Comparing the Use of Centers for Disease Control and Prevention and World Health Organization Growth Charts in Children with Cystic Fibrosis through 2 Years of Age

Zhumin Zhang, PhD[1], Suzanne M. Shoff, PhD[1], and HuiChuan J. Lai, PhD, RD[1,2,3]

Objective To examine differences between use of World Health Organization (WHO) and Centers for Disease Control and Prevention (CDC) growth reference in children with cystic fibrosis (CF) up to 2 years of age.

Study design Growth from 1-24 months in 2587 children, born 2003-2006 and recorded in the US CF Foundation Registry, was evaluated using WHO and CDC references.

Results In both boys and girls with CF aged 1-24 months, use of WHO charts resulted in ~8 percentile lower length-for-age and ~13% higher short stature rate (length-for-age <5th percentile). WHO weight-for-age was ~9 percentile lower prior to age 6 months, crossed at 6-7 months, and remained ~14 percentile higher at 8-24 months. WHO weight-for-length (WFL) percentile (WFLp) was similar before 12 months but ~10 percentile higher at 12-24 months compared with CDC. When using WHO charts, 9% of children had underweight (WFLp <50th) classified differently and this rate varied with age: 4% in the first year, 7% at 12, 13% at 15, and 16% at 18 months, respectively. Weight status assessed by WHO body mass index (BMI) charts was different from WHO WFL charts. At 24 months when switching back to CDC, 26% of children with normal WFLp on WHO charts appeared underweight on CDC charts. A 70th percentile of WHO BMI percentile was equivalent to the 50th percentile CDC BMI percentile.

Conclusions Growth status in children with CF differed when using WHO and CDC references, particularly during the second year of life. These differences need to be considered for all uses of growth assessment in CF. *(J Pediatr 2015;167:1089-95)*.

Growth charts are important clinical tools to assess and monitor growth. For infants with cystic fibrosis (CF), the US CF Foundation (CFF) recommended age-specific daily weight gain values for growth monitoring.[1] A 50th percentile goal of weight-for-length (WFL) was also recommended. For those who are undernourished, increased rates of weight gain are targeted for catch-up growth. Since 2010, most CF pediatric clinics in the US have switched to the 2006 World Health Organization (WHO) growth reference[2] for children younger than 24 months to replace the use of the US Centers for Disease Control and Prevention (CDC) growth reference,[3] in the wake of recommendations from both the CDC and the American Academy of Pediatrics.[4,5] The rationale for this recommendation is that the WHO reference represents the best possible growth potential from optimally fed babies (breastfed) residing in optimal living conditions in areas throughout the world. There are substantial anthropometric differences between the CDC and WHO reference population.[6-9] Thus, the impact of changing growth references on the interpretation of individual growth status, as well as population averages in CF, needs to be elucidated.

At age 24 months, when transitioning from WHO back to CDC reference, WFL status in children with CF with certain severe mutations was significantly better when using WHO charts compared with CDC charts.[10] However, thorough comparisons prior to age 24 months for WFL, as well as for other anthropometric variables (ie, weight and length), are not available. Estimates of nutritional status by the 2 references vary by age, the chart used, and cut-off values applied in healthy children without CF.[7-9] Similar results are expected in children with CF, but the magnitude is unknown. In addition, a goal of 50th percentile of body mass index (BMI, at age 24 months or older) or WFL (younger than 24 months) is recommended based on the CDC reference for children with CF.[10,11] Because the CDC and WHO growth charts differ, the corresponding percentile cut-off value on WHO charts will also vary.

BMI	Body mass index	LFA	Length-for-age
BMIp	BMI percentile	LFAp	LFA percentile
CDC	Centers for Disease Control and Prevention	MI	Meconium ileus
		WFA	Weight-for-age
CF	Cystic fibrosis	WFAp	WFA percentile
CFF	CF Foundation	WFL	Weight-for-length
FEV1p	Percent predicted forced expiratory volume in 1 second	WFLp	WFL percentile
		WHO	World Health Organization

From the Departments of [1]Nutritional Sciences, [2]Biostatistics and Medical Informatics, and [3]Pediatrics, University of Wisconsin–Madison, Madison, WI

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In children with CF who are at high risk of growth faltering,[12-16] the switch from use of the CDC to WHO growth charts from 0-23.9 months, then back to the CDC charts at age 2 years, may be a significant source of confusion for care providers and potentially impart undue anxiety on families because of an appearance of abrupt decline in nutritional status caused by the switch. Overall, clarification in the population with CF is necessary because of the reliance on nutritional status indicators for evaluation of individual patient care, overall assessment of effectiveness of nutritional interventions in clinical care, and the performance of CF centers with regard to nutritional management.

Therefore, the aim of this study is to apply the WHO and CDC growth reference, over 1-24 months of age in a representative population of children with CF, in order to: (1) compare differences in weight and height status (ie, weight-for-age [WFA] percentile [WFAp], length-for-age [LFA] percentile [LFAp], WFL percentile [WFLp], BMI percentile [BMIp]); (2) compare prevalence of undernutrition; and (3) identify WHO values equivalent to the 50th percentile of CDC BMI at 24 months, the age at which health care providers switch back to CDC charts.

Methods

The CFF Patient Registry documents the diagnosis and follow-up evaluations of patients with CF who are seen at accredited centers in the US. A total of 2954 children born between 2003 and 2006 were identified from the 1986-2008 CFF Patient Registry.[17] Among them, 346 children (12%) who did not have weight and length measured in the first 2 years of life were excluded. Length, weight, and WFL measurements that deviated more than 5 SDs from the CDC medians were excluded because these values were likely outliers resulting from measurement or recording errors. Very few children (n = 149, 5%) had weight and length information available in the first 2 weeks of life, therefore, comparisons between WHO and CDC growth charts at birth were not performed. The remaining 2587 children with 23 481 observations were included for analyses. The study protocol was approved by the human subjects committee at the University of Wisconsin-Madison.

Growth Evaluation Using WHO and the CDC Growth Charts

Z-score and percentile values were calculated using code written for SAS (SAS Institute, Inc, Cary, North Carolina) and used reference values for the CDC's 2000 growth charts (downloaded from http://www.cdc.gov/growthcharts) and reference values for the WHO's 2006 growth charts (downloaded from http://www.who.int/childgrowth/standards/en/). A cut-off value of the 50th percentile of WFLp and BMIp was used to define underweight.[10,11] Short stature was defined as LFAp less than the 5th percentile.[18] For CDC BMIp calculations at 24 months of age, 0.7 cm was subtracted from recumbent length to obtain standing height.[2]

Computation of WHO WFLp and BMIp Equivalents to the 50th Percentile CDC BMI at Age 24 Months

WHO values equivalent to the 50th percentile of CDC BMI at 24 months were computed for boys and girls at a given stature (5th-95th percentile) as follows. First, the weight for the given height corresponding to the 50th percentile CDC BMI was identified; then the corresponding WFLp or WHO BMIp value corresponding to this height and weight was calculated. For instance, in boys at age 24 months, 11.14 kg body weight for a given height of 82.8 cm (the CDC 5th percentile) corresponded to the 50th percentile CDC BMI. For this weight and height, WHO BMIp was the 70th percentile, WHO WFLp was the 57th percentile, and CDC WFLp was the 39th percentile.

Statistical Analyses

SAS (v 9.4; SAS Institute, Inc, Cary, North Carolina) and R (http://www.r-project.org) statistical software were used for statistical analyses. To compare growth between use of WHO and CDC growth charts in the first 2 years, repeated measures were performed using PROC GENMOD procedure in SAS using generalized estimating equations with a working assumption of independence among observations.[19] The identity link was used for continuous outcomes, and the logit link combined with the binomial variance function was used for dichotomous outcomes in generalized estimating equation models. At 24 months, paired t test and χ^2 test were conducted to test the difference between the WHO and the CDC. The analyses were performed separately for boys and girls.

Results

The study cohort (n = 2587) was comprised of the majority of children with CF (84%) born between 2003 and 2005 and reported in the 2008 US CFF Patient Registry. Among them, 1301 (50%) were boys, 599 (23%) of them had meconium ileus (MI), 1770 (68%) had pancreatic insufficiency without MI, and 218 (8%) were pancreatic sufficient. About one-quarter of these children (n = 658, 25%) were diagnosed through prenatal/neonatal screening, and another one-third (n = 965, 37%) were identified because of symptoms other than MI. In 2566 children with racial and ethnicity information available, the predominant racial background was non-Hispanic white (82%), Hispanic (11%), and non-Hispanic black (4%). The remaining 3% consisted of American Indian or Alaska Native, Asian, multiraces, and others.

Comparing LFA Status between Using WHO and CDC Growth Charts

In boys with CF, the WHO LFAp was consistently below the CDC's by an average of ~8 percentiles in the first 2 years of life (WHO 13 ± 28 vs CDC 21 ± 27th percentile, $P < .0001$; **Figure 1**, A). As a result, more boys with CF were classified as short (LFAp <5th) using WHO charts compared with the CDC (WHO 35% vs CDC 22%, $P < .0001$; **Figure 1**, B). Similar results were found in girls