

Hyperphagia severity in adult patients with Bardet-Biedl syndrome – a mixed-methods cross-sectional study in the United Kingdom

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Background

- Bardet-Biedl syndrome (BBS) is a rare genetic disease caused by primary ciliary dysfunction, leading to retinal degeneration, rod-cone dystrophy, polydactyly, renal dysfunction, hypogonadism, and neurodevelopmental/neurocognitive manifestations¹
- Impaired cilia function may also disrupt melanocortin-4 receptor (MC4R) pathway signalling, leading to hyperphagia and early-onset obesity¹
- Hyperphagia, a pathological insatiable hunger leading to excessive and unusual food intake and persistent, obsessive food-seeking behaviours, is a prominent and frequent symptom associated with BBS, substantially impacting quality of life¹⁻⁴
- Quantifying the severity of hyperphagia in individuals with BBS remains challenging due to the limited availability of assessment tools

Objectives

- To assess the level of hyperphagia severity in adults with BBS and obesity living in the UK using an exploratory mixed-methods approach

Methods

- This sub-analysis of a non-interventional, cross-sectional study included 39 adults with BBS and obesity
- Participants were excluded if they were currently prescribed or had previously taken setmelanotide or if they had a BMI <30 kg/m²
- Participants completed a 14-item hyperphagia questionnaire⁵ combining multiple-choice and open-ended questions, with each item score ranging 1–4 (scan QR code to view questionnaire and interview questions in the supplementary information); a subset participated in follow-up semi-structured, expert-led interviews
- Interview transcripts were systematically coded by a qualitative researcher and jointly reviewed with a BBS clinical expert to assign severity ratings. Interviews were designed to contextualise and overcome known limitations of self-reporting in this population, including the disability paradox, stigma, and cognitive difficulties

Results

- A total of 39 adults completed the questionnaire and 13 completed the semi-structured, expert-led, interviews
- Participants were 41.0% male, 56.4% were aged 18–34 years, 82.1% were of White ethnicity and had a mean (SD) age at diagnosis of BBS of 8.7 (8.1) years, summarised in **Table 1**

Table 1: Demographics of adults with BBS and obesity*

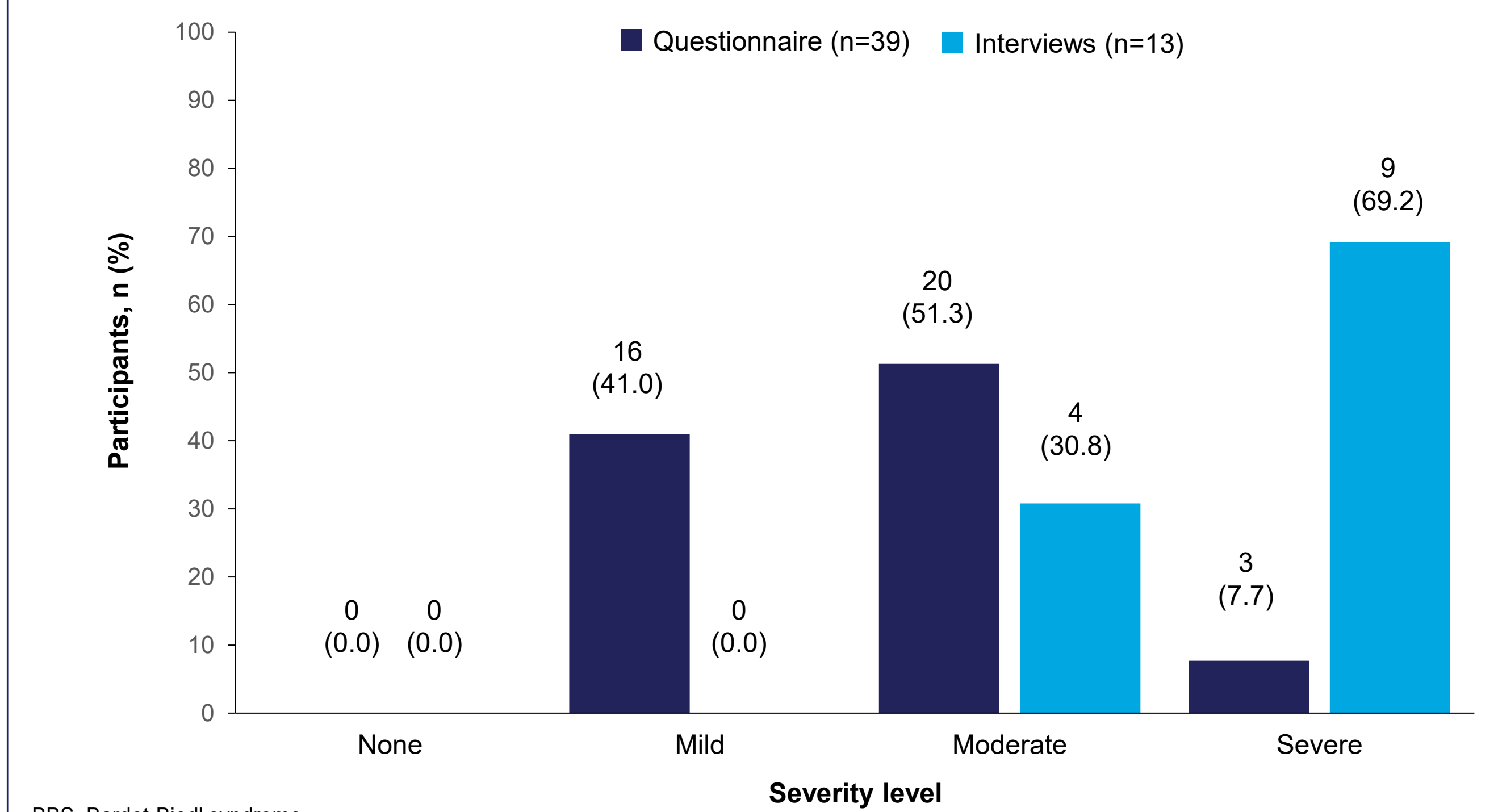
	Participants (n=39)
Sex, male, n (%)	16 (41.0)
Ethnicity, White, n (%)	32 (82.1)
Age at BBS diagnosis, years, mean (SD)	8.7 (8.1)
Age at time of study, n (%)	
18–24	12 (30.8)
25–34	10 (25.6)
35–44	7 (17.9)
45–54	4 (10.3)
55–64	5 (12.8)
≥65	0 (0.0)
Not specified	1 (2.6)
BMI at time of study, kg/m², mean (SD)	40.0 (7.0)

*Obesity defined as BMI ≥30 kg/m². BBS, Bardet-Biedl syndrome; BMI, body mass index; SD, standard deviation.

Results (continued)

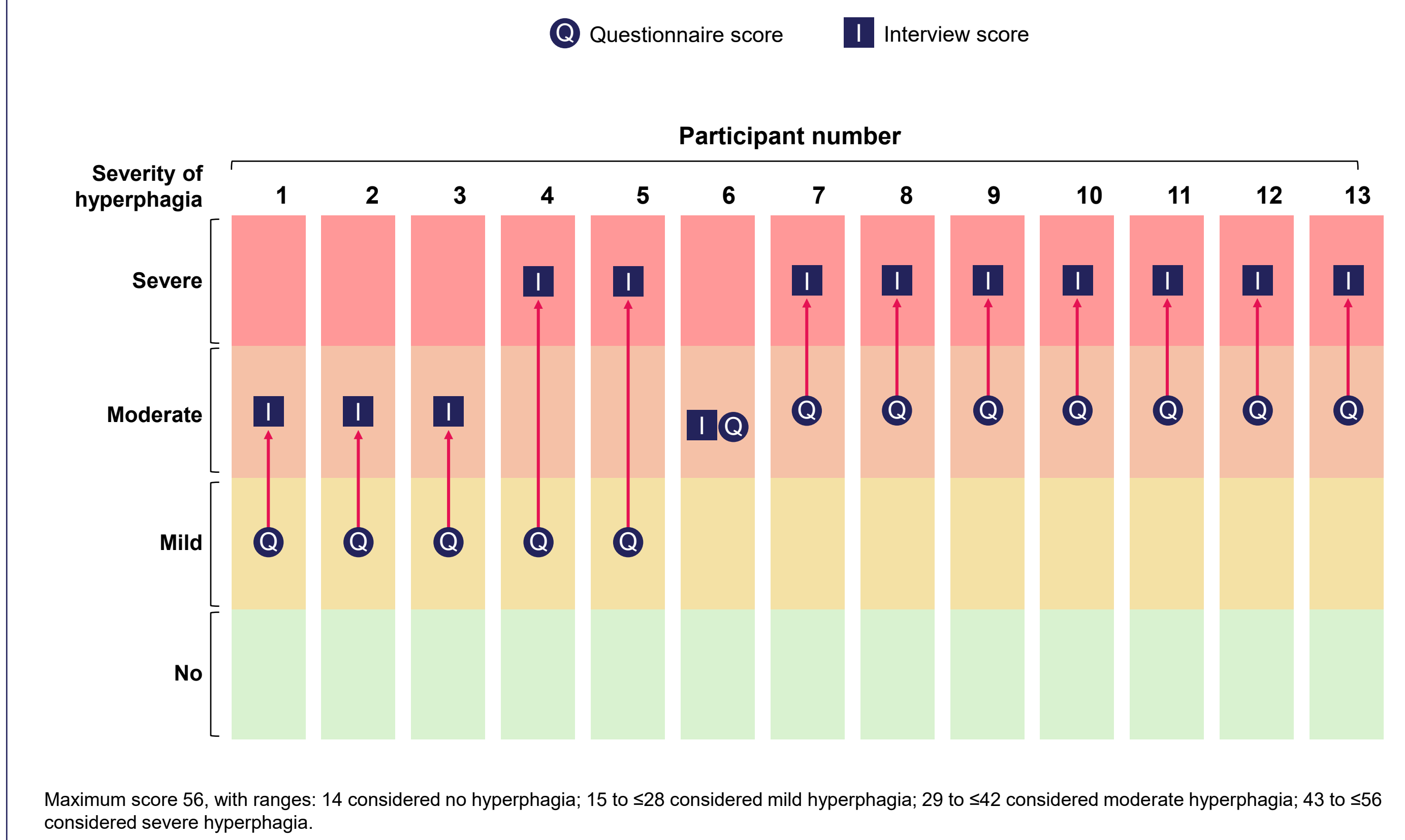
- Questionnaire data classified 7.7% of participants as having severe hyperphagia, whereas semi-structured, expert-led interviews classified 69.2% of participants as having severe hyperphagia (**Figure 1**)

Figure 1: Hyperphagia severity level questionnaire and interview analyses (n=39) of adults with BBS and obesity



- Among the 13 participants who completed both assessments, interviews systematically assigned a higher hyperphagia severity level than questionnaires (**Figure 2**)
- Notably, 92.3% (12/13) classified a higher severity level by interview compared with only 1 participant showing the same severity classification across both methods

Figure 2: Difference between self-reported questionnaire and semi-structured interview scores



Conclusions

- BBS is a rare disease, and as this was a single-country study, with a relatively small sample size, the results may not be generalisable to the wider BBS population. Future, larger studies should be conducted to replicate and validate our findings
- Semi-structured interviews suggest a high prevalence of severe hyperphagia in adults with BBS and obesity in the UK, while reliance on self-reported questionnaires alone may lead to underreporting of hyperphagia severity in this population
- To ensure a more valid and clinically meaningful assessment, we recommend incorporating semi-structured interviews reviewed by a BBS expert, which may improve both the diagnosis and management of hyperphagia in adults with BBS

Disclosures: PLB has participated on an Advisory Board for BBS UK; has participated in a webinar and symposium hosted by Rhythm Pharmaceuticals, Inc.; and serves as CEO of Axovia Therapeutics, a BBS-focused gene therapy company. JM has no conflicts of interest to disclose. SF has participated in the following events supported by Rhythm Pharmaceuticals, Inc.: the BBS Launch Meeting, an advisory board/BBS roundtable meeting, and the BBS Summit meeting. EG and EL are employees of Eric Low Consulting Ltd, East Lothian, UK, contracted by Rhythm Pharmaceuticals, Inc. NT is an employee of Rhythm Pharmaceuticals, Inc. and may hold stock and options in Rhythm Pharmaceuticals, Inc.

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