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Summary

- Hyperphagia is a salient feature in patients with Bardet-Biedl syndrome (BBS) and places a substantial and multifaceted burden on the lives of patients and their caregivers including their physical and mental health, productivity, and social relationships

Introduction

- The melanocortin-4 receptor pathway is implicated in BBS, a rare genetic obesity syndrome, whereby patients present with hyperphagia¹ and early-onset, severe obesity^{1,2}
- Hyperphagia and obesity substantially negatively impact the quality of life of those living with BBS, as well as their families^{3,4}
- The extent and severity of the burden of hyperphagia and obesity have not been well characterized in patients with BBS and their caregivers and are likely under-recognized²

Objective

- To quantify the physical, emotional, and productivity-related impacts of hyperphagia and obesity in patients living with BBS and their caregivers

Methods

- CARE-BBS was a multicountry survey conducted in the US, UK, Germany, and Canada with adult caregivers of patients with BBS
- Eligible participants must have been a caregiver for ≥6 months of a patient with BBS who had obesity or weight ≥95th percentile and uncontrollable hunger (hyperphagia)
- Caregiver-reported outcome measures were used to assess the burden of hyperphagia and obesity among patients and caregivers
 - Symptoms of Hyperphagia*: Caregiver version
 - A 5-item questionnaire to assess the frequency of hunger symptoms observed by the caregiver in the person in their care
 - 3-point scale includes the responses "never," "1 or 2 times," and "3 or more times" over the past 24 hours
 - Calculated as a total score across 5 items, with higher scores indicating more severe hyperphagia
 - Impacts of Hyperphagia*: Caregiver version
 - An instrument with 2 sections: 1 section with 5 items for caregiver proxies of the patient experience, 5-item section for caregiver self-report
 - 4-point scale includes responses ranging from "not at all" to "a great deal" over the past 7 days
 - Scored separately for patient-proxy impact and caregiver impact, with higher scores indicating greater negative impact of hyperphagia
 - Impact of Weight on Quality of Life (IWQOL)-Kids[†]: parent proxy⁵
 - A 27-item parent proxy questionnaire assessing health-related quality of life (HRQL) in patients across 4 domains including physical comfort, body esteem, social life, and family relations
 - Total score ranges from 0 to 100, with higher scores representing better HRQL
- Descriptive analyses were performed with mean, median, and standard deviation (SD) reported for continuous variables; counts and percentages were determined for binary and categorical variables
- Validated instruments were scored according to respective standardized methods
- Data were pooled across countries

Results

Participant Demographics

- There were 242 caregivers of patients with BBS who met the eligibility criteria and completed the survey; Table 1 shows the demographics for caregivers and patients with BBS
- Caregivers were predominantly male (54.1%), fathers (51.7%), and not the sole caretaker of the person with BBS (82.2%)
- Uncontrollable hunger contributed to BBS diagnosis in 230 of 242 patients (95%)

Table 1. Participant Demographics and Characteristics

	Value
Caregivers (N=242)	
Caregiver age, mean (SD), y	41.9 (6.7)
Male, n (%)	131 (54.1)
Female, n (%)	111 (45.9)
Relationship to person with BBS, n (%)	
Mother	101 (41.7)
Father	125 (51.7)
Other	16 (6.6)
Sole caretaker of person with BBS, n (%)	43 (17.8)
Patients with BBS (N=242)	
Age, mean (SD), y	12 (3.7)
Male, n (%)	131 (64.0)
Female, n (%)	111 (40.0)
Hyperphagia contributed to diagnosis of BBS, n (%)	230 (95)
Modified BMI Z score, mean (SD)	4.1 (4.5)
Obesity classification categories,* n (%)	
Overweight	27 (12.1)
Class I	74 (33.0)
Class II	43 (19.2)
Class III	80 (35.7)

*Obesity classes were defined as overweight, 85th to <95th percentile; obesity class I, 95th percentile to <120% of 95th percentile; obesity class II, 120% to <140% of the 95th percentile; obesity class III, ≥140% of the 95th percentile. Characteristics and demographics were similar across countries. BBS, Bardet-Biedl syndrome; BMI, body mass index; SD, standard deviation.

Impacts of Hyperphagia and Obesity

- The majority of caregivers reported observing hyperphagic behaviors multiple times a day (Figure 1)
- Negotiating for food (89.6%) and waking for food during the night (88.4%) were the most frequently reported behaviors
- Caregivers reported patients with BBS, on average, eat approximately twice as many meals (mean [SD], 6.4 [1.5]) as the other members of the household (3.2 [0.6])

Figure 1. Symptoms of Hyperphagia* questionnaire results: signs and behaviors of hyperphagia.

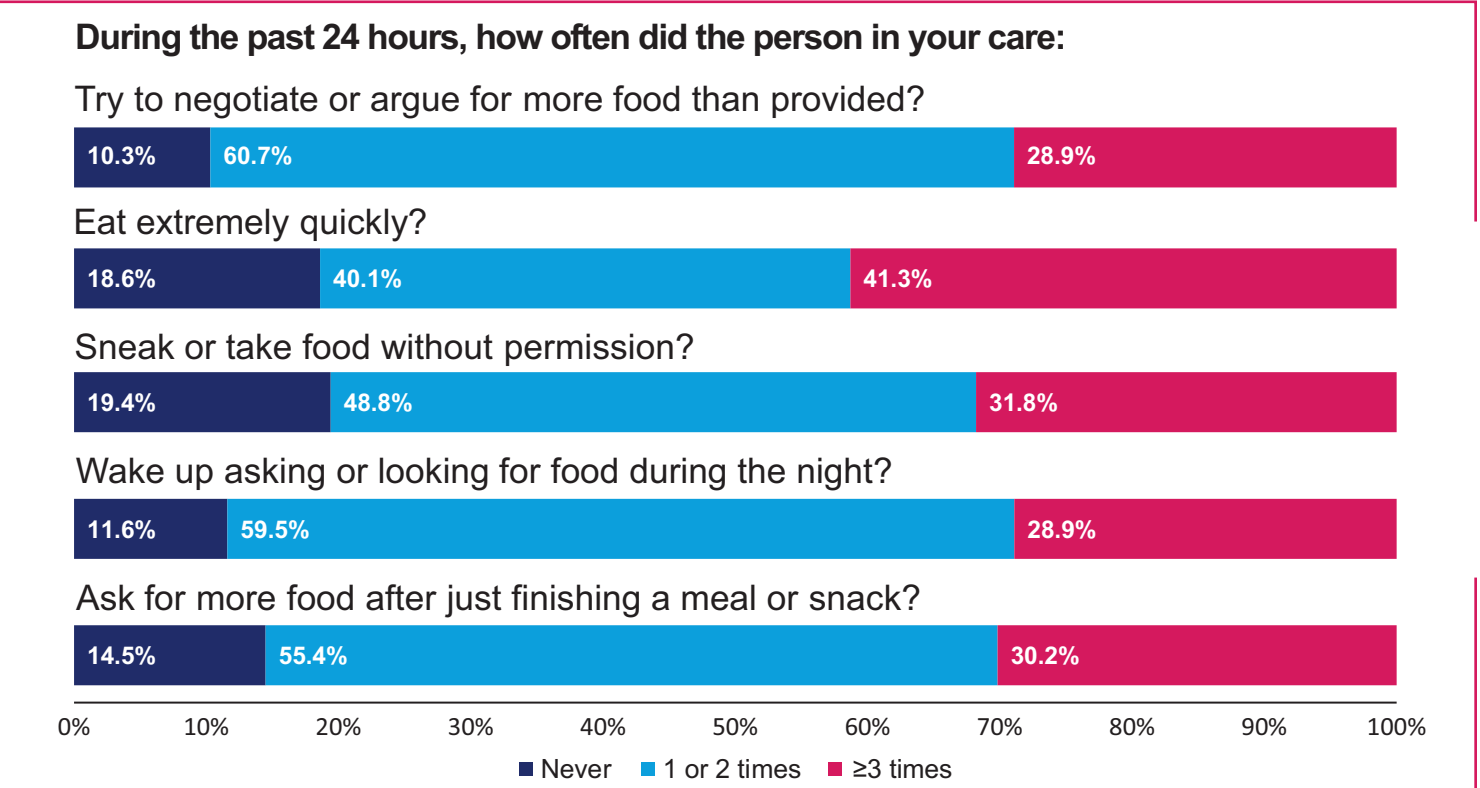
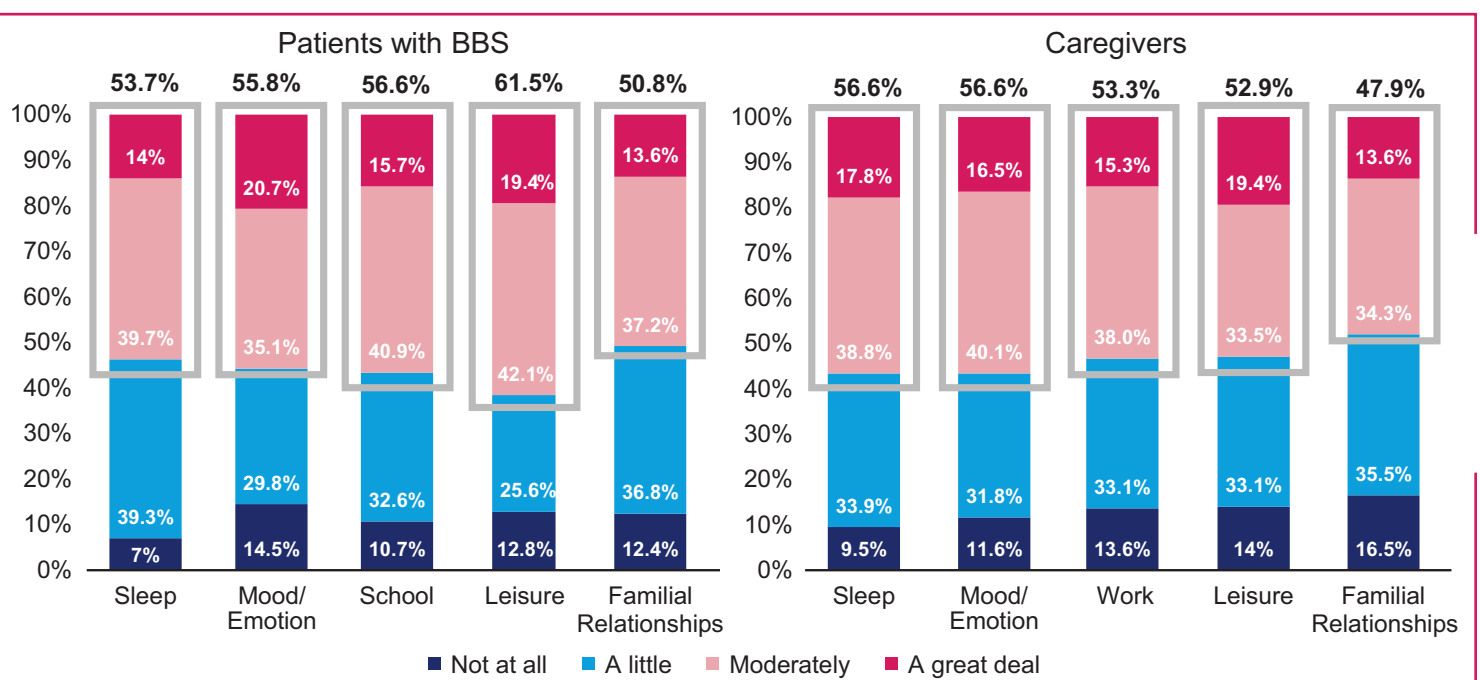


Table 2. IWQOL-Kids[†] (Parent Proxy): Impacts of Weight on Quality of Life of Patients

	Score, mean (SD)
Overall	44.2 (17.0)
Physical comfort	41.9 (17.5)
Body esteem	40.9 (18.3)
Social life	41.7 (18.1)
Familial relationships	53.8 (25.7)

Scores reported are caregiver responses from IWQOL-Kids and range from 0 to 100, with higher scores indicating better quality of life. IWQOL-Kids, Impact of Weight on Quality of Life-Kids; SD, standard deviation.

Figure 2. Impacts of Hyperphagia* questionnaire results among patients with BBS and caregivers.



Gray boxes and respective percentages indicate cumulative responses for those who were at least moderately affected by hyperphagia. Results are over the past 7 days. BBS, Bardet-Biedl syndrome.

- Hyperphagia caused difficulty concentrating at school in 97.7% of the total number of school-aged children with BBS (n=177)
- Symptoms associated with BBS caused 82.3% of children (n=181) to miss ≥1 day of school a week
- Responses from the IWQOL-Kids[†] highlight substantial weight-related impacts on quality of life, with body esteem, social life, and physical comfort reported as being the most impacted (Table 2)
- On the Impacts of Hyperphagia* questionnaire, hyperphagia had a moderate-to-severe negative impact on most patients with BBS across all domains (Figure 2)
- Caregivers similarly reported hyperphagia to have negatively affected their own mood/emotion, work, and leisure and recreational activities

Conclusions

- The substantial, multifaceted, negative impact of hyperphagia is evident throughout the lives of patients with BBS and their caregivers, extending beyond their physical health to their emotional well-being, work or school performance, and personal relationships
- The impact of obesity on quality of life reported in this population of patients with obesity due to BBS is greater than that reported for children with general obesity⁶
- This research furthers the evidence of the burden of hyperphagia and obesity through quantification of its extent and severity
- Quantifying the burden of hyperphagia and obesity in BBS demonstrates the need and use for interventions that can treat the symptoms of these health conditions and improve the lives of patients and their caregivers

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