Understanding the Burden of Classical Homocystinuria (HCU) From the Patient's Perspective: A Qualitative Study

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RESULTS

- Eleven adult patients, 7 caregivers of pediatric patients, and 2 pediatric patients participated in the concept elicitation interviews (**Table 1**)
- Most participants were female and White. The majority of pediatric patients were diagnosed with newborn screening where most adult patients were not. Almost half the adult patients and the majority of the pediatric patients were non-responsive to B6.

Table 1. Participant Characteristics

Characteristics	Adult patients (n=11)	Caregivers of pediatric patients (n=7)		Pediatric patients (n=2)
		Caregiver	Children cared for	
Age in years, Median (Range)	33 (24–65)	41 (37–50)	9 (5–17)	14 (13–15)
Gender, Female, n (%)	8 (72.7)	6 (85.7)	5 (71.4)	0
Race[a], n (%)				
White	7 (63.6)	7 (100.0)	7 (100.0)	2 (100.0)
Black | African American	2 (18.2)	0	0	0
Asian	2 (18.2)	0	0	0
Other	2 (18.2)	0	0	1 (50.0)
Age at diagnosis, Median (Range)	5.0 (0–54)	n/a	0.0 (0–12)	2.0 (0–4)
Diagnosed through newborn screening program, n (%)	4 (36.4)	n/a	4 (57.1)	1 (50.0)
Vitamin B6-responsiveness, n (%)				
Responsive	5 (45.5)	n/a	2 (28.6)	0
Non-responsive	5 (45.5)	n/a	4 (57.1)	2 (100.0)
Not sure	1 (9.1)	n/a	1 (14.3)	0
Perceived HCU severity today, n (%)				
Mild	3 (27.3)	n/a	3 (42.9)	0
Moderate	6 (54.5)	n/a	2 (28.6)	2 (100.0)
Severe	2 (18.2)	n/a	1 (14.3)	0
Very Severe	0	n/a	1 (14.3)	0

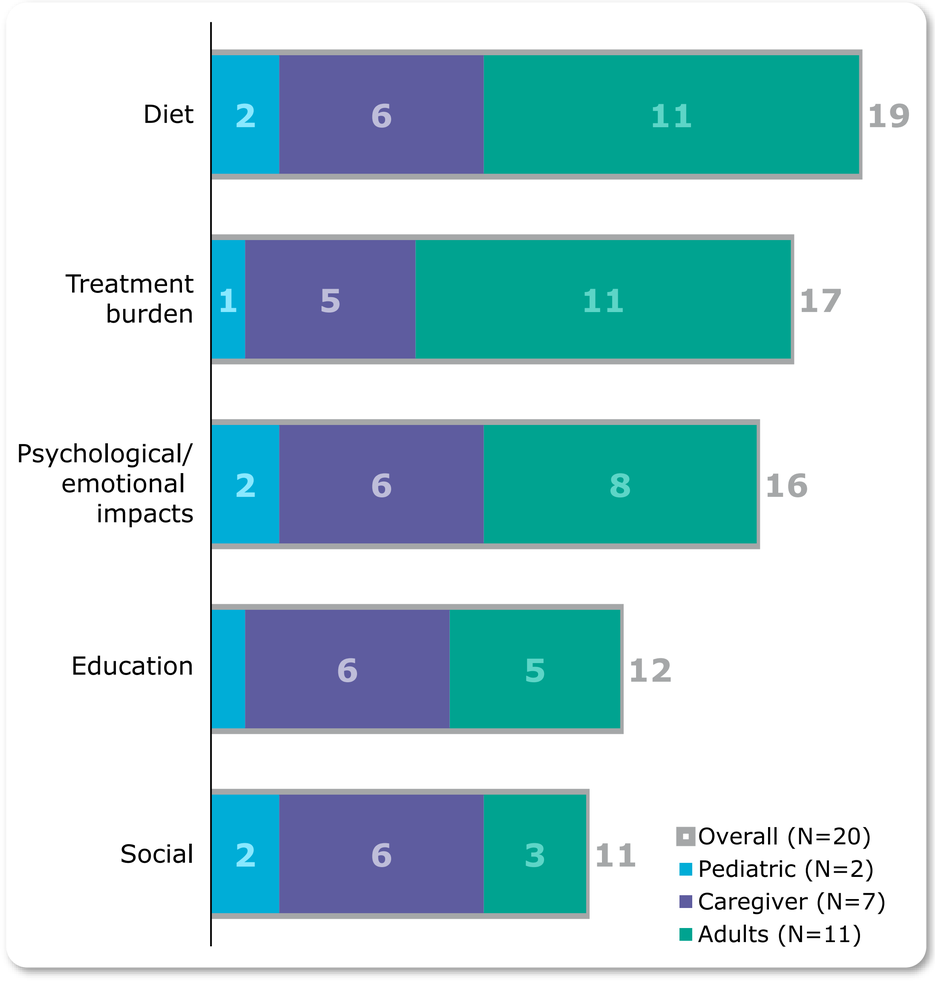
[a]Not mutually exclusive.
HCU, classical homocystinuria.

Impacts of HCU

- Diet/treatment-related impacts were most frequently reported as most bothersome, followed by psychological/emotional impacts, and educational/social impacts. Adherence to a strict low protein diet was a key challenge for 95% of patients due to limited food options, feeling hungry constantly, and coping with the foul-tasting and expensive formula (**Figure 1**).
- Psychological impacts (eg, anxiety, depression, and frustration) were often attributed to concerns about diet management and worsening HCU symptoms
- Most pediatric patients and caregivers reported social and educational impacts, such as difficulty finding words or struggling at school due to brain fog and learning difficulties
- Eyesight and skeletal problems and limited stamina impacted daily activities of 15% of participants and physical activities of 30% of participants

> "It's a huge impact. […] the stress about it is the fact that everything that you put in to that one salad, even if it's vegetables […] ends up being like, that one meal puts you out for your entire day's worth of grams of protein, the allotted allowable amounts. Then you're sitting there, well, I'm still hungry, but I cannot eat any more food." — *Adult 1*

Figure 1. Impacts of HCU

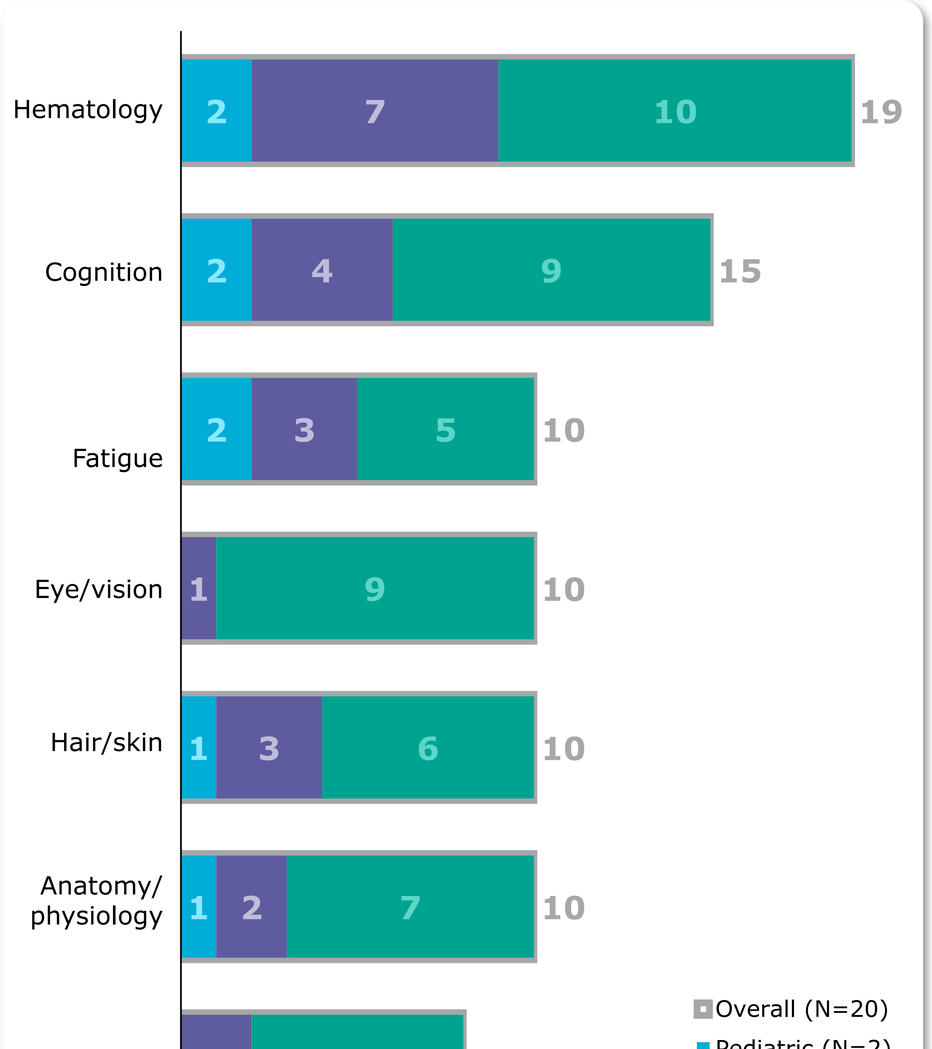


Signs and Symptoms of HCU

- The most frequently endorsed signs and symptoms of HCU were related to hematology, cognition, fatigue, eye/vision issues, hair and skin problems, or abnormal anatomy and physiology (**Figure 2**)
- Hematology reports included needing to monitor their homocysteine levels, managing their levels with adherence to treatment, and reports of levels related to impacts on speech and cognition
- Cognition-related symptoms and fatigue were most frequently reported as among the most bothersome symptoms, followed by eye issues and hair and skin symptoms
- Most adult and pediatric patients experienced cognitive symptoms, and participants across all groups considered these bothersome. Reports of "brain fog", learning disabilities, difficulty focusing, memory difficulties, and difficulties processing information were reported.
- Almost all adult patients reported eye symptoms, and several considered these to be among the most bothersome

> The most bothersome is the anxiety, just worrying about medical things. […] It's just the thought that my heart isn't working properly or that I'm going to have a stroke or some of this because I'm aware of what can happen right here if not treated. — *Adult 3*

Figure 2. Signs and Symptoms of HCU



> Having to live […] with a very restricted diet and having to drink a terrible formula that's disgusting. I mean really that's the biggest impact that I have. — *Caregiver 1*

> [My parents] were having to spend $2000 per month to keep the medication that I needed. They were making payments on that after I had moved out of the house and gone to college and gotten a job. — *Adult 2*

> If they could have a less restricted diet, that would be amazing. […] they could just fit in more with their peers and eat food a lot more similar to what they're eating and have options at a restaurant besides French fries. […]. So that they could enjoy being a kid. — *Caregiver 2*

> If they [homocysteine levels] are high, my speech is not clear. I can't think as clearly. Everything's very cloudy. — *Pediatric 1*

> The more elevated [my homocysteine levels] are, the thicker, I would say the brain fog is. The two I would say to go hand in hand. […] could just be acting on something like autopilot and kind of like a disassociating. — *Adult 4*

Meaningful Desired Changes from New HCU Treatment

Most patients and caregivers desired a treatment that would allow them to take less formula and have a more relaxed diet (n=7 adult patients, 3 caregivers, 1 pediatric patient). Many reported that making the diet more manageable would be a meaningful change and make a difference in their everyday life.

CONCLUSIONS

- ✓ Qualitative interviews with adult patients, pediatric patients, and caregivers elicited in-depth descriptions of how patients with HCU are affected and burdened by various aspects of their disease experience
- ✓ Patients were generally most bothered by restrictions and burdens of the low-protein diet, treatments, cognitive symptoms, and the psychological and emotional impacts of HCU
- ✓ Patients desired more manageable dietary treatments and felt that diet-related changes would meaningfully improve their lives

DISCLOSURES
DB: employed by HCU Network America and has received research grant support and/or speaker/consultancy fees from Travere Therapeutics, Inc. **RP**: employee of Evidera, part of PPD clinical research business, Thermo Fisher Scientific, which received funding from Travere Therapeutics, Inc. **CC**: employee of Evidera, part of PPD clinical research business, Thermo Fisher Scientific, which received funding from Travere Therapeutics, Inc. **KM**: employee and stockholder of Travere Therapeutics, Inc. **LP**: employee and stockholder of Travere Therapeutics, Inc.

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INTRODUCTION

- Classical homocystinuria (HCU) is a rare genetic disorder characterized by the inability to process homocysteine[1]
- Untreated HCU can lead to multi-system complications including blood clots, cognitive impairment, and eye and skeletal abnormalities[1]
- HCU is managed with a low-protein diet and special medical formula supplementation,[2] but 80% of patients have difficulty adhering to the restrictive diet and only 50% consistently take their formula due to poor taste, expense, and supply issues[3]
- Very few studies have explored how individual patients individually experience different aspects of HCU[3]

Aim

- To better understand the signs and symptoms of classical HCU directly from patients or their caregivers and hear how the restrictive diet and treatments have impact on day-to-day psychological, emotional, and social areas of life

METHODS

- Twenty US-based adult patients, pediatric patients aged 12–17 years, and caregivers of pediatric patients aged 5–17 years participated in concept elicitation interviews
- One-on-one, semi-structured, 90-minute concept elicitation interviews were conducted via telephone or web-based conferencing. Interview guides were informed by a targeted literature review and input from patient and clinician experts.
- Participants were asked open-ended questions about symptoms and impacts related to their (or their child's) HCU. Interviewers then probed further about the symptoms and impacts reported and asked probing questions about symptoms and impacts not spontaneously mentioned.
- Participants were asked to identify the three symptoms and impacts that bothered them (or their child) most, and what they would want to change with a new treatment for HCU
- Interview transcripts were analyzed following a thematic approach[4] using ATLAS.ti v9.8
- Qualitative results were quantified by whether participants endorsed (ie, experienced) or did not endorse (ie, did not experience) each issue

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