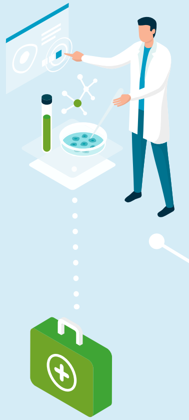
European Commission

European Reference Networks



Working for patients with rare, low-prevalence and complex diseases

Share.Care.Cure.

Health

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European Reference Networks

Working for patients with rare, low-prevalence and complex diseases

Share.Care.Cure.

The EU stands with rare disease patients to bring them help, hope and a brighter future

Sandra Gallina
Director General DG SANTE

The toll of rare diseases as a whole is huge – they are estimated to strike 3.5% – 5.9% of the world's population and, in the EU alone, up to 36 million people are living with one of the over 6,000 distinct rare diseases. Each rare disease, however, has a low prevalence. The definition of a rare disease in the EU is one that affects fewer than 5 persons out of 10,000.

Having a rare disease may mean that you have a condition your doctor or other healthcare professional cannot identify. It may mean that your symptoms are misdiagnosed – sometimes for years – while you suffer and watch your condition worsen. Having a rare disease often means not knowing what is wrong with you, or what to do about it to ease your pain and discomfort. It can be frustrating and lonely. It can feel hopeless.

The EU stands with rare disease patients and is bringing EU-added value by pooling our resources, sharing knowledge and working together.

First, we want to help patients get the accurate diagnosis they need. Then to make sure they have treatment and care that will help miniamize discomfort and help them live as fully as possible. And lastly, we want to work together to find cures. Currently, there is no known cure for 95% of rare diseases. Through strong EU action such as revising the pharmaceutical legislation, we offer rare disease patients a better future.

The European Commission has supported numerous actions in the field of public health and healthcare systems to help Member States develop national responses, strategies and plans. These include the very successful European Reference Networks (ERNs) which were set up in 2017 to pool knowledge and resources to tackle rare and complex diseases, also in medical domains where expertise is rare. The European Commission played a fundamental role in creating the framework for the ERNs, providing grants to support the networks, coordinators and the technical networking facilities.

ERNs are virtual networks connecting healthcare providers, professionals and patient organizations across the EU and Norway. Based on the EU Directive on Cross Border Health Care, the ERNs represent one of the greatest achievements of the rare disease community in Europe and have become an inspiration for global action, thanks to the efforts of the healthcare providers, patients' organizations, the European Commission and the EU Member States.

No country alone has the knowledge and capacity to treat all rare and complex conditions. Thanks to the ERNs, patients across the EU have access to the best expertise available. Through these networks, the experts reach the patient, without the patient having to travel to experts who may be located far away. The European Union connects the dots, maximizing synergies between Member States and encouraging the sharing of knowledge and resources.

There are currently 24 ERNs for rare and complex diseases, formed through partnerships between healthcare system managers, patient advocates, and clinical leaders. Now set up and fully functioning, these networks are continuing to make progress and are experimenting with new ways of cross-border cooperation.

After six years of existence, the ERNs are currently being evaluated. The results of the evaluation will be available at the end of 2023 and will help identify additional ways of improving the ERN model and shaping their future.

Their true potential will only be reached when the ERNs are consolidated into our national health systems. Then, they will truly be able to deliver EU-added value and have the possibility of bringing hope and help to millions of rare disease patients across the EU. That's why EU Member States, Norway and Ukraine have joined forces with the Commission on a three-year action to help consolidate these networks, beginning at the end of 2023. This action will receive some EUR 15 million in EU funding.

Additionally, the Commission has funded a new generation of grants to support the ERNs with more than EUR 77 million under the EU 4Health Programme. These grants will help fund the setting up and operation of 24 fully-fledged patient registries with thousands of entries and will result in hundreds more patient cases being discussed in international panels via a dedicated IT tool known as the 'Clinical Patient Management System'. ERNs are key actors in data collection and scientific collaboration in research on rare diseases.

Funding will also help make high-level accredited training courses available for health professionals and will help provide new or updated clinical patient guidelines and clinical decision support tools for the benefit of the patients.

By connecting experts and patient populations, ERNs also pave the way for clinical studies and test therapeutic interventions, putting them at the forefront of innovation in numerous rare disease fields. Pharmaceutical companies may be reluctant to invest in developing drugs for rare disease patients because the market for these drugs would be extremely limited. This is the reason why the Commission is providing incentives to manufacturers to develop orphan medicines and bring them to market and has just revisited the relevant legislation to improve these incentives.

It took over a decade for the idea of cross-border healthcare cooperation for complex and rare conditions, powered by ERNs, to germinate and find its way into EU legislation. The four years ahead will mark the years of consolidation of the ERNs and their stronger embedding into national healthcare systems. We can expect impactful ERN actions to make the difference for patients living with rare diseases and their families, to expand the use of registries and spread the knowledge on rare diseases to broader audiences.

The need for more European coordination in health has been growing and satisfying that growing desire is at the heart of the Commission's proposal to build a strong European Health Union.

The next stage of the networks' development should harness this drive for better patient outcomes and greater cross-border cooperation on healthcare to ensure that the ERN system is reaching its full potential by 2030. Living with a rare disease should not mean living with uncertainty about diagnosis, care, and treatment and living with a rare disease should never mean facing it alone.

Sandra Gallina
Director General DG SANTE

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Background

Any disease affecting fewer than five in 10,000 people in the EU is considered rare. More than 6,000 rare diseases affect the daily lives of up to 36 million people in the EU.

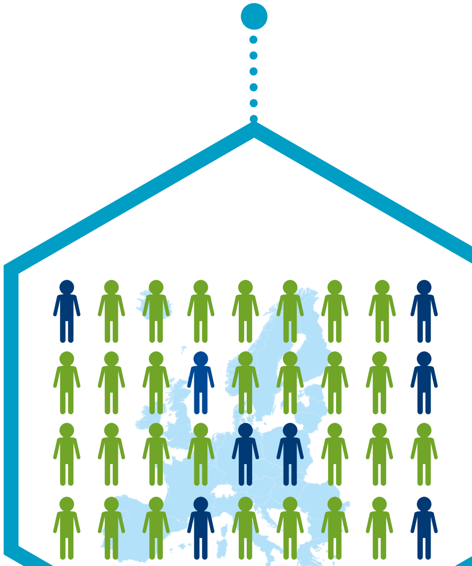
In the field of oncology alone, for example, there are almost 300 different types of rare cancers and each year more than half a million people in Europe are diagnosed with one of them.

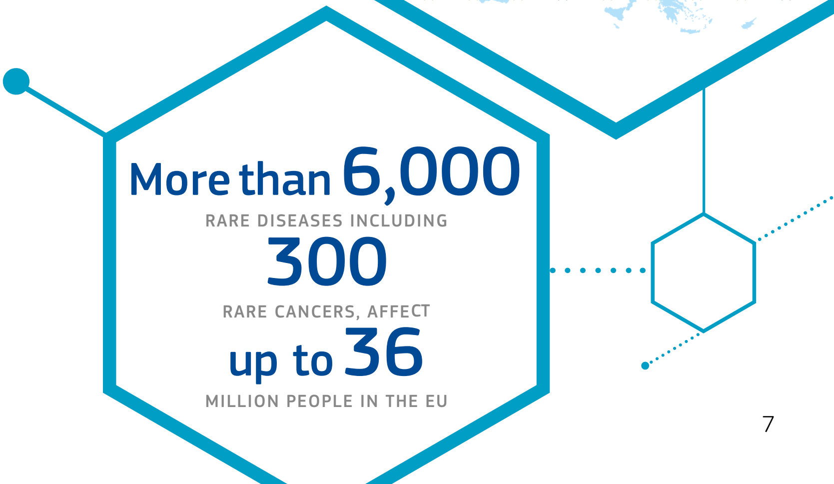
Many of those affected by a rare or complex condition do not have access to diagnosis and high-quality treatment. Expertise and specialist knowledge may be scarce because patient numbers are low.

The EU and national governments are committed to improving the recognition and treatment of these rare and complex conditions by strengthening European-level cooperation and coordination and supporting national plans for rare diseases.

The 2011 Directive on Patients' Rights in Cross-border Healthcare not only enables patients to be reimbursed for treatment in another EU Member State, but also makes it easier for patients to access information on healthcare and thus increase their treatment options. The Directive became law in EU Member States in 2013 and laid the foundations for cross-border collaboration in areas such as rare diseases and ERNs or eHealth.

Against this background, with the support of the EU Health Programme (and, since 2021, EU4Health), the 24 European Reference Networks, comprising nearly 900 highly specialised health care units, began work in 2017. Since then, thousands of patients with rare or complex diseases have been helped by the programme, and today the ERNs have grown to include more than 1,600 health care units from almost 400 hospitals across all 27 EU Member States and Norway.





What are European Reference Networks?

European Reference Networks (ERNs) are virtual networks connecting healthcare providers, health care professionals and patients across the EU and Norway. They aim to tackle complex or rare diseases and conditions which require highly specialised treatment and a pooling of knowledge and resources.

No country alone has the knowledge and capacity to treat all rare and low prevalence complex diseases. ERNs enable patients and doctors across the EU to access the best expertise and timely exchange of life-saving knowledge, without having to travel to another country. The networks facilitate sharing the latest knowledge and experience in rare diseases present in the EU to member hospitals, researchers, and patient groups.

To review a patient's diagnosis and treatment, ERN coordinators convene 'virtual' advisory panels of medical specialists across different disciplines, using a dedicated IT platform – the Clinical Patient Management System (CPMS). Discussions are carried out in the CPMS allowing healthcare providers from all over the EU to work together online to discuss, diagnose and treat patients with rare, low prevalence and complex diseases. ERNs also coordinate and facilitate educational and training activities, develop clinical practice guidelines and other clinical decision support tools, work together on knowledge generation and dissemination through communication activities and are focal points for research and innovation in the area of rare and low prevalence complex diseases. In addition, ERNs are populating EU-registries with high quality data from patients with rare diseases, creating a unique, highly valuable data source to foster research and devise the next generation of treatments for rare and complex diseases.

The ERNs were launched in March 2017. Currently there are 24 ERNs comprising more than 1,600 highly specialised healthcare units from almost 400 hospitals in all EU Member States, plus Norway. They work on a range of thematic areas, from rare bone disorders and childhood cancers to rare vascular diseases, benefitting thousands of EU patients suffering from a rare or complex health condition.

The ERN initiative receives support from several EU funding programmes, including the EU4Health Programme, Connecting Europe Facility and Horizon Europe.

EU Member States lead the ERN process: they are responsible for recognising centres at national level and endorsing applications. A Board of Member States (BoMS) is responsible for developing the EU ERN strategy and approving the creation of networks and inclusion of new members.

The 24 ERN coordinators collaborate within the ERN Coordinators group (ERN-CG), which was set up in 2017. This strategic group establishes a common ground on several key technical and organisational aspects of the ERNs. The ERN-CG and BoMS collaborate closely with various working groups - including knowledge generation; integration into national health systems; monitoring; legal and ethical issues, and IT advice - which report their proposals to the ERN-CG and BoMS for final discussion and decision.

ERN on bone disorders (ERN BOND)

Rare bone diseases encompass disorders of bone formation, modelling, remodelling and removal, and defects of the regulatory pathways of these processes. They result in short stature, bone deformity, teeth anomalies, pain, fractures and disability, and can adversely influence neuromuscular function and haemopoiesis.

ERN BOND brings together all rare bone diseases - congenital, chronic and of genetic origin - which affect cartilage, bones and dentin. The network currently focuses on osteogenesis imperfecta (OI), X-linked hypophosphataemic rickets (XLH) and achondroplasia (ACH) as exemplars, based on disease prevalence, diagnostic and management difficulty, and novel emergent therapies. In future, as systematic approaches are established, ERN BOND will move on to rarer diseases.

Working with patients, ERN BOND develops patient-reported outcome and experience measures, as well as guidelines for the development and dissemination of best practice. As new therapeutics are developed, the network aims to ensure rapid access to studies for affected patients.

ERN BOND enables skill development through eHealth and telemedicine platforms, alongside working visits, training courses and dissemination activities. The network aims to reduce diagnosis time through fewer inappropriate tests, more accurate diagnosis and new viable treatments.

NETWORK COORDINATOR

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ERN on craniofacial anomalies and ENT disorders (ERN CRANIO)

ERN CRANIO focuses on rare and complex craniofacial anomalies, and ear, nose and throat (ENT) disorders. These conditions cover malformations of the brain, skull and face, including specific disorders such as Craniosynostosis and Craniofacial Microsomia, cleft lip and cleft palate, orodental abnormalities, and ENT disorders.

The network operates across different areas of work including dissemination, evaluation, eHealth, training and education, quality of care, registry development and outcome measurement.

ERN CRANIO aims to pool disease-specific expertise, knowledge and resources from across the EU/EAA to achieve health goals that may otherwise be unachievable in a single country. Such health goals include the development of clinical skills, increased patient access to high-quality expert care, and making improved diagnosis-specific information available to healthcare professionals, patients, and their families and carers.

In doing so, ERN CRANIO also seeks to reduce health inequalities by standardising practices and making high-quality care, information and resources accessible to healthcare providers, patients, and their families and carers across Europe.

NETWORK COORDINATOR

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Adding value for patients and professionals

Patients with rare and complex diseases can spend years without a clear diagnosis, and it can be a frustrating and dispiriting experience for patients, their families and carers. Many of those living with these conditions are children with impaired development who move through the health system, sometimes seeing several specialists during the course of their childhood, in search of a diagnosis.

ERNs improve public and professional awareness of rare diseases and complicated presentations of illness, increasing the likelihood of early and accurate diagnosis and effective treatment where available.

The networks are a platform for the development of guidelines, training and knowledge sharing. ERNs can help facilitate large clinical studies to improve understanding of diseases and develop new drugs by gathering a large pool of patient data.

The degree of patient engagement varies from Network to Network, but all ERNs ensure that patients' representatives are involved, for example, in developing clinical practice guidelines, clinical trials and care pathways.

For specialist health professionals, ERNs are an opportunity for networking with like-minded experts from across the EU/EEA, helping to reduce the professional isolation faced by many experts in rare diseases. The ERN system is underpinned by innovation in healthcare delivery, helping to develop new care models and changing the way treatments are delivered, through eHealth solutions and tools and ground-breaking medical solutions and devices. ERNs are incubators for the development of digital services, and the provision of virtual healthcare and telemedicine.

ERNs help to boost economies of scale and ensure more efficient use of resources, with a positive impact on the sustainability of national healthcare systems. The networks are a visible demonstration of what solidarity can achieve in Europe.

ERN on endocrine conditions (Endo-ERN)

Rare endocrine conditions include too much, too little or inappropriate hormonal activity, hormone resistance, tumour growth in endocrine organs, and diseases with consequences for the endocrine system. The epidemiological distribution is highly variable, spanning ultra-rare, rare and low-prevalence conditions. Patients with a low-prevalence disorder may require highly specialised care from a multidisciplinary team led by an endocrinologist.

The network has established eight main thematic groups covering the full spectrum of congenital and acquired conditions. These are: adrenal disorders; disorders of calcium and phosphate homeostasis; disorders of sex development and maturation; genetic disorders of glucose and insulin homeostasis; genetic endocrine tumour syndromes; disorders of growth and genetic obesity syndromes; hypothalamic and pituitary conditions; and thyroid disorders.

Endo-ERN continues to build on the work of several pre-existing European networks, including those established through the European Society of Endocrinology (ESE) and the European Society for Paediatric Endocrinology (ESPE), and those developed through European Cooperation in Science and Technology (COST) actions.

Aiming to deliver improved diagnostic trajectories, treatment, quality of care and measurable outcome for patients with rare endocrine conditions, Endo-ERN facilitates multidisciplinary and cross-border collaboration in complex care, research and education, whilst ensuring patients' voices are heard.

NETWORK COORDINATOR

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ERN on rare and complex epilepsies (EpiCARE)

Epilepsy affects at least six million people in Europe. Traditionally it has been treated as a single disease, but although the first clinical manifestations in the form of epileptic seizures may look similar, epilepsies can originate from a large number of different neurological aetiologies. Treatment choices, outcomes and the overall prognosis depend on which aetiologies are at work, and a prompt diagnosis, whenever possible, plays an important role.

When appropriately prescribed, traditional anti-seizure medications help nearly 70 percent of those affected to remain seizure free - but for patients suffering from refractory epilepsy, the clinical outlook is poor. Rare and complex epilepsies require multi-disciplinary management from the onset. Well-established care pathways and close collaboration with well-structured national networks for epilepsy care is essential.

The medical teams of ERN EpiCARE work to improve and increase diagnoses of the causes of rare epilepsies; enhance early identification of patients with treatable rare causes; increase access to specialised care; further develop and design innovative clinical trials for new anti-seizure medication through the European Collaboration for Epilepsy Trials (ECET); deliver full access to, and use of, early pre-surgical evaluation and epilepsy surgery; and foster research on innovative diagnostic tools and causal treatments.

Several times each month the network organises patient case discussion sessions with the participation of EU experts in genetics, neuropsychology, drug management and pre-surgical evaluation. ERN EpiCARE has launched numerous knowledge generation activities, including interactive educational webinars and updates on clinical practice guidelines. The network with other ERNs and EU-funded initiatives such as the European Joint Programme on Rare Diseases (EJP RD), SOLVE-RD; ERICA and the transversal working groups on neurological disorders particularly involving ERN-RND and ERN EURO-NMD.

From the outset, the network has collaborated closely with all related scientific bodies such as the International League Against Epilepsy (ILAE), the European Paediatric Neurology Society (EPNS) and the European Academy of Neurology (EAN). In order to increase awareness of best practices and care pathways, ERN EpiCARE works with patient advocates from European Patient Advocacy Groups (ePAGs) to produce, for example, information leaflets on rare epilepsies, and patient centred clinical trials.

NETWORK COORDINATOR

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How ERNs are approved

EU Member States play the lead role in the designation and development of European Reference Networks. To achieve ERN status, network members respond to a call from the European Commission, following which an Independent Assessment Body (IAB) assesses their application and compiles a report. The Board of Member States (BoMS) then decides whether or not to approve the ERN application.

The BoMS comprises nominees from all EU Member States plus Norway and plays an active role in developing the ERN strategy. It continues to monitor ERN members, assesses applicants wishing to join existing networks, and approves any future networks. As a result of the 2019 call for applications, more than 600 additional healthcare providers from 20 EU Member States and Norway were admitted as members of ERNs in 2022.

18 ERN indicators have been adopted by the BoMS and are submitted by ERNs on a regular basis. They provide solid continuous monitoring to measure improvements in quality and outcomes while highlighting successes and potential pitfalls.

Countries which do not have representation in an approved ERN may participate through healthcare providers designated by their Member State either as ‘associated’ or ‘collaborative’ national centres. These affiliated partners have access to good practice guidelines for diagnosis, care and treatment, and are involved with research activities.

ERNs must fulfil certain key criteria:

- Patient-centred and clinically led
- A minimum of **10 members** in at least **8 countries**
- Strong, independent assessment
- Fulfilment of Network and Member criteria
- Endorsement and approval by national authorities

ERN on kidney diseases (ERKNet)

Rare and complex kidney diseases encompass a wide range of congenital, inherited, and acquired disorders. It is estimated that at least two million Europeans are affected by rare kidney diseases, with glomerulopathies and congenital renal malformations accounting for about one million cases each. In addition, inherited tubulopathies, tubulointerstitial diseases and thrombotic microangiopathies represent a number of rare and ultra-rare disorders of high clinical relevance.

State-of-the-art diagnostic tools can provide valuable information on disease prognosis and therapeutic options. However, access to testing is not universal. Due to delayed diagnosis and inadequate treatment, many rare kidney diseases unnecessarily progress to kidney failure.

ERKNet aims to enhance the management of patients with rare kidney diseases, especially new and complex cases, through online consultation services. The network's expert working groups establish consensus-based diagnostic algorithms for patients with suspected rare kidney diseases, including standard criteria for genetic testing in cases of suspected inherited kidney disease. In addition, the working groups define clinical pathways for therapeutic management after a thorough review of available treatments.

Since awareness and knowledge among healthcare professionals are essential for identifying and treating rare kidney diseases, ERKNet has introduced a three-year postgraduate curriculum based on clinical training, webinars and e-learning, which provides a state-of-the-art education on the entire spectrum of rare kidney diseases. Those who successfully complete the course will be recognised as 'European Rare Kidney Disease Specialists'.

ERKNet has established ERKReg, the European Rare Kidney Disease Registry. This online registry provides demographic information and facilitates collaborative clinical research by identifying cohorts of patients with rare kidney diseases across Europe. Moreover, the registry provides clinical performance statistics and benchmarking across the specialist centres, supporting harmonised and optimised care for rare kidney disorders in all ERKNet hospitals and clinics.

NETWORK COORDINATOR

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ERN for rare neurological diseases (ERN-RND)

ERN-RND creates and shares knowledge and coordinates care for patients affected by rare neurological diseases involving the most common central nervous system pathological conditions. It covers cerebellar ataxias and hereditary spastic paraplegias; Huntington's disease and other choreas; frontotemporal dementia; dystonia, (non-epileptic) paroxysmal disorders and neurodegeneration with brain iron accumulation; leukoencephalopathies; and atypical parkinsonian syndromes.

The network unites expert centres and affiliated partners in 24 European countries, as well as patient representatives. It focuses on highly specialised healthcare services such as next generation sequencing diagnostics, deep brain stimulation and advanced therapies, and generates and disseminates both overarching and disease group-specific knowledge.

ERN-RND develops clinical best practice guidelines for some RNDs, best practice recommendations for neurorehabilitation and transition, as well as care standards such as the composition of multidisciplinary teams.

Disease expert groups develop and agree care pathways including diagnostic flowcharts and therapeutic algorithms, as well as disease scales to assess different aspects of rare neurological diseases.

Patients with unclear diagnoses are discussed via the CPMS. ERN-RND is one of four networks participating in the Solve-RD - Solving the Unsolved Rare Diseases project, and its training and education programme underpins an RND curriculum for healthcare professionals. The network facilitates trial-readiness and care quality through an ERN-RND registry, including data on all patients seen at ERN-RND centres and providing a unique overview of existing genotype-based cohorts.

ERN-RND cooperates with the European Academy of Neurology (EAN); the European Paediatric Neurology Society (EPNS); the European section of the International Parkinson and Movement Disorder Society (MDS); the European Federation of Neurological Associations (EFNA); and the European Academy of Childhood Disability (EACD). With the other two 'Neuro-ERNs' - EURO-NMD and EpiCARE – ERN-RND has established nine working groups.

NETWORK COORDINATOR

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ERN on inherited and congenital (digestive and gastrointestinal) anomalies (ERNICA)

ERNICA covers two diagnostic groups: malformations of the digestive system and malformations of the diaphragm and abdominal wall. The malformations of the digestive system work stream comprises four working groups on oesophageal diseases, intestinal diseases, intestinal failure and gastroenterological diseases. The malformations of the diaphragm and abdominal wall work stream is made up of two working groups: malformations of the diaphragm, and abdominal wall defects.

Working groups are co-led by ERNICA healthcare professionals and patient representatives. Nine areas of work are applicable to all diagnostic groups - management, dissemination, evaluation, standards of care, training, research, eHealth, foetal medicine; and networking.

ERNICA aims to pool disease-specific expertise, knowledge and resources from across the EU/EAA, in order to achieve health goals that may otherwise be unachievable in a single country. These health goals include development of clinical skills; increased patient access to high-quality expert care; and increased diagnosis-specific information available to healthcare professionals, patients and their families and carers.

In doing so, ERNICA also seeks to reduce health inequalities across Europe by standardising practices and making high-quality care, information and resources accessible to healthcare providers, patients and their families and carers across Europe.

NETWORK COORDINATOR

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Integration, coordination and collaboration: Member States and ERNs

2022 saw 620 new healthcare providers (HCPs) joining ERNs, bringing the total membership to more than 1600. That's good news for patients who now have greater access than ever before to highly specialised healthcare services, and for clinicians who benefit from collaboration with other experts across the EU and Norway.

However, the expansion also brings challenges around coordination and partnership - and that's where the Board of Member States (BoMS) plays a crucial role. The Board has guided the ERNs from infancy to adulthood - it was responsible for approving them when they were first established in 2017 and will approve any future additional ERNs. Integrating the work of ERNs into national health systems, and ensuring their priorities are aligned, is also a priority.

"The situation has changed significantly," says BoMS Co-Chair Professor Till Voigtländer. *"ERNs have matured and are now fully operational. The ERN Coordinators' group has been working very actively and efficiently, demonstrating its merits as an important collaborating partner for the Board."*

"ERN coordinators and their teams are actively addressing questions such as the best and most economical ways of monitoring performance, developing and organising ERN registries, sharing and disseminating knowledge, training, and complying with high ethical and legal standards," adds Professor Voigtländer. *"They have also been instrumental in developing the Clinical Patient Management System, which is key to support faster and better diagnosis, treatment and care for people living with rare diseases."*

The Board is also charged with approving new HCPs, and the latest additions result from a rigorous journey which began with a call for applications in 2019. The process was further complicated by Brexit and the subsequent loss of expertise from UK-based HCPs. With the new HCPs on board, attention now focuses on assessing and improving the quality of care provided by ERNs and HCPs.

An essential element in the continuous quality improving system of ERNs is AMEQUIS - the Assessment, Monitoring, Evaluation and Quality Improvement System. An independent evaluation and assessment body will evaluate ERNs to identify strengths and weaknesses, ensuring that the views of all those involved are heard, including patients and their families. BoMS will play a crucial role in this journey as it will be their job to agree on improvement plans for ERNs and HCPs, if and where needed.

Starting in 2022, the Joint Action on the integration of ERNs will require even greater collaboration between Member States, who will establish the building blocks of the future of ERNs, fully integrated into national health systems and perfectly harmonised with European partners. The Commission will coordinate the process with the ERN Coordinators' group playing a vital implementation role. Integration, coordination and collaboration will ensure the success of ERNs over the next phase of their journey.

"We now have more stakeholders than ever before involved in the ERN project, including hospital managers and patient advocacy groups" says Professor Voigtländer. *"That's good news, and we should be very happy about it. However, Member States can't cope with this workload alone. It is time to intensify our collaboration, because only when we all work together we will get the most out of the ERN project - a venture that is already the envy of the rest of the world."*

Professor Till Voigtländer

ERN on respiratory diseases (ERN LUNG)

Rare and complex lung diseases require multidisciplinary care and psycho-social support. Their complexity can be due to the underlying genetic mechanism of the disease or the secondary changes and damage done to other organ systems. Early diagnosis and access to specialist care improves outcomes for many of these conditions.

ERN LUNG addresses all rare and complex diseases of the respiratory system, including interstitial lung diseases (ILD); cystic fibrosis (CF); non-CF bronchiectasis (nCF-BE); pulmonary hypertension (PH); primary ciliary dyskinesia (PCD); alpha-1 antitrypsin deficiency (AATD); mesothelioma (MSTO); and chronic lung allograft dysfunction (CLAD).

The network seeks to improve expertise across Europe to advance standards of care, quality of life and prognosis for the entire spectrum of rare pulmonary diseases. Members of ERN LUNG develop and disseminate guidelines, promote common treatment approaches, enhance cross-border access to diagnosis and treatment, initiate and support registries, and assemble sufficiently large cohorts for clinical studies, drug development and natural history studies.

ERN-LUNG provides patients with access to interdisciplinary teams, providing online second opinions on complex cases without requiring patients to travel. This is achieved through an online expert advice system, by online case panel discussions, and – if needed – by cross-border referral.

NETWORK COORDINATOR

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ERN on skin disorders (ERN Skin)

Many skin conditions have a severe impact on patients and can be associated with a risk of cancer. Diagnosis of rare and complex skin diseases consists of a full assessment of the skin and mucous membrane, as well as other systems, in addition to skin biopsies. Only experienced dermatologists can differentiate between these complex conditions, and the absence of an expert diagnosis is a barrier to treatment. This can be a profound physical and psychological burden for patients.

ERN Skin brings together leading experts in the field of rare child and adult skin diseases to exchange knowledge, update and develop best practice guidelines, improve professional training and patient education, and set up research programmes.

It aims to improve healthcare organisation with the pooling of resources, including a platform with expert collaborative discussions on difficult cases. For every disease covered, core multidisciplinary teams include at minimum a dermatologist, a nurse, a psychologist, a geneticist, a dietician and a pathologist, along with other specialists as required.

ERN Skin also develops rare skin disease registries, allowing participation in research programmes and clinical trials with well-characterised patients, as well as the stimulation of therapeutic research with sufficiently large cohorts of patients. In addition, a comprehensive socio-economic study on the individual burden of diseases will be conducted.

NETWORK COORDINATOR

Professor Christine Bodemer
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ERN on adult cancers (solid tumours) (ERN EURACAN)

The Surveillance of Rare Cancers in Europe (RARECARE) defines rare cancers as malignant disorders with an incidence of fewer than six per 100,000 per year. They account for around 20-25 percent of all new cancer diagnoses and 30 percent of cancer deaths.

Experts agree that patients with rare cancers should, from initial diagnosis, be referred to certified reference centres. This enables them to benefit from the most up-to-date, multidisciplinary expertise - from effective therapies to evidence-based treatment guidelines - and ensures appropriate care for all patients, regardless of the initial point of access.

EURACAN covers more than 300 rare adult solid cancer types, grouping them into ten domains corresponding to the RARECARE classification and ICD10. The network collaborates closely with patient representatives from European Patient Advocacy Groups (ePAGs) to provide information and perspectives on patients' needs and expectations.

Since its inception, EURACAN has reached 26 EU and EAA countries, aiming to standardise patient management and improve survival rates by generating and sharing best practice tools, and regularly updating diagnostic and therapeutic clinical practice guidelines in collaboration with several scientific societies. The network has developed communication tools in all languages for patients and physicians, while the STARTER project (STarting an Adult Rare Tumour European Registry) is creating a crucial tool for the future - the EURACAN federated registry model.

EURACAN builds on existing networks and successful clinical trials through the European Organisation for Research and Treatment of Cancer (EORTC), the European Neuroendocrine Tumour Society (ENETS), the Connective Tissues Cancer Network (Conticanet) and several previous EU research programmes, including the EURACAN-initiated SPECTA/Arcagen and TRacKING projects.

NETWORK COORDINATOR

Professor Dr. Jean-Yves Blay

Centre Léon Bérard, Lyon, France

Europe:
a global centre of excellence

European Reference Networks came into operation in March 2017, with the primary purpose of improving the lives of people in Europe who are living with rare and complex diseases.

However, ERNs have a global impact far beyond Europe. They enhance global best practice where it exists and shape it where it does not. The networks are helping to make Europe a hub of activity in rare and complex conditions by implementing best practice diagnostic or treatment guidelines where they exist and developing them where they do not.

By connecting experts and patient populations, ERNs also facilitate clinical studies and test therapeutic interventions, putting them at the forefront of innovation in numerous rare disease fields.

The ERN model is an example to others, developing state-of-the-art eHealth tools to aid cross-border collaboration in Europe, with the potential to foster international collaboration and improve healthcare access.

ERN on Haematological diseases (ERN-EuroBloodNet)

Haematological diseases involve abnormalities of blood and bone marrow cells, lymphoid organs and coagulation factors, and almost all of them are rare. They can be subdivided into six categories: rare red blood cell defects; bone marrow failure; rare coagulation disorders; haemochromatosis and other rare genetic disorders of iron synthesis; myeloid malignancies; and lymphoid malignancies.

Diagnosis of rare haematological diseases (RHDs) requires considerable clinical expertise and access to a broad range of laboratory services and imaging technologies. These tests allow precise disease classification according to WHO criteria using international scoring systems and, where possible, biomarkers.

Given these requirements and the fact that some RHDs are very rare, diagnosis is frequently overlooked or delayed, especially in elderly patients. Treatment is also often difficult due to the specialised infrastructures and teams required and the difficulty accessing specific treatments such as allogenic stem cell transplantation or coagulation factors. Preventive programmes are in place in some countries for certain conditions, but there is an urgent need for harmonisation in the field of screening.

In its first five years ERN-EuroBloodNet, in close collaboration with the European Hematology Association (EHA), has successfully conducted multiple transversal and RHD disease-specific actions aimed at improving access to healthcare for RHD patients; promoting guidelines and best practice; improving training and knowledge-sharing; offering clinical advice where national expertise is scarce; and increasing the number of clinical trials in the field. The involvement of ePAGs and patient associations from the outset contributes to patients' empowerment, therapeutical education and advocacy training, in keeping with ERN-EuroBloodNet's patient-centred approach.

NETWORK COORDINATOR

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Professor Béatrice Gulbis
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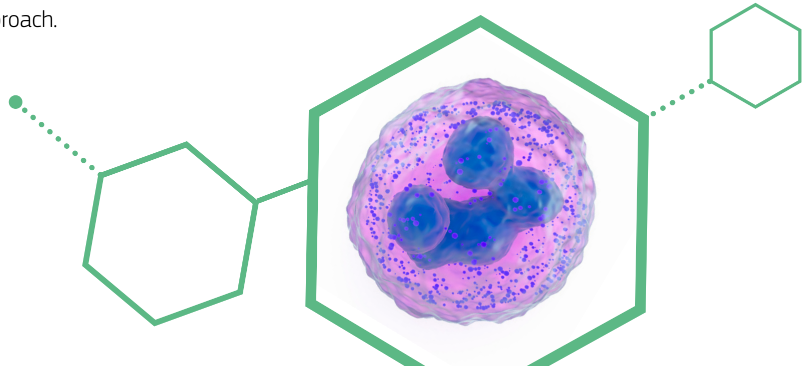

ERN on uro-recto-genital diseases and conditions (ERN eUROGEN)

Rare and complex uro-recto-genital conditions can require surgical correction, often during the neonatal period or in childhood. Urinary and faecal incontinence are a heavy burden on paediatric, adolescent and adult patients. Affected individuals require life-long care provided by multidisciplinary teams of experts who plan and perform surgery and provide post-operative care with additional support from physiotherapy and psychology teams when needed.

ERN eUROGEN provides independently evaluated best practice guidelines and improves the sharing of outcomes. For the first time, it aims to offer the capacity for tracking long-term outcomes for patients over a 15-20 year period through the ERN eUROGEN Registry.

The network collects data and materials where they are lacking; develops new clinical guidelines; builds evidence of best practice; identifies variations in current clinical practice; develops education and training programmes; sets the research agenda in collaboration with patient representatives; and shares knowledge through participation in virtual consultations on the CPMS and through multidisciplinary teams. New specialists for rare and complex uro-recto-genital diseases benefit from specific training and clinical exchange visits offered by the ERN eUROGEN exchange programme.

Ultimately, the network seeks to advance innovation in medicine and improve diagnostics and treatment for rare and complex uro-recto-genital patients through the 'Share. Care. Cure' strategy.

NETWORK COORDINATOR

Wout Feitz
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Collaboration in action

Online platforms, telemedicine and ehealth tools play a valuable role in facilitating collaboration. ERNs are connected through a dedicated IT platform, the Clinical Patient Management System (CPMS), a web-based clinical software application which allows healthcare providers from all over the EU to work together virtually to diagnose and treat patients with rare, low prevalence and complex diseases.

Network coordinators can convene 'virtual' advisory boards of medical specialists using telemedicine tools to review a patient's condition for diagnosis or treatment. This allows health professionals, who would previously have handled rare and complex cases in isolation, to consult peers and seek a second opinion from a colleague. A central feature of these tools is interoperability.

Thanks to advances in video conferencing, physical geography is no long a barrier to working in remote teams. Networks also use dedicated systems to share tissue samples or high-resolution images of complex conditions, which can also be used to build up an archive of cases for further study. The CPMS is covered by European and national legislation on data protection and patients' privacy rights (GDPR).

For example, once pathology or radiology data are securely shared, members of the network can log in, view the images and comment in a closed environment. The treating physician remains responsible for their patient but can tap into the ERN as a valuable and supportive resource.

Affiliated Partners

ERNs aim to deliver genuine added value to all EU Member States. The relevant legislation enables countries without representation in an approved ERN to participate through healthcare providers that are designated by their Member State as 'associated' and/or 'collaborative' national centres.

Member States may also wish to designate a national coordination hub to liaise with all ERNs. The ERN Board of Member States sets up the common framework for the designation and integration of those types of centres into the ERNs. Nevertheless, it is essential that the designation of Affiliated Partners by Member States be undertaken through open, transparent and robust procedures, and all ERNs must have in place a clear policy objective for the active engagement and participation of Affiliated Partners.

ERN on neuromuscular diseases (ERN EURO-NMD)

Neuromuscular diseases (NMDs) occur from early childhood to late adulthood and are characterised by muscle weakness and wasting. They may also be associated with other symptoms including fatigue, pain, numbness, blindness, swallowing difficulties, breathing difficulties and heart disease. Most NMDs are progressive and debilitating, with reduced lifespan and quality of life.

There are significant gaps and disparities in access to diagnostics and treatment across Europe. Major challenges in improving outcomes include the delay in referral from primary care to a specialist centre and managing the transition from paediatric to adult services.

EURO-NMD unites Europe's leading experts to provide patients with access to specialist care through virtual and in-person consultations. The network aims to reduce time to diagnosis, improve diagnostic yield and increase access to appropriate care pathways.

In the first half of 2021, a total of 12,882 new patients consulted EURO-NMD partners, and partners participated in 258 clinical trials. Since 2018 the number of new patients consulting network partners has risen by 37.5 percent and the participation of EURO-NMD partners in clinical trials has increased by 63 percent.

In addition, the network continuously develops new guidelines and provides healthcare professionals and patients with disease-specific best practice information. The knowledge generated and curated by the network is widely available online and through publicly-available webinars, as well as via eHealth tools such as CPMS discussions. A Moodle-based learning management system (LMS) is currently under construction.

Building on a strong legacy of cooperation, the network continues to foster collaborations with the potential to drive research and therapy development to address unmet patient needs. Promoting transnational data sharing through ethically robust, high quality registries and research data platforms is also a priority.

NETWORK COORDINATOR

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ERN on eye diseases (ERN-EYE)

Rare Eye Diseases (REDs) are the leading cause of visual impairment and blindness for children and young adults in Europe. More than 900 REDs are listed in the portal for rare diseases and orphan drugs (ORPHANET), including more prevalent diseases such as retinitis pigmentosa - which has an estimated prevalence of 1 in 5,000 - as well as some very rare conditions described only once or twice in medical literature.

In close collaboration with ePAGs, ERN-EYE addresses these diseases in four thematic groups: rare diseases of the retina; neuro-ophthalmology rare diseases; paediatric ophthalmology rare diseases; and rare anterior segment conditions. In addition, six transversal working groups are addressing issues common to the four main themes. Additional working groups focus on specific areas, including genetic testing, registries, research, education, communication, low vision and patients groups, and national integration.

One of the most important ERN tools is the CPMS, a virtual clinic IT platform with a dataset dedicated to REDs. ERN-EYE focuses on improving patients' diagnosis and care across the EU through connecting and enforcing expert networking; knowledge and information exchange; development of educational and training programmes such as webinars or e-Learning program); creation of a European interoperable registry (REDdistry); and development of guidelines and good practices documents.

NETWORK COORDINATOR

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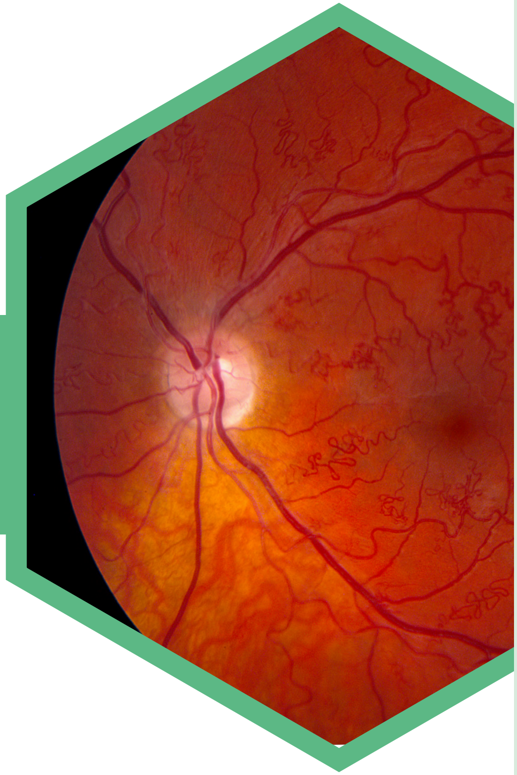

ERN on genetic tumour risk syndromes (ERN GENTURIS)

Genetic tumour risk syndromes are disorders in which inherited genetic variants strongly predispose individuals to the development of tumours. The lifetime risk of cancer can be as high as 100 percent. While there is considerable diversity in the organ systems that may be affected, individuals affected by these conditions share similar challenges: delay in diagnosis, lack of prevention for patients and healthy relatives, and therapeutic mismanagement. At present, only a small minority of people with genetic tumour risk syndromes has been diagnosed as such.

ERN GENTURIS is working to improve identification of these syndromes; minimise variation in clinical outcomes; design and implement EU-guideline; develop the GENTURIS registry; support research; and empower patients. The network educates the public and healthcare professionals via its website, by organising regular webinars and courses, and by fostering sharing of best practice across Europe. Both virtual and face-to-face access to multidisciplinary care will be improved, in order to share and discuss complex cases. The network is enhancing the quality and interpretation of genetic testing and increasing patient participation in clinical research programmes.

ERN GENTURIS cooperates with other ERNs to improve the care of patients with genetic tumour risk syndromes who develop conditions that fall within the expertise of another network.

NETWORK COORDINATOR

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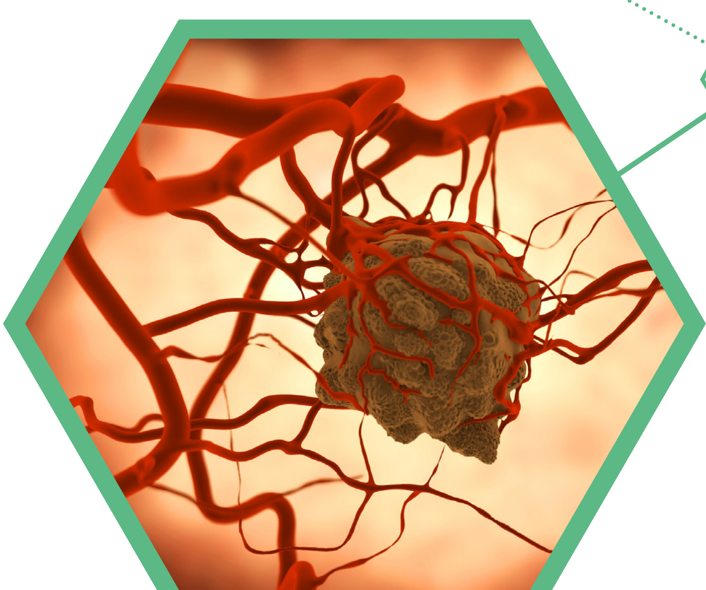

Leading a European Reference Network

Professor Hélène Dollfus

Professor Hélène Dollfus is a professor in medical genetics and a consultant in medical genetics at the Strasbourg University Hospital (HUS) in France, where she is the head of the medical genetics department. She has been the coordinator of ERN-EYE since it was established in 2017, and served one mandate as the Chair of the CG.

"Coordinating an ERN, working alongside the European Commission, is quite an adventure," says Prof Dollfus. *"The network is highly innovative and covers a wide range of initiatives focused on patient care. It's a huge challenge, but it's very exciting and we're starting to see some promising results."*

Prof Dollfus is proud that ERN-EYE is living up to its founding vision. *"It's a great achievement that specialists in rare eye diseases from all over Europe have teamed up under the guidance of our exceptional devoted management team,"* she explains. *"In addition, patient representatives are actually major partners with whom we work hand in hand. I feel that we have already learned a lot from each other and have sown the seeds for ERN-EYE to be successful in the future."*

Not only does Prof Dollfus head up ERN-EYE, she is also the current chair of the ERN coordinators' group, which brings together all 24 coordinators to discuss common challenges and share experiences. *"We are at an interesting stage of ERNs' development. We can assess and evaluate the achievements of the first five years with some satisfaction, but we are now entering a new period of expansion which will require enlarged management teams and more resources to support healthcare professionals provide increasingly efficient services to patients with rare diseases,"* she says.

As from January 2022, most ERNs have at least doubled in size as more members are added from all over the EU. *"Integrating the ERNs into Member States' health care systems is a major challenge that we are all eager to achieve. Training exchanges have been a significant success, and most of us are continually producing and updating guidelines,"* says Prof Dollfus.

"As ERNs, our goal is for rare disease data to be shared as widely as possible through the growing number of registries, to benefit both patients and practitioners. We want to see enhanced research collaborations across the EU - not only for clinical trials, but also on scientific research including genomics developments."

Prof Dollfus is looking forward to the next stage in the development of ERNs. *"My vision is for a seamless, cohesive and productive maturation phase for all the ERN beehives, whilst fulfilling our mission to bring care to each rare disease patient in the EU."*

ERN on uncommon and rare diseases of the heart (ERN GUARD-Heart)

Rare cardiac diseases can present throughout a person's life, and most of them are usually either genetic (inheritable) disorders or those which develop during embryogenesis (congenital heart defects). These conditions are characterised by a wide range of symptoms and signs which vary not only from disease to disease, but also from patient to patient. Most of these cardiac diseases carry a unique susceptibility to sudden death at a young age, and may occur in otherwise healthy people.

ERN GUARD-Heart has identified five thematic areas: familial electrical diseases in adults and children; familial cardiomyopathies in adults and children; special electrophysiological conditions in children; congenital heart defects; and other rare cardiac diseases. These themes follow the International Classification of Diseases (ICD10) and Orphanet and are subject to the clinical guidelines of the European Society of Cardiology (ESC).

The network seeks to strengthen the coordination of expertise and resources, in order to facilitate the pooling of multidisciplinary knowledge which is then mapped and disseminated to the public.

Healthcare services are provided through a shared eHealth platform, which ensures patients get wider access to expertise and healthcare professionals around Europe. By fostering closer cooperation between experts, new scientific knowledge is acquired and shared to support the development of new diagnostic and therapeutic procedures, and to identify new rare cardiac diseases.

NETWORK COORDINATOR

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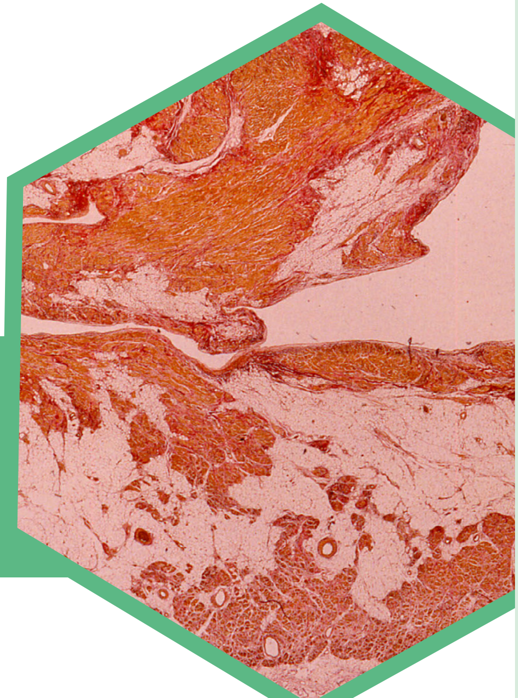

ERN on congenital malformations and rare neurodevelopmental disabilities (ERN ITHACA)

ERN ITHACA (Intellectual disability, TeleHealth, Autism and Congenital Anomalies) echoes the diagnostic 'odyssey' experienced by so many patients with developmental anomalies. The network brings together more than 70 clinical genetics department across EU academic hospitals, including experts in rare neurodevelopmental disorders (NDDs) - mainly intellectual disability (ID) and autism spectrum disorder (ASD) - as well as rare multiple congenital anomalies.

ERN ITHACA covers the clinical and biological/genetic diagnosis of these developmental anomalies, the coordination of multidisciplinary care and treatment, and prenatal diagnosis and foetal pathology.

Rare developmental anomalies affect many children and adults - for example, approximately two percent of newborns will be affected by ID and at least one percent by ASD (with or without ID). Roughly half of patients with ID, and more than one in ten with ASD, have a monogenic or a chromosomal disorder. Congenital malformations affect one in 40 babies, often as part of complex syndromes which also display NDDs. More than 5,000 rare syndromes have been described.

ERN ITHACA unites medical experts and ePAG representatives, providing collaborative support for clinical research, developing best practice consensus and guidelines, and improving the early diagnosis, care and cure of patients. The network has also established the International Library of Intellectual disability and Anomalies of Development (ILIAD) patient registry.

The network develops telemedicine and tele-expertise to facilitate collegial discussions between referring doctors and researchers across the EU, and produces training and e-learning tools for health professionals, lay persons and ePAGs.

NETWORK COORDINATOR

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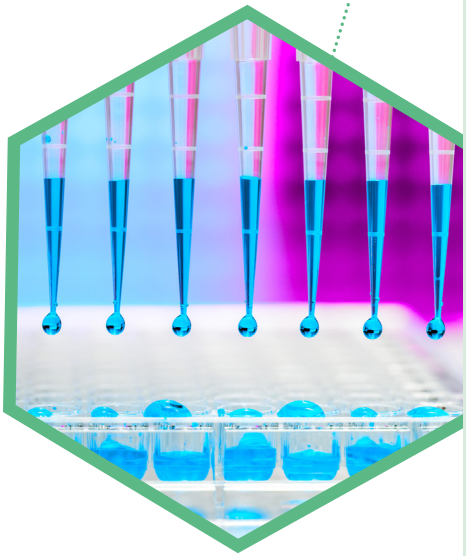
ERN on hereditary metabolic disorders (MetabERN)

Rare inherited metabolic diseases (IMDs), of which there are more than 1400, are individually rare but collectively frequent. Many metabolic diseases have severe - sometimes life-threatening - implications for patients. These conditions include disorders of all organs, can affect people of any age, and require multidisciplinary collaboration between a range of professionals.

Early diagnosis can improve outcomes, but only five percent of known IMDs are currently included in newborn screening programmes in Europe and there is a need for national programmes to be harmonised. Many IMDs lack knowledge about their natural history and the efficacy and safety of therapies, while long-term follow-up is incomplete.

MetabERN seeks to improve the lives of people affected by this highly heterogenous group of diseases by dividing them into seven main categories. The network represents the most comprehensive, pan-metabolic, pan-European, patient-orientated network, aiming to transform how care is provided to patients with IMDs in Europe.

MetabERN uses the Clinical Patient Management System (CPMS) as a referral platform for clinical decision-making processes and for fostering translational research programmes across IMDs. With its fully operational unified European registry for IMDs (U-IMD), developed with a grant from the EU Consumers, Health, Agriculture and Food Executive Agency (CHAFEA), MetabERN effectively generates patient data for research purposes. This allows a detailed assessment of the natural history of IMDs, as well as the investigation of further research questions, including prospective analysis of preventive and therapeutic interventions in patients with IMDs. Moreover, U-IMD is the first observational, non-interventional patient registry to encompass all 1400+ IMDs.



NETWORK COORDINATOR

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National policies on rare diseases

EU Member States hold primary responsibility for organising and delivering health services and medical care in their own countries. EU health policy aims to complement national policies, to ensure health protection in all EU policies and to work towards a European Health Union.

In 2009, the European Council of Health Ministers recommended that member countries establish and implement plans or strategies to support patients with rare diseases. These plans should be designed to:

- Guide and structure actions in rare diseases within national health and social systems
- Integrate initiatives at local, regional and national levels into plans or strategies to ensure a comprehensive approach
- Define priority actions with objectives and follow-up mechanisms

The EU4Health programme 2021-2027 provides project funding to support Member States to implement their national health plans in line with the vision for a European Health Union. By 2022, 23 Member States (plus Switzerland and Norway) had adopted national health plans for rare diseases.

ERN on paediatric cancer (haemato-oncology) (ERN PaedCan)

Paediatric cancer is rare and comes in multiple subtypes. Each year across Europe, 35,000 children and young people are diagnosed with cancer and 6,000 paediatric cancer patients die - the leading fatal disease for children aged over one. More than half a million long-term survivors of childhood cancer are alive today in Europe, with two-thirds of them experiencing long-term health and psycho-social problems due to their disease.

Average survival rates have improved in recent decades - progress for some conditions has been dramatic, while for others the outcomes remain very poor. Significant survival inequalities are a challenge, with worse outcomes in Eastern Europe.

ERN PaedCan works to improve access to high-quality healthcare for children and adolescents with cancer whose conditions require specialist expertise and tools not widely available due to low case volumes and lack of resources. It builds on previous EU-funded projects ENCCA, PanCare and ExPO-r-Net.

Members include a strong interactive network of paediatric hospitals and units specialised in paediatric and adolescent cancer care. Together with the European Society for Paediatric Oncology (SIOPE), European Standard Clinical Practice (ESCP) guidance protocols have been established as a common reference for upfront treatments in all major paediatric cancer care settings, and a virtual paediatric oncology tumour board uses eHealth tools to share expertise and advice. Education and training are fostered through webinars, meetings and exchange programmes.

ERN PaedCan strives to achieve equity in childhood cancer outcomes across Europe and to help implement SIOPE's Strategic Plan, strongly supported by the Horizon Europe Cancer Mission, Europe's Beating Cancer Plan and the Pharmaceutical Strategy for Europe.

The network aims to increase childhood cancer survival and quality of life by fostering cooperation, research and training, with the ultimate goal of reducing current inequalities in childhood cancer survival and healthcare capabilities in EU Member States.

NETWORK COORDINATOR

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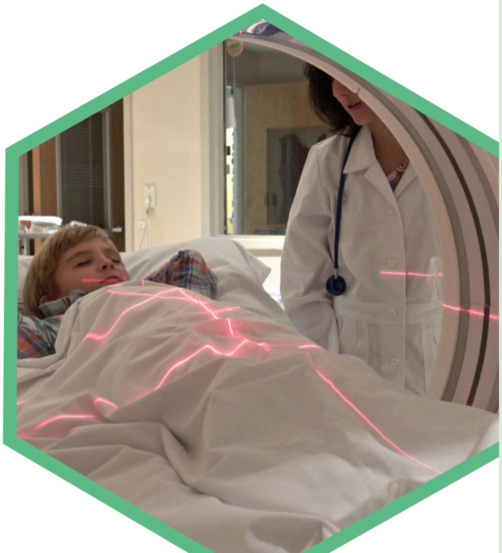

ERN on hepatological diseases (ERN RARE-LIVER)

Rare liver diseases can cause progressive liver injury, leading to fibrosis and cirrhosis. The complications of cirrhosis can lead to death and, in many cases, the only effective treatment is liver transplantation. Fatigue, pruritus in cholestatic conditions, and pain and abdominal swelling in cystic conditions significantly affect patients' quality of life.

In paediatric patients, delays in diagnosis, failure to thrive and attain developmental milestones, and the challenge of transition in care through adolescence are additional complicating factors.

ERN RARE-LIVER addresses three disease themes: autoimmune liver disease; metabolic, biliary atresia and related liver disease; and structural liver disease. For the first time in liver disease, the network fully integrates adult and paediatric care with a focus on the needs of transitional populations and the implications for families with a genetic diagnosis.

Up-to-date guidelines are a priority. Care guidelines, supported by the standardisation of key diagnostic and prognostic tests, are implemented in collaboration with the European Association for the Study of the Liver (EASL) and the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN).

ERN RARE-LIVER aims to address the significant challenges of clinicians' awareness of rare liver disorders and equitable access to rapidly evolving treatment options.

NETWORK COORDINATOR

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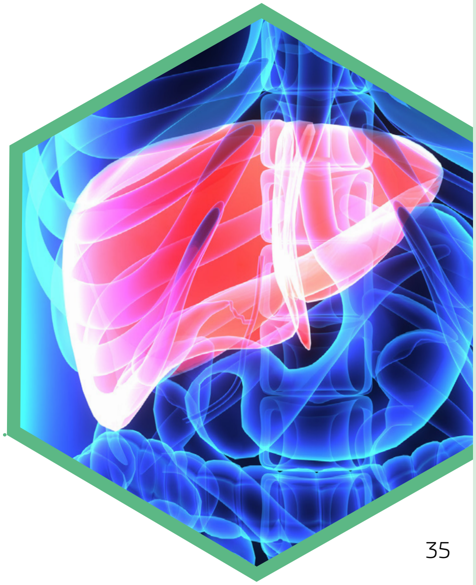

ERN on connective tissue and musculoskeletal diseases (ERN ReCONNET)

Rare connective tissue and musculoskeletal diseases (rCTDs) comprise different diseases and syndromes which have a considerable impact on patient well-being. They include hereditary conditions; systemic autoimmune diseases such as systemic sclerosis; mixed connective tissue diseases; inflammatory idiopathic myopathies; undifferentiated connective tissue diseases; and anti-phospholipid syndrome.

ERN ReCONNET is developing a framework for the delivery of high quality, innovative, sustainable and equitable standards of care and practice which will give European patients with rCTDs better access to healthcare.

Thanks to collaboration between full members, ePAG representatives and affiliated partners, ERN ReCONNET has developed peer-reviewed publications including the latest clinical practice guidelines; unmet needs in patient education; optimisation of patient care pathways; and the impact of COVID-19 on rCTDs. The network has also delivered a methodology for creating organisational models for rare disease patient care pathways; a European registry infrastructure for data harmonisation in rCTDs which aims to integrate all existing and newly developed registries on rCTDs across Europe; webinars for healthcare professionals and patients on ERN ReCONNET topics; and lay versions of clinical practice guidelines.

Patient representatives are deeply involved in all ERN ReCONNET activities, playing a key role in drafting and reviewing publications, providing essential information on patients' needs to improve pathways, and helping to improve disease knowledge and management. They participate both as webinar panelists and attendees, develop lay versions of publications, support assessment procedures for new members, and are involved in governance.

The close collaboration of the different stakeholders involved in the network represents one of the main added values of ERN ReCONNET, which will continue improving the lives of people living with rCTDs.

NETWORK COORDINATOR

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Azienda Ospedaliero Universitaria Pisana, Italy

Focusing on improving patients' health outcomes: the role of patient organisations

ERNs are about patients. Patient organisations and in particular EURORDIS - a non-governmental patient-driven alliance of 984 rare disease patient organisations in 74 countries - have played an active role in the development of the networks for more than a decade. Collectively, they have helped ensure that ERNs prioritise enhancing clinical excellence and improving patients' health outcomes, whilst ensuring equitable access to quality care across Europe.

"We were there at the birth of the idea in the High-Level Working Group on Health Services and Medical Care, where ERNs were translated into the Cross-Border Healthcare Directive," says Inés Hernando, ERN and Healthcare Director at EURORDIS. *"We have walked the long road with Member States and the European Commission, from the birth of the concept into legislation, through the mobilisation and clustering of clinical leads, up to the launch of the 24 ERNs grouped in therapeutic areas, and we are now supporting their implementation by collaborating closely with the patient advocates and clinical leads involved in the networks."*

As a consistent partner in nurturing the concept of ERNs, EURORDIS continues to work with the rare disease patient community, clinical leads and ERN project management teams to ensure that patients are routinely and systematically involved in ERN activities and governance. ERN clinical leads and patient advocates are gradually building a culture of shared leadership and are learning how to best collaborate to ensure that ERNs contribute to improving the lives of people living with rare diseases.

"There are currently no treatments for many rare diseases," explains Ms Hernando. *"However, the culture of learning that ERNs have started to build is transforming them into a hotbed of innovation. By defining outcomes for specific diseases that can be systematically measured and shared across different expert centres and countries, ERNs will open the door to quality improvement and adoption of optimal medical or surgical interventions."*

ERNs are expected to break the isolation that rare disease communities face, raise the visibility of experts across Europe and complement the capacities of national health systems to diagnose, treat and manage patients. *"For this to happen at scale, there must be clear and transparent referral pathways. Member States need to establish the mechanisms and processes to facilitate uptake and adoption of ERNs' knowledge assets - for example, in the development of rare disease care pathways,"* she says.

Patients have high hopes that ERNs can make a real impact on their lives: *"Discussing complex cases and sharing experience and expertise in the ERNs is an important first step, but countries should make better and more extensive use of the knowledge that these networks create and curate, in order to improve the lives of the 30 million people living with a rare disease in Europe,"* adds Ms Hernando. The Member States have a key role to play at this stage. *"Now is the time to nurture and support the networks in line with their ambitions, and to integrate them into national health systems, to improve survival and quality of life outcomes for as many patients as possible."*

ERN on immunodeficiency, autoinflammatory and autoimmune diseases (ERN RITA)

ERN RITA brings together the leading European centres with expertise in the diagnosis and treatment of rare immunological disorders. These constitute potentially life-threatening conditions requiring multidisciplinary care using complex diagnostic evaluation and highly specialised therapies. The network divides these conditions into four sub-themes or work streams – primary immunodeficiency (PID), autoimmune disorders, paediatric rheumatological disorders and autoinflammatory disorders.

Immunological therapies are being discovered and implemented rapidly. Polyvalent immunoglobulin therapy has revolutionised the outlook for antibody deficient patients; specific anti-cytokine treatments have transformed the lives of patients with rare autoimmune and autoinflammatory conditions; and stem cell and gene-based therapies originally for PIDs are now applied to all the diseases covered by the network.

The network builds on the work of the existing European scientific societies which have developed patient registries, clinical guidelines, research collaborations, educational activities and links with patient organisations for all four disease streams.

ERN RITA strives to reduce inequalities in health care faced by patients seeking to access diagnostic testing and innovative treatments such as biologic therapies, immunoglobulin replacement and cellular therapies such as stem cell transplantation. It aims to link pre-existing registries; develop pan-European clinical guidelines; establish a task force of geneticists for quality control of next generation sequencing technology; agree a common tool for pharmacovigilance in these rare conditions; convene a task force for the correct use and monitoring of biologic treatments in immune-mediated diseases; bring together and improve stem cell therapies for patients; foster collaborations between patient associations; and bring together paediatric and adult specialists across the four themes.

NETWORK COORDINATOR

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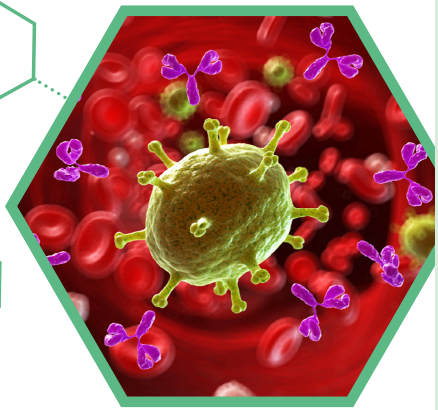

ERN on transplantation in children (ERN TransplantChild)

Paediatric transplantation (PT) includes both solid organ transplantation (SOT) and haematopoietic stem cell transplantation (HSCT), and is the only curative procedure for several rare diseases. Optimal post-transplant care requires the concerted efforts of a multidisciplinary team. After transplantation, patients face chronic immunosuppression to avoid rejection, which requires monitoring for post-transplant complications in order to extend children's lifespans and improve their quality of life.

ERN TransplantChild brings together experts in PT and post-transplantation care to improve outcomes for children and their families. The network aims to reduce both the time spent in hospital and the use of complex, long-term treatments, and it works to improve psychological support services as children transition to adulthood.

The network strives to make the latest techniques and medical, pharmacological and therapeutic advances available, whilst facilitating the dissemination of harmonised clinical practice guidelines and the development of personalised PT medicine.

ERN TransplantChild seeks to reduce the efforts associated with transplantation - such as re-transplantation and pharmacological treatments - and is harmonising PT care to minimise the risks of post-transplantation complications. Together, Europe's leading PT experts are working to reduce mortality and morbidity related to transplantation in children.

NETWORK COORDINATOR

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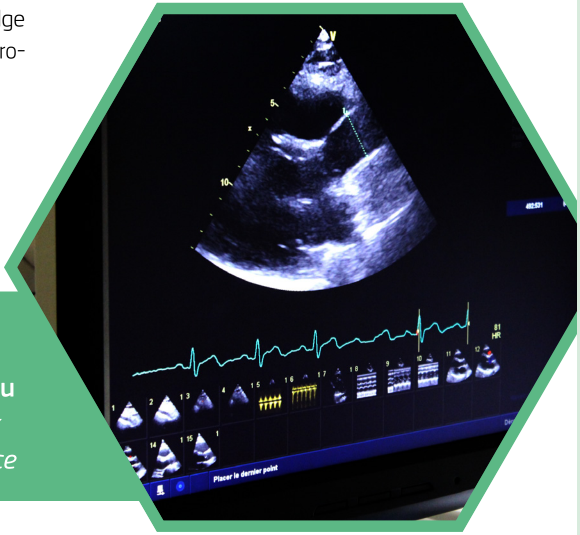
ERN on multisystemic vascular diseases (VASCERN)

Rare multisystemic vascular diseases include disorders which affect all types of blood vessels, with consequences for several body systems which require a multidisciplinary approach to care. VASCERN comprises six rare disease working groups on hereditary haemorrhagic telangiectasia (HHT-WG); heritable thoracic aortic diseases (HTAD-WG); medium sized arteries (vascular Ehlers Danlos Syndrome) (MSA-WG); paediatric and primary lymphedema (PPL-WG); vascular anomalies (VASCA-WG); and neurovascular diseases (NEUROVASC-WG). In addition, there are several thematic working groups which address communication, registries, ethics and issues related to pregnancy. A dedicated ePAG enables patient advocates to be involved in all VASCERN activities.

VASCERN's objectives include networking, sharing and spreading expertise; promoting best practices, guidelines and clinical outcomes; patient empowerment; and improving knowledge through clinical and basic research.

Healthcare professionals involved in VASCERN have already made educational materials, such as webinars and the 'Pills of Knowledge' series of videos, available online for both doctors and patients. The network has published consensus statements and clinical decision-making tools - including patient pathways, and 'Dos and Don'ts' factsheets - to provide advice on the proper diagnosis and care of patients with rare diseases. Digital eHealth services such as the VASCERN mobile app have been developed in collaboration with all the expert centres and patient organisations of the ePAG. Exchanges between member institutions are being set up, and the network continues to share knowledge both with members and with healthcare professionals outside the ERN.



NETWORK COORDINATOR

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ERN Directory

Endo-ERN	ERN on endocrine conditions (Endo-ERN)	www.endo-ern.eu	info@endo-ern.eu
ERKNet	ERN on kidney diseases (ERKNet)	www.erknet.org	contact@erknet.org
ERN BOND	ERN on bone disorders (ERN BOND)	www.ernbond.eu	https://ernbond.eu/contact/
ERN CRANIO	ERN on craniofacial anomalies and ENT disorders (ERN CRANIO)	www.ern-cranio.eu	ern-cranio@erasmusmc.nl
ERN EpiCARE	ERN on rare and complex epilepsies (EpiCARE)	www.epi-care.eu	https://epi-care.eu/contact-us/
ERN EURACAN	ERN on adult cancers (solid tumours) (ERN EURACAN)	www.euracan.eu	contact@euracan.eu
ERN EuroBloodNet	ERN on haematological diseases (EuroBloodNet)	https://eurobloodnet.eu	coordination@eurobloodnet.eu
ERN eUROGEN	ERN on uro-recto-genital diseases and conditions (ERN eUROGEN)	www.eurogen-ern.eu	eurogen@uroweb.org
ERN EURO-NMD	ERN on neuromuscular diseases (ERN EURO-NMD)	www.ern-euro-nmd.eu	info@ern-euro-nmd.eu
ERN EYE	ERN on eye diseases (ERN EYE)	www.ern-eye.eu	contact@ern-eye.eu
ERN GENTURIS	ERN on genetic tumour risk syndromes (ERN GENTURIS)	www.genturis.eu/	genturis@radboudumc.nl
ERN GUARD-HEART	ERN on diseases of the heart (ERN GUARD-Heart)	www.guardheart.ern-net.eu	contact@guardheart.ern-net.eu
ERNICA	ERN on inherited and congenital (digestive and gastrointestinal) anomalies (ERNICA)	www.ern-ernica.eu	ern-ernica@erasmusmc.nl
ERN ITHACA	ERN on congenital malformations and rare neurodevelopmental disabilities (ERN ITHACA)	www.ern-ithaca.eu	https://ern-ithaca.eu/contact/
ERN LUNG	ERN on respiratory diseases (ERN LUNG)	www.ern-lung.eu	info@ern-lung.eu
ERN PaedCan	ERN on paediatric cancer (haemato-oncology) (ERN PaedCan)	www.paedcan.ern-net.eu	ernpaedcan@ccri.at
ERN RARE-LIVER	ERN on hepatological diseases (ERN RARE-LIVER)	www.rare-liver.eu	ern.rareliver@uke.de
ERN ReCONNET	ERN on connective tissue and musculoskeletal diseases (ERN ReCONNET)	www.reconnet.ern-net.eu	ern.reconnet@ao-pisa.toscana.it
ERN RITA	ERN on immunodeficiency, autoinflammatory and autoimmune diseases (ERN RITA)	www.ern-rita.org	contact-rita@ern-net.eu
ERN-RND	ERN for rare neurological diseases (ERN-RND)	www.ern-rnd.eu	info@ern-rnd.eu
ERN Skin	ERN on skin disorders (ERN Skin)	www.ern-skin.eu	coordination@ern-skin.eu
ERN TRANSPLANT-CHILD	ERN on transplantation in children (ERN TransplantChild)	www.transplantchild.eu	coordination@transplantchild.eu
MetabERN	ERN on hereditary metabolic disorders (MetabERN)	www.metab.ern-net.eu	https://metab.ern-net.eu/contact/
VASCERN	ERN on multisystemic vascular diseases (VASCERN)	www.vascern.eu	contact@vascern.eu


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