Dietary Goals and Current Challenges in the Management of Classical Homocystinuria: Insights From Multinational Real-World Experience

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Poster# 9

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RESULTS

Patients

- The dietitians who participated in this expert panel worked with a total of approximately 130 patients at the time of this virtual meeting
- Most patients managed by this expert panel were non-responsive to vitamin B6

Establishing Dietary Management

- General methods for establishing dietary management were similar across dietitians, sites, and countries represented in the panel (**Figure 1**), although each patient received a highly individualized diet
- Dietary management plans varied in terms of vitamins B6, B12, folic acid, and betaine administration
  - Target levels of tHcy and Met were similar across all dietitians
- Frequency, evaluation, and follow-up management for clinic visits for each dietitian had broad similarities (**Figure 2**)

Figure 1. Dietary Management Planning

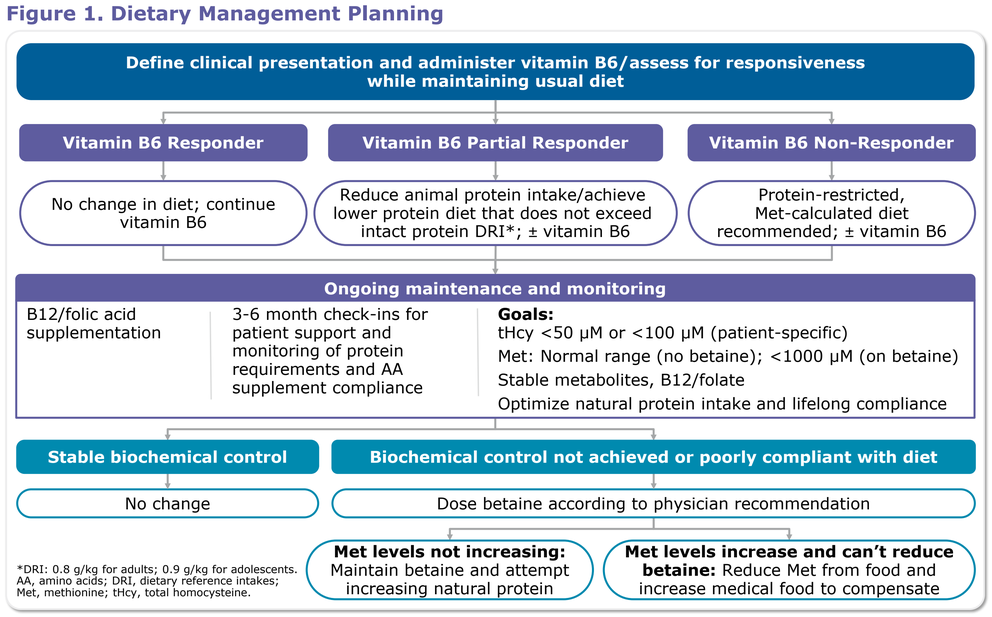


Figure 2. Typical Clinic Visit

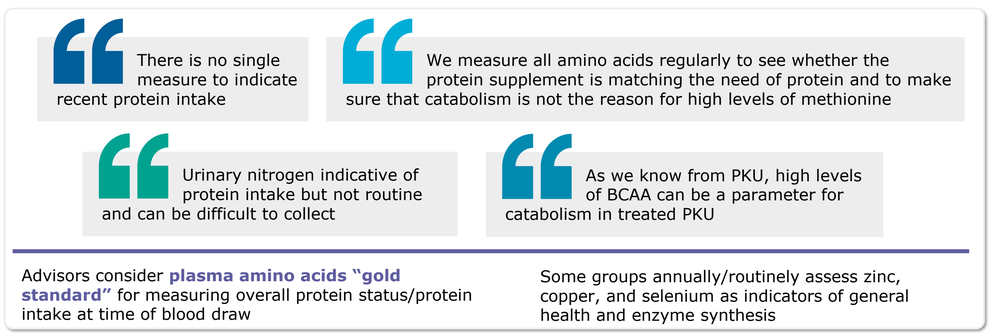
Frequency	Evaluation				Management
	Lab results	**Medications**	**Dietary review**	**Physical exam**	
› Physician and dietitian meet with patient every 3-6 months	› Routine bloods, plasma AA, tHcy, B12, folate, iron, zinc, selenium, magnesium	› Review medication compliance, challenges	› Review protein/Met, calories, compliance, challenges	› Body weight/ composition; developmental, skeletal, ocular, and CV health	› Provide dietary counseling › Review/adjust management goals

AA, amino acids; CV, cardiovascular; Met, methionine; tHcy, total homocysteine.

Dietary Management Assessments

- Dietitians provided their opinions on laboratory markers available to assess nutritional outcomes for patients with HCU (**Figure 3**)

Figure 3. Dietitians' Opinions on Laboratory Markers to Assess Nutritional Outcomes



BCAA, branched chain amino acids; PKU, phenylketonuria.

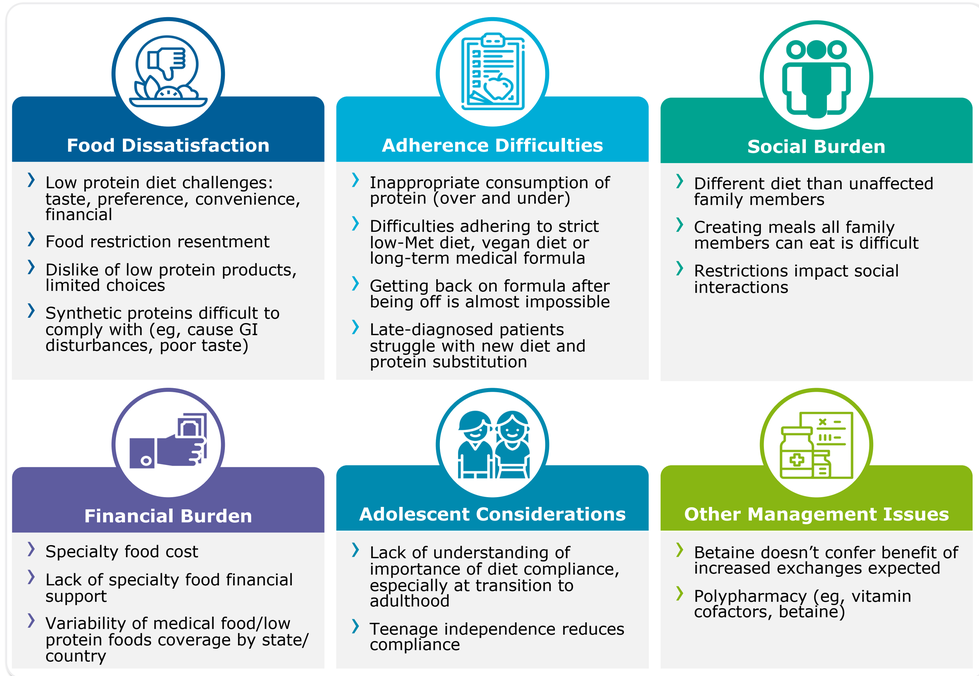
Challenges with Food Tracking and Dietary Compliance

- Dietitians expressed that inaccurate recording of diets was a challenge due to lack of accurate diet recording tools, omission of diet record by patient/family, and/or lack of detail or genuine reporting
  - Sufficient support to provide records should be provided to patients (eg, reminders, phone calls, coaching)
  - Provision of guidance/equipment for food measurement may be helpful
  - New tools/apps could enhance data collection (**Table 1**)
- Numerous challenges with and impact of dietary management compliance were identified (**Figures 4, 5**)

Table 1. Tools and Resources Available to Help Track Patients' Protein Intake

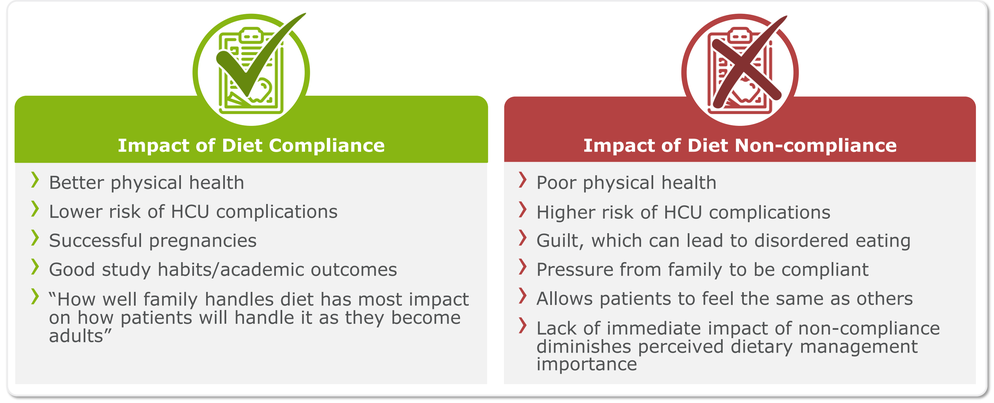
Tools and Resources to Track Protein Intake	
› 24-hour recalls	› Information from caregiver
› Food diaries/tracking apps	› Nutritional information from food companies
› Food photographs and weight	› Analysis packages (eg, MetabolicPro in US; Prodi in Germany; Nutritics in UK and Ireland)
› Food Frequency Questionnaire (FFQ; adapted from other diseases)	› Resources such as working groups for pediatric dietitians (eg, ADP, Germany)

Figure 4. Challenges with Dietary Management in HCU



GI, gastrointestinal.

Figure 5. Impact of Dietary Compliance and Non-compliance



CONCLUSIONS

- Despite geographic and cultural differences, there were broad similarities in dietary management in HCU
- Dietitians experienced in treating patients with HCU agreed on the importance of restricting methionine while providing a personalized diet for patients with HCU
- Despite intensive dietary management, patients frequently had poor adherence with a methionine-restricted diet
- Improved tracking/testing tools, more palatable medical and low-protein foods, financial coverage of medical food, and low-protein food options may improve adherence and outcomes in patients with HCU
- Continued exploration of improved treatments would be beneficial for patients

DISCLOSURES

CB: Paid consultant for Travere Therapeutics, Inc. **FG:** Employee and stockholder of Travere Therapeutics. **DG:** Paid consultant for Travere Therapeutics, Inc. **AH:** Paid consultant for Travere Therapeutics, Inc. **AJ:** Paid consultant for Travere Therapeutics, Inc. **JM:** Paid consultant for Travere Therapeutics, Inc. **MS-M:** Paid consultant for Travere Therapeutics, Inc. **SH:** Paid consultant for Travere Therapeutics, Inc. and receives salary support from Travere Therapeutics, Inc.-sponsored research.

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INTRODUCTION

- Homocystinuria (HCU) is a slowly progressive genetic disease due to mutations in the cystathionine β-synthase (CBS) gene, which leads to elevated homocysteine in the body[1]
- HCU leads to complications in the eye, skeleton, brain, and vasculature[1]
- Current standard-of-care includes protein-restricted diet (±formula), betaine, and vitamin B6 when appropriate[2]
- Current guidelines recommend keeping total homocysteine (tHcy) levels below 100 µM[2]; despite treatment, many patients are unable to achieve this threshold
- Objectives of this expert panel were to obtain insights on:
  - Dietary management of HCU across different treatment centers
  - Challenges associated with dietary management (for both dietitians and patients)
  - Definitions of successful dietary management outcomes

METHODS

- Eight metabolic dietitians who manage patients with HCU from four countries (USA, UK, Ireland, Germany) met virtually to discuss real-world treatment practices and challenges for HCU dietitians and patients
  - Dietitians received open-ended questions regarding items such as clinical characteristics of patients, specific practices used during treatment, challenges related to diet, and definitions of successful dietary management outcomes
  - Experts were encouraged to answer questions in their own words and answers were transcribed and grouped by topic
- Six of the eight dietitians participated in follow-up discussions for additional insights

DEFINING SUCCESS

Successful Dietary Management Outcomes and Compliance

- Dietitians use biochemical markers and diet components to define an optimized diet as well as compliance
  - A **stabilized diet** would maintain tHcy, methionine (Met), B12, folate, and amino acid (AA) levels in acceptable target ranges; in contrast, most patients do not have stable tHcy levels
  - **Variations in laboratory markers** can occur due to illness, changes in routine, and in fasting versus fed states
- Compliance was defined as a flexible term, but with an ultimate aim of minimizing risk in an achievable way
  - **Consistent compliance** is cumbersome, burdensome, and difficult to achieve; it requires patient understanding and acceptance of the importance of dietary restrictions
  - Many dietitians felt most patients have either moderate-good or moderate-poor control, but do not fluctuate between good and poor control
  - A **fully optimized diet** would be one in which the patient can have a good variety of foods, enjoy what they are eating, eat outside their home, and have good biochemical control of tHcy and Met

Successful Drug Response

- Limited side effects
- Normal Met levels, without Met deficiency
- Ability to increase natural protein intake and decrease synthetic protein after metabolic targets are reached
- Most felt natural protein could be added once patients reached tHcy <50 µM, with 1 advisor indicating a threshold of <80 µM and 2 advisors indicating a threshold of <100 µM
- "Free" patients from close diet surveillance
- With current dietary management, it is often not possible to reduce tHcy levels without reducing Met to potentially dangerous levels, thereby indicating the need for new management alternatives

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