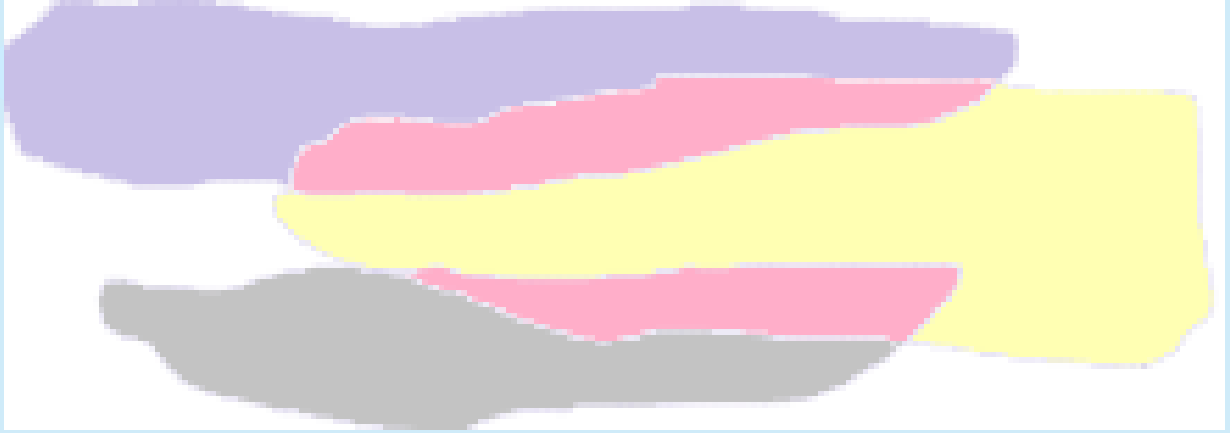


Rett syndrome from childhood to old age

RETT SYNDROME IN NORDIC LIGHT
Stockholm 19-20 April 2018

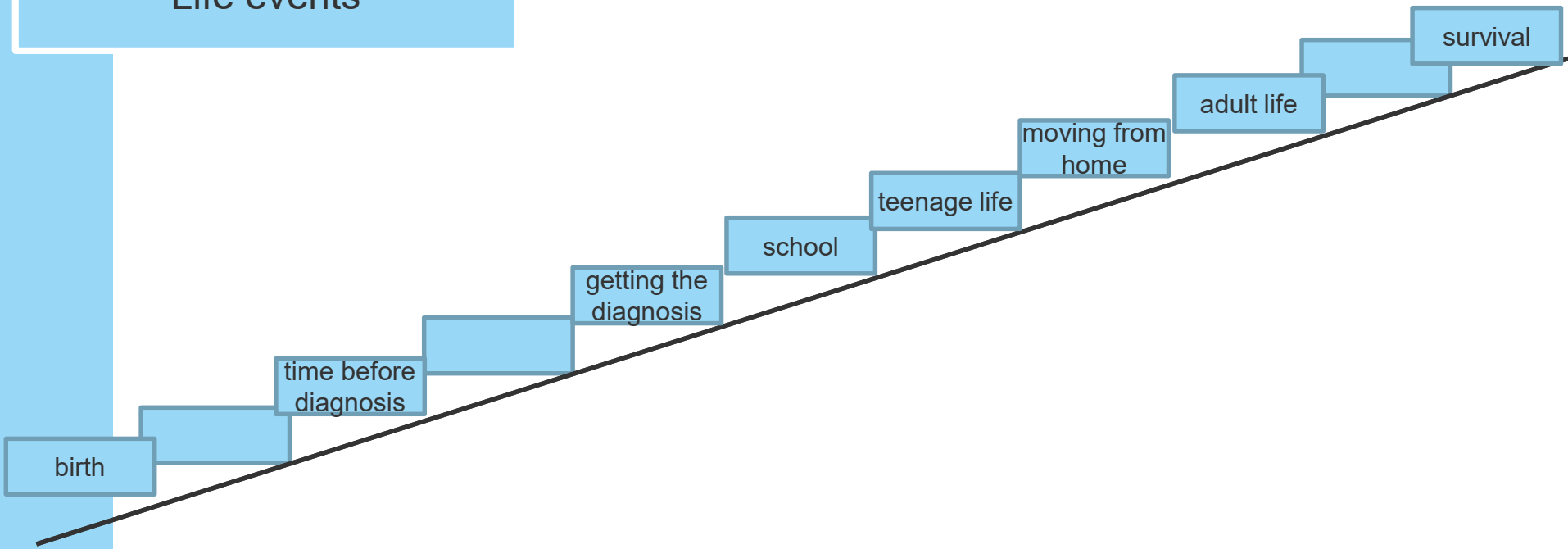
Nordic Rett Conference – Research and Practice

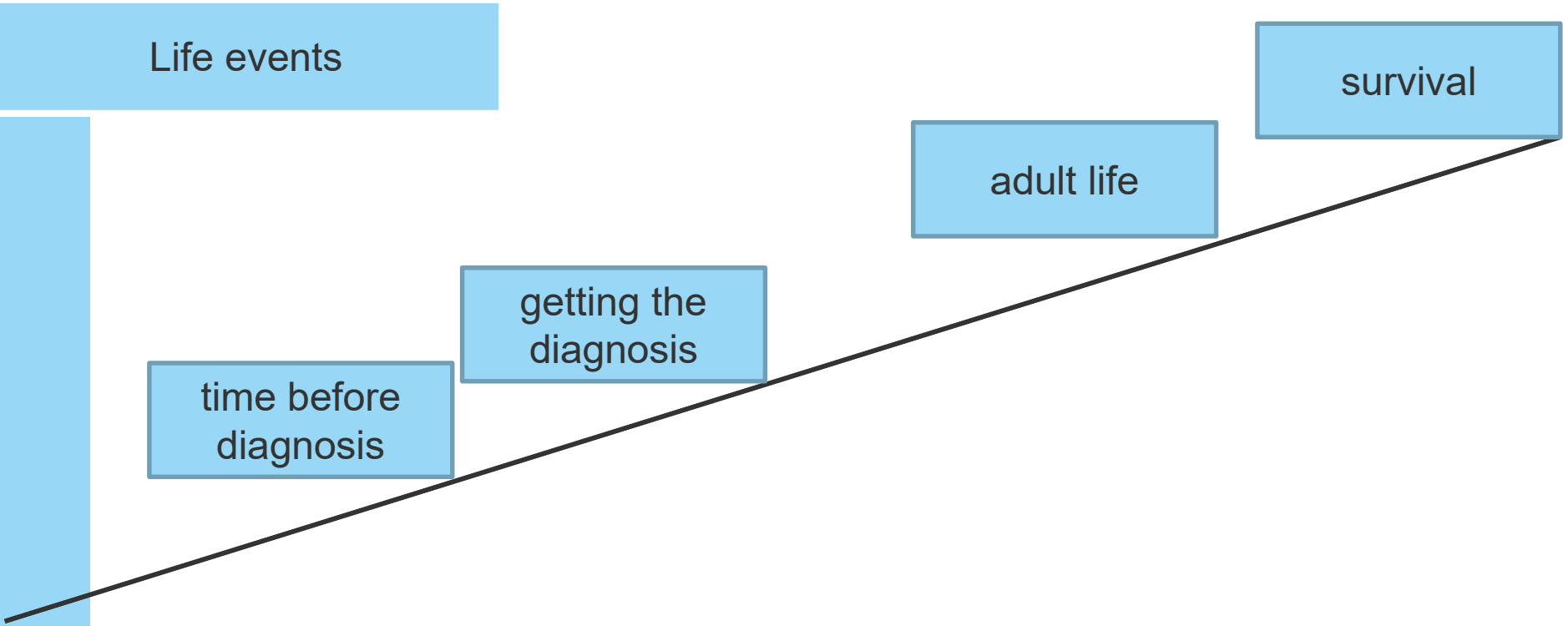
Anne-Marie Bisgaard, M.D., PhD
Center for Rett syndrome, Kennedy Center
Department of Paediatrics and Adolescent Medicine,
Rigshospitalet, Copenhagen, Denmark

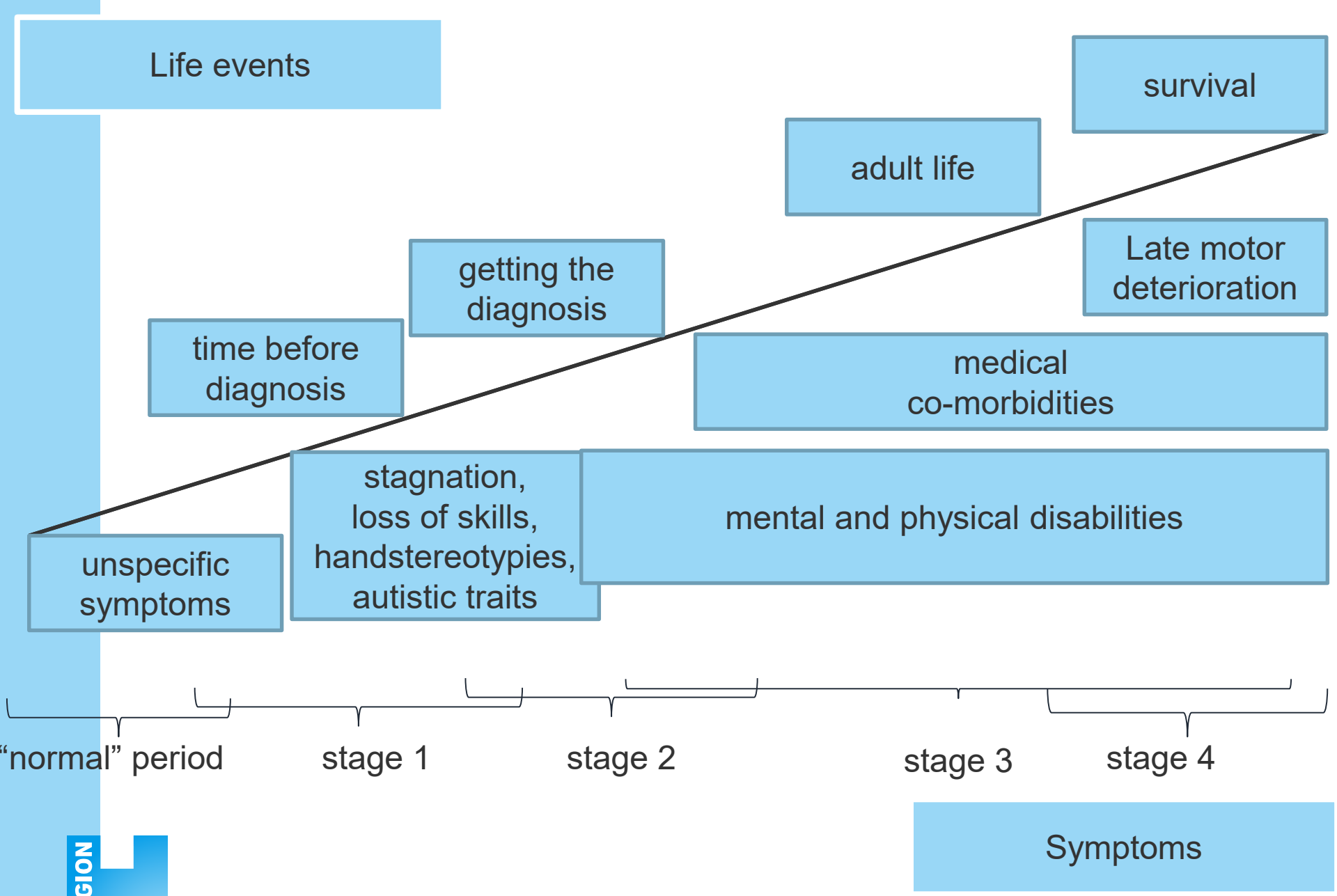
We are here to make the pieces fit together

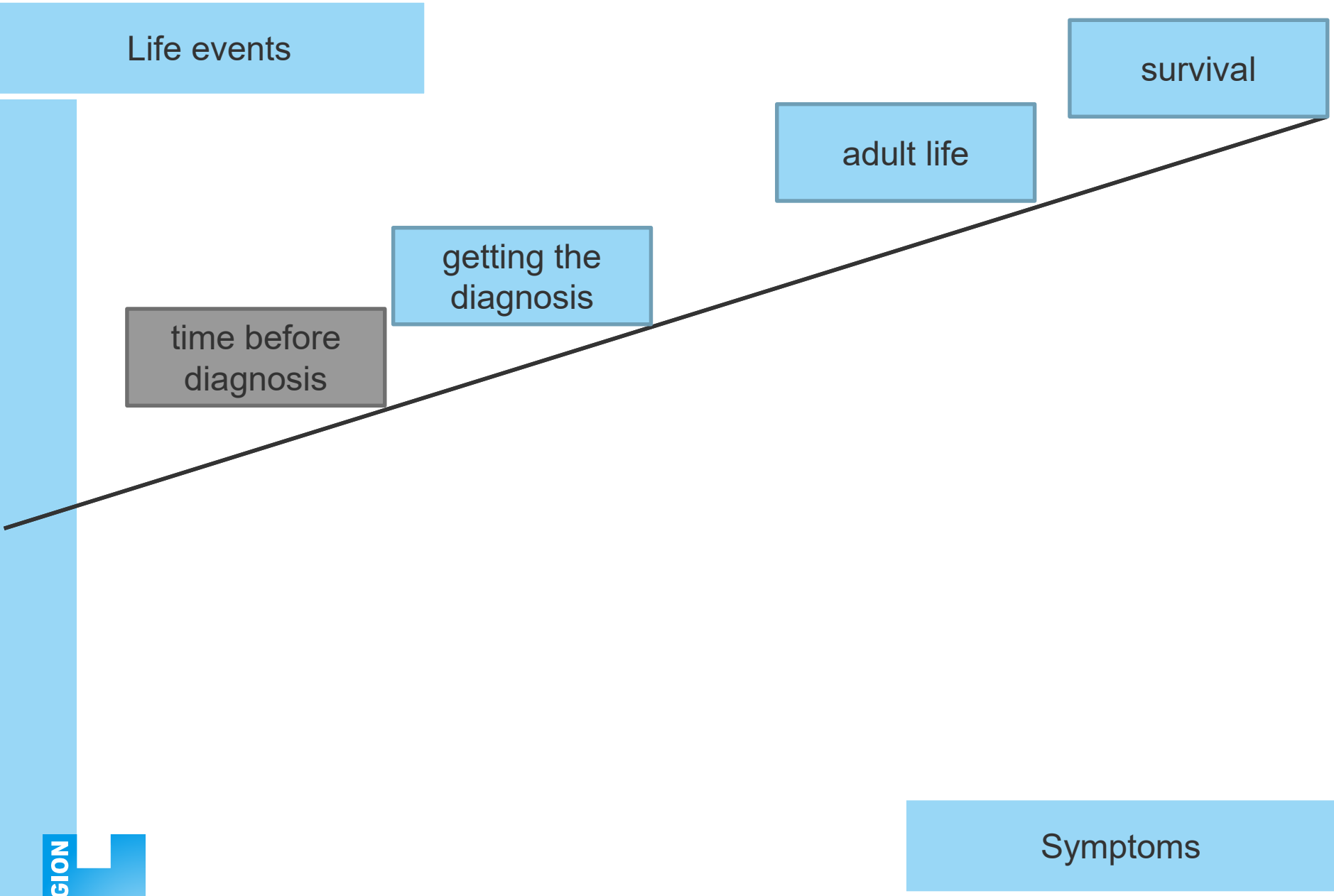
- to improve the quality of life for the child, adult and family
  - diagnose as soon as possible
  - provide the best counselling and treatment tailored the individual
    - medical issues
    - habilitation, special equipment/aids
    - communication (alternative)
    - participation in everyday life and social life
    - etc.
  - lifelong care planning

Life events


birth
time before diagnosis
getting the diagnosis
school
teenage life
moving from home
adult life
survival


Life events
time before diagnosis
getting the diagnosis
adult life
survival


Life events
survival
adult life
Late motor deterioration
getting the diagnosis
time before diagnosis
medical co-morbidities
stagnation, loss of skills, handstereotypies, autistic traits
mental and physical disabilities
unspecific symptoms
“normal” period
stage 1
stage 2
stage 3
stage 4
Symptoms


Life events
survival
adult life
getting the diagnosis
time before diagnosis
Symptoms

Life events

time before diagnosis

We use to say that development is apparently normal in the first 6 -18 months of life

Studies have, however, showed that early development might be delayed before the onset of classical symptoms and there might be some other concerns

Symptoms

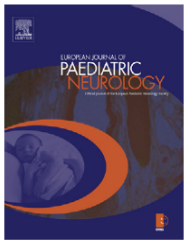
Life events

time before diagnosis

EUROPEAN JOURNAL OF PAEDIATRIC NEUROLOGY XXX (2015) 1–9

ELSEVIER

Official Journal of the European Paediatric Neurology Society



Original article

Is it possible to diagnose Rett syndrome before classical symptoms become obvious? Review of 24 Danish cases born between 2003 and 2012

Anne-Marie Bisgaard [a,*], *Bitten Schönewolf-Greulich* [a], *Kirstine Ravn* [b], *Gitte Rønde* [c]

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[b] *Molecular Genetic Laboratory, Department of Clinical Genetics, 4062, Rigshospitalet, University of Copenhagen, Blegdamsvej 9, 2100 Copenhagen Ø, Denmark*

[c] *Department of Paediatrics, Roskilde Hospital, University of Copenhagen, Køgevej 7-13, 4000 Roskilde, Denmark*

Symptoms

Life events

time before diagnosis

24 girls born in 2003-2014 with a *MECP2* mutation

- reviews of medical files and questionnaires from parents
  - regarding early development and symptoms
  - parents concerns before the diagnosis
  - severity scoring

Age of diagnosis ranged from 15 months to 5.3 years (mean 2½ years)

Parents were concerned from 3 months to 4.8 years (mean 1½ years)

Symptoms

time before diagnosis

Symptoms in the “normal” period:

- The majority of girls had combinations of concerning symptoms such as developmental delay and a collection of subtle signs such as

Specific RTT symptoms
- abnormal hand movements and hand skills
- less or poor social interaction
- being quiet and easy to please

Unspecific symptoms
- floppiness, hypermobility
- hair pulling
- teeth grinding
- gastroesofageal refluks/vomiting
- squint

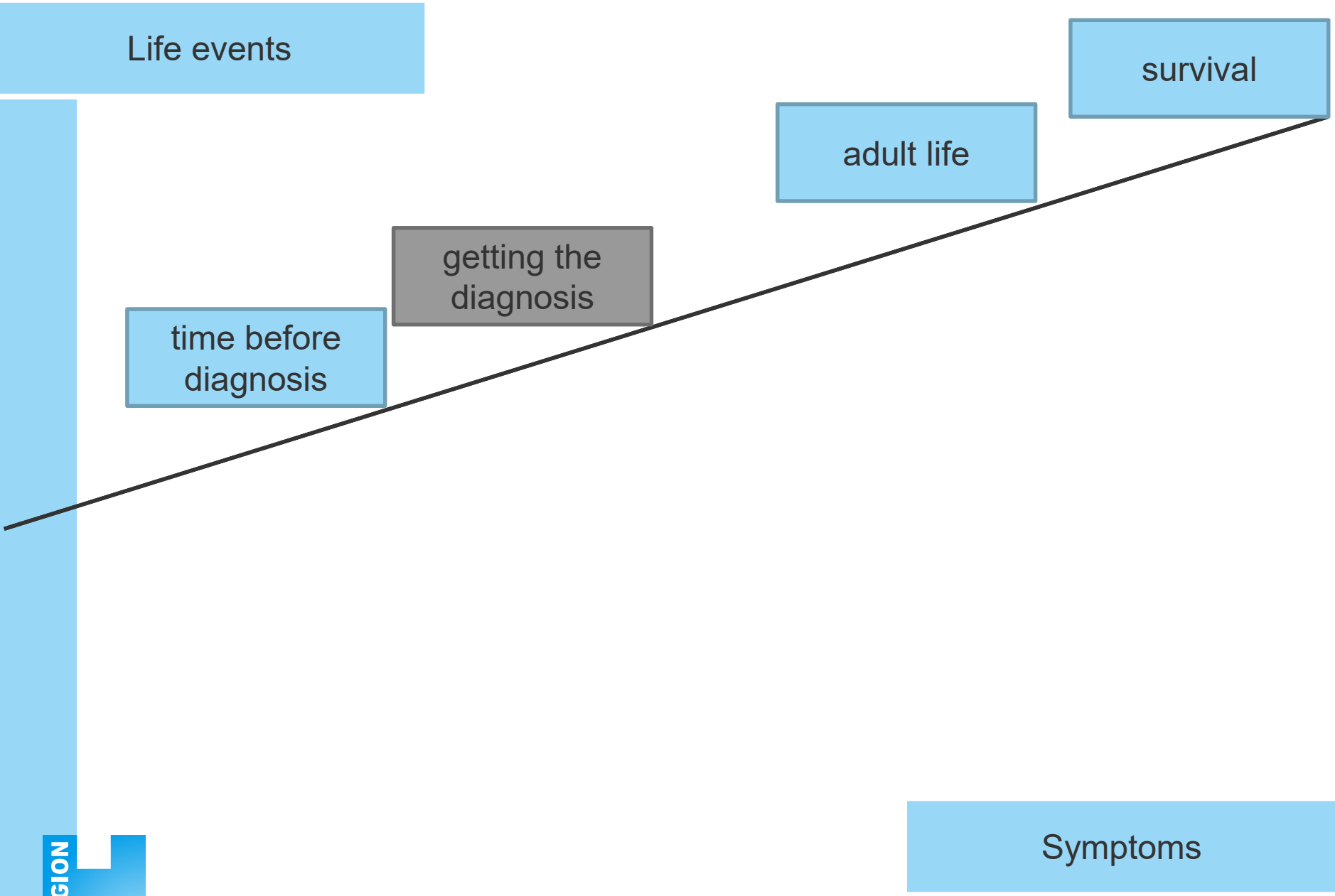
Symptoms

Life events

time before diagnosis

- 29% (7 girls) were referred to psychiatric department on suspicion of autism
  two of them got an autism diagnosis
- 29% (7 girls) were investigated for muscular or mitochondrial disease

Symptoms


Life events
survival
adult life
getting the diagnosis
time before diagnosis
Symptoms

Life events

getting the diagnosis

- The majority of girls get the diagnosis when the classical Rett-symptoms are obvious (Fehr S, 2010; Tarquinio D et al, 2015)

- Our study
  - mutation analysis was done in 87.5% because of regression and hand stereotypies
  - the diagnosis was mainly suspected by a neuropaediatrician (and child psychiatrist/psychologist, ophthalmologist and parents (3))

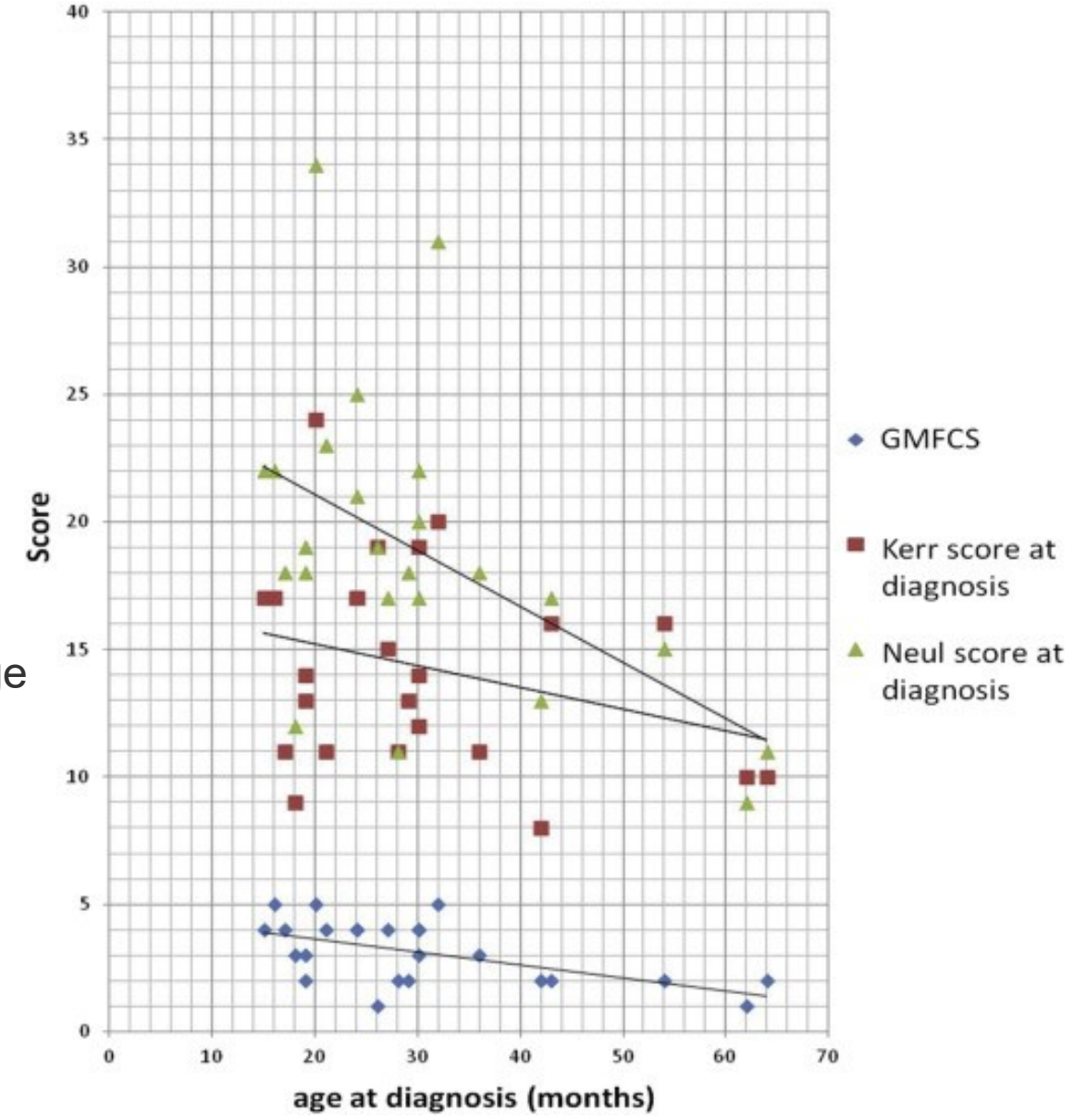
Parents' description of the diagnosis

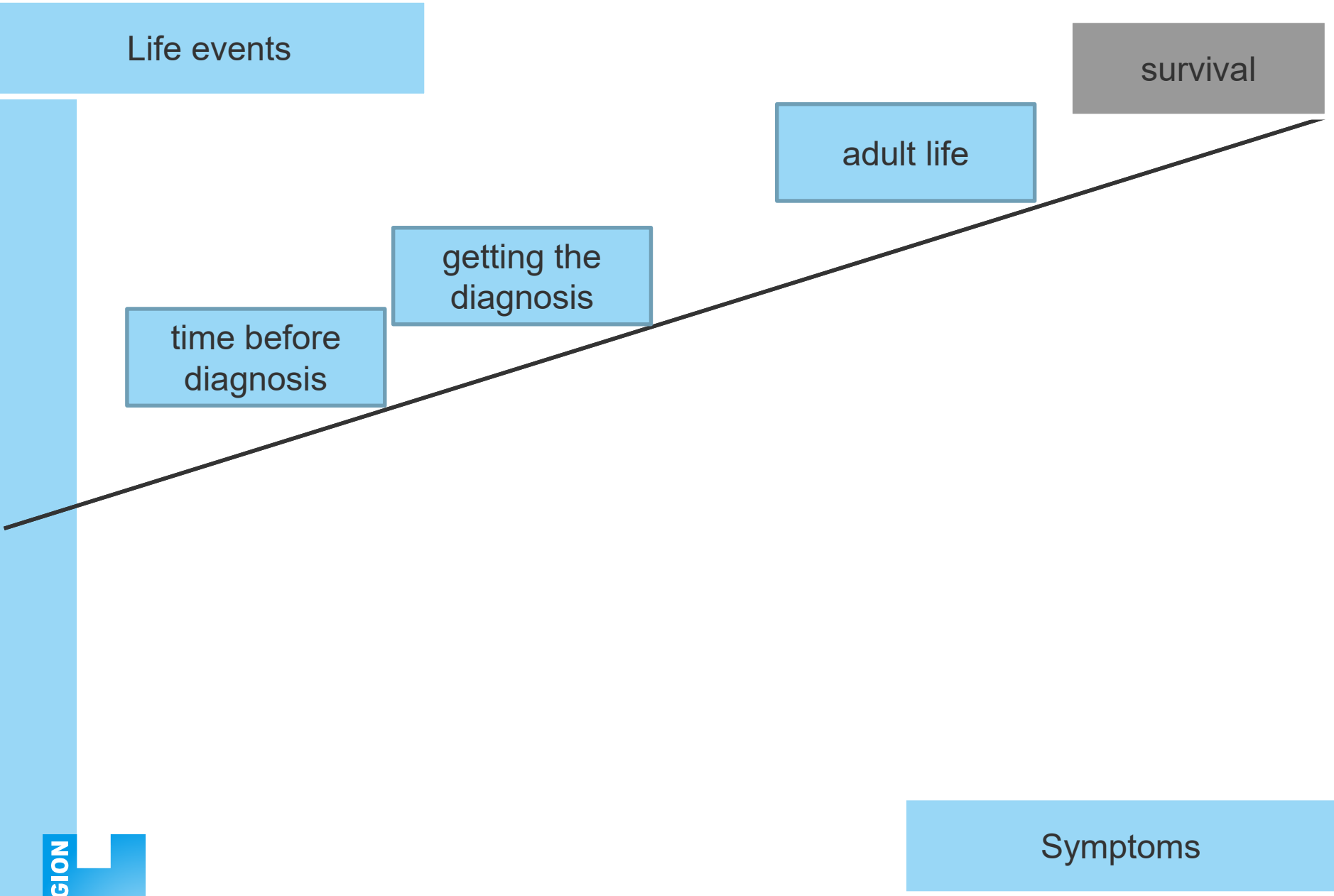
Symptoms

The more severe

the younger age at diagnosis

We have to acknowledge the more subtle and unspecific symptoms




Life events
survival
adult life
getting the diagnosis
time before diagnosis
Symptoms

DMCN Developmental Medicine & Child Neurology

Free Access

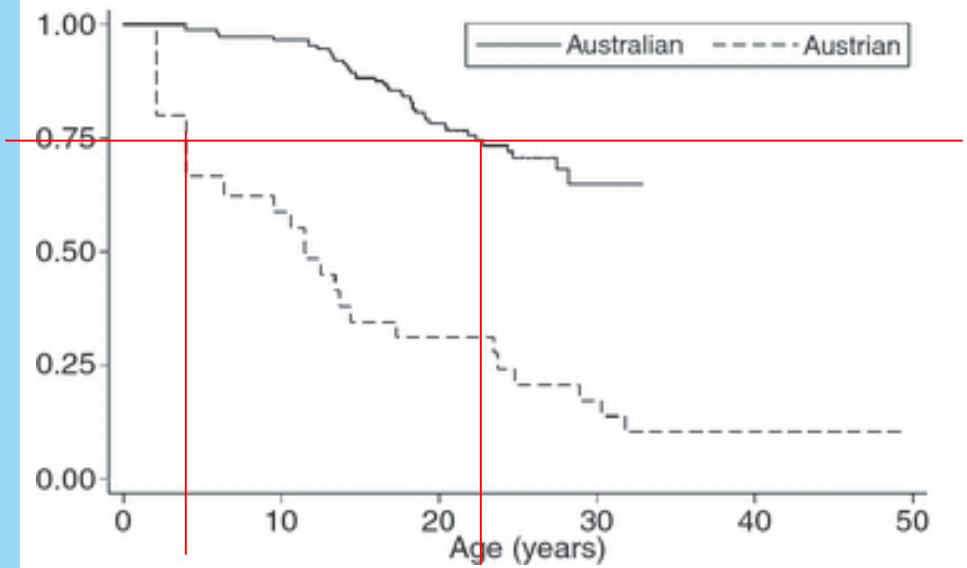
Survival with Rett syndrome: comparing Rett's original sample with data from the Australian Rett Syndrome Database

MICHAEL FREILINGER, AMI BEBBINGTON, INES LANATOR, NICK De KLERK, DANIELA DUNKLER, RAINER SEIDL, HELEN LEONARD, GABRIEL M RONEN

First published: 6 September 2010
| https://doi-org.ep.fjernadgang.kb.dk/10.1111/j.1469-8749.2010.03716.x | Cited by:20

The probability of survival
up to the age of 25 years was 21%,
compared with 71% in the Australian cohort

Survival in Rett syndrome has changed



- Austrian cohort - 22
  - born 1954-1964
    - 3 women alive (48, 48, 49 y)
- Australian cohort - 332
  - born from 1976

Published in final edited form as:
Pediatr Neurol. 2015 November ; 53(5): 402–411. doi:10.1016/j.pediatrneurol.2015.06.003.

The changing face of survival in Rett syndrome and *MECP2*-related disorders

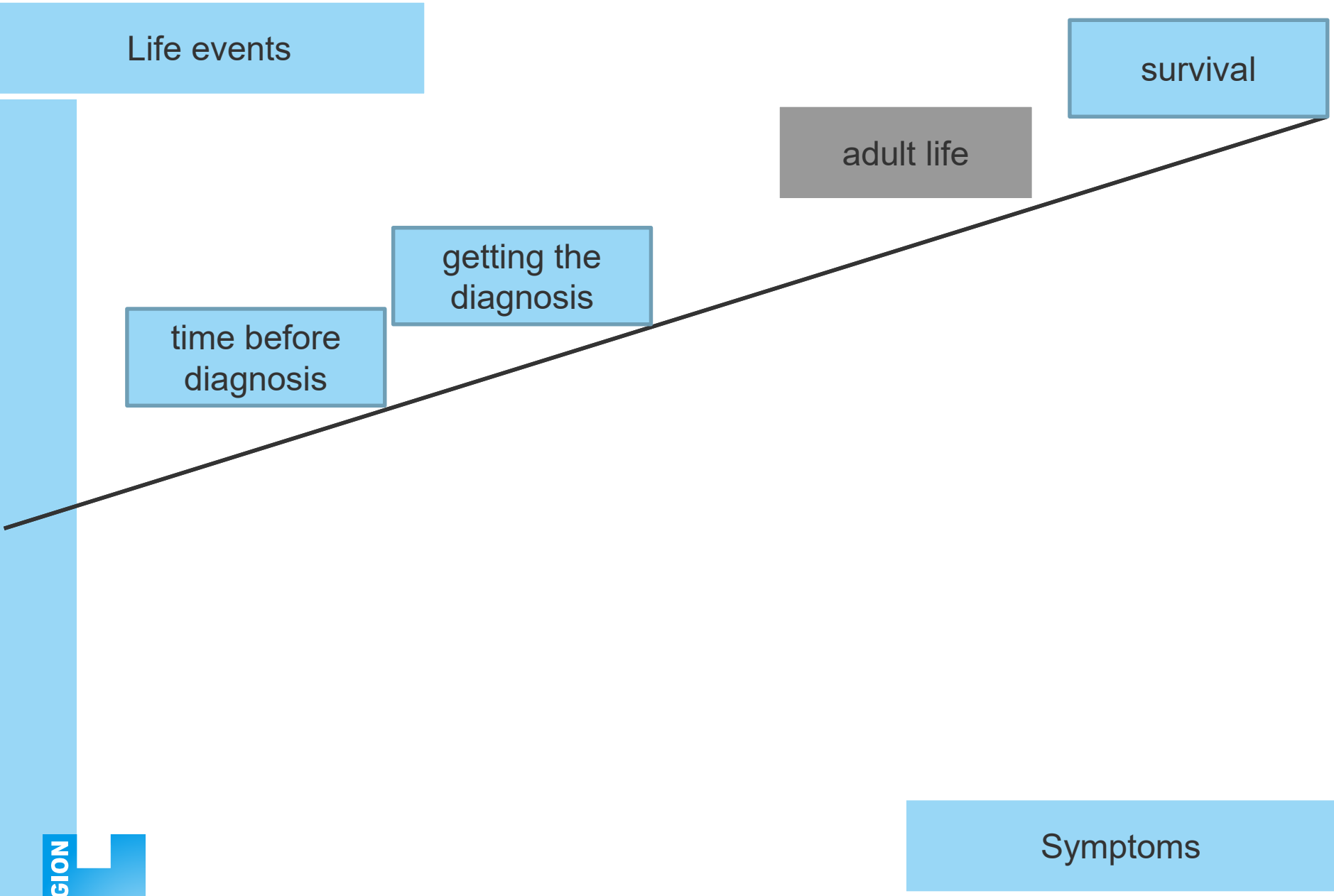
Daniel C. Tarquinio, DO[1], **Wei Hou, PhD**[2], **Jeffrey L. Neul, MD, PhD**[3], **Walter E. Kaufmann, MD, PhD**[4], **Daniel G. Glaze, MD**[3], **Kathleen J. Motil, MD, PhD**[3], **Steven A. Skinner, MD**[5], **Hye-Seung Lee, PhD**[6], and **Alan K. Percy, MD**[7]

- Survival for classic and atypical RTT was greater than 70% at 45 years (>1000 participants)
- Causes of death have changed
    - In the past: poor health and nutrition
    - Now: cardio-respiratory issues

Some risk factors are associated with risk for mortality: supports the need to focus on

- nutrition
- gastrointestinal issues (reflux, constipation, gallbladder dysfunction)
- scoliosis monitoring
- aspiration risk (ex. proper positioning when eating/drinking)
- epilepsy
- prevent or manage contractures, dystonic postures, proper positioning
- ambulation

Improve quality of life


Life events
survival
adult life
getting the diagnosis
time before diagnosis
Symptoms

DISABILITY AND REHABILITATION, 2016
http://dx.doi.org/10.3109/09638288.2016.1170896

Taylor & Francis
Taylor & Francis Group

ORIGINAL ARTICLE

Functional abilities in aging women with Rett syndrome – the Danish cohort

Bitten Schönewolf-Greulich, Michelle Stahlhut, Jane Lunding Larsen, Birgit Syhler and Anne-Marie Bisgaard

Centre for Rett Syndrome, Kennedy Centre, Department of Clinical Genetics, Rigshospitalet, University of Copenhagen, Glostrup, Denmark

ABSTRACT

Rett syndrome (RTT) is a neurodevelopmental disorder, which mainly affects females and results in multiple disabilities. Many clinical descriptions of the symptoms and functional abilities have been made medically, though mainly in children with RTT. Previous reports have established that even though the syndrome causes severe psychomotor disability, women with RTT can live long into adulthood.

Purpose: We aim to describe what to expect from aging women with RTT regarding some of the basic functional abilities that are used in daily activities and that could have an impact on quality of life in these women.

Methods: A team of two medical doctors, a physiotherapist and an educational psychological adviser, performed clinical evaluations of 27 women with RTT in Denmark above 30 years of age and confirmed *MECP2* mutation.

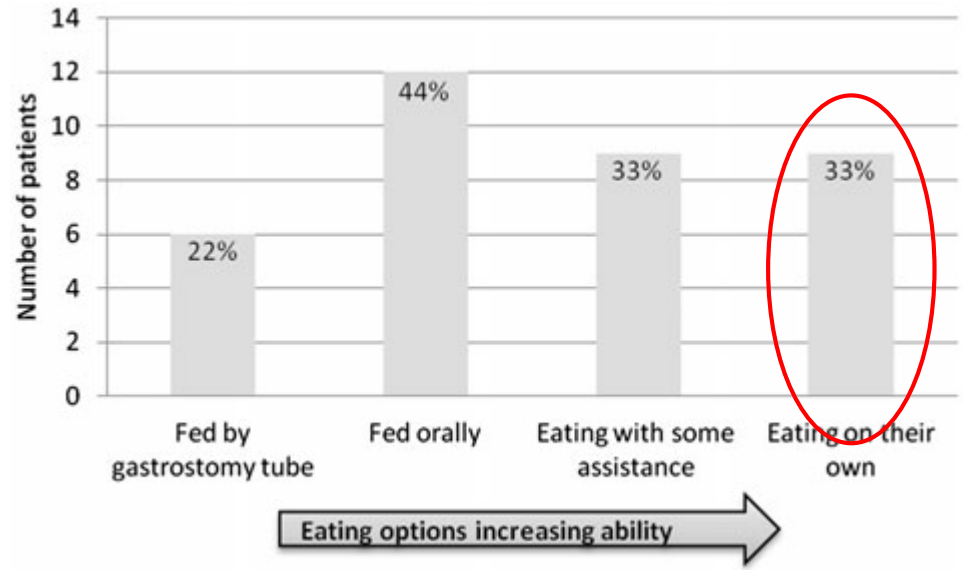
Results: We found that 63% of the women were able to walk outside their homes and only 11% were not able to walk at all. However, 67% could not transfer from sitting to standing position without support. There was profound difficulties communicating, but 85.1% of the women could either consistently point with their hand or eyes to things of their interest.

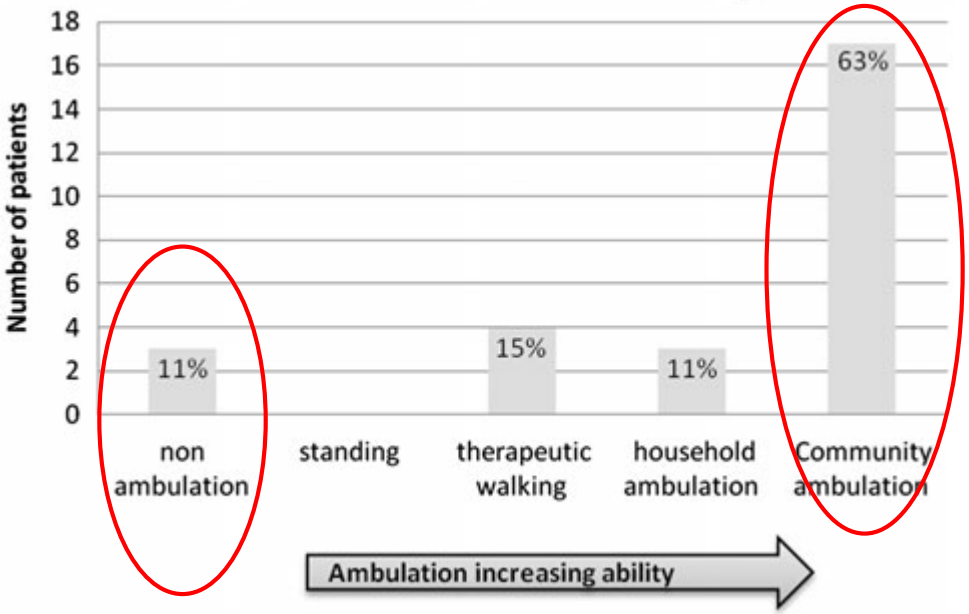
Conclusions: Women with RTT are very dependent on caregivers who maintain and rehabilitate their functional abilities. They can often walk short distances unassisted, but do have trouble transferring and thus getting up from a chair on their own. They have severe problems communicating and they often perform subtle signs that can be difficult to recognize.

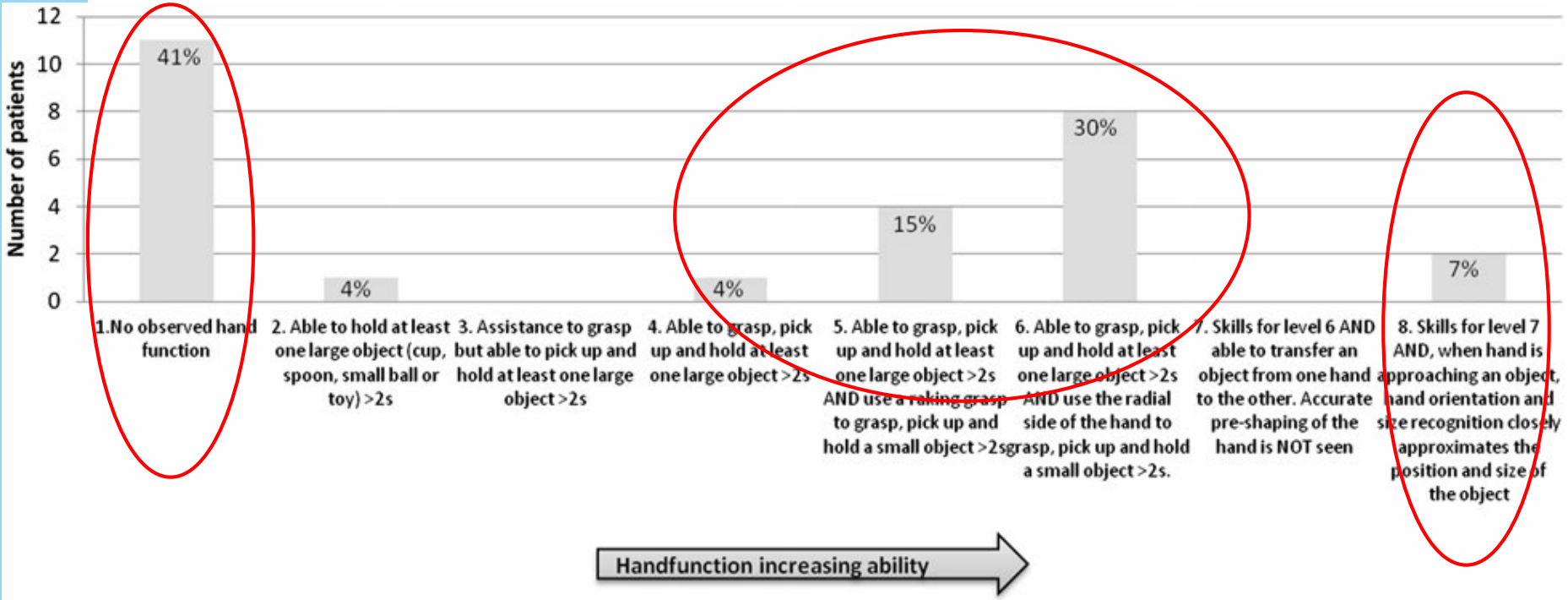
ARTICLE HISTORY
Received 29 September 2015
Revised 22 March 2016
Accepted 22 March 2016
Published online 11 May 2016

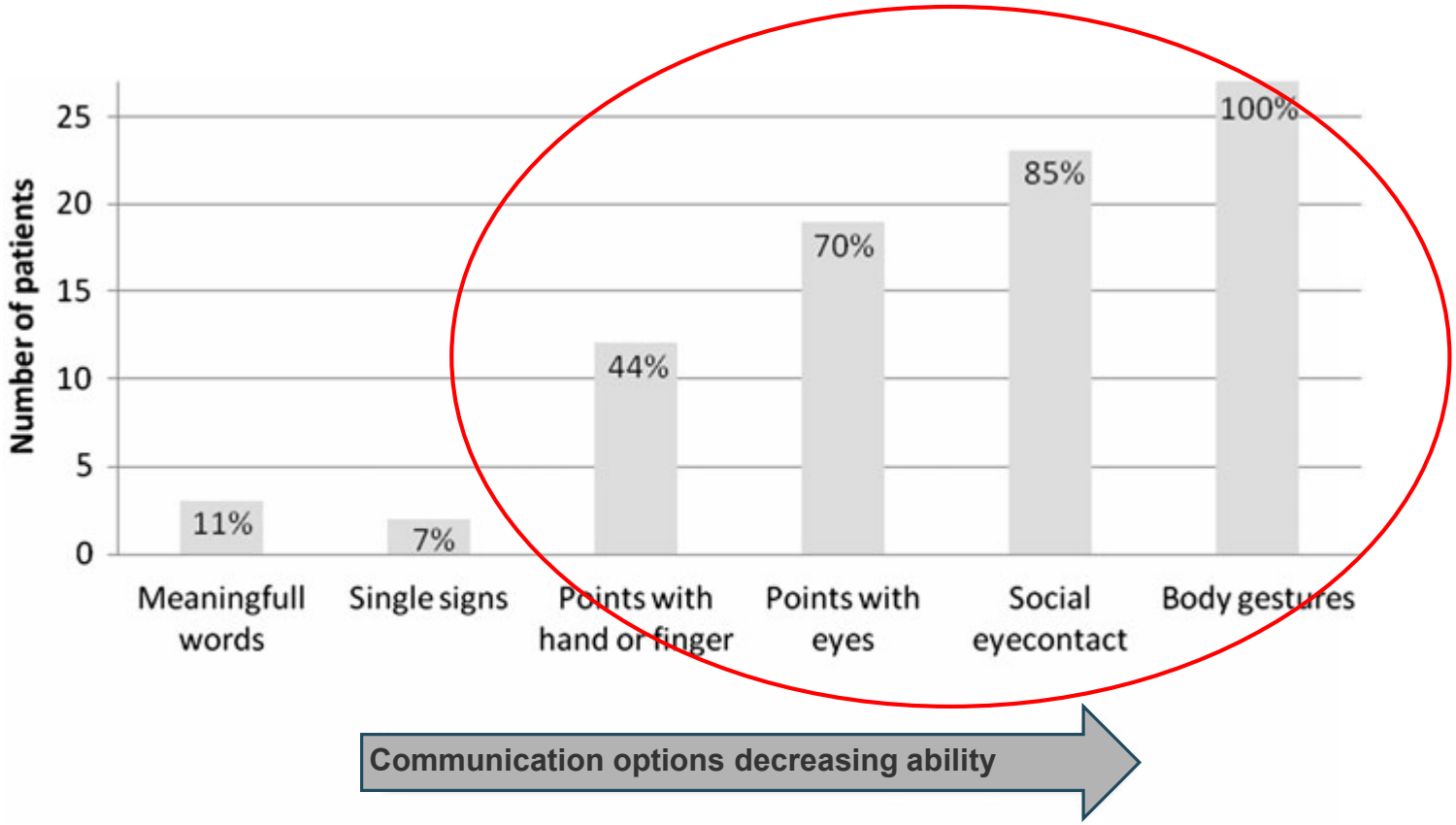
KEYWORDS
Aging; communication; functional ability; hand function; intellectual disability; *MECP2;* methyl CpG binding protein 2; Rett syndrome

Overall, the results showed a high dependency in most functional abilities


Number of patients
14
12
10
8
6
4
2
0
22%
44%
33%
33%
Fed by gastrostomy tube
Fed orally
Eating with some assistance
Eating on their own
Eating options increasing ability

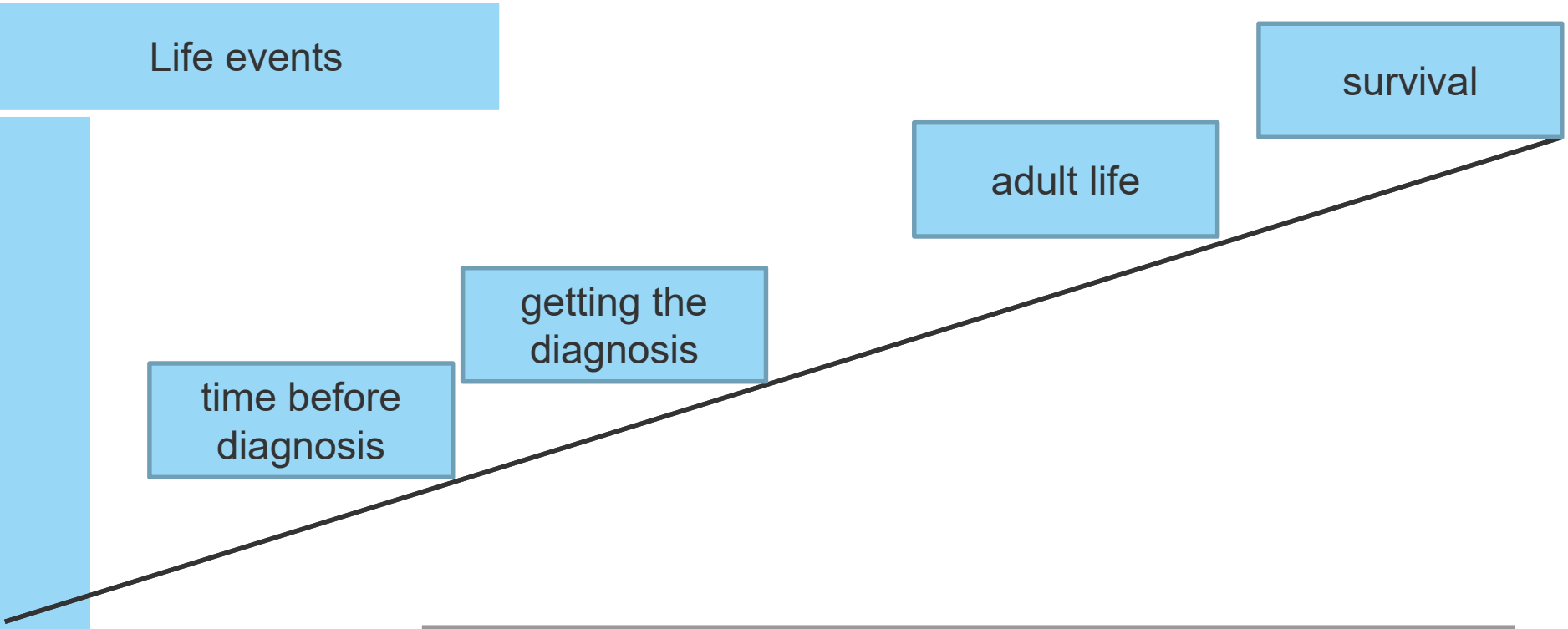

Number of patients
18
16
14
12
10
8
6
4
2
0
11%
15%
11%
63%
non ambulation
standing
therapeutic walking
household ambulation
Community ambulation
Ambulation increasing ability


Number of patients
12
10
8
6
4
2
0
41%
4%
4%
15%
30%
7%
1.No observed hand function
2. Able to hold at least one large object (cup, spoon, small ball or toy) >2s
3. Assistance to grasp but able to pick up and hold at least one large object >2s
4. Able to grasp, pick up and hold at least one large object >2s
5. Able to grasp, pick up and hold at least one large object >2s AND use a raking grasp to grasp, pick up and hold a small object >2s
6. Able to grasp, pick up and hold at least one large object >2s AND use the radial side of the hand to grasp, pick up and hold a small object >2s.
7. Skills for level 6 AND able to transfer an object from one hand to the other. Accurate pre-shaping of the hand is NOT seen
8. Skills for level 7 AND, when hand is approaching an object, hand orientation and size recognition closely approximates the position and size of the object
Handfunction increasing ability


Number of patients
25
20
15
10
5
0
11%
7%
44%
70%
85%
100%
Meaningfull words
Single signs
Points with hand or finger
Points with eyes
Social eyecontact
Body gestures
Communication options decreasing ability

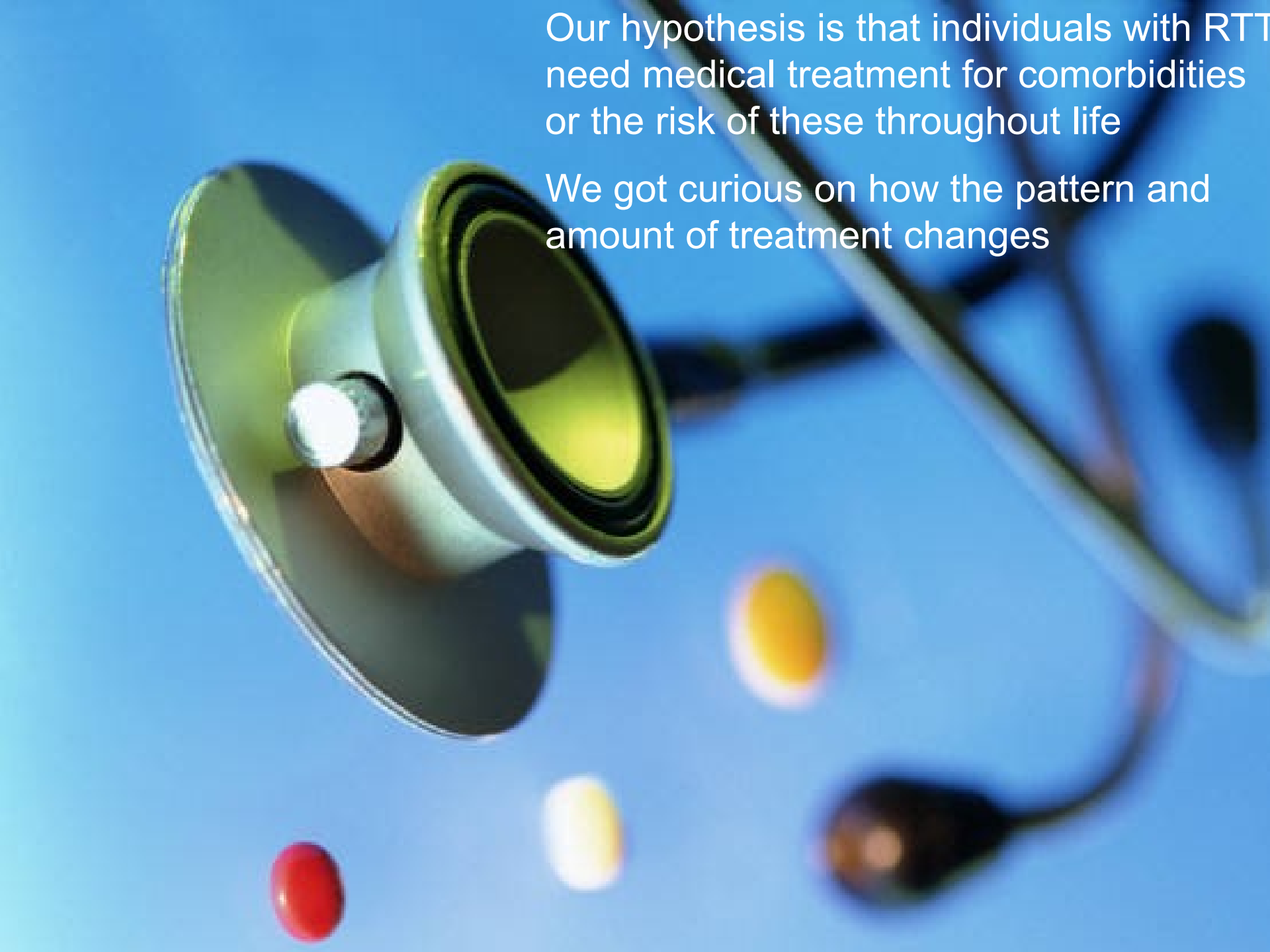
Overall, the results showed a high dependency in most functional abilities

However, the adults also showed us that they are able to do more things if we give them the time and believe in them



treatment of medical issues ~ need for live long follow-up

Symptoms



Our hypothesis is that individuals with RTT need medical treatment for comorbidities or the risk of these throughout life

We got curious on how the pattern and amount of treatment changes

88 individuals with RTT and a *MECP2* mutation– divided into three age groups

	Number of participants	Age range	Mean	Median
Group 1: 2-14 years	28	2-12	6.8	7
Group 2: 15-29 years	29	15-27	19.6	19
Group 3: 30-60 years	31	30-60	40.9	41.5

Number of medically treated comorbidities

	Number	Mean
Group 1: 2-14 years	0-4	1.89
Group 2: 15-29 years	1-7	3.14
Group 3: 30-60 years	1-6	3.55

Top 3 medically treated comorbidities and supplements

	Constipation	Epilepsy	Gastroeso-phagealreflux		D-vitamin/calcium
In total (88)	76% (67)	56.8% (50)	16% (14)		77.3% (68)
	⬇	⬇	⬇		⬇
2-14 years (28)	28.4% (19)	22% (11)	14.3% (2)		20.6 % (14)
15-29 years (29)	35.8% (24)	38% (19)	50.0% (7)		36.8% (25)
30-60 years (31)	35.8% (24)	40% (20)	35.7% (5)		42.6 % (29)

Medically treated comorbidities mainly in adulthood

	Pain (daily on pain killers)	Osteoporosis	Muscle stiffness and dystonia	Behavioural problems, psychosis	Depression	Menstrual disturbances
In total (88)	7% (8)	6.8% (6)	6.8% (6)	6.8% (6)	4.5% (4)	5.7% (5)
	⬇	⬇	⬇	⬇	⬇	⬇
2-14 years (28)	0% (0)	0% (0)	0% (0)	0% (0)	0% (0)	0% (0)
15-29 years (29)	14.3% (1)	16.7% (1)	33.3% (2)	16.7% (1)	0% (0)	100% (5)
30-60 years (31)	85.7% (6)	83.3% (5)	66.7% (4)	83.3% (5)	100% (4)	0% (0)

What we have learned from this study

- Almost all individuals with RTT are medically treated for comorbidities in childhood, adolescents and in adult life
- The amount and pattern of treated comorbidities changes throughout life
- Individuals with RTT should be followed lifelong by professionals
  - who have knowledge of the risk of the comorbidities in RTT and how to treat them

Take home messages

- Children with RTT might have many different symptoms before the characteristic RTT symptoms occur
- It is important to listen to the parents and their concerns
- Many with RTT live long in to adulthood
- Lifelong care planning
    - medical issues
    - communication
    - socially
    - in the social system

We owe everyone who are affected with Rett syndrome to do our best

Thank you for your attention☺