HURDLES TO HIGHLY SPECIALISED HEALTHCARE

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I RECEIVE UN/RESTRICTED RESEARCH AND EDUCATION GRANTS AND TRAVEL HONORARIA FROM ACTELION, BIOMARIN, GENZYME, PTC, SHIRE, SYNAGEVA/ALEXION, BIOASIS.

I AM THE PRESIDENT OF THE BRAINS FOR BRAIN FOUNDATION WHICH RECEIVES GRANTS FOR ITS INSTITUTIONAL ACTIVITIES FROM THE COMPANIES LISTED ABOVE BUT WITHOUT ANY OBLIGATION.

I HAVE NO ECONOMICAL OR STOCK MARKET INTERESTS ON ANY RARE DISEASE PRODUCT
The Centre or Expertise: Health Care Provider

Healthcare Provider (e.g.: Centre of Expertise)

→ Already exist and provide highly specialised healthcare (e.g.: procedures)

→ For a regional or national ‘catchment area' or 'population'.

→ Within ‘basket of treatments’ available in their Member State

→ Designated to provide these services by their Member State under their national legislation

Healthcare Provider ‘X’

Types of ‘procedures’
- Specialist surgery
- Genetic testing
- Implantation of a medical device
- Proton or photons therapy
- Medication prescribing
- Sophisticated neuroimaging
- etc …
With permission of parents
M.P. at 5 months

(Kindly from Prof. O. Gabrielli, Ancona Italy)
A.P. at 4y before therapy

• Coarse face
• Joint stiffness
• Hepato-splenomegaly
• Mitral insufficiency
• Corneal Clouding
• Hydrocephalus (shunt)

(kindly from Prof. O. Gabrielli, Ancona Italy)
... at 4y ...

- Clinically is normal
- Only a light corneal clouding
- Growth at 90°/le (usually <3°/le)

(kindly from Prof. O. Gabrielli, Ancona Italy)
A.P. today

- Limited joint stiffness
- Soft skin
- Reduction of the hepatosplenomegaly
- Stable valvulopathy

(kindly from Prof.O.Gabrielli, Ancona Italy)
...M.P today...

(kindly from Prof. O. Gabrielli, Ancona Italy)
The DIAGNOSIS OF NPC DISEASES

FROM THE GERMAN NPC ASSOCIATION, personal Communication
RARE DISEASES MAIN PROBLEM: Delayed Or Difficult Diagnosis

According to patients surveyed, it takes:
- on average **7.6 years in the US**
- on average **5.6 years in the UK**
for a patient with a rare disease to receive a proper diagnosis.

According to patient/caregiver respondents, in order to get a proper diagnosis, a patient typically visits up to
- **8 physicians: 4 primary care and 4 specialists**
and receives **2 to 3 misdiagnoses**

Data from Rare Diseases Impact Report April – 2013 SHIRE
THE REALITY IN RARE DISEASES
Delayed Or Difficult Diagnosis

INDEX OF SUSPICION MUST BE HIGH
It’s necessary to increase awareness
When addressing Rare Diseases (according to physicians surveyed)

- **92%** in the US
  - The majority of physicians reported it is more difficult to address the needs of a rare disease patient in a typical office visit.
- **98%** in the US
  - Nearly all physicians stated more office visits are required to diagnose a rare disease patient.
- **88%** in the UK
  - The majority of physicians said it takes more office visits to adequately address symptoms.
- **88%** in the UK
  - The majority of physicians said they found it difficult to do so.

- **54%** in the US
  - More than half of physicians stated there aren’t enough opportunities to network with other physicians who treat rare diseases.
- **88%** in the UK
  - While it may be necessary to coordinate with other physicians when managing a patient with a rare disease, the majority of physicians said they found it difficult to do so.

Data from Rare Diseases Impact Report April – 2013 SHIRE
When addressing Rare Diseases (according to patients and caregivers)

Around half of patients with a rare disease and their caregivers stated they received conflicting information from different healthcare professionals about treatment options.

More than half of patients and caregivers stated they needed to provide their healthcare professionals with information on their rare disease.

Data from Rare Diseases Impact Report April – 2013 SHIRE
Rare Disease Patients Face Also Other Common Problems

- Lack of quality information on the disease
- Lack of scientific knowledge of the disease
- Heavy social consequences for patients/communication problems
- Lack of appropriate quality healthcare
- Inequities and difficulties in access to treatment and care
HCPs Face Also Other Common Problems

- Lack of quality information on the disease
- Lack of scientific knowledge of the disease
- Heavy social consequences for patients/communication problems
- Lack of appropriate quality healthcare
- Inequities and difficulties in access to treatment and care
CHALLENGES FOR EUROPEAN HEALTH SYSTEMS

• **Pressure on healthcare systems:**
  - Citizens’ expectations for high-quality care
  - Demographic changes
  - Increased prevalence of chronic diseases
  - Increased mobility of citizens and patients
  - Staff shortages, unequal territorial distribution
  - Reactive model of healthcare delivery
  - Rising healthcare costs

*From G.Florio  DGINFO WEB 2011*
GLOBAL CHALLENGES

• Rising costs
• Changing demographics
• Filling the resource gap
• Easy access
• Focus on quality
• Becoming customer-driven
GLOBAL HEALTHCARE TRENDS

• Move from being supply driven towards a demand driven consumer model
• Informed patients and the rise of social media
• Patients exercising choice
• Patient-centered medical home
• Hospitals as networks
• Personalized medicine
• Translational research and the advent of personalized medicine
• Transition Programs

Deloitte: 2014 Global Healthcare Outlook
CGI: Healthcare Challenges and trends 2104
RARE DISEASES HAVE TO FACE GLOBAL COST RAISING PROBLEMS AND SHORTAGE IN HUMAN RESOURCES

Figure 1: World population over 60 (in millions)

Source: DTTL Global Life Sciences and Health Care Industry Group analysis of United Nations data statistics

Deloitte: 2014 Global Healthcare Outlook
Despite the desirability of coordinating care, incorporating it into day-to-day practice is not simple. Neither existing care delivery systems nor the professional systems are based on principles of coordinating services. The main obstacles for implementing coordinated care are deeply rooted in the prevailing organisational and policy systems. These include:

- Insufficient public funding to provide sufficient services;
- Unequal access – the counteracting mechanisms of means testing and co-payments may influence people’s access to long-term care in opposite directions, as do specific eligibility criteria for social care between local authorities and/or regions;
- Complexity of the system – multiple stakeholders may have different roles, tasks, interests and power positions;
- Lack of overall responsibility for coordinated provision of care and services and for outcomes as a barrier to decision making;
- Frictions in collaboration between organisations and professionals that usually reflect the fragmentation of the various systems involved;
- Human resources – staff shortages, shortcomings in quality of staff;
- Non-corresponding cultures – there are significant differences between the social and healthcare sectors, in areas such as qualifications, ways of working and systems;
- Quality management – social services lack quality systems and policies more often than is the case in the health services. Quality definitions sometimes conflict between parties, so they are often not agreed upon.

Source: Adapted from Niels and Berman, 2004
CHALLENGES FOR THE PATIENT’S PATHWAY

1. Proximity of doctor or emergency services
   Family doctor or a local medical center

2. Basic diagnostics
   Use of common diagnostics

3. Suspected diagnosis
   Due to low prevalence or lack of diagnostic means, doubts related to the diagnosis persist

4. Referral to specialist
   Could be a specialist doctor or a reference entity for the suspected issue

5. Further diagnostics
   Could be standard/usual diagnostic resource or a very specific one

6. Final diagnosis
   The suspected diagnostic is confirmed or a new diagnostic is given

7. Treatment
   Should follow clinical guidelines. For non-treatable conditions, a palliative plan will be established

8. Monitoring & Follow-up
   Preliminary results monitored. Self-monitoring could be used.

9. Relapse or worsening
   The treatment isn’t having the expected results or further issues arise

10. Updated Treatment
    The treatment is rethought based on non-achieved results and on new diagnosis. The treatment follows clinical guidelines.

11. Cure or Death
    The treatment cycle ends with the patient feeling well (cure or with palliative successful measures) or with their death
**Figure 1:** Directive 2011/24/EU on the application of patients’ rights in cross-border healthcare (objectives and constitutive elements)

- **Legal certainty about rights and entitlements to care in another Member State**
  - Conditions for reimbursement of cross-border health care (benefit basket, level, formalities)
  - Prior authorisation (scope, undue delay, administrative procedures)
  - Guarantees of information and equal treatment (prices)

- **Access to safe and high-quality cross-border healthcare**
  - Information on applicable quality and safety standards and on available providers
  - Access to medical record
  - Guarantees of non-discrimination, complaints and compensation, professional liability, data protection

- **Cooperation on healthcare between Member States**
  - Basic duty of mutual assistance and cooperation
  - Mutual recognition of medical prescriptions
  - Areas of cooperation: European reference networks, Rare diseases, e-health, Health technology assessment, border regions

Source: W Palm
Main conclusions of the report

- Extremely low number of citizens are aware of their general rights to reimbursement
- Some current systems of prior authorisation are more extensive than current number of requests appear to justify.
- Not always clear which treatments require prior authorisation
- Some MSs apply lower reimbursement tariffs than those used in the home MS (disincentive for citizens)
- Significant differences between NCPs (National Contact Point) in their performance and the quality of info they provide
### Table 1: Conditions for reimbursement of cross-border health care under Directive 2011/24/EU

<table>
<thead>
<tr>
<th>In all circumstances</th>
<th>No or unclearly defined list(^{(1)})</th>
<th>Clearly defined list(^{(2)})</th>
<th>Never(^{(3)})</th>
<th>Member States applying a lower reimbursement rate</th>
<th>Member States requiring a 'domestic' referral for reimbursing claims</th>
</tr>
</thead>
<tbody>
<tr>
<td>CY</td>
<td>AT, BE, BG, DE, DK, EL, ES, FR, IE, IT, LU, PL, SI</td>
<td>HR, HU, LV, MT, PT, RO, SK, UK</td>
<td>CZ, EE, FI, LT, NL, SE</td>
<td>AT, DE(^{(4)}), FI, NL</td>
<td>IE, MT, IT, EE, LT, LV, RO, SK, SI, PL</td>
</tr>
</tbody>
</table>

Source: Author’s own analysis based on information drawn from the National Contact Points (February 2016).

Notes: (1) This means that the scope as defined in the Directive is not further detailed, or only partially (in several instances the criterion of “overnight stay” remains unspecified); (2) This does not necessarily mean that the scope as defined is in conformity with the principles of necessity and proportionality; (3) Some countries still preserve the legal possibility of introducing prior authorisation and defining its scope at a later stage; (4) Germany applies a 5% reduction as an administrative fee to process claims.
**Figure 2:** Eurobarometer survey results on patients’ reasons for not using cross-border health care, 2007 and 2015

For which of the following reasons are you unwilling to go to another EU country to receive medical treatment?

- I'm not sure if I will be reimbursed: 2015 (16), 2007 (20)
- I have no information on patient safety and quality of care abroad: 2015 (20), 2007 (20)
- I can't afford it: 2015 (47), 2007 (61)
- I don't have enough information about the availability and quality of medical treatment abroad: 2015 (21), 2007 (61)
- I'm not aware of my rights when something goes wrong: 2015 (23), 2007 (61)
- I would have language problems: 2015 (27), 2007 (49)
- It is more convenient to be treated in my home country: 2015 (49), 2007 (49)
- I'm satisfied with health care I receive in my home country: 2015 (55), 2007 (83)

Source: Eurobarometer 2015 and 2007
SCATTERED EXPERT CENTRES ACROSS EU
OPEN PROBLEMS

- Late diagnosis
- Scarcity of awareness
- Not knowledge by medical professionals
- Scarse collaboration among Centers
- Difficult collaboration among specialists
- Need of a transition program
- Specialized expertise
Clinical services in a virtual environment ...
Knowledge sharing network.
COMPETITION TO IMPROVE THE HEALTH SYSTEMS

• Introducing, increasing or changing competition in health services is a delicate policy exercise.
• Accreditation of providers and the detailed design of payment systems are of specific importance.
• Key elements to consider when introducing, changing or increasing competition are ensuring market transparency, with availability of information on quality and prices, careful monitoring of access and equity effects, promoting health literacy, and enforcement of competition rules to prevent the creation, strengthening and abuse of dominant positions.

• Competition among health care providers is distinct from patient choice.
• Patient choice may be combined with different degrees of competition among health care providers;
• Patient choice works best in situations where patients can easily assess the quality of the services provided.
HOW THE ERNS CAN HELP TO CHANGE?

<table>
<thead>
<tr>
<th>How the ERNS can help to change</th>
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<tbody>
<tr>
<td>BY IMPLEMENTING A COMPREHENSIVE APPROACH TO RARE DISEASES</td>
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<tr>
<td>BY DEVELOPING APPROPRIATE PUBLIC HEALTH POLICIES AND INTERNATIONAL</td>
</tr>
<tr>
<td>COLLABORATION</td>
</tr>
<tr>
<td>BY GAINING AND SHARING SCIENTIFIC KNOWLEDGE ABOUT ALL RARE DISEASES,</td>
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<tr>
<td>NOT ONLY THE MOST “FREQUENT” ONES</td>
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<tr>
<td>BY RAISING PUBLIC AWARENESS</td>
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<tr>
<td>BY FACILITATING THE NETWORKING OF PATIENT GROUPS TO SHARE THEIR</td>
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<td>EXPERIENCE AND BEST PRACTICES</td>
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<tr>
<td>BY SUPPORTING THE MOST ISOLATED PATIENTS AND THEIR PARENTS TO</td>
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<tr>
<td>CREATE NEW PATIENT COMMUNITIES OR PATIENT GROUPS</td>
</tr>
<tr>
<td>BY PROVIDING COMPREHENSIVE QUALITY INFORMATION TO THE RARE DISEASE</td>
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<tr>
<td>COMMUNITY</td>
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HOW THE ERNS MIGHT HELP

Proximity doctor or emergency service
Online sign posting of where the expert centres are in Europe.
Cross-Border Healthcare Pathways

Referral to Specialist
European evidence based clinical protocol is available.
Triage patient referral – review
Virtual MDT review of rare disease and co-morbidities
Second opinion of complex case and specialist care plan given to HCP
Additional specific diagnostics required to be completed by HCP.

Treatment
Reference Best Practice of Diagnostic and Care, on which the treatment will be based.
Capture data either as part of a protocol research for that disease or as part of a post-marketing real world evidence data collection.

Monitoring and follow up
Data will be collected all along in the patient registration file which is a common tool across HCP in the ERN, collecting common data set, sharing patient summaries.
ERN to ERN consultation of other more rare and less distinct clinical features and co-morbidities
RARE INHERITED METABOLIC DISEASES: MetabERN

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Helios Dr. Horst Schmidt Klinik
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17 COUNTRIES
Ireland and Austria will not be able to participate at this point in time

The MetabERN is endorsed by and partners with the Society for the Study of the Inborn Errors of Metabolism (SSIEM)
MetabERN STRUCTURE

**MetabERN General Assembly**
(Representatives from all involved HC providers, patient groups and other third party stakeholders involved)

**Medical Executive Board**
(consisting of coordinator and leadership of sub-networks)

**ERN Advisory Board**
(including umbrella patient organisations, policy-makers, foundations, trade organisations, ethics specialists)

**External Experts Board**
(Clinical Trials C, Ethic conflicts C, Registries C, Patient recorded outcomes C, Physical activity C, QoC C, Social Services C, etc.)

- Aminoacid and organic acids related disorders
  - Medical Executive Board
  - Advisory Board
  - TBD
  - TBD

- Carbohydrate, fatty acid oxidation and ketone bodies disorders
  - Medical Executive Board
  - Advisory Board
  - TBD
  - TBD

- Lysosomal disorders
  - Medical Executive Board
  - Advisory Board
  - TBD
  - TBD

- Peroxisomal and lipid related disorders
  - Medical Executive Board
  - Advisory Board
  - TBD
  - TBD

- Disorders of pyruvate metabolism, Krebs cycle defects, mitochondrial oxidative, phosphorylation disorders, disorders of thiamine transport and metabolism
  - Medical Executive Board
  - Advisory Board
  - TBD
  - TBD

- Congenital disorders of glycosylation and disorders of intracellular trafficking
  - Medical Executive Board
  - Advisory Board
  - TBD
  - TBD

- Other metabolic disorders
  - Medical Executive Board
  - Advisory Board
  - TBD
  - TBD
PATIENT-CENTRED STRUCTURE OF THE Metab-ERN

Society: culture – legislation – education policy - social & health policy

Marike Groenendijk
MetabERN ACTIVITIES

- Prevention and Screening
- Diagnosis/New Diseases Diagnosis
- Management/Quality of Life and Transition Guidelines and Pathways
- Epidemiology/Registries and Outcome
- Education and Training
- Virtual Counselling
- Dissemination/Stakeholders Relations
- Clinical Trials
- Patient Empowerment
- Research
CONCLUSIONS

• Rare Diseases represent a big social burden affecting about 10% of the population. However, EU is committed to increase the awareness and research in order to give the chance to the patients to receive adequate therapies.

• Patients and families are still facing an Odissey which is due by the scarce knowledge of professionals, legislators and society in general about rare diseases.

• Rare Diseases Health Care System must compete with the global health system which is rapidly changing.

• The growth of the Health Cost is affecting negatively the Rare Diseases System.
CONCLUSIONS

- The scarcity of medical resources and the loss of professionality will have a tremendous negative impact on patients affected by rare Diseases.

- Rare Diseases require multidisciplinary teams and expanded networks of excellence.

- The forthcoming ERNs will be instrumental to answer most of the patients’ and families’ needs and empower them.

- The forthcoming ERNs will represent the only chance to rationalize resources and help the national Health System in containing costs and optimizing management of patients.