

Brazilian Food Reference Guide for Phenylalanine Content: A Study Based on the Perception of PKU Patients and Health Providers

Bruna B. dos Santos¹ , Bibiana M. de Oliveira¹ ,
Vaneisse C. Lima Monteiro¹ , Soraia Poloni², Tassia Tonon²
and Ida V. D. Schwartz^{1, 2, 3, 4} 

Abstract

The mainstay of management of phenylketonuria (PKU) is restriction of dietary phenylalanine (Phe) intake. The present study sought to assess the perception and understanding of health care providers and lay users (patients/family members/caregivers) regarding the national reference database for checking the Phe content of foods, provided by the Brazilian Health Regulatory Agency (Anvisa), whose data are presented in the Table of Phenylalanine Content of Foods (TCFA-Anvisa) and recently in the Phenylalanine Content of Foods Dashboard (PCCFA-Anvisa); and to identify factors which interfere with the usability of these resources. Two online questionnaires, one for providers (n=33) and another for lay users (n=194), were used to collect sociodemographic information, knowledge about dietary management of PKU, sources of information about the Phe content of foods, and perception and understanding of the Anvisa tools. TCFA-Anvisa and PCCFA-Anvisa were not used as main sources of information by either group. Among the participants who had used these tools (15 providers; 35 lay users), most considered the PCCFA-Anvisa to be superior or partially superior to the TCFA-Anvisa. The main limitations reported were related to layout and limited variety of foods. We suggest that the limitations identified in this study be considered for future improvement of these resources.

Keywords

Inborn Errors of Metabolism, Phenylketonurias, Dietary Therapy.

Introduction

Phenylketonuria (PKU) is an inborn error of metabolism characterized by deficient activity of phenylalanine hydroxylase, the enzyme which catalyzes conversion of phenylalanine (Phe) into tyrosine (Tyr). As a result of this metabolic defect, plasma Phe rises to toxic levels. Intake of this amino acid must thus be restricted by patients [1].

The prevalence of PKU varies across populations. It is influenced by genetic factors and by the effectiveness of neonatal screening programs [2]. Its overall prevalence is estimated at 1:10,000 live births worldwide [3]. In Brazil, according to data from the Brazilian Society of Neonatal Screening survey conducted in 18 states, the prevalence was 1:15,839 in 2001 and 1:24,780 in 2002 [4].

Patients who adhere to a Phe-restricted diet since shortly after birth achieve normal intellectual and neurological

development, while those diagnosed late and/or who do not adhere to treatment are subject to severe neurological conditions, including microcephaly, cognitive impairment, and epilepsy [5].

¹Universidade Federal do Rio Grande do Sul, Programa de Pós-Graduação em Genética e Biologia Molecular, Porto Alegre, RS, Brazil.

²Hospital de Clínicas de Porto Alegre, Serviço de Genética Médica, Porto Alegre, RS, Brazil.

³Universidade Federal do Rio Grande do Sul, Departamento de Genética, Porto Alegre, RS, Brazil.

⁴Hospital de Clínicas de Porto Alegre, Centro de Pesquisa Clínica, Núcleo de Investigação Clínica em Medicamentos, Porto Alegre, RS, Brazil.

Received January 29, 2022. Accepted for publication June 20, 2022.

Corresponding Author:

Bruna Bento dos Santos, E-mail: bruna.bdsantos@hotmail.com



Other manifestations include delayed neurological and psychomotor development, irritability or apathy, loss of interest in one's surroundings, seizures, agitation, tremor, spasticity, ataxia, irreversible cognitive deficits, emotional impairment, cutaneous hypopigmentation due to decreased melanin synthesis, chronic eczema, and a characteristic odor in the urine, skin, and hair due to the buildup of phenylacetic acid [6].

In addition to Phe restriction, dietary treatment of PKU comprises supplementation with a Phe-free amino acid formula and intake of low-protein foods. Blood Phe levels are the main biomarker to guide treatment. Dietary prescriptions for these patients need to be carefully adjusted and monitored, as protein deficiency and excess Phe restriction also have negative consequences, including growth restriction, anorexia, alopecia, lethargy, and eczematous rashes [7].

One of the major challenges faced in estimating nutrient intake in the PKU diet is the reliability of the methods used for estimation. In an attempt to provide accurate data on Phe intake for this population, several tools for querying the Phe content of foods have been developed. Despite the best efforts of several authors and institutions, many factors still interfere with the usability of these resources. According to Elmadfa et al. [8], regional and seasonal differences in soil quality and meteorological aspects are some of the factors that modify the nutritional composition of foods and, consequently, limit the use of such tools, especially across different regions and countries.

Another issue that restricts the use of tables, lists, and dashboards that list the Phe content of foods to their territory of origin is the regionalization of cuisine and diet. The absence of foods typical to a certain region not only makes it difficult to estimate nutrient intake but can also reduce prescription of these foods, directly interfering with the culinary traditions of patients and their families.

Given the dietary restrictions imposed by PKU and the absence of reliable information on the Phe content of foods grown and made in Brazil, in 2010, the Brazilian Health Regulatory Agency (Anvisa) developed a Table of Phenylalanine Content in Food (TCFA-Anvisa). In June 2019, the agency published its Phenylalanine Content of Foods Dashboard (PCCFA-Anvisa). This new resource was developed in response to the demands made by representatives of PKU patients' associations and health care providers during a workshop on usability of the TCFA, held in December 2018 [9].

Within this context, the present study aimed to evaluate perceptions and understanding of these two Anvisa reference guides for Phe content of foods, as well as to identify the factors that interfere with usability of these resources.

Methods

This cross-sectional study was approved by the Hospital de Clínicas de Porto Alegre Research Ethics Committee (Protocol: 19-0208). All participants or their legal guardians agreed to participate by completing the study questionnaire on the Google Forms platform.

An initial meeting was held at the XXX Brazilian Congress of Medical Genetics (Rio de Janeiro, May 2018) to discuss the research project and its data collection instruments, previously developed by the study team. The study team, health care providers, and family members of patients with PKU took part in the meeting. The lead investigator of the study presented the project, while the other team members recorded the views of health care providers and family members, who also raised questions about the usability of TCFA-Anvisa.

Based on this experience, the data collection instruments were modified to meet the demands of the study population. New questions were also added to collect sociodemographic information on the participants and to inquire on the content of the TCFA-Anvisa, as well as the new PCCFA-Anvisa, published in June 2019.

The definitive versions of the data collection instrument were distributed between December 2019 and October 2020 to health care providers and from May to October 2020 to patients/family members/caregivers. The questionnaire for providers consisted of 29 items, while the version for lay users (patients, family members, and caregivers) had 38 items. Both evaluated: (1) sociodemographic status; (2) knowledge about dietary management; (3) sources of information on Phe content in foods; and (4) perception and understanding of the Anvisa tools. The questionnaires will be made available upon request to the author.

Participants were recruited using the snowball sampling technique. Initially, some participants were invited to participate in the study through the contact list of the Medical Genetics Service, the Outpatient Metabolic Disorders Clinic of Hospital de Clínicas de Porto Alegre, and PKU patients' associations. The link to the questionnaire was also posted on the social networks (Facebook and Instagram) of patients' associations and neonatal/genetic screening referral centers across the country. Contacted participants were encouraged to share the study with others who were part of the target audience.

We obtained 37 responses from health care providers who prescribed Phe-restricted diets and 215 responses from patients/family members/caregivers. Due to inconsistency in the data, 4 providers and 21 lay users were excluded from analysis. Thus, the final sample consisted of 33 providers (29 dietitians and 4 physicians) and 194 lay users (20 patients with a confirmed diagnosis of PKU, 148 family members, and 26 caregivers).

Data were analyzed using descriptive statistics, presented as absolute and relative frequency or mean and standard deviation.

Results

Health care providers (prescribers of Phe-restricted diets)

Thirty-three prescribers of Phe-restricted diets participated in the study: 29 dietitians (88%) and 4 physicians. Nineteen participants (57%) were affiliated with a neonatal screening referral center. The sample included representatives of all five Brazilian regions.

When asked which sources of information on the Phe content of foods they referred to, unofficial lists shared among professionals working in the field and materials published by unidentified institutions were cited by most providers ($n=17$). The TCFA-Anvisa ranked second ($n=14$), followed by a table developed by the Federal University of Minas Gerais Center for Action and Research in Diagnostic Support ($n=7$), a United States Department of Agriculture table ($n=3$), the Brazilian Food Composition Table ($n=2$) and the Federal University of São Paulo Table ($n=1$).

Twenty-eight providers (85%) also used nutrition facts labels when prescribing diets to patients with PKU; nevertheless, 12/28 (43%) considered that the content of these labels is not enough to serve as a single source of information, while 16/28 (57%) considered them to be partially sufficient.

Regardless of the sources of information mentioned, 32 (97%) participants stated that they had difficulties in prescribing foods for patients with PKU because they did not know their nutritional composition.

Given this scenario, 28 (85%) participants stated that, if they had access to a list that described the Phe content of a wider range of foods, they would be able to include new options in the diet of their patients with PKU. Among the other participants, 4 (12%) stated that they would consider the possibility of including new foods in the prescribed diet and 1 (3%) would not. Regarding the inclusion of foods that are classified as prohibited for patients with PKU in the Phe content tables, 31 (94%) professionals considered this to be important, 1 (3%) considered it partially important and 1 (3%) did not answer.

The second section of the data collection instrument asked specifically about the Anvisa reference tools for Phe content of foods. The results showed that the TCFA-Anvisa had been checked at least once by 23 providers (70%). As for the PCCFA-Anvisa, 20 providers (61%) were aware of its publication and 17 (51%) had checked it at least once.

Fifteen participants (45%) had already checked both tools. Of these, 12 (80%) considered the PCCFA-Anvisa superior to the TCFA-Anvisa. Twelve (71%) of the 17 participants who checked the dashboard considered it useful for dietary prescription, even though it is not linked to a nutritional calculation program. Five (29%) considered it only partially useful.

When asked about their understanding of the terms used in the panel, 8 (47%) found them easy to understand, 6 (35%) found them somewhat easy and 3 (18%) found them hard to understand.

Regarding the identification of processed foods available in supermarkets/grocery stores within the PCCFA-Anvisa, 7 (41%) stated that they were able to identify such foods, 9 (53%) only partly and 1 (6%) was unable to do so. In addition, 4 providers (23%) reported that PCCFA-Anvisa allowed the prescription of a greater variety of foods to patients with PKU compared to other similar tools, and 12 (71%) reported that it partially served this purpose. When comparing the PCCFA-Anvisa and the TCFA-Anvisa, 6 (40%) participants stated that the dashboard allowed them to prescribe a greater variety of foods compared to the

table. Five providers (33%) reported only partial superiority in this regard, and 4 (27%) did not perceive any such improvement.

Four providers in the sample (24%) reported that the PCCFA-Anvisa made it possible to prescribe a greater intake of Phe-rich foods to patients with PKU. Five others (29%) reported only partial improvement in this regard, and 8 (47%) did not perceive any such improvement.

In the opinion of most providers (9; 53%), the dashboard only partially covered the staple foods that are part of their patients' diets. Seven providers (41%) considered that the dashboard contained all main foods included in their patients' diets, while 1 (6%) claimed it did not.

Eleven (65%) participants considered the unit of measurement used to report the Phe content of food (mg/100 g) adequate, 4 (23%) considered it partially adequate, and 2 (12%) considered it inadequate. The providers' opinion on the units of measurement they considered best suited for the Phe content tools is described in the supplementary material (Table S1).

Twenty-five (76%) participants considered that the Anvisa Phe content checkers should be made available to patients/family members/caregivers and prescribers, while 3 (9%) believed the dashboard should only be available to health professionals. Five participants (15%) did not answer this question. Providers' criticisms, suggestions, and other comments about the PCCFA-Anvisa are available in the supplementary material (Table S2).

Patients with phenylketonuria, family members, and caregivers

A total of 194 participants comprised the lay-users group: patients ($n=20$; 10%), family members ($n=148$; 76%), and caregivers ($n=26$; 14%). The vast majority (176, 91%) identified as female. The mean age was 26.6 ± 6.0 , 39.4 ± 9.4 , and 35.0 ± 7.9 years for patients, family members, and caregivers, respectively.

Of the patients included or with ties to participating family members/caregivers, 31 (16%) had serum Phe levels above 6 mg/dL and 8 (4%) above 10 mg/dL on the most recent sample collected prior to enrollment in the study. Fifty-eight (30%) participants did not know or did not want to answer the question, while the others ($n=97$; 50%) had Phe levels equal to or lower than 6 mg/dL. The age of the patients was not assessed in this analysis.

Most of the participants lived in the Southeast region of the country. The remainder were distributed, in descending order, across the South, Northeast, Center-West, and North regions (Figure 1). The specialist care centers where the patients were being treated are listed in Table 1.

One hundred and eighty-nine participants (97%) lived in households with internet access. At the time of the survey, 84 (43%) participants had had internet access in their homes for more than 10 years, 36 (18%) for 5 to 10 years, 33 (17%) for 2 to 5 years, and 12 (6%) for less than 2 years. Seventeen participants (9%) could not specify the time, and 7 (4%) did not answer the question. Of the 5 participants without internet access at home, 2 lived in São Paulo, 1 in Amazonas, 1 in Piauí, and 1 in Espírito Santo.



Figure 1. Geographical distribution of study participants. Data refer to participants of the lay users group (patients with phenylketonuria, their families, and caregivers, all living in Brazil).

When participants in the lay group were asked which sources of information about Phe content in foods they referred to when following the diet prescribed by their dietitians, answers varied widely (Table 2).

Despite having shown a preference for different sources of information, 170 participants (88%) said they use the information on food labels to adhere to the prescribed diet. Among the others, 18 (9%) did not use nutrition labels and 6 (3%) did not know how to answer.

Most patients, family members, and caregivers (159; 82%) knew what a “Phe content of foods table” was. Twenty-two participants (11%) said they did not know what it was about, and 12 (6%) did not know how to answer the question. One (<1%) did not answer the question.

Of the 159 participants who were aware of the table, 79 (49%) had first learned about it more than 5 years ago, 27 (17%) between > 3 and 5 years, 32 (21%) between > 1 and 3 years, 13 (8%) between 1 year and 6 months, and 8 (5%) had been aware

of it for less than 6 months. Most of these participants (116; 73%) were first introduced to the concept of a phenylalanine content table by a dietitian. Other sources of this knowledge were, in descending order: the internet (14; 9%), phenylketonuria patients’ associations (12; 7%), other patients/family members/caregivers (10; 6%); and physicians (6; 4%). One (<1%) participant stated that another source was responsible for introducing him to this resource but did not specify which source.

Of the participants who claimed to know what a Phe content of foods table was, 82 (51%) considered that the tables covered the main foods included in a PKU diet, 68 (43%) considered that the tables did not cover the main foods, and 9 (6%) did not know how to answer the question.

Eighty-five participants (54%) considered that the Phe content tables that they know covered foods typical of their regional cuisine, 69 (43%) considered that the tables did not, and 5 (3%) did not know how to answer. Figure 2 illustrates the perception of patients with phenylketonuria, their family members, and

their caregivers regarding the inclusion of regional foods in the tables (stratified by region of Brazil).

One hundred and fifty (94%) participants stated that, if they had access to a Phe content table which covered a wider range of foods, they would include new foods in their (or the patient's) diet. Three (2%) would not, and 6 (4%) did not know how to answer.

Considering the overall sample (n=194), 177 participants (91%) stated that they would exclude a food from their diet upon discovering, through the table, that it was rich in Phe. Among the others, 12 (6%) would not do so and 5 (3%) did not know how to answer. When participants were asked whether it is important to know the Phe content of foods considered "prohibited" for patients with PKU, 187 (96%) answered "yes".

Table 1. PKU patients included in the study: Brazilian state of living and treatment center.

State of living (n)	Treatment center (number of times mentioned)
Amazonas (1)	Policlínica Codajás (1)
Bahia (11)	APAE Salvador (10) APAE Anápolis (1)
Ceará (14)	Hospital Infantil Albert Sabin (13) Unspecified (1)
Brazilian Federal District (11)	Hospital de Apoio de Brasília (11)
Espírito Santo (6)	CEDAB/APAE Vitória (5) Unspecified (1)
Goiás (14)	APAE Anápolis (11) Hospital de Apoio de Brasília (3)
Maranhão (2)	APAE São Luís (1) Unspecified (1)
Mato Grosso (1)	APAE Anápolis (1)
Mato Grosso do Sul (1)	IPED/APAE Campo Grande (1)
Minas Gerais (13)	NUPAD/UFMG (6) Hospital das Clínicas da UFMG (3) IEDE (1) Unspecified (3)
Pará (3)	UREMIA (3)
Paraíba (6)	Hospital Infantil Arlinda Marques (5) APAE Anápolis (1)
Paraná (13)	FEPE (13)
Pernambuco (9)	Hospital Barão de Lucena (9)
Piauí (3)	Hospital Infantil Lucídio Portella (2) IGEIM (1)
Rio de Janeiro (17)	IEDE (14) Hospital Infantil Joana de Gusmão (1) Ceapd (1) Unspecified (1)
Rio Grande do Sul (16)	Hospital de Clínicas de Porto Alegre (13) Hospital Materno Infantil Presidente Vargas (2) Santa Casa de Misericórdia de Porto Alegre (1)
Rondônia (4)	Nativida Neonatal Screening Center (4)
Santa Catarina (15)	Hospital Infantil Joana de Gusmão (13) Hospital de Clínicas de Porto Alegre (1) Private medical genetics clinic (1)
São Paulo (34)	APAE São Paulo/Instituto Jô Clemente (18) UNICAMP (5) Hospital das Clínicas de Ribeirão Preto (3) Hospital das Clínicas da Faculdade de Medicina da USP (2) IGEIM (2) Hospital das Clínicas de Botucatu (1) Unspecified (3)

APAE: Associação de Pais e Amigos dos Excepcionais; CEDAB: Centro de Diagnóstico Dr. América Buaziz; IPED: Instituto de Pesquisas, Ensino e Diagnósticos; NUPAD: Núcleo de Ações e Pesquisa em Apoio Diagnóstico; UFMG: Federal University of Minas Gerais; IEDE: Instituto Estadual de Diabetes e Endocrinologia Luiz Capriglione; UREMIA: Unidade de Referência Materno, Infantil e Adolescente; FEPE: Fundação Ecumênica de Proteção ao Excepcional; IGEIM: Instituto de Genética e Erros Inatos do Metabolismo; UNICAMP: State University of Campinas; USP: University of São Paulo.

Table 2. Sources of information on Phe content of foods mentioned by patients, family members, and caregivers.

Source	Number of times mentioned
Unofficial tables, lists, and other materials shared among diet prescribers or published by unidentified institutions	123
Food labels	25
TCFA-Anvisa	20
Internet searches	12
Multidisciplinary team at specialized treatment centers	7
Tips from family members of other patients with PKU	5
Material provided by APAE São Paulo	5
Material provided by FEPE	4
USP table	4
NUPAD/UFGM table	4
Books	2
Tips from group chats	2
Material provided by APAE Anápolis	1
APAE Salvador cookbook	1
Material provided by Nativida Neonatal Screening Center	1
Material provided by UNICAMP/CIPOI	1

APAE: Associação de Pais e Amigos dos Excepcionais; FEPE: Fundação Ecumênica de Proteção ao Excepcional; USP: University of São Paulo; NUPAD: Núcleo de Ações e Pesquisa em Apoio Diagnóstico; UFGM: Federal University of Minas Gerais; UNICAMP: State University of Campinas; CIPOI: Centro Integrado de Pesquisas Oncohematológicas na Infância.

The second section of the questionnaire focused specifically on the Anvisa reference guides for checking the Phe content of foods. Overall, 83 (52%) of the lay participants knew that Anvisa provides this type of resource. Of these, 45 (54%) were aware that the PCCFA-Anvisa had been published.

Of the 83 participants who knew that Anvisa provides its own tools for checking the Phe content of foods, 74 (89%) had checked the TCFA-Anvisa at least once. Of the 45 patients who knew about the PCCFA-Anvisa, 37 (82%) had already checked it at least once.

Answers to the items of the third section of the questionnaire, intended only for participants who had already checked both the TCFA-Anvisa and the PCCFA-Anvisa (n=35), are summarized in Figure 3. All participants who answered this section said they would check the tool more often if it were made available through a mobile-friendly app. Thirty-four participants (92%) considered that the dashboard should be used by patients, family members, caregivers, and prescribers. Two (5%) believed that the tool should only be used by prescribers, and 1 (3%) did not answer the question.

Considering only the responses of those 159 participants who knew what a Phe content of foods table was, their opinions regarding which units of measurement would be most suitable for such a table are described in the supplementary material (Table S1). Patients, family members, and caregivers' criticisms, suggestions, and other comments regarding the PCCFA-Anvisa are available in the supplementary material (Table S2).

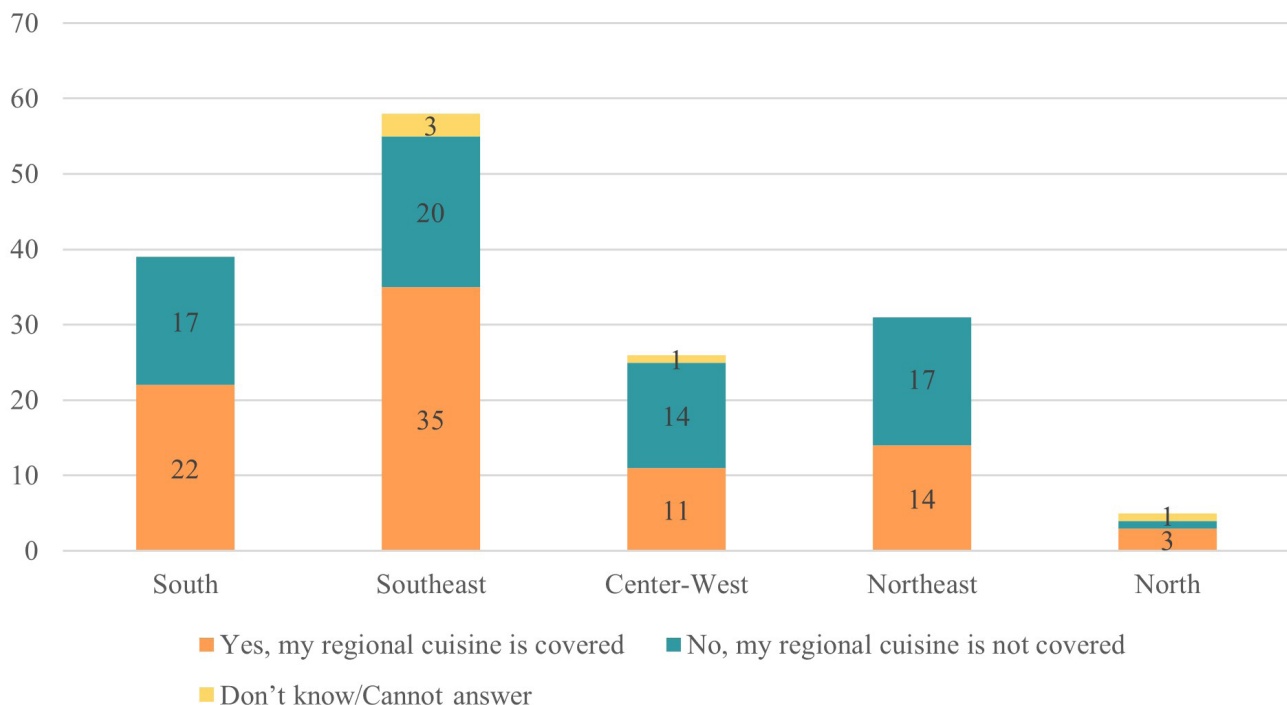


Figure 2. Perception of patients with PKU, their family members, and caregivers regarding the addition of foods typical to the region of Brazil in which they live to the Phe content of food tables available in the literature (n=159).

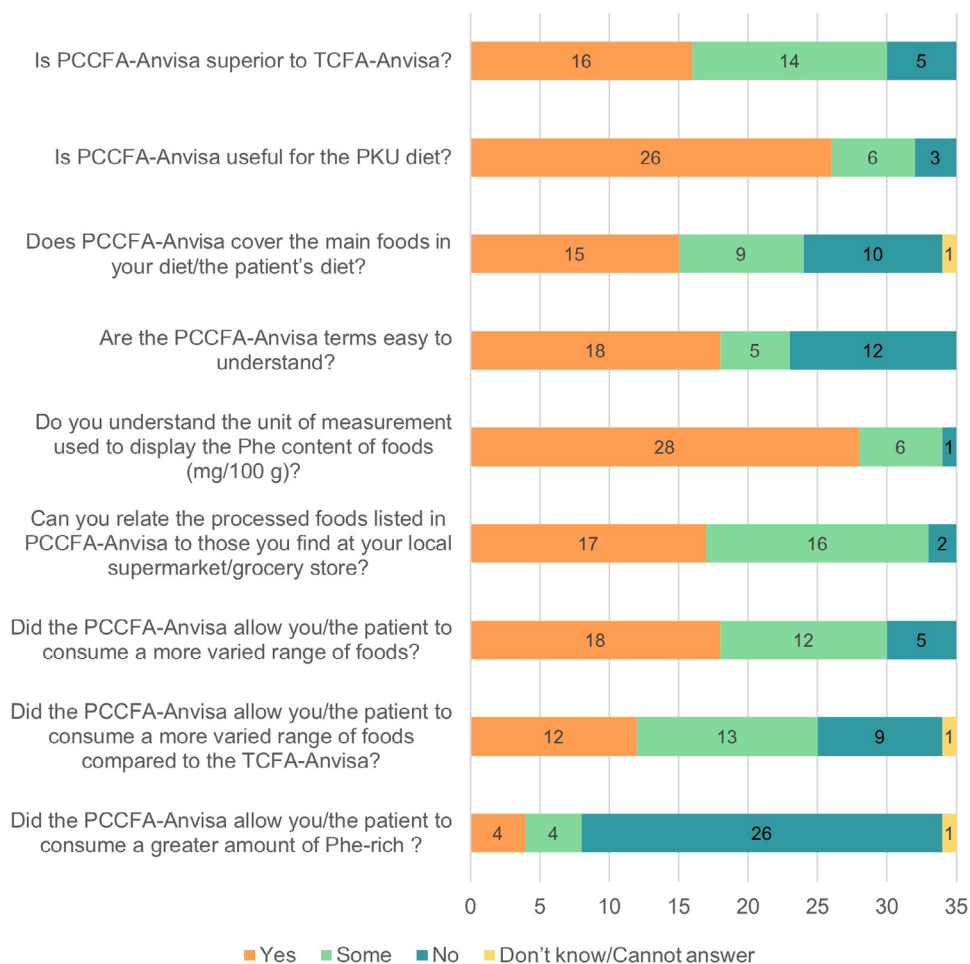


Figure 3. Perception and understanding of patients with PKU, their family members, and caregivers regarding the Anvisa tools for determining Phe content of foods and the impact of these resources on their PKU diet (n=35) PCCFA-Anvisa: Phenylalanine Content of Foods Dashboard (*Painel para Consulta do Conteúdo de Fenilalanina em Alimentos*); TCFA-Anvisa: Table of Phenylalanine Content of Foods (*Tabela de Conteúdo de Fenilalanina em Alimentos*); PKU: Phenylketonuria; Phe: Phenylalanine.

Discussion

In this study, only 15 of 33 health professionals who prescribe a Phe-restricted diet knew and had used both the TCFA-Anvisa and the PCCFA-Anvisa. Among PKU patients, their families, and caregivers, these tools were even less popular, as only 35 of 194 participants checked them. The PCCFA-Anvisa still remains relatively unknown when compared to the TCFA-Anvisa, especially among lay users, probably due to the short time elapsed between publication of this new resource and enrollment in the study.

Regarding sources of information on Phe content in foods, the most often cited titles were unofficial lists shared among professionals working in the field and materials published by unidentified institutions. The Anvisa database ranked second among providers and third among lay participants.

This finding, in addition to (1) the difficulty reported by professionals in prescribing foods to patients with phenylketonuria due to the lack of information on nutritional composition; (2)

the high percentage of participants who would like access to a table listing the Phe content of a wider range of foods; (3) the positive perception of participants regarding the importance of including foods classified as “prohibited” in the tables; and (4) the absence of regional cuisine as pointed out by 44% of the lay participants suggests that the initiative of providers in developing their own reference materials to check the Phe content of foods for their patients with PKU arises from an urgent need to meet the demands of their patient population, because the official tools available are not sufficient.

It is also noteworthy that a significant portion of both groups uses data from food labels to prescribe or choose foods for the PKU diet. However, Phe content is not listed on nutrition facts labels.

Dissatisfaction regarding the lack of regional foods in the Phe content tables seemed to be higher among participants from the Center-West and Northeast of Brazil compared to other regions. However, the variation in sample sizes for each region of the country may reduce the reliability of this result.

The Anvisa database was developed to serve as a guide and reference for health care professionals who prescribe and prepare diets and follow these patients in a clinical setting. Having a national reference table is essential for the dietary management of Brazilian patients with PKU, since regional and seasonal differences in soil quality, as well as meteorological aspects, modify the nutritional composition of foods and consequently limit the use of such tools to their region/country of origin [8].

Furthermore, the absence of foods typical to Brazilian cuisine in international tables not only makes it difficult to estimate nutrient intake but, even worse, can also prevent inclusion of these foods in the PKU diet, directly interfering with the culinary traditions of patients and their families.

The PCCFA-Anvisa, which was designed taking into account the opinions of representatives of PKU patients' associations and health professionals, seems to fill some of the gaps that remained even after the publication of TCFA-Anvisa. For most participants in both groups, the PCCFA-Anvisa is superior or partially superior to the TCFA, and the terms used in the dashboard were considered by most respondents to be easy or somewhat easy to understand.

A significant portion of the criticisms and suggestions from both groups revolved around the search engine and the layout of the dashboard, which shows that, although the new tool represents an improvement over the table, it still has room for enhancement.

Developing a mobile-friendly app for the dashboard and updating the lists of processed and unprocessed foods, with a special focus on the addition of gluten-free, vegan, regional, and controlled/prohibited foods, were the two main items that should be considered to improve usability of the PCCFA-Anvisa.

The possibility of exporting data in PDF format or publishing the Anvisa's database in book format were options mentioned by the participants to overcome their lack of internet access or difficulties in browsing and represent short-term solutions to improving the usability of the Phe content references provided by Anvisa.

Lack of information also appears to be a problem. Twenty-two participants in the lay group did not know what a Phe content table was, while 12 did not know how to answer the question. Although this number does not represent the majority of the sample, it highlights the need to include the subject in nutritional education for PKU patients, since this type of resource, if used with proper professional guidance, can improve patients' treatment adherence and quality of life.

The inclusion of household measurements was also suggested by providers and patients/family members/caregivers alike. The absence of this feature seems to be another factor limiting the wider use of Phe content references.

Conclusion

PCCFA-Anvisa was an important initiative to consolidate the Agency's tools as a national reference for checking the

phenylalanine content of various foods. However, although the study suggests that participants perceive the dashboard as being superior to TCFA-Anvisa, many factors still hinder its usability.

This investigation found that the key demands of patients, family members, and health care providers are development of a mobile application through which the PCCFA-Anvisa can be accessed, with a more modern and intuitive layout, and constant updates to the list of foods covered by the dashboard.

Acknowledgements

The authors thank the participants for their time and availability.

Funding

The authors thank the National Health Surveillance Agency (Anvisa), the National Council for Scientific and Technological Development (CNPq); and the Research and Events Incentive Fund of Hospital das Clínicas de Porto Alegre (FIPE) for financial support.

Authors' Contributions

BBS and IVDS were responsible for study design and data collection. All authors participated in the analysis and interpretation of data and in writing of the manuscript. All authors approved the final version of the manuscript and declare that there are no conflicts of interest.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Supplementary Material

The following online material is available for this article:

Table S1 – Most appropriate units of measurement for Phe content of food tables, in the opinion of study participants.

Table S2 – Criticisms, suggestions, and other comments from the study participants regarding the Anvisa Phenylalanine Content of Foods Dashboard (PCCFA-Anvisa).

References

1. Blau N. Genetics of phenylketonuria: then and now. *Hum Mutat.* 2016;37(6):508-515. doi:10.1002/humu.22980.
2. Monteiro LTB, Cândido LMB. Fenilcetonúria no Brasil: Evolução e casos. *Rev Nutr.* 2006;19(3):381-387. doi:10.1590/S1415-52732006000300009.
3. Albrecht J, Garbade SF, Burgard P. Neuropsychological speed tests and blood phenylalanine levels in patients with

- phenylketonuria: A meta-analysis. *Neurosci Biobehav Rev.* 2009;33(3):414-421. doi:10.1016/j.neubiorev.2008.11.001.
4. Carvalho TM. Resultados do levantamento epidemiológico da Sociedade Brasileira de Triagem Neonatal (SBTN). *Rev Méd Minas Gerais.* 2003;13(2):109-135.
 5. Chen S, Zhu M, Hao Y, Feng J, Zhang Y. Effect of delayed diagnosis of phenylketonuria with imaging findings of bilateral diffuse symmetric white matter lesions: A case report and literature review. *Front Neurol.* 2019;10:1040. doi:10.3389/fneur.2019.01040.
 6. Brasil, Ministério da Saúde, Secretaria de Atenção Especializada à Saúde, Secretaria de Ciência, Tecnologia e Insumos Estratégicos. Portaria conjunta nº 12, de 10 de setembro de 2019. http://conitec.gov.br/images/Protocolos/Portaria-Conjunta-PCDT-Fenilcetonuria_SAES.pdf. Accessed April 22, 2022.
 7. van Spronsen FJ, Blau N, Harding C, Burlina A, Longo N, Bosch AM. Phenylketonuria. *Nat Rev Dis Primers.* 2021;7(1):36. doi:10.1038/s41572-021-00267-0.
 8. Elmadfa I, Meyer AL. Importance of food composition data to nutrition and public health. *Eur J Clin Nutr.* 2010;64 Suppl 3:S4-S7. doi:10.1038/ejcn.2010.202.
 9. Agência Nacional de Vigilância Sanitária (Anvisa). Conteúdo de Fenilalanina em Alimentos. http://antigo.anvisa.gov.br/en_US/fenilalanina-em-alimentos. Accessed April 22, 2022.