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Epilepsy in Rett syndrome
– from a lifetime perspective

Mari Wold Henriksen
MD/Phd-student
Drammen hospital VVHF/University of Oslo
Norway

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A national survey on females with Rett syndrome in Norway

Main aims:

- Describe the phenotypic variation in the Norwegian Rett Syndrome population, and the development of clinical features in different phases of life.

- Examine which treatment and habilitation strategies offered to this group

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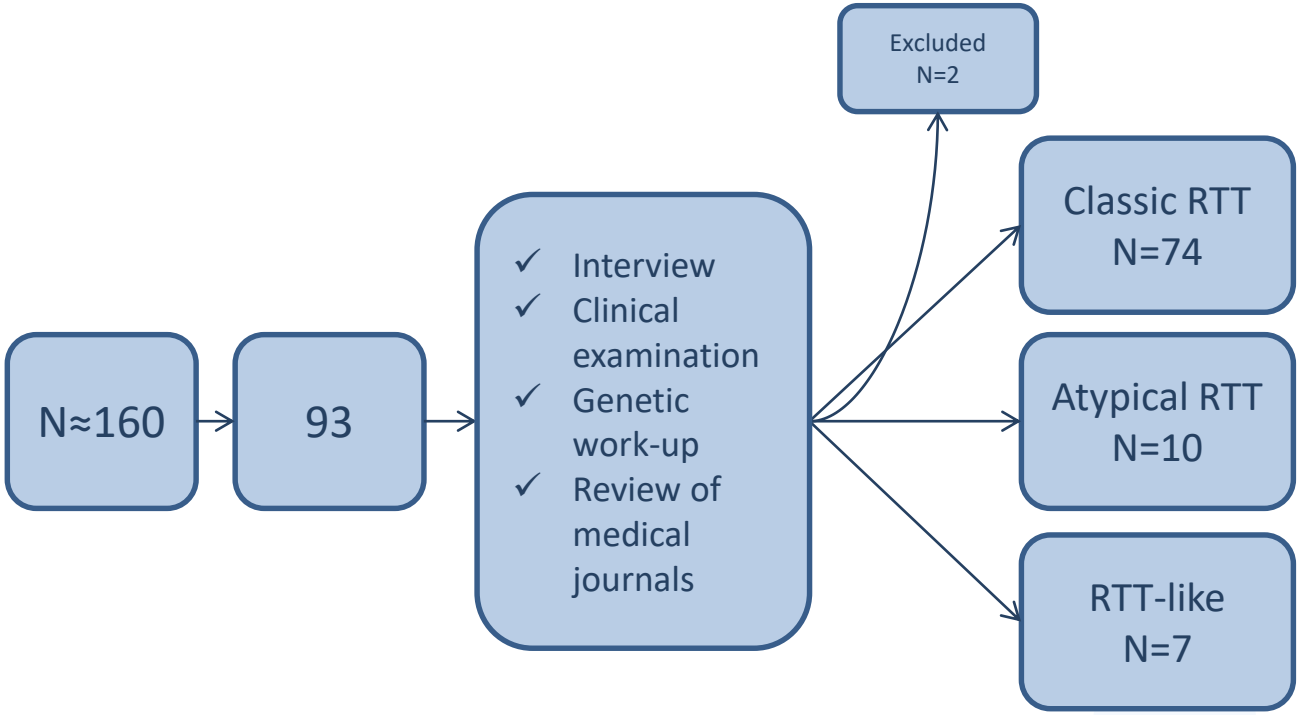
Methods



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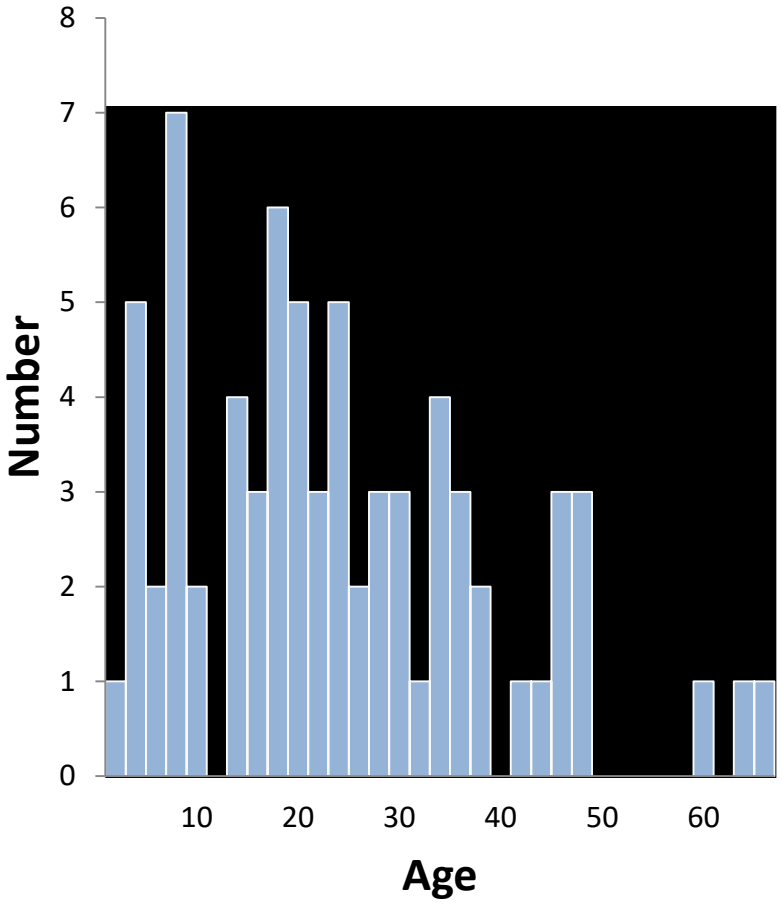

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Epilepsy in Rett Syndrome

Prevalence 70-90%

Seizure onset 3-5 years

Multiple seizure types

Pattern of remission/relapse?

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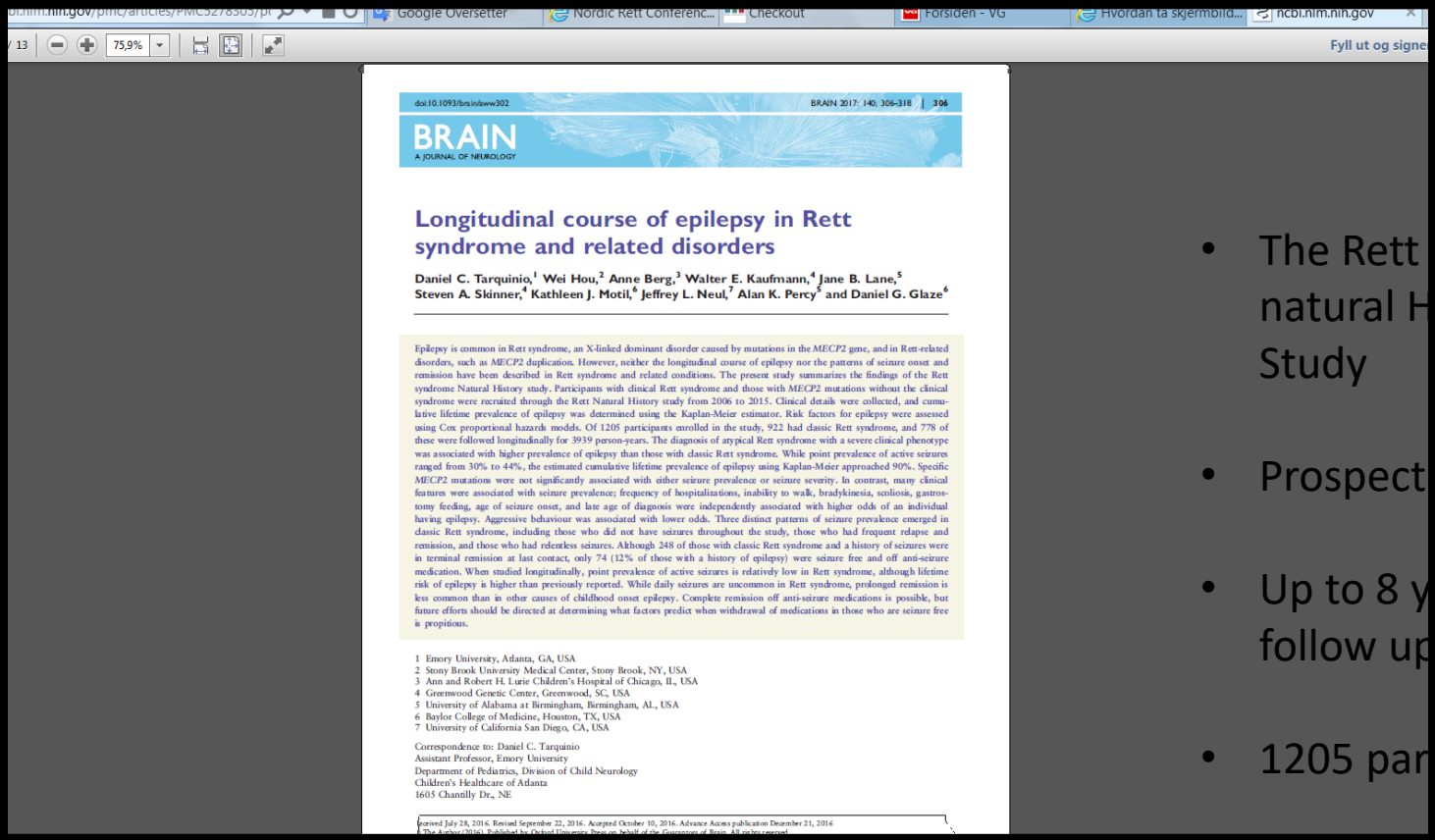

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A JOURNAL OF NEUROLOGY

Longitudinal course of epilepsy in Rett syndrome and related disorders

Daniel C. Tarquinio,[1] Wei Hou,[2] Anne Berg,[3] Walter E. Kaufmann,[4] Jane B. Lane,[5] Steven A. Skinner,[4] Kathleen J. Motil,[6] Jeffrey L. Neul,[7] Alan K. Percy[5] and Daniel G. Glaze[6]

Epilepsy is common in Rett syndrome, an X-linked dominant disorder caused by mutations in the *MECP2* gene, and in Rett-related disorders, such as *MECP2* duplication. However, neither the longitudinal course of epilepsy nor the patterns of seizure onset and remission have been described in Rett syndrome and related conditions. The present study summarizes the findings of the Rett syndrome Natural History study. Participants with clinical Rett syndrome and those with *MECP2* mutations without the clinical syndrome were recruited through the Rett Natural History study from 2006 to 2015. Clinical details were collected, and cumulative lifetime prevalence of epilepsy was determined using the Kaplan-Meier estimator. Risk factors for epilepsy were assessed using Cox proportional hazards models. Of 1205 participants enrolled in the study, 922 had classic Rett syndrome, and 778 of these were followed longitudinally for 3939 person-years. The diagnosis of atypical Rett syndrome with a severe clinical phenotype was associated with higher prevalence of epilepsy than those with classic Rett syndrome. While point prevalence of active seizures ranged from 30% to 44%, the estimated cumulative lifetime prevalence of epilepsy using Kaplan-Meier approached 90%. Specific *MECP2* mutations were not significantly associated with either seizure prevalence or seizure severity. In contrast, many clinical features were associated with seizure prevalence; frequency of hospitalizations, inability to walk, bradykinesia, scoliosis, gastrostomy feeding, age of seizure onset, and late age of diagnosis were independently associated with higher odds of an individual having epilepsy. Aggressive behaviour was associated with lower odds. Three distinct patterns of seizure prevalence emerged in classic Rett syndrome, including those who did not have seizures throughout the study, those who had frequent relapse and remission, and those who had relentless seizures. Although 248 of those with classic Rett syndrome and a history of seizures were in terminal remission at last contact, only 74 (12% of those with a history of epilepsy) were seizure free and off anti-seizure medication. When studied longitudinally, point prevalence of active seizures is relatively low in Rett syndrome, although lifetime risk of epilepsy is higher than previously reported. While daily seizures are uncommon in Rett syndrome, prolonged remission is less common than in other causes of childhood onset epilepsy. Complete remission off anti-seizure medications is possible, but future efforts should be directed at determining what factors predict when withdrawal of medications in those who are seizure free is propitious.

1 Emory University, Atlanta, GA, USA
2 Stony Brook University Medical Center, Stony Brook, NY, USA
3 Ann and Robert H. Lurie Children's Hospital of Chicago, IL, USA
4 Greenwood Genetic Center, Greenwood, SC, USA
5 University of Alabama at Birmingham, Birmingham, AL, USA
6 Baylor College of Medicine, Houston, TX, USA
7 University of California San Diego, CA, USA

Correspondence to: Daniel C. Tarquinio
Assistant Professor, Emory University
Department of Pediatrics, Division of Child Neurology
Children's Healthcare of Atlanta
1605 Chantilly Dr., NE

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- The Rett [illegible]ome natural H[illegible] Study
- Prospect[illegible]hort
- Up to 8 y[illegible] follow up
- 1205 par[illegible]nts

Aged 3 months-66 years

Pattern of remission/relapse?

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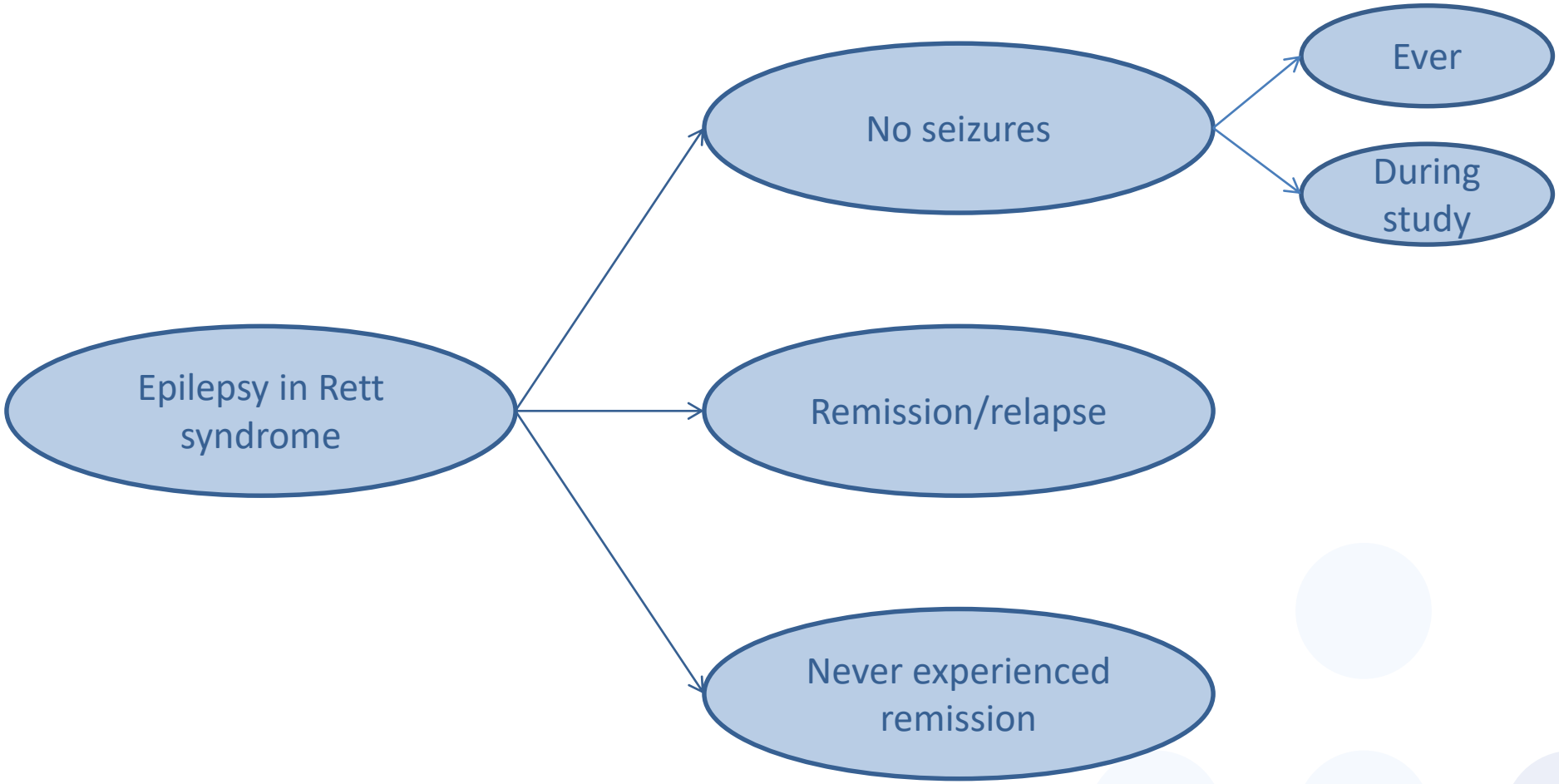

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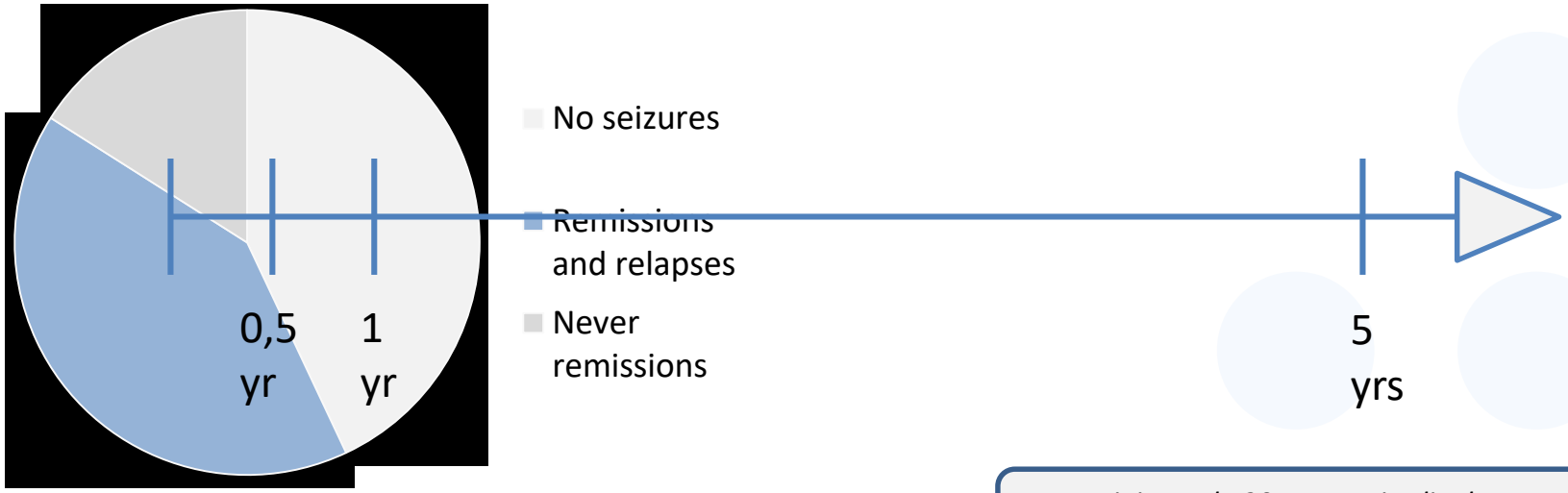
- Average duration 1 year
- 7% ≥ five years

- 41% of study population

Remission/relapse



Tarquinio et al., 2017. Longitudinal course of epilepsy in Rett syndrome and related disorders, Brain 140, 306-318

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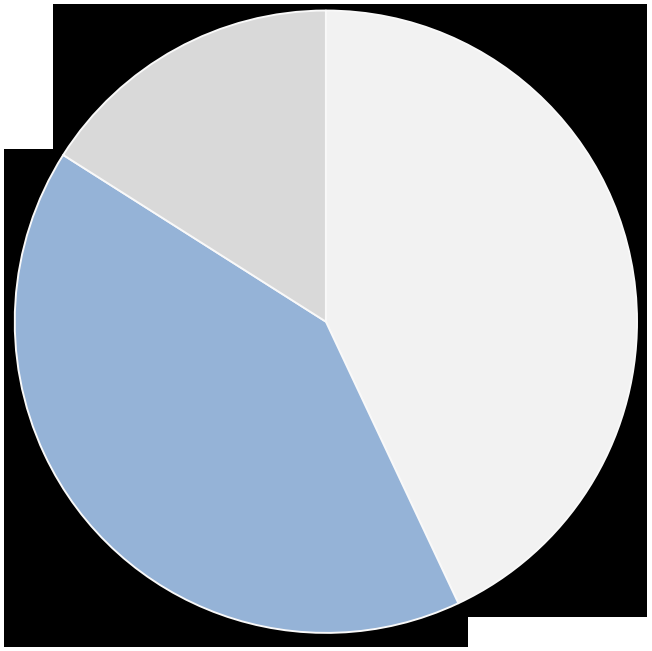
Tarquinio et al.

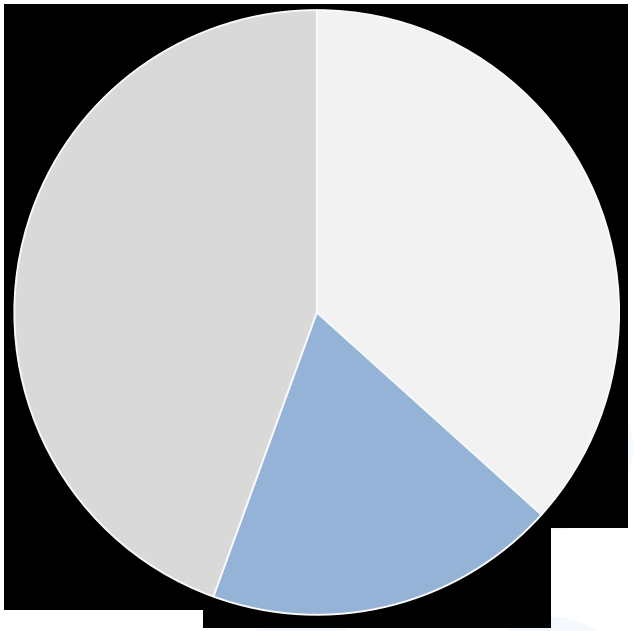


No seizures

Remissions and relapses

Never remissions

Henriksen et al.



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Epilepsy in Rett Syndrome

Prevalence 70-90%

Seizure onset 3-5 years

Multiple seizure types

Better with increasing age

Pattern of remission/relapse?

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Aim:

To describe the course and characteristics of epilepsy in adults with Rett syndrome

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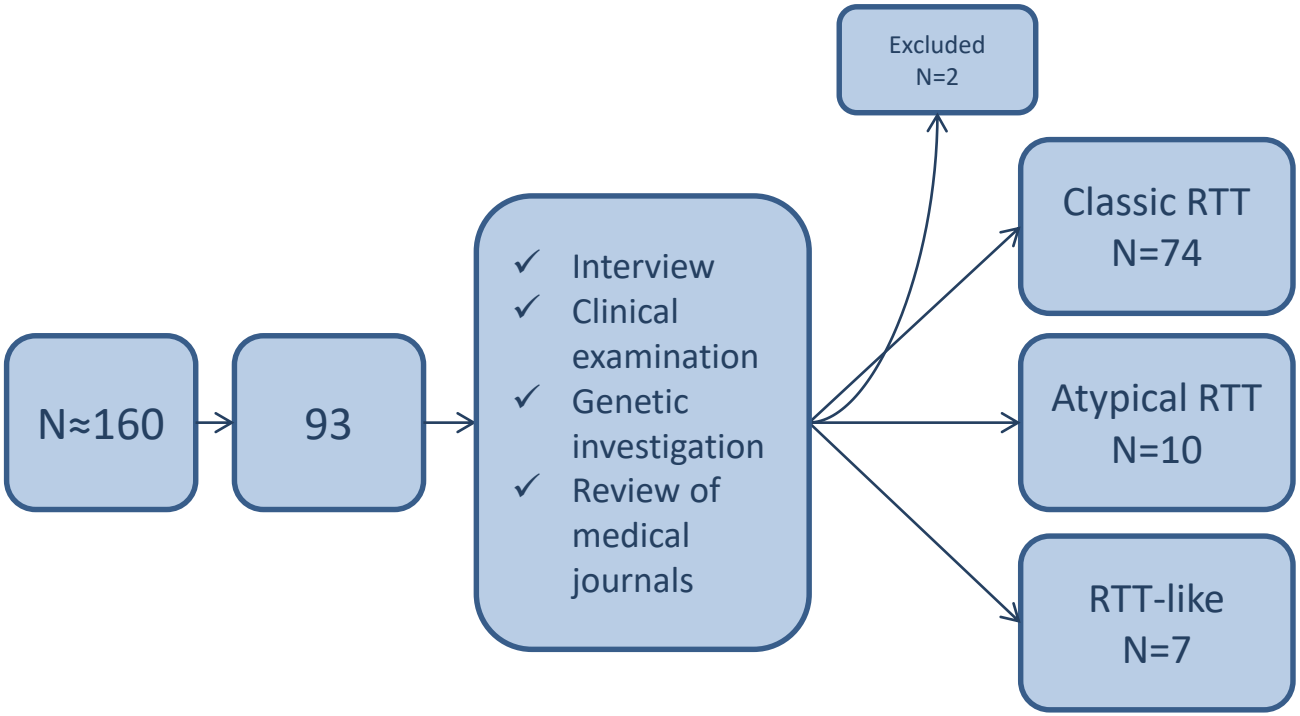

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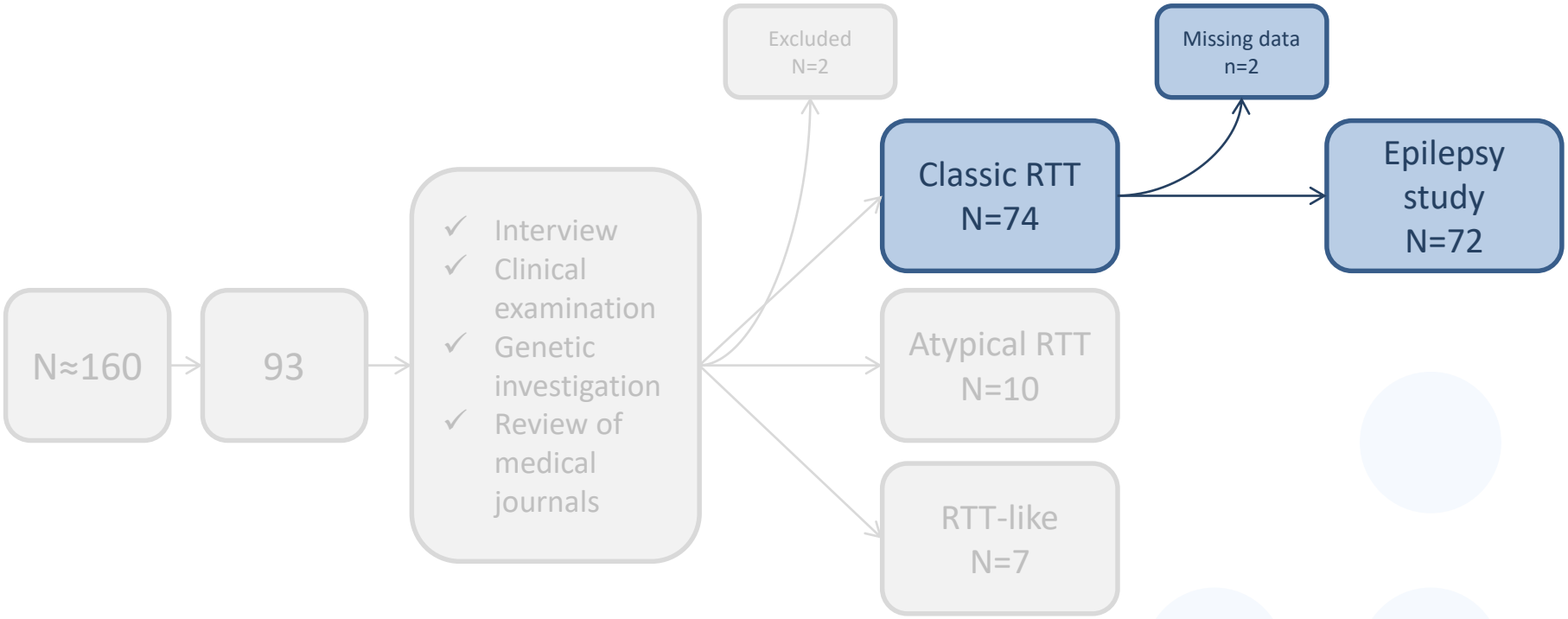

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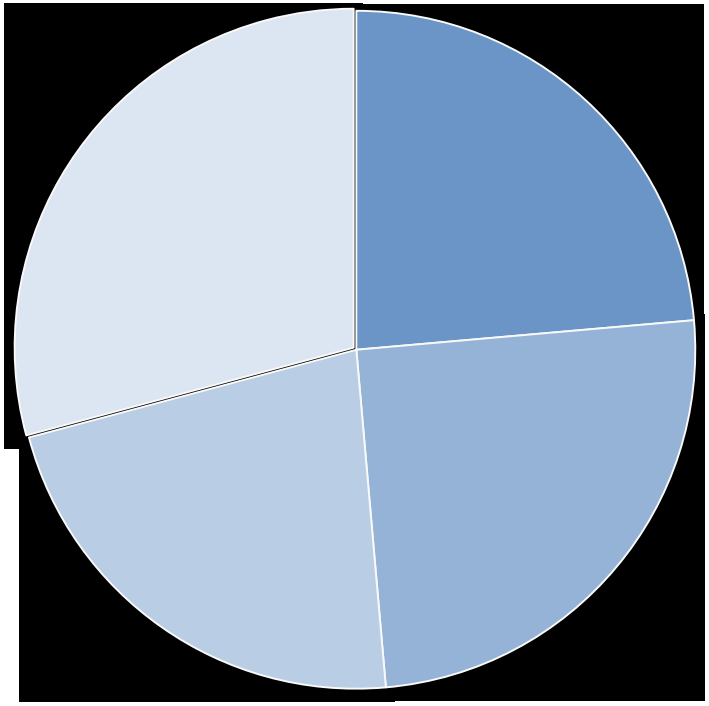
Age



Epilepsy study
N=72

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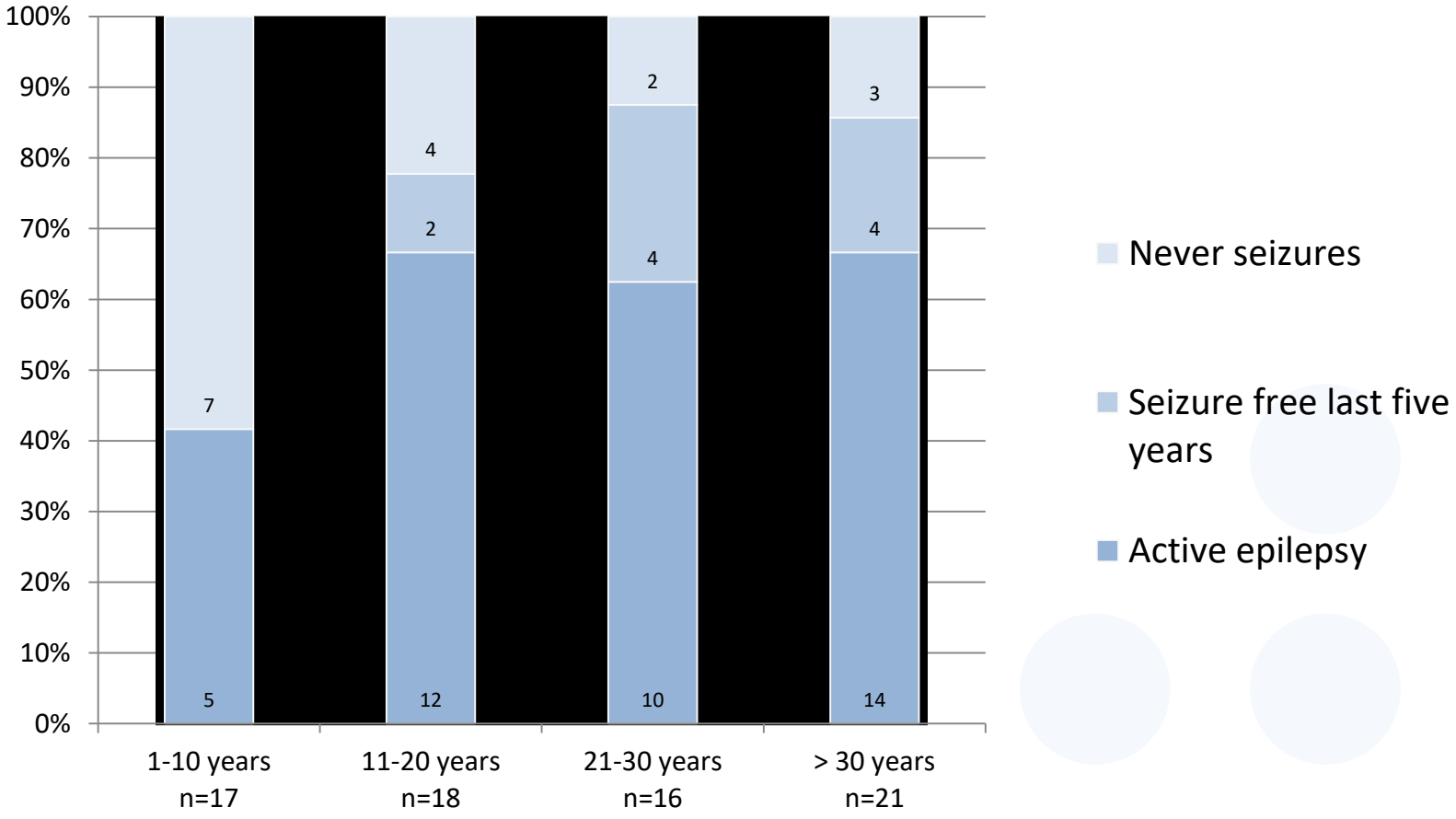
Results

Prevalence of active epilepsy



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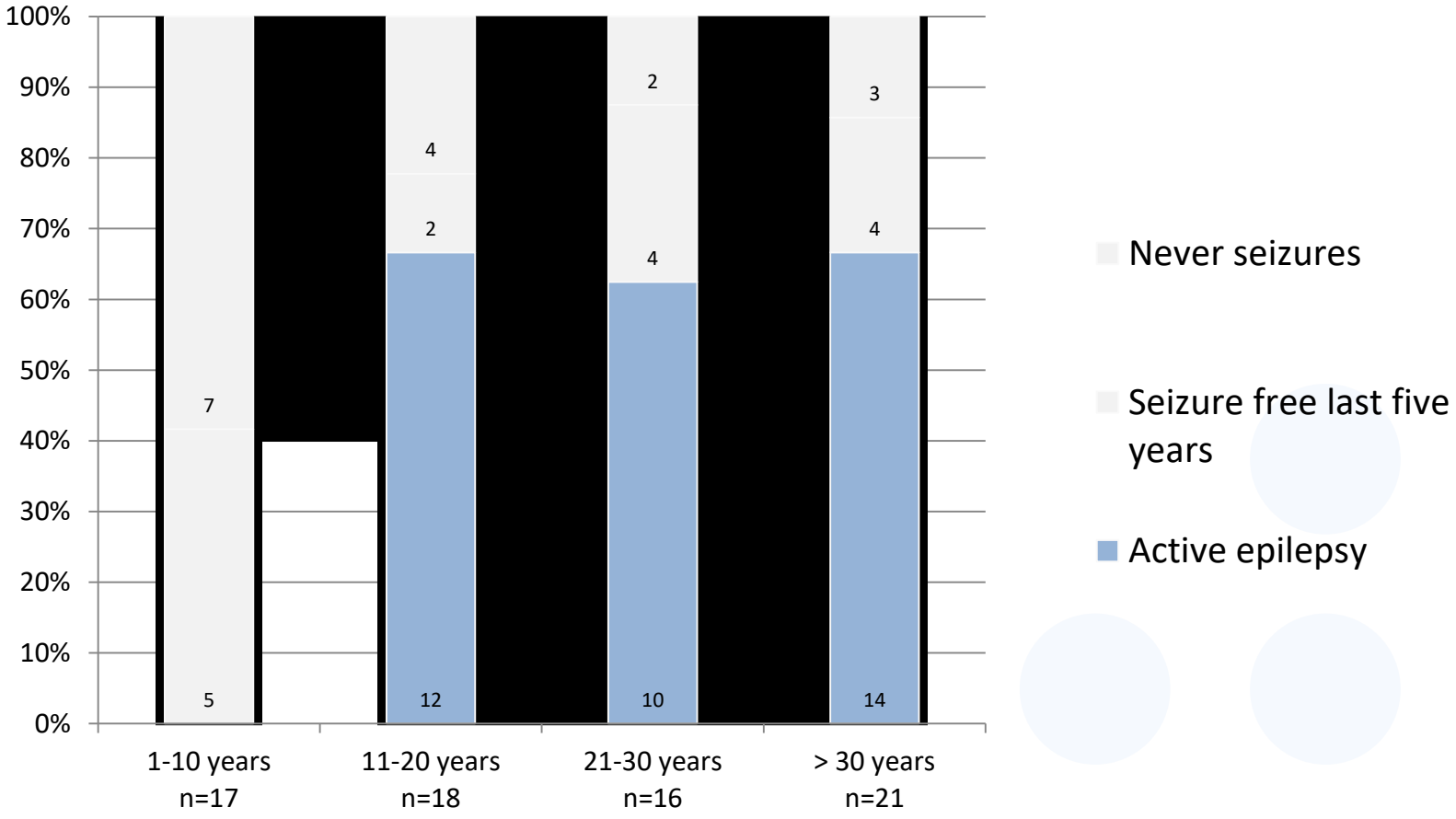
Results

Prevalence of active epilepsy



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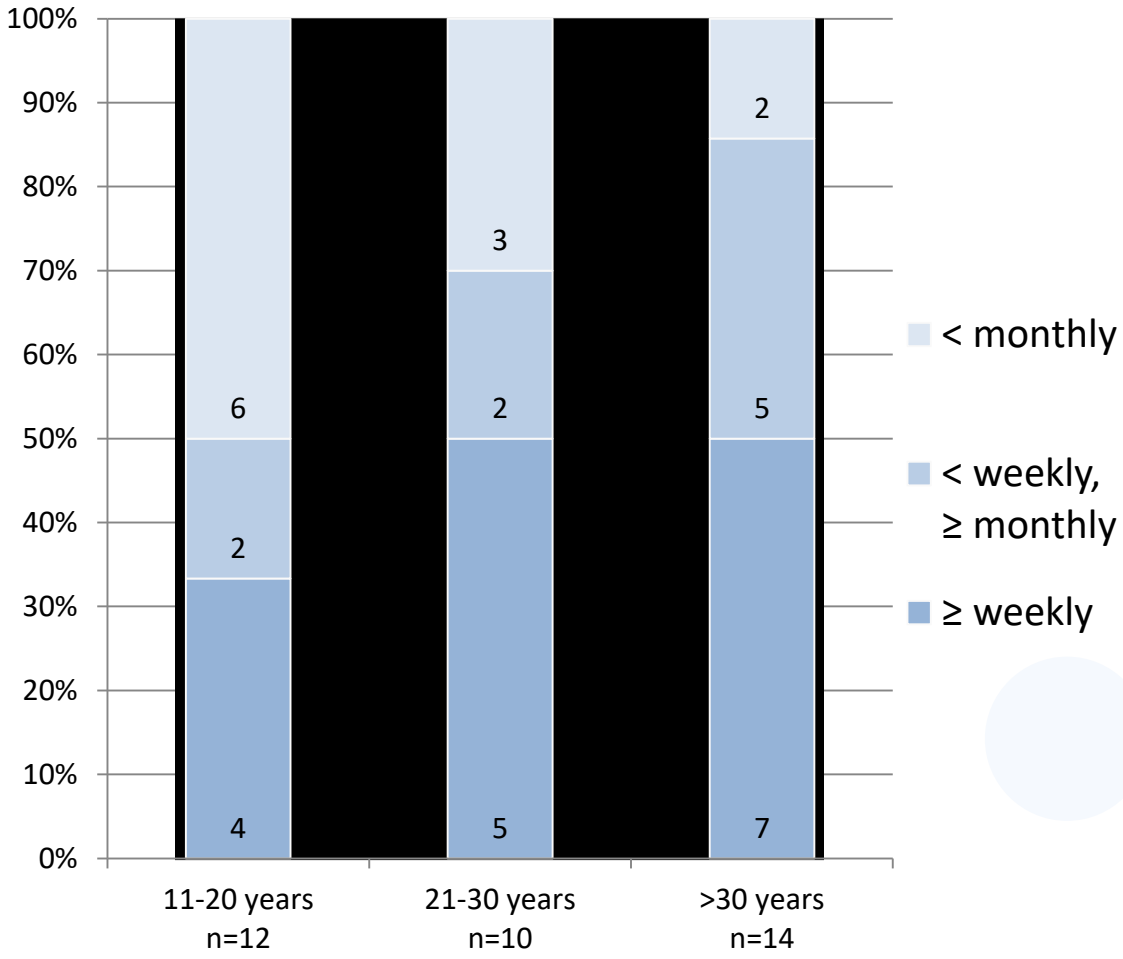
Results

Frequency of seizures



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Results

Seizure types

	N	Bilateral tonic-clonic seizures N(%)
11-20 years	12	7 (58)
21-30 years	10	7 (70)
> 30 years	14	9 (64)

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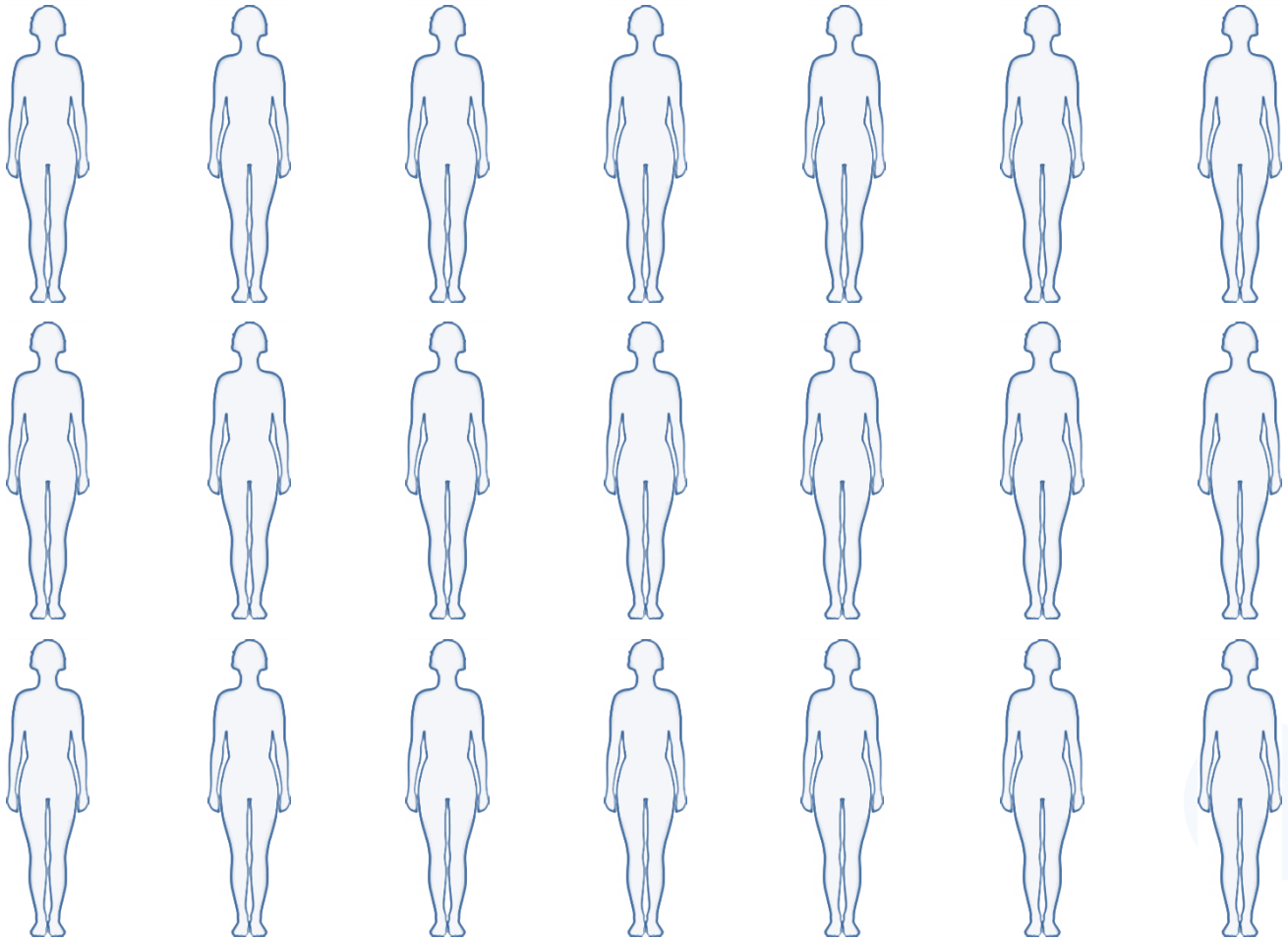

Women >30 years

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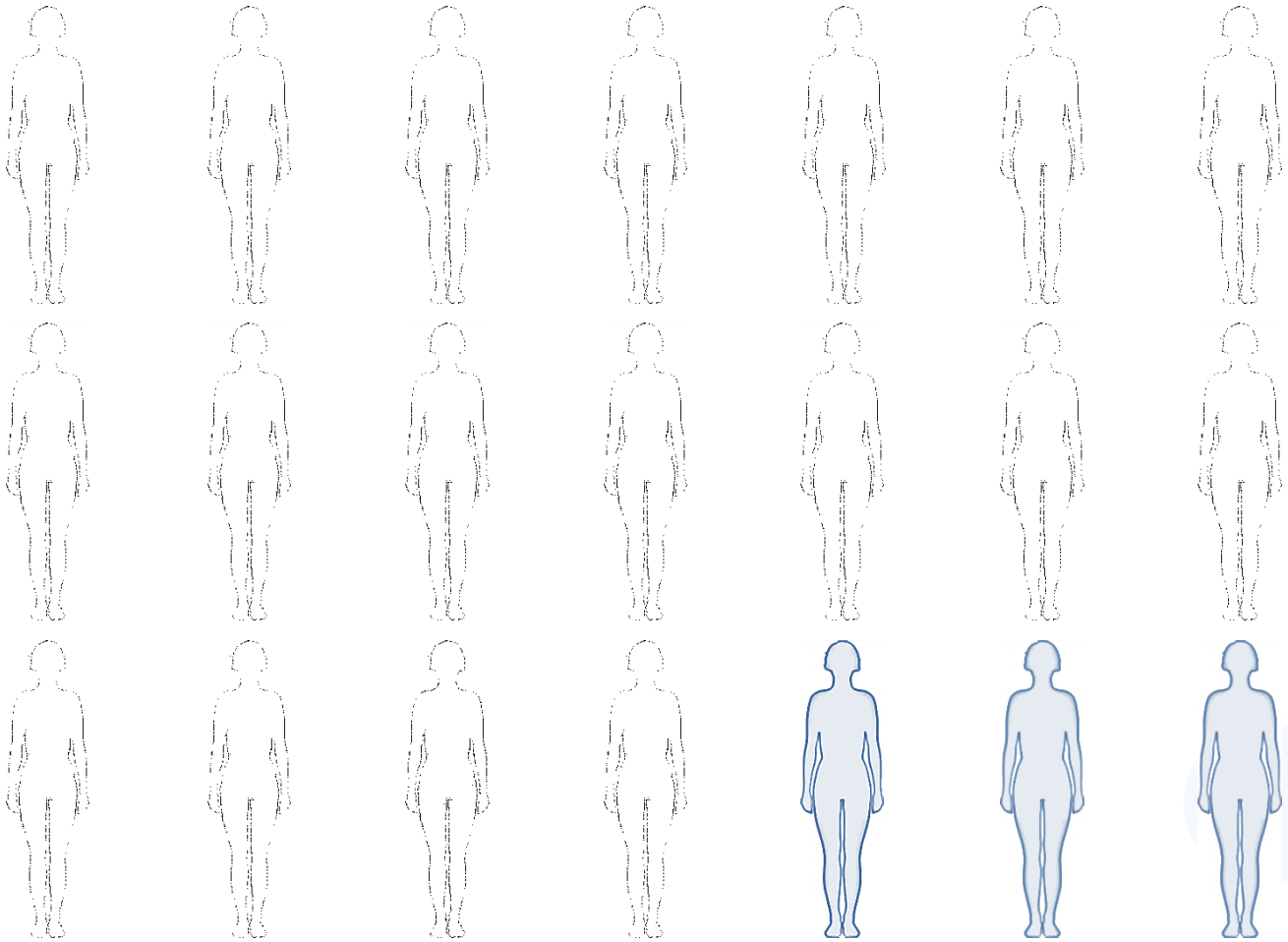
Never seizures



Women >30 years

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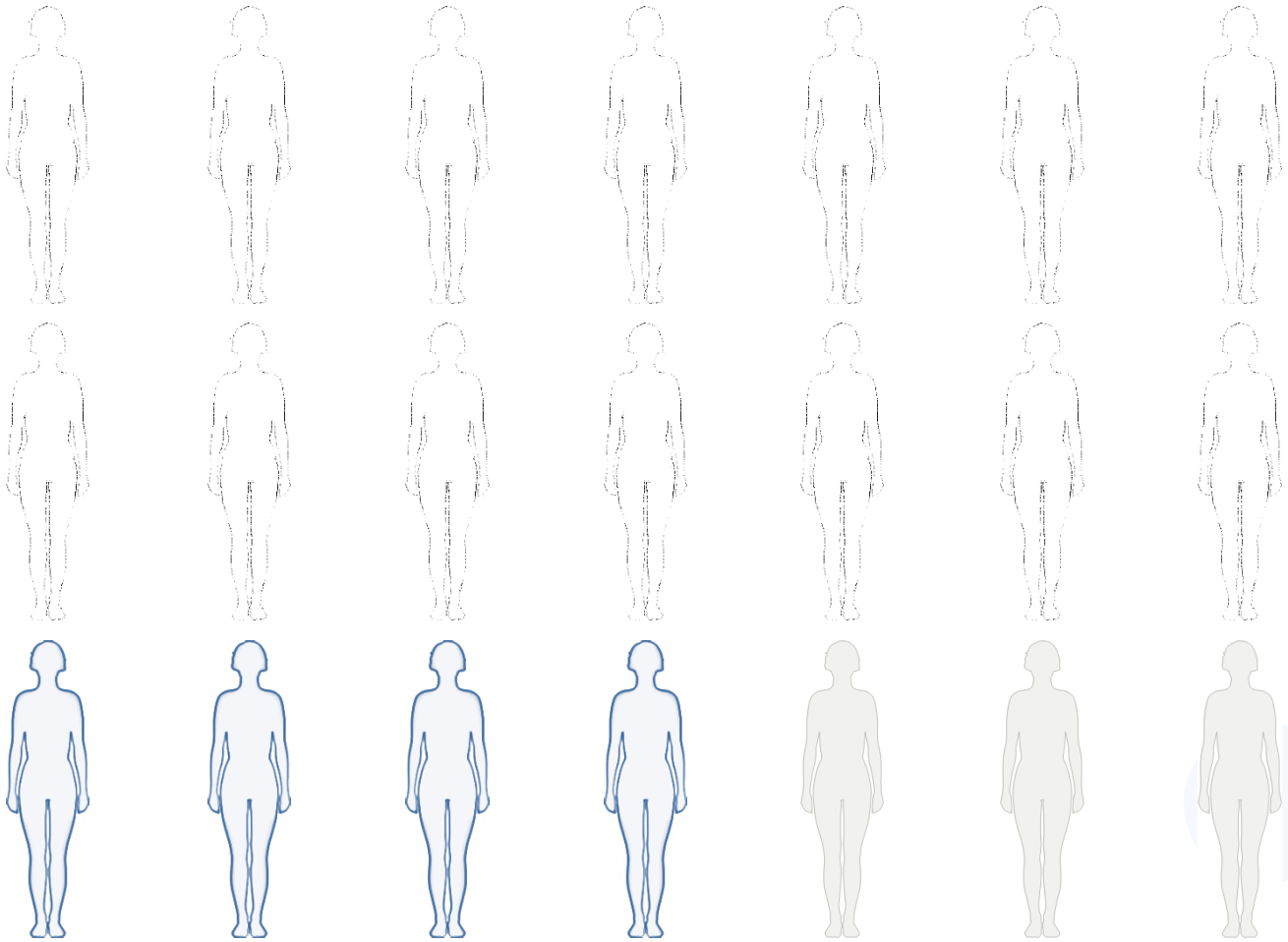
Seizure free last 5 years



Women >30 years

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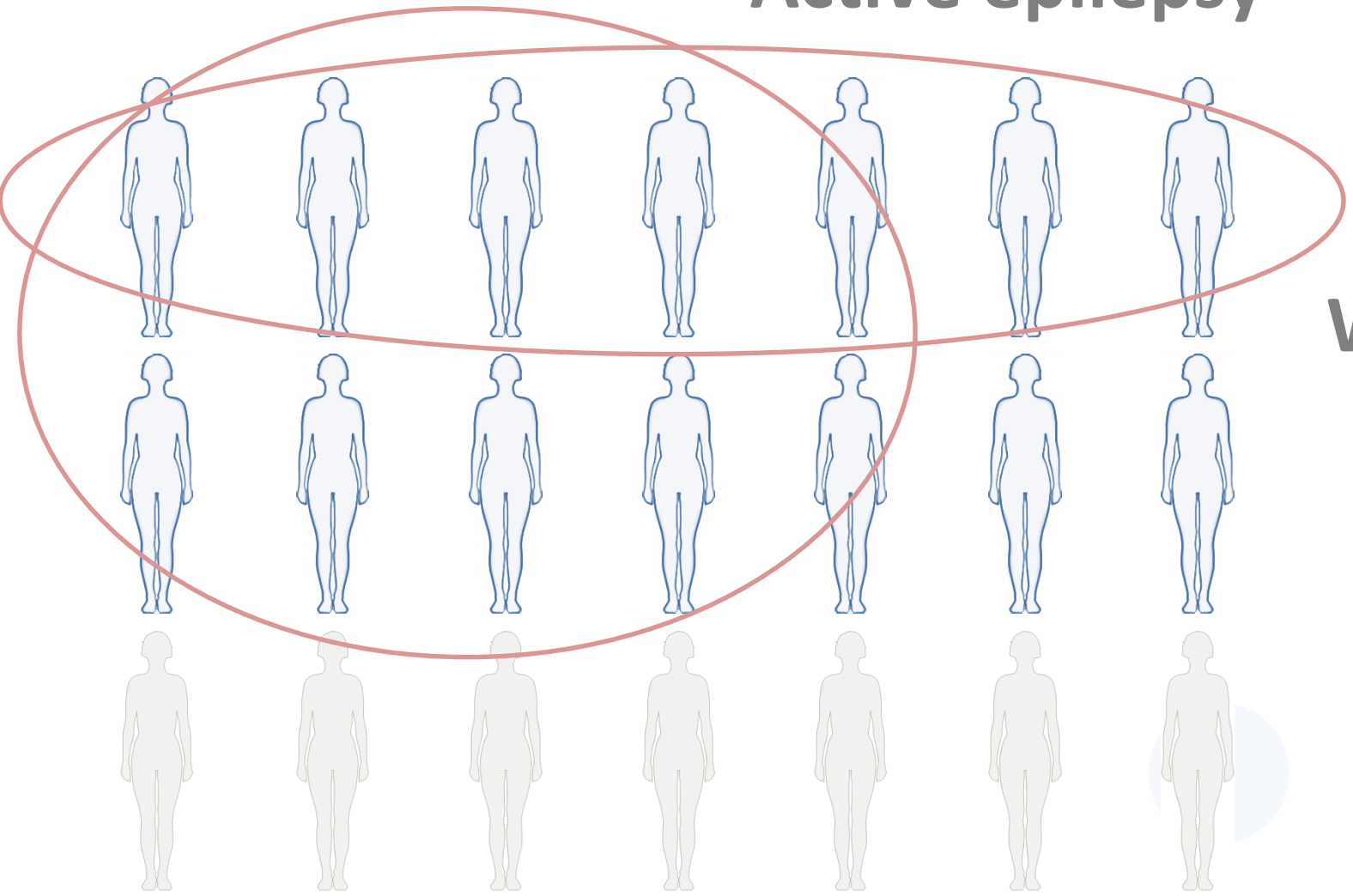
Active epilepsy



Women >30 years

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Conclusion

- Many will experience a pattern of remissions and relapses
- Epilepsy is still a major concern in many adults with Rett syndrome

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