

The Voice of 12,000 Patients

Experiences and Expectations of Rare Disease Patients
on Diagnosis and Care in Europe

A report based on the EurordisCare2
and EurordisCare3 Surveys





Foreword

We need to work together across Europe to tackle rare diseases. However, in order to work together, we need solid evidence. This book marks a great improvement in our common understanding of the needs and expectations of patients suffering from rare disease in the European Union.

The survey could not have been completed without a broad-based network. In the past, the large number of patient organisations acting in the field was both an indication of the importance of the issues as well as an obstacle to progress. EURORDIS (the European Organisation for Rare Diseases) has been a crucial new platform, grouping patient organisations as well as the most relevant networks and federations acting in the field. Patients with rare diseases in the European Union should be glad to know that they have such solid and professional representation.

The European Commission is also glad to have contributed to the support of the large surveys conducted by EURORDIS in recent years.

The information provided by the EurordisCare Survey Programme has been essential to the sound preparation of the recent Commission

Communication on a European Action in the Field of Rare Diseases.

The EurordisCare3 survey, helping shape the future of European Centres of Reference; the EurordisCare2 survey, on diagnostic delays for eight diseases; the EurordisCare1 survey, comparing health care for six diseases in 17 countries; the fourth EURORDIS Survey on Orphan Drug Availability in Europe; and the European Survey on Information Services for Rare Diseases have all put an extraordinary amount of information at the disposal of patient organisations, health professionals and political authorities.

I hope that the cooperation between EURORDIS and the European Commission will continue to be one of the foundations of success for European action in this field in the future.

Robert Madelin

*Director General, Health & Consumers
European Commission*

Preface

It is with great satisfaction and great interest that I contribute this preface to this work dedicated to the publication of the results of the EurordisCare Survey Programme.

Satisfaction firstly, as it is very exciting to see an undertaking of this kind come to fruition. The collection of information on the health needs and expectations of patients and their families in 12 different languages and in 17 countries, conducted by patient associations, is quite a feat. This would be quite a challenge with any disease, however it takes on an additional complexity when the diseases that the patients have are rare. This demonstrates once again the power of patients' associations. This work can only encourage researchers and medical research organisations to support this action, as well as to inspire them to better define their research programmes and to develop their work. This is the mission of the INSERM group GRAM*, of which I have recently been elected chairperson; and this work can only help.

Secondly, it is of great interest for the health economic and social scientist (such as myself) whose major research themes have long been focused on ways of living with illness and the involvement of patients and their caregivers. In this sense, I can therefore appreciate the extent of the contribution of these investigations.

From the point of view of methodology, in particular we must appreciate the formidable task of language and the difficulty of putting together a common questionnaire, which is relevant, understandable and applicable to multiple countries with different healthcare systems. In addition, these questionnaires deal with six, eight and 16 rare diseases, respectively, which vary in their symptoms and their manifestations. I must finally acknowledge it as a feat to simultaneously carry out 17 national surveys. In the end, the three successive surveys (each with 6000 respondents) that have been conducted, each benefited from the experience of the previous, enabling access in the 17 countries involved, to the responses from patients themselves and not only from the heads of associations.

The interest in the data collected is that they come from the experiences of patients and the declaration of their needs and expectations with respect to medical and social services. It is therefore not surprising that they are focused on care and multiple services, both medical and social.

Having a rare disease presents specific questions that need to be answered in a specific manner. Thus this detailed analysis describes the experience of delays and access to good diagnoses and appropriate care as well as

the consequences for patients and their families. It also stresses the importance of the establishment of European Centres of Expertise and identifies the wrong paths that are sometimes taken. With respect to this point, incorrect diagnosis of psychiatric problems results in increasing the delay in obtaining the correct diagnosis and is particularly illuminating. The results show that it is necessary to consider the distance to centres of reference, the link to local structures, as well as the differences that exist between countries.

Additionally, these results show that problems faced by these patients and the responses to them are not specific to rare diseases and that they exist for many other medical problems. Therefore results also have an additional value and can contribute to better understanding and responding to the needs and expectations of all patients in our societies.

Concerning the medical issues, particularly the problems associated with the announcement of the disease, recent work suggests that this is best done by doctors who have some knowledge of the disease, its treatment and its prognosis. This is also true in defining the role of general practitioners confronted with diseases, rare or less rare, for which they do not have adequate knowledge; the solution could be found by collaboration between generalists and specialists.

Concerning the social issues, similarly these surveys describe the difficulties these patients have in maintaining their professional activities, the necessity that family members stop work to take care of the patient and the travel or relocation required. Such difficulties are also experienced by a significant number of patients suffering from any chronic disease.

The wealth of information provided by this work is twofold, firstly for rare disease patients but also for all other patients and for those in associations who are struggling in each country to improve care and the conditions of their daily lives.

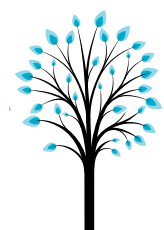
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* GRAM - Groupe de Réflexion avec les Associations des Malades (Think tank with Patient organisations)



Preface

This book is the capstone to four years of hard work and diligent research devoted to providing necessary information for healthcare authorities, healthcare professionals and patients' representatives to make well-informed public health decisions. It also marks the beginning of a new chapter in which true-life stories, statistics and the empathic nature of humankind are melded together to produce a meaningful and cohesive tool for rare disease patients, their families and caregivers to advocate for an improved quality of life for rare disease patients.

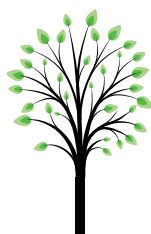
The survey data, from which the book evolved, was collected by EURORDIS under the EurordisCare Survey Programme. This programme was made possible by the support of public and private institutions such as the European Commission, the French Institute of Health and Medical Research (INSERM), the AFM-Telethon, Actelion Pharmaceuticals, OTL Pharma, Sigma Tau Pharmaceuticals and the health mutual fund UGIM. This ambitious programme would not have been possible without the dedication of hundreds of volunteers who shared their time, language skills, experience of living with a disease and their knowledge of national healthcare systems to reveal 'the voice of 12 000 patients'. In contrast to standard survey norms, the two EurordisCare surveys presented, EurordisCare2 and EurordisCare3, involved the survey population in all aspects of the survey's development.

Historically, the involvement of patients in public health research consisted solely of subject-based participation. This book, and the methodology behind it, regards patients differently. By encouraging patient input in the development, design and distribution of the surveys and treating them as de facto experts on their respective diseases and actors of their research, patient advocacy organisations like EURORDIS have successfully achieved a paradigm shift in the role of patients in the generation of quantitative data on their own health as well as on the provision of healthcare services.

Disenfranchised as a result of the rare nature of their diseases, rare disease patients had no choice but to become amongst the most empowered in the health community in order to attain a level of care to which all individuals are entitled. Rare disease patients and their representative organisations have already played an active role in shaping rare disease policies at national and European levels. Despite their involvement, a quantitative description of their experiences has largely been lacking from these policy-determining discussions. In this book, and the surveys upon which it is founded, patients were instrumental in the two investigations of (i) delays in diagnosis and (ii) unmet needs and expectations in medical and social services: two challenges faced by rare disease patients that may be overlooked by even the most dedicated non-patient stakeholders. While the publication of this book is a significant achievement in itself, it does not represent the experiences of all 30 million rare disease patients in Europe affected by one of the 5000 to 8000 rare diseases identified so far. The ultimate goal of accurate and comprehensive reporting of the needs and experiences of rare disease patients is within reach (as results in this book demonstrate), but not yet complete. We hope that this publication further inspires such investigations and helps shape policies on local, national and European levels that lead to a better quality of life for rare disease patients.

Yann Le Cam

*Chief Executive Officer
on behalf of the EURORDIS staff
and Board of Directors*



Acknowledgements

Main Contributors

This book was written by Anna Kole and François Faurisson¹, with significant contribution from Maria Mavris¹, editing by Christel Nourissier¹ and Flaminia Macchia¹, the collection of patient testimonies and patient organisation contributions by Teresa Sellan^{*2} and Gemma Loughheed¹, and the loving support of Edward and baby Mills^{*}.

The EurordisCare2 survey was designed and conducted by François Faurisson¹ and executed with the help of Simone Keita¹. Data entry was performed by Hervé Finel and statistical analysis by Sarah Zohar³.

The translation of open-ended questions regarding symptoms and diagnosis in EurordisCare2 was made possible by Eve Anderson (Sweden), Mette Bendix (Denmark), Fabrizia Bignami (Italy), Christina Black (Spain), Ingrid Palisson (the Netherlands), Alexandra Rudeanu (Romania), Sabine Schliechtig (Germany), Katja Silander (Finland) and Maria Wolaniecka (Poland). Florance Bastos^{1*} constructed the ad hoc database of symptoms for these questions.

The following people were members of the EurordisCare2 Advisory Committee:

Nora Ansell (UGIM), Fabrizia Bignami (EURORDIS), Bertrand Bonnot (Actelion), Bernard Dauvergne (OTL Pharma), Marie-Christine De la Morlais (Association Sclérose Tubéreuse de Bourneville), Jean Claude Delavier (UGIM), François Faurisson (EURORDIS), Christel Nourissier (Prader-Willi France), Françoise Salama (AFM) and Françoise Weber (Association Française du Syndrome de Marfan).

The EurordisCare3 survey was designed by Muriel Herasse¹ and François Faurisson¹. It was conducted by Muriel Herasse¹ with logistical support from Simone Keita¹ and Annie Rahajarizafy¹. Data entry was performed by members of Stefi. Patrice Régnier¹ created the informatics tool necessary for the analysis and presentation of results. Statistical analysis was performed by François Faurisson¹ with contribution from Sandrine Katzhahian³.

This report is one of the achievements of the Rare Disease Patient Solidarity Project RAPSODY, conducted by EURORDIS and its nine partners⁴. With the support of Public Health Programme of the European Commission (DG SANCO) and of Sigma Tau Pharmaceuticals, Actelion Pharmaceuticals and Groupe Initiatives Mutuelles UGIM.



The following people were members of the RAPSODY WorkPackage 5 Advisory Committee: Fabrizia Bignami (EURORDIS therapeutic development officer), Bertrand Bonnot (Actelion), Pierre Chauvin (Inserm U707, Epidemiology), François Faurisson (EURORDIS, RAPSODY EurordisCare project manager), Anja Helm (EURORDIS manager of relations with patient organisations), Muriel Hérasse (EURORDIS, RAPSODY EurordisCare project research assistant), François Houyez (EURORDIS health policy officer and RAPSODY project manager), Mathieu Lapprand (UGIM), Yann Le Cam (EURORDIS, chief executive officer and RAPSODY project leader), Sylvie Mayou (Ipsos), Rosa Sanchez (EURORDIS vice-president and RAPSODY EurordisCare project leader), Wendy Perrow (Sigma Tau Pharmaceuticals, Inc.) and Sarah Zohar (Inserm U717, Biomathematics).

Additional Contributions

Thank you to all National Alliances, patient organisations and patient organisation representatives for their voluntary contributions to the 'Results by Disease' and 'Results by Country' chapters.

Special Thanks

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1-EURORDIS; 2-Centro di Coordinamento Regionale delle Malattie Rare del Veneto; 3-INSERM Department of Biomathematics U717 Paris; 4-AFM Telethon, Barretstown, Climb, Federation Espanolas de Enfermedades Raras FEDER, Fundacio Doctor Robert, Frambu, Orphanet, Rare Disorders Denmark, State Institute for Drug Control SUKL
*volunteer

Organisations participating in **EurordisCare 2**

Marathon

Verein von Eltern und Angehörigen gegen Muskelkrankheiten bei Kindern

Fibrosis
Quística

Cystic fibrosis Finland



Duchenne Muscular Dystrophy Finland

Marfan Syndrome Finland



Interessengemeinschaft Fragiles-X e.V.

The Cystic Fibrosis
Association of Ireland(Deutschland) e.V.
gegründet 1991 - VR Stuttgart 5059MDI
MUSCULAR DYSTROPHY
IRELAND

DUCHENNE PARENT PROJECT

PWS Norway

ALAN
Association
L'association
d'aide pour les personnes
Atteintes de maladies Neuro-musculairesPrader-Willi
Angelman
Vereeniging

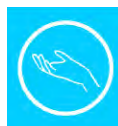
POLSKA



Asociatia Pentru o Viata Sanatoasa de Copilarie



APN

ASOCIATIA ROMANA
DE MUCOVISCOZA
ROMANIAPWS
PRADER WILLI SYNDROME

PWS



ASRIM

Organisations participating in **EurordisCare 2** and **EurordisCare 3**

ABM

Asociación Síndromes de
Ehlers-Danlos e Hiperlaxitud

Edf

SIMA
Societatea Internationala de Maladii de MușchiEhlers-Danlos - oireyhtymä
(Suomen Reumaliitto)

Fragile X oireyhtymä

Suomen
Tuberosisskleroosi
YhdistysVIVRE
MARFAN

Angelina

AFM
Association Française contre les Myopathies

PWS



Prader-Willi France



CF

Tuberos Sclerosis Deutschland e.V.
www.tuberosclerosis.de

VSN



PWS

APWR

ASOCIATIA PRADER WILLI ROMANIA



PWS

CF
RÍKSFÖRBUNDET
CYSTISK FIBROSIS

EDS

EDS Riksförbundet Sverige



PWS



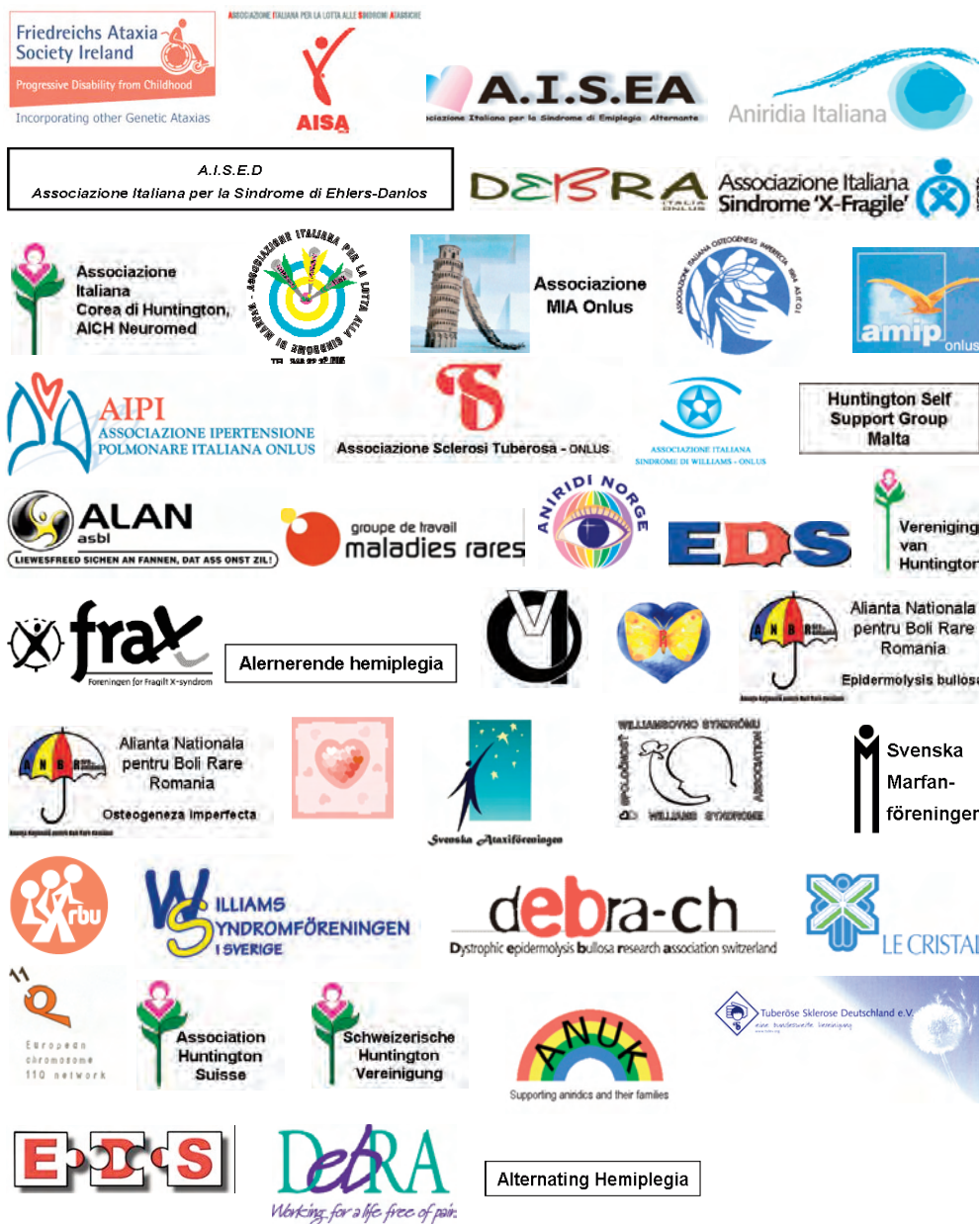
PWS-Sverige i Sverige

PWS
Prader-Willi Syndrome Association (UK)

marfan

The Fragile X Society





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Contributing Organisations

EurordisCare2

Crohn's Disease

Austria: Österreichische Morbus Crohn - Colitis Ulcerosa Vereinigung - **Finland:** CCAFIN Crohn ja Colitis ry organization - **France:** Association François Aupetit - **Portugal:** Associação Portuguesa da Doença Inflamatória do Intestino - **Switzerland:** SMCCV – ASMCC.

Cystic Fibrosis

Belgium: Belgische Vereniging voor Strijd tegen Mucoviscidose - **Finland:** Cystic Fibrosis Finland - **France:** Vaincre la Mucoviscidose - **Germany:** Wissenschaftsreferat Mukoviszidose e.V. - **Ireland:** The Cystic Fibrosis Association of Ireland - **Italy:** Lega Italiana Fibrosi Cistica - **Romania:** Asociatia Romana de Mucoviscidoza Timisoara - **Spain:** Federación Española contra la Fibrosis Quística - **Sweden:** Riksförbundet Cystick Fibros.

Duchenne Muscular Dystrophy

Austria: Marathon Verein von Eltern und Angehörigen gegen Muskelkrankheiten bei Kindern - **Belgium:** Association Belge contre les Maladies Musculaires - **Denmark:** Muskelsvindfonden - **Finland:** Duchenne Muscular Dystrophy Finland - **France:** Association Française contre les Myopathies - **Germany:** Deutsche Gesellschaft für Muskelkranke e.V - **Ireland:** Muscular Dystrophy Ireland - **Italy:** Duchenne Parent Project - **Netherlands:** Dutch Association for Neuromuscular Diseases - **Portugal:** Associação Portuguesa de Doentes Neuromusculares - **Spain:** Asociación Española de Enfermedades Musculares - **Switzerland:** Association de la Suisse Romande et Italienne contre les Myopathies - **United Kingdom:** Duchenne Family Support Group.

Ehlers Danlos Syndrome

Denmark: Ehlers - Danlos Foreningen i Danmark - **Finland:** Ehlers - Danlos Finland - **France:** Association Française des Syndromes Ehlers - Danlos - **Spain:** Asociación Sindromes de Ehlers - Danlos e Hiperlaxitud - **Sweden:** Ehlers - Danlos Syndrom Riksförbund.

Fragile X Syndrome

Belgium: Association X Fragile Belgique - **Finland:** Fragile X Finland - **France:** Le Goëland Association Nationale du X - Fragile - **Germany:** Interessengemeinschaft Fragiles - X e.V. - **Switzerland:** Association Suisse du Syndrome de l'X Fragile - Le Cristal - **Sweden:** Swedish Association Fragile X - **United Kingdom:** Fragile X UK.

Marfan Syndrome

Belgium: Association Belge du Syndrome de Marfan - **Finland:** Marfan Syndrome Finland - **France:** Association Française du Syndrome de Marfan - **Germany:** MarfanHilfe (Deutschland) e.V. - **Poland:** MarFan Polska - **Spain:** Asociación de Afectados Síndrome de Marfan - **Switzerland:** Marfan Stiftung Schweiz.

Prader - Willi Syndrome

Austria: Österreichische Gesellschaft Prader - Willi Syndrom - **Belgium:** Prader Willi Vereniging vzw - **Denmark:** Landsforeningen for Prader Willi Syndrom - **Finland:** Suomen PWS yhdistys ry - **France:** Prader Willi France - **Italy:** Associazione per l'Aiuto ai Soggetti Prader - Willi ed alle loro Famiglie - **Netherlands:** Prader - Willi/Angelman - Vereniging - **Poland:** Polskie Stowarzyszenie Pomocy Osobom z Zespołem Pradera - Willego - **Romania:** IPWSO - **Spain:** Asociación Valenciana Prader-Willi - **Sweden:** PWS - föreningen i Sverige - **Switzerland:** Schweizerische Prader - Willi - Syndrom Vereinigung - **United Kingdom:** Prader - Willi Syndrome Association UK.

Tuberous Sclerosis

Finland: Tuberous Sclerosis Finland - **France:** Association Française Sclérose Tubéreuse de Bourneville **Germany:** Tuberöse Sklerose Deutschland e.V - **Netherlands:** STSN - **Poland:** Tuberous Sclerosis Poland - **Sweden:** Svenska Föreningen för Tuberös Skleros

Contributing Organisations

EurordisCare3

Alternating Hemiplegia

Denmark: AHC - foreningen i Danmark - **France:** Association Française Hemiplegie Alternante (AFHA) - **Germany:** AHC Deutschland e.V. - **Italy:** Associazione Italiano per la Sindrome die Emiplegia Alternante - (AISEA) ONLUS. - **Netherlands:** AHC - Vereniging Nederland - **Spain:** Asociación Española del Síndrome de la Hemiplejía Alternante (AESHA).

Aniridia

Cyprus: Health professional - **Denmark:** Patients' families - **France:** Aniridie et pathologies rares de l'Iris 'Gêniris' - **Italy:** Associazione Aniridia Italiana - **Norway:** Aniridi Norge - **Spain:** Asociación Española de Aniridia.

Ataxias

Finland: Ataksia - Suomen MS - liitto ry - **France:** Association Française de l'Ataxie de Friedreich (AFAF); Connaître les Syndromes Cérébelleux (CSC) - **Ireland:** Friedreich's Ataxia Society of Ireland - **Netherlands:** Vereniging Spierziekten Nederland (VSN) - **Spain:** Federación de Ataxias de España (FADAES); Asociación Catalana de Ataxias Hereditarias - **Sweden:** Svenska Ataxiföreningen.

Chromosome 11 Disorders

Europe: European Chromosome 11q Network

Cystic Fibrosis

Croatia: Hrvatska udruga za cisti nu fibrozu - **Czech republic:** Cystic Fibrosis Czech republic- **France:** Vaincre la Mucoviscidose - **Hungary:** Országos Cisztás Fibrózis Egyesület (OCFE) - **Italy:** Associazione Sclerosis Tuberosa ONLUS - **Spain:** Asociación Catalana de Fibrosis Quística - **Sweden:** Riksförbundet Cystick Fibros.

Ehlers-Danlos Syndrome

Austria: SHG Ehlers Danlos Syndrom - **Belgium:** Kontaktgroep Marfan/Ehlers Danlos, Groupe d'entraide Syndromes Ehlers - Danlos - (GESED) - **Denmark:** Ehlers Danlos foreningen i Danmark - **Finland:** Ehlers - Danlos - oireyhtymä (Suomen Reumaliitto) - **France:** Association Française des Syndromes d'Ehlers - Danlos (AFSED) - **Germany:** Deutsche Ehlers - Danlos - Initiative e.V. - **Italy:** Associazione Italiana per la Sindrome di Ehlers - Danlos (AISED) - **Norway:** Norsk Forening for Ehlers - Danlos syndrom - **Spain:** Asociación Sindromes de Ehlers - Danlos e Hiperlaxitud - **Sweden:** EDS Riksförbund Sverige - **United Kingdom and Ireland:** Ehlers Danlos Syndrome Support Group.

Epidermolysis Bullosa

Belgium: DEBRA - Belgium (vzw – asbl) - **Croatia:** DEBRA - Croatia - Hrvatsko - drustvo za buloznu epidermolizu - **Finland:** Epidermolysis bullosa - Iholiitto - **France:** DEBRA - France Epidermolyse Bulleuse Association d'Entraide (EBAE) - **Hungary:** DEBRA - Hungary - DebRA Magyarországon - **Italy:** DEBRA Italia Associazione per la Ricerca sull'Epidermolisi Bollosa Distrofica ONLUS - **Romania:** Alianta Nationala pentru Boli Rare Romania - **Spain:** Asociación de Epidermolisis - Bullosa de España (AEBE - DEBRA) - **Switzerland:** DEBRA - CH - **United Kingdom:** DEBRA – UK.

Fragile X Syndrome

Belgium: Association X Fragile Belgique - **Cyprus:** Health professional - **France:** Le Goëland Association Nationale du X - Fragile - **Italy:** Associazione Italiana Sindrome X - Fragile ONLUS - **Norway:** Foreningen for Fragilt X - syndrom (fraX) - **Spain:** Asociación del Síndrome X - Frágil de Madrid (ASXFM); Asociación Síndrome X Frágil de Cataluña - **Sweden:** Föreningen Fragile - X - **Switzerland:** Association Suisse du Syndrome de l'X - Fragile : Le Cristal - **United Kingdom:** The Fragile X Society.

Huntington's Disease

Austria: Österreichische Huntington Hilfe - **Belgium:** Huntington Liga vzw België; Ligue Huntington Francophone Belge - **Denmark:** Landsforeningen mod Huntingtons Chorea i Danmark - **France:** Fédération Huntington Espoir - **Italy:** AICH Neuromed - Associazione Italiana Corea di Huntington - **Luxembourg:** ALAN asbl. & Groupe de travail maladies rares - **Spain:** Asociación Catalana de la Enfermedad de Huntington (ACMAH) - **Switzerland:** Association Huntington Suisse / Die Schweizerische Huntington Vereinigung (AHS – SHV).

Marfan Syndrome

Belgium: Association Belge du Syndrome de Marfan - **Denmark:** Landsforeningen for Marfan Syndrom - **France:** Association Française du Syndrome de Marfan - **Italy:** Associazione Italiana per la lotta alla sindrome di Marfan e patologie correlate - **Luxembourg:** ALAN asbl. & Groupe de travail maladies rares - **Spain:** Asociación de Afectados Síndrome de Marfan (SIMA) - **Sweden:** Svenska Marfan föreningen - **Switzerland:** Marfan Foundation SWI (Marfan Stiftung Schweiz).

Myasthenia

Cyprus: Health professional - **France:** Association Française contre les Myopathies (AFM) - groupe Myasthénie - **Hungary:** Myasthenia Gravis Önségít Betegcsoport - **Italy:** Associazione Italiana Miastenia (AIM) ONLUS - **Luxembourg:** ALAN asbl. & Groupe de travail maladies rares - **Netherlands:** Vereniging Spierziekten Nederland (VSN) - **Spain:** Asociación Española de Miastenia (AEM); Asociación española de Enfermadades Musculares (ASEM) Cataluña.

Osteogenesis Imperfecta

Belgium: Zelfhulp Osteogenesis Imperfecta - **Denmark:** Dansk Forening for Osteogenesis Imperfecta - **Finland:** Suomen Osteogenesis Imperfecta - Yhdistys - **France:** Association Française de l'Ostéogénèse Imparfaite (AOI) - **Italy:** Associazione Italiana Osteogenesi Imperfetta (As.It.O.I.) ONLUS - **Netherlands:** Vereniging Osteogenesis Imperfecta - **Romania:** Alianta Nationala pentru Boli Rare Romania - **Sweden:** Riksförbundet för Rörelsehindrade Barn och Ungdomar (Osteogenesis imperfekta).

Prader-Willi Syndrome

Cyprus: Health professional - **Czech Republic:** Patients' group - **France:** Prader Willi France - **Hungary:** Prader - Willi Baráti Társaság - **Italy:** Associazione per l'Aiuto ai Soggetti Prader - Willi ed alle loro Famiglie **Luxembourg:** ALAN asbl. & Groupe de travail maladies rares - **Romania:** IPWSO - **Spain:** Asociación Española para el Síndrome de Prader - Willi (AESPW); Asociación Catalana síndrome de Prader - Willi (ACSPW) - **Sweden:** PWS - föreningen i Sverige - **United Kingdom:** Prader - Willi Syndrome Association UK.

Pulmonary Arterial Hypertension

Austria: Selbsthilfegruppe Lungenhochdruck - **Denmark:** PAH Denmark - **France:** Association Hypertension Artérielle Pulmonaire France (HTAPF) - **Germany:** Pulmonale Hypertonie e.v. (PHeV) - **Greece:** Association of support and mutual help for sufferings from Pulmonary Hypertension - **Italy:** Associazione Ipertensione Polmonare Italiana (APII) ONLUS; Associazione Malati Ipertensione Polmonare (AMIP) ONLUS - **Netherlands:** PHA Nederland.

Tuberous Sclerosis

Denmark: Dansk forening for Tuberøs sclerose - **Finland:** Suomen Tuberosisskleroosi Yhdistys - **France:** Association Française Sclérose Tubéreuse de Bourneville - **Germany:** Tuberöse Sklerose Deutschland e.V. - **Greece:** TSA Greece - **Hungary:** Sclerosis tuberosa Baráti Társaság - **Italy:** Associazione Scleroti Tuberosa (AST) ONLUS - **Luxembourg:** ALAN asbl. & Groupe de travail maladies rares - **Spain:** Asociación Esclerosis Tuberosa de Madrid.

Williams Syndrome

Belgium: vzw Williams - Beuren syndroom; Association Belge du Syndrome de Williams - **France:** Association Française du syndrome de Williams et Beuren (ASWB France) - **Germany:** Bundesverband Williams - Beuren Syndrom (BV - WBS) - **Hungary:** Magyar Williams Szindróma Társaság - **Italy:** Associazione Italiana Sindrome di Williams (AISW) ONLUS - **Luxembourg:** ALAN asbl. & Groupe de travail maladies rares - **Romania:** Asociata Williams Syndrome - **Slovakia:** Spolocnost Williamsovho Sydrumu - **Sweden:** Williams Syndromforeningen.



Introduction

Understanding Rare Diseases as a Public Health Priority

The concept of ‘rare diseases’ was first introduced when several pathologists, specialising in metabolic diseases, made apparent that many rare diseases, although diverse, exhibit common problems with respect to recognition and management^{1,2,3}. In 1983, the passing of the FDA Orphan Drug Act in the US (in which a rare disease or condition was defined as less than 200 000 persons in the United States) reflected the recognition of a specific need to encourage the development of drugs that, whilst being necessary, would remain undeveloped under normal market conditions. This recognition followed in Europe with the European Union (EU) Orphan Drugs Regulation, in which a disease or disorder is defined as rare when it affects less than five per 10 000 citizens^{4,5}. While this number seems small, it translates into an estimated 29 million people affected by rare diseases across all 27 EU member states. Rare diseases are often chronic, progressive, degenerative, life-threatening and disabling diseases. Although they are diverse in their clinical manifestations, causes, populations they affect, severity and age of onset, the majority have identified genetic origins. Non-genetic rare diseases also exist and may be the result of bacterial or viral infections, allergies and environmental causes, or may have a degenerative or proliferative basis. Most rare diseases are of such low prevalence (often affecting one per 100 000 citizens or less) that they receive little attention, as do the individuals who suffer from them. As such, concerted efforts are required to prevent significant morbidity, perinatal or early mortality, or a considerable reduction in an individual's quality of life or socioeconomic potential.

1-PEDIATRICS Vol. 62 No. 6 December 1978, pp. 1056-1060; 2-D. N. Raine, ‘The need for a national policy for the management of inherited metabolic disease’. *J Clin Pathol Suppl (R Coll Pathol)*, 1974; 8: 156-163; 3-D N Raine. ‘Management of inherited metabolic disease’. *Br Med J*, 1972 May 6; 2(5809): 329-336; 4-EC Regulation 141/2000 on Orphan Medicinal Products; 5-Several MS use more restrictive definitions.

As stated in the World Health Organization (WHO) Constitution, ‘the enjoyment of the highest attainable standard of health is one of the fundamental rights of every human being without the distinction of race, religion, political belief, economic or social condition’, where health is defined as ‘a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity’⁶. Health authorities, healthcare providers, patients and their organisation representatives all agree that rare disease patients are denied this right and are all confronted with similar obstacles in attaining the highest possible standards of health including: (1) lack of scientific knowledge of their disease, (2) lack of access to correct diagnosis, (3) delays in diagnosis, (4) lack of appropriate multidisciplinary healthcare, (5) lack of quality information and support at the time of diagnosis, (6) undue social consequences, (7) inequities and difficulties in access to treatment, rehabilitation and care, (8) dissatisfaction with and loss of confidence in medical and social services and (9) rejection by health professionals.

EURORDIS’ mission is to facilitate participation of patients in patient groups and to federate these patient groups with the goal of achieving a more powerful unified voice. Having heard this united patient voice, in addition to suggestions from rare disease experts and national health authorities, the European Commission has recognised the common concerns related to rare diseases as a public health issue. It has been agreed that a multidisciplinary coordinated approach, including specialised social services, is necessary to improve the health and well-being of rare disease patients throughout Europe. The European Commission has proven its dedication to the support of rare diseases by enacting several European regulations and other initiatives that stress the importance of rare diseases as a key priority. These include the EU Regulation on Orphan Drugs (1999), EU Regulation on Paediatric Drugs (2006), Programme of Community Action in the Field of Public Health (2007-2013), EU Seventh Framework Programme for Research (2007-2013) and most recently the Communication on a European Action on Rare Diseases, amongst others. Despite these positive efforts at the European Commission level as well as those at the national level, challenges still remain for rare disease patients to obtain a correct diagnosis and equal access to care.

Diagnosis of Rare Diseases

The difficulty in obtaining the correct diagnosis is the first dramatic hurdle for rare disease patients and may take years or even decades to overcome. Late diagnoses delay the beginning of adapted treatments and can have severe irreversible, debilitating and life-threatening consequences. When seeking diagnosis, patients frequently consult numerous doctors, undergo multiple examinations and often receive various incorrect diagnoses resulting in inefficient and even harmful treatments. Additionally, relatively common symptoms can hide underlying rare diseases, leading to misdiagnosis. The individual consequences of improper diagnosis include the worsening in clinical status^{7,8,9} psychological damage¹⁰ often related to medical denial of the undiagnosed disease and, in some cases, death¹¹.

In addition, families endure other consequences, including lifelong feelings of guilt due to inappropriate behaviour towards the affected person prior to diagnosis or the possible birth of additional affected siblings.

Without diagnosis, a patient's medical or social needs may not receive due attention and the patient may be considered a complainer who, as a result, progressively loses confidence in medicine¹². Also, the accumulation of consultations, examinations, tests and inefficient treatments are a major financial burden for both families and society.

The delay in diagnosis for many rare diseases has scarcely been studied despite its obvious public health importance. As delays in diagnosis and subsequent consequences can vary greatly depending on the disease, the country and other individual factors, a EURORDIS survey (EurordisCare2) was launched to provide quantitative evidence on delays in diagnosis in 17 countries and investigate its main causes.

Barriers in Access to Medical and Social Services

Barriers in access to care exist for all populations in all contexts. Those affecting access to care in the rare disease community can be summarised as: barriers in scientific knowledge, organisational barriers, financial barriers and personal barriers. A lack of incentive for publicly driven research on rare diseases compared to more common diseases has resulted in a delay in fundamental scientific knowledge needed to establish appropriate treatment, whether through drug therapy or other medical attention. The causes and mechanisms for the majority of rare diseases are not well-understood, resulting in under-diagnosis, misdiagnosis or delays in diagnosis and making treatment even more difficult. Without correct diagnoses, people with rare diseases are not yet considered rare disease patients and are thus restricted in their ability to seek appropriate medical attention and social assistance in their respective healthcare systems. A health professionals' unfamiliarity with a rare disease also leads to a lack of referral to specialised services due to an inability to identify what is appropriate but also a lack of knowledge about what potential services may be needed or available.

Even if correctly diagnosed, no good clinical practice guidelines exist for the vast majority of rare diseases. Where they do exist, their practice varies from country to country due to differences in medical school curricula. Additionally, the segmentation of medical specialties is a barrier to the multidisciplinary care of a patient suffering from a rare disease.

6-Preamble to the Constitution of the World Health Organization as adopted by the International Health Conference, New York, 19-22 June, 1946; signed on 22 July 1946 by the representatives of 61 States (Official Records of the World Health Organization, no. 2, p. 100) and entered into force on 7 April 1948; 7-Accurso FJ, Sontag MK, Wagener JS. 'Complications associated with symptomatic diagnosis in infants with cystic fibrosis'. *J Pediatr* 2005;147(3 Suppl):S37-41; 8-Bennett FC, Guralnick MJ. 'Effectiveness of development intervention in the first five years of life'. *Pediatr Clin North Am* 1991;38(6): 1513-28; 9-Vogels A, Fryns JP. 'Age at diagnosis, body mass index and physical morbidity in children and adults with Prader-Willi syndrome'. *Genet Couns* 2004;15(4):397-404; 10-Merelle ME, Huisman J, Alderden-van der Vecht A, Taat F, Bezemer D, Griffioen RW, et al. 'Early versus late diagnosis: psychological impact on parents of children with cystic fibrosis'. *Pediatrics* 2003;111(2):346-50; 11-Manusov EG, Martucci E. 'The Marfan syndrome. An underdiagnosed killer'. *Arch Fam Med* 1994;3(9):822-6; 12-Kharrazi M, Kharrazi LD. 'Delayed diagnosis of cystic fibrosis and the family perspective'. *J Pediatr* 2005;147(3 suppl):S21-5.

Services required by rare disease patients are often inadequately available and unadapted due to the fact that they are not covered by their respective healthcare systems (i.e. psychotherapy, occupational therapy, dental care, optics, nutrition). This is especially true for social services. Social security systems are usually designed around common diseases and are not flexible enough to take into consideration unprecedented health needs. This is also true for adjusting reimbursements.

Physical barriers to access often affect rare disease patients with physical or mental disabilities. As services are not abundant, patients have to travel far for care or endure long periods of waiting. As a result of the aforementioned difficulties in obtaining correct diagnoses or appropriate care, patients experience frustration with the medical field in general, feeling rejected by their healthcare providers and eventually losing confidence in the medical system. The financial costs of caring for rare disease patients are often higher than those for common diseases on which most home healthcare services are based. Having to stop working either as a patient or to take care of an affected family member creates further financial burdens.

The Patient's Voice

Difficulties in obtaining correct diagnoses and barriers to access to care have been somewhat reported by health authorities and healthcare professionals¹³. To date, the patient's voice has been documented by qualitative descriptions of experiences and expectations. EURORDIS surveys give patients the opportunity to have their voice directly represented in a quantitative way. These surveys only quantify the responses of those patients who participated, and although the results of these surveys can only be extrapolated for other rare disease patients in Europe with caution, they can provide an acceptable picture of the experiences and expectations of rare disease patients at large in Europe. As no survey addressing rare diseases has previously been conducted on this scale, it will serve as an important precedent to quantitative documentation of the problems faced by patients of the 18 diseases investigated, and shed light onto some of the problems that other rare disease patients and their caregivers face.

The surveys presented in this book were conducted by patients, for patients. They are not epidemiological observational studies but a community survey performed by members of the community described. EURORDIS' mission is to enable patients to express themselves and to report their voice collectively.

EurordisCare Survey Programme

Surveys are particularly useful when researchers are interested in collecting data on aspects of behaviour that are difficult to observe directly and when it is desirable to sample a large number of subjects. Despite common aspects

and struggles, rare diseases are as diverse as the patients that suffer from them. Three surveys, EurordisCare1, EurordisCare2 and EurordisCare3 make up the EURORDIS Survey Programme, with the ultimate goal of contributing to the establishment of standards and guidelines for the management of rare diseases throughout Europe and promoting equal and adequate access to diagnosis, care and treatment for rare disease patients in all European countries. An ever-evolving process, lessons learnt from each survey helped shape the methodology for the next.

Rare disease care varies from one European country to another. While economic policy, cultural preferences and political systems explain some of these differences, the EurordisCare1 survey was designed to identify and measure these differences through a questionnaire focusing on diagnosis, treatment, level of knowledge, and the need and provision of health services for rare diseases. The lack of knowledge about rare diseases by the general public and health professionals was further investigated as a contributing factor to the unequal availability and quality of care for rare disease patients in the EurordisCare2 survey. Despite being well known throughout the rare disease community, the consequences of this lack of information have not been well documented. As a result of the poorly documented nature of these consequences, EurordisCare2 was launched to identify the main causes of delay in diagnosis, subsequent delays in the introduction of necessary treatments, possible untreated progression of the disease and severe, potentially preventable consequences.

Stakeholders have agreed that the establishment of Centres of Expertise in European countries and the coordination of these centres through the establishment of European Reference Networks are key solutions in addressing not only the unmet needs of patients in effectively reaching a diagnosis of their disease, but also the barriers they experience in accessing medical and social care. In the context of stakeholder discussions on this subject, a quantified description of the experience and needs of patients was greatly lacking. As crucial stakeholders in the development of a set of recommendations for the creation and development of national Centres of Expertise and European Reference Networks, the patient's perspective is now represented by the collection of data on these topics in the EurordisCare3 survey.

Through this book, the direct voice of patients will shape policy. As such, the survey's purpose is twofold: first, stakeholders finally benefit from having a collective patient voice through the surveys; second, patients and participating patient organisations learned from their experience by learning about the administration of surveys, the random sampling process, analysis and key issues concerning other rare disease patients.

To address the common challenges concerning timely and accurate diagnoses and accessible and quality medical and social services, stakeholder discussions have revolved around the encouragement of national plans on rare disease in which the organisation of rare disease care is structured around Centres of Expertise and European Reference Networks.

Centres of Expertise and European Reference Networks

The European Commission Directorate General of Health and Consumers (DG SANCO) has recognised the importance of establishing Centres of Expertise at the national level and the European added value of supporting European Reference Networks. Following a reflection process on patient mobility, the DG SANCO established the High Level Group on Health Services and Medical Care - Working Group on Centres of Expertise and European Reference Networks. DG SANCO equally supports the Rare Disease Task Force Working Group on Standards Care, which has produced two reports on the subject¹⁴. Although there is no common definition of a Centre of Expertise among member states¹⁵, many have identified hospitals that serve as physical expert structures for rare diseases patients.

The establishment of a Centre of Expertise for each rare disease in each country in Europe is, however, an unrealistic goal. The creation of European Reference Networks, physical or virtual networking of knowledge and expertise, would provide the potential for an even higher added value, while respecting the responsibility of member states for the organisation and management of their healthcare systems. As exemplified by the Pilot European Reference Network projects supported by the European Commission¹⁶, such networking between Centres of Expertise has major potential in (i) overcoming the limited experience of professionals confronted with very rare diseases, (ii) improving access for European citizens to treatment and care, (iii) offering patients the highest possible chance of success through the sharing of expertise and resources, (iv) maximising cost-effective use of resources, (v) helping to share knowledge and provide training for health professionals, (vi) acting as benchmarks to help develop and spread best practices throughout Europe and (vii) helping small countries with insufficient resources to provide a full-range of high-quality specialised services¹⁷.

EURORDIS' Reflection Process

EURORDIS began its reflection process on this issue in April 2006 at its annual membership meeting in Berlin, which was dedicated to 'Centres of Reference for Rare Diseases: How Can We Make It Happen?' Based on these debates, a 'Reflection Paper on Centres of Expertise' was adopted. Since that time, EURORDIS' national alliances and their members have worked together extensively on promoting the need for specialised, multidisciplinary health services for rare disease patients and in facilitating the development of common concepts, a common language and common strategies.

Their efforts have resulted in the EURORDIS position paper on 'Centres of Expertise and European Reference Networks for Rare Diseases'¹⁸, one of four specific topics addressed in EURORDIS' response to the European Commission's Public Consultation for Commission Communication

on Rare Diseases. This document, together with the founding text ‘Rare Diseases: Understanding This Public Health Priority’,¹⁹ have been elaborated thanks to a broad consultation of EURORDIS members and widely disseminated to all stakeholders and policymakers. In the context of the European Commission-funded Rare Disease Patient Solidarity project (RAPSDODY), 11 national workshops were organised to gather the recommendations of over 270 patient representatives, healthcare professionals and policymakers on Centres of Expertise and European Reference Networks. In parallel, the EurordisCare3 survey was launched in part to collect solid data on the experiences and expectations of rare disease patients and their families. The Fourth European Conference on Rare Diseases in Lisbon in November 2007 provided an occasion to report and debate with a larger audience on the positions of policymakers in the High Level Group on Health Services and Medical Care - Working Group on European Reference Networks. Finally, through a plenary discussion and focused workshop during the annual membership meeting in Copenhagen in May 2008, a ‘Declaration of Common Principles on Centres of Expertise and European Reference Networks’ (Appendix 1), describing the basic key principles of Centres of Expertise, was voted on and adopted. The declaration aims to ensure that patients have access to equal care and services wherever they are living in Europe through Centres of Expertise that shall facilitate the coordination of the multidisciplinary management of rare diseases, provide accurate diagnosis, facilitate access to social assistance, coordinate research activities and infrastructures, share their knowledge at the national and European levels, and last but not least, make patients feel welcome and safe, including them in their own management and evaluation.

This Book

Healthcare authorities need quantified data to make public health decisions. To go beyond patients’ anecdotes and investigate experience-based opinions in a quantitative way, the EurordisCare2 and EurordisCare3 surveys were intended to contribute to shaping patient-centred public health policies by describing and comparing patients’ experiences and expectations regarding (i) diagnosis and (ii) access to health services for 18 significantly relevant rare diseases across Europe. Although this is not an epidemiological analysis of the access and diagnosis of rare diseases, it is a valid synthesis of patient opinion, which should be included in the debate. The information provided in this book should be used as an information and advocacy tool in which the collective opinion of 12 000 rare disease patients is expressed.

14-www.rdtf.org; 15-‘Centres of Reference for rare diseases in Europe: State-of-the-art in 2006 and recommendations of the Rare Disease Task Force’, ec.europa.eu/health/ph_threats/non_com/docs/contribution_policy.pdf; 16-ec.europa.eu/health/ph_threats/non_com/rare_8_en.htm#1; 17-‘Centres of Reference for rare diseases in Europe: State-of-the-art in 2006 and recommendations of the Rare Disease Task Force’, ec.europa.eu/health/ph_threats/non_com/docs/contribution_policy.pdf; 18-eurordis.org/IMG/pdf/position-paper-EURORDIS-centres-excellence-networksFeb08.pdf; 19-eurordis.org/IMG/pdf/princeps_document-EN.pdf



The EurordisCare Survey Programme

Lessons Learnt from EurordisCare1

The first EurordisCare Programme survey, EurordisCare1, was conducted and analysed between November 2002 and April 2003. Its aim was to describe the experiences of rare disease patients in accessing medical services and treatment. At the time, it was considered that patient organisation representatives were the best study participants as they were not only often patients themselves, but also because they were able to integrate the experiences of, and directly represent other patients with their disease. Patient organisations were also considered more capable of responding to questions about access to services than health authorities, who are more familiar with the availability of medical services and treatments, therefore likely to underestimate limitations, such as a lack of quality of services and barriers to accessing these services (e.g. long waiting times and excessive personal cost to the patient). A 16-page questionnaire was sent to 50 European patient organisations in 17 countries covering six rare diseases: Prader-Willi syndrome (PWS), Marfan syndrome (MFS), Crohn's disease (CD), Duchenne muscular dystrophy (DMD), tuberous sclerosis (TS) and cystic fibrosis (CF) (*Table 1*). Each patient organisation designated representatives to fill out the questionnaire.

After participating in the survey, patient organisation representatives provided valuable input regarding the survey design and implementation:

- 1** - Patient organisation representatives found that some questions were difficult, or even impossible, to respond to due to inadequate knowledge of medical services provided for subtypes of their disease. In addition, there was a lack of information about treatment due to the high variability of drugs and their dosage.
- 2** - Patient organisation representatives were unable to quantify access to services, resulting in qualitative responses such as 'Physiotherapy is often difficult to obtain.' The variability of responses was difficult to evaluate.
- 3** - As the questionnaire was available in only six languages, some representatives had difficulty filling out the questionnaire.
- 4** - During discussions with a larger audience of organisation members, results were criticised as too optimistic. Many ordinary members of patient organisations felt that because many of the representatives designated to fill out the questionnaire were members of the board of their respective organisations, they were more informed as patients and underestimated the difficulty in accessing services that other patients experienced.
- 5** - Many comments were made on the questions themselves and these were taken into account when designing future surveys.

Other limitations of the EurordisCare1 study were identified. Questioning only one representative of each patient organisation resulted not only in a bias of sampling in terms of the level of information on services, but also in the representation of subtypes of each disease studied. Some concepts such as the availability of drugs were difficult to survey.

Due to the high number of treatments used, it was not possible to make a simple list of medications for survey participants to check off. The open-ended nature of this question resulted in mistakes in drug names and variability of brand names in different countries, amongst other misunderstandings. In general, survey participants did not have the opportunity to provide comments explaining the extent of the variability for certain investigated experiences. Finally, the translation of the questionnaire into six languages and retranslation of open-ended responses into a common language was a challenging process that may have introduced some errors.

	EurordisCare1	EurordisCare2	EurordisCare3
Date of execution	Nov 2002-Apr 2003	Sept 2003-June 2006	May 2006-April 2008
Source of information	Patient organisations	Patients	Patients
Length of questionnaire	16 pages	4 pages	4 pages
Number of diseases covered	6	8	16
Patient organisations involved	50	70	130
Countries covered	17	16	22
Languages of questionnaire	6	12	15
Responses	50 patient organisations	5980 patients (18 000 questionnaires distributed by patient organisations)	5995 patients (20 000 questionnaires distributed by patient organisations)

Table 1 Characteristics of the three surveys

EurordisCare2 and EurordisCare3

The EurordisCare2 study was carried out from September 2003 to June 2006 and encompassed eight diseases in 16 European countries.

The EurordisCare3 survey was conducted as part of a larger EURORDIS European Commission project, RAPSODY, between May 2006 and April 2008.

Despite the logistical convenience of surveying patient organisation representatives, it was decided, based on the experiences of and the lessons learnt from the EurordisCare1 survey, that for the EurordisCare2 and EurordisCare3 surveys patients themselves would be questioned directly. A larger sample of patient participants would enable the analysis of a more diversified target population thus representing a more accurate reality. With a survey sample possessing more diversity in characteristics such as age, gender, nationality and social status, a greater variability of responses could be obtained and potential associations between clinical experiences and demographic characteristics could be made (*Table 1*).

Involvement of Patient Organisations in EurordisCare2 and EurordisCare3

In order to most fairly represent the interest of all patients with rare diseases, the central themes of the surveys were initially discussed and suggested by the EURORDIS board of directors. The content of the questionnaire was subsequently designed by the EURORDIS staff in close collaboration with patient organisation representatives concerned by the diseases investigated. Many topics, such as the non-medical consequences of a delay in diagnosis and the rejection of patients by health professionals, illustrate the invaluable contribution of patient organisations in this programme. Without their contribution, these topics would have not been investigated.

Although no longer the direct source of information in the study, patient organisation representatives still played a crucial role in the design and implementation of both surveys. Not only were patient organisation representatives directly involved in the selection of explored topics, but they were also responsible for the evaluation of the comprehensibility of the questions. Secondly, the involvement of patient organisations enabled an innovative circuit of information. Questionnaires prepared by the EURORDIS staff were sent to patient organisations, which, using their own lists of patient members sent the questionnaires to individual patients. In this way, patients were invited to participate in the survey by someone they knew, therefore improving the number of responses received. Patients who filled out the questionnaire then returned it directly to EURORDIS anonymously. Distributing surveys via patient organisations guaranteed the inclusion of respondents with the specific disease in question without the necessity of identifying individual patients, thus maintaining total respect for the patients' privacy.

Thirdly, the close collaboration with patient organisations and the direct involvement of patients themselves made survey respondents more than observed subjects in a study but rather invested members of a large study team. Their contribution resulted in many aspects of the study design,

including translation of the survey and responses to open-ended questions, the addition of the patient organisation's logo on the questionnaire and the provision of prepaid envelopes, which resulted in a high response rate and quality participation despite the 40 to 60 minutes required to complete the questionnaire.

Why These 18 Diseases?

EURORDIS used a combined approach in its inclusion of diseases in the survey. First, the diseases and countries covered by the survey were determined by the voluntary participation of patient organisations, as a result of the implementation of the survey via patient organisations. Diseases were successively added to those investigated in EurordisCare1. More diseases were added to the list in EurordisCare2 with the elimination of two diseases: Crohn's disease (CD) (the prevalence was considered too high to be kept in the programme) and Duchenne muscular dystrophy (representatives of the muscular dystrophies network suggested that another, less explored disease, myasthenia gravis [MG], be included).

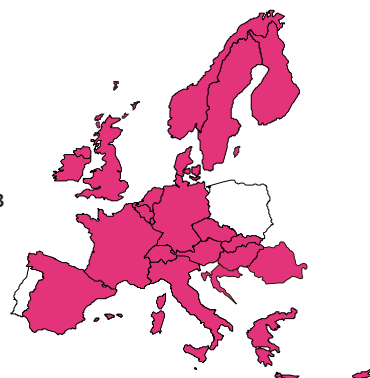
In EurordisCare3, two very rare diseases were added to the list: chromosome 11 deletion disorders and alternating hemiplegia, for which, due to their low prevalence (*Table 2*), no national organisations exist, but rather European networks. Second, surveyed diseases were chosen in order to represent a wide range of characteristics of diseases, in terms of aetiology, clinical manifestations, physical or mental impairment, age of onset and prevalence (*Table 2*).

For each disease, all existing European (whether European Union members or not) patient organisations were invited to participate. The majority accepted and refusals were mostly due to an overload of work or a lack of interest in European collaboration. The participation of patient organisations was not restricted to EURORDIS member organisations.

Figure 1
Countries
represented
in EurordisCare2



Figure 2
Countries
represented
in EurordisCare3



Two European countries represented in the EurordisCare2 survey, Poland and Portugal, were not represented in EurordisCare3 (*Figure 1*).

However, eight additional countries joined the list of countries represented in the EurordisCare3 survey: Croatia, Cyprus, the Czech Republic, Greece, Hungary, Luxembourg and Slovakia (*Figure 2*). The inclusion of these countries added diversity to the size (as small countries) and geography (Eastern European countries) of the countries represented.

Table 2 Characteristics of rare diseases studied in EurordisCare2 and EurordisCare3

	Prevalence (number of patients for 10 000 inhabitants) ¹	Age (adults, children)	Gender of patients	Main clinical domains	Possible physical handicap (Yes/No)	Possible mental handicap (Yes/No)	Inherited Dominant, recessive, X-linked, Spontaneous mutation, Unknown ²
Alternating hemiplegia (AH)	~130 families in Europe	A,C	M, F	Neuromuscular	Y	Y	U, possibly D
Aniridia (ANR)	0.17	A,C	M, F	Ophthalmological Neurological	Y ³	Y ⁴	D, R, S
Ataxia (ATX)	0.22	A,C	M, F	Cardiological	Y	N	D, R, X
Cystic fibrosis (CF)	1.20	A,C	M, F	Respiratory Digestive	Y	N	R
Crohn's disease (CD)	6-9	A	M, F	Digestive	Y	N	multifactorial
Duchenne muscular dystrophy (DMD)	0.5	A,C	M ⁵	Neuromuscular	Y	N	X
Ehlers-Danlos syndrome (EDS)	1.25	A,C	M, F ⁶	Rheumatological Cardiological Ophthalmologic	Y	N	D, R, X
Epidermolysis bullosa (EB)	1.00	A,C	M, F	Dermatological	Y	N	D, R
Fragile X syndrome (FRX)	1.42	A,C	M	Psychiatric	Y	Y	X
Huntington's disease (HD)	0.62	A	M, F	Neurological Psychiatric	Y	Y	D
Marfan syndrome (MFS)	3.00	A,C	M, F	Rheumatological Cardiological Ophthalmological	Y	N	D
Myasthenia gravis (MG)	0.85	A	M, F	Neuromuscular	Y	N	S
Osteogenesis imperfecta (OI)	0.65	A,C	M, F	Dermatological Cardiological Ophthalmological	Y	N	D, R
Prader-Willi syndrome (PWS)	1.07	A,C	M, F	Endocrinological Psychiatric	N	Y	S
Pulmonary arterial hypertension (PAH)	0.15	A	M, F	Cardiological Pneumonological	N	N	D, S
Tuberous sclerosis (TS)	0.88	A,C	M, F	Neurological Psychiatric	Y ⁷	Y	D
Williams syndrome (WS)	1.33	A,C	M, F	Cardiological Neurological	Y	Y	S
Chromosome 11q deletion disorder (Ch11)	150 published cases	A,C	M, F	Neurological	Y	Y	S

1-From the Orphanet Report Series, 'Prevalence of Rare Diseases: bibliographic data – May 2008', orpha.net/orpha-com/cahiers/docs/GB/Prevalence_of_rare_diseases.pdf; 2-From Orphanet, orpha.net; 3-Vision problems; 4-For patients with WAGR syndrome, of which aniridia is one characteristic; 5-Though defined as an X-linked recessive disease, some females display identical symptoms and benefit equally from membership in DMD patient organisations; 6-Despite the fact that Ehlers-Danlos is usually passed down as an autosomal dominant trait affecting males and females equally or as an X-linked trait affecting males more often, participants of the survey were mostly females; 7-Mental retardation and vision problems due to non-cancerous tumours on the brain and eyes

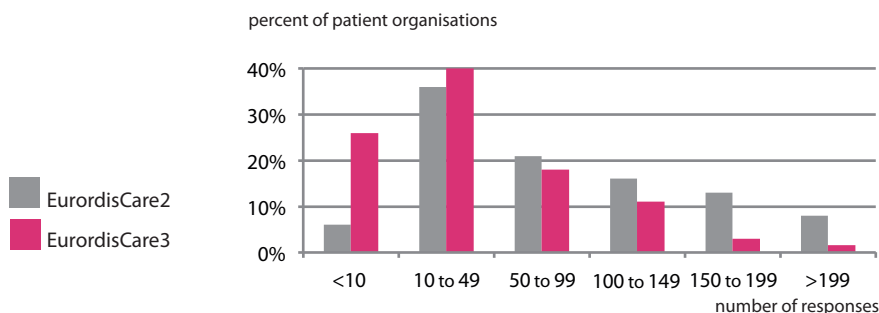


Figure 3 Number of respondents per patient organisation

In EurordisCare2, all patient members of the participating patient organisations were eligible for the study. In the case of patient organisations with more than 500 members, a sample of 500 patients was randomly selected to avoid overrepresentation. In EurordisCare3, in order to avoid disequilibrium according to the size of the association, larger associations were asked to limit the mailing of questionnaires to 300 randomly chosen patients (to ultimately obtain approximately 100 responses). All but four patient organisations accepted restricting the number of participating patients despite some initial reluctance due to a perception of inequity. Eventually, all patient organisations agreed to the rationale of sampling and the interest of randomisation. Some were very excited to acquire this new analytical tool and declared that they would use it for their own internal surveys. Figure 3 shows the range of numbers of respondents per patient organisation. In EurordisCare3, small patient organisations and diseases with a very low prevalence were more represented.

Questionnaires⁸ ?

EURORDIS volunteers translated the EurordisCare2 questionnaire into 12 languages and the EurordisCare3 questionnaire into 15 languages.

For each language, one volunteer translated the questions from English, while a second volunteer validated the translation.

A four-page black-and-white paper questionnaire was sent to the home of each patient, in their native language. This format of the questionnaire: (i) eliminated the ‘electronic bias’ of online surveys in which Internet users are more informed than the general population of patients, especially regarding questions of access to services and diagnostic tools, as a result of their ability to locate services on the Internet, (ii) eliminated the language barrier experienced during EurordisCare1 and (iii) allowed for an appropriate setting for the administration of questions that could evoke unpleasant experiences and difficulties. Although the translation, dissemination and analysis of such a large survey introduced a heavy workload for EURORDIS staff, volunteers and patient survey respondents, it was agreed that it was the best way to represent the direct voice of the patients.

With the exception of two questions in the EurordisCare2 survey, all fields in the questionnaire were either binary (requiring an answer of yes or no) or quantitative (requiring a numeric response or date). Two open-ended

questions regarding the first symptoms experienced by patients and possible initial misdiagnoses had to be codified for quantitative analyses.

As responses were varied, abundant, written in native languages, often using non-technical terms, the processing of these responses required extensive work by a medical expert and translator. Significant valuable contributions were lost due to these obstacles. It was thus decided that no open-ended questions would be included in the EurordisCare3 survey. To maximise response rates, questions regarding demographic data, which may have been considered indiscrete by some patients, were not collected in EurordisCare2. Following a successful response rate, it was decided to include such data collection in the EurordisCare3 survey.

When designing the EurordisCare3 survey, discussions with patient organisation representatives revealed that patient experiences in accessing medical and social services varied greatly depending on the kind of service sought. It was decided that a single questionnaire for the 16 considered diseases would not allow patients to accurately report on their experiences. As such, the EurordisCare3 survey was divided in two parts.

The first section (see Q1 to Q8 in Appendix 3) was dedicated to investigating the experiences of patients for eight services defined by representatives of the disease as uniquely essential. The second section (Q9 to Q14) included additional questions common to all diseases⁹.

Within this section, the thresholds used to define income groups were adjusted for the economic situation in each country.

In contrast to EurordisCare2, socioeconomic data, including income level and education level, were collected.

Additional Collection of Information

A second phase of data collection was launched after the initial analysis of survey results, enabling a more exploratory approach. In countries where national alliances exist, representatives were contacted to describe the national initiatives in the field of rare diseases, providing readers with an overall picture of the healthcare system in each country covered by the EurordisCare2 and EurordisCare3 surveys (see Results by Country and Acknowledgements). In Austria, Poland, Slovakia, Switzerland and the United Kingdom, where there are no national alliances, patient organisations, rare disease health professionals and health authorities were contacted for this information. Patient organisations participating in the surveys were contacted for their input on the daily experience of living with their disease, as well as their reactions and interpretations of the results (see Acknowledgements). Through other patient organisations, patients were asked for anonymous testimonies on topics investigated in the survey to further illustrate the patient experience. Sources used in creating clinical descriptions included the US National Organisation of Rare Disorders (NORD)¹⁰, Orphanet¹¹ and the US National Institutes of Health's Office of Rare Diseases, which were also validated by patient representatives from patient organisations.

8-See Appendix 2&3 for examples of EurordisCare2 and EurordisCare3 questionnaires; 9-Patient organisation representatives were asked to select and rank, in order of importance, medical services specific to their disease from a list of over 50 care services, specialised consultations and medical explorations. Respondents were encouraged to include additional services not included in the list. Questions regarding the eight most important medical services were uniquely catered for each disease questionnaire; 10-rarediseases.org; 11-orpha.net; 12-rarediseases.info.nih.gov

Ethical Considerations

Respondents were in no way coerced into participating in the survey. Measures to protect the confidentiality of patients were implicit in the implementation of the survey. Patients were never directly contacted by EURORDIS to fill out the surveys, only by patient organisations. As surveys were returned anonymously to EURORDIS, participating patient organisations were neither aware of which patients actually responded, nor provided with any individual responses. Despite all attempts to ensure the confidentiality of the data, some respondents wrote their addresses on the back of the response envelopes. In these cases, EURORDIS staff replied with a short message, thanking patients for their participation and explaining that all identifiable personal data would be destroyed after sending the letter. As such, anonymity was entirely maintained and data remained unidentifiable. Although overall survey results were and continue to be presented publicly, individual participants are never identified or associated with their responses. All patients, patient organisations and health authorities providing contributions to this publication were asked for their permission.

Analysis

Due to the self-administered nature of the surveys, errors were anticipated. As contacting specific participants was not possible and ‘cleaning up’ the data would dilute the authenticity of patient responses, a certain level of ‘noise’ in the data was tolerated.

It was considered that the variability of responses due to errors could lower the power of the conclusions, but not necessarily introduce any response bias. Therefore, no returned questionnaires in the EurordisCare3 survey were excluded. In the EurordisCare2 survey, however, in which the delay in diagnosis was the major variable analysed, questionnaires in which the time of the appearance of the first symptoms or the time of correct diagnosis were missing could not be considered in the final analysis.

Statistical analyses for the EurordisCare2 survey were performed by members of the Department of Biostatistics and Mathematical Computing at the French National Institute for Health and Medical Research (INSERM - U717). Variables with two or more categories, but no intrinsic order, were calculated as a total and as a percentage. In order to perform a transversal analysis for different diseases with unique difficulties in diagnosis, ‘late diagnoses’ were defined as the 25% longest delays from the time of first symptoms to the time of correct diagnosis within each disease. A descriptive analysis was performed by patient organisation, disease and country.

Investigation into factors associated with delayed diagnosis was performed by logistic regression on the global set of data. Wherever ‘overall’ values are indicated, responses from all respondents were included. Results by disease also included all survey responses. To avoid the presentation of inconclusive and biased results, country-specific averages were only calculated for countries with more than 60 responses, representing three or more diseases, of which no disease represented more than half of the responses.

All analyses of EurordisCare3 survey results were performed by EURORDIS staff. Wherever ‘overall’ values are indicated, responses from all respondents were included in the analysis. Results by disease also included all survey responses. To avoid the presentation of inconclusive and biased results,

country-specific averages were calculated only for countries with more than 60 responses, representing four or more diseases, of which no disease represented more than half of the responses. Education level was defined by the highest level of education attained in the family. Family income was defined as the net family income per month. Three thresholds were appropriately defined in the context of the economic situation in each country. The four resulting income categories appear as 'lowest', 'medium low', 'medium high' and 'highest' in the results.

A Unique Sharing of the Workload

At first glance, the design, implementation, analysis and communication of a direct patient survey adapted to numerous rare diseases and translated into many languages, to be disseminated to a number of European countries, seemed like an unreachable objective for a patient organisation such as EURORDIS. In reality it was! The time required to follow through with the design, implementation and analysis of EurordisCare2 alone was calculated as 3630 hours of work, an amount far exceeding the capacity of EURORDIS' staff. Without the external support of INSERM staff for statistical analyses, EURORDIS volunteers for daily tasks and translations, and communication and mailings to patient members by patient organisations, EurordisCare2 would not have been possible. It must not be forgotten, however, that the greatest contribution of all was that of the patients themselves. Considering that each respondent took an average of 45 minutes to complete the questionnaire, the 5980 participants contributed an additional 4485 hours of work.

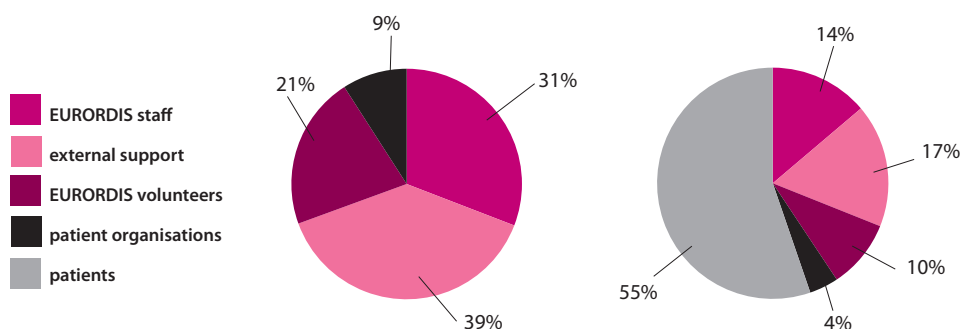


Figure 4 Contributions from EURORDIS staff, volunteers, patients, patient organisations and external support without (left) and with (right) consideration for questionnaire filling.

Survey Challenges and Limitations

The survey results presented in this report represent the largest compilation of data from rare disease patients on their experiences and opinions related to disease diagnosis and access to available care. They therefore constitute a useful reference for comparison. There are, however, several limitations to the data that should be considered.

Due to workload constraints of the EURORDIS staff, only a limited number of rare diseases could be studied. Although an attempt to select diseases with a large range of characteristics, in terms of clinical manifestations, physical or mental impairment, age of onset and prevalence was made, the rare diseases chosen for the surveys are by no means statistically representative of the 5000 to 8000 rare diseases identified today. And although the results of these surveys can only be extrapolated for other rare disease patients in Europe with caution, they can provide an acceptable picture of the experiences and expectations of rare disease patients at large in Europe.

In general, it could be argued that patients who are members of patient organisations are more informed and empowered and therefore more confident and willing to participate in such surveys, hence the responses received may underrepresent the difficulty of patients who are not members of patient organisations. We find, however, that given the existing difficulties reported in reaching a correct diagnosis and accessing appropriate care, it can only be assumed that these difficulties are increased for isolated patients who are not members of a patient organisation.

As the survey was completed individually by participants with no opportunity to clarify any questions, misunderstanding of questions may have contributed to inaccuracies in some responses.

As many questions also required respondents to recall experiences, poor memory may have also contributed to inaccurate answers.

Both limitations may have contributed to an optimistic bias in the results.

Many patient organisation representatives asked why there was no place for additional comments in the EurordisCare3 questionnaire. It was explained that for logistical reasons (based on the experience of EurordisCare2) it was not possible to synthesise such information from 15 different languages.

As it would be ethically unacceptable to collect data that would not be analysed at a later stage, this option was not included in the EurordisCare3 questionnaire design. Subsequently, EURORDIS was particularly motivated to encourage contributions by patient organisations and patient testimonies throughout this publication. Despite the attempt to streamline the survey design and implementation process, the mailing of 140 customised questionnaires via 135 patient organisations required several months of coordination. In addition, several patient organisations, initially reluctant to participate, eventually decided to join the surveys.

Dissemination of Results

Although this report was designed to serve as an advocacy tool for all stakeholders in the rare disease community, we place significant emphasis on the importance of disseminating the results of these surveys to the patients and organisations that provided them. For the EurordisCare2 survey, each patient organisation received overall descriptive results.

In addition, patient organisations received a compilation of results related to their disease and their country for comparison and ultimately for advocacy purposes. For the EurordisCare3 survey, all descriptive overall results, as well as results by association, disease and country, were made available for participating patient organisations via a local EURORDIS website, eurordis.org/eurordiscare3/.

Whether participating in the workshop or not, national and disease-specific networks were provided with a collection of 66 disease-specific and 59 country-specific PowerPoint slides to be appropriately selected in the creation of advocacy presentations. In addition, organisations were invited to attend the workshop 'Getting the Most out of the EurordisCare3 Survey' held during the 2008 annual EURORDIS membership meeting in which EURORDIS staff instructed participants on how to most effectively choose slides to illustrate findings of interest in their respective countries for their respective patient groups.

With an approval from the board of directors, the database of results of the EurordisCare3 survey is also available to academics interested in further analysing the data. In addition, global EurordisCare2 results were presented at the 2005 European Conference on Rare Diseases, in Luxembourg. The main findings of the EurordisCare3 survey were presented at the 2007 Workshop on Centres of Expertise and European Reference Networks, in Prague; the European Commission High Level Group on Health Services and Medical Care; the 2007 European Conference of Rare Diseases and the 2008 annual EURORDIS membership meeting.

Preliminary Reactions

The results of EurordisCare2 and EurordisCare3 were presented to patients, patient organisations, health professionals and health authorities on several occasions as described in the 'Dissemination of Results' section above.

Overall, patients were not surprised by the results for either survey. Only when results contradicted familiar clichés in the field of healthcare were the findings debated. In the context of improving the patient experience, these 'enlightening' findings were a first and important step in paving the way.

In general, commentaries from health professionals and policymakers surrounded potential conclusions drawn from the overall results and the application of these conclusions in shaping rare disease health policies. Preliminary reactions also included a concern that questions in the survey were subjective, making the application of results in public health policies difficult. One suggestion included the future possibility of identifying and following cohorts of rare disease patients in order to measure changes in their experiences and expectations.

As the members of rare disease patient organisations can change at any given point in time, it may not be possible to represent these changes.

It was suggested that qualitative data be presented along with the survey results. This and all other suggestions were taken into account during the publication of this book.

Presentation of Results in This Book

All quantifiable results, such as the number of days of delay in diagnosis, the percentage of patients satisfied with services or the order of preference are presented using a colour range from green to red where, in general, green represents more favourable situations and red represents the less favourable

situations. For each presentation of results, an appropriate numerical scale was used to best illustrate the results.

Despite differences between the numerical scales, the same green-to-red colour scale was used for all figures to enable readers to easily see differences across disease, country or socioeconomic groups. We use an example from the section ‘Global Results of the EurordisCare3 Survey - Consequences of the Disease’ in which the responses of patients regarding the need to move house as a consequence of their disease are discussed, to illustrate the presentation of results throughout the publication.

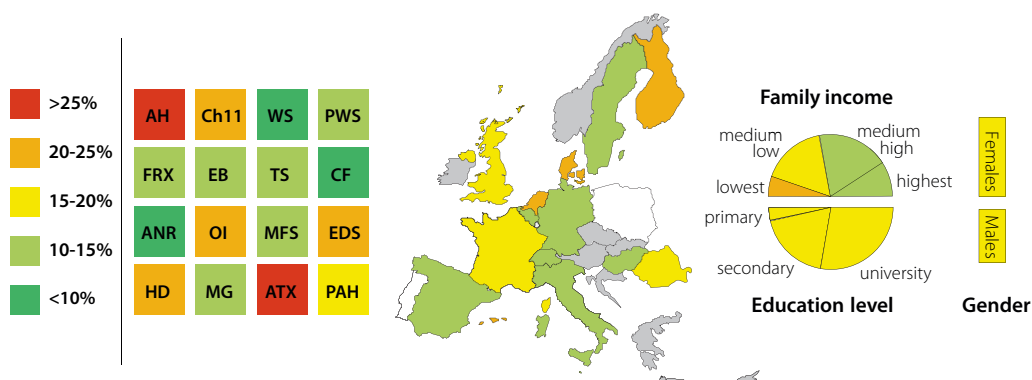


Figure 5 Distribution of patients required to move house as a result of their disease (example of presentation of results throughout the publication)

To illustrate the variation in responses across disease groups, 16 squares represent the 16 diseases included in EurordisCare3 (for EurordisCare2 a similar figure includes the eight investigated diseases). Commonly used disease abbreviations are used to simplify the figure and the full names appear on the bookmark for reference. The squares appear in the same formation throughout the text and have been arranged according to the mean age of respondents from each disease group.

The diseases with the youngest mean patient age appear in the first row and diseases with the oldest mean patient age appear in the last row.

In Figure 5, we see that survey participants concerned with alternating hemiplegia (AH) and ataxia (ATX) most frequently reported the need to move house (at least 25% of respondents from each disease group).

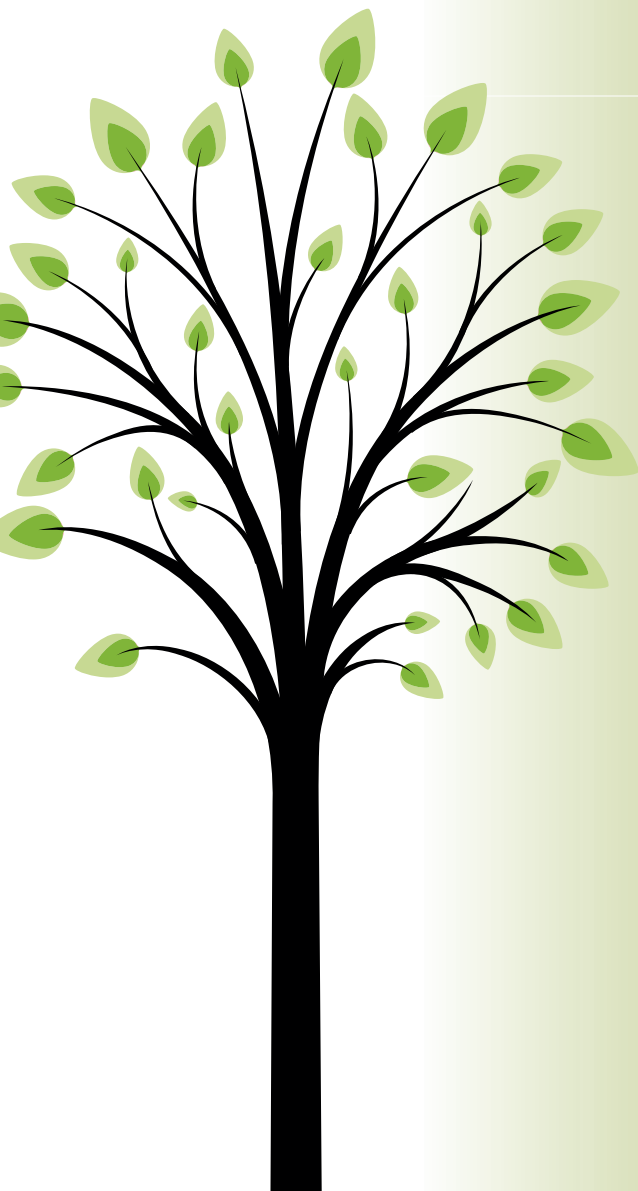
In Williams syndrome (WS), cystic fibrosis (CF) and aniridia (ANR), however, less than 10% of respondents reported this need. In this figure, no relationship between the age of respondents and the need to move house is observed (as squares are not more frequently red or more frequently green in the top or bottom rows). Variations in responses across country groups are illustrated with a map and the same green-to-red scale.

As previously explained, country data was only presented for countries with at least 60 responses, representing a sufficient number of diseases (three for EurordisCare2 results and four for EurordisCare3), for which no single disease represented more than half of the responses. If, for example, the majority of respondents from a given country were affected by cystic fibrosis (CF), the country would appear dark green in Figure 5,

and one could incorrectly conclude that few patients from this country needed to move house. In Figure 5, we do see less diversity across country groups than disease groups. It can be concluded that the need to move house is more strongly linked to the disease than the country of residence. Despite this overall trend, we do see that the need to move house was more frequently reported by Finnish, Danish and Dutch patients.

The sections of the pie chart and bar graph represent the distribution of the total survey respondents across demographic and socioeconomic groups and remain the same throughout the figures in the publication (i.e. more women, more respondents with a medium high income and more respondents with a university level of education participated in the survey overall).

Differences in responses across demographic and socioeconomic groups are represented by the green-to-red scale. In Figure 5, we see a relationship between income and need to move house, where respondents with the lowest income reported the need to move house twice as frequently as those with the highest. No variation is seen across education level groups or between female and males respondents.



results

Overall Results of the EurordisCare2 Survey **p42**

Overall Results of the EurordisCare3 Survey **p62**

Results **by disease** **p92**

Results **by country** **p212**

Overall Results of the **EurordisCare2** Survey

For many of the survey participants affected by a rare disease, the quest for a correct diagnosis signified a long and significant challenge. Before having obtained their diagnosis they consulted many specialists, underwent numerous medical exams and often received incorrect diagnoses along the way. This journey was not only troublesome and taxing, as patients often travelled long distances and used their own savings, but also often led to deleterious consequences for patients and their families. Overall, patients were left with no choice but to seek answers on their own, with little help from healthcare systems, in many cases. Even if obtained, diagnoses were often announced under inappropriate circumstances, where the gravity of the announcement and the subsequent consequences for the patients and their families were not considered.

The Quest for Diagnosis

When presented with a symptom or set of symptoms, it is logical that a rare disease would not be the first proposed cause by a health professional. For the same reason, it is not surprising that the time it takes to diagnose a rare disease might be longer than for a common one. With each clinical event, the time it takes to reach a diagnosis will depend upon the disease in question and the complexity of diagnostic needs. These delays, difficult enough to accept for individuals with common diseases (let alone healthy individuals), represent only the first obstacle for rare disease patients. The delays in diagnosis for the eight investigated diseases are presented below (*Table 1*). Within disease groups, delays in diagnosis varied greatly. A small percentage of respondents experienced very short delays in diagnosis and another small percentage of respondents experienced very long delays. However, the majority of patients within each disease group experienced delays somewhere in between. As a result of this range in delays, the median delays in diagnosis were calculated based on the responses of half (50%) of the respondents in each disease group as well as for three-fourths (75%) of respondents in each disease group. For example, for half of respondents affected by CF, diagnosis was determined 1.5 months after the first

appearance of symptoms. When including the 25% of respondents affected by CF that experienced the longest delays, the median increased dramatically, to at least 15 months of delay following the first appearance of symptoms.

Source of information	Delay in diagnosis for 50% of patients	Delay in diagnosis for 75% of patients
CF	1.5 months	15 months
TS	4 months	3 years
DMD	12 months	3 years
CD	12 months	5.8 years
PWS	18 months	6.1 years
MFS	18 months	11.1 years
FRX	2.8 years	5.3 years
EDS	14 years	28 years

Table 1 Median time elapsed between the first symptoms and a correct diagnosis.

The results in Table 1 not only illustrate the great differences in delays between disease groups but also between patients with the same disease. For example, half of respondents (50%) affected by MFS reported a delay of at least 18 months between the first appearance of symptoms and obtaining a correct diagnosis. An additional 25% of respondents from this same disease group did not receive a correct diagnosis until an average of at least 133 months (more than 11 years) after the first appearance of symptoms. As the aim of this survey was not to criticise the diagnosis process in general, but rather to investigate the consequences and factors associated with longer delays, these aspects are presented below in order to help propose solutions that could ultimately lead to an improvement in the health and quality of life of rare disease patients.

PRENATAL AND NEONATAL DIAGNOSIS (DIAGNOSIS DURING THE FIRST THREE MONTHS OF LIFE)

For certain rare diseases, an early diagnosis is realistic when clinical signs can be observed during pregnancy or just after birth, if a specific diagnostic test exists and is systematically proposed at birth or in the case of prior family cases. In this survey, such early diagnoses were most frequently reported by patients affected by PWS (32% of patients) and CF (36% of patients). For all other investigated diseases, less than 11% of patients received such an early diagnosis. The relatively high percentages of PW and CF patients diagnosed at an early stage could serve as a source of encouragement for other patients. At the same time, although relatively high, these percentages are low considering the consistently observed hypotonia (floppiness as a result of decreased muscle tone) in PWS neonates and the existence of reliable genetic tests for CF (systematically provided in France, Belgium and Italy). With correct screening, the number of patients reporting early diagnosis for these diseases could approach 100%.

Even when excluding Austrian respondents (the majority of which were affected by CD, an adult disease with no known hereditary form of transmission) a significant variation in early diagnosis was observed across country groups (*Figure 1*). Early diagnosis was more frequently reported by

Belgian (41%) and Italian (28%) respondents and less frequently by respondents from Denmark, Sweden, Finland, Switzerland or Poland (from 7% to 9%).

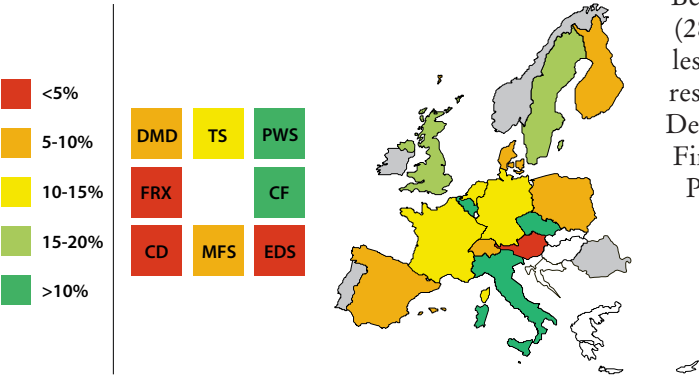


Figure 1 Percentage of respondents obtaining a diagnosis within the first three months of life

The neonatal and infancy periods are very unique periods, and for certain diseases, specific symptoms are only apparent during this time. For all patients, it is a time when contact with healthcare professionals is particularly frequent. As such, this period presents ideal circumstances for the diagnosis of a disease. In the case of PWS, one-third of respondents reported being diagnosed during the neonatal period. However, of the remaining respondents, half reported an average delay of diagnosis of 18 months and an additional 25% reported a delay of more than ten years. For many rare diseases, neonatal screening represents an undeniable opportunity to minimise diagnostic delays and therefore warrants further investigation (*Table 2*). Missing such an opportunity to minimise severe and harsh consequences is an unacceptable reality.

Disease	Delay in diagnosis for 50% of all respondents	Delay in diagnosis for 50% of respondents excluding those diagnosed during neonatal period
CF	1.5 months	9 months (63%)
PWS	1.5 years	4 years (66%)
TS	4 months	6 months (90%)
MFS	1.5 years	2 years (92%)
DMD	12 months	16 months (95%)
EDS	14 years	14 years (96%)
FRX	2.8 years	3 years (97%)
CD	12 months	12 months (100%)

Table 2 Median time elapsed between the first symptoms and correct diagnosis for all patients and for patients not diagnosed during or before the first three months of life.

CONSULTATIONS AND MEDICAL EXAMS

The quest for diagnosis includes consultations with many health professionals until the patient finally comes in contact with the one that announces the correct diagnosis. As seen in Figure 2, patients with more complex and numerous symptoms reported consulting more physicians. Of all respondents affected by EDS, 58% reported consulting over five physicians and 20% reported consulting over 20 before obtaining a correct diagnosis. The differences between country groups are even more significant: while 80% to 87% of French, Swiss and Dutch respondents reported obtaining a diagnosis after consulting a maximum of five physicians, 10% to 14% of Polish and Danish respondents reported consulting more than 20 physicians before obtaining a correct diagnosis. In addition to these numerous consultations, survey participants reported various medical and exploratory examinations in 90% of cases: biological tests (67%), radiological exams (50%), functional testing (41%) and genetic testing (28%). Each participant reported an average of at least two different exploratory exams. It is important to note that genetic testing varies significantly from country to country and was reported by 14% to 17% of Swiss, Swedish and Danish respondents and by 40% of Belgian respondents, 42% of Italian respondents, 52% of British respondents and 55% of Polish respondents. Beyond the high healthcare costs introduced by such a great number of exploratory tests that do not lead to a correct diagnosis, it is

important to recognise the disappointment that a patient or a parent experiences when each additional test does not bring them any closer to confirming the disease.

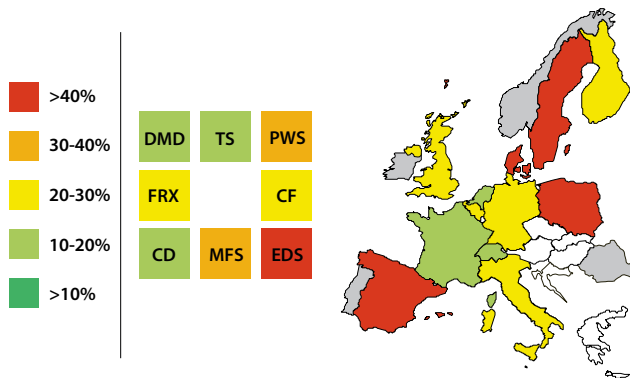
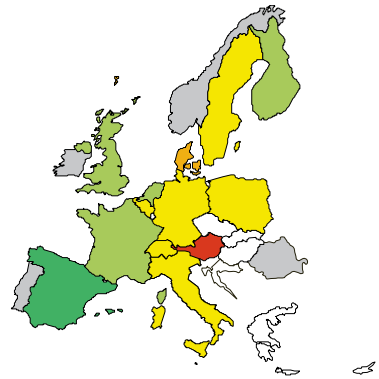
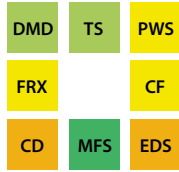
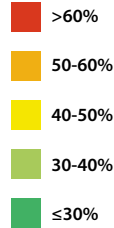


Figure 2 Percentage of respondents who reported consulting more than five physicians during their quest for diagnosis

INITIAL MISDIAGNOSIS

Initially receiving incorrect diagnoses is a common experience for many rare disease patients. Of the total number of survey participants, 41% received at least one such misdiagnosis before obtaining the correct one. The diversity in responses was more apparent among respondents affected by diseases with onset during adulthood: 25% of respondents with MFS compared to 51% of respondents with CD and 56% of respondents with EDS reported receiving an initial misdiagnosis (Figure 3). The trend in responses across country groups showed less frequent reports of misdiagnosis from patients from France, the United Kingdom, Spain, the Netherlands and Finland (Figure 3, p 46).

Figure 3 Percentage of respondents reporting initial misdiagnosis



MISDIAGNOSIS AND INAPPROPRIATE TREATMENT

It is only logical that an incorrect diagnosis be followed by inappropriate treatments. Figure 4 illustrates the frequency of surgeries reported as a result of an incorrect diagnosis. Patients with adult diseases more frequently reported this inappropriate intervention than patients affected by childhood

diseases: 29% of MFS respondents, 17% of EDS respondents and 17% of CD respondents compared to 10% of DMD respondents, 8% of CF respondents, 7% of PWS respondents and 6% of TS respondents.

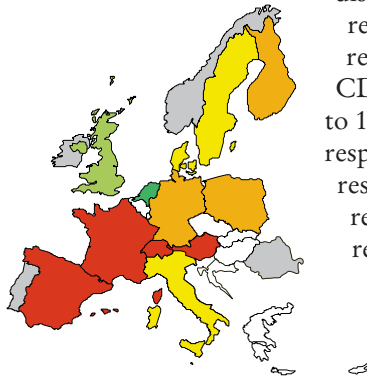
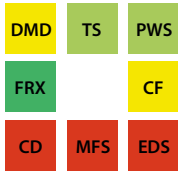
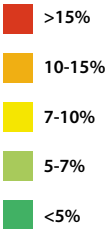


Figure 4 Percent of patients reporting surgery as a result of initial misdiagnosis

Psychological and Psychiatric Treatment Following Misdiagnosis

Rare disease patients and their families have reported cases of psychological and psychiatric treatments following misdiagnosis of a rare disease, ranging from periodic psychological therapy or support to psychiatric hospitalisations and psychiatric medication. Many parents of rare disease patients have reported being accused of being overly worried, hysterical or even abusive. In our analysis, we grouped together all such treatments reported by patients or their families following the misdiagnosis of what eventually was correctly diagnosed as a rare disease. Even if families initially accepted such treatments, in retrospect they were recognised as initial misdiagnoses just as with any non-psychiatric misdiagnosis, resulting in severe consequences such as delays in treatment.

Overall, 7% of survey participants reported such inappropriate treatments. In the case of some of the rare diseases presenting with psychiatric symptoms, such as FRX, inappropriate treatments required some type of adjustment. For other investigated rare diseases, a psychiatric or psychological diagnosis was assigned to explain the symptoms experienced by a patient, which were not recognised as rare diseases by their physician: 2% of CF patients and 5% of DMD patients received only psychological treatment for their symptoms.

Across countries, patients also reported varied experiences. More than 15% of Polish respondents reported inappropriate psychological or psychiatric treatment. Finnish, German, Danish and Dutch respondents reported these treatments less than 5% of the time, suggesting that the phenomenon is

related to cultural factors in addition to disease-related factors.

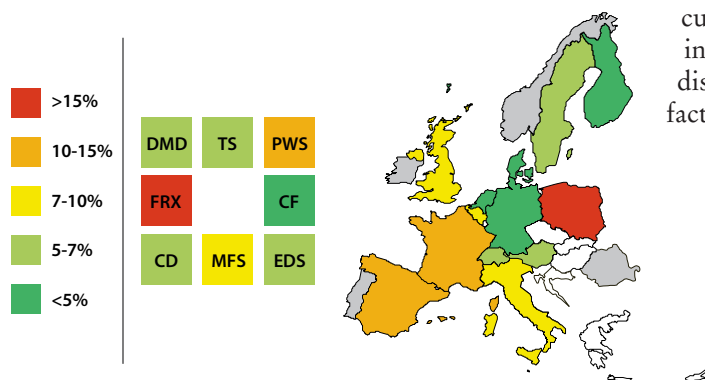


Figure 5 Psychological and psychiatric treatments in the case of the misdiagnosis of a rare disease

Misdiagnosis and the Quest for Diagnosis

Misdiagnosis of rare disease patients not only leads to inappropriate treatments but may also be followed by the cessation of the quest for another diagnosis. Although it cannot be concluded that misdiagnosis directly causes the cessation of the quest for another diagnosis, relationships between the type of misdiagnosis and delays in obtaining a correct diagnosis were observed. Patient testimonies strongly suggest that misdiagnosis introduces an additional barrier in obtaining a correct diagnosis.

Table 3 (*see p 48*) describes the percent of overall misdiagnoses and the percent of psychological or psychiatric diagnoses for each disease investigated. It also displays the delays in diagnosis reported by survey participants as a function of the type of misdiagnosis they received. Patients who initially received a false psychological or psychiatric diagnosis experienced longer delays in diagnosis, suggesting that this type of diagnosis introduced yet an even greater barrier for patients before the quest for correct diagnosis could be resumed.

	Delay in diagnosis for 50% of patients (% of respondents) *		
Diseases	Without misdiagnosis	With non-psychological or non-psychiatric misdiagnosis	With psychological or psychiatric misdiagnosis
TS	3 months (62%)	12 months (33%)	3.5 years (5%)
CF	3 months (52%)	12 months (47%)	24 months (1%)
DMD	1 year (69%)	2 years (22%)	3 years (9%)
CD	1 year (49%)	2 years (44%)	6 years (7%)
MFS	1 year (74%)	9.5 years (24%)	14 years (2%)
FRX	2 years (58%)	3.6 years (24%)	4.6 years (18%)
PWS	2.5 years (66%)	5 years (30%)	10 years (4%)
EDS	16 years (44%)	16 years (45%)	22 years (11%)

Table 3 Misdiagnoses and delays in diagnosis in relation to the type of misdiagnosis

**Patients diagnosed during the prenatal and neonatal periods are excluded from this analysis.*

Overall, non-psychological or non-psychiatric misdiagnoses were associated with delays twice as long as those reported by patients who were initially correctly diagnosed. Respondents affected by TS and CF reported delays four times longer if they initially received a psychological or psychiatric misdiagnosis and MFS patients reported delays ten times longer in this same situation. In the case of psychological or psychiatric misdiagnosis, respondents reported delays 2.5 to 14 times longer than those who initially received a correct diagnosis.

FACTORS LEADING TO A CORRECT DIAGNOSIS

In the absence of an ideal system of diagnosing rare diseases, the motivation and personal initiatives of rare disease patients themselves are often the crucial factors in obtaining a correct diagnosis. These initiatives can include the suggestion of the possibility of a rare disease to the diagnosing physician, the location of diagnostic laboratories and travel to such diagnostic structures outside the patient’s region or country.

Introducing the Possibility of a Rare Disease

For many patients, arriving at a correct diagnosis requires a crucial step:

the suggestion by either the patient, a member of the patient’s family or a healthcare professional that their disease is not one frequently encountered but possibly a rare disease. Once introduced as a possibility, the arrival at a correct diagnosis is usually accelerated.

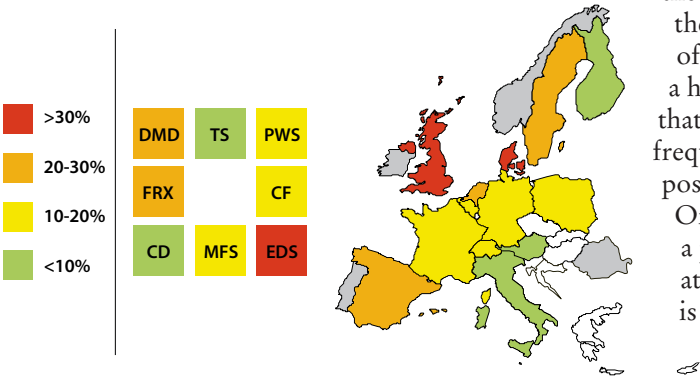


Figure 6 Percentage of patients who reported introducing the possibility of a rare disease to their healthcare professional

In 18% of cases, patients reported making this suggestion themselves. The sources from which they obtained the possibility of a rare disease varied: their family and friends, media, other patients and the Internet, amongst others. One out of three respondents affected by EDS reported suggesting the possibility of a rare disease to their healthcare professionals. Respondents affected by DMD and FRX also frequently reported taking this initiative. Danish (34%), British (31%), Dutch (24%), Swedish (23%) and Spanish (21%) respondents more frequently reported taking this initiative (Figure 6).

Identifying a Diagnostic Structure

Even when the possibility of a rare disease is suggested and a specific disease may even be suspected, patients need to be directed to a diagnostic

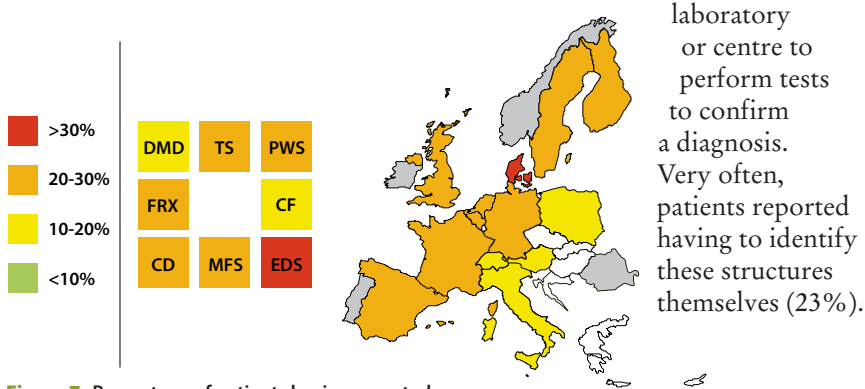


Figure 7 Percentage of patients having reported identifying a diagnostic structure from a non-health professional source

For almost all the investigated diseases, longer delays in diagnosis were reported if the suggestion of a rare disease or the identification of a diagnostic laboratory or centre came from a non-health professional source.

Disease	Delays in diagnosis for 50% of patients when the possibility a rare disease was raised by		Delays in diagnosis for 50% of patients when the location of a diagnostic structure was provided by	
	a health professional	a non-health professional	a health professional	a non-health professional
TS	6 months	11 months	7 months	4.8 months
CF	9 months	17 months	11 months	6 months
CD	12 months	30 months	12 months	32 months
DMD	15 months	18 months	14 months	24 months
MFS	24 months	36 months	24 months	51 months
FRX	31 months	41 months	33 months	41 months
PWS	48 months	108 months	50 months	57 months
EDS	156 months	227 months	144 months	240 months

Table 4 Delays in diagnosis in relation to raising the possibility of a rare disease and the location of a diagnostic structure provided by a health professional or non-health professional source

The Cost of Obtaining a Diagnosis

Despite the fact that universal access to and coverage of health care is largely practised across countries in Europe, some rare disease patients (10% overall) reported that obtaining a diagnosis was only possible with a 'high' or 'very high' personal financial contribution. The percent of respondents reporting the need for this personal financial contribution varied across disease groups as well as country groups. For five out of the eight diseases, 10% to 12% of respondents reported the need to make 'high' or 'very high' financial contributions. Respondents affected by PWS and EDS most frequently reported this need. Respondents from the Netherlands (33%),

Belgium (29%), Italy (21%) and Spain (20%) reported the need to make a 'high' financial contribution. Belgian (18%) and Dutch (13%) respondents most frequently reported the need to make a 'very high' contribution.

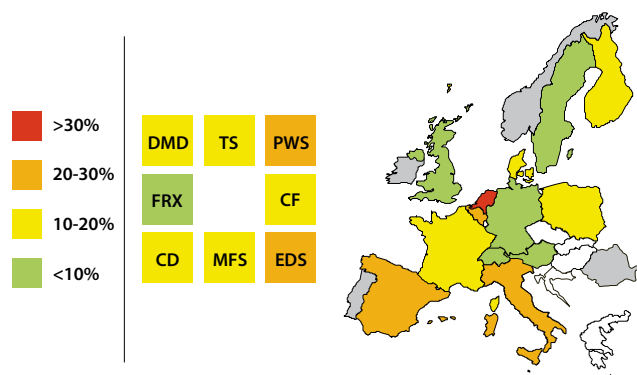


Figure 8 Percentage of patients reporting 'high' or 'very high' personal financial contribution

Structures providing the diagnoses were reported as private in 10% of cases overall and this was more often the case for respondents affected by 'adult' diseases (CD: 24%, MFS: 18%, EDS: 11%) than for paediatric diseases (from 4% to 7%). Across country groups, respondents from France, Spain and Switzerland most frequently reported seeking diagnoses from a private structure.

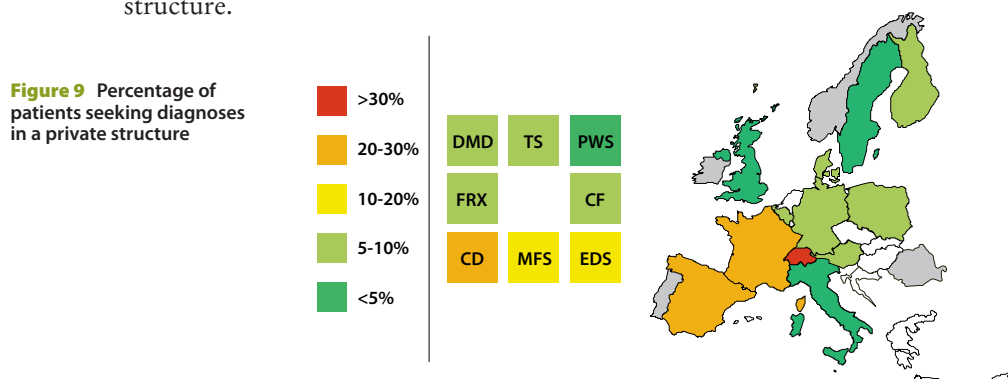


Figure 9 Percentage of patients seeking diagnoses in a private structure

Travelling to a Diagnostic Structure

Respondents reported that the diagnostic structure was located in another region in 26% of cases and in another country in 2% of cases. Respondents affected by CD less frequently reported travelling to another region for

diagnosis (16%). Respondents concerned with PWS (37%), EDS (37%) and MFS (31%) more frequently reported travelling outside of the region to obtain a diagnosis. Across country groups, Danish, Belgian and Dutch respondents most frequently reported travelling to another region (although travel to another region in these smaller countries probably involved short distances). Finnish (47%) and Polish (48%) respondents also frequently reported travelling to another region, although this travel most likely included more significant distances. Spanish and Italian respondents

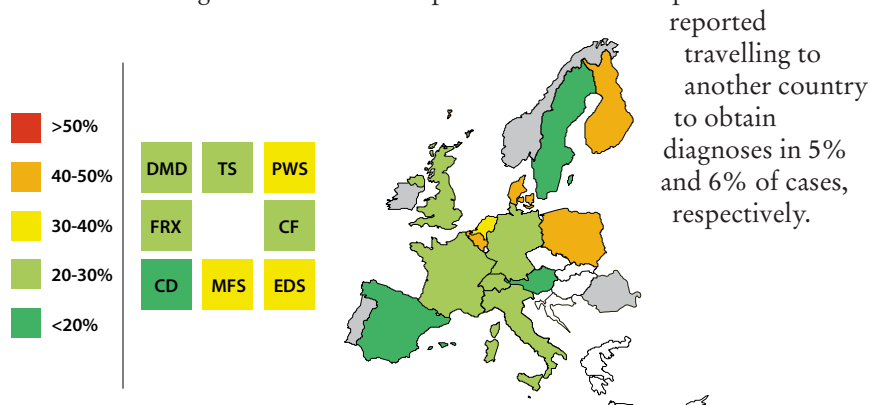


Figure 10 Percentage of respondents reporting travelling to another region to obtain diagnoses

Consequences of Delays in Diagnosis

From a medical perspective, a delay in correct diagnosis is primarily regarded as a cause of delaying appropriate treatment, unnecessarily worsening the disease state. In the day-to-day lives of patients and their families, however, the same delays in diagnosis can lead to numerous equally deleterious consequences, which include but are not limited to medical consequences, such as physical consequences, psychological consequences, cognitive consequences and death. Non-medical consequences might include the birth of another affected child, maladapted family behaviour or the loss of confidence in medicine. Patient responses regarding these consequences varied significantly across disease and country groups: 55% of respondents affected by DMD reported deleterious consequences as a result of delayed diagnosis, whereas respondents affected by EDS reported experiencing deleterious consequences in 86% of cases.

Amongst medical consequences (*Figure 11, p52*), respondents concerned with MFS and EDS most frequently reported physical consequences (41% and 64% respectively, including death in 6% of cases for MFS and 2% for EDS). Respondents concerned with EDS reported psychological consequences in 38% of cases (often the result of an extremely long non-recognition of their symptoms or disease by health professionals).

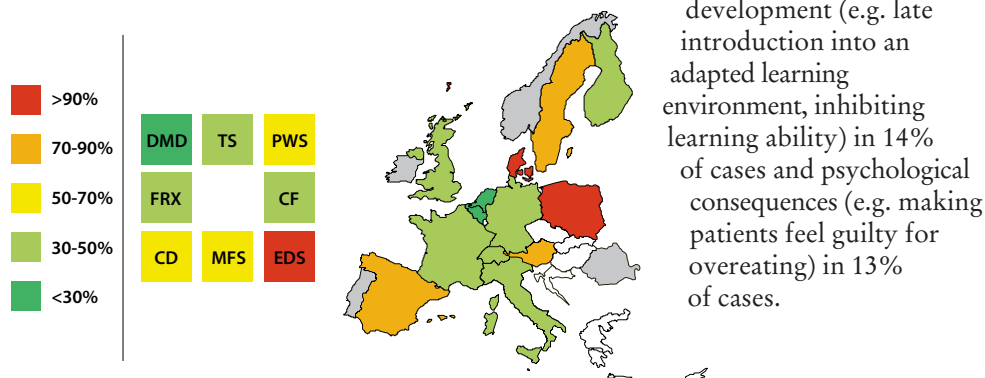


Figure 11 Cumulative percentage of reported medical consequences (physical, psychological, cognitive, death) of delayed diagnosis, by disease and country groups. (As this percentage represents a summation of all medical consequences of which patients may have experienced several, the total may exceed 100%.)

Overall, one out of three patients reported deleterious consequences (and an average of 1.5 consequences per patient). The type of consequences experienced varied significantly across countries. Austrian (52%), Danish (48%), Spanish (47%) and Polish (41%) respondents most frequently reported physical consequences (compared to 26% overall). Danish (47%), Polish (42%) and Swedish (33%) respondents more frequently reported psychological consequences (compared to 13% overall). Polish (22%), British (13%) and Finnish (10%) respondents more frequently reported intellectual consequences (compared to 8% overall).

Rarely recognised by the medical community, non-medical consequences were reported by survey participants as frequently as medical ones (*Figure 12*). When considered by type, these non-medical consequences most often included the maladapted behaviour of the patient's family (21%) and loss of confidence in the healthcare system (19%). Maladapted behaviour most often includes the lack of recognition that certain of the patient's characteristics are symptoms of the disease, and is mirrored in a lack of recognition by physicians. For example, children with DMD may often be considered lazy rather than suffering from muscle fatigue, PWS patients considered greedy as opposed to having an inability to control appetite, patients with FRX may be thought to be misbehaving rather than exhibiting disruptive behaviour as a result of their disease or patients with EDS may be suspected of pretending to have pain that is 'only in their head'.

After receiving a correct diagnosis, parents suffer tremendous guilt for inappropriately regarding symptoms as bad behaviour or even unfairly punishing their children. Respondents affected by DMD, PWS, FRX and EDS reported such maladapted behaviour in 18%, 26%, 39% and 33% of cases, respectively.

CONFIRMATORY DIAGNOSIS

The announcement of a rare disease diagnosis marks a significant turning point in the lives of patients and their families. It is understandable, therefore, that patients and their families would seek a confirmatory diagnosis from a second physician or diagnostic structure. It follows that the motivation for seeking a second opinion is even stronger for patients or families who initially received misdiagnoses. As patients with EDS frequently reported receiving a misdiagnosis, it is not surprising that the same respondents most frequently reported seeking a confirmatory diagnosis.

The varied distribution of patients having reported seeking a confirmatory diagnosis across country groups suggests that the motivation to seek a second opinion is also culturally determined (*Figure 13*).

Less than one out of ten Dutch and British respondents reported seeking a confirmatory diagnosis, whereas more than one out of three Spanish respondents reported the same action.

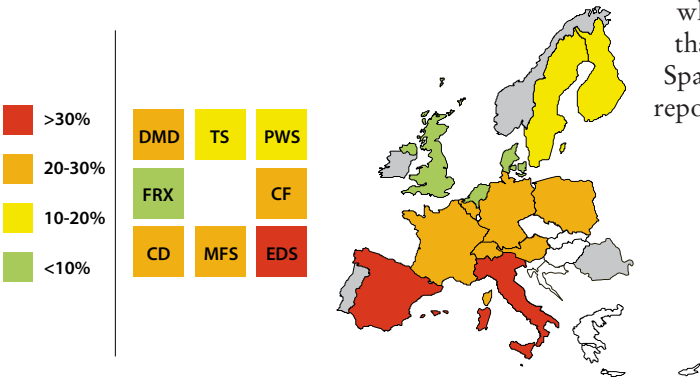


Figure 13 Percentage of patients reporting seeking a confirmatory diagnosis

MOVING HOUSE

One of several consequences following the diagnosis of a rare disease, the need to move house was reported by 10% of respondents overall, with a varied distribution across disease groups (*Figure 14*).

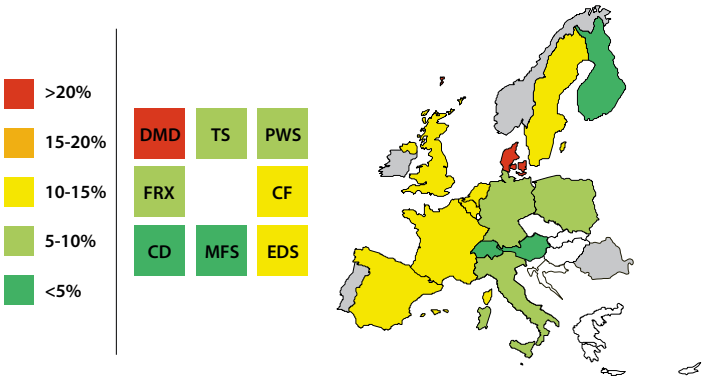


Figure 14 Percentage of respondents who reported moving house

Respondents affected by DMD (28%) and EDS (15%), for whom the progression of the disease includes significant limitations in mobility, most frequently reported the need to move (mainly in the same region), quite possibly to an adapted house (Figure 15).

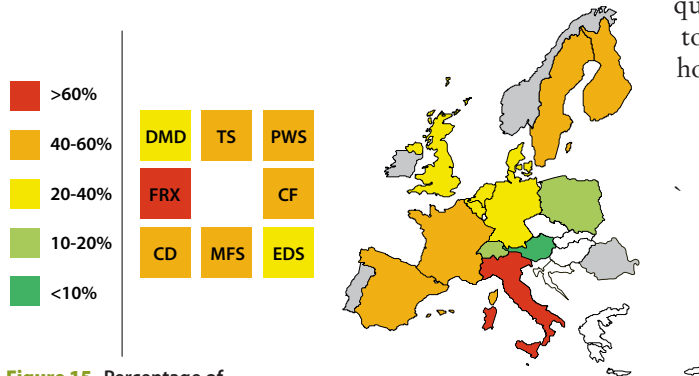


Figure 15 Percentage of respondents who reported moving house outside of their region

Announcement of Diagnosis

The conditions under which the announcement of a rare disease is given is as important to patients and their families as the announcement of the life-changing diagnosis itself and may be crucial in helping patients and their families accept the diagnosis and commit to appropriate treatment. When asked about their experiences, 23% of respondents recalled 'poor' conditions and 12% reported that they were 'unacceptable' (Figure 16). Overall, over one out of three respondents reported receiving the diagnosis in less than ideal conditions. The conditions surrounding the announcement of the diagnosis varied considerably across disease groups: 51% of respondents affected by EDS, less than 30% of respondents affected by MFS and CD, and between 30% and 40% of respondents affected by DMD, CF, FRX, PWS and TS reported receiving the diagnosis under 'poor' or 'unacceptable' conditions. Across country groups, even greater differences are observed: less than 30% of Dutch, Italian, Swiss, Polish and Finnish

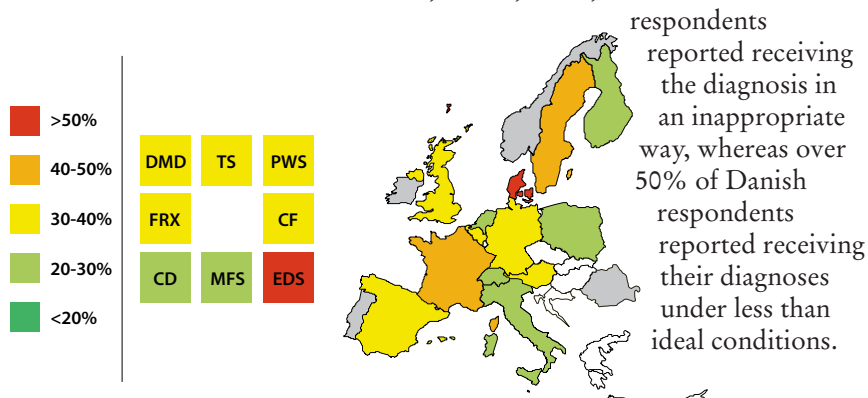


Figure 16 Percentage of respondents who reported receiving the diagnosis under 'poor' or 'unacceptable' conditions

Ideal conditions surrounding the announcement of a rare disease include comfortable conditions for patients and their families; adequate time to explain the nature of the disease, its consequences on daily life, the disease progression and prognosis; as well as adequate time for patients and their family members to freely ask any additional questions. In the case of a child receiving the diagnosis, the presence of both parents is also important, especially in the case of an inherited disease transmitted genetically by one or both parents. To meet these criteria, the announcement of a rare disease diagnosis should occur in the context of a medical consultation specifically dedicated to the announcement. Nevertheless, 32% of respondents reported the announcement of their rare disease in a different context (*Figure 17*). Respondents affected by PWS and FRX most frequently reported the announcement of the rare disease diagnosis outside of a medical consultation. Variation across country groups largely exceeded that observed across

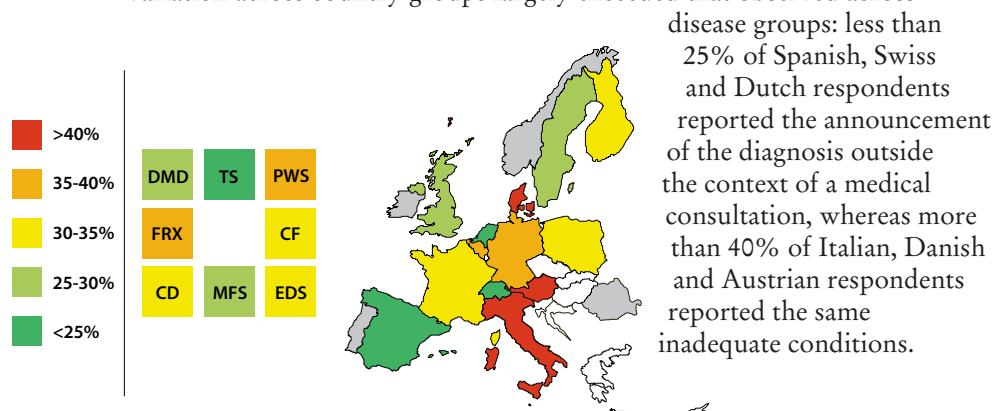


Figure 17 Percentage of respondents reporting the announcement of the diagnosis outside the context of a medical consultation

The verbal announcement of a diagnosis outside the context of a medical consultation can occur in a variety of inappropriate places (such as in the corridor or in the patient's hospital room), which do not allow confidentiality or the undivided attention of the physician announcing the diagnosis. Overall, 10% of respondents reported receiving

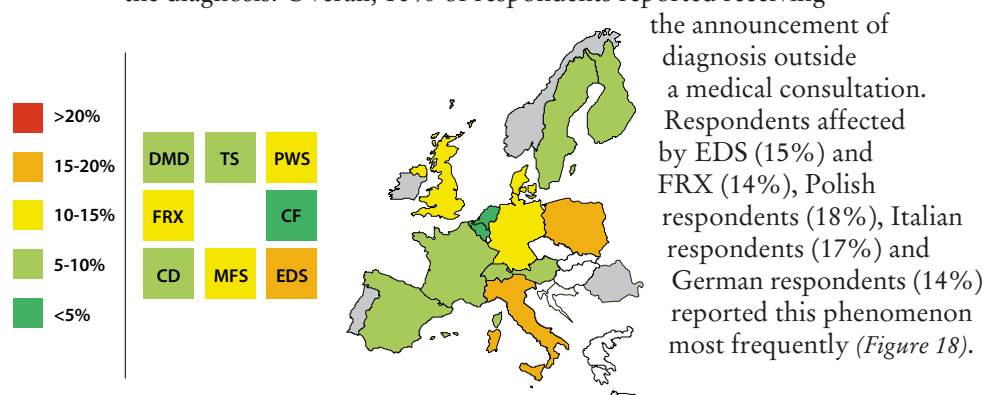


Figure 18 Percentage of respondents reporting the verbal announcement of the diagnosis outside the context of a medical consultation

Announcement of the diagnosis by telephone was reported by 10% of respondents overall and more frequently by Austrian respondents (30%), less by Italian, German, French and Belgian respondents (12% to 13%) and the least frequently by British and Swedish respondents (3% to 4%). Across disease groups, respondents affected by CD (22%) and CF (18%)

most frequently reported receiving their diagnosis by telephone (Figure 19).

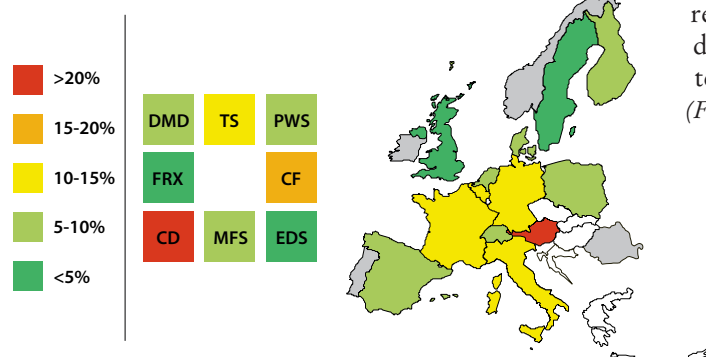


Figure 19 Percentage of respondents reporting the announcement of the diagnosis by telephone

For 10% of overall respondents, the diagnosis was announced in writing, without any personal contact at all. In some cases (7% overall), this meant the receipt of an announcement from a diagnostic structure with no accompanying explanation. Most frequently this was reported by respondents affected by FRX (19%), PWS (10%) and DMD (10%). Across countries, Swedish, Dutch and Belgian respondents frequently reported receiving the diagnostic announcement in this way (10%).

Respondents from Spain (1%) very rarely reported receiving the diagnosis in written form (Figure 20).

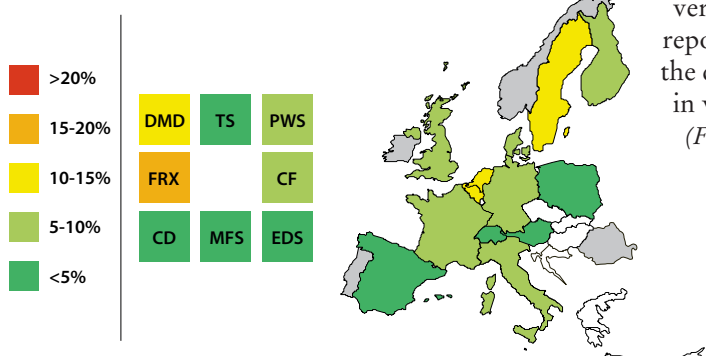
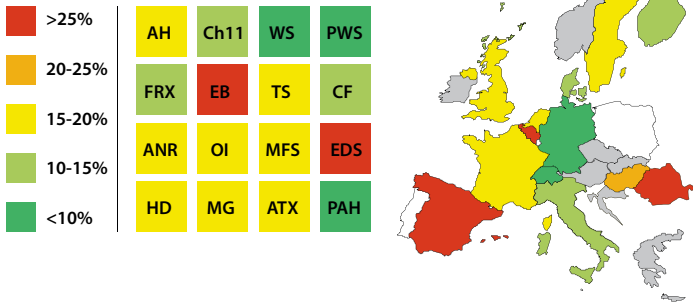


Figure 20 Percentage of respondents reporting written announcement of diagnosis without additional explanation

Written announcement of the diagnosis with an accompanying explanation was less frequently reported overall (3%), but more frequently by Danish

respondents (12%) and those affected by EDS (7%) as compared to other disease and country groups (Figure 21).

Figure 21 Percentage of respondents reporting a written announcement of the diagnosis with accompanying explanation



**ADDITIONAL SUPPORT AND INFORMATION
ACCOMPANYING THE ANNOUNCEMENT OF DIAGNOSIS**

Psychological Support

With the exception of Polish respondents (16%) a large majority of survey participants (87% overall) reported the belief that psychological support should be proposed during the time of diagnosis (Figure 22). In practice, the majority of respondents did not receive psychological support (between 60% and 80% overall). More than three out of four French, Polish, Italian

and Swiss respondents did not receive such support at the time of diagnosis (Figure 23).

If provided, such psychological support was provided by a psychologist (33% of cases), by a physician (28% of cases) or a patient organisation (24% of cases).

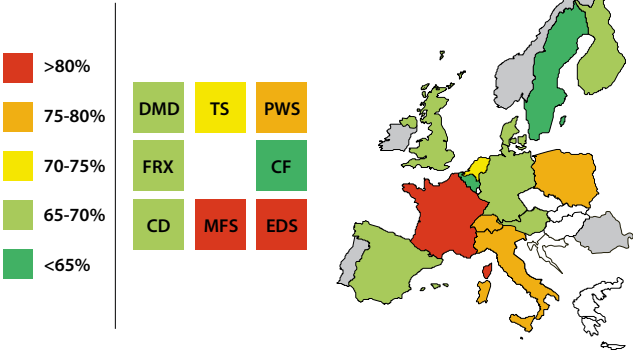


Figure 22 Percent of respondents reporting the announcement of the diagnosis without accompanying psychological support

Complete Information About the Disease

Similarly, almost all survey participants (95% overall) expressed the belief that additional information regarding the newly diagnosed disease should also accompany diagnosis.

On average, 25% of survey respondents did not receive such additional information. More specifically, more than one out of three respondents affected by PWS, TS, EDS and MFS and more than one out of three Danish and Dutch

respondents did not receive any such information (Figure 23).

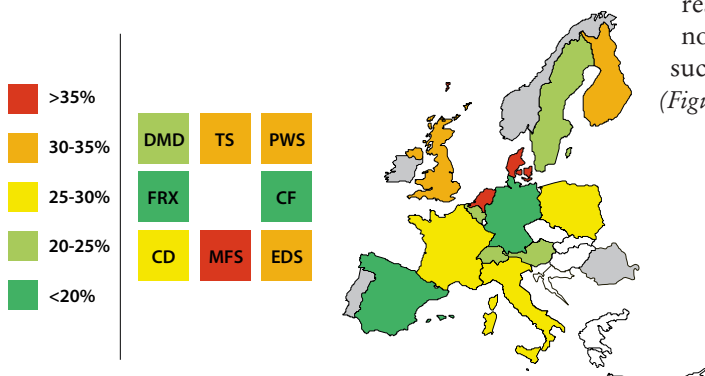


Figure 23 Percent of respondents reporting the announcement of the diagnosis without accompanying information without disease

Genetic Nature of the Disease¹

For the seven investigated diseases with a genetic mode of transmission, nearly 25% of overall respondents reported that the genetic nature of the newly diagnosed disease was not explained at the time of announcing the diagnosis. More specifically, respondents affected by EDS, TS and PWS more frequently reported that this information was lacking. Swiss, Polish,

Danish and Finnish respondents more frequently reported a lack of communication of the genetic nature of the disease more than respondents from other investigated countries (Figure 24).

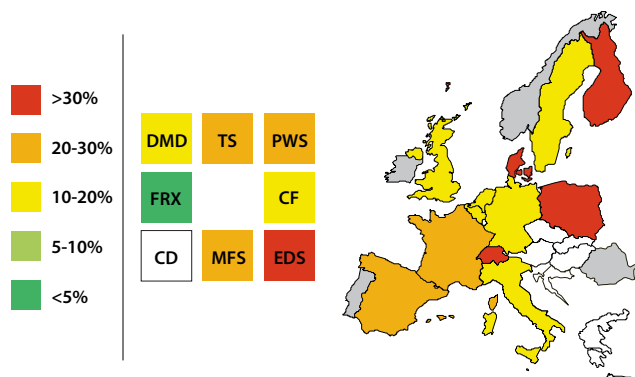


Figure 24 Percentage of respondents reporting the announcement of the diagnosis without accompanying genetic information about the disease

¹-Crohn's disease, which does not have a genetic mode of transmission and Austria, where the respondents' were mainly CD patients, are not included in this section.

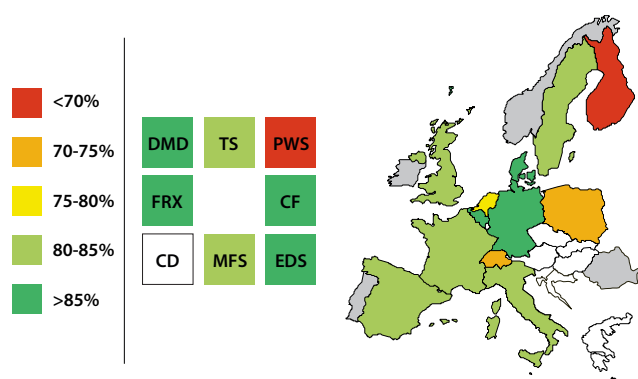
The announcement of a genetic disease has direct consequences on a patient's decision to have children. This announcement can also have an impact on any other family member's decision to have children, as they may also be carriers of the disease. The diagnosis of one family member may also lead to the diagnosis of other affected family members whose symptoms previously had gone unnoticed.

In order for the knowledge of a genetic disease in the family to effectively prevent continued transmission or to enable the diagnosis of affected family members not yet identified, genetic counselling should be offered for diagnosed patients or their families. Once genetic counselling has been offered, the communication of this information to other family members must also be guaranteed.

Genetic counselling was offered to 52% of families participating in the survey overall. Great variation was observed between disease groups: 86% of respondents affected by FRX, 77% of respondents affected by DMD and only 26% of respondents affected by EDS were offered genetic counselling services. Across country groups, the provision of genetic counselling services was most frequently reported by British (74%), Dutch (71%) and Belgian (67%) respondents and less frequently by respondents from Switzerland (32%), Denmark (35%) and Sweden (27%).

Less than half of the respondents (42%) reported that informing their family about the genetic nature of their disease was suggested by a health professional. This suggestion was especially infrequently reported by Swedish (21%), Swiss (29%) and Danish (32%) respondents.

Whether suggested by a health professional or not, 87% of respondents overall shared this information with their family members. At least one out of five Finnish, Swiss, Polish and Dutch respondents reported not informing their family about the genetic nature of their disease.



Respondents affected by PWS reported not informing their families about the genetic nature of their disease much less frequently than other respondents (*Figure 25*).

Figure 25 Percentage of respondents informing their families about the genetic nature of the disease

The communication of information on the genetic nature of the disease led to the diagnosis of other family members for 15% of respondents overall (*Figure 26*) and the identification of other carriers of the disease for 17% of

respondents overall (*Figure 27*), some of whom were already experiencing symptoms and others who were not.

Differences across country groups were quite significant: diagnoses of respondents from Poland, Belgium and the Netherlands (*figure 26*) less frequently led to diagnoses of their family members and in Italian respondents this was even less frequent (<5%). Across disease groups, differences were also observed: respondents affected by PWS (1%), CF, DMD and TS (6-8%) reported informing their families less frequently, resulting in other diagnoses, than respondents affected by MFS, FRX and EDS (32%-37%).

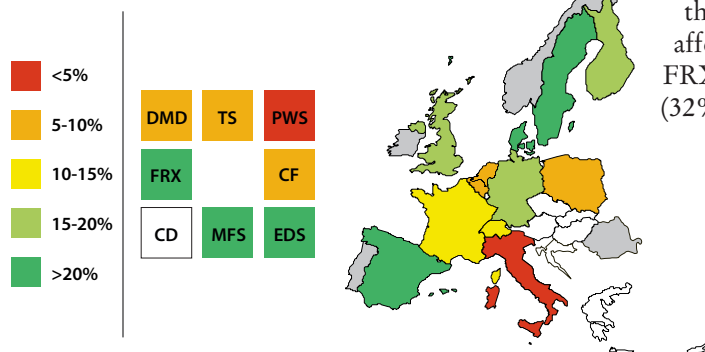


Figure 26 Percentage of respondents for whom the diagnosis led to another diagnosis in the family

Across disease groups the percentage of carriers identified as a result of another diagnosis in the family varied. The least frequent identification of carriers occurred in the families of respondents affected by PWS and MFS. Very few respondents from Poland and Switzerland reported the identification of carriers in their family following the announcement of diagnoses. This could be explained by the fact that many Polish and Swiss survey participants were also affected by PWS and MFS (*Figure 27*).

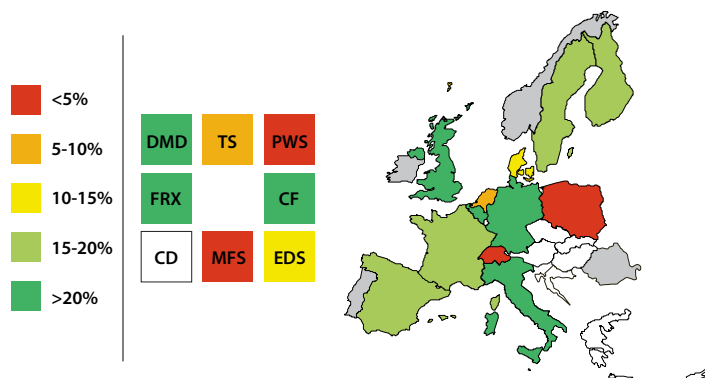


Figure 27 Percentage of respondents for whom the diagnosis led to the identification of other carriers

Overall Results of the **EurordisCare3** Survey

Considering the overall population of respondents, the average patient required more than nine different medical services. This number ranged from approximately four different medical services to nearly 12 different medical services, depending on the disease. More than half of the respondents reported the lack of referral as the greatest barrier to accessing essential medical services. The next most significantly reported reason for lack of access was the unavailability of services, followed by waiting times, distance and personal cost. Almost one-third of respondents required the assistance of a social worker in the 12 months preceding the survey. While the majority of patients reported easy or very easy access, more than one-third met one with difficulty or could not meet one at all.

Even when obtained, patients were not always satisfied with medical or social services. Overall, one out of ten patients reported that essential services they sought met their expectations poorly or did not meet them at all. In general, satisfaction with social services was even lower. For the seven social services investigated, half of the respondents reported that services met their expectations only 'somewhat' or 'not at all'. As a result of their disease, nearly one-fifth of respondents had to move house, usually to relocate to a home better adapted to their health needs. Nearly one-third of respondents reported that a patient in their family had to reduce or stop professional activity as a result of their disease; an additional one-third of respondents reported one member in the family had to reduce or stop professional activities to take care of a relative with a rare disease.

Overall, nearly one out of five patients experienced rejection by a healthcare professional. Although the types of rejection experienced ranged across disease and country groups, most patients reported a reluctance of professionals to treat them due to the complexity of the disease. Survey participants ranked the functions of Centres of Expertise and how they could be best implemented.

Medical Services

In the absence of a single aetiological treatment for most rare diseases, their management usually involves a piecemeal approach to the treatment of symptoms. As such, most rare diseases are complex, requiring a multidisciplinary approach to their care. The extent to which this multidisciplinary approach is required varies from one patient to another, depending on the severity of the particular case, as well as from disease to disease, depending on its complexity. To quantify the number of medical services required by individual patients, the average number of different medical services sought per patient over the two-year period preceding the survey was measured. Although this number represents the extent of needs for an individual patient, it does not reflect the range of services required within each disease group. Even within the same disease group, diversity may exist between patients for the various services. Therefore, for each investigated disease, the medical services required for at least one out of ten patients were documented, representing the range of medical services potentially needed to meet the needs of the disease group in question. This analysis, in combination with patient expectations regarding the structure and function of Centres of Expertise, will shed light on the most effective and desirable organisation of care for rare disease patients in general and for each rare disease specifically.

INDIVIDUAL NEEDS

Considering the overall population of respondents, the average individual needs of respondents included 9.4 different medical services. More specifically, these included four kinds of consultations, three types of medical exams and 2.4 types of additional care services. What may seem to be a considerable number of medical services to the healthy observer is a reality for rare disease patients. Their daily life revolves around locating service providers, securing appointments and obtaining the quality care required. As shown in Figure 1, significant differences in individual needs exist between patients affected by the different diseases investigated. Patients affected by FRX reported an average of 4.3 different medical services needed, whereas patients with EDS reported the need for an average of 11.8 different medical services.

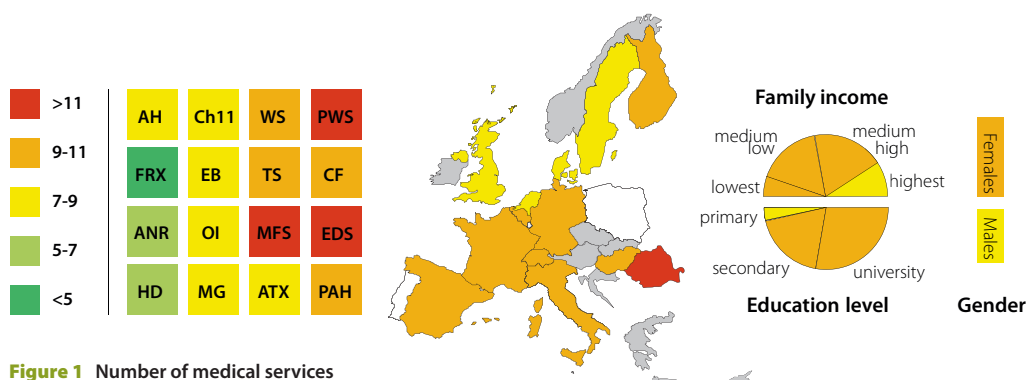


Figure 1 Number of medical services needed during the two-year period preceding the survey

Across countries (for countries with at least 60 respondents and representing more than four diseases) fewer differences were observed, suggesting that disease-specific needs play a stronger role than cultural or local economic factors in the average number of medical services required per patient. Overall, small differences in the average number of medical services required per patient were observed across socioeconomic groups.

Family Income Level

The need for consultations (4.4 consultations for respondents with lower incomes and 3.6 for those with higher incomes) and medical exams (3.2 exams reported by respondents with lower incomes and 2.9 exams for higher income respondents) decreases with the increased level of income. Little variation was observed amongst income groups for additional care services.

Education Level

The need for all three types of medical services varied depending on the level of education, with more services required by respondents with university-level education compared to respondents with primary-level education. More specifically, 4.1 consultations were needed for those with a university education and 3.8 consultations for those with a primary level of education; 3.1 exams were reported by respondents with a university level of education and 2.7 exams for those with a primary level; 2.5 additional services were required by respondents with a university level of education as compared to 2.1 additional services reported by those with a primary level of education.

Area of Residence

Slight variations in the average number of consultations (4.4 consultations for residents of country capitals and 3.9 for residents in small cities) and medical exams (3.3 exams reported by respondents residing in national capitals and 2.9 exams in small cities) also exist depending on the area of residence. These differences are even less apparent for additional care services, which are usually provided by local professionals.

Gender

Disparities between men and women were also observed. Overall, women sought consultations more frequently (4.3 consultations for women and 3.6 consultations for men), medical exams (3.3 exams reported by women compared to 2.8 for men) and additional care services (2.5 additional care services required by female respondents and 2.2 reported by men).

COLLECTIVE NEEDS ACCORDING TO DISEASE

As previously expressed in terms of the average number of medical services required by an individual patient, survey participants reported a need for an average of 9.4 different medical services in the two-year period preceding this survey. Locating service providers, securing appointments and obtaining the quality of care required for this large number of different medical services is a feat in itself. The number of medical services required by rare disease patients depends heavily on the complexity of the disease with which they are affected. Figure 2 depicts the number of medical services required by at least one out of ten patients within each disease group.

It is evident from this figure that PWS and EDS patients reported the greatest number of medical services potentially needed to meet their disease-specific needs. When considered in the context of Centres of Expertise, it may not be possible to provide such a large range of services in one centre; a network of multiple centres may be needed.

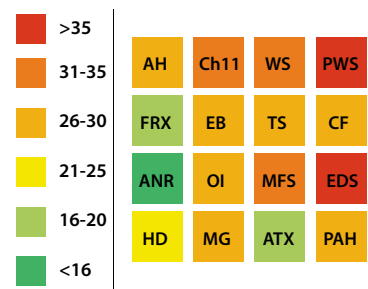


Figure 2 Number of medical services needed by at least one out of ten patients in each disease group

HOSPITALISATIONS

Rare disease patients may require hospitalisation not only for ambulatory care (acute problems related to the disease) but also for further exploration (radiology, ultrasound, biological testing, etc.), routine check-ups or for specialised care only available in a hospital setting. Hospitalisation was heterogeneous amongst the different rare disease groups, ranging from 21% of patients with FRX to 62% of patients with CF reporting being hospitalised in the two years preceding the survey (*Figure 3*). Slight differences were also observed across country groups, with more frequent hospitalisations in Germany, Italy, Hungary and Romania.

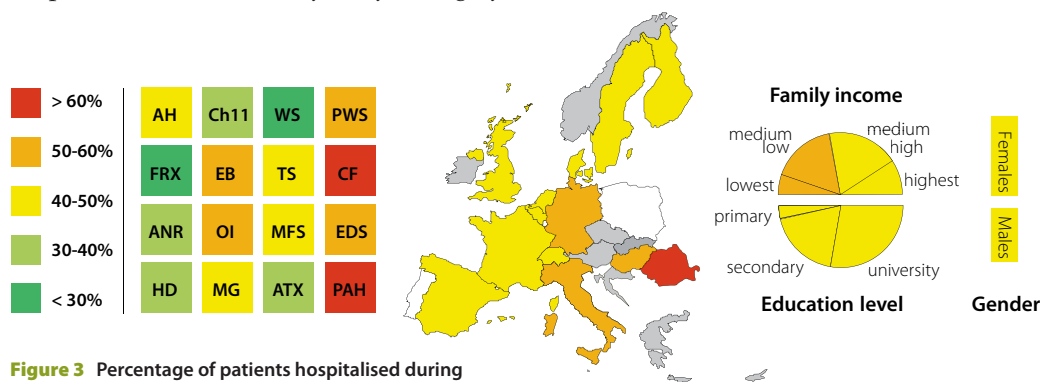


Figure 3 Percentage of patients hospitalised during the two-year period preceding the survey

Survey participants not only reported on the number of hospitalisations but also on the total number of days spent in hospital (*Figure 4*). Patients with HD reported the highest number of days spent in hospital as a result of disease-specific needs that required longer stays.

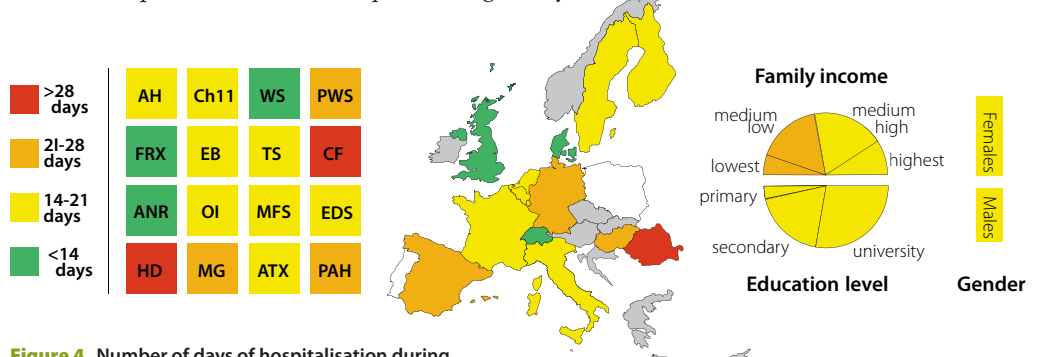


Figure 4 Number of days of hospitalisation during the two-year period preceding the survey

Patients with PAH reported the least number of days spent in hospital as a result of the fact that their disease-specific needs required shorter but more frequent hospital visits. Patients from the United Kingdom, Switzerland and Denmark reported the least number of days spent in hospital.

Although no general trends were observed across disease or country groups, these data should be considered in policy-shaping discussions concerning the organisation of care. For patients with diseases requiring frequent hospital visits, local services would be more appropriate.

Some variations in the number of patients requiring hospitalisation and the duration of their stay were observed across demographic groups.

A slightly larger percentage of patients from small towns (48%) required hospitalisation compared to patients living in large cities and capitals (45%).

More respondents from households with lower incomes required hospital stays (51%) for a longer period of time (24 days) than respondents from households with higher incomes (45%, 18 days).

ACCESS TO AND SATISFACTION WITH MEDICAL SERVICES

Access to medical services was evaluated based on patient experiences surrounding what were considered eight essential services for each disease. The responses per country, therefore, concerned at least 30 different essential services, as the total number of respondents from a given country were concerned with several diseases, each with specific (though sometimes overlapping) essential services.

The following figures show that patients' experiences across countries in accessing essential services was difficult, very difficult (*Figure 5*) or impossible (*Figure 6*).

Barriers to Access

Respondents from Germany and the Netherlands reported the lowest number of situations (less than 10%) in which they experienced difficult or very difficult access. Respondents from more than half of the investigated countries considered access difficult or very difficult in more than 15% of situations. Respondents from Finland reported a total lack of access to essential medical services in more than 20% of situations in which they sought essential medical services.

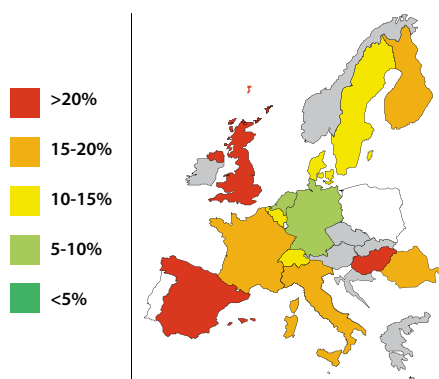


Figure 5 Difficult access

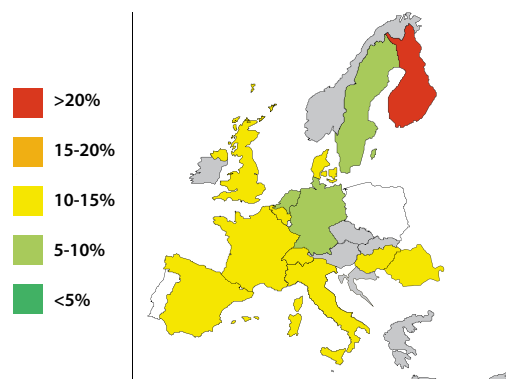
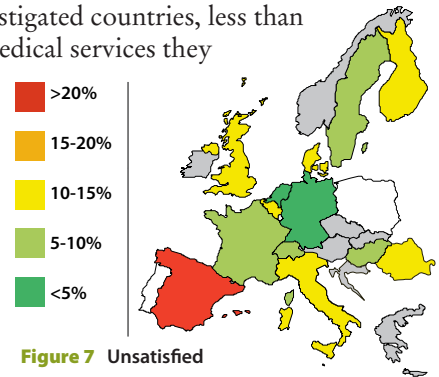


Figure 6 Impossible access

Satisfaction

Even when obtained, some patients reported dissatisfaction with the services they received. In general, a higher dissatisfaction with medical services was reported in countries with more difficult access (*compare Figure 6 and Figure 7*). With the exception of Spain (where the rate of dissatisfaction with services is higher than the rate of impossible access), the rate of dissatisfaction was lower than the rate of difficult access; in half of the investigated countries, less than 10% of respondents reported that the essential medical services they sought responded to their expectations poorly or not at all. This finding suggests that after overcoming barriers to accessing essential medical services, the expectations of patients are often met. Eliminating barriers to access could significantly contribute to meeting patients' expectations and should be considered a priority.

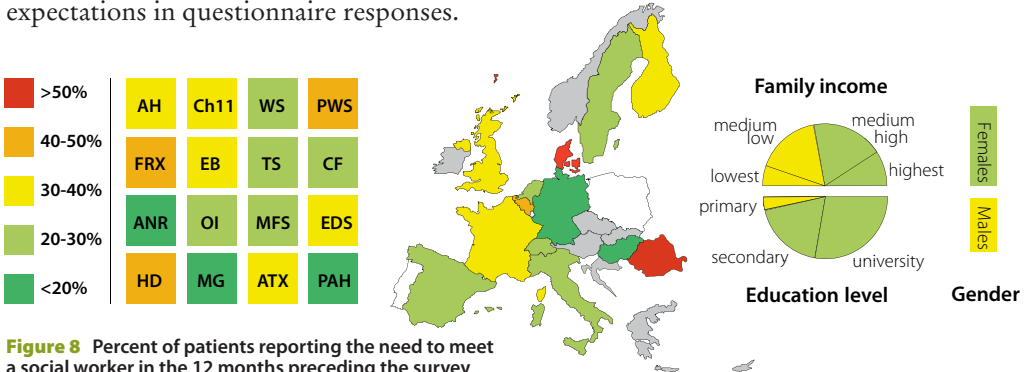


Social Services

NEEDS

The need for social services differs dramatically from country to country: in Germany 11% of respondents reported a need to meet a social worker in the 12 months preceding the survey, whereas in Denmark 54% reported the same need. Equally dramatic differences were reported across disease groups, with 19% of respondents affected by ANR compared to 59% of respondents affected by HD reporting the need to meet a social worker in the 12 months preceding the survey.

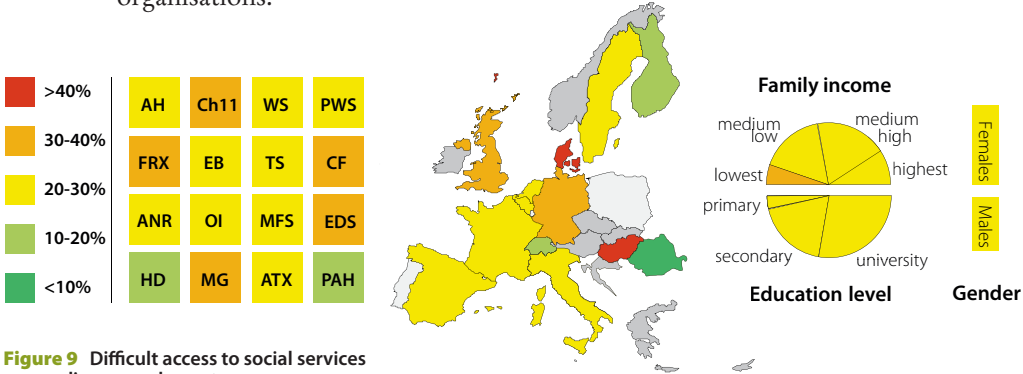
It is important to consider that cultural norms regarding social assistance may influence patient responses as much as needs resulting from a disease. In countries where social assistance is customarily not widely accepted, patients may less frequently report this need and underemphasise their expectations in questionnaire responses.



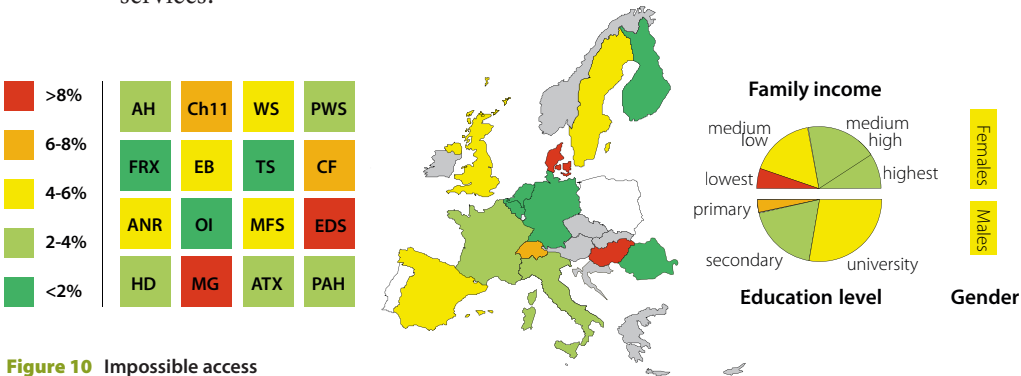
A small difference was observed between the responses of respondents from the lowest income group and the highest: respondents with lower incomes reported a slightly higher need for social services than higher income respondents (34% and 25%, respectively).

ACCESS TO SOCIAL SERVICES

Depending on the country, the structure providing social assistance varies greatly. With the exception of respondents from Germany, Sweden, Belgium and Romania, the majority of respondents reported the provision of social services in administrative structures. In Germany and Sweden, social services were usually provided in medical structures, and in Belgium and Romania, such services were provided in associative structures, such as patient organisations.



With the exception of respondents affected by HD and PAH (*Figure 9*), little variation in difficulty accessing social services was reported across disease groups; between 20% and 40% of respondents reported difficult access to social services. Survey participants from Denmark and Hungary reported a greater difficulty accessing these services, whereas Finnish and Swiss respondents reported less difficulty. Respondents from families with the lowest income level more frequently reported difficult access to social services.

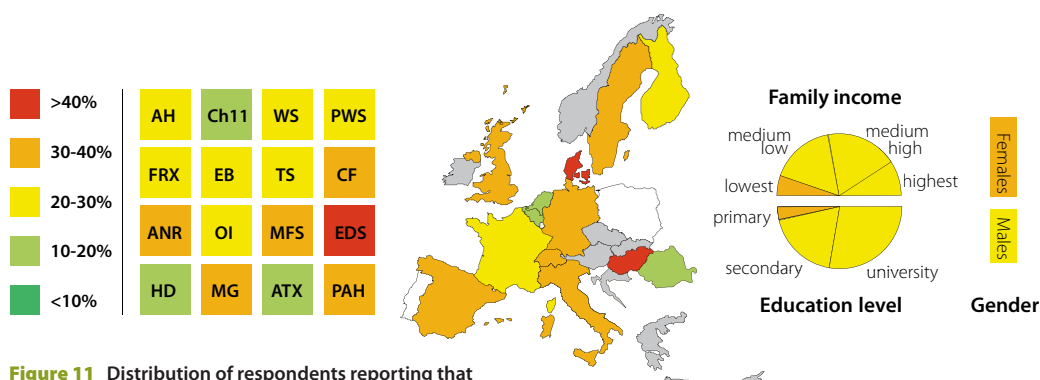


Respondents with EDS and MG most frequently reported impossible access to social services. As compared to respondents from other investigated countries, Hungarian and Danish respondents most frequently reported a total lack of access to social services. Respondents from families with the lowest income level most frequently reported a total lack of access to social services.

SATISFACTION WITH SOCIAL SERVICES

Survey participants were asked whether each of seven social services met their expectations ‘entirely’, ‘well’, ‘somewhat’ or ‘not at all’. The strikingly large (28% of situations overall) number of respondents who reported being ‘not at all’ satisfied by these social services stimulated further investigation into the characteristics of the respondents. For six of the disease groups, over 30% of respondents (and up to 46% for respondents with EDS) reported that social services did ‘not at all’ meet their expectations. Patients with Ch11, ATX and HD less frequently reported a total lack of social services satisfaction (18%, 16% and 16%, respectively) (*Figure 11*). The same diversity was observed across country groups. Respondents from Romania (14%), Belgium (16%) and the Netherlands (18%) less frequently reported a total lack of satisfaction with social services. Respondents from Denmark (45%) and Hungary (48%) reported this lack more frequently.

Little variation was observed in satisfaction with social services across education level groups; 32% of respondents with a primary level of education and 29% of respondents with a university level of education reported that social assistance met their expectations.



Patient satisfaction with social services was also related to the structure in which services were sought. Respondents who obtained services from a social worker belonging to an insurance company (31%), administrative structure (32%) or professional structure (33%) more often reported that their expectations were ‘not at all’ met. Respondents that obtained services from hospitals or associative structures, such as patient organisations, were less often disappointed (27% and 17%, respectively). The means of communication with the social worker also played a role in the satisfaction with social services: 34% of patients who communicated by telephone, 29% of patient who communicated in the social worker’s office and 24% of patients who communicated with the social worker in their own homes reported that their expectations were ‘not at all’ met.

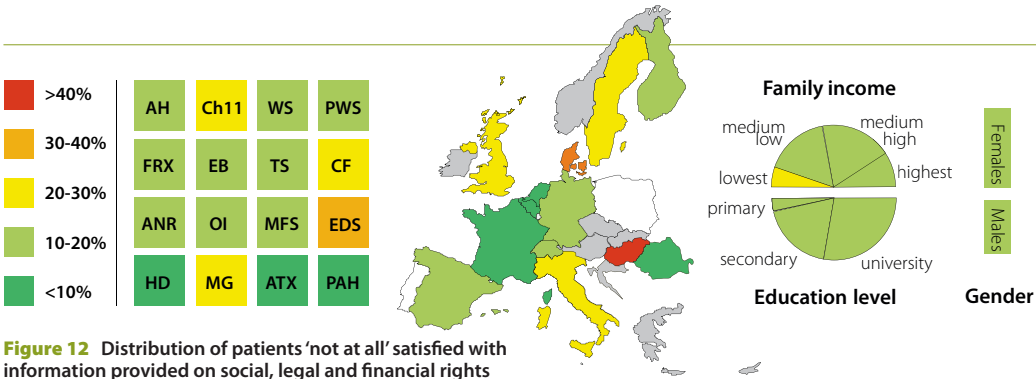
In summary, the more closely the social worker worked with patients (i.e. within the structure of a patient organisation or in the patient’s own home), the more adequately the needs of the patient were met.

Satisfaction With Specific Social Services

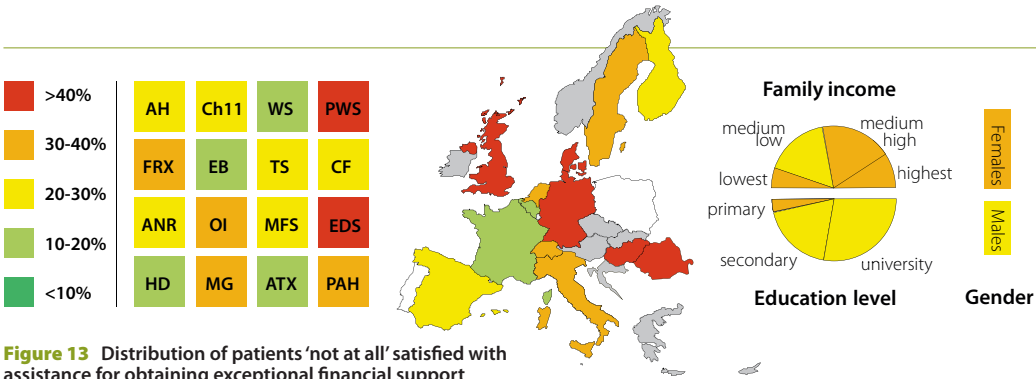
Survey participants reported their level of satisfaction for the following seven social services:

- Information on social, legal and financial rights
- Assistance with financial paperwork (assistance with financial liability or reimbursement, allowance, etc.)
- Information on specialised technical support
- Assistance with social integration (school, leisure, professional, etc.)
- Help in getting personal assistance
- Referral to other services (psychological support, home care, etc.)
- Assistance with obtaining exceptional financial support

The figures illustrate the distribution of respondents who were ‘not at all’ satisfied with each service. As all patients were not necessarily in need of each service, the percentage of respondents concerned is included in the figure legend (*Figure 12 to 18*). Services are presented in decreasing order of need.



This need was reported as the most frequently needed social service. Respondents with EDS and respondents from Denmark and Hungary most frequently reported being ‘not at all’ satisfied by the service.



Respondents with EDS and PWS most frequently reported being ‘not at all’ satisfied by the service. A greater variability of responses was observed across country groups: British, German, Danish, Hungarian and Romanian respondents most frequently reported being ‘not at all’ satisfied with the service.

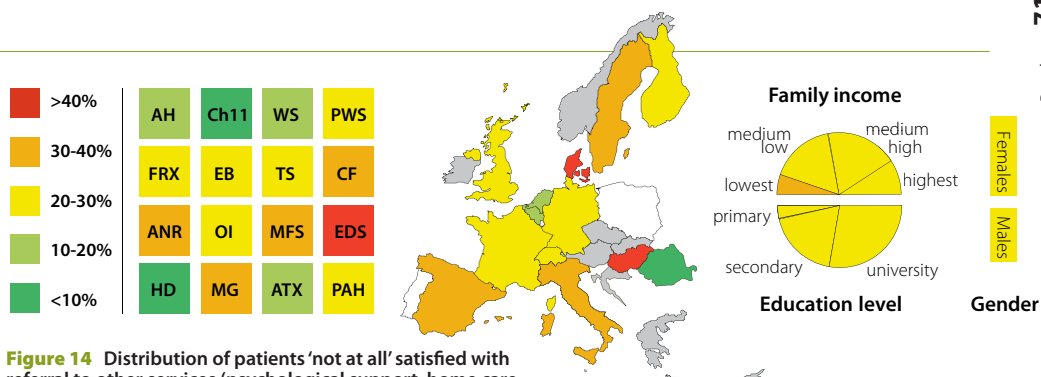


Figure 14 Distribution of patients 'not at all' satisfied with referral to other services (psychological support, home care, etc.) (out of the 75% of overall respondents concerned)

Variability of responses was observed across disease and country groups. Respondents with EDS most frequently reported being 'not at all' satisfied by the service. Danish and Hungarian respondents most frequently reported being unsatisfied with this service.

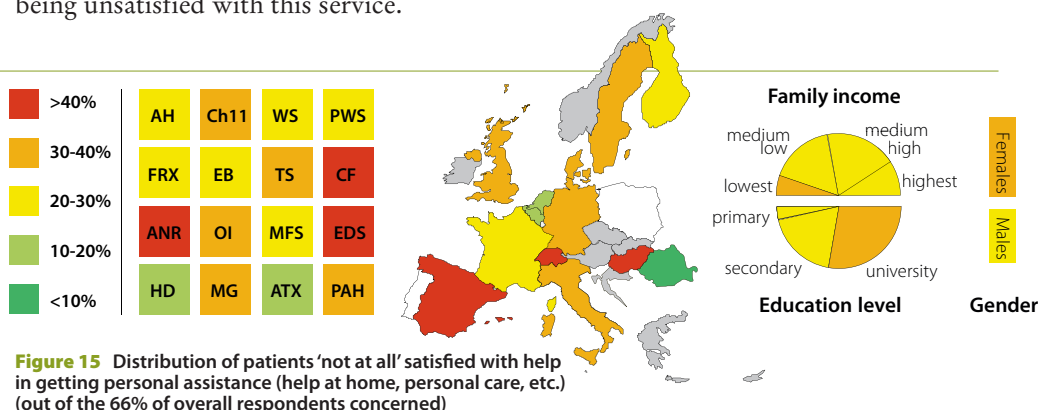


Figure 15 Distribution of patients 'not at all' satisfied with help in getting personal assistance (help at home, personal care, etc.) (out of the 66% of overall respondents concerned)

Variability of responses was observed across disease and country groups as well as economic groups. Respondents with EDS, ANR and CF most frequently reported being 'not at all' satisfied by the service. Danish, Hungarian and Swiss respondents reported being 'not at all' satisfied with this service more frequently than respondents from any other country. Respondents from families with the lowest incomes also frequently reported this dissatisfaction.

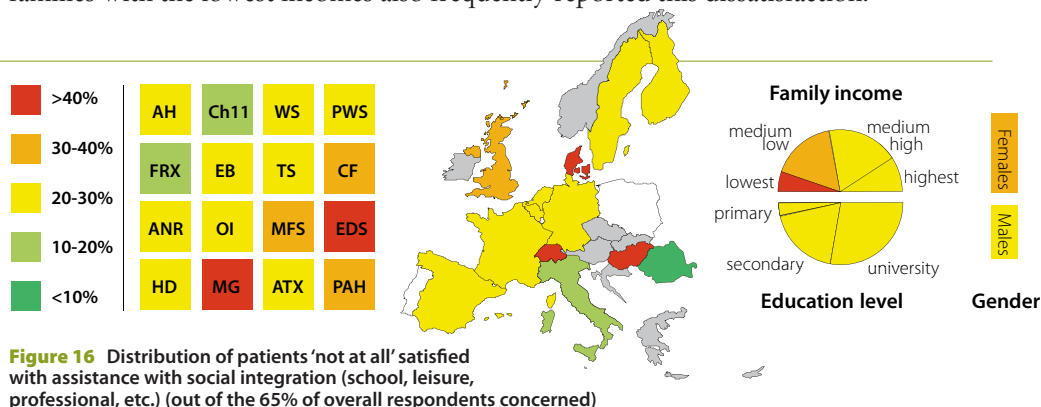
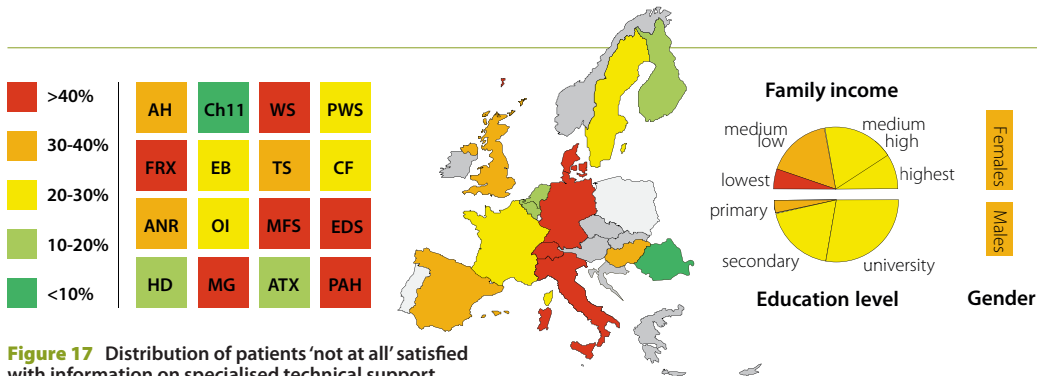


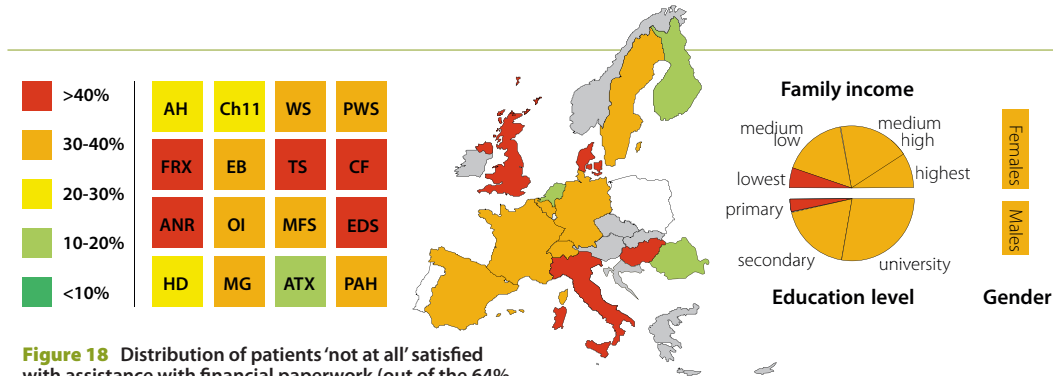
Figure 16 Distribution of patients 'not at all' satisfied with assistance with social integration (school, leisure, professional, etc.) (out of the 65% of overall respondents concerned)

Variability of responses was observed across disease and country groups as well as economic groups. Respondents with EDS and MG most frequently

reported being “not at all” satisfied by the service. Danish, Hungarian and Swiss respondents reported being “not at all” satisfied with this service more frequently than respondents from any other country. Respondents from families with the lowest family income also frequently reported this dissatisfaction.



Although less frequently needed, respondents across several disease groups and several countries frequently reported being ‘not at all’ satisfied with this social service. Respondents from families with the lowest level of income more frequently reported being ‘not at all’ satisfied with this service than other economic groups.



This social service was reported as the least frequently needed. With the exception of Dutch, Romanian and Finnish respondents, survey participants across Europe were ‘not at all’ satisfied with this service. This satisfaction varied little across socioeconomic groups. Respondents concerned with EDS, CF, TS, FRX and ANR more frequently reported being ‘not at all’ satisfied with this service as compared to respondents concerned with other diseases.

Overall, the more specific a social service is (i.e. the smaller the percentage of rare disease patients seeking the service) the more frequently respondents reported being ‘not at all’ satisfied with the services obtained.

UNRESOLVED DISPARITIES IN SOCIAL SERVICE SYSTEMS

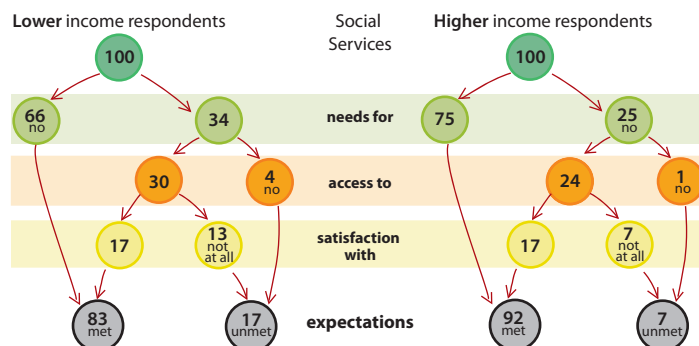


Figure 19 Comparison of needs, access and satisfaction with social services between lower and higher income groups

Despite a greater need for social services, respondents from lower income groups experienced greater barriers to access than those from higher income groups (Figure 9 and Figure 10). In addition, respondents from lower income groups more frequently reported being ‘not at all’ satisfied with the social services they received even after overcoming any barriers to access. As illustrated in Figure 19, for a given 100 lower income respondents, 34 required social services. Of these 34, only 30 were able to access services. Of the 30 able to access social services, 13 were ‘not at all’ satisfied with the services they obtained. In the end the needs of 17 out of the 100 respondents with lower income remain unresolved versus only 7 out of the 100 respondents with higher income.

Overall, an inadequate organisation of the social service systems seems to exacerbate social inequalities rather than improve them.

SATISFACTION WITH SOCIAL VERSUS MEDICAL SERVICES

In contrast to medical services, for which barriers to access were reported to present the greatest problem for patients, it was the inadequacy of the social services provided that was reported as the most significant problem facing survey participants. Overall, for the seven social services investigated (Figure 12 to Figure 18), 50% of respondents considered that these services met their expectations ‘somewhat’ or ‘not at all’; a rate of dissatisfaction five times higher than for medical services, overall.

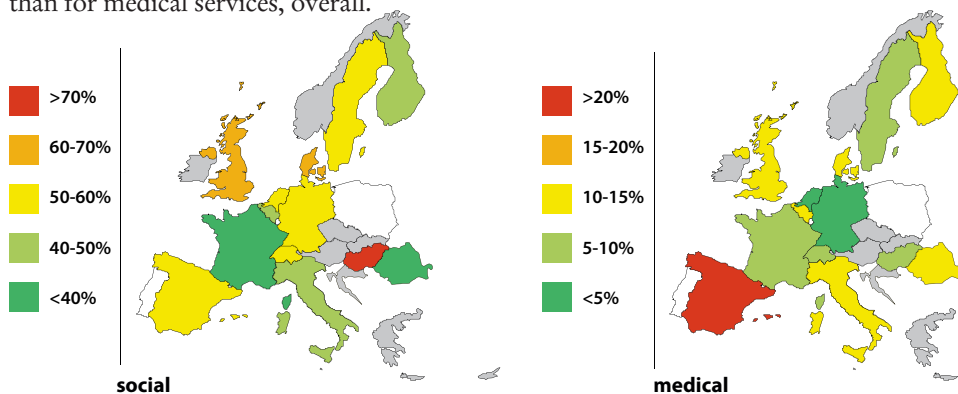


Figure 20 Dissatisfaction with social services compared to dissatisfaction with medical services

Rejection

The question regarding rejection by health professionals effectively illustrates the importance of involving patient organisation representatives in the construction of the questionnaire. Patient organisation representatives involved in this process suggested the inclusion of this question, based on the strong anecdotal evidence they had gathered from patients suggesting the frequent rejection of rare disease patients by their healthcare providers. During these discussions, patient organisation representatives relayed anecdotes such as the following:

- A PWS patient unwelcome in a general practitioner's office because of the inability to accommodate her in the waiting room due to her weight
- A TS patient asked to leave a physician's office because her behaviour made other patients uncomfortable
- A patient with a metabolic disorder diagnosed with tonsillitis was sent home with no treatment due to the reluctance of an ear, nose and throat specialist to prescribe any treatment that might be contradicted

Understanding the dynamics of rejection by healthcare professionals is a controversial subject. Some critics can view patients' feelings of rejection as subjective and therefore unreliable. Among many explanations, acts by healthcare professionals experienced as rejection by patients may be unintentional, a result of prudence, with the intention of protecting the patient; a result of the health professional's limited knowledge of the obstacles faced by rare disease patients; or a result of the healthcare structure's limited capacity to accommodate rare disease patients, who may have needs that differ from others in the practice.

The preliminary presentation of the results of this question in the survey elicited great controversy amongst all stakeholders. Many healthcare professionals and health authorities were unaware of the problem, or were greatly surprised by its scale. The intention of the investigation of this problem was not to criticise healthcare professionals or to legitimise the feelings of rejection by patients, but rather to quantify the magnitude of the problem and to investigate the reasons for rejection, in order to help adjust the structure and approach in healthcare settings to more appropriately accommodate rare disease patients.

Recalling the Constitution of the World Health Organization¹, any potential violation of the fundamental right of human beings to attain their highest attainable standard of health deserves exploration. Given the initial responses of healthcare professionals, it is possible that such a question would not have been included in the questionnaire, further highlighting the importance of the direct involvement of patient organisation representatives in the questionnaire design process.

The first and most striking aspect of the rejection experienced by patients is its scale. Overall, one out of five survey respondents (18%) reported being rejected by a healthcare professional, with a great variation reported across disease and country groups, as illustrated in the figure below (*Figure 21*).

1-See introduction

The greatest level of rejection was reported by EDS (35%) and EB (28%) patients, less for WS (9%), PAH (9%) and PWS (8%). Respondents from Belgium (33%), Spain (26%) and Romania (25%) reported rejection more frequently than patients from Germany (7%).

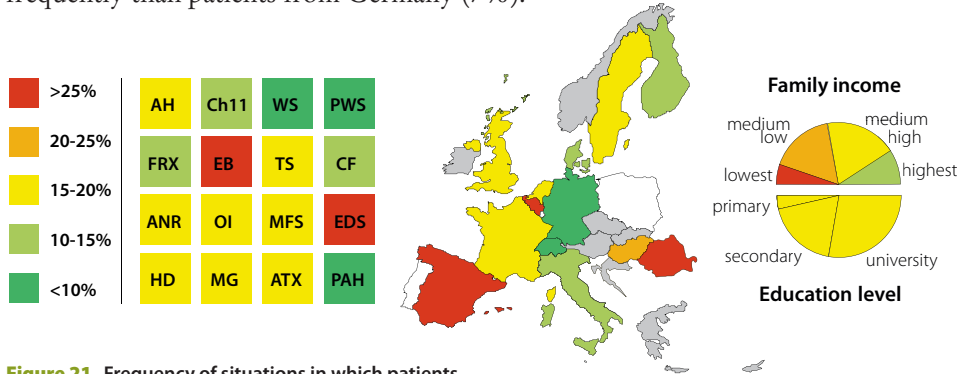


Figure 21 Frequency of situations in which patients were rejected by health professionals, by country and disease group.

CAUSE OF REJECTION

In general, patients reported experiencing rejection either as a result of the disease itself (its complexity) or as a result of characteristics associated with the disease (physical appearance, communication, behaviour). In many cases, patients reported experiencing rejection for several reasons even during the same encounter with a health professional. It is for this reason, therefore, that the total reported incidents of rejection surpass 100%.

Overall, the reluctance of health professionals to treat patients due to the complexity of their disease was the most frequently reported, in 85% of situations. Responses across disease and country groups reflected the same trend. However, respondents concerned with diseases including psychological difficulties (HD, FRX, WS, PWS, Ch11) also reported rejection due to personal characteristics associated with the disease. All Danish, Finnish and Romanian respondents who experienced rejection found that it was always due to the complexity of their disease, if sometimes in addition to other reasons.

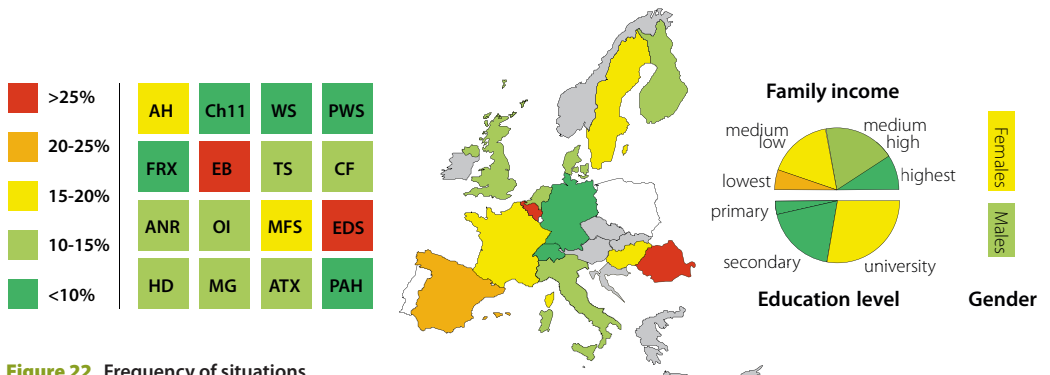
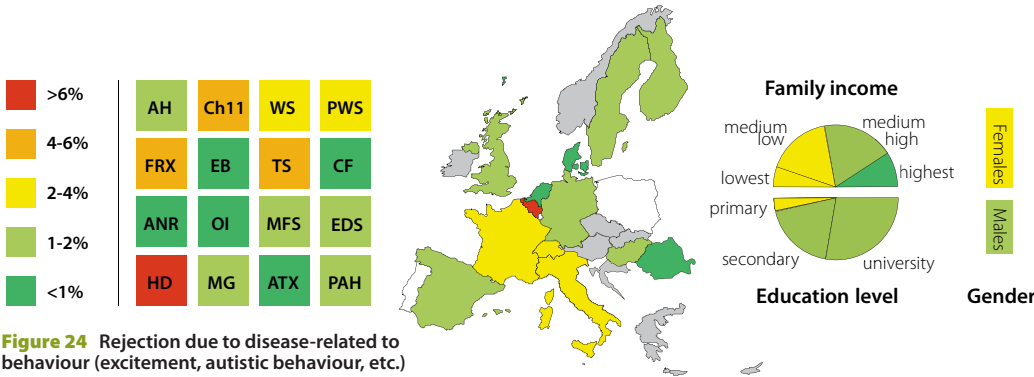
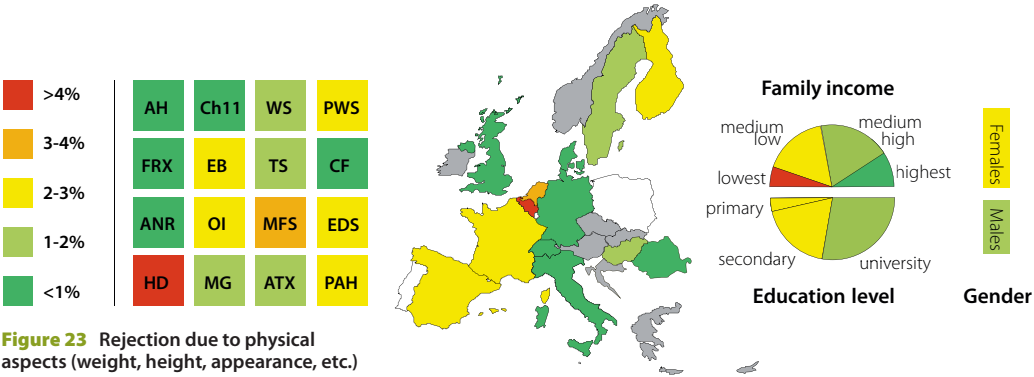
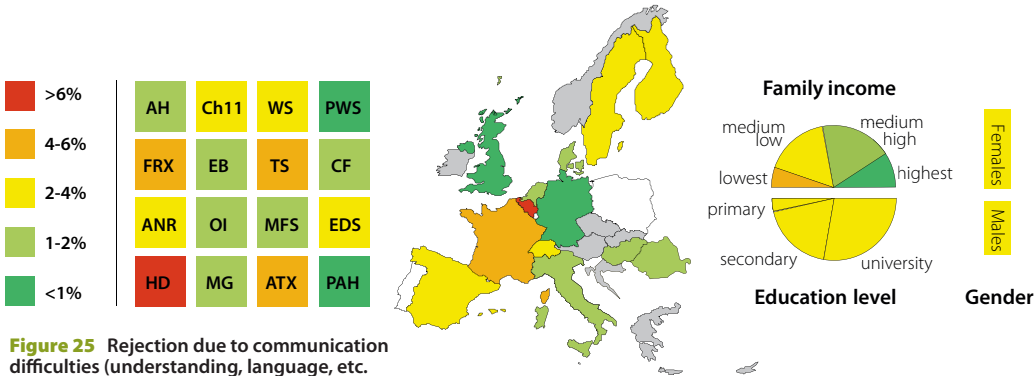


Figure 22 Frequency of situations in which patients were rejected as a result of the complexity of the disease

Still other respondents reported rejection directed toward characteristics of the patients themselves, including physical appearance (11%), disease-related behaviour (11%) and difficulty in communication (16%).



Rejection due to disease-related behaviour was mainly reported by respondents concerned with childhood diseases presenting psychological or psychiatric symptoms, as well as HD, for which respondents reported rejection due to disease-related behaviour in 9% of situations.



Differences in the experience of rejection across socioeconomic groups are often worrisome, and in some cases very surprising.

patients across countries (*Figure 27*) suggests that this difference is culturally related. In looking at the relationship between the rejection of male and female patients across countries, it is clear that a greater ratio of females to males rejected was reported in Sweden, Finland and Denmark than in Spain, Romania and Hungary. In Sweden, Denmark and Finland, countries

commonly known for their universal healthcare systems and social security systems that overall encourage equality among all socioeconomic groups, such significantly higher rejection of females (seven times higher in Finland, five times higher in Sweden and four times higher in Denmark) may be surprising for some and certainly warrants further investigation.

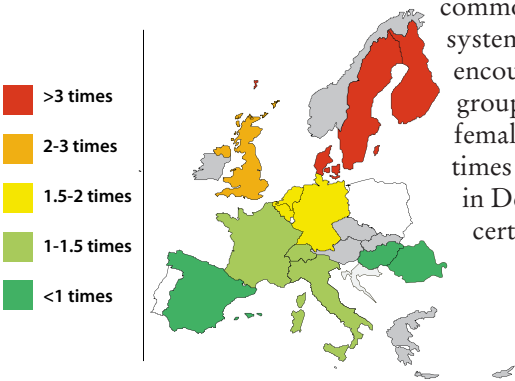


Figure 27 Rejection of females versus rejection of males. In Sweden, Finland and Denmark, females are rejected in more than three times as many situations as males.

Consequences of the Disease

The effects of a chronic illness on patients and their families are numerous, interfering with all dimensions of everyday life. In this survey, two specific consequences of being affected with a rare disease were investigated: moving house (to a more adapted home, to a specially adapted care centre, nearer disease specialists or nearer other relatives) and discontinuation or reduction of professional activity (either for patients themselves or for a family member, in order to take care of a relative).

MOVING HOUSE

Overall, 16% had to move for various reasons, with significant differences depending on the disease: 4% of respondents affected by ANR, 8% affected by WS, 10% affected by CF, 26% affected by AH and 33% affected by ATX. Differences between countries were less significant: 10% of German respondents, 12% of Swiss respondents, 21% of Italian respondents and 23% of Danish, Dutch and Finnish respondents (*Figure 28*).

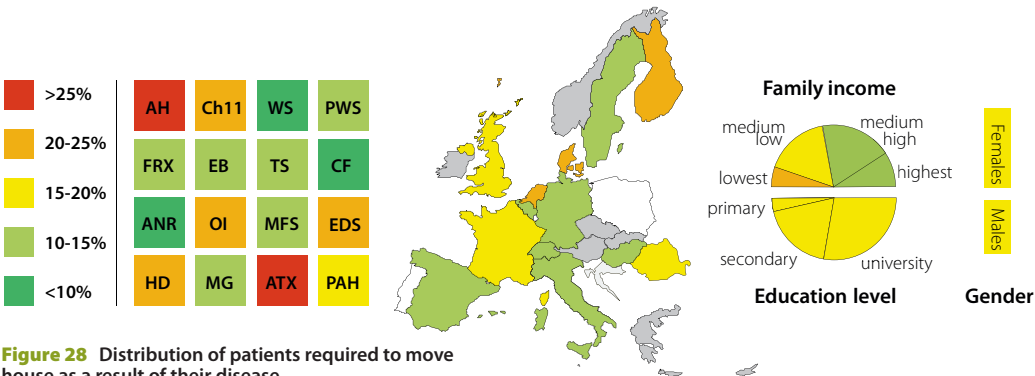
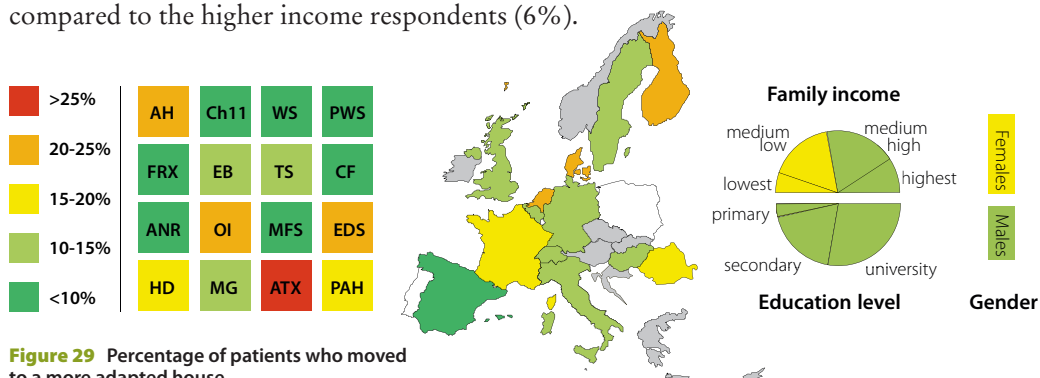


Figure 28 Distribution of patients required to move house as a result of their disease

Moving to a More Adapted House

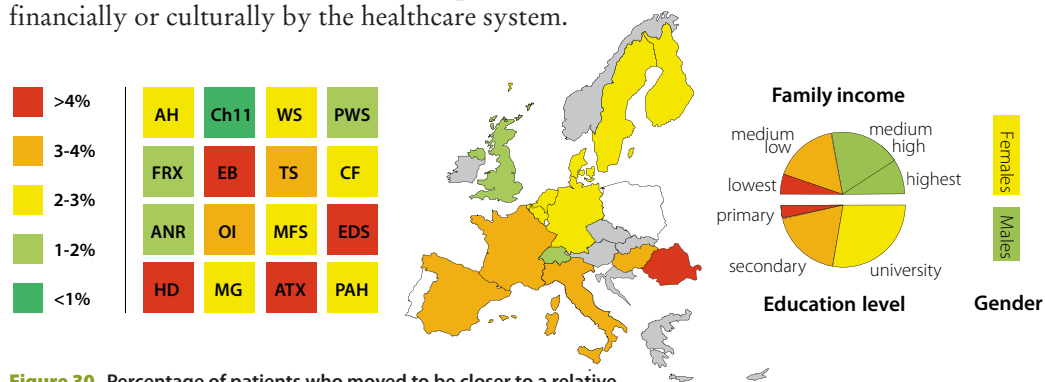
The majority of respondents who reported the need to change houses specified that the change was motivated by the need for a home more suitable to their disease-related needs. This reason for changing homes was more frequently reported by adult patients to address barriers in mobility. Across the different countries investigated, moving homes overall was less frequently reported by Spanish and British participants (*Figure 28*). This phenomenon was linked to the income of the families. The need to move house was twice as high in the lower income respondents (12%) compared to the higher income respondents (6%).



Other reasons for moving, in decreasing order, were: to move closer to a relative, to move closer to a disease specialist and to move to a specialised care centre.

Moving Closer to a Relative

In 3% of cases, respondents moved house to be closer to a relative who could provide them with psychological or logistic support. It is not surprising that this rate was higher for the four most debilitating diseases. We observed geographic variations in relation to moving to be closer to a relative; it was higher in Romania, France, Spain, Italy and Hungary. Socially, we observed even more significant variations: 7% of those who moved house were amongst the lower income group and 2% were in the higher income group. Similarly, families with a lower level of education were represented more frequently (5%) than others (3%) who moved house to be closer to a relative. These differences suggest that those who moved to be closer to a relative did so in order to address needs that were not provided either financially or culturally by the healthcare system.



Moving Closer to a Disease Specialist

Overall, 2.5% of patients moved in order to be closer to medical specialists in their diseases. For very rare diseases, such as AH and Ch11, this percentage was greater than 5%. Similar to those patients who moved to be closer to their families, variations across country groups were observed. The higher percentage observed in Finland could be explained by the distances from big cities, where specialised services are often located. The income level is also a strong determining factor, as families in the lower income bracket relocated seven times more frequently than those in the higher income bracket (4.7% versus 0.6%). In contrast, little difference with respect to the level of education obtained was found.

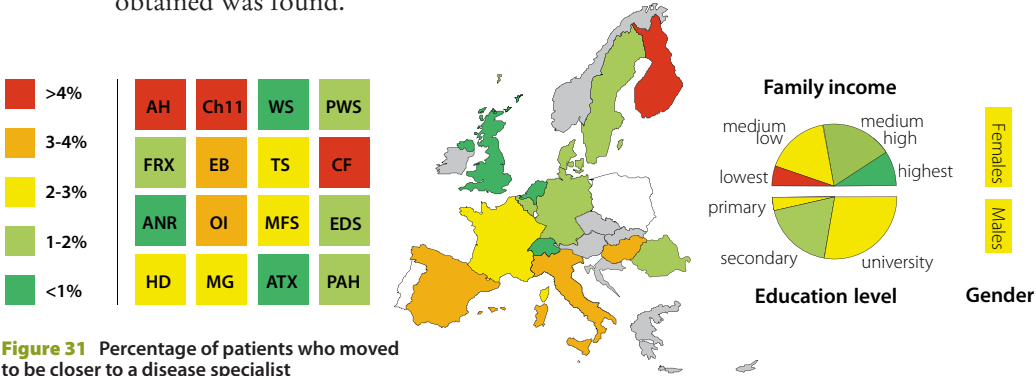


Figure 31 Percentage of patients who moved to be closer to a disease specialist

Moving to a Specialised Care Centre

Patients with neurological and/or psychiatric symptoms due to their disease were more likely to move to a specialised care centre.

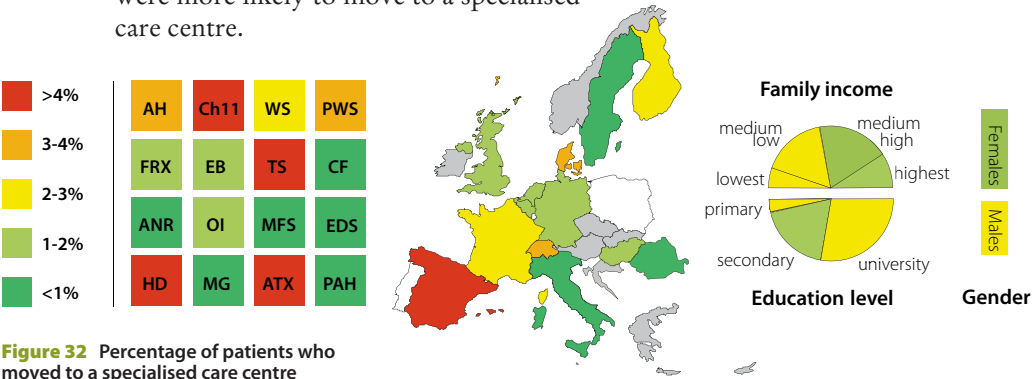


Figure 32 Percentage of patients who moved to a specialised care centre

Reduction or Interruption of Professional Activity

Overall, a reduction or interruption in professional activity due to the disease was observed in 61% of families. This percentage includes the patients themselves or a member of the family who stopped work to look after the patient, often a child.

Professional Activities of the Patient

On average, between 20% and 40% of all adult patients — lower for ANR (15%) and higher for PAH and EDS (56% to 60%) — interrupted their professional activities. The distribution of interruption of the professional

activities demonstrates that the more frequent interruptions occur in countries with a higher income per capita. In contrast, amongst the three countries with the lowest percentage of interruptions of professional activities are Hungary and Romania, which have lower income per capita.

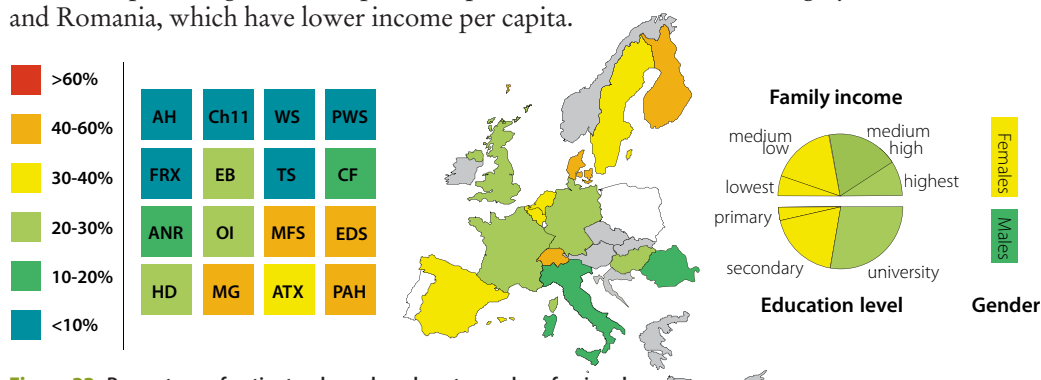


Figure 33 Percentage of patients who reduced or stopped professional activities due to their disease, across disease and country groups

Reductions in professional activities were more frequently reported by respondents from families with lower incomes (21%) compared to those with higher incomes (40%), females (36%) compared to males (18%) and those with a university education (31%) compared to a primary level of education (18%).

These figures suggest that in addition to disease-related issues, economic factors also have a great impact on the decision to reduce or interrupt professional activities, such as the wealth of the country and the possibility of social assistance.

Professional Activity of a Relative Caring for a Patient

In general, most reductions in professional activities were associated with parents stopping work in order to taking care of a sick child (54% to 71% for the six diseases affecting children).

In certain countries, an overrepresentation of minors may have resulted in a greater number of respondents who reported a reduction in professional activities to take care of a member of their family, i.e. a child of less than 18 years of age.

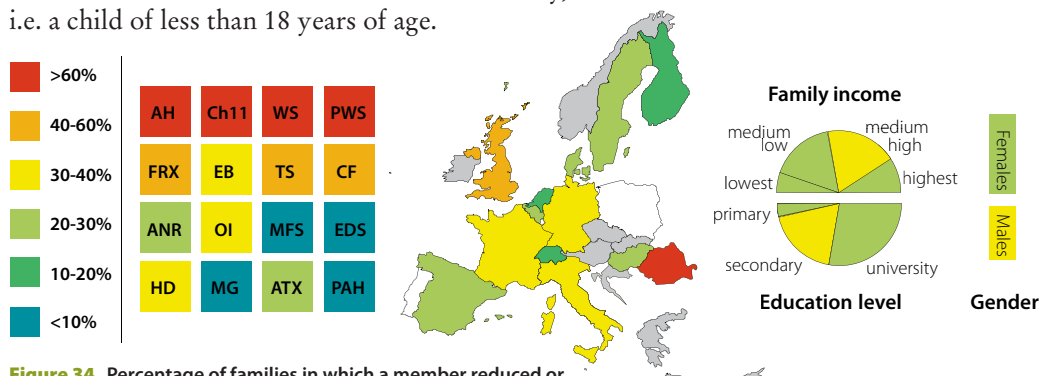


Figure 34 Percentage of families in which a member reduced or stopped professional activities in order to take care of a relative.

In lower income groups, 27% of patients interrupted or reduced their professional activities compared to 32% in the higher income group.

The gender of the patient also seems to play a role, with differences observed in relatives reducing professional activities in order to look after a male or a female. A difference is observed in both children and adults.

In the case of children, from the age of 5 years, relatives more frequently reduce their professional activities to take care of boys compared to girls (62% versus 53% in the range of 5 to 20 years).

The most striking difference is seen in the 25-to-35-year-old age group (34% versus 18%), which gradually reduces with age (12% versus 9% for more than 65 years of age). On average for patients of more than 20 years of age, 23% of male patients compared to 13% of female patients are assisted by a relative who has reduced or stopped professional activities.

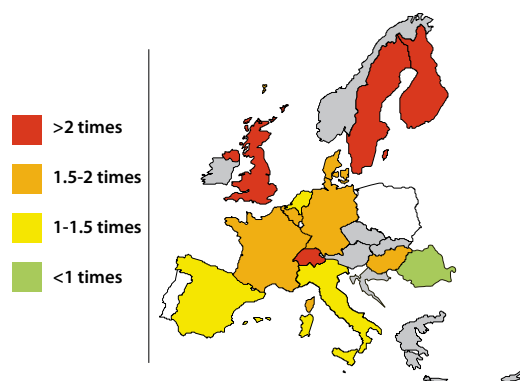


Figure 35 Ratio of reduction of activity to take care of male versus female patients

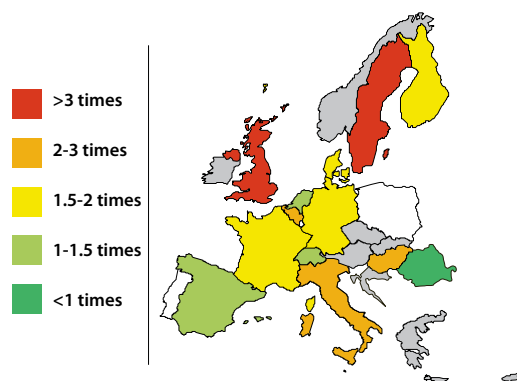


Figure 36 Reduction of activity of female versus male patients

Patient Expectations Regarding Centres of Expertise

As previously described in the section about the questionnaire design process, lessons learnt from the EurordisCare2 survey included the elimination of open-ended questions regarding treatment and medical service needs.

Although ideal for collecting patient expectations regarding the functions and implementation of Centres of Expertise, it was anticipated that similar difficulties would be encountered. Therefore, with the guidance of patient organisation representatives involved in the design of the questionnaire, the most important related issues were identified (12 additional functions provided by Centres of Expertise and nine descriptive statements describing their implementation). As a result, very few respondents considered the proposed functions of the Centres of Expertise as 'of no use', 'of little use', or disagreed with the statements regarding their implementation.

PATIENT EXPECTATIONS REGARDING PROPOSED FUNCTIONS OF CENTRES OF EXPERTISE

Given that the basic mission of a Centre of Expertise for a rare disease, or group of rare diseases, is to ensure diagnosis and follow-up of patients by offering multidisciplinary consultations, medical examinations, specialised equipment and genetic advice, survey respondents were asked to qualify 12

additional functions of a Centre of Expertise according to their specific needs (see 'Questionnaire' in Appendix). As patient organisation representatives were closely involved in the creation of these suggested functions, it is not surprising that the majority of survey participants found all 12 functions as 'useful' or 'essential'. This illustrates the high degree to which patient organisations are able to represent the needs of their patient members.

Therefore, responses to this question are presented by ranking the functions of the Centres of Expertise considered most essential. Complementing the discussions' two-year reflection process, the following conclusions provide a quantitative representation of patients' expectations regarding the functions of Centres of Expertise, which are officially acknowledged in the Declaration of Common Principles on Centres of Expertise and European Reference Networks for Rare Diseases².

The ranking of essential functions of Centres of Expertise were further analysed by country (as described p 64) and by disease (none representing more than two-thirds of responses). Amongst the 12 proposed functions of Centres of Expertise³, were considered as most essential for at least two-thirds of the respondents:

- Coordinating the sharing of medical information on the patient between all professionals who care for him/her in the specialised centre
- Coordinating the sharing of medical information between professionals of the specialised centre and local health professionals, to facilitate the continuity of the patients' follow-up
- Communicating with other specialised centres and professional networks to harmonise treatments and research at the national and European levels
- Collaborating with research teams working on the rare disease (in particular for clinical studies)

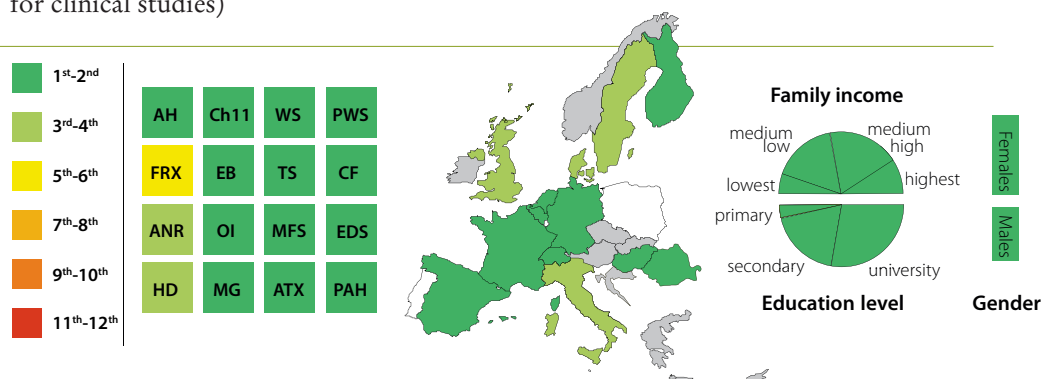


Figure 37 Rank of 'Coordinating the sharing of the patient's medical information between all professionals who care for him/her in the specialised centre' as an essential function.

This function (Figure 37) was considered as one of the most essential functions of a Centre of Expertise by patients affected by almost all investigated diseases and countries (ranked first or second), representing 70% of respondents overall. Respondents affected by FRX syndrome (ranked fifth or sixth), ANR and HD (ranked third or fourth), which also reported an overall lower need for medical services, considered this function as slightly less essential compared to patients with other investigated diseases.

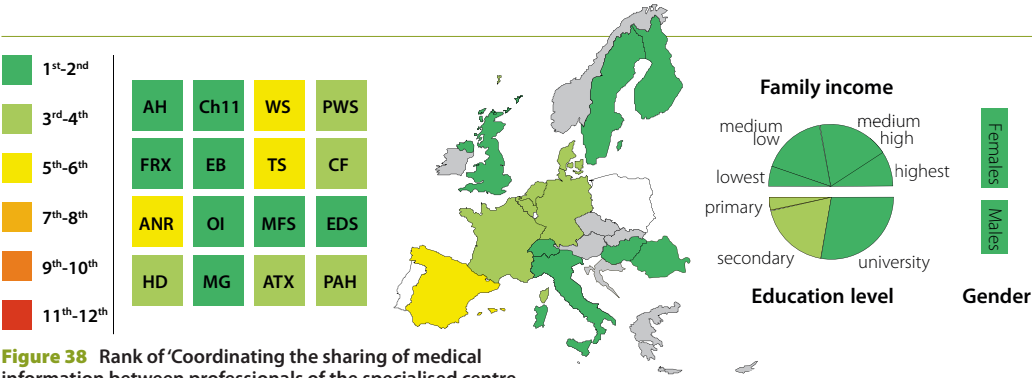


Figure 38 Rank of 'Coordinating the sharing of medical information between professionals of the specialised centre and local health professionals, to facilitate the continuity of the patients' follow-up' as an essential function

This function (*Figure 38*) was also reported as an one of the most essential functions of a Centre of Expertise by patients affected by almost all investigated diseases and countries, representing 67% of respondents overall.

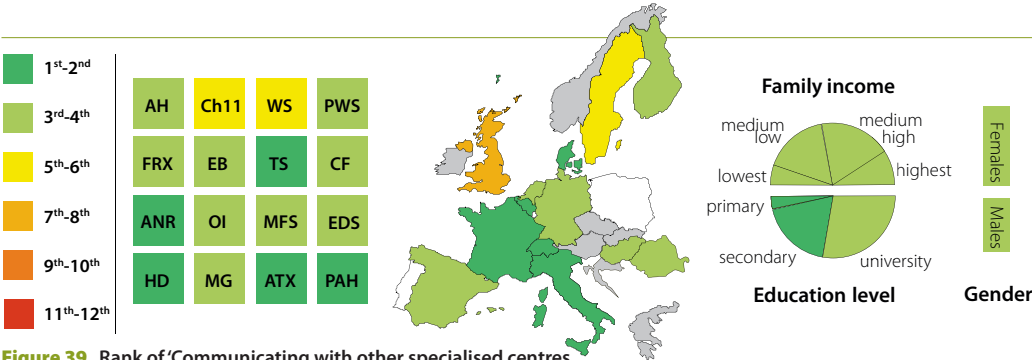


Figure 39 Rank of 'Communicating with other specialised centres and professional networks to harmonise treatments and research at the national and European levels' as an essential function.

This function (*Figure 39*) was reported as the third most essential function of a Centre of Expertise, representing 66% of respondents overall. Respondents from Sweden (ranked fifth or sixth) and the United Kingdom (ranked seventh or eighth) considered the communication with other Centres of Expertise and professional networks as less essential compared to other investigated countries.

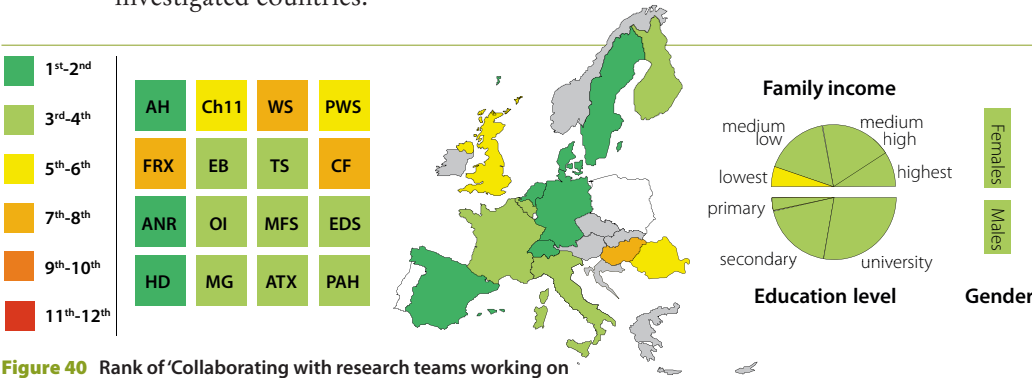


Figure 40 Rank of 'Collaborating with research teams working on the rare disease (in particular for clinical studies)' as an essential function.

This function (*Figure 40*) was reported as the fourth most essential function of a Centre of Expertise, representing 64% of respondents overall.

In general, this function was reported as a greater priority for adult patients, as parents may be more reluctant to consent to their child's participation in clinical studies.

Overall, patients more strongly emphasised the importance of the quality of care (better communication and collaboration between health structures and professionals) rather than the type of care itself when reporting on essential functions of Centres of Expertise.

Fewer respondents considered the remaining proposed functions of Centres of Expertise as essential:

- Facilitating the follow-up of patients at different stages of their life by easing the passage from paediatric care to adult care, or from adult care to geriatric care
- Offering patients the option of grouping consultations or tests on the same day in the specialised centre and organising the appointments
- Informing patients about their rights and guiding them toward social services, schools, leisure activities or vocational guidance, etc.
- Training local professionals in responding to the specific needs of patients and supplying their contact information to patients
- Creating material for teachers, employers, social services, insurance companies and the general public to inform them about patients' needs and improve the social integration of patients
- Providing frequent care related to the disease (physiotherapy, speech therapy, psychotherapy, etc.)
- Monitoring the current needs of the patient community of a rare disease through surveys or registers of patients
- Providing occasional care related to the disease (surgery, prosthesis, orthopaedics, etc.)

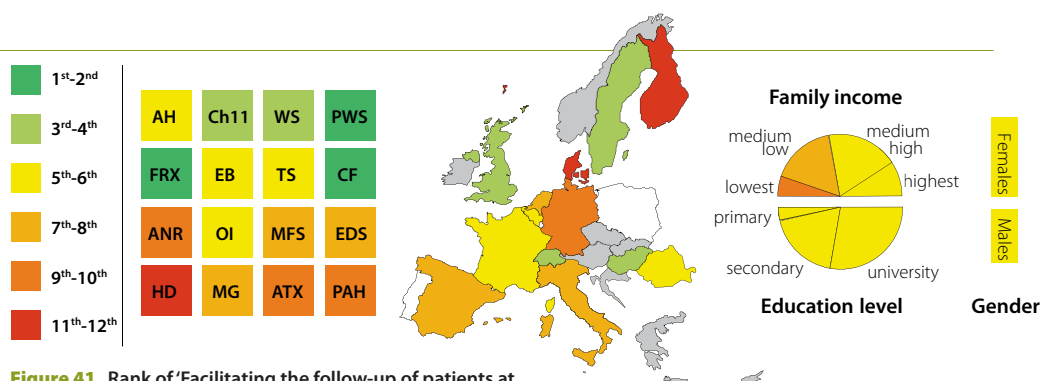


Figure 41 Rank of 'Facilitating the follow-up of patients at different stages of their life by easing the passage from paediatric care to adult care, or from adult care to geriatric care' as an essential function.

This proposed function (*Figure 41*) of Centres of Expertise was considered essential by 57% of respondents overall.

In general, this function was reported as a greater priority for paediatric patients, though the responses were quite heterogeneous for the diseases and countries investigated.

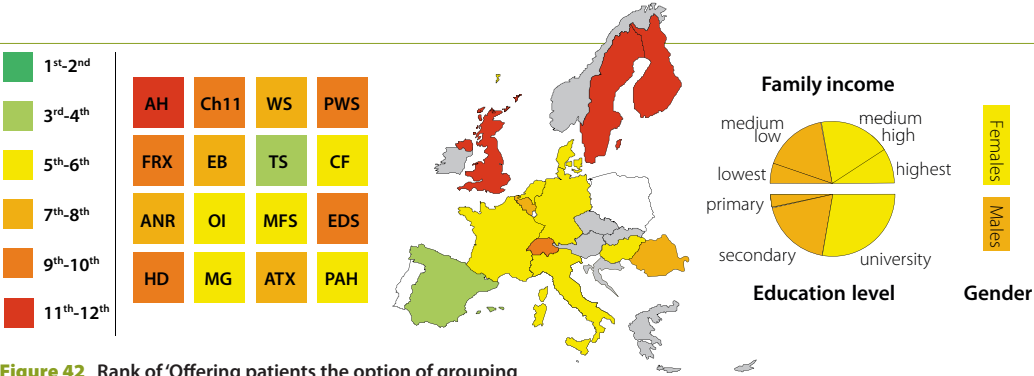


Figure 42 Rank of 'Offering patients the option of grouping consultations or tests on the same day in the specialised centre, and organising the appointments' as essential function.

Offering patients the option of grouping appointments was considered essential by 57% of respondents overall (Figure 42).

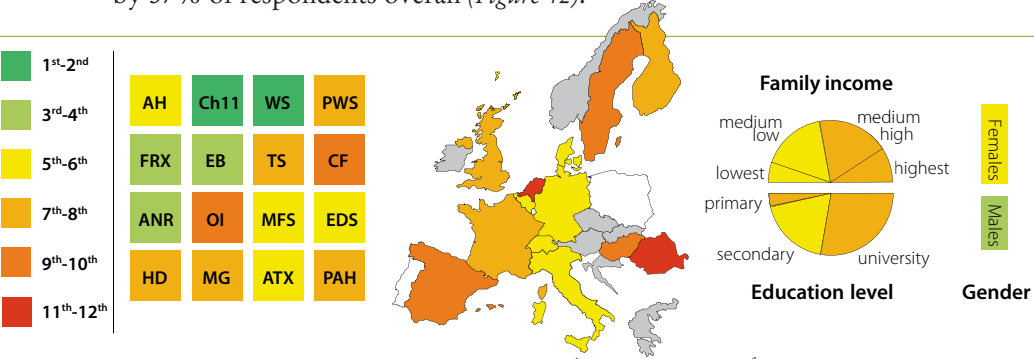


Figure 43 Rank of 'Informing patients about their rights and guiding them toward social services, schools, leisure activities or vocational guidance, etc.'

This proposed function of a Centre of Expertise (Figure 43) elicited heterogeneous responses amongst the different countries, although fewer adult patients considered the provision of this information as an essential function of Centres of Expertise. Overall, 55% of respondents considered this function as essential.

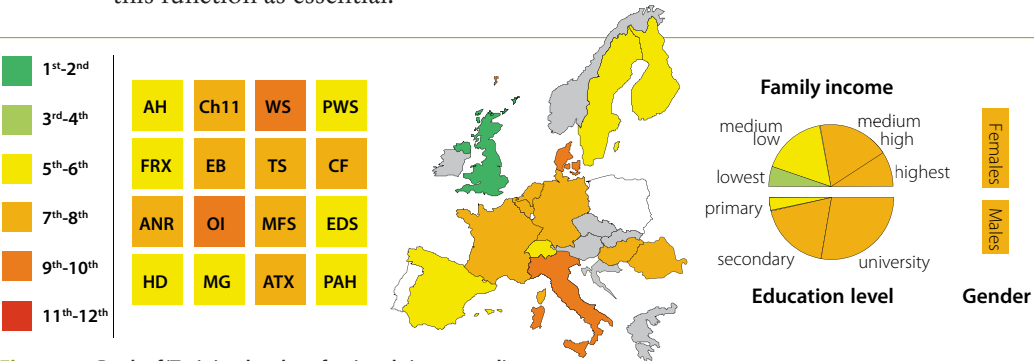


Figure 44 Rank of 'Training local professionals in responding to the specific needs of patients and supplying their contact information to patients' as an essential function.

The training of local professionals in responding to the specific needs of patients (Figure 44) was considered as a priority by 55% of respondents overall. Respondents from the United Kingdom considered this function as more essential (ranked first or second) than respondents from other countries investigated.

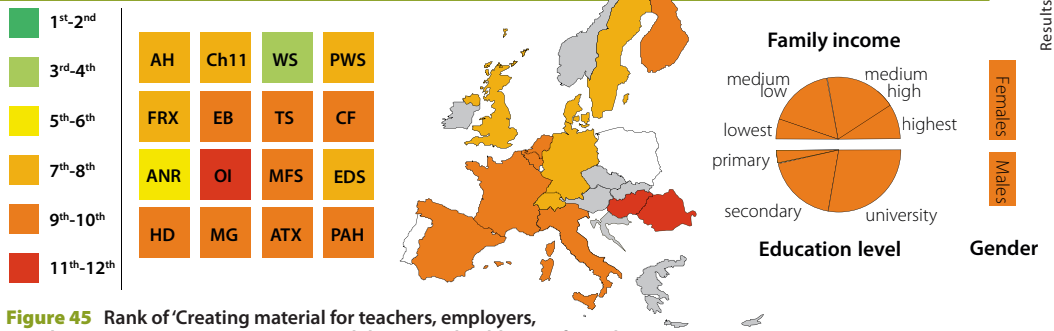


Figure 45 Rank of 'Creating material for teachers, employers, social services, insurance companies and the general public to inform them about patients' needs and improve the social integration of patients' as an essential function.

Although the creation of these materials was only considered as essential by 50% of respondents overall (Figure 45), patients from Finland and Romania ranked this function of Centres of Expertise as much more essential than respondents from other investigated countries. The opinion of patients across diseases was less heterogeneous, although patients affected by HD, ATX and CF regarded this function of Centres of Expertise as more essential than other patients.

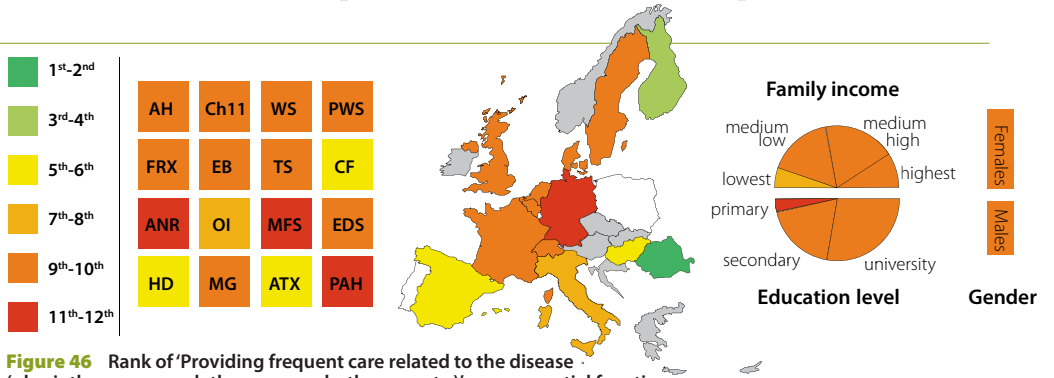


Figure 46 Rank of 'Providing frequent care related to the disease (physiotherapy, speech therapy, psychotherapy, etc.)' as an essential function.

This proposed function (Figure 46) of Centres of Expertise was considered essential by 50% of respondents overall, with a heterogeneous response among patients across different diseases and countries.

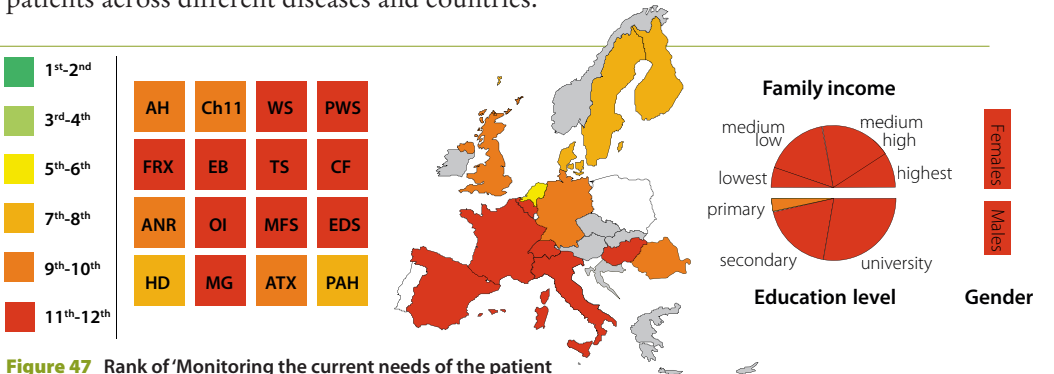


Figure 47 Rank of 'Monitoring the current needs of the patient community of a rare disease through surveys or registers of patients' as an essential function.

It is somewhat paradoxical that, as participants of a survey on patient needs, the majority of respondents would report this function of a Centre of Expertise as less essential (considered essential by 42% of respondents) (Figure 47).

Respondents from countries in southwest Europe considered this function as less of a priority compared to respondents from other investigated countries, and may consider that while the provision of medical services may be an essential function of Centres of Expertise, the monitoring and evaluation of patients' needs should be performed externally.

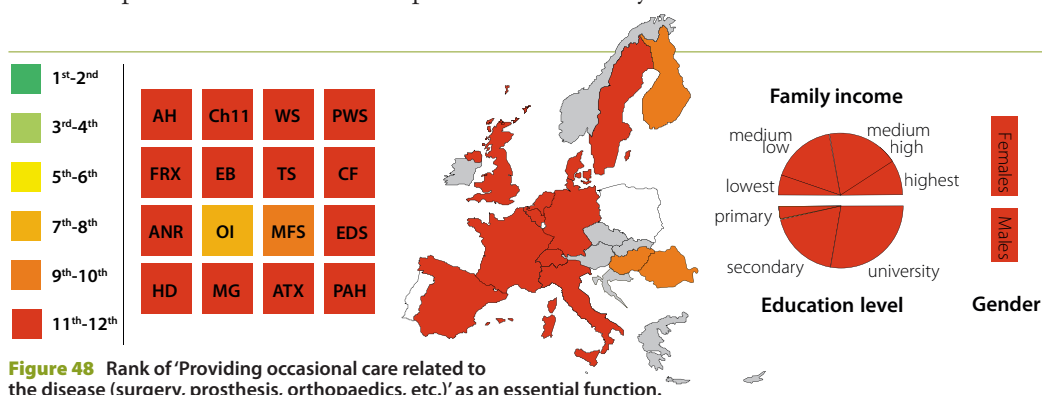


Figure 48 Rank of 'Providing occasional care related to the disease (surgery, prosthesis, orthopaedics, etc.)' as an essential function.

Patients from almost all countries and disease groups considered this function (Figure 48) as the least essential of the 12 proposed functions of a Centre of Expertise. Overall, only 37% of respondents considered the provision of infrequent care services, such as surgery, prosthesis or orthopaedics as an essential function of Centres of Expertise.

This finding supports the possibility that not all disease-specific medical services required by patients can be addressed in the same care structure, as previously introduced in the context of the range of potential medical service needs of each rare disease group.

TERMS OF ESTABLISHING A CENTRE OF REFERENCE

In addition to the potential functions provided by Centres of Expertise, survey participants were asked to rate the following nine statements regarding the potential implementation of specialised centres:

- A single national centre would be preferable because it could gather all the medical skills and competences and the most up-to-date equipment in the same location
- Rather than concentrating all the expertise and competences in a single national centre, sharing them between several centres would be preferable and more accessible to patients
- To maintain the skills and experience of its professionals, a specialised centre must follow a high number of patients affected by a specific disease
- Rare diseases are not well known by the majority of health professionals; it is therefore preferable to travel to a specialised centre for consultations and most specialised care
- The quality of relationships is as important as skills and competences, therefore, a local professional is preferable because of freedom of choice
- The main hurdles in travelling to a specialised centre are the cost of transport and/or the need to be accompanied by someone
- The main hurdles in travelling to a specialised centre are the time needed to

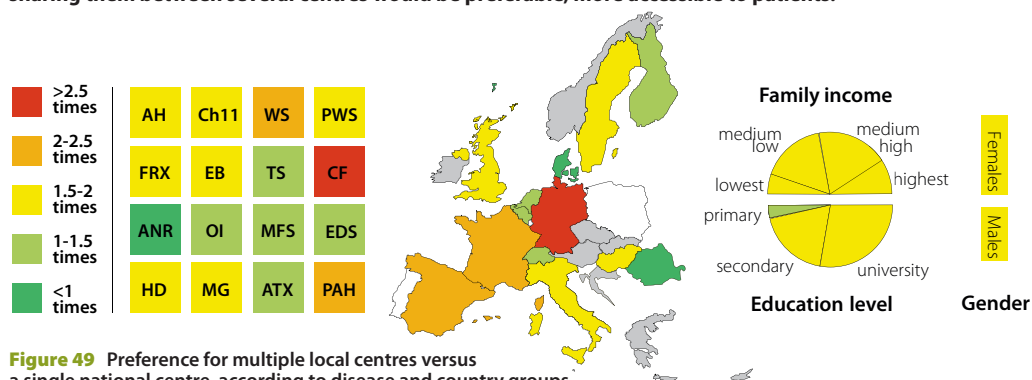
get there and/or physical difficulties encountered by the patient (pain, fatigue and injuries)

- The role of the general practitioner consists mainly of looking after health problems not related to the rare disease
- A specialised centre should involve patient organisations to benefit from their knowledge of the daily life and needs of patients

The rarity of diseases investigated in these surveys introduces both a logistical and technical dilemma regarding the number of Centres of Expertise for a given disease. On the one hand, a single national Centre of Expertise could convene the most advanced skills and resources in one place but might be difficult to access for many patients located too far away. On the other hand, the existence of a larger number of local centres could result in the dilution of the most advanced skills and resources, thus reducing the quality of services available to patients.

The first three statements included in the question regarding the potential implementation of Centres of Expertise were concerned with this dilemma. Although the first two statements represent opposing ideas, many respondents reported both the concentration of advanced skills and resources and the accessibility of centres as important. Overall, 50% of respondents agreed with the importance of a single national centre and 83% agreed with the importance of multiple local centres, demonstrating that frequently any one respondent found both options equally essential. Therefore, the relationship between these two responses has been calculated. As illustrated in Figure 49, preferences varied according to disease, country and socioeconomic groups. German respondents strongly preferred multiple centres, as indicated by a score more than 2.5 times higher than respondents favouring a single national centre, such as Romania and Denmark (less than one), where respondents slightly preferred a single national centre.

- ▶ **A single national centre would be preferable because it could gather all the medical skills and competences and the most up-to-date equipment in the same location.**
- ▶ **Rather than concentrating all the expertise and competences in a single national centre, sharing them between several centres would be preferable, more accessible to patients.**



Differences between disease groups included a strong preference for multiple centres amongst CF, PAH and WS patients and a strong preference for single national centres amongst OI, TS, EDS, MFS, ATX and ANR patients. Although there is no obvious link between the prevalence of the disease and

the preference for a single centre or multiple centres, respondents affected by one of the five diseases that present with a possible mental handicap (AH, Ch11, WS, PWS, FRX) reported a slightly greater preference for multiple centres.

Respondents living in rural areas reported a stronger preference for multiple centres and those living in larger cities and country capitals favoured single national centres. Differences were also observed with respect to income and education levels, with a stronger preference for multiple centres in the lower income groups. This preference was also observed with the higher education level group.

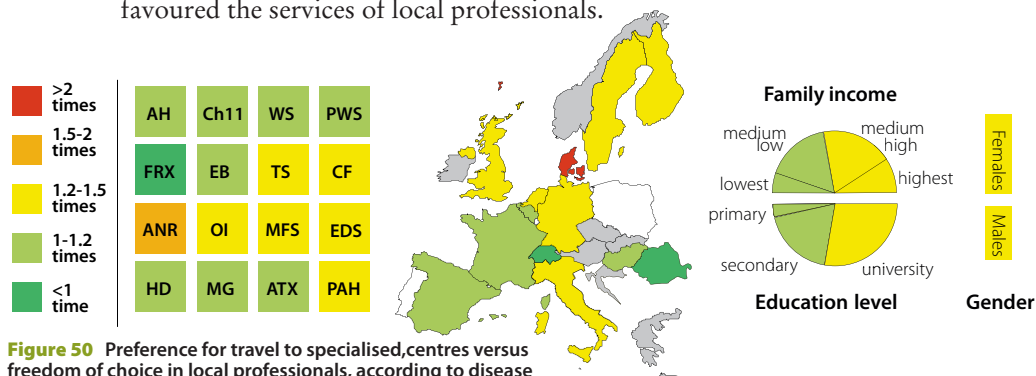
► **To maintain the skills and expertise of its professionals, a specialised centre must follow a high number of patients affected by a specific disease.**

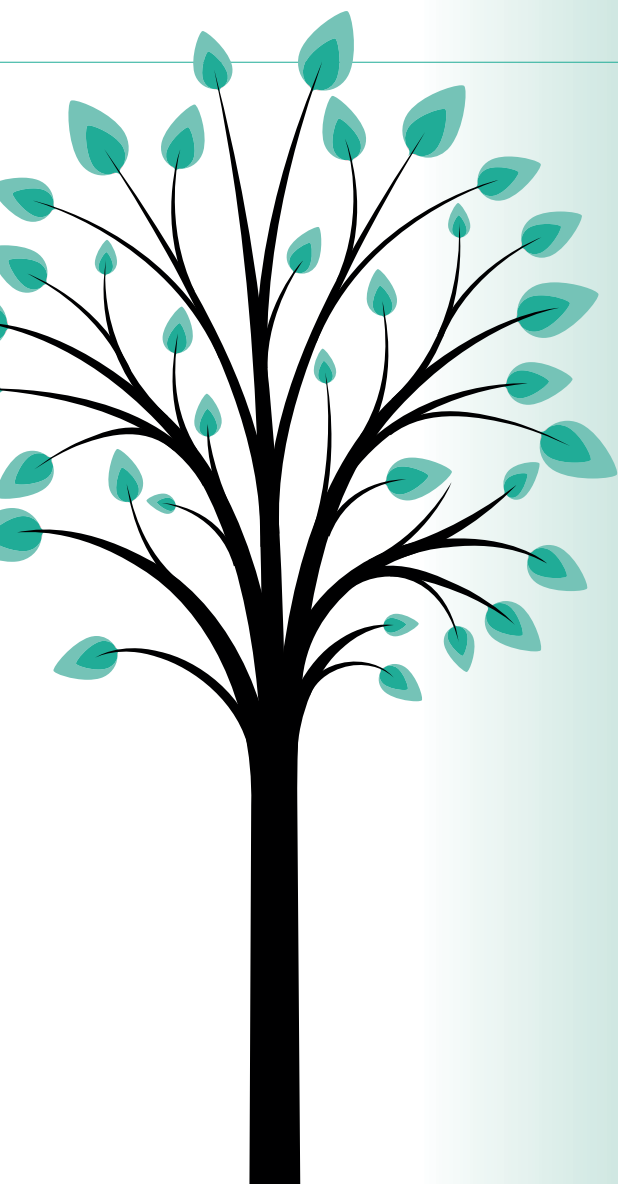
The range of responses regarding the usefulness of a high critical mass of patients followed by each centre was less significant across investigated countries and diseases. Respondents affected by PWS, ANR and MFS and respondents from Denmark, Romania and Sweden attached a slightly higher importance to this aspect of a Centre of Expertise (although no relationship was observed between valuing this aspect and a preference for either a single national centre or multiple local centres). Higher income families and respondents with higher educational levels reported this aspect as more useful regardless of the location of their residence.

► **Rare diseases are not well known by the majority of health professionals; it is therefore preferable to travel to a specialised centre for consultations and most specialised care.**

► **The quality of relationships is as important as skills and competences, therefore, a local professional is preferable because of freedom of choice.**

These two statements both relate to the question, ‘should the centralisation of highly specialised services within a Centre of Expertise be favoured over the high quality personal relationships (outside a Centre of Expertise) allowed by seeking treatment with freely chosen and more easily accessible local professionals?’ Respondents affected by ANR, PAH and OI (and to a lesser extent, patients affected by TS, CF, MFS and EDS) more strongly favoured seeking highly specialised services only from professionals in a Centre of Expertise. Patients affected by FRX more strongly appreciated the ability to see local health professionals outside of a Centre of Expertise. Overall, patients affected by diseases presenting with possible psychiatric problems favoured the services of local professionals.





Results

by Disease

Alternating hemiplegia - AH	95
Aniridia - ANR	101
Ataxia - ATX	107
Chromosome 11 disorders - Ch 11	113
Crohn's disease - CD	119
Cystic fibrosis - CF	123
Duchenne muscular dystrophy - DMD	131
Ehlers Danlos syndrome - EDS	135
Epidermolysis bullosa - EB	143
Fragile X syndrome - FRX	149
Huntington's disease - HD	157
Marfan syndrome - MFS	163
Myasthenia gravis - MG	171
Osteogenesis imperfecta - OI	177
Prader Willi syndrome - PWS	183
Pulmonary arterial hypertension - PAH	191
Tuberous sclerosis - TS	197
Williams syndrome - WS	205

Alternating Hemiplegia

Sections of this chapter were written with the collaboration of the European Association for Research on Alternating Hemiplegia (ENRAH), Alternating Hemiplegia of Childhood Deutschland E.V and Associazione Italiana per la Sindrome di Emiplegia Alternata.

Clinical Picture

Alternating hemiplegia (AH) (also called alternating hemiplegia of childhood) is a rare neurological disorder characterised by frequent, temporary episodes of paralysis on one side of the body (hemiplegia). Symptoms usually begin before 4 years of age and can range from mild, including episodes of paralysis occurring only at night and no neurological impairment, to severe, including paralysis of the legs, arms and eye muscles, mental impairment, problems with gait (step) and balance, excessive

sweating, changes in body temperature, seizures and movement disorders. The cause of AH is unknown, although some cases may be inherited as an autosomal dominant trait.



Mike,
alternating hemiplegia
© AHC Deutschland E.V.

The prevalence of AH is also unknown. Children with mild forms of AH have a good prognosis. Drug therapy may help to reduce the severity and duration of attacks of paralysis. However, those who experience more severe forms have a poor prognosis as intellectual and mental capacities do not respond to drug therapy, and balance and gait problems continue. Neurological problems may also be associated and can become increasingly severe

with age. While AH is not a progressive disease, episodes of weakness may get worse over time, recovery may become slower and walking unassisted can become difficult or impossible.

Living With Alternating Hemiplegia

Living with AH means permanent adjustment to changing and unpredictable situations for the patient, the family and anyone involved in the patient's life. A child's development is inhibited from birth, depending upon the severity of the neurological seizures and other accompanying

symptoms (e.g. epilepsy). The uncontrolled appearance of paralysis hinders the body's development, requiring a great deal of energy to continue, thus taking energy away from other developmental processes, such as learning. Skills autonomously learnt by the child, such as walking, are constantly disrupted by paralysis. As children with AH cannot rely on their own bodies, psychological problems are often experienced. The unpredictability of the intensity and the duration of the attacks are a burden for all caregivers and require constant attentive monitoring and flexible adaptation to sudden changes in the patient's condition. Activities must be managed differently depending on the presence or lack of paralysis. Not only are daily aspects

'Proper schooling has been a great challenge since the start. We have changed schools three times. We sought help from the local authorities in order to accommodate our daughter's needs, but eventually each time we found the school through friends and neighbours who had experiences with the schools. Even though our daughter has no hearing problems, she attends a school specialised for children with hearing problems — it simply offers small classes and accepted our daughter.'

Parent of child with AH, Austria

that require mobility affected, such as walking, self-sufficiency, continence, speech, eating, swallowing and danger of aspiration (accidental sucking in of food particles or fluids into the lungs), but also activities that require mental functions, such as the ability to concentrate on tasks, which is important in progressing in school. The ability to follow through with these daily functions fluctuates frequently depending upon the child's daily condition and requires a great deal of patience and flexibility from caregivers and teachers. Teachers may require some time to become acquainted with all the possible needs of a student with AH. Healthcare professionals must also take the time to develop appropriate care with patients who have very diverse and individual needs. The best source of information for these individual needs is often the parents of a patient.

For these reasons, it is particularly valuable for patients to take part in support groups that can allow them to learn from the experiences of, and obtain the necessary encouragement from other families with children with AH. Sometimes the best experts on the needs of their child, parents have become indispensable partners for doctors, teachers and caregivers of patients of AH.

Access to Medical and Social Services

PARTICIPANTS IN THE SURVEY

Responses from 79 families of AH patients from six countries were analysed in the survey (*Figure 1*).

Respondents were almost equally female and male (52% and 48%, respectively).

The mean age of patients was 15 years (mean age at diagnosis: 3.2 years).

Figure 1
Survey participants
affected by AH



NEED FOR MEDICAL SERVICES

Overall, each patient with AH needed an average of nine different kinds of medical services related to their disease (the same as the average number of services required for the 16 rare diseases surveyed). In addition to consultations mentioned in Figure 2, consultations of paediatrics (39%), rehabilitation medicine (30%), emergency services (30%) and orthopaedics (29%) were often needed. The most frequently required explorations were biological testing (56%), electroencephalogram (47%) and radiology (27%), as well as specialised imagery (20%). Other types of care included dental care (52%), physiotherapy (51%), glasses (39%), psychomotility therapy (32%), speech therapy (29%) and nursing care (27%). Hospitalisation occurred in 49% of patients for an average total duration of 15 days.

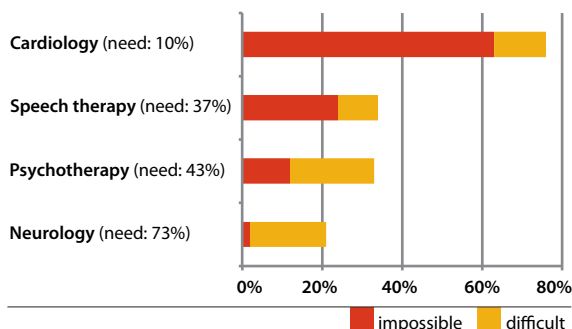


Figure 2
Need for and access to four representative medical services for AH

ACCESS TO MEDICAL SERVICES

Lack of access to medical services in 18% of situations overall for AH patients

Impossible access to services was most frequently reported for cardiology (63%) and speech therapy (24%) services, but also for psychotherapy (12%) and neurology (2%) (Figure 2). A lack of referral was the most frequent barrier to access for all services: neurology (100%), cardiology (80%), speech therapy (71%) and psychotherapy (50%). Unavailability was a hurdle for access to psychotherapy (25%) and speech therapy (14%) services. Personal cost (25%) and waiting time (25%) were also hurdles for accessing psychotherapy services.

Access to medical services was difficult in 14% of situations overall

Although possible, access was reported as difficult by patients for psychology (21%), neurology (19%), cardiology (13%) and speech therapy (10%). An insufficient number of appointments were reported for psychotherapy (28%), neurology (13%) and speech therapy (9%). Personal cost was considered excessive for psychotherapy (44%). Professional assistance for travelling to care centres was provided in 29% of cases for speech therapy services, in 17% of cases for psychotherapy and in only 13% of cases for neurology consultations, despite the fact that neurology consultations were most frequently in another region as compared to other services.

Satisfaction with medical services

Overall, 88% of patients considered that medical services, when obtained, responded fully or partially to their expectations (*Figure 3*). Patients were less frequently satisfied with neurology consultations (87%) and psychotherapy services (87%) compared to cardiology (100%) consultations and speech therapy services (100%).

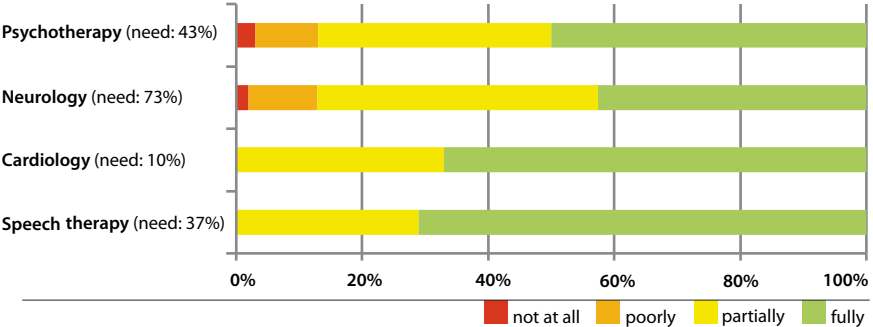


Figure 3 Satisfaction with medical services for AH patients

SOCIAL SERVICES

Amongst the 39% of families requiring social assistance, 3% failed to meet with a social worker and 21% met one with difficulty. When obtained, the level of satisfaction with social assistance was 57% overall, lowest for specialised technical support (22%) and highest for exceptional financial support (62%) (*Figure 4*).

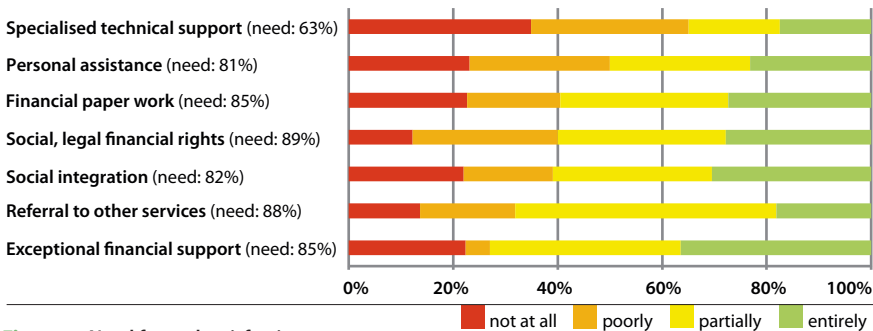


Figure 4 Need for and satisfaction with social services

REJECTION

Patients with AH experienced rejection by health professionals with similar frequency (19%) to the overall respondents for the 16 surveyed rare diseases (18%). The reluctance of health professionals due to the complexity of the disease was reported by 100% of rejected patients. Patients were also rejected for personal aspects including difficulties in communication (7%) and disease-related behaviour (7%). Even if the rejection was mainly linked to the disease rather than the patient, its extent was perceived as a refusal of health professional to treat AH patients.

'I stopped working mainly to look after my daughter, who has alternating hemiplegia.'
Parent of child with AH, Austria

The frequency and cause of rejection varied according to the patient's country of origin (Figure 5).

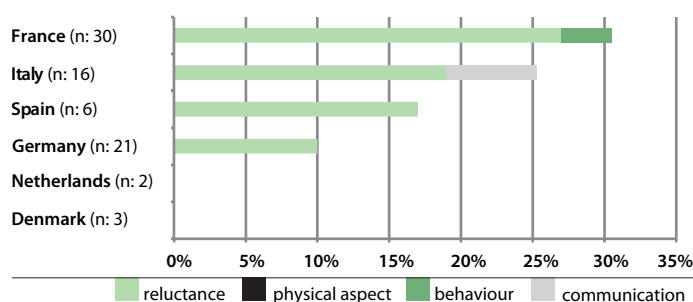


Figure 5
Cumulated frequencies of causes of rejection by country (n: total number of respondents) in AH. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

CONSEQUENCES OF THE DISEASE

As a consequence of the disease, 26% of patients had to move house. Amongst these, 70% had to move to a more adapted house, 20% moved to be closer to a relative and 15% moved to be closer to a specially adapted care centre. As a consequence of the disease, 71% of family members had to reduce or to stop their professional activity to take care of a relative with the disease.

Expectations Regarding Centres of Expertise for Rare Diseases

Not differing from the overall opinion of survey participants, respondents with AH considered the following functions provided by a centre of expertise as the four most essential:

- Coordinating the sharing of medical information on the patient between all professionals who care for him/her in the specialised centre
- Communicating with other specialised centres and professional networks to harmonise treatments and research at the national and European levels
- Coordinating the sharing of medical information between professionals of the specialised centre and local professionals, to facilitate the continuity of the patients' follow-up
- Collaborating with research teams working on the rare disease (in particular for clinical studies)

As onset of AH is usually in early childhood, patients require medical attention throughout their lifetime. Sudden changes depending on the presence or lack of paralysis require constant attentive monitoring by all people involved in the child's life, including teachers.

These aspects of the disease were reflected in the fact that survey participants with AH considered 'facilitating the follow-up of patients at different stages of their life by easing the passage from paediatric care to adult care, or from adult care to geriatric care' and 'informing patients about their rights and guiding them toward social services, schools, leisure activities, or vocational

guidance, etc.’, as the fifth and sixth-highest most essential priorities. These findings also correspond with the greater need for social services reported by AH families as compared to the overall survey population. Respondents affected by AH more often expressed that ‘the main hurdles in travelling to a specialised centre are the time needed to get there and/or physical difficulties encountered by the patient (pain, fatigue and injuries)’ as compared to respondents overall. Respondents affected by AH also more frequently expressed the importance of the following statement regarding the implementation of a Centre of Expertise: ‘Rather than concentrating all the expertise and competences in a single, national centre, sharing them between several centres would be preferable because it is more accessible to patients.’

Reactions to Results

Alternating hemiplegia is a severe and very complex disease with paroxysmal and permanent motor sensory and psycho-intellective symptoms. Consequently the required medical and social healthcare services need to be varied, integrated, coordinated and continuous. Each patient needs scheduled routine check-ups (e.g. neurological, neurophysiologic, neuro-ophthalmologic, neuro-rehabilitative, neuropsychological, genetic, metabolic, orthopaedic, specialised technical support). It is clearly more comfortable but also necessary for the coordination of care for all possible explorations to take place in one unique multi-specialist centre.

In general, physicians are not very knowledgeable about this disease. Diagnostic, therapeutic and healthcare protocols do not exist. Each referral is dependent upon the physician’s evaluation. Patients often have to ‘test’ many specialists before finding one who is familiar with the disease and is available to take care of them in an adequate way. All patients have to be accompanied (usually by family members) to seek services.

In general, medical services are more available for AH patients during infancy. As patients get older, the availability of adequate services decreases so much that care for adults with AH is almost non-existent (in particular rehabilitation and the social-educational intervention).

Patients experience rejection often because of a lack of knowledge about the disease, as it is extremely rare. Patients most frequently experience rejection due to a lack of coordination between social and medical services. For example, patients are often rejected by rehabilitation centres (in which the services of physiotherapy, speech therapy, psychological aid, etc., are available) because of numerous and sudden absences due to the frequent and unexpected crises associated with AH, resulting in high-running costs for the centres themselves.

In addition to being scarce in general, social workers often restrict themselves to fulfilling the minimum specific needs of AH patients and often only after many incessant requests. Very often, family members have no choice but to stop professional activity. A better coordination between social and medical service providers would allow social workers to be more knowledgeable and therefore more proactive in suggesting social services to which AH patients have rights.

Aniridia

Sections of this chapter were written with the collaboration of Associazione Aniridia Italiana and the Spanish Aniridia Association.

Clinical Picture

Aniridia (ANR), meaning ‘without iris’, is a rare genetic disorder affecting vision, characterised by incomplete formation of the eye’s iris (the coloured part of the eye that surrounds the black pupil). Present at birth, aniridia usually causes loss of vision in both eyes. Aniridia is caused by a dysfunction of the PAX6 gene that causes the eye to stop developing too early. The disease is most often inherited as an autosomal dominant trait, and more rarely as an autosomal recessive trait. Spontaneous mutations can also be the cause for which individuals with a deletion in the PAX6 gene may develop WAGR syndrome, which can include the development of Wilms tumour, genitourinary abnormalities and mental retardation, in addition to



Lilwen, Aniridia
© Guillaume Lancelin

aniridia. People with aniridia may also experience secondary conditions, such as sensitivity to light, nystagmus (constant involuntary movement of the eyeball), glaucoma (elevated pressure in the eyeball), cataracts, corneal disease (a variety of conditions that affect the cornea, the transparent front part of the eye that covers the iris and pupil) and optic nerve disease (conditions that affect the optic nerve, the nerve that connects the eye to the brain, making vision possible). Aniridia affects one to nine in 100 000 people, and affects males and females equally. Abnormality in the iris and nystagmus are usually apparent by six weeks of age. Glaucoma, cataract,

corneal disease and optic nerve disease develop later, often in early adulthood. Unfortunately, there is no specific treatment for aniridia, although treatments exist for many of the associated complications.

Living With Aniridia

Daily life with ANR requires constant adaptation and battle with the environment. Some of the challenges are common to those with visual impairment: studying, working, using low vision aids, moving around,

travelling and playing sport. Even the most common activities can be very difficult for a visually impaired child or adult in a world where most knowledge and information are conveyed through visual data. The exact causes and consequences of low vision are, in general, not fully understood; people with ANR may share this frustration with all visually impaired persons. Other problems, however, are specific to ANR. Nystagmus makes it difficult to maintain eye contact and may lead others to think that patients with ANR are not paying attention. For children, this may lead their teachers to think that the child is absent-minded or uninterested, resulting in a wrong appraisal of the pupil's attention. For adults, lack of eye contact

may make it hard to conduct a fluid conversation and establish relationships. People with ANR find it difficult to adapt to rapidly changing light conditions. They may be sensitive to intense light and reflections from windows, mirrors and wet, metallic or white surfaces and often have to adapt their home, work and school environments accordingly. It is not easy to explain to teachers and

workmates why and how to adapt environments as people without ANR are not aware of the discomfort it causes patients with ANR. Glare caused by reflections may lessen the ability to see details or cause visual discomfort, dry sneezing and headaches. Moving from inside to outside, switching lights on and off, moving in foggy or cloudy days, and crossing in front of car headlights produce a painful dazzling that reduces visual acuity and causes uncertainty in movement. People with ANR need to wear sunglasses with highly protective lenses, which may be needed on cloudy days or indoors and patients may feel uncomfortable, as others may perceive this as strange. Some people with ANR can wear contact lenses with an artificial iris and fixed pupil that blocks out the light. Advantages to wearing contact lenses include an unobstructed view, correction of farsightedness or nearsightedness, greater comfort and greater discretion.

'My daughter does not really want to wear glasses, especially sunglasses ... probably because other children do not have to!'
Parent of Lilwen, 5 years old, France

Access to Medical and Social Services

PARTICIPANTS IN THE SURVEY

Responses from 145 families of patients with ANR from six countries were analysed in the survey.

Fewer male patients were represented than females (42% and 58%, respectively).

The mean age of patients was 25 years (mean age at diagnosis: 2 years).



Figure 1
Survey participants
affected by ANR

NEED FOR MEDICAL SERVICES

Overall, patients with ANR needed more than five different kind of medical services related to their disease (less than the average nine medical services for the 16 rare diseases surveyed). In addition to the consultations mentioned in Figure 2, paediatrics and genetics consultations were also sought by 19% of respondents. The most frequently needed explorations were ultrasound (38%), biological testing (31%) and genetic testing (24%). As for other care services, glasses (69%), surgery (17%) and vision therapy (15%) were the most frequently reported. Hospitalisation occurred in 31% of patients for an average total duration of 13 days.

'Mine is a sporadic case. I do not have other relatives with aniridia. If the family does not receive adequate information about the disease from the physician, which was my case, if you do know what will happen to your eyes, it is even more difficult to explain and be understood by the people around you.'

Yolanda, 42 years old, Spain

ANR

ACCESS TO MEDICAL SERVICES

Lack of access to medical services in 7% of situations overall for ANR patients

Psychotherapy (32%), vision therapy (26%), nephrology (24%) and surgery (22%) were the services most frequently impossible to access for ANR patients. A lack of referral was the most frequent cause for impossible access to ultrasounds (100%), psychotherapy (86%), surgery (78%), neurology (67%), vision therapy (60%) and glasses (50%). Personal cost was reported as another significant barrier to access for ophthalmology (100%), as was difficult and extensive travel (100%), unavailability of the service (50%), waiting time (50%) and the inability to find anyone to go with (50%).

Access to medical services was difficult in 9% of situations

Patients experienced difficult access to glasses (30%) and vision therapy (27%) services. The number of appointments was considered insufficient in 36% of situations for vision therapy, 27% for psychotherapy and 25% for neurology services. Personal cost was considered excessive for glasses (74%), surgery (73%), vision therapy (67%), psychotherapy (60%) and ophthalmology (56%). Assistance of a professional for the journey to medical structure was reported most frequently for surgical services (10%), as the majority of these services (58%) were located in another region or country.

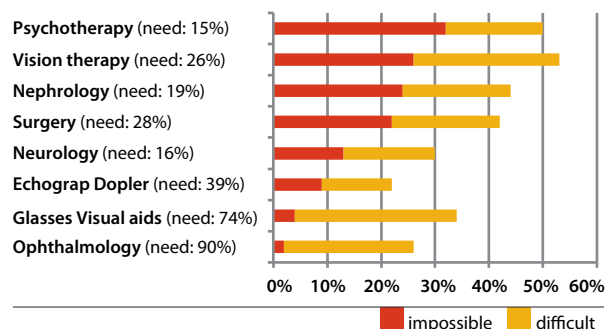


Figure 2
Need for and access to eight representative medical services for ANR

Satisfaction with medical services

Overall, 82% of patients considered that medical services responded fully or partially to their expectations. The level of satisfaction varied according to the kind of medical service, from 90% for sonograms, 86% for nephrology consultations and glasses services to 67% for psychotherapy services.

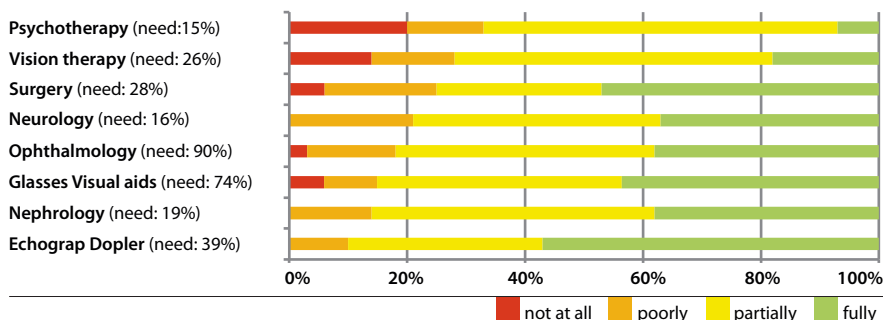


Figure 3 Satisfaction with eight representative medical services for respondents affected by ANR

SOCIAL ASSISTANCE

Among the 19% of families needing social assistance, 4% failed to meet a social worker and 22% met one with difficulty. As compared to medical services, access to social assistance was less difficult, although the level of satisfaction with this assistance was lower (Figure 4).

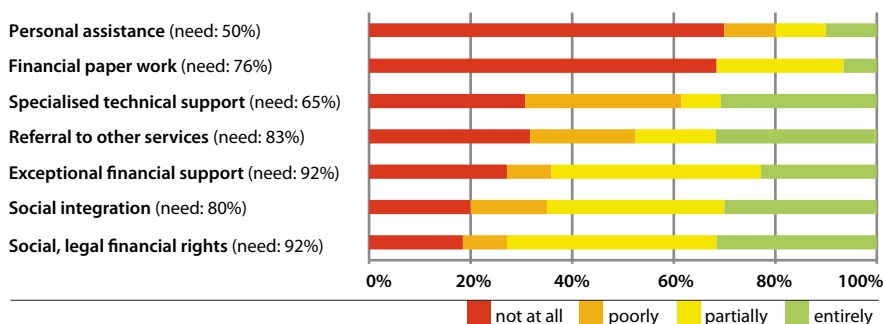


Figure 4 Satisfaction with specific social services for respondents affected by ANR

REJECTION

Patients with ANR experienced rejection by health professionals as frequently (17%) as respondents overall for the 16 surveyed rare diseases (18%). The reluctance of health professionals to treat patients due to the complexity of their disease was the main cause of rejection (88%). Patients also experienced rejection by health professionals due to communication difficulties (13%). The frequency and cause of rejection varied according to the patient's country of origin (Figure 5).

'I have been rejected by some healthcare professionals because they were not familiar with the disease, though they were not honest enough to tell me so.'
Yolanda, 42 years old, Spain

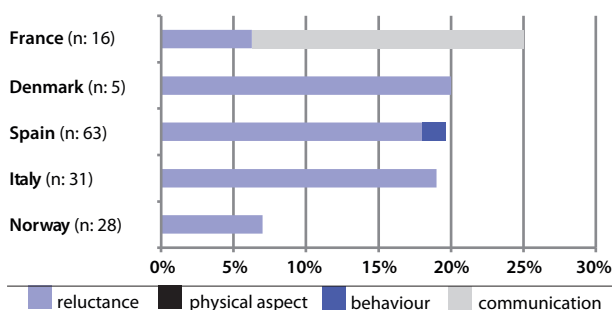


Figure 5 Cumulated frequencies of causes of rejection by country (n: total number of respondents) in ANR. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

CONSEQUENCES OF THE DISEASE

As a consequence of the disease, 4% of patients had to move house. Amongst these, families most frequently moved to be closer to a relative (33%), but also to move to a more adapted house (17%), to be nearer to disease specialists (17%) or to be closer to a specially adapted care centre (17%). As a consequence of their disease 15% of patients had to reduce or stop their professional activity and one member of 20% of the families stopped or reduced their professional activity to take care of a relative.

Expectations Regarding Centres of Expertise for Rare Diseases

Respondents with ANR considered the following three functions provided by a centre of expertise as the most essential:

- Collaborating with research teams working on ANR (in particular for clinical studies)
- Communicating with other specialised centres and professional networks to harmonise treatments and research at the national and European levels
- Coordinating the sharing of medical information on the patient between all professionals who care for him/her in the specialised centre

Patients with ANR expressed a greater need for the social service aspects of the Centres of Expertise as compared to respondents concerned by other rare diseases. The following functions of centres of expertise were ranked as the fourth and fifth most essential:

- Informing patients about their rights and guiding them towards social services, schools, leisure activities or vocational guidance, etc.
- Creating material for teachers, employers, social services, insurance companies and the general public to inform them about patients' needs and to improve the social integration of patients

The greater emphasis on these social services may be due to the fact that individuals with ANR have less of a need for a multidisciplinary approach to their care. Thus, a greater emphasis is placed on services that ease social integration in the face of a challenging physical handicap.

Patients affected by ANR agreed even less with the following statement regarding Centres of Expertise: “The role of the general practitioner consists mainly of looking after health problems not related to the rare disease.”

Reactions to Results

ANR is often associated with many other eye diseases that are treated by different specialised ophthalmologists making the treatment of the disease and coordination of treatment very complex. A lack of referral and difficulty in finding services that satisfy the needs of ANR patients are some of the barriers patients may face. The distance of medical services from the patient’s residence is a particular problem for ANR patients as most are dependent on others in their daily activities due to their severe visual impairment. After finding someone to travel with, the cost of travelling then doubles.

The main social needs for ANR patients are related to visual impairment: students with ANR need assistance in school, all patients need aids or assistance in moving or travelling, and adults with ANR need help finding an appropriate job. The main difficulty in accessing social services is due to the fact that they are scattered and it is not clear where patients have to go for a specific service. Most often patients have to see many social workers to gather this information, although social workers themselves may not be informed about social service needs and opportunities for ANR patients in many circumstances.

Ataxias

Sections of this chapter were written with the collaboration of l'Association Française de l'Ataxie de Friedreich (AFAF) and the Friedreich's Ataxia Society of Ireland.

ATX

Clinical Picture

Ataxias (ATX) are a group of genetic, progressive movement disorders caused by dysfunction of parts of the nervous system that coordinate movement. Three types of ataxias have been identified: cerebellar (ataxia due to dysfunction of the cerebellum — a region of the brain that plays an important role in the integration of sensory perception and motor control), sensory (ataxia due to loss of sensitivity to joint and body part position) and vestibular (ataxia due to dysfunction of the vestibular system — the sensory system that helps control movement and balance). Ataxias can be caused by



Magali, Friedreich's ataxia
© Magali Vigato.

non-hereditary influences such as a focal lesion (e.g. stroke or brain tumour), external substances (e.g. ethanol and some prescription and recreational drugs), vitamin B12 deficiency and other spinal disorders. Some ataxias are hereditary and are autosomal dominant (spinocerebellar ataxia, episodic ataxia and dentatorubro-pallidoluysian atrophy), autosomal recessive (Friedreich's ataxia) or X-linked (fragile X-associated tremour/ataxia syndrome). Prevalence for Friedreich's ataxia, the most prevalent inherited ataxia, is less than one in 10 000 persons and affects males and females equally. There is no specific treatment for ataxia as such, although there may be for the underlying cause. The disability of ataxia may be reduced by physical therapy, including

exercises, along with leg braces or shoe splints, if foot alignment has been affected. A cane or walker is often used in the effort to prevent falls.

Living With Friedreich's Ataxia¹

As symptoms and time of onset can vary from person to person, so do the daily struggles and triumphs of living with the syndrome. Friedreich's ataxia (FA), which usually appears in childhood, may often be diagnosed later in life. When onset occurs in childhood, it is often hard to notice.

1-The majority of survey participants had Friedreich's ataxia.

Difficulty with coordination and balance, a symptom of FA, is often mistaken for clumsiness common in all children. Physical fatigue, another symptom of FA, can also go unrecognised and children with the syndrome are simply considered lazy. Whether recognised as symptoms of FA or not, these symptoms can lead to difficulty in participating in physical activities, such as school sports, as frequent falls and fatigue are common.

Lengthy recovery times from FA and related surgeries further complicate regular school and work activities. FA patients in their teens, a period of life when image may become an important focus, can feel very insecure, as it is at this age when impaired speech may become noticeable: a symptom that may be worsened by the effects of cold, nervousness and fatigue.

The need for constant assistance also infringes on the privacy of patients with FA.

Patients with FA may require supportive measures, such as implanted metal rods that limit mobility, or the use of wheelchairs. While such supports may provide welcome relief, they may also limit a patient's independence, and may be difficult realities to accept. Some people with FA develop serious cardiac problems that can be life-threatening. Difficulty in swallowing, a possible symptom, can make eating difficult. Due to these and other physical limitations, independent living is limited.

FA may cause nystagmus (rapid involuntary eye

movements), reducing the ability to read and maintain eye contact. Writing with a pen or typing on a computer can be a time-consuming undertaking due to loss of coordination in the arms and hands.

Such symptoms make communication with others a challenge, although, recently, speech-to-text programmes have enabled patients with FA to record textual documents. All ataxias are degenerative disorders, a fact that can be very psychologically taxing on all patients as they are faced with the reality that their condition will progressively and severely worsen. Patients continuously battle to stay as active and independent as possible, modifying daily aspects of their life to overcome new challenges.

'Often the physical handicap of reduced mobility, the scarcity of competent healthcare professionals, and the lack of understanding are combined in a tragic manner: The closest speech therapist is not familiar with the disorder, the office of another is not accessible to wheelchairs and a third may even be competent and accessible, but is considered too far and reimbursement of journey is not available!'

Ataxia patient

Access to Medical and Social Services

PARTICIPANTS IN THE SURVEY

Responses from 570 patients with ATX from six countries were analysed in the survey (Figure 1). Respondents were mainly female 54%. The mean age of patients was 43 years (the mean age at diagnosis: 28 years). Respondents from most countries suffered from Friedreich's ataxia, although some respondents suffered from other types.

Figure 1
Survey participants
affected by ATX



NEED FOR MEDICAL SERVICES

Overall, each patient with ATX needed an average of nine different kinds of medical services related to their disease. In addition to consultations mentioned in Figure 2, rehabilitation medicine consultations (29%) were frequently needed. Genetics, orthopaedics, emergency services, foot medicine and psychiatry were also needed in decreasing frequency from 22% to 14% of patients. The most frequently required explorations were biological testing (55%), electrocardiogram (34%), specialised imagery (27%), ultrasounds (27%) and radiology (26%), but also functional testing (15%) genetic testing (14%) and biopsy/cytology (24%). As for other types of care, glasses (39%), dental care (30%) nursing care (25%) and occupational therapy (23%) were the most needed. Hospitalisation occurred in 34% of patients for an average total duration of 19 days.

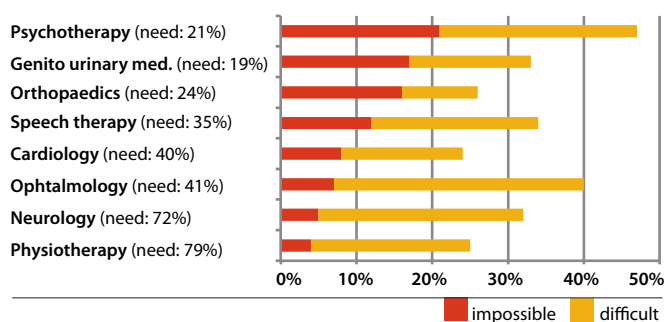


Figure 2
Need and access to eight representative medical services for ATX

ACCESS TO MEDICAL SERVICES

Lack of access to medical services in 9% of situations overall for ATX patients

Impossible access to services was most frequently reported for psychotherapy (21%), genitourinary medicine (17%), orthopaedics (16%) and speech therapy (12%). A lack of referral was the most frequent cause for impossible access to orthopaedics (67%), genitourinary medicine (67%) and psychotherapy (60%), but also for cardiology (53%), ophthalmology (50%) and neurology (40%). Unavailability of services was the predominant cause for impossible access to physiotherapy (58%). Waiting time for obtaining an appointment was considered as a hurdle in access approximately one-third of the time for ophthalmology, neurology and physiotherapy. Barriers to access related to the distance from the medical structure were mainly difficult travel for accessing physiotherapy (29%), neurology (25%) and orthopaedic (24%) consultations. The inability to find anyone to go with and difficult travel were the main barriers to access for ophthalmology, physiotherapy and speech therapy services.

Access to medical services was difficult in 23% of situations

Difficult access was significant for ophthalmology (33%), neurology (27%) and psychotherapy (26%), followed by speech therapy (22%), physiotherapy (21%), cardiology (16%), genitourinary medicine (16%) and orthopaedics (12%). An insufficient number of appointments were reported

for speech therapy, physiotherapy and neurology in more than 20% of situations. Personal cost was considered excessive for psychotherapy (52%) and orthopaedics (42%). Patients with ATX needed to be accompanied in 80% of situations, but received professional assistance in less than one-third of cases (20% for psychotherapy). Time for obtaining appointments was considered long or very long in half of situations for neurology and ophthalmology.

SATISFACTION WITH MEDICAL SERVICES

Overall, 85% patients considered that medical services, when obtained, responded fully or partially to their expectations (Figure 3).

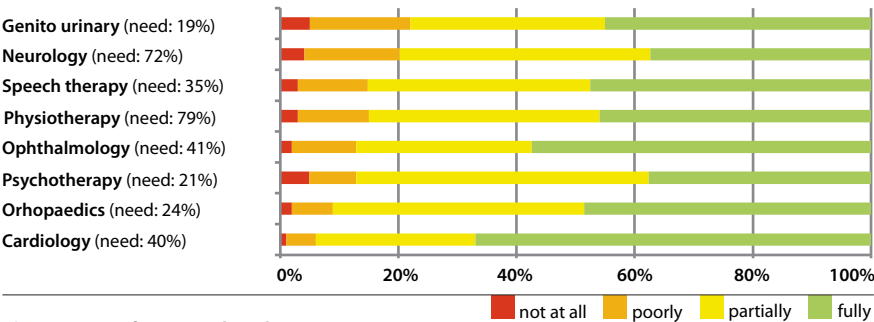


Figure 3 Satisfaction with eight representative medical services for respondents affected by ATX

SOCIAL ASSISTANCE

Amongst the 37% of families needing social assistance, 3% failed to meet a social worker and 25% met one with difficulty. When obtained, social assistance met patients' expectations two-thirds of the time (Figure 4).

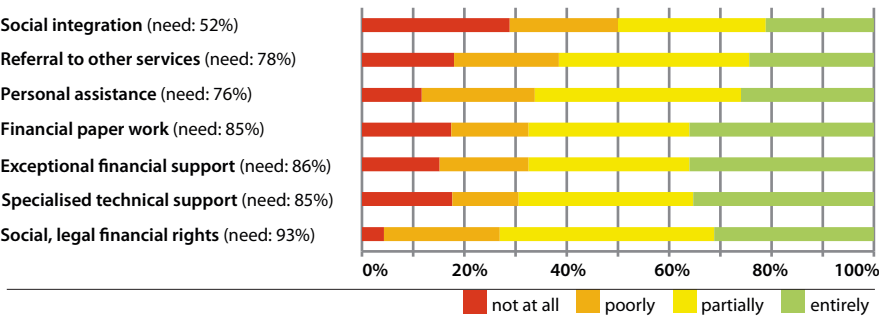


Figure 4 Satisfaction with specific social services for respondents affected by ATX

REJECTION

Patients with ATX experienced rejection by health professional 17% of the time, similar to the level observed overall for the 16 surveyed rare diseases (18%).

The reluctance of health professionals due to the complexity of the disease was reported by the majority of rejected patients (82%).

In addition, patients were rejected for personal aspects, including difficulties in communication (27%), physical aspect (10%) or disease-related behaviour (5%). Even if the rejection was mainly linked to the disease rather than the patient, its extent was perceived as a refusal of the health professional to treat ATX patients. The frequency and cause of rejection varied according to the patient's country of origin (*Figure 5*).

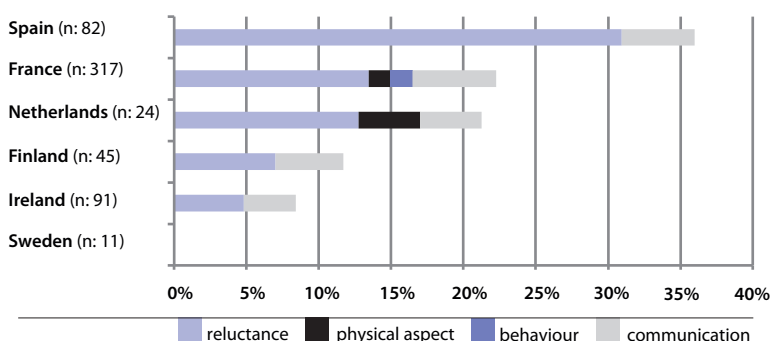


Figure 5 Cumulated frequencies of causes of rejection by country (n: total number of respondents) in ATX. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

CONSEQUENCES OF THE DISEASE

As a consequence of the disease, 33% of patients had to move house. Amongst these, 71% moved to a more adapted house, 16% moved to a specially adapted centre and 13% moved to be closer to a relative. In families of patients with ATX, 32% of patients decreased their professional activity and 23% of respondents decreased their professional activity to take care of a relative.

Expectations Regarding Centres of Expertise for Rare Diseases

Not differing from the overall opinion of survey participants, respondents with ATX considered the following functions provided by a Centre of Expertise as the four most essential:

- Coordinating the sharing of medical information on the patient between all professionals who care for him/her in the specialised centre
- Communicating with other specialised centres and professional networks to harmonise treatments and research at the national and European levels
- Coordinating the sharing of medical information between professionals of the specialised centre and local professionals, to facilitate the continuity of the patients' follow-up
- Collaborating with research teams working on the rare disease (in particular for clinical studies)

Survey participants with ATX considered 'providing frequent care related to the rare disease (physiotherapy, speech therapy, psychotherapy, etc.)' as the fifth most essential function provided by a Centre of Expertise, a higher

ranking of priority than expressed by all other respondents. As ATX patients reported difficulty in accessing psychotherapy and orthopaedic services, it is not surprising that provision of these services in a Centre of Expertise is considered as important.

Reactions to Results

Patients with ATX require many different medical services. In addition to those analysed in the survey, physical therapy, hearing specialists and endocrinology are essential. Lack of access to medical services is often due to the physician's lack of understanding of the symptoms. For example, many patients with ATX have difficulty swallowing. Physicians often underestimate the extent of the problem. Even if the severity of the symptom is recognised, physicians are not always able to refer patients to an appropriate physical therapist.

Patients' physical handicaps coupled with the scarcity of physicians familiar with ATX result in extremely difficult barriers in access to needed care. Speech therapists are usually not familiar with the specific needs of patients with ATX. Their offices are often not accessible by wheelchair and the long journeys some patients have to make to reach them are not reimbursed by their respective healthcare systems. One patient recalls, 'In order to obtain reimbursement for travel to an official Centre of Expertise, I was asked by the social security office to provide a certificate of incompetence from the neurologist of the local hospital justifying my trip to a more distant specialised centre!'

Many ATX patients report being rejected by occupational therapists because they are 'frustrating patients', unable to show clear improvement. Often therapists fail to recognise that slowing down the progression of symptoms is also a success. People with ATX often need extra time to answer questions, and physicians unfamiliar with this aspect of the disease continue to ask the patient questions or turn to an accompanying family member, referring to the patient as if they were not there. Overall, ATX patient organisations and their members continue to improve awareness of the disease among healthcare professionals, which is considered one of the major struggles faced by ATX patients.

Chromosome 11 Disorders

Sections of this chapter were written with the collaboration of UNIQUE - The Rare Chromosome Disorder (United Kingdom) and the European Chromosome 11q Network.

Ch 11

Clinical Picture

Chromosome 11 disorders (Ch11) include several extremely rare genetic diseases caused by a deletion, duplication or translocation (movement or DNA exchange) of one arm (q) of chromosome 11. Also called Jacobsen's syndrome, 11q deletion disorder is the most common type of chromosome 11 disorder. Deletion occurs when a chromosome breaks and a portion of the chromosome is lost. The incidence of 11q deletions is thought to be less than one in 100 000 people. Chromosome 11 disorders are not inherited but rather the result of a spontaneous mutation and may affect females more



Amy, 11q deletion disorder
© Unique - Rare Chromosome Disorder Support Group.

frequently than males. Symptoms vary in severity and are dependent on the size of the missing portion of the chromosome and can include slow development, physical abnormalities, cognitive difficulties, bleeding disorders and other cardiovascular problems. Mental retardation, speech problems and slow development of skills involving muscular and mental coordination are also experienced to varying degrees. Physical characteristics include short stature and facial, head, eye,

hand, foot and heart malformations, as well as undescended testicles in many males with the disorder. Onset of symptoms occurs just after birth and feeding problems are common in infancy. Although no cure for chromosome 11 disorders currently exists, management of the diseases includes regular evaluations of the heart.

Living With 11q Deletion (Jacobsen's Syndrome)¹

Clinical descriptions of Jacobsen's syndrome do not convey the finality of the diagnosis. Once genes are deleted from the end of the q arm of chromosome 11, they cannot be replaced. Consequences of this syndrome are difficult to predict early on after diagnosis and the single diagnostic label includes great variations in the way daily life may be affected.

In general, parents must prepare themselves to help their child live a highly medicalised life. Babies diagnosed with Jacobsen's syndrome are slow to

1-The majority of survey participants had 11q deletion.

develop and difficulties such as late development of speech, difficulty feeding and slow growth require extra attention from parents and health professionals.

One temporary solution to feeding and weight gain problems is a gastronomy tube through which infants can be fed directly into the stomach. To help the child learn movements such as crawling and walking, parents and health professionals must teach movements that other children learn by themselves. Even after attaining certain abilities, children with Jacobsen's syndrome can forget them, which can be frustrating. Skills and talents learned by children with Jacobson's syndrome vary greatly depending on development. Some children have very sharp observational skills, memory skills and computer skills, while others never learn to read or write. As there is such a large range of learning abilities demonstrated by children with this disease, a detailed educational assessment to identify and build on the child's strengths and weaknesses can allow them to participate in a mainstream classroom while creating an appropriate learning environment.

As speech emerges late, many people with Jacobsen's syndrome need to use alternative means of communication, such as pictures and sign language. Most people with Jacobsen's syndrome do learn to speak fluently, although some have comprehension at a higher level than that at which they can express themselves. Whether an infant, adolescent or adult, people with Jacobsen's syndrome are usually heavily dependant on others and require lifelong support. Overall, a structured environment has been found to help with behavioural problems. However many find it hard to make friends of their own age as they may have challenging behaviour or difficulties, such as tantrums and attention-seeking tendencies, difficulty handling the unfamiliar and obsessions such as hitting and biting. However through careful life adjustments, acquiring the skills for adults with Jacobsen's syndrome is slow but possible and adults with the disorder can lead happy, semi-independent, fulfilling lives.

Access to Medical and Social Services

PARTICIPANTS IN THE SURVEY

Responses from 40 families of patients with chromosome 11 disorders from nine countries were analysed in the survey (*Figure 1*).

The majority of respondents were female (63%).

The mean age of patients was 14 years (age at diagnosis: 4 years).

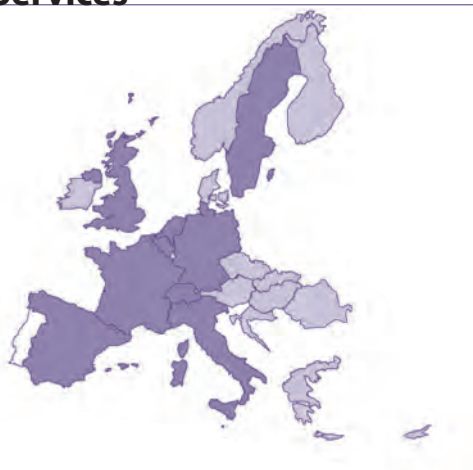


Figure 1
Survey participants
affected by Ch11

NEED FOR MEDICAL SERVICES

Overall, patients with Ch11 needed nine different kinds of medical services related to their disease (equal to the average nine medical services for the 16 rare diseases surveyed) (*Figure 2*).

Orthopaedics (45%) and ear, nose and throat medicine (45%) were the most frequently sought consultations, followed by ophthalmology (43%), cardiology (33%), haematology (25%) and neurology (20%). The most frequently needed explorations were biological testing (58%), radiology (30%) and ECG (25%).

As for other types of care, physiotherapy (48%), speech therapy (48%), glasses (40%), psychomotility therapy (23%) and nursing care (20%) were the most frequently needed. Hospitalisation occurred in 34% of patients for an average total duration of 17 days.

'The trouble with care for diseases as rare as chromosome 11 disorders is twofold — finding specialists competent about the disease and having them agree to cooperate amongst themselves in the treatment of the patient.'
Parent of child with chromosome 11 disorder

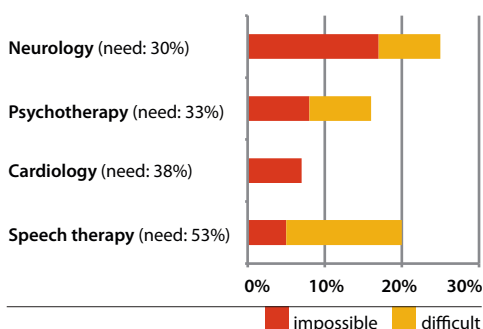


Figure 2
Need for and access to four representative medical services for respondents affected by Ch11

ACCESS TO MEDICAL SERVICES

Lack of access to medical services in 16% of situations overall for Ch11 patients

Impossible access to services was reported for neurology (17%), psychotherapy (8%), cardiology (7%) and speech therapy (5%).

A lack of referral was the only barrier to access for cardiology, neurology and speech therapy services (100%). Patients also reported impossible access to psychotherapy services due to unavailability of services (100%), waiting time (100%), personal cost (100%) and excessive or difficult travel (100%).

Access to medical services was difficult in 18% of situations

Respondents reported difficult access to speech therapy (15%), neurology (8%) and psychotherapy (8%). The number of appointments was considered insufficient for psychotherapy (17%), speech therapy (15%) and neurology (8%).

Assistance of a professional for the journey to the medical structure was available for speech therapy (21%), psychotherapy (10%) and neurology services (10%) despite the fact that the majority of these services were available in the same region.

Satisfaction with medical services

Overall, 91% of patients considered that medical services responded fully or partially to their expectations, with some variability between medical services (Figure 3): 100% for neurology and cardiology, 94% for speech therapy, 85% for cardiology and 82% for psychotherapy.

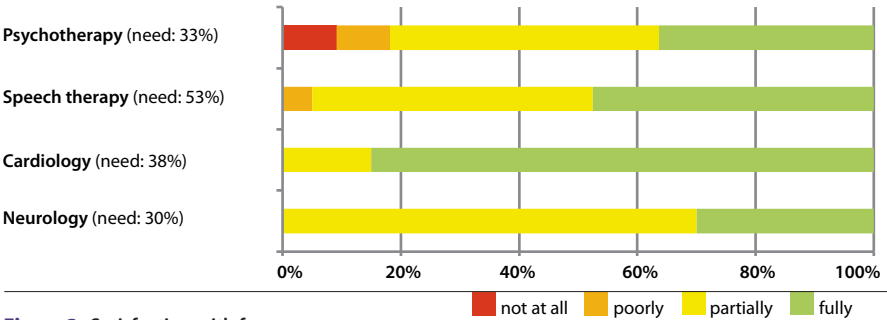


Figure 3 Satisfaction with four representative medical services for respondents affected by Ch11

SOCIAL ASSISTANCE

Social assistance was required by 35% of families of which 8% didn't meet a social worker and 38% met one with difficulty. The level of satisfaction was overall 39%, with low variability in relation to the type of assistance (Figure 4).

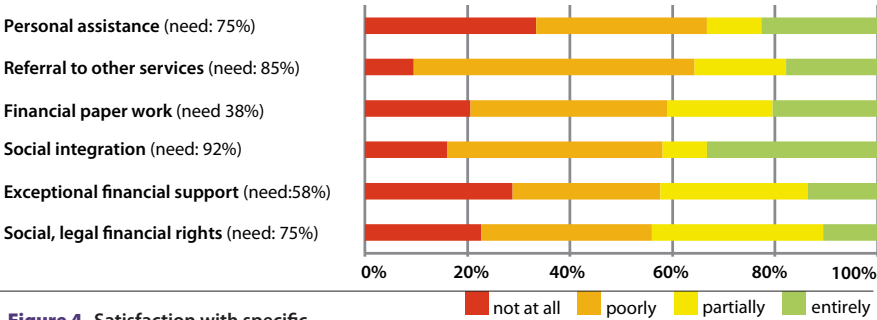


Figure 4 Satisfaction with specific social services for respondents affected by Ch11

REJECTION²

Patients with chromosome 11 disorders experienced rejection by health professional 10% of the time, less than the level observed overall for the 16 surveyed rare diseases (18%). The reluctance of the health professional due to the complexity of the disease was the main cause of rejection (75% of cases). Rejection due to disease-related behaviour was also frequently reported (50%), as was rejection due to communication difficulties (25%). The frequency and cause of rejection varied according to the patient's country of origin (Figure 5).

'The rejection experienced by patients or their families usually comes from the health professional's ignorance of the disease. It seems that professionals, especially paramedics, feel uncomfortable with these "unfamiliar" patients and try to avoid them.'

Parent of child with chromosome 11 disorder

2-Due to the low number of respondents, percentage should be considered with caution.

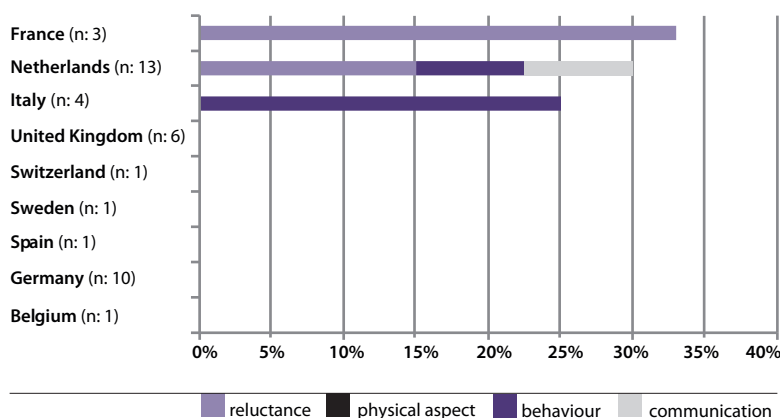


Figure 5 Cumulated frequencies of causes of rejection by country in Ch11. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

CONSEQUENCES OF THE DISEASE

In 62% of families, one member had to work less or stop his or her professional activity to take care of a relative with a chromosome 11 disorder.

As a consequence of Ch11, 21% of patients had to move house. The majority of these patients had to move to a specially adapted care centre (38%) or to be closer to disease specialists (25%).

Expectations Regarding Centres of Expertise for Rare Diseases

Differing somewhat from the overall opinion of survey participants, respondents affected by chromosome 11 disorders considered the following functions provided by a centre of expertise as the four most essential:

- Coordinating the sharing of medical information on the patient between all professionals who care for him/her in the specialised centre
- Informing patients about their rights and guiding them toward social services, schools, leisure activities or vocational guidance, etc.
- Communicating with other specialised centres and professional networks to harmonise treatments and research at the national and European levels
- Coordinating the sharing of medical information between professionals of the specialised centre and local professionals, to facilitate the continuity of the patients' follow-up

Respondents affected by the disease not only reported a greater need for social services, but also significant difficulty in accessing them.

It is not surprising, therefore, that being informed about rights and social services was reported as the second most essential function of a Centre of Expertise, a higher ranking of this priority than for respondents overall.

Reactions to Results

Abnormalities of chromosome 11 lead to a wide variety of disorders, each requiring highly specialised care, such as cardiac surgery and medical monitoring for valve malformations, ENT, surgery to correct any skull malformations, and orthopaedic treatment. An additional problem with diseases as rare as these is finding competent specialists who agree to collaborate with others in providing a patient's treatment.

The problems regarding access reported in the study arise from both the difficulty in finding competent professionals and in obtaining financial support to reach them. In addition, health professionals can be located very far away, sometimes making parents of children with chromosome 11 disorders give up.

Depending on the country of residence, financial assistance is highly variable for different essential medical aids such as glasses, splints or wheelchairs, as well as medical services such as psychotherapy and speech therapy. Limits in access can be due to long delays between appointments. The rejection experienced by patients or their families arises from an overall lack of knowledge of the diseases.

If, as reported in the study, two-thirds of responding family members reported having to stop working to care for a patient, this means that in the last third, one member was already not working, as all patients with chromosome 11 disorders require constant attention. This places a heavy burden on the sole income. Parents have to devote a lot of time travelling to different services (medical or social), which explains why some move in order to be closer to specialists of the disease.

Crohn's Disease

Clinical Picture

Crohn's disease (CD) is a chronic autoimmune disease that can affect any part of the gastrointestinal tract from the mouth to the anus. Although symptoms of CD vary among afflicted individuals, the disease is characterised by skip lesions (i.e. areas of inflammation on either side of areas of normal lining). The main gastrointestinal (relating to the stomach and intestines) symptoms are abdominal pain, diarrhoea, constipation, vomiting, weight loss or weight gain. CD can also cause complications such as skin rashes, arthritis, inflammation of the eye, difficulty swallowing, growth failure in children, fever, clubbing (a deformity of the ends of the fingers), osteoporosis (decrease in the mass of the bones) and neurological complications (such as seizures; stroke; myopathy, a disease of muscle tissue; neuropathy, a disease of the nervous system; headaches and depression). Prevalence estimates range from six to nine per 10 000, depending on the geographic area, with prevalence higher in northern European countries and possibly higher in females. The usual onset of CD is between 15 and 30 years of age, with another peak of onset between 50 to 70 years of age, although the disease can occur at any age. If appropriately controlled, patients with CD may not experience significant restrictions in daily living and the mortality rate is low. There is currently no known drug-based or surgical cure for CD, although medication, lifestyle changes and surgery may control symptoms, prevent flare-ups and keep the disease in remission, when possible.

Living With Crohn's Disease

Many patients with CD find it to be a mysterious illness. When the disease is in remission, although patients may still feel great fatigue due to immunosuppressive therapy, few aspects of daily life are affected. When the disease is active, symptoms can be severe and can significantly affect

every aspect of daily life. If undiagnosed, patients may ignore symptoms for a long time and accept their symptoms as normal or the result of psychological problems, such as stress. In addition to painful and uncomfortable constant symptoms, such as diarrhoea, fatigue, abdominal distension or discomfort, and gas, periodic ailments, such as severe iron deficiency, can lead to a long list of secondary conditions, making patients feel overwhelmed in trying to address them all.

These symptoms often make patients feel that they are not in control of their own bodies, leading to an overall loss of confidence and great anxiety.

'I was sick for years in high school, but only periodically. I would have a terrible pain, pain I now know was related to bowel obstruction, and then it would subside. At the time, paediatricians just thought I was a bundle of nerves.'

Lily, 29 years old, France

People with CD may feel ashamed about the symptoms they experience. Intimate relationships, including sexual relationships, can feel impossible and social interactions with those who do not understand the limitations for people with CD, are challenging. These realities are often hardest to accept for younger, teenage patients. People with CD may have difficulty taking public transportation, taking part in uninterrupted activities (such as going to the movies or travelling) or being in public places, as symptoms such as diarrhoea require them to have easy access to toilets. As stress and excess physical activity can trigger the flare-up of symptoms in CD patients, stressful and physically demanding activities need to be avoided.

Such limitations can grossly inhibit people with CD from working in certain environments.

Due to side effects often experienced as a result of immunosuppressive therapy, patients may stop treatment when they are feeling better, possibly taking away from its positive effects.

Diagnosis of Crohn's Disease

PARTICIPANTS IN THE SURVEY

Responses from 670 patients affected by CD from five countries were analysed (*Figure 1*). More females responded to the survey than males (62% and 38%, respectively). Half of the patients were diagnosed at 28 years of age (25% before 21 years and 25% after 36 years of age).



Figure 1
Survey participants affected by CD

AWAITING DIAGNOSIS

The time elapsed between the first clinical manifestations and diagnosis was 12 months for 50% of patients (nearly six years for 25% of the latest diagnoses). Delay in diagnosis was longer for females (20 months) than for males (12 months). During the quest for diagnosis, more than five physicians were consulted by 18% of patients and more than 20 physicians by 3%. Before obtaining the correct CD diagnosis, another diagnosis was given to 51% of patients, of which 14% received a psychiatric diagnosis. The misdiagnoses resulted in inappropriate treatments in 83% of patients: medical (57%), surgical (17%), psychological or psychiatric (5%). Misdiagnoses were associated with longer delays in reaching the final diagnosis of CD: one year without prior misdiagnosis compared to two years with initial somatic misdiagnosis and six years in the case of psychiatric misdiagnosis. For 66% of the families, delays in diagnosis were considered responsible for deleterious consequences. These consequences were associated with longer delays in reaching a final diagnosis — one year for patients without consequences, two years for patients reporting personal consequences and three years for those with familial consequences (*Figure 2*).

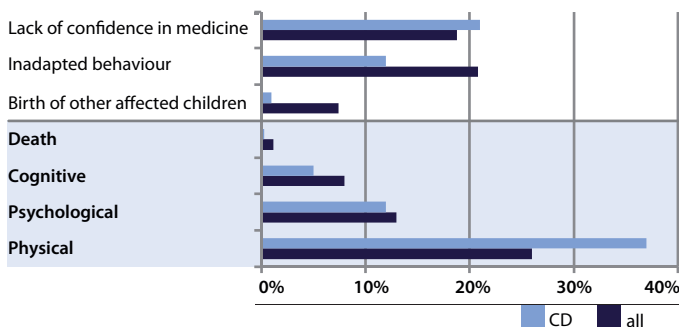


Figure 2
Consequences of delays
in diagnosis in CD patients

DIAGNOSIS

Diagnosis of CD was obtained on the basis of clinical (32%), biological (30%) or radiological (23%) data. The structure providing the diagnosis was usually a specialised centre or other hospital structure (59%), or a private practice (24%), located in the same region in 84% of cases. Access to diagnosis required a financial contribution from 58% of patients, and was considered as high or very high by 12%.

'Finding a good doctor that you trust is essential. My doctor will call me if things are bad, even at 10 p.m. on a Friday night. That is exactly what a Crohn's patient needs to feel supported.'
Lily, 29 years old, France

Over 20% of patients thought that the delay in diagnosis depended partially or primarily on the level of personal expenditure. A second opinion was sought by 22% of patients to confirm the CD diagnosis.

ANNOUNCEMENT OF DIAGNOSIS

Diagnosis was announced during a consultation in 66% of cases, or by phone in 22% of cases. Patients received the diagnosis without information on the disease 29% of the time, while 88% of patients thought this

information should have been provided. Psychological support accompanying the announcement of diagnosis was provided to only 32% of patients, and when provided it was done so by a physician (50%) or a psychologist (25%).

In contrast to this low level of support, 70% of patients considered it to be necessary.

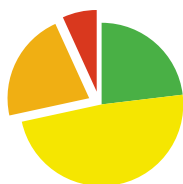


Figure 3
Satisfaction with conditions under which diagnosis was announced to CD patients.

unacceptable poor acceptable well-adapted

Reactions to Results

It is speculated that the later diagnosis of CD in women might be due to the fact that many physicians are quick to attribute CD symptoms to common causes. For example, abdominal pains may be explained as gynaecological in origin and weight loss to dieting or even anorexia nervosa. Physicians may, in general, consider pain less seriously in women than in men. Diarrhoea is also often overlooked, especially as it not comfortably discussed by patients. While waiting for a diagnosis, many patients live in fear, isolation and frustration as they are not 'officially' diagnosed with a disease but undeniably experience symptoms, such as having to leave class or take breaks from work five, 10 or even 15 times a day to use the toilet.

Patients who are initially misdiagnosed often undergo surgery or psychotherapy for anorexia nervosa. After the correct diagnosis is announced, the patient may feel anger, loss of confidence in their doctor and resentment of being 'kept' by their general practitioner who did not want to 'lose' them as a patient by sending them to a gastroenterologist — a specialist who could have more quickly made the correct diagnosis. Patients are often pushed to experiencing very severe symptoms, such as large amounts of blood in stool, an obstruction or massive weight loss, before being referred to a specialist.

Learning that you have CD is not easy, and accepting the diagnosis as well as the characteristics of the disease takes time. Acceptance may require repeated discussions with professionals who are familiar not only with the clinical aspects of the disease but also the real daily struggles, such as frequent diarrhoea or difficulty in creating intimate relationships with others. Taking the time to have these discussions allows patients to better manage the disease and improve their quality of life.

Cystic Fibrosis

Sections of this chapter were written with the collaboration of Fundacja Pomocy Rodzinom i Chorym na Mukowiscydozę (MATIO – Poland), Lega Italiana Fibrosi Cistica, L'Association Vaincre la Mucoviscidose (France) and Polskiego Towarzystwa Walki z Mukowiscydożą (Poland).

CF

Clinical Picture

Cystic fibrosis (CF) is an inherited genetic disease that affects the mucous glands of the lungs, liver, pancreas and intestines, resulting in the production of thick sticky mucus. The disease is caused by a mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene on chromosome 7. CF is an autosomal recessive disease that affects males and females equally. The overall prevalence is estimated as little more than one per 10 000 persons. It is most common amongst Europeans and Ashkenazi



Peter, cystic fibrosis
© Szilvia Molnárné Szabó.

Jews; one in 22 individuals of European descent is a carrier of one copy of the gene for CF, making it the most common genetic disease in these populations.

Onset of CF usually occurs during early childhood, although less frequently onset occurs at birth, or later in life. The thick mucus produced in people with CF can clog lungs, obstruct the pancreas and stop natural enzymes from helping the body break down and absorb food. As such, people with CF may present a variety of additional symptoms, including very salty-tasting skin, persistent cough, lung infections, wheezing or shortness of breath, poor growth/weight gain, frequent, greasy, bulky stools or difficulty in passing bowel movements.

The disease is chronic and progressive, causing increasing disability due to multi-organ failure. As such the lifespan of people with CF is shortened. Currently there is no cure for CF and treatment remains symptomatic, revolving around improving drainage of the lungs, antibiotics for lung infections, pancreatic analysis and administration of vitamins and calorie supplements for digestive and nutritional problems.

Lung transplantation may be necessary as CF worsens.

Living With Cystic Fibrosis

CF can vary greatly depending on the individual. Despite this fact, there are many common experiences shared. Nearly all patients with CF need to take daily medication, including inhalations, dietary supplements and enzymes for the duration of their lives to aid breathing and digestion. In addition to daily medication and rehabilitation, a self-care regimen is advised, from regular exercise and avoiding tobacco smoke to frequent hand-washing and daily chest physical therapy. In all, maintaining a healthy routine can be quite exhausting.

As with many illnesses that affect children, a major concern is a desire to feel 'normal'. Symptomatic coughing and frequent trips to the restroom can be disruptive, but with proper education about CF, teachers and adult supervisors can provide a healthy learning environment for children with CF.

Furthermore, physical activity should be encouraged for children with CF as it not only helps to develop and strengthen important muscles, but also adds to the 'normal' life the child desires.

Parents of children with CF can tend to be overprotective, ensuring that medications are always taken on time and limiting time playing outside, yet it is important to encourage independence and self-reliance that will be important as children become adults.

Each year more and more CF patients reach adulthood.

At this time, the responsibility for the daily routine of medication and self-care are transferred to the adult CF patient. Patients with CF may have the semblance of a normal life and they may even be able to have children under close supervision by physicians. Nevertheless, they need to cope with the eventuality of an early death. While the average life span is approximately 30 years, life expectancy varies, yet the constant awareness and preparedness for death is a real factor in causing stress and anxiety, allayed by close relationships, understanding and acceptance.

'As a parent, you try to not accept the diagnosis, because you are not able to see the disease; you don't see symptoms or particular malformations in an infant with CF.'
Giorgio, parent of a child with CF, Italy

Diagnosis of Cystic Fibrosis

PARTICIPANTS IN THE SURVEY

Responses from 1015 families of patients with CF from nine countries were analysed (Figure 1).

An equal number of female and male patients were represented in the survey (47% and 53%, respectively). The median age of patients at diagnosis was 6 years, although 25% of diagnoses occurred after 5 years of age.



Figure 1
Survey participants
affected by CF

AWAITING DIAGNOSIS

Neonatal diagnoses were obtained in 36% of patients, 45% of which resulted from disorders observed during pregnancy or at birth, 31% of which were made following neonatal testing and 17% linked to other cases in the family. For non-neonatal diagnoses, the time elapsed between the first clinical manifestations to diagnosis was nine months for 50% of patients (and as long as three years for 25% of those diagnosed the latest). This time was slightly longer for females than for males. During the quest for diagnosis, more than five physicians were consulted by 21% of families and more than ten physicians by 6% of families. Before obtaining the correct CF diagnosis, another diagnosis was given to 48% of patients, resulting in inappropriate treatments in 77% of patients (medical, 54%; surgical, 2%; psychological or psychiatric, 8%). Misdiagnoses were associated with a longer time to reach a CF diagnosis (12 months versus three months if not misdiagnosed, 24 in the case of a psychiatric misdiagnosis). For 77% of the families, a delay in diagnosis was considered responsible for deleterious

consequences.

Consequences were associated with a longer time to reach diagnosis (3.9 months in patients without consequences, 18 months for patients reporting personal or familial consequences) (Figure 2).

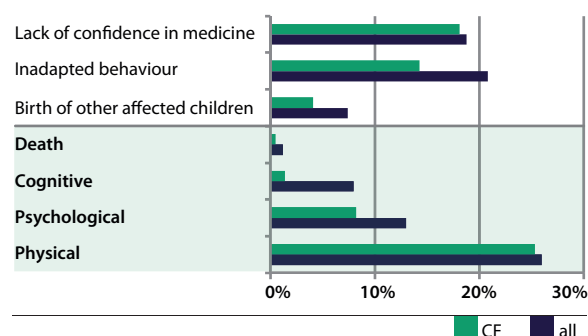


Figure 2 Consequences of delays in diagnosis in CF patients

DIAGNOSIS

Diagnosis of CF was obtained on the basis of clinical (27%), functional (11%), biological (25%) and genetic (17%) data. The structure providing the diagnosis was usually a specialised centre (24%) or other hospital structure (64%). Access to diagnosis required a financial contribution from 38% of families, and was considered a low or moderate contribution by three-quarters of these and a high or very high contribution by one-quarter. A second opinion was sought by 22% of families to confirm the diagnosis.

ANNOUNCEMENT OF DIAGNOSIS

Communication of the diagnosis occurred during a standard private consultation in 68% of cases, but also by phone in 18% (Figure 3). For 17% of patients, diagnoses were given without information on the disease. When provided, the sources were medical in 72% of cases and non-medical in 28%, including patient organisations.



Figure 3 Satisfaction with conditions under which diagnosis was announced to CF patients.

unacceptable poor acceptable well-adapted

The announcement of diagnosis was accompanied by psychological support in 40% of cases, provided by a psychologist (38%) or a patient organisation member (30%); 86% of families favoured this support.

GENETIC ASPECTS

The genetic nature of the disease was explained to families in 88% of cases, with details about the possibility of other cases in the family in 69% of cases. Genetic counselling was provided for 55% of families. Whether based on the suggestion of a health professional (48%) or not, this information was communicated to the family in 90% of cases either to the parents (63%), grandparents (39%), siblings (79%) or uncles, aunts or cousins (52%). Other diagnoses were identified in 6% of cases and other carriers were identified in 30% of cases following the communication of the diagnosis to family members.

Reactions to Results

A later diagnosis in women than in men is surprising since the life expectancy of women is shorter than that of men among patients with CF. Patients with CF, especially those who experience symptoms later in life, are not taken seriously and told that their symptoms are imaginary. Apart from those who are diagnosed during the neonatal period, many CF patients are not diagnosed until lung function is significantly altered, meaning a portion of the lung is already destroyed. Even after a CF diagnosis has been made, some related complications, such as diabetes, are not considered, despite their well-established associations. Before the possibility of neonatal screening, a delay in diagnosis often resulted in the birth of additional children with the disease. Today, the opposite is true: previously born siblings with CF are diagnosed as a result of the neonatal diagnosis of their newborn brother or sister. Patients vividly remember the announcement of the diagnosis as an unpleasant memory, especially when it occurs in a corridor in haste. It very important that the diagnosis of CF be announced calmly, several times to assure that the reality of the diagnosis is understood. It should be accompanied by psychological support and additional written information on the disease so that patients can have materials to refer to in a day an age when a lot of unreliable information is available on the Internet.

Access to Medical and Social Services

PARTICIPANTS OF THE SURVEY

Responses from 539 families of CF patients from seven countries were analysed in the survey (*Figure 4*).

An equal number of female and male patients were represented (51% and 49%, respectively). The mean age of patients was 18 years (mean age at diagnosis: 4 years).



Figure 4
Survey participants
affected by CF

NEED FOR MEDICAL SERVICES

Overall, patients with CF needed more than 11 different kinds of medical services related to their disease (more than the average nine medical services for the 16 rare diseases surveyed). In addition to consultations mentioned in Figure 5, consultations of ophthalmology, genetics, immunology, internal medicine, endocrinology, emergency services and hepato-pancreato medicine consultations were also sought by a range of 13% to 19% of patients. The most frequently needed explorations were biological testing (86%), microbiology (78%), radiology (75%), functional testing (69%), ultrasound (54%), specialised imagery (41%) and ECG (29%). As for other care services, physiotherapy (63%), injections (45%) and nursing care (32%) were the most frequently used, followed by dental care, glasses and surgery (by a range of 12% to 28% of patients). Hospitalisation occurred in 62% of patients for an averaged total duration of 29 days.

The importance of home-based care was not investigated in the survey and is very important for the CF patients ... more than all the intravenous antibiotic treatments and the physiotherapy treatments.'
Giorgio, parent of a child with CF, Italy

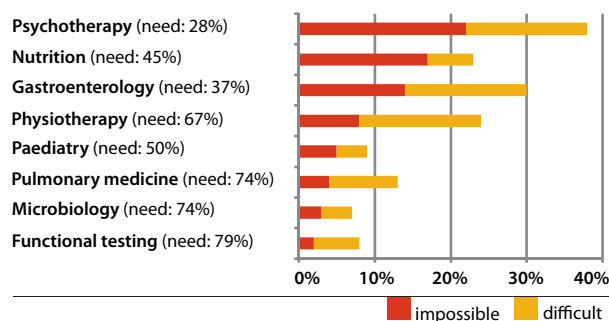


Figure 5 Need for and access to eight representative medical services for CF

ACCESS TO MEDICAL SERVICES

Lack of access to medical services in 7% of situations overall for CF patients

Psychotherapy (22%), nutrition (17%) and gastroenterology (14%) consultations were the most frequently impossible to access for CF patients. A lack of referral was the most frequent cause for impossible access to psychotherapy (52%), gastroenterology (48%), functional testing (43%) and pulmonary medicine (29%) services.

Unavailability of the service was reported as the main barrier to access for microbiology (62%), physiotherapy (50%) and nutrition (55%) services and was a significant barrier for psychotherapy (42%). Personal cost was a hurdle to access for pulmonary medicine (14%) consultations. Waiting time for obtaining an appointment was considered as a significant hurdle for access to pulmonary medicine (21%) consultations. Barriers to access related to the distance from the medical structure were mainly excessive distance for physiotherapy (46%), pulmonary medicine (29%), functional testing (29%), microbiology testing (23%), psychotherapy (21%) and nutrition (20%), and cost of the journey for pulmonary medicine (36%) and physiotherapy (32%). The inability to find anyone to go with was an additional barrier to access for physiotherapy services (25%).

Access to medical services was difficult in 9% of situations

Patients experienced difficult access to gastroenterology (16%), physiotherapy (16%) and psychotherapy (16%) services. The number of appointments for physiotherapy services was considered insufficient in 22% of situations. Personal cost was considered excessive for psychotherapy (32%) and gastroenterology (25%). The assistance of a professional for the journey to a medical structure was very infrequently reported overall (2%).

Satisfaction with medical services

Overall, 94% patients considered that medical services responded fully or partially to their expectations. The level of satisfaction varied slightly according to the kind of medical service, from 97% for microbiology to 87% for psychotherapy (*Figure 6*).

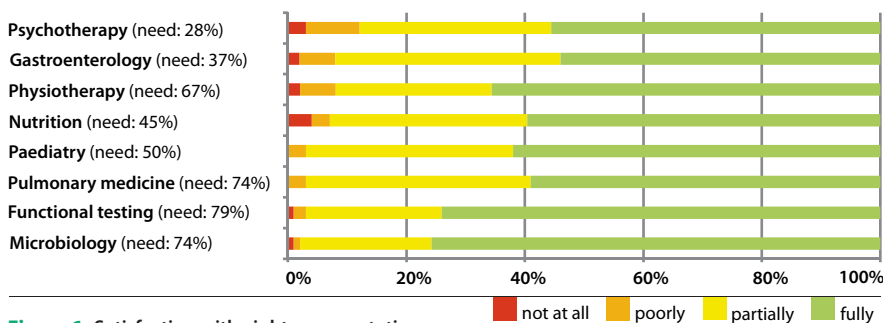


Figure 6 Satisfaction with eight representative medical services for respondents affected by CF

SOCIAL ASSISTANCE

Amongst the 26% of families needing social assistance 6% failed to meet with a social worker and 32% met one with difficulty. As compared to medical services, access to social assistance was more difficult, and the level of satisfaction with this assistance was lower (*Figure 7*).

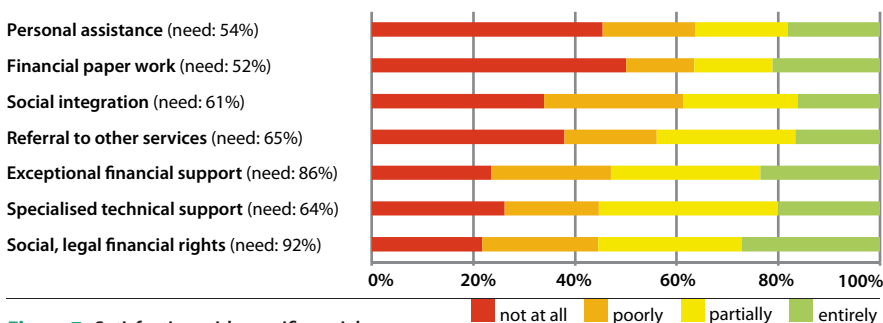


Figure 7 Satisfaction with specific social services for respondents affected by CF

REJECTION

Patients with CF experienced rejection by health professional as frequently (19%) as respondents overall for the 16 surveyed rare diseases (18%). The reluctance of health professionals to treat patients due to the complexity

of their disease was the main cause of rejection (81%) but difficulties in communication was reported by 13% of patients. The frequency and cause of rejection varied according to the patient's country of origin (Figure 8).

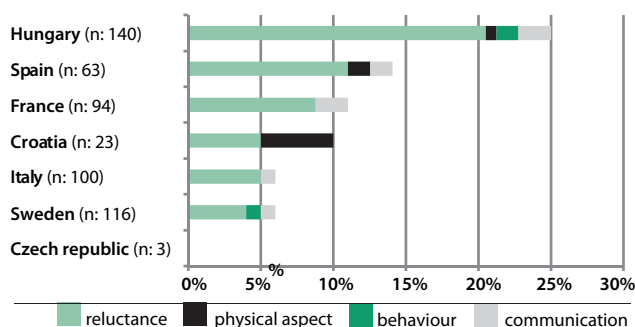


Figure 8 Cumulated frequencies of causes of rejection by country (n: total number of respondents) in CF. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

CONSEQUENCES OF THE DISEASE

As a consequence of the disease, 10% of patients had to move house. Amongst these, families most frequently moved to a more adapted house (45%), but also to be nearer to disease specialists (43%) or to be closer to a relative (26%). As a consequence of their disease, a member of the family had to reduce or stop their professional activity to take care of a relative in 48% of situations. In 15% of situations, the patient had to stop work as a result of the disease.

Expectations Regarding Centres of Expertise for Rare Diseases

Expectations regarding Centres of Expertise differed somewhat for respondents affected by CF as compared to the overall opinion of survey participants. Respondents affected by CF considered the following functions provided by a Centre of Expertise as the four most essential:

- Coordinating the sharing of medical information on the patient between all professionals who care for him/her in the specialised centre
- Facilitating the follow-up of patients at different stages of their life by easing the passage from paediatric care to adult care, or from adult care to geriatric care
- Communicating with other specialised centres and professional networks to harmonise treatments and research at the national and European levels
- Coordinating the sharing of medical information between professionals of the specialised centre and local professionals, to facilitate the continuity of the patients' follow-up

As a disease diagnosed during the early childhood years, it is not surprising that facilitating the difficult transition from paediatric to adult medical care is considered so important.

Survey participants concerned with CF considered 'offering patients the option of grouping consultations or tests on the same day in the specialised centre,

and organising the appointments' as the fifth most essential function provided by a Centre of Expertise, reflecting the multidisciplinary needs of young patients. CF respondents more frequently expressed the importance of the following statement regarding the implementation of Centres of Expertise: 'Rather than concentrating all the expertise and competences in a single, national centre, sharing them between several centres would be preferable because it is more accessible to patients.'

Reactions to Results

The large number of medical needs goes hand in hand with the complexity of the disease. As the life expectancy of CF patients has increased, new medical needs, such as the management of diabetes, or assistance with family planning, have emerged. Frequent hospitalisations for CF are usually due to the need for antibiotic treatment. When possible, delivery of such treatment at home is preferred, as patients can remain close to family and overall costs can be reduced. In many countries in Europe, access to medical care has greatly improved with the establishment of specialised centres of care for CF. However, long wait times to obtain a consultation remain a barrier to access.

Patients are often refused physiotherapy services when physiotherapists find that their sessions are too demanding. Although psychological services are often offered in specialised centres of care, patients are required to pay for their own psychological services outside the centre if they are not satisfied with the particular psychologist on staff. In these cases, CF patients often forego psychological services.

Social services for CF patients are inadequate. The number of available social workers is insufficient and they lack the expertise about CF to properly address patients' needs. Many CF patients hesitate to seek social services as they assume that they are reserved for the most severe cases of illness or financial need. It is only once they find themselves in more extreme situations that they seek assistance. To avoid this unnecessary deterioration in patients' lives, social assistance should be offered systematically and should be as available as medical services in specialised centres. Sometimes, CF patients feel as though their healthcare providers are only interested in their lungs.

Duchenne Muscular Dystrophy

Sections of this chapter were written with the collaboration of Association Française Contre les Myopathies (AFM) and the Duchenne Family Support Group (UK).

Clinical Picture

DMD

Duchenne Muscular Dystrophy (DMD) is one of the most frequent hereditary diseases. It is a degenerative genetic disease caused by a mutation of the dystrophin gene located on the X chromosome leading to an absence of dystrophin, a protein that helps keep muscles intact. As an X-linked recessive disease, it affects mainly boys. Its estimated prevalence is one in 3 500 males. DMD symptoms usually begin in childhood causing general muscle weakness, resulting in clumsiness while walking, problems getting up, difficulties climbing stairs, abnormally enlarged calves and even weakness in the hands. At about 5 to 6 years old, contractures or stiffness develop in the foot, knee and hip joints. The progressive muscle wasting leads, at about 9 to 11 years of age, to the loss of the ability to walk.



Luc and Francis, Duchene Muscular Dystrophy
© Renault family.

Orthopaedic operations are often necessary to correct the contractures or spine deformation. When walking becomes too difficult, an electric wheelchair helps the child to regain mobility and independence. DMD progresses severely, eventually affecting all voluntary muscles, as well as involuntary muscles, such as the heart and breathing muscles. Life expectancy has increased during the last decades thanks to optimal management methods. For example,

breathing difficulties can be overcome by intermittent and later continuous, mechanical ventilation. However, due to cardiac or other complications life can be significantly shortened in patients with DMD. Most boys with DMD have normal intelligence, but some have learning or behavioural difficulties. Women can be carriers of DMD, but usually do not exhibit symptoms.

A small number of female carriers of the gene can experience milder symptoms and are often called 'manifesting carriers'. Although no cure is yet available, symptomatic treatments, which include orthopaedic, respiratory and cardiac therapies, help with many complications. DMD is also the subject of many research projects and clinical trials in drug and gene therapies, whose aims are to identify a more effective and long-lasting therapy.

“Go faster; climb the stairs, concentrate”... the remorse caused by misplaced demands is rarely discussed.’
Parent of Louis, France

Living With Duchenne Muscular Dystrophy

Because DMD is usually detected early, a parent’s perspective reveals a great deal about living with the disease. Discovering that one’s child has DMD can be a considerable shock especially when, in infancy, the child can appear to be normal and healthy. Parents are encouraged to learn as much about the disease as soon as possible and engage in discussions for a long-term plan for follow-up. The better parents are informed about DMD, the more quickly they can implement helpful solutions when needs arise for their child.

Some patients with DMD begin having difficulty walking at the age of 1 to 3 years old. However, this is not always the case and some patients continue walking for some time longer and attend school. At about 8 to 11 years of age, patients become unable to walk. With the aid of wheelchairs as well as

possible structural alterations to school facilities, school continues to be a possibility. In the home, structural changes may be necessary as children slowly lose the ability to dress and bathe themselves and moving around the house becomes increasingly difficult. However, with careful preparation, modifications can be quickly made to adapt to the changing situation of the child.

Patients with DMD must be encouraged to develop independence of thought and make choices, and mistakes, on their own so that the loss of physical independence is mitigated. Activities such as painting, playing a musical instrument, reading and using a computer cannot be overestimated as beneficial outlets for creativity and self-expression for patients living with DMD. By their late teens or early 20s, the condition is severe enough to shorten life expectancy. Patients and their families must also live with the reality and psychological burden of an early death. In families with multiple siblings, parents are encouraged to reassure unaffected children by answering their questions openly and honestly. Parents themselves are encouraged to speak to other families with the diagnosis for support.

Diagnosis of Duchenne Muscular Dystrophy

PARTICIPANTS IN THE SURVEY

Responses from 913 families of DMD patients from 13 countries were analysed (*Figure 1*). The majority of respondents were male (97%). The median age of patients at diagnosis was 4 years, with a low variability: 25% of patients diagnosed before 3 years and 25% were diagnosed after 6 years of age.



Figure 1 Survey participants affected by DMD

AWAITING DIAGNOSIS

Due to the age of onset of the disease, neonatal diagnoses were rare (5.2%) resulting from other cases in the family in 50% cases, but also from neonatal testing (one in three). Not including neonatal diagnoses, the time elapsed between the first clinical manifestations and diagnosis was 16 months for 50% of patients (less than six months for 25% of patients and more than three years for another 25% of diagnoses).

During the quest for diagnosis, 88% of families consulted one to five physicians, and 10% of families consulted six to ten physicians. A significant number of various examinations and tests (biological testing, 76%; genetic testing, 39%; X-rays, 22%; and functional testing, 40%) were then performed. Before obtaining the DMD diagnosis, another diagnosis was given to 30% of patients. Although misdiagnosis for patients with DMD occurred in a lower percentage of patients than that observed overall for the 16 surveyed diseases (41%), it results in a significantly delayed diagnosis (twice as long as for another somatic diseases and three times as long in case of psychological or psychiatric diagnoses).

Inappropriate treatments resulting from misdiagnoses occurred in 54% of patients (medical, 12%; surgical, 5%; or psychiatric, 10%). For 55% of the families, a delay in diagnosis was considered responsible for deleterious consequences. The more frequent consequences included maladapted family behaviour (18%) (e.g. complaint or punishment for a boy 'medically diagnosed' as lazy) and a lack of confidence in medicine.

Consequences were associated with longer delay in diagnosis (four times longer) (*Figure 2*).

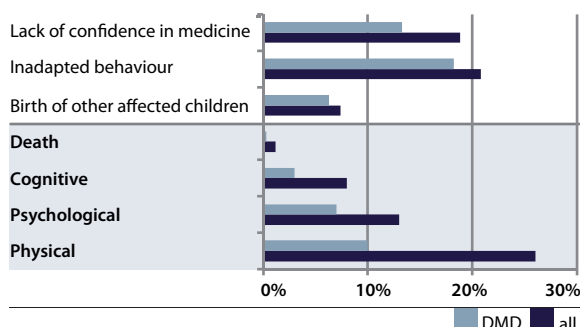


Figure 2 Consequences of delays in diagnosis in DMD patients.

DIAGNOSIS

Diagnosis of DMD was obtained on the basis of biological (39%), clinical (23%) and genetic (17%) data. The structure providing the diagnosis was usually a specialised centre (24%) or another hospital structure (64%) located in another region or country for 29% of families, and for which contact details were obtained from non-medical sources in 25% of cases. Access to diagnosis required a financial contribution from 44% of families, and was considered as high or very high by 10% of these.

A second opinion was sought by 23% of patients to confirm the diagnosis. Confirmation occurred in a private practice more often (13%) than for the first diagnosis (7%).

ANNOUNCEMENT OF DIAGNOSIS

Communication of the diagnosis occurred during a standard private consultation in 72% of cases, but also by telephone (6%) or in written form without explanation (10%). For 20% of patients, the diagnoses were given without information on the disease. When provided, the sources were medical in 66% of cases, but also patient organisations 20% of the time. Psychological support accompanied 32% of the announcements of the diagnosis and was provided by a psychologist (9%), another health professional (12%) or a patient organisation member (6%). Almost all families (92%) reported that this support should be systematically proposed.

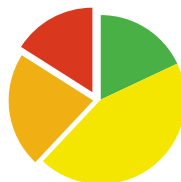


Figure 3
Satisfaction with conditions under which diagnosis was announced to DMD patients.

GENETIC ASPECTS

The genetic nature of the disease was explained to families in 87% of cases. Genetic counselling was provided for 76% of families, keeping in mind that in 5% of cases the consequence of delay in diagnosis was the birth of another affected boy. Whether based on the suggestion of a health professional (66%) or not, this information was communicated to the family in 91% of cases and resulted in the detection of carriers of the defective gene in 26% of cases and diagnosis of a relative already showing symptoms (5%) or not (3%).

'Duchenne muscular dystrophy is usually diagnosed late, at the age of 5 or 6. A second, even a third child, or a cousin may already have been born before the first has been diagnosed with the disease. Imagine the consequences for the family!'

Parent of Louis, France

Reactions to the Results

Diagnosis of DMD is technically very simple. It can, however, be easily missed as the onset of the disease is in early childhood, after the child has begun to walk. This makes symptoms such as new difficulty in walking difficult to recognise as symptoms of DMD. Sometimes when children with DMD have associated cognitive impairment, psychological misdiagnoses are inappropriately made, leading to delays in obtaining the correct diagnosis. The worst consequence of a delayed diagnosis is the birth of other affected children. Taking care of a baby and an older child with DMD is very demanding. Parents are 'on call' day and night. Neonatal diagnosis is possible, simple and inexpensive and can prevent the consequences of a delayed diagnosis. The announcement of the diagnosis is always a shock, and as such should be given under appropriate conditions — never standing in a corridor. The announcement of the disease may need to be delivered over several sessions, as adequately communicating all the necessary information is very difficult in one sitting. Competent psychologists with knowledge of genetic diseases with serious prognoses should systematically propose psychological support.

Ehlers-Danlos Syndrome

Sections of this chapter were written with the collaboration of the Association Française des Syndromes d'Ehlers Danlos and Associazione Italiana per la Sindrome di Ehlers-Danlos (A.I.S.E.D.).

Clinical Picture

Ehlers-Danlos syndrome (EDS) is a group of diverse genetic disorders caused by a mutation leading to the body's inability to produce collagen. Collagen is a protein required for the synthesis of connective tissue that makes up ligaments, tendons and cartilage and is responsible for the strength and elasticity of skin and blood vessels. The syndrome is usually inherited via an autosomal dominant mode of transmission, however in some cases transmission can be autosomal recessive or X-linked recessive. There are several subtypes of EDS and symptoms vary widely depending on the type. In the classic forms (formerly known as EDS types I and II) symptoms include unstable, flexible joints with a painful tendency to dislocate, joint pain, fragile hyperelastic skin that scars and bruises easily and hiatal hernias. Symptoms



Patient, Ehlers-Danlos
© Eurordis

that occur in rarer forms of EDS include pulmonary problems and high risk of blood vessel or organ rupture (vascular type, formerly EDS IV); congenital hip dislocation (arthrochalasia type, formerly EDS VIIB); gum disease (EDS VIII); curvature of the spine and serious eye conditions (kyphoscoliosis type, formerly EDS VI) and problems with blood clotting.

The overall prevalence of EDS is estimated at one per 10 000 individuals and certain types affect females more than males. The age of onset of EDS is neonatal or during infancy. Prognosis for people with EDS depends largely upon the type of EDS. Some individuals have

negligible symptoms while others are severely restricted in their daily life. Most individuals with EDS will have a normal lifespan; however, this is shortened in those with vascular type EDS due to the dangerous rupture of blood vessels and organs. Currently, there is no cure for EDS and treatment includes the management of symptoms and the prevention of further complications through physiotherapy and the use of pain relievers and devices that support the musculoskeletal system.

Living With Ehlers-Danlos Syndrome

Every person experiences EDS differently. For some, symptoms can appear in childhood at a time when mobility begins but stability and strength are not yet fully developed. As a result, frequent spontaneous bruising, joint

dislocations and open wounds that take a long time to heal can occur, hindering the enjoyment of playing, sports and movement in general. Due to the nature of the syndrome, children may have to miss school for medical care, social services, or chronic pain and flare-ups of other symptoms. At school, children may tire easily requiring extra time to accomplish tasks. They may also use supportive splints to aid stability, making activities even more difficult. Children who need to overcome these difficulties may develop psychological and emotional problems. As EDS is a hereditary condition, children with EDS may come from a family where one parent lives with similar difficulties.

EDS in adults can present additional complications with aging. Some adults begin life with no symptoms; they finish studies, start families and build careers. EDS in adulthood can significantly disrupt established life routines with the onset of chronic pain and fatigue throughout the entire body. Serious injuries such as the rupture of arteries, colon or uterus are not only life-threatening; they may also contribute to a patient's anxiety. Great effort must be taken to conserve energy by careful planning to accomplish tasks. Management and care of joints introduces additional challenges, requiring people with EDS to use their joints with caution, maintain good posture, keep off their feet whenever possible (i.e. while showering, dressing) and avoid heavy lifting or unnecessary effort (i.e. a continuous level working space in the kitchen to allow items to be pushed instead of lifted, a car with automatic transmission and power steering, and ironing only what is absolutely necessary). Chronic pain, if not correctly controlled, can lead to

stress and depression. People with EDS may also experience extreme frustration with the fact that, although it is a debilitating condition, EDS symptoms are not necessarily visible to family, friends, colleagues and doctors, who insist that what a patient is feeling is 'all in their mind'.

'My whole body is in constant pain so I need assistance all the time: with opening doors, carrying heavy bags and even getting in and out of the car takes guts.' Ritva, 44, Finland

Diagnosis of Ehlers-Danlos Syndrome

PARTICIPANTS IN THE SURVEY

Responses from 414 families of EDS patients from five countries were analysed in the survey (*Figure 1*). Females made up 82% of respondents and males 18%. One half of the patients were diagnosed at 29 years of age (and 25% prior to 13 years and 25% after 41 years).

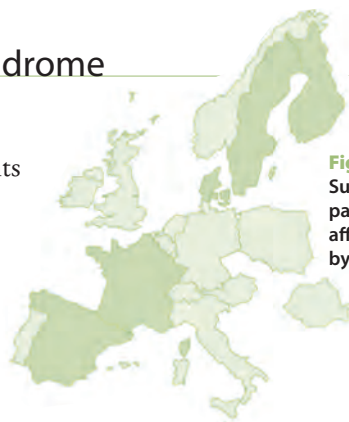


Figure 1
Survey participants affected by EDS

AWAITING DIAGNOSIS

A period of 14 years elapsed between the first clinical manifestations of the disease and diagnosis for half of patients (28 years for 25% of the latest diagnoses). This delay was longer for females (an average of 16 years) than for males (an average of four years). During the quest for diagnosis, more than five physicians were consulted by 58% of patients and more than 20 physicians by 20% of patients (as compared to 25% and 4%, respectively in the overall

survey population). A significant number of different examinations and tests (biological tests, 62%; X-rays, 61%; functional testing, 45%) were performed to reach the correct diagnosis. Before obtaining the correct EDS diagnosis, a misdiagnosis was given to 56% of patients (including a psychiatric diagnosis in 20% of these patients).

'One day I counted that I received 32 incorrect diagnoses before the correct one. They ranged from "You have nothing" to "It's all in your imagination" to very severe ones, like cancer. Some doctors told me I could live a normal life, others told me I was going to die.' Dolores, 49 years old, Spain

CONSEQUENCES OF DELAYED DIAGNOSIS

Misdiagnoses resulted in inappropriate treatment in 70% of the patients (medical, 30%; surgical, 17%; or psychiatric, 7%). In addition, misdiagnosis was associated with a longer time to reach a diagnosis of EDS (eight years without misdiagnosis, 19 years with somatic misdiagnosis and 22 years with psychiatric misdiagnosis). For 86% of the patients, the delay in diagnosis was considered responsible for deleterious consequences (Figure 2).

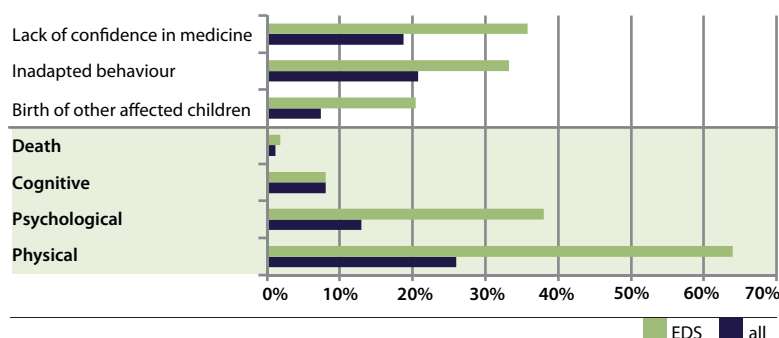


Figure 2
Consequences of delayed diagnosis for respondents affected by EDS

DIAGNOSIS

Diagnosis of EDS in the 414 EDS patients was obtained on the basis of clinical (41%), biological (20%) and functional (14%) data. The structure providing the diagnosis was a specialised centre (61%) or another hospital structure (61%) located in another region or country for 37% of patients, and for which contact details were obtained from non-medical sources in 37% of cases. Access to diagnosis required a financial contribution from 58% of patients and was considered as a low or moderate contribution by two-thirds of these respondents and high or very high by one-third. For 25% of patients, the time for reaching diagnosis depended, at least partially, on the personal cost. A second opinion was sought by 31% of patients to confirm the diagnosis (as compared to 21% overall).

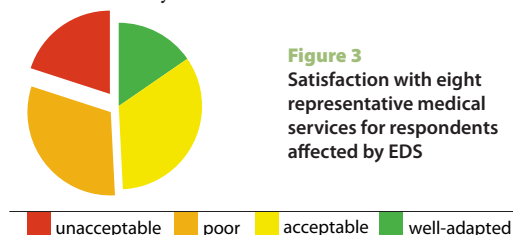


Figure 3
Satisfaction with eight representative medical services for respondents affected by EDS

ANNOUNCEMENT OF DIAGNOSIS

Diagnosis was most often given by a geneticist (55%) or directly received from a diagnostic laboratory (29%). Communication of the diagnosis occurred during a standard private consultation in 68% of cases, but also occurred orally in another manner (e.g. informally in the corridor) in 15% of cases or in written form without explanation (4%).

'As EDS is a hereditary disease, you always have to take into account that if you have children, they may inherit the disease.'
Dolores, 49 years old, Spain

For 34% of patients, the diagnoses were given without information on the disease even though 98% of patients considered that this information should be systematically provided. Psychological support accompanying the announcement of diagnosis was infrequent (19%), and when available was provided by a health professional (11%) or a patient organisation member (4%). Despite this low level of psychological support, 98% of families thought it should be systematically offered. The genetic nature of the disease was explained to families in 67% of cases, with details about the possibility of other members in the family having the same disease in 58% of cases. Genetic counselling was provided to 26% of patients. Whether based on the suggestion of a health professional (26%) or not, the patient communicated this information to other members of the family in 85% of cases, either to the parents (55%), grandparents (23%), siblings (61%), or uncle, aunt or cousin (34%). This communication resulted in diagnoses in relatives already having symptoms in 31% of cases.

Reactions to Results

Although the disease can affect men and women equally, women are more often members of patient organisations, possibly because they are more available and motivated to seek help. They are, however, often diagnosed later because their pain and hypotonia are not considered as physical symptoms but rather as psychological symptoms or common complaints. During the search for diagnosis, much help and support comes from relatives and family. Patients often report rejection by doctors, who refer them to another specialist equally unfamiliar with the disease to 'rid' themselves of the complicated case. This results in a loss of hope followed by bitterness and anger. Many patients turn to alternative medicine in order to receive the proper attention they deserve. When EDS patients are misdiagnosed, it is often up to them to seek another opinion because the disease does not progress, thus the doctor does not question the initial diagnosis. Incorrect psychiatric diagnoses cause the greatest frustration amongst patients and result in disappointment, anger and mistrust toward the health system for all the time lost. When an EDS diagnosis is finally reached, the possibility of a second opinion is rarely suggested and if sought, often leads to a break in the relationship with the first doctor. Initially, the announcement of an EDS diagnosis can be a relief. Unfortunately, the announcement is rarely accompanied by more detailed written information about the disease, crucial for a patients' understanding. Acceptance of the diagnosis can later be difficult and requires a certain amount of time and discussion with a trusted doctor.

Access to Medical and Social Services

PARTICIPANTS IN THE SURVEY

Responses from 822 families of EDS patients from 12 countries were analysed in the survey (Figure 4).

Figure 4 Survey participants affected by EDS



Respondents were mainly female (84%). The mean age of patients was 41 years (the mean age at diagnosis: 28 years).

NEED FOR MEDICAL SERVICES

Overall, each patient with EDS required an average of 12 different kinds of medical services in relation to their disease (three more than the average number of services required by the 16 rare diseases surveyed).

In addition to the consultations listed in Figure 5, orthopaedics (42%), ophthalmology (40%), rehabilitation medicine (33%) and emergency services (30%) were also frequently needed. Gynaecology, podiatry, ear-nose-throat medicine, gastroenterology, genetics, internal medicine, psychiatry, neurology, pulmonary medicine, oral and maxillofacial medicine and nutrition services were required, in decreasing frequency, by 29% to 14% of patients. The most frequently required explorations were biological testing (57%), radiology (49%), specialised imagery (41%) and electrocardiogram (37%), but also functional testing (26%), biopsy/cytology (24%), microbiology (20%), ultrasound (18%) and genetic testing (10%). As for other types of care, glasses (44%), nursing care (23%), injections (22%),

occupational therapy (19%) and prostheses (17%) were the most needed. Hospitalisation occurred in 51% of patients for an average total duration of 17 days.

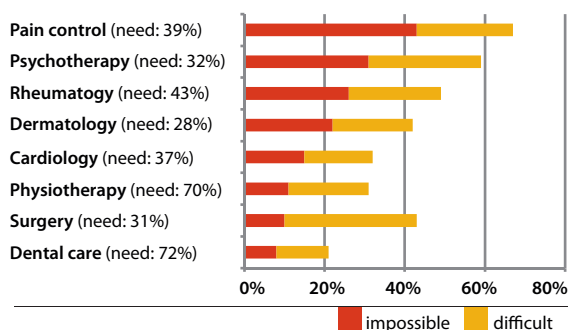


Figure 5
Need for and access to eight essential medical services for Ehlers-Danlos syndrome.

ACCESS TO MEDICAL SERVICES

Lack of access to medical services in 18% of situations overall for EDS patients

Impossible access to services was most frequently reported for pain control services (43%), psychotherapy (31%), rheumatology (26%) and dermatology (22%), followed by cardiology (15%), physiotherapy (11%) and surgery (10%). A lack of referral was the most frequent cause for lack of access to dermatology (70%), pain control (67%), cardiology (61%), rheumatology (55%) and surgical (42%) consultations. Unavailability was the predominant cause for lack of access to psychotherapy (44%) and physiotherapy (43%) services. Impossible access to dental care was most frequently due to personal cost (56%). Waiting time for obtaining an appointment was considered a hurdle to access to rheumatology (33%), cardiology (26%), physiotherapy (24%), psychotherapy (24%) and pain control services (23%). Long waiting times prevented access to rheumatology services for one out of three patients, and to cardiology, pain control, psychotherapy and physiotherapy services for one out of four patients. Access issues related to the distance from the medical structure

included difficulty in travelling to access physiotherapy (29%), rheumatology (24%), dermatology (20%) and cardiology (20%) services, and the inability to find anyone to go with (14% to 22% of respondents for the eight surveyed medical services).

Access to medical services was difficult in 23% of situations

Difficult access was significant for surgery (33%), pain control services (24%), psychotherapy (28%), rheumatology (23%), dermatology (20%) and physiotherapy (20%) services, followed by cardiology (17%) and dental care (13%). An insufficient number of appointments were reported for pain control, rheumatology, psychotherapy and physiotherapy in more 30% of situations. Personal cost was considered excessive for the eight medical services — in 29% to 33% of cardiology, physiotherapy, pain control and surgery consultations, and to an even larger extent for rheumatology (37%), psychotherapy (43%), dermatology (44%) and dental care (56%). Despite evident difficulties in travel, the assistance of a professional for the journey to the medical structure was scarce, overall 9%, and was most often provided for pain control (18%) and surgical (14%) services. Time for obtaining appointments was considered long or very long by 57% of patients for pain control (on average 11 months), 53% for rheumatology, 44% for dermatology, 41% for surgery (six months), 39% for psychotherapy and 34% for cardiology services.

Satisfaction with medical services

Overall, 81% of patients considered that medical services, when obtained, responded fully or partially to their expectations, representing the lowest level of satisfaction for the 16 surveyed rare diseases, with wide variability between services: 92% for dental care, 89% for cardiology, 72% for pain control and 70% for rheumatology (*Figure 6*).

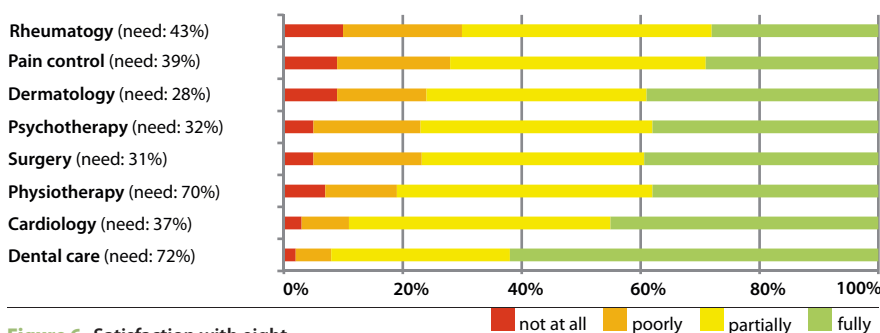


Figure 6 Satisfaction with eight representative medical services for respondents affected by EDS

SOCIAL ASSISTANCE

Amongst the 32% of families needing social assistance, 9% failed to meet with a social worker and 38% met one with difficulty. When obtained, the level of satisfaction with social assistance was significantly low, overall less than 30% (*Figure 7*).

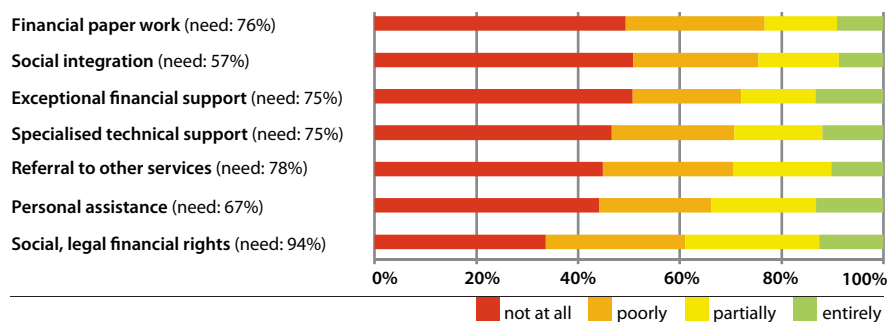


Figure 7 Satisfaction with specific social services for respondents affected by EDS

REJECTION

Patients with EDS experienced rejection by health professionals very frequently (35%); this is twice the level observed overall for the 16 surveyed rare diseases (18%). The reluctance of health professionals due to the complexity of the disease was reported by almost all rejected patients (95%). In addition, patients were rejected for personal reasons, including difficulties in communication (10%), physical aspects (8%) or disease-related behaviour (5%). Even if the rejection was mainly linked to the disease rather than the patient, its extent was perceived as the health professional's refusal to treat EDS patients. The frequency and cause of rejection varied according to the patient's country of origin (*Figure 8*).

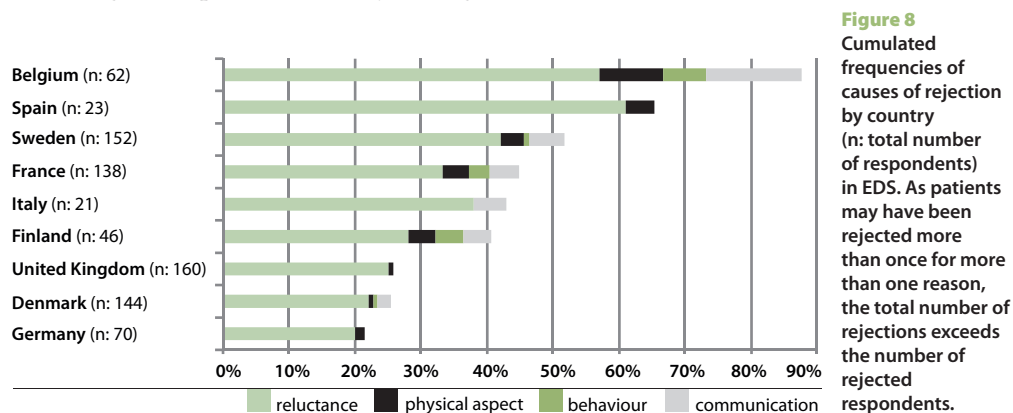


Figure 8 Cumulated frequencies of causes of rejection by country (n: total number of respondents) in EDS. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

CONSEQUENCES OF THE DISEASE

As a consequence of the disease, 22% of patients had to relocate. Amongst them, 75% moved to a more adapted house and 21% moved to be closer to a relative, i.e. for day-to-day support not provided by the social or healthcare system. As a consequence of the disease, 60% of patients with EDS had to reduce or stop their professional activity. In addition, in 8% of families one member reduced or stopped professional activities to take care of a relative.

EXPECTATIONS REGARDING CENTRES OF EXPERTISE

Not differing from the overall opinion of survey participants, respondents with EDS considered the following functions provided by a centre of expertise as the four most essential:

- Coordinating the sharing of medical information on the patient between all professionals who care for him/her in the specialised centre
- Communicating with other specialised centres and professional networks to harmonise treatments and research at the national and European levels
- Coordinating the sharing of medical information between professionals of the specialised centre and local professionals, to facilitate the continuity of the patients' follow-up
- Collaborating with research teams working on the rare disease (in particular for clinical studies)

Survey participants with EDS considered 'training local professionals in responding to the specific needs of patients and supplying their contact information to patients' as the fifth most essential function provided by a centre of expertise; a much higher ranking of priority than expressed by all other respondents. As EDS patients reported rejection by healthcare professionals most frequently amongst all the investigated diseases, it is not surprising that training non-specialist local healthcare professionals in their disease-specific needs is considered important. Compared to respondents overall, respondents affected by EDS more often expressed that 'the main hurdles in travelling to a specialised centre are the time needed to get there and/or physical difficulties encountered by the patient (pain, fatigue and injuries)'.

Reactions to Results

The complexity of EDS results in a need for many different medical services and sometimes hospitalisation during the diagnostic phase. In addition to the eight essential medical services investigated in the study, rehabilitation medicine should also be added to the list. Lack of access to these services is most often due to a lack of referral by doctors, who have insufficient knowledge of the disease and its needs. Services dedicated to pain or genetic diagnosis exist, however patients are often not referred to them. In the absence of specialised centres or hospitals with expertise in EDS, patients go to private specialists at their own expense. All too often the medical services are not adapted to the needs of EDS patients; in particular they do not take into account how severely symptoms affect the quality of life.

The frequency and reasons for rejections by health professionals described in the survey correlate well with patient organisation reports. Doctors, in particular specialists, most often refuse to treat a patient because of the complexity of the disease.

There is a great need for social services due to the disability caused by EDS. Unfortunately, the lack of recognition of the disability and inadequate number of social services adds to the difficulty in accessing them. EDS patients must frequently rely on themselves to adapt their homes or to find new appropriate accommodation that allows them to maintain independence. Very often the disease forces patients to interrupt or significantly reduce professional activities with no economic assistance. Similarly, family members may stop working in order to take care of a relative when funding or professionals for daily support are not available.

Epidermolysis Bullosa

Sections of this chapter were written with the collaboration of DebRA - United Kingdom and Associazione per la Ricerca sull'Epidermolisi Bollosa Distrofica (DebRA - Italy).

Clinical Picture

Epidermolysis bullosa (EB) is a rare inherited genetic condition in which the skin and internal body linings blister as a result of even slight rubbing or bumping, causing painful blisters and open wounds. In individuals without EB, the two layers of skin (the epidermis, the outer layer, and the dermis, the inner layer) are held together so that they do not move independently. In individuals with EB, the two layers can move independently and any friction between them creates the blisters or sores that are often compared to third-degree burns. The overall prevalence of EB is estimated at one per 10 000 persons and affects both males and females equally. There are three forms of inherited EB, EB simplex, junctional EB and dystrophic EB. These different subtypes are defined by the depth of blister within the skin layers.



Sakura,
epidermolysis bullosa
© Stefaan Van Rossem.

There are also acquired forms of EB that have very similar symptoms to the inherited forms. The onset of inherited EB usually occurs at birth or shortly after, whereas acquired EB usually appears later in adulthood. Patients with EB simplex sometimes have blistering that is confined to the feet and hands and often do not require significant medical assistance. In another form of EB simplex, however, blistering can occur all over the body and requires more medical attention. Approximately half of the patients with junctional EB do not survive past their third year of life, due to malnutrition and

anaemia caused by serious blistering in the pharynx and the oesophagus. Other individuals suffering from junctional EB do not experience any life restrictions. There is a wide variation in the severity of dystrophic EB. In general, dystrophic EB is not life-threatening in childhood. At its least severe (this is often the dominant inheritable type of dystrophic EB) the patient can lead an almost normal life. However, the severity of the disorder does increase at a later age due to scarring, fusion of fingers and wasting of skin tissue. In the recessive type of dystrophic EB, there is a high chance of developing a squamous cell carcinoma (a potentially lethal skin cancer) before the age of 35 years. Although there is no cure for EB, many complications can be avoided or minimised through prevention of infection, protection of the skin against trauma, attention to nutritional deficiencies and dietary complications, and minimisation of deformities.

'From what I know of children with EB, they seem to be blessed with big personalities that shine out and say more about them than any medical condition ever could.'

Marie, mother of two daughters with EB

Living With Epidermolysis Bullosa

Patients with EB are some of the most fragile of all rare disease patients. However with the help of healthcare professionals, careful daily hygiene and a positive outlook, patients with EB can enjoy a good quality of life. The symptoms experienced by people with EB vary, but blistering and pain are common symptoms to all types of the disease. For patients in which blistering also affects the inner body linings, such as the mouth and the oesophagus, eating solids is almost impossible, and the disposal of the body waste extremely painful. When this condition applies, malnutrition is often a consequence, further reducing the body's resistance to infection. For infants, dressing and undressing, bathing and changing are delicate tasks sometimes heartbreaking to perform. In its most severe form, EB is fatal in infancy. Younger children, who like to move around and play, must keep their skin dressed when others do not have to, such as in warm weather and around swimming pools. In severe cases of EB, scarring after blister formation may cause fusion of the fingers and toes. Both of these aspects of life with EB can provoke unwanted attention and questions from strangers.

'As a young woman, I like to dress up for an evening out, maybe wearing a nice dress with pretty shoes. But as a woman with EB Simplex, it is not that easy. Dresses do not look so good worn with trainers, and sandals do not look so good worn with blisters.'
Elizabeth, 26

Children with EB are encouraged to attend normal schools. However a school day for a student with EB may be much more of a challenge than for other students. Children with EB must begin their day much earlier than other students as frequent bathing, the application of creams and oils, and reapplication of bandages under soft clothes and shoes take extra time. If walking is too painful, mobility aids such as an electric scooter are helpful. Teachers must be aware of their fragile state and make sure that children are careful not to engage in activities that can harm them. Adults with EB also experience limitations. Some people with EB are perceived as lazy when they cannot walk far or keep up with the physical demands of adult life. They are limited in the work that they can do as they cannot stay on their feet for long periods of time. Leisure activities that require physical exertion such as sports and travelling are also not always possible due to physical limitations presented by the disease. Women with EB may decide to have children only after careful evaluation of the associated risks. Frequent visits to the hospital are needed by all patients to check skin, iron levels and nutrition. Patients with EB may be at increased risk of squamous cell cancer of the skin and should be regularly monitored.

Access to Medical and Social Services

PARTICIPANTS IN THE SURVEY

Responses from 249 families of EB patients from ten countries were analysed in the survey (*Figure 1*). More females (56%) responded than males (44%). The mean age of patients was 26 years (age at diagnosis: 5 years).

Figure 1 Survey participants affected by EB



NEED FOR MEDICAL SERVICES

Overall, patients with EB needed eight different kinds of medical services related to their disease (slightly less than the average nine medical services for the 16 rare diseases surveyed).

Not surprisingly, dermatology was the most frequently sought consultation (80%), followed by ophthalmology (34%), paediatrics (24%) and emergency services (23%) (*Figure 2*). Respondents sought the remaining 12 types of consultations (nutrition, gastroenterology, internal medicine, haematology, orthopaedics, ear-nose-throat medicine, genetics, pain control, gynaecology, oral and maxillofacial medicine, cardiology and foot medicine) 13% to 19% of the time. The most frequently needed explorations were biological testing (59%), microbiology (32%), biopsy/cytology (31%), radiology (26%), ultrasound (23%), ECG (17%), genetic testing (13%) and specialised imagery (13%). Other types of care sought included nursing care (44%), dental care (43%), surgery (29%), glasses (26%), physiotherapy (26%), psychotherapy (25%) and injection (20%). Hospitalisation occurred in 55% of patients for an average total duration of 19 days.

'I have a one-to-one helper to help set up my computer equipment for my art and design course, and once it's set up, I can work on it independently. The students in my class have accepted my condition and they get on fine with me. I get around college on my scooter, and if the lessons are upstairs and my feet hurt, I use a lift as well as a manual wheelchair to get up and down the floors with the help of my caretaker.'
Dean, United Kingdom

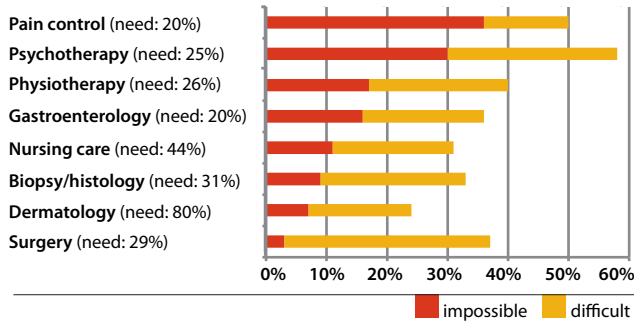


Figure 2
Need for and access to eight representative medical services for EB.

ACCESS TO MEDICAL SERVICES

Lack of access to medical services in 13% of situations overall for EB patients

Pain control services were impossible to access for 35% of patients. Access was impossible for 30% of respondents to psychotherapy, 17% for physiotherapy and 15% for gastroenterology consultations. In contrast, very few EB patients (3%) found it impossible to access surgical services. A lack of referral was the most frequent barrier to access: 100% for surgery, 75% for gastroenterology, 67% for psychotherapy, 57% for biopsy/histology and 56% pain control services. Unavailability of the service was also a significant barrier to access for pain control (56%), nursing care (42%) and dermatology (38%) services. Personal cost was the most significant barrier for psychotherapy (22%). Waiting time for obtaining an appointment was considered a hurdle in accessing dermatology

(31%), pain control (28%), physiotherapy (27%) and psychotherapy (22%) consultations. Excessive distance from the medical structure was reported as a barrier to access for dermatology (38%), psychotherapy (28%) and gastroenterology (25%) services. Difficulty in travel prevented patients from accessing gastroenterology (25%), nursing care (25%) and dermatology (23%) services.

Access to medical services was difficult in 22% of situations

Respondents experienced difficult access to surgery (34%), psychotherapy (28%), biopsy/cytology (24%) and physiotherapy (23%) consultations. The number of appointments was considered insufficient for psychotherapy (34%) and physiotherapy (21%) services. Personal cost was considered excessive for nursing care (50%), physiotherapy (50%), surgery (47%) and psychotherapy (40%). Access to the assistance of a professional for the journey to a medical structure was not frequent, overall 8%.

Satisfaction with medical services

Overall, 85% of patients felt that medical services responded fully or partially to their expectations, with low variability between medical services (*Figure 3*).

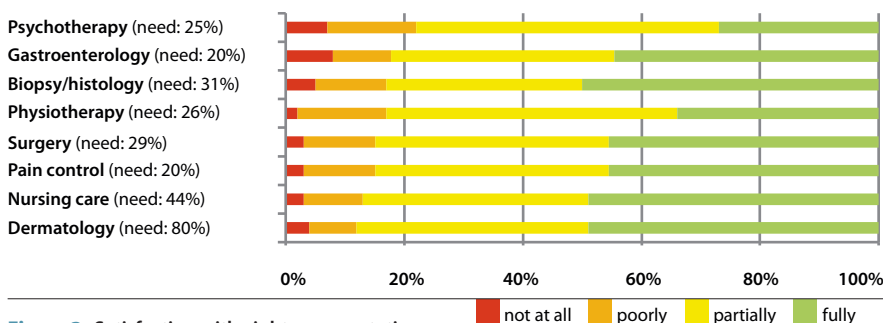


Figure 3 Satisfaction with eight representative medical services for respondents affected by EB

SOCIAL ASSISTANCE

Amongst the 32% of families needing social assistance, 4% failed to meet with a social worker and 25% met one with difficulty. The level of satisfaction overall was 55%, with low variability in relation to the kind of assistance (*Figure 4*).

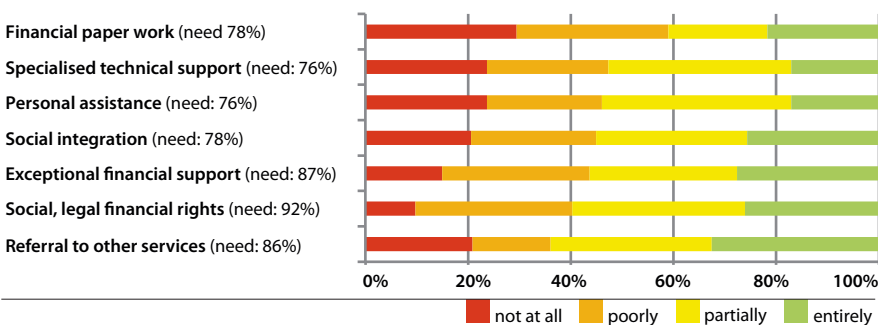


Figure 4 Satisfaction with specific social services for respondents affected by EB

REJECTION

Patients with EB experienced rejection by health professionals more frequently (28%) than respondents for the other 16 surveyed rare diseases (overall 18%). The reluctance of the health professional due to the complexity of the disease was the main cause of rejection (96% of cases). Rejection due to a physical aspect was less reported (8%). Disease-related behaviour (2%) and difficulties in communication (5%) were rarely considered as causes of rejection. The frequency and cause of rejection varied according to the patient's country of origin (*Figure 5*).

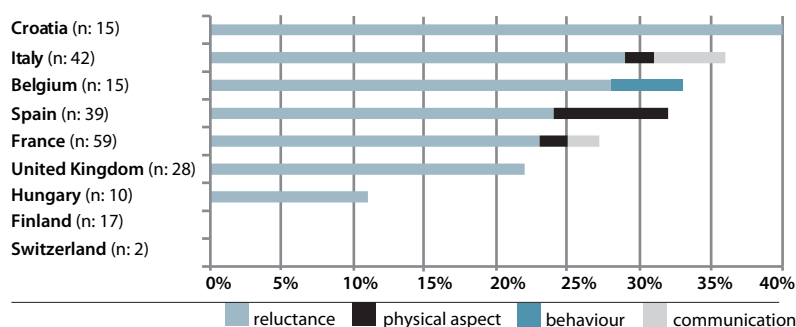


Figure 5 Cumulated frequencies of causes of rejection by country (n: total number of respondents) in EB. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

CONSEQUENCES OF THE DISEASE

In 56% of families, one member had to work less or stop his or her professional activity. In 20% of cases the patient decreased his or her professional activity and 36% of respondents decreased their professional activity to take care of a relative. As a consequence of the disease, 14% of patients had to move house. The majority of these patients had to move to a more adapted house (47%) or to move closer to a relative (35%), however patients also moved to be closer to disease specialists (24%) or to an adapted care centre (9%).

Expectations Regarding Centres of Expertise for Rare Diseases

Not differing from the overall opinion of survey participants, respondents with EB considered the following functions provided by a Centre of Expertise as the four most essential:

- Coordinating the sharing of medical information on the patient between all professionals who care for him/her in the specialised centre
- Communicating with other specialised centres and professional networks to harmonise treatments and research at the national and European levels

- Coordinating the sharing of medical information between professionals of the specialised centre and local professionals, to facilitate the continuity of the patients' follow-up
- Collaborating with research teams working on the rare disease (in particular for clinical studies)

Survey participants with EB also ranked the 'informing patients about their rights and guiding them toward social services, schools, leisure activities, or vocational guidance, etc.' as the fourth most essential function provided by a Centre of Expertise. As EB patients reported particularly difficult access to social services, it is not surprising that this function of a Centre of Expertise was considered important.

Reaction to Results

EB

In addition to those investigated in the survey, two additional services should be emphasised as important for EB patients: dental care and pain management. The lack of referral to needed services often results from the fact that general practitioners may have very little knowledge about EB and not recognise the need for specialised care. In some isolated cases, specialists have preferred to 'keep' EB patients as a result of a personal interest in investigating the disease, often at the expense of the patient's well-being.

Lack of access to essential services is not usually due to the unavailability of the services, but rather to difficulties such as the need to be accompanied or a long waiting time to obtain an appointment. The lack of satisfaction with medical services may result from the absence of one crucial professional in a multidisciplinary team. Information about the best EB treatment is often provided by patient organisations.

The rejection experienced by EB patients may be linked to the cultural and moral stigma associated with severe dermatological diseases. The pathology of the diseases means that patients have many limitations and difficulties. For example, the scarring of the hands means that in school some students might need assistance or an alternative means of writing. Unfortunately the scarcity and inadequacy of social services makes it difficult to access this type of assistance.

Fragile X Syndrome

Sections of this chapter were written with the collaboration of the Fragile X Society - UK (and their medical advisers from Contact a Family) and Associazione Italiana Sindrome X Fragile.

Clinical Picture

Fragile X syndrome (FRX) is the most common identifiable form of inherited intellectual disability. It has a prevalence of approximately one in 4000 males and one in 8000 females. FRX is caused by a mutation in the FRM1 gene, which may be passed from one generation to the next. Diagnosis is by blood test, usually testing for a mutation in the FMR1 gene using DNA analysis. Intellectual disability spans a wide range.

Approximately 80% of males have learning disabilities (mostly in the mild to moderate range). Approximately one-third of males with FRX have severe learning difficulties. Up to one-third of females with FRX have learning problems, which are usually mild or moderate but can occasionally be severe. Other problems experienced by affected individuals include delayed speech and language development with continuing speech

difficulties, attention deficits and overactivity, autistic-like features such as poor eye contact, stereotyped repetitive behaviours such as hand flapping and hand biting, repetitive speech, social anxiety, abnormal shyness and an insistence on routine. In many instances these features become less evident in adulthood.

Adults with FRX often show strength in domestic daily living skills relative to their communication and socialisation



Kevin, fragile X
© Corinne Fourier.

abilities. Clumsiness and fine motor coordination problems occur; however early motor development is often unremarkable. Oversensitivity to certain sights, sounds, smells, tastes and textures are also frequently witnessed. Boys with FRX tend to be overactive and impulsive with marked concentration problems, restlessness, fidgetiness and distractibility. Irritability, tantrums and aggressive outbursts are precipitated by environmental overstimulation, confusing situations or heightened anxiety. Physical features associated with FRX include a relatively large head, a long face with prominent ears, a largish jaw and double-jointedness. These features are rarely obvious in affected individuals. Approximately 20% of people with FRX develop epilepsy. Large testicles (macroorchidism) occur in males from early puberty. All the above features can be helped substantially by a carefully

planned and instituted combination of medical, psychological, educational and social interventions tailored to the individual's particular profile of developmental and behavioural strengths and needs.

Living With Fragile X Syndrome

Discovering that your child has learning disabilities is devastating enough for parents. However to be told that the diagnosis is FRX, which few parents have heard of, brings additional feelings of isolation and uncertainty. To then learn that your other children or future children may also be affected by the syndrome or be carriers makes acceptance of the diagnosis even harder. Learning disabilities, however mild or severe, do not always present the biggest challenges for FRX families but rather the behavioural problems that are associated with the syndrome. The short attention span, the overactivity, the sensory problems and the social anxieties translate into daily challenges. These challenges might include bringing up a child or children who do not sleep well at night, who have no sense of danger, who require constant attention to guarantee their safety and who are frightened by noisy, crowded places.

These realities limit the kinds of activities in which FRX families can participate. Attending social events with other families or even simple family celebrations can be very hard when children with FRX cannot cope with new places and experiences. Ordinary daily activities such as shopping in the supermarket can be a nightmare experience. Often children with FRX, who may not look very different from other children and in fact can appear fit and healthy with huge amounts of energy, are seen as badly behaved; parents are made to feel that that they are bad parents, incapable of disciplining their own children. FRX can also tear families apart. Marriages fail under the pressure of bringing up FRX children and families are often cut off by relatives who do not want to be told that they may be unknowing carriers of the syndrome. Finally, FRX is a lifelong condition.

Diagnosis of Fragile X Syndrome

PARTICIPANTS IN THE SURVEY

Responses from 419 families with patients affected by fragile X syndrome (FRX) from seven countries were analysed (*Figure 1*). Respondents were

mainly males (86%). The median age of patients at diagnosis was 4 years however 25% of diagnoses occurred before 2.5 years of age and 25% after 7 years of age.

'After receiving an incorrect diagnosis, our relationship with our doctor changed. We lost confidence and respect for him, and he lost some of his professional reputation.'
Laura, parent of a FRX patient



Figure 1 Survey participants affected by X Syndrome

AWAITING DIAGNOSIS

Due to the age of onset at which the first symptoms appear, neonatal diagnoses were rare (3%). The time elapsed between the first clinical manifestations and diagnosis was nearly three years for 50% of patients (more than five years for 24% of the latest diagnoses). During the quest for diagnosis, more than five physicians were consulted by 20% of families. A significant number of examinations and tests (mainly genetic testing, 50%; biological testing, 54%; and functional testing, 35%) were performed during this period. Before obtaining the correct FRX diagnosis, another diagnosis was given to 41% of patients (a psychiatric diagnosis in 40% of the cases). These misdiagnoses resulted in inappropriate treatments for 58% of patients, including surgical interventions for 8%. Misdiagnoses were associated with a longer time to reach FRX diagnosis: two years without misdiagnosis, four years with initial misdiagnosis. For 74% of families, delays in diagnosis were considered responsible for deleterious consequences. Consequences were associated with a longer time to reach diagnosis (1.5 years in patients without consequences, four years for patients reporting personal consequences and 3.3 months for those with familial consequences) (Figure 2).

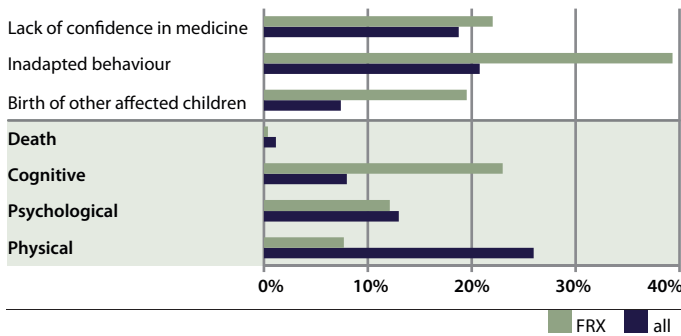


Figure 2
Need for and access to eight representative medical services for respondents affected by fragile X syndrome

DIAGNOSIS

For 50% of diagnosed patients, the possibility of a rare disease was suggested before reaching the correct diagnosis. In 20% of these cases, the suggestion of a rare disease was proposed by a non-medical individual and associated with a longer time to reach diagnosis. Diagnosis of FRX was obtained on the basis of genetic (44%) and biological (30%) data. The structure providing the diagnosis was usually a specialised centre (32%) or another hospital structure (53%), located in another region or country for 25% of patients. The contact details of this structure were obtained from non-medical sources in 22% of cases.

ANNOUNCEMENT OF DIAGNOSIS

Communication of the diagnosis occurred during a standard private consultation in 61% of cases, but also occurred orally in another manner (e.g. in the corridor) in 14% of cases, or in written form without explanation (19%).

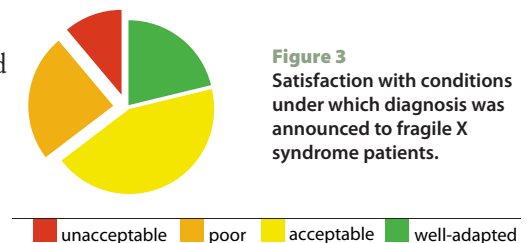


Figure 3
Satisfaction with conditions under which diagnosis was announced to fragile X syndrome patients.

Families were informed of the disease by health professionals (40%) and by patient's organisations (33%). No disease information was provided to 17% of families.

Psychological support accompanying the announcement of diagnosis was provided in only 31% of cases, while 91% of families considered it necessary.

GENETIC ASPECTS

The genetic nature of the disease was explained to families in 96% of cases, with details about the possibility of other familial cases. Following the announcement of the diagnosis to family members, other affected individuals were identified in 42% of cases and carriers of the disease in 51% of cases. Genetic counselling was provided to 86% of patients.

In 80% of the diagnoses, a health professional (in 60% of cases, during genetic counselling) suggested informing relatives about the genetic aspects of FRX. These contacts resulted in the detection of carriers (45%) and the diagnosis of relatives already having symptoms (25%).

Access to Medical and Social Services

PARTICIPANTS IN THE SURVEY

Responses from 257 families of FRX patients from nine countries were analysed in the survey (*Figure 4*).

The majority of respondents were males (92%).

The mean age of patients was 19 years (age at diagnosis: 7 years).



Figure 4
Survey participants
affected by X Syndrome

NEED FOR MEDICAL SERVICES

Overall, patients with FRX needed four different kinds of medical services related to their disease (significantly less than the average nine medical services for the 16 rare diseases surveyed). Ophthalmology was the most frequently sought consultation (34%), followed by psychological (21%), paediatric (23%) and genetic (18%) services.

The most frequently needed explorations were biological testing (23%) and genetic testing (11%). As for other types of care, dental care (35%), speech therapy (39%), glasses (26%) and psychomotility therapy (20%) were the most frequently needed. In all, 21% of patients were hospitalised for an average total duration of six days.

ACCESS TO MEDICAL SERVICES

Lack of access to medical services in 16% of situations overall for FRX patients

Impossible access to services was most frequently reported for physiotherapy (28%), speech therapy (24%), psychiatry (17%) and orthopaedics (16%). In contrast, fewer FRX patients found it impossible to access neurology (13%), ophthalmology (8%) or paediatric consultations (7%). A lack of referral was the most frequent barrier to access: 100% for psychiatry, 71% for neurology, 67% for orthopaedics, 60% for physiotherapy and 50% for paediatrics and psychotherapy. Unavailability of the service was also a significant barrier to access for psychotherapy (63%), speech therapy (63%) and psychiatry (44%), and somewhat of a barrier for neurology consultations (29%). Personal cost was considered a barrier to access a neurology consultation (29%). Waiting time for obtaining an appointment was considered a hurdle in access to neurology (43%), ophthalmology (29%) and speech therapy (29%) services (*Figure 5*).

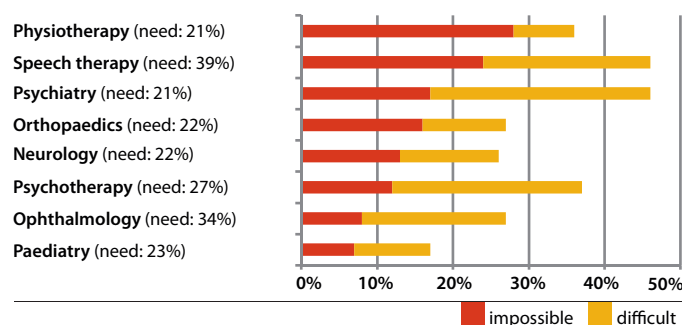


Figure 5
Need for and access to eight representative medical services for respondents affected by fragile X syndrome.

FRX

Access to medical services was difficult in 18% of situations

Respondents most frequently experienced difficult access to psychiatry (29%), psychotherapy (25%) and speech therapy (22%) consultations. The number of appointments was considered insufficient for psychiatry (28%), speech therapy (24%) and psychotherapy (23%). Personal cost was considered excessive for psychotherapy (39%), ophthalmology (32%), psychiatry (31%), neurology (27%) and speech therapy (25%). The assistance of a professional for the journey to the medical structure was available for speech therapy (13%), psychotherapy (11%), neurology and physiotherapy (9%), and more infrequent for all other services, overall 3%.

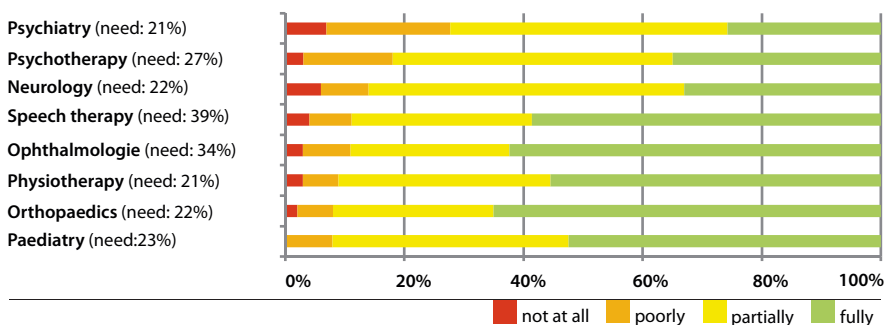


Figure 6
Satisfaction with eight representative medical services for respondents affected by fragile X syndrome.

Satisfaction with medical services

Overall, 87% of patients found that medical services responded fully or partially to their expectations, with some variability between medical services: 93% for paediatrics, 92% orthopaedics and physiotherapy, 82% psychotherapy and 73% for psychiatry (*Figure 6, p 153*).

SOCIAL ASSISTANCE

Social assistance was required by 42% of families, of which 32% met a social worker with difficulty. The level of satisfaction was overall 54%, with patients much less satisfied with specialised technical support (31%) and assistance with financial paperwork (34%), and more satisfied with social integration (59%) and social and legal financial rights (60%) services (*Figure 7*).

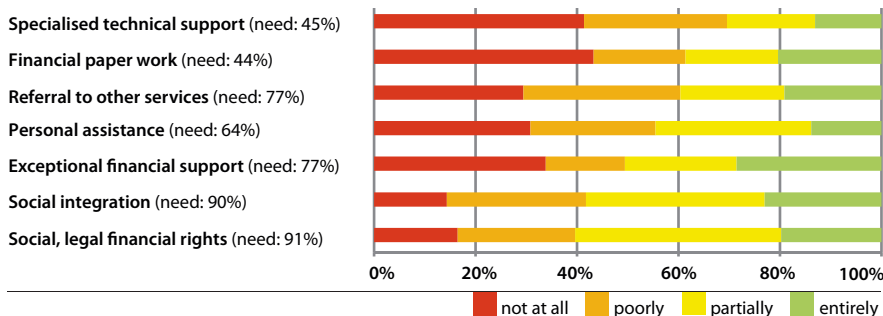


Figure 7 Satisfaction with specific social services for respondents affected by fragile X syndrome.

REJECTION

Patients with FRX experienced rejection by health professionals less frequently (overall 13%) than the level observed overall for the 16 surveyed rare diseases (18%). The reluctance of the health professional due to the complexity of the disease was the main cause of rejection (63% of cases).

'Rejection is frequently experienced because it is hard to apply care protocols that are not adapted for patients with mental retardation. Often the physician is very competent but is not trained in the psychological aspects needed in caring for patients with neurological disorders.' Laura, parent of an FRX patient, Italy

Rejection due to disease-related behaviour (50%), communication difficulties (38%) and physical aspects (6%) was less reported. The frequency and cause of rejection varied according to the patient's country of origin (*Figure 8*).

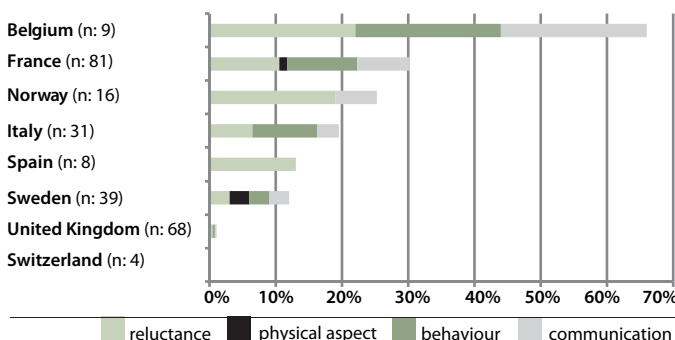


Figure 8 Cumulated frequencies of causes of rejection by country (n: total number of respondents) in FRX. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

CONSEQUENCES OF THE DISEASE

In 60% of families, one member had to reduce or interrupt professional activity to take care of a relative. As a consequence of the disease, 13% of patients had to move house. These patients had to move to a more adapted house (39%), to a specially adapted centre (19%) or to move closer to a relative (17%) or nearer to specialists of the disease (17%).

Expectations Regarding Centres of Expertise for Rare Diseases

Expectations regarding centres of expertise somewhat differed for respondents affected by FRX as compared to the overall opinion of survey participants. Respondents affected by FRX considered the following functions provided by a Centre of Expertise as the most essential in descending order:

- 'Facilitating the follow-up of patients at different stages of their life by easing the passage from paediatric care to adult care, or from adult care to geriatric care' and 'coordinating the sharing of medical information on the patient between all professionals who care for him/her in the specialised centre' were reported equally as the most important functions of a Centre of Expertise
- Communicating with other specialised centres and professional networks to harmonise treatments and research at national and European levels
- Informing patients about their rights and guiding them toward social services, schools, leisure activities or vocational guidance, etc.

As a disease diagnosed during the early childhood years, it is not surprising that facilitating the difficult transition from paediatric to adult medical care is considered important.

'Offering patients the option of grouping consultations or tests on the same day in the specialised centre, and organising the appointments' was considered one of the least essential functions of a Centre of Expertise, possibly due to the less frequent need for multidisciplinary care required by FRX patients. Respondents affected by FRX more frequently expressed that 'the main hurdles in travelling to a specialised centre are the cost of transport and/or the need to be accompanied by someone' compared to respondents overall.

Reaction to Results

In the early years of a patient's life, in-depth explorations may require frequent hospitalisation. Later, outpatient examinations are more common. Patients experience difficulties in accessing medical care, primarily due to a lack of referral because frequently the doctor does not completely

understand the needs of FRX patients or underestimates the benefits of seeking care with specialists. Even if referred, families cannot always afford the additional costs of specialised care or cannot accompany their children (who are unable to be independent) to these specialised facilities. Families are often dissatisfied with both the number and appropriateness of services available.

Rejection of FRX patients often arises from doctors' lack of knowledge of the disease. Generalists are usually more attentive and try to teach parents how to manage their affected family members. Psychologists and speech therapists have been found to reject FRX patients more frequently. This rejection can be manifested in various ways: inability to obtain an appointment with a specialist, unwelcoming attitude or superficial consultation with no detailed explanations.

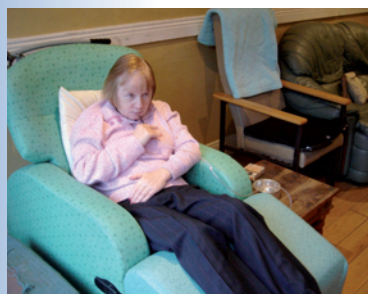
Patients and families are often sent to general social services, where the staff have no experience with FRX syndrome. It must be kept in mind that these patients are not independent and cannot travel alone to seek care. Families often move to be near medical or educational centres staffed with teams familiar with FRX.

Huntington's Disease

Sections of this chapter were written with the collaboration of the Fédération Huntington Espoir (France).

Clinical Picture

Huntington's disease (HD) is a genetic neurological disorder caused by the degeneration of brain cells, called neurons, in certain areas of the brain. The disease is characterised by jerky, random and uncontrollable body movements called chorea, a lack of coordination, a number of mental disabilities (including difficulties in planning, abstract thinking, psychomotor skills, perceptual and special skills, short-term memory and the ability to learn new skills) and changes in personality or behaviour.



Jackie, Huntington's disease
© Huntington's Association of Ireland

HD is transmitted as an autosomal dominant trait and affects males and females equally. It is estimated that the prevalence of HD is less than one in 10 000 persons. The onset of symptoms can occur at any age, but most frequently occurs in adults between the ages of 30 and 45 years.

'Tomorrow is always harder than the day before; the progression of the illness never stops. Tomorrow will be even harder yet, when the illness begins to hit the next generation. It is impossible to see the end of it.' Robert, France

The rate of disease progression

and the age of onset vary from person to person. A juvenile form of the disease also exists, affecting approximately 16% of all cases.

As the disease progresses, any function that requires muscle control is affected, causing reduced physical stability, abnormal facial expression, impaired speech comprehensibility and difficulties chewing and swallowing. Patients lose all autonomy and causes of death for most people with HD are infection, pneumonia, heart failure or choking. There is no current cure for HD. Treatment is symptomatic and includes neuroleptics for abnormal movements and psychotropic drugs for physiotherapy, if needed. Many drugs used to treat the symptoms of HD have side effects, such as fatigue, restlessness or hyperexcitability. It is extremely important for people with HD to maintain physical fitness as much as possible, as individuals who exercise and keep active tend to do better than those who do not.

Living With Huntington's Disease

Unlike many people living with a genetic rare disease with early onset, the majority of people with HD are diagnosed later in adulthood, after having established lives as healthy individuals. Thus, making adjustments to living with a rare disease can be more difficult for people with HD and their families than for those who have learnt to live with a condition from an early age. Upon diagnosis, family members of the affected are quickly faced with the dilemma of undergoing a presymptomatic diagnostic test for HD.

While a test may be able to predict the eventual onset of HD, it is not clear whether knowing will help prepare a person for the disease or cause unnecessary psychological stress during a time when the disease is still undetectable. In contrast, family members that have not inherited the disease may feel guilty in the face of their affected family member.

Physical symptoms are usually the first to appear and are accompanied by cognitive ones. Psychiatric symptoms that may remain unnoticed for some time, but which may present later as depression, apathy and irritability, prevent patients from taking care of themselves or performing normal work-related duties. As a result, children or spouses may become the primary caregivers to the affected individual, marking a change in family dynamics that may be both frustrating and difficult. Eventually, patients have difficulty carrying out routine tasks, such as having telephone conversations, cooking or doing the laundry, due to memory loss. The gradual loss of independence can be difficult to accept by a patient. Dementia, a symptom that eventually affects all individuals, may make them vulnerable to being taken advantage of or even abused by strangers. Caregivers must adapt the care of each HD patient to the patient's changing abilities because of the progressive nature of the disease. New ways of communicating must be developed, new routines created and decisions made as to what the patient is or is no longer capable of doing independently, and great patience summoned with newly emerging behavioural and physical changes. For both the caregiver and the patient, awareness to a possibly shortened life expectancy can cause great psychological burden.

Access to Medical and Social Services

PARTICIPANTS IN THE SURVEY

Responses from 207 families of HD patients from eight countries were analysed in the survey (*Figure 1*). Respondents were almost equally females and males (49% and 51%, respectively). The mean age of patients was 52 years (the mean age at diagnosis was 44 years).

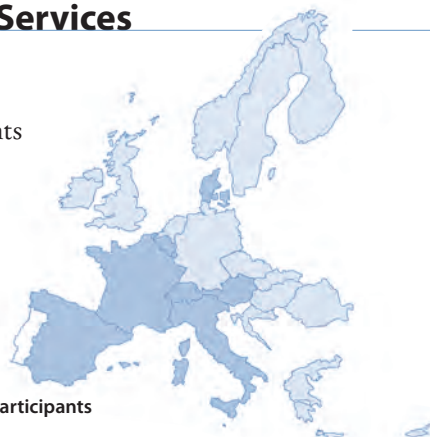


Figure 1 Survey participants affected by HD

NEED FOR MEDICAL SERVICES

Overall, each patient with HD needed an average of six different kinds of medical services related to their disease (less than the average nine medical services required for the 16 rare diseases surveyed). In addition to consultations mentioned in Figure 2, consultations in genetics (21%), rehabilitation medicine (18%) and emergency services (17%) were often needed. The most frequently required explorations were biological testing (47%), specialised imagery (33%), as well as genetic testing (18%), radiology (16%) and electrocardiogram (13%). Other types of care required included physiotherapy (35%), dental care (48%), nursing care (28%), speech therapy (36%), psychotherapy (35%) and glasses (18%). Hospitalisation occurred in 38% of patients, for an average total duration of 35 days.

ACCESS TO MEDICAL SERVICES

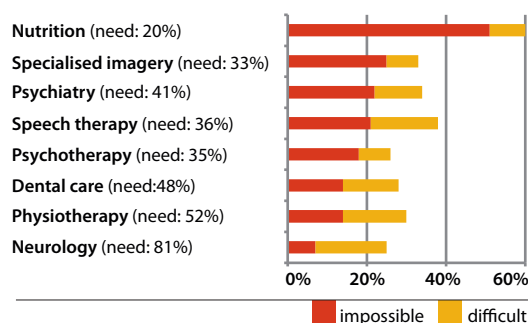


Figure 2
Need for and access to eight representative medical services for Huntington's disease

Lack of access to medical services in 18% of situations overall for HD patients

Respondents most frequently reported impossible access to nutrition (51%), specialised imagery (25%), psychiatry (22%) and speech therapy (21%) services. A lack of referral was the most frequent cause for impossible access to speech therapy (73%), specialised imagery (71%), psychiatry (61%), nutrition (57%) and psychotherapy (54%). Unavailability was a hurdle for access to psychotherapy (31%), neurology (27%) and physiotherapy (27%) services. Personal cost was a significant barrier to access to dental care (36%). Barriers to access related to the distance from the medical structure were significant for accessing neurology consultations: 55% due to excessive distance, 55% due to difficult travel, 27% due to the inability to find someone to go with and 27% due to cost of the journey.

Access to medical services was difficult in 14% of situations

Patients reported difficult access to neurology (18%) and speech therapy (17%) consultations, followed by physiotherapy (16%) and dental care (14%). An insufficient number of appointments were reported for nutrition, speech therapy, psychiatry and psychotherapy in more than 15% of situations. Personal cost was considered excessive for speech therapy (20%), neurology (28%), psychotherapy (35%) and dental care (44%). Despite the location of many consultations outside the region (21% overall for the eight medical consultations investigated), the assistance of a professional for the journey to

these medical structures was not adequate when needed for specialised imagery (14%) and psychotherapy (6%). In contrast, it was more frequently provided for consultations in the same region, for such services as dental care (16%) and speech therapy (18%). The time needed to obtain an appointment was considered long or very long in 33% of patients for psychiatry, 31% for nutrition and 27% for neurology services.

Satisfaction with medical services

Overall, 91% patients felt that medical services, when obtained, responded fully or partially to their expectations, without significant variability between services. Patients reported that specialised imagery and dental care responded fully to their expectations 70% of the time (*Figure 3*).

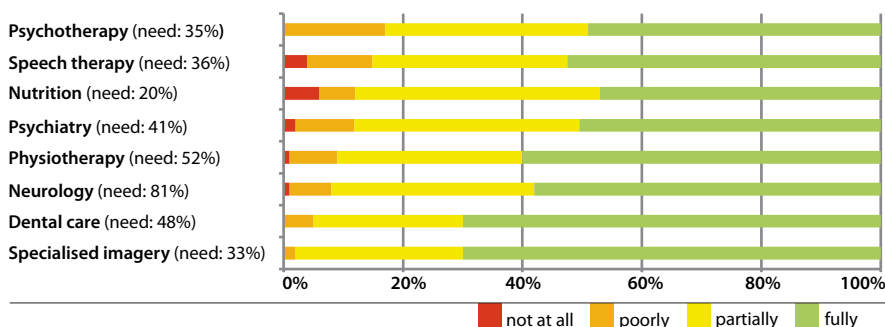


Figure 3 Satisfaction with eight representative medical services for respondents affected by HD.

SOCIAL ASSISTANCE

Amongst the 50% of families needing social assistance, 2% failed to meet with a social worker and 18% met one with difficulty.

‘To live with someone with Huntington’s disease means love, understanding, patience and devotion. But it also means discouragement, fatigue and a hatred of the illness.’
Robert, France

When obtained, the level of satisfaction with social assistance was 65% overall and was the lowest for assistance with financial procedures (38% were not satisfied with assistance for obtaining exceptional financial support and 45% were not satisfied with assistance with financial paperwork) (*Figure 4*).

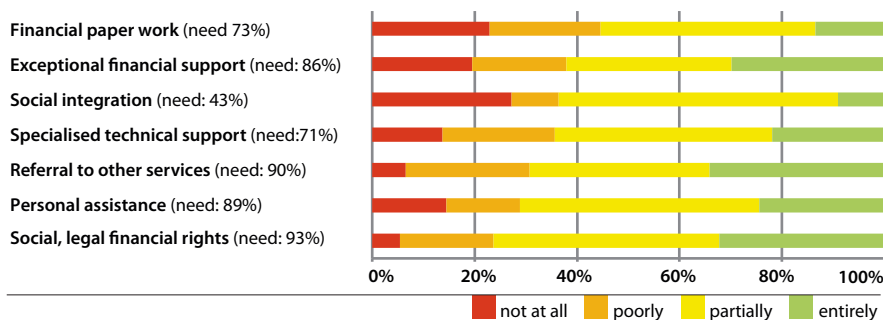


Figure 4 Satisfaction with specific social services for respondents affected by HD

REJECTION

Patients with HD experienced rejection by health professionals with similar frequency (19%) to the overall respondents for the 16 surveyed rare diseases (18%).

The reluctance of health professionals due to the complexity of the disease was reported by 58% of rejected patients. Patients were almost equally rejected for personal aspects, including difficulties in communication (50%) and disease-related behaviour (45%). In addition, patients were rejected for a physical aspect related to their disease in 23% of cases. Even if the rejection was mainly linked to the disease rather than the patient, its extent was perceived as a refusal of the health professional to treat HD patients. The frequency and cause of rejection varied according to the patient's country of origin (*Figure 5*).

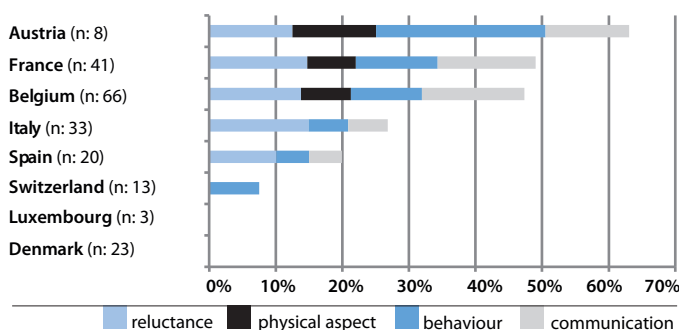


Figure 5

Cumulated frequencies of causes of rejection by country (n: total number of respondents) in HD. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

HD

CONSEQUENCES OF THE DISEASE

As a consequence of the disease, 23% of patients had to move house. Amongst these, 53% had to move to a more adapted house, 34% moved to a specially adapted care centre and 21% moved to be closer to a relative. As a consequence of the disease, 29% of patients with HD had to reduce or to stop their professional activity. An equal number of family members (30%) reduced or stopped their professional activities to take care of a relative.

Expectations Regarding Centres of Expertise for Rare Diseases

Not differing from the overall opinion of survey participants, respondents with HD considered the following functions provided by a Centre of Expertise as the four most essential:

- Coordinating the sharing of medical information on the patient between all professionals who care for him/her in the specialised centre
- Communicating with other specialised centres and professional networks to harmonise treatments and research at the national and European levels
- Coordinating the sharing of medical information between professionals of the specialised centre and local professionals, to facilitate the continuity of the patients' follow-up

- Collaborating with research teams working on the rare disease (in particular for clinical studies)

Survey participants with HD considered ‘providing frequent care related to the rare disease (physiotherapy, speech therapy, psychotherapy, etc.)’ and ‘training local professionals in responding to the specific needs of patients and supplying their contact information to patients’ as the fifth and sixth most essential functions provided by a Centre of Expertise for respondents affected by HD (higher rankings of priority than expressed by all other respondents). Although still low on the list of priorities, respondents with HD more frequently reported that they agreed with the statement ‘The role of the general practitioner consists mainly in looking after health problems not related to the disease’ compared to respondents overall.

Reaction to Results

Patients with HD require multidisciplinary care to maintain their quality of life and improve life expectancy. Despite the opinion of some doctors lacking knowledge in HD, none of the services investigated in the survey are ‘extra’. They represent the only means by which patients can maintain their independence, mental and physical well-being, and dignity. Speech therapy, for example, is not reserved for children with difficulties in pronunciation but rather enables HD patients to maintain contact with their friends and avoid isolation. In order to obtain this crucial medical service, a patient’s physician must be aware of the need for speech therapy and refer the patient to a speech therapist. In addition, patients must be referred to a speech therapist who agrees to follow them, as they are often seen as ‘unrewarding’ patients, even by their own description.

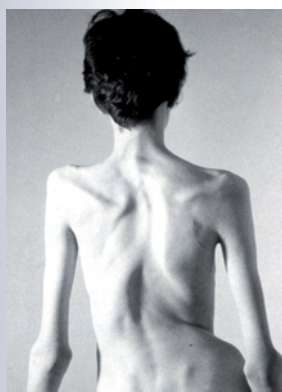
With many medical professionals, HD patients and their families encounter the problem of lack of extensive knowledge of the disease. Therefore, explanatory brochures have been produced by patient organisations and distributed by families to physiotherapists or general practitioners, allowing real progress in continued education of the disease. Similarly, social services providers, disconnected from the medical world, know little of the needs of HD patients and are often unable to assist patients in receiving the social assistance they are entitled to. Patient organisations also play a major role in supporting patients in receiving these necessary and deserved social services.

Marfan Syndrome

Sections of this chapter were written with the collaboration of the Marfan Foundation Switzerland and the Association Française du Syndrome de Marfan.

Clinical Picture

Marfan syndrome (MFS) is an autosomal dominant genetic disorder caused by a mutation in a gene that affects the formation of the connective tissue (a material that gives the organ systems form and strength). Because connective tissue is found throughout the body, Marfan syndrome can affect many body systems, including the skeleton, eyes, heart and blood vessels,



Patient, Marfan syndrome
© Marfan Foundation Switzerland.

nervous system, skin and lungs. Symptoms include increased length of the arms, legs and fingers, scoliosis, indentation or protrusion of the breastbone, dislocation of the lenses in the eye, nearsightedness and abnormalities of heart valves and the main artery. The estimated prevalence of MFS is three per 10 000 persons and affects both males and females equally. The first symptoms of MFS usually appear in childhood. Although patients with MFS can experience a range of symptoms from mild to more severe, symptoms worsen with age in most cases. Although there is no cure for MFS, a range of treatment options, including annual evaluations of the spine, breastbone and heart, are important. Visual impairments may be

corrected with glasses, contacts or surgery, and some heart valve problems may be managed with medication or surgery.

MFS

Living With Marfan Syndrome

For patients living with MFS, this means coping with a lifelong chronic disease, constant doctor's visits, repeated analyses and specialist evaluations, which accompany an incurable, but treatable disease. In spite of all this, most patients living with MFS can enjoy a good quality of life.

The range of symptoms associated with this disease varies greatly from one patient to another, as do the diversity and severity of symptoms affecting each patient. Furthermore, symptoms may change during the course of a lifetime. Modern medical treatment and regular evaluation of the aorta have almost eliminated the risk of a sudden aortic rupture and possible death due

'Affected people generally suffer from fatigue: they need repeated time-outs during their daily schedule.'
Marfan syndrom patient

to unforeseen dilatation. School life and learning may remain fairly normal once any vision-related problems are addressed and sports-related physical activities are stopped. However, issues related to self-esteem and body image may play a role in establishing relationships.

In many cases patients may be very tall, so much so that finding clothes that fit can be difficult and seats in cars, trains or planes never afford enough space. In choosing a career, MFS patients must account for very little heavy lifting and the possibility of frequent periods of rest, as well as a low-stress environment. In making the decision to start a family, patients must be prepared for a 50% chance that their child may also be born with MFS. Patients can also seek genetic counselling to explore the option of pre-implantation diagnosis.

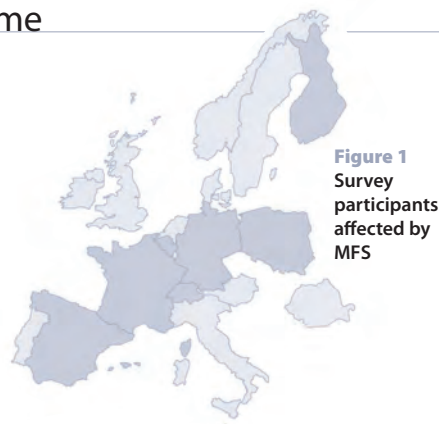
Diagnosis of Marfan Syndrome

PARTICIPANTS IN THE SURVEY

Responses from 682 families affected by MFS from seven countries were analysed (*Figure 1*).

Nearly an equal number of female and male patients were represented (53% and 47%, respectively).

The median age of patients at diagnosis was 15 years, but 25% of diagnoses occurred before 4 years of age and 25% after 32 years.



AWAITING DIAGNOSIS

Due to the age at which the first symptoms appear, neonatal diagnoses were rare (7%), and were usually due to other cases in the family.

Excluding neonatal diagnoses, the time elapsed between the first clinical manifestations and diagnosis for half of the patients was two years (and was as long as 4.5 years for 25% of patients). During the quest for diagnosis, more than five physicians were consulted by 38% of families and more than 20 physicians by 7% of families. A significant number of examinations and tests, X-rays (76%), biological testing (48%), functional testing (43%) and genetic testing (22%) were performed during this period.

Before obtaining the correct MFS diagnosis, another diagnosis was given to 25% of patients, resulting in inappropriate treatments in 81% of the patients (medical, 32%; psychological or psychiatric, 8%; or surgical, 29%).

Misdiagnoses were associated with a longer time to reach an MFS diagnosis: one year without misdiagnosis, ten years with an initial misdiagnosis (14 years if it was an initial psychiatric diagnosis). For 72% of families, a delay in diagnosis was considered responsible for deleterious consequences. Consequences were associated with a longer delay in diagnosis (13 months

in patients without consequences, four years for patients reporting personal consequences and six years for those with familial consequences) (Figure 2).

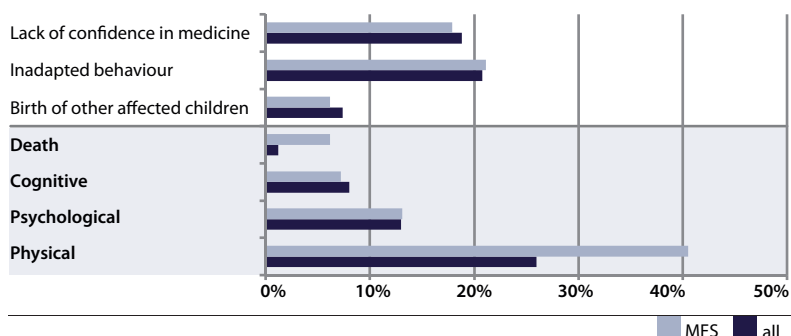


Figure 2
Consequences of
delays in diagnosis
in MFS patients.

DIAGNOSIS

Diagnosis of MFS was obtained on the basis of clinical (32%), biological (28%) and functional (12%) data. The structure providing the diagnosis was usually a specialised centre (19%) or another hospital structure (53%), but sometimes a private practice (18%). The medical structure was located in another region for 28% of patients or in another country for 3% of patients. Access to diagnosis required a financial contribution from 49% of families and was considered as high or very high by 10% of patients. In addition, 31% of patients thought that delays in diagnosis depended upon the level of personal expenditure. A second opinion was sought by 25% of patients to confirm the diagnosis. Confirmation occurred in a private practice more often (28%) than for the first diagnosis.

ANNOUNCEMENT OF DIAGNOSIS

Communication of the diagnosis occurred during a standard private consultation in 71% of cases, but also occurred orally in another manner (e.g. in a corridor) in 13% of cases, or by phone (8%). For 19% of patients, the diagnoses were given without information on the disease.

When provided, the sources were medical in 74% of cases and non-medical in 26%, including patient organisations (15%). Psychological support accompanying the announcement of diagnoses was infrequent (20%), while 86% of patients considered it necessary.

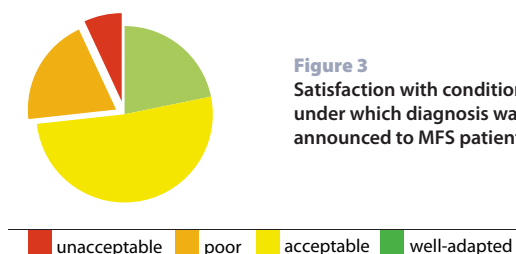


Figure 3
Satisfaction with conditions
under which diagnosis was
announced to MFS patients.

GENETIC ASPECTS

The genetic nature of the disease was explained to families in 74% of cases, with details about the possibility of other familial cases given 38% of the time. Genetic counselling was provided to 43% of patients.

'Pre-implantation diagnosis is a patient's right, but is sometimes denied under the pretext that being the carrier of a defective gene does not, in all cases, mean suffering from a severe form of the disease.'
Marfan syndrom patient

Whether based on the suggestion of a health professional (43%) or not, this information was communicated to the family in 82% of cases, leading to the diagnosis of a relative in 25% of cases if they already experienced symptoms and in 8% of cases if they did not.

Reactions to Results

MFS patients are often frustrated by the fact that doctors know that Abraham Lincoln and Niccolò Paganini both suffered from MFS, but are not able to diagnose the symptoms in a new patient. Unfortunately, frequently the diagnosis is only made at autopsy.

A lack of or delay in diagnosis in children with MFS has severe medical and non-medical consequences on the patients themselves: children with MFS may tire easily, be clumsy, write poorly, have poor eyesight and be frequently absent due to hypoglycaemia. Thus, undiagnosed children can unfairly be seen as inattentive students, careless, unintelligent or restless. The intellectual potential of young students with MFS, which can be reached in an appropriate learning environment, may be overlooked. As a result of their lack of success in school, young adults with MFS may be encouraged to pursue more physically demanding jobs, which lead to a quick physical deterioration and subsequent work accidents or substandard performance. Medical and non-medical consequences can also occur for the whole family. Physical characteristics associated with MFS (sharp facial features, deformations of the chest, very slender hands) can be difficult to accept for others, including family members, if the mutation causing the disease is spontaneous (i.e. not transmitted by a parent). Parents may be overprotective of a child with MFS. The birth of other children with MFS due to a lack of diagnosis is tragic and very hard for parents to accept, as they feel guilty not only for having transmitted the disease once but to have transmitted it twice due to a lack of knowledge needed to make an informed decision about having more children. Pre-implantation diagnosis is a right that is sometimes denied to parents based on the thinking that being a carrier does not ensure that the defective gene will be passed on.

MFS

Access to Medical and Social Services

PARTICIPANTS IN THE SURVEY

Responses from 419 families of MFS patients from eight countries were analysed in the survey (*Figure 4*). More females (60%) responded than males (40%). The mean age of patients was 37 years (age at diagnosis: 21 years).

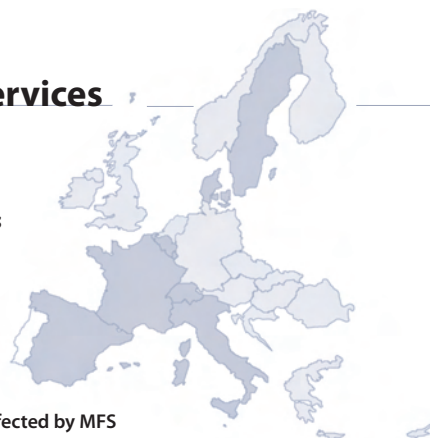
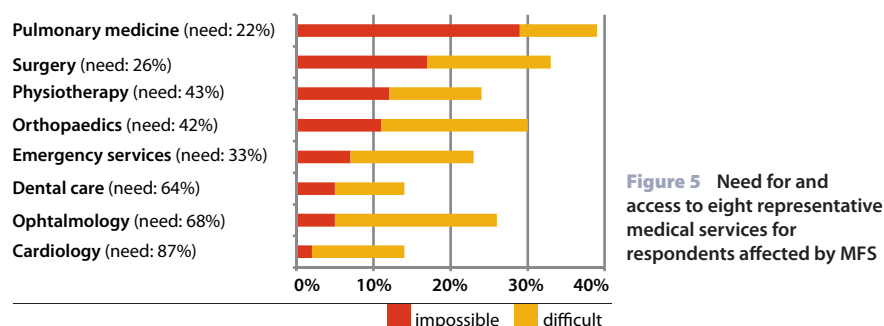


Figure 4 Survey participants affected by MFS

NEED FOR MEDICAL SERVICES

Overall, patients with MFS needed 11 different kinds of medical services related to their disease (more than the average nine medical services for the 16 rare diseases surveyed). Cardiology was the most frequently sought consultation (91%), followed by ophthalmology (68%), orthopaedics (42%) and emergency services (33%). The most frequently needed explorations were ECG (75%), biological testing (65%), ultrasounds (63%), specialised imagery (54%) and radiology (49%). As for other types of care, glasses (56%), dental care (64%), physiotherapy (43%) and surgery (26%) were the most frequently needed. Hospitalisation occurred in 43% of patients for an average total duration of 19 days (*Figure 5*).



ACCESS TO MEDICAL SERVICES

Lack of access to medical services in 8% of situations overall for MFS patients

Pulmonary medicine was impossible to access for 29% of patients. Complete barriers to access were less frequent for surgery (17%), physiotherapy (12%) and orthopaedics (11%). In contrast, very few MFS patients found it impossible to access emergency services (7%), ophthalmology services (5%), dental care (5%) or cardiology consultations (2%). A lack of referral was the most frequent barrier to access: 70% for pulmonary medicine, 68% for orthopaedics, 57% for physiotherapy, 56% for surgery and 50% for ophthalmology. Unavailability of the service was also a significant barrier to access for cardiology (33%) and physiotherapy (24%). Personal cost was considered a barrier to access for dental care (38%), ophthalmology (29%) and cardiology (17%).

Waiting time for obtaining an appointment was considered a hurdle in access to orthopaedics (26%), ophthalmology (21%) and cardiology (17%) consultations. Excessive distance from the medical structure (33%) and difficult travel (50%) were reported as barriers to access to cardiology consultations.

Access to medical services was difficult in 14% of situations

Respondents most frequently experienced difficult access to ophthalmology (21%) and orthopaedic (19%) consultations. The number of appointments was considered insufficient for physiotherapy (16%) and orthopaedics (15%). Personal cost was considered excessive for dental care (46%)

and surgery (36%). Assistance of a professional for the journey to a medical structure was available for emergency services (20%) and surgery (19%), but scarce for all other services, overall 4%.

Satisfaction with medical services

Overall, 91% of patients considered that medical services responded fully or partially to their expectations with low variability between medical services (Figure 6).

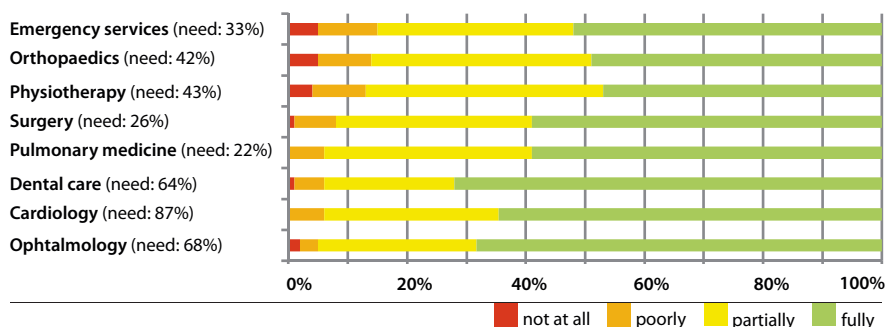


Figure 6 Satisfaction with eight representative medical services for respondents affected by MFS

MFS

SOCIAL ASSISTANCE

Amongst the 22% of families needing social assistance, 5% failed to meet a social worker, and 21% met one with difficulty.

The level of satisfaction was overall 54%, with low variability in relation to the kind of assistance (Figure 7).

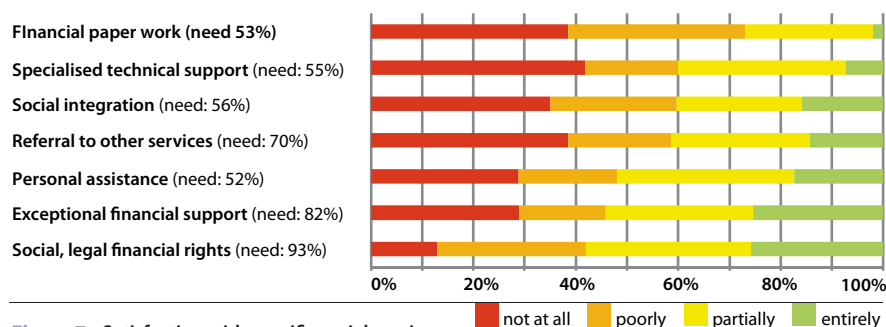


Figure 7 Satisfaction with specific social services for respondents affected by MFS

REJECTION

Patients with MFS experienced rejection by health professionals with similar frequency (19%) to the overall respondents for the other 16 surveyed rare diseases surveyed (overall 18%). The reluctance of the health professional due to the complexity of the disease was the main cause of rejection (81% of cases). Rejection due to a physical aspect was reported less frequently (16%). Disease-related behaviour (6%) and difficulties in communication (6%) were even less often considered as causes of rejection.

The frequency and cause of rejection varied according to the patient's country of origin (*Figure 8*).

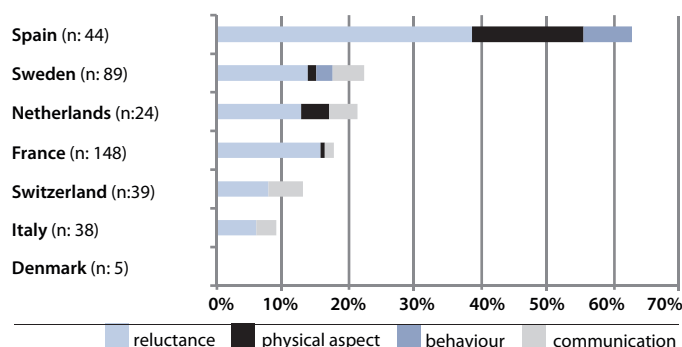


Figure 8 Cumulated frequencies of causes of rejection by country (n: total number of respondents) in MFS. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

CONSEQUENCES OF THE DISEASE

In 49% of families, one member had to reduce their workload or stop his or her professional activity. Amongst these, 40% included patients that decreased their professional activity and 9% were family members that decreased their professional activity to take care of a relative.

As a consequence of the disease, 10% of patients had to move house.

The majority of these patients had to move to a more adapted house (48%), to move closer to disease specialists (35%) or to move closer to a relative (29%).

MFS

Expectations Regarding Centres of Expertise for Rare Diseases

Not differing from the overall opinion of survey participants, respondents with MFS considered the following functions provided by a Centre of Expertise as the four most essential:

- Coordinating the sharing of medical information on the patient between all professionals who care for him/her in the specialised centre
- Communicating with other specialised centres and professional networks to harmonise treatments and research at the national and European levels
- Coordinating the sharing of medical information between professionals of the specialised centre and local professionals, to facilitate the continuity of the patients' follow-up
- Collaborating with research teams working on the rare disease (in particular for clinical studies)

As a disease that can affect many organ systems, potentially requiring multidisciplinary care, it is not surprising that respondents affected by MFS also consider 'offering patients the option of grouping consultations or tests on the same day in the specialised centre, and organising the appointments' as one of the more essential functions of a Centre of Expertise.

Respondents affected by MFS more frequently expressed that ‘the main hurdles in travelling to a specialised centre are the time needed to get there and/or physical difficulties encountered by the patient (pain, fatigue and injuries)’ compared to respondents overall.

Reactions to Results

Generally speaking, a lack of access to medical services is not the main concern for people with MFS, rather access to professionals knowledgeable about the disease. For example, finding a physiotherapist is easy, however finding a physiotherapist familiar with the restrictions imposed by the muscles and ligaments of a patient with MFS is difficult.

The needs of MFS patients are not only poorly known by health professionals, but also by reimbursement agencies, such as social security. If you consider dental service needs, the formation of caries can be followed by infections that can infect already deficient heart valves and ultimately lead to fatal inflammation of the heart. However, as carries are often considered an ‘aesthetic’ problem under health insurance schemes, reimbursement for this care is denied.

As with other health needs, people with MFS do not so much experience a total absence of social assistance, but rather the lack of sufficient knowledge of needs specific to MFS patients. Poor health or late diagnoses, inappropriate employment, sick days not taken due to fear of losing a job, exhaustion and dismissal are a few of the issues that could be prevented by the appropriate intervention of social workers. Such support requires that social workers work more closely with healthcare professionals to pre-emptively offer their support rather than waiting to be presented with a socially or medically serious case.

Myasthenia Gravis

Sections of this chapter were written with the collaboration of the Dutch Neuromuscular Diseases Association (VSN) and Associazione Italiana Miastenia (AIM).

Clinical Picture

Myasthenia gravis (MG) is a chronic autoimmune neuromuscular disorder that is characterised by weakness of the voluntary muscles. In healthy patients, when the nerve impulse originating in the brain arrives at the nerve ending, it releases a chemical called acetylcholine. Acetylcholine travels



Irene, myasthenia gravis
© Stefano Cavallari.

across the space between the nerve ending side and the muscle fibre side of the neuromuscular junction, where it attaches to many receptor sites. The muscle contracts when enough of the receptor sites have been activated by the acetylcholine. Patients with MG experience an abnormal immune response in which antibodies (proteins that normally attack foreign proteins, such as bacteria and viruses, in the body)

inappropriately attack acetylcholine receptors in the muscles. MG is not inherited, but is due to a spontaneous mutation during conception. Symptoms include drooping eyelids, blurred vision, slurred speech, difficulty chewing and swallowing, weakness in the arms and legs, chronic muscle fatigue and difficulty breathing. The estimated prevalence of the disease is two in 10 000 persons and affects both sexes equally. Although the disorder usually becomes apparent during adulthood, symptom onset may occur at any age. Weakness of the eyes is the most common first symptom and patients usually experience arm and leg weakness within three years of the initial symptoms. Currently, there is no cure for MG although symptomatic treatment is possible and includes medications (that suppress the immune system), surgery (removal of the thymus), plasmapheresis

(removal, treatment and return of blood plasma) and intravenous immune globulin therapy (providing the body with normal antibodies, altering the abnormal immune response). Although the course of the disease is variable, the mortality rate is low and patients experience a nearly normal life expectancy as a result of improved diagnostic testing, therapy and care.

Living With Myasthenia Gravis

Patients with MG do not typically show symptoms until adulthood.

Even then, the symptoms of one patient may vary distinctly from those of another. Indeed the simple fact of receiving a correct diagnosis can feel like quite an accomplishment.

'In the early days of the disease, chewing and swallowing was difficult. Several times I couldn't swallow at all and had to be urgently admitted to the hospital.'
Josipa, 63 years old, Croatia

The disease, causing a painless muscle weakness, first affects the eyes, evidenced by drooping eyelids and double vision, followed by weakness of the limbs and other body parts. While there is no cure, special surgery, treatments and prescription medication can help patients lead very satisfying and normal lives. Post-operation recovery, however, can be quite long, and determining the correct dosage for medication can be elusive, leading to frustration for some patients.

While most patients develop a stable living condition, setbacks are not uncommon. Because of muscle weakness, patients can become tired very easily and tasks such as climbing a flight of stairs or even lifting their arms above their head can be quite hard. The fact that the eyes of patients with MG are frequently affected can also limit their ability to drive a car or pursue careers in which clear vision is required. However, people with MG do tend to hold full-time jobs as long as physical exertion can be avoided.

MG

Access to Medical and Social Services

PARTICIPANTS IN THE SURVEY

Responses from 647 families of MG patients from seven countries were analysed in the survey (*Figure 1*). More females (72%) responded than males (28%). The mean age of patients was 53 years (age at diagnosis: 38 years).



Figure 1 Survey participants affected by MG

NEED FOR MEDICAL SERVICES

Overall, patients with MG needed an average of eight different kinds of medical services related to their disease (slightly less than the average nine medical services for the 16 investigated diseases).

In addition to consultations mentioned in Figure 2, consultations in ophthalmology (39%), cardiology (25%) and internal medicine (23%) were frequently needed. Ear nose and throat medicine, rheumatology, gynaecology, pulmonary medicine, dermatology, emergency services, gastroenterology, endocrinology and genito-urinary medicine were also needed in descending frequency from 19% to 11% of the time.

The most frequently required explorations were biological testing (68%), radiology (38%), ECG (34%), specialised imagery (30%), functional testing (32%) and ultrasound (26%), but also biopsy/cytology (19%) and microbiology (13%). As for other types of care, glasses (48%), dental care (29%), physiotherapy (22%), injections (22%) and plasmapheresis (14%) were most frequently required. Hospitalisation occurred in 43% of patients for an average total duration of 21 days.

ACCESS TO MEDICAL SERVICES

Lack of access to medical services in 12% of situations overall for MG patients

Plasmapheresis was impossible to access for 44% of patients.

Complete barriers to access were less frequent for psychotherapy (32%) and electromyograms (22%). A lack of referral was the most frequent barrier to access for plasmapheresis (64%), electromyograms (60%) and psychotherapy (56%). Unavailability of services was a significant hurdle in accessing neurology (33%), functional testing (26%) and psychotherapy (22%). The waiting time for obtaining an appointment was the predominant cause of impossible access to neurology (47%) but also a significant barrier to accessing gynaecological consultations (22%) and receiving eyeglasses (22%). Barriers to access related to the distance from the medical structure existed for neurology (33%), emergency services (27%) and gynaecology (22%). The inability to find someone to go with was the most significant barrier in accessing gynaecology consultations (43%) and also presented a significant barrier to accessing neurology (33%), electromyograms (27%), psychotherapy (25%) and functional testing (21%) (*Figure 2*).

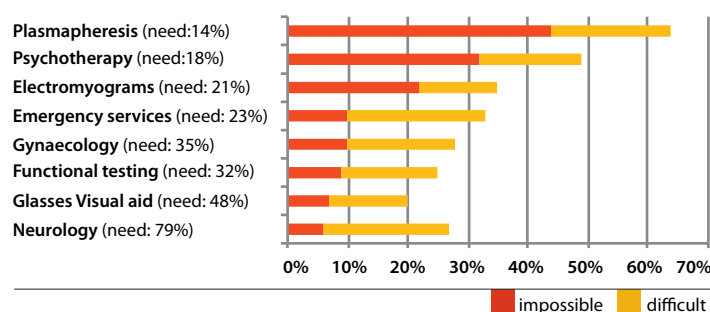


Figure 2
Need for and access to eight representative medical services for respondents affected by MG

Access to medical services was difficult in 18% of situations

Respondents experienced difficult access most frequently to emergency services (23%), neurology (21%) and plasmapheresis (20%). The number of appointments was considered extremely insufficient for obtaining glasses (67%), and less so for psychotherapy (25%), plasmapheresis (15%), neurology (14%) and gynaecology (14%). Personal cost was considered excessive for all investigated services: psychotherapy (64%), glasses (56%), gynaecology (42%), neurology (30%), functional testing (28%), emergency services (27%), plasmapheresis (25%) and electromyograms (19%). The assistance of a professional for the journey to the medical structure was available for emergency services (18%), plasmapheresis (15%) and functional testing (9%), but scarce for all other services, overall 5%.

'In the beginning, I had no psychological support. I couldn't find any information about myasthenia gravis; there were no booklets or patient support groups. I felt lost from time to time.' Josipa, 63 years old, Croatia

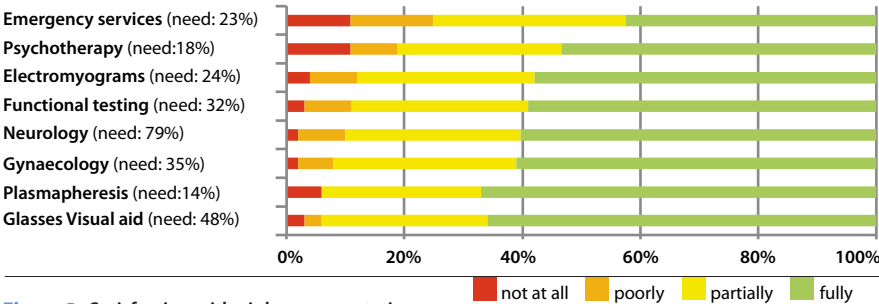


Figure 3 Satisfaction with eight representative medical services for respondents affected by MG

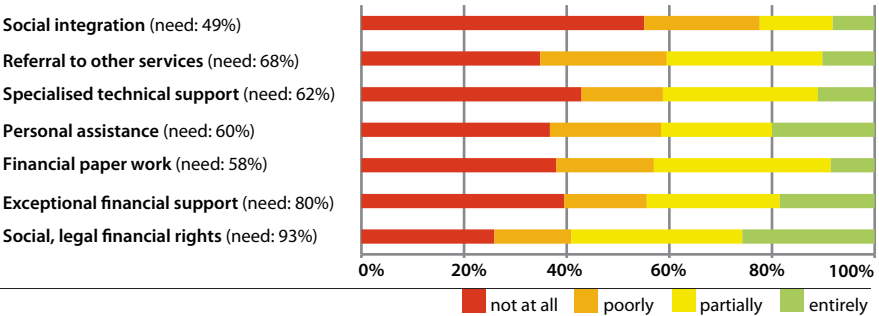
Satisfaction with medical services

Overall, 89% of patients considered that medical services responded fully or partially to their expectations, with wide variability between medical services: 94% for plasmapheresis and glasses and as little as 76% satisfaction for emergency services (Figure 3).

SOCIAL ASSISTANCE

Amongst the 16% of families needing social assistance, 9% failed to meet a social worker, and 38% met one with difficulty. The level of satisfaction with social services was 39% overall, with patients less satisfied with services encouraging social integration (22%) and more satisfied with those assisting with social and legal financial rights (59%) (Figure 4).

Figure 4 Satisfaction with specific social services for respondents affected by MG



REJECTION

Patients with MG experienced rejection by health professionals with similar frequency (17%) to the overall respondents for the 16 other surveyed rare diseases (overall 18%). The reluctance of the health professional due to the complexity of the disease was the main cause of rejection (83% of cases). Rejection due to a physical aspect (9%), difficulties in communication (11%) and disease-related behaviour (7%) were less often considered as causes of rejection. The frequency and cause of rejection varied according to the patient's country (*Figure 5*).

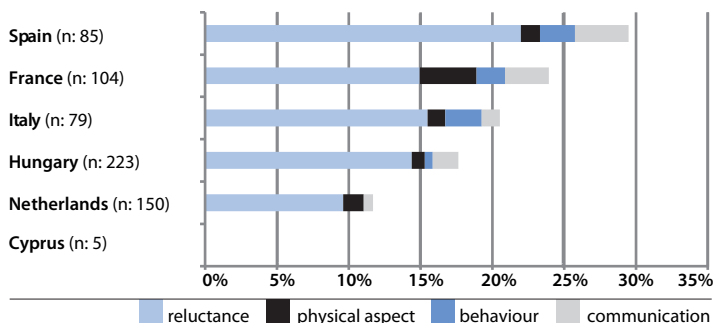


Figure 5 Cumulated frequencies of causes of rejection by country (n: total number of respondents) in MG. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

CONSEQUENCES OF THE DISEASE

In 48% of families, one member had to work less or stop his or her professional activity. Amongst these, 44% included patients that decreased their professional activity and 4% of family members who decreased their professional activity to take care of a relative. As a consequence of the disease, 13% of patients had to move house. The majority of these patients had to move to a more adapted house (54%), move closer to a relative (22%) or move closer to disease specialists (19%).

MG

Expectations Regarding Centres of Expertise for Rare Diseases

Not differing from the overall opinion of survey participants, respondents with MG considered the following functions provided by a Centre of Expertise as the four most essential:

- Coordinating the sharing of medical information on the patient between all professionals who care for him/her in the specialised centre
- Communicating with other specialised centres and professional networks to harmonise treatments and research at the national and European levels
- Coordinating the sharing of medical information between professionals of the specialised centre and local professionals, to facilitate the continuity of the patients' follow-up
- Collaborating with research teams working on the rare disease (in particular for clinical studies)

Survey participants with MG considered 'training local professionals in responding to the specific needs of patients and supplying their contact

information to patients' as the fifth most essential function provided by a Centre of Expertise, a higher ranking of priority than expressed by respondents overall.

Reaction to Results

Difficult access to health care begins with the difficulties in obtaining the correct diagnosis. Prior to determining the diagnosis, patients often undergo lengthy examinations. Once diagnosed, treatment can be very complicated. Care of MG patients is complicated because in addition to the disease, treatments (corticosteroids or immunosuppressive therapy) cause many side effects (such as glaucoma, cataracts, hypertension, renal problems, liver problems, osteoporosis, digestive problems, etc.) that require intensive monitoring.

This may also include hospitalisation for reasons such as thymectomy (surgical removal of the thymus), acute respiratory problems or highly specialised treatments such as plasmapheresis or injection of immunoglobulins, which are often administered with difficulty and only in serious cases. As with any surgery, a thymectomy requires the help of a specialised anaesthetist familiar with the risk of anaesthesia worsening the disease state.

Doctors often do not understand the potential severity of the symptoms until they are very serious. They are often not familiar with the disease and prefer to 'keep' patients rather than refer them on, either because they are not aware of specialised care centres or sometimes due to professional pride. Often the symptoms of MG patients are considered to be psychological (anxiety, depression), and ultimately ignored. Several patients reported seeking urgent care because they could not speak properly and were not taken seriously in any other health setting.

Osteogenesis Imperfecta

Sections of this chapter were written with the collaboration of Deutsche Gesellschaft für Osteogenesis Imperfecta (OIFE - Germany) and Dansk Forening for Osteogenesis Imperfecta (Denmark).

Clinical Picture

Osteogenesis imperfecta (OI) is a group of inherited genetic rare disorders affecting the connective tissue and characterised by extremely fragile bones that break or fracture easily. OI is caused by mutations in the gene involved in the production of collagen (a protein required for the synthesis of connective tissue that makes up ligaments, tendons and cartilage and is responsible for the strength and elasticity of skin and blood vessels).



Silvia, osteogenesis imperfecta
© Josep Avilés.

The types of OI range in severity. As such, symptoms also vary and can include short stature, brittle teeth, weak tissues, fragile skin, muscle weakness, loose joints, pain, curvature of the spine, bleeding, easy bruising and frequent nosebleeds. Hearing loss, breathing problems, higher incidence of asthma and risk for other lung problems are also possible complications experienced by patients.

OI is inherited as an autosomal dominant or autosomal recessive trait depending on the type.

The prevalence of the disease is estimated as less than one per 10 000 persons and affects males and females equally. The onset of symptoms usually occurs in early childhood although some patients are not diagnosed until adulthood. Life expectancy in patients with mild or moderate symptoms is not affected. In patients with more severe forms of the disease, however, life expectancy can be shortened due to respiratory failure or accidental trauma. Although there is no cure for OI, treatments exist and the focus is on minimising fractures, maximising mobility, maximising independent function and improving general health. This includes prevention of vitamin D and calcium deficiency, physical therapy, orthopaedic surgery, medication to strengthen bones and mobility aids to help with weakness or short stature.

Living With Osteogenesis Imperfecta

As there are many types of OI that range dramatically in severity, no two people with OI are alike. Some are capable of walking independently, others require the periodic use of walking aids, and still others who even after surgery and physical therapy are unable to walk and are dependent upon the use of

'The daily experience of living with osteogenesis imperfecta is about a constant fear and danger of breaking or fracturing bones — you have to concentrate on every single movement.'
Ute, Germany

a wheelchair. Almost all OI patients deal with painful bone fractures. These fractures are especially difficult to treat in infants, as locating the fracture can be difficult. Some children with OI who experience significant pain in their early years become wary of unfamiliar situations or sudden movements, fearing a possible pain-inducing accident. Parents are encouraged to help children build self-confidence by promoting positive experiences and independence despite their natural urge to protect their child.

Due to frequent bone fractures, it is unfortunately not uncommon for parents of children with OI to be mistakenly suspected of child abuse, especially prior to a child's diagnosis. Even after diagnosis when the child is required to see a physician not familiar with the disease, parents may need to be prepared to answer related questions.

Children with severe OI frequently meet qualifications for special education programmes. However because many children with OI will eventually work and live independently, it is important to integrate them into a regular classroom setting whenever possible.

As an adult with OI, independent living presents additional challenges, such as remodelling many elements in the home to allow for this.

For people in a wheelchair, these adaptations include having an access ramp or other accessible entrances. Kitchen and bathroom elements must be remodelled to accommodate either patients in wheelchairs, those of small stature or those who cannot move around easily. If adaptation of the house is too expensive, patients may have to move house. Others may need to live in an assisted centre. Either option can result in patients moving far from friends and family and from places they are familiar with.

Being affected by a disease that requires using a wheelchair means extensive planning on a daily basis. Tasks that may be simple for others, such as shopping or going on a small trip, require extra planning and effort for OI patients who are unable to walk, as many facilities lack ramps, elevators, tall counters or other elements, thus rendering the facilities inaccessible. For OI patients of any age, being in public can attract unwanted attention, as those around them are not familiar with differences in their physical appearance.

'It can be hard to get around in a wheelchair when so few places are accessible: lack of ramps, steps, tall counters and sometimes no elevators make it hard to be disabled.'
Karsten, Denmark

Access to Medical and Social Services

PARTICIPANTS IN THE SURVEY

Responses from 421 families of OI patients from eight countries were analysed in the survey (*Figure 1*). More females (61%) responded to the survey than males (39%). The mean age of patients was 35 years (age at diagnosis: 7 years).

Figure 1
Survey participants affected by OI



NEED FOR MEDICAL SERVICES

Overall, patients with OI needed eight different kinds of medical services related to their disease (slightly less than the average nine medical services for the 16 rare diseases surveyed). Patients indicated the eight most representative medical services needed for individuals with OI (Figure 2). In addition to these services, emergency services (30%), rehabilitation medicine (30%), ophthalmology (19%), rheumatology (17%) and cardiology (17%) were frequently required, followed by paediatrics (14%), internal medicine (14%), foot medicine (14%), gynaecology (12%), genetics (11%) and endocrinology (11%). The most frequently needed explorations were radiology (59%), biological testing (55%) and specialised imagery (32%), functional testing (19%), ECG (17%) and ultrasound (17%). As for other types of care, physiotherapy (62%), dental care (60%), prosthesis (36%), injections (28%), nursing care (27%), surgery (27%) and glasses (27%) were most frequently needed. Hospitalisation occurred in 53% of patients for an average total duration of 20 days.

ACCESS TO MEDICAL SERVICES

Lack of access to medical services in 16% of situations overall for OI patients

Impossible access to services was most frequently reported for pain control services (35%), pulmonary medicine (26%), and ear, nose and throat medicine (16%). In contrast, fewer OI patients found it impossible to access orthopaedics (9%), prosthesis (9%), surgery (9%) and dental care (8%) services. A lack of referral was the most frequent barrier to access for pain control services (65%), pulmonary medicine (60%), surgery (50%) and prosthesis (46%). Unavailability of the service was a barrier to access for dental care (45%) and physiotherapy (40%). Personal cost was considered the most significant barrier to access for ear, nose and throat medicine (33%), but also a barrier to access for dental care (40%), physiotherapy (27%) and orthopaedics (25%). The waiting time for obtaining an appointment was considered a hurdle in access to all services: pain control services (39%), orthopaedics (30%), surgery (30%), ear, nose and throat medicine (28%), physiotherapy (27%), prosthesis (23%), dental care (20%) and pulmonary medicine (20%).

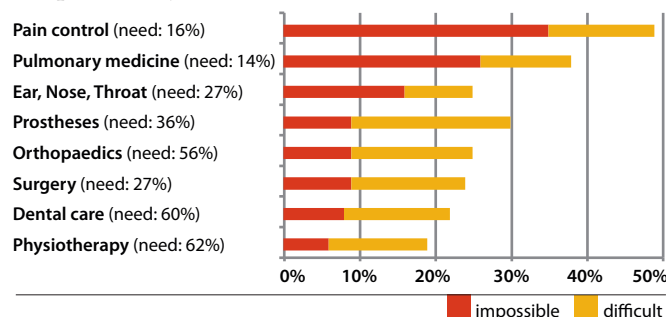


Figure 2
Need for and access to eight representative medical services for OI

Access to medical services was difficult in 18% of situations

Respondents experienced difficult access to prostheses (21%), orthopaedics (16%), surgery (15%), pain control services (14%), dental care (14%),

physiotherapy (13%), pulmonary medicine (12%) and ear, nose and throat medicine (9%). The number of appointments was considered insufficient for prostheses (25%), physiotherapy (19%), orthopaedics (14%) and pain control services (14%). Personal cost was considered excessive for all investigated services: prostheses (51%), dental care (50%), pain control services (43%), ear, nose and throat medicine (39%), pulmonary medicine (36%), orthopaedics (35%), physiotherapy (35%) and surgery (33%). The assistance of a professional for the journey to the medical structure was somewhat available for all investigated services, and above all for those in which the medical structure was often located in another region or country: surgery (24%), pulmonary medicine (16%), pain control services (15%), orthopaedics (14%), ear, nose and throat medicine (12%), physiotherapy (11%), dental care (6%) and prosthesis (5%).

Satisfaction with medical services

Overall, 91% of patients considered that medical services responded fully or partially to their expectations, with some variability between medical services: 98% for pulmonary medicine and 87% for physiotherapy and pain control services (*Figure 3*).

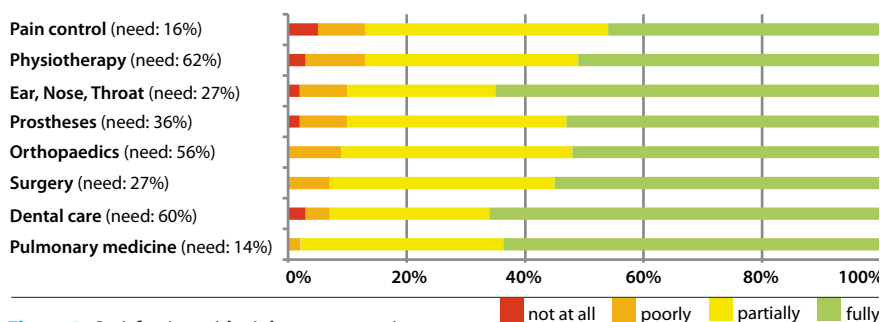


Figure 3 Satisfaction with eight representative medical services for respondents affected by OI

SOCIAL ASSISTANCE

Social assistance was required by 29% of families of which 2% failed to meet with a social worker and 29% met one with difficulty. The level of satisfaction was overall 49%. As compared to medical services, social assistance was somewhat more accessible. However, the level of satisfaction with this assistance was lower (*Figure 4*).

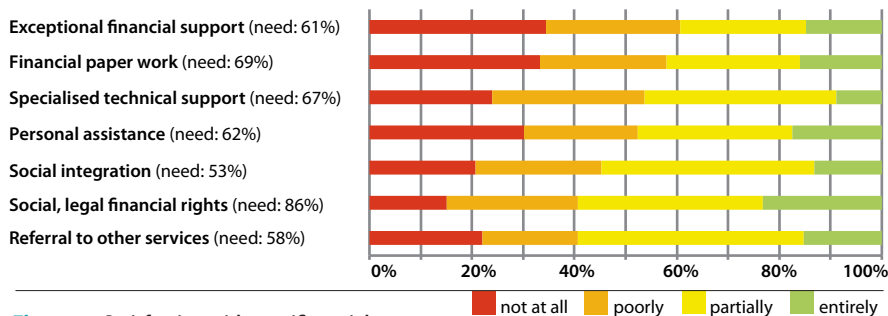


Figure 4 Satisfaction with specific social services for respondents affected by OI

REJECTION

Patients with OI experienced rejection by health professionals 17% of the time, similar to patients overall for the 16 surveyed rare diseases (18%). The reluctance of the health professional due to the complexity of the disease was the main cause of rejection (84% of cases). Rejection due to a physical aspect of the disease (12%), communication difficulties (11%) and disease-related behaviour (3%) were less reported. The frequency and cause of rejection varied according to the patient's country of origin (*Figure 5*).

CONSEQUENCES OF THE DISEASE

In 58% of families, one member had to work less or stop his or her professional activity. Amongst these, 23% included patients who decreased their professional activity and 35% were family members who decreased their professional activity to take care of a relative. As a consequence of the disease, 21% of patients had to move. The majority of these patients had to move to a more adapted house (74%); they may also have moved closer to a relative (17%), closer to disease specialists (17%) and closer to a specially adapted care centre (5%).

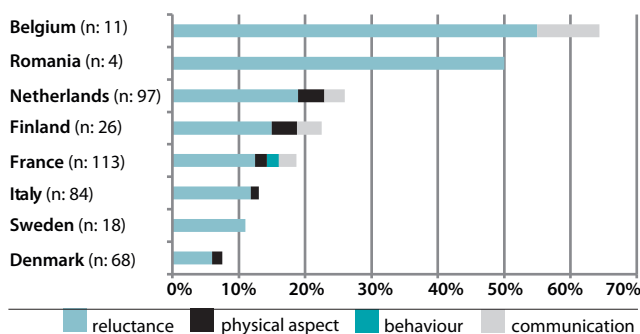


Figure 5
Cumulated frequencies of causes of rejection by country (n: total number of respondents) in OI. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

Expectations Regarding Centres of Expertise for Rare Diseases

Not differing from the overall opinion of survey participants, respondents with OI considered the following functions provided by a Centre of Expertise as the four most essential:

- Coordinating the sharing of medical information on the patient between all professionals who care for him/her in the specialised centre
- Communicating with other specialised centres and professional networks to harmonise treatments and research at the national and European levels
- Coordinating the sharing of medical information between professionals of the specialised centre and local professionals, to facilitate the continuity of the patients' follow-up
- Collaborating with research teams working on the rare disease (in particular for clinical studies)

Survey participants with OI considered 'facilitating the follow-up of patients at different stages of their life by easing the passage from paediatric care to adult care, or from adult care to geriatric care' as the fifth most essential function provided by a Centre of Expertise: a higher ranking of priority than expressed by respondents overall. As a disease diagnosed during the early childhood years, it is not surprising that respondents affected by OI reported this function as important.

Reaction to Results

In many countries the services required by OI patients are available but not specific enough to the needs of OI patients. Even in the case of specialised centres, it is quite rare that one clinic has a multidisciplinary team for such a special disorder as OI and even rarer that specialists from several clinics or even from different countries work together to help an OI patient. Parents of children with OI have to fight to obtain services for their children. Independent adults with OI, often in physical pain, are less able to do so.

Many patients report trying alternative medicine even if these treatments usually have to be paid out-of-pocket. Only recently has chronic pain in OI patients been accepted as a common problem, and therapies to control this pain are still underdeveloped. The symptom of pulmonary deficiency and the possible dependence on breathing machines to improve breathing has long been a frightening and 'taboo' topic among specialists. Many healthcare professionals are not familiar with the relationship between low oxygen levels and depression, weakness and general fatigue.

Doctors often reject patients due to the complexity of the disease. OI patients are often their own best specialists and are reluctant to accept doctors as the ultimate health authorities. Health professionals may even more often reject patients as a result of their own insecurity. Sometimes this leaves a patient with no help. Other times it provides the opportunity to find a more knowledgeable specialist, avoiding unnecessary treatments and unsuccessful surgeries.

The possibility of receiving appropriate mobility aids (small, light wheelchairs for young children or for extremely small OI patients) differs from country to country, as do public attitudes toward disabled individuals.

Prader-Willi Syndrome

Sections of this chapter were written with the collaboration of the Association Prader Willi France and the Czech Prader Willi Association.

Clinical Picture

Prader-Willi Syndrome (PWS) is a complex neurodevelopmental disease resulting from the absence of expression of several genes on the paternal copy of chromosome 15. In most cases, PWS is not genetically transmitted. Many of the manifestations of PWS are thought to be due to impaired development of the hypothalamic nuclei in the brain. These nuclei control eating behaviour, breathing, sexual development, growth, body temperature and many other functions. As a result, people with PWS present with an insatiable appetite and chronic overeating, increased body fat, severe breathing defects, immature physical development (due to growth hormone deficiency) and underdeveloped sexual characteristics. They may also suffer from mild learning disabilities, mental retardation, speech problems



Mariana, Prader-Willi Syndrome
© Tina Silvast

and psychiatric problems, including emotional instability and obsessive-compulsive behaviour. Other common concerns include strabismus, scoliosis, osteoporosis, type 2 diabetes, hypertension, skin problems, sleep disturbances and skin picking (sometimes severe). The disease affects an estimated one or less children per 10 000 at birth and occurs equally in males and females.

The first symptoms of PWS appear very early, at the time of birth. Infants with PWS typically have difficulty feeding

due to severe hypotonia and have trouble gaining weight. The child appears weak and 'floppy'. By preschool age, children with PWS develop an obsessive interest in food, and impulsive eating habits continue throughout adulthood, often leading to severe obesity, a major factor influencing morbidity and mortality. Emotional problems begin in childhood and may increase with age. Treatments for people with the disease include speech therapy, physical therapy, a strictly monitored low-calorie diet and growth hormone. Special education and behaviour-modifying medications may also be necessary. Early diagnosis and care can considerably improve life expectancy and quality of life of people with PWS.

Living With Prader-Willi Syndrome

Patients with PWS require constant attention very soon after birth. Due to a lack of proper muscle development even feeding can be a lengthy process, requiring parents to wake their baby during feeding to ensure they are receiving enough nutrients. Quickly, however, the struggle to feed a child with PWS changes to a struggle to contain their growing appetite, brought on by a hypothalamic dysfunction. From a very young age, parents may need to engage their child in physical activity per order of a physiotherapist. Upon reaching school age, speech development and learning are sometimes

delayed and children may need special education.

Children with PWS can also become intensely interested in only a few topics on which they speak about frequently, causing teachers to become frustrated and classmates to become confused. These factors seriously limit a child's ability to make friends at this age, which can make them feel lonely. The life of siblings of PWS patients can also be quite demanding, as food is regularly locked away and parents need to spend a great deal of their time caring for their child with PWS. This calls for a great deal of tolerance and maturity from children who may still be too young to fully comprehend their family situation.

Supervision of people with PWS is always necessary, even into the teenage and adult stages of life. Despite parents' best efforts to provide activities that are suitable for their child with PWS, they eventually face the question of who

will care for them when they no longer can. There is no easy answer. Yet, children with PWS can be very loving and make extra efforts to learn things that for them are very difficult, evoking great satisfaction and accomplishment for both child and parent.

'At the age of 2, the problems with his enormous appetite started. He was demanding food all the time, and ate whatever he found. We had to stop visiting most of our friends, because we had to constantly look after him and it was very stressful. We began to feel a kind of social isolation. Only a few friends understood the problem.'

Parent of a child with PWS

PWS

Diagnosis of Prader-Willi Syndrome

PARTICIPANTS IN THE SURVEY

Responses from 803 families of PWS patients from 14 countries were analysed (*Figure 1*). An equal number of female and male patients were represented in the survey (50% and 50%, respectively). The median age of patients at diagnosis was 1.7 years, although 25% of diagnoses occurred after 7 years of age.



Figure 1 Survey participants affected by PWS

AWAITING DIAGNOSIS

Neonatal diagnoses were obtained in 32% of patients, two-thirds of which resulted from disorders observed during pregnancy or at birth and one-third of which were made following neonatal testing. Overall, the delay in diagnosis was longer for females (30 months) than for males (seven months). For patients with non-neonatal diagnoses, the time to reach diagnosis was four years (less than 1.5 years for 25% and as long as 10 years for 25%). During the quest for diagnosis, more than five physicians were consulted by 33% of families and more than 20 physicians by 5% of families. A significant number of various examinations and tests (biological testing, 77%; genetic testing, 57%; X-rays, 54%; and functional testing, 72%) were performed during this period. Before obtaining the correct PWS diagnosis, another diagnosis was given to 42% of patients. Misdiagnosis resulted in inappropriate treatments in 59% of patients (medical, 16%; surgical, 7%; or psychiatric, 12%). Misdiagnoses were associated with longer time to reach PWS diagnosis: 2.5 years without misdiagnosis, six years with initial misdiagnosis (10 years in case of psychiatric misdiagnosis). For 81% of the families, a delay in diagnosis was considered responsible for deleterious consequences. Consequences were associated with longer time to reach diagnosis (two years in patients without consequences, six years for patients experiencing consequences of delay) (Figure 2).

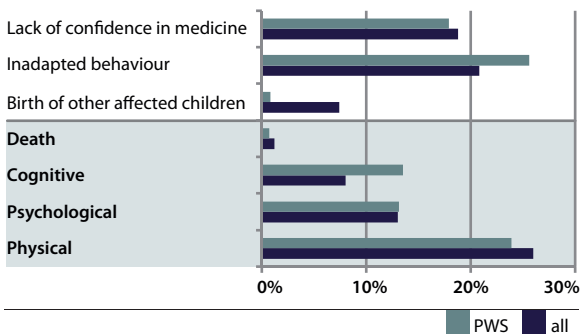


Figure 2
Consequences of delays in diagnosis in PWS patients.

PWS

DIAGNOSIS

In 56% of diagnosed patients, the possibility of a rare disease was suggested before reaching a correct diagnosis. In 10% of cases, a rare disease diagnosis was proposed by a non-medical individual. Previous suggestion of a rare disease was associated with a delay in diagnosis: four years of delay when the possibility of a rare disease was suggested by a medical individual and nine years of delay when proposed by a non-medical individual. When obtained, a diagnosis of PWS syndrome was determined on the basis of genetic (34%), clinical (28%) and biological (19%) data. The structure providing the diagnosis was usually a specialised centre (18%) or another hospital structure (70%), located in another region or country for 37% of families, and for which contact details were obtained from non-medical sources in 30% of cases (mainly obtained from the media (15%). Access to diagnosis required a financial contribution from 48% of families, and was considered a low or moderate contribution by two-thirds of respondents and high or very high by one-third.

ANNOUNCEMENT OF DIAGNOSIS

Diagnosis was most often given by a geneticist (55%) or directly received from a diagnostic laboratory (30%). Communication of the diagnosis occurred during a standard private consultation in 65% of cases, but also occurred orally in another manner (e.g. in a corridor) in 12% of cases or in written form without explanation (10%). One-third of the diagnoses were given without information on the disease. When provided, the sources were most frequently medical (41%), but also non-medical in 24% of cases, including patient organisations. Psychological support accompanying the announcement of diagnosis was infrequent (20%), and when available, provided by a psychologist (7%), a patient organisation member (5%) or physician (5%). In contrast to this low level of support, 86% of families considered it necessary.



Figure 3
Satisfaction with conditions under which diagnosis was announced to PWS patients

unacceptable poor acceptable well-adapted

GENETIC ASPECTS

The genetic nature of the disease was explained to families in 77% of cases, with details about the spontaneous mutation in 71% of cases. Genetic counselling was provided for 52% of families.

Whether based on the suggestion of a health professional (17%) or not, this information was communicated to the family in 68% of cases, either to the parents (44%), grandparents (31%), siblings (60%) or uncles, aunts or cousins (35%).

Reaction to Results

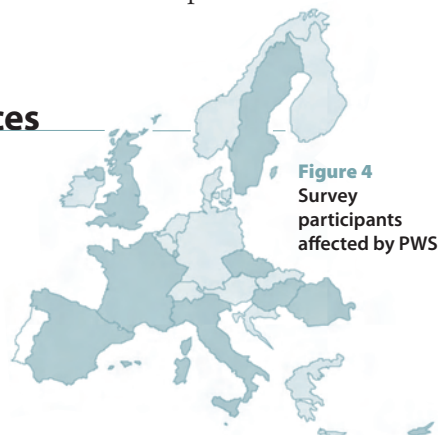
Although PWS is a genetic disease, its transmission is not predictable. While hypotonia (low muscle tone or ‘floppiness’) at birth should enable diagnosis of many cases, only 32% of patients reported this in the survey. Diagnoses missed at birth might be due to a lack of attention from the medical team or a justification such as ‘the birth was long and the child is tired’, or ‘this is a psychological problem’. Other times hypotonia is detected, but due to lack of adequate knowledge, PWS is not suggested as the cause, and the symptom is not even recorded in the medical records of the newly born child. The differences in diagnostic delays between boys and girls may be partly explained by the presence of testicular abnormalities. Without early diagnosis, the trivialisation of the disease is common and doctors ‘reassure’ the family rather than advising them to consult a more competent colleague, sometimes for fear of ‘losing’ a patient. The age at which the diagnosis is made largely plays an important role in the future health of PWS patients, as many issues must be addressed at certain developmental stages. Optimising cognitive development, in particular language, and preventing a child with PWS from becoming overweight are

examples. Intellectual deficit and obesity should not be considered as symptoms or as inevitable, but rather as consequences of late diagnosis. It is always difficult to accept the diagnosis of PWS, however the environment in which the diagnosis is made is important to parents. The announcement of the diagnosis should initially be made in the presence of both parents, accompanied by psychological support. In a second consultation (to ensure that the diagnosis is accepted and understood), potential plans for additional children and preparations to explain the diagnosis to the rest of the family should be discussed with the parents.

Access to Medical and Social Services

PARTICIPANTS IN THE SURVEY

Responses from 371 families of PWS patients from ten countries were analysed in the survey (*Figure 4*). An equal number of female and male patients were represented (51% and 49%, respectively). The mean age of patients was 18 years (age at diagnosis: 6 years).



NEED FOR MEDICAL SERVICES

Overall, patients with PWS needed more than 11 different kinds of medical services related to their disease (more than the average nine medical services for the 16 rare diseases surveyed). In addition to consultations mentioned in *Figure 5*, consultations in ophthalmology and cardiology were frequently needed (38% and 31% of patients, respectively). Genetics, ear, nose and throat medicine, rehabilitation medicine, dermatology, pulmonary medicine, emergency services, foot medicine, internal medicine and neurology consultations were also needed by a range of 11% to 24% of patients. The most frequently needed explorations were biological testing (71%), radiology (45%), ECG (34%), as well as ultrasound, genetic testing, specialised imagery, microbiology, functional testing and EEG (by a range of 18% to 28% of patients). As for other services, glasses (50%) and injections (38%) were the most frequently used, followed by psychomotility, nursing care, vision therapy and surgery (by a range of 14% to 29% of patients). Hospitalisation occurred in 56% of patients for an average total duration of 26 days.

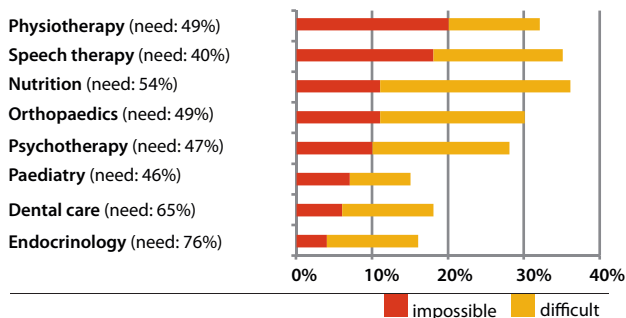


Figure 5
Need for and access to eight representative medical services for PWS

ACCESS TO MEDICAL SERVICES

Lack of access to medical services in 10% of situations overall for PWS patients

Physiotherapy (20%) and speech therapy (18%) services were the most frequently impossible to access for PWS patients. A lack of referral was the most frequent cause for impossible access for paediatrics (91%), physiotherapy (86%), nutrition (81%) and speech therapy (81%) and ranged from 61% to 79% for the four remaining investigated services. Unavailability of the service was reported as the main barrier to access for psychotherapy (33%), physiotherapy (31%) and speech therapy (30%) services. Personal cost was the most significant barrier to access for dental care (14%). Waiting time for obtaining an appointment was considered a hurdle for access to physiotherapy (31%), nutrition (24%) and psychotherapy (22%) services. In general, causes related to the distance from the medical structure were less frequent barriers to access for PWS patients than for patients with other surveyed diseases. Nevertheless, patients reported an inability to find anyone to go with, length and cost of journey as barriers to access for physiotherapy, orthopaedics, dental care and psychotherapy services.

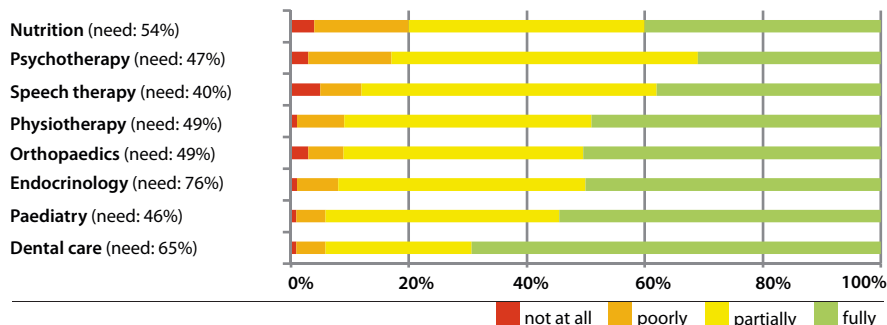
Access to medical services was difficult in 15% of situations

Patients experienced difficult access to nutrition (25%), orthopaedics (19%), psychotherapy (18%) and speech therapy (17%) services. The number of appointments was considered insufficient in more than 25% of situations for speech therapy, psychotherapy and nutrition consultations. Personal cost was considered excessive for psychotherapy (46%), dental care (34%) and orthopaedics (32%). The assistance of a professional for the journey to the medical structure was not frequently reported overall (7%) and paradoxically assistance was more frequently provided for services in the region than for consultations outside of the region. For medical consultations, 11% to 23% were located outside of the region and professional assistance ranged from 5% to 7%. In contrast, other care services were located outside the region 6% to 8% of the time and professional assistance was obtained for 8% to 14% of these journeys.

Satisfaction with medical services

Overall, 90% of patients considered that medical services responded fully or partially to their expectations. The level of satisfaction varied according to the kind of medical service, from 95% for paediatrics and dental care to 83% for psychotherapy and 80% for nutrition services.

Figure 6
Satisfaction with eight representative medical services for respondents affected by PWS



SOCIAL ASSISTANCE

Among the 42% of families needing social assistance, 3% failed to meet with a social worker and 23% met with one with difficulties. As compared to medical services, access to social assistance was more possible. However, the level of satisfaction with this assistance was lower (Figure 7).

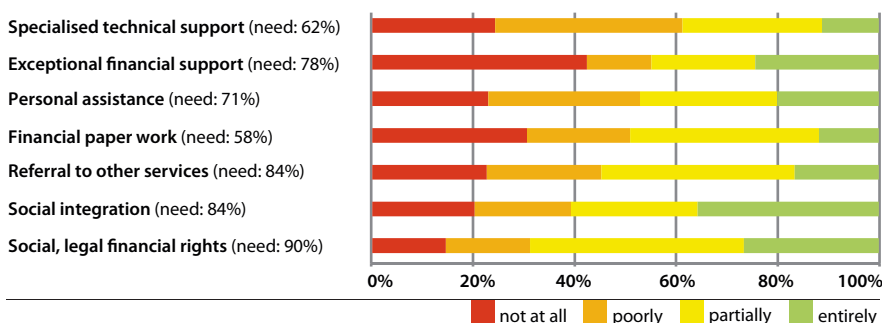


Figure 7
Satisfaction with specific social services for respondents affected by PWS

REJECTION

Patients with PWS experienced rejection by health professional less frequently (8%) than respondents overall for the 16 surveyed rare diseases (18%). The reluctance of health professionals to treat patients due to the complexity of their disease was the main cause of rejection (65%). Disease-related behaviour (32%) and a physical aspect (29%) were also reported as causes of rejection by health professionals. The frequency and cause of rejection varied according to the patient's country of origin (Figure 8).

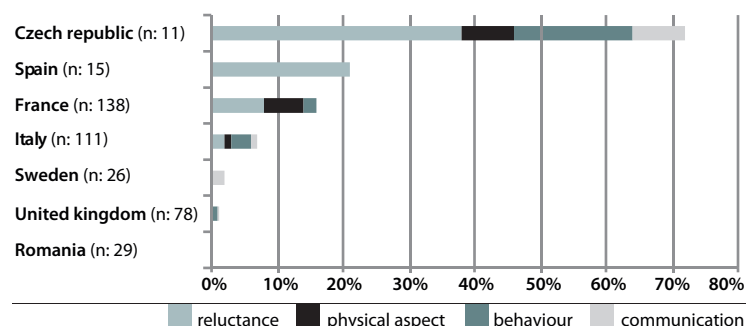


Figure 8 Cumulated frequencies of causes of rejection by country (n: total number of respondents) in PWS. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

CONSEQUENCES OF THE DISEASE

As a consequence of the disease, 11% of patients had to move house. Amongst these, families most frequently moved to a more adapted house (32%) or to be nearer to a specially adapted care centre (32%), but also to be nearer disease specialists (18%) or to be closer to a relative (11%). One member in 63% of families reduced or stopped his/her professional activity to take care of a relative.

'The effort in caring for healthy children usually decreases around the teenage years when independence increases. Care for people with Prader-Willi syndrome never ends and the affected person needs support from adults no matter what his or her age in nearly all situations.'
Parent of a child with PWS

Expectations Regarding Centres of Expertise for Rare Diseases

Expectations regarding centres of expertise somewhat differed for respondents affected by PWS as compared to the overall opinion of survey participants. Respondents affected by PWS considered the following functions provided by a Centre of Expertise as the four most essential:

- Coordinating the sharing of medical information on the patient between all professionals who care for him/her in the specialised centre
- Facilitating the follow-up of patients at different stages of their life by easing the passage from paediatric care to adult care, or from adult care to geriatric care.
- Communicating with other specialised centres and professional networks to harmonise treatments and research at the national and European levels
- Coordinating the sharing of medical information between professionals of the specialised centre and local professionals, to facilitate the continuity of the patients' follow-up

As a disease diagnosed during the early childhood years, it is not surprising that facilitating the difficult transition from paediatric to adult medical care is considered more important for survey participants concerned with PWS than for survey respondents overall.

Reaction to Results

The eight essential medical services examined in the survey are indispensable for PWS patients but do not meet all of their needs. Services should also include genetics, ear, nose and throat and rehabilitation medicine, and sometimes others. Despite the fact that these services exist, many patients do not obtain them due to a lack of understanding of the needs of PWS patients by healthcare professionals. Other types of care are 'rationed' due to limited reimbursement and delays in obtaining appointments.

Travelling to services is often difficult and becomes more tiring as the disease progresses; patients often require professional help. Once obtained, these services may be disappointing because professionals such as nutritionists, psychotherapists, speech therapists and physiotherapists rarely have the skills to address the specific needs of PWS patients. Similarly, facilities are often inappropriate. For example seats, beds, sphygmomanometers (device for measuring blood pressure) and radiological equipment may all be unsuitable in size for patients with obesity.

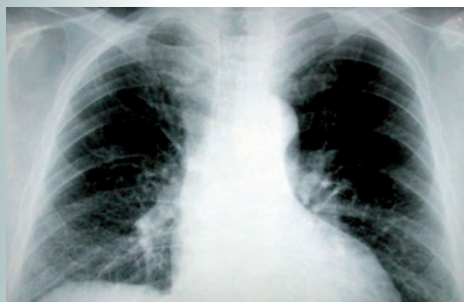
These inhospitable circumstances are often coupled with rejection by general practitioners and paramedics, who are the first in line to treat PWS patients before they even reach consultation by poorly trained specialists. The issue of rejection by medical professionals exists towards children but is particularly serious with respect to PWS adults. Unfortunately, few adults with PWS responded to the questionnaire. The true experience of older patients with PWS with respect to rejection by health professionals is probably worse than reported.

Pulmonary Arterial Hypertension

Sections of this chapter were written with the collaboration of Associazione Ipertensione Polmonare Italiana (API), the Belgian Pulmonary Hypertension Patients Association (HTAP Belgique) and the Austrian Pulmonary Hypertension Support Group (Lungenhochdruck Selbsthilfegruppe).

Clinical Picture

Pulmonary arterial hypertension (PAH) is a rare condition characterised by high blood pressure (hypertension) in the pulmonary artery, the blood vessel that carries blood from the heart to the lungs. PAH can be inherited as an autosomal dominant trait, may be a sporadic event (occurring as



Lung, pulmonary hypertension
© Clara Natoli.

a spontaneous non-inherited mutation) or can be related to other diseases of the lungs or related organs. Inherited PAH is caused by mutations in the BMPR2 gene, responsible for regulating the number of cells in certain tissues, including the arteries in the lungs. As the arteries become narrower, resistance to blood flow is increased. Genetic causes of sporadic PAH have not been identified.

Other causes of non-hereditary PAH include HIV, scleroderma (a chronic disease characterised by excessive deposits of collagen in the skin or other organs), cirrhosis and portal hypertension, sickle cell disease, congenital heart disease and others. The inherited form can affect both sexes equally, although overall, females are more frequently affected by PAH than males. Symptoms of PAH are sometimes unspecific and may lead to underdiagnosis of the condition and can include shortness of breath (dyspnoea), chest pain, fainting episodes and right heart failure.

'It took me about four years to be diagnosed. No doctor checked my heart or lungs because they did not see any reason to since I was under 30 years old.'
Sandra, 31 years old, Austria

PAH caused by spontaneous mutation is extremely rare, whereas other forms of PAH are more common, although prevalence is still less than one in 10 000 persons overall. The onset of PAH can occur at any age. Historically, survival has been poor (two to three years after diagnosis), however recent advances in drug therapies and earlier diagnosis have enabled some patients to survive for much longer.

Living With Pulmonary Arterial Hypertension

One of the most difficult aspects of living with PAH is that is often at a late stage by the time it is accurately diagnosed. Shortness of breath, lack of energy, increased heart rate and swollen ankles are some of the symptoms of PAH shared by common ailments that make diagnosis difficult and leads physicians to confuse a patient's suffering with anxiety, depression, being overworked or even menopause. During the search for the cause of the symptoms, patients can become frustrated and personal relationships may suffer. Once diagnosed, many new treatments are available that can significantly improve prognosis.

Despite improved treatments, patients with PAH often face limitations in their energy levels, requiring them to restrict activities such as work, sports and climbing stairs. For young patients with PAH these limitations are sometimes difficult to explain to those not aware or familiar with their condition. Some people with PAH feel uncomfortable in crowded places and are prone to panic attacks. Travelling can also be complicated due the need for oxygen in planes. Long stays away from a patient's home can introduce challenges as a result of changes in climate and the need to bring all the necessary medications. Women with PAH are often advised not to become pregnant, a suggestion that may be difficult to accept. Historically, PAH has been considered chronic and incurable, however with the correct lifestyle adjustments and proper treatment, many PAH patients can lead normal lives.

PAH

Access to **Medical** and **Social Services**

PARTICIPANTS IN THE SURVEY

Responses from 456 families of PAH patients from seven countries were analysed in the survey (*Figure 1*). Females made up 72% of respondents and males represented 28%. The mean age of patients was 50 years (age at diagnosis: 43 years).

Figure 1
Survey participants
affected by PAH



NEED FOR MEDICAL SERVICES

Overall, patients with PAH needed more than ten different kind of medical services related to their disease (less than the average nine medical services for the 16 rare diseases surveyed). In addition to the consultations mentioned in Figure 2, internal medicine (27%), ophthalmology (23%) and emergency services (19%) consultations were required. Ear, nose and throat medicine, gynaecology, dermatology, rheumatology, gastroenterology and rehabilitation medicine were also needed by a range of 10% to 13%

of patients. The most frequently needed explorations were ECG (77%), biological testing (75%), ultrasound (68%), functional testing (61%), radiology (59%) and specialised imagery (42%), but also Doppler tests, biopsies/cytology and genetic testing (for a range of 13% to 26% of respondents). As for other care services, nursing care (31%), injections (27%), dental care (26%), glasses (24%) and physiotherapy (20%) were needed. Hospitalisation occurred in 74% of patients for an average total duration of 21 days.

'After being diagnosed with PAH I was able to accept the problems I was experiencing because I better understood the reasons behind them.'
Sandra, 31 years old, Austria

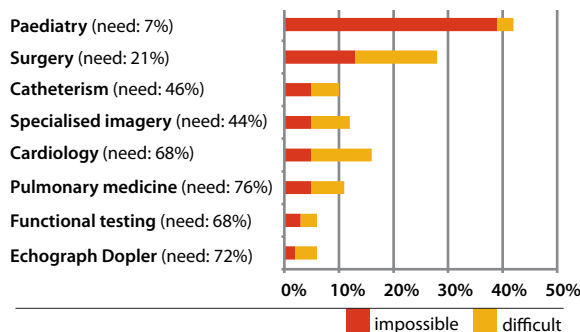


Figure 2
Need for and access to eight representative medical services for PAH

ACCESS TO MEDICAL SERVICES

Lack of access to medical services in 10% of situations overall for PAH patients

Paediatric consultations (39%) and surgical services (13%) were the most frequently impossible to access for PAH patients. A lack of referral was the most frequent cause for impossible access to specialised imagery (70%), surgery (63%), ultrasound (63%), paediatrics (62%), cardiology (50%), catheterism (50%), functional testing (38%) and pulmonary medicine (31%) consultations. Unavailability of the service and personal cost were not reported as significant barriers to access for services related to PAH. Waiting time for obtaining an appointment was considered a hurdle for access to cardiology (14%), pulmonary medicine (13%), ultrasound (13%) and functional testing (13%). Excessive distance from the medical structure was reported as a barrier to access for ultrasounds, cardiology, functional testing and pulmonary medicine (for a range of 13% to 25% of patients). Patients also reported the inability to find anyone to go with, unsuitable transport, and length and cost of the journey as barriers to access to cardiology, pulmonary medicine, ultrasound and functional testing services.

Access to medical services was difficult in 15% of situations

Patients reported difficult access to surgery (15%) and cardiology (11%) consultations. The number of appointments was rarely considered insufficient for services related to PAH.

The personal cost incurred for services was considered as excessive by more than 15% of patients for cardiology, specialised imagery, functional testing and pulmonary medicine. The assistance of a professional for the journey to the medical structure was relatively frequently reported overall (14%), as the majority of investigated services were located in another region (overall 45%).

Satisfaction with medical services

Overall, 97% of patients felt that medical services responded fully or partially to their expectations. The level of satisfaction did not vary significantly for the eight services investigated (*Figure 3*).

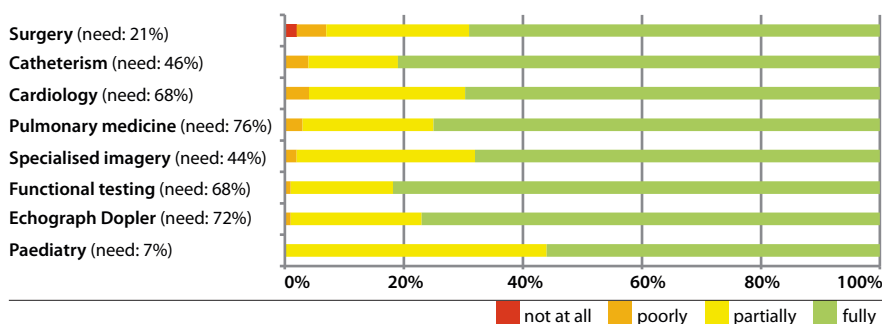


Figure 3 Satisfaction with eight representative medical services for respondents affected by PAH

SOCIAL ASSISTANCE

Amongst the 19% of families needing social assistance, 4% failed to meet with a social worker and 17% met with one with difficulties.

As compared to medical services, social assistance was more accessible, however the level of satisfaction with this assistance was much lower (*Figure 4*).

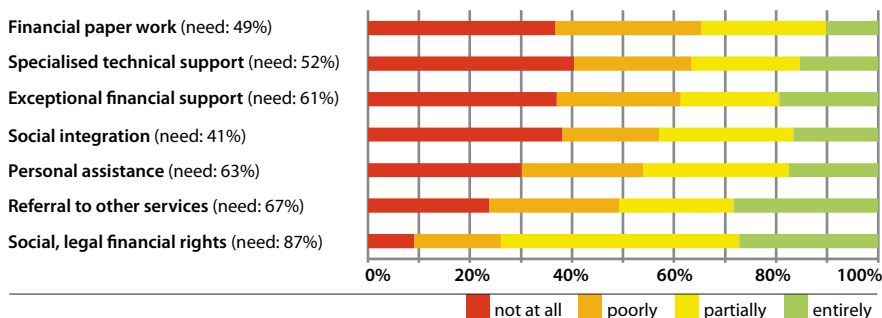


Figure 4 Satisfaction with specific social services for respondents affected by PAH

REJECTION

Patients with PAH experienced rejection by health professionals less frequently (9%) than respondents overall for the 16 surveyed rare diseases (18%). The reluctance of health professionals to treat patients due to the complexity of their disease was the main cause of rejection (71%). A physical aspect of the disease (21%) and disease-related behaviour (12%) were also reported as causes of rejection by health professionals. The frequency and cause of rejection varied according to the patient's country of origin (*Figure 5*).

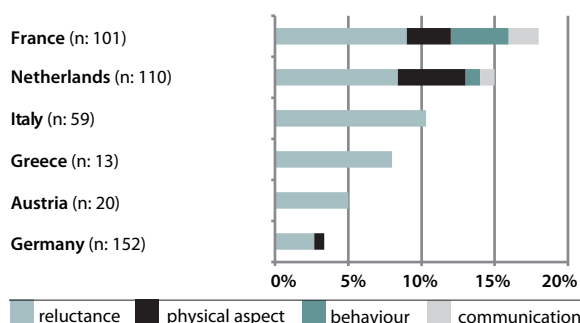


Figure 5 Cumulated frequencies of causes of rejection by country (n: total number of respondents) in PAH. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

CONSEQUENCES OF THE DISEASE

As a consequence of the disease, 15% of patients had to move house. Amongst these, families most frequently moved to a more adapted house (82%) or to be closer to a relative (18%), but also to be nearer to disease specialists (10%).

One member in 63% of families reduced or stopped his/her professional activity; 7% were family members who stopped working to take care of a relative, and 56% were patients themselves.

Expectations Regarding Centres of Expertise for Rare Diseases

Not differing from the overall opinion of survey participants, respondents affected by PAH considered the following functions provided by a Centre of Expertise as the four most essential:

- Coordinating the sharing of medical information on the patient between all professionals who care for him/her in the specialised centre
- Communicating with other specialised centres and professional networks to harmonise treatments and research at the national and European levels
- Coordinating the sharing of medical information between professionals of the specialised centre and local professionals, to facilitate the continuity of the patients' follow-up
- Collaborating with research teams working on the rare disease (in particular for clinical studies)

Survey participants with PAH considered ‘collaborating with research teams working on the rare disease (in particular for clinical studies)’ as the fifth most essential function provided by a Centre of Expertise; a higher ranking of priority than expressed by respondents overall.

Reaction to Results

Although PAH is a serious and life-threatening condition, it is often not ‘visible’: patients look healthy and can remain stable for years. Treatment for PAH most often includes vasodilators, which even gives patients a nice pink complexion. The majority of PAH symptoms are quite non-specific, such as shortness of breath and fatigue. It is possible that some physicians underestimate the level of suffering experienced by PAH patients.

As the disease mostly affects women, there are many issues related to birth control that patients must face. Pregnancy can be fatal to both mother and child. Some PAH medications are very invasive and may require pain control. Physicians often ‘keep’ patients for themselves, especially just after onset of the disease. Only when prognosis worsens do physicians refer patients to specialised centres.

PAH patients may need someone to accompany them while seeking care. Long waiting times for most exams means both patients and their companions must sacrifice work time or leave children unattended at home. These barriers are only exaggerated when travel for care is in another region or country, possibly involving an overnight stay and the greater expenses required. PAH patients ultimately experience severe disability and need help with everyday activities. Most patients have to leave their employment at some point and require social assistance.

Tuberous Sclerosis

Sections of this chapter were written with the collaboration of the Tuberous Sclerosis Association of Greece and Associazione Sclerosi Tuberosa (Italy).

Clinical Picture

Tuberous sclerosis (TS) is a rare genetic disorder that is characterised by non-cancerous tumours of the brain, eyes, heart, kidneys or lungs. These tumours can cause neurological symptoms such as epilepsy (recurrent unprovoked seizures), mental retardation and behavioural problems, as well as kidney disease, lung disease, skin abnormalities and vision problems. Symptoms such as seizures, delayed development and skin lesions usually appear shortly after birth, but may remain very discrete in children. TS results from mutations in one of two genes (TSC1 and TSC2), which play a role in cell division and the production of proteins that suppress tumour growth. The mutation may occur spontaneously for unknown reasons or be inherited as an autosomal dominant trait. The estimated prevalence of TS is one in 10 000 people and affects males and females equally. Prognosis for people with TS can range depending on the severity of symptoms. Individuals with mild forms of TS do not have a shortened life expectancy while individuals with more severe forms may have serious disabilities. Currently, there is no cure for TS, however with appropriate medical care (such as lung transplant or surgical removal of tumours) most individuals with the disorder can look forward to a normal life expectancy.

TS

Living With Tuberous Sclerosis

Historically, TS was diagnosed as a childhood disease and only the most severely affected individuals were identified. Diagnosis of TS is still most frequently made when an infant presents with epileptic seizures in the first year of life. However, it is increasingly more common for adults to be diagnosed with TS either when their child is diagnosed and/or when they themselves begin to have medical issues.

There is no one manifestation of TS that allows healthcare professionals to diagnose an individual with the disease. TS affects individuals differently, making each patient unique, but also difficult to diagnose and treat. In addition, many features known to be present in TS, such as seizures and mental disability, are so common in the general population that they are not recognised as being symptoms of TS.

Because TS affects multiple organs, consultations with a variety of specialists familiar with TS is recommended to ensure comprehensive care. In addition, as many aspects of TS do not appear until later in life or tend to change throughout a lifetime, continued evaluation is suggested. The frequent visits to doctors and specialists can be hard on children and their parents,

especially because of the unexpected nature of the next symptomatic expression of the disease.

Many adults with TS also have seizures, and appropriate care and treatment are essential in minimising the impact of seizures on quality of life and the ability to work.

Adults with TS may experience anxiety, depression and attention deficit difficulties, all posing significant problems if not treated properly. People with TS may feel misunderstood by those who are unfamiliar with the disease, especially when they show no physical external

symptoms. However when external tumours are apparent, social interactions including dating and forming interpersonal relationships can be difficult because of the reaction that skin lesions or seizures cause in others. Women with TS and their partners must consider the various risks of having children, including having a child with TS, accelerating the progression of kidney tumours and cysts in the lungs, as well as the detrimental effects of antiepileptic drugs (taken to prevent seizures) on the foetus. Individuals with TS may feel alone and without peer support and are encouraged to share their experiences with other patients via patient organisations and support groups.

'Most of the time, there are no obvious signs of this disease and people expect normal behaviour. Others do understand why I can have mood swings, be aggressive or nervous when I go shopping, to a restaurant, for a walk, etc.'

Katerina, 40 years old, Greece

Diagnosis of Tuberous Sclerosis

PARTICIPANTS IN THE SURVEY

Responses from 469 families of TS patients from six countries were analysed (*Figure 1*). An unequal number of female and male patients were represented in the survey (44% and 56%, respectively). The median age of patients at diagnosis was 13 months, but 25% of diagnoses occurred after 72 months of age.



Figure 1 Survey participants affected by TS

AWAITING THE DIAGNOSIS

Neonatal diagnoses were obtained in 11% of patients, mainly due to symptoms observed during pregnancy or at birth. In other cases, the time elapsed between the first clinical manifestations and diagnosis was six months for 50% of patients (3.5 years for 25% of the later diagnoses). Overall, the delay in diagnosis was longer for females (five months) than for males (three months). During the quest for diagnosis, more than five physicians were consulted by 13% of families. Before obtaining the correct TS diagnosis, another diagnosis was given to 38% of patients, resulting in treatments for 76% of patients — medical (59%), psychiatric (5%) or surgical (6%). Misdiagnoses were associated with a longer time to reach TS diagnosis: three months without misdiagnosis, 15 months with an initial misdiagnosis (42 months in the case of a psychiatric diagnosis). For 62% of families, a delay in diagnosis was considered responsible for deleterious consequences. Consequences were associated with a longer delay in diagnosis (2.7 months in patients without consequences, 12 months for patients reporting personal consequences and 22 months for those with familial consequences (Figure 2).

'I experienced significant delays in getting a correct diagnosis — it took three years. I received a number of incorrect diagnoses.'
Katerina, 40 years old, Greece

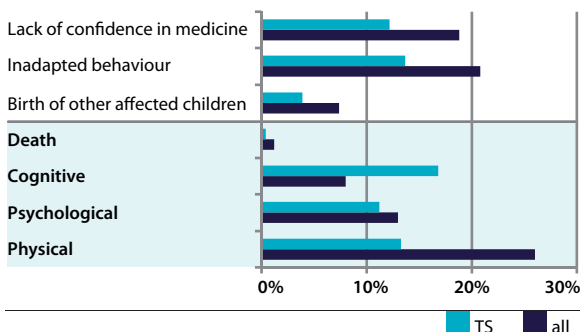


Figure 2
Consequences of delays in diagnosis in TS patients.

DIAGNOSIS

Diagnosis of TS was obtained on the basis of biological (31%), clinical (31%) and functional (19%) data. The structure providing the diagnosis was located in another region or country for 28% of cases. Access to diagnosis required a financial contribution from 42% of families, and was considered high or very high by 11%. Some patients (18%) considered that the time to reach a correct diagnosis was dependant on their ability to pay. A second opinion was sought by 18% of families to confirm the diagnosis. This confirmatory diagnosis was more frequently obtained in private practice than the first one (17% versus 5%).

ANNOUNCEMENT OF DIAGNOSIS

Communication of the diagnosis occurred during a standard private consultation in 76% of cases, but also occurred orally in another manner (e.g. in a corridor) in 6% of cases or by phone (14%). For 34% of patients, the diagnoses were given without information on the disease.



Figure 3
Satisfaction with conditions under which diagnosis was announced to TS patients.

unacceptable poor acceptable well-adapted

When provided, the sources were medical in 46% of cases and non-medical in 20%, including patient organisations. Psychological support accompanied 28% of the announcements of diagnosis, provided by a psychologist (9%), a patient organisation member (8%) or physician (5%). In contrast to this low level of support, 90% of families considered it necessary.

GENETIC ASPECTS

The genetic nature of the disease was explained to families in 74% of cases, with details about the spontaneous mutation in 49% of cases. Genetic counselling was provided for 57% of families. Whether based on the suggestion of a health professional (39%) or not, this information was communicated to the family in 84% of cases either to the parents (57%), grandparents (29%), siblings (72%), or uncles, aunts or cousins (34%).

Reaction to Results

Delays in diagnosis are often experienced by patients due to a lack of communication between general practitioners and specialists and the tendency of general practitioners to want to keep their patients despite their lack of knowledge of the disease. Patients describe frustration at having been misdiagnosed by doctors who focused only on the psychological symptoms of the disease. Incorrect diagnoses frequently lead female patients, unaware of their disease, to have children. Doctors do not routinely suggest confirmatory diagnoses, and patients take the initiative to have a second opinion without informing the first practitioner for fear of offending them. Often those with economic means have the chance consult other specialists, while the rest are limited to one 'medical pathway'. The announcement of diagnosis could be improved by taking more time to conduct it in a calm environment with the support of a psychologist. Additionally, information about patient support groups could minimise the isolation parents and patients may feel upon receiving the news. One patient recalls, 'The first doctor we went to was a geneticist who just opened a medical dictionary and read exactly what was written about the disease without caring about what he was telling us.'

Access to Medical and Social Services

PARTICIPANTS IN THE SURVEY

Responses from 393 families of patients with TS from nine countries were analysed in the survey (*Figure 4*). An equal number of female and male patients were represented (50% and 50%, respectively). The mean age of patients was 20 years (age at diagnosis: 5 years).



Figure 4 Survey participants affected by TS

NEED FOR MEDICAL SERVICES

Overall, patients with TS needed more than ten different kind of medical services related to their disease (more than the average nine medical services for the 16 rare diseases surveyed). In addition to the consultations mentioned in Figure 5, ophthalmology (47%), cardiology (45%), haematology (21%), genetics (21%), psychiatry (21%) and emergency services (17%) were needed. The most frequently needed explorations were biological testing (69%), specialised imagery (63%), EEG (54%), ultrasound (48%), ECG (44%), radiology (26%), genetic testing (19%) and microbiology (19%). As for other care services, dental care (36%), speech therapy (21%), glasses (19%), psychomotility therapy (18%), physiotherapy (17%), nursing care (15%), psychotherapy (14%) and surgery (12%) were required. Hospitalisation occurred in 46% of patients for an average total duration of 16 days.

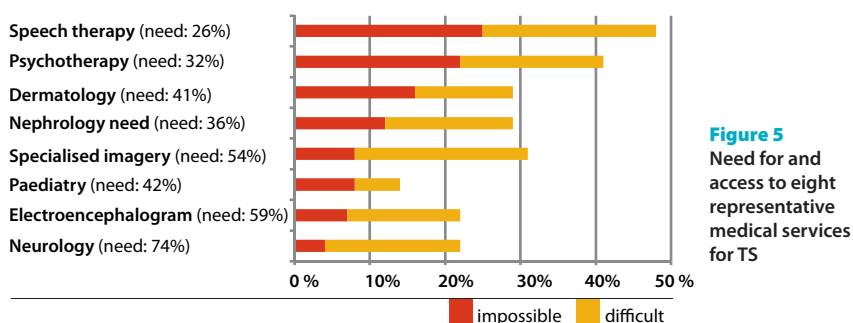


Figure 5
Need for and access to eight representative medical services for TS

ACCESS TO MEDICAL SERVICES

Lack of access to medical services in 10% of situations overall for TS patients

Speech therapy (25%), psychotherapy (22%), dermatology (16%) and neurology (12%) services were the most frequently impossible to access for TS patients. A lack of referral was the most frequent cause for impossible access for nephrology (82%), EEG (69%), neurology (67%), specialised imagery (65%), dermatology (61%), psychotherapy (58%), speech therapy (56%), and paediatric (46%) services.

Unavailability of the service was reported as a significant barrier for access to psychotherapy (35%), speech therapy (28%), and dermatology (22%). Personal cost was considered as a hurdle for access to specialised imagery (18%) and psychotherapy (15%). Waiting time for obtaining an appointment was a considerable barrier to access for specialised imagery (29%) and neurology (17%).

In general, causes related to travel to a medical structure were less frequent barriers to access for TS patients than for patients with other surveyed diseases. Nevertheless, patients reported excessive distance as a barrier to specialised imagery (24%), psychotherapy (15%), EEG (13%), dermatology (13%) and nephrology (12%). Inability to find anyone to go with was also reported as a barrier to access for neurology (17%), EEG (13%), nephrology (12%), specialised imagery (12%) and dermatology (9%).

Access to medical services was difficult in 15% of situations

Even when possible, access remained difficult for speech therapy (23%), specialised imagery (23%), psychotherapy (19%), neurology (18%), nephrology (17%), EEG (15%) and dermatology (13%) services. The number of appointments was considered most insufficient for speech therapy (23%), psychotherapy (20%) and nephrology (13%). Personal cost was frequently considered excessive for all the investigated medical services: speech therapy (46%), neurology (45%), psychotherapy (41%), dermatology (39%), EEG (30%), specialised imagery (29%), nephrology (27%) and paediatrics (25%). The assistance of a professional for the journey to a medical structure was not frequently reported overall (7%) despite the fact that many patients had to travel to another region or country to access services (overall 19%).

Satisfaction with medical services

Overall, 91% patients considered that medical services responded fully or partially to their expectations. The level of satisfaction varied according to the kind of medical service, from 93% for psychotherapy, dermatology and nephrology to 88% for paediatrics and 86% for electroencephalogram services (Figure 6).

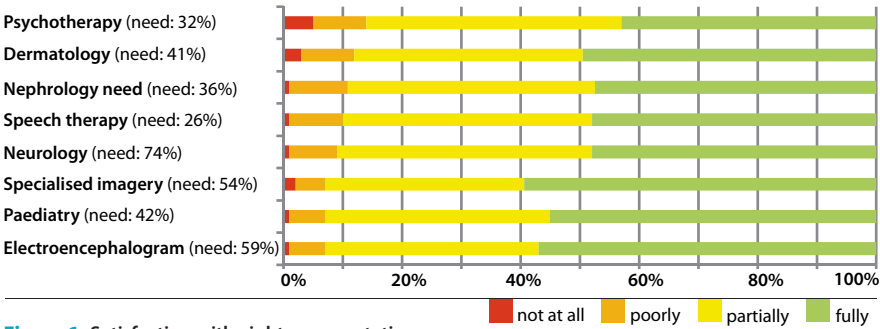


Figure 6 Satisfaction with eight representative medical services for respondents affected by TS

SOCIAL ASSISTANCE

Amongst the 25% of families needing social assistance, only 1% failed to meet with a social worker and 23% met one with difficulty. As compared to medical services, access to social assistance was less restricted, however the level of satisfaction with this assistance was lower.

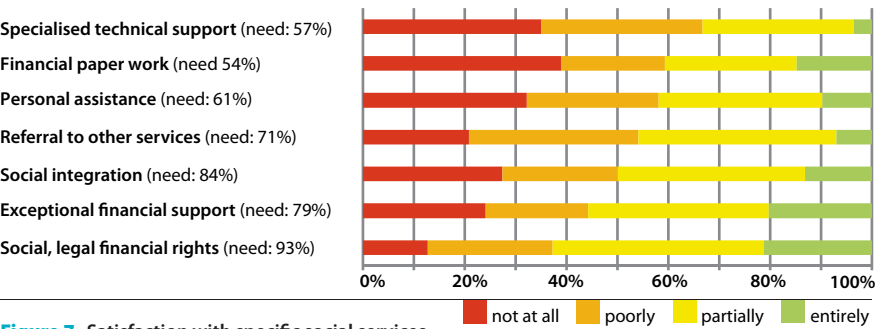


Figure 7 Satisfaction with specific social services for respondents affected by TS

REJECTION

Patients with TS experienced rejection by health professional as frequently (18%) as respondents overall for the 16 surveyed rare diseases (18%). The reluctance of health professionals to treat patients due to the complexity of their disease was the main cause of rejection (84%). Disease-related behaviour (30%) and communication difficulties (25%) were also reported as causes of rejection. The frequency and cause of rejection varied according to the patient's country of origin (*Figure 8*).

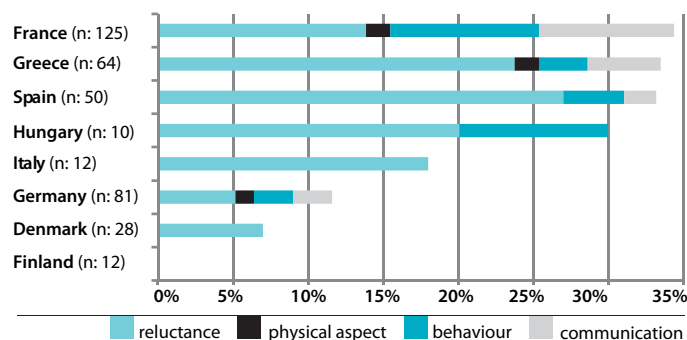


Figure 8 Cumulated frequencies of causes of rejection by country (n: total number of respondents) in TS. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

CONSEQUENCES OF THE DISEASE

As a consequence of the disease, 15% of patients had to move house. Amongst these, families most frequently moved to a more adapted house (38%) or to be nearer to a specially adapted care centre (39%), but also to be nearer disease specialists (17%), or to be closer to a relative (20%). In 56% of families one member reduced or stopped his/her professional activity to take care of a relative, and 6% of patients had to reduce or stop their professional activity themselves.

Expectations Regarding Centres of Expertise for Rare Diseases

Not differing from the overall opinion of survey participants, respondents affected by EDS considered the following functions provided by a Centre of Expertise as the four most essential:

- Coordinating the sharing of medical information on the patient between all professionals who care for him/her in the specialised centre
- Communicating with other specialised centres and professional networks to harmonise treatments and research at the national and European levels
- Coordinating the sharing of medical information between professionals of the specialised centre and local professionals, to facilitate the continuity of the patients' follow-up
- Collaborating with research teams working on the rare disease (in particular for clinical studies)

As TS is a disease that can affect many organ systems, it is not surprising that survey participants with TS also considered 'offering patients the option

of grouping consultations or tests on the same day in the specialised centre, and organising the appointments' as an important function provided by a Centre of Expertise, a higher ranking of priority than expressed respondents overall. Respondents affected by TS also ranked 'facilitating the follow-up of patients at different stages of their life by easing the passage from paediatric care to adult care, or from adult care to geriatric care' as an important function. Patients with TS more frequently agreed strongly with the following statement as compared to respondents overall: 'Quality of relationships is as important as skills and competences, therefore, a local professional is preferable because of freedom of choice.'

Reaction to Results

In addition to the eight essential services included in the survey, pneumology is also important for TS patients. Access to services is impossible when physicians do not realise the importance of referring patients to different specialists due to their lack of knowledge on TS or due to a lack of availability of local services. Parents of children with TS are frustrated and angry if they cannot access a service that could improve their child's wellbeing. Access to social assistance is inconsistent, depending on the location of patients. Sometimes public institutions do not provide the service even if it obligated to by law. Other times social workers are not adequately trained to address the specific needs of TS patients because of a lack of experience. The frequent turnover of social workers makes it very difficult for patients to build a constructive relationship between the patient and their social worker. Parents often have no choice but to reduce or stop their professional activities to take care of a child with TS. Although in some countries a parent's salary is covered by the employers' contribution to social security, those who work in the private sector risk getting fired.

Williams Syndrome

Sections of this chapter were written with the collaboration of Associazione Italiana Sindrome di Williams (AISW-Italy) and the Williams Syndrome Association of Ireland.

Clinical Picture

Williams syndrome (WS) is a rare genetic disease characterised by narrowed arteries leading to cardiovascular problems, mental retardation, learning difficulties, a distinctive cheerful facial appearance and unique behavioural and cognitive traits, including being hypersocial, having occasional negative outbursts, sensitivity to noise, being gifted in music, lacking depth perception and an inability to visualise how different parts assemble into

larger objects.

Characteristic physical features of WS include puffiness around the eyes, a short nose, wide mouth, full cheeks and lips, a small chin, a long neck, sloping shoulders, short stature, limited mobility in the joints and curvature of the spine. WS is caused by the deletion of several genes from chromosome 7 that occurs spontaneously. The prevalence of WS is estimated at one to five per 10 000 persons and can affect males and females



Fanny & Bérangère, Williams syndrome
© Elisabeth de Lavergne.

equally. The onset of symptoms usually occurs just after birth or during infancy and begins with physical characteristics, irritability, colic and feeding problems, and progresses to abdominal pain in adolescents, diabetes, high blood pressure, heart failure and hearing loss in adults. Medical complications associated with the disorder may shorten the lifespan of some people with WS. Treatment is based on the individual's symptoms, but usually includes monitoring cardiovascular problems.

Living With Williams Syndrome

Being told that your child has WS can be devastating news. The day-to-day experience of living with WS, however, is not. People with WS are extremely outgoing, kind and caring and are very tuned in to other people's feelings, wanting everyone to be happy. Concentration difficulties can lead to frustration and consequent temper tantrums. Fine motor control functionality can be very limited, i.e. problems arise in areas such as closing buttons, doing up zips, etc.

People with WS will usually suffer from hypersensitivity to noise and can become paranoid about particular noises. People with WS tend to develop a good command of language, with a large vocabulary. However, caregivers of WS patients need to be aware that they do not always understand exactly what they are saying. This can pose a problem for teachers in schools.

'Almost no patients with Williams syndrome live independently. They continue to live with their parents as long as possible. If their parents pass away they often stay with another relative.'

Patient with Williams Syndrome

As they grow older, they have great difficulty forming social relationships with others of their own age and usually relate much better to adults. Anxiety can become a serious concern as WS people grow into adulthood. Severe apprehension in adult WS patients often leads to serious depression requiring medical intervention.

Some think this stems from their caring, sensitive natures.

They can be very affected, for example, by the mood of a piece of music. While the range of ability levels can vary widely within the WS group, many people with WS can perform very well academically, musically and in the sporting arena. WS competitors have represented their country at Special Olympics games all over the world. They have achieved remarkable grades in secondary level education and some have taken their place in the world of employment. Parents of children with WS are encouraged to support them so they can reach their highest potential in whichever field they express interest.

WS

Access to Medical and Social Services

PARTICIPANTS IN THE SURVEY

Responses from 390 families of WS patients from nine countries were analysed in the survey (*Figure 1*).

An equal number of female and male patients were represented (50% and 50%, respectively).

The mean age of patients was 17 years (age at diagnosis: 5 years).



Figure 1
Survey participants affected by WS

NEED FOR MEDICAL SERVICES

Overall, patients with WS needed nine different kinds of medical services related to their disease (equal to the average nine medical services for the 16 rare diseases surveyed). In addition to consultations mentioned in Figure 2, ophthalmology (47%), orthopaedics (28%), ear, nose and throat medicine (28%), and genetics (20%) consultations were often required. Haematology, psychiatry, nephrology, internal medicine, neurology, nutrition and genito-urinary medicine were also needed by a range of 10% to 14% of the respondents. The most frequently needed explorations were ECG (58%), biological testing (46%), ultrasound (42%) and radiology (32%), but also Doppler tests, genetic testing, specialised imagery, EEG and microbiology (by a range of 10% to 17%). As for other care services, dental care (65%), glasses (50%) and physiotherapy (20%) were sought frequently by patients with WS. Hospitalisation occurred in 29% of patients for an average total duration of 10 days.

'Psychomotility and speech therapists, if they are even available in the area, frequently have long waiting lists and don't guarantee adequate service. Their availability can be less than one hour a week, compared with the real necessity of two or three hours per week of therapy.'
Patient with Williams Syndrome

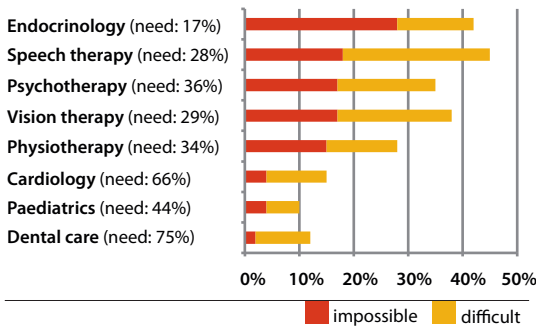


Figure 2 Need for and access to eight representative medical services for respondents affected by WS

ACCESS TO MEDICAL SERVICES

Lack of access to medical services in 10% of situations overall for WS patients

Endocrinology (28%), speech therapy (18%), vision therapy (17%), psychotherapy (17%) and physiotherapy (15%) services were most frequently impossible to access for WS patients. A lack of referral was the most frequent cause for impossible access for all the eight investigated services: speech therapy (75%), endocrinology (72%), paediatrics (57%), physiotherapy (55%), psychotherapy (46%), cardiology (45%), vision therapy (42%) and dental care (40%). Unavailability of the service was also reported as a hurdle to access: cardiology (36%), physiotherapy (30%), psychotherapy (21%), vision therapy (21%), speech therapy (15%) and paediatrics (14%). The waiting time for obtaining an appointment was considered a hurdle for access to cardiology (27%), vision therapy (21%), paediatrics (14%) and physiotherapy (10%). Barriers related to travel to the medical structure were only reported for cardiology consultations, psychotherapy and physiotherapy services.

Access to medical services was difficult in 15% of situations

Although possible, access was reported as difficult by patients for speech therapy (27%), vision therapy (21%) and psychotherapy (18%). The number of appointments was only considered insufficient for speech therapy (13%), psychotherapy (4%) and physiotherapy (12%). The personal cost incurred for services was considered as excessive for psychotherapy (48%), dental care (25%), speech therapy (18%), endocrinology (17%) and physiotherapy (17%). Assistance of a professional for the journey to a medical structure was reported for psychotherapy (18%), physiotherapy (15%) and speech therapy (15%).

Satisfaction with medical services

Overall, 96% of patients felt that medical services responded fully or partially to their expectations. The level of satisfaction did not vary significantly for the eight services investigated (*Figure 3*), although patients reported that in 13% of cases speech therapy services did not meet their expectations.

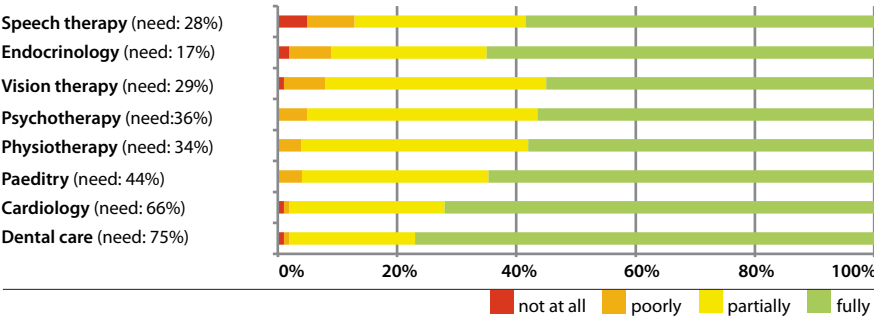


Figure 3 Satisfaction with eight representative medical services for respondents affected by WS

SOCIAL ASSISTANCE

Amongst the 28% of families needing social assistance, 4% failed to meet a social worker and 21% met one with difficulty. As compared to medical services, social assistance was somewhat more accessible, however the level of satisfaction with this assistance was lower (*Figure 4*).

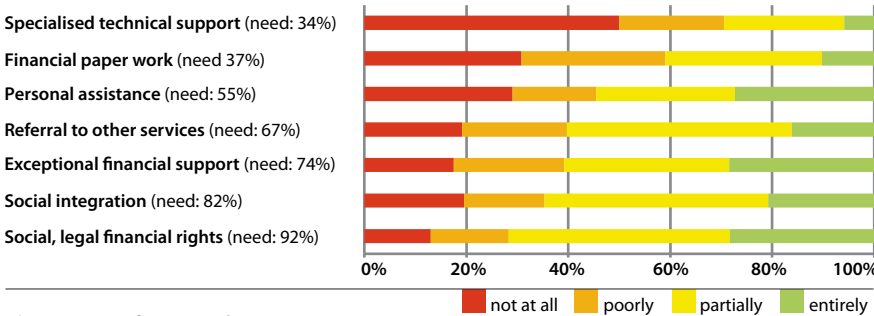


Figure 4 Satisfaction with specific social services for respondents affected by WS

REJECTION

Patients with WS experienced rejection by health professionals less frequently (9%) than respondents overall for the 16 surveyed rare diseases (18%). The reluctance of health professionals to treat patients due to the complexity of their disease was the main cause of rejection (63%). Communication difficulties (34%), disease-related behaviour (29%) and a physical aspect of the disease (20%) were also considered to be reasons health professionals rejected patients with WS. The frequency and cause of rejection varied according to the patient's country of origin (*Figure 5*).

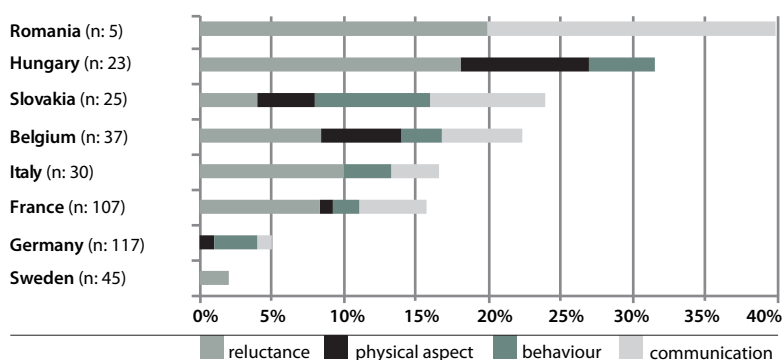


Figure 5 Cumulated frequencies of causes of rejection by country (n: total number of respondents) in WS. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

CONSEQUENCES OF THE DISEASE

As a consequence of the disease, 8% of patients had to move house. Amongst these, families moved to a more adapted house (28%), to be closer to a relative (28%) or to a specially adapted care centre (28%), but also to be nearer disease specialists (10%). One member in 60% of families reduced or stopped his/her professional activity to take care of a relative.

WS

Expectations Regarding Centres of Expertise for Rare Diseases

Expectations regarding centres of expertise reported by respondents affected by WS were quite different compared to the overall opinion of survey participants. Respondents affected by WS considered the following functions provided by a Centre of Expertise as the four most essential in descending order:

- Coordinating the sharing of medical information on the patient between all professionals who care for him/her in the specialised centre
- Informing patients about their rights and guiding them toward social services, schools, leisure activities or vocational guidance, etc.
- Facilitating the follow-up of patients at different stages of their life by easing the passage from paediatric care to adult care, or from adult care to geriatric care

- Creating material for teachers, employers, social services, insurance companies and the general public to inform them about patients' needs and improve the social integration of patients

Overall survey participants with WS considered functions related to social integration as more important compared to respondents overall.

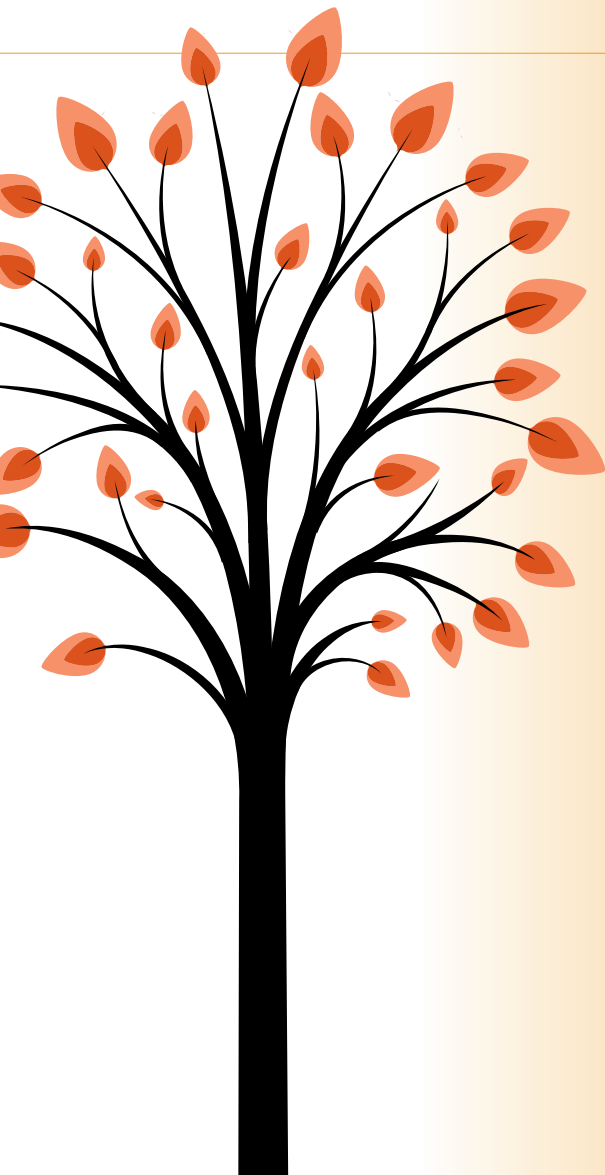
Reaction to Results

In general, WS is not very well known and rehabilitation is still experimental. Neuropsychiatrists often underestimate the severity of the associated mental retardation and think that intervention at infancy is not necessary.

WS patients need frequent check-ups (heart, kidney, thyroid, eye, posture, blood pressure, possibly gluten intolerance, calcaemia, glycaemia and endocrinological), particularly at puberty.

Physicians hesitate to give referrals for services they think are not available. In fact, the most ideal therapy is still not completely understood.

Psychomotility and speech therapy specialists, if they exist nearby, usually have very long waiting lists and limited services that do not always meet the specific needs of WS patients. Specialists familiar with WS are greatly lacking; for example, neuropsychiatrists usually only treat children and adolescents. When patients have difficulty in accessing medical services, they use alternatives, contact private specialists or continue the 'do-it-yourself' approach of going to numerous medical structures, hospitals and specialised centres to find the services they need. Most health professionals underestimate WS patients' need for cognitive rehabilitation. Social services specific to the needs of WS patients are also scarce and inadequate. Parents are often forced to reduce professional activity to care for a family member with WS, as many patients continue to be dependant on a caretaker their entire lives.



** To avoid the presentation of inconclusive and biased results, country-specific averages were calculated only for countries with more than 60 responses, representing three or more diseases, of which no disease represented more than half of the responses.*

Results by Country

Austria	215
Belgium	218
Croatia*	223
Cyprus*	224
Czech Republic*	225
Denmark	226
Finland	231
France	236
Germany	241
Greece*	246
Hungary	247
Ireland*	250
Italy	251
Luxembourg*	256
Netherlands	258
Norway*	263
Poland	264
Portugal*	268
Romania	270
Slovakia*	273
Spain	274
Sweden	279
Switzerland	284
United Kingdom	290



Austria

Sections of this chapter were written with the collaboration of Orphanet Austria, the Austrian patient organisation for cystic fibrosis (Sarko SHG), Huntington Vienna and the Austrian patient organisation for Alpha 1 Antitrypsin Mangel disease (Alpha 1 Österreich).

Socioeconomic Data

Total population: 8 316 487 (2007)
Area of country: 83 872 sq km
Population density: 99/sq km (2007)
GDP: 279.5 billion \$ (2006)
GDP/capita: 36 000 \$ (2006)
% of GDP spent on health: 3.4% (2005)
of physicians/100 000 inhabitants: 337 (2006)

National Initiative in the Field of Rare Diseases

In the Austrian healthcare system, decision making is divided between the federal government and the Länder, legislatively autonomous states, which then delegate most tasks to district or local community authorities. The structure is characterised by inequalities between the various Länder as well as between rural and urban areas. Membership in a health insurance fund is mandatory and based upon the type of employment or region. More than two-thirds of healthcare financing originates from contributions and tax revenue. Approximately one-third is provided directly by private households. Health services are provided by public, private non-profit and private for-profit organisations or individuals. Citizens covered by a health insurance fund can freely choose between service providers in the outpatient sector, of whom the majority work in individual practices.

A national plan on rare diseases is in the early stages of development in the Austrian Ministry of Health and members of the Orphanet Austria team are contributing to these discussions. No national definition for rare diseases exists, and all stakeholders accept the European Orphan Drug Regulation definition of a prevalence of one in 2000 individuals. Some patient groups in Austria have been created with the support of Dachverband der Selbsthilfegruppen, the Association of Self-Help Groups, and Selbsthilfe-Unterstützungsstelle für gesundheitsbezogene Selbsthilfegruppen (SUS) in Vienna. Most patient organisations distribute information through written materials or web sites. Orphanet Austria is also frequently referenced as a source of rare diseases information. Neonatal screening occurs for all newborns and includes many tests for metabolic diseases. Genetic counselling is not recognised as a medical subspecialty.

Diagnosis in Austria

PARTICIPANTS IN THE SURVEY

DMD (6)	TS	PWS (19)
FRX		CF
CD (109)	MFS	EDS

Figure 1
Diseases
included in
the survey
and the
number of
responses
in Austria

Responses from 134 families of patients with three diseases were analysed (*Figure 1*). An equal number of female and male patients were represented in the survey (55% and 45%, respectively).

AWAITING THE DIAGNOSIS

During the quest for diagnosis, more than five physicians were consulted by 25% of families. Physicians prescribed tests for 89% of patients including biological tests (80%), genetic tests (6%), functional tests (20%) and X-rays (68%).

Before obtaining the correct diagnosis, another diagnosis was given to 65% of patients (compared to 41% overall) (*Figure 2*) resulting in inappropriate treatments in 83% of patients including medical (46%), surgical (22%) and psychological or psychiatric (5%).

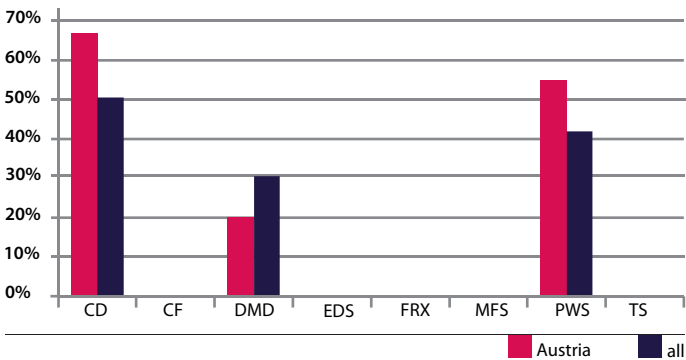


Figure 2 Percentage
of patients initially receiving
a misdiagnosis in Austria

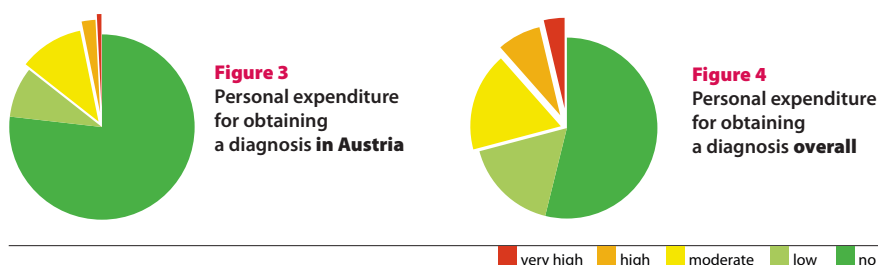
DIAGNOSIS

The structures providing the diagnoses were usually hospital consultations (54%) and specialised centres (16%), followed by private practices (8%). These were located in another region (14%) or another country (1.6%).

Access to diagnosis required a further financial contribution, however the personal cost in Austria was lower than that observed overall.

Many respondents reported free diagnoses or low expenses (86%) and only a few considered costs to be high or very high (3%).

A second opinion was sought to confirm the diagnosis by 22% families.



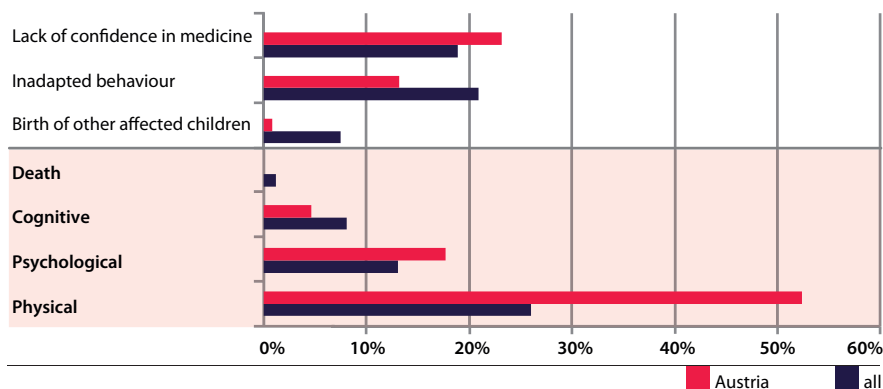
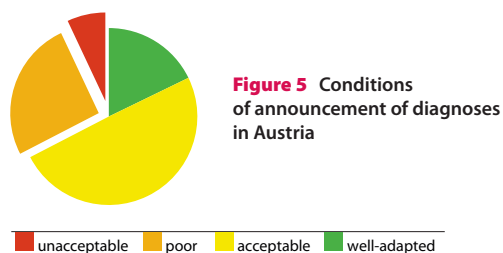
ANNOUNCEMENT OF DIAGNOSIS

For 20% of patients, diagnoses were given without complete information on the disease and 97% of respondents considered that this information was necessary.

In 95% of cases, respondents considered that psychological support was required at the time of the announcement, whereas 67% of patients did not receive such support.

The conditions in which the diagnosis was delivered were considered poor or unacceptable by 33% of respondents (*Figure 5*).

For 75% of families, the delay in receiving a correct diagnosis was considered responsible for deleterious consequences. More physical (52%) and psychological (18%) consequences were observed in Austria compared with the overall results.





Socioeconomic Data

Total population: 10 584 534 (2007)

Area of country: 30 528 sq km

Population density: 344/sq km (2006)

GDP: 316.2 billion % (2006)

GDP/capita: 35 090 (2006)

% of GDP spent on health: 3.1 % (2005)

of physicians/100 000 inhabitants: 449 (2006)

Belgium

Sections of this chapter were written with the collaboration of the Belgian Association for Children and Adults With Metabolic Diseases (BOKS, asbl).

National Initiative in the Field of Rare Diseases

Most Belgians have access to high quality health care despite a system characterised by heterogeneity and fragmentation. Compulsory health insurance is combined with a primarily private system of healthcare delivery, based on independent medical practice, freedom of choice of physician and predominantly fee-for-service payment with reimbursement. With no referral system in place, often patients' point of contact is a specialist. The federal government's primary responsibilities are executive, however these also include the supervision and financing of the compulsory health insurance, registration of pharmaceuticals and their price control. Health promotion, implementation of hospital standards, coordination of homecare, environmental health and social support are delegated to the French, Flemish and German communities.

Despite discussions on the creation of a national plan for rare diseases in Belgium by the Management Committee of the Fund for Rare Diseases and Orphan Drugs, managed by the King Baudouin Foundation of Belgium, no such plan exists yet. This group, officially recognised in December 2007, also organised a national symposium on orphan drugs after which a strategy to increase awareness of the problems presented by rare diseases and reimbursement of orphan drugs was developed. Other ad hoc working parties have been created to address the issues related to orphan diseases and to developing strategic solutions. Although no non-medical services exist specifically for rare diseases, many such services are provided from chronic diseases, some of which are rare. Neonatal screening is performed for 11 metabolic diseases at the national level.

The non-profit organisation Rare Diseases Organisation Belgium, privately founded in January 2008, created a web site to encourage the dissemination of information on rare diseases in Belgium. The Royal Decree of 8 July 2004 on the reimbursement of orphan medicinal products resulted in the creation of a Committee of Doctors for Orphan Medicinal Products within the healthcare service of the INAMI (National Invalidity Insurance Institute). INAMI is the body responsible for issuing opinions on orphan medicinal products when an opinion is required. The Committee of Doctors evaluate individual rights to reimbursement as well as the existing reimbursement conditions for these products and draw up an annual activity report. Several drafts for other legal acts relating to orphan medicinal products are currently under discussion. The FNRS (National Fund for Scientific Research) funds, in addition to fundamental research, applied research on rare diseases for the French-speaking scientific community.

Diagnosis in Belgium

PARTICIPANTS IN THE SURVEY

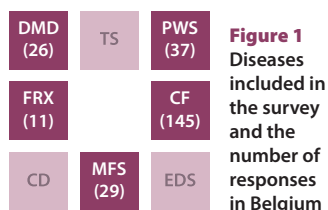


Figure 1
Diseases included in the survey and the number of responses in Belgium

Responses from 248 families of patients with five diseases were analysed (*Figure 1*). Female and male patients were represented in the survey (34% and 66%, respectively), however there was an underrepresentation of females, surprisingly due to CF patients (35% females compared to 65% overall for CF).

DIAGNOSIS OVER THE FIRST THREE MONTHS OF LIFE

A total of 41% of patients in Belgium received neonatal diagnoses, compared to 15% overall, this was the highest rate observed in the survey. This very high rate is due both to neonatal testing (21% compared to 4% overall) and to observations during pregnancy or at birth (14% compared to 7% overall). Early diagnoses linked to other cases in the family are the same as the overall result in Europe (4%).

AWAITING THE DIAGNOSIS

Before obtaining the correct diagnosis, another diagnosis was given to 44% of patients (*Figure 2*) resulting in inappropriate treatments in 75% of patients, including medical (36%), surgical (12%) and psychological or psychiatric (7%). During the quest for diagnosis, more than five physicians were consulted by 22% of families and more than ten physicians by 7% of families. They prescribed tests for 94% of patients, including biological tests (65%), genetic tests (40%), functional tests (41%) and X-rays (58%).

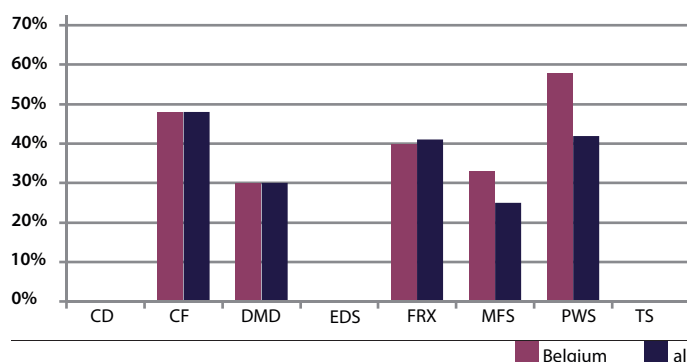


Figure 2 Percentage of patients initially receiving a misdiagnosis in Belgium

DIAGNOSIS

The structures providing the diagnoses were most frequently hospital consultations (71%), specialised centres (17%) and private practices (7%). They were rarely located in another region (13% compared to 26% overall) or in another country (1.6%). Diagnosis is expensive for Belgian patients and is rarely free (14% compared to 54% overall). Twice the number of patients considered that their expenditure was moderate in Belgium compared to the overall results

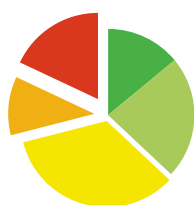


Figure 3
Personal expenditure
for obtaining
a diagnosis in Belgium



Figure 4
Personal expenditure
for obtaining
a diagnosis overall

very high high moderate low no

and more than double considered that their expenditure was high or very high (29%) compared to the overall responses (*Figure 3 & 4*).

A second opinion was sought by 28% of families to confirm the diagnosis, which was slightly more than the overall 21%, mainly for CF and PWS patients.

ANNOUNCEMENT OF DIAGNOSIS

A total of 22% of Belgian respondents obtained their diagnosis without receiving complete information on the disease and 98% considered this information to be necessary. No psychological support was received by 60% of patients, which is low compared to 91% of respondents who expected this type of support but still represents the best value in the survey.

The genetic nature of the disease was explained to families in 88% of cases, with details about the possibility of other cases in the family in 67% of cases. Genetic advice resulted in the diagnosis or identification of a carrier in the family in 36% of cases. A total of 30% of Belgian families considered the conditions of the announcement to be poor or unacceptable (*Figure 5*).

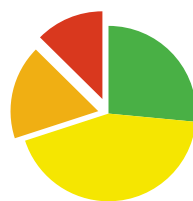


Figure 5
Conditions of
the announcement
of diagnoses
in Belgium

unacceptable poor acceptable well-adapted

CONSEQUENCES OF DELAYED DIAGNOSIS

For 78% of the families, delays in diagnosis were considered responsible for at least one deleterious consequence.

As observed overall, familial consequences 'surpass' individual consequences (*Figure 6*).

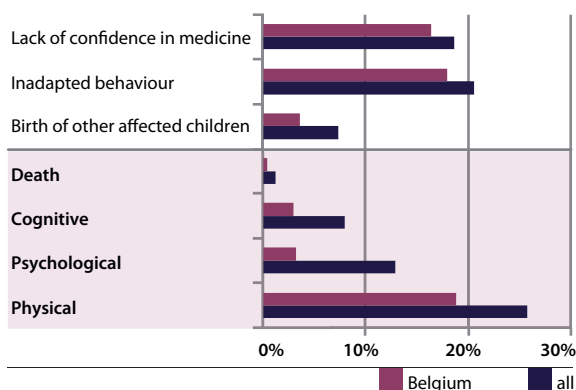


Figure 6 Medical and non-medical
consequences of delayed diagnoses
in Belgium

Access to **Medical** and **Social Services** in Belgium

PARTICIPANTS IN THE SURVEY

AH	Ch11 (1)	WS (37)	PWS
FRX (9)	EB (15)	TS	CF
ANR	OI (11)	MFS (54)	EDS (62)
HD (66)	MG	ATX	PAH

Figure 7
Diseases included in the survey and the number of responses in Belgium

Responses from 255 families of patients with eight diseases were analysed in the survey (*Figure 7*). The numbers of female and male patients represented (60% and 40%, respectively) were slightly unbalanced. The mean age of patients was 37 years (mean age at diagnosis: 24 years).

NEED FOR MEDICAL SERVICES

Belgian patients needed an average of 9.5 different kinds of medical services related to their disease. Hospitalisation occurred in 47% of patients for an average total duration of 20 days.

MEDICAL SERVICES

Access to eight services considered essential for each disease was easy in 77% of cases and difficult in 12% of cases (*Figure 8*) and impossible in 11% of cases. This was mainly due to lack of referral (53%), unavailability (18%), personal cost (10%) and location of the structures, including a location too far away (13%), no one to go with (12%) and difficulty in travelling (15%). The medical services responded to patients' expectations fully (61%) or partially (27%), poorly (9%) or not at all (3%), which were comparable to overall results (*Figure 9*).

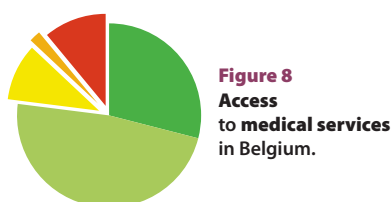


Figure 8
Access to medical services in Belgium.

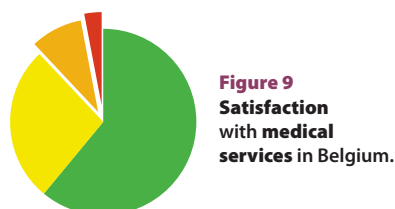


Figure 9
Satisfaction with medical services in Belgium.

impossible very difficult difficult easy very easy not at all poorly partially fully

SOCIAL ASSISTANCE

Amongst the 48% of families that required social assistance, 1% failed to meet with a social worker, whereas 78% met with one easily and 22% with difficulty (*Figure 10*).

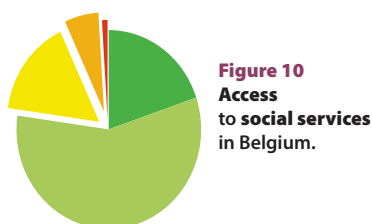


Figure 10
Access to social services in Belgium.

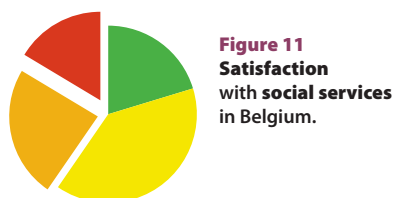


Figure 11
Satisfaction with social services in Belgium.

impossible very difficult difficult easy very easy not at all poorly partially fully

Compared to the European situation, this assistance was provided more frequently by associative and insurance structures, with 60% of Belgians being satisfied with this assistance and 16% not at all satisfied (*Figure 11*).

REJECTION

Belgian patients experienced rejection by health professionals more frequently (34% compared to 18% overall).

Overall, the reluctance of health professionals to treat patients due to the complexity of their disease was the main cause of rejection (77%), followed by communication difficulties (26%), a physical aspect (19%) and disease-related behaviour (16%) (*Figure 12*).

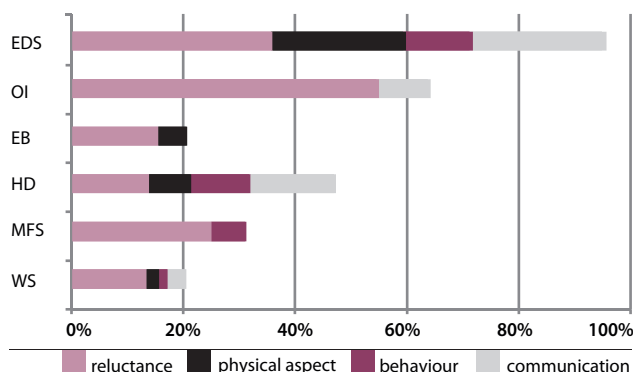


Figure 12 Cumulated frequencies of cause of rejection, by disease, in Belgium. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

CONSEQUENCES OF THE DISEASE

As a consequence of the disease, 14% of Belgian patients had to move house. Amongst these, families most frequently moved to a more adapted house (58%), but also to be nearer to disease specialists (12%) or to be closer to a relative (19%). As a consequence of their disease, 36% of patients had to reduce or stop their professional activity. In 26% of cases one member of the family had to stop work to take care of a relative.



Socioeconomic Data

Total population: 4 453 500 (2008)
 Area of country: 56 542 sq km (2008)
 Population density: 81/sq km (2008)
 GDP: 74 419 billion \$ (2008)
 GDP/capita: 16 758 \$ (2008)
 % of GDP spent on health: 7.4% (2006)
 # of physicians/100 000 inhabitants: 244

Croatia

Sections of this chapter were written with the collaboration of the Croatian Society of Patients With Rare Diseases.

National Initiative in the Field of Rare Diseases

The Croatian health system is based on a compulsory, employment-based, national health insurance system managed by the Croatian Institute for Health Insurance (CIHI). Some patients are required to provide co-payment for health services, although most citizens are exempt. Some health services, such as those provided by private institutions, must be paid for in full out of pocket. A small number of private insurance companies provide supplemental coverage. Most health facilities in Croatia, however, are owned either by the state or the county. However, healthcare reforms after the Communist era introduced extensive privatisation of primary care, some homecare services, pharmacies and dental clinics. Patients have a free choice of their primary level physicians. Significant differences in healthcare availability exist depending on a patient's place of residence, due to an uneven concentration of specialist medicine in large cities. Individual financial circumstances also create inequality in healthcare availability and the custom of informal payments remains. Progress toward a national plan for rare diseases is still in its preliminary stages in Croatia. Nevertheless, patient organisations and their representatives continue in their efforts to bring this issue to the attention of health authorities. In 2008, the Croatian Society for Rare Disease was established as part of the Croatian Medical Society. The European Union regulation definition of rare diseases, a prevalence of less than 1 per 2000 people, is used by stakeholders in many practical contexts. It is not, however, recognised in any official legislative documents. A wide range of social services, respite care and recreational services have been developed, though not specifically for rare disease patients but patients affected by any disease. As such, not all services are adapted to the needs of rare disease patients.

Public information sources on rare disease, including helplines and web sites, are solely provided by patient organisations and other non-governmental organisations (NGO). Rare disease patient organisations do receive financial support from local and national health authorities such as the Office for Cooperation with NGO. Additional support for rare disease organisations comes from cooperation with the Ministry of Health, the Ministry of Social Care and Work and other governmental bodies relevant to the field of rare diseases. The Croatian Institute for Health Insurance is responsible for the approval of orphan drugs. All available orphan drugs are reimbursed by the Croatian health insurance fund for rare diseases. Neonatal screening exists for PKU and hypothyroidism. Genetic testing is available in two main genetic testing centres in Zagreb. Genetic counselling is recognised as a medical profession.



Socioeconomic Data

Total population: 794 600 (2008)
 Area of country: 9 251 sq km
 Population density: 85/sq km (2008)
 GDP: 21 382 billion \$ (2007)
 GDP/capita: 27 429 \$ (2007)
 % of GDP spent on health: 6% (2005)
 # of physicians/100 000 inhabitants: 234 (2007)

Cyprus

Sections of this chapter were written
 with the collaboration of
 the Thalassaemia International Federation.

National Initiative in the Field of Rare Diseases

Health care in Cyprus is a balanced mix of public and private systems in which half of health spending is carried out in the public sector and half in the private sector. The two systems are continually seeking to better coordinate their services. Until recently, health services were provided by public health provision, private fee-for-service provision, employer trade union funds and private health insurance. The government is now in the process of switching to a National Health Insurance Scheme (NHIS) that will cover all citizens through both the public and the private sector. Although no official national plan exists for rare diseases in Cyprus, several national measures for the prevention, diagnosis and management of rare diseases exist. These include neonatal screening for PKU and congenital hyperthyroidism, prenatal and school screening for thalassaemia, the establishment of centres of expertise for thalassaemia, and the existence of genetic clinics and counselling. The European Orphan Drug Regulation definition of a rare disease as one with a prevalence of one in 2000 individuals is used by all stakeholders. Rare disease patient organisations receive an annual allowance. Several funding initiatives specifically dedicated to rare disease research are made possible through the government-sponsored Cyprus Research Promotion Foundation and the Cyprus Institute of Neurology and Genetics. Compassionate use of orphan drugs is also reimbursed.



Socioeconomic Data
 Total population: 10 424 926 (2008)
 Area of country: 78 866 sq km
 Population density: 132/sq km (2008)
 GDP: 248 902 billion \$ (2007)
 GDP/capita: 24 236 \$ (2007)
 % of GDP spent on health: 7.1% (2005)
 # of physicians/100 000 inhabitants: 351 (2006)

Czech Republic

Sections of this chapter were written with the collaboration of the Czech Republic State Institute for Drug Control.

National Initiative in the Field of Rare Diseases

The healthcare system in the Czech Republic, which is supervised and regulated by the government, includes social health coverage with universal membership, funded by economically active individuals, their employers and the state. Contributions for non-working individuals are covered by the state. All permanent residents are entitled to health insurance, and those who do not qualify to participate can take out voluntary health insurance but only with the General Health Insurance Fund (GHIF). The Ministry of Health primarily has an administrative role but also manages and controls the country's large hospitals. A number of small hospitals are owned and operated by regional communities. Almost all outpatient and pharmacy services have been privatised.

The European Orphan Drug Regulation definition of one in 2000 people is accepted and used in any legislation concerning rare diseases and orphan drugs. Although there is currently no national plan specifically for rare diseases, the Ministry of Health intends to set up a working group to discuss the relevant issues in preparation for the Czech European Presidency in 2009. Under the Act on Social Services for people with Disabilities (Act No. 108/2006 Sb.), which came into force in 2007, rare disease patients have had an improvement in access to social services. A few RD patient groups also organise recreational services, such as summer camps for children or rehabilitation/therapeutic weekends for adult patients. The only public information available on rare diseases includes web sites of individual patient organisations that may receive funding from grants from the Ministry of Health and Ministry of Labour and Social Affairs.

Neonatal screening is routinely performed for PKU, congenital adrenal hyperplasia (CAH) and congenital hypothyroidism. Pilot screening studies have been conducted for other metabolic disorders (2005) and cystic fibrosis (2006). Specific therapeutic programmes (Section 49 of the Act on Pharmaceuticals) allow for the use of non-authorised medicinal products. In most cases orphan drugs available on the market are fully reimbursed, and since 2008 a limit of 5000 CZK (200 €) per year has been introduced for co-payment by patients. This limit applies to prescription-only medicines and fees for visits to outpatient healthcare facilities (30 CZK — 1.23 € — per visit) and hospitals (60 CZK — 2.46 € — per day in hospital). Genetic counselling and testing services are available for families at risk for certain rare diseases such as Huntington's disease, Charcot-Marie-Tooth disease (CMT) and particular metabolic disorders, amongst others.



Denmark

Socioeconomic Data

Total population: 5 475 791 (2008)

Area of country: 43 094 sq km

Population density: 129/sq km (2008)

GDP: 198 5 billion \$ (2006)

GDP/capita: 37 000 \$ (2006)

% of GDP spent on health: 9.1% (2006)

of physicians/100 000 inhabitants: 292

Sections of this chapter
were written with the collaboration
of Rare Disorders Denmark.

National Initiative in the Field of Rare Diseases

The Danish healthcare system is a universal publicly financed system being run by regional authorities in close cooperation with the government and the local authorities. There are, however, disparities between services offered by the different municipalities, as the system is decentralised into five regions. The Danish healthcare service can be divided into primary health care and the hospital sector. Primary care 'house doctors', or general practitioners, act as gatekeepers with regard to hospital treatment and specialised care.

There is no official definition of rare diseases in Denmark, but health professionals, patients and health authorities define a disease as rare if it affects, at most, 1000 patients. This definition differs from the European Orphan Drug Regulation definition of a prevalence of 1 in 2000 people. Although there is currently no national plan for rare diseases, the rare disease alliance, Rare Disorders Denmark, has pushed for the creation of such a plan. The Danish Centre for Rare Diseases and Disabilities is a state-funded knowledge centre on rare disorders that gathers, processes and disseminates information on rare diseases and disabilities, as well as offering counselling to patients and professionals on social problems linked to rare diseases.

Two national rare disease centres have been established and are responsible not only for specialised diagnosis and patient treatment, but also for quality development, research, clinical databases and developing national guidelines for the treatment for rare disorders. However, in reality, the centres concentrate on specialised diagnosis and patient treatment. Limited funding for patient organisations is possible from the Ministry of Health and from the Ministry of Social Affairs.

National screening programmes include neonatal screening for PKU and some metabolic disorders as well as prenatal screening for trisomy 21 and other disorders, at the end of the second trimester of pregnancy. Genetic counselling exists as a service in the public health system.

Diagnosis in Denmark

PARTICIPANTS IN THE SURVEY

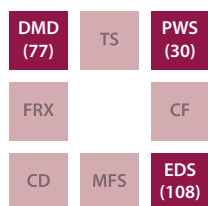


Figure 1
Diseases included in the survey and the number of responses in Denmark.

Responses from 215 families of patients with three diseases were analysed (*Figure 1*). An unequal number of female and male patients were represented in the survey (62% and 38%, respectively).

DIAGNOSIS IN THE FIRST THREE MONTHS OF LIFE

Neonatal diagnoses were obtained in 8% of patients (compared with 15% overall). This was due both to the low observations during pregnancy or at birth (1.5%) and infrequent neonatal testing (1%). Early diagnoses linked to other cases in the family were comparable to overall results (3%).

AWAITING THE DIAGNOSIS

Before obtaining the correct diagnosis, another diagnosis was given to 58% (*Figure 2*), resulting in inappropriate treatments for 53% of patients, including medical (20%), surgical (7%) and psychological or psychiatric (3%) treatments.

During the quest for diagnosis, more than five physicians were consulted by 50% of families and more than 10 physicians by 30% of families. They prescribed tests for 91% of patients, including biological tests (66%), genetic tests (17%), functional tests (53%) and X-rays (36%).

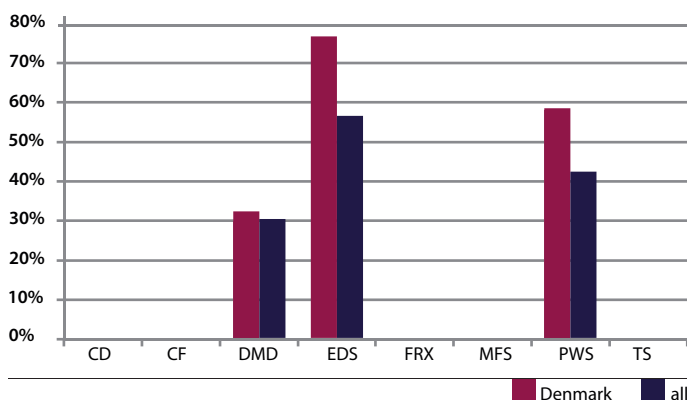


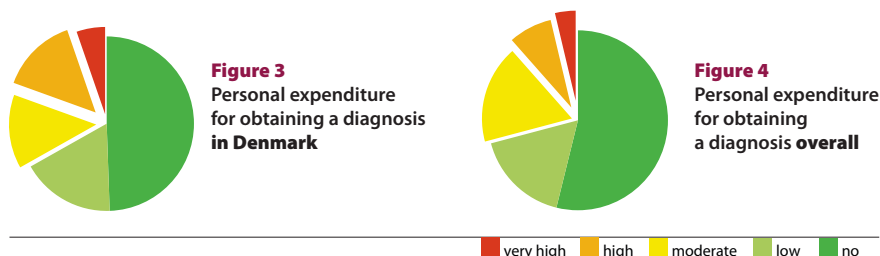
Figure 2 Percentage of patients initially receiving a misdiagnosis in Denmark

DIAGNOSIS

The structures providing the diagnoses were hospital consultations, (46%), private practices (8%) and specialised centres (25%). A total of 40% of Danish patients obtained their diagnosis outside their region but rarely in another country (1%).

Personal expenditure for obtaining a diagnosis was slightly higher than observed on average in Europe, with high or very high expenditure in 20% (compared to 12%) (Figure 3 & 4).

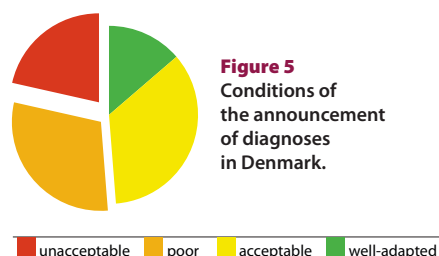
A second opinion was sought by 18% of families to confirm the diagnosis.



ANNOUNCEMENT OF DIAGNOSIS

A total of 38% of Danish patients obtained their diagnosis without receiving complete information on the disease, though 98% considered this information to be necessary. Similarly 94% considered psychological support at the time of receiving the diagnosis as necessary, whereas 67% of patients did not receive such support.

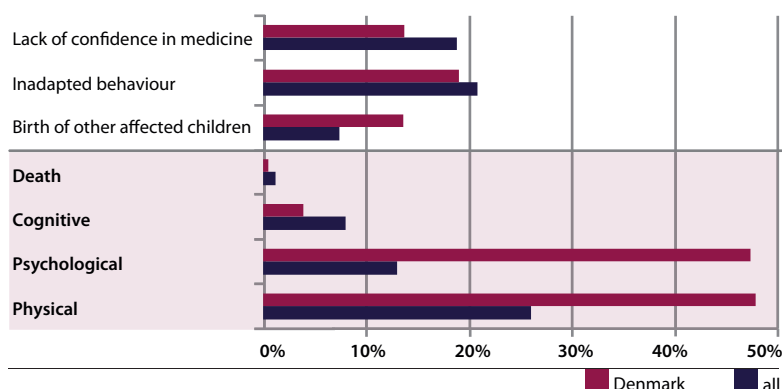
The genetic nature of the disease was explained to families in 67% of cases, with details given about the possibility of other cases in the family in 35% of cases. Genetic advice resulted in the diagnosis or identification of a carrier in the family in 35% of cases. The conditions of the announcement of the diagnosis were considered poor or unacceptable in 51% of cases (Figure 5).



CONSEQUENCES OF DELAYED DIAGNOSIS

For 78% of the families, a delay in diagnosis was considered responsible for deleterious consequences. The personal consequences included physical (48%) and psychological consequences (47%), and 17% reported the birth of other children suffering from the disease (Figure 6).

Figure 6 Medical and non-medical consequences of delayed diagnoses in Denmark



Access to **Medical** and **Social Services** in Denmark

PARTICIPANTS IN THE SURVEY

AH (3)	Ch11	WS	PWS
FRX	EB	TS (28)	CF
ANR (5)	OI (68)	MFS (5)	EDS (44)
HD (23)	MG	ATX	PAH (1)

Figure 7
Diseases included in the survey and the number of responses in Denmark

Responses from 177 families from Denmark of patients with eight diseases were analysed in the survey (*Figure 7*). The numbers of female and male patients represented were 76% and 24%, respectively. Females were overrepresented in many diseases: 90% in EDS, 80% in MFS, 60% in OI and 100% in PAH. The mean age of patients was 39 years (mean age at diagnosis: 23 years).

NEED FOR MEDICAL SERVICES

Overall, Danish patients needed 8.6 different kind of medical services related to their disease (slightly less than the average 9.4 medical services in the overall survey) and also required fewer tests (2.3 compared to three). Hospitalisation occurred in 45% of patients for an average total duration of 12 days.

MEDICAL SERVICES

Access to the eight services (essential for each disease) was easy in 71% of cases and difficult in 13% of cases. It was impossible in 17% of cases due to lack of referral (47%), but also unavailability (37%), waiting time (18%), personal cost (10%) and location of the structures, including a location too far away (5%), no one to go with (8%) and difficulty in travelling (12%) (*Figure 8*).

When obtained, the medical services responded well to patients' expectations in 89% of cases and poorly in 12% of cases (*Figure 9*).

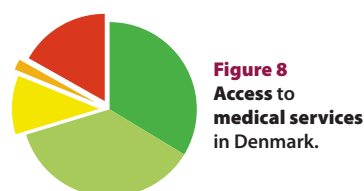


Figure 8
Access to medical services in Denmark.

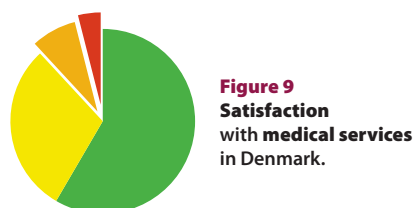


Figure 9
Satisfaction with medical services in Denmark.

impossible very difficult difficult easy very easy not at all poorly partially fully

SOCIAL ASSISTANCE

Amongst the 54% of Danish families needing social assistance, 8% failed to meet with a social worker, whereas 47% met with one easily and 45% with

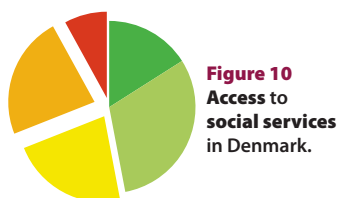


Figure 10
Access to social services in Denmark.

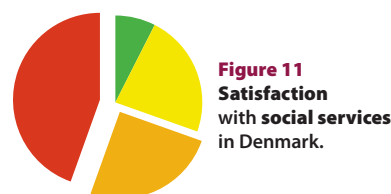


Figure 11
Satisfaction with social services in Denmark.

impossible very difficult difficult easy very easy not at all poorly partially fully

difficulty (Figure 10). Compared to the overall European situation, this assistance was provided more frequently by community care structures. A total of 31% of Danish were satisfied with this assistance, while 45% were not at all satisfied (Figure 11).

REJECTION

Danish patients experienced rejection by health professional less frequently than respondents overall for the 16 surveyed rare diseases (14% compared to 18% overall). Overall, the reluctance of health professionals to treat patients due to the complexity of their disease was the main cause of rejection (100%), followed by communication difficulties (8%), a physical aspect (5%) and disease-related behaviour (3%) (Figure 12).

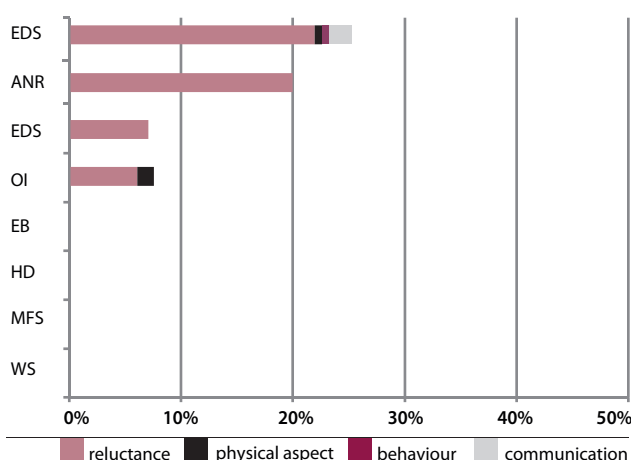


Figure 12 Cumulated frequencies of cause of rejection, by disease, in Denmark. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

CONSEQUENCES OF THE DISEASE

As a consequence of the disease, 21% of Danish patients had to move house. Amongst these, families most frequently moved to a more adapted house (73%), to be nearer to disease specialists (7%) or to be closer to a relative (11%). As a consequence of their disease, 54% compared to 29% overall of patients had to reduce or stop their own professional activity. In 21% of cases, one member of the family had to stop working to take care of a relative.

Finland



Socioeconomic Data

Total population: 5 320 102 (2008)

Area of country: 338 145 sq km

Population density: 16/sq km

GDP: 163 billion \$ (2005)

GDP/capita: 34 819 \$ (2005)

% of GDP spent on health: 7.5% (2005)

of physicians/100 000 inhabitants: 316 (2006)

Sections of this chapter were written with the collaboration of the Finnish Association for Persons With Intellectual Disabilities and the Finnish Association of People With Physical Disabilities

National Initiative in the Field of Rare Diseases

The Finnish healthcare system is decentralised. The Ministry of Social Affairs and Health directs and guides social and health services at the national level, while over 400 municipalities have the responsibility of implementing social and health services. The municipalities may produce services themselves or arrange them in cooperation with neighbouring municipal authorities.

A municipality may also contract services from another municipality or they may be provided privately or by associations, in order to offer alternatives. Regional cooperation between municipalities is required in areas of primary and specialised health care. The composition of services is not defined in precise detail by law, which means that services may differ from one municipality to another. The healthcare system in Finland is financed from several sources, but mainly through tax contributions. National Health Insurance provides coverage for expenses due to sickness, for example, part of the cost of medicine as well as fees for consultations with physicians in the private sector.

In Finland a rare disease is defined as one with a prevalence of a maximum of 100 people per one million inhabitants. To date, small steps have been taken to establish a national plan for rare diseases and it is anticipated that one should be developed in the next three or four years. The new healthcare law proposal contains many possibilities to improve diagnostics, care and rehabilitation in the area of rare diseases.

Outside of an official plan for rare diseases, a network of resource centres, the Finnish Harvinaiset Network, has been operating in Finland since 1991. Each centre was founded by a non-governmental organisation that also ensures its functioning and management. The network of centres aims at ensuring better awareness of the needs of people with rare diseases and delivering services to meet these needs through extensive collaboration with all stakeholders. The centres have set tasks to organise rehabilitation training and group meetings, advise and guide individuals and families, produce information materials and organise courses for professionals.

Like other activities of Finnish health and welfare associations, Finland's Slot Machine Association (RAY) funds this activity. The network has also created an Internet portal focusing on rare diseases uniting major stakeholders and allowing them to cooperate in the field of rare disorders and disabilities.

The Finnish Harvinaiset Network for Rare Diseases and SATA Committee of the Finnish Ministry of Social Affairs and Health are working on initiatives to improve access to treatment. Some private organisations fund rare disease research projects. Genetic counselling is recognised as a medical subspecialty.

Diagnosis in Finland

PARTICIPANTS IN THE SURVEY

DMD (45)	TS (34)	PWS (54)
FRX (42)	CF (26)	
CD (156)	MFS (50)	EDS (27)

Figure 1
Diseases included in the survey and the number of responses in Finland

Responses from 434 families of patients with eight diseases were analysed (*Figure 1*). An equal number of female and male patients were represented in the survey (52% and 48%, respectively)

DIAGNOSIS OVER THE FIRST THREE MONTHS OF LIFE

Neonatal diagnoses were obtained in only 8% of patients, less than the 15% observed overall.

This low rate is linked to low detection during pregnancy or at birth (3% compared to 7% overall) and the almost complete absence of neonatal tests (1% of patients compared to 4% overall).

AWAITING THE DIAGNOSIS

During the quest for diagnosis, more than five physicians were consulted by 29% of families and more than ten physicians by 9% of families. Physicians prescribed tests for 93% of patients, including biological tests (80%), genetic tests (23%), functional tests (39%) and X-rays (52%).

Before obtaining the correct diagnosis, another diagnosis was given to 32% of patients (*Figure 2*). These misdiagnoses resulted in inappropriate treatments for 71% of patients, including medical (38%), surgical (11%) and psychological or psychiatric (4%).

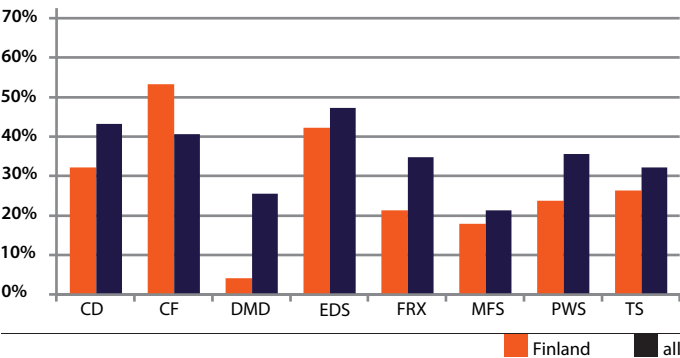


Figure 2
Percentage of patients initially receiving a misdiagnosis in Finland

DIAGNOSIS

The structures providing the diagnoses were hospital consultations (53%), specialised centres (26%) and private practices (6%). In 47% of cases they were located in another region. This was the highest reported rate, however they were rarely in another country (0.8%).

Patients reported lower access to free diagnoses in Finland than seen overall (26% compared to 54%) (Figure 3 & 4), however expenditure was most often considered low or moderate (62%) and less frequently high (11%). A second opinion was sought by 11% of families to confirm the diagnosis.

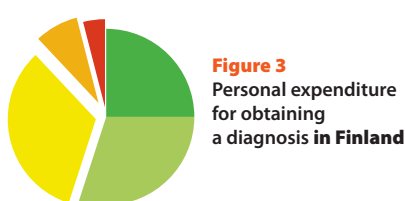


Figure 3
Personal expenditure
for obtaining
a diagnosis in Finland

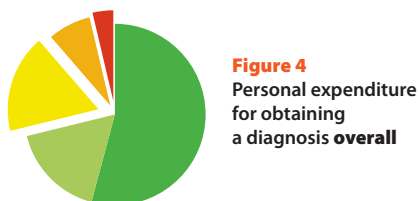


Figure 4
Personal expenditure
for obtaining
a diagnosis overall

very high high moderate low no

ANNOUNCEMENT OF DIAGNOSIS

For 30% of Finnish patients, diagnoses were given without complete information on the disease, though 97% considered this information necessary. A total of 91% of Finnish patients considered psychological support necessary at the time of the announcement, whereas 70% of patients did not receive such support.

The genetic nature of the disease was explained to families in 62% of cases, with details on the possibility of other cases in the family in 49% of cases.

The conditions of announcement were considered slightly better in Finland than overall (29% considered the conditions poor or unacceptable compared to 35% having the same opinion overall) (Figure 5).

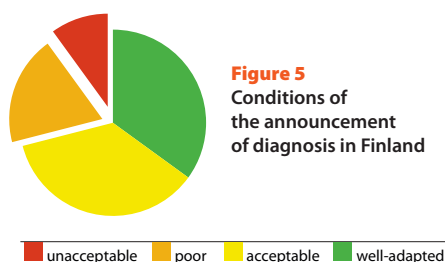


Figure 5
Conditions of
the announcement
of diagnosis in Finland

unacceptable poor acceptable well-adapted

CONSEQUENCES OF DELAYED DIAGNOSIS

For 57% of the families, delays in diagnosis were considered responsible for deleterious consequences.

The lowest frequency for all types of consequences except cognitive consequences is observed (Figure 6).

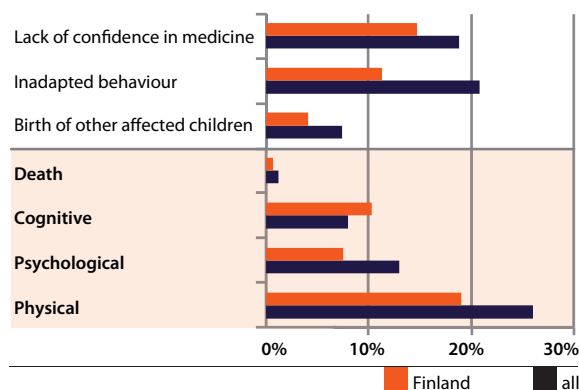


Figure 6 Medical and non-medical
consequences of delayed diagnoses
in Finland

Finland all

Access to **Medical** and **Social Services** in Finland

PARTICIPANTS IN THE SURVEY

AH	Ch11	WS	PWS
FRX	EB (17)	TS (12)	CF
ANR	OI (26)	MFS	EDS (46)
HD	MG	ATX (45)	PAH

Figure 7
Diseases
included in
the survey
and the
number of
responses
in Finland

Responses from 146 Finnish families of patients with five diseases were analysed in the survey (*Figure 7*). The proportion of female and male patients represented were 75% and 25%, respectively. There were more females represented in all diseases except TS. The mean age of the patients was 45 years (mean age at diagnosis: 30 years).

NEED FOR MEDICAL SERVICES

Overall, Finnish patients needed 9.3 different kinds of medical services related to their disease (the same as the average 9.4. medical services for all countries surveyed). Hospitalisation occurred in 43% of patients for an average total duration of 14 days.

MEDICAL SERVICES

Access to the eight essential medical services for each disease was easy in 63% of cases, difficult in 17% of cases and impossible in 20% of cases (*Figure 8*). This was due mainly to unavailability of the service (49%), personal cost (42%), lack of referral (35%), waiting time (39%) and location of the structures, including a location too far away (20%), no one to go with (19%) and difficulty in travelling (27%).

When obtained, the medical services responded mostly well (90% of respondents) to the expectations of patients, though some felt they responded poorly (10%) (*Figure 9*).



Figure 8
Access to
medical services
in Finland

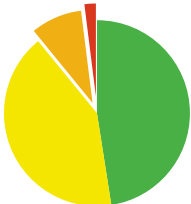


Figure 9
Satisfaction
with medical
services in Finland

impossible very difficult difficult easy very easy

not at all poorly partially fully

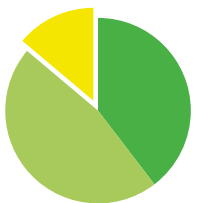


Figure 10
Access to
social services
in Finland.



Figure 11
Satisfaction
with social services
in Finland.

impossible very difficult difficult easy very easy

not at all poorly partially fully

SOCIAL ASSISTANCE

Amongst the 33% of Finnish families needing social assistance all met with a social worker however 87% met one easily and 14% met with one with difficulty (*Figure 10*).

Finnish patients were satisfied with this assistance in 54% of cases and in 22% of cases were not at all satisfied (*Figure 11*).

REJECTION

Finnish patients experienced rejection by health professional less (14%) than the overall (18%) of respondents for the 16 surveyed rare diseases.

The reluctance of health professionals to treat patients due to the complexity of their disease was the main cause of rejection (100%), followed by communication difficulties (25%), physical aspects (15%) and disease-related behaviour (10%) (*Figure 12*).

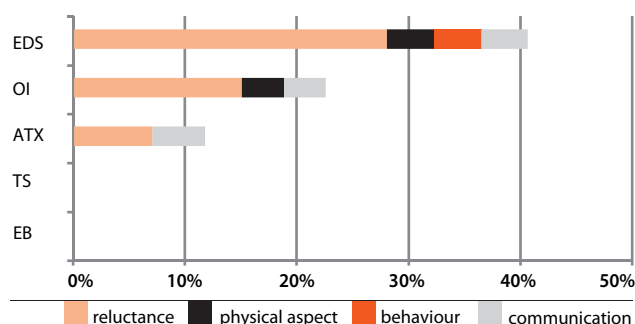


Figure 12 Cumulated frequencies of cause of rejection, by disease, in Finland. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

CONSEQUENCES OF THE DISEASE

As a consequence of the disease, 23% of Finnish patients had to move house. Amongst these, families most frequently moved to a more adapted house (76%), to be nearer to disease specialists (18%) or to be closer to a relative (12%). As a consequence of their disease, 45% of patients had to reduce or stop their professional activity. A member of the family had to stop working to take care of a relative in 11% of cases, compared to 33% overall. However there were more adults diseases represented in Finland than overall.



France

Socioeconomic Data

Total population: 64 473 140 (2008)
 Area of country: 549 000 sq km
 Population density: 114/sq km (2008)
 GDP: 1 871 trillion \$ (2006)
 GDP/capita: 30 100 \$ (2006)
 % of GDP spent on health: 11.2% (2005)
 # of physicians/100 000 inhabitants: 336 (2006)

National Initiative in the Field of Rare Diseases

The French centrally regulated healthcare system guarantees universal coverage via an employment-based healthcare insurance system. Many citizens opt for supplemental private insurance to pay for services not covered by the national system. France is often praised for its responsive healthcare providers and patient and provider freedoms. France is the only European country to have a national plan specifically for rare diseases. All stakeholders accept the European Orphan Drug Regulation definition of one in 2000. In the framework of the national plan for rare diseases, the official recognition and evaluation of Centres of Expertise (called Centres of Reference in France) is supported. New disease-oriented research networks and research projects are promoted through a national call for proposals. The dissemination of rare disease information is supported in the form of a rare diseases database (Orphanet), helplines and rare diseases identity cards. A national neonatal screening programme includes several rare diseases, including PKU, cystic fibrosis and congenital hypothyroidism. Compassionate use (called ATU in France) and reimbursement measures for this use of orphan medicinal products exist. Patient organisations are funded by several governmental institutions for their work in overcoming difficulties faced by rare disease patients and there exists social and psychological support for rare disease patients in need.

Diagnosis in France

PARTICIPANTS IN THE SURVEY

DMD (194)	TS (140)	PWS (218)
FRX (89)		CF (175)
CD (197)	MFS (162)	EDS (198)

Figure 1
Diseases
included in
the survey
and the
number of
responses
in France

Responses from 1373 families of patients with eight diseases were analysed (*Figure 1*). An equal number of female and male patients were represented in the survey (44% and 56%, respectively)

DIAGNOSIS OVER THE FIRST THREE MONTHS OF LIFE

The neonatal diagnoses rate (15%) is comparable to that observed overall (16%), with disorders observed during pregnancy or at birth (9% compared to 7%), following neonatal testing (3% compared to 4%) or linked to other cases in the family (2% compared to 3%).

AWAITING THE DIAGNOSIS

Before obtaining the correct diagnosis, another diagnosis was given to 40% of patients with no difference based on the disease reported (*Figure 2*). These misdiagnoses resulted in inappropriate treatments for 74% of patients, including medical (36%), surgical (15%) and psychological or psychiatric (10%).

During the quest for a diagnosis, more than five physicians were consulted by 20% of families and more than ten physicians by 9% of families. Physicians prescribed tests for 88% of patients, including biological tests (63%), genetic tests (25%), functional tests (40%) and X-rays (56%).

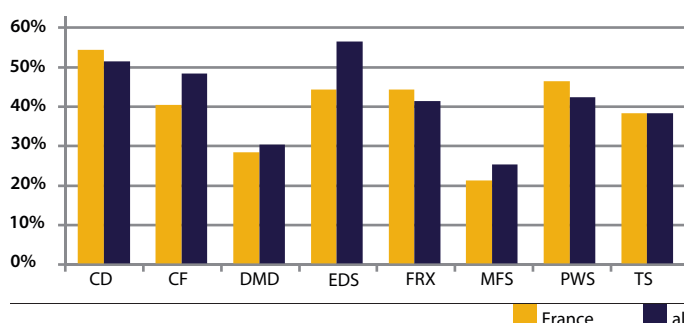
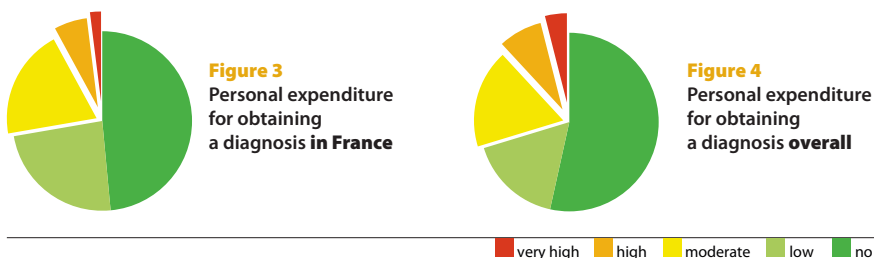


Figure 2 Percentage of patients initially receiving a misdiagnosis in France

DIAGNOSIS

The structures providing the diagnoses were hospital consultations (71%), private practices (15%) or specialised centres (7%). Those located in another region (19%) represented a value less frequent than for the overall survey (26%) or in another country (1.9 %).

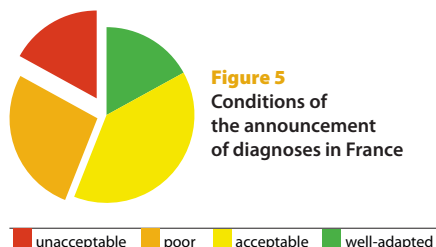
Personal costs for patients are comparable to those observed overall: free diagnosis was slightly less (49% compared to 54%), whereas patients considered expenditure to be low or moderate in 44% of cases and high or very high in 8% of cases (*Figure 3 & 4*). A second opinion was sought by 22% of families to confirm the diagnosis.



ANNOUNCEMENT OF DIAGNOSIS

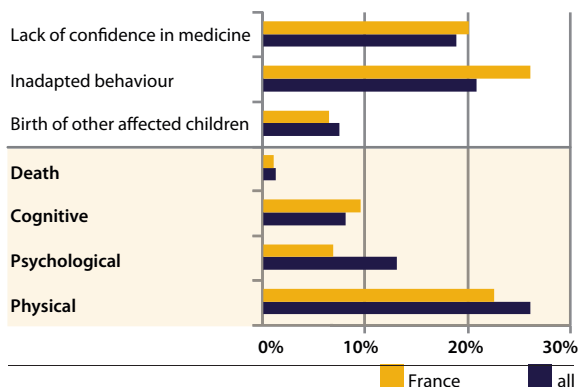
For 27% of patients, diagnoses were given without complete information on the disease, though 97% of respondents considered this information to be necessary.

A total of 90% of respondents felt that psychological support was required at the time of receiving the announcement, whereas only 17% of patients received such support. The genetic nature of the disease was explained to families in 74% of cases, with details about the possibility of other cases in the family given in 51% of cases. A total of 44% of respondents considered that the announcement was made under poor or unacceptable conditions (*Figure 5*).



CONSEQUENCES OF DELAYED DIAGNOSIS

For 74% of the families, delays in diagnosis were considered responsible for deleterious consequences. French families reported non-adapted behaviour (26%) and psychological consequences (7%) as due to delays in receiving the correct diagnosis (*Figure 6*).



Access to **Medical** and **Social Services** in France

PARTICIPANTS IN THE SURVEY

AH (103)	Ch11 (3)	WS (107)	PWS (97)
FRX (81)	EB (59)	TS (125)	CF (94)
ANR (16)	OI (113)	MFS (148)	EDS (138)
HD (41)	MG (104)	ATX (317)	PAH (101)

Figure 7
Diseases
included in
the survey
and the
number of
responses
in France

Responses from 1647 French families of patients with 16 diseases were analysed in the survey (*Figure 7*).

The proportions of female and male patients represented were 56% and 44%, respectively.

The mean age of patients was 34 years (mean age at diagnosis: 19 years)

NEED FOR MEDICAL SERVICES

Overall, French patients needed 9.4 different kinds of medical services related to their disease. Hospitalisation occurred in 45% of patients for an average total duration of 21 days.

MEDICAL SERVICES

Access to the eight essential services for each disease was easy in 74% of cases, difficult in 16% of cases and impossible in 10% of cases (*Figure 8*). Difficulties were mainly due to a lack of referral (67%), unavailability (16%), as well as waiting time (10%), personal cost (6%) and the location of the medical structures, including a location too far away (8%), no one to go with (5%) and difficulty in travelling (7%).

When obtained, the medical services responded well to patients' expectations in 91% of cases and poorly in 9% of cases (*Figure 9*).

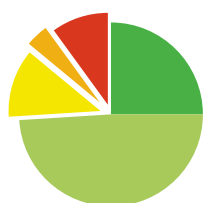


Figure 8
Access to
medical services
in France

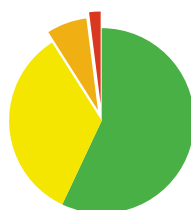


Figure 9
Satisfaction with
medical services
in France

impossible very difficult difficult easy very easy not at all poorly partially fully

SOCIAL ASSISTANCE

Amongst the 31% of French families that required social assistance, 3% failed to meet with a social worker, 76 % met with one easily and 21 % met with one

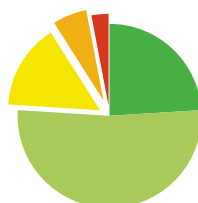


Figure 10
Access to
social services
in France



Figure 11
Satisfaction with
social services
in France

impossible very difficult difficult easy very easy not at all poorly partially fully

with difficulty (Figure 10). A total of 60% of French families were satisfied with this assistance and 23% were not at all satisfied (Figure 11).

REJECTION

Rejection by health professionals experienced by French patients (19%) was similar to that observed for respondents overall for the 16 surveyed rare diseases (Figure 12). The reluctance of health professionals to treat patients due to the complexity of their disease was the main cause of rejection (78%), followed by communication difficulties (23%), disease-related behaviour (16%) and physical aspects (12%).

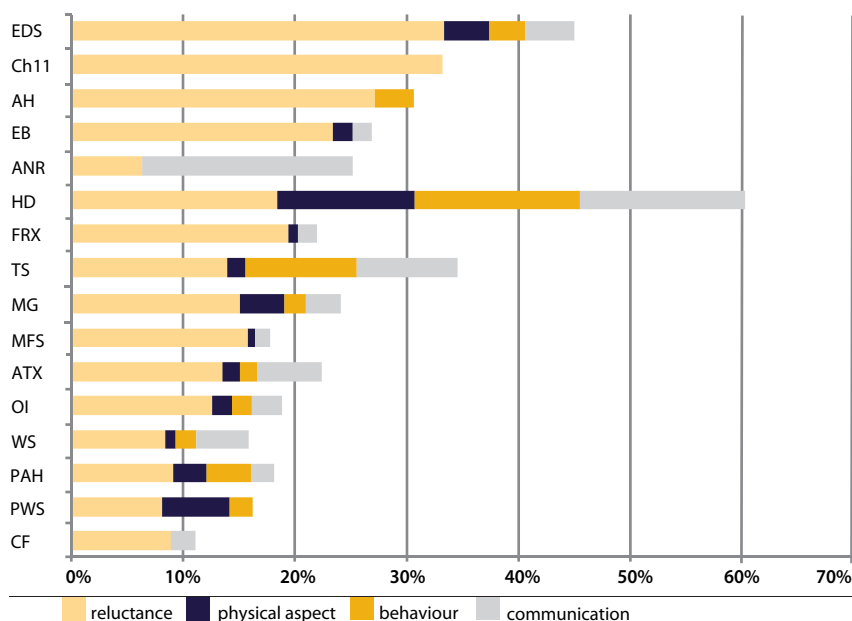


Figure 12 Cumulated frequencies of cause of rejection, by disease, in France. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents

CONSEQUENCES OF THE DISEASE

As a consequence of the disease, 19% of French patients had to move house. Amongst these, families most frequently moved to a more adapted house (59%), to be nearer to disease specialists (15%) or to be closer to a relative (21%). As a consequence of their disease, 26% of patients had to reduce or stop their professional activity. One member of the family had to stop work in order to take care of a relative in 31% of cases.



Socioeconomic Data
 Total population: 82 217 800 (2007)
 Area of country: 357 021 sq km
 Population density: 230/sq km (2007)
 GDP: 2.81 trillion \$ (2007)
 GDP/capita: 34 181 \$ (2007)
 % of GDP spent on health: 10.7% (2005)
 # of physicians/100,000 inhabitants: 336 (2006)

Germany

Sections of this chapter were written with the collaboration of the German Alliance for Rare and Chronic Diseases (ACHSE e.V.).

National Initiative in the Field of Rare Diseases

Germany's healthcare system provides almost universal access with a choice of physicians. Over 90% percent of the population receives health care through the country's healthcare insurance system administered by semi-private sickness funds operating under the constraints of a federal statute.

Membership in this programme is compulsory for all those earning less than a certain low level of income that is periodically revised. Those above the threshold may opt out of the state system and choose private insurance instead, but most remain in the state system. Although the federal government plays an important role in specifying national healthcare policies the country's healthcare system is administered by national and regional self-governing associations of payers and providers.

There is no official German definition for rare diseases and the European Orphan Drug Regulation definition of one in 2000 people is widely accepted. There is currently no national plan for rare diseases in Germany, however an in-depth evaluation of the needs of rare disease patients as a preparatory step to establishing a national plan for rare diseases has recently been commissioned by the Federal Ministry of Health. The results of this study will be used as a road map towards a national plan. The German Rare Disease Alliance (ACHSE) has made the achievement of a national plan a priority of its advocacy actions. ACHSE also offers several information services including a helpline, a general web site, an information platform on rare diseases (with links to quality information and fora on particular rare diseases) and is developing an information service for physicians.

The regional insurance associations are obliged to spend a certain amount of the insurance premiums received to support patient organisations in general (although not specifically for rare diseases). Some rare diseases are part of the neonatal screening program, while for others, such as cystic fibrosis, efforts are being made to have them introduced. The introduction of § 116b Social Law - Book 5 in the German Code of Social Law is a step towards an interdisciplinary daycare for treatment of rare diseases within the hospital, giving patients better access to specialised care. The actual implementation of such treatment centres is still an exception in most hospitals.

Access to off-label medication is currently secured by court decisions but only if there are no alternatives and the condition is very severe.

Regulations on compassionate use still need to be implemented in order to ensure reimbursement of costs and acceptable liability risks for doctors and industry. Germany has a national funding scheme for rare disease research as

part of the E-Rare Network. The Ministry of Research financed ten Research Networks on Rare Diseases for a period of three years with a total budget of 31 million € until 2008 with a possible two-year extension. The Deutsche Forschungsgesellschaft (DFG) and other research funds also spend considerable amounts of money directly or indirectly on research in the field of rare diseases albeit without particularly supporting rare disease research efforts. Genetic counselling is offered within the statutory healthcare system if it has implications for treatment decisions.

Diagnosis in Germany

PARTICIPANTS IN THE SURVEY

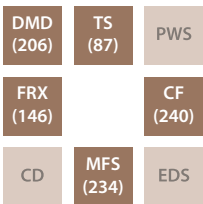


Figure 1
Diseases included in the survey and the number of responses in Germany

Responses from 913 families of patients with five diseases were analysed (*Figure 1*). An unequal proportion of female and male patients were represented in the survey (32% and 68%, respectively). This was due to number of respondents with DMD and FRX.

DIAGNOSIS IN THE FIRST THREE MONTHS OF LIFE

The neonatal diagnoses rate (12%) in Germany is slightly lower than that overall (15%) and is linked to less neonatal testing (2% compared to 4% overall).

AWAITING THE DIAGNOSIS

Before obtaining the correct diagnosis, another diagnosis was given that resulted in 69% of patients receiving inappropriate treatments, including medical (26%), surgical (14%) and psychological or psychiatric (5%) (*Figure 2*). During the quest for diagnosis, more than five physicians were consulted by 21% of families and more than ten physicians by 6% of families. Physicians prescribed tests for 88% of patients including biological tests (60%), genetic tests (26%), functional tests (41%) and X-rays (47%).

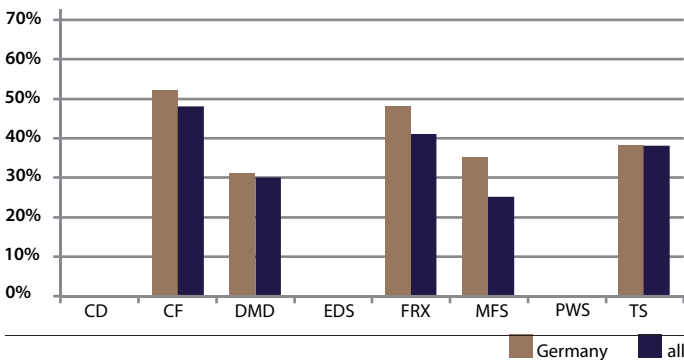
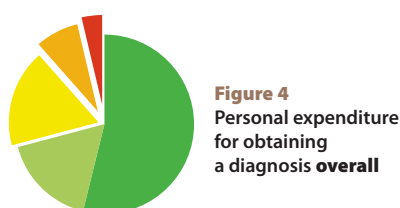
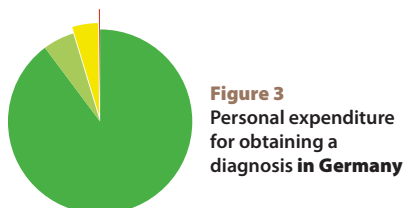


Figure 2
Percentage of patients initially receiving a misdiagnosis in Germany

DIAGNOSIS

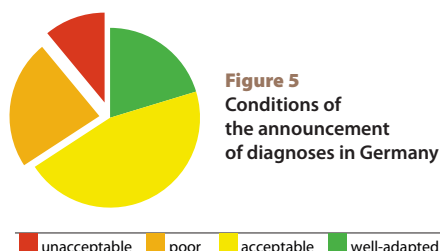
The structures providing the diagnoses were specialised centres (44%), hospital consultations (32%) or private practices (9%). Specialised centres play an important role in providing diagnosis in Germany. These were located in another region in 28% of cases or in another country in 1.6% of cases. In 90% of situations, access to diagnosis was free in Germany. Patients considered expenditure to be high or very high in only 0.2% of situations, compared with 11.5% overall (*Figure 3 & 4*). A second opinion was sought by 24% families to confirm the diagnosis.



very high high moderate low no

ANNOUNCEMENT OF DIAGNOSIS

For 15% of patients, diagnoses were given without complete information on the disease, however 95% considered this information to be necessary. A total of 87% considered that psychological support was required at the time of the announcement, whereas 67% of patients did not receive such support. The genetic nature of the disease was explained to families in 83% of cases, with details about the possibility of other cases in the family in 62% of cases. Genetic advice resulted in the diagnosis or identification of a carrier in the family in 39% of cases. German families considered the conditions of announcement to be poor or unacceptable in 34% of cases (*Figure 5*).



unacceptable poor acceptable well-adapted

CONSEQUENCES OF DELAYED DIAGNOSIS

For 68% of families, delays in diagnosis were considered responsible for deleterious consequences, similar to the overall of 71%. There were fewer medical consequences than non-medical consequences (*Figure 6*).

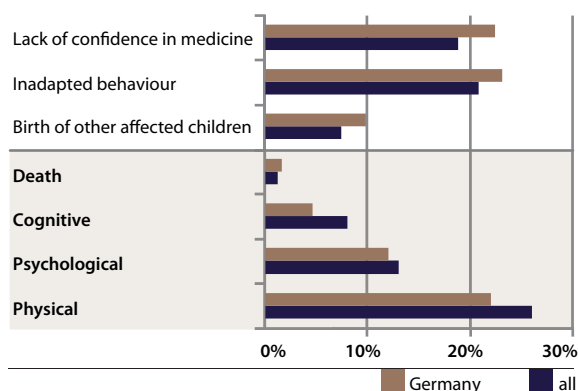


Figure 6 Medical and non-medical consequences of delayed diagnoses in Germany

Access to **Medical** and **Social Services** in Germany

PARTICIPANTS IN THE SURVEY

AH (21)	Ch11 (10)	WS (117)	PWS
FRX	EB	TS (81)	CF
ANR	OI	MFS	EDS (70)
HD	MG	ATX	PAH (152)

Figure 7
Diseases
included in
the survey
and the
number of
responses
in Germany

Responses from 451 German families of patients with six diseases were analysed in the survey (*Figure 7*). The proportion of female and male patients represented were 62% and 38%, respectively. The uneven distribution was mostly observed in PAH and EDS. The mean age of patients was 31 years (mean age at diagnosis: 20 years).

NEED FOR MEDICAL SERVICES

On average, German patients needed 10.8 different kinds of medical services related to their disease, representing more than the average of 9.4 medical services for all countries. Hospitalisation occurred in 53% of patients for an average total duration of 22 days.

ACCESS TO MEDICAL SERVICES

Access to the eight essential services for each disease was easy in 71% of cases, difficult in 10% of cases and impossible in 8% of cases (*Figure 8*). Difficulty was mainly due to a lack of referral (53%), unavailability (15%) and location of the structures, including a location too far away (2%), no one to go with (13%) and difficulty in travelling (11%). The medical services respond to patients' expectations fully (68%), partially (28%), poorly (4%) or not at all (1%) (*Figure 9*).



Figure 8
Access to
medical services
in Germany

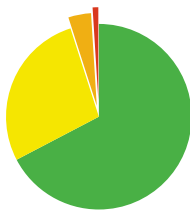


Figure 9
Satisfaction
with medical
services
in Germany

impossible very difficult difficult easy very easy

not at all poorly partially fully



Figure 10
Access to
social services
in Germany



Figure 11
Satisfaction
with social
services
in Germany

impossible very difficult difficult easy very easy

not at all poorly partially fully

SOCIAL ASSISTANCE

Amongst the 11% of families that required social assistance, all met with a social worker, 63% met with one easily and 37% met with one with difficulty (*Figure 10*). Compared to the European situation, this assistance was provided less frequently by community care structures and more by insurance or professional structures.

A total of 41% of German respondents were satisfied with this assistance, whereas 32% were not at all satisfied (*Figure 11*).

REJECTION

German patients experienced rejection by health professional less frequently (7% compared with 18%) than respondents overall for the 16 surveyed rare diseases. The reluctance of health professionals to treat patients due to the complexity of their disease was the main reason for rejection (75%), followed by disease-related behaviour (16%), a physical aspect (13%) and communication difficulties (9%).

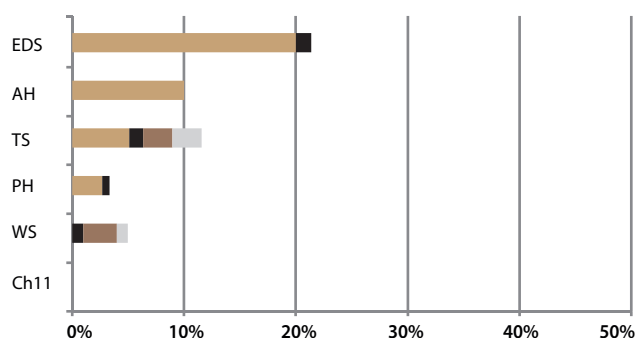


Figure 12 Cumulated frequencies of cause of rejection, by disease, in Germany. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

CONSEQUENCES OF THE DISEASE

As a consequence of the disease, 12% of German patients had to move house. Amongst these, families most frequently moved to a more adapted house (65%), to be nearer to disease specialists (11%) or to be closer to a relative (17%). As a consequence of their disease, 29% of patients had to reduce or stop their professional activity. In 34% of cases, a member of the family had to stop work in order to take care of a relative.



Socioeconomic Data

Total population: 11 216 708 (2008)
 Area of country: 131 990 sq km
 Population density: 84/sq km (2008)
 GDP: 343 billion \$ (2008)
 GDP/capita: 30 745 \$ (2008)
 % of GDP spent on health: 10% (2005)
 # of physicians/100 000 inhabitants: 438 (2006)

Greece

Sections of this chapter were written with the collaboration of the Greek Alliance of Rare Diseases (PESPA).

National Initiative in the Field of Rare Diseases

Although theoretically an employer-based system, in which all employees are enrolled in one of 35 social insurance funds, the Greek system, in essence, is highly centralised and regulated. Despite attempts made to decentralise decision making, with 17 regions responsible for implementing policy and managing the delivery of health care and 52 districts charged with the provision of many primary and secondary healthcare services, the majority of the power remains with the central government. Employers cannot choose their industry-specific social insurance to fund the services and costs vary greatly. The Greek National Health Service (NHS) operates parallel to the social insurance funds, acting essentially as a back-up mechanism; however in some rural areas it may be the principal provider of health services. Despite overlapping health plans, the Greek system falls short of universal coverage. As such, many Greeks routinely provide physicians with 'informal' payments for better access or better care. Using the European Orphan Drug Regulation Definition of one in 2000 people, an estimated 880 000 people live with a rare disease in Greece. In 2007, a commission made up of patient representatives, health professionals and government officials was created to help draft the Greek National Plan for Rare Diseases, for which an outline was officially presented to Parliament in February 2008 by the Greek Minister of Health. The state provides some psychological and social assistance to people living with rare diseases in a limited number of hospitals but relies a great deal on private associations to provide information to rare disease patients and private healthcare providers to provide additional everyday needs such as physiotherapy, occupational therapy and speech therapy. Public information measures only exist for the most prevalent rare diseases in Greece, including cystic fibrosis, thalassaemia and haemophilia. Neonatal screening exists for familial hypothyroidism, PKU and G6PD deficiency. A National Programme of Haemoglobinopathies (i.e. thalassaemia, sickle cell anaemia) includes carrier detection, prenatal diagnosis and patient diagnosis. Other diseases for which diagnostic testing is available in the public sector labs include cystic fibrosis, Duchenne and Becker muscular dystrophies, spinal muscular atrophy, fragile X disease, haemophilia, Gaucher disease and Fabry disease.

There are no more than six qualified private centres located in Athens offering mainly prenatal diagnostic services. The majority of private hospitals outsource specialised diagnostic services abroad (mainly to England). Genetic counselling is not recognised as a medical subspecialty in Greece. The National Organisation for Medicines (EOF) ensures the public health and safety of all medical products, including orphan drugs.



Socioeconomic Data

Total population: 10 041 000 (2008)

Area of country: 93 030 sq km

Population Density: 109/sq km (2008)

GDP: 199 billion \$ (2008)

GDP/capita: 19 800 \$ (2008)

% of GDP spent on health: 7.8% (2005)

of physicians/100 000 inhabitants: 332 (2006)

Hungary

Sections of this chapter were written with the collaboration of the Hungarian Williams Syndrome Association.

National Initiative in the Field of Rare Diseases

After a considerable reform following the collapse of the Communist era, Hungary's healthcare system has been transformed into a decentralised system financed by social insurance-based funds and supplemented by taxation. The national Health Insurance Fund (HIF) operates as a single-party payer supervised by the government and universally covers all citizens regardless of employment status, thus providing access to all ambulatory and secondary hospital health care.

The majority of primary care family physicians work as contracted private entrepreneurs. Patients make co-payments for certain services, including pharmaceuticals, dental care and rehabilitation, significantly contributing to healthcare financing. The practice of 'informal' payments has continued since the Communist era and significantly contributes to the total of out-of-pocket healthcare financing.

Within the National Centre for Healthcare Audit and Inspection, a new department, the National Centre of Surveillance for Congenital Anomalies and Rare Diseases responsible for the development of a national plan for rare diseases has been formed and is awaiting ratification by the Hungarian Parliament. In cooperation with the National Centre for Surveillance of Congenital Anomalies and Rare Diseases, an expert group has been formed to promote the implementation of new EU recommendations in the area of rare diseases. These and all other health authorities, professionals and organisations, including the National Institute of Pharmacy, use the European Union regulation definition of rare diseases, a prevalence of less than 1 per 2000 people. Some non-medical services for rare disease patients are available at the local level or by non-profit organisations, but demand remains much higher than the number of services available. As such, the Hungarian Federation of People with Rare and Congenital Diseases (HUFERDIS) is encouraging the creation of a Hungarian Rehabilitation Centre for Rare Disease Patients, based on such centres in other European countries, such as Norway.

The majority of public information measures, including web sites, newsletters, helplines and conferences are driven by patient organisations and additional efforts are needed. National support of patient organisations comes in part from the '1% Law', under which taxpayers can request 1% of their previous year's taxable income to be transferred to the non-profit organisation of their choice (which may include a patient organisation) without any loss to their earnings. In general, other resources for patient organisations are National Civil Fund grants aimed at strengthening

the operation of civil service organisations. Although these grants contribute to the support of many patient organisations, they are not entirely sufficient to facilitate the operation of desired programmes in the civil service sector. Some national grants are available from the limited budget of the National Medical Scientific Board and from the Hungarian Scientific Research Fund for Rare Disease Research.

Within the Scientific Health Council, a committee on the treatment of rare conditions has been established to help ensure rare disease patients receive adequate care by registering patients at appropriate treatment centres. Currently, 26 diseases are included in a neonatal screening program started in 1975. Physicians specialised in clinical genetics or human genetics provide genetic counselling services at the local level, regional level or specialised genetic centres. It is suggested that counsellors with non-medical degrees be trained to increase the availability of genetic counselling services.

Access to **Medical and Social Services** in Hungary

PARTICIPANTS IN THE SURVEY

AH	Ch11	WS (23)	PWS (2)
FRX	EB (10)	TS (10)	CF (140)
ANR	OI	MFS	EDS
HD	MG (223)	ATX	PAH

Figure 1
Seven diseases included in the survey and the number of responses in Hungary

Responses from 408 Hungarian families of patients with six diseases were analysed in the survey (*Figure 1*). The proportions of female and male patients represented were 66% and 34%, respectively. Females made up 79% of the population of MG respondents. The mean age of patients was 36 years (mean age at diagnosis: 23 years).

NEED FOR MEDICAL SERVICES

Overall, Hungarian patients needed 9.4 different kinds of medical services related to their disease (same as the average 9.4. medical services in the overall survey) with a slightly higher representation for consultations and tests and lower representation for care. Hospitalisation occurred in 55% of patients for an average total duration of 25 days.

MEDICAL SERVICES

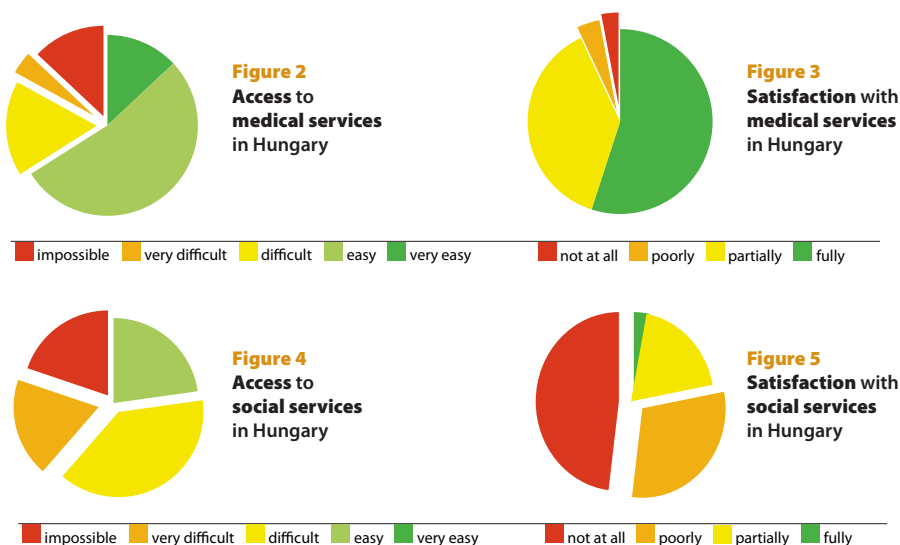
Access to the eight essential services for each disease was easy in 66% of cases, difficult in 21% of cases and impossible in 13% of cases (*Figure 2*). Difficulty was mainly due to unavailability (44%), lack of referral (24%), waiting time (18%), personal cost (17%) and location of the structures, including a location too far away (33%), no one to go with (36%) and difficulty in travelling (16%).

Once obtained, the medical services responded well to patients' expectations in 93% of cases and poorly in 7% of cases (*Figure 3*).

SOCIAL ASSISTANCE

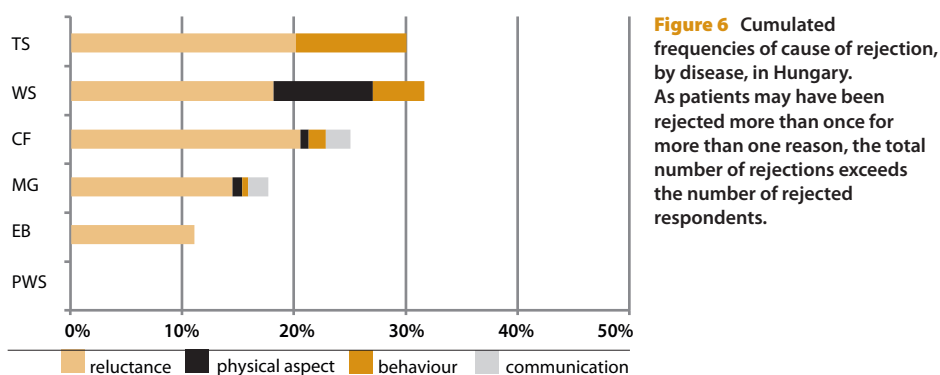
Amongst the 19% of Hungarian families that required social assistance, 20% (compared to 4% overall) failed to meet with a social worker, 23 %

(compared to 69%) met with one easily and 58% (compared to 27% overall) met with one with difficulty (Figure 4). Only 22% of Hungarian families were satisfied with this assistance, and 48% were not at all satisfied (Figure 5).



REJECTION

Hungarian patients experienced rejection by health professionals to a similar extent as the overall respondents (21% compared to 18%) for the 16 surveyed rare diseases. The reluctance of health professionals to treat patients due to the complexity of their disease was the main reason for rejection (80%), followed by communication difficulties (8%), disease-related behaviour (6%) and physical aspects (6%) (Figure 6).



CONSEQUENCES OF THE DISEASE

As a consequence of the disease, 14% of Hungarian patients had to move house. Amongst these, families most frequently moved to a more adapted house (48%), to be nearer to disease specialists (26%) or to be closer to a relative (21%). As a consequence of their disease, 21% of patients had to reduce or stop their own professional activity. In 29% of cases, one member of the family had to stop work in order to take care of a relative.



Socioeconomic Data
 Total population: 4 422 100 (2008)
 Area of country: 70 273 sq km
 Population density: 60.3/sq km (2008)
 GDP: 177 billion \$ (2006)
 GDP/capita: 45 600 \$ (2006)
 % of GDP spent on health: 8.2% (2005)
 # of physicians/100 000 inhabitants: 278 (2006)

Ireland

Sections of this chapter were written with the collaboration of Fighting Blindness, Ireland.

National Initiative in the Field of Rare Diseases

The Irish healthcare system, funded in part by general taxation, is characterised by a mix of public and private health service funding and provision. Overall formulation and evaluation of the healthcare system lies with the government, exercised through the Department of Health and Children (DOHC). In conjunction with the DOHC, the Health Service Executive is in charge of the strategic planning of health services.

All residents with a European Health Insurance Card are entitled to free maintenance and treatment in public Health Service Executive and voluntary hospitals. Outpatient services are also provided free of charge, although depending upon income, age, illness or disability, a subsidised fee is required for certain types of care received. The Medical Card, available to those receiving welfare payments, low earners, persons aged 70 or more, and those with certain long-term or severe illnesses, entitles holders to free hospital care, general practitioner visits, dental services, optical services, aural services, prescription drugs and medical appliances. Many support the idea of extending the availability of the Medical Card to cover every resident in Ireland. The European Orphan Drug Regulation definition of one per 2000 is used by all members of the health community.

Although there is currently no national plan for rare diseases, patient organisations are undertaking a lobbying campaign calling for this action. Recreational services are provided by support groups in specific disease areas. Public information measures about rare diseases include patient organisation web sites and information from rare disease national alliances, the Genetic and Rare Disorders Organisation (GRDO). The Medical Research Charities Group (MRCG) supports small patient groups in securing research funding for rare diseases. The Irish Platform for Patient Organisations, Science and Industry (IPPOSI) provides information and policy support to patient groups. Both organisations are funded in part by the government and through membership fees. Neonatal screening is not widely available and the GRDO, IPPOSI and the MRCG are all campaigning for better access to these services amongst many others pertaining to rare diseases and orphan drugs. Only six genetic counsellors provide services in the National Centre for Medical Genetics and most recently the budget for this service has been further cut.



Socioeconomic Data
 Total population: 59 619 290 (2008)
 Area of country: 301 338 sq km
 Population density: 197.6/sq km
 GDP: 1 888 trillion \$ (2007)
 GDP/capita: 32 319 \$ (2007)
 % of GDP spent on health: 8.9 (2005)
 # of physicians/100 000 inhabitants: 420 (2006)

Italy

Sections of this chapter were written with the collaboration of the Italian Alliance for Rare Disorders (UNIAMO).

National Initiative in the Field of Rare Diseases

The Italian healthcare system is a universal, regionally based public system. The National Ministry outlines funding needs based on historical funding patterns while the regional governments set their own budgets and organise healthcare delivery. The regions establish one or more Local Health Authorities (LHA), which are responsible for the provision of care. Private health insurance is available but not common. Financing comes from both payroll taxes and general revenues. Inpatient care and primary care are free of charge but co-payments are required for some services. Italians must register with a general practitioner in their LHA. A wide range of primary care, specialised care and additional health services are provided under the national system although some inequality exists between regions and overcrowding in hospitals is widespread.

Health authorities and professionals use the European Orphan Drug Regulation definition of a rare disease as having a prevalence of less than one per 2000 people. Discussion regarding a national plan for rare diseases is ongoing, with a scheduled approval in October 2008. Availability of non-medical services for rare disease patients varies considerably from region to region, with high quality services in some regions and no such services in others. Web sites, helplines and patient forums have been created by national alliances and single rare disease organisations as well as some public health institutions. No single coordinating body currently exists specifically for rare diseases and orphan drugs. Many state and regional agencies collaborate on these initiatives together. For example, Istituto Superiore di Santi (ISS) is responsible for the National Rare Disease Registry and Agenzia Italiana del Farmaco (AIFA) engages in discussions regarding orphan drugs and experimental therapeutic treatments and manages a special orphan drug research fund based on a pharmaceutical industry advertisement tax. Orphan drugs put on the market are distributed directly by or near hospitals, free of charge, in all regions of the country. Regions adopt their own policies for off-label use.

The National Ministry, the regions and AIFA provide important funding for rare disease research initiatives. Telethon, a non-profit organisation, is responsible for raising and distributing funds for the advancement of research toward diagnosis, cure and prevention of human genetic diseases

in universities and non-profit research institutes. It has also played a key role in raising awareness of rare diseases in Italy. Reimbursements for orphan drugs are based regionally and compassionate use is granted in very particular cases of patients suffering from very rare diseases. Neonatal screening exists for a few metabolic diseases. Genetic testing and counselling are provided for the most prevalent genetic diseases in Italy and diagnostic centres provide genetic counselling.

Diagnosis in Italy

PARTICIPANTS IN THE SURVEY

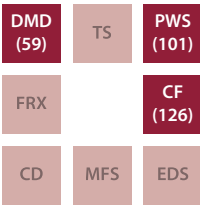


Figure 1
Diseases included in the survey and the number of responses in Italy

Responses from 286 families of patients with three diseases were analysed (*Figure 1*). An equal number of female and male patients were represented in the survey (47% and 53%, respectively).

DIAGNOSIS OVER THE FIRST THREE MONTHS OF LIFE

Neonatal diagnoses were obtained in 28% of patients, almost twice that observed for overall (15%), in particular for detection during pregnancy or at birth (14% compared with 7%) and neonatal testing (10% compared with 4%).

AWAITING THE DIAGNOSIS

Before obtaining the correct diagnosis, another diagnosis was given to 45% of patients, resulting in inappropriate treatments in 75% of cases, including medical (35%), surgical (7.5%) and psychological or psychiatric (7%) (*Figure 2*). During the quest for diagnosis, more than five physicians were consulted by 29% of families and more than ten by 9% of families. Physicians prescribed tests for 94% of patients, including biological tests (84%), genetic tests (42%), functional tests (51%) and X-rays (44%).

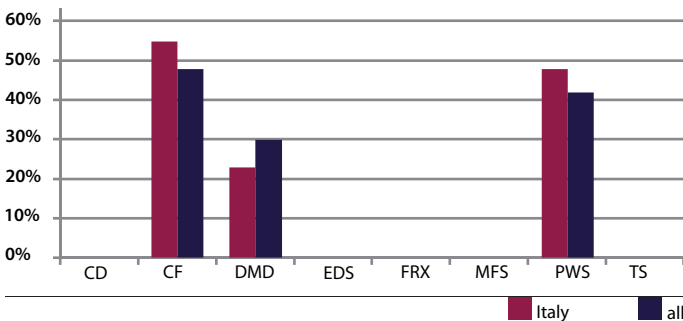
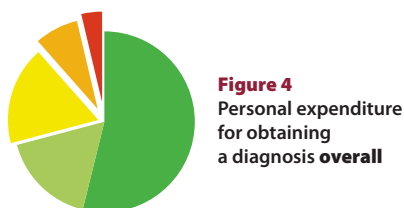


Figure 2
Percentage of patients initially receiving a misdiagnosis in Italy

DIAGNOSIS

The structures providing the diagnoses were hospital consultations (73%), specialised centres (23%) and rarely private practices (1% compared to

10% overall). These were located in another region in 21% of cases and in another country in 5.4%, representing almost three times the overall value of 1.9%. Personal cost was globally higher than that observed overall (*Figure 3 & 4*). Free diagnoses or low expenses were reported by 58% of respondents, whereas high or very high expenditure was reported by 21%. A second opinion was sought to confirm the diagnosis in one in three families, compared to one in five overall.

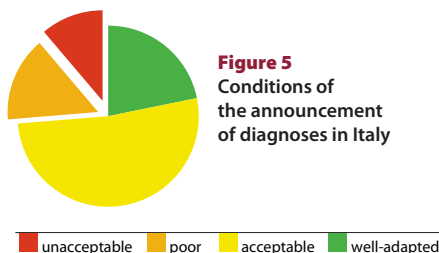


very high high moderate low no

ANNOUNCEMENT OF DIAGNOSIS

For 26% of patients, diagnoses were given without complete information on the disease; however 98% of respondents considered this information to be necessary. A total of 93% considered that psychological support was necessary at the time of the announcement of the diagnosis, whereas 78% of patients did not receive such support.

The genetic nature of the disease was explained to families in 86% of cases, with details given about the possibility of other cases in the family in 61% of cases. Genetic advice resulted in the diagnosis or identification of a carrier in family in 27% of cases. Respondents considered the conditions of the announcement to be poor or unacceptable in 26% of cases (*Figure 5*).



unacceptable poor acceptable well-adapted

For 77% of the families, delays in diagnosis were considered responsible for deleterious consequences, such as psychological consequences (6% compared to 13% overall) and birth of another affected child (2% compared to 7% overall).

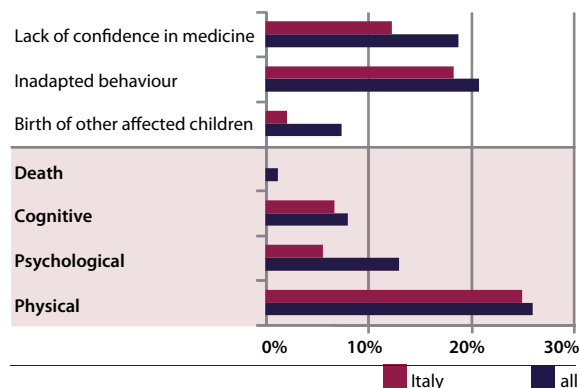


Figure 6 Medical and non-medical consequences of delayed diagnoses in Italy

Access to **Medical** and **Social Services** in Italy

PARTICIPANTS IN THE SURVEY

AH (16)	Ch11 (4)	WS (30)	PWS (111)
FRX (31)	EB (42)	TS (12)	CF (100)
ANR (31)	OI (84)	MFS (38)	EDS (21)
HD (33)	MG (79)	ATX	PAH (59)

Figure 7
Diseases
included in
the survey
and the
number of
responses
in Italy

Responses from 691 Italian families of patients with 15 diseases were analysed in the survey (Figure 7). The proportion of female and male patients represented were 55% and 45%, respectively. The mean age of patients was 29 years (mean age at diagnosis: 16 years).

NEED FOR MEDICAL SERVICES

Overall, Italian patients needed 9.7 different kinds of medical services related to their disease, which was close to overall value. Hospitalisation occurred in 53% of patients for an average total duration of 21 days.

MEDICAL SERVICES

The access to eight essential services for each disease was easy in 70% of cases, difficult in 17% of cases and impossible in 14% of cases (Figure 8). Difficulty was mainly due to lack of referral (59%), unavailability (20%), as well as waiting time (20%), personal cost (9%) and location of the structures, including a location too far away (15%), no one to go with (5%) and difficulty in travelling (10%). When obtained, the medical services responded well to patients' expectations in 90% of cases and poorly in 10% of cases (Figure 9).

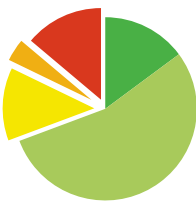


Figure 8
Access to
medical services
in Italy



Figure 9
Satisfaction
with medical
services
in Italy

impossible very difficult difficult easy very easy not at all poorly partially fully

SOCIAL ASSISTANCE

Amongst the 26% of Italian families that required social assistance, 3% failed to meet with a social worker, whereas 69% met with one easily and 28% met with one with difficulty (Figure 10).

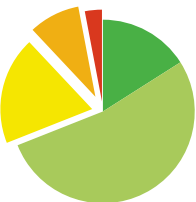


Figure 10
Access to
social services
in Italy



Figure 11
Satisfaction
with social
services
in Italy

impossible very difficult difficult easy very easy not at all poorly partially fully

Community care structures play a more important role in Italy than overall in Europe (71% compared with 53%). A total of 53% of Italian families were satisfied with this assistance while 32% were not at all satisfied (*Figure 11*).

REJECTION

Italian patients experienced rejection by health professionals slightly less frequently (14% compared to 18%) than respondents overall for the 16 surveyed rare diseases.

The reluctance of health professionals to treat patients due to the complexity of their disease was the main cause of rejection (85%), followed by disease-related behaviour (15%), communication difficulties (14%) and physical aspects (5%) (*Figure 12*).

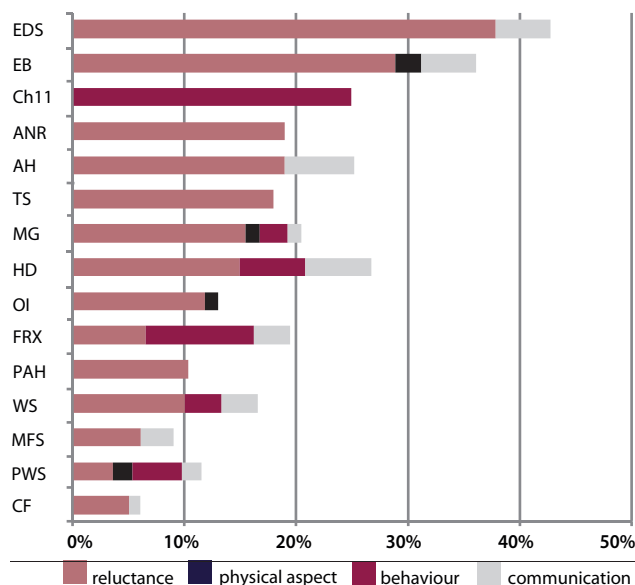


Figure 12 Cumulated frequencies of cause of rejection, by disease, in Italy. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

CONSEQUENCES OF THE DISEASE

As a consequence of the disease, 12% of Italian patients had to move house. Amongst these, families most frequently moved to a more adapted house (54%), to be nearer to disease specialists (25%) or to be closer to a relative (25%).

As a consequence of their disease, 19% of patients had to reduce or stop their professional activity. In 36% of cases, a member of the family had to stop working in order to take care of a relative.



Luxembourg

Sections of this chapter were written with the collaboration of the Task Force for Rare Diseases Luxembourg.

Socioeconomic Data

Total population: 480 222 (2007)
 Area of country: 2 586 sq km
 Population density: 186/sq km (2007)
 GDP: 32.6 billion \$ (2006)
 GDP/capita: 60 870 \$ (2007)
 % of GDP spent on health: 7.7% (2005)
 # of physicians/100 000 inhabitants: 260 (2002)

National Initiative in the Field of Rare Diseases

Luxembourg's healthcare system is based on three fundamental principles: compulsory health insurance, free choice of the provider by the patient and compulsory provider compliance with the fixed and set fees-for-services. While the standard contribution level is set by the government, the Union of Sickness funds manages and provides statutory health insurance for 99% of the population. Voluntary health insurance has always played a limited role in Luxembourg in terms of reimbursement. Nevertheless, approximately 75% of the population purchase complementary health insurance schemes to pay for services categorised as unnecessary. Preventive services are the responsibility of the Ministry of Health. Interventions are provided by public services, private practitioners and non-profit associations paid from the ministry's budget. Similar to its neighbouring countries, Luxembourg's healthcare system is mainly publicly financed through social health insurance. Providers are usually contracted. Reimbursement is valid regardless of the setting in which the patient has received the care. It is important to note that per capita expenditure calculations are based on the resident population, which can be misleading because 37.3% of Luxembourg's insured workers are foreign workers; Luxembourg's per capita GDP is actually the highest in the OECD countries.

The European Union Orphan Drug Regulation definition of a rare disease of less than one per 2000 people is accepted by all stakeholders. In 2005, a national Task Force on Rare Diseases Luxembourg was created to analyse the needs of rare disease patients in the country. The task force is in the final stages of proposing a national plan for rare diseases based on a survey analysing the major strengths and weaknesses of the healthcare system and the experiences of rare disease patients. The task force is also near completion of a national rare disease platform that offers specific medical and social services, a rare disease hotline, counselling, self-help groups, specialised information on rare diseases and guidelines of best practices, as well as recreational activities for patients and their families. The task force is currently elaborating a guide to all medical, paramedical and social services available for rare disease patients and their families, scheduled to be available online in 2009. Many projects of the task force aim also to support and empower patient organisations. The patient organisation ALAN asbl, offers guidance for services particular to rare disease patients as well as psychological support in form of self-help groups, counselling, a helpline and pain management for children and adults.

Respite care is partially reimbursed by the social security system, however, a number of rare disease patients cannot benefit from them because the services do not address the complexity of the care needed. One main objective of the task force is the creation of a national medical commission to consult on issues regarding access and reimbursements of orphan drugs and the development of guidelines of best practice in collaboration with international networks. Lions Clubs in Luxembourg contribute to research funding by organising an annual rare disease telethon.

Money raised is pooled with that of the French "Association Française contre les Myopathies" (AFM), which redistributes the funds for research projects in Luxembourg. Genetic counselling is recognised as a profession, and patients have access to genetic counselling if prescribed by a general practitioner. However a great number of patients seek genetic testing and counselling services abroad. The reimbursement of genetic counselling is not always guaranteed.



Socioeconomic Data

Total population: 16 375 000 (2008)
 Area of country: 41 526 sq km
 Population density: 395/sq km
 GDP: 671 billion \$ (2006)
 GDP/capita: 35 078 \$ (2007)
 % of GDP spent on health: 9.2% (2005)
 # of physicians/100,000 inhabitants:
 314 (2006)

Netherlands

Sections of this chapter were written with the collaboration of the Dutch National Alliance for Genetic and Rare Diseases (VSOP).

National Initiative in the Field of Rare Diseases

A recent health reform in the Netherlands has replaced the previous social health insurance programme and alternative private health insurance option with a requirement that all Dutch citizens must purchase a basic health insurance plan from one of 41 private insurance companies with subsidies based on disability, illness and ability to pay. The new Dutch system operates on the theory of managed competition, where the provision of health care and health insurance is private, but in an artificial marketplace, highly regulated by the government. Patients are able to choose their family physician but must register with a specific primary care practice. Family physicians act as gatekeepers to the system and must give their approval before patients can access hospital and specialist care.

The European Orphan Drug Regulation definition of one per 2000 people is used by all stakeholders in the rare disease community. The Dutch Steering Committee on Orphan Drugs, as appointed by the Ministry of Health, is in charge of encouraging the development of orphan drugs and improving the provision of information on rare diseases. Along with the Dutch Genetic Alliance, this committee, which includes patients among other stakeholders, is pushing the Dutch parliament to put the subject of a national plan on the political agenda in several ways, including the establishment of centres of expertise and research programmes dedicated specifically to rare diseases. Non-medical services for rare disease patients vary greatly depending on the organisation of care for the disease or the existence of a Centre of Expertise or active patient organisation.

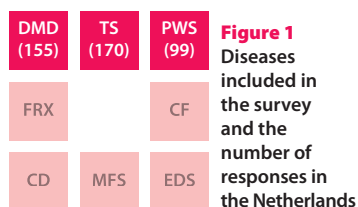
The Dutch Genetic Alliance, an umbrella patient organisation, aims to optimise the implications of research in the fields of genetics, medical biotechnology and life sciences via participation in national and international committees active in (i) advocating the interests of member organisations, (ii) stimulating publication and research in the field and (iii) raising awareness in the field through its information centre. The Dutch Genetic Alliance has founded Erfocentrum, through which a helpline and several information web sites have been established. The Federation of Patients and Consumer Organisations in the Netherlands (NPCF) and the Chronically Ill and Disabled Council of the Netherlands have similar missions, although these are destined for patient organisations, in general. Currently, 17 rare diseases are screened for at birth and new diseases may soon be added to this list. Genetic counselling is recognised as a medical profession and genetic testing and counselling is available at all university

medical centres. Access to most orphan drugs is adequate, although in some cases it takes a long time for a registered drug to be filed for reimbursement. Of the, currently, 46 different orphan medicinal products with marketing authorisation in Europe, 30 are reimbursed.* For six orphan drugs a reimbursement dossier can be filed. A special information booklet about how to obtain an orphan drug was written for patients by the Dutch Steering Committee on Orphan Drugs in 2007.

* As of October 2008.

Diagnosis in the Netherlands

PARTICIPANTS IN THE SURVEY



Responses from 424 families of patients with three diseases, occurring early in the life, were analysed (*Figure 1*). An uneven number of female and male patients were represented in the survey (32% and 68%, respectively). This was mainly due to the proportion (37%) of DMD patients.

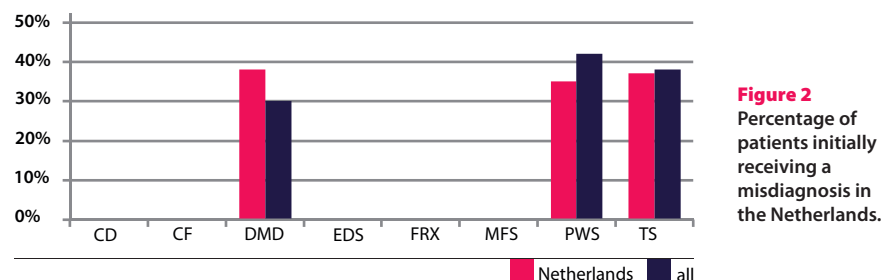
DIAGNOSIS OVER THE FIRST THREE MONTHS OF LIFE

Neonatal testing was more frequent in the Netherlands than overall (8% compared to 4%). However other neonatal diagnoses were less frequent, such as either disorders observed during pregnancy or at birth (3% compared to 7% overall) and diagnoses linked to other cases in the family (1.4% compared to 3% overall).

AWAITING THE DIAGNOSIS

Before obtaining the correct diagnosis, another diagnosis was given to 37% of patients, resulting in inappropriate treatments for 52% of patients. This included medical (25%), surgical intervention (3%) and psychological or psychiatric (2%) treatments (*Figure 2*).

During the quest for diagnosis, more than five physicians were consulted by 13% of families and more than ten by 3%. Physicians prescribed tests for 99% of patients, including biological tests (68%), genetic tests (38%), functional tests (59%) and X-rays (50%).



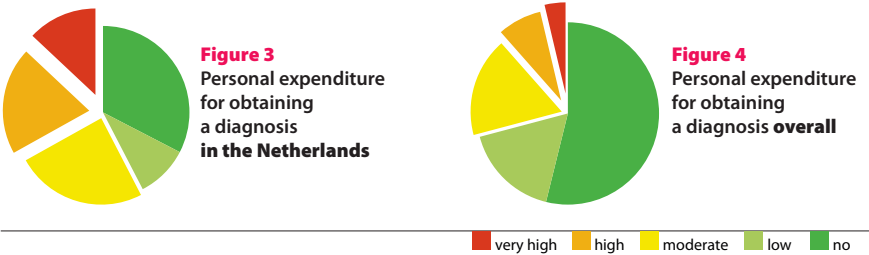
DIAGNOSIS

Compared to the overall situation, the hospital setting plays a crucial role in providing diagnoses (80% compared to 61% overall) to patients in

the Netherlands and private practice is almost non-existent (1% compared to 10% overall). These were frequently located in another region (38%) and rarely in another country (0.5%).

Personal expenditure for diagnosis in the Netherlands is dramatically high (Figure 3). Free access to medical services is scarce and expenditure was considered moderate by 58% and very high by 13% (compared to 4% overall) (Figure 4).

A second opinion was sought by 9% of families to confirm the diagnosis (low compared to 21% overall).

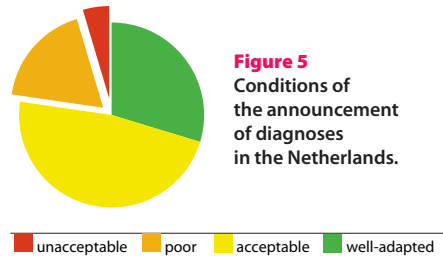


ANNOUNCEMENT OF DIAGNOSIS

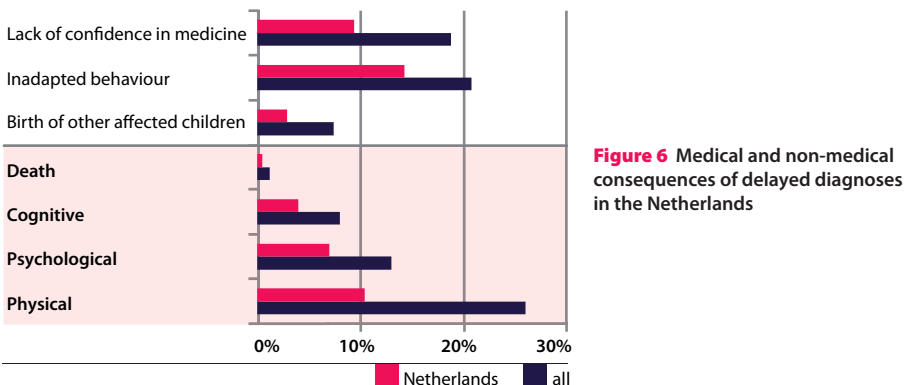
For 37% of patients, diagnoses were given without complete information on the disease, although 93% of respondents considered this information to be necessary. A total of 83% of respondents considered that psychological support was required at the time of the announcement, whereas 73% of patients did not receive such support.

The genetic nature of the disease was explained to families in 83% of cases, with details about the possibility of other cases in the family given in 71% of cases. Genetic counselling resulted in the diagnosis or identification of a carrier in family in 15% of cases.

Dutch patients reported a low rate of poor or unacceptable conditions of the announcement of the diagnosis (23% compared with 35% overall) (Figure 5).



For 56% of the families, delays in diagnosis were considered responsible for deleterious consequences (Figure 6).



Access to **Medical** and **Social Services** in Netherlands

PARTICIPANTS IN THE SURVEY

AH (3)	Ch11 (13)	WS	PWS
FRX	EB	TS	CF
ANR	OI (97)	MFS	EDS
HD	MG (150)	ATX (24)	PAH (110)

Figure 7
Seven diseases included in the survey and the number of responses in the Netherlands

Responses from 397 Dutch families of patients with six diseases were analysed in the survey (*Figure 7*). The proportion of female and male patients represented were 66% and 34%, respectively. There were more females represented in MG and PAH. The mean age of patients was 50 years (mean age at diagnosis: 33 years).

NEED FOR MEDICAL SERVICES

Overall, Dutch patients needed 7.6 different kinds of medical services related to their disease (fewer than the average 9.4 medical services).

Hospitalisation occurred in 45% of patients for an average total duration of 18 days.

MEDICAL SERVICES

Access to the eight essential services for each disease was easy in 89% of cases, difficult in 6% of cases and impossible in 6% of cases (*Figure 8*).

This was mainly due to lack of referral (39%), unavailability (14%), waiting time (11%), personal cost (5%) and location of the structures, including a location too far away (18%), no one to go with (11%) and difficulty in travelling (18%).

When obtained, the medical services responded well to patients expectations in 95% of cases and poorly in 5% of cases (*Figure 9*).

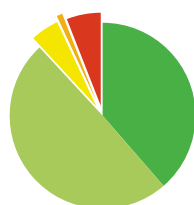


Figure 8
Access to medical services in the Netherlands

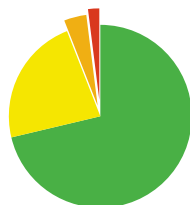


Figure 9
Satisfaction with medical services in the Netherlands

impossible very difficult difficult easy very easy not at all poorly partially fully

SOCIAL ASSISTANCE

Amongst the 24% of Dutch families that required social assistance, 1% failed to meet with a social worker, 72% met with one easily and 27% met with one with difficulty (*Figure 10*).

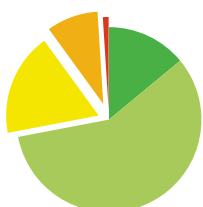


Figure 10
Access to social services in the Netherlands.



Figure 11
Satisfaction with social services in the Netherlands.

impossible very difficult difficult easy very easy not at all poorly partially fully

Half of the Dutch respondents (50%) were satisfied with this assistance, while 19% were not at all satisfied (*Figure 11*).

REJECTION

Dutch patients experienced rejection by health professional to a degree similar (17% compared to 18%) to respondents overall for the 16 surveyed rare diseases (*Figure 12*). The reluctance of health professionals to treat patients due to the complexity of their disease was the main cause of rejection (71%), followed by physical aspects (18%), communication difficulties (11%) and disease-related behaviour (3%).

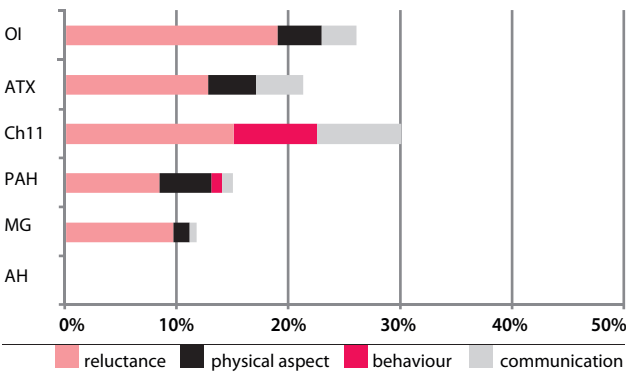


Figure 12 Cumulated frequencies of cause of rejection, by disease, in the Netherlands. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents

CONSEQUENCES OF THE DISEASE

As a consequence of the disease, 22% of Dutch patients had to move house. Amongst these, families most frequently moved to a more adapted house (74%), to be nearer to disease specialists (4%) or to be closer to a relative (13%). As a consequence of their disease, 40% of patients had to reduce or stop their professional activity. In 13% of cases, one member of the family had to stop work to take care of a relative.

Norway



Sections of this chapter were written with the collaboration of the Frambu, the Norwegian national centre for rare disorders and disabilities.

Socioeconomic Data
 Total population: 4,777,100 (2008)
 Area of country: 385,252 sq km
 Population density: 12/sq km (2008)
 GDP: 212.0 billion \$ (2007)
 GDP/capita: 17 060 \$ (2007)
 % of GDP spent on health: 9% (2006)
 # of physicians/100,000 inhabitants: 313 (2006)

National Initiative in the Field of Rare Diseases

Norway has a universal, tax-funded, single-payer national health system. Although the state has overall authority over the healthcare system, some management and funding responsibilities have been delegated to regional and local governments. In general, local governments are responsible for primary health care, while four regional health authorities are responsible for specialist care. Norwegians do not have free choice of a physician but must choose a general practitioner from a government list.

This general practitioner then acts as a gatekeeper for all other services and providers, and specialists may only be seen with a referral. Citizens can usually change physicians a maximum of twice a year.

Health authorities and professionals use a prevalence of less than 500 persons in Norway to define a rare disease. In the national strategy rehabilitation plan the situation for rare diseases is included. But a group from one of the four regional health authorities is currently revising the plan for rare diseases and will present suggestions for the future in spring 2009. Patients in need of respite care or recreation services can apply to their local health authorities.

The Norwegian Directorate of Health coordinates national centres of excellence for rare diseases. The Directorate of Health, certain centres of excellence and patient organisations have created web sites as public information tools. As the state prefers and encourages the creation of larger organisations, sizable patient organisations receive financial support but many new organisations with few members do not receive any. Neonatal screening for PKU and congenital hypothyroidism exists. Genetic counselling is free and genetic testing is available on (reasonable) demand. In principle, all drugs, including orphan drugs, are reimbursed by the state. Some hospitals apply for extra funding from the state for very costly drugs.



Poland

Sections of this chapter were written with the collaboration of the MATIO Cystic Fibrosis Foundation of Poland.

Socioeconomic Data

Total population: 38 116 000 (2007)
 Area of country: 312 679 sq km
 Population density: 122/sq km (2007)
 GDP: 620.9 billion \$ (2007)
 GDP/capita: 16 600 \$ (2007)
 % of GDP spent on health: 3.2% (2005)
 # of physicians/100 000 inhabitants: 246 (2006)

National Initiative in the Field of Rare Diseases

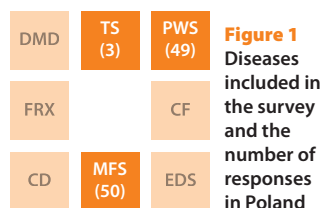
The Ministry of Health's key responsibility includes the establishment of health policies. The system has traditionally been centralised in its approach, although constant efforts have been made to decentralise authority and promote efficiency. The system is state-financed through the National Health Fund (NFZ), to which every employed citizen is required to contribute. Employee contributions are deducted directly from salaries by employers. People who are covered by the national health insurance system, and their dependents, are entitled to free primary health care, specialist outpatient care, hospital treatment, dental treatment and ambulance transport, although informal out-of-pocket payments are very common. Standards of medical care are adequate in Poland, although hospital facilities are of a lower standard than in many Western countries. Emergency services are lacking in some rural areas and most specialist forms of health care are available only in larger cities. Patients are able to consult specialists directly without a primary care provider's referral, although a system oriented towards primary care services is being established to strengthen the function of general practitioners as gatekeepers. Many would argue that the low maintenance of the healthcare system by the state reflects efforts to push the system towards privatisation. Indeed, private healthcare provision has increased dramatically in the last two decades.

The official definition of rare diseases in Poland is an incidence of one per 3000 births. Currently, plans and strategies exist only for single diseases (some of which are rare). The Commission of Systemic Diseases, a working group of the Committee of Human Development, working within the framework of the independent government-funded research organisation the Polish Academy of Sciences, focuses on rare disease issues, including the development of a national rare disease programme for Poland. A first action toward this goal was the appointment of an Orphanet Advisory Board to the committee in cooperation with the Polish Paediatric Society. State-sponsored social services exist but lack funding, appropriate training and qualification of employees, and awareness about the needs of rare disease patients.

Information on these social services, including recreational and rehabilitation activities, is most often distributed by patient organisations. Rare disease web sites and helplines are also created by patient organisations. No national initiatives exist to support patient organisations as a whole, but smaller grants exist for projects such as the organisation of workshops and conferences. In 2005 a national forum on the treatment of orphan diseases was created, mainly dedicated to the treatment of lysosomal storage diseases. Neonatal screening of PKU and hypothyroidism exists and a recent newborn screening program for cystic fibrosis will be introduced in all regions of Poland by 2009. Genetic testing is available in public as well as private healthcare facilities.

Diagnosis in Poland

PARTICIPANTS IN THE SURVEY



Responses from 102 families of patients with three diseases were analysed (*Figure 1*). An equal number of female and male patients were represented in the survey (49% and 51%, respectively).

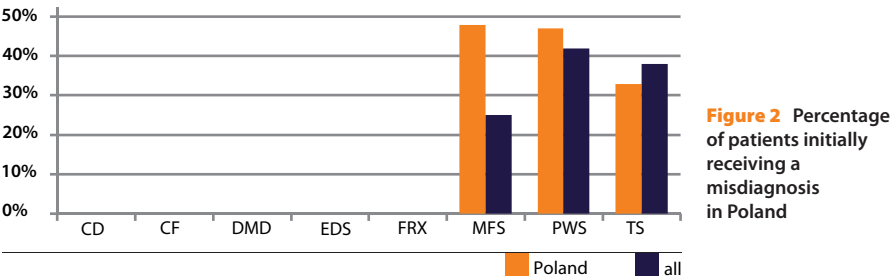
DIAGNOSIS OVER THE FIRST THREE MONTHS OF LIFE

Neonatal diagnoses were obtained in 9% of patients, lower than that observed overall (15%). This was primarily due to less neonatal testing (1% compared to 4%) and fewer observations during pregnancy or at birth (3% compared to 7% overall).

AWAITING THE DIAGNOSIS

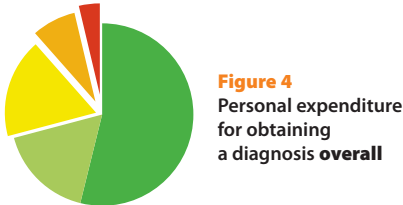
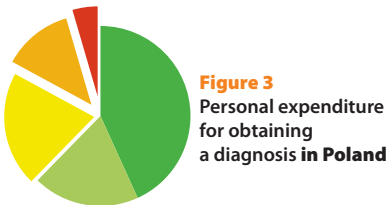
Before obtaining the correct diagnosis, another diagnosis was given to 47% of patients and resulted in 78% of patients receiving inappropriate treatment, including medical (29%), surgical (11%) and psychological or psychiatric (18% compared to 7% overall) (Figure 2).

During the quest for diagnosis, more than five physicians were consulted by 45% of families and more than ten physicians by 22% of families. Physicians prescribed tests for 99% of patients, including biological tests (69%), genetic tests (55%), functional tests (52%) and X-rays (56%).



DIAGNOSIS

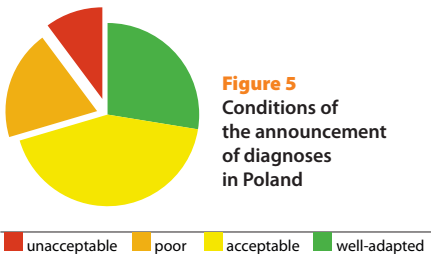
The structures providing the diagnoses were hospital consultations (47%), specialised centres (24%) and private practices (5%). These were located in another region in 45% of cases and in another country in 2.2% of cases. Diagnosis was considered slightly more expensive in Poland (Figure 3), with less free diagnosis. Respondents felt more frequently than the overall average that their expenditure was moderate to high (Figure 4). A second opinion was sought by 27% of families to confirm the diagnosis.



ANNOUNCEMENT OF DIAGNOSIS

For 26% of patients, diagnoses were given without information on the disease and 46% (compared to 95% overall) of respondents considered this information to be necessary.

The announcement of the diagnosis was accompanied by psychological support in 23% of cases and 16% (compared to 87% overall) considered this support necessary.



The genetic nature of the disease was explained to families in 63% of cases, with details about the possibility of other cases in the family in 61% of cases. Genetic advice resulted in the diagnosis or identification of a carrier in the family in Poland (10% compared to 32% overall). A total of 30% of respondents considered the announcement of the diagnosis to be poor or unacceptable (*Figure 5*).

CONSEQUENCES OF DELAYED DIAGNOSIS

A total of 93% of the families considered that the delays in diagnosis were responsible for deleterious consequences.

Each family reported an average of two different deleterious consequences (*Figure 6*).

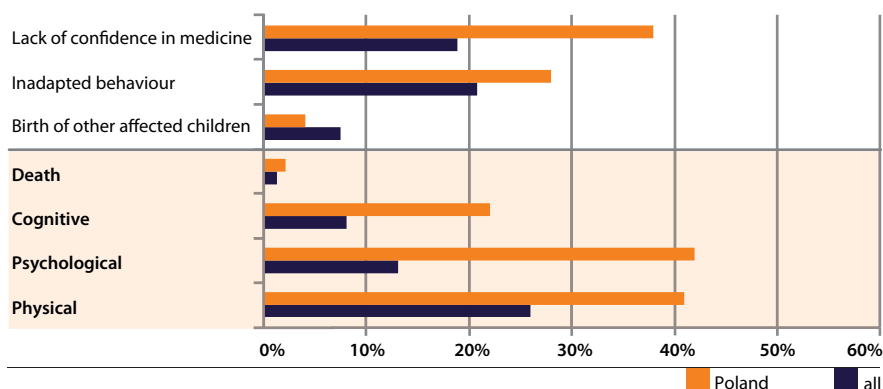
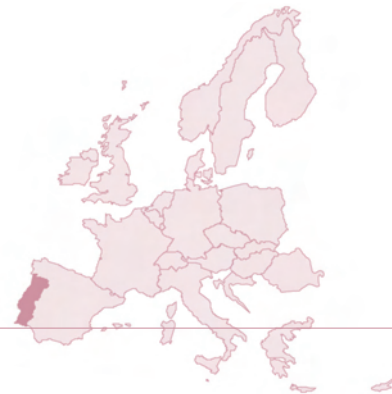


Figure 6 Cumulated frequencies of cause of rejection, by disease, in Poland. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents



Portugal

Sections of this chapter were written with the collaboration of the Portuguese Association for Haemophilia.

Socioeconomic Data

Total population: 10 617 575 (2007)
 Area of country: 92 345 sq km
 Population density: 114/sq km (2007)
 GDP: 230.6 billion \$ (2007)
 GDP/capita: 23 464 \$ (2006)
 % of GDP spent on health: 10.2% (2006)
 # of physicians/100 000 inhabitants: 342 (2006)

National Initiative in the Field of Rare Diseases

The Ministry of Health is responsible for developing health policy and overseeing and evaluating its implementation. However, for some diseases there are specific programmes that are coordinated and developed by the Directorate General of Health and the High Commissariat for Health. Regional health administrations are responsible for the implementation of national health policy objectives and coordinating all levels of health care. These are divided further into 18 sub-regions. Disparities in health services exist between regions, although all citizens are expected to have equal access to the services. These disparities arise from the socioeconomic diversity across regions in the country.

Portugal's national health service is predominately financed by taxes and universally covers most citizens through employer-based health insurance schemes. All Portuguese citizens are covered by the National Health Service and may also be eligible for other public insurance schemes or have private health insurance. Even under the national service, co-payments for diagnostic tests, hospital admissions, consultations with specialists and prescription drugs are required and can be quite high. Primary care physicians, hospital doctors and specialists are all public employees but are allowed to practice privately, and many do. Recent healthcare reforms have attempted to improve deficiencies in the healthcare system by creating one in which publicly and privately owned providers coexist to better meet the healthcare needs of Portugal's citizens.

The European Orphan Drug Regulation definition of one in 2000 individuals is accepted and used by most stakeholders. In 2007, during the Fourth European Conference on Rare Diseases, the Portuguese Plan for Rare Diseases was presented. Since this formal presentation, approval by the Health Ministry is still being awaited. Many measures outlined in the plan are already underway. Although social services do exist for all citizens in need, there are no specific services for rare disease patients who systematically have to wait much longer than others to receive the help they need. A few recreational services for handicapped patients are available but again not for rare disease patients specifically. Respite care is not yet a common practice in Portugal. It is frequently patient organisations that provide these services to the specific population they represent.

Sparse public information about rare diseases is available on the Portal da Saúde (health portal) of the Portuguese Ministry of Health. Information is also available on Portuguese web site of Orphanet. Information on specific rare diseases is available on the diverse web sites of the Portuguese rare disease patient organisations. Some Portuguese patient organisations receive financial support from the state, and there are many programmes that sponsor specific activities proposed by patient organisations. National measures for prevention, diagnosis and neonatal screening of several hemoglobinopathies exist. Prevention, diagnosis and care measures exist for other rare diseases, although not on a national level. The Directorate General of Health and Infarmed (National Authority on Medicines and Health Products) are two coordination bodies for rare diseases and orphan drugs. Initiatives to improve access to treatment for some rare diseases currently exist. The complete implementation of the national plan will increase the number of diseases for which this is a reality. The proposed plan also includes increased funding initiatives specifically for rare disease research. Genetic testing is provided for female carriers or patients of several rare diseases, including many rare bleeding disorders, Von Willebrand disease and Huntington's disease. Medical doctors specialised in genetics provide genetic counselling, which is not recognised as a medical subspecialty.



Socioeconomic Data

Total population: 22 246 862 (2008)
 Area of country: 238 391 sq km
 Population density: 93/sq km (2008)
 GDP: 264 billion \$ (2008)
 GDP/capita: 12 285 \$ (2008)
 % of GDP spent on health: 5.5% (2006)
 # of physicians/100,000 inhabitants: 190 (2006)

Romania

Sections of this chapter were written with the collaboration of the Romanian Prader Willi Association and the Romanian National Alliance for Rare Diseases (RONARD).

National Initiative in the Field of Rare Diseases

Romania's healthcare system, once state-owned and tax-based, is now more decentralised. The Ministry of Public Health is the central authority, responsible for setting public health priorities. The system is now funded through two sources: (a) social insurance through the National Health Care Insurance Fund, to which employers and employees make mandatory contributions, and (b) taxes (including taxes on alcohol and tobacco) that are directed by the Ministry of Public Health policies towards the national health programmes and capital investments in health. Private health insurance has developed slowly, and due to low public funding approximately 36% of healthcare spending is out of pocket. Informal payments are very common for obtaining improved treatment. Primary healthcare services are mainly delivered by private general practitioners acting as gatekeepers to specialised services. Secondary and tertiary care are mostly publicly owned and administered by the state. Long-term lack of funding of the healthcare system during the Ceausescu regime and the low quality of medical equipment has resulted in decreased healthcare standards, in particular in rural areas.

Romanian health authorities and professionals use the European Orphan Drug Regulation prevalence of less than one in 2000 people to define rare diseases. At the end of 2007, the Romanian Prader Willi Association and the Romanian National Alliance for Rare Diseases (RONARD) (initiated by the Romanian Prader Willi Association) concluded a partnership agreement with the Ministry of Public Health (MPH) for the creation of the first National Plan for Rare Diseases in Romania. The National Plan foresees as one of its first missions the establishment of an interdisciplinary commission for rare diseases, the first priority on the MPH agenda. As a consequence of creating the National Plan, the MPH health programme enlarged coverage of orphan drugs beginning in July 2008. The creation of rare disease registries has also been a product of this work. Non-medical services exist for all patients with disabilities in Romania, but not specifically for rare disease patients.

The Romanian Prader Willi Association acts a centre of information not only for Prader Willi, but also for all other rare diseases. Through this centre, counselling services, support groups and training are also available. The National Plan will guarantee the development of the Romanian Prader

Willi Association centre into a reference and training centre. Currently neonatal screening exists for several diseases, although availability is not yet complete at the national level. Genetic counselling can only be provided by physicians specialising in genetics. Until recently all genetic testing was done abroad through foreign hospitals and clinical centre partnerships.

Access to **Medical** and **Social Services** in Romania

PARTICIPANTS IN THE SURVEY

AH	Ch11	WS (5)	PWS (29)
FRX	EB (22)	TS	CF
ANR	OI (4)	MFS	EDS
HD	MG	ATX	PAH

Figure 1
Diseases included in the survey and the number of responses in Romania

Responses from 60 Romanian families of patients with four diseases were analysed in the survey (*Figure 1*).

The proportions of female and male patients represented were 54% and 46%, respectively.

The mean age of patients was 18 years (mean age at diagnosis: 11 years).

NEED FOR MEDICAL SERVICES

Overall, Romanian patients needed 16.3 different kinds of medical services related to their disease, more than the average 9.4 medical services.

Hospitalisation occurred in 73% of patients for an average total duration of 33 days.

MEDICAL SERVICES

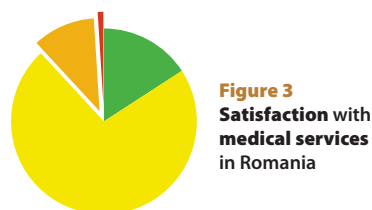
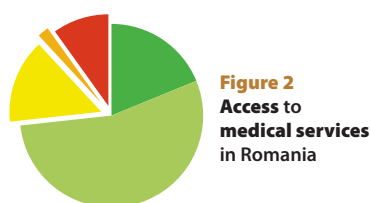
Access to the eight essential services for each disease was easy in 72% of cases, difficult in 17% of cases and impossible in 10% of cases (*Figure 2, p272*). Difficulty was mainly due to lack of referral (59%), unavailability (34%), waiting time (34%), personal cost (3%) and location of the structure, including a location too far away (52%), no one to go with (55%), cost of the journey (66%) and difficulty in travelling (7%).

When obtained, the medical services responded well to patients' expectations in 89% of cases and poorly in 11% of cases (*Figure 3, p272*).

SOCIAL ASSISTANCE

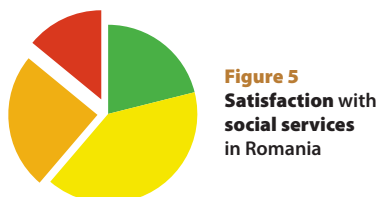
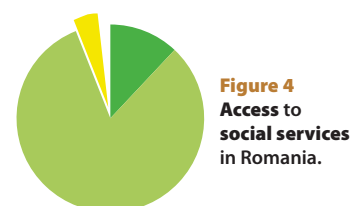
Amongst the 53% of Romanian families needing social assistance, all met with a social worker, and 94% met with one easily and 6% met with one with difficulty.

In Romania, social assistance is provided mainly from ‘private’ sources, associations (71%) and religious (7%) establishments. Romanian families (61% compared to 50% overall) were satisfied with this assistance, 14% not at all (28% overall).



impossible very difficult difficult easy very easy

not at all poorly partially fully

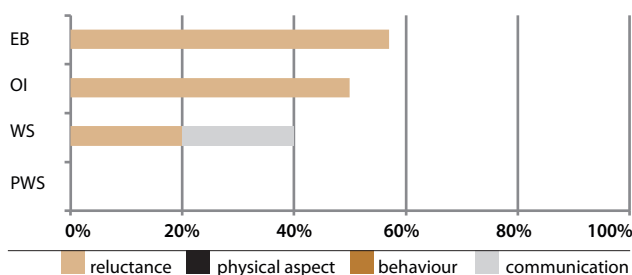


impossible very difficult difficult easy very easy

not at all poorly partially fully

REJECTION

Romanian patients experienced rejection by health professional in 25% of cases (compared to 18% overall) for the 16 surveyed rare diseases (*Figure 6*). The reluctance of health professionals to treat patients due to the complexity of their disease was the main cause of rejection (100%), followed by communication difficulties (7%).



As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents

CONSEQUENCES OF THE DISEASE

As a consequence of the disease, 19% of Romanian patients had to move house. Amongst these, families moved to a more adapted house (55%), to be nearer to disease specialists (9%) or to be closer to a relative (46% compared to 18% overall). As a consequence of their disease, 20% of patients had to reduce or stop their professional activity. In 73% of cases, a member of the family had to stop work in order to take care of a relative (compared to 33% overall).



Socioeconomic Data
 Total population: 5 388 000 (2006)
 Area of country: 49 035 sq km
 Population Density: 111/sq km (2001)
 GDP: 110 billion \$ (2007)
 GDP/capita: 17 060 \$ (2007)
 % of GDP spent on health: 7% (2006)
 # of physicians/100 000 inhabitants: 317 (2006)

Slovakia

Sections of this chapter were written with the collaboration of the Slovakian Cystic Fibrosis Association (Klub Cystickej Fibrozy).

National Initiative in the Field of Rare Diseases

Today, Slovakia's healthcare system is characterised by a mixture of decentralised and centralised structures, although the transition from state monopoly has been gradual. Until recently, the Ministry of Health continued to own, run and control most inpatient care facilities and some outpatient specialist facilities. Today, many of the state's responsibilities have been transferred to the regions or municipalities. The previously tax-based system has now become one ensuring universal coverage and access to free-of-charge healthcare services based on mandatory health insurance with marginal co-payments for related services. A very strong sense of entitlement and a strong resistance to health insurance and/or healthcare provision schemes that ration access to health services still exists, and informal payments supplementing the once inadequate services remain common.

Since its transition after the Communist era, most providers of primary health care and many specialists providing secondary care have gone into private practice and links between primary healthcare providers and secondary health care have weakened. As such, healthcare delivery has since become fragmented. Primary care physicians act as gatekeepers to specialist care services, although patients with chronic illnesses who are registered in a specialist's clinic have direct access to the appropriate specialist physicians. Although no official definition of rare diseases exists, health authorities and health professionals accept the European Orphan Drug Regulation definition of prevalence below one per 2000 persons. No national plan for rare diseases and no progress have yet been made, although the Ministry of Health has announced a focus on rare diseases as a new aspect of its policy. Many non-medical services are provided though not specifically for rare diseases. The majority of web sites, helplines and patient counselling services that exist for rare diseases are operated by non-governmental organisations, but a few such projects are supported by the state and its municipalities. Neonatal screening exists for PKU and the addition of other conditions is being considered. Some discussion has occurred on the establishment of a Committee on Rare Disease at the Ministry of Health; however no action has been taken yet. Rare disease patients are reimbursed for most of their medications. Initiatives to improve access to treatment have come from patient organisations and some have received governmental support. Patients may have access to unauthorised treatments through a special application via the Ministry of Health. Genetic counselling is recognised as a medical speciality and is easily accessible and free of charge.



Socioeconomic Data

Total population: 45 200 737 (2007)
 Area of country: 504 030 sq km
 Population density: 90/sq km (2007)
 GDP: 1.310 trillion \$ (2007)
 GDP/capita: 33 700 \$ (2007)
 % of GDP spent on health: 8.2% (2005)
 # of physicians/100 000 inhabitants: 330 (2006)

Spain

Sections of this chapter were written with the collaboration of the Spanish Alliance for Rare Diseases (FEDER).

National Initiative in the Field of Rare Diseases

In Spain's recently decentralised national healthcare system, primary responsibility regarding health care was transferred to 17 regional governments, with some regions achieving autonomy more recently than others. Whilst the Spanish Ministry of Health and Consumer Affairs retains responsibility for certain strategic areas, most policymaking power and the organisation of health services occurs at the regional level.

Coverage under the mainly tax-funded national system is nearly universal, however long waiting times and problems with the quality of care have led to a growing number of private insurance alternatives (resulting in double coverage, since opting out of the state system is not allowed). Spanish patients are assigned to a local primary care doctor. If more specialised care is needed, then the primary care physician is responsible for referring patients to a network of specialists. Patients cannot see providers outside this network if they do not have private health insurance. This restriction has forced some residents to move houses in order to change physicians or find networks with shorter waiting lists in the event of illness.

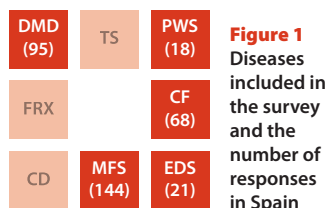
The European Orphan Drug Regulation definition of a rare disease, i.e. a prevalence of less than one per 2000 individuals, is accepted by health authorities and care professionals in Spain. A national plan for rare diseases has been developed by the Ministry of Health and Consumer Affairs and a working group, made up of representatives from health authorities, medical societies and patient organisations, aims to finalise it in 2009. No respite care or recreation programmes dedicated specifically to rare diseases currently exist in Spain. A medico-social centre for rare disease patients and their families is anticipated in the city of Burgos in 2009. The Rare Disease Epidemiological Network (REPIER) created a National Provincial Atlas of Rare Diseases, which was updated in 2006. The public health institute of Spain, Instituto de Salud Carlos III, includes the Research Institute for Rare Diseases. Calls for proposals provide opportunities for patient organisations to apply for grants to fund their activities and infrastructure.

In two regions, Valencia and Andalucía, pre-implantatory genetic diagnosis programmes for rare diseases are being developed. Neonatal screening for some rare diseases exists in certain regions of the country. A national decree regarding the appointment and accreditation of centres of expertise, although not specifically for rare diseases, has been created. Nevertheless, several centres for specific rare diseases have been designated as a result of this law. The Biomedical Research Network on Rare Diseases, CIBERER,

based in Valencia, includes 46 research teams and specific funds for rare disease research. Through calls for proposals, the Minister of Health has also financially supported several clinical trials on rare diseases. Genetic counselling is not recognised as a medical subspecialty in Spain.

Diagnosis in Spain

PARTICIPANTS IN THE SURVEY



Responses from 346 Spanish families of patients with five diseases were analysed (*Figure 1*). The lower number of female respondents as compared to males (41% and 59%, respectively) may be due to the size of the DMD representation (as an X-linked recessive trait, DMD primarily affects males).

DIAGNOSIS OVER THE FIRST THREE MONTHS OF LIFE

The low rate of diagnosis at an early stage (8% as compared to 15% overall) is mainly due to the scarcity of neonatal testing (1.5 % in Spain as compared to 4% overall) and fewer disorders observed during pregnancy or at birth (3% as compared to 7% overall).

AWAITING THE DIAGNOSIS

Before obtaining the correct diagnosis, 23% of all Spanish respondents were misdiagnosed, a lower percentage than the overall survey finding (*Figure 2*). Misdiagnoses resulted in inappropriate treatments for 87% of patients, including medical (37%), surgical (26%) and psychological or psychiatric (10%). During the quest for diagnosis, more than five physicians were consulted by 24% of families and more than ten physicians by 10% of families. Physicians prescribed tests for 95% of patients, including biological tests (81%), genetic tests (32%), functional test (48%) and X-rays (60%).

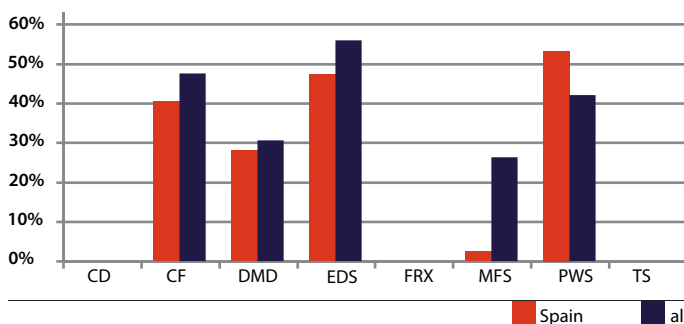
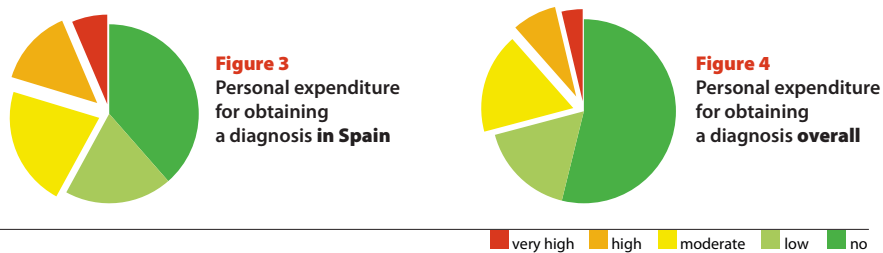


Figure 2 Diseases included in the survey and the number of responses in Spain

DIAGNOSIS

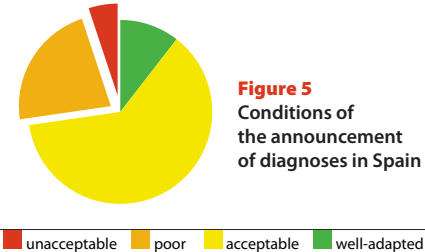
The structures providing diagnoses were reported as private practices (15%), hospital consultations (71%) and specialised centres (6%). These were located in another region in 13% of cases and in another country in 4.8% of cases. In 39% of situations, access to diagnosis was free in Spain.

Patients considered expenditure to be high or very high in 20% of cases (compared to 12% overall) (Figure 3 & 4). A second opinion was sought by 33% families to confirm the diagnosis.



ANNOUNCEMENT OF DIAGNOSIS

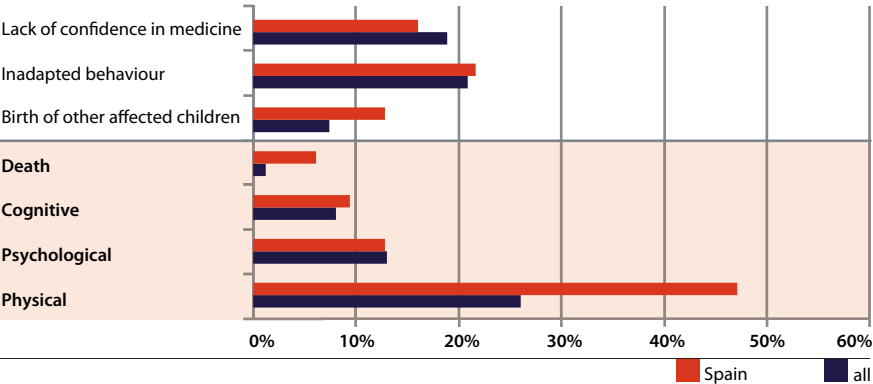
For 18% of patients, diagnoses were given without complete information on the disease, though 99% considered this information to be necessary. A total of 95% of patients considered that psychological support was required at the time of the announcement, whereas 70% of patients did not receive such support. The genetic nature of the disease was explained to 79% of patients and genetic counselling was provided to 50% of patients. Genetic advice resulted in the diagnosis or identification of a carrier in the family in 17% of cases. Although the percentage of Spanish patients who informed family members of the possibility of other cases (83%) is lower than reported overall (91%), the percentage of new cases identified as a result of the provision of this information was much higher amongst Spanish respondents (24%) than the overall (15%). Spanish families considered the conditions of the announcement of diagnosis to be poor or unacceptable in 12% of cases and well adapted in 68% of cases (Figure 5).



CONSEQUENCES OF DELAYED DIAGNOSIS

For 69% of the families, a delay in diagnosis was considered responsible for deleterious consequences (the same as for respondents overall, 71%). The consequences of a delayed diagnosis included physical consequences (47%), death (6%) and the birth of other children suffering from the disease (13%) (Figure 6).

Figure 6
Medical and non-medical consequences of delayed diagnoses in Spain.



Access to **Medical** and **Social Services** in Spain

PARTICIPANTS IN THE SURVEY

AH (16)	Ch11 (1)	WS	PWS (15)
FRX (8)	EB (39)	TS (50)	CF (23)
ANR (63)	OI	MFS (44)	EDS (23)
HD (20)	MG (85)	ATX (82)	PAH

Figure 7
Diseases
included in
the survey
and the
number of
responses
in Spain

Responses from 469 Spanish families of patients with 13 diseases were analysed (*Figure 7*).

More females than male patients were represented (55% and 45%, respectively).

The mean age of respondents was 29 years (mean age at diagnosis: 16 years).

NEED FOR MEDICAL SERVICES

Spanish patients required 10.6 different kinds of medical services related to their disease (i.e. more than the average 9.4 medical services). Hospitalisation occurred in 42% of patients for an average total duration of 22 days.

MEDICAL SERVICES

Access to the eight most essential services for each disease was easy in 67% of cases, difficult in 20% of cases and impossible in 13% of cases (*Figure 8*). This difficulty was mainly due to lack of referral (67%), unavailability of services (18%), long waiting times (14%), personal cost (11%) and location of the structures, including a location too far away (14%), no one to go with (11%) and difficulty in travelling (11%).

When obtained, medical services responded well to patients' expectations in 79% of cases (compared to 89% overall) and poorly or not at all in 21% of cases (*Figure 9*).



Figure 8
Access to
medical services
in Spain

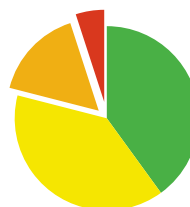


Figure 9
Satisfaction
with medical
services
in Spain

impossible very difficult difficult easy very easy not at all poorly partially fully

SOCIAL ASSISTANCE

Amongst the 29% of Spanish families requiring social assistance, 6% failed to meet with a social worker, 72% met with one easily and 22% met one with difficulty (*Figure 10*).

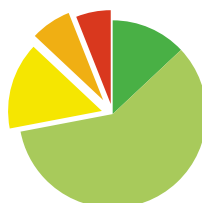


Figure 10
Access to
social services
in Spain



Figure 11
Satisfaction
with social
services
in Spain.

impossible very difficult difficult easy very easy not at all poorly partially fully

A total of 49% of Spanish respondents were satisfied with this assistance, whereas 30% were not at all satisfied (*Figure 11*).

REJECTION

Spanish respondents experienced rejection by health professionals in 26% of cases (compared to 18% overall). The reluctance of health professionals to treat patients due to the complexity of their disease was the main cause of rejection (94%), followed by a physical aspect (10%), communication difficulties (8%) and disease-related behaviour (7%).

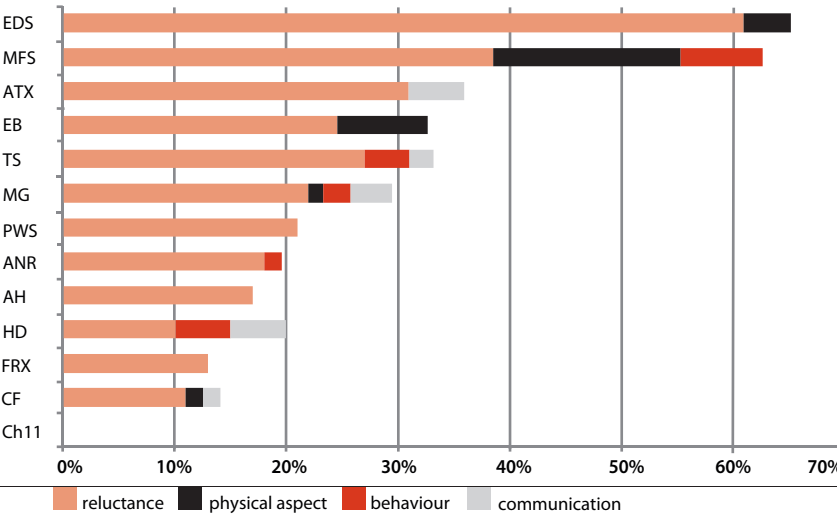


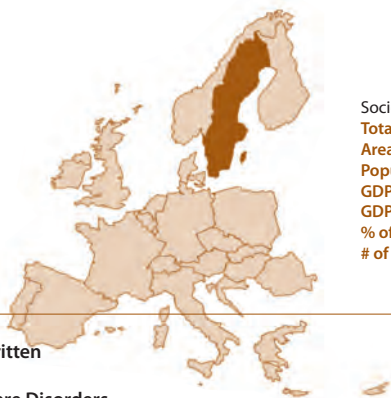
Figure 12 Cumulated frequencies of cause of rejection, by disease, in Spain. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

CONSEQUENCES OF THE DISEASE

As a consequence of the disease, 15% of Spanish patients had to move house. Amongst these, families most frequently moved to a more adapted house (26%), to be nearer to disease specialists (21%) or to be closer to a relative (22%). As a consequence of their disease, 32% of patients had to reduce or stop their professional activities. In 23% of cases one member of the family stopped working to take care of a relative.

Sweden

Sections of this chapter were written with the collaboration of the Swedish Association of Rare Disorders.



Socioeconomic Data
 Total population: 9 223 766 (2008)
 Area of country: 449 964 sq km
 Population density: 20/sq km 2008
 GDP: 455 billion \$ (2007)
 GDP/capita: 36 900 \$ (2007)
 % of GDP spent on health: 9.2% (2005)
 # of physicians/100 000 inhabitants: 328 (2006)

National Initiative in the Field of Rare Diseases

Sweden's healthcare system is a decentralised, publicly operated system organised on three levels, with regional country councils planning the development and organisation of care together with the central government, and the provision of services at the local level. Services are primarily funded through taxation and supplemented by small user charges. For specialised care, country councils cooperate to form six large medical care regions. Regulations, waiting times and patient fees vary from region to region. Few private hospitals exist, and the number of private general practitioners and health centres varies greatly throughout the country. Long waiting times for elective treatment not covered by the national system of care may be behind the recent trend in private health insurance. The Swedish National Board of Health and Welfare defines a rare disease as 'one found in a maximum of 100 people per one million inhabitants'. Stricter than the European Orphan Drug Regulation definition of one per 2000 people, the board believes that the attention paid to very rare diseases will be undermined if more common diagnoses are included in the definition. Currently there is no national plan for rare diseases. The Swedish rare disease national alliance, Riksförbundet Sällsynta diagnoser, holds the creation of such a plan as one of their most important goals. There are no non-medical services exclusively for rare disease patients but rather a general social support system provided by the local authorities, county councils and the state. The Swedish Rare Disease Database, provided by the Swedish National Board of Health and Welfare, includes medical information on approximately 230 rare diseases. Ågrenska, a national patient organisation for rare diseases, serves as an important source of comprehensive information for families who have children with rare diseases. Furthermore, almost every national specific rare disease patient organisation has a respective web site. There are no national helplines for rare diseases in Sweden. No national initiatives exist to support nationwide patient organisations because decentralisation is strongly emphasised in the Swedish healthcare system, and organisations are expected to work on the municipal or county council level and thus receive funding from local or regional authorities. As such, great variation exists in activities between patient organisations.

All newborns are screened for PKU. National centres of expertise for a few rare diseases exist, with the primary goal of improving access to treatment. Genetic counselling is not recognised as a medical subspecialty although a small number of health professionals have been trained to provide genetic counselling.

Diagnosis in Sweden

PARTICIPANTS IN THE SURVEY

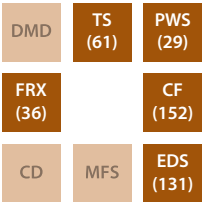


Figure 1
Diseases included in the survey and the number of responses in Sweden

Responses from 409 families of patients with five diseases were analysed (*Figure 1*). An equal number of female and male patients were represented in the survey (54% and 46%, respectively).

DIAGNOSIS OVER THE FIRST THREE MONTHS OF LIFE

The neonatal diagnosis rate (17%) in Sweden is comparable to that observed overall (15%).

AWAITING THE DIAGNOSIS

Before obtaining the correct diagnosis, another diagnosis was given to 50% of patients, which resulted in inappropriate treatment in 59% of patients, medical (32%), surgical (10%) and psychological or psychiatric (6%) (*Figure 2*). During the quest for diagnosis, more than five physicians were consulted by 40% of families and more than 10 physicians by 21% of families. Physicians prescribed tests for 91% of patients, including biological tests (62%), genetic tests (15%), functional tests (50%) and X-rays (56%).

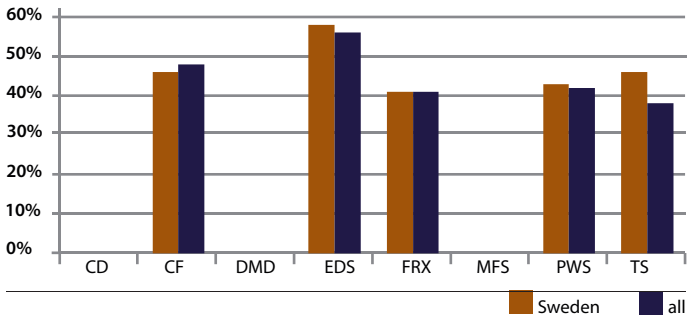
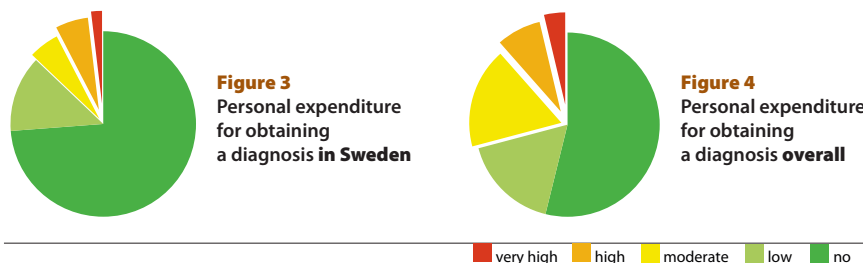


Figure 2
Percentage of patients initially receiving a misdiagnosis in Sweden

DIAGNOSIS

The structures providing the diagnoses were comparable to those observed for other countries, except for the lack of private practices. Swedish patients travelled to another region in 17% of cases (compared to 26%) or to another country in 1% of cases (compared to 2%).

Access to diagnosis is less expensive for Swedish patients than overall in Europe (*Figure 3 & 4*). Free diagnoses were more frequent. Patients considered expenditure to be moderate in 13% of cases (compared to 29% overall). A second opinion was rarely sought to confirm the diagnosis.



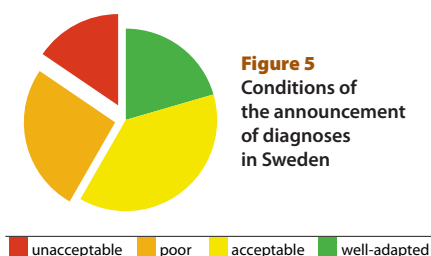
ANNOUNCEMENT OF DIAGNOSIS

For 24% of patients, diagnoses were given without providing complete information on the disease, though 99% of patients considered this information to be necessary. A total of 91% considered that psychological support was required at the time of the announcement; however 63% of patients did not receive such support.

The genetic nature of the disease was explained to families in 83% of cases, with details given about the possibility of other cases in the family in 27% of cases.

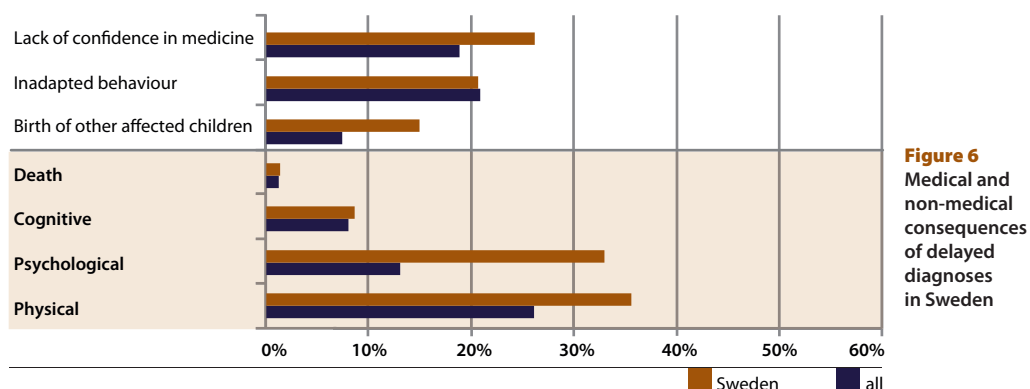
Genetic advice resulted in the diagnosis or identification of a carrier in the family in 36% of cases.

The conditions under which the diagnosis was announced were considered poor in 42% of cases (compared to 35% overall) (*Figure 5*).



CONSEQUENCES OF DELAYED DIAGNOSIS

For 79% of families, delays in diagnosis were considered responsible for deleterious consequences (*Figure 6*). In addition, on average two types of consequences were reported, with the worst being psychological consequences (33% compared to 13% overall) and the birth of affected children (15% compared to 7% overall).



Access to **Medical** and **Social Services** in Sweden

PARTICIPANTS IN THE SURVEY

AH	Ch11 (1)	WS (45)	PWS (26)
FRX (39)	EB	TS	CF (116)
ANR	OI (18)	MFS (89)	EDS (152)
HD	MD	ATX (11)	PAH

Figure 7
Diseases included in the survey and the number of responses in Sweden

Responses from 497 French families of patients with nine diseases were analysed in the survey (*Figure 7*). The percentage of female and male patients represented were 62% and 38%, respectively. There was a high proportion of female EDS patients (94%). The mean age of patients was 32 years (mean age at diagnosis: 17 years).

NEED FOR MEDICAL SERVICES

Overall, Swedish patients needed nine different kinds of medical services related to their disease (similar to the average 9.4 medical services overall). Hospitalisation occurred in 47% of patients for an average total duration of 19 days.

MEDICAL SERVICES

Access to the eight essential services for each disease was easy in 78% of cases, difficult in 13% of cases and impossible in 9% of cases (*Figure 8*). This was primarily due to unavailability (43%), lack of referral (39%), waiting time (24%), personal cost (14%) and location of the structures, including a location too far away (10%), no one to go with (14%) and difficulty in travelling (14%). When obtained, the medical services responded well to patients' expectations in 92% of cases and poorly in 8% of cases (*Figure 9*).

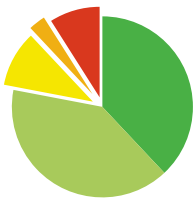


Figure 8
Access to medical services in Sweden.

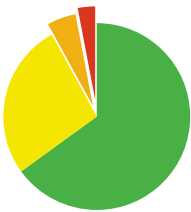


Figure 9
Satisfaction with medical services in Sweden.

impossible very difficult difficult easy very easy

not at all poorly partially fully

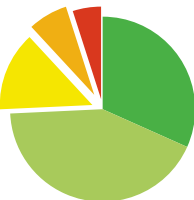


Figure 10
Access to social services in Sweden



Figure 11
Satisfaction with social services in Sweden

impossible very difficult difficult easy very easy

not at all poorly partially fully

SOCIAL ASSISTANCE

Amongst the 29% of Swedish families that required social assistance, 5% failed to meet with a social worker, 75% met with one easily and 21% met with one with difficulty (*Figure 10*).

A total of 46% of Swedish families were satisfied with this assistance, 31 % not at all (*Figure 11*).

REJECTION

Swedish patients experienced rejection by health professionals at a rate (18%) similar to that observed for respondents overall for the 16 surveyed rare diseases (*Figure 12*). The reluctance of health professionals to treat patients was mainly due to the complexity of their disease (95%), followed by communication difficulties (12%), disease-related behaviour (6%) and physical aspects (8%).

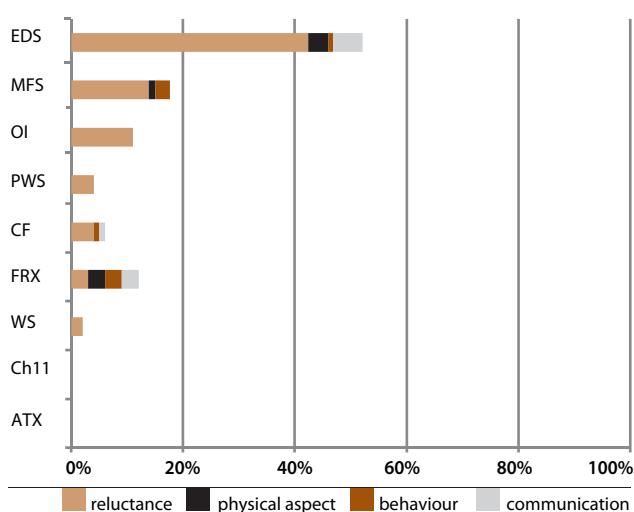


Figure 12 Cumulated frequencies of cause of rejection, by disease, in Sweden. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

CONSEQUENCES OF THE DISEASE

As a consequence of the disease, 12% of Swedish patients had to move house. Amongst these, families most frequently moved to a more adapted house (74%), to be nearer to disease specialists (12%) or to be closer to a relative (22% compared to 18%). As a consequence of their disease, 36% of patients had to reduce or stop their professional activity. In 28% of cases, a member of the family had to stop work to take care of a relative.



Switzerland

Sections of this chapter were written with the collaboration of Orphanet Switzerland.

Socioeconomic Data

Total population: 7 591 400 (2007)
 Area of country: 41 281 sq km
 Population density: 181/sq km
 GDP: 296 billion \$ (2007)
 GDP/capita: 38 706 \$ (2007)
 % of GDP spent on health: 11.4% (2005)
 # of physicians/100 000 inhabitants: 361 (2006)

National Initiative in the Field of Rare Diseases

The Swiss healthcare system is a combination of public, subsidised private and completely private systems. The federal government has the regulatory responsibility of preventing widespread disease, creating a system of universal insurance, promoting medical research and training and certifying medical professionals. Twenty-six cantons are individually responsible for the implementation of federal laws, inpatient and outpatient care, and the provision of health services and education, and are collectively responsible for the market authorisation and control of medications. Some health services are further delegated to the municipalities. The compulsory health insurance system, regulated by the Federal Office for Social Insurance, is based on the principle of managed competition in which insurance companies are required to offer a certain range of treatments at a rate dependent on the cost of basic health care in that region, and cannot make a profit from these compulsory activities. Many companies additionally offer supplementary insurance policies for services not covered, and more advantageous insurance payment rates. However, joining a managed care plan may restrict a citizen's choice of healthcare provider. Hospitals are managed at the canton level. Many are public and those that are private are often partly subsidised. Patients are free to choose primary or specialised care providers within their canton. Currently, the Swiss Hospital Association and the health insurance funds are negotiating a federal plan for continuous promotion of the quality of hospital services. The European Orphan Drug Regulation definition of a rare disease as one affecting one person among 2000 is accepted and used by stakeholders.

National initiatives in a country where 26 cantons each promote their own public health policies are difficult to accomplish. Although there is currently no plan for a national plan for rare diseases, several promising initiatives have been introduced in the field. Though not officially recognised as such, several specialised care centres have been established as centres of reference by reputation. At both the national canton levels, several organisations (e.g. Pro Infirmis and Insieme) are dedicated to people with mental or physical handicaps, including rare disease patients. The Telethon Suisse (www.telethon.ch) raises funds specifically for rare diseases. Orphanet Switzerland, a partner of the Orphanet rare disease database, is the only specific project for rare diseases supported by the Swiss Conference of the Cantonal Ministers of Public Health. Additional web sites and helplines for people with handicaps exist, but are not specifically dedicated to rare diseases. Orphanet Switzerland helped identify approximately 100 rare disease patient organisations.

Although these organisations have not yet been federated under a national alliance, there is a strong interest in initiating this step and a first meeting will be organised in 2009. Again, the organisation of a national alliance is complicated by the fragmentation cantons and three major languages used by Swiss citizens.

A nationwide newborn screening program includes neonatal screening for PKU, congenital hypothyroidism, galactosaemia, congenital adrenal hypoplasia, biotinidase deficiency, medium-chain acyl-CoA dehydrogenase (MCAD) deficiency and hearing tests. A Swiss Orphan drug regulation has been in place since 2006 under which an orphan drug status applies to products treating diseases that affect no more one in 2000 persons.

Companies acquiring orphan drug designation for their products are exempted from certain administrative taxes but are not granted market exclusivity. Although no specific national budget exists for rare disease research, the Fondation Telethon Action Suisse and some private funding organisations do contribute to rare disease research. Several public and private centres provide genetic testing, though not all tests are reimbursed by insurance. An initiative to increase this list is underway. Genetic counselling is not officially recognised as a medical subspecialty, but is rather provided by medical doctors specialised in medical genetics.

Diagnosis in Switzerland

PARTICIPANTS IN THE SURVEY

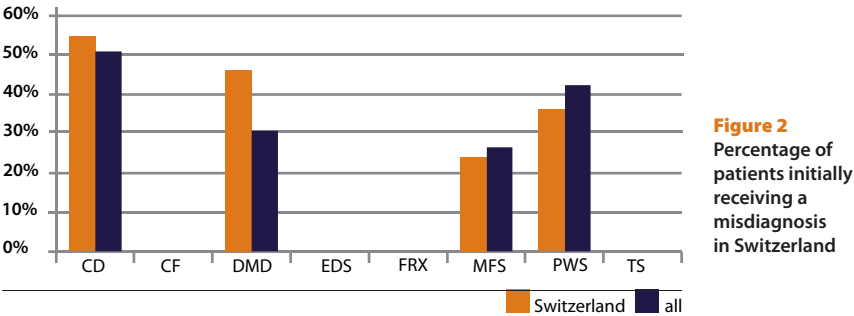
DMD (14)	TS	PWS (40)
FRX (3)		CF
CD (92)	MFS (49)	EDS

Figure 7
Diseases
included in
the survey
and the
number of
responses in
Switzerland

Responses from 198 families of patients with five diseases were analysed (*Figure 1*). An equal number of female and male patients were represented in the survey (54% and 46%, respectively). The neonatal diagnoses rate (9%) in Switzerland is slightly lower than that overall (15%) and is linked to less neonatal testing (1% compared to 4% overall).

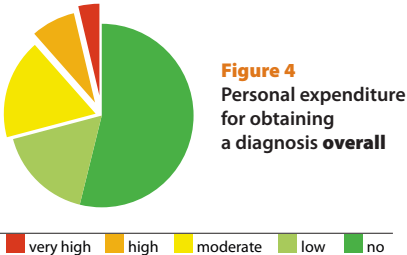
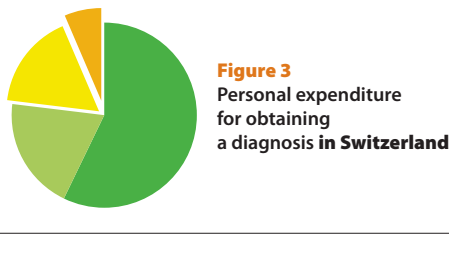
AWAITING THE DIAGNOSIS

Before obtaining the correct diagnosis, another diagnosis was given to 43% of patients, resulting in inappropriate treatments for 79% of patients, including medical (44%), surgical (16%) and psychological or psychiatric (6%) (Figure 2). During the quest for diagnosis, more than five physicians were consulted by 16% of families and more than ten physicians by 7% of families. Physicians prescribed tests for 82% of patients including biological tests (66%), genetic tests (14%), functional tests (29%) and X-rays (53%).



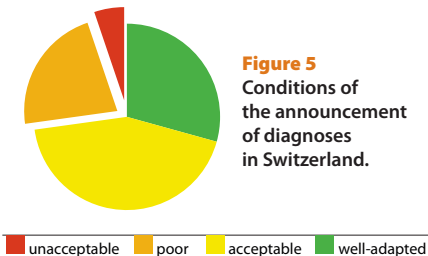
DIAGNOSIS

The structures providing the diagnoses included private practices in 33% (compared to 10% overall), hospital consultations (32% compared to 61%), specialised centres (22%) or other structures (15%). They were located in another region in 21% of cases or in another country in 2.2% of cases. Personal cost to the patient was slightly lower in Switzerland than overall (Figure 3 & 4); personal expenditure was considered low in 78% of cases and very high in 0.6% of cases. A second opinion was sought by 21% of families to confirm the diagnosis.



ANNOUNCEMENT OF DIAGNOSIS

For 21% of patients, diagnoses were given without providing any information on the disease, whereas 98% of patients considered this information to be necessary. A total of 75% felt psychological support was required at the time of the announcement, although 77% of patients did not receive such support.



The genetic nature of the disease was explained to families in 46% of cases, with details given about the possibility of other cases in the family in 67% of cases. Genetic advice resulted in the diagnosis or identification of a carrier in the family in 15% of cases.

Swiss families considered the conditions of the announcement to be poor or unacceptable in 27% of cases (*Figure 5*). A second opinion was sought by 21% of families to confirm the diagnosis.

CONSEQUENCES OF DELAYED DIAGNOSIS

For 69% of the families, delays in diagnosis were considered responsible for at least one deleterious consequence (*Figure 6*).

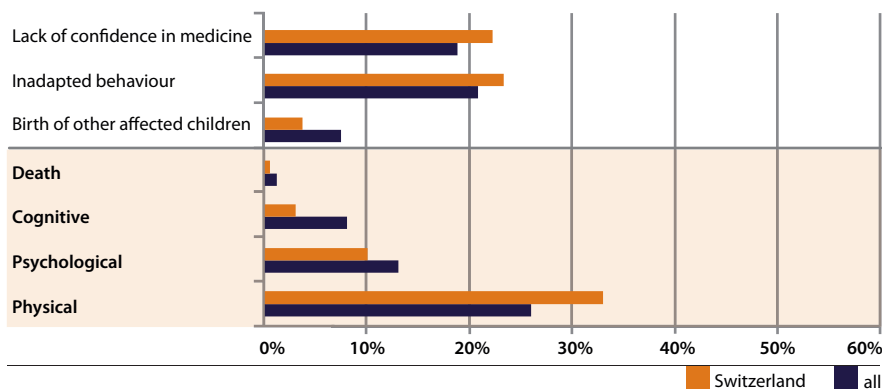


Figure 6 Medical and non-medical consequences of delayed diagnoses in Switzerland

Access to **Medical** and **Social Services** in Switzerland

PARTICIPANTS IN THE SURVEY

AH	Ch11 (1)	WS	PWS
FRX (4)	EB (2)	TS (1)	CF
ANR	OI	MFS (39)	EDS
HD (13)	MG	ATX	PAH

Figure 7
Diseases included in the survey and the number of responses in Switzerland

Responses from 60 Swiss families of patients with six diseases were analysed in the survey (*Figure 7*). The proportion of female and male patients represented were 51% and 49%, respectively. The mean age of patients was 37 years (mean age at diagnosis: 22 years).

NEED FOR MEDICAL SERVICES

Overall, Swiss patients needed 9.3 different kinds of medical services related to their disease (the same as the average 9.4. medical services for all the diseases surveyed). Hospitalisation occurred in 43% of patients for an average total duration of 11 days.

MEDICAL SERVICES

Access to the eight essential services for each disease was easy in 76% of cases, difficult in 12% of cases and impossible in 12% of cases (*Figure 8*). Difficulty was mainly due to lack of referral (52%) and personal cost (30%) but also waiting time (15%), unavailability (7%) and location of the structures, including a location too far away (26%), no one to go with (22%) and difficulty in travelling (26%).

When obtained, the medical services responded well to patients' expectations in 94% of cases and poorly in 6% of cases (*Figure 9*).

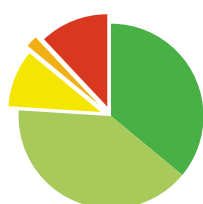


Figure 8
Access to
medical services
in Switzerland.

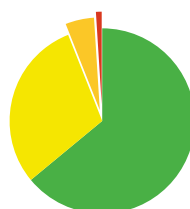


Figure 9
Satisfaction
with medical
services
in Switzerland

impossible very difficult difficult easy very easy

not at all poorly partially fully

SOCIAL ASSISTANCE

Amongst the 27% of Swiss families needing social assistance, 7% failed to meet with a social worker, 78% met with one easily and 14% met with one with difficulty (*Figure 10*).

A total of 48% of Swiss families were satisfied with this assistance; however a total of 40% were not at all satisfied (compared to 28% overall) (*Figure 11*).

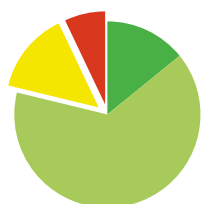


Figure 10
Access to
social services
in Switzerland.



Figure 11
Satisfaction
with social
services
in Switzerland.

impossible very difficult difficult easy very easy

not at all poorly partially fully

REJECTION

Swiss patients experienced rejection by health professionals at a rate (14%) similar to that observed overall (18%) for the 16 surveyed rare diseases (*Figure 12*).

The reluctance of health professionals to treat patients due to the complexity of their disease was the main cause of rejection (50%), followed by communication difficulties (25%) and disease-related behaviour (25%).

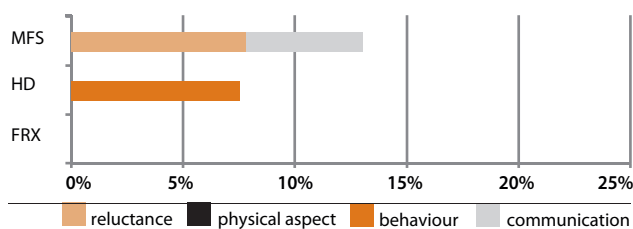
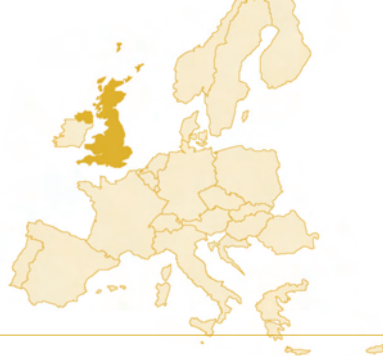


Figure 12 Cumulated frequencies of cause of rejection, by disease, in Switzerland.

As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents

CONSEQUENCES OF THE DISEASE

As a consequence of the disease, 10% of Swiss patients had to move house. Amongst these, families most frequently moved to a more adapted house (50%) or to be closer to a relative (17%). As a consequence of their disease, 45% of patients had to reduce or stop their professional activity. In 17% of cases, a member of the family had to stop work in order to take care of a relative.



United Kingdom

Sections of this chapter were written
with the collaboration of DebRA International.

Socioeconomic Data

Total population: 60 512 000 (2007)
Area of country: 244 820 sq km
Population density: 246/sq km (2007)
GDP: 2.270 trillion \$ (2006)
GDP/capita: 37 328 \$ (2006)
% of GDP spent on health: 8.2% (2005)
of physicians/100 000 inhabitants: 230 (2006)

National Initiative in the Field of Rare Diseases

In the United Kingdom, four separate but cooperating National Health Services (NHS) exist, which are managed by the Department of Health in England, Wales, Scotland and Northern Ireland. Under this tax-funded, fully government-run system most primary and secondary care services are free (with the exception of small co-payments for prescription drugs, dental care and optician services) for all legal residents. The National Institute for Health and Clinical Excellence (NICE) has been created to advise medical practitioners as to how various conditions should be treated and whether or not a particular treatment should be funded. The highly centralised system has resulted in long waits for primary and specialised care. Some residents have opted for private health insurance to supplement the public system. The working definition of a rare disease by the National Commissioning Group (NCG), which designates clinical services for rare conditions, is not more than 1000 patients. There is no national plan for rare diseases in particular but rather individual conditions apply for designation through the NCG. Social services, respite care and recreation services exist in the UK and are mostly provided at the local level by the relevant rare condition patient group as are any available web sites and helplines. The UK Department of Health has a limited scheme to provide low-level core funding for some patient groups. Various groups are recognised by the government for consultation purposes. Neonatal screening is offered for phenylketonuria (PKU), congenital hypothyroidism (CHT), sickle cell disease (SCD), cystic fibrosis (CF) and medium-chain acyl-CoA dehydrogenase deficiency (MCADD).

No specific coordinating body exists for rare diseases, although the Genetic Interest Group undertakes this role in the case of genetic conditions, many of which are rare. The NHS fully funds those treatments that it recognises as being reimbursable. Compassionate use of unlicensed medication is possible. No specific statutory funding schemes for rare disease research exist, although there may, from time to time, be calls for applications in specific areas that relate to rare conditions. In addition, patient groups often have their own research grant schemes.

Genetic testing and counselling is provided via regionally based services. In the case of some conditions, testing and counselling is provided via a specialist Centre of Expertise, often arising from a research interest. Genetic counselling is recognised as a profession and specific training is offered at a number of academic centres.

Diagnosis in the United Kingdom

PARTICIPANTS IN THE SURVEY



Figure 1
Diseases included in the survey and the number of responses in the United Kingdom

Responses from 446 families of patients with three diseases were analysed (*Figure 1*). An unequal number of female and male patients were represented in the survey (28% and 72%, respectively), likely due to the DMD and FRX patients.

DIAGNOSIS OVER THE FIRST THREE MONTHS OF LIFE

The neonatal diagnosis rate (20%) in the United Kingdom is higher than the overall rate (15%) and is linked to more neonatal testing (6% compared to 4% overall) and to disorders observed during pregnancy or at birth (11% compared to 7% overall).

AWAITING THE DIAGNOSIS

Before obtaining the correct diagnosis, another diagnosis was given to 35% of patients, resulting in inappropriate treatments for 45% of patients, including medical (11%), surgical (6%) and psychological or psychiatric (10%) treatment (*Figure 2*).

During the quest for diagnosis, more than five physicians were consulted by 20% of families and more than ten physicians by 6% of families. Physicians prescribed tests for 82% of patients, including biological tests (57%), genetic tests (52%), functional tests (28%) and X-rays (20%).

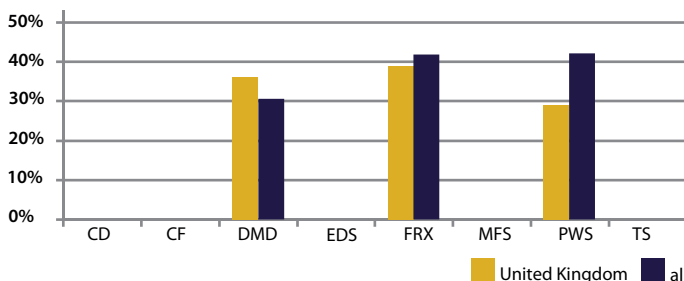


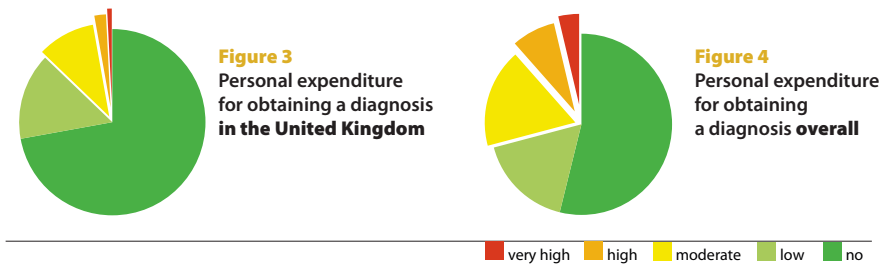
Figure 2 Percentage of patients initially receiving a misdiagnosis in the United Kingdom

DIAGNOSIS

The structures providing the diagnoses included hospital consultations (76%), specialised centres (15%), private practices (0.6%) and other structures (8%).

They were located in another region in 20% of cases and in another country in 1.6% of cases.

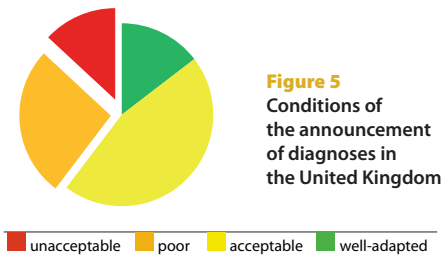
In 71% of situations, access to diagnosis was free in the United Kingdom. Patients considered expenditure to be high or very high in only 3% of situations compared with 11.5% overall (Figure 3 & 4). A second opinion was sought by 7% families to confirm the diagnosis.



ANNOUNCEMENT OF DIAGNOSIS

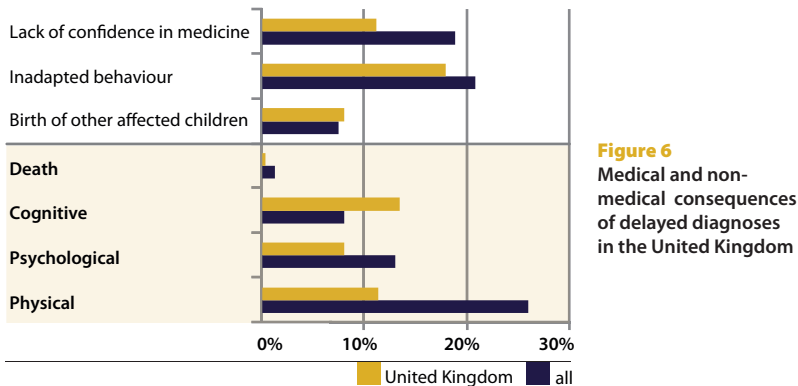
For 31% of British patients, diagnoses were given without complete information on the disease, though 98% considered this information to be necessary. A total of 93% considered that psychological support was necessary at the time of the announcement, whereas 69% of patients did not receive such support.

The genetic nature of the disease was explained to families in 89% of cases, with details about the possibility of other cases in the family offered in 74% of cases. Genetic advice resulted in the diagnosis or identification of a carrier in the family in 41% of cases. British families considered the conditions of announcement of the disease to be poor or unacceptable in 39% of cases (Figure 5).



CONSEQUENCES OF DELAYED DIAGNOSIS

For 82% of families, delays in diagnosis were considered responsible for deleterious consequences (compared to the overall of 71%) (Figure 6).



Access to **Medical** and **Social Services** in United Kingdom

PARTICIPANTS IN THE SURVEY

AH	Ch11 (6)	WS	PWS (78)
FRX (68)	EB (28)	TS	CF
ANR	OI	MFS	EDS (160)
HD	MG	ATX	PAH

Figure 7
Diseases included in the survey and the number of responses in United Kingdom

Responses from 340 British families of patients with five diseases were analysed in the survey (*Figure 7*). The percentage of female and male patients represented were 56% and 44%, respectively. The mean age of patients was 32 years (mean age at diagnosis: 15 years).

NEED FOR MEDICAL SERVICES

Overall, British patients needed 7.8 different kinds of medical services related to their disease, less than the average 9.4 medical services for all the diseases surveyed. Hospitalisation occurred in 45% of patients for an average total duration of 14 days.

MEDICAL SERVICES

Access to the eight essential services for each disease was easy in 63% of cases, difficult in 23% of cases and impossible in 13% of cases (*Figure 8*). This was mainly due to lack of referral (51%), unavailability (43%), waiting time (31%), personal cost (9%) and location of the structures, including a location too far away (7%), no one to go with (13%) and difficulty in travelling (24%).

When obtained, the medical services responded well to patients' expectations in 86% of cases and poorly in 14% of cases.

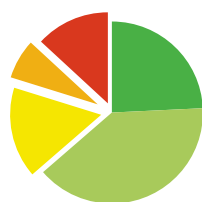


Figure 8
Access to medical services in the United Kingdom



Figure 9
Satisfaction with medical services in the United Kingdom

impossible very difficult difficult easy very easy

not at all poorly partially fully

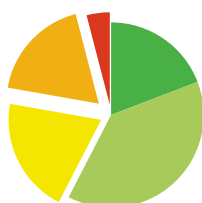


Figure 10
Access to social services in United Kingdom



Figure 11
Satisfaction with social services in the United Kingdom.

impossible very difficult difficult easy very easy

not at all poorly partially fully

SOCIAL ASSISTANCE

Amongst the 38% of British families that needed social assistance, 4% failed to meet with a social worker, 57% met one easily and 38% met one with difficulty (*Figure 10, p 293*). A total of 38% of British families were poorly satisfied with this assistance and 34% were not at all satisfied (*Figure 11, p 293*).

REJECTION

British patients experienced rejection by health professionals at a rate similar (16%) to that observed for respondents overall for the 16 surveyed rare diseases (*Figure 12*). The reluctance of health professionals to treat patients due to the complexity of their disease was the main cause of rejection (94%), followed by disease-related behaviour (8%), communication difficulties (2%) and physical aspects (2%).

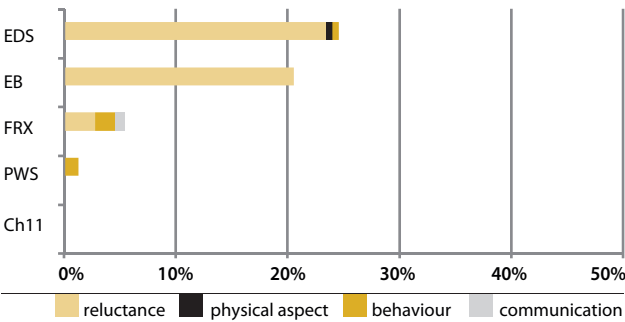
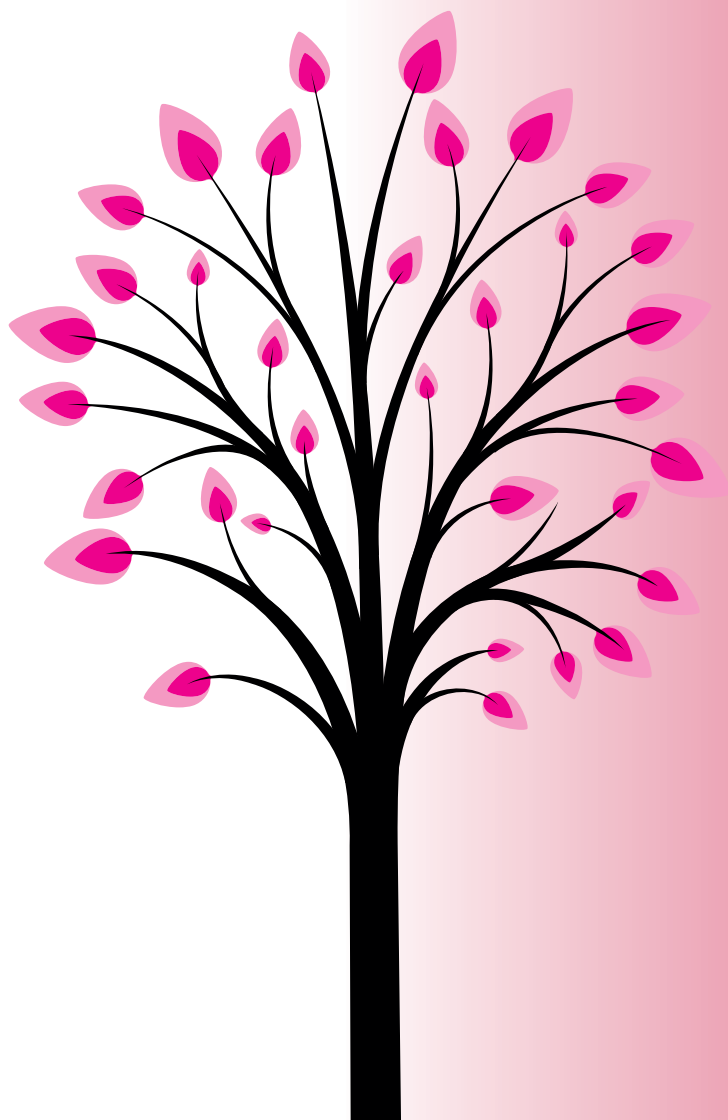


Figure 12 Cumulated frequencies of cause of rejection, by disease, in the United Kingdom. As patients may have been rejected more than once for more than one reason, the total number of rejections exceeds the number of rejected respondents.

CONSEQUENCES OF THE DISEASE

As a consequence of the disease, 19% of British patients had to move house. Amongst these, families most frequently moved to a more adapted house (36%), to be nearer to disease specialists (4%) or to be closer to a relative (9%). As a consequence of their disease, 26% of patients had to reduce or stop their own professional activity. In 34% of cases, a member of the family had to stop work in order to take care of a relative.



Conclusions

The results of the EurordisCare2 survey directly reflect the challenges encountered by patients in a quantitative way. Forty percent of patients were initially misdiagnosed, leading to severe consequences such as inappropriate medical interventions, including surgery and psychological treatment. One-quarter of patients reported waiting between five and 30 years from the appearance of the first symptoms to receiving the correct diagnosis of their disease, and the same proportion reported having to travel to a different region to reach the diagnostic facility. In almost half of the cases, the diagnosis was reported as being announced under inadequate or totally unacceptable conditions. In one-quarter of cases, the genetic nature of the disease was not communicated to the patient or family — an astounding and unacceptable reality given the genetic origin of most rare diseases.

A general lack of awareness and a specific lack of knowledge of rare diseases may be the result of inadequate training during medical studies, reflecting a need for strengthened advocacy and, above all, continued education of currently practicing healthcare professionals about rare diseases. Even if the patients' suffering and the inappropriate medical interventions they undergo are disregarded, the waste of resources on such unnecessary and harmful procedures should surely be recognised.

Above all, excessive delays in diagnosis and subsequent inappropriate interventions cause rare disease patients to lose confidence in the healthcare system and in medical professionals, thus exacerbating the inequality they already face in receiving high quality care compared with patients suffering from more frequently occurring diseases.

'Tomorrow is always harder than the day before. Progression of the illness never stops. Tomorrow will be even harder still, when the illness begins to hit the following generation. It is impossible to see the end of it.'
Robert, France

Results of the EurordisCare3 survey continue to lend quantitative support to the common struggles voiced by rare disease patients. The average patient required more than nine different medical services over the two-year period preceding the survey. More than one-quarter of patients reported difficult, very difficult or impossible access to services. A lack of referral was the most frequently reported cause of impossible access. One out of ten patients reported that



the essential services they sought poorly met their expectations or did not meet them at all, a rate of satisfaction that may be acceptable for other service arenas, but not health care. Almost one-third of respondents required the assistance of a social worker in the 12 months preceding the survey. While the majority of these patients reported easy or very easy access, more than one-third met one with difficulty or could not meet with one at all. Of those who did seek social services, one-half reported that their expectations were met only 'somewhat' or even 'not at all'. Moving house and reducing professional activity were some of the daily changes patients and their families were required to make as a result of a rare disease. Nearly one out of five respondents reported being rejected when seeking medical services, usually due to the reluctance of the healthcare professional to treat them because of the complexity of their disease.

The complexity of rare diseases necessitates multiple types of care offered by various specialists, often in different locations, who rarely communicate regarding the care of their common patients. The scattered nature of these medical needs makes accessing them difficult because the referring physician may not know, firstly, what specialised needs the patient could benefit from and, secondly, where to find them. Many physicians refuse to even see a patient with a rare disease in the fear that they are not adequately trained to serve their needs, even if the needs presented by the patient are not related to the rare disease, but a simple and common health concern.

In addition to the numerous medical services rare disease patients face, social services are at times equally important. As social service systems are often separate from healthcare systems, social workers are even less familiar with the unique needs of rare disease patients and, as a consequence, are less prepared to meet their expectations. Rare disease patients recognise the benefits of concentrating medical and social services in Centres of Expertise and those participating in this survey were no exception. Similarly, those who participated in other stakeholder discussions have agreed on the most essential services provided by these centres. Patients have also agreed on several key aspects in the establishment of Centres of Expertise,

'Problems with access to care result from the difficulty in finding specialists in the disease but also in obtaining financial support to reach them. Services can be very far from home. Sometimes, when faced with these compounded difficulties, parents just give up.'

Parent of a child with a chromosome 11 disorder

although the implementation of these centres is more complicated, as they depend upon the country in which they will be established. In the meantime, patient organisations can reflect on a common set of principles that define their relationship with such Centres of Expertise in their respective home countries.

These trends were observed across and within country and disease groups. Some are inarguably consistent across the majority of participants; others vary between subgroups and still others introduce newly identified trends in the needs and experiences faced by rare disease patients and warrant further investigation. Many observations have motivated us and may motivate others to research subtopics in further detail. In the meantime, several very important conclusions can be drawn as a result of our analysis.

Despite their great diversity, rare diseases are severe to very severe, chronic, degenerative and usually life-threatening. They are often disabling psychologically or physically, often seriously compromising the quality of life of patients or their families due to a decrease or total loss of autonomy. Many rare diseases are very painful. The suffering of rare disease patients and their families is only aggravated by psychological despair and the lack of therapeutic hope. Almost all rare diseases are incurable, but for many, symptoms can be treated to improve the quality of life and life expectancy.

From a medical perspective, rare diseases are characterised by their large number, broad diversity and symptoms that vary not only from disease to disease, but also within the same disease. The same condition can have very different clinical manifestations from one affected person to another, and for many there are large numbers of subtypes. For most rare diseases the aetiological mechanisms are still unknown because of a lack of research on the physiopathology of the disease. For these reasons, it is accepted that the diagnosis of rare diseases is more problematic than for more frequently occurring diseases. Their rarity alone contributes to the lack of understanding of their initial cause, mode of transmission and prognosis. Often, physicians must be competent in several fields to be able to comprehend their complex and multidisciplinary nature. From our analysis, however, it is clear that the reasons for many delays in diagnosis are not clinically related. Instead they include gender, the existence and nature of an initial misdiagnosis, and the need for the families to themselves suggest the possibility of a rare disease or to identify the diagnostic structure. Being a woman should have no influence on a physician's clinical ability to diagnose a disease. It is, therefore, difficult to accept that overall women experience much greater delays in diagnosis than men. The more rapid diagnosis of men illustrates that the capacity to do so exists and that if the reasons that women experience greater delays in diagnosis could be understood and overcome, then overall delays in diagnosis for rare disease patients could be decreased. Patients who were initially misdiagnosed or who were forced to reach a diagnosis with little assistance from medical professionals also experienced greater delays. Again, these patient characteristics should in no way influence a healthcare professionals' ability to diagnose a disease, therefore their association with delays in diagnosis must be investigated and eliminated.

Similarly, non-clinical factors demonstrated as being responsible for delays in diagnosis are associated with the rejection of patients by healthcare professionals. Specifically, three factors significantly were associated with an increased rate of rejection: having a disease that involves chronic or significant pain, level of income and gender. Participants in the study were asked whether they needed 'pain control services'. Those who did were much more frequently rejected by health professionals (41.9% of cases) than those who did not (15.5% of cases). Patients who reported being in either low or the lowest income brackets reported rejection in 22.9% of cases compared to 14.7% of cases for patients who reported being in the two higher income brackets.

'No doctor was willing to listen to my problems carefully, and I often had the impression doctors diagnosed me with anything just to satisfy me.'
Sandra, 31 years old, Austria



Women reported rejection in 17% of cases whereas men only reported rejection in 13.9% of cases. Most importantly these three factors compound each other: rejection was reported in 6.6% of cases for men with the highest income who experienced no chronic pain. Women with the lowest incomes who experienced chronic pain reported rejection in 69.7% of cases. The most vulnerable populations are the most frequently rejected. Again, although it is important to point out and try to understand the reason behind inequalities, it is even more important to first recognise that rejection is not inevitable for many, and it can therefore be minimised for all.

That it can be very low in one subgroup does not mean that it will inevitably be higher in another, but rather that it should be low for all patients — male or female, rich or poor, educated or not, experiencing chronic pain or not.

'I have experienced intolerance, cruelty and misunderstanding because I am different. This causes me great insecurity and a desire to be like others.'
Yolanda, 42 years old, Spain

Rare disease patients are subject to marginalisation in classic healthcare systems designed for non-rare diseases. They are confronted with unequal obstacles in attaining the highest possible standards of health they deserve (as agreed upon in the WHO Constitution)¹. Patients and

their families are often forced to educate themselves about rare diseases when the health professionals they consult are not able to. They are often the ones to introduce the possibility that their illness may be a rare disease to their health care professionals. In 18% of cases, patients reported making this suggestion themselves. The sources from which they obtained the information varied, including family and friends, media, other patients and the Internet, amongst others. It is often because of this suggestion that the correct diagnosis is finally reached. Even when the possibility of a rare disease is suggested and a specific disease may even be suspected, patients need to be directed to a diagnostic laboratory or centre to perform tests to confirm a diagnosis. Very often, patients also reported having to identify these facilities themselves (23%).

The restructuring of the classic system designed for the management of frequent diseases can be accomplished through the establishment of Centres of Expertise. Although the specific functions and implementation of Centres of Expertise may differ from country to country or disease group to disease group, the concentration of expertise in a place where the (i) management of the disease is multidisciplinary and coordinated, (ii) accurate diagnosis can be provided, (iii) access to social assistance can be facilitated, (iv) research and knowledge about the disease can be shared on national and European levels and (v) patients can feel welcome, safe and included in decisions related to their disease management and evaluation can help rare disease patients attain the 'state of complete physical, mental and social well-being and not merely the absence of disease or infirmity'², to which they are entitled.

1-Preamble to the Constitution of the World Health Organization as adopted by the International Health Conference, New York, 19-22 June, 1946; signed on 22 July 1946 by the representatives of 61 States (Official Records of the World Health Organization, no. 2, p. 100) and entered into force on 7 April 1948. 2-Ibid

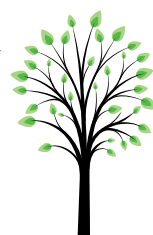
It may be surprising, however, that rare disease patients' perception of the quality of their lives is linked more to the quality of care provided than to the gravity of the illness or the degree of the associated disabilities. Overall, respondents to this survey emphasised the importance of the quality of services they expected in a Centre of Expertise rather than quantity of services available. Patients did not frequently report an expectation that Centres of Expertise be highly technical centres of knowledge. They did not emphasise the importance of the need for Centres of Expertise to follow a high volume of patients to maintain the skills and experience of its professionals, nor the requirement that they monitor patient needs through surveys or patient registries. More frequently, survey participants emphasised the importance of improving the way in which existing care and therapy was provided through better coordination and communication between professionals within the Centres of Expertise, with professionals in other Centres of Expertise and local professionals (such as the patient's general practitioner, social workers and caregivers).

Given these priorities expressed by survey participants, it follows that Centres of Expertise should not focus on a disease, but rather on the patients with the disease. This is not so much a question of changing the care that is given but rather the frame of mind in which it is given. When considering the patient as a whole, not just their disease, the need for the integration of social services and medical services in a single facility becomes very obvious.

Prescription of a treatment is only helpful if it is correctly adhered to. Such adherence is often associated with transportation to a distant care facility, significant costs and accompaniment by another person, with both the patient and the companion taking time away from work. Not all rare disease patients have the necessary support systems at hand to correctly adhere to their treatment and may, rightly so, require social assistance to meet these needs. It is especially for this reason that social services should be accessible in the same care facilities as medical services. They should be offered in parallel and systematically to all who need them. The integration of such services in Centres of Expertise and making their availability transparent should eliminate disparities across socioeconomic groups rather than reinforcing them, as is currently the case. People should not have to be more educated or have a higher income to better navigate social services or have them more frequently offered.

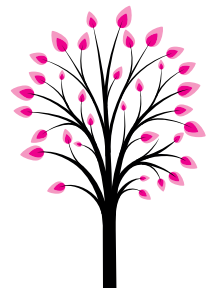
It is well established that late diagnoses delay the beginning of adapted treatments leading to severe, irreversible, debilitating and life-threatening consequences. Furthermore, treatments applied in a misdiagnosed disease may be inappropriate, ineffectual or even harmful, further compounding the adverse effects on the health of the patient and further delaying a correct diagnosis.

In addition, the initial misdiagnoses and delayed eventual diagnoses of patients have even further negative repercussions for the general medical knowledge of a rare disease. Delays in diagnosis and inadequate care create a vicious cycle in the treatment of rare diseases.



When patients are diagnosed in the late stages of a rare disease, the body of knowledge about the disease fails to portray key early symptoms or manifestations. Very frequently, clinical descriptions of rare diseases are based on advanced stages of the disease observed after an absence of intervention. Diagnoses based on these descriptions are consequently, and not surprisingly, late. To use the example of PWS, moderate to severe mental retardation can develop, particularly in cases with no treatment. Early diagnosis can provide PWS patients the opportunity to optimise their learning environment and improve cognitive development while their cognitive capacity is still flexible. With repeated documentation, such benefits of early intervention could be included in clinical descriptions, be put into practice and break the vicious cycle, allowing for earlier diagnosis and more robust treatment.

Non-medical consequences resulting from excessive delays in diagnosis, such as the birth of another affected child or the inappropriate treatment of an affected child, profoundly affect patients, but are seldom if ever taken into account in the implementation of many healthcare policies. In the case of screening policies, many health authorities argue that the availability of diagnosis should only be offered in cases where specific treatment exists. From this survey as well as countless patient testimonies, it is well established that not knowing one's illness is not only a psychologically frustrating and tiring experience, but also one that can lead to inappropriate treatments and other severe and unacceptable consequences. Prior to the publication of these results, these consequences were not well known by policymakers, health care professionals and other healthcare authorities. The consequences were rarely recorded in medical records, as they were considered to fall outside the sphere of the patient's acute medical needs and relevant medical information, and were not considered as relevant medical history. The issue of the right to diagnosis remains a significant debate in the rare disease community. The majority of patients feel they have a right to know their diagnosis, whether treatment for their disease exists or not. Many healthcare professionals feel that it is unethical to announce to a patient the diagnosis of a disease for which nothing can be done. What is certain is that the continued collection of experience and expectations on this topic (as well as all others related to rare diseases) can only help all stakeholders make informed decisions.



The Way Forward:

From the Voices of 12 000 Patients to Patient-Centred Health Care for Rare Diseases

EURORDIS' mission is to build a strong pan-European community of patient organisations and people living with rare diseases, to be their voice at the European level and to — directly or indirectly — fight against the impact of rare diseases on their lives.

EURORDIS has and will continue to organise interactive consultation processes empowering patient representatives to seek multidisciplinary and comprehensive care as well as promoting the development of adequate public care policies. Twelve thousand rare disease patients have directly expressed their experiences, needs and expectations through their participation in the EurordisCare2 and EurordisCare3 surveys.

EURORDIS' ongoing and future advocacy actions are based not only on these survey results but also on the outcome of activities started in 2006, which will continue to involve its members, medical experts and policymakers until 2011.

To improve the quality and access to diagnosis and care for rare disease patients in Europe, and to build on the success of the EU policy on orphan drugs, EURORDIS has progressively identified and promoted two cornerstones: National Strategies or Action Plans for Rare Diseases and European Reference Networks of Centres of Expertise for Rare Diseases. These two policy areas are closely linked.

Together they form the framework on which long-term goals in the field of rare diseases, such as the development of patient registries, multicentric clinical research,

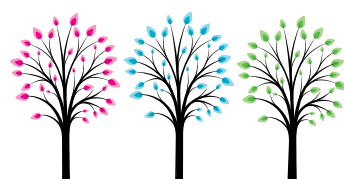
a common approach to screening, common protocols for diagnosis and care, and common social guidelines, will be built.

A RESOURCE-INTENSIVE WORK IN PROGRESS SINCE 2006

Contributing to the EU High Level Group on Health Services and Medical Care and the EU Directive on Patients' Rights in Terms of Cross-Border Care

EURORDIS has contributed to the debate on the EU Directive on Patients' Rights in Cross-Border Healthcare in order to promote a legal instrument enforcing a patient's right to seek care across the EU, a significant step towards a European-wide organisation of health care.

A section of this directive is dedicated to the creation of European Reference Networks.



From 2006 until 2008, EURORDIS has taken an active role, as an invited partner, in the work of the EU High Level Group on Health Services and Medical Care through its Working Group on European Reference Networks. Together with the members of this working group as well as with the representatives of the DG SANCO Rare Disease Task Force, EURORDIS has contributed to the definition of the key concepts of Centres of Expertise and European Reference Networks, their expected missions, the criteria for their identification and selection, and their evaluation process. The rarity of the patients as much as the scarcity of experts and knowledge on rare diseases are the main reasons that they are at the forefront of these reflection processes. EURORDIS has played a key role in advocating to the commission in favour of piloting European Reference Networks in the arena of rare diseases.

Promoting a Patient-Centred Dialogue Between All Interested Parties at National and European Levels on Centres of Expertise and European Reference Networks

In 2007, EURORDIS was instrumental in developing the dialogue between interested parties both at national and EU levels. EURORDIS and its national alliances or partners, organised national and European workshops in 11 countries¹, altogether convening 370 patient representatives, experts and policymakers. Each national workshop was built around the same agenda. Each started with presentations of the key concepts developed by the EU High Level Group on Health Services and Medical Care and the quantitative analysis of the Rare Disease Task Force. Participants addressed the same questions regarding the application of these concepts to their specific healthcare systems and contributed to the articulation of a policy on Centres of Expertise with European networks.

In July 2007, a two-day European workshop took place in Prague, bringing together 90 participants from all over Europe, with a delegate from each previous national workshop as well as European policymakers and stakeholders. This capstone workshop built on a preliminary analysis of the EurordisCare3 survey as well as on the outcomes of the national workshops refining key recommendations on Centres of Expertise and European Reference Networks based on patients' feedback and stakeholder dialogue. These coordinated 'top-down' and 'bottom-up' dialogue processes were essential in creating a shared concept and common vocabulary regarding Centres of Expertise and European Reference Networks amongst all stakeholders. It was also a significant contribution to the ongoing policy development process of the EU High Level Group, the Commission and some member states.

Contributing to the Commission Communication on a European Action in the Field of Rare Diseases and the Council Recommendations on Rare Diseases

EURORDIS initiated the call for a comprehensive and long-term policy framework for rare diseases at both the EU and member state levels since its European Conference on Rare Diseases 2005 Luxembourg, under the EU

1- Czech Republic, Denmark, France, Germany, Italy, Luxembourg, Netherlands, Portugal, Spain, Sweden, United Kingdom. See http://www.eurordis.org/IMG/pdf/EU_workshop_report_3.pdf

presidency. One year later, it called for the establishment of an EU High Level Group on Rare Diseases to define and steer such a policy. It also publicly advocated for rare diseases to be considered by the European Commission and the Council as a public health priority in the EU Public Health Programme 2008 to 2013. This was an essential step in the initiation of the actions that followed.

Since the beginning of its development in 2007, EURORDIS has participated in the drafting of a Commission Communication on a European Action in the Field of Rare Diseases. EURORDIS intensively used the European Conference on Rare Diseases 2007 Lisbon as a launching pad for the Commission's Public Consultation 'Rare Diseases: Europe's Challenges'. It further mobilised its network of patient groups, national alliances, European federations, industry and academic partners as well as all other stakeholders to promote this public consultation and turn it into a success. The result was an outstanding 600 high-quality contributions by February 2008. Since this time, EURORDIS has continuously taken an active part in meetings of the Communication Drafting Group and relevant Rare Disease Task Force meetings and followed through with all opportunities to advocate for a prompt adoption of the document.

EURORDIS has played a leading role in promoting the Council Recommendations on Rare Diseases to ensure their political momentum and service as a European reference document used by all member states to develop and implement national strategies and action plans in the area of rare diseases. With the goal of improving quality and access to diagnosis and care, two key pillars in these recommendations include the creation of Centres of Expertise with European Reference Networks, and the sharing of expertise at the European level.

EURORDIS has relentlessly advocated at the highest political levels of the commission and the rotating EU presidency in order to speed up the development and adoption of these policies. Patients are waiting. To fight against the impact of rare diseases on their lives, patients not only need a sound policy framework that includes a strategy and action plans but also the tools and time to turn the framework into a reality.

VISIONS FOR THE FUTURE

Contributing to the National Strategies and Action Plans on Rare Diseases
EURORDIS' political priority for the upcoming years is to promote national strategies and action plans on rare diseases articulated within a European policy framework in the areas of research, information, Centres of Expertise, access to rare disease therapies, sharing of expertise and patient empowerment.

EURORDIS acts first with and through its network of national alliances on rare diseases in 16 countries to promote and contribute to these national strategies and action plans.



EURORDIS is participating in EUROPLAN, the European Project for Rare Disease National Plans Development, a Directorate General of Health and Consumers-funded project coordinated by the Italian Health Institute that aims to develop recommendations on how to define a strategy and an action plan for rare diseases at the national level. This project, which began in June 2008 and will continue until mid-2011, is essential to the implementation of this most significant recommendation from the European Commission's Communication on a European Action in the Field of Rare Diseases.

The EUROPLAN project already brings together representatives from 22 member states (19 as partners and three as observers, thus far). As the only patient organisation involved, EURORDIS will be specifically responsible for identifying and supporting 15 multi-stakeholder National Conferences on Rare Diseases across Europe, and ensuring that during the conferences the strategy underlying the commission communication as well as the best measures identified through the mapping and benchmarking exercises involving all member states, are explained to all participants.

EURORDIS participation, closely linked to the participation of national alliances, should allow a patient-centred contribution to the development of national strategies. In addition, the feedback from the debates and the discussions about the feasibility of these measures in different national contexts will be summarised and reported to develop common European recommendations.

The creation of national rare disease strategies and action plans presents an opportunity for the introduction of policies that can encourage earlier diagnosis and adequate quality of and access to care. These plans may include supporting raising awareness of rare diseases in general practitioners trained in each country. They can support and even require the systematic screening for certain rare diseases for which clear early clinical signs have been identified or reliable genetic tests exist, leading to earlier appropriate medical interventions and significant improvement in the quality of a patient's life. These plans can encourage the identification, selection, support and evaluation of Centres of Expertise, centres in which patients can feel welcome, find a concentration of specialists and ultimately be treated with the comprehensive, multidisciplinary approach they require.

Providing a Common Political Platform to Advocate for Centres of Expertise and European Reference Networks

Alongside this and other commission-supported activities, EURORDIS has and will continue to organise discussions empowering patient representatives in seeking multidisciplinary and comprehensive care.

EURORDIS initiated a broad, direct consultation of its membership base during its 2006 membership meeting in Berlin entitled 'Centres of Reference: How Can We Make It Happen?.' The meeting included workshops on rare disease specialised care centres, patient databases

and registries and patient-driven research. This first cycle of grassroots patient organisation policy development ended in 2008, 'a pivotal year to grasp the nettle', with the EURORDIS membership meeting 2008 in Copenhagen entitled 'Acting Together for Patient-Centred Care for Rare Diseases: A European Workshop Empowering Patients, Families and Their Organisations Toward Multidisciplinary Medical and Social Care in Centres of Expertise and European Reference Networks on Rare Diseases'. This meeting included workshops on challenges and expectations for European Reference Networks for rare diseases, innovative partnership between patient organisations and Centres of Expertise and innovative social approaches to cope with rare diseases.

During the Copenhagen meeting, 120 patient organisation representatives from 26 countries drafted the Declaration of Common Principles on Centres of Expertise and European Reference Networks. This document represents the patients' call for health policy supporting the establishment of Centres of Expertise and a list of their key functions, proposed and agreed on by patients, to be ultimately considered as functions of all Centres of Expertise.

This declaration is based on all previous discussions, the results from the EurordisCare3 survey, the direct input of all of EURORDIS's member organisations since 2006, the conclusions of the two-year participative bottom-up reflection process, and the work of the EU High Level Group on Health Services and Medical Care and the DG SANCO Rare Disease Task Force.

The declaration (Appendix) will be officially launched on February 28th, Rare Disease Day 2009, as an advocacy tool for all rare disease patient groups, national alliances, European federations on rare diseases and medical experts working in the field of rare diseases.

Providing Tools and Processes to Facilitate the Dialogue Between Professionals and Patient Groups at Local and European Levels

Also during the 2008 Copenhagen membership meeting, discussions on the relationship of patient organisations with their Centres of Expertise in their respective countries resulted in the drafting of a Charter for Good Practice Collaboration Between Patient Groups and Centres of Expertise. The charter will eventually serve as a guide and an operational tool for patient representatives providing a working basis for collaboration with medical experts within their respective Centres of Expertise.

The charter will be launched for a three-year experimental phase throughout Europe.

With the support of POLKA, Patient Preferred Policy Scenarios for Rare Diseases, EURORDIS' newest project supported by the Directorate General of Health and Consumers, a Working Group on Centres of Expertise and European Reference Networks will be created with the participation of patient representatives, healthcare professionals

and policymakers. This group will be charged with the continued development of the charter, the creation of new patient online tools on Centres of Expertise and European Reference Networks, and an overall mission of supporting and guiding the implementation of an EU policy for European Reference Networks from a patient perspective.

Gaining a Track Record of Experience on Partnership Between Patients' Representatives, Centres of Expertise and European Reference Networks

EURORDIS is involved in several European Reference Networks either as a partner (e.g. nEUrope: the European Reference Network for Rare Paediatric Neurological Diseases) or as adviser (e.g. the European Reference Network for Cystic Fibrosis as well as that for histiocytosis). As such, EURORDIS is directly involved in the preliminary stages of pilot networks learning directly from their successes and challenges as they are encountered and contributing to the solutions ultimately included in a sound long-term EU policy.

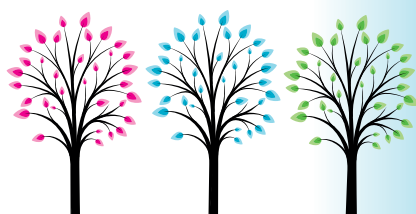
In parallel, EURORDIS will share the experience gained by its members, in particular, the 16 national alliances, the 25 rare disease-specific European federations and the national patient organisations with experience in partnering with Centres of Expertise.

EURORDIS knows that these EU and national policies are necessary but will not come easily, particularly when it comes to financial aspects. EURORDIS knows that the relationship between patients and healthcare professionals can very rewarding but also challenging when it comes to discussing essential choices on how to organise centres or networks and how to work with its ultimate end users — patients and their families. While promoting national policies on Centres of Expertise and supporting partnership between patient groups and these centres, EURORDIS paramount objective will be to promote mutually supportive relationships between patient representatives and medical experts in order to better serve patients and their families and to reduce the impact of rare diseases on their lives.

We all need each other. Patients and families need healthcare professionals. Healthcare professionals need the support of patient advocates. Policymakers need the guidance and support of patient advocates and healthcare professionals. Partnership is the only way forward to better define patient healthcare pathways and more patient-centred care.

Yann Le Cam

*Chief Executive Officer
EURORDIS*



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

www.eurordis.org



D E C L A R A T I O N

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



15 November 2008

Rare Diseases Europe

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

In 2008, EURORDIS adopted this Declaration of "Common Principles on Centres of Expertise and European Reference Networks for Rare Diseases", in order to improve patient care throughout Europe.

Rare disease patients call upon National Health Authorities to endorse, publicise and implement the following Declaration to contribute to the identification of Centres of Expertise and to support them financially.

Rare diseases are often complex diseases

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

Rare disease patients are too often excluded from health systems and socially marginalised, in spite of their tenacious personal commitment^{(5) (6)}

6. Centres of Expertise shall be places where patients feel welcome and safe⁽⁷⁾ and where patients are received by knowledgeable and understanding professionals
7. Centres of Expertise shall facilitate and improve the autonomy of the patient
8. Centres of Expertise shall provide access⁽⁸⁾ to social assistance⁽⁹⁾, which respond to the special needs of the disease⁽¹⁰⁾



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

9. Centres of Expertise and European Reference Networks shall actively involve patients and their representatives in the establishment and performance, management and evaluation of the centre ⁽¹¹⁾. These evaluations should be made publicly available
10. Centres of Expertise shall exchange information with local professionals ⁽¹²⁾, including general practitioners ⁽¹³⁾
11. Centres of Expertise and European Reference Networks shall disseminate information on the diseases to social and other relevant stakeholders involved ⁽¹⁴⁾
12. Centres of Expertise shall provide training ⁽¹⁵⁾ to all stakeholders involved, including health care professionals, patients and their representatives
13. Centres of Expertise and European Reference Networks shall provide guidelines on the most appropriate care management for patients, closely integrating both medical and social aspects. They should involve patients and give them an active role as recognised partners at all stages.
14. Centres of Expertise and European Reference Networks shall facilitate the coordination of both basic and clinical research activities and infrastructures, including clinical trials, registries, biobanks, exploration of innovative techniques, etc. They should also be required to publish and disseminate research results, irrespective of whether the results are positive or negative
15. Access to Centres of Expertise must be ensured to all patients, regardless of their country or region of origin

The following figures are based on the **EurordisCare3 Survey** on access to health services, for which a total of 5995 responses were received from 22 countries for 16 diseases, thanks to the active involvement of 130 patient organisations.

- (1) Each patient went through an average of four different types of medical consultation, three kinds of examination and 2.4 types of treatment over the last two years, in relation to his/her disease.
- (2) During the same period, almost half of these (47%) spent time in hospital for an average of three times for 20 days in total.
- (3) 94% of patients consider that "coordinating the sharing of medical information on the patient between all professionals who care for him/her in the specialised centre" is essential (70%) or useful (24%).
- (4) 95% of patients consider that "communicating with other specialised centres and professional networks to harmonise treatments and research at the national and European level" is essential (67%) or useful (28%).
- (5) An average of 59% of the respondents (up to 64% for the low income group) had to reduce or stop their professional activity because of their disease or to take care of a relative affected by a rare disease.
- (6) On average, 16% of patients (up to 24% for the low income group) were forced to move house because of their disease.
- (7) One out of 5 patients (18%) experienced rejection linked to their disease from healthcare professionals. The patient perceived reason of rejection is linked to the disease (80% of cases due to reluctance because of the complexity of the disease), and/or to the physical conditions of the patient: 10% for disease-related behaviour, 11%, for communication difficulties and 15% for physical aspect.
- (8) Every year, 28% of the patients needed the assistance of a social worker. For about one-quarter of these, access to this assistance was difficult: difficult access (18%), very difficult (9%) or even impossible (4%).
- (9) 92% of patients consider that "informing patients about their rights and guiding them toward social services, schools, leisure activities or vocational guidance" is essential (55%) or useful (37%).
- (10) Globally, social assistance services respond inadequately to the expectations and needs of rare diseases patients (only 37% of patients are satisfied), especially when the demands are specific to the disease: 27% for assistance to obtain exceptional financial support, such as the purchase of a wheel chair, 32% for assistance with social integration, school, leisure or professional integration. This inadequacy of the social assistance is more severe for the low income patients (only 26% of satisfied).
- (11) 96% of patients agree that "a specialised centre should involve patient organisations in order to benefit from their knowledge of daily life and needs of patients".
- (12) 90% of patients consider that "creating material for teachers, employers, social services, insurance companies and the general public to inform them about patients' needs and improve social integration of patients" is useful or essential.
- (13) 44% of patients disagree that "the role of general practitioners consists mainly in looking after health problems not related to the rare disease".
- (14) 95% of patients consider that "coordinating the sharing of medical information between health professionals of the specialised centre and local health professionals" is useful or essential.
- (15) 93% of patients consider that "training local professionals to respond to the specific needs of patients" is useful or essential.

Appendix 2 The EurordisCare2 questionnaire

	EurordisCare 2 Survey of the delay in diagnosis for 10 rare diseases in Europe	 EURORDIS European Organisation for Rare Diseases
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Dear friends, we are contacting you as a member of a patient organisation collaborating in this survey.

As you know, Rare Diseases are still poorly known both by the general public and by most health professionals. This lack of information often leads to late diagnoses which delay the beginning of adapted treatments and can be responsible for the disease's progression or to severe consequences. While rare disease patients often face this delay in diagnosis, it remains badly documented and its consequences are insufficiently taken into account by the health authorities.

In collaboration with 75 European associations including yours, EURORDIS * is undertaking this survey to study the delay in diagnosis for 10 rare diseases (Crohn's disease, Cystic fibrosis, Duchenne muscular dystrophy, tuberous sclerosis, Ehlers-Danlos syndrome, Marfan syndrome, Prader Willi syndrome, X fragile syndrome, retinitis pigmentosa, Williams syndrome). This survey, named EurordisCare 2, will cover all European countries (as far as possible!!).

This study's objective is to identify the main causes of delay in diagnosis and to find solutions to reduce this delay by appropriate measures such as: medical training, raising public awareness, systematic screening, etc. Delay in diagnosis can vary greatly depending on the disease, and on the country, but also on individual factors: each patient has his own history. **For this reason, this questionnaire is addressed to the only information holders: the patients and families concerned. Each answer is significant. The quality and the repercussions of this study depend on the number of answers and on their widespread origin. If you have any problems answering this questionnaire, please contact us at eurordiscare@eurordis.org**

To save time, your members should return the completed questionnaire directly to Eurordis using the pre-paid envelope herewith. Each participating association will of course have access to the anonymous data concerning its own members.

The number of answers received per country and per disease, will be regularly updated and available at www.eurordis.org in the section "EurordisCare 2".

We hope to be able to present the synthesis of this investigation in the summer of 2004 and would therefore thank you in advance for answering very quickly, as the questionnaires received after June 15th may not be taken into account.

* Eurordis is a European alliance of rare disease patient associations which brings together more than 200 associations in 17 countries. A prior survey, "EurordisCare 1", of access to care for six rare diseases. 50 patient organisations participated - the results can be consulted on our site www.eurordis.org

• Questionnaire(s)** completed by

☐ the patient ☐ a relative ☐ another member of the association ☐ other: _____

** If several people suffer from the disease in your family, please complete a questionnaire per person and return them to us in the same envelope. You can photocopy this form or ask your association or eurordiscare@eurordis.org for extra copies

• Patient's date of birth: / / (day/month/year) • Sex: ☐ Male ☐ Female

• When the disease first manifested itself, what was the patient's professional category or that of the patient's parents if symptoms occurred during childhood?

<input type="checkbox"/> Middle or senior management	<input type="checkbox"/> Student	<input type="checkbox"/> Teacher
<input type="checkbox"/> Bluecollar worker	<input type="checkbox"/> Unemployed	<input type="checkbox"/> Farmer
<input type="checkbox"/> Craftsman, tradesman	<input type="checkbox"/> Retired	<input type="checkbox"/> Employee
	<input type="checkbox"/> Liberal professions	<input type="checkbox"/> Other

• When the disease first manifested itself, where did the patient live, or his parents if symptoms occurred during childhood?

<input type="checkbox"/> country or village	<input type="checkbox"/> town of 1000 to 10 000 inhabitants	<input type="checkbox"/> town of 10 000 to 50 000 inhabitants
<input type="checkbox"/> town of 50 000 to 100 000 inh.	<input type="checkbox"/> town of 100 000 to 500 000 inhabitants	<input type="checkbox"/> city of more than 500 000 inhabitants

3

• Was the diagnosis already known at birth, or within the first 3 months?

☐ No Yes, specify the circumstances

☐ Other cases in the family ☐ Disorders during the pregnancy or at the birth ☐ Systematic neonatal screening

If yes go directly to: 7. (bottom of page 3)

4

• What were the first manifestations of the disease?

Nature of the symptoms	When did these symptoms start?	How many time did these symptoms occur before the final diagnosis?			
	age: or date:/... (month/year)	<input type="checkbox"/> 1 to 5 times	<input type="checkbox"/> 6 to 20 times	<input type="checkbox"/> more than 20 times	<input type="checkbox"/> persistent disorders
	age: or date:/... (month/year)	<input type="checkbox"/> 1 to 5 times	<input type="checkbox"/> 6 to 20 times	<input type="checkbox"/> more than 20 times	<input type="checkbox"/> persistent disorders
	age: or date:/... (month/year)	<input type="checkbox"/> 1 to 5 times	<input type="checkbox"/> 6 to 20 times	<input type="checkbox"/> more than 20 times	<input type="checkbox"/> persistent disorders

• How many doctors did you consult between the first manifestations and the final diagnosis?

☐ 1 to 2 ☐ 3 to 5 ☐ 6 to 10 ☐ 11 to 20 ☐ more than 20: _____

• Which types of examination were carried out during this period? (several answers possible)

<input type="checkbox"/> none	<input type="checkbox"/> biological examinations (blood test, urine test, CSF test, biopsy)	<input type="checkbox"/> genetic testing
<input type="checkbox"/> radiological examinations, (ultrasound, NMR, scanner, other imagery...)	<input type="checkbox"/> functional explorations (respiratory, muscular, electroencephalogram)	<input type="checkbox"/> others: _____

• In view of these disorders, were you given other diagnosis before that of your disease?

☐ No ☐ Yes, specify:

Diagnosis:	When?	By whom?
1	age: or date:/... (month/year)	<input type="checkbox"/> a general practitioner <input type="checkbox"/> a specialist (specify): _____
2	age: or date:/... (month/year)	<input type="checkbox"/> a general practitioner <input type="checkbox"/> a specialist (specify): _____
3	age: or date:/... (month/year)	<input type="checkbox"/> a general practitioner <input type="checkbox"/> a specialist (specify): _____

• Following these diagnosis, were treatments undertaken? (several answers possible)

☐ No Yes, specify:

<input type="checkbox"/> medicinal	<input type="checkbox"/> surgical
<input type="checkbox"/> psychological	<input type="checkbox"/> others: _____

• What were the consequences of the delay in diagnosis? (several answers possible)

☐ none

<input type="checkbox"/> physical consequences	<input type="checkbox"/> birth of other children suffering from the disease
<input type="checkbox"/> psychiatric consequences	<input type="checkbox"/> family behaviour not adapted
<input type="checkbox"/> intellectual consequences	<input type="checkbox"/> loss of confidence in medicine
<input type="checkbox"/> death	<input type="checkbox"/> other: _____

5

- When was the possibility of a rare disease first raised?

Age of the patient: or Date: (month/year)

- Who raised this possibility?

<input type="checkbox"/> a physician	<input type="checkbox"/> another health professional	<input type="checkbox"/> the media/ press	<input type="checkbox"/> Internet
<input type="checkbox"/> a teacher	<input type="checkbox"/> a rare disease patient	<input type="checkbox"/> a close relative	<input type="checkbox"/> other.....

6

- When was the final diagnosis carried out?

Age of the patient: or Date: (month/year)

- By whom was the diagnosis given?

<input type="checkbox"/> a general practitioner	<input type="checkbox"/> a specialist specify the speciality: <input type="text"/>
---	--

- On which type of data was the diagnosis based? *(several answers possible)*

<input type="checkbox"/> clinical (examination of the patient, symptoms, evolution...)	<input type="checkbox"/> biological (blood or urine test, biopsy...)	<input type="checkbox"/> functional (respiratory, muscular, EEG...)
<input type="checkbox"/> radiological (scanner, ultrasound, scintigraphy, NMR...)	<input type="checkbox"/> genetics	<input type="checkbox"/> other: <input type="text"/>

- In which type of facility was the diagnosis carried out?

<input type="checkbox"/> private practice	<input type="checkbox"/> hospital consultation
<input type="checkbox"/> specialised centre	<input type="checkbox"/> other: <input type="text"/>

- How did you find this facility?

<input type="checkbox"/> recommended by a physician	<input type="checkbox"/> by another health professional	<input type="checkbox"/> media, press
<input type="checkbox"/> recommended by a patient	<input type="checkbox"/> Internet, Web site	<input type="checkbox"/> other: <input type="text"/>

- In relation to your home at that time, where was this facility located?

<input type="checkbox"/> in the same city	<input type="checkbox"/> in the same region	<input type="checkbox"/> in another region	<input type="checkbox"/> in another country
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- Did you seek a second opinion to confirm this diagnosis?

<input type="checkbox"/> No	<input type="checkbox"/> Yes, when ? <input type="text"/>
<p>• Age of the patient: <input type="text"/> or Date: <input type="text"/> (month/year)</p>	
<p>• Who provided this confirmatory diagnosis?</p> <p><input type="checkbox"/> a general practitioner <input type="checkbox"/> a specialist specify: <input type="text"/></p>	
<p>• Where was this confirmatory diagnosis carried out?</p> <p><input type="checkbox"/> private practice <input type="checkbox"/> hospital consultation</p> <p><input type="checkbox"/> specialised centre <input type="checkbox"/> other: <input type="text"/></p>	

- Did seeking diagnosis require any personal expenditure?

<input type="checkbox"/> no	<input type="checkbox"/> low	<input type="checkbox"/> moderate	<input type="checkbox"/> high	<input type="checkbox"/> very high
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- Do you think that the delay in diagnosis depends on the level of personal expenditure?

<input type="checkbox"/> not at all	<input type="checkbox"/> slightly	<input type="checkbox"/> partially	<input type="checkbox"/> primarily
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7

- Did knowledge of this diagnosis lead you to move?

<input type="checkbox"/> No	<input type="checkbox"/> Yes
<input type="checkbox"/> within the same region	<input type="checkbox"/> to another area <input type="checkbox"/> to another country

• Who announced the disease diagnosis to you?		
<input type="checkbox"/> an analysis laboratory	<input type="checkbox"/> a general practitioner	<input type="checkbox"/> a specialist
<input type="checkbox"/> a geneticist	<input type="checkbox"/> other:	
• How?		
<input type="checkbox"/> orally in consultation	<input type="checkbox"/> orally, elsewhere (corridor...)	<input type="checkbox"/> by phone
<input type="checkbox"/> in writing with explanations	<input type="checkbox"/> in writing without explanations	<input type="checkbox"/> other:
• Was the announcement of the diagnosis accompanied by psychological support?		
<input type="checkbox"/> No	Yes, specify by whom:	
<input type="checkbox"/> by a general practitioner	<input type="checkbox"/> by a specialist	<input type="checkbox"/> by a psychologist
<input type="checkbox"/> by an association member	<input type="checkbox"/> other:	
• Should this support be systematically offered?		
		<input type="checkbox"/> No <input type="checkbox"/> Yes
• Did you then receive complete information about the disease? <i>(several answers possible)</i>		
<input type="checkbox"/> No	Yes, specify by whom:	
<input type="checkbox"/> by a general practitioner	<input type="checkbox"/> by a specialist	<input type="checkbox"/> by a geneticist
<input type="checkbox"/> by an association member	<input type="checkbox"/> other:	
• Should this information be systematically provided at that time?		
		<input type="checkbox"/> No <input type="checkbox"/> Yes
• Globally, the conditions in which the diagnosis was announced of the diagnosis seemed:		
<input type="checkbox"/> well-adapted	<input type="checkbox"/> acceptable	<input type="checkbox"/> poor <input type="checkbox"/> unacceptable

• Was the genetic nature of the disease identified?		
<input type="checkbox"/> No	Yes	
<input type="checkbox"/> not inherited (new mutation or isolated case)		
<input type="checkbox"/> transmitted with possibility of other carriers in the family (recessive gene)		
<input type="checkbox"/> transmitted with possibility of other people suffering in the family (dominant gene)		
• When? Age of the patient: _____ or Date: .../.../... (month/year)		
• Following the diagnosis of the disease did you obtain genetic advice?		
<input type="checkbox"/> No	<input type="checkbox"/> Yes	
• Once diagnosed did you contact other members of your family to inform them of the genetic nature of the disease? <i>(several answers possible)</i>		
<input type="checkbox"/> No	Yes, specify which:	
<input type="checkbox"/> brothers, sisters	<input type="checkbox"/> father, mother	
<input type="checkbox"/> uncles, aunts, cousins	<input type="checkbox"/> grandparents, grandchildren	
	<input type="checkbox"/> more distant relative	
• Was this step suggested by doctors or health professionals?		
<input type="checkbox"/> No	Yes, specify on which occasion:	
<input type="checkbox"/> during the diagnosis	<input type="checkbox"/> during genetic counselling	<input type="checkbox"/> later
• Did this step lead to diagnoses among other members of your family?		
<input type="checkbox"/> No	Yes, specify	Family link:
<input type="checkbox"/> Suffering from the disease and already having symptoms		
<input type="checkbox"/> Suffering from the disease while not yet having symptoms		
<input type="checkbox"/> Not suffering from the disease but liable to transmit it		

Thank you for your collaboration...

Appendix 3 The EurordisCare3 questionnaire



Eurordis survey on patients' experience and expectations concerning access to health services in Europe.



Dear friends,

We are writing to you, patient or patient's relative, who is member of the Ehlers-Danlos Syndrome Support Group UK which is collaborating with Eurordis on this survey.

Access to health services is part of the difficulties associated with rare diseases that are encountered daily by patients and their families. Access to health services faces various obstacles: identification of skilled professionals, access to structures that are sometimes far away, acceptance of financial liability or reimbursement of the medical services and journey, etc. The difficulties encountered can vary a lot according to the disease, the country, and individual factors: each patient has his/her own history.

We are leading this survey in order to assess the current situation and define expectations of patients affected by Ehlers-Danlos syndrome and 15 other rare diseases in Europe (Alternating hemiplegia, Aniridia, Ataxias, Cystic fibrosis, Epidermolysis bullosa, Fragile X syndrome, Huntington disease, Marfan syndrome, Myasthenia, Osteogenesis imperfecta, Prader-Willi syndrome, Pulmonary arterial hypertension, Tuberous sclerosis, Williams syndrome, and 11q disorders). Our aim is to make the patient voice heard, while several European countries are leading a reflection on the reorganisation of the offer for care for rare diseases. The quality of this survey and the attention that it will get from health policy makers depends on the number of responses we receive. **Patients' opinion is the priority.**

Questions concerning your personal experience were defined in collaboration with organisations of every disease to better adapt them to specific situations. Questions concerning your expectations, and those that help to identify the origin of the disparities of access to health services due to individual situations are common to all diseases. **It is essential to answer all questions.** If a section is not relevant (sections 1 to 8, 11 and 12), please select "no" in the first line of the section, before moving on to the next one. Unless mentioned otherwise, each question requires a single answer.

The distribution of the questionnaire by your organisations, who have exclusive access to your contact details, allows us to specifically survey the patients of the diseases studied. Once completed, this anonymous questionnaire can be returned directly to Eurordis (using the included prepaid envelope), which will ensure the complete confidentiality of the information and responses. Eurordis will complete the analysis of this data and commits not to share your personal data with anyone. Every organisation will receive the statistical results of the analysis corresponding to the responses of their members.

(contact : mherasse@eurordis.org)

Thank you for replying quickly to ensure all responses are taken into account in the analysis (before September 30th 2007).

1 Have you needed to consult a **cardiologist** over the last 12 months? ☐ YES ☐ NO → go to 2

Did you have access to these consultations? ☐ YES ☐ NO

Why? (several responses possible)

Access to these consultations was:

- ☐ very easy ☐ easy ☐ difficult ☐ very difficult

Overall, the number of consultations was:

- ☐ well adapted ☐ sufficient ☐ insufficient ☐ very insufficient ☐ no opinion

The personal cost incurred was:

- ☐ nil ☐ partial ☐ total specify £ / consultation You found this amount: ☐ acceptable ☐ excessive

Most of the consultations took place:

- ☐ at home ☐ private practice ☐ hospital ☐ clinic ☐ specialised centre for your disease

specify where:

- ☐ same region ☐ other region ☐ other country miles from home You found this distance: ☐ acceptable ☐ excessive

Journey completed: ☐ alone ☐ with a relative / friend ☐ with professional assistance or transport

You found the time to obtain the first consultation:

- ☐ very short ☐ short ☐ long ☐ very long specify how long month

These consultations responded to your expectations:

- ☐ fully ☐ partially ☐ poorly ☐ not at all

Why? (several responses possible)

- ☐ Specialist could not be found or unavailable ☐ yes ☐ no
- ☐ Lack of referral ☐ yes ☐ no
- ☐ Excessive waiting time specify month ☐ yes ☐ no
- ☐ Personal cost incurred too high specify £ / consultation ☐ yes ☐ no
- ☐ Location of the consultations too far specify miles from home ☐ yes ☐ no
- ☐ specify where ☐ same region ☐ another region ☐ another country
- ☐ Excessive time of journey ☐ yes ☐ no
- ☐ Nobody was available to accompany you ☐ yes ☐ no
- ☐ Cost of journey too high ☐ yes ☐ no
- ☐ Lack of suitable transport ☐ yes ☐ no
- ☐ Travelling too difficult (pain, fatigue, injuries) ☐ yes ☐ no

2 Have you needed to consult a **rheumatologist** over the last 12 months? ☐ YES ☐ NO → go to 3

Did you have access to these consultations? ☐ YES ☐ NO

Why? (several responses possible)

Access to these consultations was:

- ☐ very easy ☐ easy ☐ difficult ☐ very difficult

Overall, the number of consultations was:

- ☐ well adapted ☐ sufficient ☐ insufficient ☐ very insufficient ☐ no opinion

The personal cost incurred was:

- ☐ nil ☐ partial ☐ total specify £ / consultation You found this amount: ☐ acceptable ☐ excessive

Most of the consultations took place:

- ☐ at home ☐ private practice ☐ hospital ☐ clinic ☐ specialised centre for your disease

specify where:

- ☐ same region ☐ other region ☐ other country miles from home You found this distance: ☐ acceptable ☐ excessive

Journey completed: ☐ alone ☐ with a relative / friend ☐ with professional assistance or transport

You found the time to obtain the first consultation:

- ☐ very short ☐ short ☐ long ☐ very long specify how long month

These consultations responded to your expectations:

- ☐ fully ☐ partially ☐ poorly ☐ not at all

Why? (several responses possible)

- ☐ Specialist could not be found or unavailable ☐ yes ☐ no
- ☐ Lack of referral ☐ yes ☐ no
- ☐ Excessive waiting time specify month ☐ yes ☐ no
- ☐ Personal cost incurred too high specify £ / consultation ☐ yes ☐ no
- ☐ Location of the consultations too far specify miles from home ☐ yes ☐ no
- ☐ specify where ☐ same region ☐ another region ☐ another country
- ☐ Excessive time of journey ☐ yes ☐ no
- ☐ Nobody was available to accompany you ☐ yes ☐ no
- ☐ Cost of journey too high ☐ yes ☐ no
- ☐ Lack of suitable transport ☐ yes ☐ no
- ☐ Travelling too difficult (pain, fatigue, injuries) ☐ yes ☐ no

3 Have you needed to consult a **dermatologist** over the last 12 months? ☐ YES ☐ NO → go to **4**

Did you have access to these consultations? ☐ YES ☐ NO Why? (several responses possible)

➤ Access to these consultations was:

☐ very easy ☐ easy ☐ difficult ☐ very difficult

➤ Overall, the number of consultations was:

☐ well adapted ☐ sufficient ☐ insufficient ☐ very insufficient ☐ no opinion

➤ The personal cost incurred was:

☐ nil ☐ partial ☐ total specify £ / consultation You found this amount: ☐ acceptable ☐ excessive

➤ Most of the consultations took place:

☐ at home ☐ private practice ☐ hospital ☐ clinic ☐ specialised centre for your disease

specify where:

☐ same region ☐ other region ☐ other country miles from home You found this distance: ☐ acceptable ☐ excessive

Journey completed: ☐ alone ☐ with a relative / friend ☐ with professional assistance or transport

➤ You found the time to obtain the first consultation:

☐ very short ☐ short ☐ long ☐ very long specify how long month

➤ These consultations responded to your expectations:

☐ fully ☐ partially ☐ poorly ☐ not at all

• Specialist could not be found or unavailable... ☐ yes ☐ no

• Lack of referral... ☐ yes ☐ no

• Excessive waiting time... specify month ☐ yes ☐ no

• Personal cost incurred too high... specify £ / consultation ☐ yes ☐ no

• Location of the consultations too far... specify miles from home ☐ yes ☐ no

specify where ☐ same region ☐ another region ☐ another country

• Excessive time of journey... ☐ yes ☐ no

• Nobody was available to accompany you... ☐ yes ☐ no

• Cost of journey too high... ☐ yes ☐ no

• Lack of suitable transport... ☐ yes ☐ no

• Travelling too difficult (pain, fatigue, injuries)... ☐ yes ☐ no

4 Have you needed to consult a **pain control medicine specialist** over the last 12 months? ☐ YES ☐ NO → go to **5**

Did you have access to these consultations? ☐ YES ☐ NO Why? (several responses possible)

➤ Access to these consultations was:

☐ very easy ☐ easy ☐ difficult ☐ very difficult

➤ Overall, the number of consultations was:

☐ well adapted ☐ sufficient ☐ insufficient ☐ very insufficient ☐ no opinion

➤ The personal cost incurred was:

☐ nil ☐ partial ☐ total specify £ / consultation You found this amount: ☐ acceptable ☐ excessive

➤ Most of the consultations took place:

☐ at home ☐ private practice ☐ hospital ☐ clinic ☐ specialised centre for your disease

specify where:

☐ same region ☐ other region ☐ other country miles from home You found this distance: ☐ acceptable ☐ excessive

Journey completed: ☐ alone ☐ with a relative / friend ☐ with professional assistance or transport

➤ You found the time to obtain the first consultation:

☐ very short ☐ short ☐ long ☐ very long specify how long month

➤ These consultations responded to your expectations:

☐ fully ☐ partially ☐ poorly ☐ not at all

• Specialist could not be found or unavailable... ☐ yes ☐ no

• Lack of referral... ☐ yes ☐ no

• Excessive waiting time... specify month ☐ yes ☐ no

• Personal cost incurred too high... specify £ / consultation ☐ yes ☐ no

• Location of the consultations too far... specify miles from home ☐ yes ☐ no

specify where ☐ same region ☐ another region ☐ another country

• Excessive time of journey... ☐ yes ☐ no

• Nobody was available to accompany you... ☐ yes ☐ no

• Cost of journey too high... ☐ yes ☐ no

• Lack of suitable transport... ☐ yes ☐ no

• Travelling too difficult (pain, fatigue, injuries)... ☐ yes ☐ no

5 Have you needed **physiotherapy or rehabilitation** over the last 12 months? ☐ YES ☐ NO → go to **6**

Did you have access to this type of care? ☐ YES ☐ NO Why? (several responses possible)

➤ Access to this type of care was:

☐ very easy ☐ easy ☐ difficult ☐ very difficult

➤ Overall, the number of sessions was:

☐ well adapted ☐ sufficient ☐ insufficient ☐ very insufficient ☐ no opinion

➤ The personal cost incurred was:

☐ nil ☐ partial ☐ total specify £ / session You found this amount: ☐ acceptable ☐ excessive

➤ Most of the sessions took place:

☐ at home ☐ private practice ☐ hospital ☐ clinic ☐ specialised centre for your disease

specify where:

☐ same region ☐ other region ☐ other country miles from home You found this distance: ☐ acceptable ☐ excessive

Journey completed: ☐ alone ☐ with a relative / friend ☐ with professional assistance or transport

➤ You found the time to obtain the first appointment:

☐ very short ☐ short ☐ long ☐ very long specify how long month

➤ This type of care responded to your expectations:

☐ fully ☐ partially ☐ poorly ☐ not at all

• Professional could not be found or unavailable... ☐ yes ☐ no

• Lack of prescription... ☐ yes ☐ no

• Excessive waiting time... specify month ☐ yes ☐ no

• Personal cost incurred too high... specify £ / session ☐ yes ☐ no

• Location of the sessions too far... specify miles from home ☐ yes ☐ no

specify where ☐ same region ☐ another region ☐ another country

• Excessive time of journey... ☐ yes ☐ no

• Nobody was available to accompany you... ☐ yes ☐ no

• Cost of journey too high... ☐ yes ☐ no

• Lack of suitable transport... ☐ yes ☐ no

• Travelling too difficult (pain, fatigue, injuries)... ☐ yes ☐ no

6 Have you needed **psychological support** over the last 12 months? ☐ YES ☐ NO → go to **7**

Did you have access to this type of care? ☐ YES ☐ NO Why? (several responses possible)

➤ Access to this type of care was:

☐ very easy ☐ easy ☐ difficult ☐ very difficult

➤ Overall, the number of sessions was:

☐ well adapted ☐ sufficient ☐ insufficient ☐ very insufficient ☐ no opinion

➤ The personal cost incurred was:

☐ nil ☐ partial ☐ total specify £ / session You found this amount: ☐ acceptable ☐ excessive

➤ Most of the sessions took place:

☐ at home ☐ private practice ☐ hospital ☐ clinic ☐ specialised centre for your disease

specify where:

☐ same region ☐ other region ☐ other country miles from home You found this distance: ☐ acceptable ☐ excessive

Journey completed: ☐ alone ☐ with a relative / friend ☐ with professional assistance or transport

➤ You found the time to obtain the first appointment:

☐ very short ☐ short ☐ long ☐ very long specify how long month

➤ This type of care responded to your expectations:

☐ fully ☐ partially ☐ poorly ☐ not at all

• Professional could not be found or unavailable... ☐ yes ☐ no

• Lack of prescription... ☐ yes ☐ no

• Excessive waiting time... specify month ☐ yes ☐ no

• Personal cost incurred too high... specify £ / session ☐ yes ☐ no

• Location of the sessions too far... specify miles from home ☐ yes ☐ no

specify where ☐ same region ☐ another region ☐ another country

• Excessive time of journey... ☐ yes ☐ no

• Nobody was available to accompany you... ☐ yes ☐ no

• Cost of journey too high... ☐ yes ☐ no

• Lack of suitable transport... ☐ yes ☐ no

• Travelling too difficult (pain, fatigue, injuries)... ☐ yes ☐ no

3 Have you needed to consult a **dermatologist** over the last 12 months? ☐ YES ☐ NO → go to 4

Did you have access to these consultations? ☐ YES ☐ NO

Access to these consultations was:

☐ very easy ☐ easy ☐ difficult ☐ very difficult

Overall, the number of consultations was:

☐ well adapted ☐ sufficient ☐ insufficient ☐ very insufficient ☐ no opinion

The personal cost incurred was:

☐ nil ☐ partial ☐ total specify £ / consultation You found this amount: ☐ acceptable ☐ excessive

Most of the consultations took place:

☐ at home ☐ private practice ☐ hospital ☐ clinic ☐ specialised centre for your disease

specify where:

☐ same region ☐ other region ☐ other country miles from home You found this distance: ☐ acceptable ☐ excessive

Journey completed: ☐ alone ☐ with a relative / friend ☐ with professional assistance or transport

You found the time to obtain the first consultation:

☐ very short ☐ short ☐ long ☐ very long specify how long month

These consultations responded to your expectations:

☐ fully ☐ partially ☐ poorly ☐ not at all

Why? (several responses possible)

Specialist could not be found or unavailable ... ☐ yes ☐ no

Lack of referral ... ☐ yes ☐ no

Excessive waiting time ... ☐ yes ☐ no specify month

Personal cost incurred too high ... ☐ yes ☐ no specify £ / consultation

Location of the consultations too far ... ☐ yes ☐ no specify miles from home

specify where ☐ same region ☐ another region ☐ another country

Excessive time of journey ... ☐ yes ☐ no

Nobody was available to accompany you ... ☐ yes ☐ no

Cost of journey too high ... ☐ yes ☐ no

Lack of suitable transport ... ☐ yes ☐ no

Travelling too difficult (pain, fatigue, injuries) ... ☐ yes ☐ no

4 Have you needed to consult a **pain control medicine specialist** over the last 12 months? ☐ YES ☐ NO → go to 5

Did you have access to these consultations? ☐ YES ☐ NO

Access to these consultations was:

☐ very easy ☐ easy ☐ difficult ☐ very difficult

Overall, the number of consultations was:

☐ well adapted ☐ sufficient ☐ insufficient ☐ very insufficient ☐ no opinion

The personal cost incurred was:

☐ nil ☐ partial ☐ total specify £ / consultation You found this amount: ☐ acceptable ☐ excessive

Most of the consultations took place:

☐ at home ☐ private practice ☐ hospital ☐ clinic ☐ specialised centre for your disease

specify where:

☐ same region ☐ other region ☐ other country miles from home You found this distance: ☐ acceptable ☐ excessive

Journey completed: ☐ alone ☐ with a relative / friend ☐ with professional assistance or transport

You found the time to obtain the first consultation:

☐ very short ☐ short ☐ long ☐ very long specify how long month

These consultations responded to your expectations:

☐ fully ☐ partially ☐ poorly ☐ not at all

Why? (several responses possible)

Specialist could not be found or unavailable ... ☐ yes ☐ no

Lack of referral ... ☐ yes ☐ no

Excessive waiting time ... ☐ yes ☐ no specify month

Personal cost incurred too high ... ☐ yes ☐ no specify £ / consultation

Location of the consultations too far ... ☐ yes ☐ no specify miles from home

specify where ☐ same region ☐ another region ☐ another country

Excessive time of journey ... ☐ yes ☐ no

Nobody was available to accompany you ... ☐ yes ☐ no

Cost of journey too high ... ☐ yes ☐ no

Lack of suitable transport ... ☐ yes ☐ no

Travelling too difficult (pain, fatigue, injuries) ... ☐ yes ☐ no

5 Have you needed **physiotherapy or rehabilitation** over the last 12 months? ☐ YES ☐ NO → go to 6

Did you have access to this type of care? ☐ YES ☐ NO

Access to this type of care was:

☐ very easy ☐ easy ☐ difficult ☐ very difficult

Overall, the number of sessions was:

☐ well adapted ☐ sufficient ☐ insufficient ☐ very insufficient ☐ no opinion

The personal cost incurred was:

☐ nil ☐ partial ☐ total specify £ / session You found this amount: ☐ acceptable ☐ excessive

Most of the sessions took place:

☐ at home ☐ private practice ☐ hospital ☐ clinic ☐ specialised centre for your disease

specify where:

☐ same region ☐ other region ☐ other country miles from home You found this distance: ☐ acceptable ☐ excessive

Journey completed: ☐ alone ☐ with a relative / friend ☐ with professional assistance or transport

You found the time to obtain the first appointment:

☐ very short ☐ short ☐ long ☐ very long specify how long month

This type of care responded to your expectations:

☐ fully ☐ partially ☐ poorly ☐ not at all

Why? (several responses possible)

Professional could not be found or unavailable ... ☐ yes ☐ no

Lack of prescription ... ☐ yes ☐ no

Excessive waiting time ... ☐ yes ☐ no specify month

Personal cost incurred too high ... ☐ yes ☐ no specify £ / session

Location of the sessions too far ... ☐ yes ☐ no specify miles from home

specify where ☐ same region ☐ another region ☐ another country

Excessive time of journey ... ☐ yes ☐ no

Nobody was available to accompany you ... ☐ yes ☐ no

Cost of journey too high ... ☐ yes ☐ no

Lack of suitable transport ... ☐ yes ☐ no

Travelling too difficult (pain, fatigue, injuries) ... ☐ yes ☐ no

6 Have you needed **psychological support** over the last 12 months? ☐ YES ☐ NO → go to 7

Did you have access to this type of care? ☐ YES ☐ NO

Access to this type of care was:

☐ very easy ☐ easy ☐ difficult ☐ very difficult

Overall, the number of sessions was:

☐ well adapted ☐ sufficient ☐ insufficient ☐ very insufficient ☐ no opinion

The personal cost incurred was:

☐ nil ☐ partial ☐ total specify £ / session You found this amount: ☐ acceptable ☐ excessive

Most of the sessions took place:

☐ at home ☐ private practice ☐ hospital ☐ clinic ☐ specialised centre for your disease

specify where:

☐ same region ☐ other region ☐ other country miles from home You found this distance: ☐ acceptable ☐ excessive

Journey completed: ☐ alone ☐ with a relative / friend ☐ with professional assistance or transport

You found the time to obtain the first appointment:

☐ very short ☐ short ☐ long ☐ very long specify how long month

This type of care responded to your expectations:

☐ fully ☐ partially ☐ poorly ☐ not at all

Why? (several responses possible)

Professional could not be found or unavailable ... ☐ yes ☐ no

Lack of prescription ... ☐ yes ☐ no

Excessive waiting time ... ☐ yes ☐ no specify month

Personal cost incurred too high ... ☐ yes ☐ no specify £ / session

Location of the sessions too far ... ☐ yes ☐ no specify miles from home

specify where ☐ same region ☐ another region ☐ another country

Excessive time of journey ... ☐ yes ☐ no

Nobody was available to accompany you ... ☐ yes ☐ no

Cost of journey too high ... ☐ yes ☐ no

Lack of suitable transport ... ☐ yes ☐ no

Travelling too difficult (pain, fatigue, injuries) ... ☐ yes ☐ no

Your expectations regarding specialised centres

The basic mission of a specialised centre for a rare disease is to ensure diagnosis and follow-up of patients by offering - in the same location - multidisciplinary consultations, medical examinations, specialised equipment and genetic advice.

12 According to your needs, how would you qualify the other following functions that could be provided by a specialised centre ?	of no use	of little use	useful	essential	no opinion
Providing occasional care related to the rare disease (surgery, prosthesis, orthopaedics, etc).	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Providing frequent care related to the rare disease (physiotherapy, speech therapy, psychotherapy, etc).	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Offering patients the option of grouping consultations or tests on the same day in the specialised centre, and organising the appointments.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Coordinating the sharing of medical information on the patient between all professionals who care for him/her in the specialised centre.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Facilitating the follow-up of patients at different stages of their life by easing the passage from paediatric care to adult care, or from adult care to geriatric care.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Informing patients about their rights and guiding them toward social services, schools, leisure activities, or vocational guidance, etc.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Creating material for teachers, employers, social services, insurance companies and the general public to inform them about patients' needs and improve the social integration of patients.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Collaborating with research teams working on the rare disease (in particular for clinical studies)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Monitoring the current needs of the patient community of this rare disease (through surveys or registers of patients)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Training local professionals in responding to the specific needs of patients and supplying their contact information to patients.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Coordinating the sharing of medical information between health professionals of the specialised centre and local health professionals, to facilitate the continuity of the patients' follow-up.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Communicating with other specialised centres and professional networks to harmonise treatments and research at the national and European levels.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

13 Could you please rate the following statements regarding the potential implementation of specialised centres?	strongly disagree	partially disagree	partially agree	strongly agree	no opinion
A single, national centre would be preferable because it could gather all the medical skills and competences and the most up-to-date equipment in a same location.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Rather than concentrating all the expertise and competences in a single, national centre, sharing them between several centres would be preferable, because more accessible to patients.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
To maintain the skills and experience of its professionals, a specialised centre must follow a high number of patients affected by a specific disease.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Rare diseases are not well known by the majority of health professionals; it is therefore preferable to travel to a specialised centre for consultations and most specialised care.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Quality of relationships is as important as skills and competences, therefore, a local professional is preferable because of freedom of choice.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
The main hurdles in travelling to a specialised centre are the cost of transport and/or the need to be accompanied by someone.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
The main hurdles in travelling to a specialised centre are the time needed to get there and/or physical difficulties encountered by the patient (pain, fatigue, and injuries).	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
The role of the general practitioner consists mainly in looking after health problems not related to the rare disease.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
A specialised centre should involve patient organisations to benefit from their knowledge of daily life and needs of patients.	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

14 Questionnaire completed by <input type="checkbox"/> the patient <input type="checkbox"/> a relative <input type="checkbox"/> personal care assistant <input type="checkbox"/> other
age of the patient <input type="text"/> years gender <input type="checkbox"/> male <input type="checkbox"/> female age of the patient at diagnosis <input type="text"/> years
Where does the patient live ?
<input type="checkbox"/> village or city of less than 1000 inhabitants <input type="checkbox"/> city of 1000 to 100 000 inhabitants <input type="checkbox"/> city of more than 100 000 inhabitants <input type="checkbox"/> capital city
Were you forced to move because of the disease ? <input type="checkbox"/> no <input type="checkbox"/> yes, specify :
<input type="checkbox"/> to a more adapted house <input type="checkbox"/> to a specially adapted care centre <input type="checkbox"/> to get nearer to specialists of the disease <input type="checkbox"/> to get closer to a relative

15 Structure of the family : total number of adults <input type="text"/> total number of children <input type="text"/> number of patients <input type="text"/>
Highest level of education in the family : <input type="checkbox"/> primary education <input type="checkbox"/> secondary / professional education <input type="checkbox"/> university / higher education
Activities of patient or parents : <input type="checkbox"/> working <input type="checkbox"/> unemployed <input type="checkbox"/> never working <input type="checkbox"/> retired <input type="checkbox"/> student
Occupations of patient or parents (present occupation if working, last occupation if not) : <input type="checkbox"/> farmer / fisherman <input type="checkbox"/> craftsman / tradesman
<input type="checkbox"/> senior management <input type="checkbox"/> middle management <input type="checkbox"/> office work or services <input type="checkbox"/> skilled worker <input type="checkbox"/> unskilled worker
Specify if sector is : <input type="checkbox"/> health / research professional <input type="checkbox"/> teacher
Net family income per month, from all sources (salary, allowances, etc.) : <input type="checkbox"/> < £ 540 <input type="checkbox"/> from £ 540 to £ 1,400 <input type="checkbox"/> from £ 1,400 to £ 3,600 <input type="checkbox"/> > £ 3,600
Because of the disease, did one member of the family have work less or stop his/her professional activity ?
<input type="checkbox"/> no <input type="checkbox"/> yes, specify : <input type="checkbox"/> as patient <input type="checkbox"/> to take care of a relative

Thank you for your collaboration

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This book is intended for a large dissemination to all stakeholders in the field of rare diseases;

Electronic versions can be downloaded from www.eurordis.org

Results of EurordisCare3, by association, disease and country, are available on website: eurordis.org/eurordiscare3/.

In addition, with approval from the board of directors, the database of results of the EurordisCare3 survey is also available to academics interested in further analysing the data.

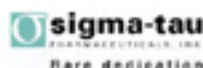
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Healthcare authorities need quantified data to make public health decisions. To go beyond patients' anecdotes and investigate experience-based opinions in a quantitative way, the EurordisCare2 and EurordisCare3 surveys were conducted to contribute to shaping patient-centred public health policies by describing and comparing patients' experiences and expectations regarding rare disease diagnosis and care for a variety of significantly relevant rare diseases across Europe. Accompanied by figures, illustrations, and patient testimonies, the survey findings are presented in a user-friendly manner to serve as an information and advocacy tool for patients, patient organisations, health professionals, and health authorities. With its publication on Rare Disease Day 2009, this book not only encourages media attention and subsequent communication of the issues to the general public, but also helps illustrate state-of-the-art-public health solutions to reducing delays in diagnosis and improving access to care in the context of two major European Union policy developments: the European Commission Communication on a European Action in the Field of Rare Diseases, and the Directive on the application of patients' rights in cross-border health care.

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