

Growth hormone (GH) dosing patterns in children with isolated GH deficiency and multiple pituitary hormone deficiency enrolled in the NordiNet[®] International Outcome Study

- Marta Šnajderová**
Charles University and University Hospital Motol, Prague, Czech Republic
- Effie Pournara**
Novo Nordisk Health Care AG, Zurich, Switzerland
- Birgitte Tønnes Pedersen**
Novo Nordisk A/S, Søborg, Denmark
- Oliver Blankenstein**
Charité-University Medicine Berlin, Berlin, Germany

Disclosure statement:

MS and OB are members of the NordiNet[®] International Outcome Study Committee. EP and BTP are employees of Novo Nordisk.

Introduction

- Growth hormone deficiency (GHD) may be either isolated growth hormone deficiency (IGHD) or included in multiple pituitary hormone deficiency (MPHD) where levels of other pituitary hormones are also decreased or absent.
- Current treatment guidelines for patients with IGHD or MPHD¹ recommend treatment with growth hormone (GH) at least until completion of linear growth.
- To guide treatment optimisation for patients with IGHD and MPHD, it is important to monitor GH treatment in clinical practice, where treatment and outcomes may vary from randomised controlled trials.
- Data from observational studies support the benefits of GH treatment; after 2 years, height gains in patients with IGHD or MPHD are similar^{2,3} and 75% achieve final height within their target height range.³
- The NordiNet[®] International Outcome Study (IOS) captures data on patients treated with GH (Norditropin[®] [somatotropin; recombinant GH], Novo Nordisk A/S, Denmark) in a real-life clinical setting⁴ and may help guide treatment optimisation.

Aim and methods

- We investigated GH dosing patterns in children with IGHD and MPHD over a 7-year period, using data from the NordiNet[®] IOS (NCT00960128), a non-interventional study evaluating the long-term effectiveness and safety of Norditropin[®].⁴
- Average GH dose during the full treatment period and duration of GH treatment were calculated and categorised as low (0–25 µg/kg/day), medium (>25–40 µg/kg/day) and high (>40–70 µg/kg/day). The proportions of patients with low, medium and high average GH dose were analysed, as were the proportions with a decrease or an increase of >10%, or no change in GH dose from baseline within the first and second year of treatment (as this is the time period during which doctors closely monitor growth and adverse events, and thus adjust the dose as needed).
- Descriptive statistics were applied on age, body mass index (BMI) standard deviation score (SDS), height SDS and insulin-like growth factor-I (IGF-I) SDS for all patients and by diagnosis, gender and dose group.
- Linear regression was performed to analyse the relationship between baseline height SDS or BMI SDS at treatment start and GH dose during the full treatment period.

Results

- Overall, data for 6297 patients were analysed, 5503 (66.4% boys) with IGHD and 794 (60.1% boys) with MPHD. Baseline demographics are shown in Table 1.
- At baseline, across both indications, boys were older and taller than girls. Furthermore, all patients with IGHD were younger and shorter, and had higher baseline IGF-I SDS than patients with MPHD (Table 1).
- Average GH dose during the full treatment period was higher in patients with IGHD than MPHD, whilst average mean doses during the full treatment period were similar between boys and girls (Table 2).
- The majority (76.7%) of all patients were in the medium-dose group at baseline (Table 1). At baseline, the medium-dose group comprised over three-quarters (78.6%) of all patients with IGHD and almost two-thirds (63.6%) of all patients with MPHD. Of the remaining patients with IGHD, 11.2% were in the low-dose group and 10.2% were in the high-dose group. For MPHD these proportions were 28.3% and 8.1%, respectively.

Table 1. Baseline characteristics of boys and girls with IGHD and MPHD.

	Sex	Low GH dose (13.36%)		Medium GH dose (76.7%)		High GH dose (9.94%)							
		IGHD (N=616)	MPHD (N=225)	IGHD (N=4325)	MPHD (N=505)	IGHD (N=562)	MPHD (N=64)						
		n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)		
Age at GH treatment start, years	Boys	419	9.8 (4.6)	123	10.5 (4.4)	2875	9.2 (4.0)	319	9.7 (4.4)	361	9.1 (3.9)	35	9.5 (4.5)
	Girls	197	9.5 (3.9)	102	10.4 (4.6)	1450	8.5 (3.7)	186	9.4 (4.0)	201	8.8 (3.9)	29	8.6 (4.1)
Height SDS	Boys	374	-2.5 (1.0)	110	-1.7 (1.5)	2599	-2.6 (0.9)	291	-2.4 (1.2)	333	-2.6 (1.0)	33	-2.3 (0.9)
	Girls	167	-2.5 (1.0)	91	-1.6 (1.5)	1325	-2.8 (1.0)	165	-2.5 (1.2)	183	-2.8 (0.9)	25	-2.6 (1.2)
BMI SDS	Boys	386	0.6 (1.5)	111	1.3 (1.3)	2613	-0.3 (1.3)	292	-0.1 (1.5)	334	-0.5 (1.2)	33	-0.9 (1.2)
	Girls	173	0.5 (1.4)	91	1.1 (1.6)	1338	-0.3 (1.2)	164	0.1 (1.3)	184	-0.7 (1.1)	25	-0.3 (1.2)
IGF-I SDS	Boys	195	-1.7 (1.9)	59	-2.8 (2.4)	1376	-1.7 (1.6)	147	-2.5 (2.2)	166	-1.5 (1.4)	18	-1.8 (2.5)
	Girls	103	-2.0 (1.9)	60	-2.5 (2.0)	716	-1.7 (1.5)	80	-2.3 (1.6)	92	-1.6 (1.6)	10	-0.3 (1.6)

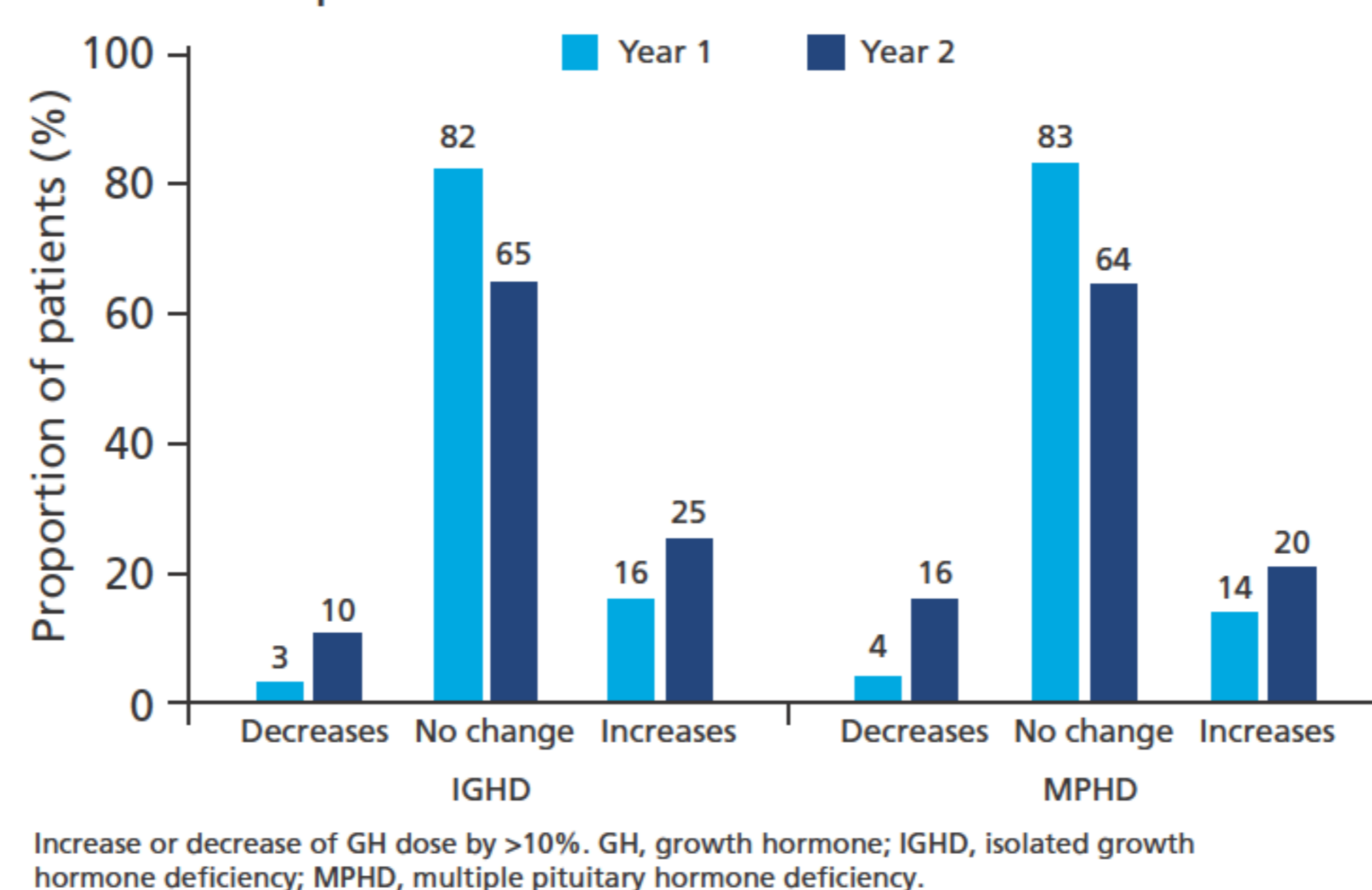
Low GH dose (0–25 µg/kg/day), medium GH dose (>25–40 µg/kg/day) and high GH dose (>40–70 µg/kg/day). Percentages represent the proportion of all patients within each GH dose group. BMI, body mass index; GH, growth hormone; IGF-I, insulin-like growth factor-I; IGHD, isolated growth hormone deficiency; MPHD, multiple pituitary hormone deficiency; SD, standard deviation; SDS, standard deviation score.

Table 2. Mean doses (µg/kg/day) for boys and girls with IGHD and MPHD across the treatment period.

	IGHD				MPHD			
	Boys		Girls		Boys		Girls	
	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Full treatment period	3655	31.9 (6.6)	1848	32.4 (6.8)	477	29.3 (8.0)	317	28.7 (9.4)
Year 1	3800	31.3 (7.0)	1912	31.8 (7.2)	487	29.6 (8.1)	333	29.4 (9.4)
Year 2	3200	32.4 (7.4)	1619	32.9 (7.5)	415	30.3 (9.0)	289	30.5 (9.4)
Year 3	2655	32.5 (7.6)	1353	33.2 (8.1)	341	30.2 (8.7)	235	30.0 (10.2)
Year 4	2094	32.2 (7.7)	1073	33.0 (8.0)	279	29.5 (9.6)	181	29.0 (10.2)
Year 5	1594	31.8 (7.6)	749	32.6 (8.1)	202	28.3 (10.0)	145	27.4 (10.2)
Year 6	1171	31.4 (7.9)	533	32.5 (8.7)	150	28.2 (9.9)	102	26.9 (10.1)
Year 7	804	31.1 (8.1)	359	31.9 (8.7)	107	27.9 (9.3)	84	27.2 (9.6)
Exposure time, years	4008	3.6 (2.7)	1990	3.5 (2.7)	508	3.7 (2.7)	349	3.8 (3.0)

GH, growth hormone; IGHD, isolated growth hormone deficiency; MPHD, multiple pituitary hormone deficiency; SD, standard deviation.

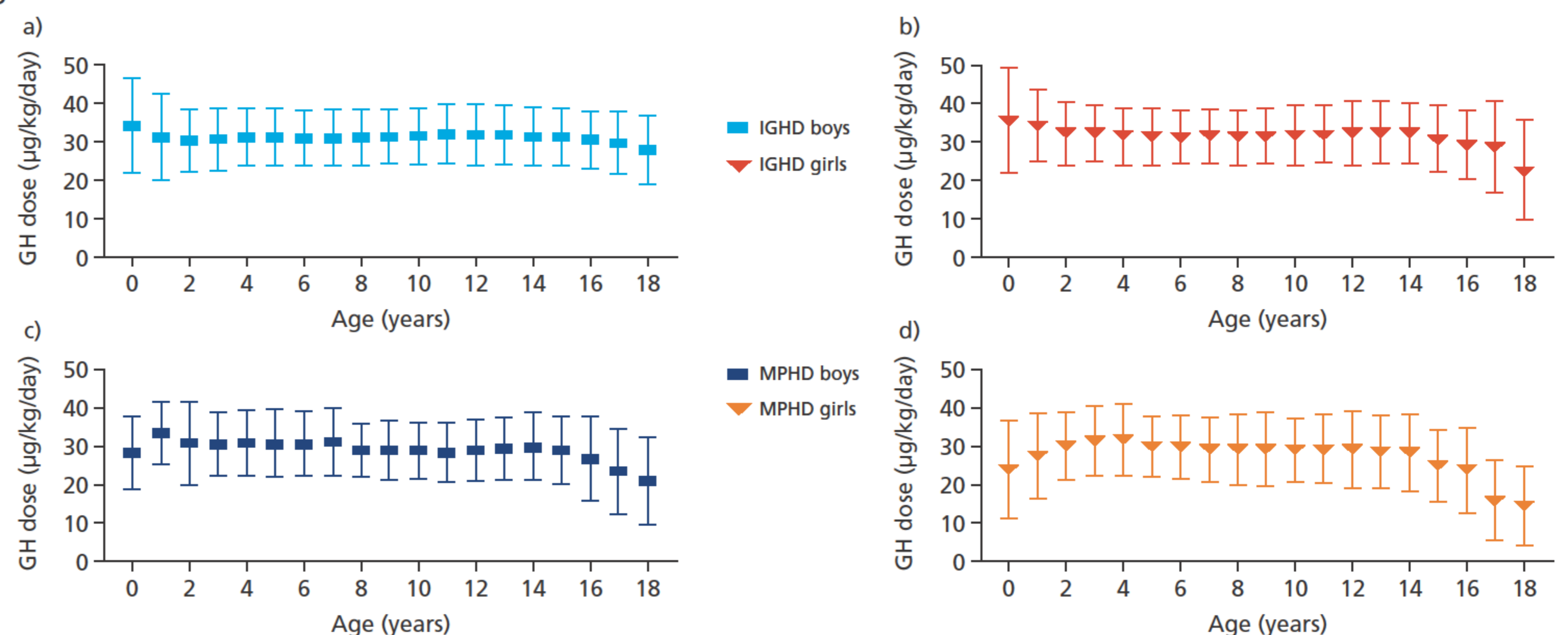
Figure 1 Change in GH dose during first and second year of treatment in patients with IGHD and MPHD.



Increase or decrease of GH dose by >10%. GH, growth hormone; IGHD, isolated growth hormone deficiency; MPHD, multiple pituitary hormone deficiency.

- During the first year of GH treatment, GH dose was unchanged for the majority of patients (>80%) with IGHD or MPHD (Figure 1).
- During the second year of GH treatment, the proportion of patients with no change in dose was similar in both IGHD and MPHD. GH dose increased for 25% and 20%, and decreased for 10% and 16% of patients with IGHD and MPHD, respectively (Figure 1).
- Mean GH doses were stable across most of the age range but decreased in boys and girls with IGHD or MPHD from the age of 14 and 15 years, respectively (Figure 2).
- Mean height SDS at baseline was lower in the medium- and high-dose groups than in the low-dose group for patients with IGHD and MPHD (Table 1).
 - Baseline height SDS was significantly inversely correlated with GH dose in patients with IGHD ($p=0.0319$) and MPHD ($p<0.0001$).
- Across the full treatment period, patients with a lower BMI SDS at baseline were on higher GH doses, as illustrated by significant inverse correlations in patients with either IGHD ($p<0.0001$, $n=5028$) or MPHD ($p<0.0001$, $n=716$).

Figure 2 Mean (SD) GH dose by age, diagnosis and sex: a) boys with IGHD; b) girls with IGHD; c) boys with MPHD; d) girls with MPHD.



GH, growth hormone; IGHD, isolated growth hormone deficiency; MPHD, multiple pituitary hormone deficiency; SD, standard deviation.

References

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Conclusions

- Patients with MPHD received lower mean GH doses than patients with IGHD.
- Significant inverse correlations were observed between GH dose and baseline height SDS or BMI SDS in both cohorts of IGHD and MPHD patients.
- The majority of patients with IGHD or MPHD received a GH dose of 25–40 µg/kg/day during the analysis period.



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