

Lundberg E¹, Kriström B¹, Albertsson Wikland K²

¹Dep of Clinical Science/Pediatrics, Umeå University, ²Department of Physiology/Endocrinology, Institute of Neurosciences and Physiology, Sahlgrenska Academy at University of Gothenburg, Gothenburg, Sweden.

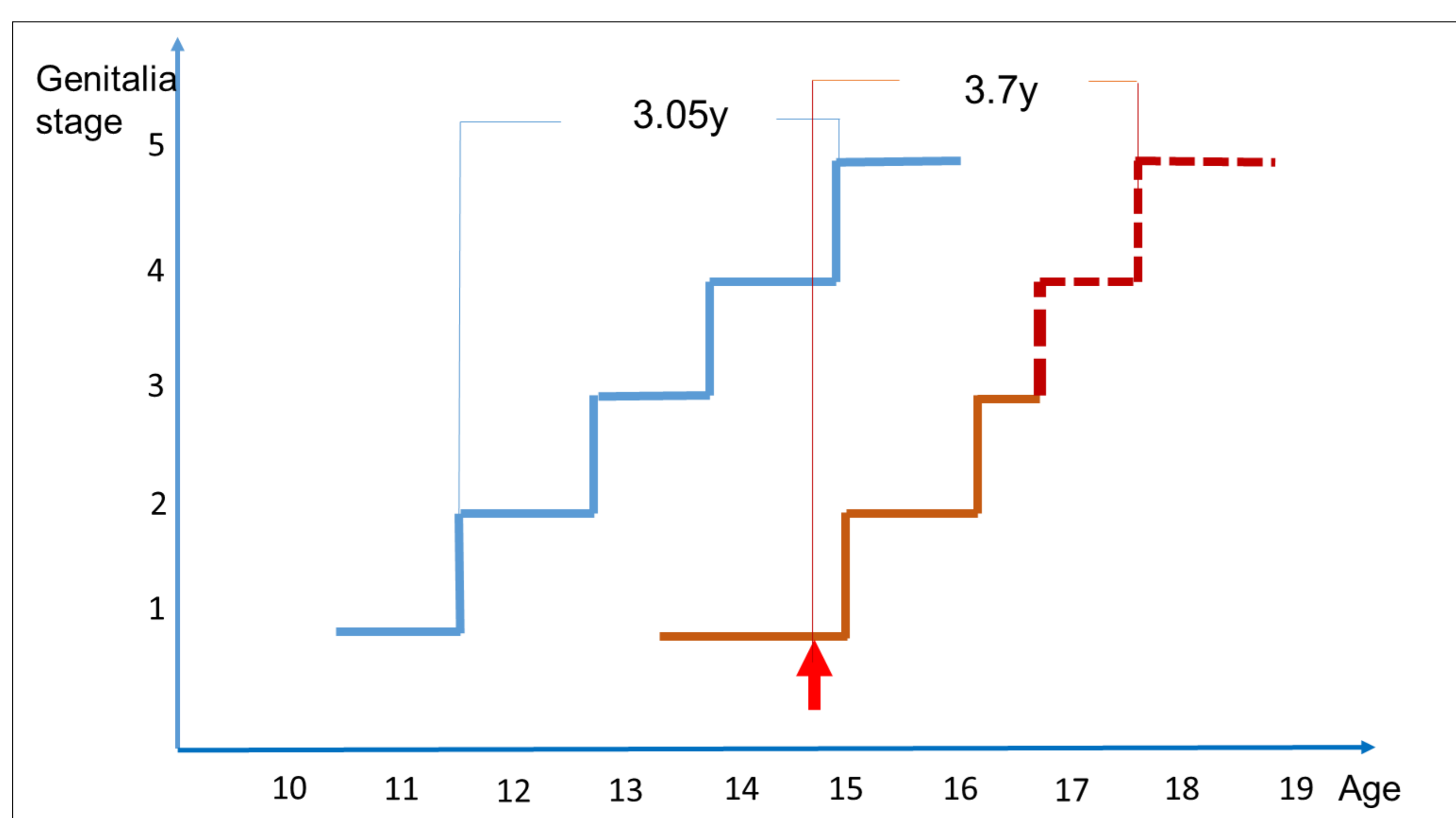
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Aim: By mimicking normal pubertal physiology¹ induce pubertal development, pubertal height gain and increase adult height in children with multiple pituitary hormone deficiencies (MPHD)

Background: Masculinisation tempo on sex-steroid replacement in boys with MPHD and pubertal growth spurts on adequate GH-treatment regimens were unknown in 1989 and are still not optimal.

Study population: 10 boys with organic or idiopathic MPHD and \geq one prepubertal year on rhGH treatment 33 μ g/kg/day were randomized to rhGH 33 or 67 μ g/kg/day (Genotropin[®]) during puberty with low testosterone doses used together in a hypothesis driven prototype trial^{2,3}. Sex-steroid replacement was oral testosterone undecanoate (Undestor[®]) in increasing doses (10, 20, 40mg/d) followed by parenteral Testoviron depot[®].

Results



Genitalia development in boys with MPHD on therapy. Median age and duration for each stage (red line) compared to normal values according to Tanner¹ (blue line).

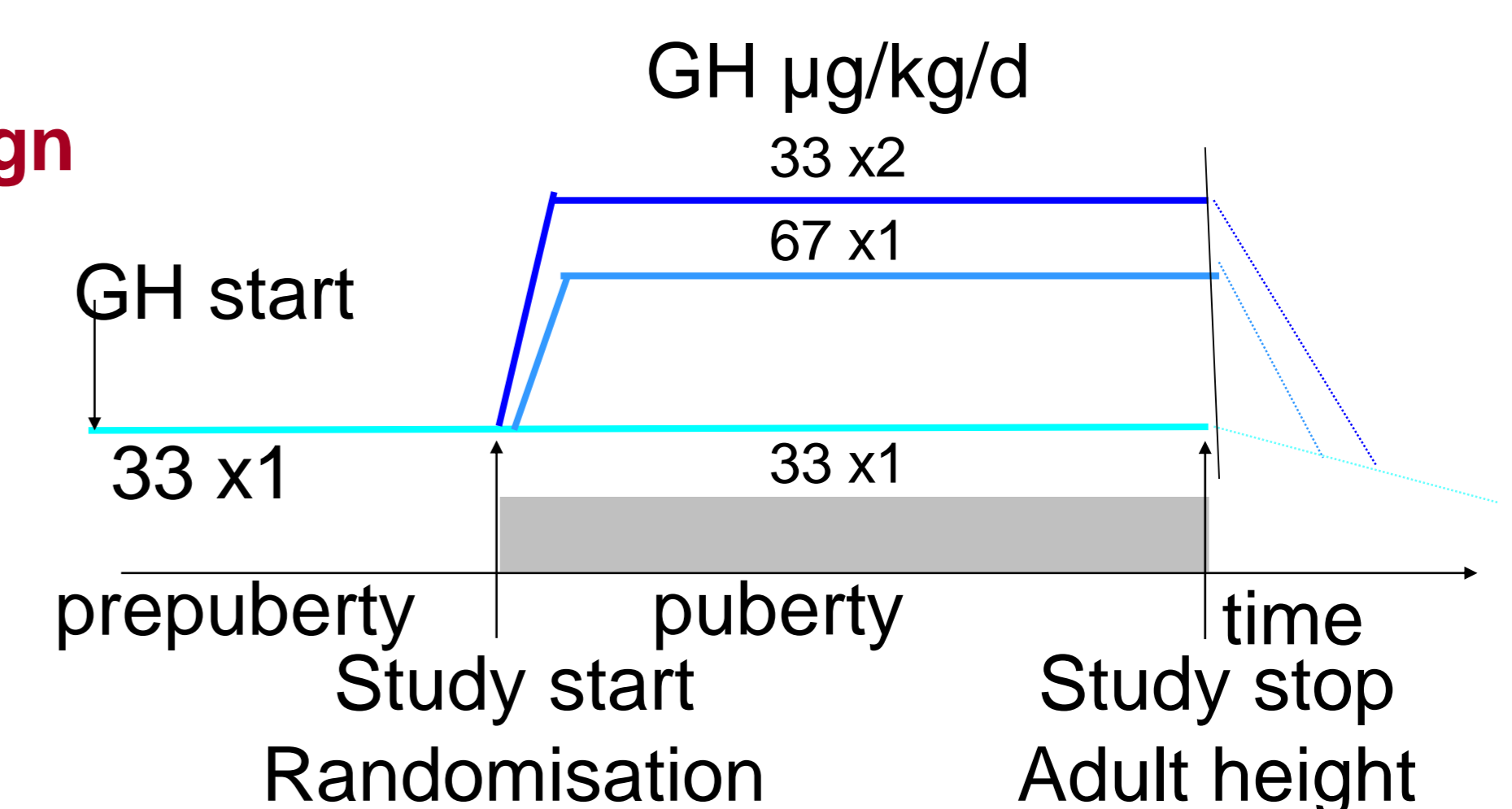
Total (n)	Genitalia Stage	Median (y)	Range (y)	Mean values Tanner and Marshall (y)
10	Ind	14.8	12.6-15.1	
10	G2	15.0	13.7-16.8	11.64
10	G3	16.2	14.7-17.4	12.85
7	G4	16.5	15.8-19.6	13.77
7	G5	17.7	16.9-19.6	14.92
Total (n)	Interval	Median (y)	Range (y)	Mean values Tanner and Marshall (y)
10	Ind-G2	0.6	0.1-1.1	
10	G2-G3	1.15	0.5-2.4	1.12
7	G3-G4	0.9	0.3-2.2	0.81
7	G4-G5	1.4	0.7-2.7	1.0
7	G2-G5	3.7	1.9-5.6	3.05
10	Ind-Gmax	3.7	1.9-5.6	

Median age and duration of genitalia stages in boys with MPHD, receiving increasing doses of oral testosterone compared to Tanner¹ mean values from healthy boys.

Conclusion

- Tempo of genitalia development, pubertal growth spurt and Adult Height can be normalized in MPHD boys by using a physiological substitution therapy with low dose testosterone and adequate GH-doses.
- Induction with oral testosterone was favourable for genital development and growth but was insufficient for complete maturation.
- This treatment regimen allows earlier induction of puberty, comparable to puberty in healthy boys.

Study design



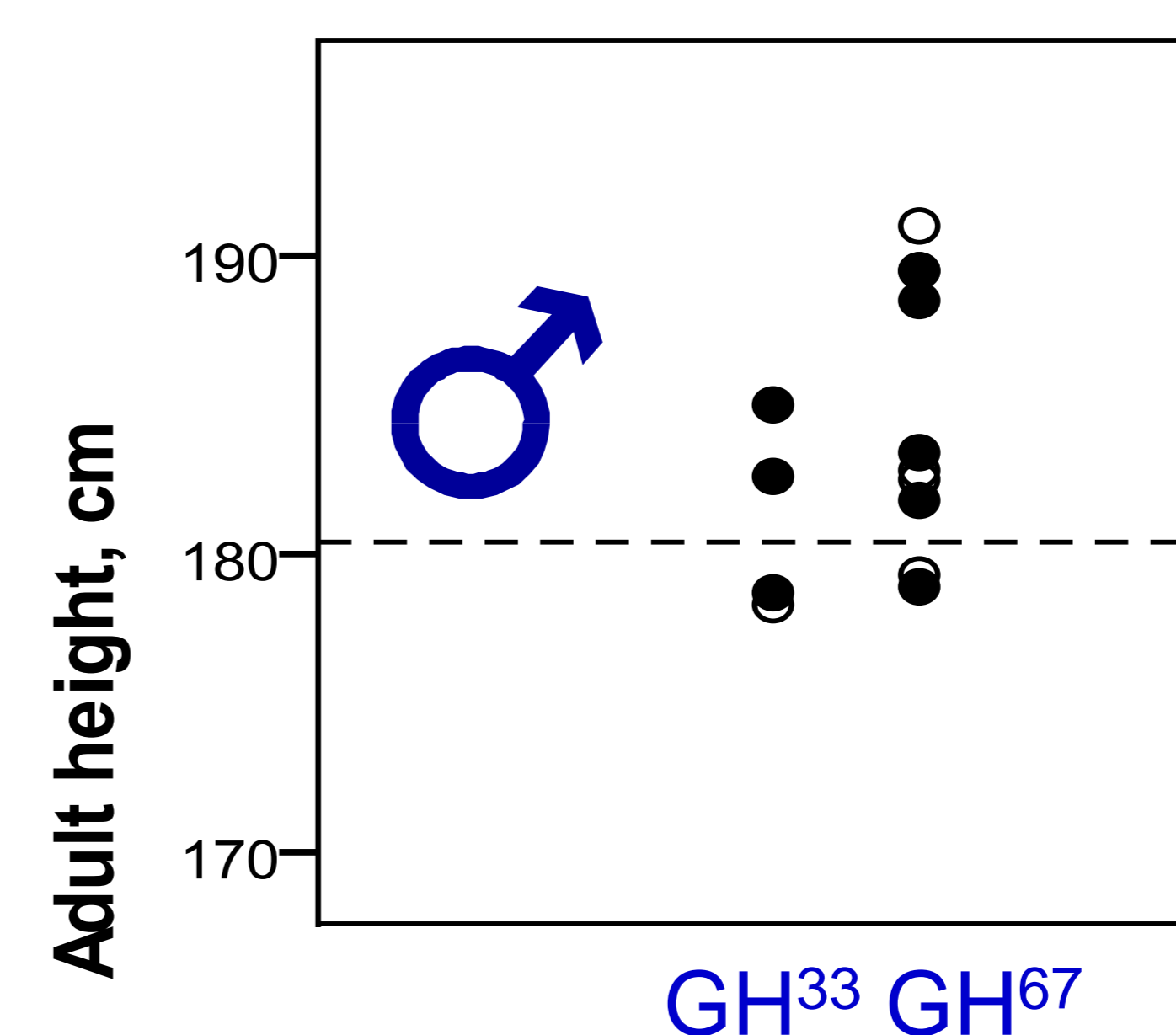
Height methods and outcome

Pubertal height gain was estimated as change in height_{SDS} at start of testosterone (calculated vs prepubertal height reference⁴) to Adult Height.

Pubertal gain in height_{SDS}, median +1.2 (-0.4 to 2.5); in cm 23.1 (15.7-33.4).

Adult Height_{SDS} was median 0.3 (-0.3 to 1.4); and in cm 182.3 (178.2-189.5).

Adult height (cm)



Mean population male height⁴ 180.4 (broken line)

Referenser:

- ¹Marshall&Tanner, Arch. Dis. Child.1970;45:13-21
- ²Albertsson-Wikland et al. Acta.Paed.1999;88(suppl):80-84
- ³Albertsson-Wikland et al. Horm. Res.Paed. 2014;82:158-170
- ⁴Albertsson-Wikland et al. Acta Ped 2002; 91:739-54