

## 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 5<sup>th</sup>, 10<sup>th</sup>, 25<sup>th</sup>, 50<sup>th</sup>, 75<sup>th</sup>, 90<sup>th</sup>, and 95<sup>th</sup> percentiles. The KS-specific nomograms were then overlaid 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  $\pm$  SD of  $9.1 \pm 10.6$  measures per patient) between 2-20 years of age. Patients were followed for a mean of  $4.2 \pm 3.9$  years, yielding 8,936 total height measurements for this analysis. Prior to 5 years of age, the 5<sup>th</sup> percentile for KS is below the CDC 5<sup>th</sup> percentile, while the 50<sup>th</sup> and 95<sup>th</sup> percentiles 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 5<sup>th</sup> percentile for KS is at the CDC 5<sup>th</sup> percentile.

**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.