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## Background

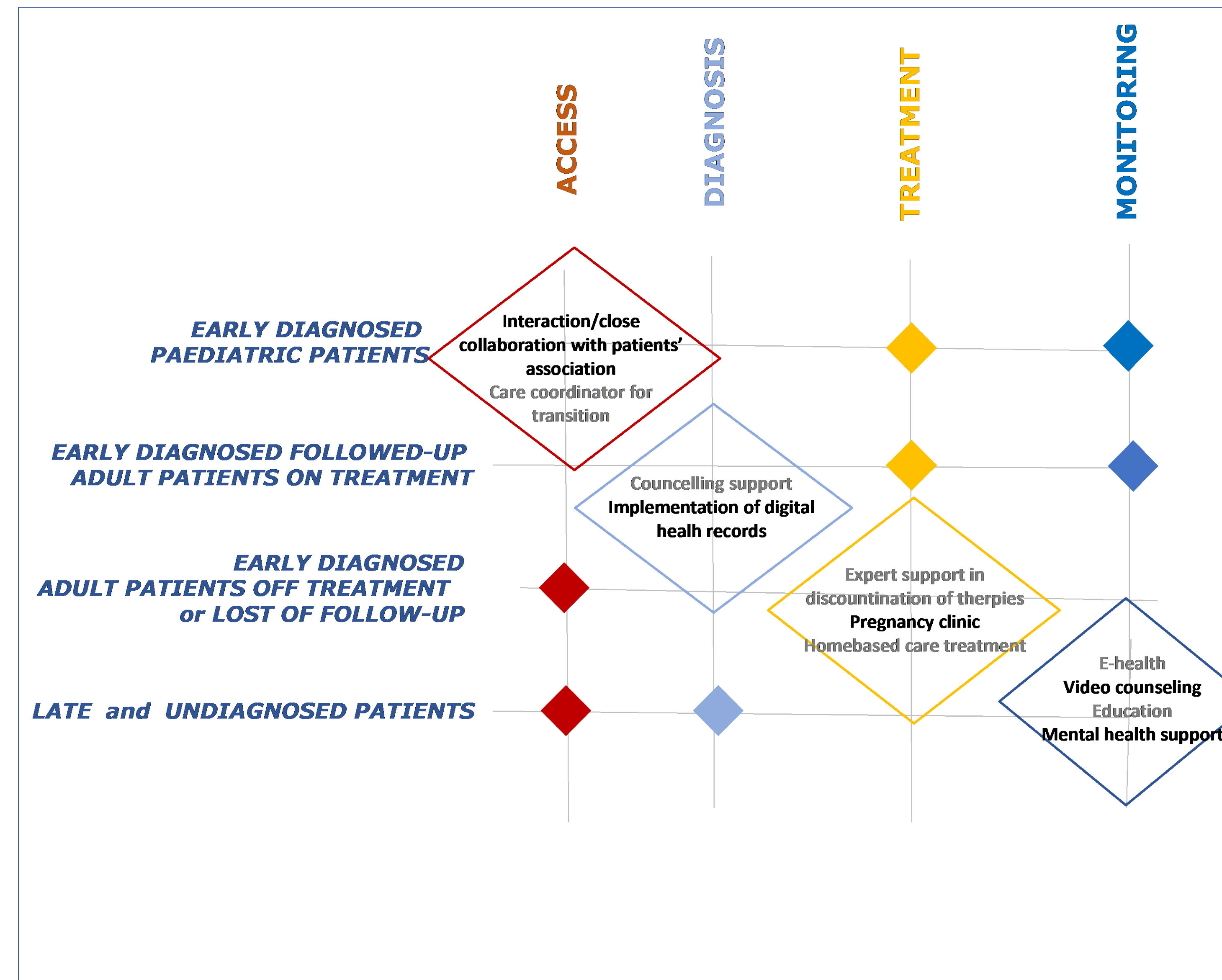
Phenylketonuria (PKU) is a rare autosomal recessive inborn error of phenylalanine (Phe) metabolism caused by pathogenic variants in the gene encoding phenylalanine hydroxylase (PAH). PAH deficiency causes abnormal accumulation of Phe in the blood and in the brain. High blood Phe levels are strongly linked to neurocognitive dysfunction, and if not treated PKU causes intellectual disabilities, motor deficits, microcephaly, autism, eczematous rash, seizures, developmental problems, aberrant behavior, and psychiatric symptoms. In Europe PKU prevalence is about 10:100,000 newborns with higher rate in Turkey and Ireland, and a very low rate in Finland. In most European countries, the national newborn screening (NBS) programs include Phe measurement. The aim of the NBS is to discover hyperphenylalaninemia (HPA), and this is defined as any blood Phe >120 µmol/L. The early detection of HPA and its treatment can prevent neurological damages. Despite the high diffusion of NBS, there are still late diagnosed patients or undiagnosed patients such as immigrant children from countries where NBS is lacking, or adults born before the introduction of the NBS.

## Methods

In defining and optimising patient care pathways (PCPs) the role of patient representatives (PRs) is very important; it is crucial in the contest of rare diseases where the complexity of the disorders is higher, comorbidity and multi-organ involvement are present, multidisciplinary care is needed, and patients may experience inequality in the access to specialised diagnostic/treatment procedures. In this work we have analysed the role of PRs in the design and optimization of Phenylketonuria's (PKU) PCP. We applied RarERN Path© methodology to PKU PCP within the Value of Treatment (VOT) for Rare Brain Disorders project (European Brain Council). PRs of PKU Associations of Ireland and Germany were involved. The PCPs in place in centers of excellence (COE) were analysed, and patients provided input through a semi-structured questions survey exploring organization of care and perception of criticalities when receiving healthcare services. A first draft of the optimized PCP for PKU was discussed in a plenary meeting attended by neurologists and PRs. Finally, PRs were requested to provide additional suggestions through a second ad-hoc survey.

## Results

Patients Representatives contributed to the design of an optimized PCP, providing unique information on the main organizational challenges in COEs and on the coordination of care between COE and non-hospital care at European level.



## Patients said about patient care pathways, how to improve the care for their PKU:

*“Many patients were born before newborn screening. Other than their intellectual and physical disabilities, the underlying condition PKU often has not been adequately looked after. It is a significant milestone that the Patient Care Pathways shed a light on them and explicitly highlight their need to having access to treatment and better quality of life.”*

*„Too often, we PKU patients have been told we should be grateful for the value of early diagnosis and an effective nutritional therapy. However, PKU is not a solved problem and too much gratefulness is delaying progress. It is so important that the Patient Care Pathways outline many of the residual unmet needs in PKU care.“*

*„For years I did not recognize how I was mentally chocked by the diagnosis. I functioned, however was unable to cope. Thanks to trauma screening and mental health support I learned to accept my sons' disease and the treatment as something normal. It means the world to me that the Care Pathways acknowledge the individual needs of both patients and caregivers.“*

## Conclusion

To formally involve PRs in the co-design of the PCP is necessary because it allows to complement clinicians' perspective about “ranking” and “weight” of what really matters throughout the PCP. PKU case is particularly interesting in this respect.

## Acknowledgements

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