REF: Whitehouse A, Jacoby P, Reddihough D, Leonard H, Williams K, Downs J. The effect of functioning on Quality of Life Inventory-Disability measured quality of life in children with intellectual disability is not mediated or moderated by parental psychological distress. Quality of Life Research. 2021 Oct;30(10):2875-2885. doi: 10.1007/s11136-021-02855-9. Epub 2021 May 3.

The effect of functioning on Quality of Life Inventory-Disability measured quality of life in children with intellectual disability is not mediated or moderated by parental psychological distress

ABSTRACT:

Purpose: The measurement of quality of life (QOL) in children with intellectual disability often relies upon proxy-report via caregivers. The current study investigated whether caregiver psychological distress mediates or moderates the effects of impairment on their ratings of QOL in children with intellectual disability.

Methods: Caregivers of 447 children with an intellectual disability reported their child's day-to-day functioning, their own psychological distress using the Kessler Psychological Distress Scale, and the Quality of Life Inventory-Disability (QI-Disability), a measure of QOL for proxy-report of a child's observable behaviours that indicate quality of life. Linear regression was used to assess the effects of the child's functional abilities on their QI-Disability score and causal mediation analysis to estimate the extent to which these effects were mediated by caregivers' psychological distress.

Results: A minority of caregivers (n=121, 27.1%) reported no psychological distress. Lower day-to-day functional abilities, such as being fully dependent on others to manage their personal needs were associated with lower total QOL scores. There was no significant mediation effect of caregiver psychological distress on the association between child functioning and total QOL scores. Moderation analyses revealed small and largely non-significant interaction coefficients, indicating that caregiver

psychological distress did not influence the strength of the relationship between child functioning and total QOL scores.

Conclusion: Caregiver psychological distress did not mediate or moderate the relationship between the level of functional abilities and QOL in children with intellectual disability. QI-Disability measured observable child behaviours which may reduce the influence of caregiver factors on the accurate measure of QOL for children with intellectual disability.

PLAIN ENGLISH SUMMARY

Caregivers of a child with intellectual disability often report on their child's quality of life when planning what clinical care and disability supports are needed. It is possible that caregiver feelings influence how they rate the child's quality of life and ratings may not be accurate. We tested whether caregiver feelings affected their rating of the child's quality of life, measured with the Quality of Life Inventory-Disability. Caregiver feelings did not alter the relationships between the child's abilities to walk, talk or look after their personal needs and child QOL. This is possibly because the Quality of Life Inventory-Disability measures observable child behaviours which may reduce any effects of caregiver feelings on their ratings.

Keywords: Quality of life, intellectual disability, functional impairment, proxy-report, caregiver mental health

INTRODUCTION

Children with intellectual disability are vulnerable to a wide range of physical and mental health problems [1-3], many of which persist into adulthood [4]. The cause of intellectual disability is often unknown but advances in genetic testing including genome sequencing, next generation sequencing and use of gene panels for clinical diagnosis is identifying a genetic cause for a growing number of children [5,6], beyond the more readily recognised disorders such as Down syndrome. Although not causative, some children have been exposed to risk factors such as preterm birth or intrauterine growth restriction [7]. Common developmental conditions may be accompanied by intellectual disability which, for example, affects approximately 50% of children with cerebral palsy [8]. Each child experiences difficulties with adaptive behaviours, a set of conceptual, social and practical skills that are necessary for everyday living. Many children also experience challenges to physical and mental health and wellbeing. Each of these difficulties can impact the child's quality of life (QOL) and as such, it is important to understand both aspects of the condition and QOL.

QOL refers to satisfaction with life experiences, some that are universal and others that vary by the specific population group [9]. Accordingly, the domains of QOL identified as important for children [10] and adolescents [11] with cerebral palsy have included condition-specific domains such as pain and discomfort. We recently extended this literature by exploring the domains of QOL important to children with cerebral palsy and comorbid intellectual disability, finding novel domains of "predictability and routines" as well as "nature and the outdoors" [12]. Based on these latter data and together with the domains identified as important for children and adolescents with autism spectrum disorder [13], Down syndrome [14] and Rett syndrome [15], we developed and validated the Quality of Life Inventory-Disability (QI-Disability), a QOL scale designed to capture important domains of QOL across the spectrum of intellectual disability [16-18].

QI-Disability was designed as a proxy report measure, given that many children and adolescents with intellectual disability may be restricted in their abilities to reflect inwardly, think abstractly, and thereafter

communicate their feelings and experiences [19]. Although not exclusive, proxy-reported data makes an important contribution to the care and support of children and adolescents with intellectual disability. However, we acknowledge that there could be differences between parent and child reports [20]. In a study of 201 caregivers of a child with cerebral palsy, relationships between the level of impairment measured by the Gross Motor Classification System and CP-QOL scores were partially mediated by parental psychological distress for nine of the 11 CP-QOL domain scores. These findings suggest that parents may report lower child QOL when they are experiencing psychological distress [21]. To reduce this potential effect, QI-Disability items were derived from behaviours reported in qualitative data that could be observed [12,15,13,14] rather than proxy-reported interpretations of how they believed the child or adolescent felt [16]. Alternatively, the parental mental health status could moderate the relationship between functional abilities and child QOL, indicating the circumstances when this relationship could be true [22]. Investigations of potential moderator variables influencing quality of life in children with a disability are sparce but different coping strategies have been identified as both a mediator and moderator in the relationship between stress and quality of life in parents who have a child with autism [23]. The possibility that factors related to the proxy-respondent could influence these relationships cannot be excluded.

We have previously reported that greater levels of impairments were associated with poorer QOL, particularly when children were fully dependent when managing daily tasks and experienced difficulties making eye contact when speaking [24]. Using an expanded dataset, this current study was designed to build upon these findings and investigate whether caregiver psychological distress was a mediator on the pathway between functional impairment and child and adolescent QOL and also whether psychological distress moderated the association between impairment and QOL.

METHODS

Data sources

This work forms part of a large cross-sectional study to investigate the determinants of QOL in children with confirmed intellectual disability and a diagnosis of ASD, cerebral palsy, Down syndrome or Rett syndrome, as described in detail elsewhere [24]. In summary, participating families were primary caregivers of children registered with disorder-specific databases or through community organisations and networking. The questionnaire was administered using the Research Electronic Data Capture (REDCap) tool with some families providing data using a paper format or telephone interview. Ethics approval for this study was provided by Human Research Ethics Committees at The University of Western Australia (RA/4/20/4276) and the Child and Adolescent Health Services (RGS2390), and primary caregivers provided informed consent to participate in the study.

Measures

Exposure variables – Novel items with categorical responses were developed to describe functional abilities, adapted from the Index of Social Competence [25]. These included items to evaluate

1. Mobility: responses were categorised as ability to walk at least 500 metres with no difficulty, ability to walk independently but for shorter distances, ability to walk with assistance or unable to walk.
2. Communication: responses were categorised as ability to speak well, some difficulty speaking such as lack of clarity, difficulty speaking and only understood by those who know him/her well, non-verbal communication, and unable to communicate.
3. Independence in relation to personal needs: responses were categoried as independent, independent but needing monitoring or reminding, needing assistance or fully dependent.

Questions from the Eye Contact Avoidance Scale (ECAS) [26] were selected to measure the individual's eye contact during social functioning when he/she initiates communication. Eye contact when communicating with the parent, friends and family, and when communicating with unfamiliar people were each rated on a 0 to 4-point Likert scale (0=Never, 1=Rarely, 2=Sometimes, 3=Often, 4=Always)

and then 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 (>=9) levels of eye contact.

Potential confounder variables included sleep dysfunction, pain, frequency of seizures and scoliosis. The Sleep Disturbance Scale for Children [27], comprising 26 items rated on a 5-point Likert scale with a Cronbach alpha value of 0.79, was used to describe sleep. This scale has also been used populations with a developmental disability including Rett syndrome [28], autism [29] and cerebral palsy [30]. As well as giving an overall score, the instrument derives five subdomains by summing the relevant items. For this study, only the "Disorders of Initiating and Maintaining Sleep" (DIMS) and the "Disorders of Excessive Somnolence" (DOES) subscales were used. Scores were compared with normative data reported in the initial validation paper [27], to calculate z-scores and then t-scores based on the normative DIMS or DOES dataset [27].

Novel items with categorical responses were developed to describe other potential confounders including

1. Parents observed their child's experiences of pain over the previous month as "not at all", "occasionally" or "recurrently".
2. Epilepsy, a diagnosis of epilepsy was classified as "yes" or "no" and if yes, the frequency of seizures was described as "controlled", "fewer than once per month", "monthly" or "daily or weekly".
3. Scoliosis was classified as "no scoliosis", "mild or moderate scoliosis", "severe scoliosis treated with surgery" or "severe scoliosis managed conservatively".
4. Age was classified as 5 to 12 years or 13 to 18 years.
5. Other confounder variables were diagnostic group and gender.

Mediation / moderation variable - Parental distress was assessed using the Kessler Psychological Distress scale (K10) comprising 10 questions about emotional states each with a 5-level response scale [31].

Scores of the items are summed yielding a range of possible total scores from 10 to 50. Higher scores indicate higher levels of psychological distress and can discriminate individuals with anxiety and mood disorders from those who do not [31,32]. Scores were classified to represent levels of psychological distress (<15 low, 16-21 moderate, 22-29 high, 50-50 very high) [31].

Dependent variable - QI-Disability was used to measure child or adolescent QOL, a 32-item parent-report measure comprising six domains: Social Interaction (7 items), Positive Emotions (4 items), Negative Emotions (7 items), Physical Health (4 items), Leisure and the Outdoors (5 items) and Independence (5 items) [16]. Domain scores are transformed onto a scale of 0 to 100, with higher scores representing better QOL. A total score is derived by averaging domain scores. The psychometric properties of the measure have been reported including content validity [15], satisfactory convergent validity with Cronbach alpha coefficients ranging from 0.72 to 0.90 [16], and ICC values ranging from 0.58 to 0.91 after adjusting for changes in physical and emotional health status [18].

Statistical Analysis

Linear regression models were used to estimate a) total effects of the impairment variables on QI-Disability total and domain scores after adjustment for confounder variables, b) associations between parental distress and QI-Disability scores and c) the association between impairments and parental distress. We then performed mediation analysis to estimate the ACME (average causal mediation effect) which is the indirect effect of the impairment variable on QOL acting through the hypothesised mediation pathway of parental distress. The mediation analysis partitions the total effect into the ACME and a direct effect which does not involve the mediation pathway. The small amount of missing data was considered to be missing at random and complete case analysis was conducted. Statistical analyses were performed using STATA 16.0 (StataCorp LLC, College Station, Texas) with the *paramed* module used for the mediation analysis. Sensitivity analyses to address the sequential ignorability (no unmeasured confounding) assumption were performed using the STATA module *medsens*. We also investigated any moderation of the total effect in a) above by including in the regression models interaction terms

involving parental distress and the impairment variables. The mediation and moderation analyses are presented in Figure 1.

RESULTS

Between March 2018 and January 2020, 577 parents/primary caregivers were asked to complete a questionnaire, with 447 responses received. Respondents comprised 151 (33.8%) parents/primary caregivers with a child/adolescent with cerebral palsy (CP); 132 (29.5 %) with a child/adolescent with autism spectrum disorder (ASD), 90 (20.1%) with a child/adolescent with Down syndrome and 74 (16.6%) with a child/adolescent with Rett syndrome. Data describing the distributions of functioning, physical health, parent/caregiver psychological distress and QOL variables are presented in Table 1. The mean (SD) Kessler-10 score was 21.2 (7.7), with scores classified as no psychological distress for 121 (27.1%) caregivers, mild distress for 135 (30.2%), moderate distress for 121 (27.1%) and high distress for 70 (15.7%) of caregivers.

Relationships between functioning and QOL

In univariate analyses and compared to child/adolescent's with the highest level of functioning in each domain, total QOL scores were lower when the child/adolescent was unable to walk (coeff -9.85, 95%CI -12.89,-6.81), unable to communicate (coeff -13.01, 95%CI -17.57,-8.45), had the poorest level of eye contact during speaking (coeff -10.62, 95%CI -13.58,-7.65) or was fully dependent on others to manage their personal needs (coeff -14.35, 95%CI -20.84,-7.85) (Table 2). Adjusting for the other functioning and confounding variables (Total Effect, Table 2), there were smaller and no longer statistically significant coefficient values for total QOL scores for each of the mobility and communication levels compared to the reference levels. However, significantly lower QOL scores persisted for children/adolescents with the poorest level of eye contact (coeff -6.34, 95%CI-9.03, -3.65) and being fully dependent for daily needs (coeff -8.75, 95%CI-14.80, -2.70). Multivariate model coefficients for the confounding variables are reported in Supplementary Table 1.

Relationships between functioning, parent/caregiver psychological distress and QOL

Relationships between functioning and parent/caregiver psychological distress are presented in Table 3. There were no statistically significant relationships between impaired functioning and psychological distress after adjustment for confounding variables. However, higher psychological distress was associated with lower total QOL scores in a univariate model (coeff -0.47, 95%CI -0.61,-0.32) corresponding to a reduction of half a point in QOL score for each additional point on the Kessler-10 scale.

Causal mediation analysis

Table 2 (Indirect Effect) shows the results of performing causal mediation analysis to estimate the indirect effects of poor functioning on total QOL scores operating through parent/caregiver psychological distress pathway. The mediation analysis showed no significant mediation effects of impairment through the parental distress pathway for any of the domains, with estimates of direct effects and total effects being similar (Table 2). Sensitivity analyses to address the sequential ignorability assumption showed that an unmeasured confounder would have to display a correlation in excess of 0.5 for any of the significant total effects of poor functioning to be substantially mediated through parental distress.(Supplementary Figures 1-3)

Moderation by parent/caregiver psychological distress

Table 4 shows interaction coefficients describing the moderating effect of psychological distress on the association between functional impairment and QOL. The coefficients are small and not statistically significant with the exception of one interaction effect involving the mildest level of mobility impairment (coeff -0.45, 95%CI -0.76,-0.14). It is difficult to interpret this effect as other than a chance finding.

DISCUSSION

QOL is a key concept in clinical science, helping guide and monitor decisions around clinical management. QOL is typically measured via direct report of the individual, but can also be measured via proxy-report in cases where there are challenges in communication or intellectual functioning, such as in children and adolescents with intellectual disability. Concerns have been raised that the rating of a child's QOL may be influenced by factors associated with the proxy-rater, particularly in the case of caregiver ratings and any concomitant psychological distress they may be experiencing [21]. Previously, we have shown that lower levels of child or adolescent functioning were associated with poorer parent-rated QOL, as measured by the QI-Disability [24]. The current study is an important extension of these findings, showing that this association was not mediated nor moderated by caregiver psychological distress, and providing evidence that caregiver psychological distress has little influence on how they report on their child or adolescent's QOL with this measure.

Parent caregivers with a child or adolescent with intellectual disability are extremely vulnerable to psychological strain and distress, illustrated also in our sample where 27.1% reported no distress compared with approximately 70% in the general population [31]. Poorer mental health has been attributed to the child's sleep and behavioural problems [33], recurring grief [34], and challenges navigating the complex care pathways for their child's necessary supports [35]. Greater impairments in children with CP have been associated with poorer caregiver mental health [21], possibly because greater levels of care are needed, although descriptive parental distress data where not reported in this paper [21] and we could not compare with the current sample. In contrast, the levels of impairments were not associated with parent caregiver psychological distress in our sample, possibly because there are a wider range of comorbidities and behavioural challenges necessitating high levels of care across different levels of functional ability in intellectual disability. Caregiver mental health can vary by the child's diagnosis [36] and we have demonstrated better mental health in mothers with a child/adolescent with Down syndrome compared to those with a child/adolescent with Rett syndrome [37]. Accordingly, our mediation and moderation models adjusted for diagnostic group. We also did not include child/adolescent

behaviour as a functioning variable because it was identified as a component of poor QOL in the qualitative studies on which QI-Disability is based [12,15,13,14] and relevant items are incorporated into QI-Disability, although we acknowledge the important relationship between child challenging behaviour and maternal mental health [35].

The mediation and moderation analyses examined different ways caregiver psychological distress may influence the association between child/adolescent functioning and QOL. Mediation analyses tested a hypothetical causal chain in which child/adolescent functional abilities would influence the caregiver emotional state, which in turn would affect caregiver ratings of QOL. The current study found no evidence for a mediating influence of caregiver psychological distress, with similar coefficient estimates being observed for the tests of direct and total effects and very small coefficients for the indirect effects. Moderation analyses examined whether there are certain circumstances under which the effect between child/adolescent functional ability and QOL would differ, specifically the presence or severity of psychological distress experienced by the caregiver. The interaction coefficients for different levels of caregiver psychological distress were small and nonsignificant in almost all cases, indicating no moderation effect of caregiver psychological distress on the bivariate association. The one statistically significant interaction effect observed was for the mildest level of mobility impairment (i.e., walks independently but < 500m). There is little theoretical reason to support a moderating effect of caregiver psychological distress in children or adolescents with this level of mobility impairment. While we cautiously interpret this effect as a chance finding, we encourage future studies of other participant samples to test this interpretation.

The findings of this study contrast with a previous study in the area which found a weak mediating effect of caregiver depression on proxy-reported QOL of children with cerebral palsy [21]. There were two key differences between the studies. The first relates to the populations investigated. The previous study included a sample (n = 201) of children with CP, aged between 4 and 12 years. By contrast, the current study investigated a larger (n = 447) and more clinically diverse (CP, ASD, Down syndrome, Rett

syndrome) sample which spanned a greater age range (5 to 18 years). It is plausible that between-study differences in any (or combination) of these variables, in isolation or combination, could drive differences in study findings. Another critical difference between studies is the measure of QOL administered. Most QOL proxy-report measures of QOL, such as the questionnaire administered in the previous study (Cerebral Palsy Quality of Life Questionnaire for Children [10]), ask caregivers to report on their impression of the child's feelings. The QI-Disability takes a different approach by asking caregivers to rate behaviours or actions they observe in their child or adolescent [16]. It is possible that the experience of psychological distress influences a caregiver's impressions of their child's feelings, and that this confounding influence is reduced or eliminated by focusing on the ratings of observable behaviours.

The study design was strengthened by a large sample size of children and adolescents with a range of diagnostic conditions, which broadens the clinical implications of the findings. A limitation of the study design was that observations were restricted to a single cross-sectional time point and data on child functioning levels were parent reported. While mediation and moderation analyses of cross-sectional data are valid, stronger inferences from the results of these analyses can be made with longitudinal datasets. This may be particularly salient for children with intellectual disability, for whom there are significant changes across childhood (and adulthood), particularly in key life stages such as transition to school [38] and the onset of puberty [39,40]. The collection of longitudinal datasets, which facilitate an examination of changes within an individual over time, will be an important extension to the findings presented here.

The development of supports that can enhance QOL for children and adolescents with intellectual disability is a key public health aim. Central to this aim is the accurate measurement of QOL to guide priorities for clinical management and monitor progress according to the goals set. While self-report is preferable, proxy report via caregivers remains common in paediatric practice [19], particularly for children and adolescents with intellectual disability where the ability to reflect inwardly and communicate complex concepts remains poorly understood. There are two main findings in the current study. First, our contemporary dataset indicates that high prevalence of mental health difficulties for caregivers with a

child/adolescent with intellectual disability is persisting and the imperative remains to find effective supports for this group. Second, our statistical models suggest that reporting of child QOL using instruments that measure observable QOL-linked behaviours, such as the QI-Disability, may not be influenced by caregiver psychological distress, and may therefore be particularly applicable for use with children with intellectual disability within clinical practice and research.

DECLARATIONS

All procedures performed were in accordance with the ethical standards of the institutional research committees and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. The study was approved by the Human Research Ethics Committees at The University of Western Australia (RA/4/20/4276) and the Child and Adolescent Health Services (RGS2390), and primary caregivers provided informed consent to participate in the study.

Professor Andrew Whitehouse, Associate Professor Peter Jacoby, Professor Dinah Reddihough and Professor Katrina Williams have no financial or non-financial interests to declare.

Associate Professor Helen Leonard has consulted for Marinus, Newron, Anavex, GW Pharmaceuticals and AveXis and remuneration has been made to her department. She has been an investigator on clinical trials with Newron and Anavex. These interests have had no role in the current work.

Associate Professor Jenny Downs has consulted for Newron, Anavex, GW Pharmaceuticals and AveXis and remuneration has been made to her department. She has been an investigator on clinical trials with Newron and Anavex. She has non-financial relationships with Marinus, Ovid/Takeda and Ultragenyx. These interests have had no role in the current work.

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Table 1: Frequency distribution (%) of categorical and mean (SD) values for continuous variables describing the individuals in the study (n=447).

		All (n=447)	Cerebral Palsy (n=151)	Autism spectrum disorder (n=132)	Down syndrome (n=90)	Rett syndrome (n=74)
Age (N=447)	5 to 11 years	230 (51.5)	65 (43.0)	76 (57.6)	52 (57.8)	37 (50.0)
	12 to 18 years	217 (48.5)	86 (57.0)	56 (42.4)	38 (42.2)	37 (50.0)
Gender (N=446; 0.003% missing)	Female	223 (50.0)	60 (40.0)	35 (26.5)	54 (60.0)	74 (100.0)
Mobility (N=447)	Walks with no assistance	134 (30.0)	12 (8.0)	91 (68.9)	31 (34.4)	0
	Walks short distances only	160 (35.8)	41 (27.2)	39 (29.6)	58 (64.4)	22 (29.7)
	Walks with assistance	35 (7.8)	19 (12.6)	2 (1.5)	0	14 (18.9)
	Unable to walk	118 (26.4)	79 (52.3)	0	1 (1.1)	38 (51.4)
Communication (N=446; 0.003% missing)	Speaks well	46 (10.3)	13 (8.6)	25 (18.9)	6 (6.7)	2 (2.7)
	Some difficulty speaking	134 (30.0)	32 (21.2)	52 (39.4)	43 (47.8)	7 (9.6)
	Difficult to understand	87 (19.5)	18 (11.9)	29 (22.0)	34 (37.8)	6 (8.2)
	Nonverbal only	119 (26.7)	49 (32.5)	19 (14.4)	6 (6.7)	45 (61.6)
	None	60 (13.5)	39 (25.8)	7 (5.3)	1 (1.1)	13 (17.8)
Personal Needs (N=447)	Looks after personal needs	15 (3.4)	6 (4.0)	7 (5.3)	2 (2.2)	0
	Requires checking	88 (19.7)	11 (7.3)	42 (31.8)	33 (36.7)	2 (2.7)
	Needs assistance	112 (25.1)	23 (15.2)	50 (37.9)	36 (40.0)	3 (4.1)
	Fully dependent	232 (51.9)	111 (73.5)	33 (25.0)	19 (21.1)	69 (93.2)
Eye contact (N=435; 0.04% missing)	Good	153 (35.2)	49 (35.3)	20 (15.2)	44 (48.9)	40 (54.1)
	Average	173 (39.8)	55 (39.6)	61 (46.2)	32 (35.6)	25 (33.8)
	Poor	109 (25.1)	35 (25.2)	51 (38.6)	14 (15.6)	9 (12.2)
Seizure Frequency (N=441; 0.014% missing)	None	267 (60.5)	62 (41.1)	110 (83.3)	85 (94.4)	10 (14.7)
	Controlled	45 (10.2)	25 (16.6)	6 (4.6)	3 (3.3)	11 (16.2)
	Less than once a week	66 (15.0)	35 (23.2)	9 (6.8)	0	22 (32.4))
	Daily or weekly	63 (14.3)	29 (19.2)	7 (5.3)	2 (2.2)	25 (36.8)
Pain (N=446; 0.003% missing)	None	167 (37.4)	44 (29.3)	58 (43.9)	36 (40.0)	29 (39.2)
	Occasional	202 (45.3)	69 (46.0)	63 (47.7)	46 (51.1)	24 (32.4)

	Recurrent	77 (17.3)	37 (24.7)	11 (8.3)	8 (8.9)	21 (28.4)
Scoliosis (N=436; 0.025% missing)	None	331 (75.9)	96 (63.6)	128 (97.7)	85 (94.4)	22 (34.4)
	Mild/moderate	50 (11.5)	23 (15.2)	2 (1.5)	4 (4.4)	21 (32.8)
	Severe, has had surgery	36 (8.3)	19 (12.6)	1 (0.8)	1 (1.1)	15 (23.4)
	Severe, no surgery	19 (4.4)	13 (8.6)	0	0	6 (9.4)
DIMS (N=440; 0.16% missing)	Abnormal	210 (47.7)	77 (52.7)	69 (52.7)	31 (34.8)	33 (44.6)
DOES (N=443; 0.01% missing)	Abnormal	103 (23.3)	36 (24.3)	24 (18.3)	15 (16.7)	28 (37.8)
Psychological Distress (Range 10 to 50) (N=447)	Kessler-10 score	21.2 (7.7)	21.5 (7.9)	21.9 (7.9)	19.0 (6.3)	22.1 (8.1)
Primary Caregiver's Education (N=443; 0.01% missing)	Tertiary	203 (45.8)	66 (43.7)	63 (48.1)	48 (53.9)	26 (36.1)
Family Type (N=446; 0.003% missing)	Single Parent	66 (14.8)	24 (15.9)	21 (15.9)	11 (12.2)	10 (13.7)
Siblings (N=447)	None	65 (14.5)	23 (15.2)	19 (14.4)	17 (18.9)	6 (8.1)
	1-2	309 (69.1)	101 (66.9)	91 (68.9)	58 (64.4)	59 (79.7)
	3 or more	73 (16.3)	27 (17.9)	22 (16.7)	15 (16.7)	9 (12.2)
Quality of life (Range 0 to 100) (N=447)	Total score	69.2 (12.7)	66.6 (13.5)	68.3 (10.9)	77.5 (11.7)	66.1 (11.2)

DIMS: Disorders of Initiating and Maintaining Sleep
DOES: Disorders of Excessive Somnolence

Table 2: Relationships between functioning and total QOL scores, taking into account the effects of confounder variables* and mediation by maternal distress level (k10).

		Univariate model **Coefficient [95% CI]** ***p-value***	Total Effect* **Coefficient [95% CI]** ***p-value***	Direct Effect **Coefficient [95% CI]** ***p-value***	Indirect Effect **Coefficient [95% CI]** ***p-value***
Personal Needs	Looks after his/her personal needs independently	ref	ref	ref	ref
	Needs checking and reminding	-4.24 (-11.03,2.55) 0.221	-3.61 (-9.02,1.80) 0.191	-3.83 (-9.18,1.53) 0.161	0.21 (-0.58,1.00) 0.597
	Is provided with assistance but helps	-9.52 (-16.21,-2.83) 0.005	-7.49 (-13.08,-1.91) 0.009	-7.38 (-2.91,-1.85) 0.009	-0.12 (-0.92,0.69) 0.777
	Is dependent on other persons	-14.35 (-20.84,-7.85) <0.001	-8.75 (-14.80,-2.70) 0.005	-8.73 (-14.72,-2.75) 0.004	-0.01 (-0.89,0.86) 0.975
Mobility	Able to walk at least fair distances (at least 500m)	ref	ref	ref	ref
	Walks independently but < 500m	-2.07 (-4.90,0.75) 0.149	-2.37 (-4.93,0.19) 0.070	-2.35 (-4.88,0.19) 0.070	-0.02 (-0.40,0.36) 0.911
	Needs assistance to walk	-3.67 (-8.22,0.88) 0.114	1.87 (-2.96,6.71) 0.448	2.07 (-2.72,6.86) 0.397	-0.19 (-0.92,0.53) 0.598
	Unable to walk	-9.85 (-12.89,-6.81) <0.001	-1.55 (-5.90,2.81) 0.487	-1.77 (-6.09,2.54) 0.421	0.23 (-0.43,0.89) 0.500
Communication	Speaks well and understood	ref	ref	ref	ref
	Some difficulty speaking such as lack of clarity	2.15 (-1.83,6.13) 0.289	0.76 (-2.51,4.04) 0.648	0.98 (-2.27,4.22) 0.555	-0.21 (-0.72,0.29) 0.411
	Only understood by those who know him/her well	-2.41 (-6.67,1.84) 0.266	0.62 (-3.26,4.50) 0.753	0.84 (-3.00,4.68) 0.667	-0.22 (-0.81,0.37) 0.466
	Nonverbal communication	-4.84 (-8.89,-0.80) 0.019	2.51 (-1.78,6.80) 0.252	2.62 (-1.63,6.87) 0.227	-0.11 (-0.75,0.53) 0.739
	Unable to communicate	-13.01 (-17.57,-8.45) <0.001	-2.66 (-7.45,2.13) 0.276	-2.33 (-7.07,2.42) 0.336	-0.34 (-1.08,0.41) 0.377
Eye Contact	High	ref	ref	ref	ref
	Medium	-4.32 (-6.94,-1.71) 0.001	-2.30 (-4.55,-0.05) 0.046	-2.48 (-4.71,-0.25) 0.029	0.18 (-0.17,0.54) 0.309
	Poor	-10.62 (-13.58,-7.65) <0.001	-6.34 (-9.03,-3.65) <0.001	-6.35 (-9.01,-3.70) <0.001	0.02 (-0.38,0.41) 0.938

* from multivariate model including all functioning variables, and adjusting for seizure frequency, scoliosis, sleep disturbances, pain, age group, diagnostic group and gender.

Table 3: Relationships between functioning and parent/caregiver psychological distress. Coefficient values represent the mean change in Kessler-10 score for each level of the independent variable relative to the reference level.

Predictor		**Outcome – Kessler-10 Coefficient (95% CI) p-value**	
		Univariate models	**Multivariate model****
Personal Needs	Can look after his/her personal needs independently	ref*	ref
	Needs checking and reminding	-1.54 (-5.76,2.67) 0.471	-1.12 (-5.21,2.97) 0.591
	Is provided with assistance but helps	1.52 (-2.63,5.67) 0.471	0.61 (-3.62,4.84) 0.776
	Is dependent on other persons	1.21 (-2.81,5.22) 0.555	0.07 (-4.53,4.68) 0.975
Mobility	Able to walk at least fair distances (at least 500m)	ref	ref
	Walks independently but shorter distances than 500m	0.21 (-1.57,2.00) 0.816	0.11 (-1.88,2.11) 0.911
	Needs assistance to walk	2.47 (-0.41,5.36) 0.093	1.03 (-2.74,4.80) 0.592
	Unable to walk	-0.20 (-2.13,1.72) 0.836	-1.20 (-4.59,2.19) 0.488
Communication	Speaks well and understood	ref	ref
	Some difficulty speaking such as lack of clarity	0.82 (-1.80,3.44) 0.539	1.12 (-1.44,3.67) 0.391
	Only understood by those who know him/her well	1.67 (-1.13,4.46) 0.243	1.16 (-1.87,4.19) 0.451
	Nonverbal communication	2.04 (-0.62,4.70) 0.133	0.57 (-2.78,3.93) 0.737
	Unable to communicate	2.37 (-0.64,5.38) 0.122	1.77 (-1.98,5.51) 0.354
Eye Contact	High	ref	ref
	Medium	0.09 (-1.60,1.78) 0.913	-0.97 (-2.73,0.79) 0.277
	Low	1.93 (0.01,3.85) 0.048	-0.08 (-2.17,2.01) 0.938

* ref – reference category

* *multivariate model includes all functioning variables, seizure frequency, scoliosis, sleep disturbances, pain, age group, diagnostic group and gender

Table 4: Moderation of the functioning effects on QOL by maternal distress level. Coefficients of interactions between k10 and impairment level from multivariate model adjusted for confounders*.

		Coefficient [95% CI] ***p-value***
Personal Needs	Looks after his/her personal needs independently	ref
	Needs checking and reminding	-0.55 (-1.27,0.16) 0.128
	Is provided with assistance but helps	-0.54 (-1.26,.0.18) 0.142
	Is dependent on other persons	-0.38 (-1.14,0.37) 0.320
Mobility	Able to walk at least fair distances (at least 500m)	ref
	Walks independently but < 500m	-0.45 (-0.76,-0.14) 0.005
	Needs assistance to walk	-0.30 (-0.76,0.17) 0.208
	Unable to walk	-0.33 (-0.75,0.10) 0.133
Communication	Speaks well and understood	ref
	Some difficulty speaking such as lack of clarity	0.03 (-0.45,0.51) 0.912
	Only understood by those who know him/her well	0.30 (-0.24,0.84) 0.281
	Nonverbal communication	0.51 (-0.03,1.05) 0.065
	Unable to communicate	0.33 (-0.24.0.90) 0.257
Eye Contact	High	ref
	Medium	-0.18 (-0.47,0.12) 0.247
	Poor	0.01 (-0.330.35) 0.944

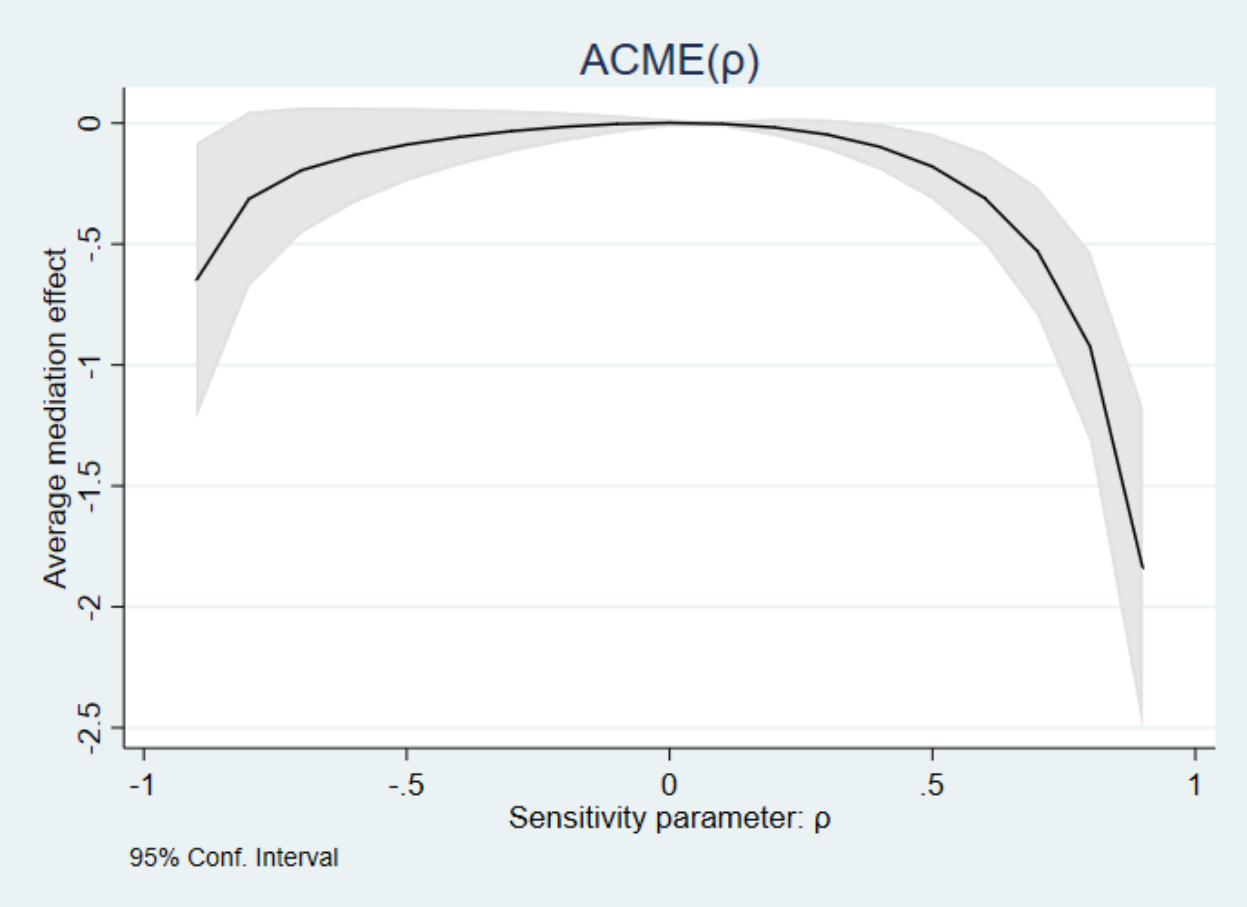
* adjusting for seizure frequency, scoliosis, sleep disturbances, pain, age group, diagnostic group and gender

Supplementary Table 1: Coefficients* of confounder variables from multivariate model estimating the direct effect of functioning variables on total QOL

		Coefficient (95% CI)	p-value
Age	5 to 11 years	Ref	
	12 to 18 years	-1.85 (-3.87, 0.17)	0.072
Gender	Male	Ref	
	Female	1.06 (-1.10, 3.21)	0.336
Seizure Frequency	None	Ref	
	Controlled	-0.71 (-4.28, 2.87)	0.697
	Less than once a month	1.24 (-2.47, 4.95)	0.513
	Monthly	-0.48 (-4.97, 4.01)	0.833
	Daily or weekly	-2.13 (-5.41, 1.15)	0.202
Pain	None	Ref	
	Occasional	-0.40 (-2.47, 1.67)	0.706
	Recurrent	-1.83 (-4.78, 1.13)	0.225
Scoliosis	None	Ref	
	Mild/moderate	-2.63 (-6.13, 0.87)	0.140
	Severe, has had surgery	-2.56 (-7.04, 1.92)	0.262
	Severe, no surgery	-4.60 (-9.97, 0.77)	0.093
Sleep	DIMS (continuous)	-0.09 (-0.14, -0.03)	0.003
	DOES (continuous)	-0.23 (-0.30, -0.16)	<0.001
Diagnostic Group	ASD	Ref	
	Cerebral Palsy	3.00 (-0.18, 6.18)	0.064
	Down syndrome	6.23 (3.23, 9.22)	<0.001
	Rett syndrome	2.18 (-2.19, 6.56)	0.327

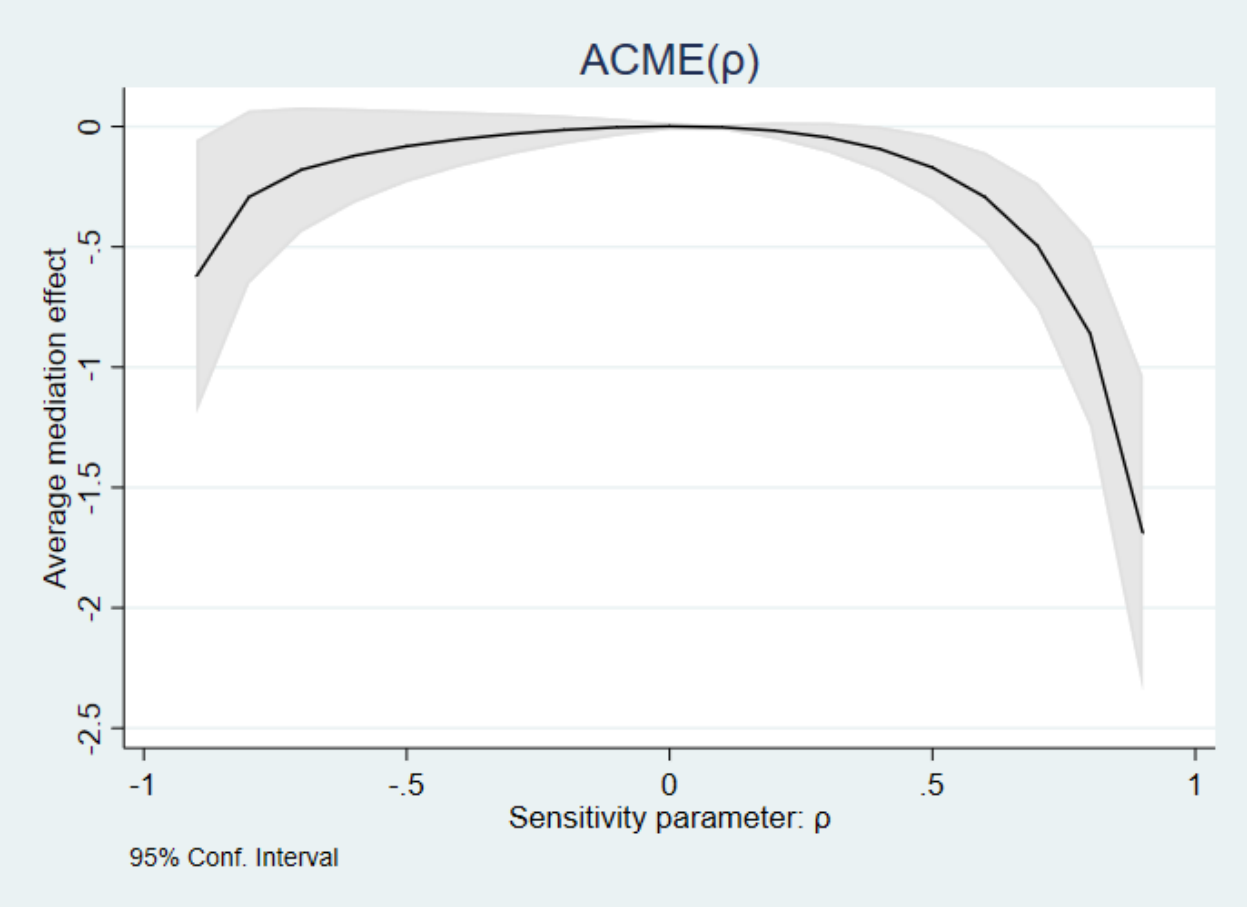
* Coefficients are the difference in QOL score for the factor level compared to the reference level. For continuous covariates they are the increase in QOL score per unit increase in covariate score

Supplementary Figure 1 - Sensitivity graph showing influence of an unmeasured confounder on the mediation effect of Personal Needs (Level 3 – Is provided with assistance)



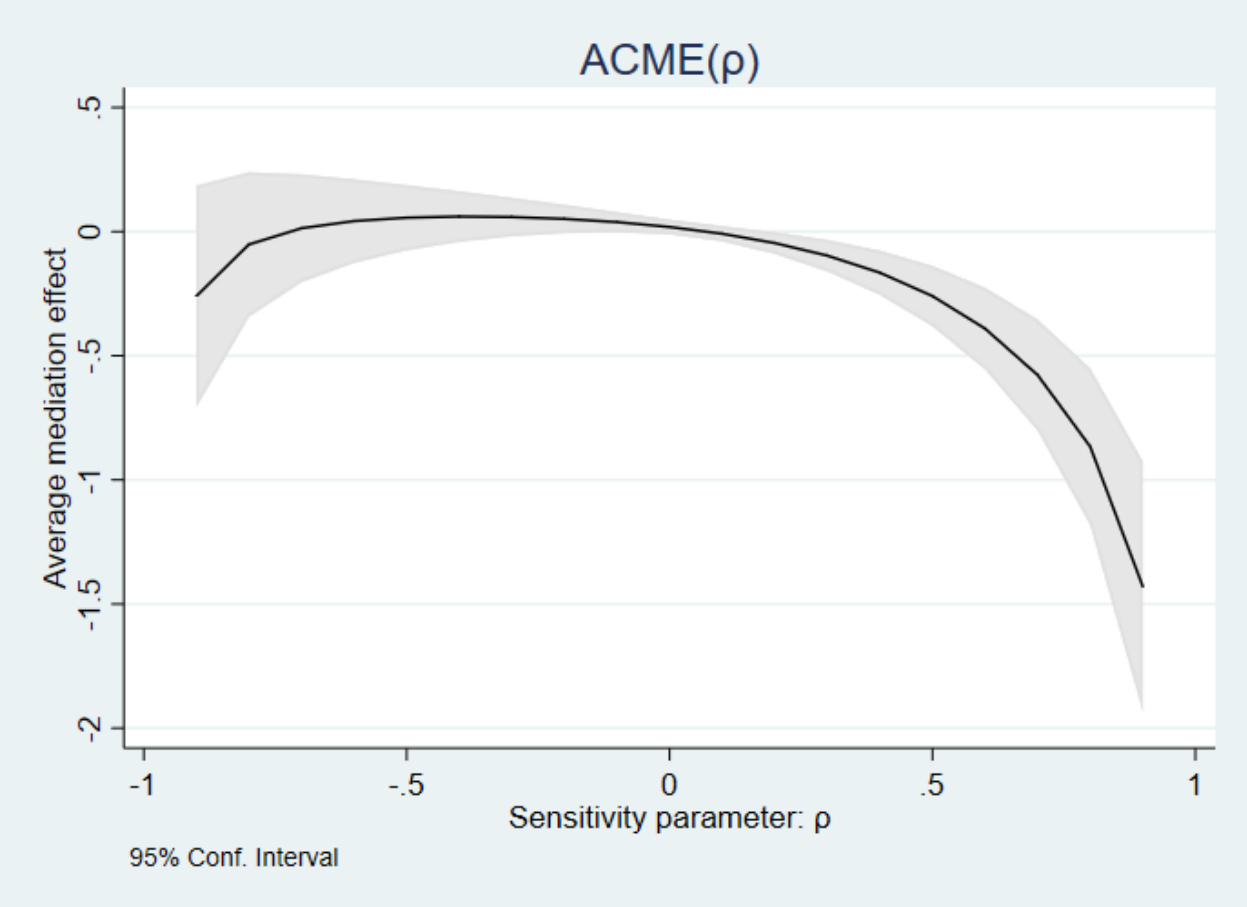
ρ is the strength of confounding indicated by the correlation between residuals of the outcome-mediator and the outcome-predictor models

Supplementary Figure 2 - Sensitivity graph showing influence of an unmeasured confounder on the mediation effect of Personal Needs (Level 4 – Is dependent on other persons)



ρ is the strength of confounding indicated by the correlation between residuals of the outcome-mediator and the outcome-predictor models

Supplementary Figure 3 - Sensitivity graph showing influence of an unmeasured confounder on the mediation effect of Eye Contact (Level 3 – Poor eye contact)



ρ is the strength of confounding indicated by the correlation between residuals of the outcome-mediator and the outcome-predictor models