

Validation of US Cerebral palsy growth charts using a British cohort

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Abbreviations

BCPE Box-Cox Power Exponential, BMI Body mass index, BCCG Box-Cox-Cole-Green
CP Cerebral palsy, GAMLSS Generalized Additive Models for Scale and Shape
GMFCS Gross motor function classification system, LMS Lambda-Mu-Sigma
SD Standard deviation, UK United Kingdom, UK-WHO Combined World Health
Organization and UK 1990 growth reference, Z Standard deviation

ABSTRACT

Aims

Growth charts for cerebral palsy (CP) have been constructed using data for 24,920 Californian patients, covering ages 2-20 years, with separate charts for the five Gross Motor Function Classification System (GMFCS) severity levels. Our aim was to test how British children with CP fit these charts, compared to conventional local charts.

Methods

The US CP growth reference was reanalyzed using the LMS (Lambda-Mu-Sigma) method to allow calculation of standard deviation (Z) scores. Growth data for 195 children in Glasgow with CP were retrieved and converted to Z scores using the CP reference as well as the UK-WHO growth reference.

Results

Measurements diverged progressively from the UK-WHO reference with increasing severity, with mean height for GMFCS V being close to the 2nd UK-WHO percentile. Compared to the CP reference mean height and weight Z scores were between 50th and 75th for all severity levels, while BMI was just below the 50th percentile.

Interpretation

British children with severe CP appear very small when plotted on non-CP charts, but fit well to US CP charts for weight and BMI and reasonably well for height. The LMS look-up tables will make it possible to calculate Z scores and produce charts in local formats.

What This Study Adds

- Children with severe cerebral palsy (CP) appear very small when plotted on standard charts
- UK children with CP fit well to US CP charts for weight and BMI
- UK children with CP appear tall relative to US CP charts for height
- It is now possible to calculate CP Z scores and produce charts in local formats.

BACKGROUND

Cerebral palsy (CP) is one of the most common physical disabilities in children, with a prevalence of around 2 per 1,000 children.¹ It is characterized by a variable degree of motor and postural impairment due to a non-progressive insult to the developing brain, which is also commonly accompanied by cognitive or sensory impairment². Healthcare professionals use growth charts as a tool for monitoring how a child is growing in comparison to children of the same age and sex and to identify children whose weight or height falls significantly below normal percentiles, which may indicate the need for investigation or treatment. It has been known for some time that children with severe CP do not grow or gain weight as expected for unaffected children³. CP is commonly associated with feeding difficulty, due to oromotor impairment, affecting the ability to chew and swallow safely⁴ and the extent of feeding difficulty has been shown to predict growth outcomes⁵. The wider recognition of this has led to many children receiving gastrostomy tube feeding in recent years, with clear benefits for their state of nutrition and quality of life^{6,7}. However, despite gastrostomy feeding, many children with severe CP remain very small, leading to recognition that even with even with careful clinical nutritional monitoring and intervention nutrition, children with severe cerebral palsy grow slowly for intrinsic rather than nutritional reasons.

A large study of children with CP who had accessed the services provided by the California Department of Developmental Services within a 15-year period, 1988-2002, summarized the growth of 24,920 children and found clear gradients for height and weight between the most and the least severe⁸. The same group used these data to develop growth charts for height, weight and BMI, specifically for children with CP aged 2 to 20 years⁹. Charts showing percentiles for height-for-age, weight-for-age and BMI-for-age were statistically modeled using 141,961 measurements of height and weight. Specific charts were developed, for both genders, for each of the five levels of the Gross Motor Function

Classification System (GMFCS) for severity of CP motor involvement¹⁰; level 5, representing the most severe motor disability was further stratified by the presence or not of a feeding tube. Thus there were a total of twelve separate growth charts.

Although published in 2011 there has so far only been one published validation of the weight curves¹¹ and their international relevance is unclear. Our aim therefore was to retrieve a growth data set for British children with CP in order to explore how well they fit the US CP charts compared to the mainstream UK charts.

METHODS

Patients

The NHS Greater Glasgow and Clyde Community Pediatric Services have a large caseload of children with CP, seen first usually to make the diagnosis and then monitored through the school years to coordinate their care needs. All contacts with children managed by GGC Community Pediatric Services were recorded in their Support Needs System electronic database. All children with CP diagnosis recorded within that database born between 1997 and 2013 were identified and available weight and height data downloaded. All weights were recorded on electronic, clinical grade standing, sitting or wheelchair scales. Standing height was measured where possible, usually using a wall mounted measure with a rigid T piece or occasionally a rigid free standing scale. Children who could not stand were measured using a flexible rule laid on the couch under the child. Lengths were not usually measured at all where children had fixed contractures to both legs, were too long for the measurer or too heavy to lift.

For children with any growth data the child's consulting supervising community pediatrician was contacted and asked to notify us both of their GMFCS level and whether they were tube fed. These records were also linked to a specialized CP database which included some but not

all the children managed by the service, where GMFCS level was recorded, but not tube feeding status.

The GMFCS levels were defined as follows¹²:

- Level I: Walks without restrictions; limitations in more advanced gross motor skills
- Level II: Walks without assistive devices; limitations in walking outdoors and in the community
- Level III: Walks with assistive mobility devices; limitations in walking outdoors and in the community
- Level IV: Self-mobility with limitations; children are transported or use power mobility outdoors and in the community
- Level V-NT: Self-mobility is severely limited even with the use of assistive technology, though not tube fed
- Level V-TF: Level V-NT and tube fed.

Enteral feeding turned out to be poorly recorded, and some children started or stopped tube feeding as they got older . So for our purposes the two level V categories were merged and plotted in V-NT charts. Once the data were matched to a GMFCS level child identifiers were deleted and the analyses were undertaken on this anonymized data set. The analysis was classified as service evaluation, so no ethical permissions were required.

Further analysis of the US source data

The US CP charts were constructed using Generalized Additive Models for Scale and Shape (GAMLSS) and the Box-Cox-Power-Exponential (BCPE) distribution family¹³ as implemented with the *gamlss* package¹³ in the *R* language. The fitted chart percentiles (from the 1st through to the 99th) were tabulated by age in tenths of a year from 2 to 20 years, giving tables with 181 rows and 99 columns. There were separate tables of weight, height and BMI by sex, for each of the GMFCS levels. The advantage of this approach was that the

percentiles were adjusted for distributional skewness and kurtosis, but the disadvantage was the lack of convenient software to convert the measurements and percentiles to exact standard deviation (Z) scores.

For the present analysis the tables were recalculated to match tables for the LMS method¹⁴, using the *LMSfit* function in the *sitar* package. The LMS method corresponds to the GAMLSS Box-Cox Cole-Green (BCCG) family, a special case of the BCPE family that adjusts for distributional skewness but not kurtosis. However in practice BCPE percentiles are usually very similar to LMS/BCCG percentiles, and any differences are restricted to the most extreme (i.e. top and bottom) percentiles. This reanalysis converted the references to LMS tables compatible with LMSgrowth¹¹ software, which in turn allowed a) individual measurements to be converted to Z scores, and b) the GMFCS chart percentiles to be adjusted to match the UK 9 percentile format¹⁵. It also meant that the GMFCS charts could be compared directly with the UK-WHO charts, the combined World Health Organization and UK 1990 growth reference as used in the UK for school age children¹⁶. A small pilot of manual plotting on the GMFCS IV and V charts suggested that the fit to the charts was reasonable, but that data for a wider range of ages and severities were needed.

Analysis of data from the UK cohort

Anthropometric measures for children with known GMFCS levels were converted to Z scores using LMSgrowth software¹⁷, both on the relevant GMFCS chart and the UK-WHO chart. These data were first analyzed per measurement, as the larger numbers allowed examination of narrow age categories as well as all the GMFCS levels. In addition, the Z scores for weight and height were averaged by child, along with the mean ages of measurement, and the analyses were then repeated for the child means.

We defined the fit to either reference in terms of the discrepancy of the mean value from the expected zero as described in a recent paper: ¹⁸ a poor fit being a discrepancy of greater than 0.67 standard deviations (SD) and a good fit being within 0.33 SD.

We hypothesized that compared to UK-WHO, children with mild CP would fit well on average, but that percentiles would be progressively lower with greater CP severity, and more so with increasing age. Compared to the CP reference we hypothesized that the CP children would on average be close to average for all grades of severity, with no variation by age. However we also had to consider the possibility that the CP weight and BMI Z scores would be below average, due to selective weighing of children with poor weight gain.

RESULTS

There were 336 children coded as having CP in the database, born between 1997 (when growth was first recorded) and 2013. Of these 293 had at least one measurement and 195 had a GMFCS level recorded. The remainder did not have a score entered on the database and their pediatrician had not replied to our request for this extra information. This provided 480 heights and 596 weights (see web table) with median (range) 2 (0-11) weights and 2 (0-15) heights per child children, aged 2-17 years.

Using the UK-WHO reference, height and weight Z scores declined with increasing CP severity, with median height Z score for GMFCS V close to the UK-WHO 2nd percentile (figure 1). In contrast, with the CP reference and the appropriate GMFCS level chart, median height and weight were between the 50th and 75th percentiles for all GMFCS levels, while BMI was consistently close to the 50th percentile. Table 1 shows the corresponding Z score means and SDs. In terms of formal criteria, the fit to the CP reference was good or acceptable (i.e., within 0.67 SD) at all levels for weight and BMI, and for height at all levels except III and V. Using the UK-WHO, there was a poor fit for height from GMFCS levels II to V, for weight at levels IV and V, and BMI at level V. The SDs of the Z scores for UK-WHO were

usually greater than 1 (range 0.9 to 2), while they were less than 1 (range 0.5 to 1) for the CP reference.

Compared to the UK charts by age of measurement there was large divergence in height from age 2 years, with little overall evidence of an age trend. However it was really only those with more severe CP who were consistently discrepant from the UK 1990 reference (figure 2) and their discrepancy tended to increase with age (table 2). In contrast there was a trend to increasing weight and BMI Z scores with age in all severities when compared to the CP reference (table 2). These analyses were repeated in the per child dataset and similar effects were seen (data not shown).

DISCUSSION

Recognizing the limited growth potential of many severely disabled children is important to avoid invasive feeding approaches when they are not needed. While some children will require gastrostomy feeding due to unsafe swallow, there is the risk that others are tube fed due to a misperception that they are nutritionally compromised. Recent studies have demonstrated that when tube fed these children often have very modest requirements¹⁹ and tend to become overfat²⁰. Equally, it is important not to simply assume that all is well in child with CP with falling percentiles. What is needed is a valid reference for comparison and these charts appear to go a long way in providing this, although they can only be seen as a description of how such children grow, rather than a standard of optimal growth.

Compared to the UK reference, the height and weight deficit of children with CP was very pronounced and present from age 2 years. To our surprise the deficits increased only slightly with age, even in those with the most severe CP, which suggests that the slow growth trajectory in CP is set very early on. The fit to the UK reference was much better generally for BMI, though the most severe children still fitted poorly. In contrast children showed acceptable fits to the California CP charts, though they tended to be somewhat taller in all

GMFCS levels, and those with more severe CP also tended to be heavier. The fit for BMI was better and showed the closest fit for those with more severe CP, with mean values tending to be slightly below the 50th percentile.

There were limitations in this study. Not all children with CP had growth data recorded electronically and many had only one or two data points. Working within a clinical system and dependent on the good will of many pediatricians, we were only able to identify a GMFCS level for two thirds of the children, but this should not have introduced any systematic bias. It still yielded data on nearly 200 children with a median of 2 weights and 2 heights per child, and spanning the whole of childhood. The relative sparsity of the data per child will inevitably raise concerns about their representativeness, with the risk that more measurements were collected at times when there were concerns about growth or weight gain. Thus in using single measurements there was a risk of bias due to children with poor growth being measured more often than others²¹. However, when using average values per individual child the numbers were small. Analysis of the data using both methods reassuringly yielded very similar results. We had very few data for later adolescence, at which point they may have been harder to measure. However the data points we had at these ages were consistent with earlier ages.

The SDs of the Z scores based on the UK-WHO reference were all greater than the expected value of one, which may reflect a non-healthy sample being compared to a healthy reference. However based on the CP reference the SDs were all less than one, suggesting *less* than the expected level of variation. Taken together with the relatively high height and weight Z scores, this suggests that UK children are bigger and less variable in anthropometric measures than the reference Californian children. Measurement of height and length is often challenging in children with CP, so that these differences might reflect differences in measurement method. The equipment used in both settings was not standardized and in the

UK the most severe and the oldest children tended not to be measured at all. Contractures used to significantly limit measurement in CP, but these are now much less common due to early physiotherapy and splinting. However these factors would be expected to differentially affect length for the children with the most severe CP, when in fact mean heights/lengths were higher for all severities.

Part of the explanation may be related to general demographics. The Californian population was more heterogeneous with regard to ethnicity, with a large proportion of Hispanic individuals who tend to be shorter than non-Hispanic white persons of the same age²². To our knowledge differences in CP growth by ethnicity have not been studied directly, but a recent study by the Surveillance of Cerebral Palsy in Europe did find that anthropometric measures differed across countries in a pattern that seemed to relate to differing rates of enteral feeding²³. Beyond general demographic considerations, it should be recognized that the British children were predominantly born and managed in the years 2000-2010, around 10 years after most of the Californian children were measured. Studies from both the US and the UK^{24 25} have documented significant trends toward increased weight and BMI of children as measured in general pediatric practices from the early 1990s. In addition the study period is recognized as one of increased awareness of the risks of malnutrition in children with CP. However, again this trend is seen consistently in all severities, particularly for height, and it seems unlikely that children with milder CP will have previously experienced undernutrition in childhood. However, many of these children at all severities will have been born preterm, so it is possible that these differences could reflect better recent nutritional care as neonates.

The Californian reference data showed that children who were tube fed were both heavier and taller than equally severe children who were not, which suggests that at least some of the growth deficit in severe CP reflects a nutritional deficit⁸. In our sample we

could not reliably identify tube feeding status, and the British GMFCS V group showed an acceptable fit to the GMFCS V-NT California reference. Further research is necessary to validate the use of charts that are stratified by mode of feeding and to clarify how to classify children who commence or cease enteral feeding over time.

Surprisingly, the best fit for the UK CP children was to the BMI charts. BMI is not widely used in this population but it can be highly illuminating in small children where there is concern about possible undernutrition. However, it is the measure most prone to error and in our practice we would always recommend use of skinfolds as well, as a more direct assessment of fat stores.

In conclusion, UK children with severe CP plotted on conventional charts appear very small. They fit the US CP charts much better, though tending to be heavier and taller than average. Presenting the US CP charts as LMS tables will make it possible to calculate GMFCS level specific Z scores, as well as to create paper charts using local chart formats.

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Conflict of Interest Statement

Jordan Brooks headed the team who developed the Cerebral Palsy charts and Tim Cole constructed the UK 1990 growth reference. Neither of them derive income from their charts. The other authors have no conflicts of interest relevant to this article to disclose.

Contributors statement

Charlotte Wright conceived the idea for the study analyzed the UK data and drafted the paper. Jordan Brooks developed the US CP charts, constructed the tabulated percentile tables and assisted in drafting the paper. Tim Cole reanalyzed the tabulated percentile tables to construct the LMS lookup tables, assisted in drafting the paper and approved the final manuscript as submitted. Emily Ingram did the initial literature search and pilot appraisal of the CP charts and approved the final manuscript as submitted. Lucy Reynolds identified the British children with CP, downloaded their growth data, supplied the linked GMFCS data and approved the final manuscript as submitted.

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Table 1: Z scores for height, weight and BMI based on UK 1990 and US Cerebral Palsy References, by GMFCS level

Bold = good fit to standard (<0.33SD discrepancy from expected 0)

Underlined = poor fit (>0.67 discrepancy)

Individual measurements GMFCS	Number of		UK 1990 reference						Cerebral Palsy Reference					
	Heights	Weights	Height		Weight		BMI		Height		Weight		BMI	
			Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
I	150	157	-0.63	1.07	-0.30	1.23	0.09	1.28	0.38	0.54	0.07	0.79	-0.34	0.67
II	131	135	<u>-1.03</u>	1.28	-0.37	1.50	0.37	1.38	0.40	0.61	0.25	0.94	-0.13	0.73
III	60	72	<u>-0.86</u>	1.14	-0.59	1.53	0.07	1.59	<u>0.80</u>	0.56	0.50	0.86	-0.12	0.79
IV	56	81	<u>-1.79</u>	1.43	<u>-1.63</u>	1.95	-0.41	1.96	0.49	0.62	0.20	1.02	-0.18	0.82
V	83	151	<u>-1.68</u>	1.56	<u>-1.52</u>	1.77	<u>-0.80</u>	1.75	<u>0.71</u>	0.62	0.62	0.85	-0.26	0.74
Average per child	Number of children													
I	52		-0.46	0.90	-0.22	1.08	0.03	1.15	0.48	0.46	0.13	0.71	-0.38	0.61
II	43		<u>-0.81</u>	1.25	-0.35	1.38	0.25	1.30	0.51	0.60	0.26	0.86	-0.18	0.69
III	26		<u>-1.10</u>	1.05	-0.59	1.43	0.11	1.39	<u>0.67</u>	0.50	0.50	0.80	-0.11	0.68
IV	28		<u>-1.70</u>	1.34	<u>-1.38</u>	1.85	-0.32	1.89	0.54	0.58	0.35	0.97	-0.12	0.82
V	46		<u>-1.84</u>	1.60	<u>-1.69</u>	1.61	<u>-0.86</u>	1.71	0.66	0.62	0.54	0.70	-0.24	0.66

Table 2: Z scores for individual height, weight and BMI based on UK 1990 and US Cerebral Palsy references, by age and severity

	Age (yrs)	UK 1990 reference						Cerebral Palsy Reference					
		Height		Weight		BMI		Height		Weight		BMI	
		Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
GMFCS	2-4	-1.06	1.17	-0.37	1.27	0.38	1.22	0.51	0.56	0.26	0.83	-0.26	0.57
I-III	4-6	-0.85	1.05	-0.51	1.43	0.13	1.51	0.49	0.49	0.14	0.92	-0.37	0.74
	6-8	-0.83	1.14	-0.55	1.43	0.04	1.34	0.42	0.50	0.10	0.87	-0.34	0.72
	8-10	-0.86	1.12	-0.38	1.41	0.18	1.38	0.27	0.56	0.18	0.85	-0.13	0.76
	10-12	-0.68	1.27	-0.22	1.80	0.35	1.67	0.28	0.70	0.25	1.07	0.07	0.89
	12-14	-0.34	1.40	0.01	1.45	0.18	1.37	0.62	0.79	0.46	0.85	0.03	0.71
	14-17	-0.62	1.28	-0.20	0.96	0.15	1.16	0.68	0.80	0.43	0.67	0.03	0.69
	P [†]		0.05		0.14		0.76		0.70		0.15		0.001
IV-V	2-4	-1.29	1.44	-1.22	1.61	-0.40	1.68	0.70	0.62	0.24	0.88	-0.38	0.67
	4-6	-1.68	1.83	-1.73	2.31	-0.57	2.11	0.58	0.77	0.20	1.14	-0.33	0.83
	6-8	-2.14	1.35	-1.61	1.45	-0.75	2.12	0.51	0.57	0.41	0.71	-0.34	0.83
	8-10	-1.67	1.49	-1.30	1.87	-0.73	1.29	0.71	0.63	0.75	0.93	-0.18	0.61
	10-12	-1.89	1.14	-1.60	2.09	-1.07	2.06	0.62	0.51	0.73	1.04	-0.10	0.89
	12-14	-1.96	1.37	-1.52	1.50	-0.72	2.01	0.68	0.64	0.88	0.68	0.25	0.85
	14-17	-2.94	1.32	-2.43	1.52	-1.27	2.11	0.44	0.55	0.75	0.65	0.14	0.81
	P [†]		0.07		0.04		0.13		0.88		<0.001		0.001

†Linear regression

LEGENDS TO FIGURES

Figure 1: Fit of individual measurements to CP and UK charts, by severity (GMFCS)

Figure 2: Fit of individual measures to UK 1990 charts, by age and severity (GMFCS)