MS AMY EPSTEIN (Orcid ID : 0000-0003-4441-0901)
DR SUSAN MARGARET REID (Orcid ID : 0000-0001-9415-5246)
PROFESSOR HELEN LEONARD (Orcid ID : 0000-0001-6405-5834)
DR JENNY DOWNS (Orcid ID : 0000-0001-7358-9037)

Article type : Original Article

[Original article: 4 tables, 1 figure]

Functioning, participation, and quality of life in children with intellectual disability: an observational study

KATRINA WILLIAMS[1,2,3,4]
PETER JACOBY[5]
ANDREW WHITEHOUSE[5]
RACHEL KIM[6]
AMY EPSTEIN[5]
NADA MURPHY[5]
SUE REID[3,4]
HELEN LEONARD[5]
DINAH REDDIHOUGH[3,4,7]
JENNY DOWNS[5,8]

1 Paediatric Education and Research, Monash University, Melbourne, Victoria; **2** Developmental Paediatrics, Monash Children's Hospital. **3** Developmental Disability and Rehabilitation Research, Murdoch Children's Research Institute, Melbourne, Victoria; **4** Department of Paediatrics, University of Melbourne, Victoria; **5** Telethon Kids Institute, The University of Western Australia, Perth, Western Australia, Australia. **6** Department of

Sociology, Princeton University, Princeton, NJ, USA. **7** Royal Children's Hospital, Parkville, Victoria; **8** School of Physiotherapy and Exercise Science, Curtin University, Perth, Western Australia, Australia.

Correspondence to Jenny Downs, Telethon Kids Institute, University of Western Australia, PO Box 855, West Perth, Western Australia, 6872, Australia. E-mail: Jenny.Downs@telethonkids.org.au

PUBLICATION DATA

Accepted for publication 00th Month 2020.

Published online 00th Month 2020.

ABBREVIATION

ASD	Autism spectrum disorder
ICF	International Classification of Functioning, Disability and Health
PEM-CY	Participation and Environment Measure for Children and Youth
QoL	Quality of life

AIMS To investigate associations between functioning, community participation, and quality of life (QoL) and identify whether participation mediates the effects of functioning on QoL.

METHOD The caregivers of 435 children (211 females, 224 males; mean age 12y; SD 3y 11mo; age range 5–18y) with intellectual disability and autism spectrum disorder, cerebral palsy, Down syndrome, or Rett syndrome reported on their child's functioning (dependence for managing personal needs, mobility, communication, eye contact when speaking), frequency of participation, and QoL. Linear regression and mediation analyses were used to evaluate the relationships between child functioning, participation, and QoL.

RESULTS Children with greater dependency for managing personal needs and limited eye contact when speaking experienced poorer QoL. Less impaired functioning was associated with more frequent participation, which, in turn, was associated with a 3-point gain in QoL for each additional point in frequency of participation (coefficient=2.67, 95% confidence interval 1.56–3.78). The effect of impaired functioning on QoL was partially mediated by participation in children with greater dependency in managing personal needs and those with mildly impaired communication.

INTERPRETATION Greater levels of impairments with poorer functioning, notably a high level of dependence, were associated with poorer QoL. Poorer QoL can be partly explained by less frequent community participation.

[First page footer]

DOI: 10.1111/dmcn.xxxxx
[Left page footer]
Developmental Medicine & Child Neurology 2020, 62: 000–000
[Right page footer]
Functioning, Community Participation, and QoL *Katrina Williams et al.*

What this paper adds

- More impaired functioning was associated with poorer quality of life (QoL).
- More frequent community participation was associated with better QoL.
- QoL scores were partly explained by the frequency of community participation.

[main text]

Children with intellectual disability live with a range of difficulties in motor, communication, and social functioning and in independently managing activities of daily living. For example, children with Down syndrome have mild-to-moderate intellectual disability; some can speak and manage activities of daily living, whereas other cannot.[1] Rett syndrome is a rare genetic disorder mainly affecting females and disability is more severe than in Down syndrome; some children can walk and self-feed, whereas others cannot walk or require enteral feeding.[2] Children with intellectual disability are vulnerable to poor health and difficulties with activities such as walking or communication.

The International Classification of Functioning, Disability and Health (ICF) model integrates impairments, health, and activities with domains of participation, personal factors, and how the child lives within the environment.[3] Each of the ICF domains are essential to daily living and are considered interrelated.[3] For example, health conditions are associated with the child's functioning as observed in some children with cerebral palsy (CP) and intellectual disability who may be non-ambulatory and frequently experience comorbidities such as epilepsy and severe respiratory infections.[4] Capacity to perform activities such as walking or communication could in turn be associated with participation.[3] Participation

describes meaningful involvement in life situations in the home, at school, and in the community and provides opportunities for the development of functional skills, connecting with others, developing independence, and engaging in enjoyable and meaningful activities.[5] There are two essential components: attendance, usually defined by frequency; and involvement, which relates to the child's engagement and motivations associated with the activity.[6,7] Relationships between activities and participation are not well understood across the spectrum of intellectual disability.

It has been suggested that the concept of quality of life (QoL) encompasses all of the ICF domains.[8] QoL refers to satisfaction with life experiences including domains that are universally applicable (e.g. physical and mental well-being) with additional domains relevant for particular populations.[9] QoL is often a crucial endpoint to include in both clinical practice and research. Founded on qualitative data,[10–13] we recently developed and validated the Quality of Life Inventory-Disability[14] which enhances our capacity to understand QoL across the range of presentations of intellectual disability. However, there is limited evidence on the determinants of QoL in intellectual disability. For example, the available literature suggests that poorer social and communicative functioning in children with autism spectrum disorder (ASD) are associated with poorer child QoL, as measured by a generic QoL instrument;[15] however, associations between these determinants and QoL were not reported specifically for children with intellectual disability. Complex relationships between various aspects of functioning (such as mobility, communication, independence in relation to caring for personal needs, and ability to make eye contact), participation, and QoL have been investigated in children with CP in the SPARCLE (Study of PARticipation of Children with cerebral palsy Living in Europe) study[16,17] but not specifically in children with intellectual disability.

Using the newly validated QoL tool (Quality of Life Inventory-Disability) and guided by the ICF framework, this study sought to evaluate the associations between functioning and QoL in children with intellectual disability, taking into account confounders such as health issues, age, and diagnosis. Participation is a modifiable factor and could be an important target for improving QoL, exploiting the notion of the disability paradox where appropriate contextual interventions can reduce the adverse impacts of impairments and difficulties with functioning on QoL.[18] Therefore, we also sought to identify whether community participation was a mediator for associations between functioning and a child's QoL.

METHOD

Design and procedure

We used a cross-sectional study design. Families were recruited if they had a child (range 5–18y) with confirmed intellectual disability and a diagnosis of ASD, CP, Down syndrome, or Rett syndrome. Participating families were primary caregivers of children registered with one of five databases. Caregivers of children with ASD and intellectual disability were recruited from the Western Australian Autism Biological Registry[19] or the Western Australian Autism Register;[20] additional families were recruited through community organizations and networks as well as social media advertisements. Caregivers of children with CP and intellectual disability were recruited from the Victorian Cerebral Palsy Register, a population-based register of individuals with CP born in Victoria, Australia since 1970.[21] Caregivers of children with Down syndrome born from 1980 to 2004 were recruited from the Down syndrome 'NOW' database, a Western Australian population-based resource initially established in 1997;[22] additional families were contacted through community organizations and networks, social media advertisements, and network sampling. The families of children with Rett syndrome were recruited from the Australian Rett Syndrome Database, a longitudinal, population-based register established in 1993.[23] After initial telephone contact with the caregivers, the questionnaire was administered using the Research Electronic Data Capture tool. Some families provided data using a paper format or telephone interview with a member of the research team with psychology training (AE, NM).

Ethical approval for this study was provided by the Human Research Ethics Committees at the University of Western Australia (no. RA/4/20/4276) and the Child and Adolescent Health Services (no. RGS2390); primary caregivers documented informed consent to participate in the study.

Measures

Functioning variables

Mobility was categorized as: can walk at least 500 metres with no difficulty; can walk independently but for shorter distances; can walk with assistance; or unable to walk. Communication was categorized as: can speak well and are understood; have some difficulty speaking, such as lack of clarity; have difficulty speaking; are only understood by those who know them well; non-verbal communication; and cannot communicate. Questions from the Eye Contact Avoidance Scale[24] were used to measure the child's eye contact during social functioning when they initiate communication. Eye contact when communicating with the parent, friends, and family, and when communicating with unfamiliar people were each rated on a 5-point Likert scale (0=never, 1=rarely, 2=sometimes, 3=often, 4=always) and then

Commented [SC1]: Typesetter: B head

Commented [SC2]: Typesetter: C head

summed to give a total possible score of 12. A ternary variable was then created to indicate low (0–5), medium (6–8), and high functioning (≥9). Parents categorized their child's function in relation to personal needs as: independent; independent but needing monitoring or reminding; needing assistance or fully dependent.

Confounding variables

The following physical health variables were identified that might potentially be associated with both functioning and QoL and therefore confound any relationships. A diagnosis of epilepsy was categorized as 'yes' or 'no'; if yes, the frequency of seizures was described as 'controlled', 'fewer than once per month', 'monthly', or 'daily or weekly'. Scoliosis was categorized as 'no scoliosis', 'mild or moderate scoliosis', 'severe scoliosis treated with surgery', or 'severe scoliosis managed conservatively'. The Disorders of Initiating and Maintaining Sleep and the Disorders of Excessive Somnolence subscales of the Sleep Disturbance Scale for Children[25] were used to describe sleep. Subscale scores were compared with the normative data reported in the initial validation paper to calculate z-scores and then T scores.[25] Parents observed their child's experiences of pain over the previous month as 'not at all', 'occasionally', or 'recurrently'. Other potential confounding variables were diagnostic group, sex, and age (classified as 5–12y or 13–18y).

Mediator variable

Commented [SC3]: Typesetter: C head

Participation was assessed using the Participation and Environment Measure for Children and Youth (PEM-CY),[6] a parent-reported measure that evaluates participation in three contexts: at home; at school; and in the community. The 10-item community module was used in this study. For each of the 10 items, parents were asked how frequently their child attended activities (such as neighbourhood outings, organized or unstructured physical activities) and the scores were averaged to give a summary score (total possible score of 7).

Dependent variable

Child QoL was measured using the Quality of Life Inventory-Disability, a 32-item parent-reported measure assessing the QoL of children with intellectual disability.[14] The questionnaire comprises six domains: social interaction (seven items); positive emotions (four items); negative emotions (seven items); physical health (four items); leisure and the outdoors (five items); and independence (five items). Items were rated on a 5-point Likert scale and parents were asked to recall observations of their child's well-being and enjoyment of life over the past month. Items were linearly transformed to a scale of 0 to 100, with higher scores representing better QoL. Domain scores were calculated by averaging item scores;

total scores were calculated by averaging domain scores. Evidence for the initial reliability and validity of the Quality of Life Inventory-Disability has been published previously.[14,26]

Statistical analysis

Commented [SC4]: Typesetter: B head

Linear regression models were used to: (1) examine univariate associations between the functioning variables and total and domain QoL scores, (2) estimate the total effects of the functioning variables on QoL scores after adjustment for the confounders, and (3) estimate the direct effects, not involving a participation pathway, of the functioning variables on QoL scores by including in the models the hypothesized mediating variable describing participation (PEM-CY frequency). We then performed mediation analysis to estimate the average causal mediation effect, which is the indirect effect of the functioning variables acting through the participation pathway. We also used linear regression models to examine the associations between QoL scores and PEM-CY and, separately, the associations between PEM-CY and the functioning variables (Fig. 1). Our functional ability variables are categorical; statistical output of their relationships with the QoL and PEM-CY scores are presented as coefficients for the effect of each level relative to the reference level. The small amount of missing data was missing at random and complete case analysis was conducted. Statistical analyses were performed using Stata v16.0 (StataCorp LLC, College Station, TX, USA) with the 'paramed' module used for the mediation analysis.

RESULTS

Commented [SC5]: Typesetter: A head

Between March 2018 and October 2019, a family questionnaire was administered to 577 parents/primary caregivers. Of those, 435 families completed the questionnaire including families of 133 out of 162 (82.1%) children with ASD, 151 out of 229 (65.9%) children with CP, 89 out of 97 (91.8%) children with Down syndrome, and 62 out of 89 (69.7%) children with Rett syndrome. Most (90.4%) respondents were biological mothers, 244 (56.4%) worked full-time or part-time, and 332 (76.3%) families were dual-parent households. The mean age of the children was 12 years (SD=3y 11mo, range 5–18y); there were 211 females and 224 males. The data describing the distributions of child functioning, physical health, and QoL variables are presented in Table 1 and Table 2.

Relationships between functioning and QoL

Commented [SC6]: Typesetter: B head

Total QoL score

In the univariate analyses, total QoL scores were substantially lower when the child was unable to walk (coefficient=−10.15, 95% confidence interval [CI] −13.28 to −7.03), unable to communicate (coefficient=−13.01, 95% CI −17.62 to −8.40), had the poorest level of eye

contact during speaking (coefficient=−9.73, 95% CI −12.79 to −6.66), or was fully dependent on others to manage their personal needs (coefficient=−14.54, 95% CI −21.12 to −7.97), compared to individuals with the highest level of functioning in each domain (Table 3). Adjusting for each of the functioning and confounding variables (Table 3, total effect), there were smaller coefficient values for total QoL scores for each of the levels of mobility and communication compared to the reference levels; however, significantly lower QoL scores persisted for children with the poorest level of eye contact (coefficient=−6.02, 95% CI −8.75 to −3.29) and being fully dependent on others for daily needs (coefficient=−8.99, 95% CI −15.23 to −2.75).

Commented [SC7]: Typesetter: Please insert Table 3 here.

Relationships between functioning, participation, and QoL

Univariate relationships between functioning and participation are presented in Table 4. Compared to the highest levels of functioning, full dependency for managing personal needs, walking with assistance or being unable to walk, using non-verbal communication strategies or being non-verbal, and low eye contact scores were associated with less frequent community participation (Table 4). More frequent community participation was associated with higher total QoL scores in a univariate model (coefficient=5.45, 95% CI 4.30–6.60).

Commented [SC8]: Typesetter: Please insert Table 4 here.

When including frequency of community participation in the model to estimate the direct effects of functioning on QoL, the effects of poorer functioning on total QoL scores were attenuated slightly across most levels of each of the functional domains (Table 3, direct effect) but remained statistically significant for the higher levels of needs dependence and for poor eye contact. Frequency of participation was associated with nearly three additional points in the total QoL score for each additional point in frequency of community participation (coefficient=2.67, 95% CI 1.56–3.78). Applying the traditional Baron and Kenny approach, these results support a conclusion of partial mediation of the effects of poor functioning through the participation pathway.[27]

Causal mediation analysis

Table 3 (indirect effect) shows the results of performing causal mediation analysis to estimate the indirect effects of poor functioning on total QoL scores operating through the participation pathway. A statistically significant degree of mediation (indirect effect coefficient=−1.55, 95% CI −3.10 to 0.00) was observed for the highest needs dependence effect. The 'difficulty in speaking' communication level was associated with a significant indirect effect on QoL (indirect effect coefficient=0.92, 95% CI 0.05–1.78).

DISCUSSION

Commented [SC9]: Typesetter: A head

Within a cohort of children and adolescents with intellectual disability, our study investigated the relationships between functioning, participation, and QoL, critical relationships that can inform understanding of how best to support children with disability. For these children, greater impaired functioning was associated with poorer QoL. More frequent participation was associated with higher QoL overall and was a partial mediator for the association between functioning and QoL.

Poorer functioning across all domains was associated with poorer QoL in the univariate analyses; in the multivariate models, negative associations between dependence for managing personal needs, poor eye contact during speaking, and QoL persisted, whereas mobility and communication impairments were less influential. Dependency for managing personal needs was associated with lower QoL scores, suggesting that child involvement in regular routine tasks, such as dressing, contributes to well-being and life satisfaction, perhaps by increased agency and some control over preferences. Using a modified Eye Contact Avoidance Scale developed for children with fragile X syndrome,[24] poorer ability to maintain eye contact when speaking was associated with lower QoL scores. This important element of non-verbal communication can be challenging for children with intellectual disability, particularly those with ASD. In typically developing children, eye contact is used to regulate social behaviours during interactions and convey emotions; differences in the quality or quantity of this communicative skill can lead to disruptions in communication.[28] Intervention research has recently shifted focus from seeking changes to the child's eye gaze behaviours to seeking modification of the social environment around the child, such as evaluation of parent-mediated interventions that focus on parental adaptation of their own communication styles to that of their child with ASD.[29] Our findings suggest that development of intervention strategies for communication partners across settings could promote QoL in this group.

The SPARCLE study, an important predecessor to our study, included analyses of parent-reported QoL in children with CP,[16] and later when they were adolescents,[17] using the generic QoL measure KIDSCREEN. Poorer mobility skills were associated with poorer scores on the physical well-being domain during childhood,[16] whereas poorer motor and communication skills were associated with generally better QoL scores during adolescence.[17] These data are not directly comparable with our study because only a proportion of children had intellectual disability; however, their findings suggest that QoL is more nuanced than being dependent simply on functional abilities.

More frequent participation was independently associated with better QoL, adjusting for health and functioning factors. Findings indicated that a 2-point increase in the frequency of

participation would be associated with a 5.34-point increase in QoL, which is greater than the minimal clinically important difference value of 4.83.[30] We also found evidence that participation was a mediator for QoL in children with greater needs dependency and those with mildly impaired communication, although the effects were small. It is important to identify modifiable factors that could improve QoL so that services can achieve optimal outcomes and funding be directed to accomplish this. Our data provide some evidence that support for greater attendance at participation opportunities has the potential to increase QoL. Participation in the community, such as social and recreational experiences that are fun and interesting, can contribute to the development of emotional well-being and social networks, and are particularly important to counter social isolation.[31,32] Engagement in meaningful community experiences was described as beneficial to QoL in our previous qualitative studies in children with intellectual disability.[10–13] Participation interventions that are tailored appropriately for a child's interests and level of disability might include sport-, recreation-, or arts-based activities and would also include opportunities for the child's choice, control, and personal engagement.[5] Our findings are consistent with the disability paradox where impairments are not necessarily associated with poor QoL and suggest that activity and participation restrictions might be avoided or moderated by appropriate contextual interventions.[18] Longitudinal monitoring and evaluation of mechanisms to support participation in the community by children with more severe impairments is an important topic of future research.

The strengths of this study included use of a comprehensive suite of independent and potential confounder variables, and a validated QoL measure for children with intellectual disability. Recruited mostly from population-based registries, our large sample of children represented a wide spectrum of clinical and disability issues. We acknowledge some limitations. Measurement of QoL was based on parental reporting and this may differ from what the child may report or feel.[33] Self-reporting is preferable but there is still substantial reliance on parent/proxy reports in paediatric practice, particularly in the field of intellectual disability where the child's ability to reflect inwardly and thereafter communicate their feelings are less well understood. It is important to determine ways to elicit self-reporting about QoL. PEM-CY scores indicated that participation was infrequent, occurring several times in the previous month on average, but it is possible that this was associated with social desirability bias[34] and was less frequent than reported. We characterized participation by caregiver ratings of frequency rather than involvement[6] because frequency is observable whereas ratings of involvement could be more subjective for severely affected children. We

acknowledge that involvement in participation is an important ingredient of participation that is not characterized in this study. Finally, we report that cross-sectional findings and longitudinal studies and trials are necessary to identify whether participation has an effect as an intervention over time. We acknowledge that this study design can suggest associations but cannot confirm causal relationships.

CONCLUSIONS

This study is the first to examine associations between functioning, participation, and QoL in a large cohort of children with intellectual disability. Greater dependence for activities of daily living and poorer eye contact during speaking, but not mobility and communication, were associated with poorer QoL. More frequent participation was associated with better QoL and we found some evidence that community participation in part mediated the relationship between some aspects of functioning and QoL. These data provide some evidence to support participation interventions for children with intellectual disability as a way of improving QoL, in keeping with the disability paradox. Studies that evaluate the effects on QoL after interventions aimed at supporting the development of social communication strategies and increasing participation in the community are warranted.

ACKNOWLEDGEMENTS

We extend our thanks to the families for their participation in this study. This study is currently funded by the National Health and Medical Research Council (no. 1103745). We acknowledge the support of Dr Emma Glasson, who supported the recruitment of families from the Western Australia Autism Registry. The Victorian Cerebral Palsy Register receives funding from the Victorian Department of Health and Human Services and from the Victorian Government's Operational Infrastructure Support Program for support of register staff. The authors acknowledge the support of Disability Services Commission WA in establishing the Down syndrome database, and community organizations Developmental Disability WA and the Down Syndrome Association of Western Australia for their support. We thank the Australian Paediatric Surveillance Unit and the Rett Syndrome Association of Australia for their ongoing support in case ascertainment for the Australian Rett Syndrome Database. The Australian Rett Syndrome Study was previously supported by the National Institutes of Health grant no. 5R01HD043100-05 and National Health and Medical Research Council project grant nos. 303189 and 1004384. AW and HL are each supported by a Senior Research Fellowship from the National Health and Medical Research Council (nos. 1077966

Commented [SC10]: Typesetter: A head

and 1117105 respectively). Dinah Reddihough is funded by a University of Melbourne Award. The funders of this research have had no roles in the study design, data collection, data analysis, manuscript preparation, and/or decision to publish.

REFERENCES

1. Leonard S, Msall M, Bower C, Tremont M, Leonard H. Functional status of school-aged children with Down syndrome. *J Paediatr Child Health* 2002; **38**: 160–5.
2. Leonard H, Cobb S, Downs J. Clinical and biological progress over 50 years in Rett syndrome. *Nat Rev Neurol* 2017; **13**: 37–51.
3. World Health Organization. International classification of functioning, disability and health (ICF). Geneva: World Health Organization, 2001.
4. Reid SM, Meehan EM, Arnup SJ, Reddihough DS. Intellectual disability in cerebral palsy: a population-based retrospective study. *Dev Med Child Neurol* 2018; **60**: 687–94.
5. Imms C, Granlund M, Wilson PH, Steenbergen B, Rosenbaum PL, Gordon AM. Participation, both a means and an end: a conceptual analysis of processes and outcomes in childhood disability. *Dev Med Child Neurol* 2017; **59**: 16–25.
6. Coster W, Bedell G, Law M, et al. Psychometric evaluation of the Participation and Environment Measure for Children and Youth. *Dev Med Child Neurol* 2011; **53**: 1030–7.
7. Imms C, Adair B, Keen D, Ullenhag A, Rosenbaum P, Granlund M. 'Participation': a systematic review of language, definitions, and constructs used in intervention research with children with disabilities. *Dev Med Child Neurol* 2016; **58**: 29–38.
8. McDougall J, Wright V, Rosenbaum P. The ICF model of functioning and disability: incorporating quality of life and human development. *Dev Neurorehabil* 2010; **13**: 204–11.
9. Solans M, Pane S, Estrada M-D, et al. Health-related quality of life measurement in children and adolescents: a systematic review of generic and disease-specific instruments. *Value Health* 2008; **11**: 742–64.
10. Davis E, Reddihough D, Murphy N, et al. Exploring quality of life of children with cerebral palsy and intellectual disability: what are the important domains of life? *Child Care Health Dev* 2017; **43**: 854–60.
11. Epstein A, Leonard H, Davis E, et al. Conceptualizing a quality of life framework for girls with Rett syndrome using qualitative methods. *Am J Med Genet A* 2016; **170**: 645–53.

12. Epstein A, Whitehouse A, Williams K, et al. Parent-observed thematic data on quality of life in children with autism spectrum disorder. *Autism* 2019; **23**: 71–80.

13. Murphy N, Epstein A, Leonard H, et al. Qualitative analysis of parental observations on quality of life in Australian children with Down syndrome. *J Dev Behav Pediatr* 2017; **38**: 161–8.

14. Downs J, Jacoby P, Leonard H, et al. Psychometric properties of the Quality of Life Inventory-Disability (QI-Disability) measure. *Qual Life Res* 2019; **28**: 783–94.

15. Kuhlthau K, Orlich F, Hall TA, et al. Health-related quality of life in children with autism spectrum disorders: results from the autism treatment network. *J Autism Dev Disord* 2010; **40**: 721–9.

16. Arnaud C, White-Koning M, Michelsen SI, et al. Parent-reported quality of life of children with cerebral palsy in Europe. *Pediatrics* 2008; **121**: 54–64.

17. Rapp M, Eisemann N, Arnaud C, et al. Predictors of parent-reported quality of life of adolescents with cerebral palsy: a longitudinal study. *Res Dev Disabil* 2017; **62**: 259–70.

18. Albrecht GL, Devlieger PJ. The disability paradox: high quality of life against all odds. *Soc Sci Med* 1999; **48**: 977–88.

19. Taylor LJ, Maybery MT, Wray J, Ravine D, Hunt A, Whitehouse AJO. Brief report: do the nature of communication impairments in autism spectrum disorders relate to the broader autism phenotype in parents? *J Autism Dev Disord* 2013; **43**: 2984–9.

20. Glasson EJ. The Western Australian register for autism spectrum disorders. *J Paediatr Child Health* 2002; **38**: 321.

21. Reid SM, Meehan E, McIntyre S, Goldsmith S, Badawi N, Reddihough DS. Temporal trends in cerebral palsy by impairment severity and birth gestation. *Dev Med Child Neurol* 2016; **58**(Suppl. 2): 25–35.

22. Bourke J, Ricciardo B, Bebbington A, et al. Physical and mental health in mothers of children with Down syndrome. *J Pediatr* 2008; **153**: 320–6.

23. Downs J, Torode I, Wong K, et al. The natural history of scoliosis in females with Rett syndrome. *Spine (Phila Pa 1976)* 2016; **41**: 856–63.

24. Hall SS, Venema KM. A screening tool to measure eye contact avoidance in boys with fragile X syndrome. *J Autism Dev Disord* 2017; **47**: 2254–64.

25. Bruni O, Ottaviano S, Guidetti V, et al. The Sleep Disturbance Scale for Children (SDSC). Construction and validation of an instrument to evaluate sleep disturbances in childhood and adolescence. *J Sleep Res* 1996; **5**: 251–61.

26. Epstein A, Williams K, Reddihough D, et al. Content validation of the Quality of Life Inventory-Disability. *Child Care Health Dev* 2019; **45**: 654–9.

27. Baron RM, Kenny DA. The moderator–mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *J Pers Soc Psychol* 1986; **51**: 1173–82.

28. Senju A, Johnson MH. Atypical eye contact in autism: models, mechanisms and development. *Neurosci Biobehav Rev* 2009; **33**: 1204–14.

29. Pickles A, Le Couteur A, Leadbitter K, et al. Parent-mediated social communication therapy for young children with autism (PACT): long-term follow-up of a randomised controlled trial. *Lancet* 2016; **388**: 2501–9.

30. Jacoby P, Epstein A, Kim R, et al. Reliability of the Quality of Life Inventory-Disability measure in children with intellectual disability. *J Dev Behav Pediatr* 2020. DOI: 10.1097/DBP.0000000000000815 (Online ahead of print).

31. Bigby C. Social inclusion and people with intellectual disability and challenging behaviour: a systematic review. *J Intellect Dev Disabil* 2012; **37**: 360–74.

32. Adair B, Ullenhag A, Keen D, Granlund M, Imms C. The effect of interventions aimed at improving participation outcomes for children with disabilities: a systematic review. *Dev Med Child Neurol* 2015; **57**: 1093–104.

33. Davis E, Nicolas C, Waters E, et al. Parent-proxy and child self-reported health-related quality of life: using qualitative methods to explain the discordance. *Qual Life Res* 2007; **16**: 863–71.

34. Streiner DL, Norman GR. Health measurement scales: a practical guide to their development and use. Oxford: Oxford Medical Publications, 1996.

Table 1: Categorical independent and dependent variables for the children in the study cohort (*n*=435)

Commented [AB11]: Typesetter: please fit on one page

Variable	Description	All (*n*=435)	ASD (*n*=133)	CP (*n*=151)	Down syndrome (*n*=89)	Rett syndrome (*n*=62)
Age	5–12y	221 (50.8)	77 (57.9)	65 (43.0)	51 (57.3)	28 (45.2)
	13–18y	214 (49.2)	56 (42.1)	86 (57.0)	38 (42.7)	34 (54.8)
Sex	Female	211 (48.5)	35 (73.7)	60 (60.3)	54 (39.3)	62 (100)
Personal needs	Can look after their personal needs independently	15 (3.4)	7 (5.3)	6 (4.0)	2 (2.2)	0 (0.0)
	Need checking and reminding	88 (20.2)	42 (31.6)	11 (7.3)	33 (37.1)	2 (2.3)
	Are provided with assistance but help	112 (25.8)	51 (38.4)	23 (15.2)	35 (39.3)	3 (4.8)
	Are dependent on other persons	220 (50.6)	33 (24.8)	111 (73.5)	19 (21,4)	57 (91.9)
Mobility	Can walk fair distances (≥500m)	135 (31.0)	92 (69.2)	12 (7.8)	31 (34.8)	0 (0.0)
	Walk independently but <500m	156 (35.7)	39 (29.3)	41 (27.2)	57 (64.0)	19 (30.6)
	Need assistance to walk	32 (7.4)	2 (1.5)	19 (12.6)	0 (0.0)	11 (17.7)
	Cannot walk	112 (25.8)	0 (0.0)	79 (52.3)	1 (1.1)	32 (51.6)
Verbal communication[a]	Speak well and are understood	46 (10.6)	25 (18.8)	13 (8.6)	6 (6.7)	2 (3.3)
	Have some difficulty speaking, such as lack of clarity	133 (30.6)	52 (39.1)	32 (21.2)	42 (47.2)	7 (11.5)
	Are only understood by those who know them well	86 (19.8)	30 (22.6)	18 (11.9)	34 (38.2)	4 (6.6)
	Non-verbal communication	109 (25.1)	19 (14.3)	49 (32.4)	6 (6.7)	35 (57.4)
	Unable to communicate	60 (13.8)	7 (5.3)	39 (25.8)	1 (1.1)	13 (21.3)
Eye contact during speaking[b]	High	157 (36.1)	20 (15.0)	61 (40.4)	44 (49.4)	32 (51.6)
	Medium	170 (39.1)	62 (46.6)	55 (36.4)	31 (34.8)	22 (35.5)
	Low	108 (24.8)	51 (38.4)	35 (23.2)	14 (15.7)	8 (12.9)
Epilepsy	None	271 (77.5)	111 (83.5)	62 (41.1)	85 (95.5)	13 (21.0)
	Under control	42 (9.7)	6 (4.5)	25 (16.6)	3 (3.4)	8 (12.9)
	Less than once a month	39 (9.0)	5 (3.8)	25 (16.6)	3 (3.4)	9 (23.1)
	Monthly	23 (5.3)	4 (3.0)	10 (6.6)	0 (0.0)	9 (15.5)
	Daily or weekly	60 (13.8)	7 (5.3)	29 (19.2)	1 (1.1)	23 (37.1)
Scoliosis	None	337 (77.5)	130 (97.7)	96 (63.6)	84 (94.4)	27 (43.6)
	Mild or moderate	47 (10.8)	2 (1.5)	23 (15.23)	4 (4.5)	18 (29.0)
	Severe scoliosis managed surgically	35 (8.0)	1 (0.8)	19 (12.6)	1 (1.1)	14 (22.6)
	Severe scoliosis managed conservatively	16 (3.7)	0 (0.0)	13 (8.6)	1 (0.0)	3 (4.8)
Pain[a]	Not observed	164 (37.8)	59 (44.4)	44 (29.3)	36 (40.4)	25 (40.3)
	Observed occasionally	196 (45.2)	63 (47.4)	69 (46.0)	45 (50.6)	19 (30.6)
	Observed recurrently	74 (17.0)	11 (8.3)	37 (24.7)	8 (9.0)	18 (29.0)

Data are *n* (%). [a]1 missing; [b]12 missing; ASD, autism spectrum disorder; CP, cerebral palsy.

Table 2: Continuous independent and dependent variables for the children in the study cohort (*n*=435)

Variable	Description	All (*n*=435)	ASD (*n*=133)	CP (*n*=151)	Down syndrome (*n*=89)	Rett syndrome (*n*=62)
DIMS[a]	T score	72.1 (20.0)	74.1 (20.3)	76.3 (21.0)	65.2 (16.2)	67.9 (18.9)
DOES[b]	T score	60.0 (15.8)	57.2 (15.8)	60.6 (15.4)	58.9 (12.4)	69.1 (17.6)
PEM-CY	Frequency score	1.9 (1.0)	2.1 (0.9)	1.6 (0.9)	2.4 (0.9)	1.8 (0.9)
Quality of life	Total score[a]	69.3 (12.9)	68.4 (11.0)	66.6 (13.5)	77.6 (11.7)	65.8 (11.8)

Data are mean (SD). [a]7 missing; [b]4 missing. ASD, autism spectrum disorder; CP, cerebral palsy; DIMS, disorders of initiating and maintaining sleep; DOES, disorders of excessive somnolence; PEM-CY: Participation and Environment Measure for Children and Youth.

Table 3: Relationships between functioning and total quality of life scores, considering the effects of confounding variables and mediation by the participation variable

Predictor	Description	Univariate model coefficient (95% CI)	*p*	Total effect[a] coefficient (95% CI)	*p*	Direct effect[b] coefficient (95% CI)	*p*	Indirect effect[c] coefficient (95% CI)	*p*
Personal needs	Look after their personal needs independently	ref[d]	–	ref	–	ref	–	ref	–
	Need checking and reminding	−4.24 (−11.10 to 2.62)	0.225	−3.76 (−9.38 to 1.85)	0.188	−4.51 (−9.99 to 0.97)	0.106	0.58 (−0.71 to 1.86)	0.378
	Are provided with assistance but help	−9.34 (−16.09 to −2.58)	0.007	−7.64 (−13.43 to −1.86)	0.010	−7.69 (−13.32 to −2.05)	0.008	−0.11 (−1.41 to 1.19)	0.870
	Are dependent on other persons	−14.54 (−21.12 to −7.97)	<0.001	−8.99 (−15.23 to −2.75)	0.005	−7.60 (−13.70 to −1.49)	0.015	−1.55 (−3.10 to 0.00)	0.050
Mobility	Can walk at least fair distances (≥500m)	ref	–	ref	–	ref	–	ref	–
	Walk independently but <500m	−2.11 (−4.98 to 0.76)	0.150	−2.41 (−5.07 to 0.24)	0.075	−1.85 (−4.45 to 0.74)	0.161	−0.51 (−1.16 to 0.14)	0.122
	Need assistance to walk	−3.68 (−8.44 to 1.09)	0.130	1.15 (−3.84 to 6.13)	0.651	1.95 (−2.91 to 6.81)	0.431	−0.79 (−1.98 to 0.41)	0.197
	Cannot walk	−10.15 (−13.28 to −7.03)	<0.001	−2.16 (−6.64 to 2.32)	0.344	−1.17 (−5.55 to 3.21)	0.559	−0.98 (−2.09 to 0.12)	0.082
Communication	Speak well and are understood	ref	–	ref	–	ref	–	ref	–
	Have some difficulty speaking, such as lack of clarity	2.19 (−1.84 to 6.23)	0.285	1.09 (−2.27 to 4.46)	0.522	0.17 (−3.12 to 3.47)	0.918	0.92 (0.05–1.78)	0.038
	Are only understood by those who know them well	−2.32 (−6.63 to 1.98)	0.290	1.08 (−2.88 to 5.04)	0.594	0.61 (−3.24 to 4.48)	0.755	0.43 (−0.50 to 1.37)	0.364
	Non-verbal communication	−4.85 (−9.00 to −0.70)	0.022	2.55 (−1.83 to 6.93)	0.253	1.83 (−2.44 to 6.11)	0.399	0.72 (−0.34 to 1.78)	0.183
	Unable to communicate	−13.01 (−17.62 to −8.40)	<0.001	−2.97 (−7.80 to 1.86)	0.227	−2.48 (−7.19 to 2.22)	0.300	−0.48 (−1.62 to 0.66)	0.408
Eye contact	High	ref	–	ref	–	ref	–	ref	
	Medium	−3.10 (−5.81 to −0.39)	0.025	−2.96 (−4.35 to 0.23)	0.078	−2.20 (−4.43 to 0.03)	0.053	0.13 (−0.40 to 0.66)	0.630
	Poor	−9.73 (−12.79 to −6.66)	<0.001	−6.02 (−8.75 to −3.29)	<0.001	−5.46 (−8.13 to −2.79)	<0.001	−0.53 (−1.20 to 0.13)	0.116

The coefficient values represent the mean change in Quality of Life Inventory-Disability score for each level of the independent variable relative to the reference level (n=427 participants in the univariate models and n=416 in the multivariate models). [a]From the multivariate model, including all functioning variables and adjusting for seizure frequency, scoliosis, sleep disturbances, pain, age group, diagnostic group, and sex; adjusted r^2=44%. [b]From the multivariate model, including all functioning variables and participation, and adjusting for seizure frequency, scoliosis, sleep disturbances, pain, age

group, diagnostic group, and sex; adjusted r^2=47%. [c]From the mediation analysis using the Stata command 'paramed', which describes the effect operating via the mediation pathway. [d]Reference category. CI, confidence interval.

Table 4: Univariate relationships between functioning and participation. The coefficient values represent the mean change in PEM-CY score for each level of the independent variable relative to the reference level

Predictor	**Description**	**Outcome PEM-CY (out of 7) coefficient (95% CI)**	***p***
Personal needs	Can look after their personal needs independently	ref[a]	–
	Need checking and reminding	0.19 (−0.29 to 0.67)	0.433
	Are provided with assistance but help	−0.12 (−0.59 to 0.34)	0.625
	Are dependent on other persons	−0.80 (−1.26 to −0.34)	<0.001
Mobility	Can walk at least fair distances (at least 500m)	ref	
	Walk independently but shorter distances than 500m	−0.18 (−0.39 to 0.02)	0.087
	Need assistance to walk	−0.65 (−1.00 to −0.30)	<0.001
	Unable to walk	−0.88 (−1.10 to −0.65)	<0.001
Communication	Speak well and are understood	ref	–
	Have some difficulty speaking, such as lack of clarity	0.30 (0.00–0.59)	0.047
	Are only understood by those who know them well	−0.16 (−0.47 to 0.16)	0.321
	Non-verbal communication	−0.43 (−0.74 to −0.13)	<0.001
	Unable to communicate	−0.96 (−1.30 to −0.62)	<0.001
Eye contact	High	ref	–
	Medium	0.10 (−0.11 to 0.30)	0.371
	Low	−0.25 (−0.48 to −0.01)	0.042

[a]Reference category. PEM-CY, Participation and Environment Measure for Children and Youth; CI, confidence interval.

Figure legend

Figure 1: Participation-mediated pathway between functional abilities and quality of life.