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Our lives with PKU: German patient voices - "Nothing about us without us"

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ABSTRACT

Objectives: Many publications describe experiences of healthcare professionals (HCPs) on managing phenylketonuria (PKU), but literature on the perspectives of individuals with PKU is limited. Nevertheless, patient insights and strategies to address challenges of living with PKU can provide guidance to HCPs and the PKU community to further optimise PKU care.

Methods: A virtual meeting was held to elucidate the lived experience of patients with PKU and brainstorm best practice recommendations from the patient perspective. The meeting was moderated by a psychologist and attended by seven adults with PKU and one caregiver. Based on the outcomes of this meeting and subsequent online rating rounds, consensus statements (≥75 % agreement) reflecting patient focused considerations were developed using a modified Delphi approach.

Results: Consensus was reached for 18 statements on five topics: the PKU diet, experience with HCPs throughout life, impact of PKU on everyday life, connecting with the PKU community, and future aspirations to facilitate life with PKU.

To minimise the burden of diet, avoidance of hunger and offering new treatment options were identified, together with adequate education and support. Maintaining metabolic control throughout adulthood could be facilitated by easier access to clinics beyond in-person visits and by availability of treatment teams specifically equipped to provide PKU-adult care. To further support adults in reaching target blood Phe concentrations and personal goals, pegvaliase can be offered to those eligible. Finally, exchanging experiences with others from the PKU community through social media and live/virtual meetings may help individuals with PKU and caregivers to improve their knowledge and skills to manage PKU.

Conclusion: These consensus statements provide unique insights on how challenges faced by individuals with PKU may be addressed and may provide guidance to HCPs as well as the PKU community and caregivers on ways to improve patient care and support.

1. Introduction

Phenylketonuria (PKU) is a rare metabolic disorder caused by phenylalanine hydroxylase (PAH) enzyme deficiency. If left untreated, the resulting elevated blood and brain phenylalanine (Phe) concentrations can induce severe neurodevelopmental, behavioural, and psychiatric complications [1,2]. To prevent these, often irreversible, negative consequences, prompt initiation of medical nutrition therapy (MNT)

Abbreviations: BH4, tetrahydrobiopterin; DIG PKU, Deutsche Interessengemeinschaft Phenylketonurie und verwandte angeborene Stoffwechselstörungen; HCP, healthcare professional; MNT, medical nutrition therapy; PAH, phenylalanine hydroxylase; PAL, phenylalanine ammonia lyase; Phe, phenylalanine; PKU, phenylketonuria; US, United States.

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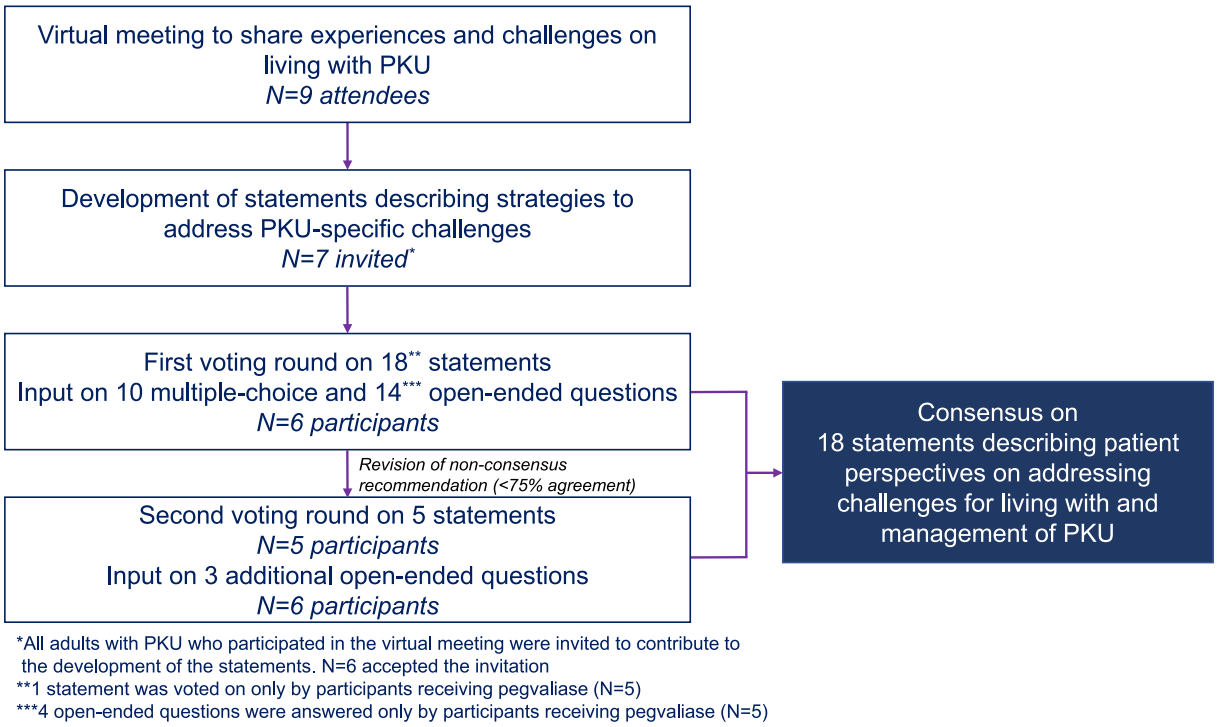

Fig. 1. Overview of the consensus statements development process.

upon diagnosis of PKU with newborn screening is recommended to reduce blood Phe concentrations [2,3]. MNT for PKU encompasses a Phe-restricted diet that consists of natural foods low in protein complemented with modified low-protein foods from specialised manufacturers and Phe-free protein supplements (also referred to as medical food) [3–7]. For those eligible, pharmacological treatment such as sapropterin dihydrochloride (for individuals with residual PAH activity) or pegvaliase (for adults with blood Phe concentrations above blood Phe target ranges), may be initiated to lower blood Phe concentrations [8–11].

As European guidelines recommend lifelong control of blood Phe concentrations to below a target value of ≤360 μmol/L until 12 years of age and <600 μmol/L for older individuals [2,12], regular in-clinic follow-up remains important beyond childhood, irrespective of treatment regimen. However, motivation to attend clinic visits and to maintain metabolic control tends to decline during adolescence and adulthood, exposing many individuals to the negative effects of elevated blood Phe concentrations [6,7,13–18].

Many publications describe the perspectives of healthcare professionals (HCPs) on the management of PKU. While such insights are important for implementing best practices in clinics, the experiences and input of individuals with PKU are also indispensable to further optimise PKU care. However, current literature on the perspectives of individuals with PKU is limited. To address this lack of evidence/insights, expert opinion of six adults with PKU and one psychologist from Germany was collected using a modified Delphi technique. The resulting consensus statements shed light on how the daily challenges and struggles faced by individuals with PKU may be addressed and can give guidance to HCPs as well as the PKU community and caregivers on ways to improve patient care and support.

2. Methods

A virtual meeting was held on 29 June 2023 to elucidate the lived experience of patients with PKU and brainstorm best practice recommendations from the patient perspective across various topics. This meeting was sponsored by BioMarin and moderated by a psychologist experienced in supporting individuals with PKU and attended by seven adults with PKU and one mother of an adult child with PKU. All participants were living in Germany. The individuals with PKU and caregiver were recruited to participate either via their treatment centres, the German patient association 'Deutsche Interessengemeinschaft Phenylketonurie und verwandte angeborene Stoffwechselstörungen' (DIG PKU), or in-person at a local PKU meeting. After receiving further information about the purpose of the meeting, interested parties could indicate their willingness to participate.

Based on the outcomes of the virtual meeting, statements on strategies to address challenges faced by people with PKU were developed. All seven adults with PKU were invited as panel members to rate these draft statements on an online platform, with the aim of consensus generation (≥75 % agreement) using a modified Delphi approach. Statements for which no consensus was reached could be revised and revoted in consecutive rounds. Additionally, all panel members were asked to answer multiple-choice and open-ended questions on the platform on their experiences and challenges faced with PKU and its management throughout different phases of their lives.

Overall, outcomes from discussions during the virtual meeting complemented with the information provided by the panel members via the online platform were used to describe patient perspectives on five overarching topics: the PKU diet, experience with HCPs throughout life, impact of PKU on everyday life, connecting with the PKU community, and future aspirations to facilitate life with PKU.

3. Results

Of the seven adults with PKU who participated in the virtual meeting, six participated in the first voting round. The panel members (4 females, 2 males) were aged 36–58 years and achieved varying levels of education (from lower secondary school to grammar school). The same six panel members also participated in the second rating round (one participant only answered open-ended questions in the second round). Of the 18 draft statements, 13 were accepted in the first voting round. In the second round, 5 statements were revised and revoted, leading to consensus (≥75 % agreement) for all 18 statements (Fig. 1).

Table 1
Challenges of medical nutrition therapy for individuals with phenylketonuria (PKU) throughout childhood, adolescence and adulthood.

Childhood	Adolescence	Adulthood
• Accessing non-permitted food at school (e.g., swapping with others)* [20] • Prohibitive parenting style*	• Becoming responsible for PKU care* [21] • Peer pressure to consume forbidden foods* [21]	• No suitable food when eating out* [19] • Feelings of shame when consuming medical food at restaurants, work or while travelling* [19]

Challenges shown in this table were encountered by the panel (indicated with *) and/or described previously in literature.

Additionally, 10 multiple-choice and 17 open-ended questions were asked during the voting process, to shed more light on the panel members' personal experiences. The final approved statements, key discussion topics of the virtual meeting, and related literature are discussed by topic below.

4. Key discussion topics

4.1. Topic 1: The PKU diet throughout life

4.1.1. Challenges encountered by individuals with PKU

In agreement with previous publications, the panel emphasised that adhering to MNT is challenging, burdensome, and becomes more complicated when growing up. Universal barriers to diet acceptance across all ages commonly described in the literature and experienced by the panel members include problems with availability and costs of medical food, lack of motivation, inadequate dietary education, limited medical supervision and support from environment, and a perceived lack of association between dietary adherence and well-being [5,6,19]. Poor palatability and little variability of medical food are also important contributors to impaired diet adherence [5,6,19] although the panel members acknowledged that the taste of medical food and the choice and variety of suitable foods have improved since their youth. Interestingly, the majority of panel members indicated having experienced hunger when adhering to the diet, mostly during childhood and adolescence, but some also as adults. Noteworthy, the panel represents a selected sample of adults with a long history of PKU (some were among the first cohorts to be identified through newborn screening), making it possible their childhood experiences were more difficult than the situation of today's children with PKU.

The impact of additional factors complicating MNT, such as inconvenience, time demands, interference with social life and embarrassment, and how these manifest, evolve throughout the different phases of life, along with changes in an individual's environment (e.g., school, college, work) and circumstances (autonomy, interactions with others) (Table 1) [5,6,19].

4.1.1.1. Quotes (translated from German) on diet-related challenges encountered by panel members

> *"Everything was very tightly controlled by my parents and a few relatives. Lots of prohibitions: no children's birthdays, no school trips, no visits from friends, no trust in this regard from my parents."*

> *"It was often the case, especially when we were young, that we were special to others and not that others were special to us. It was often the case that many people were jealous of what we ate and not the other way around. Which is why we swapped our low-protein Nutella (cocoa spread) bread for sausage rolls."*

> *"It is a huge financial burden!!"*

> *"I try not to get into a situation where I'm very hungry because then it's super difficult to stick to the diet! If I eat on time it's easier because there are now a lot of good-tasting 'permitted' foods."*

> *"I was very homely, had few friends and rarely went out to eat, was shy when it came to new contacts, had some mental health issues and lower self-esteem. I always ate vegetarian food when accompanied by others. I tried to stick to the diet and not punish myself by having values below 10 [mg/dL], which was around 11-14 g [protein] per day. My hobbies like crafts and reading distracted me in addition to my two dogs."*

4.1.2. Patient perspectives on addressing challenges with the PKU diet throughout life

> ***Statement #1:*** **It is important that parents are well-educated and trained in PKU management and motivated to provide optimal care. Caregivers should support children with following the diet and help to prepare adolescents and young adults for independent PKU management. (100 % consensus).**

Various studies have shown a correlation between parents being poorly educated on PKU management and elevated blood Phe concentrations in their children [22–24]. Others have demonstrated how knowledge of caregivers and their attitude towards MNT influences their child's nutritional behaviour [25,26], underlining the importance of knowledgeable parents. Furthermore, children with PKU often display problematic eating habits that may necessitate considerable parental effort to address. Strategies to improve nutritional behaviour, such as eating together, establishing consistent routines with adequate time per meal, encouraging familiarisation with new foods, allowing play with food (e.g., decorating cookies), and inviting friends to eat low protein foods require motivated and well-organised parents [27]. For adolescents with PKU, the challenge of becoming independent and taking responsibility for PKU and its management may be further complicated by a desire to fit in, peer pressure, feelings of anger, guilt and embarrassment, as well as PKU-related neurocognitive or -psychiatric complications [6,21]. Parents can help facilitate the complex transition to self-care by educating their children and adolescents on PKU management and teaching them practical skills (e.g., preparing Phe-free meals). While supervision can gradually decrease when adolescents start acquiring skills for self-management, some level of support often remains necessary throughout the teenage years to avoid major pitfalls [21,28].

> ***Statement #2:*** **Healthcare professionals (HCPs) and caregivers should make sure that individuals with PKU are not experiencing hunger when following the diet, especially during childhood. (100 % consensus).**

> ***Statement #3:*** **Mobile applications may help track food intake and support adherence to diet. (100 % consensus).**

Feeling not fully satisfied or hungry can lead to unhealthy food choices or disturbed eating patterns. Disordered eating may evolve to clinical eating disorders, which have been suggested to occur more frequently in individuals with PKU than in the general population [27,29]. Therefore, HCPs and caregivers should be attentive to signs of malnutrition, regularly inquire if individuals feel satisfied after meals, and propose solutions to avoid hunger. Dietary advice and written nutrition protocols can further guide and educate individuals with PKU and their caregivers towards healthy eating habits. Recently, mobile applications, either for general dietary support (e.g., YAZIO®) or PKU-specific (e.g., Mevalia®, PKU Bite®) have emerged as additional tools to identify suitable food and track protein and nutrient intake [30]. While these are valuable instruments facilitating everyday life, some panel members suggested that additional features that allow scanning of

Table 2
Challenges encountered by individuals with phenylketonuria (PKU) related to healthcare professionals (HCPs) and metabolic clinics.

- Lack of contact with the same physician who is familiar with the individual's habits, condition, and history*
- Inadequate communication within the treatment team and with other HCPs [5]
- Local HCPs (e.g., primary care providers) poorly educated on PKU, its treatment, and the specific needs of affected individuals* [5,25]
- Failure to refer individuals with psychological issues to a mental health provider* [5,14]
- Geographical barriers or busy lifestyle (e.g., unable to get time off from work) interfering with clinic visits* [14]
- Lack of a formal plan for transitioning to adult care* [21]
- PKU clinics focused on treating children with lack of educational materials for adults* [14,28,33,34]

Challenges shown in this table were either experienced by the panel (indicated with *) and/or described previously in literature.

nutritional value tables and automatic conversion into Phe could further enhance user experience.

Statement #4: **New treatment options that become available throughout life should be offered to eligible individuals to give them the opportunity to liberalise or normalise their diet. (100 % consensus).**

Pharmacological treatment options may partly alleviate the challenges associated with MNT and counter declining adherence. If treatment successfully reduces blood Phe concentrations to within or below the target recommended range, individuals may experience increased dietary freedom and worry less about their disease. Nevertheless, nutritional counselling and education remains necessary to ensure individuals follow a normal, healthy diet with sufficient protein and nutrient intake [31].

4.2. Topic 2: Experience with HCPs throughout life

4.2.1. Challenges encountered by individuals with PKU

Following a PKU diagnosis, individuals are generally followed up in a metabolic clinic by a multidisciplinary team consisting of a paediatrician and a dietitian, ideally complemented with a nurse, a psychologist, and a social worker [13,32]. During childhood, parents are the main communicators with the paediatric care team and are the primary caregivers to manage all aspects of PKU (such as ensuring adherence to MNT and obtaining blood spots) [25]. From adolescence onwards, individuals with PKU become more involved with the metabolic clinic themselves and gain further insights and skills to manage their disease and diet. While some individuals successfully transition to adult care upon entering adulthood, others are either still treated by their paediatric HCPs, partly because adult-specific metabolic clinics are scarce in many countries, or completely discontinue treatment and/or become lost to clinical follow-up [13,28,33,34].

Generally, the metabolic clinic and treatment team are essential for maintaining optimal health in individuals with PKU and for keeping them engaged with the treatment. Table 2 lists HCP- and clinic-related factors that may impede optimal PKU care, as identified by the panel and literature.

4.2.1.1. Quotes (translated from German) on challenges encountered by panel members related to HCPs and metabolic clinics

> *"In general, we haven't been looked after at all since we were 17 years old. We also did not take any blood tests, let alone receive any information. When the diet ended, so did the care".*

> *"As far as I know, we didn't have a real contact person on site who really knew about PKU, which made it very difficult.[…] Even the treating physicians didn't know exactly what the correct target value was. They said up to 15 [mg/dL] is OK, but that's negligent if you have that value for 20 years".*

4.2.2. Patient perspectives on improving interactions with HCPs throughout life

Statement #5: **The treatment team should establish an open, honest and continuous patient-provider partnership and be easily reachable outside of clinic visits. (100 % consensus).**

By establishing a relationship of mutual trust, the treatment team may prevent individuals with PKU from becoming lost to follow-up and stimulate treatment continuation [21,34,35]. Contact with the same providers, who are knowledgeable about an individual's circumstances, can improve confidence in the clinic, especially when easily reachable (e.g., via phone or email) in case of concerns or questions. The panel identified dietitians as the most trusted and used source of information for individuals with PKU, in line with several other studies [22,25,30]. To further optimise care and engagement with the clinic, strategies such as digital solutions (e.g., telemedicine, reminder calls or emails), offering flexibility, focussing on positive empowerment, and setting personalised treatment goals beyond blood Phe control can be employed [21,36]. The panel members further suggested to organise more time-efficient, PKU-dedicated in-clinic appointments (shortening waiting times) and to set up more specialised outpatient PKU clinics with trained personnel (shortening the distance and travel time to clinics). These structural solutions were also previously identified in a United States (US) PKU expert HCP survey [36]. Finally, one panel member noted that health insurance providers should provide better support to cover costs related to diet, treatment, and travel to the clinic.

4.2.2.1. Quotes (translated from German) on interactions with HCPs and clinics

> *"In fact, communication outside of the clinic visit now often takes place via email or SMS. This makes communication easier and I get answers to inquiries quickly."*

> *"As far as I can remember, the contact with the dietitian was always more intensive than with the doctors. She knew/knows me and my story."*

> *"I have a very good (and nice) diet assistant who is always available to me (by phone or in person) and who always supports me a lot!"*

> *"There should be more metabolic outpatient clinics, but [therefore] more doctors would have to be trained in the specific disease. And always be up to date with the latest research."*

Statement #6: **Adults with PKU should be followed in an adult-focused clinic. The transition to adult care should be prepared slowly in early adolescence and relevant healthcare professionals should be present to support. (83.3 % consensus).**

Adults with PKU could benefit from adult-specific facilities offering adult-directed educational tools and management of medical and psychological comorbidities. The transition to adult care requires a multidisciplinary effort and as many individuals appreciate the familiar relationship with their paediatric treatment team, introducing the new adult physicians during consultations with the familiar paediatrician may help individuals to adapt to the new treatment environment [34].

Table 3
Impact of phenylketonuria (PKU) on the everyday life of affected individuals and their parents across various domains.

Impacted domain	Parents	Individuals with PKU
Work	• Need to reduce working hours or completely quit work* [5] • Need to change career* [5]	• Limited career choices* • Not accomplishing full potential* [5] • Feeling different from colleagues* [5] • Unable to work full-time due to time burden of treatment*
Family	• Changes in family planning (decision not to have any more children) [5] • Fear of neglecting non-PKU siblings* [5] • Arguments with children about diet adherence* [5,43]	• Changes in family planning o Decision to have children* o Timing of pregnancy*
Social life	• Less time for social activities* [5] • Complicated relationship with partner, family, and friends* [5]	• Inability to eat out [5] o No suitable food available o Embarrassment over diet* • Feeling socially excluded or isolated from peers, friends, or family* [5] • Lack of spontaneity* [5] • Missing social events* [5]
Mental health	• Psychological burden of knowing that inadequate care can be detrimental for the child's functioning* [5]	• Feelings of guilt when not successfully adhering to treatment* [7,21]

Everyday struggles shown in this table were either identified by the panel (indicated with *) and/or described previously in literature.

However, the feasibility of this strategy depends on country-specific coverage by insurance providers, as in some regions, including Germany, reimbursement is limited to one doctor per consultation.

Other strategies for clinics to promote a successful transition to self-management, and consequently improved self-confidence and self-efficacy, include beginning with PKU-specific education in early childhood, preparing the transition process during early adolescence (for some as early as the age of 12 years), and developing and implementing transition policies [21,34].

4.3. Topic 3: Impact of PKU on everyday life

4.3.1. Burden of PKU on everyday life of affected individuals and their caregivers

It is well documented that the diagnosis and management of PKU has a substantial impact on the daily lives of individuals with PKU and their caregivers. Besides the time-consuming workload of preparing low-Phe food, calculating protein intake and, specifically for parents, supervising the diet and ensuring appropriate food consumption, aspects such as attending clinic visits, monitoring blood Phe, and psychological stress contribute to the burden. The considerable time and effort individuals with PKU and their caregivers put into disease management affects their lives in various domains such as school, professional careers, and social life (Table 3) [5,7,37–39]. Furthermore, poor metabolic control with elevated blood Phe concentrations may affect basic skills such as planning, concentration, and memory and can contribute to mental health (depression, anxiety) and behavioural (aggression) issues. This impaired functioning complicates organising everyday life and can further impair the ability to adhere to MNT and clinic visits, trapping individuals in a vicious cycle [5,7,40–42].

4.3.1.1. Quotes (translated from German) on burden of PKU on everyday life of caregivers

"My dad was working all the time, he was self-employed, he didn't know about the illness and stayed out of it. My mom took over everything and was therefore at home and a housewife."

"My parents divorced when I was 8 years old. The PKU was also part of the problems."

4.3.1.2. Quotes (translated from German) on burden of PKU on everyday life of patients

"When I wanted to become a dietitian, I was told by the education centre that I was not suitable for this education due to my metabolic disorder."

"I decided early on (with my wife) not to have children. because I didn't want to share my experience of having permanent hunger with my child."

"Eating out is not possible spontaneously because I have to check in advance whether a restaurant offers something suitable. When we're invited, especially when we're with acquaintances, I always find out in advance what we're going to eat and often bring something myself. Planning and preparing food takes a lot of time."

"I try to eat a lot of fruit and vegetables as much as my Phe tolerance allows. If I know that we are going out to eat, we look for restaurants in advance that have vegetarian, PKU-friendly options. I also save Phe during the day so that I have more options when eating out."

4.3.2. Patient perspectives on alleviating impact of PKU and its management on everyday life

***Statement #7:* Healthcare professionals should discuss all PKU management options with their patients to support them in making informed decisions about their care. (100 % consensus).**

***Statement #8:* If effective, pegvaliase may reduce the effort and time needed to manage PKU and lead to more normality in life. (100 % consensus).**

With growing research and evidence, PKU management strategies and guidelines continue to evolve, making it necessary to inform every individual with PKU regularly on all treatment options (becoming) available to them, irrespective of prior or current treatment. Even individuals who are lost to follow up may become motivated to return to treatment upon hearing about new therapies [32]. Both the benefits and possible adverse events or challenges of a therapy should be discussed to allow an informed decision regarding an individual's best treatment option. While advancements have been made to improve MNT products, it remains extremely difficult to achieve metabolic control without intensive clinical support, even for those strictly adhering to the diet [7,44]. Sapropterin dihydrochloride (KUVAN®), a synthetic cofactor of tetrahydrobiopterin (BH4) required for normal Phe metabolism, can lower blood Phe concentrations in a subset of patients, although some degree of Phe-restriction through MNT often remains necessary to achieve and maintain metabolic control [8,9]. Pegvaliase (PALYNZIQ®) is a PEGylated recombinant phenylalanine ammonia lyase (PAL) enzyme approved to lower blood Phe in adults with PKU [10,11] that may alleviate part of the burden associated with PKU care, particularly by allowing a liberated or normalised diet [45–47]. While some aspects of pegvaliase treatment, including the induction-titration scheme when starting the therapy, the risk and management of hypersensitivity reactions and side effects (especially during the first 6 months), the need for a trained observer, subcutaneous administration, and prolonged time

to efficacy may be challenging and impact daily life as well [7,48,49], a patient-preference study showed that patients tend to accept these risks over the restricted diet [50]. Data from a case series demonstrated improvements in everyday life in those who achieved sustained reduced blood Phe concentrations with pegvaliase [51]. However, while pharmaceuticals may be beneficial for eligible individuals with PKU, not everyone has access to these products.

4.3.2.1. Quotes (translated from German) on experience with pegvaliase

"I'm much more active, my self-confidence has increased, I'm happy when we go out to eat and I'm trying out a lot more, getting to know a lot of dishes and learning to cook "normal" dishes. I feel much more liberated and it is still not normal for me to be able to eat everything. My partner still reminds me of it sometimes. The first time I went shopping unrestricted in the supermarket, I was totally overwhelmed because the selection was so large and I didn't know a lot of foods or whether I liked them." (13 months on pegvaliase).

"I can now eat anything I want without paying attention to the diet.[…] I can do my job properly and concentrate on my work. I could fulfil my dream job. […]It changed my life for the better. I have been given a new life." (37 months on pegvaliase).

4.3.2.2. Quotes (translated from German) on challenges with pegvaliase

"Well, of course you shouldn't forget that you may have to inject yourself constantly and every day. That's not normal either. But I'd recommend it to anyone for whom it has an active effect." (18 months on pegvaliase).

"I brought three of my colleagues on board to look after and observe me during working hours when I inject and in the hour after the injection, which of course limited the work a little. In general, however, the feedback was good and my boss also understood it." (17 months on pegvaliase).

***Statement #9:* Individuals with PKU should be supported and encouraged to pursue their educational, professional and personal goals. (100 % consensus).**

Several studies have shown that school performance and career achievements of most individuals with well-controlled PKU are comparable to those of the general population, suggesting that early and continuously treated individuals with PKU have an equal ability to achieve their personal academic and professional goals [18,42,52]. However, not all studies confirm these findings, suggesting that additional support may be needed to achieve academic or professional goals in some cases [5,52,53].

4.4. Topic 4: Connecting with the PKU community

4.4.1. Patient perspectives on improving PKU management through the PKU community

***Statement #10:* Digital platforms for direct and personal interactions can make communicating with other members of the PKU community easier (e.g., mobile chat applications). (100 % consensus).**

***Statement #11:* Patient organisations should try to reach a younger target audience via social media platforms that are popular among adolescents. (100 % consensus).**

In addition to education of individuals with PKU and their parents by the treatment team, exchange of information with peers is deemed valuable [21,22]. Social media and PKU patient organisations were identified by the panel as important sources of information and communication with peers. HCPs should encourage involvement of families in patient organisations and participation in initiatives such as PKU camps or educational meetings [21,22,49]. Individuals with PKU not only benefit from receiving support from peers, but also from providing guidance to others (e.g., improving mood and self-esteem) [21,22]. While Facebook groups may be helpful to share general PKU information [25], they are less suitable to address individual-specific topics or relatively new management regimens (e.g., pegvaliase). For these topics, direct questions to others in a similar situation through, for example, mobile chat applications such as WhatsApp may be valuable to rapidly exchange ideas. Social media platforms such as Instagram and TikTok are more frequently used by adolescents than Facebook [54]. Patient organisations or support groups should therefore extend their focus from Facebook to these alternative social media platforms when trying to reach a younger audience.

***Statement #12:* Educational meetings for individuals with PKU and their caregivers organised by patient organisations or treatment clinics are helpful to gain insights into PKU management and to promote networking opportunities. They should be organised in-person as well as virtually to reach a larger audience. (100 % consensus).**

Meetings for individuals with PKU and caregivers offering seminars (e.g., on calculating amount of Phe in food) and workshops (e.g., cooking classes) are valuable to acquire the necessary knowledge and practical skill set required to maintain metabolic control [49,55]. Besides educating individuals with PKU and their caregivers on managing PKU, such events offer networking opportunities. Younger individuals can exchange ideas with peers, which may improve preparedness for autonomy and self-care, while parents may connect with other caregivers or adults with PKU and learn from their experiences, potentially improving the care for their children. To meet the expectations of those individuals who are unable to travel due to geographical, logistical or financial barriers as well as of those preferring personal, real-life contact, networking and educational events are ideally offered as hybrid-events (both in-person and virtually) at different locations across a country.

4.4.1.1. Quotes (translated from German) on the importance of exchanging experiences and providing networking opportunities in the PKU community

"You never have the chance to exchange ideas with other individuals with PKU. That made things worse. From time to time you would become less and less motivated to stick to the diet. You just didn't want to be special anymore."

"The clubs/organizations thrive on committed members; not only a board can organise meetings. The more people who actively participate, the more diverse the programme! If you have special wishes and ideas, you should probably try to get involved in the club and help implement it in order to spread the burden across more shoulders."

"There certainly are many teenagers and young adults who want to celebrate PKU, so to speak, and I would also suggest organising youth events there in the form of parties, music festivals, etc."

"It's great to be able to exchange ideas, share thoughts and fears and hear that other parents feel the same way…"

4.5. Topic 5: Future aspirations to improve PKU care

The outcomes of the virtual meeting and online rating sessions indicate that continued efforts are needed from multiple stakeholders to improve the lives of individuals with PKU. The panel proposed several ideas, representing their vision on ideal future PKU care.

As established above, the panel believes clinics and the treatment

Table 4
Patient recommendations to optimise phenylketonuria (PKU) care (Statements 13–18).

- Individuals with PKU and their parents/caregivers should be better informed about PKU, new treatment options, current research and treatment guidelines. (100 % consensus)
- Individuals with PKU and their families should be informed about tools (e.g., mobile applications, databases, trackers) that can help with following the Phe-restricted diet. (80 % consensus)
- More detailed nutritional advice in the treatment centres is desired. (100 % consensus)
- The treatment team (doctors and nutritionists) should maintain a closer, more trusting relationship with those affected and their families to ensure continuity of treatment. (100 % consensus)
- The treatment team (doctors and nutritionists) should involve those affected and their families in the planning and execution of the transition from paediatric to adult care. (100 % consensus)
- More opportunities should be created to connect individuals with PKU and their families with other affected people. In the long term, this could create a network for those affected, where they can exchange their experiences and support each other. (100 % consensus)

team should be easily reachable beyond on-site visits and explore the possibility of telemedicine, but also that receiving comprehensive, adult-oriented care from a multidisciplinary team that evaluates a person's health status beyond PKU is needed. They emphasise that individuals have unique struggles and personal goals and should thus receive tailored care without comparisons to other patients. Additionally, there is a strong desire for transparency and information in lay language on novel treatment options or promising research results, as well as on all possible costs related to managing their PKU (e.g., co-payments). Further, to alleviate the financial burden of living with PKU, the panel expressed the need for better and more efficient coverage by health insurance companies, for children as well as adults. This includes broader reimbursement, not limited to costs for MNT and pharmaceutical treatments, but also for expenses arising from concomitant diseases related to PKU, and faster processing of requests for reimbursement or exemptions of co-payment. The pharmaceutical industry also plays a fundamental role in reducing the financial stress associated with PKU: the panel hopes for affordable medicines and larger package sizes of products to allow long-term treatment, which may reduce the co-payment fraction. Other efforts needed from the industry include further research on the disease and treatment options, continued development of diverse and palatable medical food and low-protein products, and better, local production of treatment supplies (medicines, food, syringes) to avoid delivery and accessibility issues. Technological advancements such as systems for self-monitoring of blood Phe concentrations and improved, user-friendly mobile applications to track Phe intake could further simplify the daily lives of individuals with PKU. Finally, the need to offer more assistance for caregivers (e.g., mental support, household help) to relieve stress associated with managing a child's PKU was identified, as well as the need for more meeting opportunities with others affected, not only to discuss PKU management in general, but also to exchange experiences and acquire skills for specific treatment options such as pegvaliase.

Table 4 summarises the panel's overall recommendations on improving the care and support for individuals with PKU and their caregivers.

5. Conclusion

The outcome of this modified Delphi, based on expert opinion of six individuals with PKU and a psychologist from Germany, provides unique insights into how affected individuals experience the disease and identifies solutions tailored to their needs, thereby also focussing on the long phase of adulthood in PKU, a period that has received less attention in research and literature to date. The consensus statements represent their perspectives on strategies to address challenges encountered across five domains: the PKU diet, experience with HCPs, impact of PKU on everyday life, connecting with the community, and future aspirations. Within the rapidly evolving landscape of PKU care, expert opinion, including patient experience, is critical for further optimising the management of those living with this disease.

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CRediT authorship contribution statement

Karin Lange: Conceptualization, Investigation, Methodology, Writing – original draft, Writing – review & editing. **Jens Böhmer:** Investigation, Methodology, Writing – original draft, Writing – review & editing. **Yvonne Deich:** Investigation, Methodology, Writing – original draft, Writing – review & editing. **Daniel Dickneite:** Investigation, Methodology, Writing – original draft, Writing – review & editing. **Pascale Fuchs:** Investigation, Methodology, Writing – original draft, Writing – review & editing. **Verena Naunheim:** Investigation, Methodology, Writing – original draft, Writing – review & editing. **Angelika Scholz:** Investigation, Methodology, Writing – original draft, Writing – review & editing. **Christian Heimbold:** Conceptualization, Investigation, Methodology, Writing – original draft, Writing – review & editing.

Declaration of competing interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ymgmr.2025.101201.

Data availability

The de-identified individual participant data that underlie the results reported in this article (including text, tables, figures, and appendices) will be made available together with the research protocol and data dictionaries, for noncommercial, academic purposes. Additional supporting documents may be available upon request. Investigators will be able to request access to these data and supporting documents via a website (www.BioMarin.com) beginning 6 months and ending 2 years after publication. Data associated with any ongoing development program will be made available within 6 months after approval of relevant product. Requests must include a research proposal clarifying how the

data will be used, including proposed analysis methodology. Research proposals will be evaluated relative to publicly available criteria available at www.BioMarin.com to determine if access will be given, contingent upon execution of a data access agreement with BioMarin Pharmaceutical Inc.

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