Morawska Alina (Orcid ID: 0000-0002-9404-5423)

Mitchell Amy Elizabeth (Orcid ID: 0000-0003-3352-3046)

Psychosocial functioning in children with phenylketonuria: Relationships between quality of life and parenting indicators

Running head: Psychosocial functioning in phenylketonuria

Alina Morawska[1*], Amy E Mitchell[1], Evren Etel[1], Grace Kirby[1], James McGill[2,4], David Coman[2,4],Anita Inwood[2,3]

[1]Parenting and Family Support Centre, School of Psychology, The University of Queensland
[2]Queensland Lifespan Metabolic Medicine Service, Queensland Children's Hospital
[3]School of Nursing and Social Work, The University of Queensland
[4]School of Medicine, The University of Queensland

*Corresponding Author:
Alina Morawska, 13 Upland Rd, Parenting and Family Support Centre, School of Psychology, The University of Queensland, Brisbane, 4072, Australia.
Email: alina@psy.uq.edu.au Ph: +61 7 3365 7304

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Morawska contributed to the study design and literature review and was the primary author of the manuscript. A.E. Mitchell contributed to the study design, data collection and interpretation, and drafting of the article. E. Etel was responsible for data analysis and contributed to drafting of the article. G. Kirby was responsible for data collection and revising the manuscript. J. McGill contributed to study design. D. Coman contributed to study design and revising the manuscript. A. Inwood contributed to study design and data collection and revising the manuscript.

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Abstract

Objective: This study aimed to assess the impact of phenylketonuria (PKU) and its treatment on parent and child health-related quality of life (HRQoL), and to identify the parenting-related correlates of parent and child HRQoL, as well as metabolic control. Methods: Eighteen mothers of 2 to 12-year-old children with PKU participated and completed a series of self-report questionnaires including the Phenylketonuria Impact and Treatment Quality of Life Questionnaire (PKU-QOL). Results: Mothers reported that the most significant impact of PKU on HRQoL was in relation to impact of their child's anxiety during blood tests on their own HRQoL, and guilt related to poor adherence to dietary restrictions and supplementation regimens. Higher reported intensity of child emotional and behavioural difficulties and parenting stress were associated with higher scores for PKU symptoms on the PKU-QOL, higher scores for emotional, social and overall impact of PKU, and higher scores for impact of dietary restriction. Where mothers reported greater use of overreactivity as a parenting strategy, children tended to have better lifetime phenylalanine (Phe) levels; however, the overall impact of PKU and the impact of supplement administration on mothers' HRQoL was worse for these families. Conclusions: These findings have implications for a holistic family-centred approach to the care of children with PKU and their families.

Keywords: child, child behaviour, chronic illness, metabolic, parenting, phenylketonuria

Phenylketonuria (PKU, OMIM 261600) is a rare (1:10,000; Scriver and Kaufman, 2001) autosomal recessive inborn error of metabolism resulting from phenylalanine hydroxylase (PAH) deficiency, and characterized by elevated blood phenylalanine (Phe) levels (Enns et al., 2010). Phe restriction is tightly controlled and monitored during early childhood, since elevated Phe levels in children <12 years contribute to poorer short- and long-term neurodevelopmental outcomes (Enns et al., 2010). Tailored dietary intervention is the treatment cornerstone, and typically involves moderate to severe restriction of natural protein intake combined with supplementation with Phe-free amino acid formulas to support adequate nutrition and growth (Inwood et al., 2017).

Treatment and support for PKU need to go beyond a narrow focus on metabolic control, instead adopting a holistic approach to supporting child and family psychosocial wellbeing and quality of life (Feillet et al., 2010, Vegni et al., 2010, Medford et al., 2018, Borghi et al., 2019). Parents play an essential role in children's chronic health condition management (Morawska et al., 2015) and are responsible for implementing the child's PKU management plan, which represents a considerable and ongoing burden (Carpenter et al., 2018). Notably, parents report higher intensity of childhood behaviour problems compared to healthy controls (Jusiene and Kučinskas, 2004, Ambler et al., 2018). Parents of children with chronic health conditions also tend to experience more psychosocial problems and poorer health themselves compared to parents of healthy children (Pinquart, 2018), and some have identified elevated levels of parental distress for parents of children with PKU (Vetrone et al., 1989, Kazak et al., 1988, Gunduz et al., 2015, Medford et al., 2017, Ionio et al., 2018) although others report minimal differences (Kazak et al., 1988, Ambler et al., 2018).

Relationships between parenting indicators, such as parenting stress and parenting strategies, and metabolic control in children with PKU are, likewise, unclear. Medford et al. (2018) identified 29 studies examining these associations, finding inconsistent results. For

example, Fehrenbach and Peterson (1989) found that children with good metabolic control had families with firmly fixed rules, whereas Ievers-Landis et al. (2005) reported that authoritarian parents had children with higher Phe levels. Notably, parents of children with PKU may adopt a permissive style of parenting (Jusiene and Kučinskas, 2004). Parenting styles, specifically accepting and autonomy-allowing parenting (cerebral palsy; Aran et al., 2007) and parent responsiveness (diabetes; Botello-Harbaum et al., 2008), have been associated with variations in quality of life for children with other chronic health conditions (Im et al., 2019), and parenting stress is associated with worse child and parent quality of life (e.g., cerebral palsy; Lee et al., 2019, inborn errors of metabolism; Yamaguchi et al., 2018).

Goldbeck and Storck (2002) highlighted parental quality of life as the most relevant indicator of adjustment for parents of children with chronic health conditions. Predictors of poor quality of life in PKU include low perceived social support (ten Hoedt et al., 2011, Fidika et al., 2013), high family stress (Fidika et al., 2013), high perceived stress (Irannejad et al., 2018), high levels of depression and anxiety (Mahmoudi-Gharaei et al., 2011), loss of friendship, and younger child age (ten Hoedt et al., 2011). However, no studies have examined PKU-specific health-related quality of life (HRQoL; e.g., anxiety associated with poor adherence, difficulty implementing special diets), even though targeted measures are more likely to be directly related to parenting and psychosocial wellbeing and potentially better able to be modified by interventions.

This study had two main aims: (1) to comprehensively assess the impact of PKU and its treatment on parent and child HRQoL and to describe the PKU-specific HRQoL of parents and young children with PKU in Queensland, Australia, and (2) to identify the parenting-related correlates of parent and child HRQoL, as well as metabolic control. We focused on parenting stress, child behaviour, parent efficacy and parenting practices based on the broader

HRQoL literature which indicates the importance of these factors to children's chronic health condition management.

Method

Participants

Parents of children with PKU receiving care through the Queensland Lifespan Metabolic Medicine Service (QLMMS) at the Queensland Children's Hospital (QCH), Brisbane, Australia, were invited to participate. Inclusion criteria were: (i) having a child diagnosed with PKU at newborn screening who requires a protein-restricted diet and supplementation with a phenylalanine-free amino acid formula, (ii) child aged 2-12 years old. Exclusion criteria were: (i) difficulties reading an English-language newspaper, (ii) parental disability affecting cognition, (iii) child disability, (iv) child under the care of the Department of Communities.

Overall, 39 parents were invited to participate, 23 parents enrolled, and 18 (response rate = 46%) completed questionnaires. Participants were mothers, mostly (94%) married and living with their child's father. Seven (39%) reported having complete responsibility for PKU management, 2 (11%) shared equal responsibility with their child, and 9 (50%) indicated management was somewhat shared with their child. None reported that their child was completely responsible for PKU management. Classical PKU was the most common biochemical phenotype (see Table 1).

Procedure

Ethics clearance was granted by (blinded). Eligible parents were sent a letter explaining study aims, along with study information and consent forms. A researcher telephoned all parents to answer any questions, obtain written consent, and email a link to the online questionnaires. Participants were free to withdraw at any stage.

Measures

PKU management information (diagnosis, medications/formula, PKU management plan/s, Phe levels) was obtained from the child's treating team.

Demographic and health information. The Family Background Questionnaire (Sanders and Morawska, 2010) was used to obtain demographic and general child health information.

Phe levels. Phe levels are measured from dried blood spots (DBS) collected by parents on a 2-4 weekly basis (dependent on age). Lifetime Phe level represents the mean of all Phe levels from birth to the age of testing.

Quality of life. Parent and child HRQoL was assessed using the 54-item parent version of the Phenylketonuria Impact and Treatment Quality of Life Questionnaire (PKU-QOL; Regnault et al., 2015). It comprises four modules assessing impact across 30 domains: PKU symptoms (11 domains); PKU in general, including emotional, practical, social and overall impacts (9 domains); administration of Phe-free protein supplements (5 domains); and dietary protein restrictions (5 domains). Domain scores <25 indicate little/low impact; 25-50 indicate moderate impact; 50-75 indicate major impact; and scores >75 indicate severe impact. The instrument has satisfactory validity (Regnault et al., 2015). Internal consistency was good for most multi-item domain scores in this sample (emotional impact, α=.70; practical impact, α=.78; social impact, α=.78; overall impact, α=.83; anxiety - blood test, α=.83; practical impact of dietary protein restriction, α=.87), but low for others (impact of anxiety-blood test, α=.59; practical impact of supplements, α=.52; management of dietary protein restriction, α=.35).

Parenting stress. The Parenting Stress Index – Short Form (PSI-SF; Abidin, 2007) is a 36-item measure of parenting stress. Parents rate items on a 5-point scale ranging from 1 (strongly agree) to 5 (strongly disagree). Higher scores indicate higher levels of stress. Internal consistency was good for Parental Distress (α=.86), Parent-Child Dysfunctional Interaction (α=.91), and Difficult Child (α=.83) subscales, and the total score (α=.95).

Child behaviour and parenting efficacy. The Child Adjustment and Parent Efficacy Scale (CAPES; Morawska et al., 2014) assessed child behavioural and emotional adjustment and parenting efficacy. Parents rate 27 child behaviour items using a 4-point response scale from 0 (not true at all) to 3 (true most of the time). Item scores are summed to yield a total Intensity score, comprising Behaviour Difficulties and Emotional Maladjustment scores, with higher scores indicating higher levels of difficulties. Parents also rate their self-efficacy in dealing with 20 of the behaviours using a scale from 1 (certain I can't do it) to 10 (certain I can do it). Scores are summed to provide a parenting efficacy score, with higher scores indicating higher levels of parenting efficacy. CAPES demonstrated good internal consistency in this study for Emotional Maladjustment (α=.89), Behavioural Difficulties (α=.91), Total Intensity (α=.90) and Parent Self-Efficacy (α=.93).

Parenting. The 30-item Parenting Scale (Arnold et al., 1993) assessed use of dysfunctional parenting strategies: laxness (permissive discipline), overreactivity (authoritarian discipline), and verbosity (reliance on talking). Each item was rated on a 7-point scale ranging from more to less effective. Higher scores indicate higher levels of dysfunctional parenting strategies. In this study, the scale demonstrated good internal consistency (total score, α=.83; laxness, α=.80; overreactivity, α=.83), except for verbosity (α=.40) which was excluded from analyses.

Statistical analyses

Means, median scores and interquartile ranges of PKU-QOL domain and module scores were computed and interpreted based on impact severity and reference values from a European sample (Bosch et al., 2015). Pearson's correlations examined associations among demographic variables, parenting indicators, lifetime Phe levels and scores for PKU-QOL modules and selected domains. Multiple regression analyses explored predictors of PKU-QOL modules and selected domains which correlated with more than one parenting indicator.

Considering the small sample size, only two predictor variables were included in each regression model. All analyses were performed using IBM SPSS 24.

Results

Health related quality of life (PKU-QOL)

PKU-QOL scores are presented in Table 2. Within the PKU Symptoms module, mothers rated their child's overall health status as poor (*n*=2, 11.1%), fair (*n*=3, 16.8%), good (*n*=5, 27.8%) or very good (*n*=8, 44.4%).

Across the other three modules, the highest mean scores were for parental guilt related to poor adherence to (a) dietary restrictions and (b) Phe-free amino acid supplementation, as well as impact of the child's anxiety during blood tests, with scores indicating major impact. Elevated scores were also found for emotional impact of PKU, anxiety about blood Phe levels and practical impact of the dietary protein restriction, all indicating moderate impact.

PKU-QOL scores according to severity of PKU

Between-group comparisons were conducted for subgroups based on PKU severity. PKU-QOL scores did not differ between groups (see Table 2). However, mothers of children with classical PKU reported greater (moderate) levels of financial impact of PKU, and greater (severe) impact of guilt related to poor adherence to dietary restrictions and Phe-free amino acid supplement intake compared to those with mild PKU and hyper-phe (little/no impact and major impact, respectively).

We compared our data to those in a European sample from seven countries (Bosch et al., 2015). For parents of children with classical PKU, PKU-QOL scores indicate similar levels of impact, although some differences are evident. Specifically, in our sample, scores for child health status and lack of concentration domains indicate little or no impact, whereas scores for the European sample indicate moderate impact. On the other hand, anxiety scores indicate moderate impact of PKU in our sample, whereas they indicate little or no impact in the

European sample. The major difference is observed in the impact of the child's anxiety during blood tests: the mean score indicates a major impact in our sample, but little or no impact in the European sample. Mothers reported a moderate level of anxiety about their child's Phe levels in our sample, compared to a major level of anxiety in the European sample. The highest mean score of all domains was for guilt related to poor adherence to dietary restrictions and Phe-free amino acid supplement intake, indicating severe impact, whereas scores in the European sample indicate moderate to major impact.

Correlations between parenting indicators and PKU-QOL

Table 3 presents correlations between parenting indicators and parent PKU-QOL modules and selected domains. We examined correlations between parenting indicators and total scores of the four PKU-QOL modules: PKU Symptoms, PKU in General, Administration of Phe-free Protein Supplements, and Dietary Protein Restriction. We also examined the correlates of three specific domains, drawn from the PKU in General module: Emotional Impact of PKU, Social Impact of PKU and Overall Impact of PKU.

Correlates of lifetime Phe levels

Examining relationships with PKU-QOL module scores, lifetime Phe levels were significantly correlated only with Dietary Protein Restriction impact scores, indicating that higher lifetime Phe levels are associated with mothers reporting greater impact of dietary protein restriction. Lifetime Phe levels were significantly correlated with greater child tiredness and slow thinking, parental impact of child's anxiety during blood tests and anxiety about blood Phe levels, financial impact of PKU, and greater impact of dietary protein restriction management (see Supplementary Table).

Lifetime Phe levels were also correlated with CAPES emotional maladjustment scores, PSI parent-child dysfunctional interaction, PSI difficult child, and PSI total scores, indicating that higher lifetime Phe levels were associated with increased parent-report of child

emotional difficulties and parenting stress. Lifetime Phe levels were also negatively correlated with an overreactive parenting style, such that greater overreactivity was associated with lower lifetime Phe levels and better metabolic control.

Identification of potential predictors of PKU-QOL

Multiple regression analyses (see Table 4) indicated that, after accounting for parenting stress scores, CAPES Intensity scores were significant predictors of parent-reported PKU symptoms. Intensity of emotional and behavioural problems also significantly predicted emotional impact of PKU on mothers, after controlling for parenting stress. These effects together accounted for 71% of the variance in PKU symptoms and 66% of the variance in emotional impact of PKU. On the other hand, parenting stress was the significant predictor of social impact of PKU, after controlling for the intensity of child behavioural and emotional problems. These effects together explained 69% of the variance in the social impact of PKU. In terms of overall impact of PKU, although parenting stress and overreactivity were positively correlated with overall impact of PKU, neither explained significant variance in overall impact of PKU in the regression model.

Discussion

This study is one of the first to examine relationships between parental HRQoL and parenting practices, parenting stress, and child behavioural and emotional difficulties in families of children with PKU. Areas of greatest impact on child and parent HRQoL converge on mothers' psychological health and functioning, whereas PKU-QOL child symptoms were rated as being very low. Mothers even rated the impact of their child's anxiety around blood tests on themselves as being twice as great as the impact on the child.

The scores in the domains of guilt related to non-adherence to dietary restrictions and supplement intake, emotional impact of PKU, and practical impact of dietary restriction were in line with the PKU-QOL scores of parents in the European sample (Bosch et al., 2015).

Overall, and similarly to the European sample, this study demonstrated that mothers of children with PKU in Australia experience high levels of guilt related to poor adherence to dietary restrictions and supplement intake, and high levels of emotional impact of PKU and practical impact of dietary protein restriction.

Mothers reporting higher intensity of child emotional and behavioural difficulties also tended to report higher levels of PKU symptoms (PKU-QOL) for their children, higher levels of emotional, social and overall impact of PKU, and higher levels of impact of dietary restriction in their daily lives; and these remained significant even after controlling for mothers' parenting stress. These findings build on previous research in other childhood chronic health conditions. For example, Wilson et al. (2009) reported that child misbehaviour was positively associated with time parents spent in diabetes management and perceptions of the impact of child illness on discipline strategies. Although further exploration of these associations are still needed, our findings support Wilson et al. (2009)'s suggestion that child misbehaviour may lead to increased parental involvement, which in turn may affect parental perception of time spent in management, children's symptoms, and illness impact.

Mothers reporting higher levels of parenting stress also tended to report higher levels of PKU symptoms (PKU-QOL) for their children, higher levels of emotional, social, and overall impact of PKU, and higher levels of impact of dietary restriction in their daily lives; and these remained significant even after controlling for intensity of child misbehaviour. In general, findings on the association between parenting stress and quality of life among parents of children with chronic illness are varied (Borghi et al., 2019). However, our findings are in line with recent studies in other childhood chronic health conditions showing the negative association between parenting stress and the primary caregiver's quality of life (Lee et al., 2019, Yamaguchi et al., 2018).

In terms of parenting practices, mothers who reported higher use of overreactivity as a parenting strategy tended to have children with better lifetime Phe levels, indicating better metabolic control; however, the overall impact of PKU and the impact of supplement administration on these mothers was worse. When caring for a child with a chronic illness, parental perceptions that the child is vulnerable due to illness can affect parenting behaviours in the form of overindulgence, overprotection, control and intrusiveness (Hullmann et al., 2010, Thomasgard and Metz, 1993). However, the literature reporting on relationships between authoritarian parenting and metabolic control in children with PKU remains inconsistent (Fehrenbach and Peterson, 1989, Ievers-Landis et al., 2005). Our findings are in line with Fehrenbach and Peterson (1989), showing an association between more parenting overreactivity and better lifetime Phe levels for children with PKU. Ievers-Landis et al. (2005), on the other hand, reported an association between authoritarian parenting and worse metabolic control; however, their results were related to diet (not supplements).

Limitations

Our sample size was small; however, PKU is a rare condition, and we successfully recruited almost half of the eligible population of parents in the state of Queensland, Australia; nevertheless, statistical power was limited, and larger studies are needed to progress research with this clinical group. Furthermore, this study was cross-sectional in design, meaning that causality cannot be inferred and thus the direction of the relationships needs to be examined in future longitudinal studies. Our study only included parent-report measures of all psychosocial variables, as gathering observational data was impractical given the geographical dispersion of the sample. Future studies should examine parent-child interaction in more detail, specifically focusing on coercive parenting practices.

Conclusions

We found that mothers of children with PKU in Queensland, Australia share similar concerns to parents internationally. Findings suggest that increasing support for parents in managing difficult child behaviour and parenting stress could contribute to improved HRQoL and better PKU management. Parenting strategies and coping approaches are readily modifiable via evidence-based intervention, and are potentially important intervention targets to improve metabolic control and longer-term outcomes for children.

Key Messages

- Guilt related to poor adherence to dietary restrictions and supplementation regimens was the most significant impact of PKU on HRQoL.
- Greater child emotional and behavioural difficulties and parenting stress were associated with greater impact on HRQoL
- Greater use of overreactivity as a parenting strategy associated with better lifetime phenylalanine (Phe) levels; but greater impact on HRQoL.

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Table 1: Demographic and clinical characteristics of participants (*N* = 18)

Variables		*M*	*SD*
Parent's age (years)		38.67	5.96
Child's age (years)		6.89	3.68
Number of children in household[a]		2.22	0.73
Lifetime Phe levels[b]		289.11	59.89
		%	*N*
PKU diagnostic category[c]	Classical PKU	44.4	8
	Mild PKU	27.8	5
	Hyper-phe	27.8	5
Child's sex	Male	33.3	6
	Female	66.7	12
Parent Relationship	Married	94.4	17
	Widowed	5.6	1
Household	Original family	94.4	17
	Sole parent family	5.6	1
Parent's education	High school or less	22.2	4
	Trade/College	27.8	5
	University degree	22.2	4
	Postgraduate degree	27.8	5
Parent's employment	Full-time/part-time	83.3	15
	Not working/job seeking	16.7	3
Meet essential expenses[d]	Yes	83.3	15
	No	11.1	2
	Don't know	5.6	1
After expenses can afford	Not much	5.6	1
	Some things	50	9
	Most things	44.4	8
Child problems	Emotional/behavioural	11.1	2
	Developmental delay	5.6	1
	Asthma	16.7	3

[a] Range 1-4.
[b] Range 182-429.
[c] Diagnostic category based on Phe level at time of diagnosis: classical PKU >1200umol/L, mild = 600-1200 umol/L, hyper-phe = 120-600umol/L.
[d] Able to meet essential household expenses during the past 12 months.

Table 2: PKU-QOL parent version scores

						Classical PKU			Mild PKU			Hyper-phe		
Domains / Modules	*n*	Mean (*SD*)	Range	Median	Q1-Q3	*n*	*M*	*SD*	*n*	*M*	*SD*	*n*	*M*	*SD*
PKU symptoms	18	23.23 (16.18)	2.27-61.36	19.32	12.50-34.09									
Child health status	18	23.61 (26.39)	0-75	25	0.00-50.00	8	21.9	28.1	5	20.0	20.9	5	30.0	32.6
Headaches	18	4.17 (9.59)	0-25	0	0.00-0.00	8	0.0	0.0	5	5.0	11.2	5	10.0	13.7
Stomach aches	18	22.22 (25.57)	0-75	25	0.00-31.25	8	15.6	26.5	5	30.0	20.9	5	25.0	30.6
Tiredness	18	34.72 (31.08)	0-100	25	0.00-56.25	8	25.0	35.4	5	50.0	25.0	5	35.0	28.5
Irritability	18	36.11 (23.04)	0-75	37.5	25.00-50.00	8	31.3	17.7	5	40.0	28.5	5	40.0	28.5
Aggressiveness	18	15.28 (17.45)	0--50	12.5	0.00-25.00	8	18.8	22.2	5	15.0	13.7	5	10.0	13.7
Moodiness	18	27.78 (24.08)	0-100	25	18.75-31.25	8	21.9	16.0	5	35.0	37.9	5	30.0	20.9
Sadness	18	20.83 (27.45)	0-100	12.5	0.00-31.25	8	15.6	22.9	5	30.0	41.1	5	20.0	20.9
Anxiety	18	25 (32.08)	0-100	12.5	0.00-50.00	8	31.3	39.5	5	25.0	17.7	5	15.0	33.5
Lack of concentration	18	29.17 (33.49)	0-100	25	0.00-50.00	8	21.9	36.4	5	35.0	22.4	5	35.0	41.8
Slow thinking	18	16.67 (29.7)	0-100	0	0.00-25.00	8	21.9	41.1	5	10.0	13.7	5	15.0	22.4
PKU in general	13	27.78 (15.58)	6.67-58.42	26.5	15.67-36.67									
Emotional impact	18	43.75 (20)	12.50-81.25	46.88	25.00-62.50	8	42.2	22.6	5	50.0	20.3	5	40.0	18.0
Practical impact	15	11.39 (12.35)	0-45.83	8.33	0.00-16.67	6	9.7	18.0	5	10.8	10.0	4	14.6	4.2
Social impact	16	19.04 (18.19)	0-60	15	5.00-32.50	7	19.0	22.6	5	24.3	17.2	4	12.5	11.9
Overall impact	13	21.57 (11.98)	5-42.12	21.67	8.33-32.50	5	15.3	12.8	5	25.8	13.2	3	25.0	5.0
Anxiety – blood test (child)	18	31.94 (33.55)	0-100	25	0.00-56.25	8	32.8	32.0	5	20.0	44.7	5	42.5	25.9
Impact of child's blood test anxiety on parent	19	63.89 (23.75)	37.50-100	62.5	43.75-87.50	4	65.6	27.7	1	100.0		4	53.1	12.0
Anxiety - blood Phe levels	18	41.67 (27.12)	0-100	37.5	25.00-56.25	8	43.8	32.0	5	55.0	20.9	5	25.0	17.7
Financial impact	18	27.78 (30.78)	0-100	25	0.00-50.00	8	43.8	39.5	5	15.0	13.7	5	15.0	13.7
Information	18	31.94 (22.37)	0-75	25	18.75-50.00	8	34.4	22.9	5	25.0	25.0	5	35.0	22.4
Administration of Phe-free protein supplements	16	28.75 (15)	5-61.67	25	17.08-41.25									
Adherence	18	12.5 (15.46)	0-50	0	0.00-25.00	8	9.4	12.9	5	10.0	13.7	5	20.0	20.9
Management	18	16.67 (25.72)	0-75	0	0.00-25.00	8	12.5	18.9	5	15.0	33.5	5	25.0	30.6
Practical impact	18	23.61 (20.06)	0-83.33	25	8.33-33.33	8	27.1	27.7	5	26.7	7.0	5	15.0	13.7
Guilt - poor adherence	18	68.06 (26.85)	0-100	75	50.00-81.25	8	81.3	17.7	5	65.0	37.9	5	50.0	17.7
Relationships within family	16	20.31 (27.72)	0-75	0	0.00-43.75	8	18.8	29.1	5	20.0	32.6	3	25.0	25.0
Dietary protein restriction	15	32.48 (12.75)	14.76-61.19	29.05	26.43-41.55									
Adherence	18	5.56 (10.69)	0-25	0	0.00-6.25	8	3.1	8.8	5	5.0	11.2	5	10.0	13.7
Management	17	22.55 (11.22)	0-41.67	20.83	14.58-31.25	8	22.9	15.1	5	18.3	3.7	4	27.1	8.0
Practical impact	15	45.4 (21.11)	3.57-89.29	42.86	28.57-57.14	8	42.0	26.3	4	54.5	13.5	3	42.9	14.3
Food enjoyment (child)	18	22.22 (25.57)	0-75	25	0.00-31.25	8	21.9	28.1	5	20.0	20.9	5	25.0	30.6
Guilt – poor adherence	18	65.28 (29.88)	0-100	75	43.75-81.25	8	78.1	24.8	5	55.0	41.1	5	55.0	20.9

Note. A lower score indicates less severe PKU symptoms as measured by the PKU-QOL, lower impact of PKU, better adherence.

Table 3: Correlations between child and parent PKU-QOL scores, lifetime blood phenylalanine levels and parenting indicators

	M (SD)	Child's PKU symptoms	PKU in general	Emotional impact of PKU	Social impact of PKU	Overall impact of PKU	Admin. of Phe-free protein supplements	Dietary protein restriction
n		18	13	18	16	13	16	15
Parent's age	38.67(5.96)	.06	-.37	-.09	.11	-.39	-.30	-.11
Child's age	6.89(3.68)	.35	.03	.26	.22	-.27	.02	.18
Lifetime Phe levels	289.11(59.89)	.42	.50	.35	.43	-.12	-.14	.61*
PS								
- Laxness	2.83 (0.8)	.08	.34	.14	.26	.25	-.03	.19
- Overreactivity	3.08 (0.87)	.05	.34	.36	.21	.67*	.51*	.05
- Total	3.30 (0.59)	.06	.30	.24	.21	.45	.35	.07
CAPES								
- Parent efficacy	153.84 (22.46)	-.19	.09	-.02	-.01	-.21	-.07	-.04
- Emotional maladjustment	2.28 (2.27)	.51*	.18	.45	.50*	.10	.21	.44
- Behavioural difficulties	18.94 (9.94)	.77***	.21	.72**	.65**	.61*	.38	.58*
- Intensity	21.22 (10.54)	.84**	.25	.78***	.71**	.62*	.40	.64*
PSI								
- Parental Stress	27.67 (9.62)	.59*	.30	.64**	.78***	.50	.11	.55*
- P-C Dysfunctional Interaction	20.72 (8.75)	.60**	.61*	.70**	.81***	.59*	.18	.69**
- Difficult Child	24 (7.47)	.76***	.51	.73**	.70**	.56*	.11	.64*
- Total	72.39 (23.76)	.70**	.55*	.74***	.82***	.65*	.15	.68**

Note. PS = Parenting Scale; CAPES = Child Adjustment and Parent Efficacy Scale; PSI = Parenting Stress Index; P-C = Parent-Child; Phe = phenylalanine.
*** < .001 ** < .01 *< .05

Table 4: Regression analyses explaining variance in selected domains of child and parent PKU-QOL

	Child's PKU symptoms (n = 18)			Emotional Impact of PKU (n = 18)			Social Impact of PKU (n = 16)				Overall Impact of PKU (n = 13)		
Predictor	β	*SE*	*p*	β	*SE*	*p*	β	*SE*	*p*	Predictor	β	*SE*	*p*
CAPES Intensity	1.12	0.33	0.004	0.95	0.44	0.049	0.33	0.39	0.41	PS Overreactivity	5.64	3.07	0.10
PSI Total	0.10	0.15	0.51	0.31	0.20	0.14	0.49	0.18	0.015	PSI Total	0.31	0.18	0.13
R^2	0.71			0.66			0.69				0.57		
R^2_{adj}	0.67			0.61			0.65				0.49		

Note. PS = Parenting Scale; CAPES = Child Adjustment and Parent Efficacy Scale; PSI = Parenting Stress Index.