Phenylketonuria: optimizing care
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Citation for published version (APA):
CHAPTER 8
Future Perspectives
FUTURE PERSPECTIVES

Optimizing care in phenylketonuria (PKU) remains an important goal. Since the introduction of newborn screening and early and subsequent continuous dietary treatment, much research has been performed on the physical and social wellbeing of patients with PKU. This thesis has focussed on a number of these aspects and this chapter provides an overview of future perspectives based on our results.

First, an uniform approach is warranted when treating patients with PKU. Even though dietary treatment is the mainstay in the care for PKU, there are still differences to overcome in how this care is implemented. To overcome such differences (inter)national consensus procedures, resulting in clinical pathways and/or guidelines are probably the best tools. A Dutch national consensus has been reached on how the care for PKU is best provided. However, to guarantee up-to-date information about the care trajectories stated in the clinical pathway for PKU it is necessary for clinicians to remain in dialogue about the content, and the clinical pathway needs to be regularly updated. Furthermore, a need for international consensus also exists and efforts to achieve an uniform European PKU guideline have been made.

Second, the burden of living with PKU and disease management needs further investigation. Health related quality of life (HRQoL) is hypothesized to be impaired. The available questionnaires that we used in our research (both the generic HRQoL questionnaires as the questionnaires aimed at the chronically ill) are not disease specific. Unfortunately, for this reason we were not able to pinpoint if and which domains of HRQoL are affected in patients with PKU. The development of a PKU specific and internationally validated questionnaire is of great importance, because an adequate HRQoL questionnaire is evaluative and discriminative specifically for the researched group of patients, in this case in PKU. A disease specific questionnaire may also be useful in detecting changes in quality of life when new treatment options are introduced.
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Third, the burden of time placed on caregivers of pediatric patients related to disease management is significant and it takes away time from leisure. Future research on this matter is of use in optimizing care for the patients with PKU as it may provide insight in effects of new treatment options and it may be used as a new outcome measure in future research. From a clinical approach it is of importance to be aware of the effect of the imposed dietary treatment on the lives of patients with PKU. Awareness may improve physician-patient relationship and perhaps increase understanding of dietary adherence problems.

Fourth, a systematic review and meta-analysis showed that bone health in patients with PKU is less impaired than was previously hypothesized, although low bone mineral density (BMD; Z-score below -2) was slightly more prevalent than in the general population. We found the same results for BMD Z-scores in our own Dutch PKU population. Bone turnover markers (BTM) were found to be elevated, both formation and resorption markers, suggesting that the bone turnover in our population is affected. The fracture history of our patients showed that their lifetime fracture prevalence was comparable to the general population and none of the patients had osteoporosis. These results suggest that bone health in patients with PKU is uncomplicated. However, the patients investigated were relatively young and it is possible that the combination of finding a higher prevalence of low BMD and a change in BTM may lead to adverse outcomes of bone health when patients become older. Further research is of importance to investigate the cause of the slightly higher prevalence of low BMD and altered BTM in blood, and to relate outcomes to the dietary treatment that patients are subjected to. Female patients over the age of fifty years will be a particular important group to be studied in the future as women over 50 years of age already have a higher prevalence of osteoporosis related fractures, and women with PKU might have an even greater risk based on our findings.

Fifth, improvements of the present dietary treatment options, need to be developed in order to try to reduce the burden of dietary restriction on the patient and decrease risks of nutrient deficiencies. Examples of complications of dietary treatment are alterations in micronutrient (vitamin D, selenium, zinc, arginine) and fatty acid (eicosapentaenoic
acid) intakes and blood levels. The effects imposed on the patient by chronic restriction in natural protein should be carefully examined in larger cohort studies, as should the possible complications of nutrient deficiencies.

Finally, not studied in this thesis, but of great importance, to improve care for patients with PKU, further advances in research on new pharmacological treatment options are warranted. PEG-PAL, gene therapy and hepatocyte transplantation are all potential therapies that may achieve more dietary freedom, or even help patients to go off diet completely, by increasing Phe tolerance.