Introduction of the IDEFICS Study and methodology – GAMLSS

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- on behalf of the IDEFICS consortium -

Consensus Workshop on the Metabolic Syndrome in Children – the IDEFICS results

CIP 2015 – 4th Global Congress for Consensus in Pediatrics & Child Health
Budapest, 20 – 22 March 2015
Identification and prevention of Dietary- and lifestyle-induced health Effects in Children and infants

➢ Objectives:
  - Enhance knowledge of health effects of changing diet & altered social environment & lifestyle of children, 2-10 years, in Europe,
  - Develop, implement & evaluate specific intervention approaches to reduce prevalence of diet- & lifestyle-related diseases & disorders.
Core variables

- Questionnaires (parent)
  - Social factors, lifestyle + PA (100%)
  - Eating behaviour + FFQ (94%)
  - Medical history (77%)

- 24-hour dietary recall + school meals
  - SACINA (68%): computer-based 24-hour dietary recall

- Physical activity
  - Accelerometer (46%): 3 days

Core variables & add-ons

- Physical examination
  - Anthropometry (100%)
  - Blood pressure (91%)
  - Musculoskeletal disorders (47%)
    (calcaneal ultrasonometry)

- Biological markers
  - Blood (57% venous + 20% capillary)
  - Saliva / mouth swab (86%)
  - Urine (86%)

- Add-ons, e.g.
  - Sensory taste perception
  - Physical fitness
  - Food advert effects
  - (Pre-) school environment: GIS
Design of IDEFICS

- Exhaustive examination programme including numerous biological/clinical parameters
- Population-based sample of 18,745 newly recruited European children 2.0 - 10.9 years old

IDEFICS study valuable data source
Reference curves

- For many clinical parameters reference values are still missing in children
- Due to physical development of children age-dependent growth curves (e.g. for height) are needed

➤ Method of choice for estimating reference curves: GAMLSS
GAMLSS - an innovative approach for calculating reference values
Obsesity determinants and reference standards for health parameters in pre-adolescent European children: Results from the IDEFICS study

- Percentile reference values for anthropometric body composition indices in European children from the IDEFICS study
- Percentiles of fasting serum insulin, glucose, HbA1c and HOMA-IR in pre-pubertal normal-weight European children from the IDEFICS cohort
- Blood lipids among young children in Europe: results from the European IDEFICS study
- Blood pressure reference values for European non-overweight school children: The IDEFICS study
- Metabolic syndrome in young children: definitions and results of the IDEFICS study
  - C-reactive protein reference percentiles among pre-adolescent children in Europe based on the IDEFICS study population
  - Reference values for leptin and adiponectin in children below the age of 10 based on the IDEFICS cohort
  - Physical fitness reference standards in European children: The IDEFICS study
  - Reference values of bone stiffness index and C-terminal telopeptide (CTX) in healthy European children
  - Reference values of whole-blood fatty acids by age and sex from European children aged 3-8 years

- Generalised additive model for location, scale and shape
- Rigby and Stasinopoulos (2005)
- Regression model
- Generalisation of the LMS method (Cole and Green, 1992)
- General class of distribution:
  - Highly skew
  - Kurtotic
- More than one covariate
- `gamlss` package in the statistical software R
- Used by WHO for growth curves
A semi-parametric GAMLSS assumes:

- \( y_i, i = 1, \ldots, N \), independent observations with probability density function \( f(y_i | \theta^i) \) conditional on \( \theta^i \) which is vector of \( K \) parameters related to the covariates

\[
g_k(\theta_k) = X_k \beta_k + \sum_{j_k=1}^{J_k} h_{j_k k}(x_{j_k k})
\]

- Link function \( g_k, k = 1, \ldots, K \)
- Parameter \( \theta = (\theta_1, \ldots, \theta_K) \) of a distribution \( D(\theta) \)
- Design matrix \( X_k \) with parameter vector \( \beta_k \)
- Spline \( h_{j_k k} \) of a vector \( x_{j_k k} \in \mathbb{R}^N \) of \( 1, \ldots, J_k \)
Four distribution parameters

For $K = 4$

**Location:**

$$g_1(\mu) = X_1 \beta_1 + \sum_{j_1=1}^{J_1} h_{j_11}(x_{j_11})$$

**Scale:**

$$g_2(\sigma) = X_2 \beta_2 + \sum_{j_2=1}^{J_2} h_{j_22}(x_{j_22})$$

**Skewness:**

$$g_3(\nu) = X_3 \beta_3 + \sum_{j_3=1}^{J_3} h_{j_33}(x_{j_33})$$

**Kurtosis:**

$$g_4(\tau) = X_4 \beta_4 + \sum_{j_4=1}^{J_4} h_{j_44}(x_{j_44})$$
Distributions in GAMLSS

<table>
<thead>
<tr>
<th>BCCG (LMS)</th>
<th>BCPE</th>
</tr>
</thead>
<tbody>
<tr>
<td>transformed normal</td>
<td>transformed power exponential</td>
</tr>
<tr>
<td>$K = 3$</td>
<td>$K = 4$</td>
</tr>
</tbody>
</table>

1 shape parameter  2 shape parameters
Median $\mu$: location parameter
Median $\mu$: location parameter
Median $\mu$: location parameter
Coefficient of variation $\sigma$: scale parameter
Coefficient of variation $\sigma$: scale parameter
Coefficient of variation \( \sigma \): scale parameter
Skewness $\nu$: shape parameter
Skewness $\nu$: shape parameter
Skewness $\nu$: shape parameter
Kurtosis $\tau$: shape parameter

- Special feature of GAMLSS
Model selection

- A variety of distributions at hand (e.g. BCPE, BCCG)
- Model influence on distribution parameters as
  - constant,
  - linear function of age and height or
  - cubic spline of age and height
- Stepwise model selection using Bayesian Information Criterion (BIC)

> Results in a model for each distribution with lowest BIC
Model diagnostics

- Information criterion: BIC
- Visual impression
- Comparison of models: boys ↔ girls
- Percentage of cases below the percentiles

- Distribution of residuals
  - Q-Q plots
  - Wormplots (Buuren and Fredriks, 2001)
Model diagnostics
Conclusion

- We applied GAMLSS successfully for more than 35 variables
- Derivation of percentile curves and z-scores
- Particularly useful, if
  - Shape adjustments are required
  - More than one covariate should be modeled (e.g. for blood pressure)
- Model diagnostic tools available to avoid overcomplex models
References


Thank you for your attention!
Appendix
For boys

<table>
<thead>
<tr>
<th>Distribution</th>
<th>Parameter</th>
<th>BIC</th>
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<tbody>
<tr>
<td>BCCG</td>
<td>age+cs(height)</td>
<td>42 652</td>
</tr>
<tr>
<td></td>
<td>cs(height)</td>
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<td>cs(height)</td>
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<tr>
<td>BCPE</td>
<td>age+cs(height)</td>
<td>42 661</td>
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<tr>
<td></td>
<td>cs(height)</td>
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<td>cs(height)</td>
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<tr>
<td>Normal distribution</td>
<td>age+cs(height)</td>
<td>43 154</td>
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<tr>
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<td>cs(height)</td>
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Bone stiffness index (SI)

- Percentiles depending on height: P3, Median, P97
Bone stiffness index (SI)

- Age- and height-specific

50th percentiles for girls
Shape parameter $\tau$
Shape parameter $\tau$
Shape: kurtosis