New Standards for Craniofacial Growth

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INTRODUCTION

- The Craniofacial Growth Consortium Study (CGCS) consists of the largest sample of longitudinal craniofacial growth records assembled.
- Longitudinal growth data in untreated subjects provide:
  - Craniofacial growth knowledge
  - Norm or craniofacial growth standards for orthodontic diagnosis and treatment planning
  - Control group when evaluating interventions during the growth period.
- Understanding the timing of growth milestones (e.g., age at peak growth velocity, age at cessation of growth) is critical for developing individualized orthodontic growth modification strategies.
- The objective of this poster is to discuss our approach to building and presenting new percentile growth curves for craniofacial measures.

SAMPLE AND MODELLING

Sample

- 17,256 lateral cephalograms from the Craniofacial Growth Consortium Study (Sherwood et al., 2021).
- Females and males ages 2.5 to 28 years
  - 1055 Males, 1044 Females (median 9 cephalograms per individual)
- Triple-determined 2D landmarks from lateral cephalograms
- 12 interlandmark distance measurements
  - Derived traits represent mandibular, facial, and basicranial traits

Modelling

- Double logistic growth model (Bock et al., 1973), with pre-pubertal and adolescent growth stages
  - Six parameters, including asymptotic measure (f) and prepubertal contribution (a_1), and separate initial rates (b_1 and b_2) and ages (c_1, c_2) at peak growth velocity.

$$y = \frac{a_1}{1 + \exp(-b_1(age - c_1))} + \frac{f - a_1}{1 + \exp(-b_2(age - c_2))}$$

  - Multilevel models with separate intercept terms for individual.
- Bayesian inference address the challenges of parameter estimation (e.g., via maximum likelihood)
  - Models estimated using stan programming language (Gelman et al. 2015; Carpenter et al. 2017) via the *rethinking* package in R.
  - Four parallel chains sampled for 10^4 iterations yields ~4,000 effective samples and $\hat{R}$ values of 1.

Percentiles

- Percentile curves were estimated from growth models
- 10-fold cross validation was carried out to test the adequacy of the growth model and estimated percentiles for these traits.
- For each of 10 folds, a Bayesian the model was fit to 90% of the data, and the remaining 10% was used as a test set.
- For each test observation, we determined if that observation fell within the middle 50% and 98% posterior prediction intervals.

Web Interface

- R-Shiny (shiny.rstudio.com) was used to build a web-interface to provide users the ability to estimate sex-specific percentile scores on 12 twelve traits for individuals

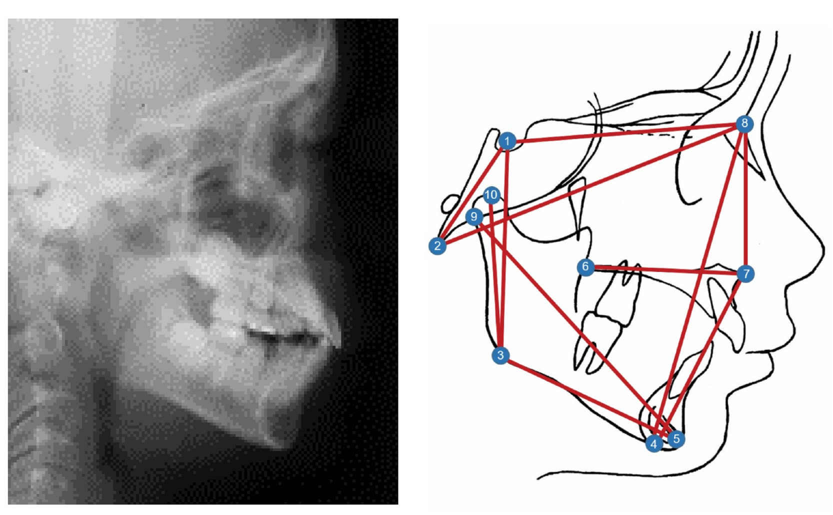


Figure 1. Example cephalogram and cephalometric points and measures.

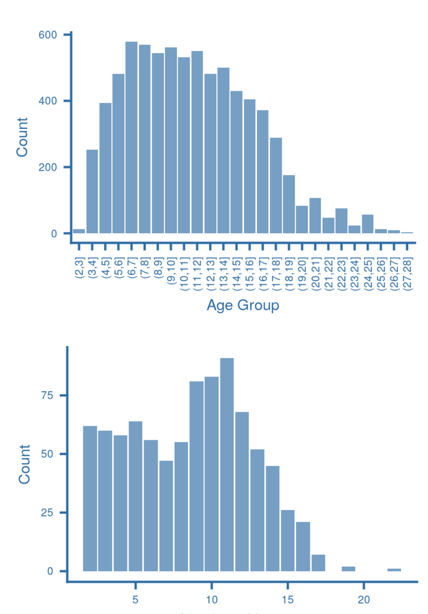


Figure 2. Count of images per individual and distribution by age.

RESULTS

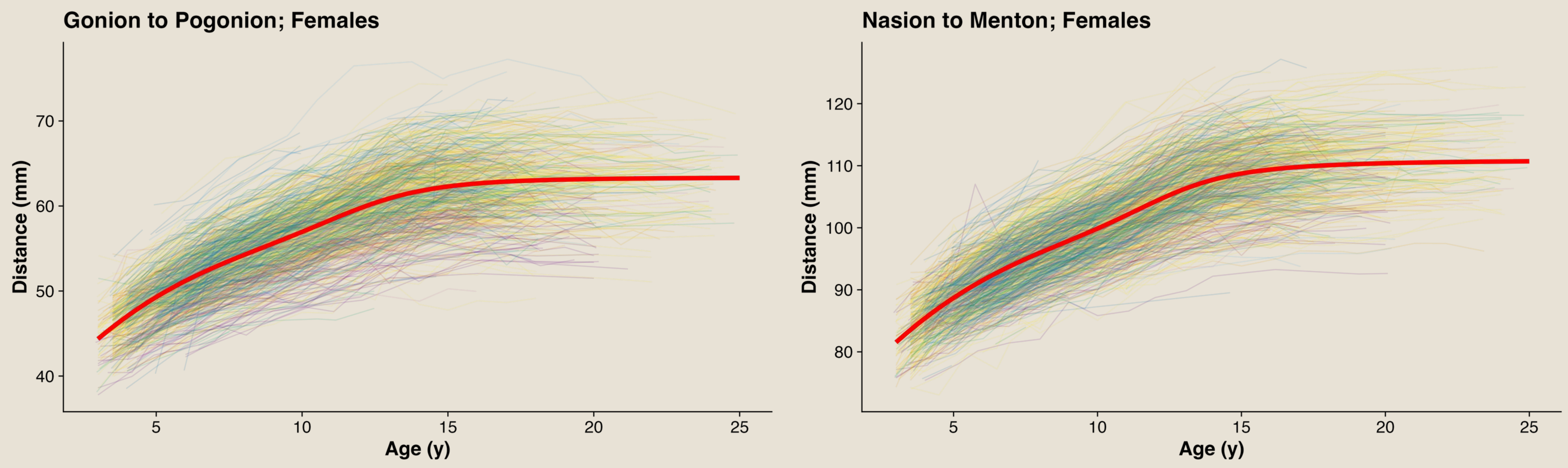
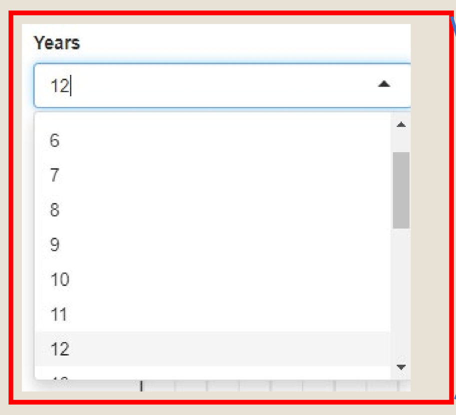


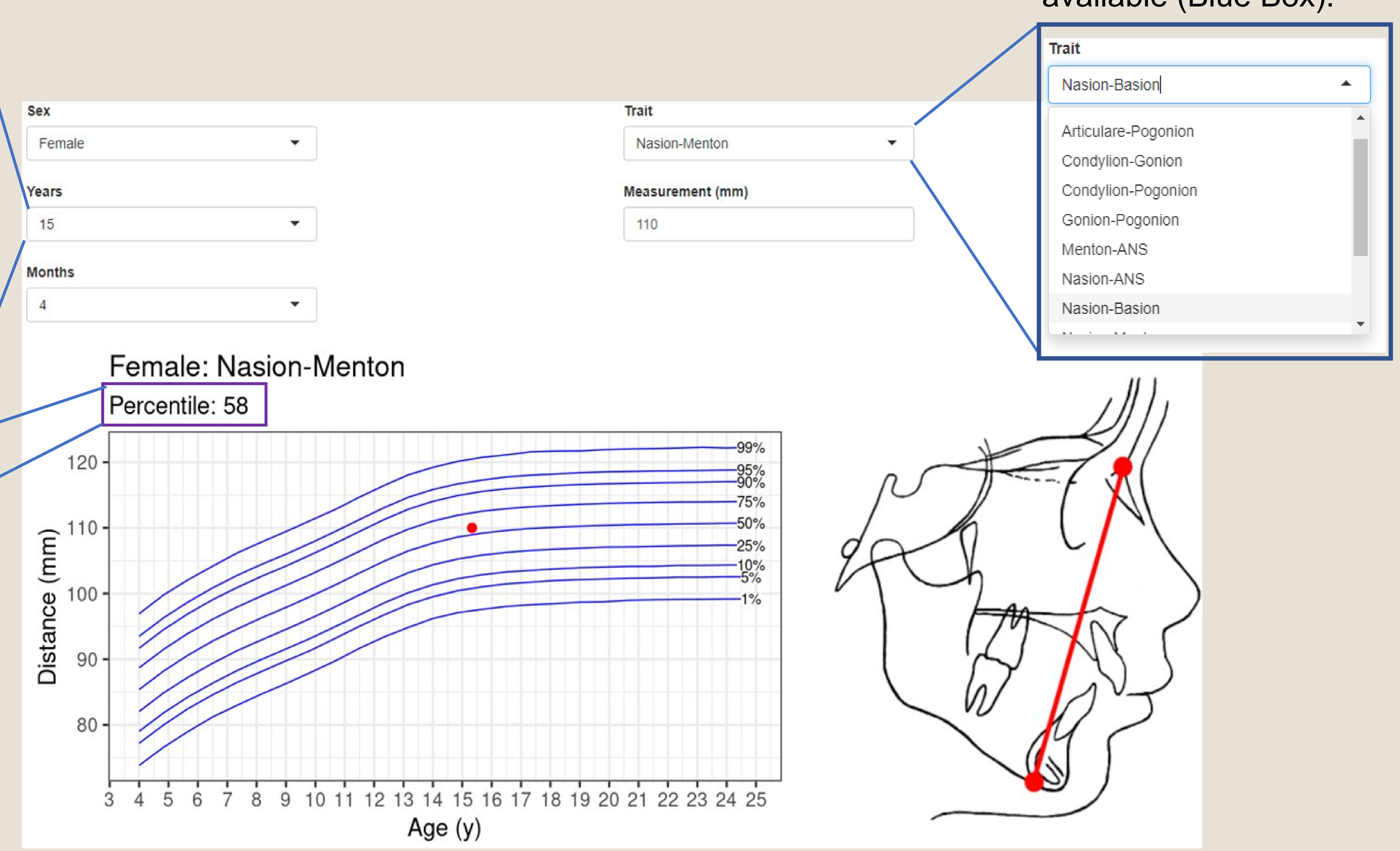
Figure 3. Examples of double-logistic growth curves (upper images) for two craniofacial traits in females (Distance from Gonion to Pogonion; Distance from Nasion to Menton) using the CGCS sample

Craniofacial Percentile Web Application

Users can choose sex (male or female) and age from 4-25 years, in one-month increments (Red Box).



Twelve craniofacial traits commonly used in clinical settings are currently available (Blue Box).



Percentile score is provided (purple box) and displayed graphically

Use QR code (above) to access Web Application

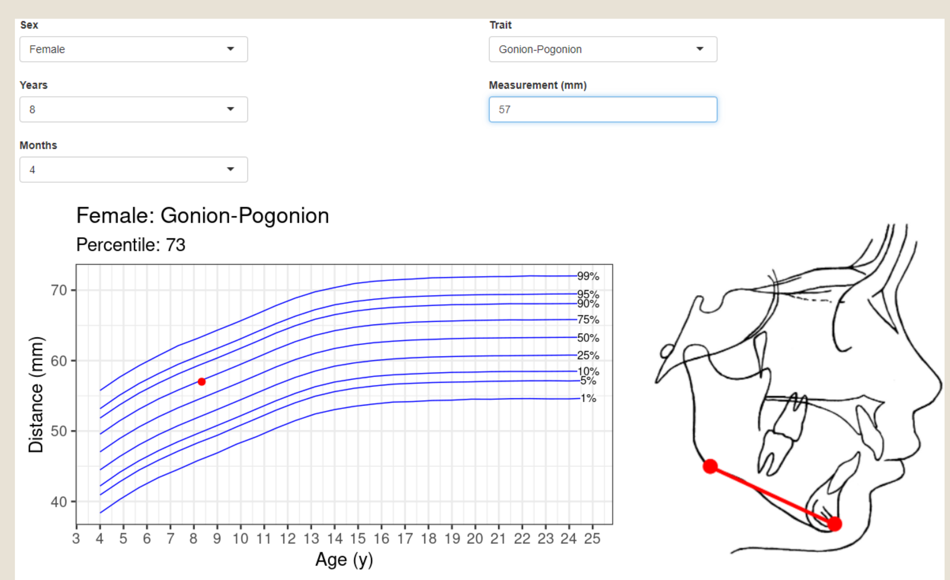


Figure 4. The initial traits investigated include those considered standard for cephalometric analysis such as basicranial length or multiple measures of mandibular length (pictured here).

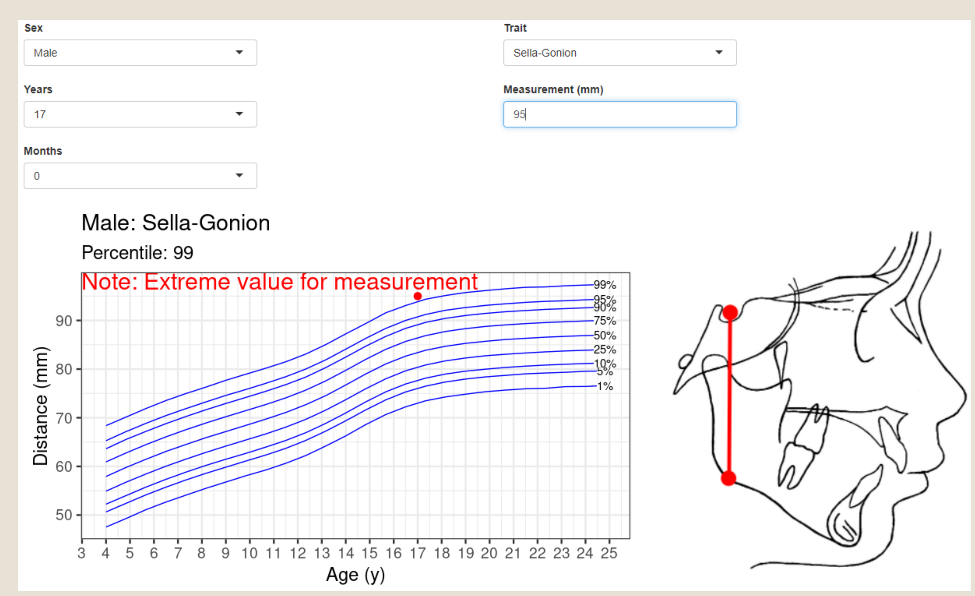


Figure 5. The program will alert the user if a trait value falls above the 99th, or below the 1st, percentile for the chosen trait.

CONCLUSIONS

- We have previously shown that Bayesian multilevel modelling addresses many challenges of craniofacial growth estimation using polynomials (Sherwood et al., 2021).
  - Double-logistic growth models include biologically meaningful parameters of PGV, aPGV, and age at growth cessation.
- Population-level percentile interval standards can be estimated from measurements based on the CGCS as a representative sample.
- Cross validation showed that approximately half of observations in the test set were found within the middle 50% posterior predictive interval and 98% were in the corresponding 98% interval.
- Percentile curves can be used by clinicians to rapidly identify and localize possible growth disparities in young patients. The percentiles provided cover a range of craniofacial traits and are based on a large, geographically diverse sample. R-shiny provides a simple means for interactive web-based clinical tools.

REFERENCES

Beaumont MA, Zhang W, Balding DJ. 2002. Approximate Bayesian Computation in Population Genetics. Genetics 162:2025–2035.

Bock RD, Wainer H, Petersen A, Thissen D, Murray J, Roche A. 1973. A parameterization for individual human growth curves. Hum Biol 45:63–80.

Carpenter B, Gelman A, Hoffman MD, Lee D, Goodrich B, Betancourt M, Brubaker M, Guo J, Li P, Riddell A. 2017. Stan: A probabilistic programming language. J Stat Softw 76

Gelman A, Lee D, Guo J. 2015. Stan: a probabilistic programming language for Bayesian inference and optimization. J Educ Behav Stat:1076998615606113

Sherwood, R.J. H.S. Oh, M. Valiathan, K.P. McNulty, D.L. Duren, R.P. Knigge, A.M. Hardin, C.L. Holzhauser, K.M. Middleton. 2021. Bayesian Approach to Longitudinal Craniofacial Growth: The Craniofacial Growth Consortium Study. Anat. Rec. 304:991-1019. PMID:33015973. PMCID: PMC8577187

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