



Prediction of Social Participation Factors Affecting the Quality of Life of Mothers with Children with PKU Using a Random Forest Model: A Cross-sectional Study in Hamadan, Iran, in 2018

Sahar Dehdar Karsydani¹, Sassan Amari², Naser Kamyari³, Mostafa Eghbalian⁴, Zahra Mortazavi⁵, Elahe Salarpour⁶, Saideh Sadat Mortazavi^{5*}

¹University Research and Development Center, Tehran University of Medical Sciences, Tehran, Iran

²Department of Nursing, Faculty of Nursing and Midwifery, Hormozgan University of Medical Science, Bandar Abbas, Iran

³Department of Public Health, School of Health, Abadan University of Medical Sciences, Abadan, Iran

⁴Yazd Cardiovascular Research Center, Shahid Sadoughi University of Medical Sciences, Yazd, Iran

⁵Department of Occupational Therapy, Faculty of Rehabilitation, Hamadan University of Medical Sciences, Hamadan, Iran

⁶Endocrinology and Metabolism Research Center, Hormozgan University of Medical Sciences, Bandar Abbas, Iran

*Corresponding Author: Saideh Sadat Mortazavi, Email: s.mortazavi.ot@gmail.com

Abstract

Background: Parents of children with chronic medical conditions, including those with phenylketonuria (PKU), face emotional stress. In this study, we will focus mainly on the social relationships, social participation, and quality of life of mothers of children with PKU using the random forest (RF) method.

Method: In this cross-sectional study, data were collected from the Association for the Protection of PKU in Hamadan province. We utilized the RF method for data analysis using the packages “Metrics” and “random forest SRC” in R software (version 3.2.2).

Results: In total, 201 mothers who had children with PKU were included in this study. More than half (52.2%) of the mothers were aged between 18 and 35 years. Based on the random forest method, the most important predictors of the social interactions and social participation of mothers who had children with PKU were, in order, environmental health, social relationships, mental health, physical health, income, the number of family members, educational status, mothers’ job status, and age of mothers.

Conclusion: The first four variables (environmental health, social relationships, mental health, and physical health) were the most effective predictors.

Keywords: Random forest, Phenyl ketonuria, Mental health

Citation: Dehdar Karsydani S, Amari S, Kamyari N, Eghbalian M, Mortazavi Z, Salarpour E, et al. Prediction of social participation factors affecting the quality of life of mothers with children with PKU using a random forest model: a cross-sectional study in Hamadan, Iran, in 2018. *Health Dev J.* 2023; 12(1):25–30. doi:10.34172/jhad.92376

Received: October 25, 2023, **Accepted:** May 12, 2024, **ePublished:** July 17, 2024

Introduction

Phenylketonuria (PKU) is a scarce inherited chronic untreatable disorder associated with intellectual disability and neurological abnormalities (1). The incidence is estimated as 1:21 000 (2), 1:10 000 (1), and 1.5:10 000 (3) in Latin America, Europe, and Iran, respectively.

Recent studies have mentioned that the parents of a child with chronic medical conditions, such as PKU, face enormous emotional stress (4,5). These studies indicate that babyhood, social functioning, general health, physical functioning, parental impact–time, emotional functioning, physical health, psychosocial health, quality of life, etc. can raise special challenges for the parents of children with PKU (1-5). In fact, caregivers’ physical and mental health is important for the success of therapeutic

interventions delivered to PKU patients. Previous studies have pointed out the importance of the emotional burden of the diagnosis of PKU (6) and other parameters related to parental psychological performance with regard to PKU (7).

Simon et al used the Wilcoxon Test for the analysis of the quality of life and social services offered to 67 PKU patients over 17 years old in Germany in 2008 (8). In the cross-sectional study of Fidika et al, 89 parents completed the self-report measures of PQoL, family stress, social support, and parental coping scale. Regression and mediation analyses were performed to determine the impact of these potential predictors on PQoL (9). Alavi et al conducted a study on 39 children and adolescents with thalassemia major children and their parents, who



completed a quality-of-life questionnaire (PedSQL) assessing four dimensions, including physical, emotional, social, and school performance using inferential statistics (paired t-test, Mann-Whitney, and Spearman Solidarity) (10).

Theoretically, there are several advantages for random forest (RF) models over regression. First, the RF algorithm automatically selects important variables (11) and has no restrictions on the number of variables entering the model, which is different from stepwise variable selection in logistic regression. Second, missing values and imbalanced data can be handled automatically by RF. Third, RF works better than logistic regression in large data sets, where numerous variables are present. Nevertheless, RF has a main disadvantage. Unlike the decision Trees analysis, the Tree structure in RF is highly complex and an invisible “black box”. So, there is an unknown relationship between a particular level of a variable and the outcome (11).

In this study, the main goal was to identify the predictors of social participation and QoL of mothers who had PKU children using an RF model in an Iranian population, Hamadan.

Materials and Methods

In this retrospective study, 201 women who had PKU children were included. The data were collected from the Protection of Phenylketonuria Patients' Association in Hamadan Province. The response variable in this study was social participation. We also used the World Health Organization Quality of Life (WHOQOL) questionnaire (12) to assess mothers' physical health, psychological health, social relationships, and environmental health. Additional information included premature birth, maternal health (physical and mental), mother's age, mother's job status (employed or housewife), marital status (married, single), marital condition (peaceful, discordant, divorced, and widowed), mother's education (illiterate, high school diplomas, bachelor's degrees or higher), monthly income of the family members, number of PKU children, social participation (the degree of participation in a community or society, measured by the female social participation questionnaire), physical health (overall physical well-being as the most visible health dimension, measured by the WHOQOL), psychological health (emotional, behavioral, and social maturity of a person, measured by the WHOQOL), social relations (relationships established in a company, organization, etc., determined by the WHOQOL), and environmental health (environmental public health, etc. determined by the WHOQOL).

The data were analyzed using the packages of “Metrics”, and “random forest SRC” in R software (version 3.2.2). The metrics of the RF package in R software are commonly used in supervised machine learning. This

method works in such a way that it fits into multifaceted data gathered using different sampling and by choosing different cut-points and combining the input of the independent variable. Finally, the model that has the best sensitivity and specificity is selected as the final model. In order to select the most important variables, we used the %IncMSE index.

Results

Table 1 shows the demographic characteristics of mothers who had children with PKU. As Table 1 shows, 72.7% of the mothers had premature birth; 90.9% of the mothers were healthy, and 52.2% of them had an age between 18 and 35 years. Most (76.1%) of the mothers were housewives; 93.0% lived with their husbands, and 83.3% of these mothers enjoyed a peaceful life with their spouses. The highest frequency of maternal education was diploma (42.9%), and 41.4% of them were illiterate. The highest frequency of monthly income was 400-900 thousand tomans; 50.5% of the families had 1-3 members; 36.3% of the mothers had just one child with PKU, and 3.0% of them had two children with PKU.

In this study, the mean \pm SD of the social participation score of mothers was 81.51 ± 6.74 ; the mean \pm SD of the

Table 1. Demographic characteristics of mothers who had children with PKU

Predictors		Number	Percent
Premature birth	1	144	72.7
	2	54	27.3
Mother's good health	Yes	178	90.9
	No	18	9.1
Mother's age	18-35	105	52.2
	35-55	82	40.8
	>55	11	5.5
Mother's job status	Employed	45	22.4
	Housewife	153	76.1
Marital status	Married	187	93.0
	Single	11	5.5
Marital condition	Peaceful	165	83.3
	With conflicts	22	11.1
	Divorced	6	3.0
	Widowed	5	2.5
Mother's education status	Illiterate	82	41.4
	Diploma	85	42.9
	Bachelor's degree and higher	31	15.7
Income status (monthly, Tomans)	<400	47	23.7
	400-900	76	38.4
	>900	75	37.9
Number of family members	1-3	100	50.5
	3-6	65	32.8
	6-9	33	16.7

physical health score was 9.86 ± 2.23 ; the mean \pm SD of the psychological health score was 19.21 ± 3.46 ; the mean \pm SD of the social relationship score was 25.41 ± 3.94 ; the mean \pm SD of the environmental health score was 25.54 ± 5.25 , and the mean \pm SD of the environmental health score was 80.01 ± 12.81 .

Based on the RF method, the following variables could predict the status of the social participation of the mothers of children with PKU. The most important ordered predictors were environmental health, social relationships, mental health, physical health, income, number of family members, maternal educational status, maternal job status, and maternal age (Table 2).

According to the RF method, variables had a meaningful relationship with social participation (Figure 1). When the physical health score ranged from 4 to 8, social participation showed a decline; for a physical health score between 8 and 11, social participation increased, and again participation declined when the physical health score exceeded 12. Regarding the mental health score, when the score was between 9 and 17, social participation showed a decline, and in cases where the mental health score was above 15, social participation increased. With regard to social communication, a direct association was observed between this variable and social participation. The environmental health scores of 11-14 and >14 predicted a decline and an increase in social participation, respectively. The average social participation score was lower in mothers aged 35-55 years than in mothers aged 18-35 years, and the social participation of mothers over the age of 55 years was greater than that of mothers under 55 years old. The social participation of employed mothers was higher compared to that of housewives. Also, higher maternal education and family income predicted higher social participation. On the other hand, the social participation of mothers seemed to remain unchanged by increasing the number of family members.

Discussion

This study was performed to identify the factors influencing the social participation and life quality of mothers of children with PKU. For this purpose, we used the RF model. This model disclosed a total of nine variables, including four quantitative variables (environmental health, social relationships, physical health, and mental health) and five qualitative variables (mother's job, mother's education, mother's age, number of family members, and monthly income). Among four quantitative variables (Figure 1), maternal social participation showed the strongest association with mental health and environmental health, displayed by their clear and distinct climax points. At first, the effectiveness patterns of both variables showed a declining trend, which subsequently increased. The index of the mental health variable was 17. The social

Table 2. Ordered variables based on their effects on social participation (i.e., the response variable)

Variables	Random forests	
	Order	%IncMSE
Mother's age (year)	IX	1.03
Mother's job status	VIII	1.11
Mother's education status	VII	2.02
Income	V	2.12
Number of family members	VI	2.88
Physical health	IV	12.07
Mental health	III	14.74
Social relationships	II	24.02
Environmental health	I	40.01

The order of importance of the variables, the variable with a higher numerical value is more important. Effective variables are Bold.

relationship variable (i.e., the third strongest predictor of social participation) showed an increasingly influential pattern, while the pattern related to physical health (the fourth effective predictor) revealed a downward trend. The effectiveness patterns of the five qualitative variables were almost equal, except for maternal jobs, where higher levels of this variable predicted higher maternal social participation.

One of the factors that affects the QoL of parents with PKU children is the condition of the disease. Several studies have suggested that QoL in PKU patients is lower than that of healthy people (13). The existence of a sick child increases the prevalence of physical illnesses such as pain (14) and psychiatric problems such as depression, stress, and anxiety in family members, especially mothers (15). In some studies, the life quality of mothers of ill children has been reported to be lower than that of mothers of healthy children (10,13). Some studies have shown that there is a correlation between the life quality of these mother and the severity of their children's disabilities, where more severe disabilities foretell poorer QoL (14,16,17). In a study in Italy, it was found that mothers of children with apathy disorders had relatively poor QoL (16). In the current study, we witnessed that with an increase in the mental health of mothers, their social participation also increased. In a 2011 study on the parents of PKU children by Mahmoudi-Gharaei et al, stress, depression, and anxiety levels were higher in these parents, and the birth of a PKU child was considered to impose a heavy burden on these parents since they had to be highly vigilant about the special dietary requirements of their child (18). In 2010, Dijkers evaluated the factors affecting the social interactions and participation, as well as familial relationships of families with members suffering from hereditary illnesses, reporting that the mental health of individuals was linked with their social participation (19).

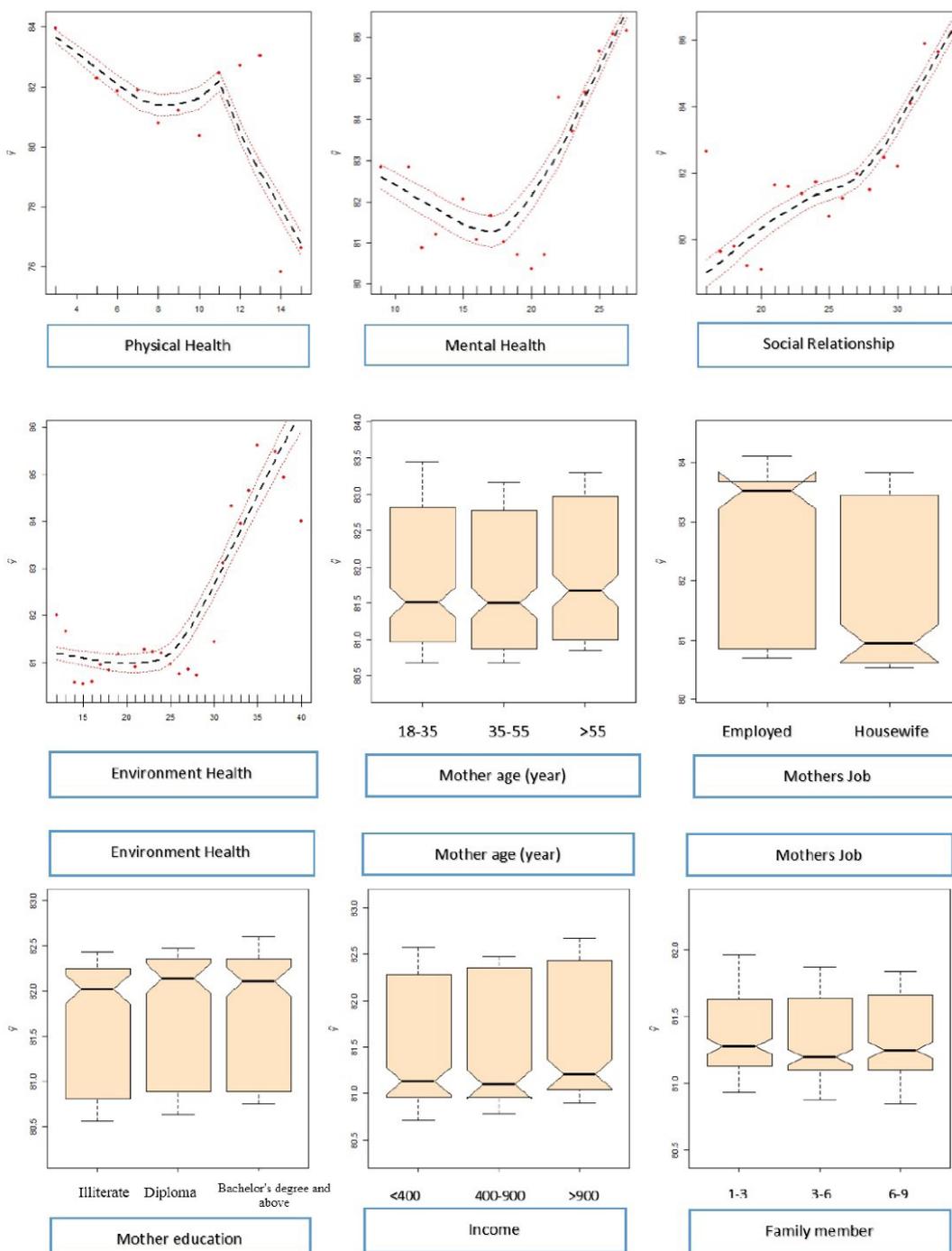


Figure 1. Mean score of the social participation of mothers of children with PKU and its correlation with selected variables according to the Random Forests method

In the present study, an improvement in environmental health was observed to enhance maternal social participation. Studies have shown that the level of social participation is related to social and physical environment, as well as excessive physical activities and individual and environmental factors (19,20). In line, people who have higher physical health scores generally show less social participation. Many studies have also shown that the social participation of physically healthy people is higher than individuals suffering

from physical illnesses (21-23). As suggested by Xiang and colleagues' study, QoL is linked with the low social participation of the parents of underpaid and overactive children with specific medical conditions (24,25). The discrepancy between these findings may be due to the fact that mothers of PKU children do not care about their illnesses. As Bourke-Taylor and colleagues asserted, most mothers often sacrifice themselves for their children and prefer their children's happiness to their own (26). Individuals aged between 35-55 years had the lowest

social participation rate, and mothers over 55 years old had the highest social participation. Mothers who worked outside reported higher social interactions, especially with home caregivers. Also, increased levels of education and income predicted higher levels of social participation.

In previous studies investigating the parents of children with hyperactivity, attention deficit disorder, asthma, and diabetes, a positive relationship was noticed between parents' education and social participation. In explanation, it can be said that individuals with higher education have better career choices, so their needs and expectations are better met depending on their conditions. On the other hand, educated people have access to necessary information about the disease and its therapeutic modalities (25). Previous studies acknowledge that higher monthly income is associated with the life quality of parents of children with disabilities. Of course, other than income, health-related and non-health costs, such as housing and other household expenditures, also affect QoL (26). Fazer's assessment of life revealed a direct and meaningful relationship between QoL and income, where lower income intensified the feeling of misery, leading to isolation and lack of social participation (27). Gunduz and colleagues suggested that low-income families suffered from stress and depression due to the pressure imposed by the high costs of specific diets, which could negatively affect the mother's social partnership (28). With an increase in the number of family members, social participation has increased. The results of studies by Ozel et al and Alaea et al (30,31) confirmed that PKU children's condition was directly influenced by their families' knowledge and maternal quality of care. More opportunities for studying about the disease and gaining knowledge in the field can help provide better familial care to these patients.

We observed a significant negative relationship between the number of PKU children in a family and providing satisfactory familial care. With an increase in the number of PKU children in a family, the focus on nutritional control on the level of dietary phenylalanine becomes harder and weaker, exacerbating physical, psychological, and financial stress on family members (29,31). However, with a higher number of family members and their participation in the care process, it is expected that the physical and mental pressure on the mother can be diminished, increasing the opportunity for maternal social participation. Therefore, in order to improve maternal QoL, appropriate programs should be considered to help these mothers better care for their children along with having opportunities for participating in social events.

Acknowledgments

The data presented here were the results of a research project with number 9403058031 carried out with the financial support of the research vice-chancellor of Hamedan University of Medical

Sciences. We would like to thank the Hamadan University of Medical Sciences for their approval and support of this study.

Authors' Contribution

Conceptualization: Sahar Dehdar Karsydani, Mostafa Eghbalian, Saideh Sadat Mortazavi.

Data curation: Zahra Mortazavi, Elahe Salarpour, Sassan Amari.

Formal analysis: Mostafa Eghbalian, Naser Kamyari.

Funding acquisition: Mostafa Eghbalian, Saideh Sadat Mortazavi.

Investigation: Sahar Dehdar Karsydani, Mostafa Eghbalian, Saideh Sadat Mortazavi.

Methodology: Zahra Mortazavi, Elahe Salarpour, Mostafa Eghbalian, Sassan Amari.

Project administration: Sahar Dehdar Karsydani, Mostafa Eghbalian, Saideh Sadat Mortazavi.

Resources: Sahar Dehdar Karsydani, Mostafa Eghbalian, Saideh Sadat Mortazavi.

Software: Mostafa Eghbalian, Naser Kamyari.

Supervision: Saideh Sadat Mortazavi.

Validation: Sahar Dehdar Karsydani, Mostafa Eghbalian, Saideh Sadat Mortazavi.

Visualization: Sahar Dehdar Karsydani, Mostafa Eghbalian, Saideh Sadat Mortazavi.

Writing-original draft: Sahar Dehdar Karsydani, Sassan Amari, Saideh Sadat Mortazavi.

Writing-review & editing: Sahar Dehdar Karsydani, Mostafa Eghbalian, Saideh Sadat Mortazavi.

Competing Interests

The authors declare no conflict of interest.

Funding

None.

References

1. Bosch AM, Burlina A, Cunningham A, Bettiol E, Moreau-Stucker F, Koledova E, et al. Assessment of the impact of phenylketonuria and its treatment on quality of life of patients and parents from seven European countries. *Orphanet J Rare Dis.* 2015;10:80. doi: [10.1186/s13023-015-0294-x](https://doi.org/10.1186/s13023-015-0294-x).
2. Vieira Neto E, de Souza Maia Filho H, Monteiro CB, Carvalho LM, Tonon T, Vanz AP, et al. Quality of life and adherence to treatment in early-treated Brazilian phenylketonuria pediatric patients. *Braz J Med Biol Res.* 2017;51(2):e6709. doi: [10.1590/1414-431x20176709](https://doi.org/10.1590/1414-431x20176709).
3. Habib A, Fallahzadeh MH, Kazeroni HR, Ganjkarimi AH. Incidence of phenylketonuria in southern Iran. *Iran J Med Sci.* 2010;35(2):137-9. doi: [10.30476/ijms.2010.39771](https://doi.org/10.30476/ijms.2010.39771).
4. Hafetz J, Miller VA. Child and parent perceptions of monitoring in chronic illness management: a qualitative study. *Child Care Health Dev.* 2010;36(5):655-62. doi: [10.1111/j.1365-2214.2010.01102.x](https://doi.org/10.1111/j.1365-2214.2010.01102.x).
5. Nabors LA, Kichler JC, Brassell A, Thakkar S, Bartz J, Pangallo J, et al. Factors related to caregiver state anxiety and coping with a child's chronic illness. *Fam Syst Health.* 2013;31(2):171-80. doi: [10.1037/a0031240](https://doi.org/10.1037/a0031240).
6. Lord B, Ungerer J, Wastell C. Implications of resolving the diagnosis of PKU for parents and children. *J Pediatr Psychol.* 2008;33(8):855-66. doi: [10.1093/jpepsy/jsn020](https://doi.org/10.1093/jpepsy/jsn020).
7. Ionio C, Salvatici E, Confalonieri E, Milani L, Mascheroni E, Riva E, et al. Mothers and fathers facing their children's phenylketonuria. *Child Health Care.* 2018;47(1):83-100. doi: [10.1080/02739615.2016.1275643](https://doi.org/10.1080/02739615.2016.1275643).
8. Simon E, Schwarz M, Roos J, Dragano N, Geraedts M, Siegrist J, et al. Evaluation of quality of life and description of the sociodemographic state in adolescent and young

- adult patients with phenylketonuria (PKU). *Health Qual Life Outcomes*. 2008;6:25. doi: [10.1186/1477-7525-6-25](https://doi.org/10.1186/1477-7525-6-25).
9. Fidika A, Salewski C, Goldbeck L. Quality of life among parents of children with phenylketonuria (PKU). *Health Qual Life Outcomes*. 2013;11:54. doi: [10.1186/1477-7525-11-54](https://doi.org/10.1186/1477-7525-11-54).
 10. Alavi A, Parvin N, Kheyri S, Hamidzadeh S, Tahmasebi S. Comparison of perspective of children with major thalassemia and their parents about their quality of life in Shahrekord. *J Shahrekord Univ Med Sci*. 2007;8(4):35-41. [Persian].
 11. Geng M. A Comparison of Logistic Regression to Random Forests for Exploring Differences in Risk Factors Associated with Stage At Diagnosis Between Black and White Colon Cancer Patients [dissertation]. University of Pittsburgh; 2006.
 12. The WHOQOL Group. Development of the World Health Organization WHOQOL-BREF quality of life assessment. *Psychol Med*. 1998;28(3):551-8. doi: [10.1017/s0033291798006667](https://doi.org/10.1017/s0033291798006667).
 13. Khayatizadeh M. A comparative study about quality of life in mothers of children with cerebral palsy, mental retardation and mothers of normal children. *Daneshvar Medicine*. 2009;16(83):49-58. [Persian].
 14. Arnaud C, White-Koning M, Michelsen SI, Parkes J, Parkinson K, Thyen U, et al. Parent-reported quality of life of children with cerebral palsy in Europe. *Pediatrics*. 2008;121(1):54-64. doi: [10.1542/peds.2007-0854](https://doi.org/10.1542/peds.2007-0854).
 15. Olsson MB, Hwang CP. Depression in mothers and fathers of children with intellectual disability. *J Intellect Disabil Res*. 2001;45(Pt 6):535-43. doi: [10.1046/j.1365-2788.2001.00372.x](https://doi.org/10.1046/j.1365-2788.2001.00372.x).
 16. Mugno D, Ruta L, D'Arrigo VG, Mazzone L. Impairment of quality of life in parents of children and adolescents with pervasive developmental disorder. *Health Qual Life Outcomes*. 2007;5:22. doi: [10.1186/1477-7525-5-22](https://doi.org/10.1186/1477-7525-5-22).
 17. Warschburger P, Buchholz HT, Petermann F. Psychological adjustment in parents of young children with atopic dermatitis: which factors predict parental quality of life? *Br J Dermatol*. 2004;150(2):304-11. doi: [10.1111/j.1365-2133.2004.05743.x](https://doi.org/10.1111/j.1365-2133.2004.05743.x).
 18. Mahmoudi-Gharaei J, Mostafavi S, Alirezai N. Quality of life and the associated psychological factors in caregivers of children with PKU. *Iran J Psychiatry*. 2011;6(2):66-9.
 19. Dijkers MP. Issues in the conceptualization and measurement of participation: an overview. *Arch Phys Med Rehabil*. 2010;91(9 Suppl):S5-16. doi: [10.1016/j.apmr.2009.10.036](https://doi.org/10.1016/j.apmr.2009.10.036).
 20. Levasseur M, Desrosiers J, Whiteneck G. Accomplishment level and satisfaction with social participation of older adults: association with quality of life and best correlates. *Qual Life Res*. 2010;19(5):665-75. doi: [10.1007/s11136-010-9633-5](https://doi.org/10.1007/s11136-010-9633-5).
 21. Monbaliu E, De Cock P, Maillieux L, Dan B, Feys H. The relationship of dystonia and choreoathetosis with activity, participation and quality of life in children and youth with dyskinetic cerebral palsy. *Eur J Paediatr Neurol*. 2017;21(2):327-35. doi: [10.1016/j.ejpn.2016.09.003](https://doi.org/10.1016/j.ejpn.2016.09.003).
 22. Nooijen CF, Stam HJ, Sluis T, Valent L, Twisk J, van den Berg-Emons RJ. A behavioral intervention promoting physical activity in people with subacute spinal cord injury: secondary effects on health, social participation and quality of life. *Clin Rehabil*. 2017;31(6):772-80. doi: [10.1177/0269215516657581](https://doi.org/10.1177/0269215516657581).
 23. Takada K, Sashika H, Wakabayashi H, Hirayasu Y. Social participation and quality-of-life of patients with traumatic brain injury living in the community: a mixed methods study. *Brain Inj*. 2016;30(13-14):1590-8. doi: [10.1080/02699052.2016.1199901](https://doi.org/10.1080/02699052.2016.1199901).
 24. Davey H, Imms C, Fossey E. "Our child's significant disability shapes our lives": experiences of family social participation. *Disabil Rehabil*. 2015;37(24):2264-71. doi: [10.3109/09638288.2015.1019013](https://doi.org/10.3109/09638288.2015.1019013).
 25. Xiang YT, Luk ES, Lai KY. Quality of life in parents of children with attention-deficit-hyperactivity disorder in Hong Kong. *Aust N Z J Psychiatry*. 2009;43(8):731-8. doi: [10.1080/00048670903001968](https://doi.org/10.1080/00048670903001968).
 26. Bourke-Taylor H, Howie L, Law M. Impact of caring for a school-aged child with a disability: understanding mothers' perspectives. *Aust Occup Ther J*. 2010;57(2):127-36. doi: [10.1111/j.1440-1630.2009.00817.x](https://doi.org/10.1111/j.1440-1630.2009.00817.x).
 27. Kahneman D, Deaton A. High income improves evaluation of life but not emotional well-being. *Proc Natl Acad Sci*. 2010;107(38):16489-93. doi: [10.1073/pnas.1011492107](https://doi.org/10.1073/pnas.1011492107).
 28. Gunduz M, Arslan N, Unal O, Cakar S, Kuyum P, Bulbul SF. Depression and anxiety among parents of phenylketonuria children. *Neurosciences (Riyadh)*. 2015;20(4):350-6. doi: [10.17712/nsj.2015.4.20150319](https://doi.org/10.17712/nsj.2015.4.20150319).
 29. Abd-Elkodoos RF, Badr-Eldein SA, Ismail GM. Family caregiver's knowledge and practices of children with phenylketonuria at Abo El Reesh hospital. *Med J Cairo Univ*. 2012;80(2):61-9.
 30. Ozel HG, Lammardo AM, Motzfeldt K, Robert M, Rocha JC, Van Rijn M, Ahring K, Bélanger-Quintana A, MacDonald A, Dokoupil K. Use of sapropterin in the management of phenylketonuria: seven case reports. *Molecular genetics and metabolism*. 2013;108(2):109-11. doi: [10.1016/j.ymgme.2012.11.012](https://doi.org/10.1016/j.ymgme.2012.11.012).
 31. Alaei M, Asadzadeh-Totonchi G, Gachkar L, Farivar S. Family social status and dietary adherence of patients with phenylketonuria. *Iran J Pediatr*. 2011;21(3):379-84.