DEVELOPMENT OF A KLINEFELTER SYNDROME SPECIFIC STATURE-FOR-AGE GROWTH CHART
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Background: Condition-specific growth curves can assist in the assessment of pathologic growth in children with various genetic disorders. Klinefelter syndrome (KS) is associated with tall stature; however, the growth pattern in KS prior to reaching adult height is not well described, and a KS-specific growth chart does not currently exist.

Purpose: To generate a KS-specific stature-for-age growth chart for males ages 2-20 years.

Methods: Electronic health records for all male patients with a billing diagnosis of KS (excluding other genetic diagnoses) and at least one outpatient encounter from 2009-2019 at one of six US pediatric institutions participating in PEDSnet were obtained. Measures of height were reviewed for error, including units of measure, duplicates, and non-physiologic outliers. Nonparametric quantile regression was used to model the effect of age on height (R v4.2.1, quantregGrowth), with testosterone prescription and normalization of number of patient encounters as covariates. A stature-for-age growth chart for KS ages 2-20 years was constructed at the 5th, 10th, 25th, 50th, 75th, 90th, and 95th percentiles. The KS-specific nomograms were then overlayed on the Center for Disease Control (CDC) height-for-age reference chart for visual comparison.

Results: Eighty-five percent (986/1,161) of patients with KS had at least one usable height measurement (mean ± SD of 9.1 ± 10.6 measures per patient) between 2-20 years of age. Patients were followed for a mean of 4.2 ± 3.9 years, yielding 8,936 total height measurements for this analysis. Prior to 5 years of age, the 5th%ile for KS is below the CDC 5th%ile, while the 50th and 95th%iles are similar to the CDC reference. After 5 years of age, stature in KS at all percentiles increases greater than the CDC reference percentiles; however, approaching final height the 5th%ile for KS is at the CDC 5th %ile.

Conclusions: Individuals with KS follow unique stature-for-age nomograms relative to the CDC data, particularly in early childhood at lower percentile curves and in later childhood at higher percentile curves. Future directions include generating growth velocity, weight-for-age and BMI-for-age growth curves from this cohort. These growth curves will aid in the clinical assessment of growth for boys with KS.