



Prescribing issues experienced by people living with phenylketonuria in the UK



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ABSTRACT

Background: Foods for Special Medical purposes (Phe-free protein substitutes [PS] and low protein foods [LPFs]) are central to successful dietary management of patients with phenylketonuria (PKU). In the UK, PS and LPFs are prescribed by primary care general practitioners (GPs) and dispensed by high street pharmacists or via home delivery companies. As patients and carers commonly reported access issues with PS and LPFs through the National Society for PKU (NSPKU) helpline, the NSPKU collected more information about the extent of prescriptions issues via a questionnaire.

Methods: A cross sectional online survey was carried out consisting of 7 multiple choice and 3 open questions. The questionnaire was available via the NSPKU website over a 9-month period (15th May 2018–31st January 2019). Carers or patients with PKU were invited to participate if they had any problems accessing PS and LPF.

Results: There were 252 responses. 65% for children and 35% for adults, aged ≥ 18 y with PKU. 59% ($n = 146/246$) of responses described difficulties accessing basic LPF (bread, pasta) and 33% ($n = 81/248$) PS. 36% ($n = 88/248$) said problems had re-occurred > 1 y, and 40% ($n = 99/248$) for < 3 months. 59% ($n = 146/246$) had supply issues with LPF and 33% ($n = 81/246$) with PS. 18% ($n = 42/234$) reported that the local NHS authority had refused, restricted or had a policy to block treatment access; 27% ($n = 63/234$) cited GPs declining requests or restricting prescription amounts. 21% ($n = 49/234$) could not access all their products via a pharmacy, 40% ($n = 93/234$) said their home delivery system failed, and 15% ($n = 34/234$) of the dispensed prescribed products were out of date, incorrect, damaged or poor quality. For patients and carers these issues caused: stress (87%, $n = 210/241$); they considered PKU was not taken seriously by professionals (66%, $n = 160/241$); they reduced patient access to LPF and PS (53%, $n = 128/241$); and affected the patients' health (53%, $n = 128/241$).

Discussion: Access to PKU dietary treatment is frequently disrupted for reasons relating to GP prescriptions and unreliable dispensing and delivery practices. These issues require immediate attention by UK health professionals in order to create a fairer and more efficient system for everyone.

1. Introduction

Phenylketonuria (PKU) is an autosomal recessive genetic disorder, that causes deficiency of the phenylalanine (Phe) hydroxylase enzyme leading to an abnormal accumulation of phenylalanine. Individuals with PKU who are untreated or inadequately treated during infancy and childhood have profound damage to the developing brain with a very low intelligence quotient (IQ), hyperactive behaviour with autistic features, and seizures [1]. In contrast, individuals who are well treated in early life, have normal intellectual ability but are still at risk of mental health problems and white matter pathology that adversely

affects motor function that is associated with elevation of Phe at any time in life [2]. In the UK, the only treatment routinely available for patients with PKU is a lifelong, Phe restricted diet. Foods such as meat, fish, eggs, cheese, nuts, seeds, bread and pasta are high in Phe and must be avoided. In classical PKU, most patients tolerate < 10 g/day natural protein [3]. The low Phe diet consists of fruit, some vegetables, sugar and oils. Even chemical sweeteners, namely aspartame must be avoided as they contain Phe. 'Foods for Special Medical Purposes' (Commission delegated regulation (EU) 2016/128 of 25 September 2015 supplementing Regulation (EU) No 609/2013 of the European Parliament and of the Council as regards the specific compositional and information requirements

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for food for special medical purposes), including protein substitutes (PS) and low protein foods (LPF) are an essential part of treatment.

In PKU, PS provide a non /low Phe protein replacement, mainly based on amino acids and they are usually supplemented with vitamins, minerals and long chain fatty acids. They prevent protein deficiency, support growth, and their amino acid composition helps optimise metabolic control by promoting anabolism and altering Phe transport both at gut epithelial level [4] and the blood brain barrier [5]. Special LPF made from food starches (e.g. bread and pasta), are an important source of energy, aid satiety, provide variety, help diet acceptability and so improve adherence. Dietary management should not be attempted without access to these special dietary products.

Access systems to PS and LPFs varies throughout the world. In most countries in Europe, PS is paid for by the health service or is available by insurance [6]. For LPF, reimbursement policies are inconsistent, varying from full reimbursement in Italy, monthly financial allowances in Belgium, Norway and Denmark, and self-payment in Spain, Germany, The Netherlands and Poland [6]. In the UK, PS and LPFs are reimbursed via NHS prescription for the dietary management of PKU. To gain reimbursement status, PS manufacturers must supply evidence to demonstrate their safety, efficacy, acceptability and tolerance. A 'recommended list' of approved products by the Advisory Committee on Borderline Substances (ACBS) is published as Part XV of the Drug Tariff and so this guides prescribers (mainly community GPs) about the suitability of products for PKU. The NSPKU also produces a guide outlining the maximum number of units per month of LPF which can be prescribed based on patient age and special circumstances such as pregnancy.

Over 85% of UK patients with PKU are cared for by specialist hospital centres [3]. The specialist PKU dietitians advise GPs about the dietary requirements and prescription needs of each patient. Monthly prescriptions are issued by GPs and they are dispensed either via local pharmacists (who may offer a home delivery service) or via one of 5 different specialist home delivery companies linked to the suppliers of PS and LPF. In England, only patients aged under 16 years, over 60 years, or pregnant or experiencing other special circumstances are entitled to 'free' prescriptions; others must pay a fee for each item that is prescribed by their GP (in Northern Ireland, Scotland and Wales prescriptions are dispensed without charge).

For some time, specialist PKU dietitians in the UK and the NSPKU have been aware that continuity of supply of 'Foods for Special Medical Purposes' via NHS prescription is problematic for patients with PKU, with patients being left without supplies leading to disruption to their essential treatment. In order to ascertain information about the nature of the access problems and to develop an understanding about the potential frequency of supply problems, the NSPKU surveyed people with PKU and their caregivers through an online survey to record access problems.

2. Material and methods

We carried out a cross sectional online survey. The questionnaire, which focused on supply issues with low-Phe/Phe-free PS and LPF, was voluntarily completed and submitted by adults with PKU, parents/caregivers of children with PKU or health care professionals caring for their treatment. The questionnaire was placed on the UK NSPKU website, Facebook and twitter accounts between 15th May 2018 and 31st January 2019. During this nine-month period, respondents could complete the questionnaire more than once for new or ongoing issues. Although the study time period was not selected for any reason, the authors are not aware of any reason why this period would be atypical or unusual.

This non-validated questionnaire comprised of 10 questions, including single choice, multiple choice and 2 open-ended questions: one question asked for information about respondent postcode (to identify problems related to area of residence and this is not reported) and the

Table 1

Open-ended question "Do you want to tell us in your own words about the problem and the effect it has had on you?" This question followed a multiple-choice question about the type of problem that had been experienced. This question is described in full as it may have influenced the responses to the open-ended question.

What kind of problem are you experiencing? (Tick any that apply to you)
<ul style="list-style-type: none"> ● The NHS authority (e.g. the Clinical Commissioning Group/Health Board) for my area is refusing or restricting prescribing for PKU products. ● The NHS authority for my area has made a policy that creates an obstacle for getting my prescriptions. ● The GP will not prescribe the products I want. ● The GP restricts the quantity of products I can get. ● The GP's receptionist/administrative staff are unhelpful or obstructive. ● The GP refuses to allow repeat prescriptions. ● My dietitian or consultant will not prescribe the products I need. ● I have a prescription, but I cannot get the products I want from the chemist. ● I have a delivery service - but the system doesn't work. ● I have prescription foods delivered which are out of date, or wrong, or damaged or poor quality. ● Other

other asked to describe the problems with access to PS and LPF that they had experienced. This last question was thematically analysed and presented in Table 1.

Demographic information was also collected about type of respondent (patient, parent/caregiver, or health professional), age categorization of patient (child or adult aged $\geq 18y$), male or female, and patient risk category (aged ≤ 4 years; 5-12y, pregnant, pre-conception). Respondents answered questions about any dietary products they had difficulty in accessing, the length of time the problem had occurred, the type of problem that was being experienced and the impact that this problem had caused. This questionnaire was developed using issues that had already been reported to the NSPKU helpline patients and parents/caregivers.

There were 204 useable responses to the open-ended question.

The whole survey dataset was imported into 'NVIVO pro' software V.11, a programme for qualitative data analysis. Each survey response was created as a case (allowing responses to be filtered by any characteristics or response which was captured in the survey). Each open-ended question was created as a node, and the individual responses within each question were read individually and coded at a very fine level of detail according to one or more nodes created in response to emerging patterns in the data.

2.1. Data cleaning and recoding

Data was recoded from Google forms to SPSS format using a variety of manual transformations and SPSS syntax.

2.2. Analysis

The closed questions (multiple choice and single choice) were analysed using descriptive statistics only. The open-ended question was analysed using inductive thematic analysis [7] which centres on identifying patterns in the text which seem most relevant to the research objectives. Ideas, comments, statements or ideas which recurred were coded in NVIVO and these codes were organised into a hierarchical pattern of nodes with the top-level parent nodes being considered as probable themes. Codes and themes were reviewed and refined throughout the analysis process (e.g. merging and splitting codes).

2.3. Ethics

Ethical consent was not sought as it was clarified at the beginning of the questionnaire that anonymous information may be shared with the NHS, MPs, government, or health care organisations to improve care for

people with PKU. Potential respondents were also advised that the NSPKU may publish data from the survey in an anonymized form. Adults with PKU and caregivers gave their consent by their voluntary completion and submission of the online questionnaire. If names or hospitals were mentioned in verbatim abstracts, these were removed in the presentation of analysis.

3. Results

There were 252 responses to this questionnaire in a 9-month time scale. Not all responses included an answer to every question. Sixty-five per cent ($n = 160/245$) of the responses described prescription issues with children and 35% ($n = 86/245$) adults. Sixty-five per cent ($n = 160/245$) of the responses were about females and 35% ($n = 86/245$) males. Twenty per cent ($n = 50/252$) of the issues associated with dietary foods affected children aged ≤ 4 years; 37% ($n = 92/252$) children aged 5-12y, 1% ($n = 2/252$) pregnant women, and 4% ($n = 10/252$) women planning pregnancy. The questionnaires were completed by parents (37%, $n = 91/249$); patients (25%, $n = 62/249$) and health professionals on behalf of the patients/carers, 39%, 97 of 249).

Fifty nine per cent ($n = 146$ of 246) of respondents said that they were having prescription problems with basic LPF (e.g. pasta and bread), 41% ($n = 100$ of 246) with pre-prepared LPFs (e.g. biscuits, cakes), and around a third (33%, $n = 81$ of 246) with PS. The rate of problems for each category was similar between adults and children.

Thirty five per cent ($n = 88$ of 248) said the problems had re-occurred for > 1 year; 22% ($n = 55$ of 248) over the last year; 19% ($n = 47$ of 248) over the last 3 months, 13% ($n = 31$ of 248) over the last 4 weeks and 9% ($n = 21$ of 248) in the last week. The duration of problems was similar between children and adults.

Table 2 presents types of problems experienced when accessing LPF and PS.

Thematic analysis of the open-ended questions identified nine themes with more than five coding references, and these were taken as the main themes. These were: delivery service ($n = 50$), lack of co-ordination ($n = 28$), difficulty with specific LPF/PS ($n = 25$), running out of LPF (including rationing) ($n = 17$), GP related issues ($n = 17$), stress and hassle ($n = 14$), issues with ordering LPF ($n = 12$), problems with food supply affecting dietary adherence ($n = 7$); and ignorance about PKU ($n = 6$).

3.1. Theme 1: Delivery service ($n = 50$ comments)

There were more responses about children than adults (Table 2). There were many references to poor standards of home delivery service including missed deliveries, incomplete deliveries, wrong items supplied, and lack of communication about rescheduling deliveries. Most of the comments related to one home delivery service (*Dial A Chem*[®]). Caregivers and patients gave detailed feedback about their issues and frustrations with the home delivery services.

Verbatim extracts from parents and caregivers responses about delivery service

Sometimes Dial A Chem email us to check if we need things from this list - sometimes we do not hear from them and we run out of low protein food. We work hard to maintain control in our 3 children. It is unacceptable to run out of low protein food. No children should have to go hungry.

.....Almost ran out of protein substitute. Vitaflo at Home did a stock check - only had small supply left but they still aimed to send it after the child would have run out. The dietitian sorted this.

.....Each month we seem to have a problem with the delivery service and sometimes the GP. The actual items I get is often different from the ones I have ordered. Items can be missing, but

Table 2
Types of problem experienced when accessing LPF or PS in PKU.

Type of problem	Number of responses	% of responses	Number of child problems	% of responses	Number of adult problems	% of responses
I have a delivery service – but the system doesn't work	93	40	77	51	16	19
The GP restricts the quantity of products I can get	53	23	22	15	31	37
I have a prescription, but I cannot get the products I want from the chemist.	50	21	25	17	25	30
The GPs receptionists/administrative staff are unhelpful or obstructive	49	21	26	17	23	28
The GP will not prescribe the products I need	39	17	15	10	24	29
I have prescription foods delivered which are out of date, or wrong, or damaged or poor quality	33	14	22	15	11	13
The NHS authority (e.g. the CCG/Health Board) for my area is refusing or restricting prescribing for PKU products	30	13	9	17	17	21
The NHS authority for my area has made a policy that creates an obstacle for getting my prescriptions	12	5	5	3	7	8
The GP refuses to allow repeat prescriptions	10	4	5	3	5	6
My dietitian or consultant will not prescribe the products I need.	5	2	2	1	3	4
Other	31	13	18	12	13	16
Total responses	405	100	230	101	175	100
Total number of choices	234		151		83	

there is never an explanation as to why they are missing or if they will be replaced. I am not sure if this is the GP changing items or if this is the home delivery changing items? If items are missing, there is no note to say when they will be replaced or if they will ever be replaced. Similarly, if they are different no note or explanation is given.

they cannot get my Mevalia bread; have taken 2 months so far to give me my Promin pizza mix and are saying that do not know if they will be able to get it. They then told me they cannot get my Promin burger mix. All of these are vital items when on 3–4 exchanges (3–4 g protein) a day.

3.2. Theme 2: Lack of co-ordination (n = 28 comments)

A major theme was the lack of co-ordination between the key organisations involved in PKU prescription (GP, GP receptionist, chemist, ordering and delivery services). There were many instances of confused communication, leaving patients at risk of no supplies of LPF or PS. One sub theme also stood out (with 13 coding references), about the role that dietitians play in acting as the coordinator to rectify any problems in access to LPF and PS.

Verbatim extracts about lack of co-ordination

Home delivery company failed to deliver infant protein substitute. The home delivery company did not do an appropriate stock check. Almost ran out of infant protein substitute. The hospital organised emergency supplies.

.....The items are not at the chemist as expected or they order the wrong products from the repeat prescription or I do not get informed of a supply issue and then we have no supply of protein supplement or other foods. I decided it would be easier to have home delivery of the protein supplement, but the GP's team kept sending the prescription electronically to our local chemist."

.....No idea when I'll get my food items, often having to chase them and constantly going backward and forward between GP and pharmacy to know which actual pharmacy it has been delivered to and whether I'll be getting it! The only time I have to call during open hours is my half an hour lunchtime. I'm actually trying to get back on diet and have more low protein foods but this struggle makes everything so much more difficult and it's why you don't want to be on diet, so you don't have to rely on prescriptions and GPs.

3.3. Theme 3: Difficulty with specific foods/protein substitute (n = 25 comments)

The caregivers/patients described how not being able to get the right foods at the right time caused disruption in the provision of dietary treatment. Inability to access one specific flavour of PS or being unable to obtain a specific LPF that is mixed with a PS (e.g. low protein yoghurt or milk) may lead to treatment disruption, poor metabolic control and distress for the patient/caregiver.

Verbatim extracts about difficulty with specific low protein foods

My daughter, if she does not get her bread on time, she is hungry and then she eats foods she is not allowed that leads to poor phenylalanine control. I have tried to order fresh bread from Dial A Chem - they consistently fail to deliver on time. I order fresh bread from my chemist - they go around the houses to order it - and they fail to get it to me on time. I am now back with Dial A Chem. They knew my GP had sent the prescription to the chemist in error but did nothing to chase this up. They said I should put my child on packet low protein bread - which she will not eat. My dietitian has to sort this out for me every time.

.....Home delivery service keeps delivering wrong flavour of PKU Lophlex LQ. It has happened 3 times in 3 months. My daughter will not drink the wrong flavoured protein substitute. It is very frustrating.

.....I am pregnant on very low exchanges and chemist says

3.4. Theme 4: Running out of low protein food /protein substitute (n = 21 comments)

The survey data showed that 47% (n = 115 of 247) of responses referred to running out of LPF and 21% (n = 51 of 247) of responses referred to running out of PS. Many responses referred to people running out of key LPF for considerable periods or in some cases rationing their food supplies. There was one sub theme 'Missing meals or hunger' (4 coding references) where adults and children had to go without food or consumed low protein fruit and vegetables only, in the absence of appropriate LPF.

Verbatim extracts about running out of low protein food

Always running out of essential low protein food. GP will not supply enough. Dial A Chem delayed order as had no Mevalia bread. We had to supply food for the patient.

.....A little boy aged 18 months has recently been unwell/weight loss, was prescribed SOS 15 (a glucose polymer). A delivery was organised with Vitaflo at Home. The family ran out of SOS 15. Vitaflo at Home did not deliver as they could not get hold of mum. They did not inform the dietitian of this.

.....I have a daughter who is now 15 y old and is very hungry. We order foods from the Pharmacy but for the last 2–3 months they are telling us they are out of stock. We have had to beg for basic items of food. PKU is hard enough, PKU and teenagers is even harder, to face this battle is soul destroying.

.....My food rarely gets to me within 4 weeks after ordering which means I tend to run out of items such as pasta and rice.

3.5. Theme 5: GP issues (n = 17 comments)

GPs play a key role in patients' access to supplies of LPF and PS. The most common problems were with the GP receptionists (who often act as gatekeepers to the prescriptions which are issued). Some receptionists, but also some GPs, did not seem to understand that LPF could not be purchased in supermarkets (the analogy to gluten free food, for people with coeliac disease, was mentioned in responses, and gluten free foods are widely available in shops and supermarkets, unlike LPFs). GPs sometimes refused to prescribe the appropriate range or quantity of LPFs, and it appeared that cost was a barrier.

Verbatim extracts about GP related issues

I've had to move GP surgeries three times in 1 year to try to find one that would prescribe me products and refer me to the metabolic clinic.

.....My daughter is 17 now and I never get what I ask for, quantity wise. They feel they know what my child consumes per month therefore re-write my order for me. It's always the ones who type the prescriptions up. Numerous times a year I have to go in and speak to receptionist to get them to write a note in my daughter's file but it reoccurs again and again

.....3 times my foods have been wiped off my list and the reason is due to them saying it is all gluten free. I have had to go in the receptionists and explain what PKU is and that it is LPF not gluten free

3.6. Theme 6: Stress and hassle (*n* = 14 comments)

Survey data indicated that 85% (*n* = 210 of 247) of responses said their problems were stressful, 77% (*n* = 191 of 247) time consuming, and 66% (*n* = 162 of 247), said they think that PKU is not taken seriously by professionals. Forty-seven per cent (*n* = 116 of 247) found the problems depressing or degrading and 15% (*n* = 37 of 247) said the problems made them want to give up on their diet. Some said they faced continual worry, stress and demands on their time in chasing up issues to do with the supply of LPF and PS.

Verbatim extracts about stress and hassle associated with dietary prescriptions

I have constant stress & anxiety. Feel unsupported, overlooked & alone. Consultant aware but not been able to sort. Deliveries arrive late & my son has days without supplies eating just fruit & veg at times & always hungry.

.....It causes a lot of stress and worries because we know how we feel and act when we can't keep our levels down.

.....It is stressful every month when being told by chemist they can't get certain items, when I ring manufacturers, they say no problems in supply or tell chemist to order direct and it would come the next day but chemist won't.

.....It's really worrying when you've been waiting for supplements for a week and they still don't arrive to be told there is a manufacturing problem and you've only got a couple of days' supply left. The emotional rollercoaster that this causes is really worrying.

3.7. Theme 7: Issues with ordering low protein food (12 comments)

Ordering PKU food was sometimes problematic and it was not uncommon for patients to find that products were out of stock (or to be informed that they were) and not to have full flexibility in what they could order (e.g. minimum or maximum amounts). Survey data showed that 52% (*n* = 129 of 247) said this affected the variety in the diet.

Verbatim extracts about issues with ordering LPF

I have found a document that states I am allowed 50 units per month of prescription items (excluding supplements and milk substitutes), but sometimes my prescription requests are refused without reason.

.....Always a problem on the prescription i.e. wrong item or only 1 of bread, milk etc. when we have asked numerous times for larger quantities... the receptionist thinks that I'm over reacting as I could get these items in supermarkets which we know isn't the case as my son has PKU only 5 exchanges so most foods are prescription.

3.8. Theme 8: Problems with food supply affecting adherence (*n* = 7 comments)

The unpredictability of supply and unavailability of key PKU food items causes the low Phe diet to be particularly arduous and it led to inadvertent low dietary adherence, poor metabolic control and even cessation of dietary treatment.

Verbatim extracts about issues with food supply affecting adherence

I went back on diet, did really well but got fed up with GPs restricting and refusing to give me the prescription. This happened a few times; also if I got products I got asked if I couldn't have a

cheaper version. I got fed up fighting a losing battle with GPs that I came off diet and stayed off it.

.....Miscommunication between the home delivery company and the family. The family do not speak English as their first language and have 2 small boys with severe/classical PKU. Lack of calories leads to poor metabolic control. They were allowed to run out of low protein milk (through home delivery not checking stock levels) which caused very high blood Phe levels.

.....I got told by the receptionist that I am no longer allowed to put orders in for food products as they have a limit and I'm only allowed basics due to cost such as bread, pasta etc. As I have classical PKU I feel it has affected me because I know my levels are high and I am trying to get back on the diet desperately but every time when I think I am sorted something like this happens. I did try to arrange appointment to see my GP to make him aware but couldn't get it....

3.9. Theme 9: Ignorance of PKU (*n* = 6 comments)

Responses described how they had to 'educate' health professionals (e.g. GPs, receptionists, and pharmacists) about their low Phe diet. One sub theme 'entitlement to PKU foods' (2 coding references) relates to specific knowledge about what foods people with PKU are entitled to obtain on prescription.

Verbatim extracts about ignorance of PKU

Just started university and the student GP is not understanding at all about what is needed; just makes starting uni {university} more stressful and complicated than it needed to be, having to explain to health care professionals what PKU is - it's hard enough explaining to everyone else.

4. Discussion

Although this survey was not based on a random sample of the PKU population, but rather a self-selected sample from visitors to the NSPKU website who were invited to complete a questionnaire if they were experiencing problems with prescriptions, it illustrates the issues, barriers and frustrations that patients with PKU have in accessing essential PS and LPF to enable them to adhere with dietary management in the UK. Dietary product prescription refusal, obstacles that caused delays in products being dispensed and received by the end users, and failure of health professionals within the community, pharmacists or home delivery companies to support patients on low Phe diets all led to patient hunger, treatment disruption, unintentional dietary non-adherence, and poor blood Phe control, and it even led to treatment abandonment. Poor metabolic control can negatively impact development and behaviour in childhood, mental health and neurological status in teenagers and adults, as well as potentially causing birth defects in pregnant women such as cardiac defects and microcephaly and low IQ in the offspring [8–10]. Over 60% of the prescription problems related to people in high risk categories based on age, pregnancy and women planning pregnancy.

It was particularly worrying that both the NHS authority (e.g. the Clinical Commissioning Group or Health Board) and the GPs had refused to prescribe PS and LPF or limited the quantity of products that patients had access to. Refusal of LPF prescription was commonly associated with misunderstanding or consideration that some LPFs such as low protein cake mixes, or cereals bars were luxury items. However, if followed by GPs, the NSPKU guidelines suggest monthly upper limits on the number of LPF's that can be prescribed. These guidelines help ensure expenditure is controlled on LPF items, enable patients to receive enough LPFs to meet energy requirements but they limit excess

amounts. The problem of PS and LPF access was more prevalent in adults with PKU, even though in the UK, lifelong dietary treatment has been recommended since 1993, [11] and the recent PKU European guidelines strengthened this recommendation with further supporting evidence [2,12]. In our survey 15% of the respondents said access problems made them want to abandon their PKU diet and some respondents even described how the frustrations of accessing 'Foods for Special Medical Purposes' had led to cessation of dietary treatment. They had to live with food insecurity, knowing that their supplies of PS or LPF's was limited or of uncertain availability. Unfortunately, adult patients who stop the PKU diet may experience poor executive functioning, information processing (reaction times, attention) and low mood (increased inhibition, anxiety, depression and low self-esteem) compared with adults who have continued Phe restriction throughout life and healthy controls [13–17]. A UK NHS system that permits individual GPs and clinical commissioning groups to refuse access to the only permitted and commissioned treatment of patients with PKU is flawed.

Failure of the home delivery services to provide a reliable service for patients with PKU was highlighted as an issue by many patients and caregivers. Home delivery services were used more by children than adults with PKU. Whilst home delivery services have been shown to be safer [18], the survey responses (mainly associated with one home delivery service) indicate that they are not always reliable. Lack of communication with caregivers or patients, and poor co-ordination with GP practices or pharmacists, leaving patients without LPF and PS supplies were common occurrences. Some responses described receiving damaged, short shelf-life or out of date LPF. Patients using high-street pharmacists reported similar difficulties. None of the home delivery services were able to supply the entire range of LPF and PS. Multiple supply sources lead to confusion and inefficiency and these have been reported previously [19].

Accessing 'Foods for Special Medical Purposes' was a stressful process (cited in 85% of the responses), with many responses identifying that this activity was time consuming and time wasting. Many said they considered their prescription problems were not taken seriously by health care professionals. It was not uncommon for patients or parents to feel humiliated by staff within primary care or frustrated by the cumbersome system. A survey conducted in Scotland also identified the negative experiences and obstructions which people with PKU have experienced when attempting to access prescribable LPF [20]. It is difficult for adults and caregivers to find time to teach and communicate community health professionals about their (or their child's) dietary requirement when they may be working and have limited availability to speak to the GP practice team.

It is time to re-evaluate how patients with PKU access their LPF and PS in the UK. Supply systems should be introduced whereby patients/caregivers have minimum contact with health professionals who have little knowledge or experience of caring for PKU, and these non-specialists should not take decisions on the appropriateness of specialist dietary products for an individual patient. The specialist centres, particularly specialist dietitians, should play a more prominent and direct role in the provision of PS and LPF, although they will need additional resources in order to conduct this task. It should be examined if all specialist dietary products could be delivered from a single 'hub', supported by all the dietary companies. Also, an annual programmed 'credit card' system specifically for LPF could be explored, enabling patients to order LPF online, offering them flexibility, choice and immediate access to LPF.

5. Limitations

Our sample of respondents were self-selected rather than drawn from a random sample, and it is unknown to what extent the problems reported are reflective of the entire population of patients with PKU. It is also possible that the survey respondents were more informed or

vocal about PKU issues than the general PKU population as many were users of the NSPKU website. This survey specifically collected information about problems with access to PS and LPF rather than collecting information about any systems or services that worked well. The prescriptions issues were complex and qualitative research methods (such as one to one interviews) would be appropriate for a deeper understanding of patients' and carers' experiences. We did not collect any quantitative data about blood Phe control or neurocognitive outcomes. We also did not seek the views of the GPs, pharmacists or home delivery service providers.

6. Conclusions

A fundamental review of how specialist dietary products are prescribed, supplied and controlled for patients with PKU is urgently needed. Consideration should be given to specialist dietitians providing prescriptions for patients with PKU patients, directing responsibility from a community driven system to the specialist treatment centres. Otherwise, the disconnect between those who control treatment access and those who understand it will continue. The delivery systems for LPF are fragmented. A system overhaul with cooperation by all suppliers to consider one central delivery system, which is properly resourced must be considered to improve service reliability and reduce the patient and caregiver anxiety associated with PS and LPF access. Further research is also needed amongst people with PKU, with larger random samples, to gain reliable estimates of the frequency of these problems in the PKU population.

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Declaration of competing interest

Suzanne Ford has received either funding to attend conferences or honoraria from Nutricia, Vitaflo International, Biomarin, and Mevalia. She is a member of a Nutricia Advisory Board on PKU.

Mike O'Driscoll has no conflicts of interest.

Anita MacDonald has received research funding and/or honoraria from Nutricia, Vitaflo International, Biomarin, Galen Pharmaceuticals and Mevalia. She is a member of the European Nutrition Expert Panel (Biomarin), member of Sapropterin Advisory Board (Biomarin), member of the Advisory Board entitled ELEMENT (Danone-Nutricia), and member of an Advisory Board for Arla and Applied Pharma Research.

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