4p- Growth

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1 Methods

To prepare the data, all lengths were converted to centimeters and all weights were converted to kilograms. Subject-specific trajectories were examined for outlier measurements and such measurements were deleted or corrected based on clinical judgment. OFC was only analyzed between birth and 24 months of age. Length was analyzed between birth and 18 years of age. When a subject had multiple length measurements at age 18 or older, only the first of these was included. All ages corresponding to length measurements beyond age 18 were truncated to 18 years of age.

We used two approaches to construct growth curve references. First, we used generalized additive models for location, scale, and shape to construct growth percentiles. Second, we allowed individual longitudinal growth curves using a subject-specific, shape-invariant model approach. Separate models were fit for weight, length, and OFC. For weight and length separate models were fit for $\leq$24 months of age and $\geq$24 months of age. For OFC, a model for $\leq$24 months was fit. Stratificaiton by gender was investigated in two ways: (1) fitting separate models for each gender and (2) including gender as a covariate.

Generalized Additive Models for Location, Scale, and Shape (GAMLSS) assume that the measurement at any age follows a normal distribution. The location (scale), variance, skewness, and kurtosis are all allowed to change over time. The result is that any percentile can be calculated using the value of these functions at a given age.

The subject-specific, shape-invariant model provides a common shape for all subjects' growth over time. Up to three parameters can vary from subject to subject. First, the height of the curve can change. Second, the timing of growth can change (when growth starts/ends). Last, the rate of growth can change. The shape used for each model was a natural smoothing spline. Model fitting was performed for each measurement and age group using Akaike Information Criterion as a measure of model fit. Model selection included number of spline knots and which marginal and subject-specific parameters to include.

2 Results

Patients in dataset	68
Withdrew	1
Missing Ages	2
Analyzed	65
Total number of measurements	
Weight	960
Length	677
OFC	300

Growth centiles are shown in Figures 1–5. The approximate CDC growth curves corresponding to the median and quartiles for boys and girls combined are added as a reference (in purple).

Individual growth patterns are shown in Figures 6–10. The fitted spline curves based on subject-specific trajectories in each case are shown in blue. The approximate CDC growth curves corresponding to the median and quartiles for boys and girls combined are added as a reference (in purple).

The following models were chosen:

Measurement and age group	Knots	Marginal Parameters	Subject Parameters
Weight, $\leq$24 months	3	height, timing	height, timing
Weight, $\geq$24 months	4	height, timing	timing
Length, $\leq$24 months	2	height, timing	height, timing
Length, $\geq$24 months	4	height	height, timing, rate
OFC, $\leq$24 months	3	height, timing	height, timing

Figure 1: GALMSS: Weight 0–24 months

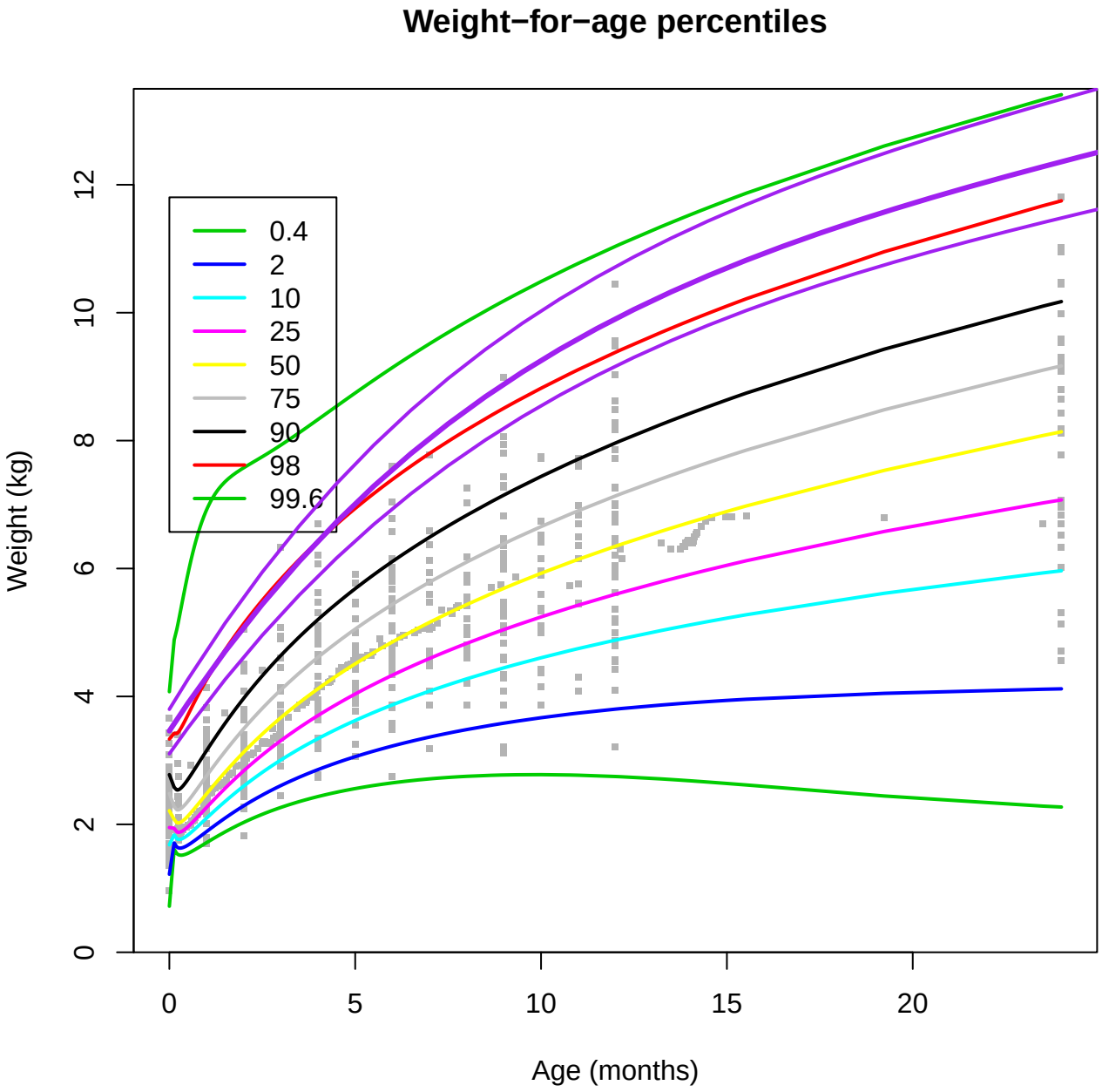

Figure 2: GALMSS: Weight 2–18 years

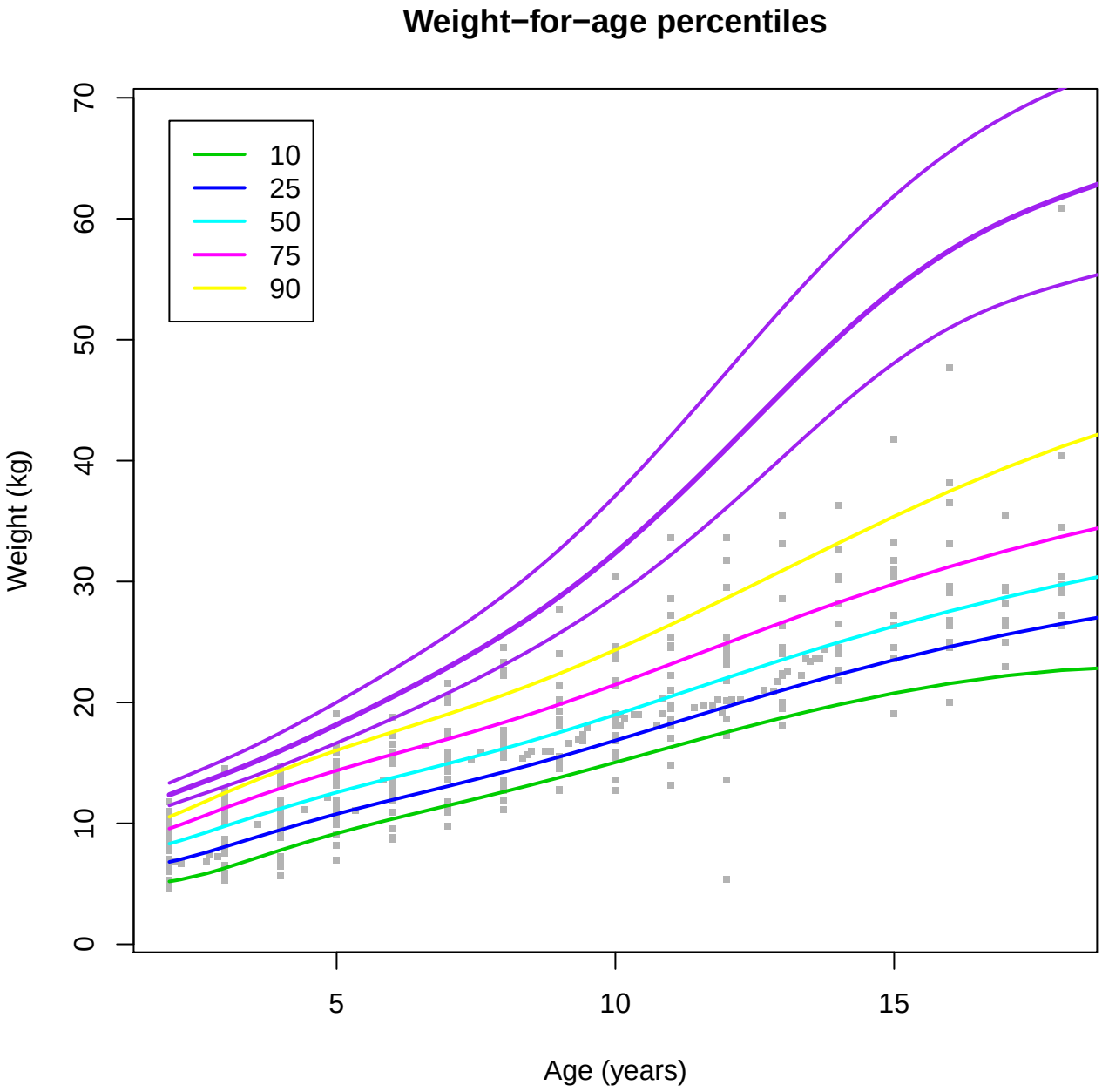

Figure 3: GALMSS: Length 0–24 months

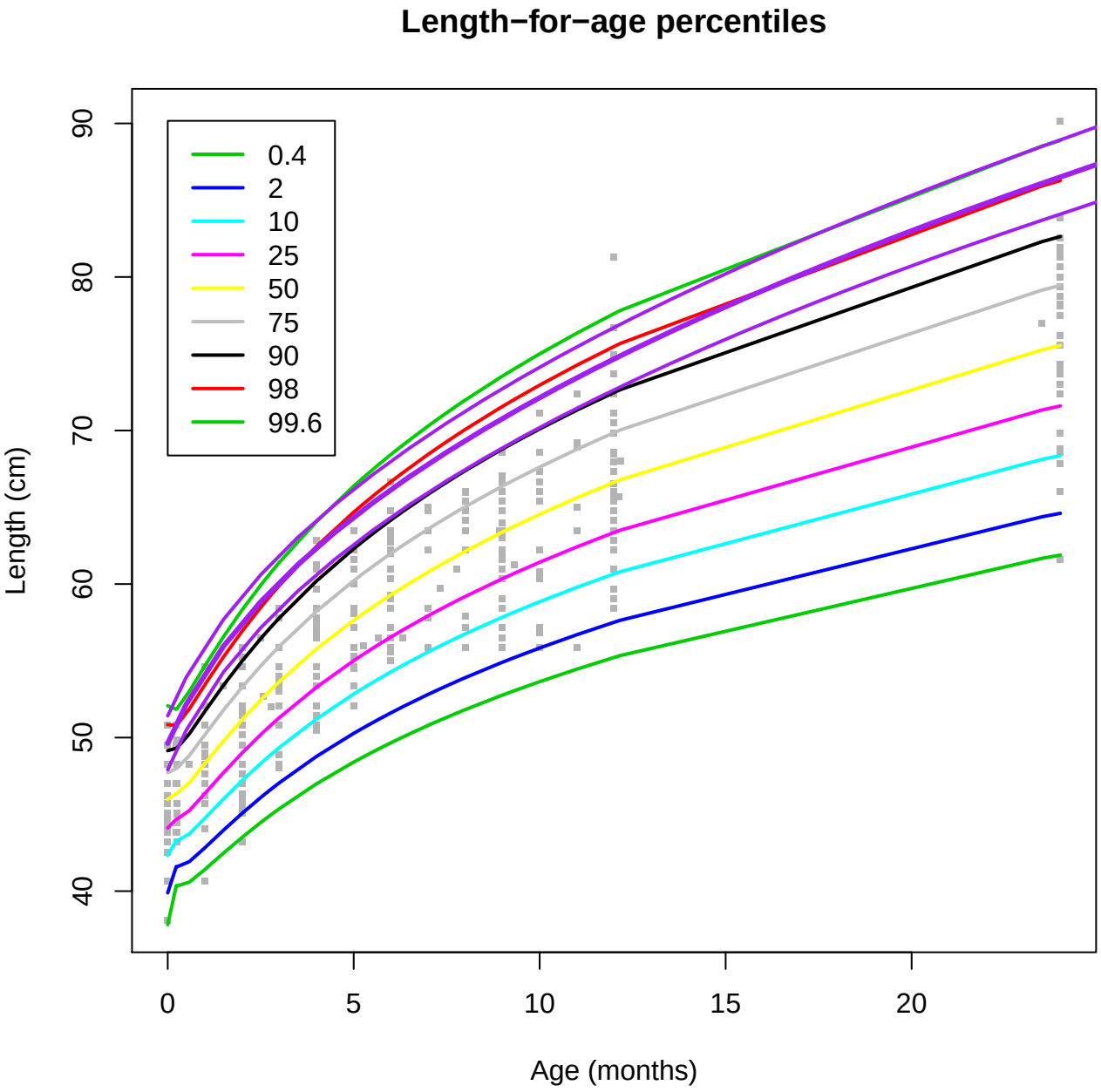

Figure 4: GALMSS: Length 2–18 years

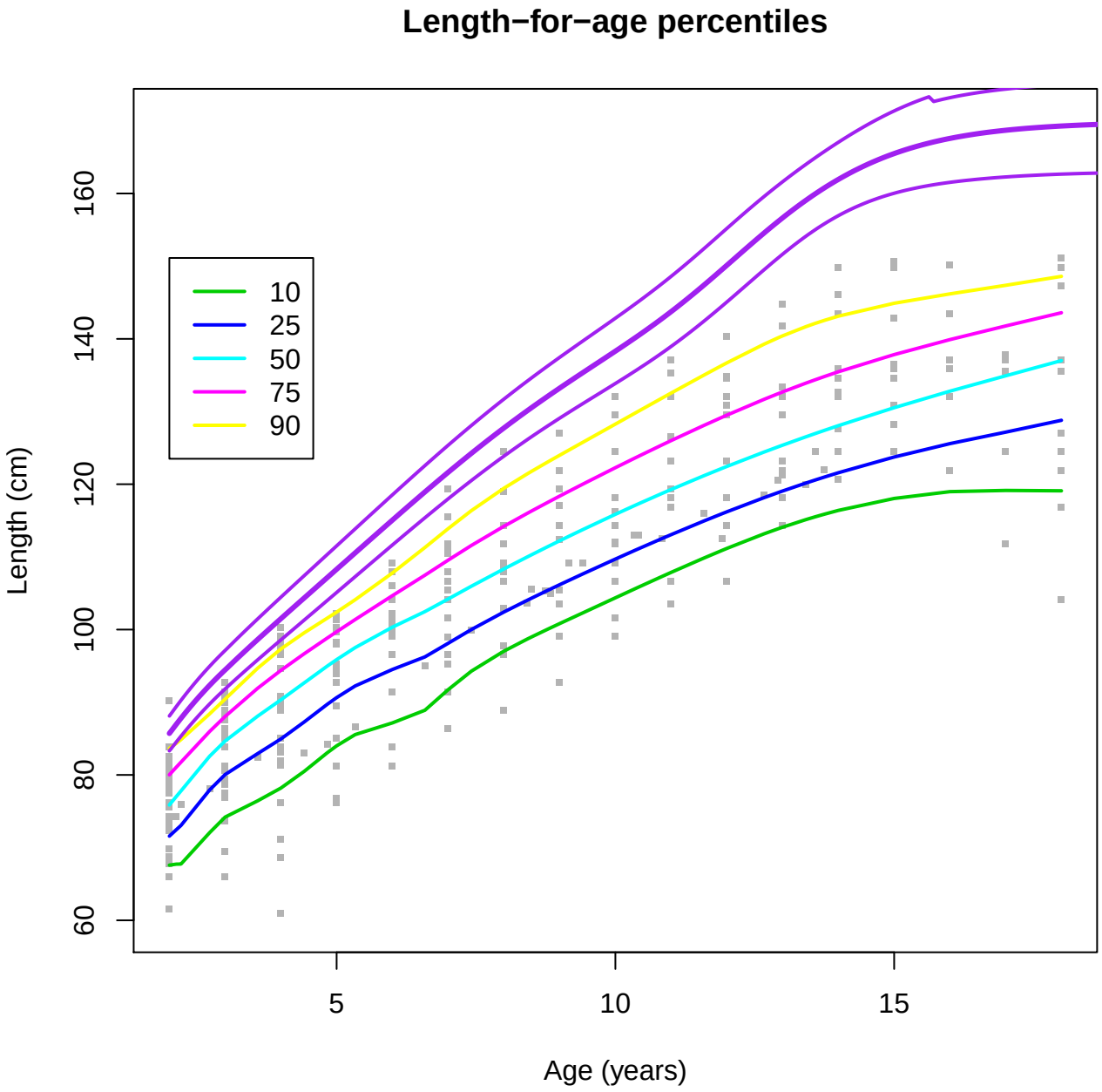

Figure 5: GALMSS: OFC 0–24 months

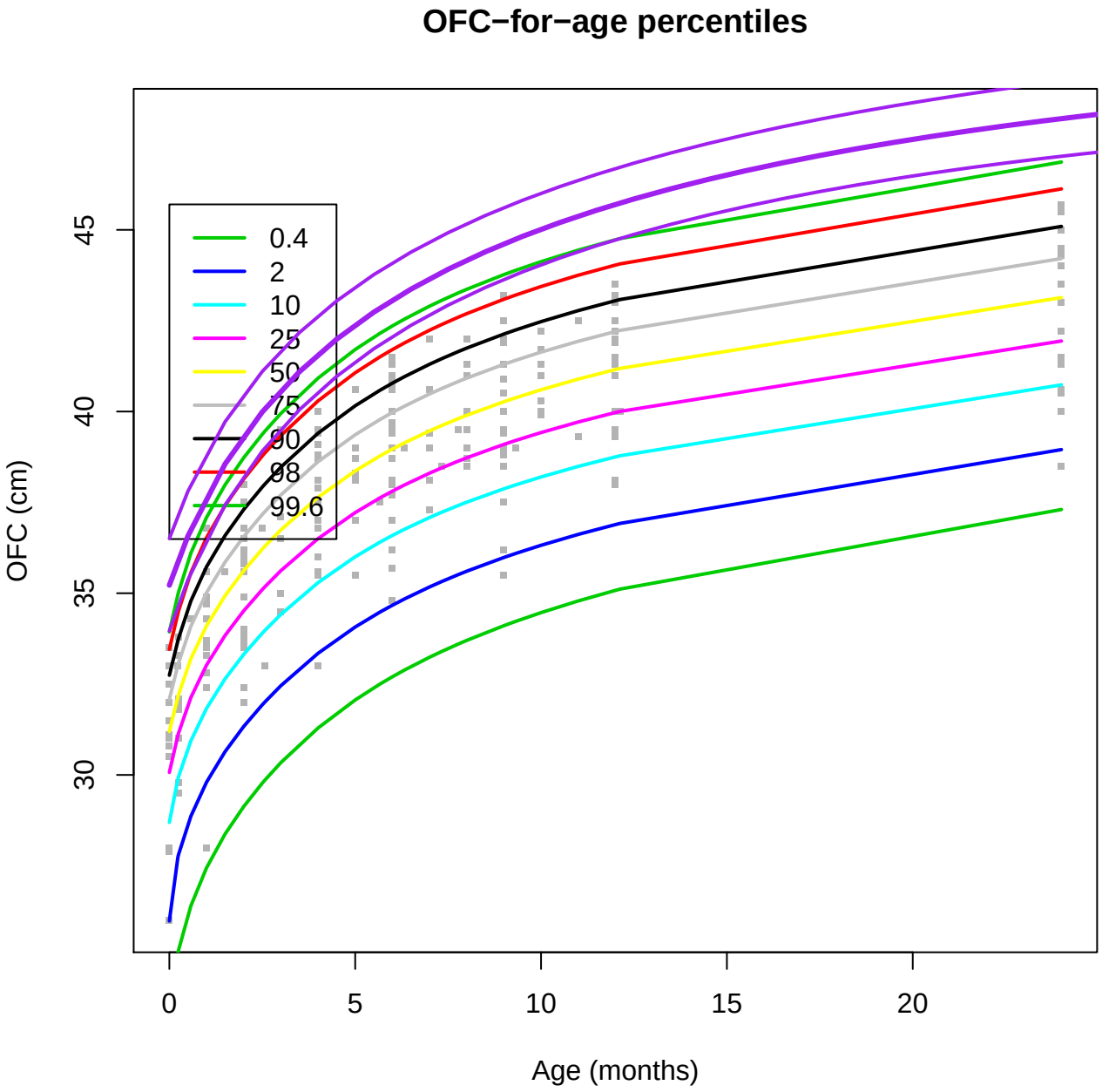

Figure 6: Subject-specific model: Weight 0–24 months

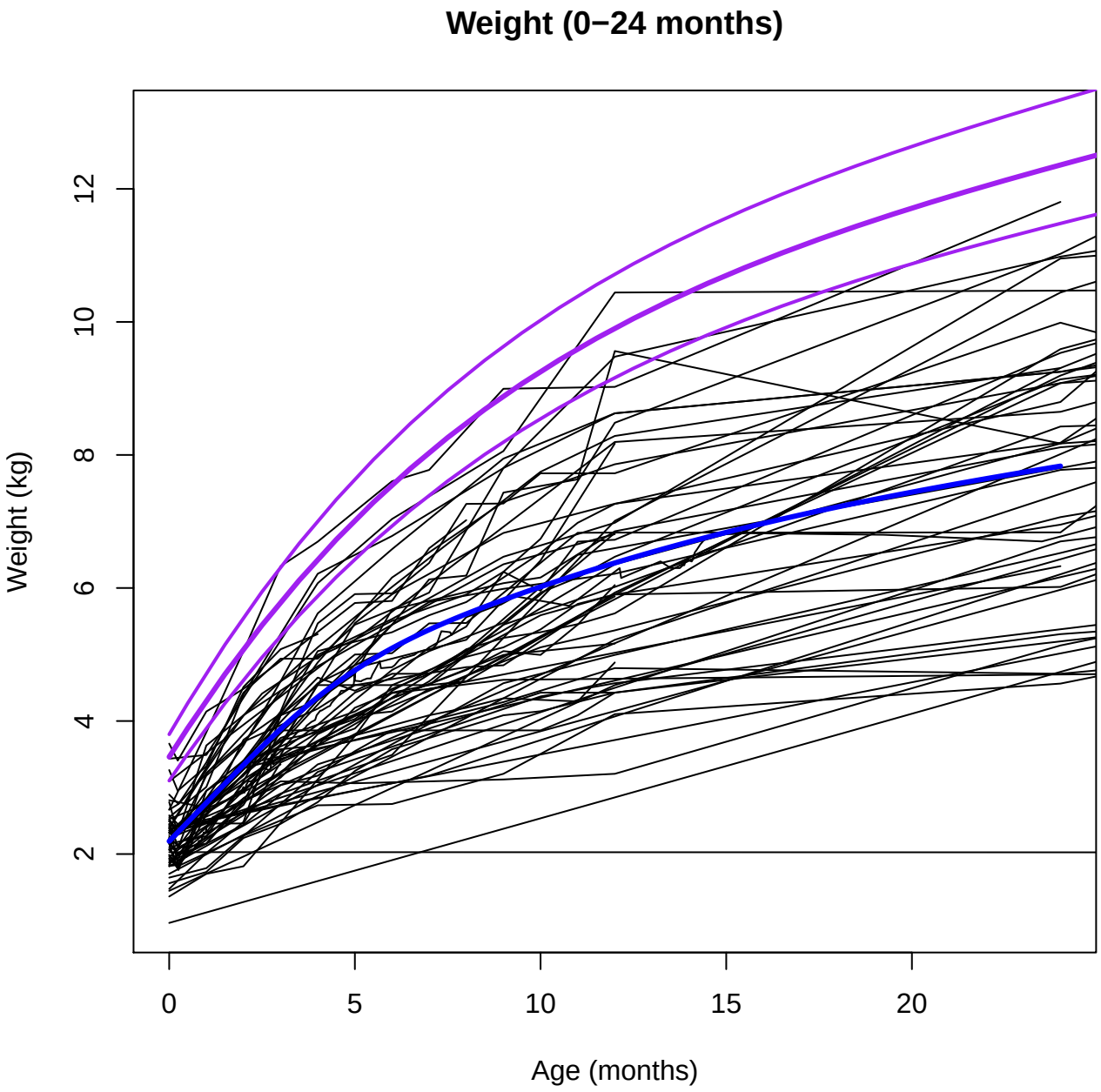

Figure 7: Subject-specific model: Weight 2–18 years

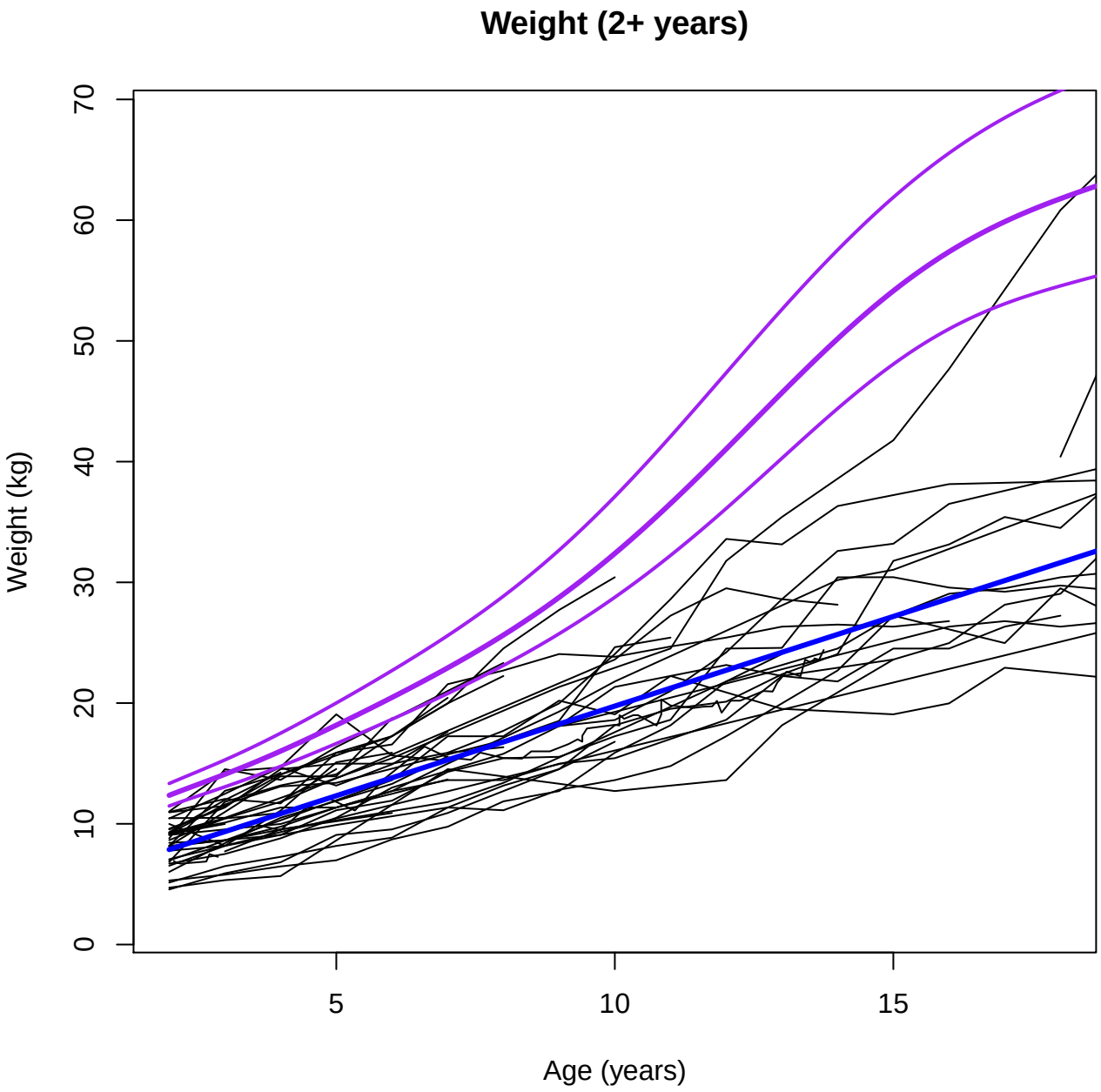

Figure 8: Subject-specific model: Length 0–24 months

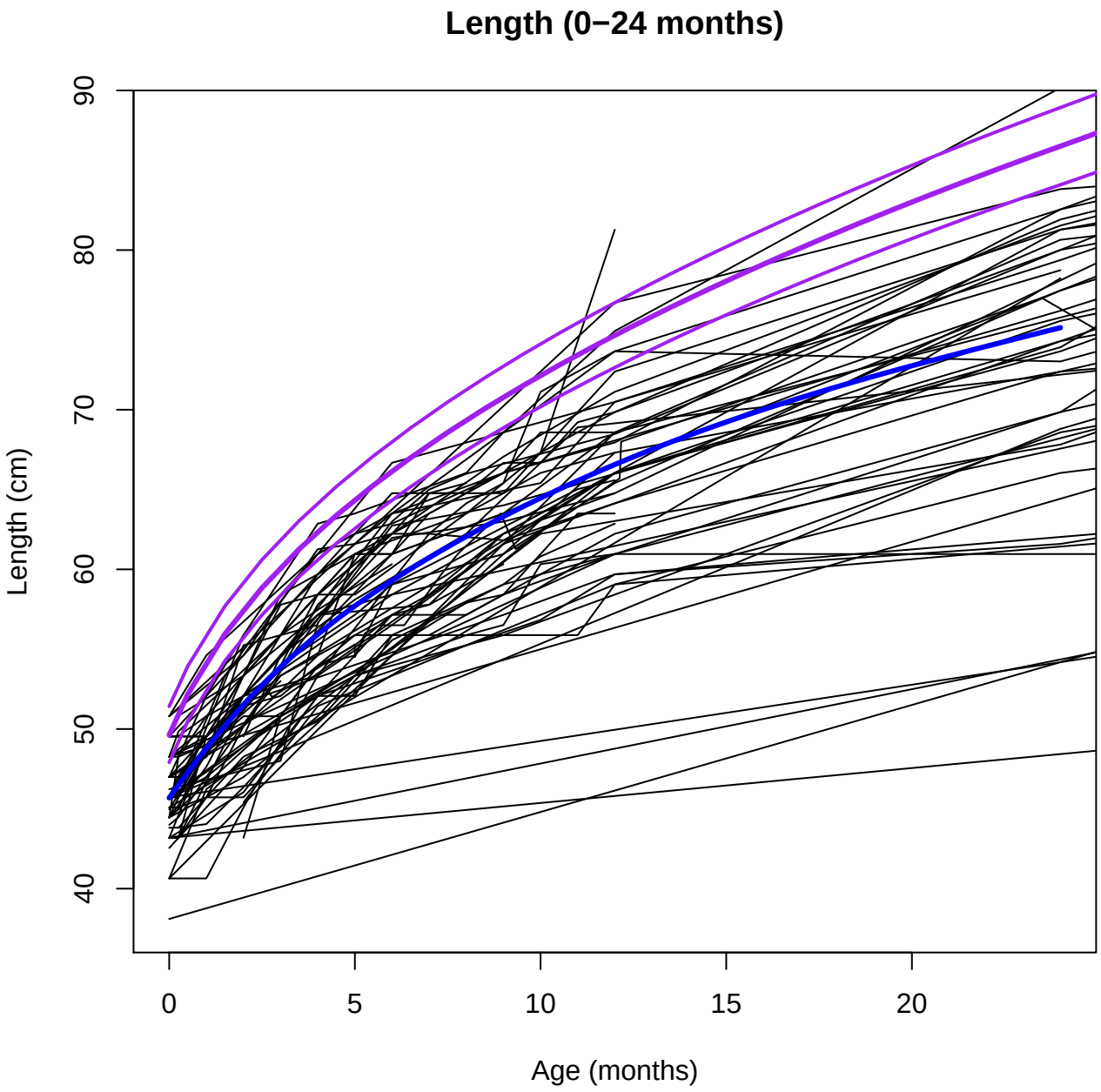

Figure 9: Subject-specific model: Length 2–18 years

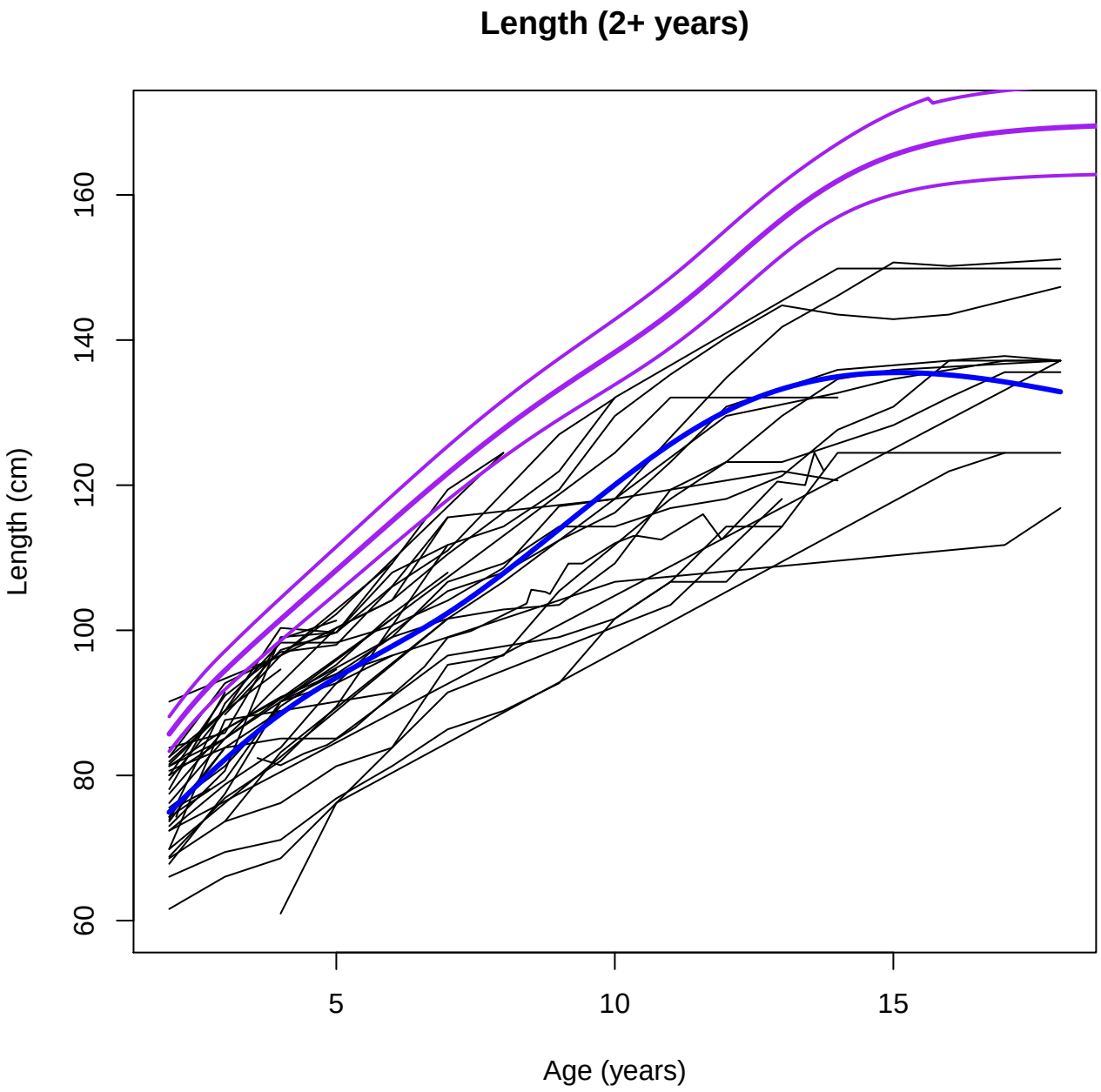

Figure 10: Subject-specific model: OFC