
European Commission

EUROPEAN REFERENCE NETWORKS

Helping patients with rare or low-prevalence complex diseases

# 1.Patient Workshop

## Thursday 12 December 2024

## AM – Intro – Part 1

## Hosted by Pr. Maria Puiu, Dorica Dan, Tanja Zdolšek Draksler

ERN ITHACA Anne Hugon

European Reference Networks ITHACA

# Agenda

## Patient Workshop - Thursday 12 December

9:00 Opening - **Maria Puiu, Anne Hugon**

9:10 Added value of ERN ITHACA to engage patient organisation at national level Rare Diseases Roumania, state of art - **Dorica Dan**

9:20 Activity report and added value from PAB activities in ERN ITHACA - **Dorica Dan, Anne Hugon**

Part 1: Learning from each other workshop - Best practice sharing

9:30 Introduction - **Tanja Zdolšek Draksler**

9:35 *Clinics and Patient care*

1. NoRo in community or how to upscale your resources? - **Dorica Dan**
2. Multidisciplinary clinic for patients with macroglossia in BWS - **Monica Bertoletti**
3. PKS Clinic: a multidimensional approach to Pallister-Killian Syndrome care - **Samantha Carletti**
4. Care coordination for all rare conditions in Ireland – A comparison between 22q11 Deletion Syndrome and 2q24 Deletion Syndrome - **Lyndsey Walsh, Anne Lawlor**

10:30 **Coffee break**

## Patient Workshop - Thursday 12 December (PM)

11:00 *Global collaboration and guidelines*

5. The Value of WaihonaPedia for your community, guide for community leaders - **Gerritjan Koekkoek**
6. Parent co-led initiative in creating the first global Clinical Practice Guideline (CPG) for a rare neurodevelopmental disorder called SATB2-Associated Syndrome (SAS) - **Erika Stariha**

11:30 *Data collection and registries*

7. GASR - Global Angelman Syndrome eRegistry - **Ellen Koekoeckx**
8. Building a research portal for rare disease collaboration: CHAMP1 Approach - **Daniele Palumbo**
9. Solving rare diseases: How global collaboration and data are advancing Kleefstra Syndrome research - **Tanja Zdolšek Draksler**

12:10 General discussion - **Tanja Zdolšek Draksler, Dorica Dan**

12:40 **Lunch**

Part 2: The Patient Journey — Navigating Diagnosis, Grief, and Mental Health

13:30 Mental health and wellbeing and rare conditions - **Kristen Johnson**

Session 1: Diagnosis

14:00 Role of genetic counseling in managing the impact of a diagnosis - **Sofia Douzgou Houge, Adela Chirita**

14:15 Communicating diagnosis: Addressing the needs of patients, families, and doctors - **Eduardo Tizzano**

14:30 Diagnostic journey of a rare disease patient, a parent perspective - **Erika Stariha**

14:45 Patient advisory board feedback on communicating diagnosis, discussion - **Ellen Koekoeckx**

Session 2: Parallel sessions

| | **Group 1**<br>Identifying and mapping resources to boost family resilience | **Group 2**<br>Different faces of grief |
|---|---|---|
| 15:30 | Introduction:<br>**Ioana Streata,**<br>**Ammi Sundqvist Andersson**<br>Moderation and participation:<br>**Dorica Dan,**<br>**Monica Bertoletti** | Introduction:<br>**Andrada Ciuca**<br>Moderation and participation:<br>**Kasia Katarzyna Świeczkowska,**<br>**Marie-Christine Rousseau,**<br>**Esther Szabo,**<br>**Samantha Carletti,**<br>**Gerritjan Koekkoek** |

17:00 Summary of groups 1 and 2, results and final conclusions - **Dorica Dan, Tanja Zdolšek Draksler**

17:15 **Cocktail reception**

# Welcome and opening session, Pr. Maria Puiu

- ITHACA Consortium-Center represented by Pr. Maria Puiu, and will be hosted at the **Bucharest University of Economic Studies**.

  - **Ro-NMCA-ID** (Romanian Network for Multiple Congenital Abnormalities with Intellectual Deficiency)  HCP ROMANAI , TIMISOARA Lead by Pr Puiu Maria

  - **Ro-NMCA-ID is based on five existing structures with previous collaboration.**
    - The four hospitals have expertise in diagnostic, preventive and treatment procedures in genetic diseases,
    - while NoRo center offers educational and supportive therapy


WELCOME TO
ROMANIA!
BRAN
CASTLE

Welcome to Romania!

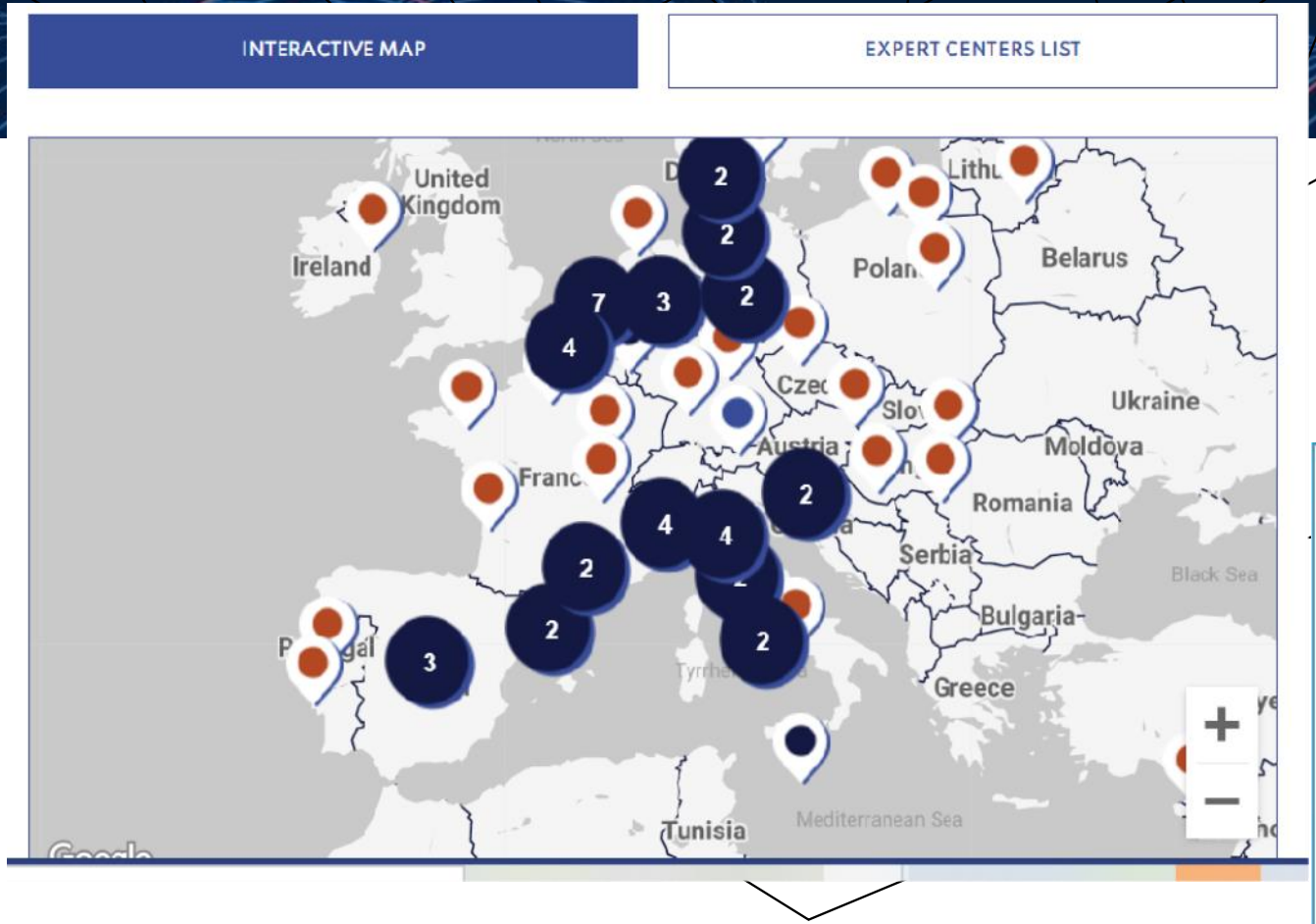
**Dear ERN ITHACA Board Members, Dear Colleagues and Friends,....**

We are honored to welcome you to Romania, a country where tradition and innovation go hand in hand.

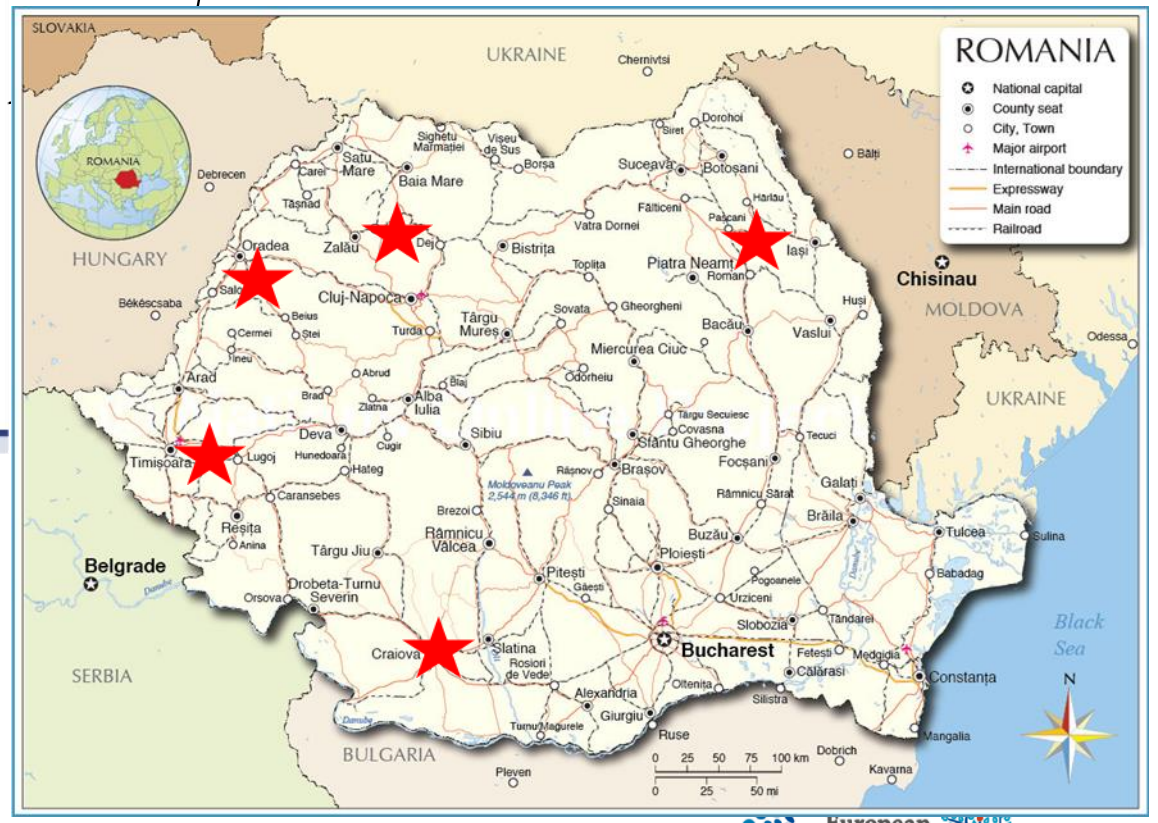
Your presence reflects our shared commitment to research and support for patients with rare genetic diseases.

We wish you a pleasant stay and productive discussions!

Together, we make a difference!




**Ro-NMCD-ID is created as a Romanian network of ERN ITHACA since 2016 (because we are inspired!)**




**Ro-NMCD-ID is recognized as the National Coordination Center for Rare Diseases in Romania from 2023 (because we are the best!).**

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# State of the Art for RDs in Romania

## Added value of ERN ITHACA to engage patient organisation at national level.

## - Rare Diseases Romania –

*Dorica Dan, president RPWA, RONARD*

*ePAG chair ITHACA, vice-president EURORDIS, RareResourceNet*

*Coordinator NoRo Center*



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# Challenges at national level

1. **>1.000.000 patients with RDs in Romania**. Many rare diseases are still **undiagnosed/ late diagnosed**
2. **ICD 10** used in the HCS do not cover a large number of rare diseases
3. **No national registry** for rare diseases
4. **No legislation** for integrated care
5. Romania perform **neonatal screening only for 3 diseases**
6. **Innovative treatments** are available for patients with a big delay
7. **Not enough specialized social services** for patients
8. **No Centers of Expertise in all ERNs**
9. No organization for **undiagnosed patients**
10. Only **2 national networks** established until now
11. **Disability assessment** for RDs patients needs improvement
12. 50% of population in **rural areas**


# Improvements

38 centers of expertise accredited by MoH since 2016 (MoH Order 540/2016); members in 11 ERNs

NoRo Center accredited as a CoE since 2016; member of RO-NMCA-ID and member of ERN ITHACA since 2017; member of RareResourceNet;

55 Patient Organizations for RDs, members of RONARD;

National Plan for Rare Diseases included in the Nat. Strategy4HealthH

National Council 4 RD has 3 members of RONARD with voting rights

Very good collaboration between PO & CoE;

New working groups for RDs established by MoH (Off Label)

Pilot Project to increase the number of diseases in screening

The list of innovative treatments have been updated;

A systemic approach to involve community nurses in case management for rare diseases

Coorperation with Medical Universities from Timișoara, Craiova and Cluj to train professionals and to create virtual case management platform for community nurses

12. Ro-NMCA-ID was designated as a **National Coordination Hub**

# 20 years in brief

European Reference Network for rare or low prevalence complex diseases

Network Intellectual Disability and Congenital Malformations (ERN ITHACA)

ITHACA

**2003**

RPWA

**2007**

RONARD

**2008**

1st Partnership MoH - ANBRaRo

**2010**

– 1ST NPRD / NO FUNDING

**2011**

•NoRo Center (EEA&Norway grants)
•ARCrare

**2013**

•2ND Partnership MoH - ANBRaRo
•NCRD

**2014**

2ND NPRD included in the NSH 2014-2020

**2016**

Acreditation of Centers of Expertise

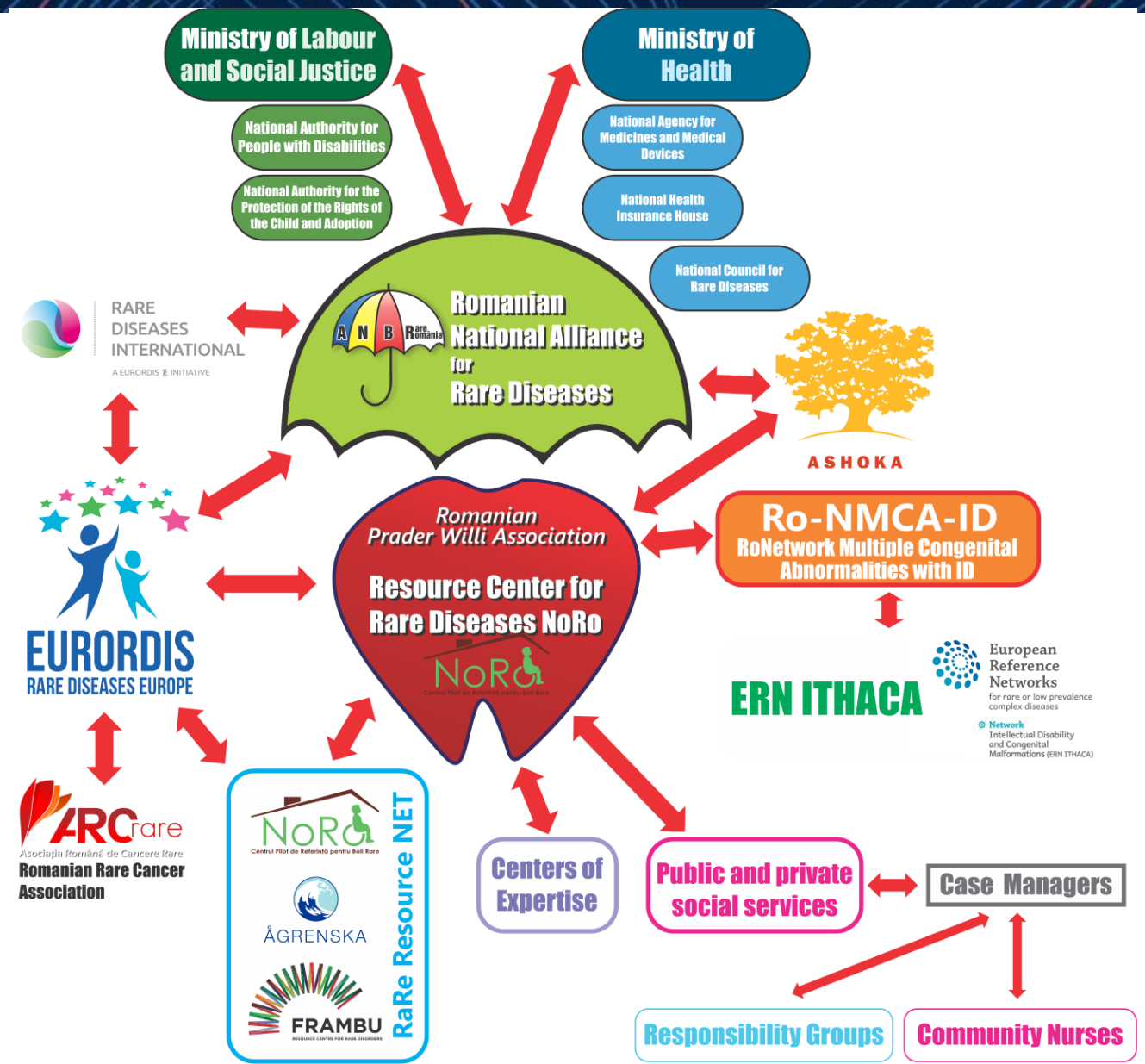
**2020**

3rd Partnership MoH - ANBRaRo-APWR

**2023**

•NPRD
•NSH 2022- 2030

# Working in networks




## Ro-NMCA-ID centres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# NoRo is part of Ro-NMCA-ID

**Ro-NMCA-ID is based on five existing structures with previous collaboration.** The **four hospitals have expertise in diagnostic, preventive and treatment procedures in genetic diseases**, while **NoRo center offers diagnostic, educational and supportive therapy.**

**These centers are:**

1. **Louis Turcanu Paediatric Emergency Hospital Timisoara** (Regional Centre for Medical Genetics Timis - coordinator Prof Maria Puiu);
2. **County Emergency Hospital Craiova** (Regional Centre for Medical Genetics Dolj -coordinator: Assoc. Prof. Mihai Ioana)
3. **“Sfanta Maria” Paediatric Emergency Hospital Iasi** (Regional Centre for Medical Genetics Iasi - coordinator: Prof Cristina Rusu)
4. **Municipal Hospital ”Dr. Gavril Curteanu” Oradea** (Regional Centre for Medical Genetics Bihor- coordinator Dr. Claudia Jurca)
5. **NoRo Pilot Reference Centre for Rare Diseases in Zalau** (coordinator: Dorica Dan);

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# NoRo – A Resource Centre in RareResourceNet

***A one-stop shop style service designed for people living with a RD and their carers***

- ✓ Complementary to health care and social services
- ✓ Holistic care and support
- ✓ Create a bridge between patients/families and various stakeholders providing health care, social care and social support




## Holistic care?

**Addressing the multidimensional health, psychosocial, educational, and daily life needs, abilities and wishes** of people with a RD and their carers

- ✓ **Documentation, information, referral and counselling** services on health and social issues
- ✓ **Training courses** for patients/families and professionals
- ✓ **Case management** services
- ✓ **Rehabilitation, Therapies, Therapeutic recreation** and **respite care** services
- ✓ **Occupational therapy** and day care
- ✓ **Rehabilitation and abilitation**
- ✓ **Medical/psychological consultations**

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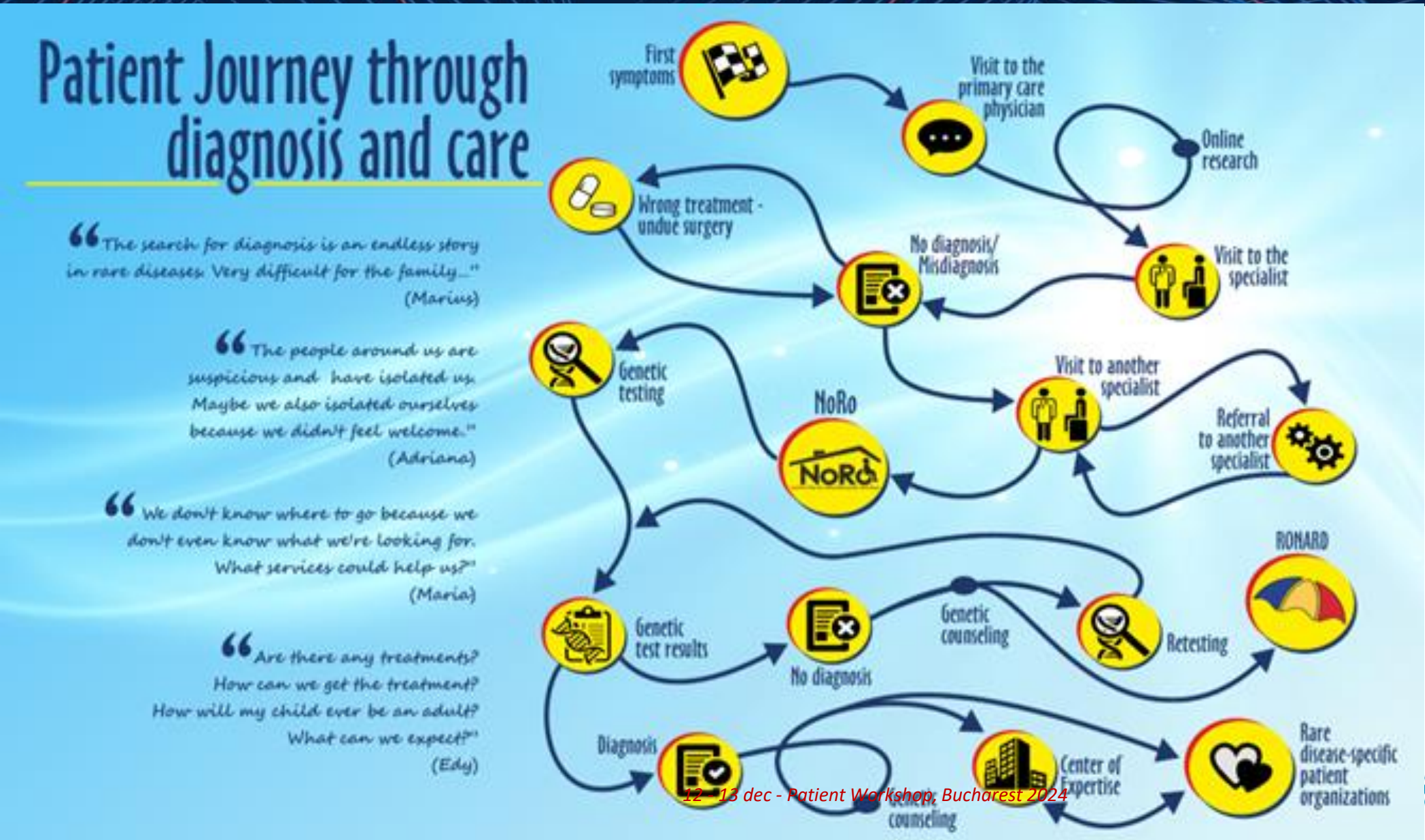
# Care pathways for RD in Romania




1. Advocacy
2. Trainings
3. Information campaigns
4. Provide care services
5. Connect with others
6. Facilitate access to treatment and care
7. Coordinate care
8. Collaborate
9. Communication
10. Monitor

# Conclusions

- ✓To build an efficient, integrated care system for patients living with RD take a lot of **efforts, time and solidarity;**
- ✓**ERNs represent a huge achievement for all of us**;
- ✓Still, **there is a need for recognition** for healthcare providers and ePAGs participating in the ERNs;
- ✓Our role as ePAGs is to **make the voice of our community heard** at ERN level and also at national level;
- ✓We also **need a better collaboration between ERN, ePAGs, CoE, MoH, NAs and EURORDIS to facilitate the integration of ERNs into national healthcare systems;**
- ✓**The involvement of National Alliances** have to be amplified in order to transfer best practices from ERN into the NHCS;
- ✓**It is about time to prove our solidarity as EU citizens** and ensure that **all rare disease patients in the EU enjoy equal opportunities to diagnosis, accessible treatments, specialized social care, education access and integrated care!**

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Helping patients with rare or low-prevalence complex diseases

# ERN ITHACA & activities

Anne Hugon

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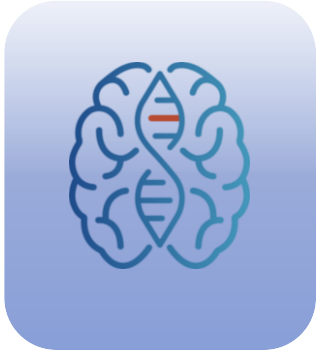
# Overview and key facts : ITHACA





- Scope
  - Disorders of human development (over 6000 diseases)
    - Of genetic, genomic/chromosomal or environmental origin (including teratogens) :
      - Congenital malformations (single/multiple)
      - Fetal pathology
      - Prenatal diagnosis of fetal anomalies

    - ***Registries***
  - Disorders of human neurodevelopment (over 2500 genes)
    - Intellectual disability
    - Autism spectrum disorder
    - Psychiatric manifestations of developmental disorders

- ERN network (www.ern-ithaca.eu)
  - A network of Medical Genetics Departments in EU academic hospitals
  - 71 members in 25 EU Countries + Norway
  - > 100.000 patients seen/year



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# OVERVIEW AND KEY FACTS

## Aims of ERN ITHACA

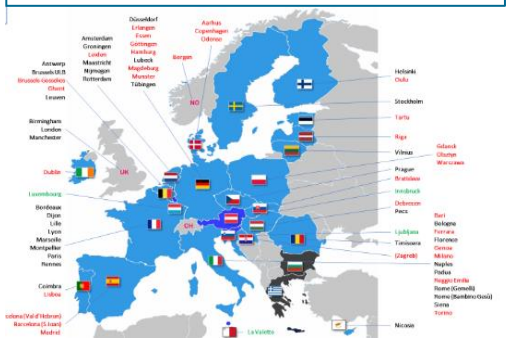
- Improving the diagnosis of patients with rare developmental or neurodevelopmental disorders
- Improving and disseminating knowledge the field
- Improving patients' quality of life and appropriate daily care


## ERN ITHACA disease areas

- Developmental (**malformations** & **dysmorphisms**) and neurodevelopmental (**intellectual disability** & **autism**) disorders from genetic, genomic or environnmental origin
- Includes prenatal diagnosis and foetal pathology of RD
- NDDs affect more than 3% of the EU population, half of whom have a RD of genetic origin and fall within the scope of ITHACA.
- ITHACA covers more than 5000 different Rare Diseases, including more than 2500 monogenic causes of intellectual disability or autism.
- Spina bifida and related abnormalities are a specific area of activity with inter-ERN connectivity

## ERN ITHACA members

- 71 HCPs in 25 EU countries & Norway, including 3 Hubs
- Most Members are clinical Genetics Departments in Academic Hospitals
- Connexions with affiliated partner networks in Switzerland an Turkey (other coming)
- Patient Advisory Board counts more than 60 PAGs and ePAGs



## Clinical Pracice Guidelines & Consensus statements

- 5 CPG written by ERN ITHACA (and several in their final stage)
  - Disorder specific guidelines
  - Transversal guidelines
- 1 guideline co-authored and several endorsed

## Workshops

- EuroNDD : bi-annual multidisciplinary 2-day workshop on NDD, rotating
- EuroDysmorpho : 4-day workshop, annual, rotating
- Fetal pathology Winter school : annual, in Paris

## Dissemination & education

- ITHACA e-Training Programme: 14 free webinars on demand. New Webinars now on a monthly basis
- APOGeE free online Handbook on medical genetics
- MOOC BIG (bioinformatics in genetics)
- MOOC" Diagnosing RD: from the Clinic to Research and back" (with EJPRD)
- Support to Manchester Dysmorphology meeting (bi-annual)
- Writing/editing > 80 clinical summaries for ORPHANET
- Contribution to Orphanet classification update and enrichment of HPO thesaurus
- "Genetics survival guide" (collaboration with Dundee University)

## Research & Registries

- Over 160 call for collaborative call for collaboration in clinical research
- ILIAD RD registry
  - Focus on rare monogenic neurodevelopmental disorders
  - Public access by end 2024

*12 - 13 dec - Patient Workshop, Bucharest 2024*

ITHACA
European Reference Network
for rare or low prevalence complex diseases
Network Intellectual Disability and Congenital Malformations (ERN ITHACA)

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# SANTE Evaluation WG

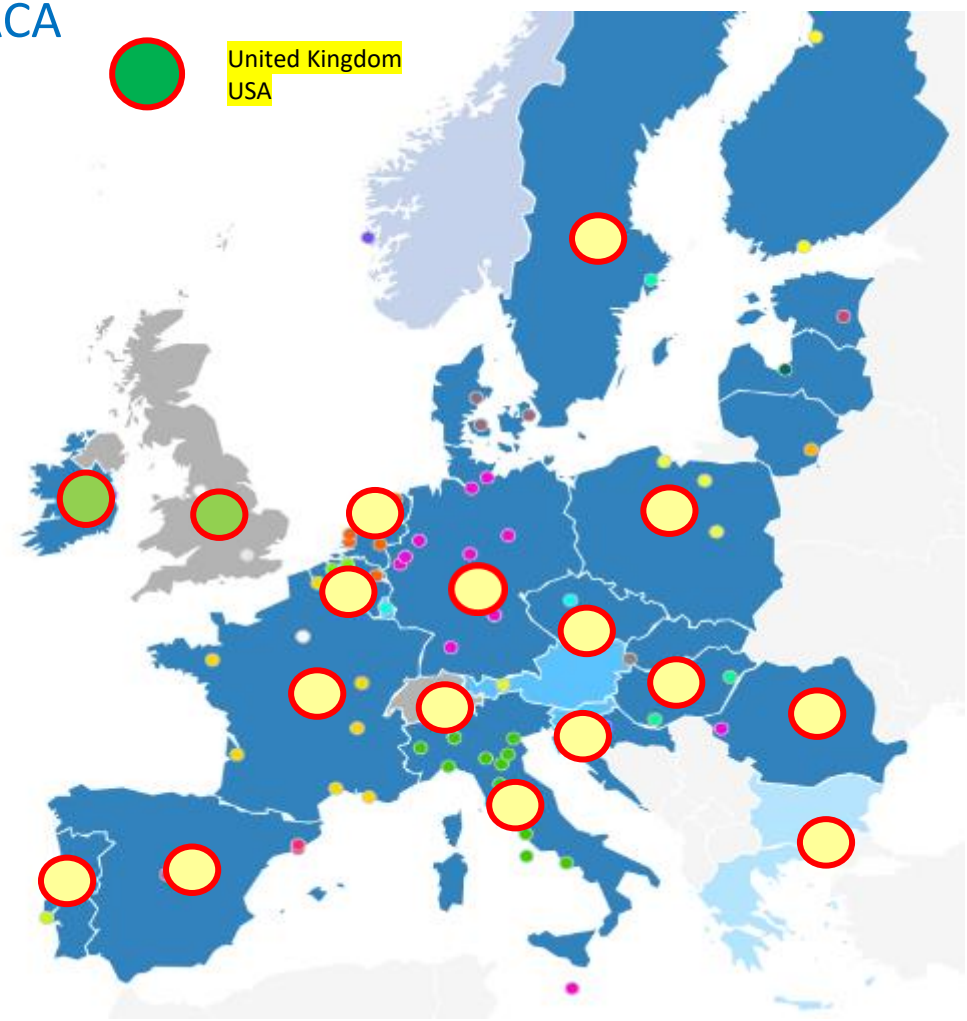
- Consultation ERN-ITHACA Patient Advocates group on the ERN evaluation methodology – measurable elements
- deadline for receiving comments directly in the online file is the 6th of January 2025
- File exclusively reserved to the ePAG representatives for ERN-ITHACA : **ERN Evaluation Measurable Elements – For Comments – ePAG_ERN ITHACA.docx**
- https://emptekom.sharepoint.com/:w:/s/FWCHADEAHealthExperts23-26/ES4FZsWAuA9HrKoiAMEhOrAB-Gt4pbX12N_vmckoMaje0A?rtime=LJAbDcgV3Ug
- Particularly focus on Measurable Elements (MEs)
  - Related to patient care (at all 3 levels) for rare and complex diseases
  - Integration of patient associations at the level of the ERNs as networks and of the Clinical Centres, accredited as Centres of Expertise (HCP/Clinical Centre)

# ePAGS 47 - ITHACA PAB > 50 PO National, EU, International

## Engagement with patient organizations, a success story within ITHACA

| | | | | | |
|---|---|---|---|---|---|
| 22q11.2 | Acrodysostosis | ADNP | Angelman | Beckwith-Wiedemann | Chromosomal disorders |
| Chromosomal abnormalities | Corpus Callosum | Costello and cardio-facio-cutaneous syndrome | Cowden (mental health) | Coffin-Lowry | Cdls Cornelia Delange |
| CDKL5 | Dravet | Fragile X | Goldenhar | Kleefstra | MED13L |
| Mowat-Wilson | Noonan | PACS1 | Pallister-Killian | Pitt Hopkins | Prader Willi |
| Phelan-McDermid | Rett | SAT2B | Smith-Lemli-Opitz | Smith-Magenis | Spina Bifida |
| Tuberous Sclerosis Complex | Williams | White-Sutton | Brain malformations, genetic on NDD | ID rare diseases | Ultra rare condition |

| | | | | |
|---|---|---|---|---|
| Undiagnoses, no names | RD Borys the Hero Foundation | RD Alliance IT,ES,CZ,NL,FR,RO | (SWAN, UDNI, Wilhelm Foundation) | Etc ..... Specific conditions |



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# ePAGs - Involvement & very active, growing fast !

Work in Progress !!

- PAB 15 meetings per year + SC + Tfs
- Division tasks in small WG
  - Task : Administrative; ToR; Elections process; Partnership
  - Task : Evaluation, Monitoring Patient involvement
  - Task : Partnership, Mentoring
  - Task : Annual Patient workshop
  - Task : Webinars and Materials resources
  - Task : Production of various publications
  - Lay versions, Care Pathways, Patient Journeys

- *A large scale of activities and back office work*
  - Reception of new PO and Presidents
  - Enlargement of the PAB
  - ePAGS //partners, the largest ERN PAB
  - Preparation of meetings and minutes and all activities
  - Referal of families for care

**Achievements**

- Guidelines,
- Web Site Patient
- Doc Resources
- Dedicated seminars
- Training workshops, coaching
- Publications flyers, ePAG ToR ...
- SC EuroNDD 2024 - 2026

WG1-3 Transversal PB

WG5. NDD NeuroDev Disorders

WG8. Training & Education

WG11. Guidelines

WG13. SBoD - Spina Bifida and other dysraphisms

WG14. PAB - Patient Advisory Board



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# ePAGs - Interactive Patient Workshop, dec 12 Bucharest

- ERN ITHACA's mission to foster a patient-centered network that addresses the needs of individuals living with rare congenital malformations and intellectual disability syndromes, both diagnosed and undiagnosed
- Strength collaboration between healthcare providers and patient advocacy groups
- Improve support and care for people affected by rare genetic diseases
- An interactive event combines presentations, speakers, abstract showcases and in-depth discussions to encourage meaningful engagement among all participants.

**Sharing Best Practices**

- **Abstract** to be discuss on effective strategies on how to engage patient organisation and support rare disease patients. **Highlights innovative initiatives, best practices, and collaborative efforts**

**Patient journey**

- Explore the **patient experience from diagnosis to coping with mental health**
- highlighting genetic counselling and effective communication with families and healthcare teams, supported by findings from the Patient Advisory Board survey.

**Building Resilience**

- Explore whole **resources and strategies** to help patients and **families build resilience** and cope with emotional challenges.
- **Mental health, diagnoses, and genetic counseling.**
- Strategies to **strengthen family resilience and address the multifaceted aspects of grief**

**Collaborative space**

- Built supportive network for patient-centred care within ERN ITHACA to promote patient-centred care across Europe.



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# JARDIN Joint action & ePAGS Involvement

## “JARDIN” a Joint Action

- on Integration of ERNs into National Healthcare Systems https://jardin-ern.eu
- Develop strategies for systematic dissemination of information on the ERNs, with a specific emphasis on people living with rare diseases as well as ...

✓WP5: National governance…

✓WP6: National care pathways and ERN referral

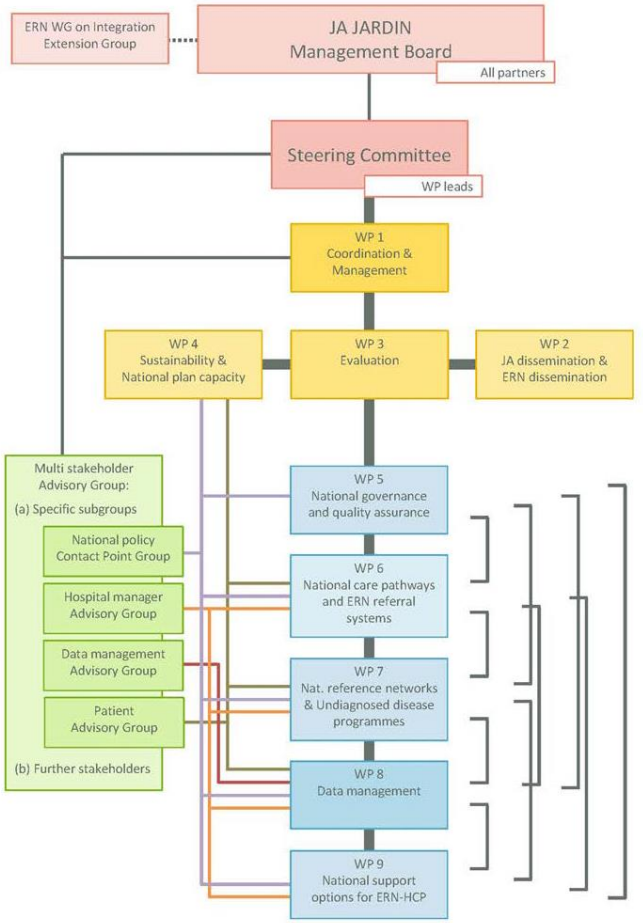
✓6.1 & 6.2 1/Spina Bifida 2/ NDD

✓WP7: Undiagnosed disease programs or equivalent strategies

✓WP8: Data management

✓WP9: National support options for ERN-HCP

Ithaca & ePags



# ePAGs - involved in National Workshop on Patient Rights

## National workshops


National Workshop on Patients Rights in cross-border healthcare (CBHC) and European Reference Networks

➔ In each country ERN ITHACA ePGAS and HCP are represented

ERNs Secretary: Information about the workshops at national level focusing on patients' rights in cross-border healthcare
In the context of enhancing the implementation of Directive 2011/24/EU on, the Commission is organising a series of 10 workshops at national level focusing on patients' rights in cross-border healthcare and European Reference Networks (ERNs).

European Commission
**DG Health and Food Safety**
Unit B3 – Health monitoring and cooperation, Health Networks
12, rue Guillaume Kroll
L-1882 Luxembourg



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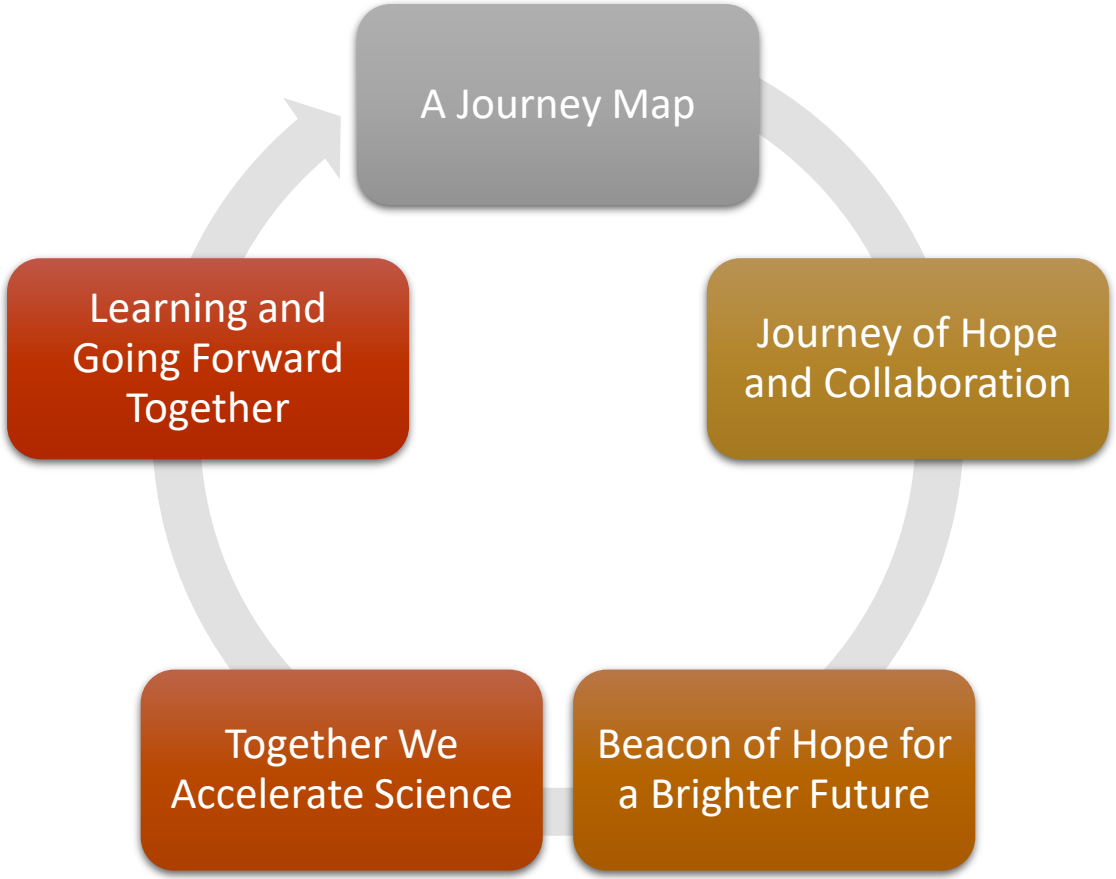
# Success Story : Impact on patient care, EuroNDD 2024


## Elevating Care and Research in Genetic NeuroDevelopmental Disorders (NDD), a Great Success

- Second-of-its-kind European workshop focused on the complex care and research of genetic neurodevelopmental disorders.
- Over 250 experts including clinicians, patients, and researchers from across Europe
- Held at the University Institute of Lisbon (ISCTE), April 4-5, 2024
- Highlights of interdisciplinary collaboration and patient-centric approaches that led to practical innovations in diagnostics and therapies

- EuroNDD 2024 aligned with and supported by ERN ITHACA's initiatives to enhance patient care across Europe
- Next EuroNDD 2026 Warsaw

→ Partnership ePAGS community


A Journey Map
Journey of Hope and Collaboration
Beacon of Hope for a Brighter Future
Together We Accelerate Science
Learning and Going Forward Together

# ! Steering Committee members, here for you

Tomasz "Tomek" Grybek

Dorica Dan
Chair

Sue Routledge

Tanja Zdolsek Draksler
Co-Chair

Katarzyna "Kasia" Swieczkowska

European Patient Advocacy Group

ITHACA

https://ern-ithaca.eu Register to the Web site to get NewsLetter!



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# “Learning from each other”

Tanja Zdolsek Draksler

European Commission

EUROPEAN REFERENCE NETWORKS

Helping patients with rare or low-prevalence complex diseases

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# “Learning from each other” - Tanja Zdolsek Draksler

## Flash talks “Learning from each other” Introduction Abstracts

- Clinics and Patient care
  - ✓ 1. NoRo in community or how to upscale your resources? by Dorica Dan
  - ✓ 2. Multidisciplinary clinic for patients with macroglossia in BWS, by Monica Bertoletti
  - ✓ 3. PKS Clinic: A Multidimensional Approach to Pallister-Killian Syndrome Care, by Samantha Carletti
  - ✓ 4. (online) Care coordination for all rare conditions in Ireland – A comparison between 22q11 Deletion Syndrome and 2q24 Deletion Syndrome, by Lyndsey Walsh and Anne Lawlor
- Global collaboration and guidelines
  - ✓ 5. The Value of WaihonaPedia for your community, guide for community leaders, by Gerritjan Koekkoek
  - ✓ 6. Parent co-led initiative in creating the first global Clinical Practice Guideline (CPG) for a rare neurodevelopmental disorder called SATB2-Associated Syndrome (SAS), by Erika Stariha
- Data collection and registries
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  - ✓ 8. Building a Research Portal for Rare Disease Collaboration: CHAMP1 Approach, by Daniele Palumbo
  - ✓ 9. Solving Rare Diseases: How Global Collaboration and Data are Advancing Kleefstra Syndrome Research, by Tanja Zdolšek Draksler

- Timeline :
- Call for abstracts launch: September 13th 2024
- Deadline for submission: October 21st 2024
- Results published: November 15th 2024

## Call for Abstracts: Learning From Each Other Workshop

### Showcase Best Rare Disease Projects and Activities
(in the scope of ERN ITHACA ePAGs)

We are pleased to announce the call for abstracts for presenting rare disease activities-good practices at the upcoming **ERN ITHACA Patient Workshop (December 12th 2024, Romania)**.

The focus is on sharing and promoting innovative, high-impact projects. The focus is on sharing and advancing impactful projects and activities within the rare disease community. To provide a patient centred network which will meet the needs of those with rare congenital malformation and intellectual disability syndromes, both diagnosed and undiagnosed. We invite ERN ITHACA ePAGs (patient advocates, patient representatives, and rare disease organizations involved in ERN ITHACA) to submit abstracts that highlight innovative initiatives, best practices, and collaborative efforts aimed at improving the lives of those affected by rare diseases.

## Criteria for Acceptance

1. Impact and Best Practice Potential
2. Innovative Approach
3. Collaboration and Community Engagement
4. Evidence of Success or Potential
5. Transferability and Scalability

## Abstracts committee (4):

- Tanja Zdolsek Draksler, PhD (research perspective
- Sue Routledge (family perspective
- Ioana Streata, MD (clinician perspective)
- Anne Hugon (ERN ITHACA perspective

- 12 abstracts received
- 3 rejected, 9 accepted
- Presentations divided into groups:
  - Clinics and Patient care
  - Global collaboration and guidelines
  - Data collection and registries
- Book of abstracts published on ERN ITHACA web-page

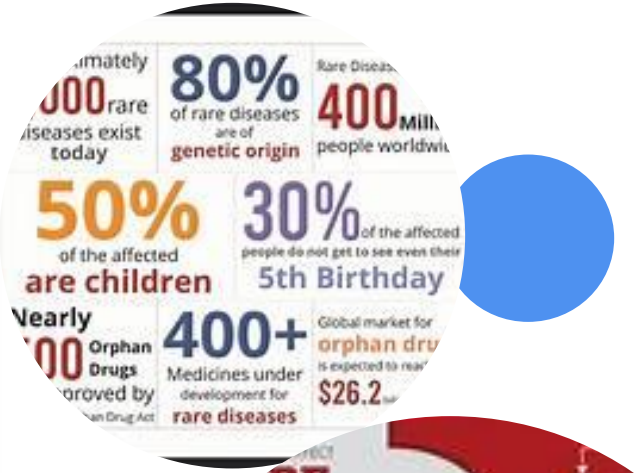
# 1. NoRo in community or how to upscale your resources?

Dorica Dan

# NoRo in community

Dorica Dan – president RONARD/ RPWA/ ARCrare
vicepresident Eurordis, ePAG chair ERN ITHACA

# NoRo – A Pilot Reference Centre for RDs since 2011



NoRo online

**Center of Expertise since 2016**
**Part of RO-NMCA.ID and ITHACA since 2017**

# RD Management

Complex, Organized, Proactive, Integrated

**Care delivery system**

Healthcare delivery system
Therapies, Education & Social Services, Rehabilitation
Patient organizations, Family & Community support


**Case Management**

**Care delivery system:**
- Infrastructure
- Resources

**Providers:**
- Knowledge
- Collaboration
- Org. structure
- **Therapies,treatment, care, education, etc.**

**What can be done?**

- Identify the needs and map the resources
- Support groups
- Social & medical care
- Therapies & Therapeutic education
- Advocacy

Short-term outcomes

**Long-term outcomes:** Quality of life

# NoRo- A Resource center for rare diseases/ Center of Expertise & RO-NMCA.ID

**What?**

- It is a "one stop shop service", combining therapies, therapeutic education, training, medical and social services;
- Connected with majority of Centes of Expertise in Romania and ERN + RareResourceNet

**How?**

## Integrated & holistic health and social care

*Medical services (Ambulatory):*
*paediatric psychiatry , genetics.*
*60 children and 17 young adults +*
*31 employees*

Social services
*1. Day care centre*
*2. Trial for flight*
*3. RD Patient groups +*
*case management*

*Trainings and working in community*

*Patients*
*Parents*
*Professionals*

## Advocacy & up scaling

**Strategy - NPRD**
Integration into National Policies & Strategies
Local Strategy – New services

**Quality of care**
Standards of social services
Standards for medical services

**Training**
Case management for RDs+ community support network (nurses, doctors)
Psychological Structure

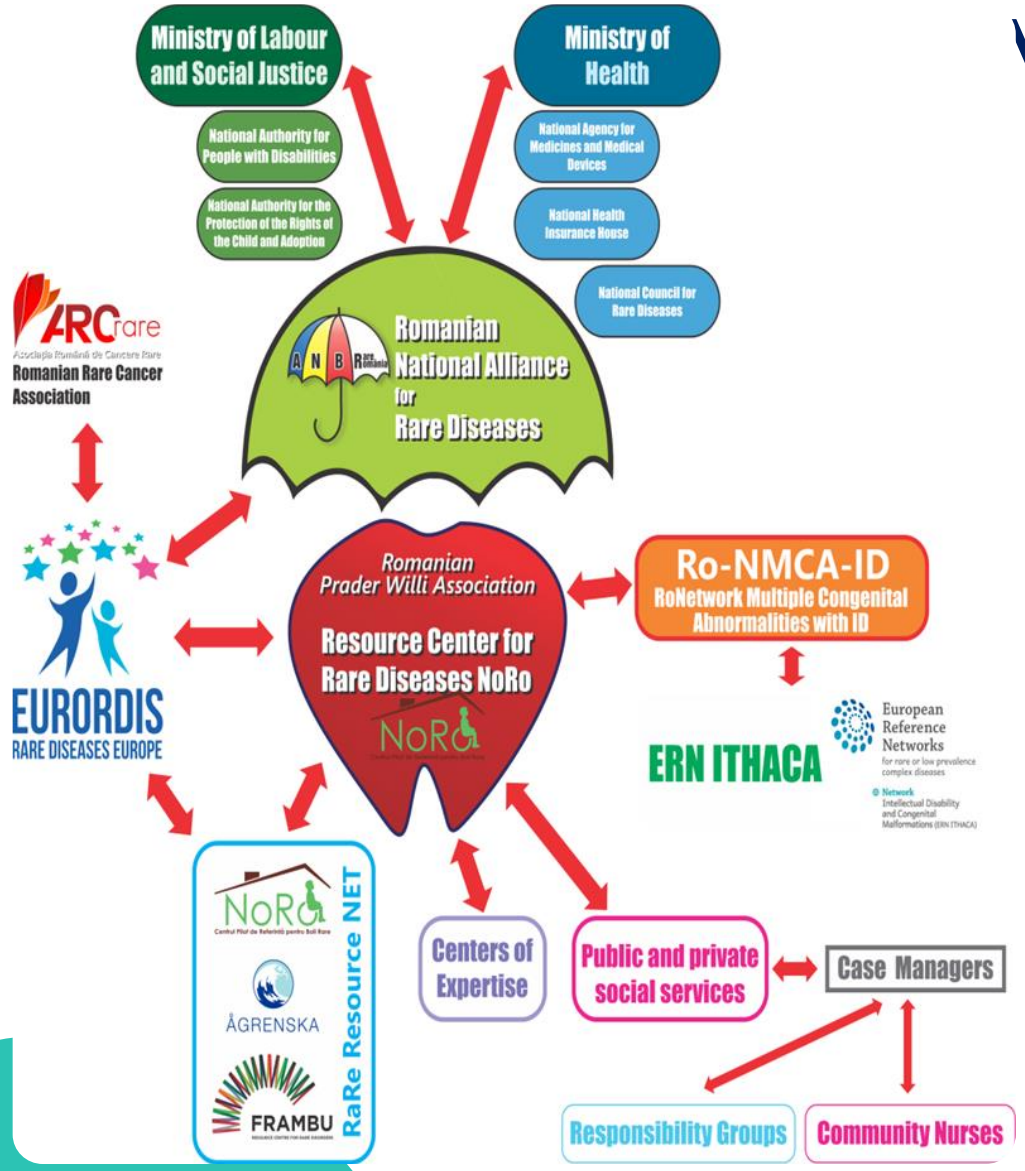
**Communication**
Workshops, RDD, trainings, conferences, publications, Radio NoRo , RDSJ ;

**Recognition**
The Prize for innovation in Health
Recognition from Romanian Presidency,Count Holistic

**Opportunities created for integrated care**

**Impact**

- Integrated services
- *Intersectorial Partnerships*
- NPRD
  Legislation for community nursing
  Social Assistance Law
- Case managers: 1/50 persons with disability
  Case management for RD patients
- Training curricula developed for ECHO trainings
- Sustainability
  Involve local and national authorities




# Working in networks

- ✓**Interinstitutional collaboration** is essential
- ✓Be **close to your beneficiaries**!
- ✓Ensure sustainable and **timely access to diagnosis, treatment and care**
- ✓Better integration of the different components of a health care system and **improved coordination of care**
- ✓A **multidisciplinary approach** to provide care for PLWRD is critical!

**50% of the Romanian population in the rural area!!!**


## Living with Rare Diseases

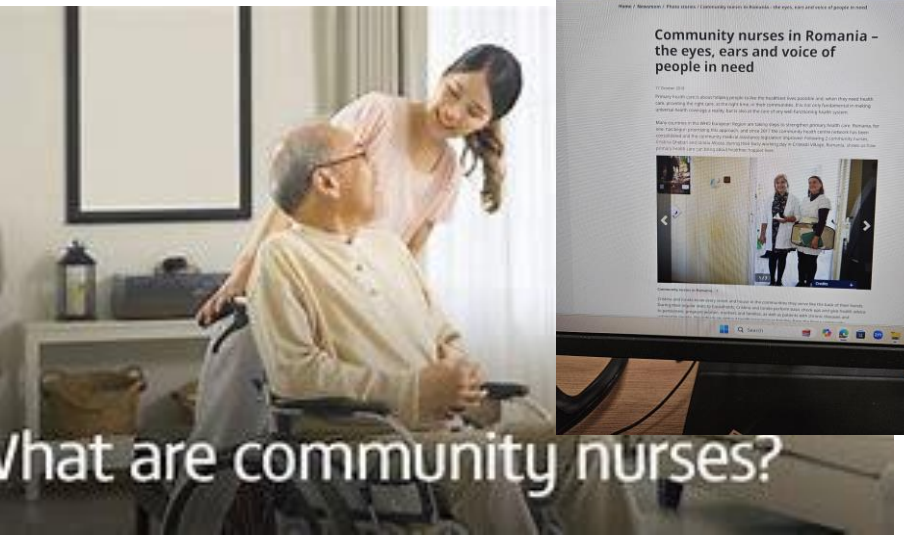
**People affected by rare diseases may face challenges such as:**[3,4]

- **Lack of information**
- **Difficulty in obtaining a diagnosis, or misdiagnosis**
- **Psychological burden**
- **Few physicians experienced in treating rare disease**
- **Limited support services for the patient and family**

Patients and their families may feel isolated and frustrated, and can be emotionally and financially devastated.[4]

**For more information on disease burden and prevalence please visit www.diseaselens.com**

## Training of community nurses in case management of RDs




## METHODOLOGY

Connect with Expert Medical Specialists to Build Capacity in Primary Care and Reduce Health Disparities

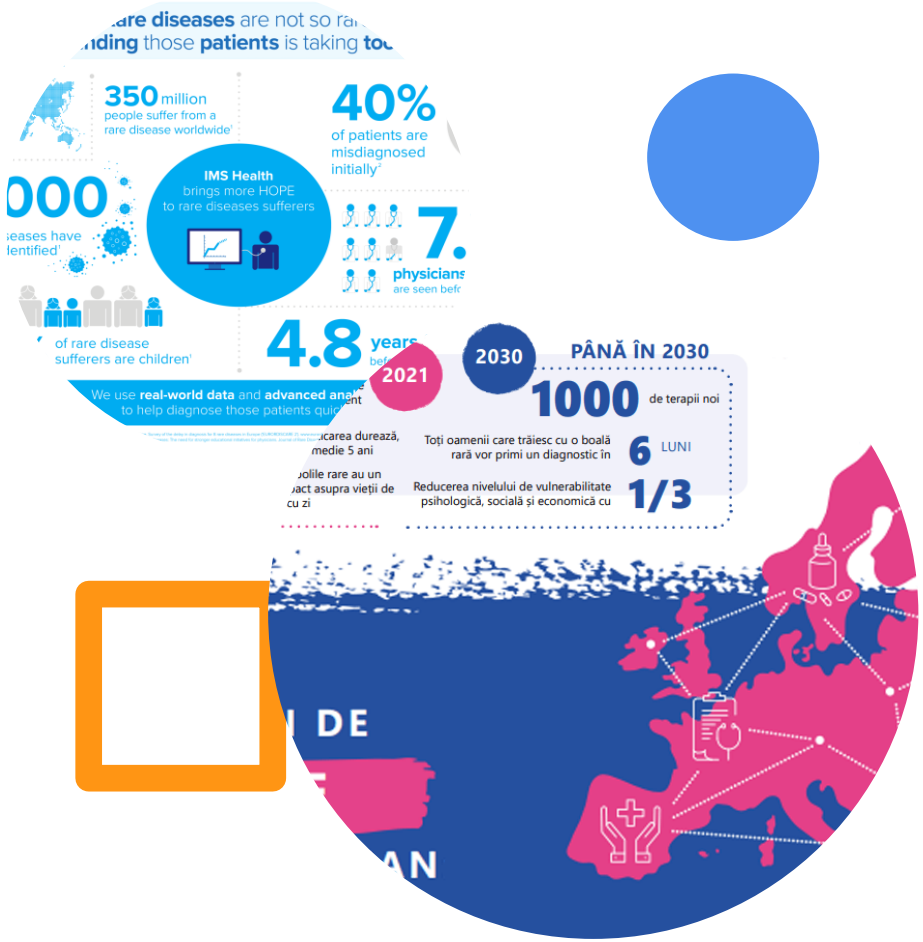

**ECHO is all teach, all learn.**

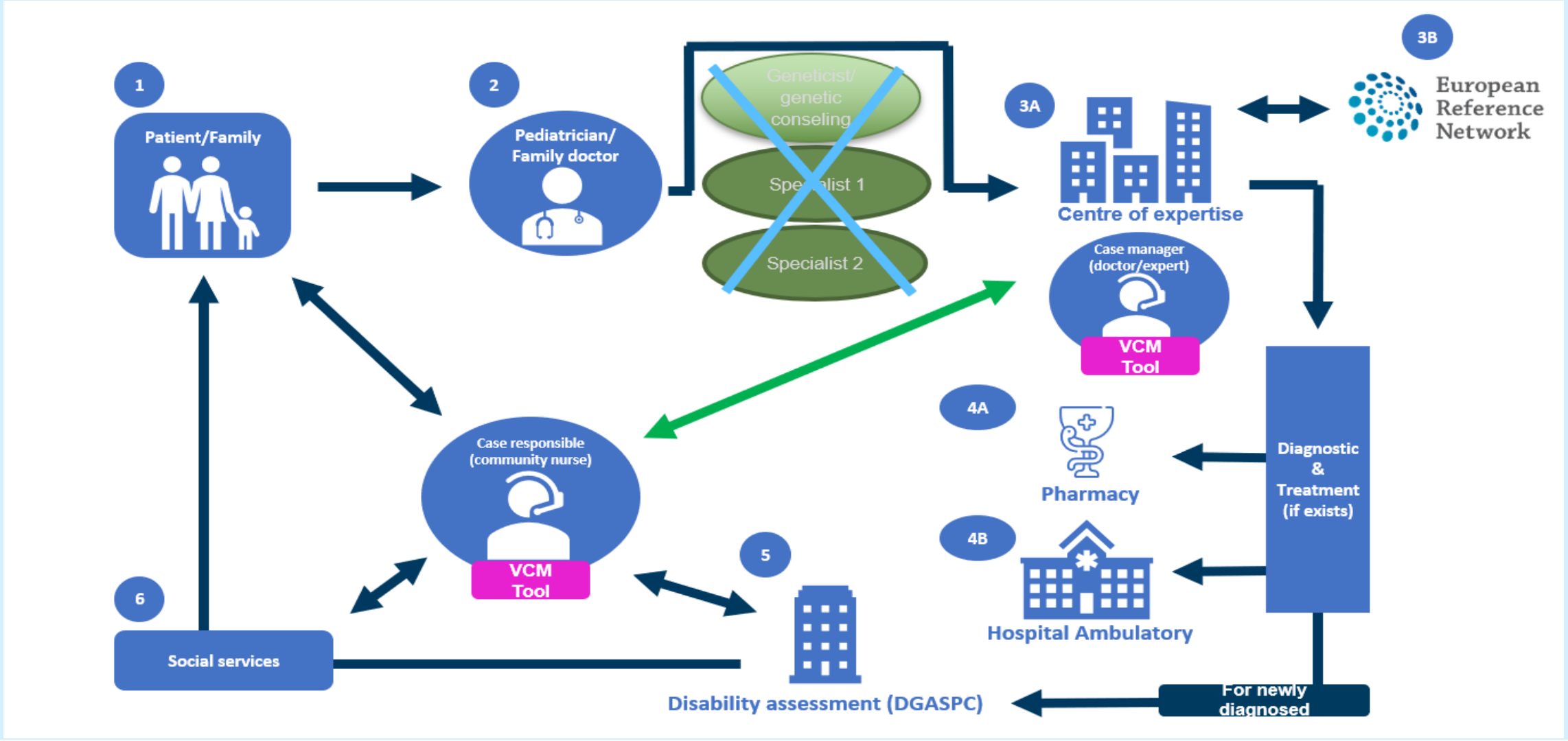
- Interactive
- Co-management of cases
- Peer-to-peer learning
- Collaborative problem solving

engaging and interactive educational toolkits that are practical, actionable "how-to" guides to transform and improve your practice

# How to upscale our impact in community?

1. Extend and develop **new services**
2. Include our **priorities in national strategies**
3. Exchange experience and collaboration with schools and kindergartens in the community, where our children are integrated to ensure **continuity of care** and ensure their inclusion in society
4. **Collaborate** with all the stakeholders in RDs
5. **Involve patients at every stage** ensured that their perspectives were integrated, in the **local, regional and national strategies**
6. **Contribute to EU and international strategies**






**Improved knowledge** for community nurses about case management for patients with RDs, access and care coordination.

Patients are **better connected** with care services that they need. **Reducing the waiting time for diagnostic and care.**

Connected with relevant experts at national and EU level via ERNs. Increased number of patients.

# RESULTS

**>3000**
PATIENTS RECEIVED THERAPIES AT NORO

**1228**
PATIENTS IN REGISTRY

**60** OF CHILDREN IN THE NORO CHILDREN'S DAY CENTER

**15** YOUNG PEOPLE AT NORO DAY CENTER FOR ADULTS

**>4500**
PATIENTS IN CLINICAL CONSULTATIONS

**2400**
PATIENTS IN CASE MANAGEMENT

**3500**
PEOPLE EDUCATED IN WORKSHOPS AND CONFERENCES

**850**
PROFESSIONALS TRAINED ON RARE DISEASES

**>3000**
PATIENTS IN HELPLINE NORO

ACCREDITATION STANDARDS FOR CENTRES OF EXPERTISE FOR RARE DISEASES IN 2016

**214**
PATIENTS IN ONLINE THERAPIES AND THERAPEUTIC GROUPS

**1154**
COMMUNITY NURSES TRAINED

TRAINING CURRICULUM FOR DOCTORS INCLUDES NOW RARE DISEASES

JOB DESCRIPTION FOR COMMUNITY NURSES INCLUDES CASE MANAGEMENT FOR RD

THE 3RD NPRD INTEGRATED INTO THE NATIONAL STRATEGY FOR HEALTH

**>300**
JOURNALISTS HAVE BEEN TRAINED AT RDSJ

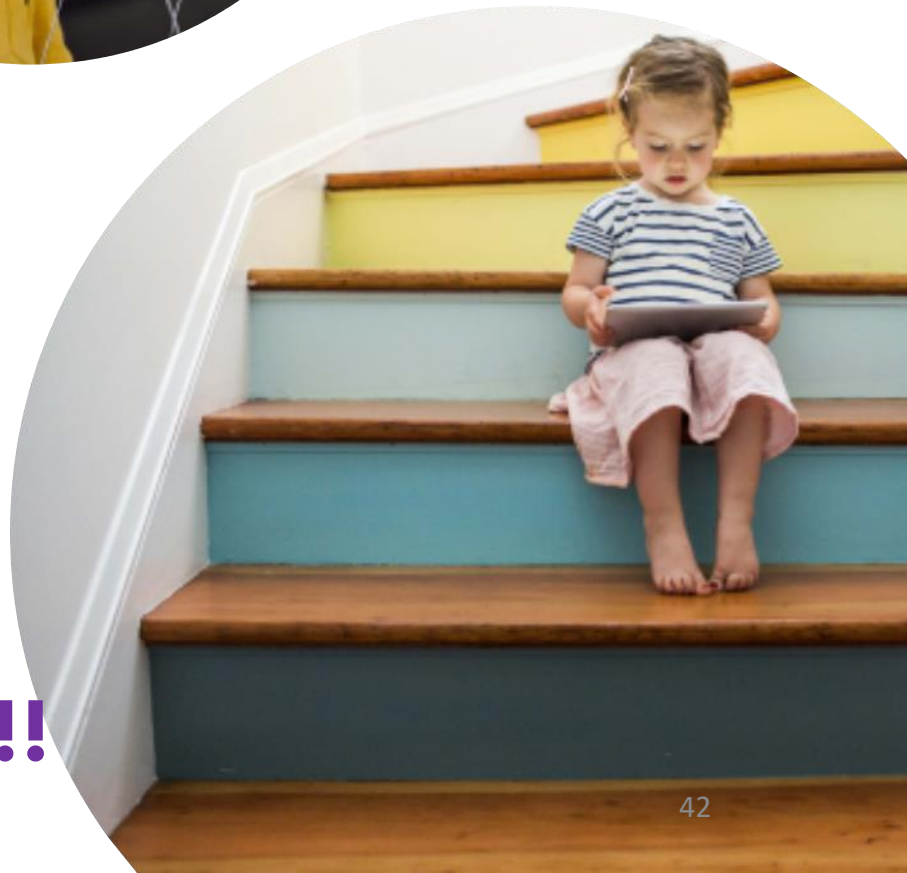
NATIONAL COUNCIL FOR RARE DISEASES IN FRAME OF THE MINISTRY OF HEALTH OF YEAR 2014 and 3 GROUPS OF WORK created by MINISTRY OF HEALTH

**151**
THERAPEUTIC EDUCATION GROUPS

**35** ONLINE SUPPORT GROUPS

# Lessons learned:

1. Address the **root cause of the problems**
2. **Interinstitutional collaboration**
3. **Community support networks**
4. **Promotion and recognition of the case manageme RDs**
5. **F2F meetings** might be completed with **virtual monitoring**
6. **Digital tools for patients' monitoring**
7. **Case management** implementation **reveal the needs of the community** ; these needs should be integrated in local strategy and **communicate to local authorities in order to create new/provide services.**
8. **Combining services and advocacy**
9. Collaborate in different **networks and networks of networks**
10. Don't forget to **include patients at all levels! We all teach and all learn in RDs every day ..**
11. **Funding is just 1 piece of this puzzle…**



**Thank you!!!**

# 2. Multidisciplinary clinic for patients with macroglossia in BWS

Monica Bertoletti

MB

# Multidisciplinary clinic for macroglossia in Beckwith-Wiedemann syndrome


results

main problems

when

main consequences

how

who

needs

Aibws Odv → ERN ITHACA

Smile House (S. Paolo Hospital, Milan) → ERN CRANIO

Monica Bertoletti per AIBWS

# 3. PKS Clinic: A Multidimensional Approach to Pallister-Killian Syndrome Care

Samantha Carletti


Innovative Solutions for Pallister-Killian Syndrome

# PKS Clinic:
# A Holistic Model for Rare Disease Care

# Introduction

PKS CLINIC EUROPE

The PKS Clinic was established to address the multidimensional needs of patients with Pallister-Killian Syndrome (PKS), a rare genetic disorder characterized by multi-organ anomalies, epilepsy, neuromotor developmental delay, and intellectual disability. It offers a comprehensive, patient-centered approach to care, research, and family support.

# Key Objectives

PKS CLINIC EUROPE

| | |
|---|---|
| CARE | • Provide comprehensive, multidisciplinary care. |
| REGISTRY | • Establish a European PKS Registry to enhance research. |
| SUPPORT | • Support families through psychological resources and practical assistance. |
| EDUCATE | • Train healthcare professionals to improve diagnostic and therapeutic capabilities. |

# Innovative Approach


**The PKS Clinic integrates cutting-edge research and family support programs to create a holistic care model.**

**It combines:**

- Comprehensive 3-day hospitalization with multidisciplinary evaluations.
- Centralized data collection through the PKS Registry.

# Impact and Scalability


- Improved quality of care and family support.
- Established a replicable and scalable model for rare disease care.
- Enhanced research capabilities through the PKS Registry.
- Addressed gaps in care with innovative telemedicine and remote support solutions.

# Collaboration and Community Engagement


The PKS Clinic fosters collaboration among:

Medical professionals across disciplines.

Families of patients with PKS.

National and international research institutions.

It also aims to prioritize community engagement through psychological resources and educational initiatives.

PKS CLINIC EUROPE

# Conclusion

The PKS Clinic is more than a healthcare facility; it is a movement towards integrated, holistic care for rare diseases. By addressing the urgent needs of PKS patients and their families, it serves as a model of excellence, innovation, and compassion that can inspire systemic change in rare disease care worldwide.

# 4. Care coordination for all rare conditions in Ireland – A comparison between 22q11 Deletion Syndrome and 2q24 Deletion Syndrome

Lyndsey Walsh and Anne Lawlor

# Care coordination for all rare conditions in Ireland – A comparison between 22q11 Deletion Syndrome and 2q24 Deletion Syndrome

Anne Lawlor & Lyndsey Walsh

ERN-ITHACA – Workshop

Bucharest December 2024


# Meet Aine
# 22q11.2 Deletion Syndrome

Aine is 41 and has a diagnosis of 22q11.2 Deletion Syndrome. She has a wide range of variable symptoms including mild ID, and has ongoing physical and mental health issues.

She is a Special Olympian in 10-pin bowling and athletics, having represented Ireland in the Special Olympics World Games in 2003. She's a proud silver medallist and recently joined a basketball team.

In the I am Number 17 campaign she describes herself on her journey with rare disease as “brilliant”, “warrior”, “funny”, “resilient”.

# Meet Arabella
# 2q24.2 Microdeletion Syndrome

Arabella is 10 and has a diagnosis of 2q24.2 Deletion Syndrome.  She has a wide range of variable symptoms including moderate intellectual disability, autism, sensory processing differences and is non-speaking.

She is a proficient AAC user and her main mode of communication is an AAC communication device.  She loves all things sensory seeking, she loves going to shopping centres, lifts, escalators and penguins.

She loves school and attends a ‘Special School’ in Waterford.

**Commonalities**

- Developmental Delay
- Intellectual disability
- Autism
- Seizures – Epilepsy
- Feeding difficulties
- Growth differences
- Heart conditions
- Cleft Palate
- Eye conditions

# Multi-System Conditions and a Spectrum of Profile

# Minor disparate symptoms over time add up to significant disabilities – Need for joined-up thinking

Hospital


Community Services

School

Person living with a rare condition and family

# UNIQUE

**Rare Condition Guides e.g. Chromosome, Single Gene, Advice for Parents, Explainers**

**www.rarechromo.com**


## Chromosome 2

- 2p Deletions
- 2p Duplications
- 2p15p16.1 Microdeletion Syndrome
- 2p16.3 (NRXN1) deletions
- 2q Duplications
- 2q13 Microdeletions
- 2q13 Microduplications
- 2q23.1 Microdeletion Syndrome
- 2q24.3 Microdeletions
- 2q32 Deletions And Microdeletions
- 2q33.1 Deletions And Other Deletions Between 2q31 And 2q33
- 2q37 Deletion Syndrome
- 2q37 Deletions In Adults And Adolescents
- KIF1A
- MYT1L syndrome (MYT1L variants and 2p25.3 deletions)
- Ring 2
- SATB2 Syndrome (Glass syndrome)
- SCN2A Related Conditions

## Single Gene Disorder Guides

- 2p16.3 (NRXN1) deletions
- ADNP Related Syndrome
- Alazami Syndrome
- ANKRD11 And KBG Syndrome
- ARID1B Syndrome
- ATR-X
- Au-Kline syndrome (HNRNPK LOF variants and 9q21.32 microdeletions)
- Bainbridge-Roper Syndrome ASXL3
- BBSOAS (NR2F1)
- Bohring-Opitz Syndrome (BOS)
- BRPF1-related disorder
- BWCFF Baraitser-Winter Cerebrofrontofacial Syndrome
- CACNA1A-related disorders
- CACNA1C Timothy syndrome
- Cantu Syndrome
- CASK-related disorders
- CDK13-related disorder
- Chitayat Syndrome (ERF Variant)

## Chromosome 22

- 11 22 Translocation
- 22q11 deletion syndrome easy read
- 22q11.2 Deletion Syndrome (Velo-Cardio-Facial Syndrome)
- 22q11.2 Distal Deletion Syndrome
- 22q11.2 Microduplications
- 22q12q13 Duplications
- 22q13 Deletions Phelan McDermid Syndrome
- Cat Eye Syndrome CES
- Emanuel Syndrome
- Ring 22

## Chromosome_X

- CASK-related disorders
- DDX3X Syndrome
- Disclosing_about_XXX_for_girls
- Disclosing_about_XXX_for_parents
- HNRNPH2-NDD

# 22q11DS – Our Clinical Team & Co-Production

- Wesley Mulcahy –- Complex Care Coordinator 22q
- Dr. Suzanne Kelleher – Consultant Paediatrician
- Anne Lawlor - 22q Ireland Lead, Parent and Expert by Lived Experience

Involving service users and patients in their healthcare - *'a meeting of minds coming together to find shared solutions and involves people who use services working together with staff, from the start to the end of any project that affects them'* (HSE Ireland 2023)

# 22q Clinic – A transferrable model of care for all rare conditions

**Winner – HSE Excellence in Quality and Patient Safety**

# Care Coordination – what is it?

## Integrated care – maximising potential

**Continuity of Care**

**Regular Follow-Up**

**Multidisciplinary Approach**

**Individualized Care Planning**

**Care Transitions**

**Addressing Psychosocial Needs**

**Advocacy**

**Family-Centred**

**Education**

**Research and Innovation**

Sláinte Leanaí Éireann

Children's Health Ireland

@nch_info | #ourchildrenshospital

# Outcomes of Complex Care Coordination to date

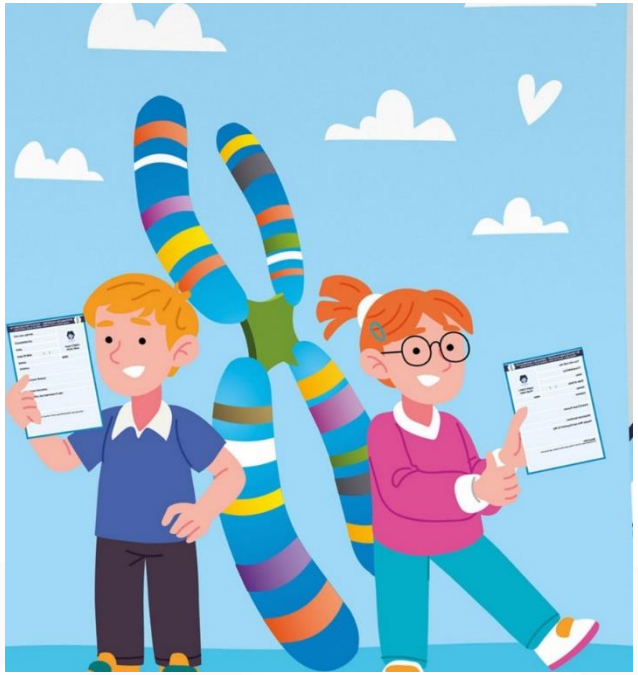
## 25 Qualitative Interviews and 3 Focus Groups

- 1. Improved Patient Care
- 2. Improved family satisfaction with healthcare provided & decreased stress
- 3. Cost-savings to the HSE
- 4. Increased capacity building of clinicians
- 5. Increased Healthcare Service Innovation

# What makes our project unique?

## 22q leading the way in integrated care for a rare disease population

- PPI approach successfully used to co-design the job description
- Exemplary transferable model of care:
  - Clinic attended by Consultant, HSCP and parent with lived experience
  - Single point of contact for health related concerns
  - Multiple appointments in one day (Dental, Immunology, General Paeds)
  - Parent support and training classes
  - Recommended transition service structure
  - Capturing of unmet needs of young people with complex healthcare conditions
  - Resourcing a patient registry for research and anticipated healthcare needs
  - Successful grant applications to improve health literacy and self management tools
  - Upskill community colleagues
  - Research output



**Improving Patient Experience**


Coffee break

# 5. The Value of WaihonaPedia for your community, guide for community leaders

Gerritjan Koekkoek

WaihonaPedia

See and Learn. Know and Share.

# CITIZEN HEALTH DATA SPACE?

# Who am I?

Family: 3 kids

1 Cornelia de Lange syndrome

Chairman dutch cdls

Vice chair cdls world federation

ePag ERN Ithaca

Director WaihonaPedia.org

# What is the value of family data?

- ✓ The detailed knowledge on n=1 (the individual)
- ✓ 4 cases:

# CASE 1: EXPLORE THE NEEDS

✓ Every question on Facebook or TikTok

✓ Every Story, Movie shared  on on Facebook or TikTok

**A Clearer Research Agenda:** Storytelling and shared experiences help uncover hidden needs and solutions, making research more focused.

# CASE 2: VALIDATE KNOWLEDGE

- ✓ Apply recommended therapy
- ✓ Share the results by stories
- ✓ Share by PROMS

**The Power of Validation:** By applying knowledge to your own situation, you help identify weak points and make the collective understanding stronger.

# CASE 3: TOGETHER FOR INSIGHT

- ✓ Organize family meetings to exhange insights and needs
- ✓ Use the reports from these meetings

**A Treasure Trove of Information:** When families and scientists work together, the potential for discovery is limitless.

# CASE 4: COLLECT INDIVIDUAL JOURNEYS

✓ Construct this by evaluating the stories, questions, proms from birth to now

**A More Complete Picture:** Long-term tracking helps uncover patterns and changes that might not be visible in shorter studies.

# What issue?

- ✓ Lived experiences information and patient needs are not organized!
- ✓ Communities by diagnose, no inter diagnose
- ✓ Communities by countries, language, culture barriers
- ✓ Families do not yet use PROMS for each other!
- ✓ Unfair investment policies:
  not valueing science (knowledge) of families, only health care providers, university research is funded
- ✓ Unfair investment balance by national alliances:
  Focus on generic problems only
  Does not solve the challenges of the rare!

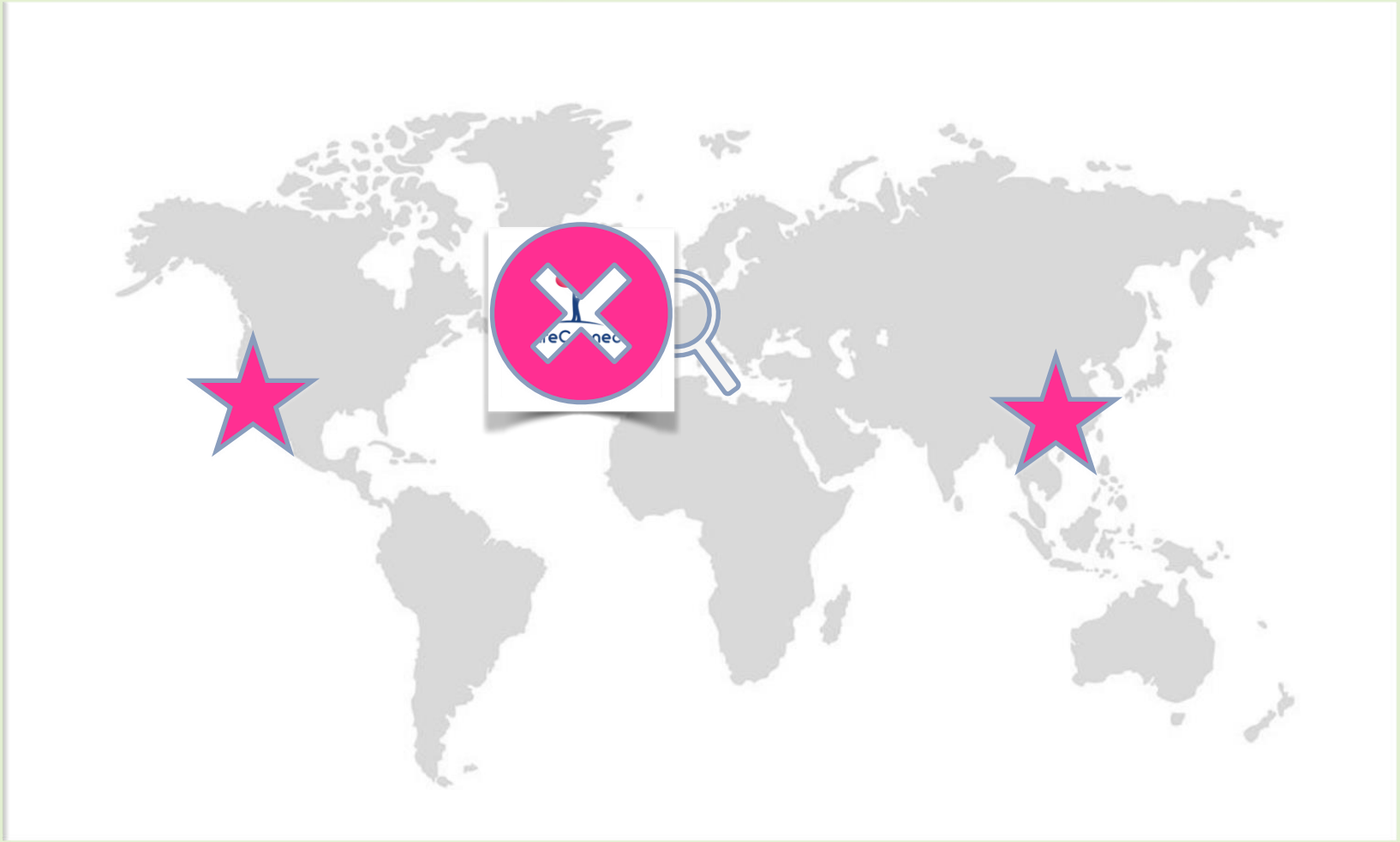
# Current state

- ✓ Silos of websites
- ✓ Use of Social media
- ✓ Digital Sovereignty at risk

# Global / European risks

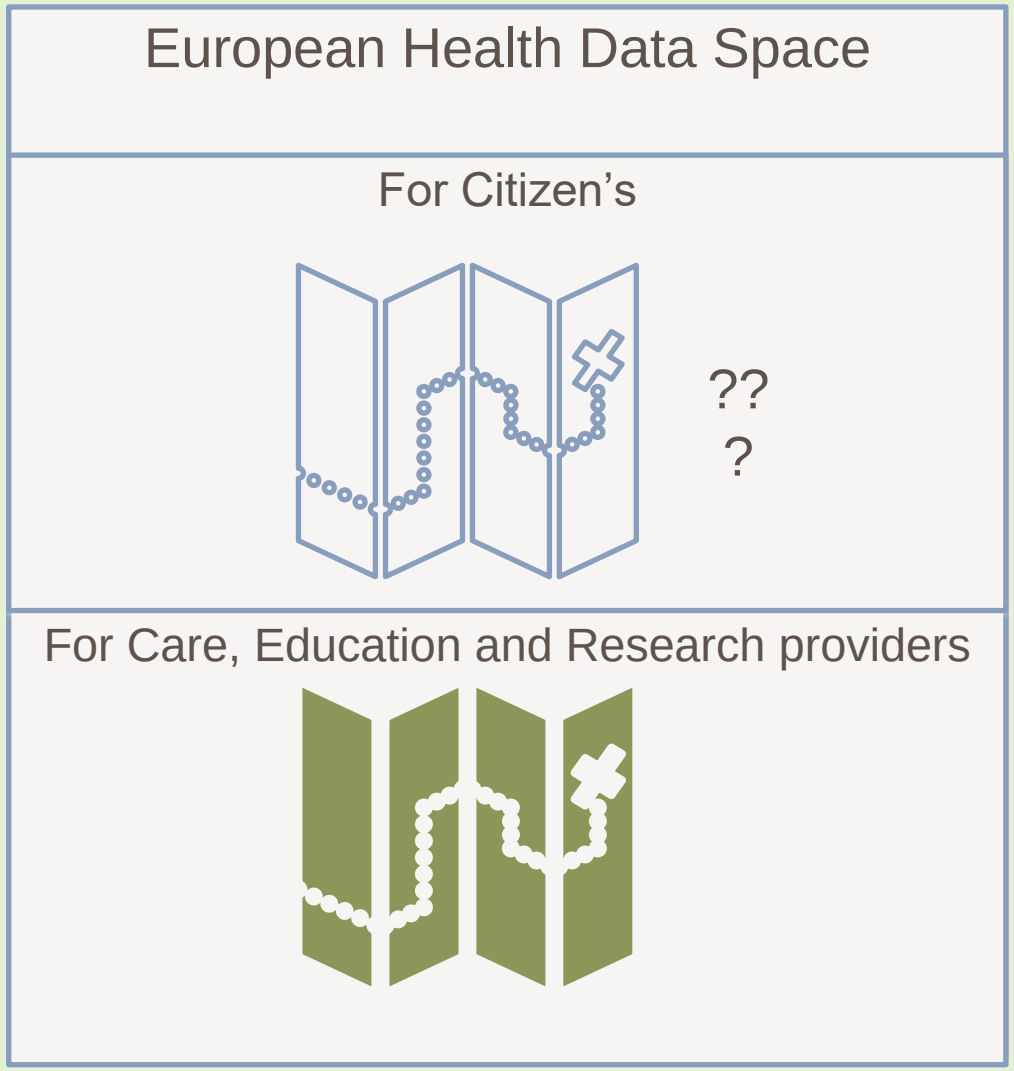
- ✓ S
  W
  th
  atforms
- ✓ S
  In
  ar
  int
  a
  family

# WHERE IS THE OIL, CONTROLLED BY?



# COLLABORATION

- ✓ Eurordis
- ✓ ERN Ithaca
- ✓ National Alliances
- ✓ Communities




WaihonaPedia

# 6. Parent co-led initiative in creating the first global Clinical Practice Guideline (CPG) for a rare neurodevelopmental disorder called SATB2-Associated Syndrome (SAS)

Erika Stariha

**Erika Stariha**
*MSc Clin Pharm*

SATB2 EUROPE

- Global collaboration-

# Parent co-led initiative for creating the first global Clinical Practice Guideline for a rare neurodevelopmental disorder - SATB2-Associated Syndrome

ITHACA

European Reference Network
for rare or low prevalence complex diseases
Network Intellectual Disability and Congenital Malformations (ERN ITHACA)

# How it all started...

We need clinical guidelines

# How it all started...

HOW do you create a clinical guideline for a RARE NDD?

Establishing Foundation

Finding the ‚right“ ERN

Advocating early on

**We need clinical guidelines**

European Reference Network for rare or low prevalence complex diseases

Network Intellectual Disability and Congenital Malformations (ERN ITHACA)

**Don‘t wait for the right opportunity: create it!**

George Bernard Shaw

Attending ESHG congress Vienna 2022

# How it all started...

HOW do you create a clinical guidelines for a RARE NDD?

Become an ePAG at ERN ITAHCA

Establishing Foundation

Start creating the network through parents from zero

**We need clinical guidelines**

Finding the „right“ ERN

Advocating early on

European Reference Network for rare or low prevalence complex diseases

Network Intellectual Disability and Congenital Malformations (ERN ITHACA)

# Creating our SATB2 universe

**CLINICIANS**

**Speech lanugage pathologists,**

**Behavioiural experts**

**PARENTS**
(all SATB2 organisations)

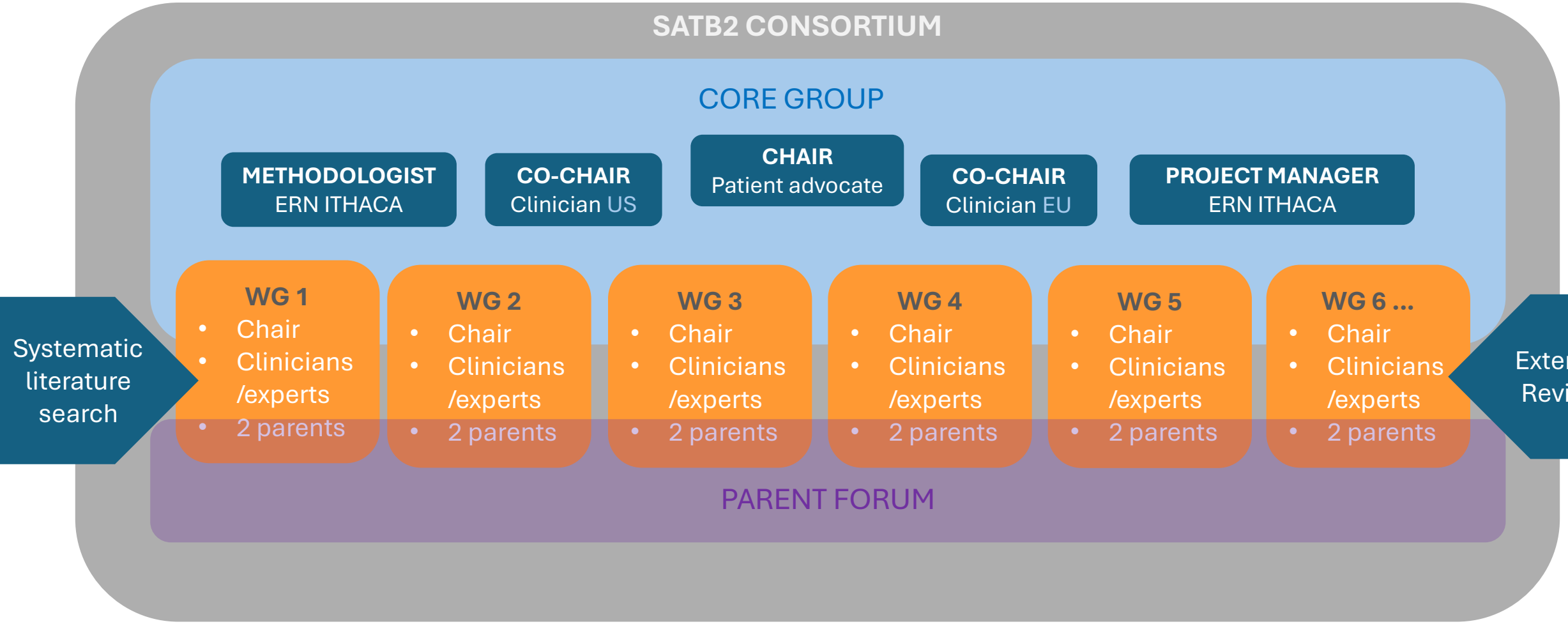
**CHAIR** ?

**ERN ITHACA**
methodology and managing guidance and support

**Around 80 people (60 experts, 20 parents) from Europe (also UK), USA, Canada, Brazil, Australia**

ITHACA
European Reference Network
for rare or low prevalence complex diseases
Network Intellectual Disability and Congenital Malformations (ERN ITHACA)

# How are we organised?



# Methodology – Overall Process

60 confirmed experts, some will be added after CQ selection

20 parents in Parent forum

DONE

Survey in **8 languages**!

**30 responses from experts** and **240 from parents**

FORMING THE CONSORTIUM

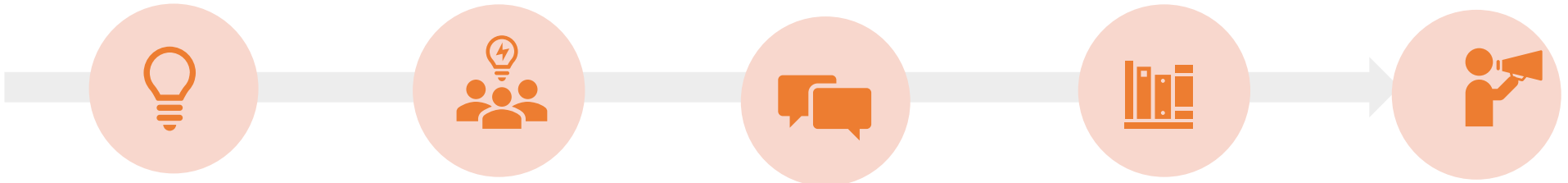
FRAMEWORK, COLLECTION & ANALYSIS OF CLINICAL ISSUES/QUESTIONS

PRIORITIZATION OF CLINICAL QUESTIONS: **ONLINE SURVEY & REPS TOOL**

LITERATURE SEARCH (EXTERNAL) AND SELECTION

WORKING GROUPS FORMATION

LITERATURE SUMMARY, WRITING



RECOMMENDATIONS WITHIN WORKING GROUPS

CONSENSUS MEETING, ROUND OF COMMENTS

EXTERNAL REVIEW

PUBLICATION

DISSEMINATION, ACCESS

# The journey

When we started this journey we
had no idea HOW and IF
we will reach the final destination…

On every **step** we are **learning**, yet –

**where the will is, there the way is!**

# FINAL DESTINATION

... is not „just“ the Guideline itself.

**Building a collaborative group of people – our „SATB2 universe“**

# Thank you

erika.stariha@satb2europe.org

# 7. GASR - Global Angelman syndrome eRgistry

Ellen Koekoeckx

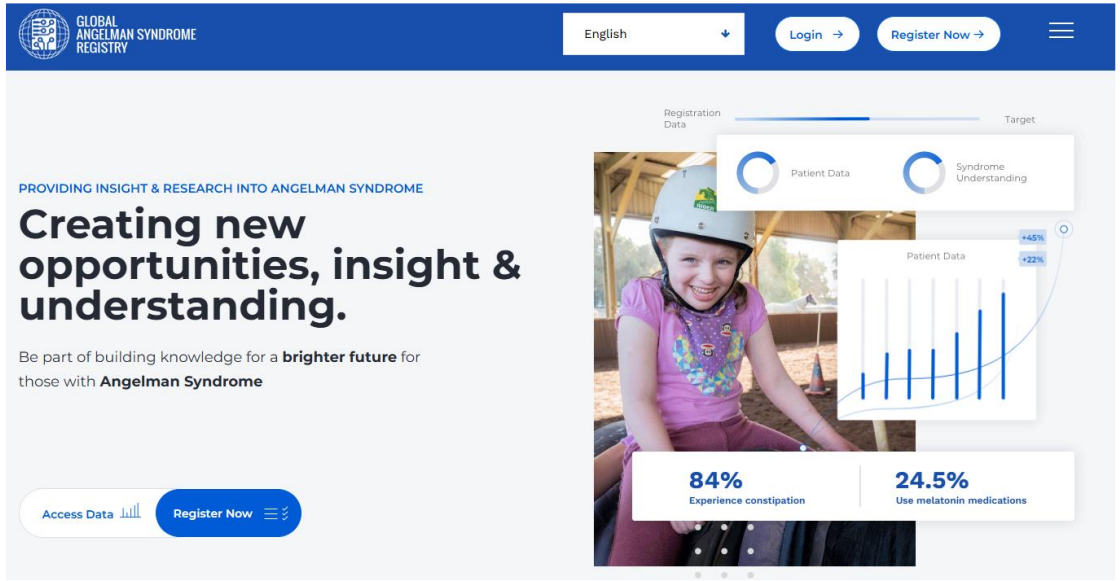
# Global Angelman Syndrome Registry

**Ellen Koekoeckx**
**Global Advisor – Foundation for Angelman Syndrome Therapeutics**

fast

# What is the Global Angelman Syndrome Registry?

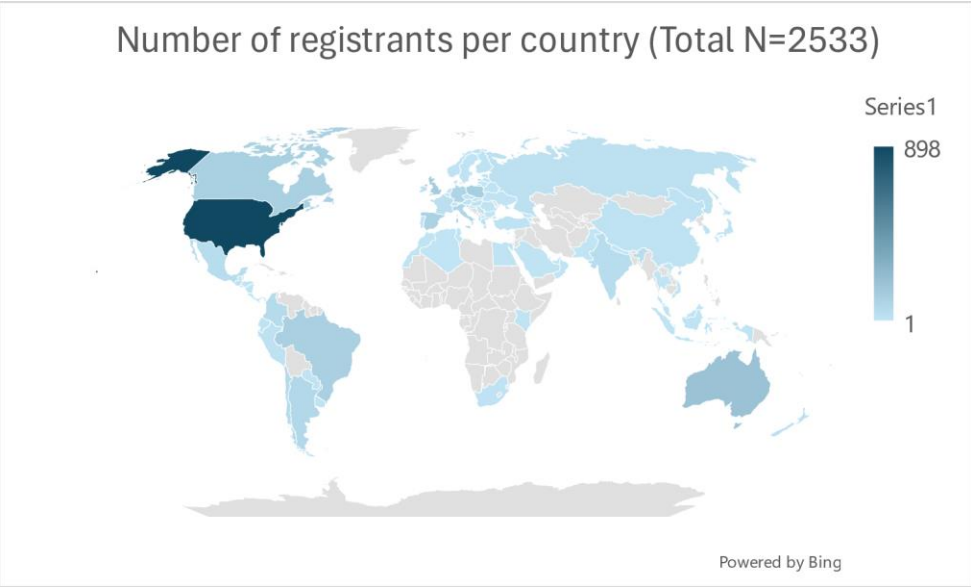
- **Caregiver reported registry for individuals living with Angelman syndrome**
- **Web based**
- **International – available in 7 languages**
  - English
  - Spanish
  - Hindi
  - Italian
  - traditional Chinese
  - Brazilian Portuguese
  - Polish

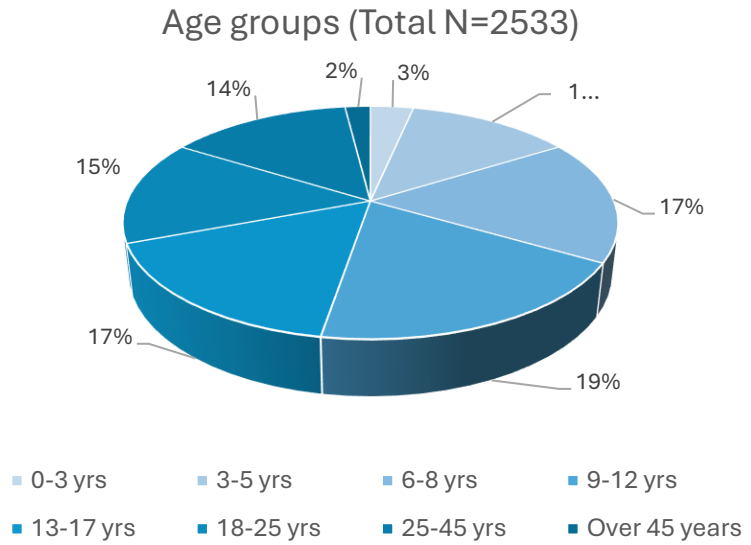


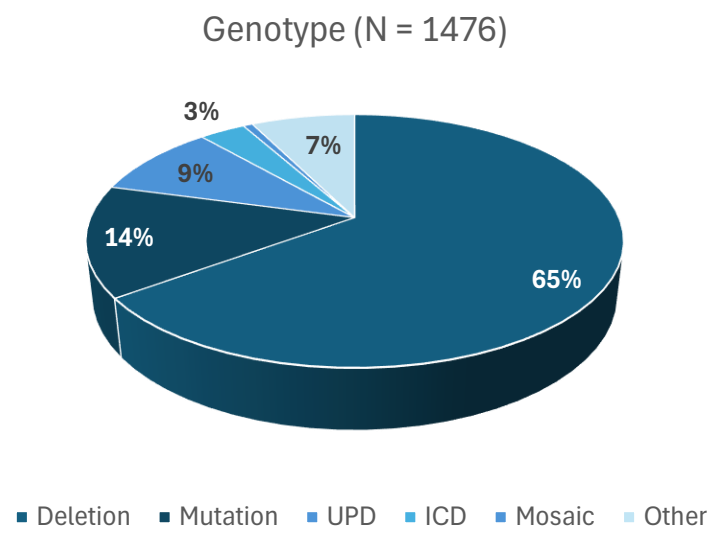

Register Now → angelmanregistry.info

# Who is in the Global Angelman Syndrome Registry?

- **2533 participants** worldwide from 95 countries – **LATEST UPDATE: 2577**



# How is the data collected?

GLOBAL ANGELMAN SYNDROME REGISTRY

## Basic demographics

- Parent/Guardian
- Location
- Contact information
- Patient
- Genotype
- Consent

## Baseline (first visit)

All modules are completed in the initial data entry:

- Newborn and infancy history
- History of diagnosis
- Medical history
- Epilepsy
- Medications, interventions & therapies
- Clinical trials & studies
- Illness or medical problems
- Communication
- Behavior and development
- Sleep
- Data collection for other studies

## Longitudinal

Update every 6 months:

- Epilepsy
- Medications, interventions & therapies
- Clinical trials & studies

Update every year:*

- Illness or medical problems
- Communication
- Behavior and development
- Sleep

* Every 2 years as of 10 year

## Clinical data (in pilot)

fast

# What is the role of GASR in Angelman syndrome research?

- **Counting—through the quick registration in the Registry**
  Angelman Syndrome is hugely underdiagnosed, especially in adults and in countries with less available testing

- **Accessible and flexible!**
  Open to everyone living with Angelman syndrome  and meets European compliance standards
  Can participate at any time from any place with internet access

- **Data on ALL individuals living with Angelman syndrome**

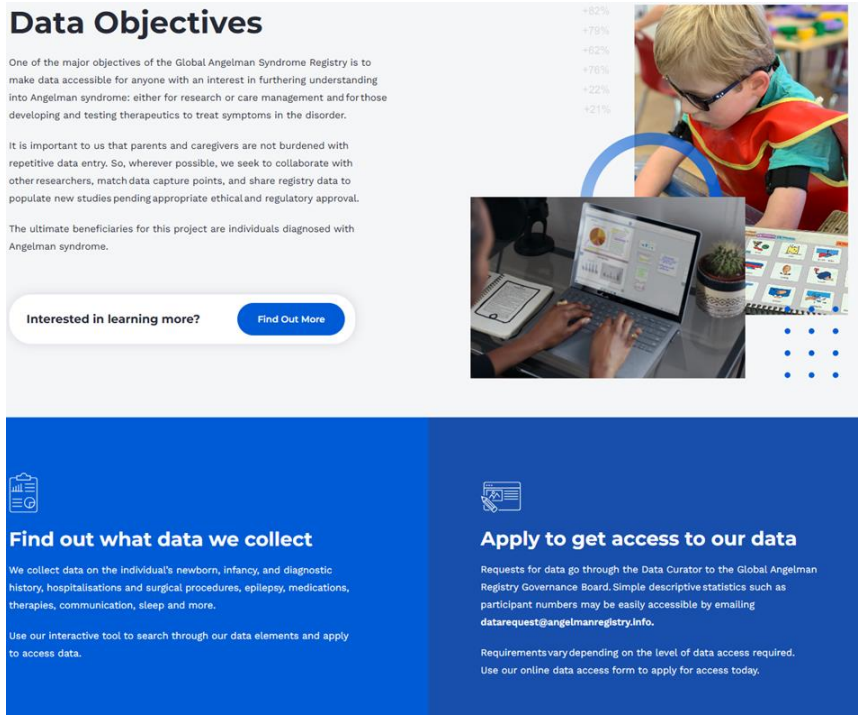
- **Parent/Caregiver data**
  Caregivers know their loved ones best!

- **De-identified data easily shared with researchers and can be combined with other datasets**

- **Clinical trial recruitment**

# How is the data accessed?

- Since 2016, there have been **105 requests** for GASR datasets
- Most requestors are:
  - Researchers
  - Clinicians
  - Industry



# How is the data used?

GLOBAL ANGELMAN SYNDROME REGISTRY

Sleep Medicine 117 (2024) 9–17

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

## Factors associated with sleep disturbances in children and adolescents with Angelman Syndrome

Geraldine Leader[a], Chloe Killeen[a], Sally Whelan[a,*], Rory Coyne[a], Megan Tones[b], Arlene Mannion[a]

[a] Irish Centre for Autism and Neurodevelopmental Research, School of Psychology, National University of Ireland, Galway, Ireland
[b] Research Office, Queensland University of Technology, Brisbane, Australia

Tones et al. Orphanet Journal of Rare Diseases (2023) 18:330
https://doi.org/10.1186/s13023-023-02904-1

Orphanet Journal of Rare Diseases

LETTER TO THE EDITOR — Open Access

## Does the registry speak your language? A case study of the Global Angelman Syndrome Registry

Megan Tones[1*], Nikolajs Zeps[1], Yvette Wyborn[1], Adam Smith[1], Roberto A. Barrero[1], Helen Heussler[2], Meagan Cross[3], James McGree[4] and Matthew Bellgard[1,5*]

Napier et al. Orphanet Journal of Rare Diseases (2017) 12:134
DOI 10.1186/s13023-017-0686-1

Orphanet Journal of Rare Diseases

LETTER TO THE EDITOR — Open Access

## A web-based, patient driven registry for Angelman syndrome: the global Angelman syndrome registry

Kathryn R. Napier[1], Megan Tones[2], Chloe Simons[3], Helen Heussler[4], Adam A. Hunter[1], Meagan Cross[3] and Matthew I. Bellgard[1*]

JIDR Journal of Intellectual Disability Research
Published on behalf of mencap and in association with IASSID

Journal of Intellectual Disability Research — doi: 10.1111/jir.12975

VOLUME 66 PART 11 pp 865–879 NOVEMBER 2022

## Association between early and current gastro-intestinal symptoms and co-morbidities in children and adolescents with Angelman syndrome

G. Leader,[1] S. Whelan,[1] N. N. Chonaill,[1] R. Coyne,[1] M. Tones,[2] H. Heussler,[3] M. Bellgard[2] & A. Mannion[1]

1 Irish Centre for Autism and Neurodevelopmental Research, School of Psychology, National University of Ireland, Galway, Ireland
2 eResearch Office, Queensland University of Technology, Brisbane, Queensland, Australia
3 Children's Health Queensland Hospital and Health Service, Brisbane, Queensland, Australia

Journal of Autism and Developmental Disorders
https://doi.org/10.1007/s10803-024-06367-6

ORIGINAL ARTICLE

## Association Between Challenging Behaviour and Sleep Problems in Adults Enrolled in the Global Angelman Syndrome Registry

Heather Coleman[1] · Arlene Mannion[1] · Sally Whelan[1] · Megan Tones[2] · Helen Heussler[3,4] · Matthew Bellgard[2] · Geraldine Leader[1]

JIDR Journal of Intellectual Disability Research
Published on behalf of mencap and in association with IASSIDD

Original Manuscript

## Research protocol: The initiation, design and establishment of the Global Angelman Syndrome Registry

M. Tones, M. Cross, C. Simons, K. R. Napier, A. Hunter, M. I. Bellgard, H. Heussler

First published: 06 April 2018 | https://doi.org/10.1111/jir.12482 | Citations: 12

ORIGINAL PAPER | Published: 10 February 2021

## Caregivers Report on the Pathway to a Formal Diagnosis of Angelman Syndrome: A Comparison Across Genetic Etiologies within the Global Angelman Syndrome Registry

Laura Roche, Megan Tones, Mark G. Williams, Meagan Cross, Chloe Simons & Helen Heussler

*Advances in Neurodevelopmental Disorders* 5, 193–203 (2021) | Cite this article

# Important considerations

- **Translations:** Providing translations in multiple languages is essential to maximize participation and ensure proper consent.
- **Country Registries:** Each country may prefer to maintain its own registry. Explore ways to align datasets and facilitate imports into a global registry.
- **Caregiver and Clinic Reporting:** Ideally, caregiver-reported data should be linked with clinic-reported data using Global Unique Identifiers.
- **Survey Design:** Focus on collecting only essential data. Long surveys may lead to caregiver fatigue, reducing engagement.
- **Recruitment and Engagement**: Develop a robust strategy to reach caregivers and patients broadly, ensuring participation. Plan for ongoing engagement over the years to maintain involvement and data continuity.
- **Data Collection and Analysis Platform:** Choose a platform that is affordable, flexible, and capable of adapting to technological advancements over time. This ensures sustainability and efficiency in data handling.
- **Stakeholder Feedback and Registry Improvement**: Actively involve stakeholders, including caregivers, clinicians, and researchers, in providing feedback and suggesting improvements for the registry. This will enhance buy-in and ensure the data collected continues to meet the needs of the community and other stakeholders.
- **Reporting and Motivation:** Regular reporting is critical to maintain motivation and involvement from participating countries.
- **Data Protection Compliance:** Ensure adherence to the strictest global data protection laws.
- **Data Access:** Limit access to identifiable data to authorized curators only.

# The team

- Project design
- Funders
- Data owners

- Design & development
- Data hosting
- Data curation

Children's Health Queensland Hospital and Health Service

Principal Investigator
Assoc Prof H Heussler

- Data curation

Project Ethics

University of East London

Initial project design oversight
Prof Matthew Bellgard

Audit, compliance and certification
GDPR, SOC2 Privacy & Security, CCPA, HIPAA, TI 2024

# Thank you!

For general information about FAST: ellen.koekoeckx@cureangelman.org
For information about the global registry: curator@angelmanregistry.info

# 8. Building a Research Portal for Rare Disease Collaboration: CHAMP1 Approach

Daniele Palumbo

# Building a Research Portal for Rare Disease Collaboration

The CHAMP1 Approach to overcome the burden

CHAMP1

RESEARCH FOUNDATION - EUROPE

**Daniele Palumbo**

dp@champ1foundation.eu

# Who ~~am I~~ are We

Dad of Francesco and Tommaso
CHAMP1 Dad
Husband
IT architect
Open Source enthusiast
Nerd
Problem solver

CHAMP1 ALLIANCE

And not only ~~me~~ us.

Dad of Emma & Ella
Maths & English teacher
CHAMP1 dad
Husband
Ski instructor
3D printing enthusiast.
Always curious, learning

# Before the portal

- CHAMP1 is a rare disease as many others
  - 200 cases worldwide
- Papers are scattered
  - several “well known” websites
- Healthcare professionals may not realize others are also working on the same gene
- Most healthcare professionals are unfamiliar with CHAMP1
- Projects are not shared
- Shared link with other diseases are not easy to be find out

http://research.champ1foundation.org

# Terminology

Coding for non-techy

- No-code development platform - Wikipedia
- Low-code development platform - Wikipedia

App to App language

- API - Wikipedia

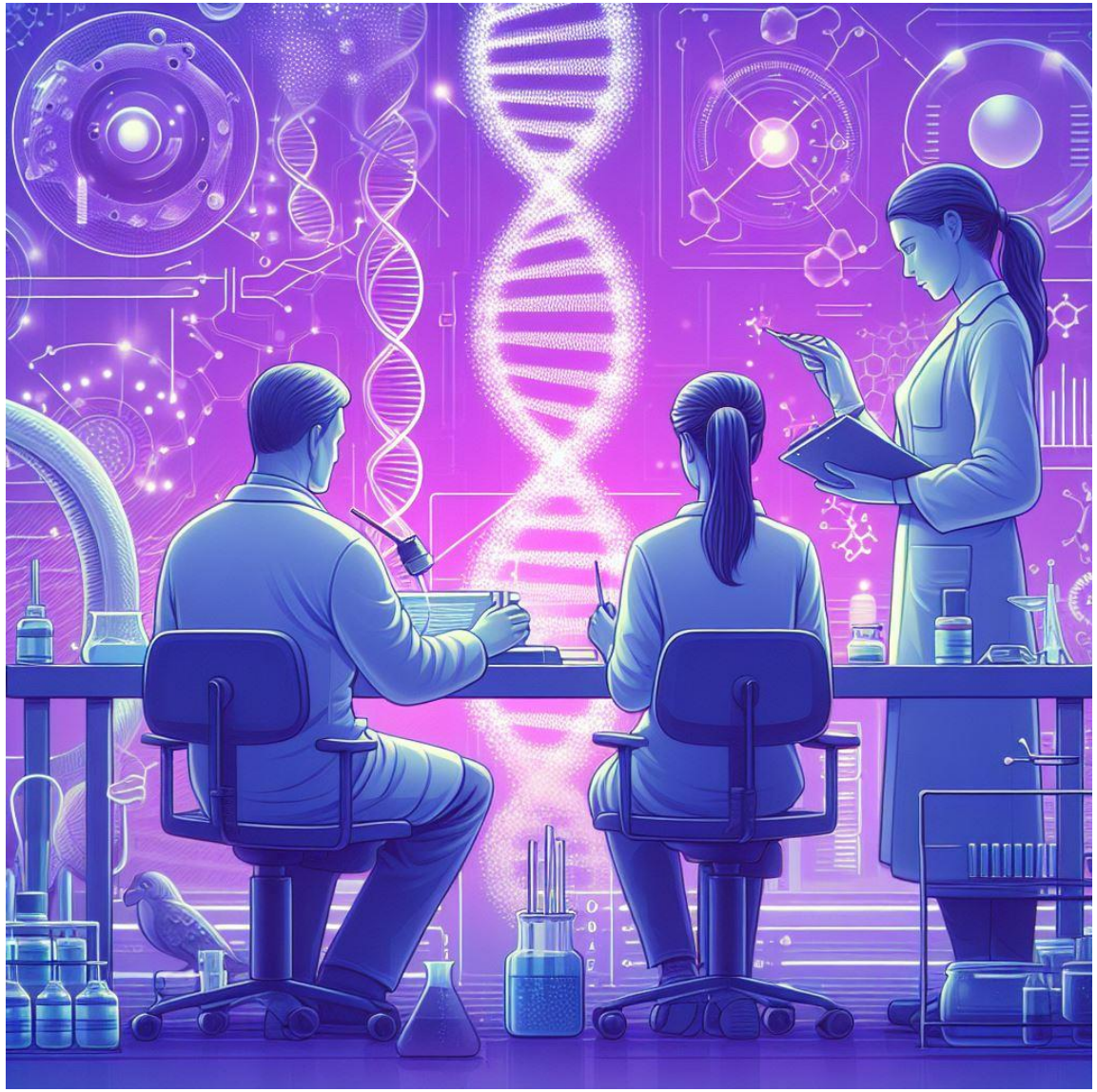
Outside of my garden!

- Software as a service - Wikipedia

Do you need to know the name of every tool in the kitchen?

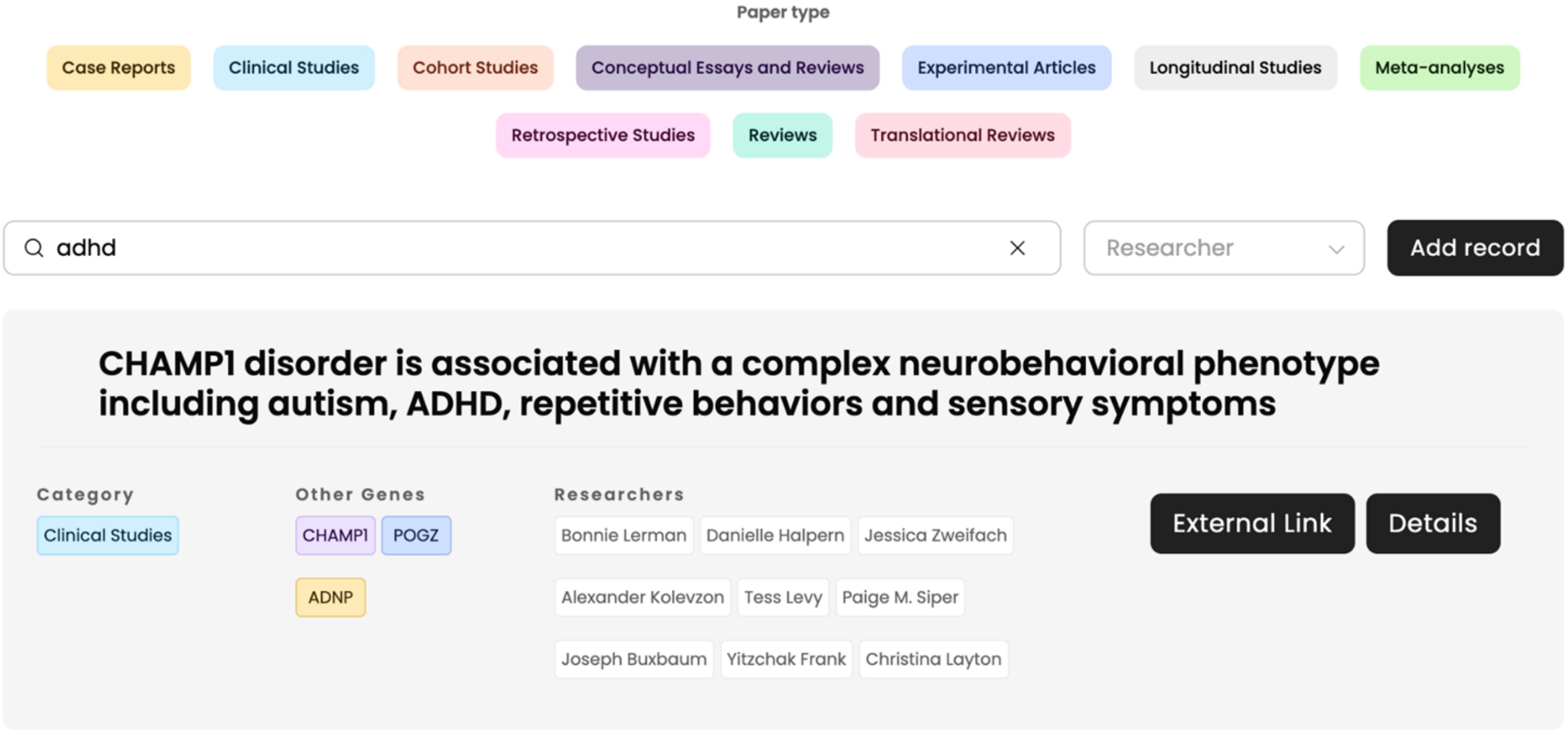
# The research portal

- Login & privacy
- Affiliations
- Researchers contacts
- Papers, with linked researchers
- Projects, with linked affiliations
- NDAs management
- Call to actions
- Integration with the main website
- PITA: the privacy policy & consent!

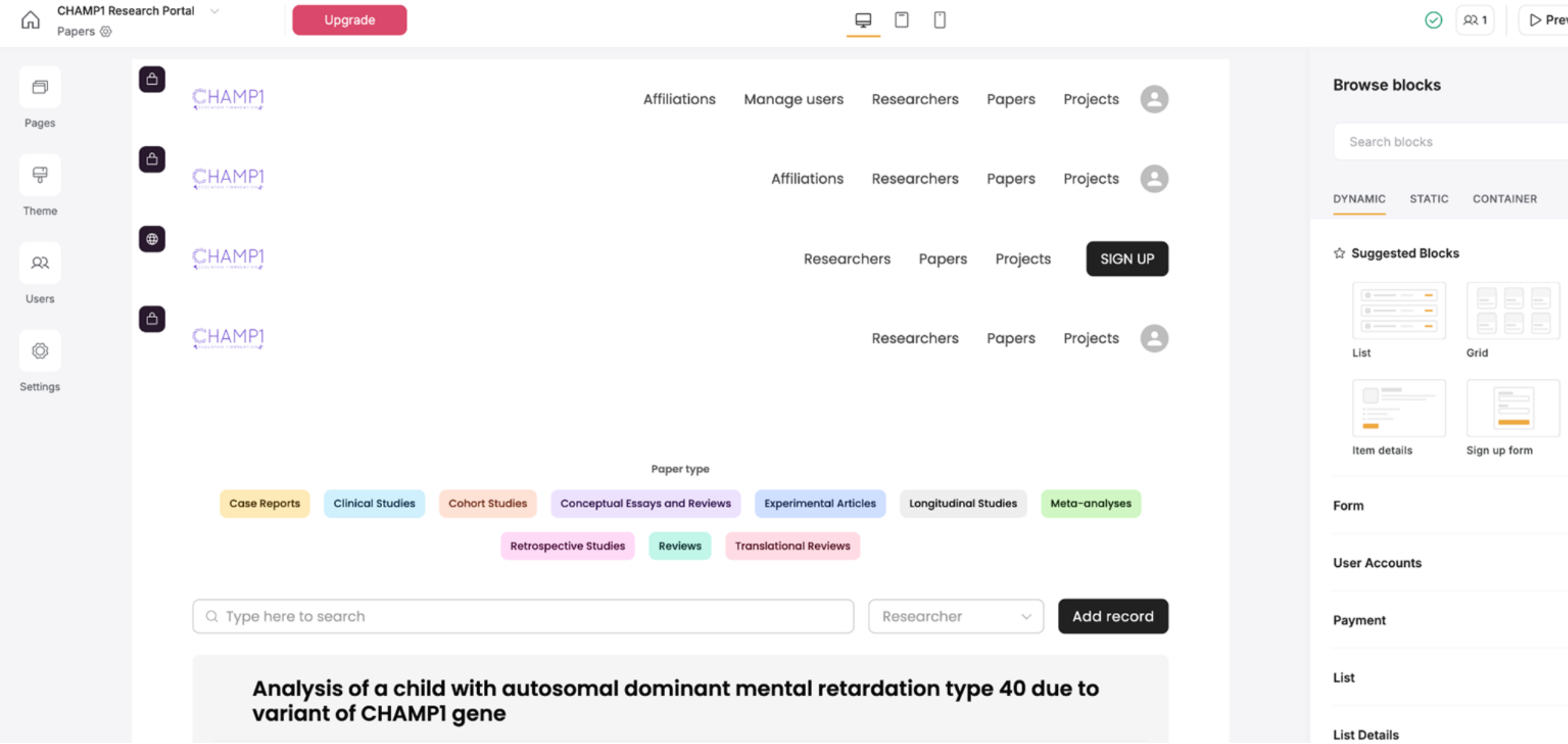


## A caregiver portal is on the way!

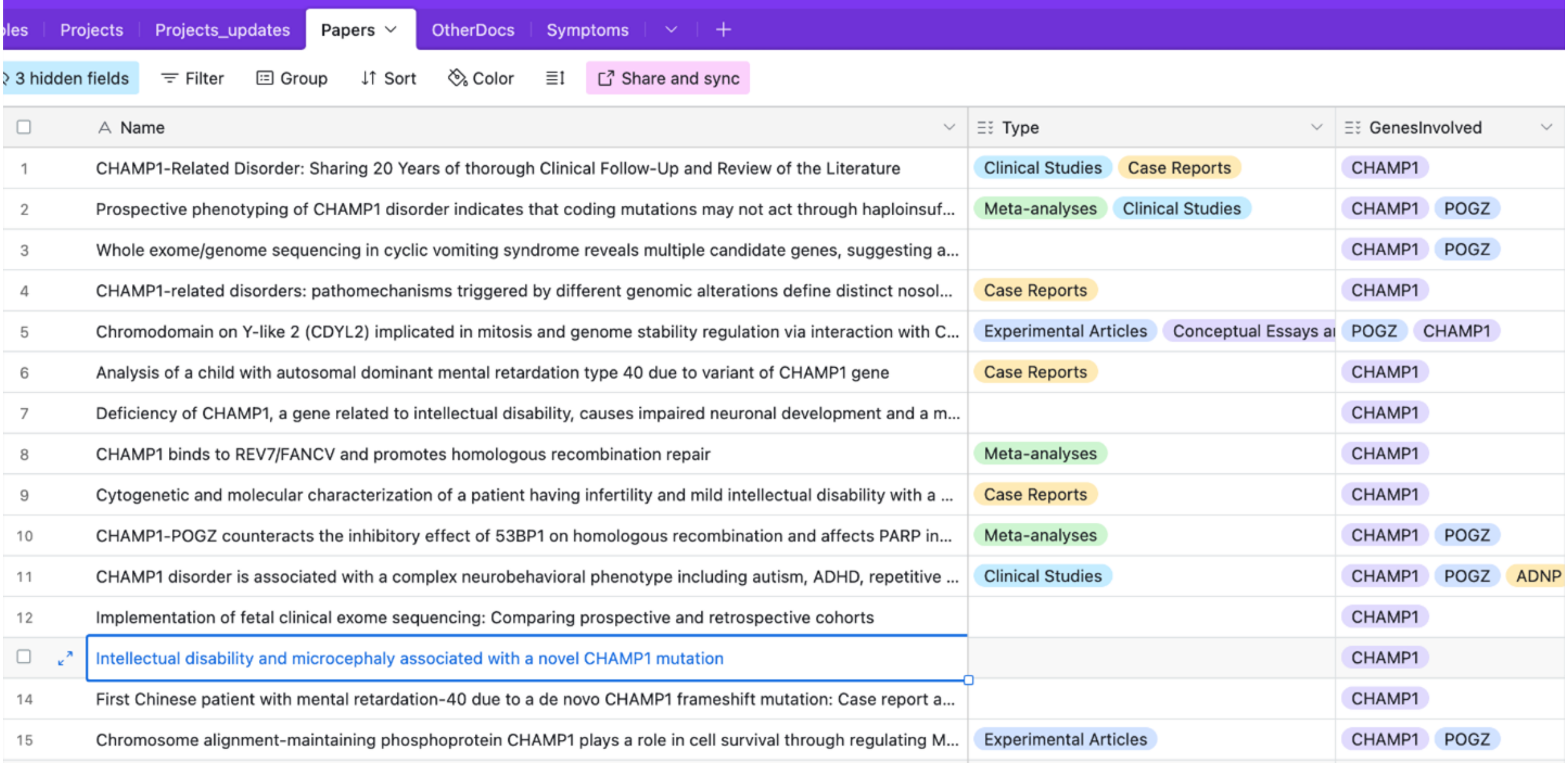
Rome wasn’t built in a day - but the Research Portal was!




Papers from the website




Softr backend




| | Name | Type | GenesInvolved |
|---|---|---|---|
| 1 | CHAMP1-Related Disorder: Sharing 20 Years of thorough Clinical Follow-Up and Review of the Literature | Clinical Studies, Case Reports | CHAMP1 |
| 2 | Prospective phenotyping of CHAMP1 disorder indicates that coding mutations may not act through haploinsuf... | Meta-analyses, Clinical Studies | CHAMP1, POGZ |
| 3 | Whole exome/genome sequencing in cyclic vomiting syndrome reveals multiple candidate genes, suggesting a... | | CHAMP1, POGZ |
| 4 | CHAMP1-related disorders: pathomechanisms triggered by different genomic alterations define distinct nosol... | Case Reports | CHAMP1 |
| 5 | Chromodomain on Y-like 2 (CDYL2) implicated in mitosis and genome stability regulation via interaction with C... | Experimental Articles, Conceptual Essays a | POGZ, CHAMP1 |
| 6 | Analysis of a child with autosomal dominant mental retardation type 40 due to variant of CHAMP1 gene | Case Reports | CHAMP1 |
| 7 | Deficiency of CHAMP1, a gene related to intellectual disability, causes impaired neuronal development and a m... | | CHAMP1 |
| 8 | CHAMP1 binds to REV7/FANCV and promotes homologous recombination repair | Meta-analyses | CHAMP1 |
| 9 | Cytogenetic and molecular characterization of a patient having infertility and mild intellectual disability with a ... | Case Reports | CHAMP1 |
| 10 | CHAMP1-POGZ counteracts the inhibitory effect of 53BP1 on homologous recombination and affects PARP in... | Meta-analyses | CHAMP1, POGZ |
| 11 | CHAMP1 disorder is associated with a complex neurobehavioral phenotype including autism, ADHD, repetitive ... | Clinical Studies | CHAMP1, POGZ, ADNP |
| 12 | Implementation of fetal clinical exome sequencing: Comparing prospective and retrospective cohorts | | CHAMP1 |
| | Intellectual disability and microcephaly associated with a novel CHAMP1 mutation | | CHAMP1 |
| 14 | First Chinese patient with mental retardation-40 due to a de novo CHAMP1 frameshift mutation: Case report a... | | CHAMP1 |
| 15 | Chromosome alignment-maintaining phosphoprotein CHAMP1 plays a role in cell survival through regulating M... | Experimental Articles | CHAMP1, POGZ |

Papers from Airtable

# How to do the same

- Ask - also AI are helpful
- Don’t be afraid to re-do pieces
- Plan very carefully the base
- Don’t lose yourself in details
- Information is the gold of the 2000s

And remember, it's like playing Lego!

It’s easier than you can think of!

# Now & Then

- Empower caregivers
- Empower healthcare professionals
- Include the known gene data
- Include the known mutations
- Keep data updated
- Include external resources
- Involve other Patient Advisory Group and suggest them the same - **AHA!**
- Platform as a Service…

Next steps to be done!

# 9. Solving Rare Diseases: How Global Collaboration and Data are Advancing Kleefstra Syndrome Research

Tanja Zdolšek Draksler

# How Global Collaboration and Data are Advancing Kleefstra Syndrome Research

Tanja Zdolšek Draksler, PhD

tanja.zdolsek@idefine-europe.org

Jožef Stefan Institute, Ljubljana, Slovenia

unesco
Centre
Under the auspices
of UNESCO

IRC AI
International Research Centre
on Artificial Intelligence
under the auspices of UNESCO

IDEFINE EUROPE

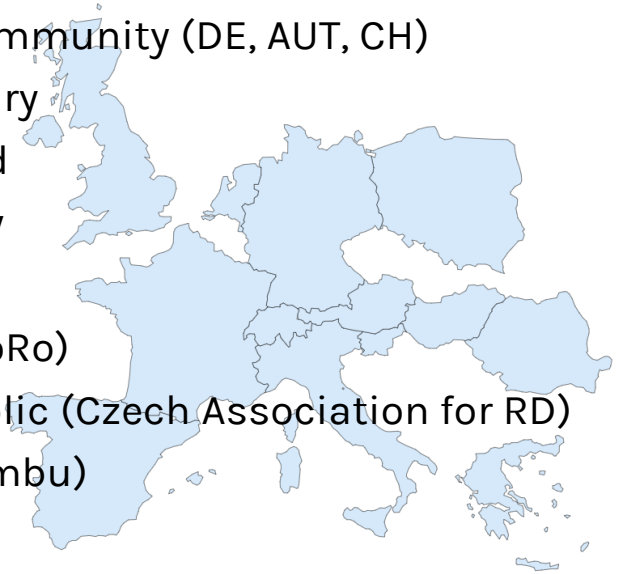
# Kleefstra Syndrome facts

- **A rare genetic neurodevelopmental disorder caused by the LoF in the EHMT1 gene (chromosome 9).**
- Affects development, involves multiple body systems (distinct facial features, developmental delay, ID, hypotonia, speech delay and communication difficulties, autism, hearing problems, vision problems, seizures…).
- A range of symptoms that can differ from person to person. Different severity (mild, moderate, severe, profound).
- Role of EHMT1: to produce the enzyme histone methyltransferase 1, that controls the activity of other genes in the body. When one copy of EHMT1 loses its function, it affects a large number of other genes involved in development and functioning of organs and tissues throughout the body.
- Individuals with Kleefstra syndrome have one standard copy of EHMT1 and one that does not work or is deleted. Almost all cases reported have been as “de novo”.
- Prevalence: <1 / 1 000 000 (old estimation, we already know that the prevalence is much higher!)

# Kleefstra Syndrome Global Community

EUROPE

- Kleefstra syndrome France
- Kleefstra syndrome Italy
- Kleefstra syndrome Spain
- Kleefstra syndrome UK
- Kleefstra syndrome Slovenia with Croatia, Serbia
- Kleefstra syndrome Netherlands (Zeldsamen)
- Kleefstra syndrome German speaking community (DE, AUT, CH)
- Kleefstra syndrome community in Hungary
- Kleefstra syndrome community in Poland
- Kleefstra syndrome community in Turkey
- Kleefstra syndrome point in Greece
- Kleefstra syndrome point in Romania (NoRo)
- Kleefstra syndrome point in Czech Republic (Czech Association for RD)
- Kleefstra syndrome point in Norway (Frambu)



North America:

- Kleefstra syndrome foundation IDefine, USA
- Kleefstra community in Canada

South America:

- Kleefstra syndrome Brazil
- Kleefstra community in Columbia

Asia: Kleefstra syndrome Japan

Kleefstra community in Australia

## The Kleefstra Syndrome Europe Alliance

a coordination hub for Kleefstra syndrome in Europe, bringing together national Kleefstra syndrome patient organizations or informal groups from Europe. The main aim is to collaborate with researchers, clinicians and other organizations globally.

Facebook groups

Kleefstra Syndrome; 9q Deletions (private group) – 1.500 members
Kleefstra Syndrome – Chromosome Mutation (private group) – 515 members
Kleefstra Syndrome All Grown UP (private group) – 260 members
Kleefstra Syndrome (public group) – 2.400 members

KLEEFSTRA SYNDROME EUROPE ALLIANCE

IDEFINE EUROPE

# Kleefstra Syndrome research teams

**Europe: preclinical + clinical research**

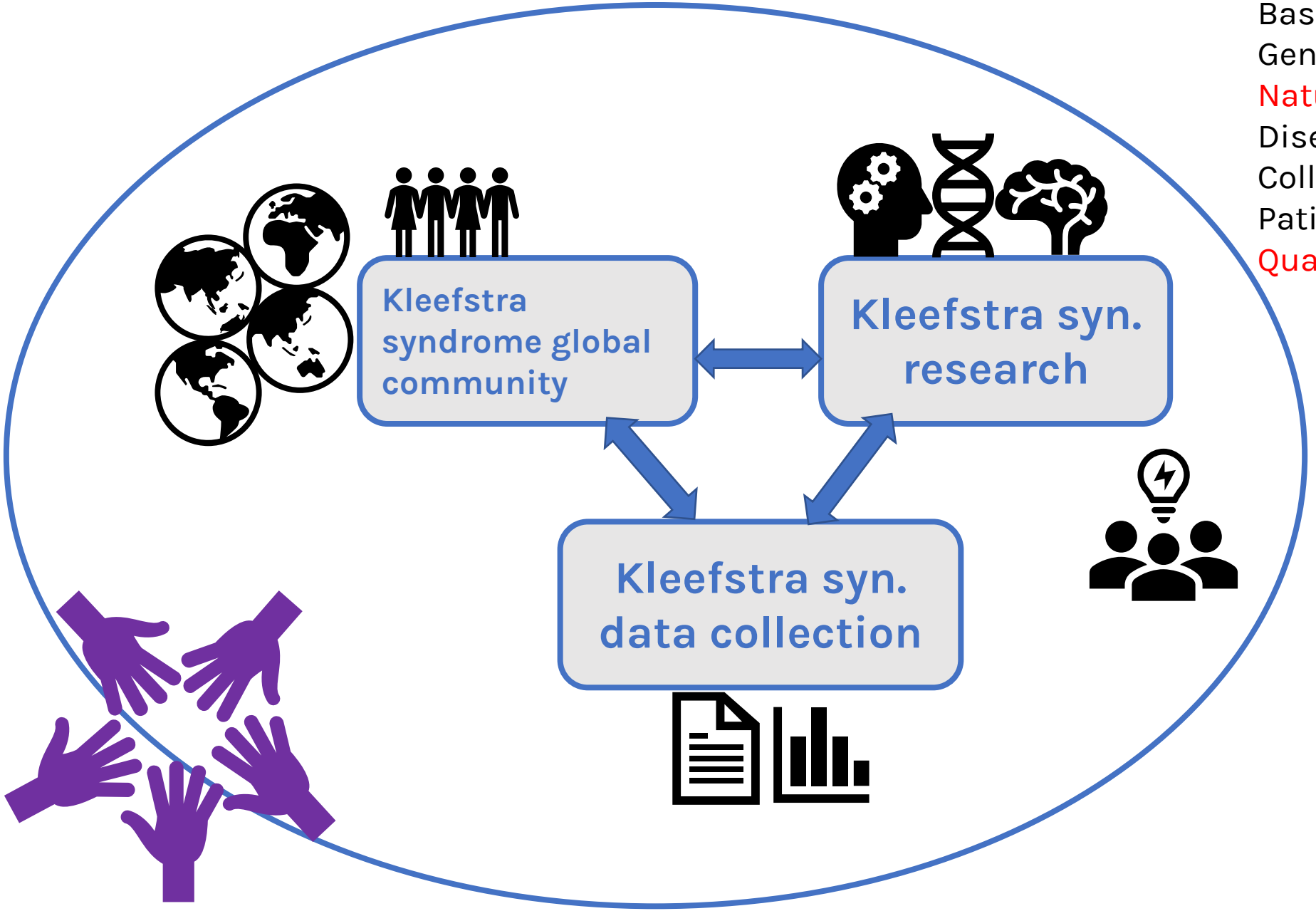
- Radboud umc, Centre of expertise for rare congenital development disorders and Radboud University, Nijmegen, The Netherlands
- Erasmus MC, Rotterdam, The Netherlands
- National institute of Chemistry, Ljubljana, Slovenia
- University of Sevilla & National Institute of Health Carlos III, Spain
- ASST Papa Giovanni XXIII, Bergamo & Policlinico di Milano & University of Milano, Italy
- RIKEN, Japan
- …

USA: Kleefstra Clinic at the Rosamund Stone Zander Translational Neuroscience Center, Boston

Australia: Speech and language research at MCRI, Melbourne

(list of researchers + list of disease models (mouse, IPSCs, fruit fly))

# Kleefstra Syndrome today




Patient Registry
Basic and clinical research
Genotype-phenotype studies
Natural history study
Disease mechanisms
Collaboration and Data Sharing
Patient-Centered Outcomes
Quality of Life Studies etc.

# Data Collection – community led

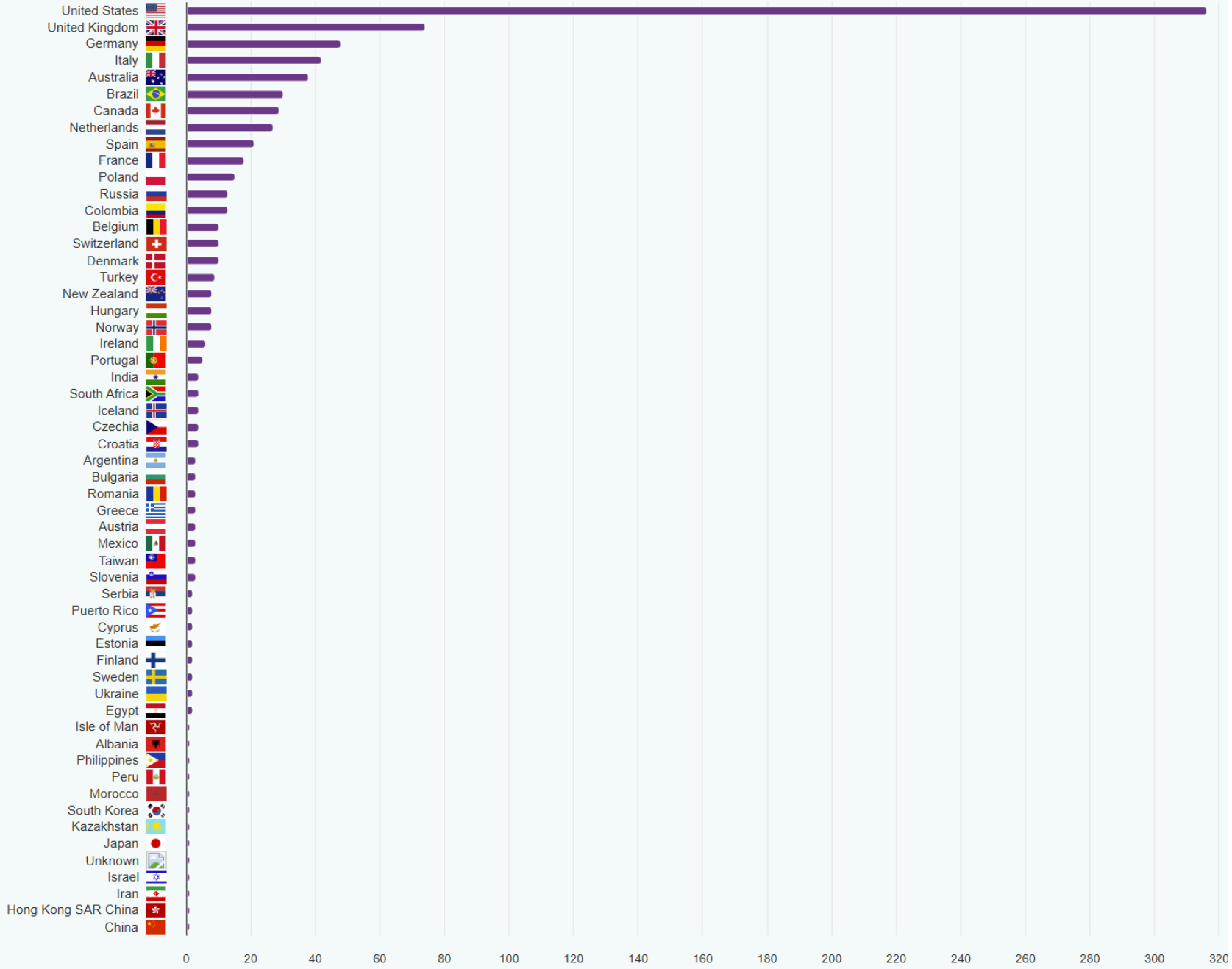
- **Kleefstra Syndrome Worldwide Map (registry)**
- GENIDA (caregiver reported outcomes)
- RARE-X (caregiver reported outcomes)
- Simons Searchlight (Registry/Biobank)
- Citizen Health (eHRs, *only for USA)

# Kleefstra Syndrome Worldwide Map

https://www.kleefstraworldmap.org/


| 368 | 429 | 13 | 810 |
|---|---|---|---|
| Male | Female | No gender | Total |

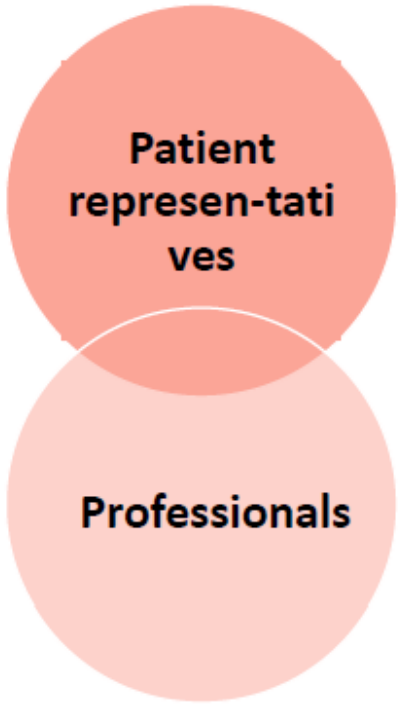
# Registrants by Country



| Group of clinical symptoms | prevalence [%] | YES/NO/I don't know | n= | mild/moderate/major/* |
|---|---|---|---|---|
| Behavior problems | 67.1 | | 158 | |
| Vision problems | 66.9 | | 166 | |
| Problems during newborn period (first four weeks) | 66.5 | | 164 | |
| Walking problems | 65.6 | | 157 | |
| Diagnosis of intellectual disability* | 64.7 | | 167 | |
| Problems during pregnancy/labour/delivery | 62.6 | | 172 | |
| Musculo-skeletal problems | 57.3 | | 157 | |
| Digestive problems | 57.1 | | 170 | |
| Feeding problems | 52.1 | | 163 | |
| Sleeping disorders | 50 | | 168 | |
| Dental anomalies | 47.8 | | 157 | |
| Skin, nails and hair problems | 44.8 | | 154 | |
| Oral/Buccal problems | 41.2 | | 153 | |
| Cardiac problems | 39.9 | | 163 | |
| Other mouvement disorders | 39.8 | | 161 | |
| Hearing problems* | 39.5 | | 167 | |
| ASD | 27.1 | | 166 | |
| Respiratory and pulmonary problems | 26.3 | | 156 | |
| Renal, bladder and urogenital problems | 25.2 | | 155 | |
| Epilepsy | 25 | | 156 | |
| Endocrine and metabolic problems | 14.3 | | 154 | |
| Tremor | 13.7 | | 161 | |
| Vascular problems | 8.4 | | 154 | |
| Sense of smell problems | 2.7 | | 150 | |
| Cancer development | 1.3 | | 150 | |

Fig. 1. **Overview of groups of clinical symptoms in the KLEFS1 cohort with prevalence numbers.** The majority of observed clinical symptoms (20/25) are frequently reported (from epilepsy to behaviour problems) ranging within the prevalence of 25% to high 67.1%. Answers from caregivers are presented as a bar chart with sample size (n). If applicable, the severity is presented on a scale of 3 stages (*mild, moderate, major*), while two groups of clinical symptoms (I*ntellectual disability* and *Hearing problems*) use 4 stages in reporting (namely *mild, moderate, severe, profound*).

# Kleefstra Syndrome Clinical Guidelines


## END PRODUCTS

- Peer-reviewed article in international journal
- Full document available on ITHACA website
- Health care provider summary
- Patient/lay version
- Surveillance scheme
- Research agenda

# General discussion and wrap up

Tanja Zdolšek Draksler

European Patient Advocacy Group

ITHACA

https://ern-ithaca.eu Register to the Web site to get NewsLetter!



European Reference Networks ITHACA