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Title: Conceptualizing a Quality of Life Framework for Girls with Rett Syndrome using Qualitative Methods

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Running title:

Quality of life in Rett syndrome

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Quality of Life

ABSTRACT

Rett syndrome is a neurodevelopmental disorder mainly affecting females and associated with a mutation on the *MECP2* gene. There has been no systematic evaluation of the domains of quality of life (QOL) in Rett syndrome. The aims of this study were to explore QOL in school-aged children with Rett syndrome and compare domains with those identified in other available QOL scales. The sample comprised 21 families registered with the Australian Rett Syndrome Database whose daughter with Rett syndrome was aged six to 18 years. Semi-structured telephone interviews were conducted with each parent caregiver (19 mothers, two fathers) to investigate aspects of their daughter's life that were satisfying or challenging to her. Qualitative thematic analysis using a grounded theory framework was conducted, and emerging domains compared with those in two generic and three disability parent-report child QOL measures. Ten domains were identified: physical health, body pain and discomfort, behavioral and emotional wellbeing, communication skills, movement and mobility, social connectedness, variety of activities, provision of targeted services, stability of daily routines, and the natural environment. The two latter domains were newly identified and each domain contained elements not represented in the comparison measures. Our data articulated important aspects of life beyond the genetic diagnosis. Existing QOL scales for children in the general population or with other disabilities did not capture the QOL of children with Rett syndrome. Our findings support the construction of a new parent-report measure to enable measurement of QOL in this group.

KEYWORDS

Rett syndrome

Quality of life

Qualitative research

Disability

Parent-proxy report

INTRODUCTION

Rett syndrome is a neurodevelopmental disorder commonly caused by a mutation on the X-linked methyl-CpG-binding protein 2 (*MECP2*) gene [Amir et al., 1999] and occurs in approximately 1 per 9,000 live female births. [Fehr et al., 2011] Hand function and language skills regress in early childhood, in conjunction with the development of stereotypies and impaired mobility. [Neul et al., 2010] These functional deficits are further complicated by the development of comorbid conditions such as epilepsy, [Bao et al., 2013] gastrointestinal disorders [Motil et al., 2012] and scoliosis [Downs et al., in press]. Some children can walk, negotiate stairs, self-feed or use eye gaze technology whereas others are unable to walk, require enteral feeding or engage in self-injurious behaviors. The disability is complex with clinical variability in how the children experience physical, social, behavioral and communication challenges, which can then restrict activities and limit participation.

Health and disability supports and services for Rett syndrome may include developmental therapies (eg, gross motor function [Lotan et al., 2012]) and medical management of comorbidities (eg, gastrointestinal and nutritional problems [Baikie et al., 2014]), although the level of evidence for these interventions is generally low. More empirical research is needed to determine which treatments, services and programs are most effective in improving outcomes for those affected by Rett syndrome. The success of these intervention studies will in part depend upon the validity of their outcome measures, and quality of life (QOL) is one such endpoint for evaluation of supports and services.

QOL refers to satisfaction with a composite of life experiences and includes domains that are either universal (eg, health, emotional wellbeing) or specific to particular populations (eg, body pain). [Verdugo et al., 2005] Generic QOL scales for

children include domains common to all children, whereas disorder-specific scales may include additional domains in relation to symptoms and treatments of the particular disorder.[Solans et al., 2008] Interviews with parents of children with autism spectrum disorder[Tavernor et al., 2013] and cerebral palsy[Young et al., 2007] have suggested that generic child QOL measures are unlikely to account for the condition-specific characteristics and needs of children with disabilities. The generic Child Health Questionnaire (CHQ)[Waters et al., 2000] has been used to measure QOL of children with Rett syndrome.[Lane et al., 2011] Children with more severe impairments had poorer physical QOL scores but better psychosocial QOL scores, possibly because these children were less likely to exhibit challenging behaviors.[Lane et al., 2011] These data provide us with the first leads on QOL in children with Rett syndrome. However, it is not yet known whether the domains of the CHQ reflect those that are important for children with Rett syndrome.

To date, there has been no systematic evaluation of the domains of QOL in Rett syndrome. The primary aim of the current study was to explore, using qualitative methods, the domains of QOL reported by parent primary caregivers to be important to school-aged children with Rett syndrome. The secondary aim was to compare these domains with those measured in other available QOL scales.

METHODS

Participants

The Australian Rett Syndrome Database (ARSD), a longitudinal and population-based registry of confirmed cases of Rett syndrome born since 1976,[Leonard et al., 1997; Wong et al., 2014] was used as a source of recruitment. Families of 389 females with Rett syndrome, of whom 73 (18.8%) had died, had

provided information to the ARSD at the time of recruitment. Of those alive, 127 girls were aged six to 18 years. Twenty-two of these families were contacted and 21 parents (two fathers) who were the primary caregivers for their daughters were recruited. One family declined to be involved for health reasons. Recruitment was purposive to provide representativeness of different forms of mobility, feeding practices, comorbidities of spinal deformity and epilepsy, and residence in Australia by state and urban or rural location (Table 1). A range of pathogenic mutations associated with milder and more severe phenotypes were represented. These included C-terminal deletion (n=3), early truncating (n=1), p.Arg106Trp (n=1), p.Arg133Cys (n=1), p.Arg168* (n=1), p.Arg270* (n=3), p.Arg294* (n=1), p.Arg306Cys (n=3), p.Thr158Met (n=5), and other (n=1). The children were aged seven to 18 years and the mean (SD) age of the child at the time of interview was 12.7 (4.0) years. Children were excluded from the QOL interviews due to their limited communication and cognitive skills, whereby the validity of QOL assessment using self-reports in this group would be unclear.[Coghill et al., 2009]

Procedure

Each of the parents participated in a semi-structured stem and leaf telephone interview. The interview schedule was based on that used in the development of a QOL measure for cerebral palsy[Waters et al., 2005] and explored aspects of life that were important for the girl's happiness, the types of activities that made her feel good about herself, and the challenges that she encountered. Parents were asked specific probing questions to identify the types of behaviors that their child exhibited, behaviors that helped the parent to interpret how she was feeling and whether an experience was satisfying or otherwise (eg, she is happy watching a video in the lounge). Probing questions that followed these perceptions of emotion included:

“How do you know?”; *“What does that look like to an outside observer?”*; and *“Why do you think that is?”*. This strategy was used to avoid inferring emotion from a child who might not be able to verbally communicate in order to confirm parents’ assumptions.

The interview schedule was piloted with a mother who was not included in the study sample. The interviews were conducted by a researcher with a psychology background (AE), lasted approximately 30-60 minutes and were digitally recorded. Recordings were transcribed and sent to each parent for member checking [completed by 18/21 (86%)]. Ethical approval of this study was prospectively reviewed by the Human Research Ethics Committee at the University of Western Australia, Western Australia (RA/4/1/6931) and parents provided informed consent to participate in this study.

Analyses

A grounded theory framework was used to identify the themes within the interview transcripts.[Liamputtong 2009] Observable behaviors were coded by AE using NVivo[2014]. Primary QOL domains as well as elements within those domains were subsequently identified. Two researchers (AE, JD) reviewed the domains, discussed the interpretation of each domain, and checked the coding of text from the transcripts. Consensus of primary domains and domain elements was achieved through joint discussion.

Domains were then compared with those in two generic and three condition-specific parent-report QOL measures. The generic measures included the CHQ[Waters et al., 2000] and the KIDSCREEN Health Related Quality of Life Questionnaire.[Ravens-Sieberer et al., 2007] The condition-specific measures

included the Cerebral Palsy Quality of Life questionnaires (CP QOL Child and Teen)[Davis et al., 2009; Waters et al., 2005] and the Quality of Life of People with Profound Multiple Disabilities questionnaire (QOL-PMD).[Petry et al., 2009]

RESULTS

Quality of life domains

Parents identified ten domains as important components of their daughter's QOL. Tables 2, 3 and 4 provide sample quotes from each of the domains.

Health and wellbeing

Physical Health referred to body health and wellness. Elements within this domain included illnesses such as pneumonia; difficulties with sleep; aspects of eating; comorbidities such as scoliosis and epilepsy; and the impact of health on daily life. For example, parents commonly reported that a period of recovery following seizures was needed before their daughter was able to return to her usual emotional state and tackle day-to-day activities.

Body Pain and Discomfort included elements contributing to discomfort such as gastrointestinal issues, musculoskeletal conditions and environmental factors. For example, pressure areas developed following prolonged periods of sitting or bed rest and abdominal discomfort was observed during bouts of constipation. Different methods of alleviating pain and discomfort were also discussed, such as regular adjustment of room thermostat settings to maintain their daughter's comfort in relation to body temperature.

Behavioral and Emotional Wellbeing referred to behaviors associated with different emotional states such as smiling and crying, and disorder-related behaviors such as bruxism, stereotypies and self-injury. Parents evaluated their daughter's

emotional wellbeing and behaviors, taking into account the contexts in which the behaviors occurred. For example, parents sometimes identified increases in their daughter's repetitive hand movements as expressions of either her excitement while watching a familiar video or her agitation at being in a noisy environment.

Daily activities

Communication Skills referred to aspects of verbal and nonverbal communication. Elements within this domain included spoken words and sounds, body language (eg, gestures, eye contact) and the use of communication aids. Communication difficulties hindered the child's ability to make choices and express her feelings, and hampered parents' abilities to identify different triggers of pain and unhappiness. Many parents relied on the subtleties of their daughter's nonverbal communication to indicate whether or not she was content in her environment and to guide appropriate attention to any stressors.

Movement and Mobility referred to the use of motor skills. Elements within this domain included moving independently or with assistance (eg, walker, standing frame, wheelchair). Pleasurable aspects of mobility were identified, such as body language indicating anticipation of standing or walking. For those who were unable to walk, many parents observed that their daughter expressed satisfaction with having her body position changed.

Stability of Daily Routines referred to sequences of activities that were consistently followed. Elements within this domain included seeking comfort from familiar or repeated activities as well as the ability to anticipate schedule changes. Parents reported that their daughter responded more favorably to familiar people and within environments that she recognized, both inside and outside of the home. For

example, falling asleep to the same genre of music, recognizing her teacher at school each morning, or sitting at the same desk in her classroom were identified as comforting activities. Parents also observed their daughter's happiness while watching favorite television shows and singing and dancing to familiar songs. Several families reported that their daughter showed a preference for things that she knew well, whereas it took a long time for her to become accustomed to and accept things that were less familiar.

Community immersion and services

Social Connectedness referred to interpersonal interactions such as engagement, acceptance and participation in social activities that occurred within the home, school and the general community. Elements within this domain included engagement during mealtime conversations and inclusion in social gatherings with people of different ages and abilities. Observable responses to being included indicated that these social interactions were satisfying.

The Natural Environment referred to the child's interest in the outdoors. Elements included time spent with animals, the exploration of plant life, the sensation of land elements (eg, sand, water), and contact with diverse weather patterns (eg, wind, rain, sunshine). Stories were shared of the girls' pleasure and satisfaction when swimming at the beach, feeling the sensation of mud on their feet while walking through a creek dam, and helping to feed the animals on the family farm. Families also spoke about the importance of time spent with pets or companion dogs. These were noted as being some of the girls' happiest moments as they became immersed in their natural environments.

Variety of Activities referred to participation in various physical, social and recreational endeavors. Elements within this domain included at-home pursuits of watching television, singing and listening to music, and reading books with family members. Out-of-home pursuits included participation in dance lessons, swimming, biking and horseback riding. Some children were able to achieve more physically and socially demanding tasks when provided with strong motivators (eg, she resisted walking unsteadily up a steep incline, but was less resistant if at the end she was able to mount and ride her horse).

Provision of Targeted Services referred to families' access to quality support services. Elements within this domain included the availability, expertise and quality of care received from medical professionals, school supports (eg, teachers and classroom aides), therapists, community programs (eg, public pools, dance classes) and respite services. For example, some parents were concerned about insufficient training undertaken by teachers and classroom aides working alongside their daughters. A lack of information passed down from one year to the next to prepare staff for the start of the school year delayed the establishment or continuation of personalized programs, thereby limiting the student's opportunities and potential for progression.

Comparison to existing measures

Concept mapping of our data against the five QOL measures is shown in Table 5. The domains of 'Stability of Daily Routines' and 'The Natural Environment' were newly identified. Some of the domains within the comparative QOL measures also emerged as domains that were important to girls with Rett syndrome (eg, Physical Health, Social Connectedness, Movement and Mobility). However, the elements within our domains provided targeted perspectives of QOL for children with severe

disability and illustrated the unique challenges experienced by children with Rett syndrome. None of the comparative measures addressed all of the elements as were identified in our data.

DISCUSSION

We have previously used qualitative methods to describe each parent's unique journey to diagnosis of their daughter with Rett syndrome, both in China [Lim et al., 2012] and in Australia.[Knott et al., 2012] This new qualitative study has brought together the facets of life that are important for children with Rett syndrome beyond the period of their diagnosis. We identified ten QOL domains, the composite of which is broadly consistent with theoretical frameworks for QOL [Felce and Perry 1995; Verdugo et al., 2005] as well as those identified for adults with intellectual disability.[Verdugo et al., 2005] However, two domains were newly identified and each domain also included elements unique to Rett syndrome. We therefore propose a new framework for conceptualizing QOL in girls with Rett syndrome.

It is not surprising that three of our domains related to health and wellbeing because Rett syndrome is associated with a suite of comorbidities,[Neul et al., 2010] often in relation to seizures and pain or discomfort from gastrointestinal disorders. Whilst sensitivity to pain can be decreased in Rett syndrome, sensitivity can also be increased particularly in relation to visceral causes.[Downs et al., 2010] Parents observed a range of emotional states and specific challenging behaviors such as bruxism, aggression or self-injury,[Mount et al., 2001] which affected QOL by limiting opportunities to engage in social and leisure time activities.

Functional abilities such as communication and mobility are severely affected in Rett syndrome, with significant dependency on others to complete tasks of daily

living.[Leonard et al., 2001] Nonverbal communication methods (eg, body language) and assistive devices such as communication boards and eye gaze technology were able to support QOL. Nevertheless, it was often challenging to interpret what was wanted or needed, thereby affecting how accurately and effectively those needs were met. Considerable emphasis was placed on opportunities for mobility. Those with very limited mobility appeared to respond positively to regular changes in position and those who could walk (either independently or assisted) appeared to derive satisfaction and pleasure in walking. Involvement in gross motor recreation programs (eg, swimming) across mobility levels was generally enjoyable. The importance of movement highlighted the potential value of fostering motor opportunities in individuals with severe physical disabilities to enhance QOL.

The newly identified domain of ‘Stability of Daily Routines’ illustrated greater feelings of security and enjoyment when participating in familiar activities at a regularly scheduled time, with people who understood the girls well and within a recognizable environment. Childhood routines are considered useful in the daily lives of all children in assisting their learning of self-regulation and organizational skills.[Sytsma et al., 2001] Routines at bedtime form part of a suite of sleep hygiene strategies that can help reduce sleep problems in Rett syndrome.[Piazza et al., 1991] Alternatively, excessive reliance and rigidity of routines can limit variety of activities and hinder enjoyment of daily life, as can be seen in children with autism spectrum disorder or Prader Willi syndrome.[Greaves et al., 2006] Childhood routines in Rett syndrome have not been studied, but in our sample routines appeared to be associated with reducing stress. To our knowledge, this domain in QOL has not been identified previously. It is interesting to observe that the concept of ‘Stability of Daily Routines’ co-occurred with engagement in a variety of activities. For example, the girls

participating in swimming and horseback riding programs derived pleasure from these new experiences that extended their personal skills, whilst structured scheduling allowed the girls to anticipate their weekly agenda.

Our remaining domains illustrated meaningful connections between the girls and their communities and services, previously described as important for women with Rett syndrome.[Walker et al., 2014] Friendships were highly valued, as illustrated by needs to seek out contact with familiar others and communicating interest and engagement through body gestures and eye contact, a feature often observed in Rett syndrome.[Hagberg 2002] Available access to and quality of services has the potential to optimise participation.

Our other newly identified domain was ‘The Natural Environment’. The girls observed and explored environmental features including plants, animals and weather. Contact with nature has the potential to promote mental health and wellbeing [Mitchell 2013; Ulrich 1986; Ulrich et al., 1991] and enhance recovery following episodes of illness[Ulrich 1984] for those in the general population. The mechanisms could relate to reduction in stress or the provision of alternate stimuli that enhance cognitive processes such as memory and attention, each with positive effects on mood.[Bratman et al., 2012] Effects of the natural environment on those with Rett syndrome have not been formally assessed, but our data suggest that these experiences are an important contributor to QOL.

Many QOL measures have been developed for children.[Solans et al., 2008] However, we have identified the QOL-PMD as the only measure for children with profound and multiple disabilities.[Petry et al., 2009] Psychometric properties of the QOL-PMD were satisfactory,[Petry et al., 2009] but ratings of items appear to be based on judgments rather than observed behaviors (eg, “*The individual’s mental*

health status is good”). Parents are able to act as proxies for their children if age or disability preclude child self-report.[Davis et al., 2007] However, in keeping with the concept that QOL is an individual’s perception, it is therefore argued that parent reports should be based on ratings of what they believe their child’s perceptions to be rather than their own perceptions of the child’s QOL. We mapped our data to the QOL-PMD and found that the domains in common with Rett syndrome did not capture many of the elements that emerged from our dataset. The CP QOL-Child [Waters et al., 2005] and CP QOL-Teen [Davis et al., 2009] measures were designed for cerebral palsy using best practice methodologies and are relevant to a range of severity levels of cerebral palsy. However, some domains and many of our domain elements were not contained in the CP QOL measures. The CHQ is a generic instrument [Waters et al., 2000] widely used in a range of chronic conditions, including disability. However, items are biased towards health and function[Felce and Perry 1995; Verdugo et al., 2005] and elements in our domains mapped poorly to the CHQ. The generic measure KIDSCREEN[Ravens-Sieberer et al., 2007] is widely used in disability research and again we found incomplete mapping with our data.

Some of our domain elements reflect specific aspects of behavior, as articulated in measures such as the Rett Syndrome Behaviour Questionnaire.[Mount et al., 2002] For example, the item *“Spells of screaming for no apparent reason during the day”* could reflect part of the domain of ‘Behavioral and Emotional Wellbeing’, while the item *“Spells of apparent anxiety/fear in unfamiliar situations”* could reflect part of the domain of ‘Stability of Daily Routines’. However, the Rett Syndrome Behaviour Questionnaire was not developed to measure QOL. Rather, it was created to describe the neurological and behavioral features of Rett syndrome and to enable differentiation from those affected by intellectual disability due to other

causes.[Mount et al., 2002] Moreover, measures of clinical severity such as the Rett Syndrome Severity Scale assess symptoms such as the severity of epilepsy or scoliosis as well as hand use or the ability to walk.[Hoffbuhr et al., 2001] Though these symptoms may contribute to QOL, such measures do not articulate how the child is enjoying life. Whilst individual items could be used as global item indicators for QOL, this would be a piecemeal approach. In contrast, our data highlight the importance of developing a QOL scale for a severe neurodevelopmental disability such as Rett syndrome, which would comprise multiple items that appropriately represent each of the relevant QOL domains.

We recruited families whose broad experiences enabled our data to reach thematic saturation. Our response fraction (95.5%) and member checking response fraction (86%) were extremely high, indicating the importance of allowing families the opportunity to discuss and promote their daughter's QOL. By definition, QOL is a subjective experience and the children's own views of their QOL are important to consider. However, Rett syndrome is associated with poor expressive language abilities[Hagberg 2002] and presumed cognitive impairment that necessitated proxy reporting. Children may be restricted in their abilities to reflect inwardly, think abstractly, and thereafter communicate their feelings and experiences,[Bibace and Walsh 1980] which are identified as important mechanisms for the evaluation of QOL. Uniquely, our interview schedule contained probing questions in relation to each contributor of QOL, such as asking, "*How do you know this?*" to identify the parent's rationale for their descriptions. We coded feelings of satisfaction or otherwise based on parents' direct observations of their daughter's behaviors. Finally, most of the parent caregivers were mothers and we acknowledge that fathers would likely have different experiences and observations to contribute.

Conclusions

This qualitative study provides unique empirical evidence for the important components of QOL in girls with Rett syndrome, a complex genetic disorder with implications for health, functioning and participation over the life course. These data could usefully inform how clinicians counsel families at diagnosis, drawing upon aspects of life such as social relationships and time spent in the natural environment that could be enormously pleasurable for affected children. The findings could also guide multi-disciplinary teams in identifying a child's need for supports and services during the school year in order to promote good quality of life. We have confirmed that existing QOL scales used for children with other disabilities do not fully capture QOL in Rett syndrome, thereby supporting the need for construction of a new appropriate measure. This is a fundamental research priority that will improve our capacity to measure the full scope of issues that are important for girls with Rett syndrome.

List of abbreviations

QOL quality of life

ARSD Australian Rett Syndrome Database

CHQ Child Health Questionnaire

CP QOL Child and Teen Cerebral Palsy Quality of Life questionnaires

QOL-PMD Quality of Life of People with Profound Multiple Disabilities questionnaire

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Table 1: Characteristics of the girls with Rett syndrome. (n=21)

	Number (%)
Age	
Middle childhood (7 to 12 years)	9 (43%)
Adolescence (13 to 18 years)	12 (57%)
Mobility level	
No assistance needed	12 (57%)
Assistance needed	6 (29%)
Wheelchair dependent	3 (14%)
Gastrostomy	
No	17 (81%)
Yes	4 (19%)
Scoliosis	
No scoliosis	9 (43%)
Conservatively managed scoliosis	7 (33%)
Surgically managed scoliosis	5 (24%)
Number of antiepileptic medications	
0	6 (29%)
1	7 (33%)
2	3 (14%)
3	4 (19%)
4	1 (5%)
Location of residence	
Urban	14 (67%)
Rural	7 (33%)

Table 2: Sample quotes from parents describing their daughter's quality of life in relation to her health and wellbeing.

Domain	Sample quotes
Physical health	<p data-bbox="436 408 1986 587">“So when she was having seizures she would have them in clusters, up to 30 in a day. So in those situations which went on for about two years with about nine or ten outbreaks, she was heavily medicated, she was very groggy, she was falling asleep all the time, she wasn't really doing many activities at school or on the weekends. And it was difficult just to take her out anywhere because mobility was affected; she was so sleepy and groggy. So we changed medications a few times and she got used to one of them and it seems to have made a difference with her.”</p> <p data-bbox="436 632 1986 735">“Usually she's unwell. And being tired as well. Also when she's exhausted she has very low tolerance for anything. So whether it's for physio[therapy], whether it's for learning, eating, whatever. If she's tired, she just can't tolerate a lot of things.”</p>
Behavioral and emotional wellbeing	<p data-bbox="436 815 1986 919">“Her self-injury... she'd be frustrated and she'd be biting her hands, which is part of the Rett's. Yes so she'll tend to really want to bite them or if she can't get access to her hands, she'll swing her arms around, bite up between the elbow and the shoulder.”</p>
Body pain and discomfort	<p data-bbox="436 999 1986 1142">“Keeping her comfortable really requires regular position changes, which is very important for her. So we'll try to, around the 2-3 hour mark if she's at home and at college I've requested, if not been a bit stronger than requesting – demanded – that she's also moved in that timeframe because she can't move herself. And that's very important for her comfort. And probably wellbeing. If she stays in the same spot she'll end up with some pressure sores and stuff.”</p>

Table 3: Sample quotes from parents describing their daughter's quality of life in relation to daily activities.

Domain	Sample quotes
Communication skills	<p>“Looking everywhere and just, whether she’s really happy looking at the TV or something like that there. And then she’ll look back at you and just trying to get it across as if to say, ‘You know I really love this’. When she’s interacting with animals and that there, she’s the same thing. It’s just all through her eyes basically. And the smile, the expressions on her face, which let you know that she’s just really happy and content to be doing the activities.”</p>
Movement and mobility	<p>“In the past she would normally never walk uphill. And we’d find her at the lowest point in the playground because she’d just gradually walk backward and end up at the lowest point. But more and more if something motivates her we find that she will walk up hills. She initiated walking up the ramp where you get on to the horse at horse riding. We were busy getting the horse ready and she walked in the gate and started to walk up the ramp.”</p>
Stability of daily routines	<p>“She likes the routine, she likes her bedroom cause that’s her bedroom, she knows that’s her room, she knows that’s her bed. She likes her routine at nighttime. She tends to like the same people to care for her as well. Once she gets attached to somebody, that’s what she likes. So we tend to find that she has very autistic traits in that respect. That at one stage say with her movies she watched Alice in Wonderland over and over and over. And we tried to put other movies on, no didn’t want to watch them, wanted to watch Alice in Wonderland again. And we just got to the point where we thought, she’s eventually going to get sick of this. And then she did, she sort of went off it for a while. And then months later we tried to put Alice back on, and she finally went ‘Okay I’ll watch it’. So she sort of likes the repetitive, she likes what she knows. So anything unfamiliar, anything new takes her an awful long time to become accustomed to, and to accept, and then to like.”</p>

Table 4: Sample quotes from parents describing their daughter's quality of life in relation to community and environment.

Domain	Sample quotes
Social connectedness	<p>“So I think she feels part of it. We’ve gone camping a couple of times with, my brother has four girls as well as I have two girls. So when they all get together and they sleep in their sleeping bags and stuff like that and sit around the camp fire, she likes that she’s included.”</p>
The natural environment	<p>“That’s her sense of freedom. And she gets to feel the wind in her hair. She looks for bird life up in the trees. Looks for kangaroos and emus. We sing songs. So that is just one of her beautiful things that she really does enjoy and does feel good about herself because she gets to be out there.”</p>
Variety of activities	<p>“[She] can swing a swing by herself. She can ride a horse by herself and swim by herself. And to see [her] on land, whenever [she] goes swimming people are just blown away by how effectively she moves through the water and how safe she is. Because on land she’s quite wobbly and can need a lot of support. And I delight in the look on [her] face as people say, ‘Oh, look at [her] swimming, that’s just incredible’. I think that must be so good for [her] to astound people.”</p>
Provision of targeted services	<p>“And the other disappointment is that when we start a new year, it requires us to schedule visits from all the therapists, the physiotherapists, occupational therapists, speech therapists, in order for the staff to then implement any of the things that have been shown to them from a previous year.”</p> <p>“That change over from one year to the next and the knowledge that gets passed from one year to the next isn’t as seamless as it should be and that is letting her down and that she sort of goes backwards a bit in those areas rather than building on the previous year.”</p>

Table 5: Quality of life domains and elements from the Rett syndrome dataset and their presence in the five comparative measures.

Rett syndrome domains	Rett syndrome elements	KIDSCREEN	CHQ ^a	CP-QOL Child ^b	CP-QOL Teen ^b	QOL-PMD ^c
Physical health	Enjoyment of food	-	-	-	-	✓
	Respiratory infection	-	-	-	-	-
	Impacts of scoliosis	-	-	-	-	-
	Impacts of epilepsy	-	-	-	-	-
	Side effects of medications	-	-	-	-	✓
	Periods of unwellness	✓	✓	✓	✓	✓
	Periods of low energy/poor sleep quality	✓	-	✓	✓	✓
Body pain and discomfort	Gastrointestinal discomfort	-	-	-	-	✓
	Prolonged sitting	-	-	-	-	✓
	Regulating body temperature	-	-	-	-	✓
	Body pain	-	✓	✓	✓	✓
Behavioral and emotional wellbeing	Bruxism	-	-	-	-	-
	Hand wringing	-	-	-	-	-
	Self-injury	-	-	-	-	-
	Fear and anxiety	✓	✓	-	-	-
	Sensory hyper-sensitivity (eg, excessive noise/light)	-	-	-	-	-
Communication skills	Eye contact	-	-	-	-	-
	Facial expressions	-	-	-	-	-
	Body language	-	-	-	-	-
	Communication aids	-	-	✓	✓	✓
	Can make needs known	✓	-	✓	✓	✓
Movement and mobility	Opportunities for movement	-	-	-	-	-
	Mobility aids	-	-	✓	-	✓
	Pleasure in movement	✓	✓	-	-	-
Stability of daily routines	Familiar activities and places	-	-	-	-	-
	Predictable routines	-	-	-	-	-
	Consistent carers	-	-	-	-	-
Social connectedness	Inclusiveness in social settings	✓	✓	✓	✓	-
	Responsiveness in social settings	✓	-	✓	✓	✓
	Enjoyable time with family members	✓	✓	✓	-	✓
	Enjoyable time with familiar others	✓	✓	✓	✓	✓
The natural environment	Animals (eg, pets, wildlife)	-	-	-	-	-
	Plants	-	-	-	-	-
	Land elements and weather	-	-	-	-	-
Variety of activities	Motivation to engage	✓	-	-	-	✓
	Responsiveness to music for entertainment	-	-	-	-	-
	Responsiveness to music to soothe when upset	-	-	-	-	-
	Enjoys a range of activities	-	✓	✓	✓	✓
Provision of targeted services	Informed service providers	-	-	-	-	-
	Accessibility of services	-	-	✓	✓	✓
	Individualized programs	-	-	-	-	-
	Continuity of care	-	-	-	-	-
	Accessibility to equipment	-	-	✓	-	✓
	Availability of respite services	-	-	✓	-	-

^a CHQ – Child Health Questionnaire; ^b CP QOL - Child and Teen Cerebral Palsy Quality of Life questionnaires; ^c QOL-PMD - Quality of Life of People with Profound Multiple Disabilities questionnaire.