

Sex differences in growth response to GH treatment: more prepubertal and less pubertal gain in girls diagnosed with IGHD, ISS, SGA.

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Aim

To describe and identify factors explaining growth response to GH-treatment, separately in girls and boys from GH-start before and during puberty to adult height (AH).

Background

Due to fewer girls than boys being GH-treated, after 50yrs the knowledge about sex-differences in both GH-response and GH-responsiveness before and during puberty remains limited.

Material

Children (3-18 yrs) diagnosed with IGHD, ISS, SGA from our GH-SAFETY-database, including all rhGH-treated children during 1986-2009 in Sweden, from National-GH-Registry and from rhGH-clinical-trials were included¹.

Inclusion criteria for the present study was complete data for the following variables: gestational age(GA) ≥ 32 weeks; birth size > -4 SDS²; longitudinal heights and weights from birth to AH, age and height/weight at pubertal stage B2/testis 4ml; mid-parental height (MPH); GH_{max}AITT/12-24h-GHprofile; rhGHstart at age ≥ 3 yrs; available rhGH-dose ($\mu\text{g}/\text{kg}/\text{day}$); resulting in 604 patients, 420 boys and 184 girls.

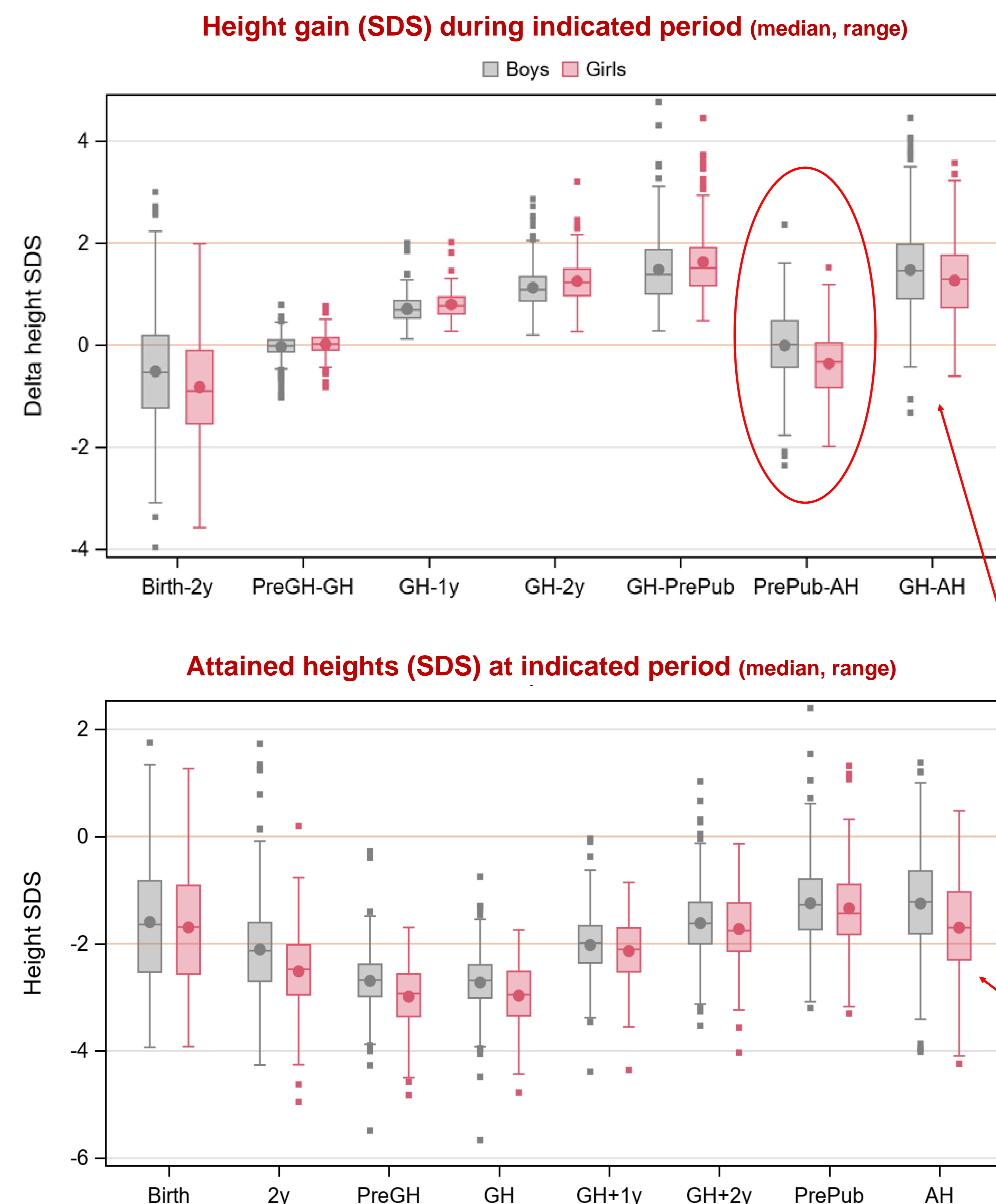
Methods

Growth response outcomes were: change vs population³ ($\Delta\text{height}_{\text{SDS}}$), and vs parents ($\text{DiffH-MPH}_{\text{SDS}}$) for the GH-treatment periods: prepubertal1yr, 2yrs, prepubertal period (GHstart to last prepubertal visit using prepubertal reference), pubertal (last prepubertal visit to AH using reference at age 18yrs for AH_{SDS}), and total height gain_{SDS} (GHstart to AH). Fisher's non-parametric permutation test and linear regression was applied. Value for significance was $p < 0.05$.

Conclusion

- Prepubertal period: girls responded more than the boys, being more GH-responsive⁴ being younger and shorter vs parents and population at GHstart; in addition, they received higher GH-doses
- Pubertal period: the group of girls lost 20% of the prepubertal attained height_{SDS} during puberty, whereas maintained in the group of boys on similar GH-doses. However, 50% of the boys and 75% of the girls had no pubertal gain (see ellipse in the figure)
- Adult height_{SDS} was for girls and boys -1.7 respectively -1.25; while mean total gain in height_{SDS} for girls vs boys was 1.3 vs 1.5

Results



	Boys=420 Mean(SD)	Girls=184 Mean(SD)	p-value
Birth/infancy			
BirthLength _{SDS}	-1.60(1.14)	-1.70(1.15)	0.31
BirthWeight _{SDS}	-1.06(1.09)	-0.98(1.18)	0.42
Infancy Δ Height _{SDS} 0-2yrs	-0.51(1.11)	-0.82(1.09)	0.0019
DiffH-MPH _{SDS} 2yrs	-1.12(1.03)	-1.38(1.02)	0.0042
Pretreatment/at GHstart			
Δ Height _{SDS} Pretreatment	-0.03(0.23)	0.02(0.23)	0.015
GH _{max} AITT/GHprofile	16.1(19.1)	15.7(14.4)	0.81
Age(yr)GHstart	8.65(2.12)	7.86(2.17)	<.0001
Height _{SDS} GHstart	-2.72(0.52)	-2.97(0.58)	<.0001
Outcome on rhGH treatment			
Δ Height _{SDS} 1 ^{yr}	0.71(0.26)	0.80(0.29)	0.0011
GHdose($\mu\text{g}/\text{kg}/\text{day}$)1 ^{yr}	35.9(9.2)	39.1(12.2)	0.0029
Δ Height _{SDS} Prepubertal	1.48(0.65)	1.63(1.12)	0.012
GHdose($\mu\text{g}/\text{kg}/\text{day}$)Prepubertal	35.8(8.0)	39.0(11.6)	0.0002
Δ Height _{SDS} Pubertal	-0.005(0.69)	-0.36(0.68)	<.0001
GHdose($\mu\text{g}/\text{kg}/\text{day}$)Pubertal	30.1(10.0)	30.3(9.8)	0.80
Δ Height _{SDS} GHstart-AH	1.47(0.80)	1.27(0.80)	0.0037
GHdose($\mu\text{g}/\text{kg}/\text{day}$)GHstart-AH	32.5(7.9)	33.9(8.8)	0.051
At adult height			
Height,cm	172.2(6.0)	157.2(5.4)	<.0001
Height _{SDS}	-1.25(0.92)	-1.70(0.89)	<.0001
DiffH-MPH _{SDS}	-0.26(0.93)	-0.57(0.83)	0.0002