consequences: physical, psychological and intellectual consequences. Physical consequences were reported in more than _ patients in the case of Marfan syndrome and Ehlers Danlos syndrome; psychological and deterioration in cognitive development mainly in Prader Willi syndrome, Fragile X syndrome and tuberous sclerosis. More dramatically, diagnosis delay was considered to be responsible for the death of the patient in 6 % of cases in the case of Marfan syndrome.

Besides individual consequences, familial consequences represent a hidden but dramatic issue: the birth of an affected sibling affected more than 8% of patients in cases of Marfan syndrome and Ehlers Danlos syndrome. Unacceptable behaviour of relatives was reported in 1 out of 10 to 1 out of 4 patients in cases of 7 diseases.
The conditions of the announcement of the diagnosis were far from satisfying: the diagnosis was announced in unsatisfactory terms or conditions in 33% of cases, and in unacceptable ones in 12.5% of cases. The genetic nature of the disease was not communicated to the patient or family in 25% of cases. This was paradoxical, given the genetic origin of 80% of rare diseases.

→ **CONCLUSIONS**

- Diagnostic delays exist and may have serious consequences.
- Disclosure of the diagnosis needs improvement: a point of attention for the medical community.
- There are differences between the countries. It is not clear whether they are cultural or structural.
- Obtaining the exact diagnosis is only the beginning of the hurdle that patients and their parents have to go through when suffering from a rare disease.

EurordisCare® is a research programme initiated by Eurordis in 2002, involving rare disease patient organisations, to survey and compare access to care between European countries and between different rare diseases.

3.2 Primary immune-deficiency: a clear illustration of diagnosis delays

The Impact of Diagnosis Delays in Primary Immune-deficiencies (PIDs):
Primary Immune-deficiencies are a group of more than 100 diseases of the immune system. They are genetic conditions that range in severity and bare the clinical hallmarks of persistent, recurring infections. Delayed diagnosis and insufficient treatment leads to increased morbidity, mortality, and inflated medical costs - not to mention a life of chronic illness, permanent organ damage, PIDs can appear at any age and know no racial or ethnic boundaries. Symptoms are often overlooked because they appear to be common childhood illnesses - sinus and ear infections, pneumonia, fever and bronchitis. Physicians often treat ailments without addressing the underlying cause.

34 IPOPI - International Patients Organisation for Primary Immune-deficiencies, IPOPI Poster 40, Bianca Pizzera Plantanida

A poster jointly submitted by the key organisations representing the EU and international PID nurse, patient and physician community

10 WARNING SIGNS OF PRIMARY IMMUNODEFICIENCY (figure 10)

Primary Immune-deficiency

Primary Immunedeficiency (PI) causes children and young adults to have infections that come back frequently or are unusually hard to cure. In America alone, up to 1/2 million suffer from one of the 100 known Primary Immunedeficiency diseases. If you or someone you know are affected by two or more of the following warning signs, speak to a physician about the possible presence of an underlying Primary Immunedeficiency.

1	eight or more new ear infections within one year.	Recurrent, deep skin, or organ abscesses.	6
2	Two or more serious sinus infections within one year.	Persistent thrush in mouth or elsewhere in skin, after age 1.	7
3	Two or more months on antibiotics with little effect.T	Need for intraveinous antibiotics to clear infections.	8
4	Two or more pneumonias within one year.	Two or more deep-seated infections	9
5	Failing of an infant to gain weight or grow normally.	A family history of Primary Immunedeficiency.	10