Development of new Austrian height and weight references

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Introduction

Reference curves used in Austria:

- First Zurich longitudinal study (Prader et al, 1989)
  - 274 children (longitudinal) from birth years 1954 to 1956
  - middle and upper class, mostly not breastfeeded
- Germany: Kromeyer-Hauschild et al (Mon.schr.KHK, 2001)
- WHO: de Onis et al (Bulletin WHO, 2007)
- Germany: Rosario et al (Ann.Hum.Biol., 2011)

Girls' height at 10 years (cm)	3rd perc	**50th perc**	97th perc
Prader et al (1989)	126.2	**138.2**	148.7
Kromeyer-Hauschild et al (2001)	128.9	**141.2**	153.4
de Onis et al (2007)	126.6	**138.6**	150.7
Rosario et al (2011)	128.6	**141.3**	154.1

Introduction

Clinical use of reference curves in paediatrics:

- monitor a child's somatic development
- decision making in diagnostic work-up for shortness
- based on Standard Deviation Scores (SDS)
- height and body proportions

Data (1/4)

- targeted sample size: ≥ 12,000
- according to age- and sex-specific population proportions in 9 provinces (Statistik Austria, 2009)
- Austrian Federal Ministry of Education, Arts and Culture
- External health care system consulting company
- 117 kindergartens, primary schools, secondary schools, and vocational schools
- November 2009 to June 2011
- sampling & statistics financed by Merck Ges.m.b.H.

Data (2/4)

- sampling whole classes
  - higher sample size
  - outside planned age range of 4 to <19 years
- 15,368 recruited
- exclude 67 (0.44%), e.g.: plaster cast, trisomy 21
- 15,301 eligible
- 14,544 of 4 to <19 years (7,415 boys and 7,129 girls)
- + 442 half year outside
- cross-sectional!

Data (3/4)

- measurements:
  - height
  - sitting height
  - weight

Data (4/4)

- measurements:
  - height
  - sitting height
  - weight
- derived quantities:
  - subischial leg length = height – sitting height
  - ratio of sitting height / leg length
  - BMI = weight / height^2
- all variables measured completely

GAMLSS Method (1/9)

- **G**eneralized **A**dditive **M**odels for **L**ocation, **S**cale and **S**hape
  - Rigby & Stasinopoulos (Stat. Med., 2004)
  - Rigby & Stasinopoulos (Appl. Statist., 2005)
  - Stasinopoulos & Rigby (J. Stat. Software, 2007): R-package
- GAMLSS model has two components:
  a) parametric distribution at each value of independent var.
  b) model dependence of distributional parameters on independent variable

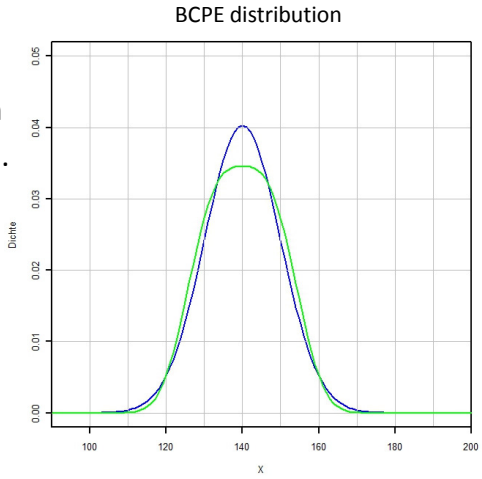
GAMLSS Method (2/9)

a) at each age parametric distribution:

- normal, log-normal, …
- more general, e.g.:
  - Box-Cox t-distribution
  - **B**ox-**C**ox **P**ower **E**xpon. (BCPE)

→skewness

→kurtosis



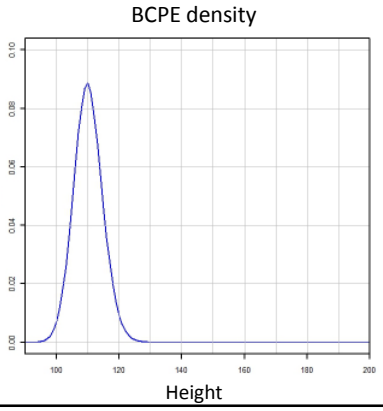
GAMLSS Method (3/9)

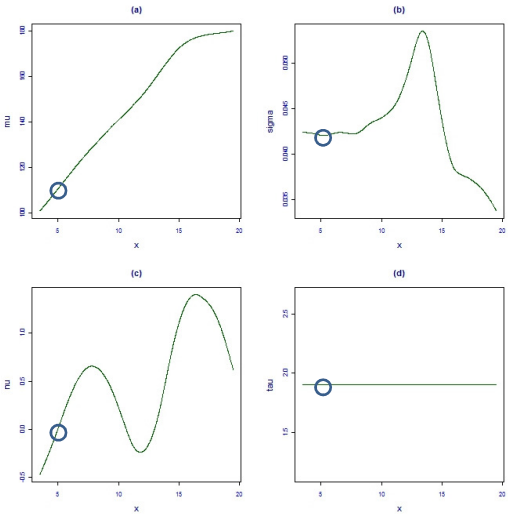
b) distributional parameters depending on age:

- linear, polynomial
- smoothing functions:
  - fractional polynomials
  - **cubic splines**

GAMLSS Method (4/9)

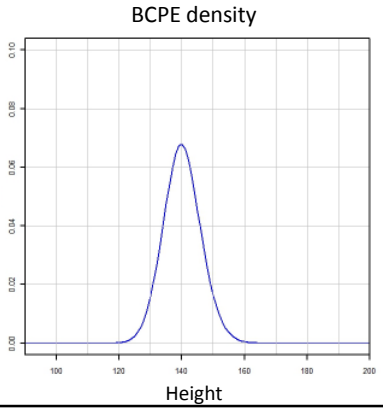
- Example: height (boys)
- 5 years

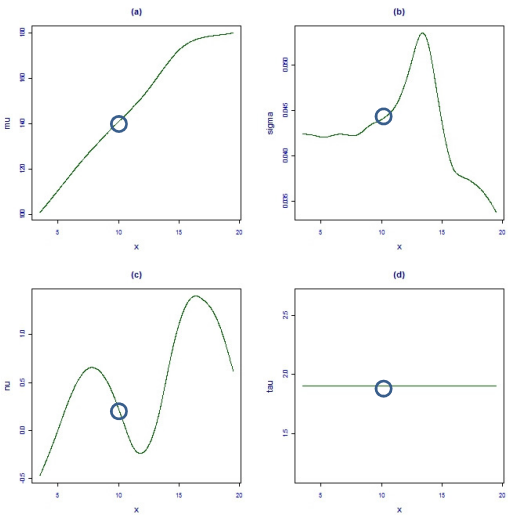




GAMLSS Method (5/9)

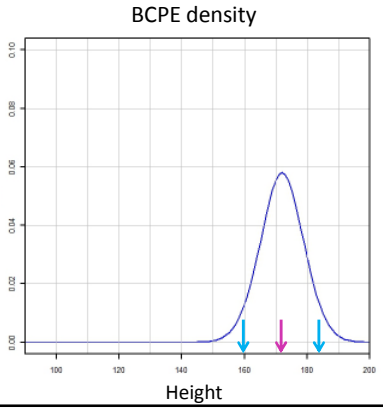
- Example: height (boys)
- 10 years

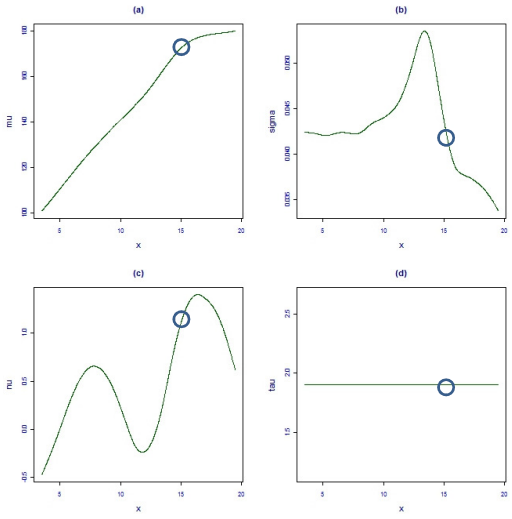




GAMLSS Method (6/9)

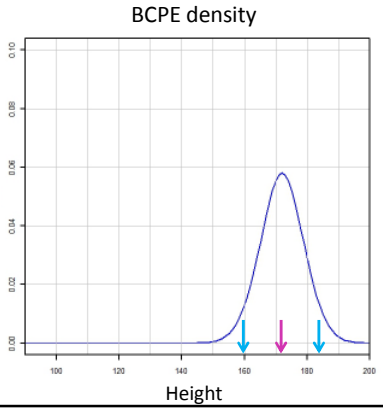
- Example: height (boys)
- 15 years

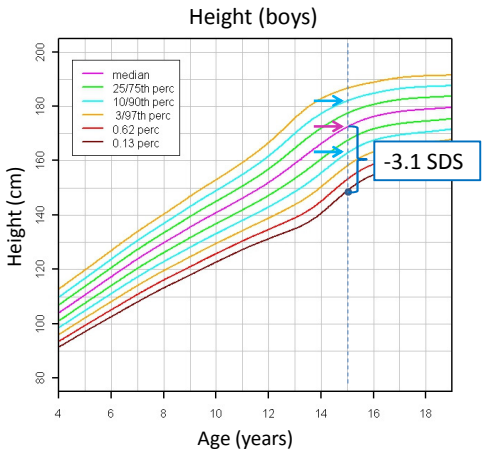




GAMLSS Method (6/9)

- Example: height (boys)
- 15 years





GAMLSS Method (7/9)

- estimation of Standard Deviation Scores (SDS) for concrete measurement *X*:

$$Z = \begin{cases} \frac{1}{\sigma\nu}\left[\left(\frac{x}{\mu}\right)^{\nu} - 1\right] & \text{if } \nu \neq 0 \\ \frac{1}{\sigma}\log\left(\frac{x}{\mu}\right) & \text{if } \nu = 0 \end{cases}$$

Rigby & Stasinopoulos (Stat. Med., 2004)

$$\text{SDS} = \Phi^{-1}\left(\left(1 + sign(z)\, G_{1/\tau}\left(\frac{1}{2}\left|Z/c\right|^{\tau}\right)\right)/2\right)$$

Φ standard normal distribution function

$G_{1/\tau}$ standard Gamma distribution function with parameter $1/\tau$

$$c = \left[2^{-2/\tau}\Gamma(1/\tau)\left(\Gamma(3/\tau)\right)^{-1}\right]^{1/2}$$

Γ Gamma function.

GAMLSS Method (8/9)

- further corrections needed:
  - correct for truncation of distribution function (see Appendix A in Rigby & Stasinopoulos, 2004)
  - correct for extreme observations removed before model estimation

$$SDS_{corr} = \Phi^{-1}\left(\left(\Phi(SDS)\cdot(n - o_l - o_u) + o_l\right)/n\right)$$

n: original # observations
o_l: # omitted at lower end
o_u: # omitted at upper end

e.g. for $o_l = o_u = 2$: SDS_{corr} = -2.5 for *SDS* = -2.84 (n=500)
or *SDS* = -2.52 (n=5000)

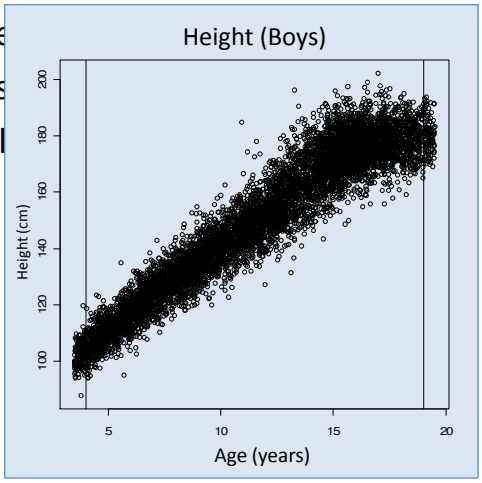
GAMLSS Method (9/9)

- separate model for each sex
- separate model for each outcome variable
- LMS-method by Cole & Green (Stat.Med., 1992)
  = special case of GAMLSS
- Borghi et al. (Stat.Med., 2006):
  evaluation of methods for WHO
- de Onis et al (Bulletin WHO, 2007):
  GAMLSS with BCPE and cubic splines for estimating WHO growth curves

Modelling (1/4)

Step 1: **data preparation**

- clarify unplausible value
- remove uneligible cases
- weight, BMI: subtract cl



Modelling (2/4)

Step 2: **starting model**

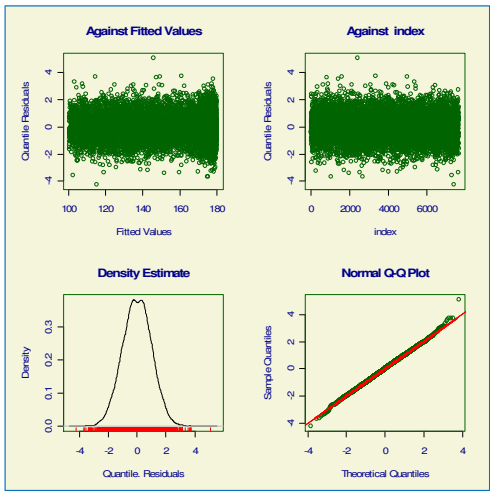
- mean and variability: 10 d.f.
- skewness and kurtosis: linear

→ remove extreme values (residuals outside +/-4 SD)

Modelling (2/4)

Step 2: **starting model**

```
Residuals: < -4 or > +4
========================
     4290     14352
 5.076757 -4.223742
         nr groesse     alter
4290    4384   184.8 10.929423
14352 14707    95.0  5.696547
```



Modelling (3/4)

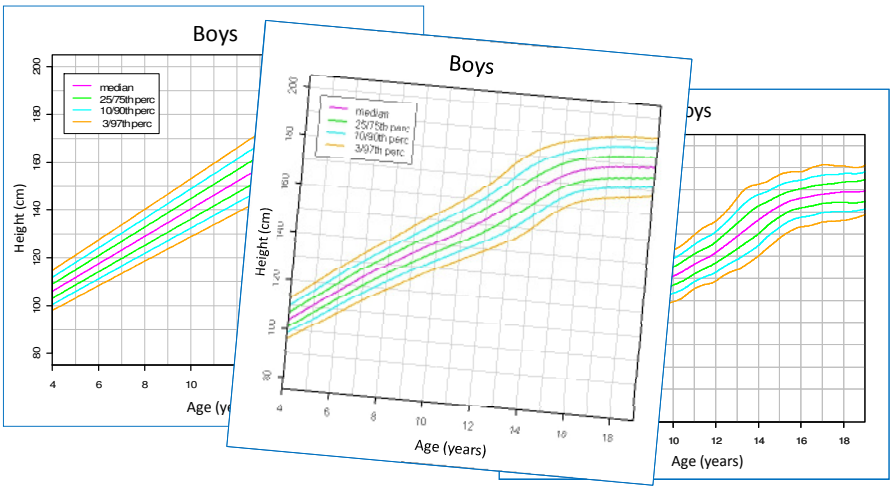
Step 3: **interim model**

- based on reduced data set
- optimization:
  - degrees of freedom for cubic splines
  - age exponent
  - using R-function `find.hyper()`
- criterion = (Generalized) Akaike Information Criterion
  = $k \cdot p - 2 \log(L)$

k = penalty, p = # parameters, L = likelihood

Modelling (3/4)

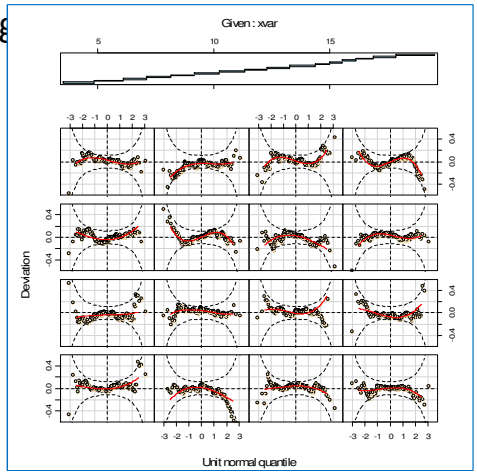
Step 3: **interim model**



Modelling (3/4)

Step 3: **interim model**

- diagnostic Tools (cf. Borg
  - residual plots
  - worm plots
    (van Buuren & Fredriks,
    Stat.Med., 2001)



Modelling (3/4)

Step 3: **interim model**

- diagnostic Tools (cf. Borghi et al, Stat. Med., 2006):
  - residual plots
  - worm plots
    (van Buuren & Fredriks,
    Stat.Med., 2001)
  - observed vs. fitted proportions below centiles
- remove further extreme values if necessary
- re-run optimization

Modelling (4/4)

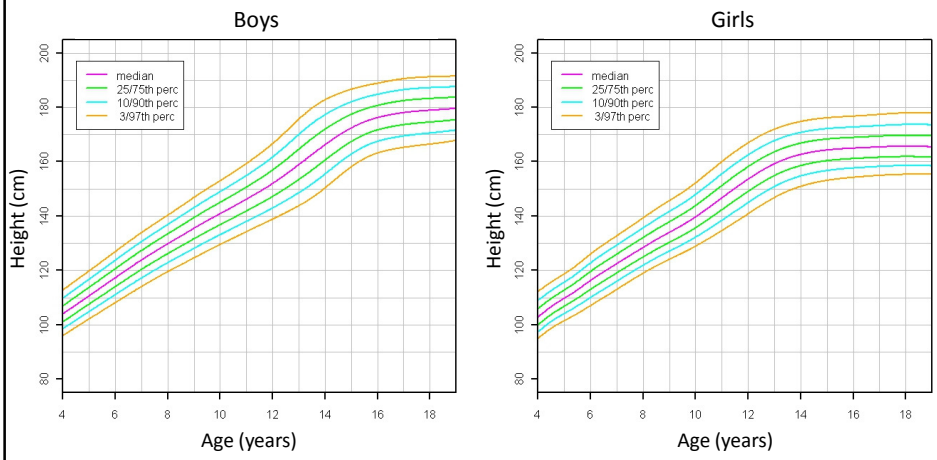
Step 4: **final model**

- consultation with paediatrician
- adapt model if necessary:
  - kurtosis more rigid (e.g. height for boys)
  - BMI generally more rigid:
    higher penalty *k* in GAIC optimization criterion

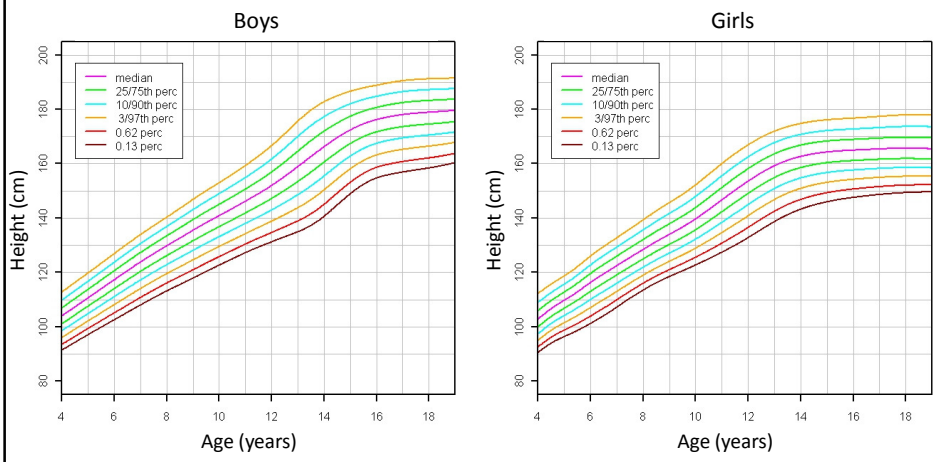
Modelling (4/4)

Boys	outliers removed	penalty *k* in GAIC	d.f. μ	d.f. σ	d.f. ν	d.f. τ	Age Expon.
Height	1+1	2	8.45	8.23	3.49	-	1.36
Weight	2+0	2	10.71	7.33	0.10	3.40	1.10
BMI	6+0	3	6.31	4.13	2.97	2.63	0.04
Sit. height	4+2	2	9.01	8.29	5.10	-	1.00
Leg length	3+2	2	8.79	7.53	4.33	-	1.01
Ratio SH/LL	8+11	2	8.19	2.80	0.79	0.17	1.00

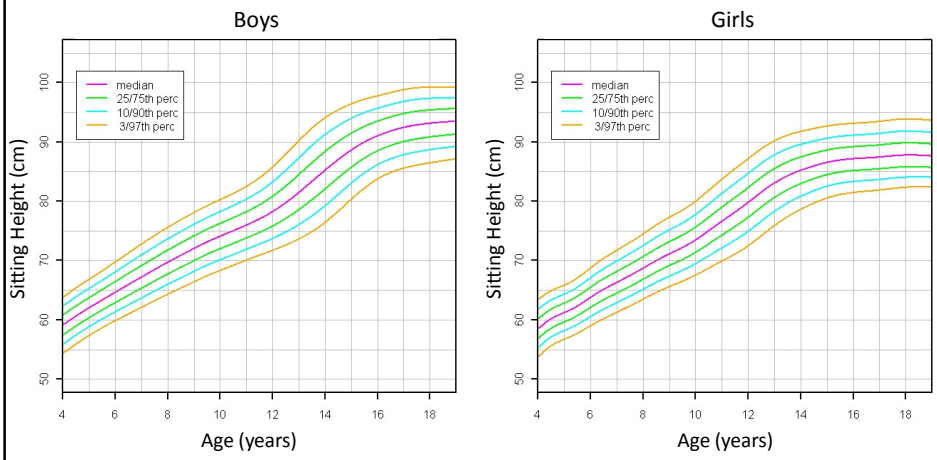
Height



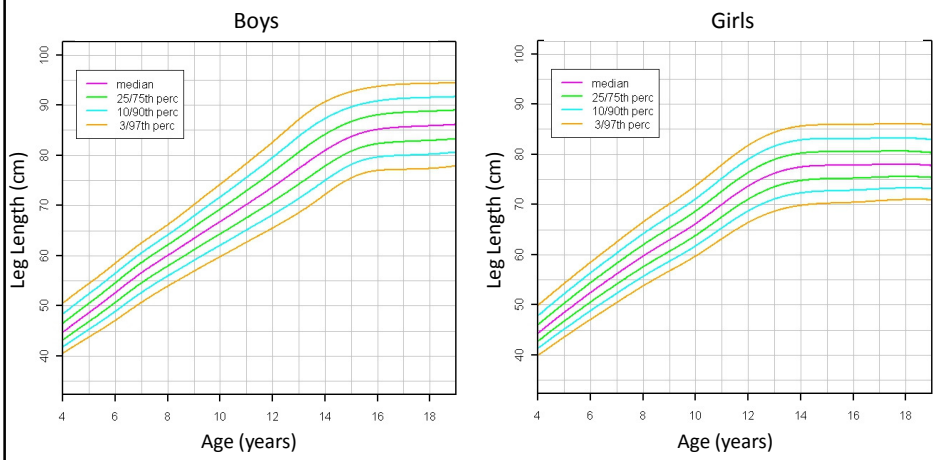
Height



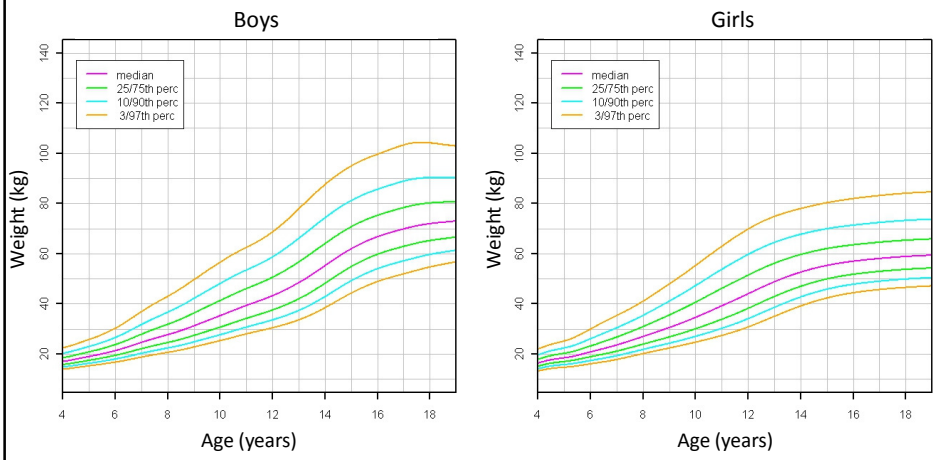
Sitting Height



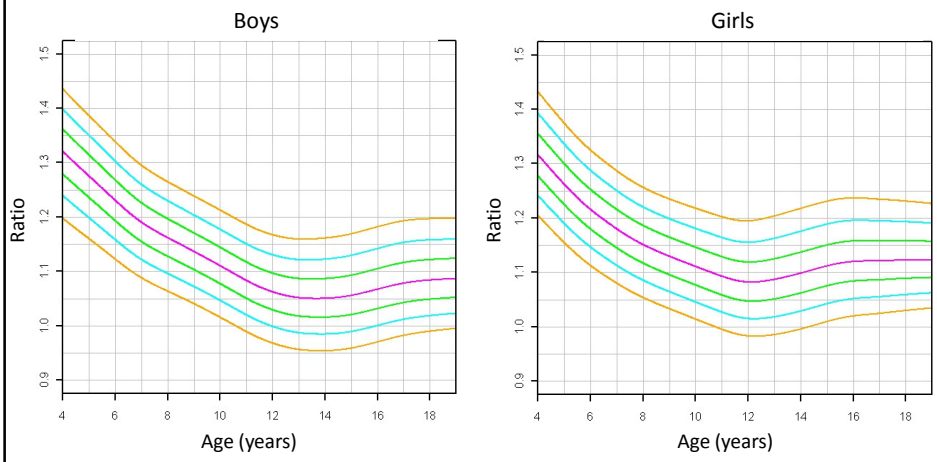
Subischial Leg Length



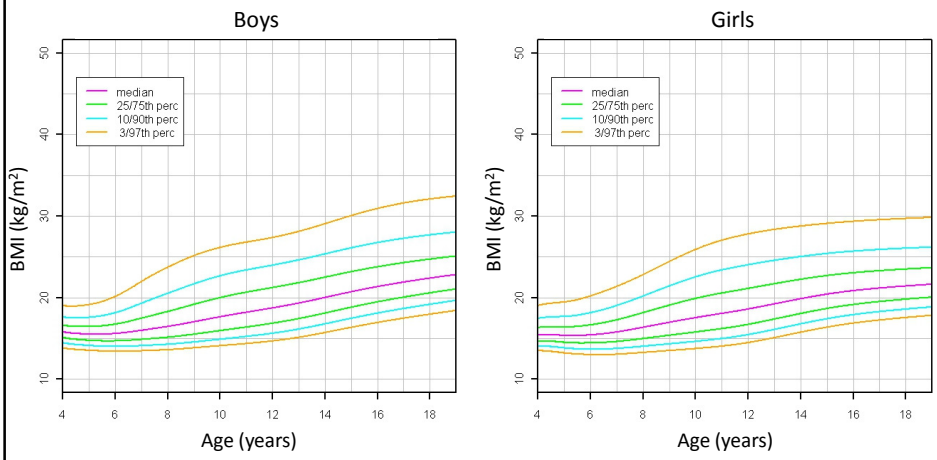
Weight



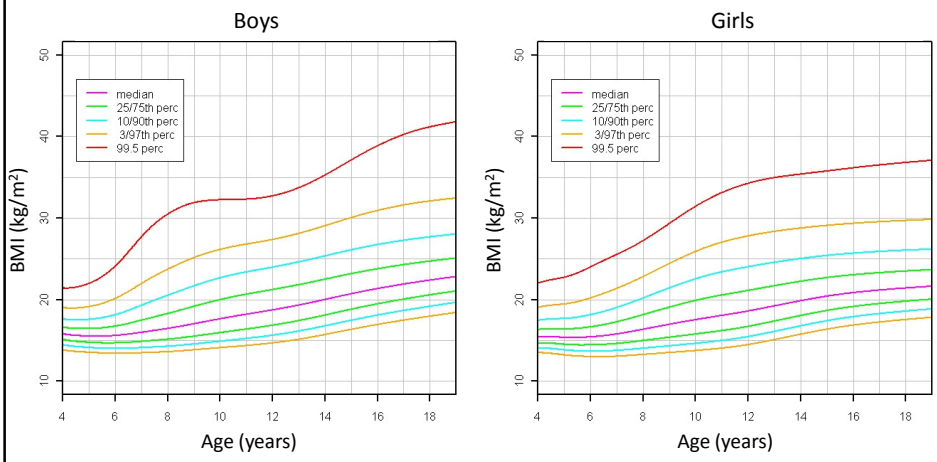
Ratio Sitting Height / Leg Length



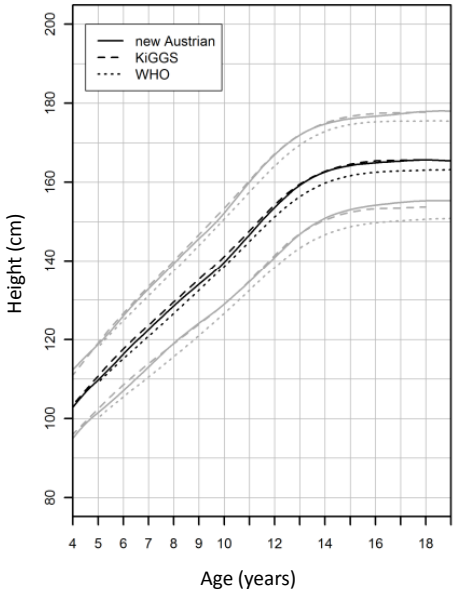
Body-Mass-Index



Body-Mass-Index



Comparisons (1/3)



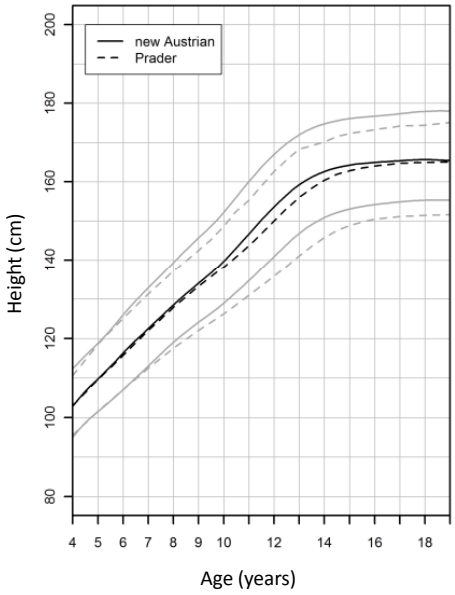
new Austrian vs. KiGGS vs. WHO

Height for Girls

black = median
grey = 3rd / 97th percentile

solid = new Austrian
dashed = KiGGS (Germany)
dotted = WHO

Comparisons (2/3)



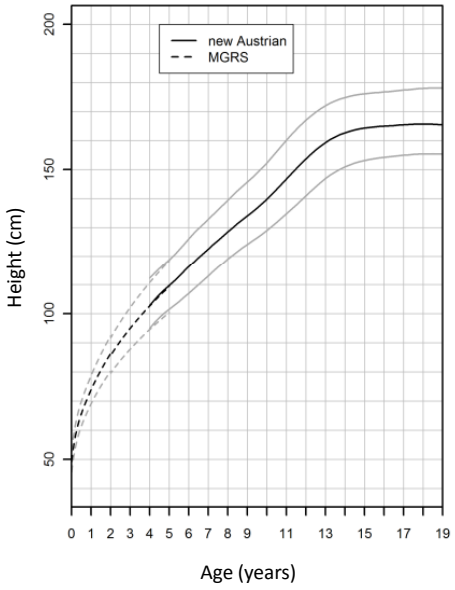
new Austrian vs. Prader

Height for Girls

black = median
grey = 3rd / 97th percentile

solid = new Austrian
dashed Prader

Comparisons (3/3)



new Austrian + MGRS

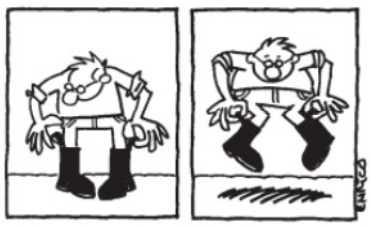
Height for Girls

black = median
grey = 3rd / 97th percentile

solid = new Austrian (4 to <19 years)
dashed = MGRS (0 to 5 years)

Sample Size Issues (1/3)

- 150 bootstrap samples
  - original sample size
  - higher / lower sample sizes
- on each bootstrap sample:
  - estimate GAMLSS model
  - calculate low percentile curve (e.g. -2.5 SDS)
- across all bootstrap samples:
  - estimate standard error of percentiles at different ages
- derive recommendation for adequate sample size



Sample Size Issues (2/3)

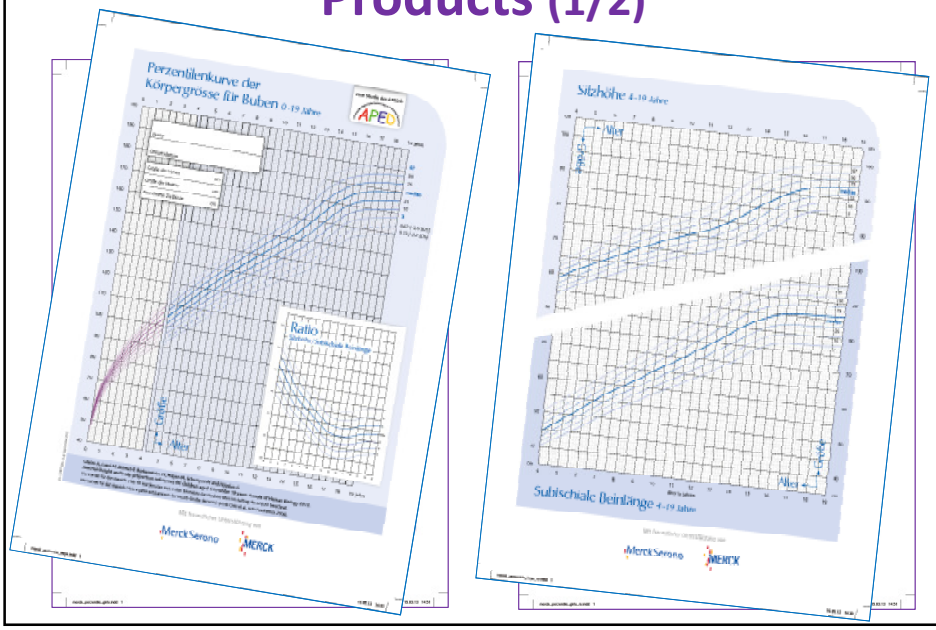
- Estimation of GAMLSS model on bootstrap samples:
  - Step 1: data preparation (before bootstrap)
  - Step 2: starting model for outlier removal
    → automatic
  - Step 3: interim model by d.f. optimization
    → automatic
  - Step 4: final model by "inspection":
    - residuals outside +/-3.5 or +/-3.0
    - or increase penalty *k* in GAIC

Sample Si

- Standard errors (cm)
  - for -2.5 SDS
  - height (boys)
- recommend sample size of ≥ 5000 per sex

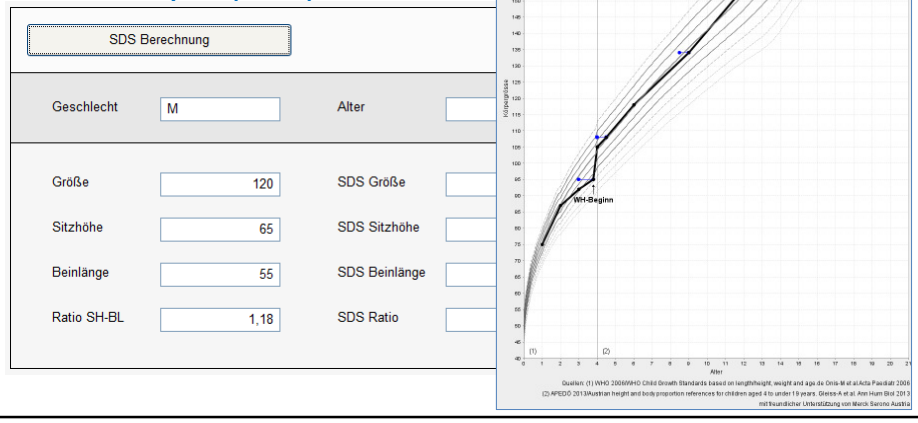
Age	n=2500	n=5000	n= 7663	n=10000
4	1.21	0.94	0.67	0.71
5	0.78	0.73	0.46	0.40
6	0.93	0.95	0.53	0.42
7	0.82	0.75	0.51	0.38
8	0.80	0.64	0.53	0.43
9	0.86	0.71	0.51	0.47
10	1.05	0.87	0.55	0.52
11	0.93	0.74	0.54	0.45
12	1.21	0.93	0.61	0.56
13	1.43	1.09	0.83	0.61
14	1.40	1.08	0.72	0.60
15	1.21	1.02	0.57	0.54
16	1.21	1.00	0.56	0.54
17	1.08	0.80	0.61	0.51

Products (1/2)



Products (2/2)

- Electronic:
  Research Documentation
  & Analysis (RDA)



Conclusions

- 14.544 individuals
- balanced w.r.t. age, sex and province
- state-of-the-art modelling
- curves suitable for the next decades
- results for height and body proportions published (Gleiss et al., Ann.Hum.Biol., 2013)
- results for weight and BMI (over-weight and obesity) submitted
- secondary use of data

References

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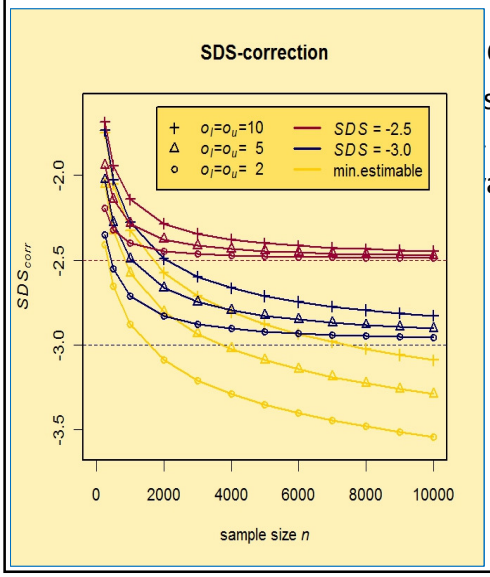
- **van Buuren**, S. & **Fredriks**, M. (Statistics in Medicine, 2001)

GAMLSS Method (8/9)



d:

stribution function
Stasinopoulos, 2004)
ations removed

$$SDS_{corr} = \Phi^{-1}\left(\left(\Phi(SDS)\cdot(n-o_l-o_u)+o_l\right)/n\right)$$

n: original # observations
o_l: # omitted at lower end
o_u: # omitted at upper end

Modelling (4/4)

Girls	outliers removed	penalty k in GAIC	d.f. μ	d.f. σ	d.f. ν	d.f. τ	Age Expon.
Height	2+0	2	10.66	6.89	4.09	1.67	0.27
Weight	1+0	2	9.32	6.59	4.34	3.90	0.28
BMI	2+0	3	6.32	3.90	0.16	2.77	0.23
Sit. height	3+2	2	13.46	7.44	3.43	0.10	0.50
Leg length	9+1	2	8.99	0.16	3.54	0.18	0.93
Ratio SH/LL	8+8	2	8.26	2.88	0.10	0.10	1.00