Recognising the burden of acquired hypothalamic obesity in patients with craniopharyngioma: cross-country insights from lived experiences to support integrated care across all life stages

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Introduction

- Acquired hypothalamic obesity (aHO) is a rare complex disease, resulting from physical injury or structural abnormality of the hypothalamus[1,2]
  - An acquired injury to, or structural abnormality within the hypothalamic region, may disrupt melanocortin-4 receptor (MC4R) pathway signalling, which can lead to hyperphagia (pathological, insatiable hunger), decreased energy expenditure and accelerated and sustained weight gain[1]
- Craniopharyngioma (CP), which typically presents during childhood, is an embryonic malformational tumour of the pituitary region and a leading cause of aHO. Hypothalamic injury related to the tumour and/or its treatment contributes to secondary chronic disease burden[3]
  - aHO can cause physical and psychological complications, resulting in a reduction in quality of life (QoL) for both patients and caregivers, with inadequate transition to adult care further increasing this burden[4]

Objectives

- This qualitative study aims to highlight the persistent and under-recognised health burden of aHO across life stages, drawing on the experiences of patients with CP from the Netherlands, Germany, and the UK

Methods

- A mixed-methods approach was employed, combining online and in-person interviews of patients with a confirmed diagnosis of CP and their family members recruited from dedicated charities/medical centres in the Netherlands (n=12), Germany (n=11), and the UK (n=10)

Results

- Baseline demographics are summarised in **Table 1**. Patients with CP (n=33) were 45.5% male and had a mean (SD) age at diagnosis of 18.3 (17.8) years

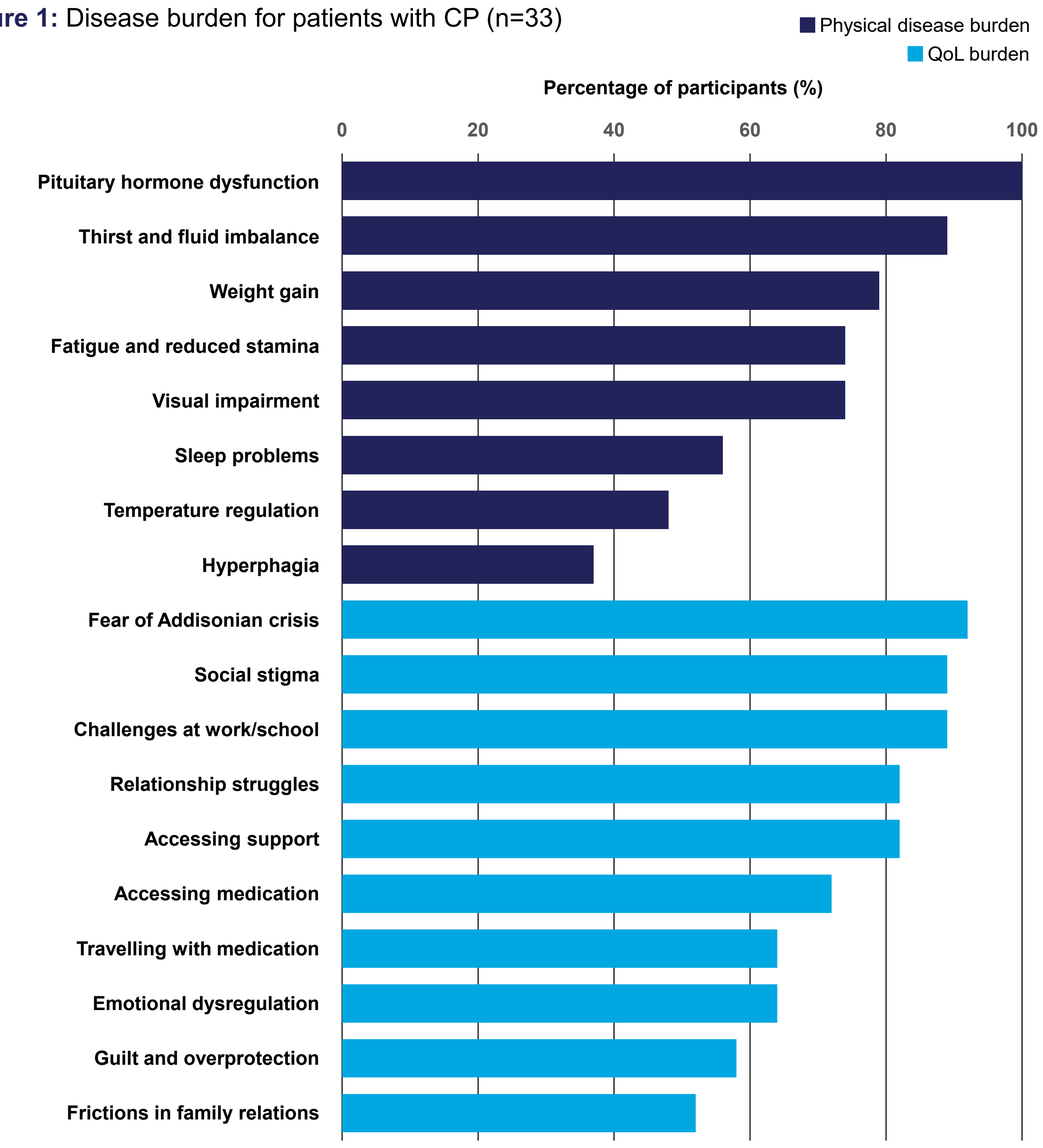
Table 1: Baseline demographics of patients with CP (n=33)

	Patients (n=33)
Sex, male, n (%)	15 (45.5)
Age at initial symptoms, n (%)	
0–11	20 (60.6)
12–18	4 (12.1)
19–30	3 (9.1)
31–40	2 (6.2)
>40	4 (12.1)
Age at diagnosis, years, median (range)	12 (3–62)
Age at time of study, median (range)	35 (7–68)

CP, Craniopharyngioma; SD, standard deviation.

- Key disease symptom burden for CP (**Figure 1**) included pituitary hormone dysfunction (100%), thirst and fluid imbalance (87.9%), and weight gain (78.8%)
- Fear of Addisonian crises (90.9%), social stigma (87.9%), and challenges at work/school (87.9%) were reported as the most frequent QoL challenges associated with CP (**Figure 1**)
- Across all three countries, many of the reported disease symptoms were associated with aHO, such as hyperphagia, fatigue and reduced stamina, and weight gain

Figure 1: Disease burden for patients with CP (n=33)



CP, Craniopharyngioma; QoL, quality of life.

- Despite centralised, structured paediatric care with early tertiary referral pathways, the patient journey uncovered several unmet needs, including the transition to adult care, which was experienced as abrupt, inconsistent, and fragmented **(Table 2)**

Table 2: Patient needs throughout the CP disease journey

	What typically happens	Patient needs at paediatric age	Patient needs at adult age
Pre-diagnosis	• Symptoms like fatigue, weight gain, visual changes, or behavioural shifts emerge but are often misattributed • Delays in diagnosis are common due to rarity and subtle onset • Lack of growth/puberty monitoring	• Recognition of early growth/puberty failure symptoms (by GP or school) • Reassurance and emotional support for parents • Quick referral to paediatric specialists	• Clear communication from GP • Faster diagnosis for unexplained fatigue, weight gain, or vision issues • Psychological validation when symptoms are vague
Diagnosis	• MRI confirms presence of a tumour; patients and families receive the diagnosis • MDT discussions begin, and initial treatment planning starts	• Multidisciplinary explanation of the disease • Support for emotional shock (family and child) • Navigation help (including endocrinology and oncology) through treatment planning	• Multidisciplinary explanation of the disease • Space to process diagnosis and long-term implications • Access to specialist team (endocrine, neuro, visual) • Involvement in care decisions and planning
First treatment	• Surgery (craniotomy or transsphenoidal) and/or radiotherapy is performed • Hormone deficiencies not already present may arise immediately	• Coordination between surgical and endocrine teams • Guidance for parents on medication and recovery • Understanding what comes next • Prepare for thirst, hunger, aHO, puberty, fertility and other challenges • Prepare for long-term self-management	• Timely access to neurosurgery and radiotherapy • Emotional support and informed consent • Early involvement of a case coordinator • Prepare for thirst, hunger, aHO, fertility and other challenges • Prepare for long-term self-management
Continuous monitoring	• Lifelong follow-up with endocrinology, ophthalmology, and imaging • Hormone doses adjusted, symptoms monitored, and daily life is restructured	• Clear schedule and explanation for tests • Ongoing psychological and school support • Parent training for medication and crisis management • Parent support • Support at school, home, sports and maturation	• Regular specialist follow-up • Self-management support tools • MDT support • Addressing fatigue, weight increase, and emotional health • Support with work, home, sports and travel • Partnerships and parenting
Recurrence of CP	• New symptoms or scan findings may indicate regrowth • Treatment restarts, often involving repeat surgery or radiotherapy and emotional strain	• Immediate access to expert teams • Honest communication adapted to age • Support for (parental) anxiety and decision making • Prepare for thirst, hunger, aHO, puberty, fertility and early growth/puberty failure	• Fast diagnostic confirmation and care restart • Managing fear and uncertainty • Peer or psychosocial support options • Prepare for thirst, hunger, aHO and other challenges
Transition to adult care	• Patients move from paediatric to adult teams, often losing integrated MDT support • Gaps in care and knowledge transfer are common • Fertility options often overlooked	• Gradual introduction to adult teams • Joint consultations during transition phase • Emotional preparation for independence • Address family planning and fertility	• Continuity in hormone treatment and monitoring • Access to adult MDT or equivalent • Support in navigating new providers and systems
Elderly care	• Patients face age-related challenges atop existing deficits • Comorbidities, cognitive decline, and simplified medication needs become central	• N/A	• Adjusting care to comorbidities and cognitive decline • Simplified medication routines • Support for caregivers and long-term planning

aHO, acquired hypothalamic obesity; CP, Craniopharyngioma; GP, general practitioner; MDT, multidisciplinary team; N/A, not applicable.

Conclusions

- This qualitative study demonstrates a substantial and lifelong disease burden in CP, with reported symptoms including pituitary hormone deficiencies, thirst and fluid imbalances, and weight gain
- Patients with CP have diverse and evolving physical, medical, and QoL needs across the lifespan, underscoring the need for improved diagnostics and for better communication and support throughout treatment and long-term follow-up
- Long-term management of CP should include bespoke hypothalamic–pituitary specialist care delivered in expert centres, incorporating targeted pharmacotherapy and coordinated multidisciplinary support
- As many reported symptoms are associated with aHO, it emerges as a key long-term neuroendocrine consequence of CP. This underscores the need for aHO to be a central focus of CP management, research, care planning, clinical guidelines, and healthcare resource allocation

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References: **1.** Roth CL, McCormack SE. *Diabetes Obes Metab*. 2024;26 Suppl 2:34–45; **2.** Müller HL, et al. *Nat Rev Dis Primers*. 2019;5(1):75; **3.** Müller HL. *J Neuro-Oncol*. 2025;173:233–244; **4.** De Alcubierre, et al. *Rev Endocr Metab Disord*. 2025;26,989–1008.

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