

# A Comparison of Published Criteria for Assuming Attainment of Adult Height in Girls who have Received Growth Hormone Treatment

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## ABSTRACT

At least six different criteria to assume attainment of adult height in girls who have received growth hormone (GH) treatment have been published in the literature. The aim of this study was to assess whether, if applied to the same population, different criteria for assuming adult height would produce the same outcome.

**Methods:** Data on Australian and New Zealand girls receiving growth hormone (GH) treatment were accessed from the nationwide OZGROW database. Girls were included in the analysis if standing height measurements were available up until the time point when bone age (BA)  $\geq 15$  yr and height velocity (HV)  $\leq 1$  cm/yr ( $n = 684$ ). Participants' height measurements were extracted from the database at the first time point that would be considered to meet the requirements of each criterion.

**Results:** ANOVA found no statistically significant differences between the value for girls' adult height assumed when using the various criteria. However, as expected, the greatest (and, thus, most accurate) estimate for adult height was obtained using the most stringent criterion, BA  $> 15$  yr and HV  $< 1$  cm/yr. The values assumed using the other adult height criteria

underestimated this height value by an average of 2.4 cm.

**Conclusion:** Statistically similar values for adult height in girls who have received GH treatment are obtained using any of the published criteria for assuming adult height that were evaluated. However, in cases where girls who have received GH treatment cannot be followed until the time point when BA  $\geq 15$  yr and HV  $\leq 1$  cm/yr, it has to be acknowledged that the assumed adult height is likely to be less than the girl's actual adult height.

## KEY WORDS

adult height, growth hormone, girls

## INTRODUCTION

Throughout the world, thousands of height restricted children are treated with growth hormone (GH). The main aim of GH treatment in children is to improve adult height. As with any medical intervention, it is important that children receiving GH treatment are regularly monitored, and that follow-up occurs to determine whether the treatment regimen implemented has improved their final outcome (i.e. adult height).

Height increases throughout childhood, then plateaus at the end of puberty, before eventually reaching a static value. Increased height outcome is achieved in children receiving GH via promotion of the growth of the long bones during childhood and early puberty. Adult height is achieved late in puberty when, under the influence of sex hormones, growth plates fuse and further linear bone growth is

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prevented. The timing of this event varies between girls and boys, and also varies somewhat amongst different children of the same gender.

Given that medical institutions are rarely able to follow-up patients receiving GH indefinitely, patients' actual adult height often cannot be measured. However, knowledge of normal growth patterns allows clinicians to estimate the general period in development when the majority of linear growth will have occurred. Measurement of height during this window allows a value for height to be obtained that is relatively close to the actual adult height. The factors most often used to assume when adult height is likely to have occurred are bone age (BA) and/or height velocity (HV). The specific values of these factors used to assume attainment of adult height often vary across different institutions and in different studies.

For example, the Bayley-Pinneau tables<sup>1</sup> suggest that a girl's height will have reached 99% of her adult height when her BA = 15 years. However, many clinicians and researchers are unable to follow up patients to this point, and will rely on height measurements taken when the patient is less mature (i.e. at a lower BA) to approximate adult height. In addition, it is important to realise that while the Bayley-Pinneau tables can be used to try to estimate the percentage of adult height that will have been attained at any particular BA, these tables are based on data derived from normally growing children, and not children with growth restrictions (who either have or have not received GH treatment), and may not reflect growth patterns in this group. As a result, many clinicians and researchers use a criterion that incorporates both a BA parameter as well as an HV parameter for assuming the timing of adult height in girls who have received GH treatment.

On review of the literature, at least six different criteria for assuming the timing of adult height in girls who have received GH treatment were found to be used in various studies<sup>2-7</sup>. In five of the six published criteria, the parameters used to assume when adult height occurred included values for both BA and HV. The specific values of these parameters accepted as approximating the timing of adult height differed in the various criteria.

Currently, it is unknown whether the specific

criterion used to assume adult height in girls who have received GH treatment would alter the actual value of this outcome. However, any discrepancies in the value of assumed adult height that do occur are likely to affect how useful the GH treatment is perceived to be. Therefore, the aim of this study was to determine whether, if applied to the same population, different published criteria for assuming attainment of adult height would produce the same adult height values.

## METHODS

### Population

Data on girls from Australia and New Zealand who had received GH treatment as part of a government-funded program were accessed from the nationwide OZGROW database ( $n = 3,152$ ). Girls were included in the analysis if standing height measurements were available up until the time point when BA  $\geq 15$  years and HV  $< 1$  cm/year. In total, data on 684 girls (22%) were available for analysis. The remainder of the patients on the database were lost to follow-up before this time point. All girls in the database had BA determined using the Greulich and Pyle method.

### Procedure

Six different criteria for assuming attainment of adult height for girls were extracted from the literature (Table 1). Each criterion was applied to the data set to determine the value for adult height that it would yield. That is, height was evaluated at the first time point recorded on the database that would be considered to meet the requirements of each criterion. In addition, the different BA and HV parameters used in the published criteria were also individually applied to the data set to determine the value for adult height that they would yield.

### Statistical analysis

Independent-groups ANOVAs were used for multiple-group comparisons. Independent-groups t-tests were used for two-group comparisons. P values  $< 0.05$  were considered statistically significant.

TABLE 1

Published criteria for determining attainment of adult height

1. BA >15 yr and HV <1 cm/yr over 1 year (Pasquino *et al.*, 2000)<sup>2</sup>
2. BA ≥15 yr and HV <1.5 cm/yr over 6 months (Lin-Su *et al.*, 2005)<sup>3</sup>
3. BA ≥15 yr or HV ≤2 cm/yr over 1 year (Carel *et al.*, 2003)<sup>4</sup>
4. BA >14 yr or HV <2 cm/yr over 1 year (Buchlis *et al.*, 1998)<sup>5</sup>
5. BA ≥14 yr and HV <2 cm/yr over 1 year (CGHAC, 2005)<sup>6</sup>
6. Last measured height after CA >13.5 yr (Chernausek *et al.*, 2000)<sup>7</sup>

BA = bone age; HV = height velocity; CA = chronological age.

TABLE 2

Assumed adult height (cm) when measured using various published criteria, as well as the various bone age (BA) and height velocity (HV) parameters (n = 684)

Criterion/parameter	Mean (95% CI)	SD	SE
Pasquino <i>et al.</i> (2000) <sup>2</sup>	151.8 (149.6-154.6)	2.6	0.3
Lin-Su <i>et al.</i> (2005) <sup>3</sup>	150.6 (148.5-153.8)	2.8	1.2
Carel <i>et al.</i> (2003) <sup>4</sup>	150.4 (148.6-151.7)	2.5	0.5
Buchlis <i>et al.</i> (1998) <sup>5</sup>	149.8 (148.1-149.7)	2.8	0.7
CGHAC (2005) <sup>6</sup>	148.7 (146.8-150.3)	3.2	1.1
Chernausek <i>et al.</i> (2000) <sup>7</sup>	147.6 (144.3-149.1)	3.6	1.8
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BA >15 yr	151.2 (147.8-155.1)	2.1	1.7
BA ≥15 yr	150.1 (147.2-152.2)	2.5	1.3
BA >14 yr	149.1 (146.9-151.8)	3.0	1.1
BA ≥14 yr	148.6 (146.8-150.2)	2.9	0.9
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HV <1 cm/yr	150.9 (148.8-152.7)	2.8	0.2
HV <1.5 cm/yr	150.4 (148.7-152.2)	2.4	0.3
HV <2 cm/yr	149.3 (148.6-150.7)	3.6	0.4
HV ≤2 cm/yr	148.2 (146.8-150.4)	3.2	0.4

## RESULTS

Table 2 lists the height values for girls in the OZGROW database obtained at the first time point that met the requirements of the various published criteria for attainment of adult height. ANOVA found no statistically significant difference in the value of girls' adult height assumed using the various published criteria ( $p = 0.380$ ). A post-hoc series of pairwise comparisons found no statistically significant differences between any of the individual criteria.

Table 2 also lists the height values of girls in the OZGROW database obtained at the first time point recorded on the database that met the requirements of the various BA and HV parameters. ANOVA found no statistically significant differences between the girls' adult height assumed using the various BA parameters ( $p = 0.428$ ) or HV parameters ( $p = 0.792$ ). A post-hoc series of pairwise comparisons found no statistically significant difference between any of the individual BA or HV parameters.

The highest value for assumed adult height (151.8 cm) was obtained using the most stringent criterion, BA >15 years and HV <1 cm/year. Compared to this value, the adult height assumed when using the other published criteria underestimated adult height by an average of 2.4 cm. Similarly, the adult height value assumed when using the various HV and BA criteria underestimated this adult height value by an average of 2.0 and 2.1 cm, respectively (Table 2).

## DISCUSSION

We found no statistically significant difference in the adult height value assumed for girls who had received GH treatment using any of the published criteria or various BA and HV parameters. However, as expected, a trend was observed, such that the more mature the BA parameter used and/or the lower the HV parameter used, the higher the adult height value assumed. A mean difference of 2.6 cm was found in the girls' height measurements taken when BA >14 years compared with when BA >15 years (Table 2). Similarly, a mean height difference of 2.7 cm was found in the girls' measurements taken when HV  $\leq$  2 cm/year compared with when

HV  $\leq$  1 cm/year.

As expected, the results of this study demonstrate that the highest (and, therefore, the most accurate) estimate for adult height in girls who had received GH treatment was obtained when using the most stringent criterion, BA >15 year and HV <1 cm/year. The other published criteria and the various individual HV and BA parameters underestimated this adult height value by an average of 2.0-2.4 cm. Such a difference would be of clinical significance. In addition, a difference of this magnitude in research findings could alter the perception of how useful the GH treatment was in maximising adult height.

## CONCLUSION

Statistically similar values are obtained for adult height in girls who have received GH treatment using any of the published criteria that were evaluated, and for the various BA and HV parameters contained within these criteria. However, in cases where girls who have received GH treatment cannot be followed until the time point when BA >15 years and HV  $\leq$  1 cm/year, it has to be acknowledged that the assumed adult height is likely to be less than the girl's actual adult height.

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