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REVIEW ARTICLE

Phenylketonuria in Brazil: a narrative review on treatment and public policies regarding patient and family demands

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Abstract

Phenylketonuria (PKU) is an autosomal recessive disorder that affects phenylalanine metabolism and, if left untreated, leads to severe intellectual disability, behavioral problems, cognitive impairments, and other dysfunctions. This study aimed to assess the clinical and social aspects of PKU, focusing on the current Brazilian context, by synthesizing existing knowledge and its implications. A literature review was conducted using different academic databases, including Scopus, Web of Science, Elsevier, and Google Scholar, using context related to terms such as "phenylketonuria", "phenylketonuria in Brazil", "phenylalanine metabolism", "history of phenylketonuria", and "neonatal screening in Brazil". Then, in order to keep our review up to date, works published in the last ten years were prioritized. Neonatal screening is widely adopted globally and began in Brazil in 1976, becoming mandatory in 2001 following the establishment of the National Neonatal Screening Program. The standard treatment begins immediately after diagnosis and consists of a protein-restricted diet supplemented with free amino acid formulas. Currently, two pharmacological therapies are available—sapropterin dihydrochloride and enzyme replacement therapy—which, although approved by *Agência Nacional de Vigilância Sanitária* (ANVISA), are still not offered by the Unified Health System (in Portuguese – *Sistema Único de Saúde* (SUS)) due to their high cost. Therefore, nutritional therapy remains the main form of treatment for PKU, despite being socially excluding and difficult to maintain over a lifetime. Public policies are urgently needed to ensure access to more effective and less restrictive treatments, aiming to improve the quality of life for individuals with PKU and minimize the consequences of the disease.

Keywords: Neonatal screening; Phenylketonuria treatment; Tetrahydrobiopterin; Phenylalanine ammonia-lyase; Protein restriction; Phenylalanine.

Highlights

- Protein-restricted diets for PKU are effective but more expensive
- Pharmacological therapies approved by ANVISA are not available through SUS
- ANVISA mandates phenylalanine content labeling in foods with 0.1% to 5% protein

1 Introduction

Phenylketonuria (PKU) (ORPHAcode[1]: 716) is a rare autosomal recessive disorder that affects the metabolism of phenylalanine. The prevalence of PKU varies among different ethnicities and geographic regions, being higher in white and East Asian populations, where it occurs in approximately 1 in 10,000 to 15,000 live births. This number is lower in some regions of Asia, such as 1: 212,535 in Thailand and 1: 120,000 in Japan. In South America, the prevalence ranges from 1: 25,000 to 1: 50,000 live births (van Spronsen et al., 2021). Its estimated prevalence in Brazil ranges from 1:15,000 to 1: 25,000 live births (Brasil, 2021a). Data on the prevalence of PKU by Brazilian state are limited and generally concentrated in a few regions, with more than a decade of lag. The available estimates show variations among states, such as Bahia state with 1: 16,334 (Amorim et al., 2011), Mato Grosso state with 3: 100,000, Rio de Janeiro state with between 3.5 and 6.1: 100,000, Santa Catarina state with 3.5: 100,000, Sergipe state with 2.3: 100,000, and Tocantins state with 3.5: 100,000 (Vargas et al., 2025).

The disease is caused by pathogenic genetic variants in the gene that encodes the enzyme phenylalanine hydroxylase, which is responsible for converting phenylalanine into tyrosine. A deficiency in this enzyme leads to an accumulation of phenylalanine and its metabolites at potentially toxic levels in the body (Brasil, 2021a; Lichter-Konecki & Vockley, 2019; Ney & Etzel, 2017; van Spronsen et al., 2021). Elevated concentrations of this amino acid in the bloodstream can damage the central nervous system, resulting in cognitive deficits and global developmental delays (Brasil, 2021a; Hofman et al., 2018; van Spronsen et al., 2021).

PKU was discovered in 1934 by the biochemist Asbjörn Fölling, who investigated urine samples from two siblings presenting with neurocognitive developmental impairment and whose urine exhibited a musty odor. He detected the presence of phenylpyruvic acid in the samples and concluded that phenylacetic acid, a byproduct of phenylpyruvic acid, was responsible for the musty smell. Fölling further analyzed urine samples from 430 children with the same mental condition. Among them, eight children presented the same substance in their urine, including two additional pairs of siblings, suggesting a hereditary genetic mutation, which Fölling named *Imbecillitas phenylpyruvica*. In 1937, the English geneticist Lionel Penrose used the term "phenylketonuria" for the first time, which later became widely known by its abbreviation PKU (Centerwall & Centerwall, 2000; Williams et al., 2008; Sacharow et al., 2021).

In the 1950s, American physician and microbiologist Robert Guthrie developed a bacterial inhibition assay that enabled the semi-quantitative determination of phenylalanine levels in the blood shortly after birth. Guthrie also observed that the test could be performed using dried blood samples impregnated on filter paper (Sacharow et al., 2021), thus initiating newborn screening.

Since its discovery, the main form of treatment has remained dietary and nutritional therapy (MacDonald et al., 2011). The dietary recommendation consists of restricting the intake of foods with high protein content and supplementing with medical formulas composed of a mixture of free amino acids devoid of phenylalanine (Lichter-Konecki & Vockley, 2019; Hofman et al., 2018; Ney & Etzel, 2017). The success of treatment with low-protein foods is primarily due to the fact that phenylalanine is an essential amino acid and, therefore, cannot be synthesized by the human body (van Spronsen et al., 2021).

Although dietary treatment has proven effective in preventing the most severe symptoms of the disease, it is not free from side effects. A diet poor in natural proteins may lead to adverse health effects such as growth restriction, alopecia, lethargy, and eczematous rashes. These symptoms serve as warning signs, indicating the need for constant nutritional monitoring and adjustment of dietary therapy (van Spronsen et al., 2021).

Another challenge in adherence to dietary treatment lies in the supplementation with the amino acid mixture. The unpleasant taste of the formula makes its consumption difficult (MacDonald et al., 2020), and the absorption of free amino acids is not as efficient as that of natural proteins (MacDonald et al., 2011). Despite continuous improvements in formulation, texture, and flavor, the latter remains unsatisfactory, often described as bitter with a residual aftertaste (van Spronsen et al., 2021; MacDonald et al., 2020).

Currently, there are some therapeutic alternatives for PKU, including enzyme replacement therapy and the use of sapropterin dihydrochloride, a synthetic analog of the tetrahydrobiopterin (BH4) cofactor (Lah & McPheron, 2021; Mahan et al., 2019; Thomas et al., 2018; van Spronsen et al., 2021). However, the most accessible and effective treatment continues to be a protein-restricted diet combined with free amino acid supplementation. Despite its efficacy, this approach presents significant adherence challenges, particularly among adolescents and adults. In addition to its high cost, the diet is socially restrictive and requires great discipline from patients (Lichter-Konecki & Vockley, 2019).

[1] The ORPHAcode is a numeric identifier assigned to each rare disease by Orphanet (2025), a European database that centralizes information on rare diseases.

This study aims to discuss the treatment of PKU in Brazil and the response of public policies to the demands of patients and their families. It also explores the evolution of neonatal screening strategies to current therapeutic options, as well as the social organization of patients in the defense of their rights.

2 Methodology

This review was conducted in a narrative format, highlighting its flexibility and the author's interpretative focus, which makes it suitable for describing and discussing the evolution and current landscape of PKU in Brazil from a theoretical and contextual perspective. The review included 28 publications between 2000 and 2025, addressing the clinical and social aspects of PKU, with the aim of synthesizing and updating existing knowledge, following the methodology described below.

The main academic databases searched were Scopus, Web of Science, Elsevier, SciELO, Dimensions AI, and Google Scholar. The main search terms used were: "phenylketonuria", "phenylketonuria in Brazil", "phenylalanine metabolism", "history of phenylketonuria", and "neonatal screening in Brazil".

Inclusion criteria included original articles, reviews, and guidelines, in English and Portuguese, with priority given to publications from the last 10 years addressing clinical, social, or political aspects of PKU. Relevant references cited in the selected articles were also evaluated. Exclusion criteria included non-peer-reviewed publications, editorials, opinion articles without a described methodology, duplicates, and studies not directly related to the article's topic.

After compiling and removing duplicates, articles were evaluated by title and abstract and eligible ones were read in full for confirmation. The analysis was qualitative, focusing on critical reading, identifying thematic axes (disease, clinical and social aspects, and incidence), and historically contextualizing the topic.

3 Results

In Brazil, neonatal screening for PKU began in 1976, initiated by Prof. Benjamin Schmidt at the Association of Parents and Friends of Exceptional Children (APAE) in São Paulo. Schmidt popularized the term "*teste do pezinho*" (heel prick test) due to the nature of the blood collection from newborns' heels. Following this, isolated initiatives started in some Brazilian states through State Laws (Bortoluzzi, 2019; Trovó de Marqui, 2016). The Child and Adolescent Statute (Brazilian Federal Law No. 8,069, dated July 13, 1990) began the formalization of the mandatory implementation of the heel prick test for PKU screening throughout the national territory. In 1992, with RDC GM/MS No. 22/1992, the legislation was complemented by adding congenital hypothyroidism to the list of screened diseases (Brasil, 2008).

However, it was only in 2001 that the Ministry of Health implemented the National Neonatal Screening Program (*Programa Nacional de Triagem Neonatal* - PNTN) through Regulation No. 822, dated June 6, 2001, with full coverage of live births. In Phase I of implementation, only PKU and congenital hypothyroidism were screened. In Phase II, hemoglobinopathies were also included. In Phase III, cystic fibrosis was added to the screening program, and in Phase IV, congenital adrenal hyperplasia and biotinidase deficiency were incorporated (Bortoluzzi, 2019; Trovó de Marqui, 2016).

On May 26, 2021, Law No. 14,154 was enacted (still not regulated), amending Law No. 8,069 of July 13, 1990 (Child and Adolescent Statute), to improve the PNTN by including a minimum list of diseases to be screened through the heel prick test, to be implemented in five phased stages. The first phase includes diseases already screened by the test: PKU and other hyperphenylalaninemias (HPA), congenital hypothyroidism, sickle cell disease and other hemoglobinopathies, cystic fibrosis, congenital adrenal hyperplasia, biotinidase deficiency, and congenital toxoplasmosis. The second phase adds galactosemias, aminoacidopathies, urea cycle disorders, and fatty acid beta-oxidation disorders. The third phase includes lysosomal storage diseases. Primary immunodeficiencies (PIs) are added in the fourth phase, and spinal muscular atrophy is included in the fifth and final phase (Brasil, 2021c).

Regarding the clinical aspects, PKU can be classified according to the concentration of phenylalanine detected in the blood under untreated conditions. The normal range of blood phenylalanine concentration is 50–110 µmol/L (micromoles of phenylalanine per liter of blood) (Sacharow et al., 2021; Blau et al., 2010). The annex to Joint Ordinance No. 12 of September 10, 2019, which approved the Clinical Protocol and Therapeutic Guidelines for Phenylketonuria, establishes the following classification: when phenylalanine levels exceed 1211 µmol/L, the condition is classified as classic phenylketonuria; levels between 484 and 1211 µmol/L are defined as mild phenylketonuria; and levels between 121 and 484 µmol/L are referred to as non-phenylketonuria hyperphenylalaninemia (Brasil, 2019).

A comprehensive study, using a cross-sectional design involving 111 patients with a biochemical phenotype of hyperphenylalaninemia, originating from 61 municipalities in the state of Bahia, revealed that 63 (56.8%) presented the classical PKU phenotype, 25 (22.5%) exhibited the mild form of the disease, and 22 (19.8%) presented non-PKU hyperphenylalaninemia. In addition, one patient was identified with PKU resulting from a deficiency in the biosynthesis of the BH4 cofactor (Amorim et al., 2011). The results of this study were very enlightening, and no studies of this nature were found in other Brazilian states. Therefore, this fact highlights the need for further studies addressing the clinical and demographic aspects of the disease in different regions of Brazil.

The current Clinical Protocol and Therapeutic Guidelines for Phenylketonuria indicate that "[…] all patients with phenylalanine levels greater than or equal to 10 mg/dL on a normal diet, and all those with persistent phenylalanine levels between 8 mg/dL and 10 mg/dL (at least in three consecutive weekly measurements on a normal diet), should follow a phenylalanine-restricted diet" (Brasil, 2019, p. 7), and the success of treatment depends on obtaining information about the amount of phenylalanine present in foods.

To make this information accessible and reliable, the Brazilian Health Regulatory Agency (*Agência Nacional de Vigilância Sanitária* - ANVISA) developed a panel for consulting phenylalanine content in both fresh and processed foods, with data obtained through appropriate methodologies, becoming a reference for diet planning for these patients (Brasil, 2020a).

Food industries are required to inform ANVISA of the phenylalanine content in foods with protein levels between 0.1% and 5%, according to Resolution RDC No. 617 of March 9, 2022. This resolution establishes the obligation to perform laboratory analyses and provide data electronically regarding phenylalanine, protein, and moisture content in processed foods as they are marketed (Brasil, 2022).

ANVISA reviews the received data and incorporates it into the panel, which currently contains phenylalanine content data for 74 fresh foods and over 2,000 processed products. The panel also offers search options by product, brand, category, and specific phenylalanine quantity, facilitating access to this information (Brasil, 2020a).

As previously presented, two pharmacological options are currently available on the market for the treatment of PKU, namely tetrahydrobiopterin (BH4), whose use depends on the responsiveness test, and enzyme replacement therapy.

The drug sapropterin dihydrochloride, a synthetic analogue of BH4, has been used in the treatment of PKU to aid in controlling blood phenylalanine levels. With its use, some patients can discontinue the diet, while others show increased tolerance to phenylalanine intake. However, only a small group of patients respond to this treatment (Brasil, 2018; van Spronsen et al., 2021), as for it to be effective, the treatment requires some residual activity of the phenylalanine hydroxylase enzyme (Mahan et al., 2019). To determine BH4-responsive hyperphenylalaninemia (HPA), a BH4 loading test must be performed, with the patient presenting initial plasma phenylalanine levels above 400 μmol/L.

In Brazil, the BH4 responsiveness test is performed according to different protocols with variability in dose (10 or 20 mg/kg/day, given as a single dose or distributed throughout the day) and evaluation period, which can last hours, days, or even months. To be considered responsive, there must be a reduction of phenylalanine greater than or equal to 30% relative to the baseline level after 24 hours following drug administration (Brasil, 2018).

For the implementation of BH4 in the portfolio of therapies provided by the Brazilian Unified Health System (*Sistema Único de Saúde* - SUS), the National Commission for the Incorporation of Technologies in SUS (*Comissão Nacional de Incorporação de Tecnologias* - CONITEC) developed a budget plan in 2018. This study is part of Medicine Recommendation Report No. 402 and compares the costs of metabolic formulas with the potential costs of sapropterin dihydrochloride (Brasil, 2018). This comparison can be seen in Table 1. The values are related to the amount of formula or medication indicated for each age group and average patient weight. The dosage of sapropterin dihydrochloride indicated in the package insert is 10 mg/kg/day (10 milligrams of medication per kilogram of patient weight per day), and the purchase price of the drug in Brazil in 2025 was R$ 196.26 per 100 mg dose. The drug is contraindicated for children under 4 years old.

Table 1 presents the estimated annual cost of the free amino acid formula and the drug sapropterin dihydrochloride, both indicated for the treatment of PKU. The dosage of the free amino acid formula was calculated based on the maximum limit recommended by the Clinical Protocol and Therapeutic Guidelines for Phenylketonuria (Brasil, 2020b), considering age and body weight.

It is important to emphasize, however, that determining the appropriate dosage of the formula to be ingested must consider the specific type of PKU, the patient's individual protein tolerance, and the daily phenylalanine intake permitted according to serum phenylalanine levels, in addition to individual characteristics such as weight, height, and age. The correct prescription, therefore, must be established by the medical team responsible for the patient's care.

Table 1. Comparison of the costs of amino acid formula with the drug sapropterin dihydrochloride (BH4) per patient per year, in Brazil, 2025.

Age (years)	Average weight (kg)	Cost per patient/year			
		Phenylalanine-free amino acid formula (R$)	Phenylalanine-Free amino acid formula (US$)*	Sapropterin dihydrochloride (R$)	Sapropterin dihydrochloride (US$)*
<1	8.4	9.840,00	1,856.46		
1	11.2	9.840,00	1,856.46		
2	13.7	14.760,00	2,784.70		
3	15.7	14.760,00	2,784.70		
4	17.8	14.760,00	2,784.70	143.267,61	27,029.58
5	19.75	9.840,00	1,856.46	143.267,61	27,029.58
6	22.2	9.840,00	1,856.46	143.267,61	27,029.58
7	25	14.760,00	2,784.70	214.901,42	40,544.38
8	27.7	14.760,00	2,784.70	214.901,42	40,544.38
9	31.65	14.760,00	2,784.70	214.901,42	40,544.38
10	33.35	14.760,00	2,784.70	214.901,42	40,544.38
11	38.15	14.760,00	2,784.70	286.535,22	54,059.17
12	43.1	19.680,00	3,712.93	286.535,22	54,059.17
13	47.65	19.680,00	3,712.93	358.169,03	67,573.96
14	51,115	24.600,00	4,641.16	358.169,03	67,573.96
15	54.8	24.600,00	4,641.16	358.169,03	67,573.96
16	56.7	24.600,00	4,641.16	429.802,83	81,088.75
17	58.6	24.600,00	4,641.16	429.802,83	81,088.75
18	60.35	24.600,00	4,641.16	429.802,83	81,088.75
19	61.05	24.600,00	4,641.16	429.802,83	81,088.75
20-24	63.6	29.520,00	5,569.39	429.802,83	81,088.75
25-29	66.6	29.520,00	5,569.39	501.436,64	94,603.55
30-34	68.1	29.520,00	5,569.39	501.436,64	94,603.55
35-44	69.2	29.520,00	5,569.39	501.436,64	94,603.55
45-54	69.85	29.520,00	5,569.39	501.436,64	94,603.55
55-64	69.2	29.520,00	5,569.39	501.436,64	94,603.55
65-74	66.85	29.520,00	5,569.39	501.436,64	94,603.55
>75	63	24.600,00	4,641.16	429.802,83	81,088.75

Source: Adapted from Brasil (2018). *Exchange rate: 1USD = 5.3004 BRL on September 18, 2025 (Banco Central do Brasil, 2025).

For the calculation of daily protein intake, the recommendation of 0.83 g/kg/day was adopted (Hengeveld et al., 2022). The cost of the free amino acid formula was estimated using the retail price of a commercially available brand (R$ 410.00 per 500 g can). The cost of sapropterin dihydrochloride was based on the final consumer price, including the 18% ICMS tax applicable in the state of São Paulo, according to the ANVISA Drug Price List[2] (R$ 5,887.71 per package containing 30 tablets of 100 mg each, equivalent to R$ 196.26 per 100 mg dose).

The excessively high cost of the medication, combined with the lack of long-term adverse event data and uncertainty about its benefits, led to the decision not to incorporate the drug into the SUS for patients with PKU over five years old. However, its availability was approved for pregnant women or those in the pre-conception phase who are responsive to the treatment and have some residual activity of phenylalanine hydroxylase. The use of this medication aims to facilitate disease control during pregnancy by maintaining plasma phenylalanine levels between 2 and 6 mg/dL. Elevated phenylalanine levels in pregnant women, known as maternal PKU, pose significant risks of congenital malformations such as microcephaly, cardiac malformations, strabismus, and vertebral abnormalities in the baby (Brasil, 2018).

[2] The ANVISA Drug Price List available at Brasil (2025).

In 2021, the medication underwent a new evaluation by CONITEC and a public consultation. Again, the committee's plenary concluded that there was no new scientific evidence and that treatment with this medication continues to be ineffective from the perspective of SUS (Brasil, 2021b). However, the medication is approved for marketing by the ANVISA and is sold by prescription. In 2024, 30 tablets of 100 mg are priced between R$ 5,777.81 and R$ 6,193.42, depending on the region and state[3].

Enzyme replacement therapy, in turn, is indicated to reduce blood phenylalanine levels in adult patients with the disease who are not controlled by dietary treatment (≥ 600 µmol/L; 10 mg/dL) (Lah & McPheron, 2021; Mahan et al., 2019). This medication is a covalent conjugate of the enzyme phenylalanine ammonia-lyase from *Anabaena variabilis* with NHS-methoxy polyethylene glycol (NHS-PEG), which converts phenylalanine into ammonia and trans-cinnamic acid, a non-toxic byproduct that is metabolized by the liver (Lah & McPheron, 2021; Mahan et al., 2019; Thomas et al., 2018).

The medication is administered subcutaneously in doses ranging from 20 to 60 mg per day, and the patient must receive training to recognize and treat anaphylactic shock, as this is the main side effect of the drug. The patient should be instructed to carry injectable epinephrine with them throughout the treatment, since anaphylaxis can occur at any time, but is mainly observed at the beginning of treatment and when the medication is increased. The initial dose is 2.5 mg of pegvaliase per week for four weeks, gradually increasing in dose and frequency until the desired effect is achieved, determined by monitoring phenylalanine levels (Lah & McPheron, 2021).

In Brazil, in 2024, the prices for a 10 mg dose of pegvaliase range from R$ 3,463.86 to R$ 3,713.01, depending on the region and state[4]. The medication was recently approved in Brazil by ANVISA (Brasil, 2025),[5] and it is still not available through the SUS. Currently, the medication is only available for purchase through importation.

Table 2 summarizes the advantages and disadvantages of each treatment currently available for PKU.

Table 2. Current Treatments for Phenylketonuria and the Advantages and Disadvantages of Each.

Type of Treatment	Relevant Information	Advantages	Disadvantages	Treatment Comparison
Dietary and Nutritional Therapy	Consists of restricting foods high in Phe* and supplementation with free amino acid formula without Phe (Lichter-Konecki & Vockley, 2019). May include GMP as an alternative to free amino acid formula without Phe (van Spronsen et al., 2021).	Effective control of blood Phe. Enables a relatively normal life if well followed.	Restrictive, requiring protein substitutes and low-protein foods (Lichter-Konecki & Vockley, 2019). Can cause nutritional deficiencies (e.g., vitamins D and B12, zinc, and selenium) (MacDonald et al., 2011). Low adherence among adolescents/ adults (Lichter-Konecki & Vockley, 2019). Free amino acid formulas are poorly palatable (van Spronsen et al., 2021; MacDonald et al., 2020).	Traditional and most accessible form. Effective control but difficult to maintain. Requires constant nutritional monitoring.
Sapropterin Hydrochloride (BH4)	Synthetic analogue of BH4. Requires that the patient has some residual Phe hydroxylase activity (Mahan et al., 2019).	May allow higher intake of Phe. Some patients can discontinue the diet (van Spronsen et al., 2021). Easy administration (oral).	Only a portion of patients respond to this treatment (van Spronsen et al., 2021). High cost and not provided by SUS. Responsiveness testing required (Brasil, 2018).	Alternative to flexibilize dietary treatment in responsive patients. More expensive than conventional diet.
Enzyme Replacement (Pegvaliase)	Converts Phe into non-toxic byproducts. Administered subcutaneously with gradual dose escalation (Lah & McPheron, 2021).	Reduces blood Phe levels. May allow a less restrictive diet (Lah & McPheron, 2021).	Side effect (risk of anaphylaxis). Requires strict medical supervision (Lah & McPheron, 2021). High cost and requires importation in Brazil. Furthermore, it is not available through SUS.	Alternative for severe PKU patients uncontrolled by diet. High cost and adverse effects limit its use.

*Phe = phenylalanine.

[3] Price quotes available on the Farmaindex website, a free public utility platform for researching and comparing medication prices (Farmaindex, 2024a).
[4] Price quotes available on the Farmaindex website, a free public utility platform for researching and comparing medication prices (Farmaindex, 2024b).
[5] News available at Moraes (2024).

Although recent therapeutic advances, such as sapropterin dihydrochloride and enzyme replacement therapy, represent promising alternatives for the treatment of PKU, access to these options in Brazil is limited by multiple factors. In addition to their high cost and the fact that they are not included in the list of medications provided by the Unified Health System (SUS), there are clinical challenges that must be considered when choosing a treatment, such as the variability of individual response to the medication, potential adverse effects, and the logistical barriers involved in its acquisition. The decision to adopt such treatments should preferably be made jointly by the patient and the medical team, considering not only economic aspects but also clinical criteria of eligibility, safety, and cost-effectiveness of the chosen therapy.

In addition to the difficulties throughout the treatment, living with a rare disease represents an ongoing challenge for both the patient and their family, particularly in the case of PKU, which is associated with the risk of neurological sequelae and delays in cognitive development. Receiving a diagnosis of PKU impacts the family dynamic, as it requires adaptations to meet the demands of treatment. The routine begins to revolve around the child, mainly due to the strict diet that differs from common cultural habits, going beyond the clinical aspect and involving changes in family daily life necessary to adapt to dietary restrictions, transforming not only eating habits but also social and family life (Soares, 2014), which can become a socially excluding experience.

In this context, socialization with people who share the same health condition gains greater relevance in the case of a rare disease, as it provides a sense of belonging. The formation of a support network provides emotional and identity support to patients and their families, helping them cope with the stigma associated with rare diseases (Nóbrega, 2020). Moreover, these support networks can also serve as means through which patients and their families organize socially to claim and protect their rights.

Thus, associations can be created to represent and empower this minority population, such as the *Associação Mães Metabólicas* (Metabolic Mothers Association), which was created due to the need for active political representation. It is a non-profit organization without government support, whose mission is to disseminate information about hereditary metabolic diseases caused by Inborn Errors of Metabolism (IEMs), such as PKU, homocystinuria, tyrosinemia, acidemias, and urea cycle disorders. Additionally, the association also conducts awareness campaigns and promotes actions aimed at the health and well-being of patients with metabolic diseases[6].

4 Conclusion

Neonatal screening, which began in Brazil in 1976 and was expanded nationwide in 2001, represented a significant advance in the early diagnosis of PKU. This measure allowed for the early initiation of treatment, contributing to the prevention or mitigation of severe complications in the cognitive and neurological development of patients.

Although effective, dietary treatment presents adherence challenges, especially among adolescents and young adults, due to the difficulty of maintenance and the social and nutritional limitations imposed by the diet. Despite recent therapeutic advances, pharmacological options such as sapropterin dihydrochloride and enzyme replacement therapy remain inaccessible to most of the Brazilian population, due to a set of factors, including its high cost, the lack of availability through the Brazilian Unified Health System (SUS), challenges in acquisition and distribution (due to importations), as well as considerations regarding risks, benefits, and individual response to treatment.

Civil society organizations, such as the Metabolic Mothers Association, provide support to affected families, promote awareness about rare metabolic diseases, and advocate for more inclusive public policies. However, there is still a need to expand the treatments offered by SUS, incorporating high-cost medications and strengthening nutritional and psychological support to ensure equity in access to treatment and a better quality of life for patients with PKU.

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Data Availability Statement

All data generated or analyzed in this study are included in this published article.

[6] Information available at: Associação Mães Metabólicas (2025).

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