European Reference Network
for rare or low prevalence complex diseases

Network Intellectual Disability and Congenital Malformations (ERN ITHACA)

Manchester Centre for Rare Disease

Manchester University NHS Foundation Trust

The role of European Reference Networks in developing and taking into account Quality of Life Indicators in health care provision

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Background

- The experience of living with a rare genetic condition is vastly more complex than its medical features: any aspect of an individual's life may be affected.
- Quality of life (QoL) refers to an individual's sense of overall well-being encompassing physical, psychological, emotional, social, and spiritual dimensions.
- There is a lack of clarity as to what actually contributes to QoL from the patient's perspective.
- In recent years, QoL has increasingly been studied in genetic conditions.
- The goal of the next frontier in healthcare for individuals living with rare genetic conditions is to improve QoL, not only by advancements in medical treatment, but with interventions aimed at modifying psychosocial and contextual factors that influence QoL.

Cohen and Biesecker, Am J Med Genet A, 2010

Previous experience

List of Genetic Conditions by Clinical Category (With Number of Studies)

- **Metabolic disorders**
  - Phenylketonuria (2)
  - Galactosemia (1)
  - Congenital adrenal hyperplasia (1)
  - Porphyrias (2)
  - Glycogen storage disease type 1 (1)
  - Hyperimmunoglobulinemia D (1)
- **Lysosomal storage disorders**
  - Fabry disease (3)
  - Gaucher disease (1)
  - Pompe disease (1)
- **Blood and vascular disorders**
  - Hereditary hemorrhagic telangiectasia (2)
  - Sickle cell disease (3)
  - Coagulopathies
    - Hemophilia (4)
    - Factor XIII deficiency (1)
    - Von Willebrand disease (1)
- **Neuromuscular and neurologic disorders**
  - Muscular dystrophies (5)
  - Charcot-Marie-Tooth disease (4)
  - Friedrich ataxia (2)
  - Familial dysautonomia (1)
  - Huntington disease (1)
- **Dermatologic disorders**
  - Neurofibromatosis type 1 (7)
  - Darier's disease (1)
  - Hailey–Hailey disease (1)
- **Connective tissue disorders**
  - Marfan syndrome (1)
  - Ehlers–Danlos syndrome (1)
- **Skeletal dysplasias**
  - Achondroplasia (1)
  - Osteogenesis imperfecta (1)
- **Chromosomal disorders**
  - Prader–Willi syndrome (1)
  - Turner syndrome (1)

List of QoL Scales (Alphabetical by Abbreviation, With Number of Studies)

Abbreviations	Scale name	#
CDLQI	Children's Dermatology Life Quality Index	2
CFQ	Cystic Fibrosis Questionnaire	5
CFQoL	Cystic Fibrosis Quality of Life Questionnaire	1
CHQ	Child Health Questionnaire	7
DISABKIDS	DISABKIDS Questionnaire	1
DLQI	Dermatology Life Quality Index	2
ITQoL	Infant/Toddler Quality of Life Questionnaire	1
MOS	Medical Outcomes Study General Health Survey	1
PedsQL	Pediatric Quality of Life Inventory	2
PLC	Profile of Quality of Life in the Chronically Ill	1
QLI	Quality of Life Index	2
SF-12	Medical Outcomes Study Short Form 12	2
SF-36	Medical Outcomes Study Short Form 36	30
SIP	Sickness Impact Profile	4
Skindex	Skin Diseases Quality of Life Index	3
TAAQoL	TNO-AZL Adult Quality of Life	2
TACQoL	TNO-AZL Children's Quality of Life	4
TAPQoL	TNO-AZL Preschool Children Quality of Life	1

Cohen and Biesecker, Am J Med Genet A, 2010

Troubleshooting

- Although widely used, generic QoL scales are biased because they measure status (i.e., level of impairment or satisfaction) in the various domains of QoL, without assessing importance of each domain. Also, most generic scales specifically assess the impact of one's health condition on the aspects of one's life primarily related to physical functioning without taking into psychological, spiritual, and social well-being.

- Disease-specific QoL scales are, by nature, health-related scales, and thus do not measure QoL as a global construct. They may prove useful in evaluating outcomes of clinical trials specific to the condition.

- There are numerous challenges around measuring QoL in children and adolescents. The instrument must be validated in the age group. A controversial issue is the reporting method.

The PedsQL™ Measurement Model for the Pediatric Quality of Life Inventory™

James W. Varni, Ph.D.

PedsMetrics™
Quantifying the Qualitative℠

About the Model

The PedsQL™ Measurement Model is a modular approach to measuring health-related quality of life (HRQOL) in healthy children and adolescents and those with acute and chronic health conditions. The PedsQL™ Measurement Model integrates seamlessly both generic core scales and disease-specific modules into one measurement system.

The PedsQL™ Generic Core Scales are:

- **Brief** (23 items)
- **Practical** (Less than 4 minutes to complete)
- **Flexible** (Designed for use with community, school, and clinical pediatric populations).
- **Developmentally Appropriate** (Ages 2-18; Child Self-Report Ages 5-7, 8-12, 13-18; Parent Proxy-Report Ages 2-4, 5-7, 8-12, 13-18).
- **Multidimensional** (Physical, Emotional, Social, School Functioning).
- **Reliable** (Total Scale Score: 0.88 Child Self-Report; 0.90 Parent Proxy-Report).
- **Valid** (Distinguishes between healthy children and children with acute and chronic health conditions; distinguishes disease severity within a chronic health condition).
- **Responsive** to clinical change over time.
- **Translated** into multiple languages including broadcast Spanish.

The **23-item PedsQL™ Generic Core Scales** were designed to measure the core dimensions of health as delineated by the World Health Organization, as well as role (school) functioning. The 4 **Multidimensional** Scales and 3 Summary Scores are:

Scales	Summary Scores
Physical Functioning (8 items)	**Total Scale Score** (23 items)
Emotional Functioning (5 items)	**Physical Health Summary Score** (8 items)
Social Functioning (5 items)	**Psychosocial Health Summary Score** (15 items)
School Functioning (5 items)	

The PedsQL™ Condition-Specific Modules

- **Complement the Generic Core Scales** for use in designated clinical populations.
- **Designed to provide greater measurement sensitivity** for circumscribed populations.
- **Disease-Specific Modules available** for asthma, rheumatology, diabetes, cancer, and cardiac conditions, with additional modules in the development and planning stages.

- Newsletter for the PedsQL™ Pediatric Quality of Life Inventory™
- Sample PedsQL™ Child-Self Report (ages 8-12)
- Sample PedsQL™ Parent-Proxy Report for Children (ages 8-12)

Development of a Needs-based Quality of Life Patient Reported Outcome Measure Specific to Patients with NF1-associated pNFs

Initiative: PRO

Name: Stephen McKenna
Contact Email: smckenna@galen-research.com
Dates: 3-1-14 to 1-1-18
Tumor Focus: plexiform neurofibroma
Application: Clinical Endpoint Tool

Background: Plexiform neurofibromas (plexiforms) are network-like, benign tumours present in a third of NF1 patients. Plexiforms have a major impact on quality of life (QoL) as they can be disfiguring and painful, and are difficult to treat. Laser treatment and surgery can be used to remove the plexiforms. However, surgery can be more challenging, as damage to nerves can sometimes occur and lead to further complications. The relative merits of these treatments as perceived by the patients are largely unknown. New treatments are becoming available for plexiforms and it is crucial to determine the value patients gain from these. No QoL measure specific to adults with plexiforms exists. This study involves developing and validating a needs-based, unidimensional QoL measure specific to this patient group – the PlexiQoL.

Goals of Project: Establishing that interventions to NF1-associated pNFs improve/benefit a patient's QoL, in addition to clinical status. The study was designed to develop a patient-based measure that determines the impact of plexiforms on need fulfilment in affected individuals. The model underlying the new measure is that illness and its treatment affect individuals by limiting their ability to meet their human needs. Needs are fundamental to life as they motivate us to take appropriate actions. For example, work is good for us as it gives us a time structure and a reason for getting out of bed, gives us the opportunity to work as part of a team and gives us status and identity. This explains why the health and well-being of unemployed people can deteriorate. The work is being conducted in parallel in the US and UK. Consequently, the final scale will be valid

PlexiQoL

PLEASE READ THIS CAREFULLY

On the following pages you will find some statements that have been made by people with plexiforms.

As you are aware, plexiforms are tumours that grow on nerves underneath the skin. They are different from the tumours you find on your skin.

We would like you to tick **'True'** if the statement applies to you and tick **'Not True'** if it does not.

Please choose the response that applies best to you

AT THE MOMENT

Please read each statement carefully and decide whether your plexiform(s) affect you in this way ***at the moment***

1. I avoid crowds where possible
   - True ❒
   - Not True ❒

2. I am unable to join in activities with my family and friends
   - True ❒
   - Not True ❒

3. I'm losing my role in life
   - True ❒
   - Not True ❒

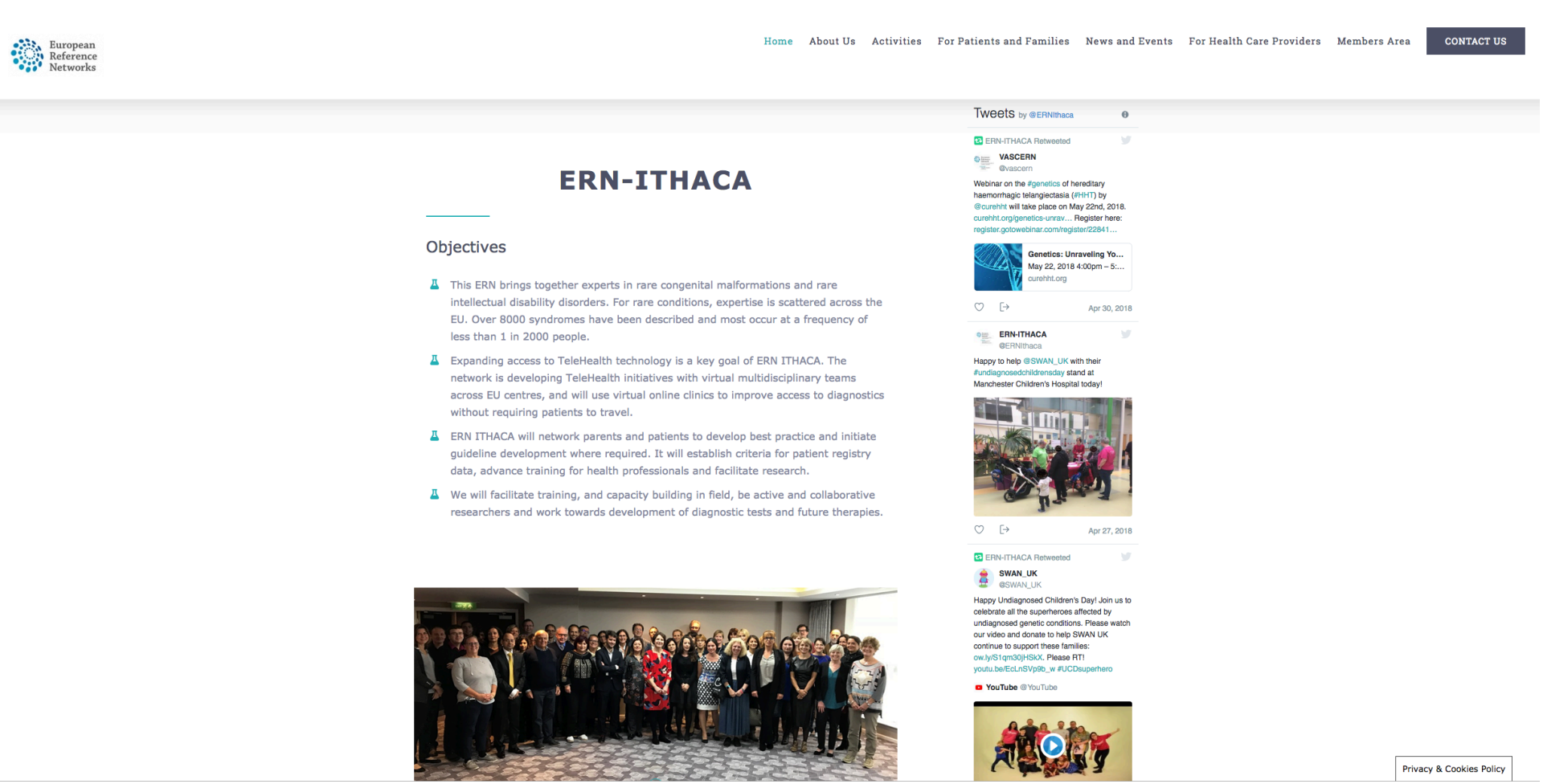
4. I am reluctant to leave the house
   - True ❒
   - Not True ❒

5. I can't live life to the full
   - True ❒
   - Not True ❒

6. I avoid looking at myself in the mirror
   - True ❒
   - Not True ❒

Limitations

- Finding an objective way to assess QoL in rare diseases is difficult and existing outcome measures often aren't valid in these populations.
- A parent-reported outcome is often very different to a standard clinical outcome. A few of these are individually reported and aren't measured using existing tools.
- Developing new tools is time consuming and expensive and they have to be validated and, in rare diseases, these specific tools cannot be used across the whole range of conditions.
- This aspect requires a lot of consultation with patients, some experts in methodology and resources, but a new rare disease outcome measure could be developed by ERNs.



ERN-ITHACA is particularly interested in the following disease areas:

- Congenital Malformations, Intellectual Disability, Developmental disorders, RASopathies, Angelman Syndrome, Rare Chromosome disorders, Rare Limb disorders, Spliceosomal disorders, Obesity disorders.

ERN-ITHACA and QoL

- We are a network dealing with multi-systemic, rare, undiagnosed conditions: reaching a diagnosis is often our best outcome
- We can concentrate on few conditions, the ones where we think our network has established expertise and liaise with the relevant patient representatives to see whether they are interested in developing new surveys
- A few HCPs of our network are piloting multidisciplinary clinics with neuropsychology assessment and these findings may direct us towards a best approach for rare patients generally
- We have put in place communication tools for patient associations to share existing resources including surveys that have proven useful (website, twitter)
- We envisage this aspect of patient care as strongly, if not exclusively, patient-led

ERNs may

- Collect patient opinions
- Share expertise in development
- Be in a good position to pilot as large numbers are required

ERN-ITHACA aims

- in the expert patient care of improving access to
  - earlier diagnosis and
  - expert health care which will have a major impact on QoL through more accurate and specific therapies

Contact us:

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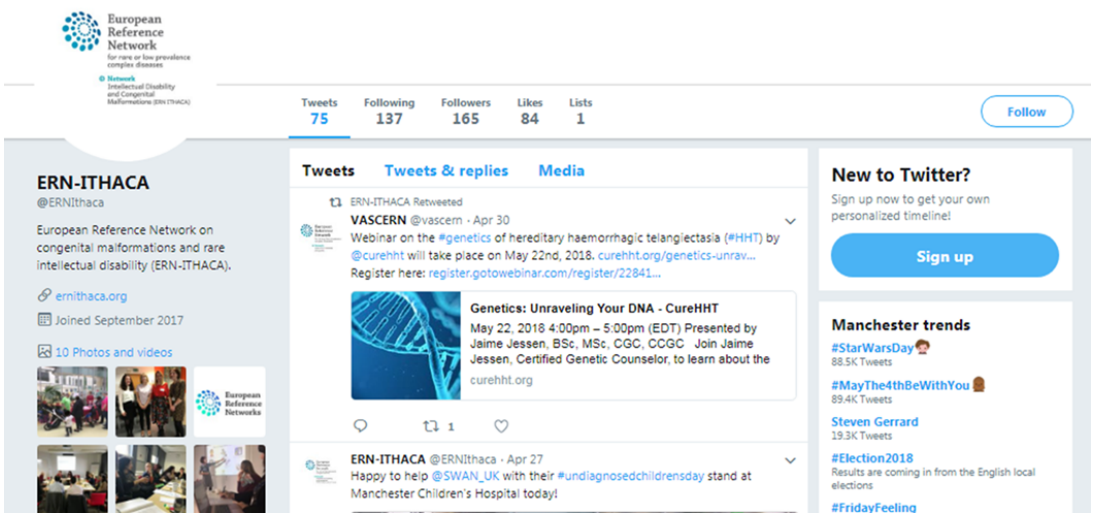

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