#### ORIGINAL ARTICLE

# The influence of secular trend for height on ascertainment and eligibility for growth hormone treatment

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#### **Summary**

Objective Assessment of short stature in many instances is based on a comparison with the Centers for Disease Control's (CDC) growth curves. The secular trend for height may limit the utility of CDC data for contemporary populations. We investigate the effect of the secular trend on Australian and US populations.

Design Describe CDC-defined height SDS distributions of contemporary populations for different ages and genders. Compare observed means and standard deviations (SDs) to expected values of 0 and 1. Compare frequency of individuals shorter than the CDC-1st centile to those shorter than 1st centile defined empirically from the contemporary population.

Subjects Healthy Kids Queensland Survey 2006: 1686 boys, 1822 girls. Australian National Children's Nutrition and Physical Activity Survey 2007: 2415 boys, 2379 girls. US National Health and Nutrition Examination Survey 2005–2006: 2160 boys, 2118 girls.

Measurements Means, SDs and normality of CDC-defined height SDS distributions. Frequency of individuals shorter than the CDC-1st centile and shorter than an empirically defined 1st centile. Results In Australia, means of CDC-defined height SDS distributions are always greater than 0 and the CDC-1st centile identifies only the shortest 0.5% of children. Means may vary with age and occasionally between genders in contemporary populations. Normality and SDs of 1 are retained.

Conclusions The secular trend has resulted in an underestimate of the number of Australian children eligible for GH treatment using the CDC-1st centile cut-off. Contemporary, local data should be used to construct standards. Using the 2nd CDC centile would approximate the 1st local centile until new standards are constructed. The secular trend does not account for the gender bias in GH therapy.

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(Received 6 July 2010; returned for revision 18 July 2010; finally revised 18 August 2010; accepted 26 August 2010)

#### Introduction

Assessment of short stature is in many instances based on a comparison with the Centers for Disease Control's (CDC) growth curves (CDC 2000). In some countries such as Australia, eligibility for subsidised growth hormone (GH) treatment also relies on CDC-standardized height data. Heights are converted to standard deviation scores (SDS, or Z scores) which are the number of standard deviation units from the CDC mean of children of the same age and sex. SDS are normally distributed with mean 0 and standard deviation 1 and allow the heights of children of different ages and genders to be directly compared thus enabling a simple clinical definition of short stature. In Australia, for example, the criteria to receive subsidised GH for short stature and slow growth ("Slow Growing") include that the height be less than the 1st centile (SDS<-2·326) on the CDC 2000 Growth Charts. 1,2 In Australia, short children are referred to growth centres where paediatric endocrinologists assess the child for the cause of their short stature. GH may be prescribed under the Pharmaceutical Benefits Scheme (PBS) for GH deficiency (<10 mU/l on stimulation testing), short stature associated with intracranial lesions or cranial irradiation, neonatal hypoglycaemia, Turner syndrome, chronic renal insufficiency, Prader-Willi syndrome, or for short stature and slow growth.

The potential problem with using CDC-based SDS is that the CDC height distributions were constructed from pooled surveys of children in the USA conducted from 1963 to 1994. As such, it is likely, given the well-known secular trend for height, hat a contemporary population will have height distributions that differ from the corresponding CDC height distributions. Also, height distributions of genders or of different age groups may have changed differentially over time. If this was the case, the CDC-defined 1st

centile height, and hence eligibility for GH treatment, may occur at a different centile position on, for example, the current Australian height distributions of boys and girls or of 5-year-olds and 13-yearolds, and reflect the true 1st centile in neither.

Height distributions have changed over time<sup>6-8,10,14,16,17</sup> and vary between populations when compared to CDC charts. 16,18-22 The height distributions we see in Australia today are different to those represented by the CDC curves. 4,5,9,15 The secular trend for mean height is well documented<sup>4-15</sup> but less is known about any changes over time, or between populations, in the standard deviation (SD) of height distributions. However, in Dutch adults (21 years old) from 1965 to 1997, it has been suggested that there is a fixed relationship between mean and SD such that the coefficient of variation approximates 3·8%. <sup>23</sup> Guedes <sup>22</sup> reported similar coefficients of variation to CDC values in Brazilian children from the Jequitinhonha Valley although there were substantial differences in median heights.

One possible effect of differences between the height distributions of a contemporary population and the CDC standard may be the almost universally observed phenomenon of gender bias in GH prescription. Across most diagnoses for which GH is used and in all countries approximately twice as many boys as girls receive GH. 24,25 A gender bias has also been reported in Australian children receiving GH.<sup>26-28</sup> It has been suggested that ascertainment bias could account for the gender bias<sup>29,30</sup> but there is substantial evidence against this conclusion. 31-33 An alternative explanation is that the growth curves of boys and girls may have changed differentially so that boys are now more likely to fall below the 1st CDC centile than girls.

This study will examine whether the secular trend and any other changes in the distributions of heights for age have adversely affected our ability to accurately identify children in Australia who should be eligible for GH treatment. In addition, the study examines whether such changes may contribute to the observed gender bias in GH prescription in Australia.<sup>28</sup>

To investigate these questions, analyses were performed on height data from general populations of Australian children: The Healthy Kids Queensland 2006 (HKQ) and the 2007 Australian National Children's Nutrition and Physical Activity (ANCNPA) surveys. To act as a comparison population in which there is only a temporal difference between it and the CDC population, the United States National Health and Nutrition Examination 2005-2006 (NHANES) survey was also used.

# Subjects and methods

#### Healthy Kids Queensland Survey

As part of the HKQ Survey 2006<sup>34</sup>, the height of participating children, 1737 boys and 1859 girls, was recorded. The children were mostly 5:00-6:99, 9:00-10:99 or 14:00-15:99 years of age as they were enrolled in years 1, 5 or 10 in Government and non-Government Queensland schools. Techniques were employed to ensure that sampling was random within the target population. In this analysis, only heights from 1686 boys and 1822 girls, who fell specifically into the above age groups, were used.

# 2007 Australian National Children's Nutrition and Physical Activity Survey (ANCNPA)

The ANCNPA survey included children aged 2-16 years from all states and territories of Australia. 35 Heights were measured for 2415 boys and 2379 girls. An initial target quota of 1000 children (50% boys and 50% girls) for each age group (2·00-3·99 years, 4·00-8·99 years, 9·00-13·99 years, and 14·00-16·99 years) was set. This was supplemented in South Australia to allow more detailed estimates for that state, increasing the final survey sample by at least 400, approximately equally divided across the age groups. Households with children aged 2-16 years were randomly selected using random digit dialing from all Australian states and territories in metropolitan, rural and remote areas. The number of children included from each state was proportional to the population of children in that state.<sup>35</sup> This data were accessed with permission from the Australian Social Sciences Data Archive (http://assda. anu.edu.au/).

## National Health and Nutrition Examination Survey 2005-2006

The NHANES 2005-2006 survey collected data, including height, from 10 348 people of all ages from January 2005 to December 2006 and targeted the civilian, noninstitutionalized US population. The sample was not random, over sampling occurred for lowincome persons, adolescents, African Americans, and Mexican Americans. Weighting values were used to adjust means to estimate true population means as described in the NHANES Analytic and Reporting Guidelines.<sup>36</sup> From the total NHANES data set, individuals younger than 17 years were selected and included 2160 boys and 2118 girls.

### **Analyses**

Heights were converted to SDS values according to sex and age at measurement using the LMS procedure and the CDC growth charts.1 The mean and standard deviation for height SDS values were calculated for boys and girls for each year of age available in each survey. Each distribution was tested for normality using the D'Agostino-Pearson test. For distributions that were found to be significantly different from Normal, measures of skewness and kurtosis were applied. Skewness implies a departure from symmetry. A symmetrical distribution has a skewness of 0; positive skewness indicates the tail to the right is longer than the tail to the left. Kurtosis is a measure of the peakedness of a distribution relative to that of a Normal distribution. Positive kurtosis indicates the distribution has a sharper peak than a Normal distribution. Means were then recorded and plotted graphically with associated standard errors to show any departures from the expected mean SDS value of 0. Similarly, standard deviations were calculated and recorded to identify any departure from expected values of 1.

The number of children of each sex whose height fell below the 1st CDC centile (SDS<-2:326) was calculated as this is a major component of the current criteria used in Australia to receive GH treatment for short stature. For comparison, empirical 1st centiles

for these distributions were calculated using the actual means and standard deviations of the SDS distributions. Assuming normality where this was appropriate, the numbers of individuals shorter than these values were determined.

Frequencies of boys and girls found to be shorter than SDS = -2.326 or the empiric 1st centile were compared using Chi square association tests. If distributions are essentially normal, it would logically follow that a secular trend of the mean to the right (increasing) should result in fewer individuals falling below the original CDC 1st centile value of -2.326.

Statistical analyses were performed using SPSS 17.0 Chicago, Illinois and Microsoft Excel 2003, Redmond, WA.

#### Results

From Tables 1–3 and Figs 1–3, it can be generally appreciated that means of height SDS from contemporary populations do not consistently reflect a value of 0. Mean height SDS values can vary significantly from 0 and may vary significantly between ages, genders and populations. The two Australian survey populations show means of height SDS, for both genders, to be consistently greater than 0 although there is some variation with age. Significant differences in height SDS can be seen between genders in some age groups although both boys and girls tend to follow the same general pattern (Figs 1 and 2). The American NHANES survey shows a similar pattern although the means are generally closer to, and sometimes fall below, the expected 0. The 4·00–5·99 years peak is only evident in boys (Fig. 3).

In contrast to the mean, the SDs of the distributions of height SDS are, with the occasional exception, consistently close to 1 for all age groups, populations, and genders (Tables 1–3). Normality, in general, was also well maintained. Positive kurtosis and negative skewness were seen occasionally in some age groups and populations. Most notable was the positive kurtosis seen in consecutive age groups, 9·00–9·99 and 10·00–10·99, in the HKQ survey (Table 1).

In both Australian surveys, approximately twice as many children were shorter than the empirical 1st centile than were shorter than the CDC 1st centile (SDS<-2·326). For the HKQ survey, 10 of 1686 boys (0.6%) and 6 of 1822 girls (0.3%) were shorter than a height SDS of -2.326 but 21 boys (1.2%) and 19 girls (1.0%) were shorter than the empirical 1st centile (Table 1). In the ANCNPA survey, 16 of 2415 boys (0.7%) and 8 of 2379 girls (0.3%) were shorter than an SDS of -2.326, whereas 28 boys (1.2%) and 17 girls (0.7%) were seen to be shorter than the empirical 1st centile (Table 2). It will be noted that more boys than girls fall below these cut-offs. If the two Australian surveys are combined, the observed gender bias seen for those shorter than the CDC 1st centile is marginally significant (P = 0.036). It is interesting to note that while approximately twice (1.86 times) as many boys as girls are seen to be shorter than the CDC 1st centile, this is reduced to only 1.36 times (P = 0.13), when the empirical 1st centile is used as the cutoff.

In both the unweighted and weighted versions of the NHANES survey, the combined numbers of children observed to be shorter than the CDC and empirical 1st centiles for height SDS were similar

Table 1. Healthy Kids Queensland: distributions of height SDSs by age

Age range	Mean†	SD‡	N, K, S§	Total	<−2·326¶	<1st centile††
Boys						
5.00-5.99	0.638***	1.017	N	200	0	1
6.00-6.99	0.356***	1.026	KS‡‡	349	2	3
9.00-9.99	0.272***	0.957	N	240	2	3
10.00-10.99	0.170***	0.951	N	443	3	8
14.00-14.99	0.324***	1.039	N	157	0	1
15.00-15.99	0.293***	0.968	N	297	3	5
Total (%)				1686	10§§ (0·59)	21¶¶ (1·25)
Girls						
5.00-5.99	0.390***	1.017	KS‡‡	246	2	2
6.00-6.99	0.256***	0.919*	N	293	1	2
9.00-9.99	0.377***	0.943	K†††	316	1	5
10.00-10.99	0.409***	0.975	K†††	444	1	5
14.00-14.99	0.214***	0.908	N	201	0	3
15.00-15.99	0.225***	0.904*	N	322	1	2
Total (%)				1822	6§§ (0·33)	19¶¶ (1⋅04)

<sup>†</sup>Null hypothesis: Mean = 0.\*0.01 < P < 0.05, \*\*0.001 < P < 0.01, \*\*\*P < 0.001.

 $<sup>\</sup>text{$^{\pm}$Null hypothesis: SD} = 1. *0.01 < P < 0.05, **0.001 < P < 0.01, ***P < 0.001.$ 

<sup>§</sup>Description of distribution. Normal (N): If not significantly different from normal distribution. Kurtosis (K), Skewness (S): If significantly different from normal distribution.

<sup>¶</sup>Number of children whose height fell below the CDC 1st centile (-2.326).

<sup>††</sup>Number of children whose height fell below the empirical 1st centile of the distribution assuming normality.

<sup>‡‡</sup>Non-normality because of a combination of positive kurtosis (peaked) and negative skewness (tail to left side, short heights).

<sup>§§</sup>Frequency difference between boys and girls, P = 0.25.

<sup>¶¶</sup>Frequency difference between boys and girls, P = 0.57.

<sup>†††</sup>Non-normality because of positive kurtosis.

Table 2. Australian National Children's Nutrition and Physical Activity Survey: distributions of height SDSs by age

Age range	Mean†	SD‡	N, K, S§	Total	<−2·326¶	<1st centile††
Boys						
2.00-2.99	0.100	0.940	N	289	3	5
3.00-3.99	0.355***	1.015	KS‡‡	316	3	3
4.00-4.99	0.481***	1.039	N	158	0	1
5.00-5.99	0.439***	0.987	N	100	0	0
6.00-6.99	0.395***	1.072	N	124	1	1
7.00-7.99	0.261*	1.150*	N	111	2	2
8.00-8.99	0.263**	0.952	N	145	0	0
9.00-9.99	0.211*	1.003	N	105	1	1
10.00-10.99	0.359***	0.957	N	122	0	0
11.00-11.99	0.389***	0.747***	N	120	0	2
12.00-12.99	0.402***	1.068	N	111	1	1
13.00-13.99	0.400***	0.954	N	118	0	3
14.00-14.99	0.257***	1.049	N	234	4	5
15.00-15.99	0.328***	1.015	N	210	0	2
16.00-16.99	0.372***	0.994	N	152	1	2
Total (%)				2415	16§§ (0.66)	28¶¶ (1·16)
Girls					,	
2.00-2.99	-0.021	0.884**	N	251	2	3
3.00-3.99	0.412***	0.925	N	306	0	3
4.00-4.99	0.627***	1.025	N	150	1	1
5.00-5.99	0.433***	0.959	N	114	0	1
6.00-6.99	0.058	1.077	N	104	2	2
7.00-7.99	0.189*	0.978	N	127	1	1
8.00-8.99	0.234**	0.916	N	128	1	1
9.00-9.99	0.103	1.005	N	121	0	0
10.00-10.99	0.406***	0.974	N	116	0	0
11.00-11.99	0.455***	0.995	N	142	0	0
12.00-12.99	0.330***	1.037	N	126	0	0
13.00-13.99	0.201*	1.001	N	130	1	1
14.00–14.99	0.383***	0.971	N	192	0	1
15:00–15:99	0.448***	0.944	N	230	0	3
16.00–16.99	0.440***	0.951	N	142	0	0
Total (%)	0 110	0,01		2379	8§§ (0·34)	17¶¶ (0·71)

<sup>†</sup>Null hypothesis: Mean = 0.\*0.01 < P < 0.05, \*\*0.001 < P < 0.01, \*\*\*P < 0.001.

and approximated 1% although these numbers varied from year to year reflecting the value of the mean (Table 3). There was no evidence of a gender bias.

The influence of the value of the mean of the height SDS distribution at each age on the number of individuals falling below the 1st centile can be gleaned from Tables 1-3. In general, it can be seen that, as might be expected given the overall normality of the distributions, if the mean varies from its expected value of 0, this significantly influences the frequency of children falling below the 1st CDC centile (SDS = -2.326). The larger the mean, the fewer individuals fall below an SDS of -2.326. This is clearly seen in the Australian surveys where an SDS of -2.326 is approximately equivalent to the 0.5th centile. Conversely, the influence of the mean is

largely removed when empirical 1st centiles are used as these, if normality is maintained, will change proportionately with the mean. In the US, short stature is defined as a height less than 2 standard deviations below the mean<sup>37,38</sup> or, occasionally, as below the 3rd centile.<sup>33</sup> As with the 1st centile definition, the proportion falling below the CDC-defined cut-off varied with the mean while the proportion falling below the empirically defined cut-offs remained relatively constant (data not shown).

# Discussion

The measurement of height, an ability to meaningfully compare heights between different ages and genders, and a robust

 $<sup>\</sup>text{$^{\pm}$Null hypothesis: SD} = 1. *0.01 < P < 0.05, **0.001 < P < 0.01, ***P < 0.001$ 

<sup>§</sup>Description of distribution. Normal (N): If not significantly different from normal distribution. Kurtosis (K), Skewness (S): If significantly different from

<sup>¶</sup>Number of children whose height fell below the CDC 1st centile (-2.326).

<sup>††</sup>Number of children whose height fell below the empirical 1st centile of the distribution assuming normality.

<sup>‡‡</sup>Non-normality because of a combination of positive kurtosis (peaked) and negative skewness (tail to left side, short heights).

<sup>§§</sup>Frequency difference between boys and girls, P = 0.11.

<sup>¶¶</sup>Frequency difference between boys and girls, P = 0.11.

Table 3. United States National Health and Nutrition Examination 2005-2006 (NHANES) Survey: distributions of height SDSs by age

Age range	UW- Mean†	W-Mean†	SD‡	N, K, S§	Total	<-2·326¶	<1st centile††
Boys							
0.00-0.99	-0.011	0.034	1.205***	K‡‡	261	5	4
1.00-1.99	0.049	0.017	0.944	N	185	2	2
2.00-2.99	0.136*	0.156*	0.843**	N	153	0	0
3.00-3.99	0.087	-0.00	1.095	N	112	1, 5	1
4.00-4.99	0.090	0.166	1.188**	N	107	1,0	0
5.00-5.99	0.339***	0.415***	0.990	N	109	0	1
6.00-6.99	0.299**	0.456***	0.970	N	104	0	2
7.00-7.99	0.129	-0.025	1.041	N	92	1, 3	1
8.00-8.99	0.021	-0.031	1.077	N	84	2	1
9.00-9.99	0.172	0.133	0.950	N	91	2, 1	2
10.00-10.99	0.153	0.113	1.010	N	93	1, 0	1
11.00-11.99	0.355***	0.402***	0.931	N	87	0	1
12.00-12.99	0.309***	0.317***	1.060	N	137	0	0
13.00-13.99	0.223*	0.154	1.187**	N	138	1	0
14.00-14.99	0.053	0.059	1.039	N	120	3	3
15.00-15.99	0.100	0.199*	0.953	N	132	0	1
16.00-16.99	0.206*	0.412***	1.023	N	155	1	1
Total (%)					2160	20, 24 (0.93), (1.11)	21 (0.97)
Girls						, , ,, ,	, ,
0.00-0.99	0.109	0.184	1.056	K‡‡	216	2	2
1.00-1.99	0.083	0.027	0.939	N	160	1	1
2.00-2.99	0.089	0.069	0.960	K‡‡	172	2	3
3.00-3.99	0.125	0.096	0.992	N.	98	0	0
4.00-4.99	0.187*	0.188*	0.985	N	131	1	1
5.00-5.99	-0.057	-0.204	1.031	N	99	4, 5	4
6.00-6.99	0.045	0.162	1.088	N	108	1	0
7.00-7.99	-0.010	-0.019	0.964	N	74	0	0
8.00-8.99	0.103	0.107	0.979	N	92	0	0
9.00-9.99	0.468***	0.440***	1.047	N	104	0	2
10.00-10.99	0.400***	0.277*	1.064	N	96	0	0
11.00-11.99	0.458***	0.498***	0.938	N	90	0	0
12.00-12.99	0.255**	0.314***	0.943	KS§§	126	1	1, 2
13.00-13.99	0.117	0.002	0.914	N	139	1, 0	1
14.00–14.99	-0.201	-0.191	1.156*	N	126	3	2
15.00-15.99	-0.046	0.001	1.040	N	140	1	1
16.00–16.99	-0.098	0.152	1.157**	N	147	5, 4	1
Total (%)					2118	22, 21 (1.04), (0.99)	19, 20 (0.90), (0

 $<sup>\</sup>dagger \text{Un-weighted (UW) or Weighted (W) Means. Null hypothesis: Mean} = 0. *0.01 < P < 0.05, **0.001 < P < 0.01, ***P < 0.001.$ 

definition of "clinically short" are of paramount importance with respect to the diagnosis and management of children with short stature. In this study, CDC-defined height SDS were examined both in terms of general efficacy as a diagnostic tool and, if not functioning effectively, as a possible cause of a gender bias in GH treatment. The well-known secular trend in height suggested that the use of height SDS could lead to inaccuracies in ascertainment and diagnosis of short children

because of the changing nature of height distributions. The potential problem associated with the secular trend of an erroneously decreased number of short children being identified has previously been flagged by Wit *et al.*<sup>38</sup> Similarly, that differences in mean heights between contemporary population samples and the CDC 2000 charts vary with age group has also been noted previously. <sup>16,20,22,39</sup> This study recognises an actual diagnostic problem associated with the use of CDC 2000 data in Australia

<sup>\$</sup>Null hypothesis: SD = 1. \*0.01 < P < 0.05, \*\*0.001 < P < 0.01, \*\*\*P < 0.001.

<sup>§</sup>Description of distribution. Normal (N): If not significantly different from normal distribution. Kurtosis (K), Skewness (S): If significantly different from normal distribution.

 $<sup>\</sup>P$ Number of children whose height fell below the CDC 1st centile (-2.326). Where this number differs between unweighted and weighted mean distributions the unweighted number is given first.

<sup>††</sup>Number of children whose height fell below the empirical 1st centile of the distribution assuming normality. Where this number differs between unweighted and weighted mean distributions the unweighted number is given first.

<sup>‡‡</sup>Non-normality because of positive kurtosis.

<sup>§§</sup>Non-normality because of a combination of positive kurtosis (peaked) and negative skewness (tail to left side, short heights).

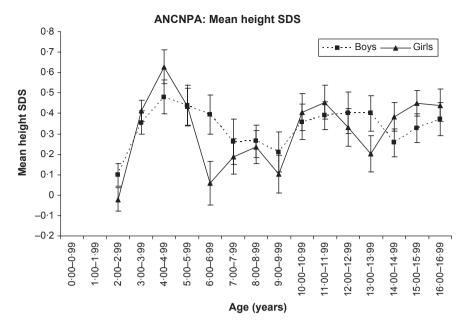


Fig. 1 Australian National Children's Nutrition and Physical Activity Survey: mean height SDS (±SE) by age.

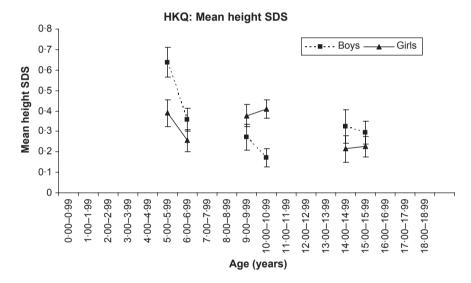


Fig. 2 Healthy Kids Queensland Survey: mean height SDS ( $\pm$ SE) by age.

and notes that it may vary with the age and at certain times also with the gender of the child being investigated.

From the evidence presented in this analysis, it is unlikely that the commonly observed gender bias in favour of boys can be explained entirely by a consistent difference between men and women in the secular trend in mean height. Such a gender bias was observed in the Australian survey populations although it was only significant when these surveys were combined. A gender bias in Australian children receiving GH treatment has previously been reported. As can be seen from Figs 1 and 2, mean height SDS vary with age but without the female values being consistently larger than the male. The situation is similar for the NHANES data (Fig. 3) for which, interestingly, there is no suggestion of a gender bias. A previous survey of children in the US state of Utah did identify a gender bias in relation to short stature. The stature of the stat

If the secular trend was primarily responsible for the gender bias, one would expect the boy/girl ratio to have increased with time. However, this does not seem to have been the case internationally. In analyses of the Pharmacia and Upjohn International growth database (KIGS) in 1998 and 2006, the boy:girl ratios for Organic GH Deficiency were 1·6 and 1·5, respectively. Similarly, the ratios for Idiopathic GH Deficiency were 2·2 and 2·1 and for Idiopathic Short Stature 2·1 and 2·1, respectively. <sup>24,25</sup>

The gender bias observed in the Australian surveys was only significant when the CDC 1st centile was used as the cut-off. This meant that the shortest 0.5% (approximately) of children were counted in contrast to the shortest 1%. It is possible that the distribution of boy's heights is skewed to the left, relative to that of girls, at the extreme end of short stature. Similarly, there may be a relative peak of boys at around the 0.5th centile that is "uncovered"

#### NHANES 2005-2006: Weighted mean height SDS

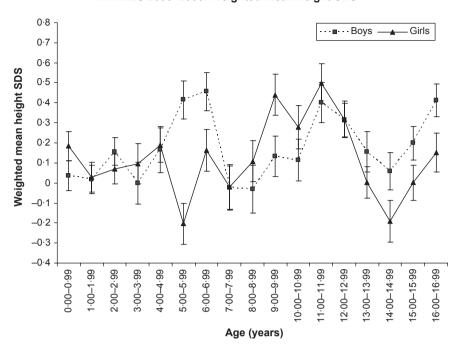


Fig. 3 National Health and Nutrition Examination Survey 2005–2006: weighted mean height SDS (±SE) by age.

when the cut-off is shifted to around this point. To test these possibilities would require a very large random survey. Alternatively, a real biological cause rather than a statistical or measurement anomaly may be at play. Population surveys of GH deficiency, rather than height, have also identified a significant gender bias towards boys. 33,40 Similarly, a gender bias has been reported with respect to structural abnormalities of the hypothalamus and pituitary in GH deficiency patients.<sup>41</sup> It is possible that such a biological cause becomes particularly evident within the shortest 0.5% of children.

The major conclusion of the current study is that the use of the CDC 1st centile as a diagnostic criterion for short stature in the contemporary Australian population underestimates those eligible for GH treatment. A similar problem in ascertainment or diagnosis of short stature is likely to occur in other populations that have experienced a significant secular trend and use CDC 2000 curves. The use of height SDS was designed to make it possible to directly compare children regardless of age or gender. However, it was evident in each of the surveys analysed here that mean height SDS values vary quite considerably across different age groups. This variation may be the result of relatively small, age-based, sample sizes although others using larger samples and the LMS smoothing method have reported similar age-related differences. 16,22 The secular trend and any age-related variation is most likely due to changes in growth tempo secondary to nutrition and lifestyle changes that have occurred since the CDC growth charts were constructed. The extremes of these changes have also been blamed for the current "obesity epidemic". 42-44

The important clinical outcome of this work is that, currently in Australia, approximately 0.5% rather than 1% of the child population is regarded as eligible for GH treatment for short stature. Secondary to this, the likelihood of a child falling below the "1st" centile possibly changes with age and sometimes between genders. Variation in mean height-SDS with age and gender also occurs within the US population although on average the proportion of individuals considered to be clinically short is similar to the historical cut-off. Height is the primary diagnostic criterion on which to base treatment for short stature or further investigations for GH deficiency. As such, paediatric endocrinologists should be aware that the use of CDC height SDS is not the unbiased normalization procedure that it is often perceived to be. Ideally, though there is some debate, heights should be normalized relative to the population from which the individuals come and a definition of short stature made in reference to that population.<sup>38,45</sup> This is a significant task but one, in this data rich age, that should be much easier to achieve and maintain than in previous generations. It has been recommended that for populations with large secular changes an update should be made every 5-10 years while 15-20 years is suggested for populations with smaller changes. 45 In the mean time, our study suggests that if the 1st centile is applied as a cut-off for short stature, in the current Australian population, this could be approximated by the CDC 2nd centile. This proposal will likely form an important part of the current debate surrounding the diagnostic criteria and approach to the treatment, or otherwise, of idiopathic short stature.

### **Conflict of interest**

Authors have nothing to declare.

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