RESEARCH ARTICLES

Effects of commencing sapropterin therapy on quality of life for children with phenylketonuria and their families: A qualitative parent interview study

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ABSTRACT

Background: Prior to 2018, sapropterin hydrochloride (BH4, Kuvan®) had not been used in Queensland, Australia, to treat sapropterin-responsive phenylketonuria (PKU). This gave our centre at the Queensland Children's Hospital the opportunity to assess the difference a new treatment makes to the quality of life of the child and family.

Study design and methods: A qualitative study design was used. Forty parents of children with a sapropterin-responsive form of PKU (one parent per family) were invited to take part in a semi-structured one-on-one interview exploring their experiences and perspectives on commencing sapropterin therapy with their child. Thirty-eight parents met the eligibility criteria, 23 consented to participate, and 21 were able to be contacted for an interview. Data collected included family background and their experiences pre and post commencement of sapropterin therapy and its impact on their child(ren), diet, and physical and psychosocial wellbeing.

Results: Four key themes emerged from thematic analysis: a) psychosocial wellbeing, b) child health and nutrition, c) family economic benefits, and d) parent-child interactions. Overall, parents reported positive experiences and reduced impact of PKU on child, parent, and family quality of life

following initiation of sapropterin therapy. The majority reported a sense of relief and optimism and expressed that they were able to manage their child's PKU more effectively than before.

Conclusions: Sapropterin therapy is associated with physical and psychosocial benefits for children and families, including improved psychosocial wellbeing, parent-child relationship quality, and child health and nutrition.

Implications for research, policy, and practice: Commencement of sapropterin therapy can result in physical and psychosocial benefits for children with phenylketonuria and their families. Longer-term follow-up studies are warranted.

What is already known about the topic?
- PKU presents numerous and diverse challenges for children and their families and can negatively impact quality of life.
- Adhering to strict dietary management requirements can be particularly challenging for children and adolescents.
- Sapropterin therapy, a relatively new treatment for PKU in Australia, can enable less severe dietary restriction and greater liberalisation of the low phenylalanine diet.

What this paper adds
- Parents report considerable overall benefits for their child and family after commencing sapropterin therapy.
- Parents perceived improved child and family psychosocial wellbeing, parent-child relationship quality, and child health and nutrition, as well as socio-economic benefits.
- Since many parents experience uncertainty and anxiety in relation to commencing sapropterin with their child, families may benefit from psychosocial support and monitoring before, during, and after the commencement of therapy.

Keywords: Child Health; Childhood Illness; Family; Metabolic; Quality of Life; Phenylketonuria.

OBJECTIVE

Prior to 2018, sapropterin had not been used in Queensland, Australia, to treat sapropterin-responsive phenylketonuria (PKU). This qualitative study aimed to explore the experiences of families of children with PKU when commencing sapropterin therapy.

BACKGROUND

Phenylketonuria (PKU) is a rare Inborn Error of Metabolism (IEM) with an incidence of approximately 1 in 10,000, resulting from a deficiency of the enzyme phenylalanine hydroxylase and characterised by elevated blood phenylalanine (Phe) levels.[1] Newborn screening for PKU leads to rapid identification and immediate commencement of dietary intervention (i.e., adherence to a low-Phe diet) to prevent severe neurological manifestations.

Dietary intervention varies from patient to patient but may involve considerable restrictions in natural protein intake from food and breastmilk or infant formula, requiring supplementation with specialised Phe-free formulas and speciality low protein foods to support adequate nutrition and growth. Most children require different (low protein) meals from the rest of the family and natural protein intake is closely monitored to ensure it stays within daily limits. The rigours of dietary management can therefore be arduous for children and families, especially at key times in children's normal psychosocial and cognitive development (e.g., toddlerhood, adolescence) which can, in turn, affect compliance.[2] Thus, metabolic control and compliance can be suboptimal during key stages of normal childhood development. Furthermore, a systematic review has suggested that outcomes with dietary treatment alone are suboptimal in terms of neurocognitive, psychosocial, quality of life, growth, nutrition, and bone pathology measures.[3] In addition to the complexity of managing dietary interventions, studies have demonstrated the impact of PKU on various aspects of quality of life and psychosocial adjustment for children and their families.[4-9]

Sapropterin dihydrochloride (Kuvan®), a synthetic form of tetrahydrobiopterin (BH_4), was approved in Australia in December 2007 as the first drug treatment for PKU.[10] It is administered orally to lower blood Phe levels and increase Phe tolerance for those individuals who have a proven sapropterin responsive form of PKU. It has been used worldwide for many years and treatment protocols have been developed, enabling varying degrees of liberalisation of the low-Phe diet.[11,12] Responsiveness is assessed by commencing sapropterin dosing (20 mg/kg/day) and checking Phe levels at 24 hours and then weekly for 4 weeks, with a decline in Phe levels of around 30% indicating responsiveness.[13]

Approximately 25-50% of patients are found to be sapropterin-responsive and can then commence long-term sapropterin therapy of 5-20 mg/kg/day in conjunction with a relatively liberalised (although still Phe-restricted) diet.[13] Long-term therapy continues as long as patients remain under the care

of a metabolic multidisciplinary team who provide regular reviews and refine diet plans to ensure Phe levels remain within the target range.

Given the significant impact of strict dietary controls on children's and families' lives, relaxation of diet has the potential to impact psychosocial wellbeing. However, studies of changes in quality of life for patients treated with sapropterin have shown mixed findings. Two studies indicated improvements in quality of life and three studies found no effects of sapropterin therapy on self-reported quality of life.[12,14,15-17] Finally, Huijbregts and colleagues found improvements in quality of life for adults with PKU but not children with PKU.[18] Feldman and colleagues suggested that the self-reported measures they used may not have been sensitive enough to detect changes and called for more research to examine the nature of changes associated with sapropterin therapy.[17] Similarly, Demirdas and colleagues noted that qualitative reports suggested that patients were experiencing substantial differences in their day-to-day life which were not being captured by the quality of life questionnaire.[15]

In summary, although sapropterin therapy often allows substantive relaxation in dietary control while maintaining Phe levels within recommended guidelines, little is known about the lived experience of children and their parents following the commencement of treatment. This is a significant gap in our understanding of how effective the treatment is for children and their families, and therefore in our ability to effectively communicate treatment expectations. Insight into the lived experience of children and families following treatment commencement may help inform educational strategies to support realistic expectations.

In 2019, sapropterin gained funding by the Pharmaceutical Benefits Scheme (PBS) in Australia to provide a treatment option for children under the age of 18 years who have a sapropterin-responsive form of PKU (≥30% reduction in Phe following a sapropterin test load), thereby providing an opportunity to explore parents' experiences when their children commenced treatment. This study used a qualitative approach aiming to provide a better understanding of the impact of commencing sapropterin therapy for children and their families via parent interviews.

METHOD

A qualitative case study design was used.

PARTICIPANTS

Forty parents of children with PKU attending the Queensland Lifespan Metabolic Medicine Service (QLMMS) at the Queensland Children's Hospital (QCH) were screened for eligibility against the following inclusion criteria: (i) parent (aged 18 years or older) of a child diagnosed with a sapropterin-responsive form of PKU, (ii) child had commenced sapropterin therapy. There were no exclusion criteria. Thirty-eight parents met eligibility criteria and were mailed a written invitation to participate, followed up by telephone call(s) to assess interest. Of 38 parents, 23 (60.5%) consented to participate in the study. Of these, two were not able to be contacted to arrange an interview, leaving a final sample of 21 parents.

Participant characteristics are reported in Table 1. Most were mothers, university educated, employed, and able to meet essential expenses. Most children were living in their original family, with two parents and one sibling, and there were more girls than boys. In the four families with multiple children (two) with PKU, both children were receiving sapropterin therapy.

All children were prescribed 20 mg/kg/day of sapropterin. Children's mean blood Phe levels in the 6-months pre- and post-commencement of sapropterin were 331.08 µmol/L (SD = 78.71) and 290.44 µmol/L (SD = 101.71), respectively. Average pre-sapropterin natural protein allowance was 11.0 g/day (SD = 7.2). A subset of 15 children (pre-sapropterin protein allowance M = 8.1 g/day) continued counting protein intake once on sapropterin therapy, with a mean increase of 6.5 g/day. The remaining 10 children (pre-sapropterin protein allowance M = 15.3 g/day) no longer counted protein intake once on sapropterin therapy and had advanced to consuming allowed core food groups as per the Australian consensus method of dietary liberalisation. All children continued to receive amino acid supplementation via Phe-free formula while on sapropterin.

PROCEDURE

Approval to conduct the research was granted by the Human Research Ethics Committees of Children's Health Queensland (HREC/20/QCHQ/67483) and the University of Queensland (2020002347). Eligible parents were mailed an invitation letter and printed information and consent forms. A member of the research team (EE) contacted each family by phone within two weeks of the mailout to discuss the study with parents, answer any questions, and obtain written consent from those who wished to take part. Parents were recruited into the study from December 2020 to April 2021, and interviews were conducted from January 2021 to April 2021.

One parent per family (the primary caregiver) was invited to take part in a semi-structured one-on-one interview exploring their experiences and perspectives on commencing sapropterin therapy with their child. Families were interviewed around sixteen months after their child commenced treatment with sapropterin (M = 16.30 months, SD = 4.67, range 7.03- 22.80 months). The interview opened with questions about family background before exploring the impact of commencement of sapropterin therapy

TABLE 1: CHARACTERISTICS OF PARENTS (*N* = 21) AND CHILDREN (*N* = 25)

Variables	*M*	*SD*
Parent age (years)[a]	41.38	9.15
Child age (years)[b]	9.13	5.59
Number of children in household (total)[c]	2.00	0.78

Variables	%	*n*
Number of children in household with PKU[d]		
1	81.0	17
2	19.0	4
PKU diagnostic category[e]		
Classical PKU (>1200umol/L)	20.0	5
Mild PKU (600-1200umol/L)	64.0	16
Hyper-Phe (120-600umol/L)	16.0	4
Child conditions		
Emotional or behavioural problems	12.0	3
Physical disability	4.0	1
Other chronic health condition	24.0	6
Child sex		
Male	28.0	7
Female	72.0	18
Parent relationship to child		
Mother	90.5	19
Father	9.5	2
Relationship status		
Married/de facto	95.2	20
Widow/er	4.8	1

Variables	%	*n*
Household		
Original family	85.7	18
Step-family (2 parents, one being a step-parent)	9.5	2
Sole parent family	4.8	1
Parent education		
High school	9.5	2
Trade/college	19.0	4
University degree	42.9	9
Postgraduate degree	28.6	6
Parent employment		
Full-time	33.3	7
Part-time	61.9	13
Not working	4.8	1
Ethnicity		
Caucasian	90.5	19
Asian	4.8	1
First Nation	4.8	1
Able to meet essential expenses[f]		
Yes	95.2	20
No	4.8	1
After expenses can afford		
Not much	0	0
Some things	38.1	8
Most things	61.9	13

[a]Range 29-65 years.
[b]Range 1.42-18.67 years.
[c]Range 1-4 children.
[d]All children with PKU in household were receiving sapropterin therapy.
[e]Diagnostic category based on Phe level at time of diagnosis: classical PKU >1,200 µmol/L, mild = 600–1200 µmol/L, hyper-Phe = 120–600 µmol/L.

on children's PKU symptoms, dietary management, and physical and psychosocial wellbeing; the practical, social, and emotional impact of PKU on child and family; impact of children's dietary restrictions/liberalisation on day-to-day life; and impact of sapropterin therapy on the need for Phe-free amino acid supplementation.

To enable the inclusion of regional and remote families in the study, families could choose to be interviewed by phone, via Zoom videoconferencing, or in-person at the Queensland Children's Hospital or The University of Queensland. Interviews took a median 21 minutes (range 14-43 minutes). Parents were given the opportunity to review the written transcript and clarify their responses at the end of their interview. Interviews continued until all parents who had consented to participate had been interviewed; no stopping criteria were used because of the small number of eligible families.

MATERIALS

PKU management information (e.g., diagnosis details, PKU diagnostic category, pre- and post-sapropterin daily protein allowance, routinely-monitored blood Phe levels) was obtained from the children's treating team (QLMMS clinicians) with parents' consent. The Family Background Questionnaire was used to collect sociodemographic information including parent age, child age and sex, ethnicity, family composition, and education.[19]

DATA MANAGEMENT AND ANALYSES

All parents elected to be interviewed via Zoom videoconferencing. Interviews were recorded via Zoom videoconferencing software and transcribed verbatim. Accuracy of transcriptions was checked by EE, and interview transcripts were de-identified using unique participant

codes prior to analysis. Original audio files and de-identified transcripts were stored separately on a secure drive within the University computer network.

Descriptive statistics were used to describe the sample using demographic and child health history data. Qualitative data were analysed in line with the framework for reflexive thematic analysis recommended by Braun and Clarke,[20] and followed Clarke and Braun's six-step protocol: (1) familiarisation with the data, (2) coding the transcripts, (3) generating initial themes, (4) reviewing emergent themes, (5) defining the themes, and (6) writing up the findings.21 The initial coding was done by JA and subsequently checked by AM and AEM to ensure inter-coder reliability. To ensure the credibility and dependability of the results, frequent discussion and revision of emerging concepts was undertaken as a team prior to the synthesis of codes and generation of themes across the whole dataset. Results were presented according to the standards for reporting qualitative research.[22]

RESEARCHER CHARACTERISTICS AND REFLEXIVITY

All study authors have extensive experience working with parents and children in both clinical and community settings. The study was conceived by AI (nurse practitioner), CA (registered nurse), AE (metabolic dietitian), SS and JS (clinical nurse and registered nurse respectively) who have between 5 and >20 years' of experience caring for children with PKU and their families. Each had a pre-existing professional relationship with the participating parents and were key members of the children's health care team at the QLMMS. The interview schedule was developed by AEM and AM, who are a paediatric nurse and clinical psychologist, respectively, both with clinical and research experience in working with families of children with chronic health conditions. The interviews were conducted by EE, a developmental psychologist, and data were analysed by JA, a clinical psychologist, with input from the broader research team. Neither EE nor JA had prior relationships with the families who took part in this study.

RESULTS

The thematic analysis revealed diverse but overarching experiences for parents whose children had commenced sapropterin therapy, and four core themes emerged: a) psychosocial wellbeing, b) child health and nutrition, c) family economic benefits, and d) parent-child interactions. Overall, parents reported positive experiences following initiation of sapropterin therapy, and the majority reported a sense of relief and optimism. Generally, parents expressed that they were able to manage their child's PKU more effectively than before.

THEME 1: PSYCHOSOCIAL WELLBEING

The time following PKU diagnosis and the period preceding the initiation of sapropterin therapy was quite turbulent for many parents. Managing a child whose diet and social interactions require constant monitoring contributed to apprehension and uncertainty, and most described feeling anxious about the future and having concerns around their child's treatment outcome. Family and child psychosocial experiences pre- and post-initiation of sapropterin therapy were captured in the following sub-themes:

1.1 Parental apprehension

Parents had mixed feelings around starting their child on sapropterin.

> *Well, it was a bit nerve-wracking because we didn't know if his body would respond…* (Parent M)

> *It was exciting….and nerve-wracking…there was a lot of unknowns still…* (Parent R)

> *I felt anxious…I felt that her levels were probably very high and of course I didn't know if the Kuvan® would bring that level down…when we got the news that she was responsive it was great. It was actually fantastic…it was a really happy and joyful time for our whole family.* (Parent B)

> *I'm a little bit lost…I am still struggling a little bit…it's been a very long process in understanding around PKU…* (Parent O)

While many parents were optimistic about the treatment outcome, some still expressed concerns about sapropterin administration and its effectiveness.

> *The most difficult part was…the number of tablets that she had to take each day…that's kind of the biggest issue…* (Parent U)

> *…let them have as much fruit and vegetables as they want without counting…I found that really hard to not count, because I was like, I – I'm not in control. I feel like I'm just hanging around waiting for the result to come back to let me know whether I'm doing it right or not…So, I did have a lot of anxiety about just letting go and trying a new way of eating…there were times where I'd be so worried that I would not be willing to try things…* (Parent C)

1.2 Social interactions

Parents expressed varying degrees of change in their family's social life. For many families, initiating sapropterin therapy and their child's positive response to treatment brought a sense of relief and freedom to engage more freely in social activities such as birthday parties and dining out due to less restrictive dietary requirements.

Socially…it has definitely had a bigger impact…she can sit for morning and afternoon tea, and she doesn't have to have, like a special kind…it's allowed her to participate – like share in a birthday celebration… (Parent O)

Kuvan® has changed the variety of food that they can eat and their social activity…a very considerable improvement for their quality of life. (Parent D)

We do enjoy…going out to eat more than before…because they can choose more…It's easier than before… (Parent J)

…having a birthday party and they might go for lunch somewhere, and we'll drop her off and…she never feels out of the group… (Parent V)

…it's much easier her going to social events, so whether that's to a friend's house or school…again, is much, much easier than it used to be… (Parent B)

1.3 Child psychological wellbeing

Parents also reported improvements in the mental, emotional, and behavioural functioning of their children post-sapropterin initiation.

…less resentful of her condition…has a lot more choice in what she can have and she's very happy…I just think that attention level…that's improved. (Parent K)

Before Kuvan®…by the afternoon…couldn't do any schoolwork and then she was talking and then she was distracting and she was getting into trouble…she can focus so much better…finished exam in time and she's excited about it…she never would have been able to do that before…and she's less emotional… (Parent Q)

…he was very withdrawn…I think his confidence probably came after Kuvan®… (Parent H)

School has been much better since the Kuvan®, so much, so much easier, don't have to worry about it… (Parent Q)

THEME 2: CHILD HEALTH AND NUTRITION

This theme underscored the changes that parents perceived in their children's physical health and food choice/nutrition post-sapropterin initiation.

2.1 Child physical health

Most parents in the study perceived marked improvements in the physical health of their children. Comparing the pre- and post-sapropterin experience, parents expressed that they noticed significant effects of treatment on the physical wellbeing of their children including lower Phe levels, more effective sleep, and higher energy levels.

…she's [child's] definitely got a lot of energy now. (Parent W)

…her energy levels, if anything, have improved…sleeps a bit more in the morning…overall she's more well post-Kuvan® than pre-Kuvan®. (Parent N)

She [child] responded really well to Kuvan® so her levels have been really, really low since she's been on that. (Parent X)

[Child] did at first complain of a sick stomach…they would have limited breakfast because they were so full. At first – where now they're a lot better, you know, they can balance, it's a little bit of liquid than a whole cup of juice to have every tablet. So that made a big difference. (Parent A)

Kuvan® has definitely made things a lot easier for us in terms of food, whether or not it's just his immune system has gotten better, but he doesn't seem to get sick very much… (Parent H)

…definitely, we can see a difference in…her level of tiredness…we are using Kuvan® to keep her level…lower, and I believe – or my observation is – that that helps her sleep better. (Parent B)

2.2 Child food choice/Nutrition

Managing children's Phe levels required parents to carefully regulate the amount of protein intake at every meal from birth, a task which parents described as both complex and demanding given the need for constant monitoring of what and how much the child eats.

…trying to manage this very complex diet again and trying to make it work. So, yes, it can be very worrying, but you want to make sure you're doing the right thing because it does affect their brain function… (Parent A)

Despite ongoing complexity around diet, most parents described their experience post-initiation of sapropterin as positive and rewarding for both the child and the family. A child's newfound ability to eat a wider variety of foods in unmeasured quantities was the greatest highlight for most parents.

It definitely makes it easier because we have more protein to play with in the day… because – increased his tolerance by 30%, [broader range of products] makes life easier for us [family] including grandparents looking after him…. (Parent I)

The food that they can eat at the moment is much more than before…I don't have to worry about if they've had too much steak for this meal… (Parent D)

It's definitely allowed us to increase her diet a lot more and probably a lot quicker than what we would have been able to do otherwise…it's definitely a lot easier being able to just buy…rather than having to get a low protein option… (Parent X)

 https://doi.org/10.37464/2024.414.1272

It's easier because she has more allowance. So, her natural protein allowance is easier. That gives her access to more foods that she likes…I don't have to weigh or measure anymore… (Parent B)

I no longer have to use pharmaceutical grain-based food…more flexibility around not having to weigh stuff…and cooking different meals, and without having to be on her like a hawk…to make sure she doesn't eat anything that she's not meant to eat. (Parent O)

THEME 3: FAMILY SOCIO-ECONOMIC BENEFITS

This theme describes parents' perceptions of socio-economic benefits of having their child commence sapropterin.

3.1 Family food expenses

Most parents expressed that sapropterin reduced the financial pressure associated with having to purchase specialty low-protein foods, which tend to be costly. Parents felt that spending less on specialty low-protein foods had a direct financial benefit for their family.

I don't have to spend much money trialling different foods, having Kuvan® took that weight off not having to be so concerned about what she was eating. (Parent O)

I think it's been beneficial, and I can see the benefits…we're not spending as much money on the specialised low protein products. (Parent U)

3.2 Family dietary freedom

Having a child with PKU typically involves cooking a variety of meals, including special low-protein meals, to cater to the dietary needs of every family member on a daily basis. When eating out, families had previously needed to grapple with the challenge of always having to ask for special menus or modified meals to accommodate their child's restrictive diet. Many of these challenges had eased since starting sapropterin.

We always sit down at the dinner table, and we always eat together…where once upon a time we'd have to speak to the waitresses and chefs to tweak it to make it acceptable for her to eat, where now we don't have to do that. It's fantastic. (Parent T)

For many parents, sapropterin brought a sense of relief and enhanced freedom to access, buy, cook, and enjoy a variety of foods with less restrictions due to protein content.

She is certainly enjoying food at the moment…family meals now look more similar… (Parent K)

Now it's more like we just cook our meal and then just add the meat in, you know it could be more of a family meal, we can eat more of the same things. (Parent F)

They've got more protein to play with…that's made life easier. They've been able to probably eat a little bit more normal food, like food that you can buy from the groceries. (Parent C)

Theme 4: Parent-child interactions

Some parents expressed feelings of stress and frustration in their effort to control their child's Phe levels prior to commencing sapropterin, which impacted how they related to the child.

I do worry, and I worry because I can see that not managing your Phe levels has this really difficult negative spiral…kids with this disorder are at much, much higher risk of mental health issues… (Parent B)

Them having the high levels was stressful me knowing that they were deliberately pushing the levels up. (Parent Q)

In contrast, most parents expressed relief and spoke of their excitement about the change in the quality of their relationship with their child after initiating sapropterin therapy. Parents reported meaningful gains including spending more quality time together at home and elsewhere, better communication, improved teamwork within the home, and better socialisation.

We see that it's a bit of a team approach at doing things…a bit more social freedom for us as a family… (Parent K)

We actually enjoy spending that time together…it's not a constant battle. (Parent Q)

When it came to the realisation that the Kuvan® was successful for [Child], it was a celebration. We went out to breakfast, and we cried over bacon and eggs together, we couldn't believe that this was real. (Parent T)

…yeah, have that, have that open chain of communication… (Parent W)

DISCUSSION

PKU presents numerous and diverse challenges for children and their families, and the advent of sapropterin therapy has the potential to dramatically change families' day-to-day experiences of managing this complex condition. Nevertheless, prior studies examining the effects of sapropterin therapy have reported mixed outcomes,[12,14-18] and no studies to our knowledge have examined the lived experience of parents whose children with PKU commence sapropterin therapy. This study used a qualitative design, with a relatively large sample size, to examine the experiences and perceptions of parents following their children's commencement on sapropterin therapy. Four main themes with multiple sub-themes were described, with each theme suggesting that parents were experiencing

considerable overall benefits for their child and their family after commencing sapropterin therapy.

Psychosocial wellbeing of both parent and child was a central theme that parents noted being important both before and after starting sapropterin therapy. Most parents described experiencing feelings of apprehension, uncertainty, and anxiety about the future and their child's treatment outcome prior to starting therapy. Many parents described having mixed feelings about their child commencing sapropterin, and some continued to have ongoing concerns about the administration and effectiveness of this treatment. Importantly, however, parents noted that they could see significant improvements in their child's mental, emotional, and behavioural functioning post-sapropterin initiation. One important element which may have contributed to improved wellbeing was the ability to participate in social activities and events more easily due to less need for dietary restriction, which brought a sense of normalcy for children and families. These results align with those of a recent UK study, which reported improvements in caregivers' mental health and reduced family impact 6-months after children's commencement of sapropterin.[23]

A second important theme related to the broader dietary choices that children now had, and parents' perceptions of their children's physical health and nutrition. The introduction of sapropterin did not eliminate the need to monitor and regulate children's diets, but it enabled a significant easing of the day-to-day burden of dietary intervention and allowed children the choice to eat a wider variety of foods. Parents also noted that their children had better sleep and higher energy levels, and, importantly, that their Phe levels remained low. PKU is associated with deficiencies in dopamine and serotonin, which are neurotransmitters important to sleep regulation;[24] however, very few studies have examined sleep in PKU. While reduced sleep quality and increased daytime sleepiness have been reported in studies with adults no differences have been found between children with early-treated PKU and healthy controls.[24-26] To the best of our knowledge there is no research examining the effect of commencing sapropterin on the sleep of children with PKU, and our data support this as an area for future research.

The third theme focused on the perceived socio-economic benefits, especially the reduction in financial burden associated with having to purchase costly specialty foods and supplements. Associated with this was a sense of freedom, both at home and when eating out, around the broader range of foods the whole family could now consume. In Australia, patients with PKU who are compliant with regular Phe monitoring and require a low-protein diet are eligible for a monthly payment of AUD$279 through the Inborn Errors of Metabolism program to assist with purchasing low-protein foods.[27] While this helps to offset costs, specialist low-protein foods remain expensive; for example, a packet of low-protein pasta (AUD$9.90-$13.50) is considerably more costly than a standard supermarket equivalent (AUD$0.90-$3.50). The dietary liberalisation that resulted from the commencement of sapropterin therapy was therefore associated with reduced financial pressures for families.

The final theme focused on perceived benefits to the parent-child relationship. Parents noted that the demands of rigorous dietary management associated with PKU had negatively impacted their relationship with their children. The commencement of sapropterin resulted in marked improvements in how families spent their time together, how well they got along, and the sense of belonging to a team.

The results of this study are consistent with previous research which has shown positive effects on psychosocial outcomes and quality of life following commencement of sapropterin,[12,14,23] and provide a unique view into the lived experience of parents and children shortly after the commencement of therapy. Overall, the experiences of parents who participated in this study were positive and suggest that families could reasonably expect to derive a range of child-, parent-, and family-level benefits from commencing therapy, many of which could persist for as long as therapy is effective. Thus, results may inform discussions with families who are considering commencing sapropterin therapy; however, additional follow-up of families is needed to understand longer-term experiences and effects.

Although parents reported significant positive changes following the commencement of sapropterin for their children and families, the lead-up to responsiveness testing and commencement of therapy emerged as a challenging time for parents, who described anxiety and worry about whether and how their child would respond to treatment. Even once children responded well and commenced therapy, some parents experienced a degree of ongoing stress and anxiety around liberalising their child's diet, and worried about keeping their child's Phe levels within the target range while they were experimenting with new foods and quantities. This has important implications for care planning for families who are being offered sapropterin therapy and suggests that families may benefit from psychosocial support and monitoring before, during, and after commencing sapropterin.

LIMITATIONS

PKU is a rare disease and, as such, it is challenging to get large numbers for a study like this from one centre. Despite this, we recruited more than half of the eligible families in Queensland and data saturation was achieved; however, the views of those parents who declined to participate, and whether they are different from parents who did participate, are unknown. Another limitation was that we were not able to compare responses of parents whose children had different sub-types of PKU and potentially differential treatment responses to sapropterin. In addition, while

we captured the views of parents, we did not interview children, and this is an ongoing gap in the literature. Gaining insight into the experience of children affected by PKU is an important consideration for future research.

CONCLUSIONS

Sapropterin is a relatively new treatment for PKU in Australia and has the potential to have great benefits to lifestyle and dietary freedom. This study demonstrated that parents overall had a positive outcome and experience of the therapy with benefits for psychosocial wellbeing, parent-child relationship quality, child health and nutrition, and socio-economic benefits.

IMPLICATIONS FOR RESEARCH, POLICY AND PRACTICE

Commencement of sapropterin therapy can result in physical and psychosocial benefits for children with phenylketonuria and their families; however, families may benefit from psychosocial support and monitoring before, during, and after commencing sapropterin. Longer-term follow-up studies are needed to understand longer-term experiences with, and effects of, sapropterin for parents and children.

Funding support: This work was supported by a grant from Children's Health Queensland – Centre for Clinical Trials in Rare Neurodevelopmental Disorders, Children's Hospital Foundation Early Career Fellowships (AEM; award ref. no. 50223, ECF0112020). The funders had no role in the study design; the collection, analysis or interpretation of data; the writing of the report; or the decision to submit the article for publication. The authors maintained full access to all data within the study and final responsibility for the decision to submit for publication.

Declaration of conflicting interest: The Parenting and Family Support Centre is partly funded by royalties stemming from published resources of the Triple P – Positive Parenting Program, which is developed and owned by The University of Queensland (UQ). Royalties are also distributed to the Faculty of Health and Behavioural Sciences at UQ and contributory authors of published Triple P resources. Triple P International (TPI) Pty Ltd is a private company licensed by Uniquest Pty Ltd on behalf of UQ, to publish and disseminate Triple P worldwide. The authors of this report have no share or ownership of TPI. Dr Morawska receives royalties from TPI. TPI had no involvement in the study design, collection, analysis or interpretation of data, or writing of this report. Dr Morawska and Dr Mitchell are employees at UQ. Dr Etel and Dr Adina were employees at UQ at the time this research was conducted. Ms Inwood has accepted travel honorariums from pharmaceutical companies. Ms Inwood has received funding to present on Pharmaceutical Advisory Boards for BioMarin Inc. The remainder of the authors have no conflicts of interest.

Acknowledgements: Our sincere thanks to the families who participated in this study.

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