BRAIN COMMUNITY JOINS CALLS FOR A RENEWED EU ACTION PLAN ON RARE DISEASES

VOT EBC European Brain Council

14 March 2022, Brussels – The European Brain Council (EBC), together with its members and partners, today launches – on the occasion of Brain Awareness Week 2022 – a call for the prioritisation of brain health, efficient care pathways and seamless, coordinated care for people living with rare brain diseases.

The call follows the EU-backed EURORDIS Rare 2030 Foresight Study recommendations, setting the roadmap for a new rare disease policy framework by 2023. 75% of rare diseases have neurological symptoms, seriously compromising the health and quality of life of people living with a rare disease. A multiplier effect of comorbidities on the impact of rare diseases requires innovative care and treatment pathways for society to cope. The EBC Value of Treatment (VOT) case study results published today highlights the value of coordinated care and specialist centers to address the challenges faced by people living with a rare neurological disease (Ataxia, Dystonia) or a neurometabolic disorder (Phenylketonuria).

WHAT ABOUT THE RARE 2030 FORESIGHT STUDY RECOMMENDATIONS?

RECOMMENDATION 1
Long-term, integrated European and national plans, and strategies

RECOMMENDATION 2
Earlier, faster, more accurate diagnosis

RECOMMENDATION 3
Access to high quality healthcare

RECOMMENDATION 4
Integrated and person-centred care

RECOMMENDATION 5
Partnerships with patients

RECOMMENDATION 6
Innovative and need-led research and development

RECOMMENDATION 7
Optimising data for patient and societal benefit

RECOMMENDATION 8
Available, accessible and affordable treatments

In line with the VOT project on rare diseases results and the conclusions of the French Ministerial conference on rare diseases and care pathways held on 28 February 2022, EBC calls on the European Commission and Member States to renew a European action plan on rare diseases. This would bring together existing efforts across different legislation and EU programmes under a coherent framework to spearhead change. It will align EU countries towards the same measurable goals to ultimately improve survival, quality of life and clinical guidelines harmonisation:

- Diagnose every person within 6 months instead of the current 5 years average and reduce premature deaths due to rare diseases;
- Increase collaboration between the ERNs and specialist centres/centres of expertise at national level and fulfill the ERNs integration into the national healthcare systems;
- Reduce the psychosocial burden of rare diseases by 1/3 by the implementation of a multidisciplinary and coordinated approach; and
- Extract value from data and bring new medicinal products, including gene and cell therapies, based on European-led research.

An ambitious EU plan will support an advanced eco-system to ensure that Europe reinforces its status as a world leader in health innovation, precision medicine, genomic health, digital health innovation and, as a result, more sustainable health systems.

WHY?

Addressing the challenges of people living with a rare disease and their families

Like any other rare disease, Ataxia, Dystonia and Phenylketonuria (PKU) all share similar challenges. Patients with rare diseases face complex biological, psychosocial, and healthcare needs with clear implications in terms of quality of life and costing. This large, affected population is one reason why rare diseases deserve significant attention, children and their families being particularly impacted. The second is the linkage between conditions. For instance, orphan drug legislation and other policies that encourage development for rare disease treatments influence the entire commercial therapeutic development pipeline.

Research infrastructures such as registries and innovative uses of alternative data can also benefit researchers across the spectrum, while adapting decision-making models related to assessment and reimbursement can ensure access to therapies beyond any single condition.

Rare diseases pose policy-level challenges for government, public health agencies and the medical research community. These include delayed diagnosis and gaps in service provision due to fragmented health services; limited treatment options, due to underinvestment in research and development (R&D); and reimbursement challenges for treatments that exist but do not meet conventional cost-effectiveness thresholds. Research needs to ensure that experts, researchers, and clinicians are connected to enhance scientific knowledge and quality information. Addressing rare diseases requires collaboration across the healthcare system to deal with systemic challenges like workforce training and awareness for frontline health care providers so that they can recognize rare diseases and direct patients to effective treatment and care. Efforts must also be made to improve the knowledge and awareness of patients, in order for them to better understand their condition and participate in research relevant to them.

FREQUENCY OF SOME RARE DISEASES?

Below an overview of estimated European prevalence rates of 22 selected rare diseases, including **ataxia, dystonia** and **PKU**:

Rare disease name	Estimated prevalence (per 100,000)	
Congenital isolated hyperinsulinism	2.0 *BP*	
Scleroderma (systemic sclerosis, localised sclerosis)	42.0 *P*	
Familial QT syndrome (Inc. Romano Ward)	40.0 *BP*	
Primary systemic amyloidosis	30.0 *P*	
Retinitis pigmentosa	26.7 *P*	
Fragile X	32.5 *P*	
Neurofibromatosis 1	21.3 *P*	
Marfan syndrome	15.0 *P*	
Sickle cell anaemia	22.0 *P*	
Sarcoidosis	12.5 *P*	
Haemophilia	7.7 *P*	
Huntington's disease and rare neurodegenerative disease	2.7 *P*	
Phenylketonuria	10.0 *BP*	Neuro-metabolic Disorder
22q11.2 Deletion syndrome (DiGeorge syndrome)	37.5 *BP*	
Duchene or Becker muscular dystrophy	4.78 *BP* / 1.53 *P*	
Prader-Willi syndrome	3.1 *BP*	
Epidermolysis bullosa	2.2 *BP**	
Mucopolysaccharidosis (type 2)	10.0 *P*	
Rare ataxias (including Friedreich's)	2.0 *P**	Rare Neurological Disease
Tuberous sclerosis	12.0 *P*	
Osteogenesis imperfecta	10.0 *P*	
Motor neuron disease	3.85 *P*	Rare Neurological Disease

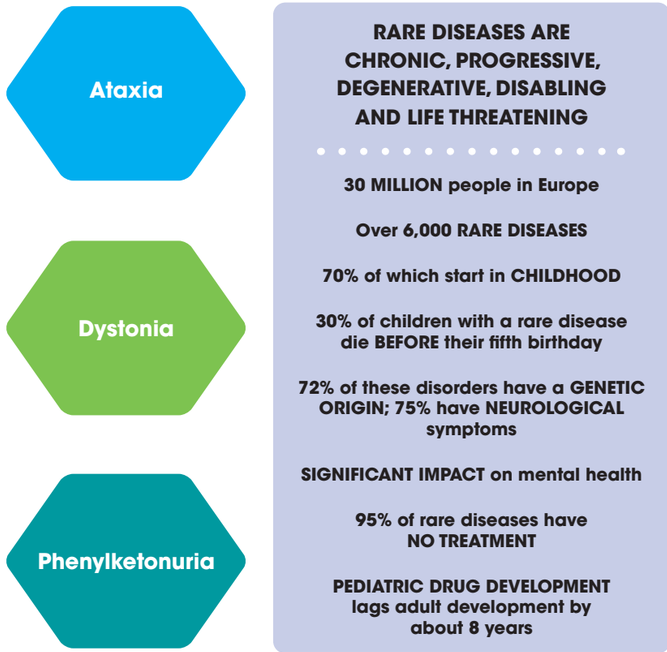
Estimates provided from the Orphanet Report Series - P = prevalence; BP = birth prevalence
*Estimates shown are for epidermolysis bullosa simplex and Friedreich's Ataxia

Byrne, N - Turner, J - Marron, R et al.
The role of primary care in management of rare diseases in Ireland. Ir J Med Sci 189, 771-776 (2020).

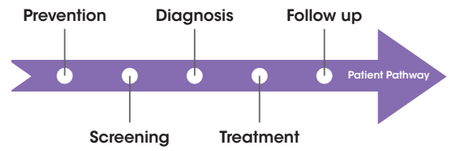
"Research into rare diseases not only improves diagnosis and outcomes for patients with rare brain diseases, but quite often open up insights into how more common diseases work. It offers the possibility of developing cures or therapies for diseases which are not rare, and therefore have a much bigger impact on the healthcare system."

Prof. Wolfgang Oertel, EBC President

WHY RARE DISEASES AND WHAT ABOUT TREATMENT GAPS?



Treatment gaps along the care pathway



- Low insight into pathological mecanisms, delayed detection and diagnosis
- Barriers to access specialized care and treatment options
- Uncoordinated care, discontinuity, drop-outs
- High prices and lack of reimbursement
- Lack of knowledge raises concern to health professionals
- Limited sharing of best practice and expertise

Note:

Study scope focuses on patient unmet needs using the care pathway as a tool to understand better the condition from onset to disease management and monitoring while identifying the treatment gaps, and to translate clinical practice guideline recommendations into health care processes, sequences for improved outcomes. Unmet needs are not only within the provision of medicines and medical devices, but also within health care systems and services.

Box 1 The Value of Treatment for rare brain diseases in Europe research project

Care coordination using the key roles of multidisciplinary teams in specialist settings and utilisation of other primary and secondary health care services are considered important for professionals and patients with complex rare conditions. Yet, research on care coordination addressing its impact is limited. The study addresses a research gap by capturing the views of patients (surveys and descriptive statistics), clinicians and health economists: data (care pathway) come from literature review, survey, or other sources such as guidelines or flowcharts based on expert consensus.

Survey key findings set the case for renewed European action on rare diseases, highlighting that:

"Less than 50% of the respondents received care from a specialist centre (centre of expertise) and most of them reported about multidisciplinary care being effective. Moreover, patients have valued the translational research aspect of these centres, been on the forefront of new diagnostic tools and management and treatment. Given this feedback, the low access to a specialist centre is a concern." **Prof. Paola Giunti,** University College London, United Kingdom

"An analysis of the cost-consequences of specialist centres for managing care of people with ataxia in several European countries was performed. The health economics evaluation has revealed that costs of specialist centres are higher due to resource use for multidisciplinary care management, complex needs (disease severity) and comorbidity, but it demonstrated benefits for patients including satisfaction and improved quality of life". **Prof. Steve Morris**, University of Cambridge, United Kingdom

"In Europe there are 500.000 people living with rare neurological diseases (RNDs), while 60% of those affected are still undiagnosed due to significant phenotype and genotype heterogeneity in clinical presentation and disease course." **Prof. Holm Graessner**, ERN-RND

"Only 16% of respondents had professionals from primary care services recognized their symptoms and referred to an appropriate specialist, while 30% was referred to a specialist without recognised their symptoms. Given this feedback, the low medical education of healthcare providers especially GPs, general neurologists, physiotherapists, is a concern for timely diagnosis and management of dystonia. This is also the case for many other rare diseases."**Prof. Maja Relja**, University of Zagreb Medical School, Croatia

"Still, large numbers of patients with PKU in Europe do not have access to a multidisciplinary team consisting of specialist physicians, nutritionists, specialty nurses, psychologists, and clinical biochemists." **Prof. Francjan van Spronsen**, MetabERN

"Most inherited metabolic disorders (IMDs) manifest in the newborn period and infancy. In PKU, newborn screening programme (NBS) has enabled early diagnosis and early intervention (major role of pediatricians) in the form of a "phenylalanine (Phe)-free" diet. However, this diet is highly restrictive, unpalatable, and can substantially affect patients' and caregivers' time and quality of life. As patients affected by PKU reach adolescence and adulthood, between 70 to 80% of them are not fully compliant with the prescribed diets." **Prof. Anita MacDonald**, Birmingham Children's Hospital, Birmingham, United Kingdom

"A biopsychosocial approach is needed for patients with rare conditions as for PKU to address not only disease-related variables, co-morbidities but also quality of life including patient perspective. Studies on rare brain diseases are revealing strong correlations between psychosocial factors and quality of life that should be investigated further in future research." **Prof. Alvaro Hermida**, Universidad de Santiago de Compostela, Santiago de Compostela, Spain

"European guidelines have been delineated, but their implementation is variable across sites (metabolic care unit services) which is characterized by variability in staffing and resources with regards to the implementation of the European PKU guidelines, genotyping of patients, monitoring Phe levels (blood tests), and access to novel therapies: patients deemed most likely to benefit from novel therapies should have access, but this requires attention to close monitoring and determining the added value of treatment, beyond dietary management alone. Given this feedback, clinical variation is a concern for adequate treatment." **Prof. Gregory Pastores**, The Mater Misericordiae University Hospital, Dublin, Ireland

"Costs of metabolic care unit service contacts for people affected by phenylketonuria are modest compared with the costs of the protein diet and novel therapies. So, we can advocate for resources to meet the added demands on the multidisciplinary care service." **Prof. Steve Morris**, University of Cambridge, United Kingdom

Policy responses

Priorities have been set up by the European Commission in the **2009 Council Recommendation on an action in the field of rare diseases**[1] calling for countries to adopt national plans or strategies aimed at guiding and structuring actions in the field of rare diseases within the framework of the health and social systems. It has been an essential means of ensuring this focus, with 25 European Member States (and countries under study) having adopted a plan or strategy at some stage[i]. It has also emphasized the importance to collaborate through networks to bridge the gap between research and care in rare diseases - the European Reference Networks[2] being one of the pillars of **the 2011 European Directive on patients' rights in cross-border healthcare** - and to build on the **most recent Clinical Guidelines** adopted for Ataxia[ii], Dystonia[iv v] and PKU[vi], the need to be forward looking has been highlighted in the case study results. Overall, where no national guidelines exist, European guidelines should be implemented to ensure that people with rare diseases have access to the support and care they need. These objectives are today to be revigorated, as there are signs in many countries that momentum and commitment to the development, implementation, and renewal of national plans is waning, in some cases.

WHAT CAN WE DO?

The patient at the core of our healthcare vision for 2030

The reality of orphan diseases is increasingly situated at the network level. Our priorities to optimise healthcare services and removing treatment gaps are based on the following trends:

1. A patient-empowering research policy (using the patient care pathway, patient reported outcomes measurement);
2. An integrated, multidisciplinary approach to rare diseases looking at payment systems, new treatment paradigms and healthcare digitization.

Provided that the supportive framework conditions are in place as proposed by the European Commission to create a strong innovation ecosystem in the area of rare diseases and a new strategy for data sharing in healthcare, the proposed solutions should be able to face and capitalize on these trends and align with the proposal for a renewed action plan on rare diseases that sets a common ambition for Europe as a whole.

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[1] Council Recommendation 2009/c151/02 - A number of recommendations issued at European level covering areas such as data epidemiology, registries and e-health, adequate identification and coding of rare diseases, care pathways, centres of expertise, practical guidelines, clinical research, disease registries, patient organisations and information services as well as transition from paediatric to adult healthcare provider in RDs were indicated as priorities to be incorporated into national plans for rare diseases.

[2] The ERNs have been established on the basis of the Directive 2011/24/EU on patients' rights in cross-border healthcare (Article 12). A set of 24 ERNs were launched in 2017, involving more than 900 highly specialised healthcare teams, located in more than 300 hospitals. They cover different disease groups from rare neurological diseases to inherited metabolic disorders, bone disorders, haematological diseases, etc. The ERNs are not directly accessible for patients, who need to consult their specialist and follow their own national care pathway. The ERNs are progressively integrated into national health systems to allow complementarity with national and regional resources and expertise.

AN ENABLING ECOSYSTEM FOR OPTIMIZING CARE AND RESEARCH

New payment systems and new treatment paradigms

Strains on the heath care budget and the emergence of new care delivery models. Gradual shift from hospital to alternative extra muros care settings (such as remote care, rehabilitation centres)	New healthcare delivery models
Greater variation in access to treatments and care resulting in more inequality across Europe for people with rare diseases	Access to medical products
Application of Whole Genome Sequencing from the research to the clinical sphere	Genomics

RESEARCH & INNOVATION CENTRES OF EXCELLENCE

HEALTHCARE DATA AS CORE ENABLER

USING REAL WORLD EVIDENCE TO MAKE RESEARCH MORE EFFICIENT

Digitisation of healthcare

Facilitation of knowledge exchange and local care delivery through digital health and monitoring of a substancial amount of data through the Electronic Health Record (EHR)	Digitalisation of healthcare
Increased potential for large sets of standardised and interoperable data	Big Data - Links between Patient Registries and Biobanks
Rise in the use of AI for diagnostics, treatment and care, opening-up the potential of 'big data'	Big Data and Artificial Intelligence
New technologies and advanced therapeutics	Innovation in Medical knowledge

HEALTHCARE PROVIDERS

OPTIMISING HEALTHCARE PROVISION STRUCTURE USING OUTCOME DATA

BIOPHARMA INDUSTRY

STIMULATING INNOVATION & INTRODUCING THE RIGHT TECHNOLOGIES

Integrated, multidisciplinary approach to rare diseases

Better collaboration between specialist centres and the first-line care (human and financial incentives)	Dedicated care manager to ensure continuity (transition) of care and compliance as per degree of disease severity and co-morbidities
Increased psychosocial support and social care	Integration of services to reduce isolation and vulnerability

Patient centricity in research and care

Demographic change of RD patients introducing new challenges, but also the need to focus on children and transition care to adult care services	Ageing population in a changing family structure
Threats to solidarity equity, and the prioritization of rare diseases	Increase inequality and treats to solidarity
Increasingly empowered rare disease patient and the patient advocacy evolution	Patient engagement
Rise in innovation-oriented, mutistakeholder, need-led (patient-led) research	Innovation in healthcare research

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EUROPEAN REFERENCE NETWORKS

European Reference Network | Neurological Diseases (ERN-RND)

European Reference Network | MetabERN
European Reference Network for Hereditary Metabolic Disorders

PATIENT ASSOCIATIONS

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