

# Development of a Klinefelter syndrome specific stature-for-age growth chart

Taylor E Marshall, MS<sup>1</sup>, Laura Pyle, PhD<sup>2,3</sup>, Anna Furniss, MS<sup>4</sup>, Shanlee M Davis, MD, PhD<sup>2,5</sup>

<sup>1</sup>University of Colorado School of Medicine, <sup>2</sup>Department of Pediatrics, University of Colorado School of Medicine, <sup>3</sup>Department of Biostatistics and Informatics, University of Colorado Anschutz Medical Campus, <sup>4</sup>ACCORDS, University of Colorado Anschutz Medical Campus, <sup>5</sup>eXtraOrdinary Kids Clinic, Children's Hospital Colorado

## BACKGROUND

- Klinefelter syndrome (KS) is a common genetic condition in males with an extra X chromosome (47,XXY)
- KS is associated with tall stature – expected adult height is 2-3 inches above mid-parental height
- Condition-specific growth charts for genetic disorders can assist with the assessment of pathologic growth
- A KS-specific growth chart does not exist

**Aim: To generate a Klinefelter syndrome specific stature-for-age growth chart for males 2-20 years of age**

## METHODS

- Data were obtained from PEDSnet – a multi-institutional clinical research network



(adapted from pedsnet.org)

### Inclusion Criteria

- Billing diagnosis of KS
- Male sex
- Age 2-20 years
- ≥ 1 outpatient visit between 2009-2019

### Exclusion Criteria

- Other genetic diagnosis
- Diagnosis of difference in sex development
- Gender dysphoria

### Data Processing

- Outliers and duplicate height values were identified and cleaned with an exponentially weighted moving average (EWMA) based algorithm (R v4.2.1, *growthcleanr*) and individual review

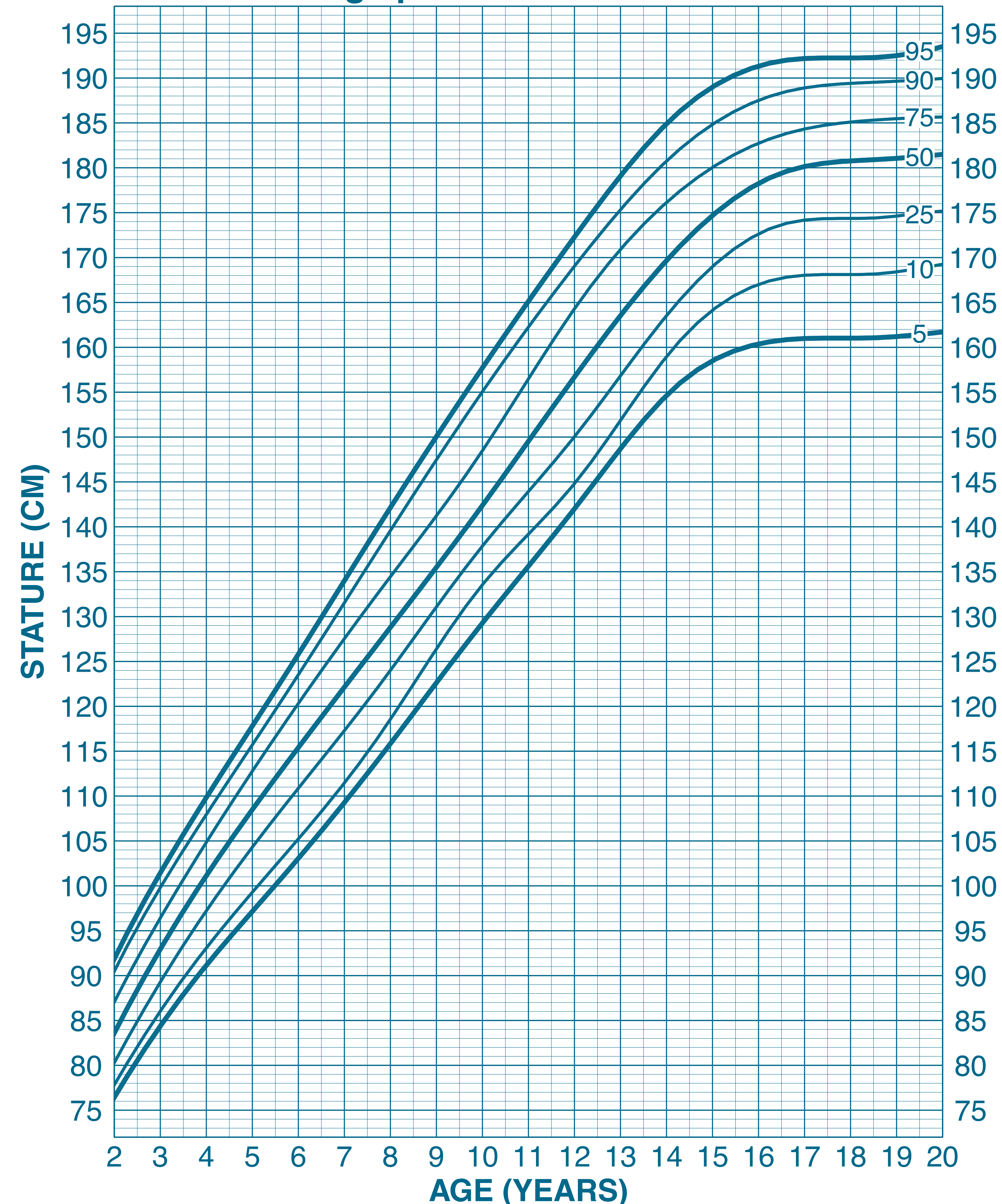
### Statistical Analysis

- Effect of age on height was modeled using non-parametric quantile regression (R v4.2.1, *quantregGrowth*)
  - Covariates – testosterone prescription, number of patient visits
  - Percentiles – 5<sup>th</sup>, 10<sup>th</sup>, 25<sup>th</sup>, 50<sup>th</sup>, 75<sup>th</sup>, 90<sup>th</sup>, 95<sup>th</sup>
- Center for Disease Control (CDC) growth curves were included for reference

## RESULTS

- **986 patients with KS** had at least one usable height measurement (mean ± SD of 9.1 ± 10.6 measures per patient over 4.2 ± 3.7 years) between 2-20 years of age, yielding **8,936 total height measurements** for this analysis

### 2 to 20 years: Klinefelter Syndrome Males Stature-for-age percentiles

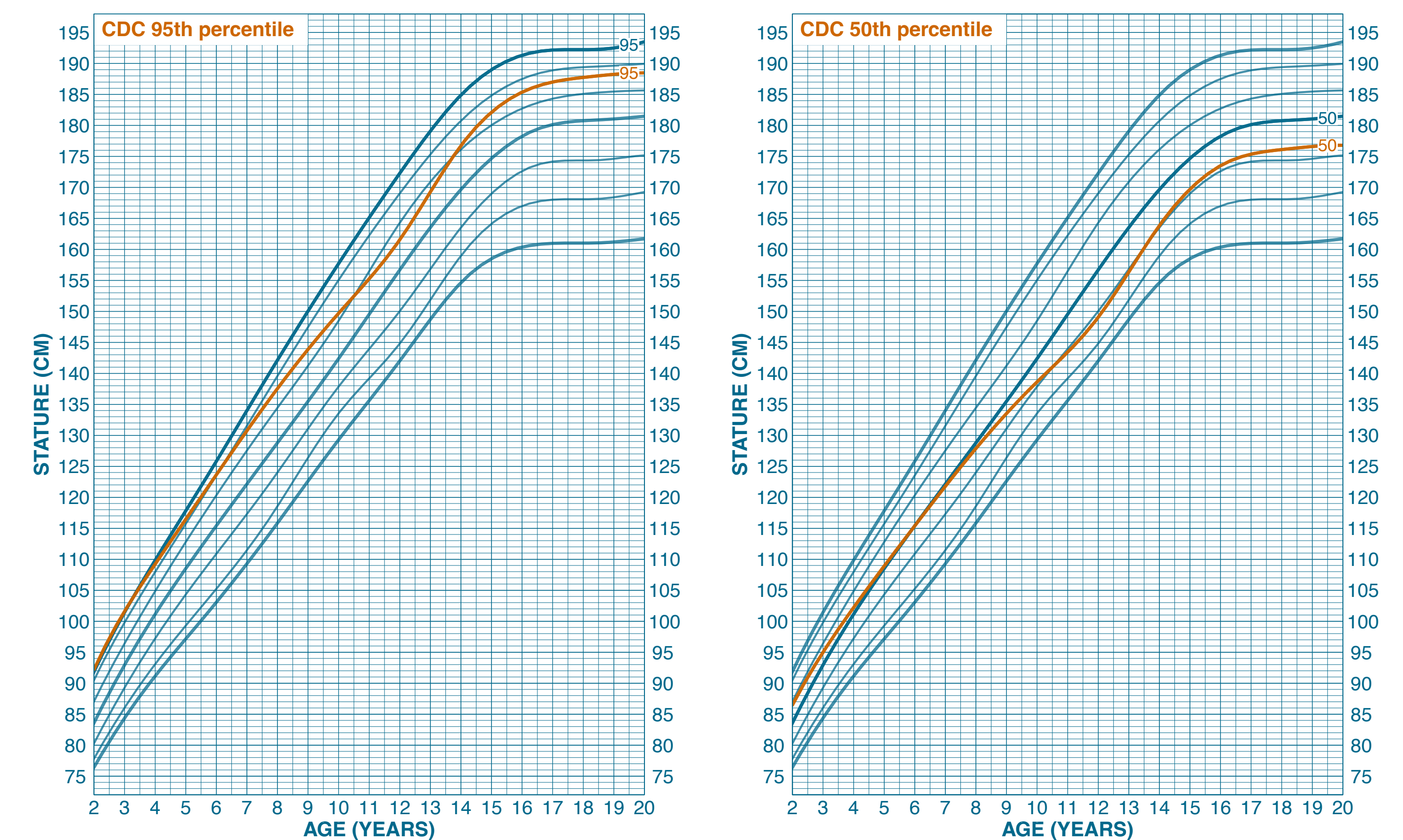


### LIMITATIONS

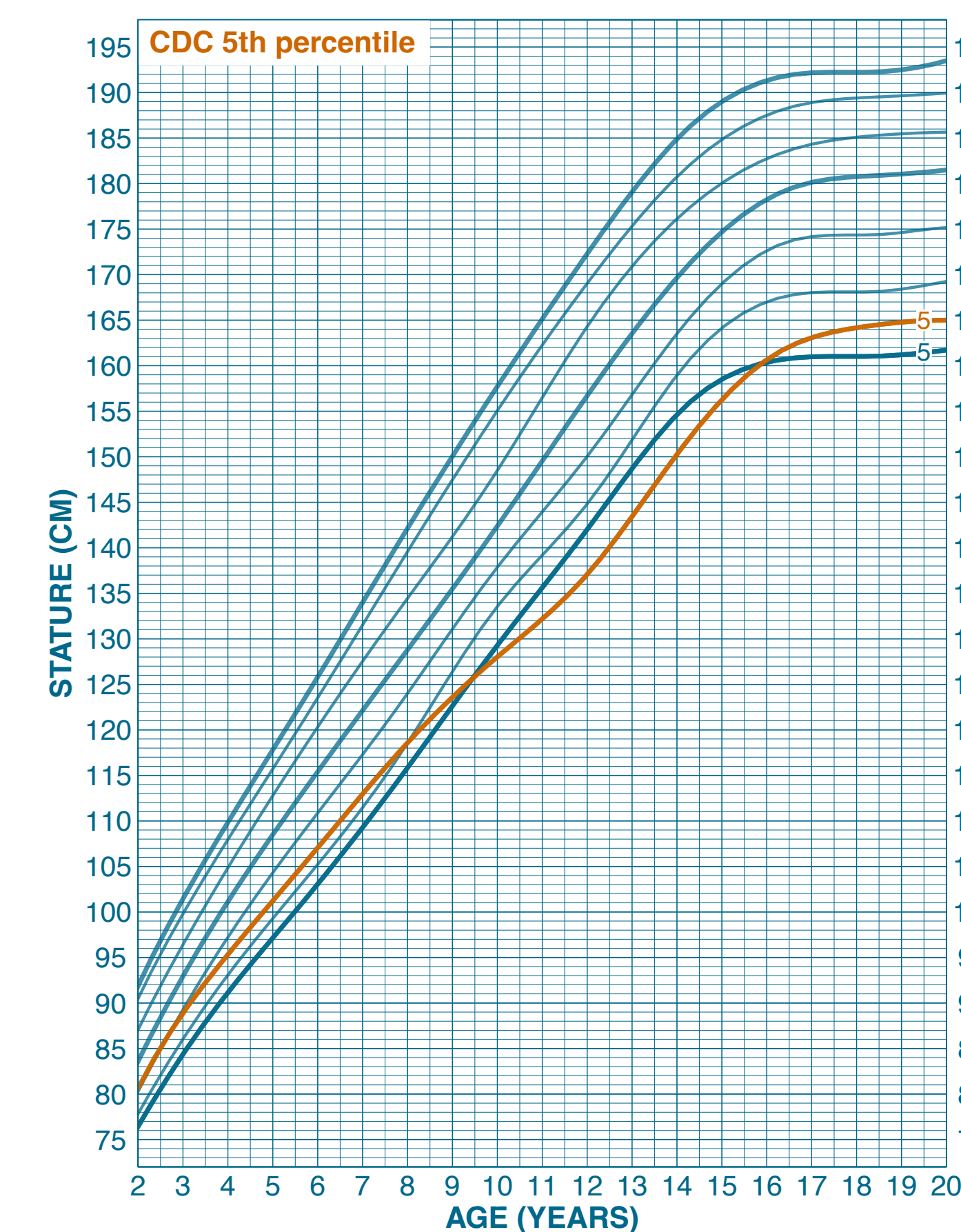
- Model is unable to account for intra-individual height trajectory
- Selection bias for known KS
- EHR errors of omission / inclusion

### FUTURE DIRECTIONS

- Height velocity, weight, and BMI-for-age KS-specific growth charts
- KS-specific growth charts for boys 0-2 years of age



The 95<sup>th</sup> (top left) and 50<sup>th</sup> (top right) percentile curves for KS are similar to the CDC reference initially; after 5 years and 9 years of age respectively, stature in KS at the 95<sup>th</sup> and 50<sup>th</sup> percentile is greater than the CDC reference



The 5<sup>th</sup> percentile (bottom left) for KS is initially below the CDC 5<sup>th</sup> percentile, from 10-16 years of age the 5<sup>th</sup> percentile curve is transiently greater in KS than the CDC reference, and approaching final stature the KS 5<sup>th</sup> percentile is below the CDC 5<sup>th</sup> percentile

## CONCLUSIONS

- Boys with KS have unique growth trajectories compared to the CDC curves
- The KS curves all seem to lack the typical pre-pubertal slowing of growth velocity, as well as an obvious pubertal growth spurt
- Tall stature is not universal in KS, particularly in infancy and early childhood

## IMPLICATIONS

- KS specific growth charts will be helpful in the clinical prediction of height potential, in facilitating discussions with families regarding expectations, and in identifying abnormal growth patterns that may warrant evaluation

## ACKNOWLEDGEMENTS, FUNDING & DISCLOSURES

- Special thanks to Dr. Shanlee Davis – my wonderful mentor – and the eXtraordinary Kids research team and patients
- None of the authors have any disclosures
- Support received from the NICHD, R03HD102773
- Project was determined by COMIRB to be Non-Human Subjects Research