# Do children and adolescents with cerebral palsy from Argentina and Germany grow differently?

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# Abstract

**Purpose:** To analyze growth patterns of children with CP between countries; to examine differences in growth; and to assess the fit of growth charts.

**Methods:** Cross-sectional study in children with CP from 2 to 19 years old, 399 from Argentina and 400 from Germany. Growth measures were converted into z-scores and compared to WHO reference and US CP growth charts. Generalized Linear Model was used to analyze the growth expressed as mean z-scores.

**Results:** 799 children. Mean age 9 years (± 4). Compared to the WHO reference, the decrease in Height z-scores (HAZ) with age in Argentina (-0.144/year) was double that in Germany (−0.073/year). For children in GMFCS IV-V, BMI z-scores (BMIz) decreased with age (−0.102/year).

Using the US CP charts, both countries showed decreasing HAZ with age, in Argentina (−0.066/year) and in Germany (−0.032/year). BMIZ increased more among children with feeding tubes (0.062/year), similar in both countries. Argentinian children with oral feeding decrease their Weight z-score (WAZ) by −0.553 compared to their peers.

With WHO charts BMIZ presented an excellent fit for GMFCS I-III. HAZ presents a poor fit to growth references. BMIZ and WAZ presented a good fit to US CP Charts.

**Conclusions**: Growth differences due to ethnicity also act in children with CP, and are related to motor impairment, age and feeding modality, possibly reflecting differences in environment or health care.


# What Is Known

- Children with CP tend to be shorter, smaller, and thinner than children with typical development.
- As the motor compromise of children with CP increases, the nutritional status tends to be more compromised.

# What Is New

- US CP charts fit well to describe growth patterns of BMI, but overestimate height. Meanwhile, conventional growth charts make children with severe CP appear very short
- German children with CP were taller and heavier than Argentinian children. Ethnic and environmental differences observed in children with TD can also been seen in children with CP.

# Introduction

Growth in typically developing (TD) children varies between countries. When comparing healthy economically-privileged children from non-European countries with those from northern European countries, the latter tend to be 5 cm taller than the WHO reference population, while non-European children fall to approximately 5 cm below the reference [1, 2]. Since the children included in the mentioned study were all considered to be relatively economically privileged, it has been suggested that these differences in growth may relate to inherent differences [1]. However other evidence suggests that these differences are likely to be environmental in origin [3, 4], as population height differences have been observed to diminish over time as populations become even more affluent[5]. Differences in

normal growth across countries may also need to be considered when assessing growth in children with chronic diseases that affect development.

Children with cerebral palsy (CP) have delayed growth and tend to be shorter and lighter than TD peers. The divergence from normal growth patterns is greatest for children with severe motor impairment and increases with age [6, 7]. Additionally, feeding difficulties, malnutrition, low growth hormone levels, and lower levels of physical activity have also been related to growth restriction [8–10].

Growth charts derived from more than 100,000 growth measures in 25,545 US children with cerebral palsy have been published [11]. Subsequent studies from other countries have reported that these charts provide a reasonable basis for monitoring growth of children with CP from Brazil and the UK [12, 13]. In particular, growth assessments of British children fitted well with the US charts regarding weight-for-age and body mass index (BMI)-for-age. British children with CP, however, were taller than the US CP growth reference [13]. Whether this difference varied with age or other characteristics (such as sex or feeding modality) was not reported in detail.

To our knowledge, differences in growth between European and South American children and adolescents with cerebral palsy have not been previously studied. The aims of the present study are: (1) to analyze and compare growth patterns of children with CP between countries; (2) to examine differences in growth with respect to age, severity of motor impairment and feeding modality and (3) To assess the fit of WHO and US CP growth reference charts in Argentinian and German children with CP.

# Method

This was a cross sectional study, with data collected retrospectively. Children with confirmed diagnosis of CP were included when weight and height measurements and diagnosis information were available. The case definition of CP developed by the Surveillance of Cerebral Palsy in Europe (SCPE) and international references was used in both countries [14, 15]. Those with a stated genetic or metabolic syndrome, (e.g. Angelman syndrome, Chromosomal aberration, etc.) potentially affecting growth, or had incomplete information were excluded.

Information on the Argentinian CP sample was obtained from the database of the INICSA (Instituto de Investigaciones en Ciencias de la Salud). Growth measurements were taken from children from five Argentinian cities (Cordoba, Ciudad Autonoma de Buenos Aires, Catamarca, Santiago del Estero and Jujuy) as part of a multicenter research study during years 2016 to 2018. Consecutive sampling was implemented in each institution, including as many children with CP as possible. Children were excluded when they did not fulfill the inclusion criteria requirements or were not available at the moment of data collection.

The German CP sample was obtained from medical records at the iSPZ Hauner (University Children's Hospital, Munich). Data were collected from children that had received medical care between 2010 and 2019. For each child only the last complete anthropometric assessment was used for comparison. All children with complete anthropometric information were included and consecutive sampling was performed.

Demographic characteristics, distribution of phenotype of CP (unilateral *versus* bilateral pattern), severity of motor impairment (GMFCS levels I-V), oral feeding vs non-oral (non-oral included children fed totally or partially with a feeding tube), and anthropometric measurements (weight and height) were obtained from the medical records of each child.

# Growth Assessment

International standards for growth assessment were followed[16]. Anthropometric measurements were collected from trained health professionals. Weight and height were collected using direct methods while children were wearing light clothes and no shoes. All measurements were taken twice and the average measurement was used for analysis.

Weight was obtained in kilograms to the nearest 100 grams using a wheelchair scale or a digital scale, depending on the child's abilities. In this study, the term height was used to refer to both height and length. Height was measured depending on the ability of the child to stand. When the child could not stand, length was measured in the supine position. Height was taken twice; if there was a difference of more than 1 cm between the two measurements, the data were excluded and the previous record of completed measure was included (n = 23). When direct height could not be obtained, it was not included in the medical records. If knee height was available, height was estimated with published equations for children with cerebral palsy using knee height when this segmental measure was available (n = 31, 3.9%) [17].

Growth measures were converted into z-scores. Z-scores for Argentinian and German children with CP were calculated based on international growth references for TD children from WHO (2007) for BMI and height [18]. Weight-for-age was not included from references for TD children as there is no information of weight-for-age for children older than 10 years old from the WHO charts. Also, z-scores for both the Argentinian and German children with CP were calculated based on the US CP growth charts for BMI, height- and weight-for-age using the procedure outlined in the UK study of Wright, Cole et al. together with LMS growth software [11, 13]. The fit of the growth curves was analyzed considering categories established in previous publications [13, 19], where mean z-score values $\leq 0.17$ SD were classified as an excellent fit, within $> 0.17$ to $\leq 0.33$ SD a good fit, and $> 0.67$ SD a poor fit. Weight-for-age z-scores were not used as they were not available for children older than 10 years of age from WHO Growth Charts (2007).

# Statistical Analysis

The normality of the continuous data was tested using the Kolmogorov-Smirnov test. Summary statistics were presented as mean with SD or medians with interquartile range (IQR) and absolute or relative frequency (percentage) with 95% confidence intervals. A bivariate analysis was performed between the z-scores for anthropometric measurements for WHO growth charts and US CP charts, and variables such as sex, GMFCS, country, etc. using t-tests. Variables with $p < 0.05$ in bivariate analysis were considered for inclusion in the multivariate analysis.

Generalized Linear Models were used to analyze the association between growth expressed as mean z-score and all relevant clinical covariates. Main effects models were used to evaluate z-score change with full adjustment (controlling for all significant covariates). We fitted interaction models to evaluate effect modification between variables found to be statistically significant in main effects models. The final models were chosen to have the best fit statistics defined by the lowest restricted maximum likelihood. Statistical significance was set at $p < 0.01$.

All analyses were performed by using IBM SPSS statistical software, V. 25 (IBM Corp, Armonk, New York, U.S.A.). Multivariable comparison graphs were developed using MedCalc V19.0 statistical software.

# Results

There were 799 growth measurements, 399 from Argentinian children with CP and 400 German children with CP. The mean age was 9 years and 5 months (SD 4 years 7 months). The characteristics of the sample are presented in supplementary Table 1.

We performed a bivariate analysis between BMIZ and HAZ of the WHO Charts, compared to country, sex, GMFCS level, Feeding and Age, and between BMIZ, HAZ and WAZ of the US CP Chart compared to the same variables (Table 1). With WHO growth charts, HAZ presented differences in feeding, between countries, GMFCS levels and age. With US CP Charts, HAZ presented significant difference between countries, GMFCS level and age, but not regarding feeding. BMIZ presented significant differences between countries and GMFCS when WHO growth references were used, and differences according to feeding with US CP charts. Age presented significant differences with both growth charts. With US CP Charts, WAZ presented significant difference between countries, GMFCS level and feeding, but not between age groups. Meanwhile, sex was not a significant variable for any z-score measurements and was not included in the multivariate analysis (Table 1).

Table 1
Bivariate analysis of variables according to z-scores values (n = 799).

| | **WHO charts, 2007** | | | | **US CP chart (2011)** | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | BMIZ | p value | HAZ | p value | BMIZ | p value | HAZ | p value | WAZ | p value |
| Country: | Mean (SD) | | Mean (SD) | | Mean (SD) | | Mean (SD) | | | |
| Germany | 0.37 [1.64] | **0.001** | -0.59 [1.48] | **< 0.001** | -0.37 [0.82] | 0.197 | 0.95*** [0.73] | **< 0.001** | 0.47 [0.89] | **0.001** |
| Argentina | -0.79*** [2.01] | | -1.96*** [1.92] | | -0.29** [0.93] | | 0.52 [0.89] | | 0.24** [1.06] | |
| Sex: | | | | | | | | | | |
| Female | -0.52 [1.73] | 0.445 | -1.30*** [1.86] | 0.740 | -0.28** [0.86] | 0.168 | 0.76 *** [0.89] | 0.448 | 0.40 [1.01] | |
| Male | -0.62 [1.92] | | -1.26*** [1.85] | | -0.37 [0.88] | | 0.72 *** [0.80] | | 0.32** [0.97] | 0.237 |
| GMFCS | | | | | | | | | | |
| Level I to III | -0.13* [1.50] | **< 0.001** | -0.60 [1.44] | **< 0.001** | -0.31** [0.82] | 0.363 | 0.82*** [0.78] | **0.001** | 0.41 [0.92] | |
| Level IV & V | -1.21*** [2.10] | | -2.35*** [1.94] | | -0.37 [0.95] | | 0.61 [0.91] | | 0.27** [1.07] | **0.056** |
| Feeding | | | | | | | | | | |
| Oral | -0.57 [1.83] | 0.695 | -1.22 *** [1.83] | **0.010** | -0.35 [0.87] | **0.031** | 0.73*** [0.83] | 0.401 | 0.32** [0.98] | |
| Non-oral | -0.67*** [2.06] | | -1.88 *** [1.92] | | -0.10* [0.89] | | 0.82 *** [0.90] | | 0.66 [1.05] | **0.017** |
| Age | | | | | | | | | | |
| 2 to 10 years old | | | | | | | | | | |
| | -0.43 [1.78] | | -0.99 *** [1.76] | | -0.48 [0.84] | | 0.88 *** [0.83] | | 0.38[0.99] | 0.341 |
| 11 to 19 years old | | **0.004** | | **< 0.001** | | **< 0.001** | | **< 0.001** | | |
| | -0.87*** [1.93] | | -1.76 *** [1.89] | | -0.08* [0.89] | | 0.49 [0.81] | | 0.31** [0.98] | |

Caption: significant differences are marked in bold. BMIZ: BMI-for-age z-score. HAZ: Height-for-age z-score. WAZ: weight-for-age z-score. GMFCS: Gross motor function classification system. Comparison to reference chart: *excellent fit (≤ 0.17 SD), **good fit (> 0.17 to ≤ 0.33 SD), ***poor fit (> 0.67 SD)

# Analysis Of Fit To The Two Growth References

WHO growth charts overall presented a poor fit, with mean values for all sub categories well below the expected value, except for BMIZ younger children and those in GMFCS level I to III. With the US CP chart BMIZ presented an excellent to good fit for all sub categories, but mean values for HAZ were considerably higher than expected (Table 1).

# Multivariate Comparison Of Mean Haz

With respect to TD reference from WHO´s reference charts for HAZ, the Generalized Linear Model (GLM) showed significant differences between countries, GMFCS levels and age ($p < 0.01$) (Table 2a). As age increased German children with CP were shorter than TD children, with a decrease of − 0.073 z-score/ per year of HAZ, meanwhile Argentinian children decreased − 0.144 z-score/ per year. Children with GMFCS I to III increased 0.087 z-score/per year their HAZ. As it can be observed in Fig. 1b, children with CP in Argentina tend to have lower HAZ than German children with CP. As age increased differences between countries also increased.

Table 2

**Generalized linear model for z-score in Argentinian and German children with cerebral palsy according to different growth charts** (n = 799).

| Model | Anthropometric measurement | Variables | β | 95%CI | p |
|---|---|---|---|---|---|
| a) WHO charts, 2007 | | | | | |
| Main effect model | Z-score BMI-for-age | Argentina, non-oral feeding, GMFCS IV & V | Reference | | |
| | | Germany | 0.041 | -0.22 to 0.30 | 0.048 |
| | | Oral Feeding | -0.440 | -0.90 to 0.02 | 0.063 |
| | | GMFCS I to III | 1.105 | 0.84 to 1.37 | **< 0.001** |
| | | Age | -0.037 | -0.06 to -0.01 | **0.007** |
| **Interaction effect model** | Z-score BMI-for-age | GMFCS IV & V *age | -0.102 | -0.13 to -0.07 | **< 0.001** |
| Main effect model | Z-score Height-for-age | Argentina, non-oral feeding, GMFCS IV & V | Reference | | |
| | | Germany | 0.852 | 0.62 to 1.08 | **< 0.001** |
| | | Oral Feeding | -0.16 | 0.21 to -0.57 | 0.451 |
| | | GMFCS I to III | 1.338 | 1.10 to 1.58 | **< 0.001** |
| | | Age | -0.061 | -0.08 to -0.37 | **< 0.001** |
| **Interaction effect model** | Z-score Height-for-age | Germany*age | -0.073 | -0.13 to -0.10 | **0.006** |
| | | Argentina*age | -0.144 | -0.18 to -0.10 | **< 0.001** |
| | | GMFCS I to III*age | 0.087 | 0.04 to 0.14 | **0.001** |
| | | Germany* GMFCS I to III | 0.767 | 0.17 to 1.36 | 0.012 |
| | | Germany* GMFCS IV &V | 0.233 | -0.34 to 0.81 | 0.428 |

Legend: Caption: significant differences are marked in bold. GMFCS: Gross motor function classification system.

| Model | Anthropometric measurement | Variables | β | 95%CI | p |
|---|---|---|---|---|---|
| | | Argentina* GMFCS I to III | 0.525 | -0.06 to 1.11 | 0.080 |
| b) US CP chart (2011) | | | | | |
| Main effect model | Z-score BMI-for-age | Argentina, non-oral feeding, GMFCS IV & V | Reference | | |
| | | Germany | -0.026 | -0.15 to 0.10 | 0.685 |
| | | Oral Feeding | -0.306 | -0.53 to -0.81 | **0.008** |
| | | GMFCS I to III | 0.148 | 0.02 to 0.28 | 0.025 |
| | | Age | 0.044 | 0.03 to 0.06 | **< 0.001** |
| **Interaction effect model** | Z-score BMI-for-age | Oral Feeding*age | 0.042 | 0.03 to 0.05 | **< 0.001** |
| | | Non-Oral Feeding*age | 0.062 | 0.04 to 0.08 | **< 0.001** |
| Main effect model | Z-score Height-for-age | Argentina, non-oral feeding, GMFCS IV & V | Reference | | |
| | | Germany | 0.321 | 0.21 to 0.44 | **< 0.001** |
| | | Oral Feeding | -0.222 | -0.43 to -0.02 | 0.034 |
| | | GMFCS I to III | 0.096 | -0.02 to 0.21 | 0.116 |
| | | Age | -0.050 | -0.06 to -0.04 | **< 0.001** |
| **Interaction effect model** | Z-score Height-for-age | Germany*age | -0.032 | -0.05 to -0.02 | **< 0.001** |
| | | Argentina*age | -0.066 | -0.08 to -0.05 | **< 0.001** |
| Main effect model | Z-score Weight-for-age | Argentina, non-oral feeding, GMFCS IV & V | Reference | | |
| | | Germany | 0.198 | 0.05 to 0.34 | **0.007** |

Legend: Caption: significant differences are marked in bold. GMFCS: Gross motor function classification system.

| Model | Anthropometric measurement | Variables | β | 95%CI | p |
|---|---|---|---|---|---|
| | | Oral Feeding | -0.429 | -0.69 to -0.17 | **0.001** |
| | | GMFCS I to III | 0.120 | -0.03 to 0.00 | 0.115 |
| | | age | -0.013 | 0.85 to 1.04 | 0.089 |
| **Interaction effect model** | Z-score Weight-for-age | Germany*Oral feeding | -0.261 | -0.57 to 0.04 | 0.095 |
| | | Argentina* Oral Feeding | -0.553 | -0.86 to -0.24 | **< 0.001** |
| Legend: Caption: significant differences are marked in bold. GMFCS: Gross motor function classification system. | | | | | |

Considering the US CP charts, differences between countries reached significance with HAZ. The GLM showed that German children decreased − 0.032 z-score/per-year, and Argentinian children decreased − 0.066 SD units/per-year. Therefore, as age increased, the HAZ decreased in both countries. Argentinian children with CP were shorter than German children (Table 2b). Figure 2b showed that HAZ presented higher values than the US CP reference population, irrespective of the GMFCS level. German children tend to be taller than Argentinian children and US CP reference chart.

# Multivariate Comparison Of Bimz

The Generalized Linear Model (GLM) for WHO's reference charts showed that for BMIZ gross motor severity and age were variables that showed significant differences ($p < 0.01$), country and feeding did not show significant differences. The interaction model between GMFCS with age was significant for levels IV to V, BMIZ decreased − 0.102 per year of age (Table 2a). Children with CP and GMFCS IV and V presented their lowest BMIZ at age 11 to 14 years old for both countries (Fig. 1a).

According to US CP charts BMIZ showed significant differences in feeding and age ($p < 0.01$). As age increased children with oral feeding increased their BMIZ 0.042 z-score per year, and children with non-oral feeding increased 0.062 z-score per year. There were no differences in BMI growth between countries or GMFCS levels (Table 2b). BMIZ was less than 0 for most groups in both countries (Fig. 2a).

# Multivariate Comparison Of Waz

GML for US CP charts showed significant differences between countries and feeding in the main effect model ($p < 0.01$). When the variables were combined in the interaction model, only Argentinian children with oral feeding presented significant differences. Argentinian children with oral feeding decrease by − 0.553 z-score units ($p < 0.001$) of WAZ, compared to their peers with non-oral feeding. WAZ was between 0 and 0.67, showing values with good fit to the references of US CP charts (Fig. 2c).

# Discussion

This study, compared growth in children and adolescents with CP from a northern European (Germany) and a southern American country (Argentina) to both the WHO reference for TD children [18], and the US CP references from Brooks et al. [11].

Children with CP in both countries are shorter, lighter and smaller than their typically developed peers and these differences increase as their GMFCS level and age increase. Previous studies have also demonstrated that children with CP grow differently from their TD peers and that GMFCS level strongly influences their growth [9, 11, 13, 20]. Studies from German and Argentinian children with CP have also recently shown this difference [21, 22].

The second main finding is that between the two countries, children with CP differed significantly in height. German children with CP with GMFCS level I to III grow similarly to their TD peers, but those with GMFCS level IV and V are significantly shorter. In contrast, all the Argentinian children with CP were shorter than their TD peer, no matter the GMFCS level and their HAZ tended to decrease with age, twice as fast as for German children. Growth differences after pubertal age have been shown for healthy children in different countries and ethnicities [1, 23]. A large meta-analysis on fifty-three different healthy populations indicated that the mean height of preadolescent healthy children differs by 3 to 5 cm. At puberty, most non-European populations fall approximately 5 cm below the reference and northern European populations exceeding the reference by a similar amount [1]. This finding may be explained proximally by population differences in the initiation and progression of puberty in TD children. In Argentina, children with TD show a two-year earlier sexual development, which leads to an earlier closure of the epiphyseal growth plate and explains a shorter final height in the general population when is compared to international references [24, 25]. Differences in the onset of puberty, which may also relate to the severity motor impairment, could partially explain differences in height between TD children and children with CP found in our study [10, 26]. The present study did not measure pubertal status or progression in children with CP, and further research would be needed to examine this possibility.

Our study demonstrates, for the first time, that the same ethnic differences that can be observed in children with TD can also been seen in children with CP. Differences in height between countries are multifactorial, but are likely to mostly relate to epigenetic, and environmental rather than genetic, factors. Secular trends in height are commonly seen within countries, related to changing socio-economic status, nutrition, and health, and these can serve as public health indicators for interactions between growth and environment [3, 4]. It has been demonstrated that social and psychological factors (such as socioeconomic status, parental education or emotional deprivation) are related to linear growth, and the effects of socio-economic crisis can increase low birthweight prevalence and can affect secular changes [27–29]. The effect of environmental factors may also explain differences in growth in children with CP from countries with difference socio-economic realities and healthcare systems, such as Germany and Argentina. Further research is needed to understand how environmental factors affect growth in children with CP.

It is puzzling that US CP charts tended to overestimate HAZ for children with CP in both countries, a similar finding to the earlier UK study [13]. For context, it should be noted that height measurements used to develop the US CP charts were taken from medical records and were not validated, and the authors recommend that height curves should therefore be viewed with caution [7, 11]. Due to the difficulties in measure height in children with CP with severe motor compromise, it is possible that the differences in height could be related to the differences in measurement methods. Beyond the possible bias, differences were greater than 0 HAZ z-score for all GMFCS levels. It is also possible that this reflects the fact that the data used for the US charts was collected longer ago and that

children with CP may grow better now than previously, due to improvements in neonatal nutrition. Future prospective multicenter studies with training measurement methods could help adjust this bias.

Besides the ethnic and sociodemographic differences, further influencing variables need to be considered for children with a chronic disease (such as CP). Compared to the US CP growth chart, children with non-oral feeding had higher BMIZ and a better fit to the charts. On the other hand, for WAZ there was a better fit for children with oral feeding, who presented lower z-score values than their peers with non-oral feeding. In the multivariate analysis, Argentinian children that were fed orally presented a significantly lower z-score than those with non-oral feeding. These findings suggest that some of the growth deficit in children with CP and GMFCS level V could be related to nutritional deficit, and when they are fed enterally, totally or partially, nutrition is more secure. This difference in growth according to the feeding modality have already been mentioned in other CP studies, showing differences between countries, and required the development of different growth charts according to feeding in the CP US Charts [11, 30].

Some limitations should be mentioned. Selection bias may exist when comparing different study populations. In Argentina, we were able to observe that the centers included had more children with GMFCS levels IV-V, whereas in the German study site patients showed a broader range of GMFCS Levels, and was predominately Level I. The prevalence of less compromised motor impairments seems to be increasing in European countries and Australia [31–33], with a similar distribution as that in our German sample. It is possible that in Argentina there is a bias due to the type of centers included, where motor disabilities were more severe. In the absence of a complete local register, it is difficult to establish if our sample distribution is representative of the Argentinian CP population. Another limitation is the possible information bias from a retrospective study. We tried to control this bias by including only patients with complete anthropometric measurements and chose their last visit if multiple measures were available. However, because of the difficulty of measuring height in children with CP, it is possible that children with more severe motor compromise were lost because measurements were not available. Due to the limitations of height measurement and the lack of relation between BMI and body fat mass [34, 35], the interpretation of BMI as an indicator of body composition should be considered with caution. To study nutritional assessment in detail, other anthropometric measures beyond weight, height and BMI are recommended [36] to assess nutritional status, such as segmental measures and skin fold. These measures were not available in all medical records.

The major strength of this study was the capacity to monitor growth in two well controlled settings. Another strength is the chance to compare children with CP form two difference settings, Argentina and Germany. Our analysis of growth possibly reflects environmental and health care differences that should be deeply studied in the field.

# Conclusion

Differences in growth pattern between Argentinian and German children with CP exist, and may be related to environmental factors. German children with CP tend to be taller than Argentinian children. All Argentinian and German children with GMFCS level IV and V tend to be smaller and shorter than their peers with TD from the WHO international references and as age increases, differences increase. When US CP charts are used, it should be considered that BMIZ presents a good fit, but that HAZ should be considered with caution.

# Abbreviations

**BMIZ** Body mass index for age z-score

**HAZ** Height for age z-score

# Declarations

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**CONFLICT OF INTEREST:** All authors have declared that they have no conflict of interest to disclose.

**AVAILABILITY OF DATA AND MATERIAL**: The datasets analyzed during the current study are not publicly available.

**CODE AVAILABILITY**: Not applicable

**AUTHOR'S CONTRIBUTIONS:** M. Ruiz Brunner designed the data collection instruments, collected data and carried out the initial analyses. M. Ruiz Brunner, S. Schroeder, and E. Cuestas conceptualized and designed the study, coordinated and supervised data collection, analysis and interpretation, drafted the initial manuscript, and reviewed and revised the manuscript. J. Brooks, C. Wrights, R. Von Kreis and F. Heinen conceptualized and designed the study and critically reviewed the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

**ETHICS APPROVAL:** Approval for the study was given by Munich University (LMU) Institutional Review Board (No. 18-759) and the Ethical Evaluation Board of Health Research (COEIS) of the province of Cordoba (REPIS No. 3262/3236). The privacy, confidentiality and security of the participants' personal data were safeguarded. The research was registered in the DRKS – German Clinical Trial Register (DKRS00016407).

**CONSENT TO PARTICIPATE:** The need for patients' written consent was deemed unnecessary by the institutional review boards as we did not contact the families to conduct this retrospective study.

**CONSENT FOR PUBLICATION:** All authors have given their consent to publish the manuscript

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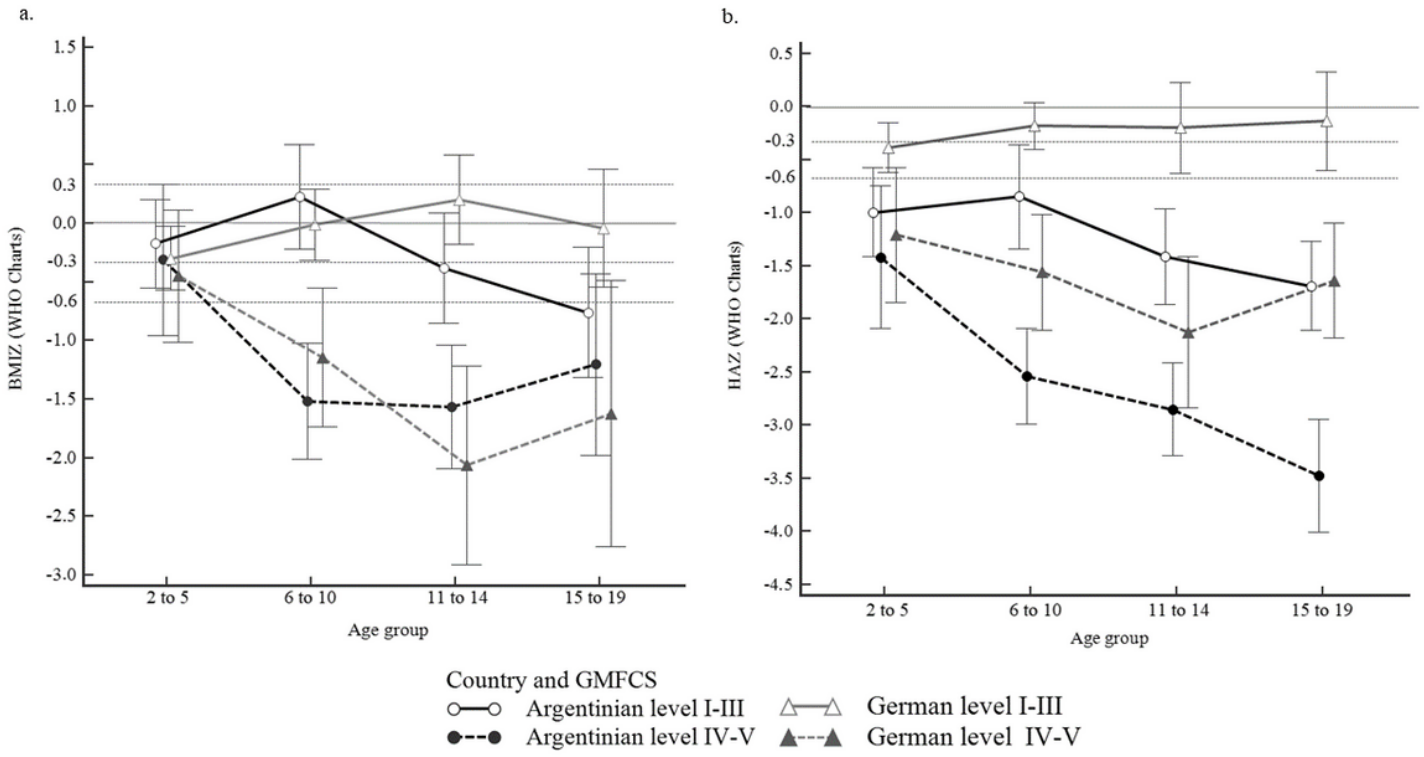
# References

1. Haas JD, Campirano F (2006) Interpopulation Variation in Height among Children 7 to 18 Years of Age. Food Nutr Bull 27:S212–S223. https://doi.org/10.1177/15648265060274S505
2. Schaffrath Rosario A, Schienkiewitz A, Neuhauser H (2011) German height references for children aged 0 to under 18 years compared to WHO and CDC growth charts. Ann Hum Biol 38:121–130. https://doi.org/10.3109/03014460.2010.521193
3. Perkins JM, Subramanian SV, Smith GD, Özaltin E (2016) Adult height, nutrition, and population health. Nutr Rev 74:149–165. https://doi.org/10.1093/nutrit/nuv105

4. Fudvoye J, Parent AS (2017) Secular trends in growth. Ann Endocrinol (Paris) 78:88–91. https://doi.org/10.1016/j.ando.2017.04.003
5. Wright CM, Parker L (2004) Forty years on: The effect of deprivation on growth in two Newcastle birth cohorts. Int J Epidemiol 33:147–152. https://doi.org/10.1093/ije/dyg187
6. Stevenson RD, Conaway M, Chumlea WC et al (2006) Growth and health in children with moderate-to-severe cerebral palsy. Pediatrics 118:1010–1018. https://doi.org/10.1542/peds.2006-0298
7. Day SM, Strauss DJ, Pierre JV et al (2007) Growth patterns in a population of children and adolescents with cerebral palsy. Dev Med Child Neurol 49:167–171. https://doi.org/10.1111/j.1469-8749.2007.00167.x
8. Stevenson RD, Roberts CD, Vogtle L (1995) The effects of non-nutritional factors on growth in cerebral palsy. Dev Med Child Neurol 37:124–130. https://doi.org/10.1111/j.1469-8749.1995.tb11981.x
9. Oftedal S, Davies PSW, Boyd RN et al (2016) Longitudinal Growth, Diet, and Physical Activity in Young Children With Cerebral Palsy. Pediatrics 138:e20161321. https://doi.org/10.1542/peds.2016-1321
10. Kuperminc MN, Gurka MJ, Houlihan CM et al (2009) Puberty, statural growth, and growth hormone release in children with cerebral palsy. J Pediatr Rehabil Med 2:131–141. https://doi.org/10.3233/PRM-2009-0072
11. Brooks J, Day S, Shavelle R, Strauss D (2011) Low weight, morbidity, and mortality in children with cerebral palsy: new clinical growth charts. Pediatrics 128:e299–e307. https://doi.org/10.1542/peds.2010-2801
12. Araújo L, Silva LR (2013) Anthropometric assessment of patients with cerebral palsy: Which curves are more appropriate? J Pediatr (Rio J) 89:307–314. https://doi.org/10.1016/j.jped.2012.11.008
13. Wright CM, Reynolds L, Ingram E et al (2017) Validation of US cerebral palsy growth charts using a UK cohort. Dev Med Child Neurol 59:933–938. https://doi.org/10.1111/dmcn.13495
14. Surveillance of Cerebral Palsy in Europe (2000) Surveillance of cerebral palsy in Europe: a collaboration of cerebral palsy surveys and registers. Surveillance of Cerebral Palsy in Europe (SCPE). Dev Med Child Neurol 42:816–824. https://doi.org/10.1111/j.1469-8749.2000.tb00695.x
15. Rosenbaum P, Paneth N, Leviton A et al (2007) A report: the definition and classification of cerebral palsy April 2006. Dev Med Child Neurol Suppl 109:8–14
16. Hall JG, Allanson JE, Gripp KW, Slavotinek AM (2007) Handbook of Physical Meausrments Second Edition. Oxford University Press, New York
17. Stevenson RD (1995) Use of segmental measures to estimate stature in children with cerebral palsy. Arch Pediatr Adolesc Med 149:658–662
18. Growth reference data for 5–19 years (WHO 2007). In: World Heal. WHO, Organ (2007) https://www.who.int/growthref/en/
19. Levin D, Marryat L, Cole TJ et al (2016) Fit to WHO weight standard of European infants over time. Arch Dis Child 101:455–460. https://doi.org/10.1136/archdischild-2015-309594
20. Oftedal S, Davies PS, Boyd RN et al (2017) Body composition, diet, and physical activity: A longitudinal cohort study in preschoolers with cerebral palsy. Am J Clin Nutr 105:369–378. https://doi.org/10.3945/ajcn.116.137810
21. Egenolf P, Duran I, Stark C et al (2019) Development of disorder-specific normative data for growth in children with cerebral palsy. Eur J Pediatr 811–822. https://doi.org/10.1007/s00431-019-03360-5
22. Ruiz Brunner M, de las M, Cieri ME, Rodriguez Marco MP et al (2020) Nutritional status of children with cerebral palsy attending rehabilitation centers. https://doi.org/10.1111/DMCN.14667. Dev Med Child Neurol Online ahead of print

23. Natale V, Rajagopalan A (2014) Worldwide variation in human growth and the World Health Organization growth standards: A systematic review. BMJ Open 4:1–11. https://doi.org/10.1136/bmjopen-2013-003735
24. Lejarraga H, Sanchirico F, Cusminsky M (1980) Age of menarche in urban Argentinian girls. Ann Hum Biol 7:579–581. https://doi.org/10.1080/03014468000004691
25. Ruiz Brunner M, de las M, Cuestas E, Cieri ME, Cuestas E (2019) Reference ranges for knee height in Argentine children and adolescents aged 2 to 18 years. Am J Hum Biol 32:e23366. https://doi.org/10.1002/ajhb.23366
26. Kao KT, Denker M, Zacharin M, Wong SC (2019) Pubertal abnormalities in adolescents with chronic disease. Best Pract Res Clin Endocrinol Metab [Epub ahead of print]. https://doi.org/10.1016/j.beem.2019.04.009
27. Niere O, Spannemann L, Stenzel P et al (2020) Plasticity of human growth – a systematic review on psychosocial factors influencing growth. Anthropol Anzeiger 77:431–443. https://doi.org/10.1127/anthranz/2020/1223
28. Mansukoski L, Johnson W, Brooke-Wavell K et al (2020) Four decades of socio-economic inequality and secular change in the physical growth of Guatemalans. Public Health Nutr 23:1381–1391. https://doi.org/10.1017/S1368980019003239
29. Terán JM, Vera C, Juárez S et al (2018) Social disparities in Low Birth Weight among Spanish mothers during the economic crisis (2007–2015). Nutr Hosp 35:129–141. https://doi.org/10.20960/nh.2095
30. Dahlseng MO, Andersen GL, Da Graca Andrada M et al (2012) Gastrostomy tube feeding of children with cerebral palsy: Variation across six European countries. Dev Med Child Neurol 54:938–944. https://doi.org/10.1111/j.1469-8749.2012.04391.x
31. Boyd RN, Jordan R, Pareezer L et al (2013) Australian Cerebral Palsy Child Study: protocol of a prospective population based study of motor and brain development of preschool aged children with cerebral palsy. BMC Neurol 13:57. https://doi.org/10.1186/1471-2377-13-57
32. Sellier E, Platt MJ, Andersen GL et al (2016) Decreasing prevalence in cerebral palsy: a multi-site European population-based study, 1980 to 2003. Dev Med Child Neurol 58:85–92. https://doi.org/10.1111/dmcn.12865
33. Himmelmann K, Sundh V (2015) Survival with cerebral palsy over five decades in western Sweden. Dev Med Child Neurol 57:762–767. https://doi.org/10.1111/dmcn.12718
34. Duran I, Schulze J, Martakis KS et al (2018) Diagnostic performance of body mass index to identify excess body fat in children with cerebral palsy. Dev Med Child Neurol 60:680–686. https://doi.org/10.1111/dmcn.13714
35. Stevenson RD (2018) Body mass index and obesity in children with cerebral palsy. Dev Med Child Neurol 60:639
36. Romano C, Van Wynckel M, Hulst J et al (2017) European Society for Paediatric Gastroenterology, Hepatology and Nutrition Guidelines for the Evaluation and Treatment of Gastrointestinal and Nutritional Complications in Children with Neurological Impairment. J Pediatr Gastroenterol Nutr 65:242–264. https://doi.org/10.1097/MPG.0000000000001646

# Figures

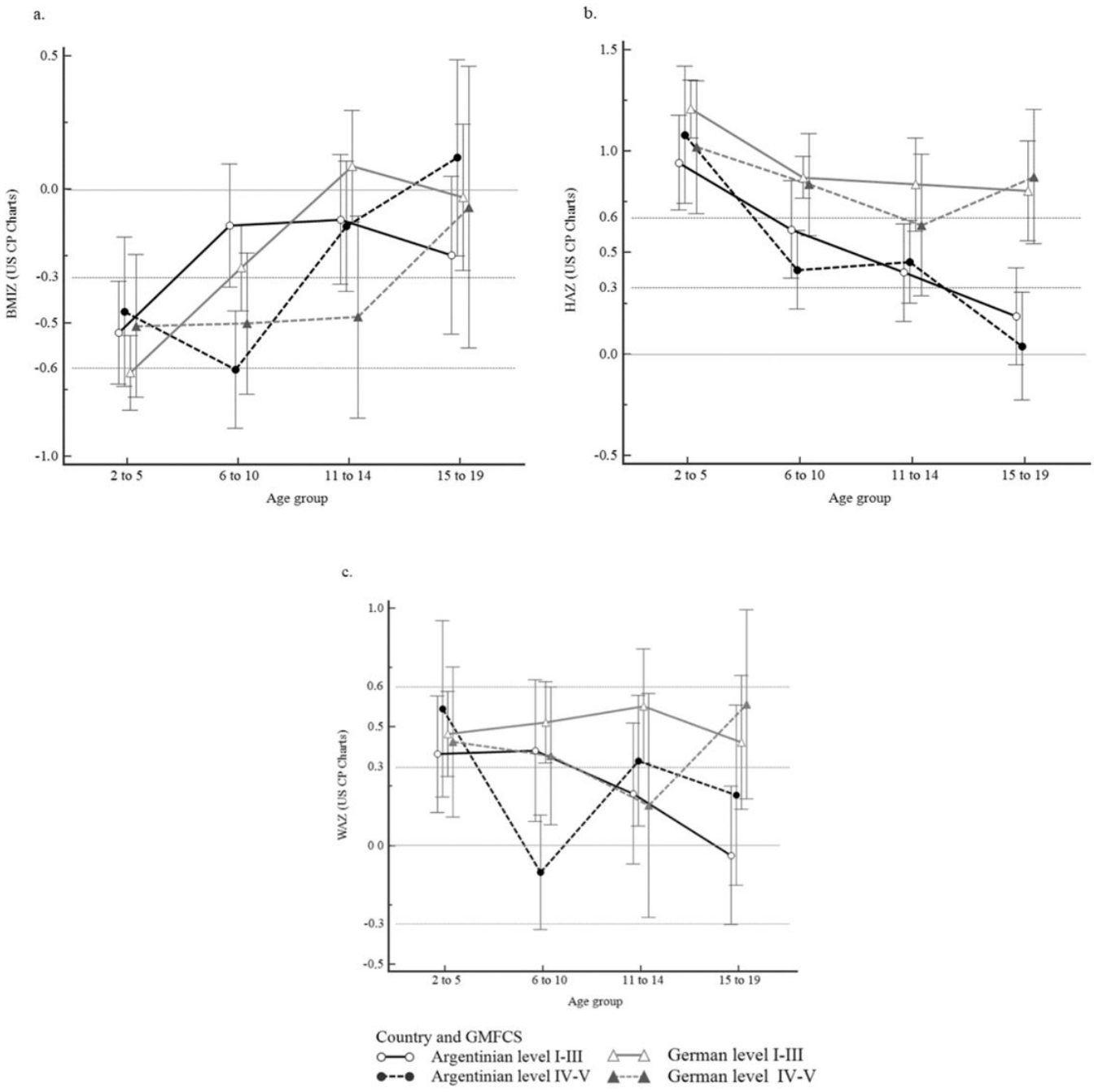



## Figure 1

Z-score (mean; 95% CI) comparison for anthropometric measures according to children with TD from **WHO growth charts (2007)** (n = 799).

Legend:

a. BMI-for-age (BMIZ) by age considering country and GMFCS level for children with CP. b. Height-for-age (HAZ) by age considering country and GMFCS level for children with. GMFCS: Gross motor function classification system. Dotted lines mark the thresholds for a good fit (<0.33 SD) and a poor fit (>0.67 SD) to the growth reference.




## Figure 2

Z-score (mean; 95% CI) comparison for anthropometric measures according to children with TD from **US CP Charts (2011)** (n = 799).

Legend:

a. BMI-for-age (BMIZ) by age considering country and GMFCS level for children with CP. b. Height-for-age (HAZ) by age considering country and GMFCS level for children with CP. c. Weight-for-age (WAZ) by age considering country and GMFCS level for children with CP. GMFCS: Gross motor function classification system. Dotted lines mark the thresholds for a good fit (<0.33 SD) and a poor fit (>0.67 SD) to the growth reference.

## Supplementary Files

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- Supplementarytable1revec140821clean.docx