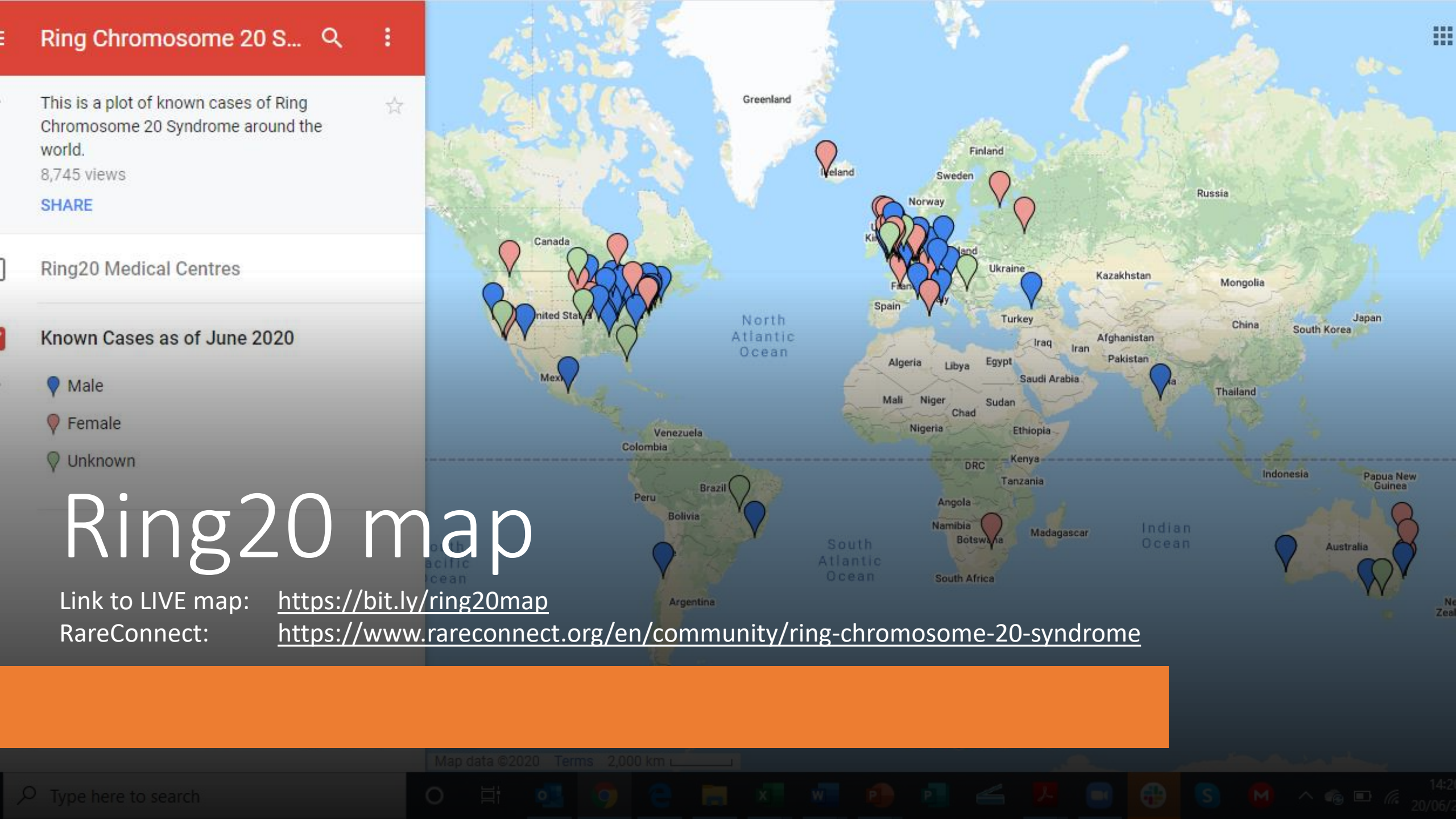
Allison Watson
Cofounder: Ring20 Research and Support UK CIO
Deputy lead for EPAG EpiCARE ERN for rare and complex epilepsies

David's journey to r(20) diagnosis



Ring20 map

Link to LIVE map: https://bit.ly/ring20map

RareConnect: https://www.rareconnect.org/en/community/ring-chromosome-20-syndrome

Birth to first seizure

- Premature labour, born on due date
- Normal childhood development
- Hyperactive pre-schooler, sensitive hearing
- 1st signs – jump up and run for no reason, appeared ‘vacant’ at times
- 1st seizure – age 6, slumped like a rag doll
- 1st EEG “Perfectly normal brain for a 6 year old”
- Diagnosed with absence seizures – prescribed Ethosuximide

6 months later…

- Sudden and severe seizure onset
- Awakening from sleep (day or night)
- Sit upright, shout “C’mon, c’mon”, stiff arms, clutching bed, head turning
- Frightened facial appearance
- Doctors suspected **night terrors**, until A&E nurse witnessed seizure
- Admitted for observation/EEG
- Prescribed Carbamazepine
- Suspected focal impaired awareness seizures (unconfirmed)

Seizure progression

- Rapidly increased from 10 per 24 hrs => 30 per 24 hrs
- Worse at night; every hour, same time
- Sodium Valproate added (exacerbated poor behaviour), Clobazam added (no effect)
- David withdrawn into his own world
- Paediatrician concerned; referred to tertiary centre
- Admitted for 24hr VEEG
- Confirmed focal impaired awareness seizures
- Prescribed **steroids**, and Topiramate, Buccal Midazolam, Diazepam (Clobazam and Sodium Valproate withdrawn)
- Seizures abated to 2-3 per day within 2 weeks

Searching for a diagnosis

- Admitted for **brain surgery workup**
- ASM's not withdrawn as clinical seizure frequency was low
- VEEG (abnormal background activity), MRI (normal), SPECT scan (cancelled)
- Neuropsychological and Neuropsychiatric tests/reports (useful for 1:1 support in school)
- Referred to Clinical Psychologist for behaviour – diagnosed ADHD and autism (prescribed Methylphenidate – didn't help)

A chance discovery…

- Curious paediatrician
- ‘Small head, sticking out ears…let’s run a chromosome test’
- SURPRISE result! Mosaic ring chromosome 20 syndrome (~42%)
- Referred to geneticist (counselling)
- Signposted to patient support group, beneficial for:
  - Information; and
  - Mutual support

ring 20
research & support uk

Epi CARE

European Reference Network
for rare or low prevalence complex diseases
Network Epilepsies (ERN EpiCARE)

European Patient Advocacy Group

The diagnostic challenge…

RECOGNISE SIGNS & SYMPTOMS

CONSIDER KARYOTYPING BEYOND EPILEPSY GENE PANEL TESTING

IMPROVE SEQUENCING TECHNIQUES

European Reference Network
for rare or low prevalence complex diseases
Network Epilepsies (ERN EpiCARE)

European Patient Advocacy Group

ring 20
research & support uk

Allison Watson
Cofounder: Ring20 Research and Support UK CIO
Deputy lead for EPAG EpiCARE ERN for rare and complex epilepsies

Seizures, triggers, treatments and support

Seizures – how they have changed over time

Early years

- Absences
- Focal impaired awareness, often clusters

Adolescence/adulthood

- Focal impaired awareness
- Prolonged NCSE (typically 30-40 mins)
- Tonic clonic (mostly at night, but some evenings)
  - Risk of injury / SUDEP

More frequent/longer seizures later in the day/eve

Typical NCSE Seizures

No warning/aura

Before seizure

- Agitated, angry, aggressive (especially towards me!)

During seizure

- Movements slow down, automatisms
- Non verbal, unable to speak/respond
- Falls asleep (5-10 mins)
- On awakening, head turning, ‘scary face’, smile/laugh

After seizure

- Confused, no awareness of seizure

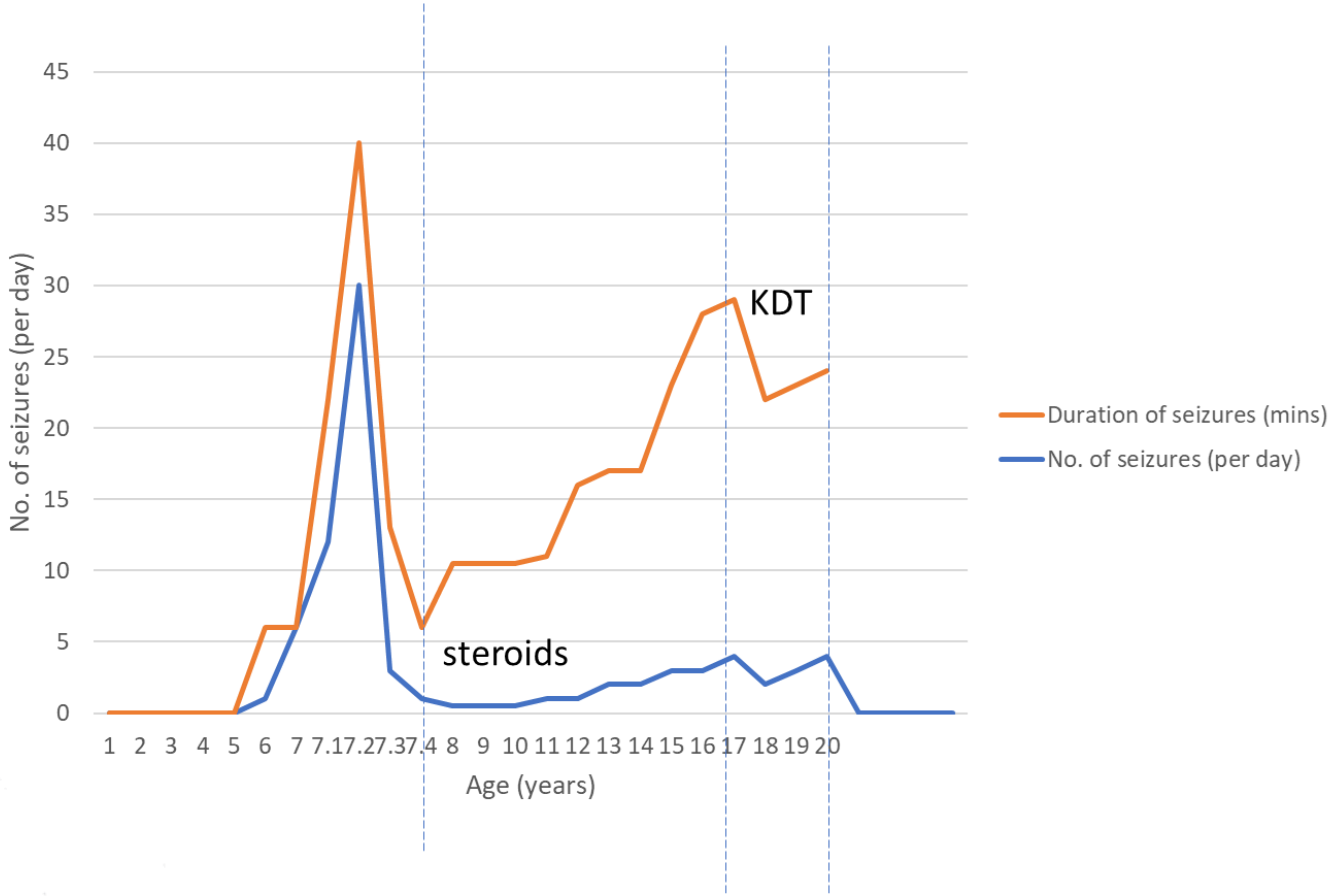
ring 20
research & support uk

Epi CARE

European Reference Network
for rare or low prevalence complex diseases
Network Epilepsies (ERN EpiCARE)

European Patient Advocacy Group

Seizure record



Triggers

Early years

- End of school day (long periods of concentration)
- Physical Exercise (at school, football, swimming)

Later years

- Taking baths/showers
- Changes in temperature (from warm room to cold outside)
- Exercise (after 10-15 mins – every time, even just walking)
- During or after a meal
- Long periods of concentration on a computer /phone/laptop

Treatments (for seizures)

Anti-seizure medications (ASMs)

- Ethosuximide
- Sodium Valproate (Epilim) with:
  - Carbamazepine (Tegretol)
  - Clobazam
- Steroids (prednisolone)
- Buccal midazolam/Diazepam (emergency)
- Carbamazepine (Tegretol slow release) +
  - Topiramate (Topamax)
  - Lamotrigine
  - Levetiracetam (Keppra)
  - Zonisamide
  - Perampanel
  - Lacosamide
- Oxcarbazepine

Other

- Steroids
  - Prednisolone
- VNS (implanted 2005)
  - ASPIRE 106
  - On 4th battery
  - Auto stim off
- KDT
  - MCT age 14
    - (suspected MCAD)
  - MAD age 17
    - (for 2 years)

Treatments vs Side Effects

Never achieved full seizure control

Adding ASM's

- Hasn't noticeably improved seizure control
- Has increased side effects (drowsiness, vacant appearance)

Seizure control vs side effects
Balance = **QUALITY OF LIFE**

Adulthood? What's needed…

Transition

Employment

- Support for travel / Reasonable adjustments

Independence

- Personal Assistant
- Supported living
- Support dog?

Mental Health

- Counselling

Marriage and children

- Genetic Counselling

ring 20
research & support uk

Epi CARE

European Reference Network
for rare or low prevalence complex diseases
Network Epilepsies (ERN EpiCARE)

European Patient Advocacy Group

The care challenge…

- SUPPORT FOR MEDICAL NEEDS
- SUPPORT AT HOME
- SUPPORT AT SCHOOL
- SUPPORT FOR SPORTS/SOCIAL
- SUPPORT IN WORK

ring 20
research & support uk

Epi CARE

European Reference Network
for rare or low prevalence complex diseases
Network Epilepsies (ERN EpiCARE)

European Patient Advocacy Group

The treatment challenge…

- NO PATIENT REGISTRY
- LIMITED RESEARCH
- NO CLINICAL PRACTICE GUIDELINES
- NO RECOMMENDED TREATMENT
- NO CLINICAL TRIALS

Addressing the 3 challenges

ACTIVELY LISTEN TO PATIENTS AND FAMILIES

BE CURIOUS, THINK OUTSIDE THE BOX

BUILD A RELATIONSHIP, OPEN DIALOGUE

WORK TOGETHER FOR BETTER OUTCOMES

European Reference Network ; 20 Patient Journey

1. Prenatal diagnosis

Parent(s) diagnosed with r(20). 50% probability of having a child with r(20) – child would likely be non-mosaic (most severe form of r(20))

2. First Symptom

Major seizure, erratic behavior. 2x EEG's (private and NHS) seizures were not detected – even though they occurred during the test.

Apparently normal childhood development though presented with: Hyperactive behavior & hearing problems – sensitivity to loud noises.

3. Second Symtoms

Sudden and severe onset of seizures, worse at night with hallucinations. Seizure's rapidly increasing from 5 to 30 per day. Cognitive regression.

4. Treatment

Treated for absence seizures based on parental recounts of history of episodes seen with child.

5. Treatment

Treated for focal (impaired awareness) seizures including multiple AEDs and steroids. Seizures significantly improved/abated with steroid treatment. Also treated for behavioral issues.

6. Brain surgery work-up

Referred for brain surgery workup. However, brain surgery is not a suitable treatment for r(20) patients – more works should be done to identify cause of epilepsy first.

7. Diagnosis (Age 8)

Diagnosis found by 'chance' to be r(20) – 2 yrs to diagnosis. Referred to geneticist. No recommended treatment protocol for r(20) – treatment on a trial and error basis

8. Treatment

Randomized to receive VNS therapy under clinical trial. Numerous AED's as adjunctive therapy with n benefit and range of side effects. Seizure frequency and duration gradually increasing during adolescence.

Need: Understanding of risks and consequences of having children. Listen to parent and take their concerns seriously. Family need reassurance and information about having a child with epilepsy.

Ideally: Counselling with pre-natal testing. In childhood, run tests to understand cause of apparent 'hyperactivity' and hearing issues treat Study EEG to diagnose seizures as a recognizable form of epilepsy.

Need: Further reassurance for patient and family. Instigate support for loss of attendance at school and cognitive regression. Need to be advise parents of risk of SUDEP and mitigating actions

Ideally: Referral to tertiary centre (paediatric neurologist). Video EEG to diagnose cause of seizures, not behavior problems or night terrors. Provide Care Plan. EHCP (or equivalent) for support at school – backed up by psychometric and neuropsychological testing. Counselling for risk of SUDEP. Advice on suitable seizure alert devices.

Need: Understand degree of behavioural problems and triggers and how to manage. And understand the seriousness and significance of brain surgery.

Ideally: Support from behaviour specialist. Identify cause for epilepsy by running genetic screening and if not identified through epilepsy panel testing or WGS, then run chromosome testing on 50-100 cells to rule out ring chromosomes prior to epilepsy surgery workup.

Note: Genetic counselling to understand the impact of the diagnosis, prognosis. Advise family of likelihood of success with polytherapy.

Ideally: Information on the diseases, genetic counselling and referral to patient support group. Explanation about level of mosaicism and what that means n terms of prognosis. Avoid polytherapy with AED's.

Prognosis for r(20)?

Will seizures continue to change?

How will seizures and co-morbidities impact on Quality of Life?

What we do NOW will influence better futures

ring 20
research & support uk

Epi CARE

European Reference Network
for rare or low prevalence complex diseases
Network Epilepsies (ERN EpiCARE)

European Patient Advocacy Group

For more information or if you can help:

email: ring20@ring20researchsupport.co.uk
website: www.ring20researchsupport.co.uk
@Ring20UK
https://www.linkedin.com/company/ring20-research-support-uk