P1-371

Growth Hormone Deficiency (GHD): Assessing Parent Burden for Child GHD Treatment: the Growth Hormone Deficiency – Parent Treatment Burden Measure (GHD-PTB)

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Introduction

- Children with growth hormone deficiency (GHD) typically have normal body proportions,[1,2] but may look chubbier, be much shorter, and younger for their age compared with most children of the same age and gender.[2]
- Many children with GHD can reach normal height with growth hormone (GH) replacement treatment.[2]
- Treatment requires daily injections, which can be painful and disruptive, and for most children, the injections are administered by an adult, usually their parent.
- Unfortunately, little is known about the burden that a child's GHD treatment places on the parent and no disease-specific measures exist to assess this impact.
  - The Growth Hormone Deficiency – Parent Treatment Burden Measure (GHD-PTB) was developed according to United States (US) Food and Drug Administration/European Medicines Agency guidelines to address this gap.[3–4]
- Items were based on qualitative interviews with 31 parents of children with GHD, aged 4 to less than 13 years, to develop the concepts assessed in the measure.[5] Cognitive debriefing interviews with an additional 13 parents confirmed relevance and readability (comprehension) of items and instructions.
- Psychometric testing was conducted to determine the measurement properties, reliability, validity, and interpretability of the measure.
- This study presents the GHD-PTB psychometric validation results.

Methods

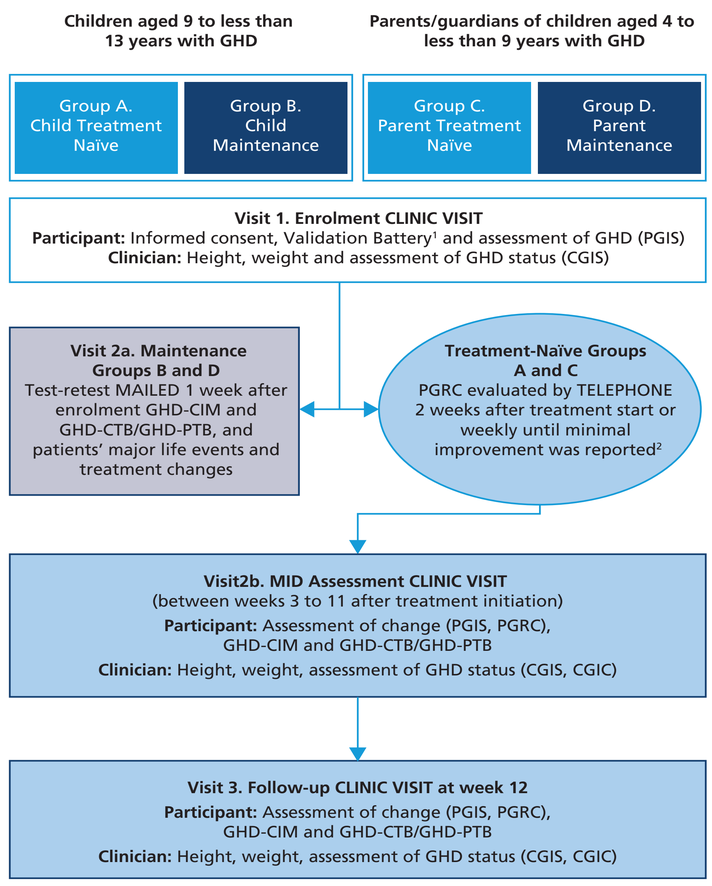
Study design

- A non-interventional, multi-clinic-based study was conducted in the USA and the United Kingdom with pre-pubertal children with GHD and parents/guardians of similar children.
- Psychometric analyses were completed according to an *apriori* statistical analysis plan to determine the Measurement Model, Reliability, validity, responsiveness, and Minimally Important Difference (MID).
- The population recruited for the validation study included pre-pubertal children with a diagnosis of GHD (aged 9 to less than 13 years), and parents/guardians of younger children with a diagnosis with GHD (aged 4 to less than 9 years).
- Each population was divided into a Treatment-Naïve group (Group A or Group C) and Maintenance group (Group B or Group D) for a total of four subgroups and no control group (**Figure 1**).
- The child patients with GHD were treated with commercially available products according to routine clinical practice at the discretion of their treating physician.
- All groups completed a baseline assessment battery in clinic, with in-person follow-up for the Treatment-Naïve group (**Figure 1**).

Statistical analysis plan

- Exploratory factor analysis procedures on the correlation matrices derived from the items comprising the GHD-PTB measures and confirmatory factor analysis to verify the final factor structure derived were performed.
- Items were considered for deletion for reasons of high correlation with other items or total score, floor or ceiling effects, poor fit or conceptual relevance considerations.
- Cronbach's alpha was used to assess internal consistency reliability. A minimum correlation of 0.70 was expected.
- Test-retest reliability was assessed using the intraclass correlation coefficient (ICC) in a subsample from the Maintenance groups who indicated experiencing no change in treatment since their last assessment.

Figure 1 • Overview of study design



1. The GHD-CIM and GHD-CTB/GHD-PTB were completed by the Maintenance Group at the enrolment clinic visit. For the Treatment-Naïve Group, the GHD-CIM was completed at the enrolment visit, and the GHD-CTB/GHD-PTB was taken home to complete 1 week after treatment start and then returned by mail.
2. Telephone assessment of improvement was conducted weekly until minimal improvement was reported. Once reported, their MID assessment clinic visit was scheduled to occur within one week.

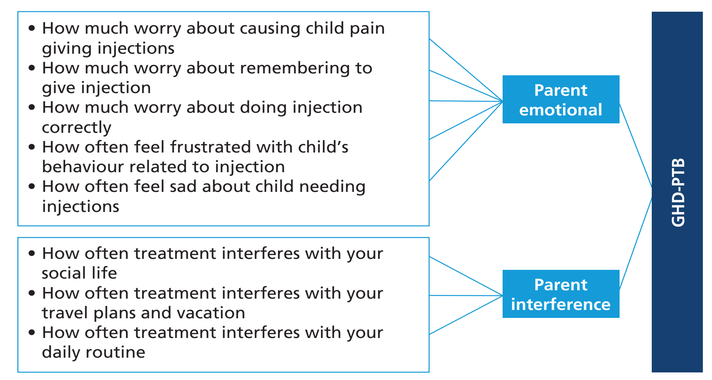
Legend: GHD-CIM, Growth Hormone Deficiency – Child Impact Measure; GHD-CTB, Growth Hormone Deficiency – Child Treatment Burden Measure; GHD-PTB, Growth Hormone Deficiency – Parent Treatment Burden Measure; PGIS, Patient Global Impression of Severity; PGRC, Patient Global Rating of Change; CGIS, Clinician Global Impression of Severity; CGIC, Clinician Global Impression of Change; MID, Minimally Important Difference.

- Convergent construct validity was assessed with Pearson's correlation, between the measure scores and the other items or instruments measuring similar concepts, and supported when the scores were substantially correlated (≥0.40).
- Known-groups validity was also tested for the hypotheses using a two-tailed test at a $p<0.05$ level and was supported when at minimum one hypothesis per subdomain was significant.

Results

- The analytic data included 98 parents (mean age of children 9.2 years and parents 41.6 years), who were predominantly mothers (80.7%), married (88.1%), and worked full-time (51.0%).
- Respondents answered all items using the full range of response options (0-"Not at all/Never" to 4-"Extremely/All of the time") for all items except one (*Child's treatment interferes with social life*), to which no-one responded 4.
- Ceiling effects, responses of "Not at all/Never" (where respondents could not get any better), ranged between 30.5% to 74.9%.
- Factor analyses identified two domains: Interference in Daily Life and Emotional Well-being (**Figure 2**).
- During item reduction, four items were dropped due to high correlations indicating conceptual redundancy resulting in a final GHD-PTB 8-item measure (**Figure 3**).
- For each domain and the Overall score, internal consistency reliability was acceptable (Cronbach's alpha >0.70) as was test-retest for Emotional and Overall (>0.70) and slightly lower than expected for Interference (0.60).
- Convergent validity hypotheses for domains and Overall were proven ($p<0.01$, $r>0.40$).
- Known groups validity hypotheses were proven for the Emotional domain, which discriminated between whether the parent gave the injections more often than the child ($p<0.05$) and the Overall domain ($p=0.5$).
- The length of time their child was on treatment did not discriminate, suggesting that treatment continues to be interfering over time.
- Marked improvements after 12 weeks of treatment were noted for Emotional and Overall domains (16.6 and 8.6 points).
- The Interference domain score had a very small improvement.
- Associated effect sizes were –0.74 (Emotional) and –0.69 (Overall), indicating that the GHD-PTB is sensitive to change at high levels.
- Preliminary recommendation for the MID is 7 points for the Overall, 10 for Emotional Well-Being and 6 for the Interference domains.

Figure 2 • Conceptual Model GHD-PTB



GHD-PTB: Growth Hormone Deficiency – Parent Treatment Burden Measure

Figure 3 • Final GHD-PTB

The following questions are about your **child's growth hormone deficiency (GHD) injections**. **Please think about how your child's treatment affected <u>you personally over the PAST WEEK</u>.**

In the past week, how much did you worry about:	Not at all	A little	Somewhat	A lot	Extremely
1. Causing your child pain when giving the injection	☐	☐	☐	☐	☐
2. Remembering to give the injection	☐	☐	☐	☐	☐
3. Doing the injection correctly	☐	☐	☐	☐	☐
In the past week, how often did you feel:	**Never**	**Rarely**	**Sometimes**	**Often**	**All of the time**
4. Frustrated with your child's behavior related to the injection	☐	☐	☐	☐	☐
5. Sad about your child needing injections	☐	☐	☐	☐	☐
In the past week, how often did your child's treatment interfere with <u>your</u>:	**Never**	**Rarely**	**Sometimes**	**Often**	**All of the time**
6. Social life (for example going out in the evening)	☐	☐	☐	☐	☐
7. Travel plans and vacations	☐	☐	☐	☐	☐
8. Daily routine	☐	☐	☐	☐	☐

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Conclusions

- The GHD-PTB was found to be reliable and valid and is considered ready for inclusion in clinical trials and clinical practice.
- Since parents are often primarily responsible for administering and ensuring compliance of treatment for young children, accurate and reliable assessment of their treatment burden can help researchers and clinicians better assess the broader range of treatment impacts.
- Less frequent treatment requirements may reduce this burden for parents.

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Conflict of interest disclosure

MB and SA are consultants to Novo Nordisk A/S. MHR, KV, and JB are employees of Novo Nordisk A/S.

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