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Nursing care in Phenylketonuria: a scoping review

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ABSTRACT

Introduction: Phenylketonuria is a rare inherited metabolic disorder which, in the absence of early diagnosis and treatment, can lead to irreversible neurological damage.
Objective: To map the available evidence on the physical and psychological impacts of phenylketonuria and its treatment, highlighting the contribution of nursing in the follow-up of these individuals and their families.
Methodology: A scoping review was conducted according to the Joanna Briggs Institute methodological guidance for scoping reviews and reported in line with the PRISMA-ScR extension, using the PCC strategy to structure the research question and identifying studies in the CINAHL, MEDLINE (via PubMed), and EBSCOhost platform, published between 2011 and 2024.
Results: Adherence to the restrictive diet emerged as the main challenge, affecting metabolic control, psychological well-being, and quality of life. The included studies consistently highlight the involvement of nurses in health literacy promotion, therapeutic education, emotional support, and care coordination, although nursing-specific interventions are often poorly described and underreported.
Conclusion: Nursing practice in rare metabolic diseases such as phenylketonuria should evolve toward more specialized and person-centered interventions that are clinically effective and tailored to the complex biopsychosocial needs of individuals with PKU and their families. However, the current evidence base provides limited detail on specific nursing interventions, underscoring the need for further research that clearly defines, implements, and evaluates nursing roles in this field.

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INFORMAÇÃO DO ARTIGO

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RESUMO

Introdução: A fenilcetonúria é uma doença metabólica hereditária rara que, na ausência de diagnóstico e tratamento precoces, pode provocar danos neurológicos irreversíveis.
Objetivo: Mapear as evidências disponíveis sobre os impactos físicos e psicológicos da fenilcetonúria e do seu tratamento, destacando o contributo da enfermagem no acompanhamento destas pessoas e suas famílias.
Metodologia: Foi realizada uma revisão de escopo de acordo com as orientações metodológicas do Instituto Joanna Briggs para revisões exploratórias e relatada em conformidade com a extensão PRISMA-ScR, utilizando a estratégia PCC para estruturar a questão de investigação e identificando estudos nas plataformas CINAHL, MEDLINE (através do PubMed) e EBSCOhost, publicados entre 2011 e 2024.
Resultados: A adesão à dieta restritiva revelou-se o principal desafio, afetando o controlo metabólico, o bem-estar psicológico e a qualidade de vida. Os estudos incluídos destacam consistentemente o envolvimento dos enfermeiros na promoção da literacia em saúde, na educação terapêutica, no apoio emocional e na coordenação dos cuidados, embora as intervenções específicas da enfermagem sejam frequentemente mal descritas e sub-relatadas.
Conclusão: A prática de enfermagem no âmbito de doenças metabólicas raras, como a fenilcetonúria, deve evoluir no sentido de intervenções mais especializadas e centradas na pessoa, que sejam clinicamente eficazes e adaptadas às complexas necessidades biopsicossociais das pessoas com PKU e das suas famílias. No entanto, a base de evidências atual fornece poucos detalhes sobre intervenções de enfermagem específicas, o que sublinha a necessidade de mais investigação que defina, implemente e avalie claramente os papéis da enfermagem neste domínio.

Introduction

Phenylketonuria (PKU) is an autosomal recessive genetic disorder caused by variants in the gene encoding the enzyme phenylalanine hydroxylase (PAH), leading to toxic levels of phenylalanine and a risk of intellectual disability and neuropsychiatric changes when not treated early.[1,2] In Portugal, PKU has been systematically screened since 1979 through the National Neonatal Screening Program, ensuring early identification of most cases and allowing early initiation of dietary treatment.[3] The national incidence is around 4-8 cases per 100,000 live births, making PKU a rare disease, but one with a significant impact throughout the life cycle of those affected and their families.[2,3]

Standard therapy is based on a strict low-phenylalanine diet, with restriction of natural protein and use of phenylalanine-free formulas and protein substitutes, sometimes supplemented with pharmacological approaches, which requires demanding adjustments to daily routines.[1] Despite advances in the organization of care and access to new treatments, adherence to the diet remains one of the main challenges, particularly in adolescence and adulthood, and is often associated with poorer metabolic control, greater psychological burden, symptoms of anxiety and depression, and impaired quality of life.[4-7] This impact also extends to caregivers, whose well-being and quality of life are influenced by the prolonged demands of the therapeutic regimen.[7,8]

Recent literature describes PKU as an "adherence disease," emphasizing the need for ongoing education, psychosocial support, and structured follow-up to promote self-management and health literacy among people with PKU.[5,7,9] In this context, nurses, who are part of multidisciplinary teams and linked to neonatal screening programs, play a central role in clinical monitoring, therapeutic education, emotional support, and care coordination throughout the different life transitions.[9-10] However, several studies highlight a lack of specific training and structured psychological and educational support resources, which may limit nurses' ability to respond in a specialized manner to the complex needs of these patients and their families.[4,7,10]

Given the exploratory nature of the topic and the expected heterogeneity of study designs, a scoping review

approach was considered the most appropriate to map the breadth of available evidence and identify gaps related to nursing practice in PKU.

Thus, the objective of this study was to conduct a scoping review to map the impacts of phenylketonuria and its treatment on the physical and psychological well-being of people with PKU, valuing the contribution of nursing and identifying gaps in knowledge and training that may guide future clinical and investigative interventions.[6,7,9]

Methodology

This scoping review followed the methodological recommendations of The Joanna Briggs Institute (JBI) for scoping reviews and was reported in accordance with the PRISMA-ScR checklist, ensuring transparency and rigor in the processes of identifying, selecting, and synthesizing evidence.[11,12] The completed PRISMA-ScR checklist is provided as supplementary material. The research question was structured according to the PCC (Problem, Concept, Context) strategy: Problem – phenylketonuria; Concept – physical and psychological impacts of the disease and its treatment; Context – healthcare with a focus on nursing practice.[11] The guiding question defined was: *What are the impacts of phenylketonuria and its treatment on the physical and psychological well-being of affected individuals, based on available evidence?*

Inclusion and exclusion criteria

Studies published between 2011 and 2024 in Portuguese, English, and Spanish were included if they focused on individuals with phenylketonuria at any stage of life and reported physical, psychological, or social impacts of the disease and/or its treatment, with explicit implications for nursing practice, healthcare provision, or multidisciplinary management. Conceptually, the review was delimited to studies that addressed the biopsychosocial impact of PKU and that contained at least some information relevant to the role, responsibilities, or potential contributions of nurses within the broader healthcare team. Opinion papers, editorials, letters to the editor, purely laboratory or genetic studies without clinical or psychosocial outcomes, guidelines without empirical data, and publications without full-text availability were excluded, in accordance with JBI recommendations for scoping reviews.[11]

Research strategy

The search strategy was developed based on the PCC mnemonic and MeSH/DeCS descriptors related to phenylketonuria, therapeutic adherence, quality of life, and nursing care. Initially, an exploratory search was conducted in PubMed to identify free terms and controlled descriptors (MeSH), which were subsequently validated in DeCS for their equivalents in Portuguese and Spanish. The full electronic search strategies for all databases and information sources are available in Supplementary Material 1.

The scoping review search was conducted in CINAHL Complete (EBSCOhost platform), MEDLINE (via PubMed), and additional databases accessible through the EBSCOhost platform between January and March 2025. Controlled vocabulary (MeSH and equivalent terms) and free-text keywords related to phenylketonuria, treatment adherence, quality of life, and nursing or healthcare were combined with Boolean operators (AND, OR) and adapted to the syntax and subject headings of each database.

For each database, the fields searched (title, abstract, subject headings) and any applied limits (publication year, language) are reported in Table 1, along with the date of the last search (08 February 2025). Gray literature was explored through manual searches of reference lists, consultation of relevant professional and patient-organization websites, and screening of conference abstracts related to metabolic diseases and nursing.

Table 1. Search strategy – MEDLINE via PubMed – date: 08/02/2025.

#	Research strategy	Results
#1	"Phenylketonuria*" [MeSH] Terms	7,610
#2	"Nursing Care" [MeSH] Terms	146,333
#3	"Nurse*"	520,208
#4	"nursing practice"	24,338
#5	"Quality of Life" [MeSH] Terms	318,524
#6	"Health Literacy"	25,802
#7	"Medication Adherence"	34,116
#8	2 OR 3 OR 4	146,333
#9	5 OR 6 OR 7	374,563
#10	1 AND 8 AND 9	7
#11	Time Range: 2011-2024 Language: English, Portuguese or Spanish	1

Study selection process / PRISMA flowchart

The selection of studies took place in two phases: reading of titles and abstracts, followed by full reading of potentially eligible texts, carried out independently by two reviewers, with discrepancies resolved by consensus, in line with the good practices recommended by PRISMA 2020.[12] The complete process of identification, screening, eligibility, and inclusion is represented in a PRISMA flowchart, specifying the number of records initially identified, duplicates removed, articles excluded, and studies included in the final synthesis.

Data extraction and synthesis/ Quality assessment

Data extraction was performed using a standardized form based on the JBI methodology, which included information on participant characteristics, study design, context, interventions, physical and psychological outcomes, and key findings related to the role of nursing. Data synthesis was performed using narrative analysis, grouping the findings into thematic categories that reflected the physical, psychological, and social impacts of PKU and the contribution of nurses.

The methodological quality of the included studies was examined using the Critical Appraisal Skills Programme (CASP) checklists appropriate to each study design, with the aim of characterizing the robustness of the available evidence rather than excluding studies on the basis of quality scores, in keeping with the exploratory nature of scoping reviews.[11,13] These appraisals were used to support the interpretation of the findings and to highlight areas where the evidence base is particularly weak or methodologically limited.

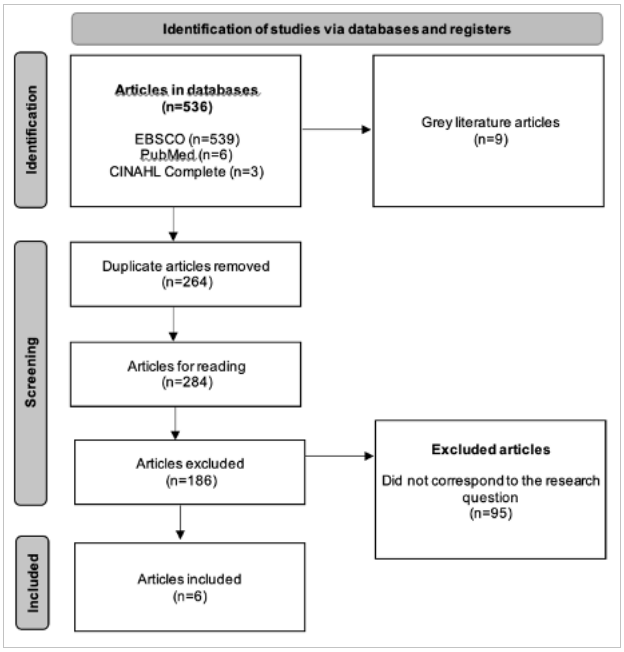
This scoping review was prospectively registered in the Open Science Framework (OSF) (https://osf.io/nru9q/) to promote methodological transparency, reproducibility, and rigor in the research process. The registration detailed the review objectives, eligibility criteria, and planned methodological procedures, thereby reducing the risk of selective reporting and enhancing the credibility of the findings.

Results

The selection process, summarized in Figure 1, initially identified 539 records (database searching: CINAHL Complete n=3; MEDLINE via PubMed n=6; EBSCOhost platform n=530) and 9 additional records from gray literature and manual searches. After removal of 264 duplicates, 284 records remained for title and abstract screening, of which 98 were excluded for not addressing PKU or its clinical/psychosocial impacts. A total of 186 full texts were assessed for eligibility; 180 were excluded for reasons such as not focusing on PKU, not reporting physical or psychological outcomes, or not providing empirical data, resulting in 6 studies being included in the final synthesis.[14]

Detailed reasons for full-text exclusion at the eligibility stage (for example, absence of PKU population, lack of relevant outcomes, or non-empirical publication type) are provided in Supplementary Table 2.

Figure 1. PRISMA flow diagram of the study selection process.



Characterization of included studies

The included studies were characterized in terms of country, setting, population, study design, main outcomes, and reported implications for nursing or healthcare practice, as summarized in Table 2. Studies were predominantly conducted in Europe (five studies, 83,3%), with one study from Asia (16,7%). Methodologically, there was a predominance of narrative and practice-oriented reviews (three studies, 50,0%), complemented by one qualitative study (16,7%), one multicenter survey (16,7%) and a retrospective observational audit (16,7%). Most investigations were carried out in hospital or specialist metabolic clinic settings, reflecting a clinical-care context (Table 2).

Table 2. Characteristics of the included studies.

Author(s)	Title	Country	Study design	Results
MacDonald et al. (2020)[15]	PKU dietary handbook to accompany PKU guidelines	Multinational (mainly European; coordinated by Neatherlands)	Practice handbook based on guidelines and expert consensus	Provides practical, step-by-step guidance for initiating and maintaining the PKU diet and emphasizes that ongoing practical support is essential for long-term adherence.
Bélanger-Quintana et al. (2011)[16]	Up to date knowledge on different treatment strategies for phenylketonuria	Multinational (Spain, Italy, Germany, UK, USA)	Narrative literature review	Summarizes pharmacological and dietary strategies, emphasizing that restrictive diets prevent mental decline but may be associated with social stigma and potential nutritional deficiencies.
Altman et al. (2021)[17]	Mental health diagnoses in adults with phenylketonuria: a retrospective systematic audit	United Kingdom	Retrospective audit (observational study)	Shows a high prevalence of mental health diagnoses in adults with PKU and that average phenylalanine levels > 600 µmol/L over the last 2 years are associated with a higher risk of low mood and other mental health problems.
Nematollahi et al. (2021)[18]	Spirituality, a path to peace: The experiences of parents who have children with Phenylketonuria	Iran	Qualitative study (content analysis)	Identifies spirituality as a central supporting factor, promoting spiritual growth, greater mental and emotional tolerance, and greater psychological well-being in families.
Cazzorla et al. (2018)[19]	Living with phenylketonuria in adulthood: The PKU ATTITUDE study	Italy	Multicenter survey study	It has been observed that many adults do not perceive PKU as a disease, which is associated with poor adherence to the diet, suboptimal levels of metabolic control, and symptoms such as fatigue and irritability.
Figueiredo & Jorge (2024)[20]	Dietary and nutritional intervention in the prevention of intellectual and cognitive disabilities in children with phenylketonuria	Portugal	Narrative literature review	It concludes that a phenylalanine-restricted diet, started early and maintained long-term, is crucial for preventing neurological damage and ensuring healthy cognitive development.

Summary of extracted data

The data extracted from the six studies were organized into thematic categories, allowing the identification of four central themes: a) *adherence to the diet*, b) *knowledge of the physical and psychological impacts*, c) *role of health professionals*, and d) *emotional and social aspects* associated with phenylketonuria, highlighting that adolescents and young adults face greater resistance to the restrictive diet, often influenced by social pressure, desire for autonomy, and perception of stigma, with repercussions on metabolic control and psychological well-being. It was observed that nurses are repeatedly identified as key figures in therapeutic education, emotional support, and care coordination, although the interventions described in most studies are not very specific and not very operationalized in terms of clinical and educational skills, which shows that PKU management remains strongly conditioned by adherence to the diet and that the impact of the disease goes beyond the biomedical dimension, involving emotional suffering, difficulties in social integration, and increased demands on families.

Discussion

This scoping review largely confirms what recent evidence has shown about the complexity of managing PKU across the life course, supporting the description of the condition as an "adherence disease," in which long-term dietary adherence directly affects metabolic control, cognitive functioning, and quality of life.[21-23] As noted in this review, adolescence and the transition to adulthood consistently emerge as periods of greater vulnerability, in which peer pressure, the desire for normality, and the perception of stigma contribute to the relaxation of dietary restrictions, higher levels of phenylalanine, and increased symptoms of depression and anxiety.[21,22,24,25]

From an evidence synthesis perspective, the included studies collectively indicate that diet-related adherence challenges, psychological distress, and social stigma are recurrent concerns among individuals with PKU and their families. At the same time, the small number of studies and their heterogeneous designs limit the extent to which patterns can be generalized, reinforcing the need for cautious interpretation of the overall findings.

The results pointing to a significant impact of PKU on the emotional and social sphere of people with PKU and their families are in line with recent systematic reviews and multicenter studies, which document significant psychological burden, difficulties in social integration, and financial impact, even in contexts with established newborn screening and specialized follow-up.[22,23,26,27] The literature shows that, although many children and adolescents have an overall acceptable quality of life, specific areas remain more compromised - such as social participation, autonomy, body image, and emotional well-being - particularly when adherence to the diet is inconsistent or when socioeconomic barriers accumulate.[22,23,26,28] The data from this review, by highlighting emotional distress, feelings of difference, and increased demands on families, reinforce the need for structured psychosocial support interventions, in line with recent recommendations that advocate for ongoing psychological support programs and approaches that integrate the family as a unit of care.[22,23,29]

In terms of implications for practice, the mapped evidence suggests several potential avenues for strengthening nursing contributions to PKU care, particularly in relation to structured therapeutic education, psychosocial support, and coordination of multidisciplinary care. These implications, however, should be viewed as hypotheses for future development and testing rather than definitive practice recommendations.

With regard to the role of healthcare professionals - and nurses in particular - the studies included suggest that they are perceived as key figures in therapeutic education, emotional support, and care coordination, but they provide little detail on specific nursing interventions, which limits their replicability and evaluation.[23,30] This finding is consistent with recent literature, which simultaneously emphasizes the centrality of nursing in neonatal screening programs, outpatient follow-up, and care transition, and the existence of gaps in specific training in hereditary metabolic diseases, health literacy, and psychosocial interventions aimed at adherence.[23,29,30,31] Intervention studies show that structured education programs and nursing interventions focused on promoting adjustment skills can improve knowledge, psychological adaptation, and adherence to the therapeutic regimen in children with PKU, which reinforces the need to develop, validate, and document advanced nursing practice models in this field.[29,30]

In summary, this review reinforces the idea that, despite diagnostic and therapeutic advances, PKU continues to require intensive and multidimensional monitoring, in which adherence to diet, psychosocial factors, and family support are determinants of health outcomes.[21-24] The most recent evidence points to the relevance of integrating specialized nursing interventions based on structured education, emotional support, digital technologies to support self-management, and family-centered approaches in order to mitigate the risk of maladjustment in adolescence and adulthood and promote a better quality of life throughout the course of the disease.[25,26,28,29]

The difficulties encountered in conducting this scoping review focused mainly on the scarcity and heterogeneity of the available evidence, which limited the direct comparison of results and the possibility of a more robust synthesis. The limited description of specific nursing interventions, often presented in a generic manner or diluted in multidisciplinary teams, made it difficult to identify the discipline's own contributions and analyze their impact on the physical and psychological outcomes of people with PKU. In addition, the diversity of methodological designs, small samples, and different assessment instruments (both for adherence and for quality of life and psychological well-being) hindered the generalization of findings, highlighting the need for more rigorous future studies with standardized measures and a clear focus on the role of nursing in rare metabolic diseases.

Implications for practice: Guide to specialized nursing interventions

The characterization of PKU as an "adherence disease" (Reach, 2025) reinforces the need for nursing practice that goes beyond traditional clinical monitoring, focusing on promoting self-management and health literacy. For these interventions to be effective, nurses must implement structured therapeutic education programs that not only impart knowledge but also develop psychological adjustment skills,[30] using digital technologies to support real-time monitoring of phenylalanine levels.[1] This approach is particularly critical in the transition to autonomy, where specific training in label interpretation and safe food choices enables adolescents to manage peer pressure[4] and the desire for normality.

At the same time, a focus on the psychosocial dimension is imperative, given that stigma and the risk of social isolation severely impact well-being,[28] requiring nurses to conduct systematic screening for symptoms of anxiety and depression.[6] Interventions should be designed to include the family as a unit of care,[7] ensuring that coordination of the clinical pathway minimizes caregiver burden[8] and identifies early socioeconomic barriers that may prevent equitable access to low-protein foods.[9]

Finally, the effectiveness of this care model depends on overcoming the gap in specific training in rare metabolic diseases,[10] and it is essential to create clinical protocols that operationalize these skills. Only through the development of advanced practice models will it be possible to offer care that is both specialized and humanized, ensuring that the complexity of treatment does not compromise the overall quality of life of individuals with PKU.[7]

Conclusion

This scope review mapped the main physical, psychological, and social impacts of phenylketonuria and its treatment, highlighting that sustained adherence to the therapeutic regimen, especially the restrictive diet, remains crucial for the clinical prognosis and well-being of people with PKU. The results show that adolescence and the transition to adulthood are periods of particular vulnerability, marked by greater resistance to the diet, the influence of social pressure, and the desire for autonomy, with repercussions on quality of life and the experience of stigma. These findings should be interpreted with caution, given the small number of included studies, their methodological heterogeneity, and the frequent lack of detailed reporting on nursing-specific activities.

This mapping suggests that nurses are important contributors to promoting autonomy and health literacy through therapeutic education, emotional support, clinical monitoring, and coordination of care across the life course. Nevertheless, the available literature describes these contributions in a relatively generic way and reveals gaps in specific training in rare metabolic diseases. It is therefore advisable to invest in advanced education in metabolic nursing, structured clinical protocols, and follow-up models that explicitly integrate psychosocial support and active family involvement, while recognizing that stronger empirical evidence is required before firm conclusions can be drawn about the effectiveness of particular nursing interventions in PKU.

Data supporting the results will be provided on request.

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