Anxiety, Depression and Quality of Life in Parents of Children with Congenital Hyperinsulinism

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Research Article

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Abstract

This study aimed to assess the mental health, family burden, and quality of life in parents of children with persisting congenital hyperinsulinism (CHI).

Forty-eight individual parents (75% female) of children with CHI completed self-reported questionnaires and screening tools for anxiety (GAD-7), depression (PHQ-8), quality of life (ULQIE), and family burden (FaBeL). Additional data on sociodemographics, social support, and child- and disease-related data were recorded.

29.8% of parents showed major depressive symptoms and 38.3% had a probable general anxiety disorder, including 20.8% who had both. Family burden was moderate and parental assessment of quality of life (PQoL) yielded average scores. Neurological impairment in an affected child ($p = .002$; $p < .001$) and lower number of working hours ($p = .001$; $p = .012$) were the most powerful predictors of elevated GAD-7 and PHQ-8 scores and poor PQoL.

Further, comorbidities in the affected child ($p = .007$) were significantly associated with lower PQoL. Mothers presented with significantly higher scores for anxiety symptoms ($p = .006$) and lower PQoL ($p = .035$) than fathers. A higher number of caretakers beyond parents was associated with decreased family burden ($p = .019$), improved PQoL ($p < .001$), and improved mental health ($p = .021$ and $p = .016$).

***Conclusions**:* Symptoms of depression and anxiety are alarmingly prevalent in parents of children with CHI. Psychological screening of parents should be initiated to ensure early identification of psychological strains and psychosocial support should be offered as needed. A good support network and regular professional activities can improve parental mental health and well-being.

What Is Known

- Psychosocial strains and reduced quality of life are common in parents of chronically ill children.

What is New:

- In this first study evaluating mental health, family burden, and quality of life in parents of children with congenital hyperinsulinism (CHI), symptoms of depression and anxiety were alarmingly prevalent.
- Parents of children with CHI should receive regular psychological screening and psychosocial support should be offered as needed.
- A good support network and regular professional activities can improve parental mental health and well-being.

Introduction

Congenital Hyperinsulinism (CHI) is a rare disorder but the major cause of persistent hypoglycemia in children [1]. Dysregulated excessive insulin secretion from pancreatic beta-cells results in recurrent, unpredictable, and often severe hypoglycemia, which poses a significant risk for hypoglycemic brain injury [2]. Neurological sequelae affect up to 50% of patients [3–7]. Parents of affected children are therefore often in fear of severe hypoglycemia and the resulting complications. Disease management in CHI is time-consuming, emotionally challenging, and demands a great amount of personal commitment. It involves frequent blood glucose assessments, dietary management with frequent carbohydrate intake and sometimes even tube feeding, pharmacological treatment, and specialized doctor's appointments. Given the rarity of the disease, the caregivers are often the only 'experts' around.

Previous studies have shown that psychosocial strains and reduced quality of life are common in parents of chronically ill children [8–12]. However, the burden of parenting a child with CHI has not yet been systematically evaluated. In this study, we aimed to assess the prevalence of depression and anxiety symptoms, family burden, and quality of life of parents caring for a child with CHI to identify predictors of adverse psychosocial outcomes that can be addressed by offering early counseling and adequate psychosocial support.

Materials And Methods

In a cross-sectional study, anxiety, depression, family burden, and quality of life in parents of children with persistent CHI were assessed in an anonymous online survey using SoSciSurvey (Leiner. 2019. Munich, Germany). Parents were eligible to participate in the study if they were proficient in German and their child had been diagnosed with persistent CHI at least six months before completing the questionnaire. Eligible parents were recruited during clinic appointments at the University Children's Hospital Duesseldorf, by email, telephone or letter. Additionally, the survey link was distributed via the newsletter of the German CHI support group 'Kongenitaler Hyperinsulinismus e.V'. Approximately 100 families were contacted and both parents were invited to participate in the study. Data collection began in June 2019 and was completed in March 2020. All individuals gave informed consent before completing the questionnaires.

Measurements

Sociodemographic data such as parental gender, age, marital status, educational level, and current employment status were surveyed. Furthermore, information on social support and CHI disease-related data, such as frequency of blood glucose measurements, hypoglycemic episodes, use of continuous glucose monitoring (CGM), neurodevelopmental outcome, and comorbidities were collected. Four standardized self-report instruments were used to assess parents' psychosocial strains:

Anxiety

The Generalized Anxiety Disorder Scale-7 (GAD-7) is a brief seven-item self-report questionnaire to evaluate symptoms of anxiety over the previous two weeks. Items are rated on a four-point scale from 0

('not at all') to 3 ('nearly every day'), providing a total sum score of 0-21 points to describe the severity of anxiety symptoms. Cut-off scores for mild, moderate, and severe anxiety were 5, 10, and 15 points, respectively [13]. The cut-off ≥ 10 points is used to determine a probable general anxiety disorder, as it was associated with high sensitivity (89%) and specificity (82%) in the validation study [13]. In the current study, the internal consistency of the GAD-7 was α = 0.88.

Depression

Depressive symptoms were assessed using the Patient Health Questionnaire (PHQ-8) [14]. It is a widely used screening instrument for self-assessment of depressive symptoms in the past two weeks and consists of eight criteria for the diagnosis of depressive disorders according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV). The ninth DSM-IV criterion on suicidal thoughts or actions is omitted in the PHQ-8. Items are scored on a four-point scale from 0 ('not at all') to 3 ('nearly every day') and a total sum score of 0-24 points is calculated to describe disease severity. Current depression is defined by a total score ≥ 5 with four categories of severity: mild depression: 5-9, moderate depression: 10-14, moderately severe depression: 15-19, severe depression: 20-24. The cut-off ≥ 10 points is used for the definition of a probable major depressive disorder, as it yielded high sensitivity (≥ 99%) and specificity (92%) for diagnosing major depression in the validation study [15]. Cronbach's alpha was calculated with 0.88.

Parental quality of life

The Ulm Quality of Life Inventory for Parents of chronically ill children (ULQIE) was used to assess parental quality of life (PQoL) [16]. It is a 29-item self-report questionnaire specifically developed for parents of children with chronic illness. The instrument consists of a total score and five subscales depicting the dimensions physical and daily functioning, satisfaction with family, emotional stability, self-development, and well-being. Answers are given regarding the past seven days on a five-point rating scale ranging from 0 ('never') to 4 ('always'). Higher scores indicate higher PQoL. Cronbach's alpha ranged from 0.66 to 0.87 for the subscales and 0.94 for the total score.

Family burden

The Family Burden Questionnaire (FaBeL), the German version of the Impact on Family Scale, [17] was used to assess the burden of the child's chronic condition on the family. The self-report questionnaire consists of 33 items on five subscales: daily/social burden, personal strains, financial burden, impact on siblings, and problems in coping. In addition, a total score excluding the six sibling-related items is computed. Answers are given on a four-point Likert rating scale ranging from 1 ('strongly agree') to 4 ('strongly disagree') with higher scores indicating higher burden. In this study, only the total score (Cronbach's alpha = 0.85) was used for comparative analysis.

Statistical Analysis

Data were analyzed using SPSS Statistics version 25.0 (IBM Inc., Armonk, NY, USA). Standard descriptive statistics were computed to assess baseline data. Cronbach's alpha was calculated for all scales to test

for internal consistency in the study sample. Normality of distribution of continuous variables was determined via Kolmogorov-Smirnov-Test. For univariate analysis, Student’s t-test, Mann-Whitney-U test, Pearson's chi-squared test, Fisher’s exact test, Spearman’s correlations, and univariate regression were calculated when applicable.

All significant variables for the total item scores from univariate analysis were entered into multivariate regression models with stepwise backward elimination to assess the impact of possible predictors on psychosocial outcome and quality of life.

Continuous variables are presented as mean with standard deviation (SD) or range for parametric variable and as median with interquartile range (IQR) for non-parametric data. Categorical variables are reported as number (n) and percent (%). A p-value <.05 was considered statistically significant.

The study was approved by the institutional review board of the Medical Faculty of the Heinrich-Heine-University Duesseldorf, Germany (2019-420-ProspDEvA), and was performed following the Declaration of Helsinki.

Results

In total, 48 parents of children with CHI participated in the study, 36 (75%) mothers and 12 (25%) fathers. The mean parental age was 41.5 years (range 26 - 54). On average, respondents had 2 (IQR 1) children. Mean weekly working hours were 25.5 (SD 10.5) for mothers and 43.9 (SD 10.9) for fathers (p <.001). In total, 33% of parents (15 mothers, 1 father, p =.033) indicated that they currently or previously received psychological care. There were no further gender-specific differences in sociodemographic status or child and disease-specific data (Tables 1 and 2). Besides themselves, parents had a median of 2 (IQR 2) additional independent caretakers for their child.

Table 1
Characteristics and associations of study participants

Variable	**Value**	**P-Value**			
		GAD-7	*PHQ-8*	*ULQIE Total Score*	*FaBeL Total Score*
Age *(mean, range)*	41.5 (26 – 54)	.395	.791	.164	.873
Female gender *(n, %)*	36 (75)	**.006**	.102	**.035**	.843
Number of children *(median, IQR)*	2 (1)	.175	.192	.219	.678
Relationship status *(n, %)*					
Married/in stable relationship	41 (85.5)	.072	.571	.77	.555
Divorced/single/widowed	7 (14.5)				
Education *(n, %)*					
Secondary education or higher	29 (60.4)	.177	.303	.86	.51
Employment status *(n, %)*					
Respondent currently employed	39 (81.3)	.971	.418	.306	.317
Partner currently employed	35 (81.4)	.97	.855	.794	.274
Both parents employed	28 (58.3)	.575	.492	.394	.293
Working full-time	18 (52.9)	.061	.06	.163	.69
Respondents' weekly working hours *(median, IQR)*	23.5 (20)	**.01**	**.004**	**.013**	.998
Partners' weekly working hours *(median, IQR)*	40 (2)	.426	.940	.379	.734
Current or prior psychological care *(n, %)*	16 (33.3)	**.031**	**.003**	.05	.959

Number (n), percent (%), interquartile range (IQR).

Variable	Value	P-Value			
Parent has chronic disease *(n, %)*	2 (4.2)	.456	.845	.191	.898
Number of independent caretakers for the affected child *(median, IQR)*	2 (2)	**.016**	**.012**	**<.001**	**.019**
Number (n), percent (%), interquartile range (IQR).					

Table 2
Children's characteristics and disease-specific data

Variable	Value	P-Value			
		GAD-7	*PHQ-8*	*ULQIE Total Score*	*FaBeL Total Score*
Age *(years, mean ± SD)*	8.8 (6.5)	.206	.915	.446	.863
Neurodevelopmental impairment	12 (25)	**.009**	**.024**	**.011**	.831
Additional diagnoses besides CHI	17 (35.4)	.107	.083	**.009**	.494
Sibling with chronic disease	5 (10.4)	.175	.773	.926	.423
Using continuous glucose monitoring (CGM)	21 (43.8)	.427	.863	.977	.547
Daily blood glucose measurements	28 (58.3)	.211	.58	.132	.928
Prior severe hypoglycemia*	26 (54.2)	.468	.248	.89	.509
Weekly hypoglycemia <60mg/dl	17 (35.4)	.589	.676	.203	.897
Values are presented as number (%) if not stated otherwise. *prior severe hypoglycemia means with seizure or loss of consciousness.					

Anxiety and Depression

The mean scores in the study population were 8.9 (SD 5.2) for the GAD-7 and 8.0 (SD 5.6) for the PHQ-8. In total, 29.8% (n=14) of parents had major depressive symptoms according to the PHQ-8 and 38.3% (n=18) had a probable general anxiety disorder according to the GAD-7, including 20.8% (n=10) who had both (Table 3). GAD-7 and PHQ-8 scores were positively correlated in the study (p <.001). Spearman's correlation showed that higher scores on both, the GAD-7 and the PHQ-8 were significantly correlated with

lower PQoL in total and on all subscales (each p ≤0.001). The analysis showed that parents who worked more weekly hours had lower GAD-7 scores (p =.01) and lower PHQ-8 scores (p =.004). Having fewer caretakers for the CHI child beyond the parents was associated with higher PHQ-8 scores (p =.021) and higher GAD-7 scores (p =.016). Mothers had significantly higher GAD-7 scores than fathers (p =.006). No association was found between PHQ-8 scores and gender. Current or prior psychological care was associated with higher scores on both GAD-7 (p =.003) and PHQ-8 (p=.031). Parents of children with neurological impairment had significantly higher scores on both the GAD-7 (p =.009) and the PHQ-8 (p =.024).

Table 3
Severity of anxiety or depressive symptoms according to GAD-7 and PHQ-8 scores

Category of severity*	**GAD-7 (n, %)**	**PHQ-8 (n, %)**
None	11 (23.4)	13 (27.1)
Mild	18 (38.3)	20 (41.7)
Moderate	11 (23.4)	9 (19.1)
Moderately severe	-	2 (4.3)
Severe	7 (14.9)	3 (6.4)
≥ 10 points	18 (38.3)	14 (29.8)
< 10 points	29 (61.7)	33 (70.2)

* Generalized Anxiety Disorder Scale-7 (GAD-7) category cut-offs for anxiety symptoms: none 0-4, mild 5-9, moderate 10-14, and severe 15-21 points. Cut-off for probable general anxiety disorder ≥ 10 points.

Patient Health Questionnaire-8 (PHQ-8) category cut-offs for depressive symptoms: none 0-4, mild 5-9, moderate 10-14, moderately severe 15-19, and severe 20-24 point. Cut-off for probable major depressive disorder ≥ 10 points.

Higher total family burden (FaBel total score) and daily/social burden (FaBeL subscale 1) were correlated with higher PHQ-8 scores (p =.01 and .017) but not with anxiety symptoms. Furthermore, there were no significant correlations between GAD-7 or PHQ-8 scores and parental or patients' age, marital status, number of children, or partners' weekly working hours. Comparative analysis showed no association between a probable general anxiety disorder (GAD-7 score ≥ 10 points) or a probable major depressive disorder (PHQ-8 score ≥ 10 points) and any sociodemographic, or child- and disease-specific data.

In multivariate regression analysis with backward elimination, neurological impairment in the affected child (p =.002 in both models) and respondent's weekly working hours (p =.001 in both models) remained

significant predictors of both the GAD-7 and PHQ-8 scores and explained 33.6% and 38.4% of the variance (Table 4).

Table 4
Multiple regression models with stepwise backward elimination

Variable	GAD-7	PHQ-8	ULQIE
Adjusted R^2 for model	.336	.384	.516
Gender	n.s.	n.i.	n.s.
Psychological care	n.s.	n.s.	n.s.
Weekly working hours	B = -.181; p = .001	B = -.221; p = .001	B = 0.016; p = .012
Addition diagnosis besides CHI	n.i.	n.i.	B = -0.496; p = .007
Neurodevelopmental impairment	B = 5.13;1 p = .002	B = 5.897; p = .002	n.s.
Number of independent caretakers	n.s.	n.s.	B = 0.183; p <.001
FaBeL total score	n.i.	n.s.	n.i.

n.i. not included, n.s. not significant.

PQoL

Parents reported the highest PQoL on the subscale for ‘satisfaction with family’ and lowest for ‘self-development’ (Table 5). Parents who had undergone prior psychological intervention or were in current psychological care had lower total PQoL (p =.050), lower ‘satisfaction with family’ (p =.016), and lower ‘emotional stability’ (p =.027). Mothers had significantly lower scores than fathers on the ULQIE total score (p =.035) and the subscales ‘satisfaction with family’ and ‘emotional stability’ (p =.027 and .009). If their child had any comorbidities or a neurodevelopmental impairment, caregivers had lower total PQoL (p =.009 and .011), lower ‘physical and daily functioning’ (p =.037 and .003), lower ‘satisfaction with family’ (p =.002 and .003) and lower ‘emotional stability’ (p =.048). If children had ongoing weekly hypoglycemia <60 mg/dL, parents had significantly lower scores on the subscale for ‘well-being’ (p =.038). Having only limited support (Table 5) and few independent caretakers for the affected child was associated with lower total PQoL (p <.001), ‘physical and daily functioning’ (p <.001), ‘emotional stability’ (p =.002), ‘self-development’ (p <.001) and ‘well-being’ (p <.001). Univariate regression showed an association between lower scores for the subscale ‘emotional stability’ and higher number of children (p =.048). Higher working hours correlated with higher total PQoL (p =.013) and ‘emotional stability’ (p =.005). No associations were found between PQoL and sociodemographic or other child- and disease-specific data. In multivariate regression analysis with stepwise backward elimination, the number of independent caretakers for the CHI child (p <.001), an additional diagnosis besides CHI (p =.007) and

weekly working hours (p =0.012) were significant predictors of the cohorts' PQoL and explained 51.6% of the variance (Table 4).

Table 5
Support system of CHI parents

Parent-reported independent caretakers of their CHI child	Total (n, %)
Caregivers at school or in kindergarten	20 (41.7)
Grandparents	24 (50)
Siblings	8 (16.7)
Other family members	32 (66.7)
Friends	38 (79.2)
Babysitter	3 (6.3)
Caregivers at sports or other leisure activities	6 (12.5)
Additional support at home or in school/kindergarten (e.g. special care or nursing service)	13 (27.1)

Family burden

On average, parents reported moderate family burden. The lowest burden was recorded on the FaBeL subscale for 'impact on siblings' and the highest burden on the subscale for 'personal strains' (Table 6). Parents who had only few independent caretakers for the CHI child reported a significantly higher total family burden (p =.019). Sociodemographic, disease- or child-related data had no impact on the FabeL total score, and no correlation was found between perceived family burden and PQoL.

Table 6
Family burden and PQoL

Scale results	Mean (SD)	Range	*Cronbach*'s alpha
FaBel Scores			
Daily/social impact	2.28 (0.63)	1.2 – 3.8	0.88
personal strains	2.45 (0.62)	1 – 3.6	0.45
financial burden	2.05 (0.69)	1 – 3.5	0.63
impact on siblings	0.59 (0.51)	1 – 3	0.69
problems in coping	1.87 (0.59)	1 – 3	0.28
FaBeL total score (without sibling items)	2.39 (0.46)	1.3 – 3.2	0.85
ULQIE Scores			
Physical and daily functioning	2.37 (0.73)	0.85 – 3.85	0.87
Satisfaction with family	2.82 (0.81)	0.67 – 4	0.83
Emotional stability	2.15 (0.98)	0 – 3.75	0.81
Self-development	1.57 (0.87)	0 – 4	0.85
Well-being	2.48 (0.75)	1 – 3.75	0.66
ULQIE total score	2.33 (0.67)	0.82 – 3.62	0.94
FaBel: four-point Likert rating scale ranging from 1 ('strongly agree') to 4 ('strongly disagree'). ULQIE: five-point Likert rating scale ranging from 0 ('never') to 4 ('always'). Higher scores indicate higher PQoL.			

Discussion

In this first study assessing the psychosocial burden of parenting a child with CHI, caregivers reported pronounced rates of anxiety and depressive symptoms.

Anxiety symptoms according to the GAD-7 mean score were significantly more prevalent in the cohort (8.9 [SD 5.2]) than in a large sample of the German general population (3.6 [SD 3.3]) [18]. Compared to data from the European Health Interview Survey, major depressive symptoms in the PHQ-8 were also significantly more common in parents of children with CHI (29.8%) compared to the German general population (9.2%) [19]. The prevalence for mild depressive symptoms was 41.7% and 29.2% for moderate to severe depressive symptoms, respectively (compared to 6.3% and 2.9% in the general population) [19].

Significantly higher levels of depression and anxiety have been reported in parents of children with numerous chronic diseases [20; 21]. In 2014, van Oers et al. found that practical problems in daily life and

parenting stress were the strongest predictors of anxiety and depression, while illness-related data had no impact on the psychological outcome [20].

Surprisingly, the frequency of hypoglycemia had no impact on anxiety and depressive symptoms in parents of children with CHI, however, in multiple regression analysis, the strongest predictor was a child's neurological impairment. It has been previously reported, that caring for a disabled child is associated with a high caregiving burden and psychological morbidity [22–24].

Comparable to our study, mothers have been reported to have significantly more symptoms of anxiety than fathers [20] and prior or current psychotherapy was a predictor of both anxiety and depression [21].

In this study, self-assessment yielded average scores for PQoL. The result is comparable to other studies using the same instrument for parents of children with chronic diseases [16; 25; 26]. Parents in our analysis reported the lowest scores for 'self-development' and highest scores for 'satisfaction with family life', as previously described [10; 16; 25; 26]. It can be assumed that parents often put their children's needs above their own, leaving them little time for personal development due to the time-consuming disease management.

Mothers reported significantly lower PQoL than fathers. This result may indicate their role as the child's primary caretaker, as there were significantly lower weekly working hours reported by mothers compared to fathers. Because treating a child with CHI is often demanding and challenging, primary caretakers carry the main burden of managing daily medical and social care, which impacts both their mental health and professional activities.

Having a child with a chronic disease was associated with reduced parental employment in several studies [27; 28] and higher rates of parents working part-time compared to parents of healthy children [29].

Interestingly, a higher number of weekly working hours was a strong predictor of decreased symptoms of depression and anxiety as well as increased PQoL in our study. Job gratification and distraction from daily coping with the child's illness may explain this finding. Despite the 'double burden', caretakers of disabled children who were satisfied with their job also indicated less parenting stress (30). Further, worse mental health was reported in unemployed mothers of chronically ill children. The authors concluded that a lack of childcare services and limited family support increased the likelihood of maternal unemployment [30; 31].

We also found that low social support and limited availability of reliable assistance in the supervision of the CHI child were associated with higher family burden, poor mental health, and decreased PQoL. Social support is important for the adjustment process to a child's chronic condition. A recent US study found that higher levels of perceived social support were associated with lower levels of anxiety in parents of children with a serious life-threatening illness [32]. In parents of children with cancer, poor social support was the most important predictor of poor mental health outcomes [33].

It is therefore crucial for parents to have a reliable support network and train others in taking care of their children to share the burden of care and improve their well-being.

Parental psychosocial problems can influence both the physical health and psychosocial functioning of the chronically ill child. Nonadherence to treatment and poor disease-related health outcomes in children with chronic diseases have been linked to their parent's mental health problems and stress [34–36]. Anxiety or depression in a parent doubles the risk for an adolescent child to also report elevated psychological distress [21]. Interestingly, despite the high psychological distress in parents of CHI children reported here, a Finnish study found no deterioration in the quality of life of the affected children themselves [37].

While annual screening for depression and anxiety has been officially recommended, e.g. in patients with cystic fibrosis and their parents [35], these recommendations are lacking for CHI and other chronic diseases. Given the high prevalence of psychosocial distress among parents of chronically ill children and the associated complications, we strongly emphasize the implementation of regular mental health screening of families affected by a child’s chronic illness to identify adverse outcomes early and to optimize referral of parents and/or patients to psychosocial counseling as needed [38].

There are some limitations to this study. First, the disease is rare, thus the sample size was relatively small, and parents with psychosocial strains may be overrepresented in this study due to a higher response rate from individuals with interest in this matter. Second, because the survey was conducted anonymously, it was not possible to evaluate whether two parents came from the same family which might bias the results. Third, the study cohort presented a relatively homogeneous group with high socioeconomic status, stable relationships, and overrepresentation of mothers. Future research in larger cohorts across socioeconomic strata is therefore needed to provide adequate information on all parents caring for a child with CHI. Fourth, the comparison of psychosocial burden between parents of children with CHI and those with other chronic diseases is limited by differences in disease characteristics and the use of different screening instruments within studies. Consecutive studies assessing parental psychosocial outcomes in CHI are therefore needed and should favorably use standardized instruments for comparability.

In conclusion, symptoms of anxiety and depression are highly prevalent among parents of children with CHI. Strong predictors of adverse mental health outcomes and lower self-reported quality of life were female gender, limited social support, low working hours, and comorbidities or neurological impairment in the affected child. Psychological screening for parents of children with CHI should be implemented to ensure early identification of psychological strains and to offer psychosocial support as needed. Parents should be encouraged and supported to train others to take care of their child to share the burden of care and allow more time for personal needs and self-development. Job gratification and distraction from daily coping with the disease through occupational activities may improve parents’ mental health.

Abbreviations

CGM: Continuous Glucose Monitoring

CHI: Congenital Hyperinsulinism

DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition

FABEL: Family Burden Questionnaire

GAD-7: Generalized Anxiety Disorder Scale-7

IQR: Interquartile Range

N: Number

PHQ-8: Patient Health Questionnaire-8

PQoL: Parental Quality of Life

SD: Standard Deviation

ULQIE: Ulm Quality of Life Inventory for Parents of Chronically ill Children

%: Percent

Declarations

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Conflict of interest/Competing interest

The authors have no relevant financial or non-financial interests to disclose.

Availability of data and material

The data that support the findings of this study are not available publicly but are available from the corresponding author on reasonable request.

Code availability

Not applicable.

Authors' contributions

MR designed the study, created the questionnaire, collected and interpreted the data, and wrote the initial manuscript. HH, RDS, FK, ET, SK, CR, and TM contributed to the study design interpreted and critically

validated the data, and revised and reviewed the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Ethics approval

The study was approved by the ethics committee of the Medical Faculty of the Heinrich-Heine-University Duesseldorf, Germany (2019-420-ProspDEuA) on March 25, 2019, and was performed in line with the principles of the Declaration of Helsinki.

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Consent for publication

Not applicable.

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