Die IDEFICS/I.Family-Kohorte: Befragungen, Messungen und eine kontrollierte Interventionsstudie

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50 Jahre Statistische Methoden in der Empirischen Forschung
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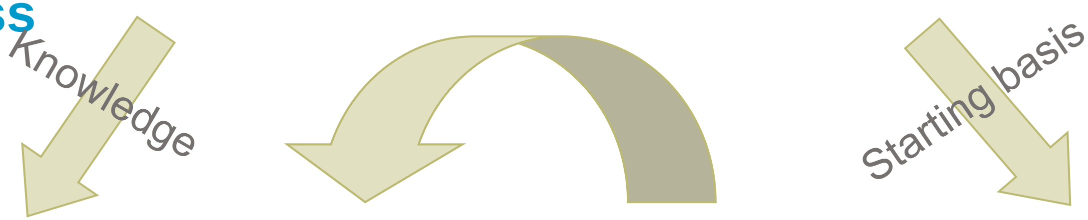
Research Purpose

Funded by the EC, FP 6, Contract No. 016181 (FOOD)

Funded by the EC, FP 7, Project No. 266044 -

Aims

- **Objectives**
  - Enhance knowledge of **health effects of changing diet & altered social environment & lifestyle** of children, 2-9 years, in Europe
  - Develop, implement & evaluate specific intervention approaches to **reduce prevalence of diet- & lifestyle-related diseases & disorders**
- **Known modifiable risk factors**
  - **Nutrition**
  - **Physical activity**
  - **Stress**



Specific intervention targets

- **Intervention study**

New knowledge on aetiological mechanisms

- **Analytical study**

Primary aim: contribute to reducing burden of nutrition- and lifestyle-related diseases

- Understand interplay between **barriers and main drivers** of a healthy food choice
- Identify **predictors of unnecessary weight gain and cardio-metabolic risk** by linking them to diet, physical activity and interacting factors
  - **Focus on IDEFICS child and his / her family**
  - **Assess how different factors affect children as they grow up**
- Develop and convey **strategies to induce changes** towards a healthy behaviour

Shift of focus: physical and socio-political environment shaping health behaviour

Study Design

ideficsstudy
Learning healthy living

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ifamily

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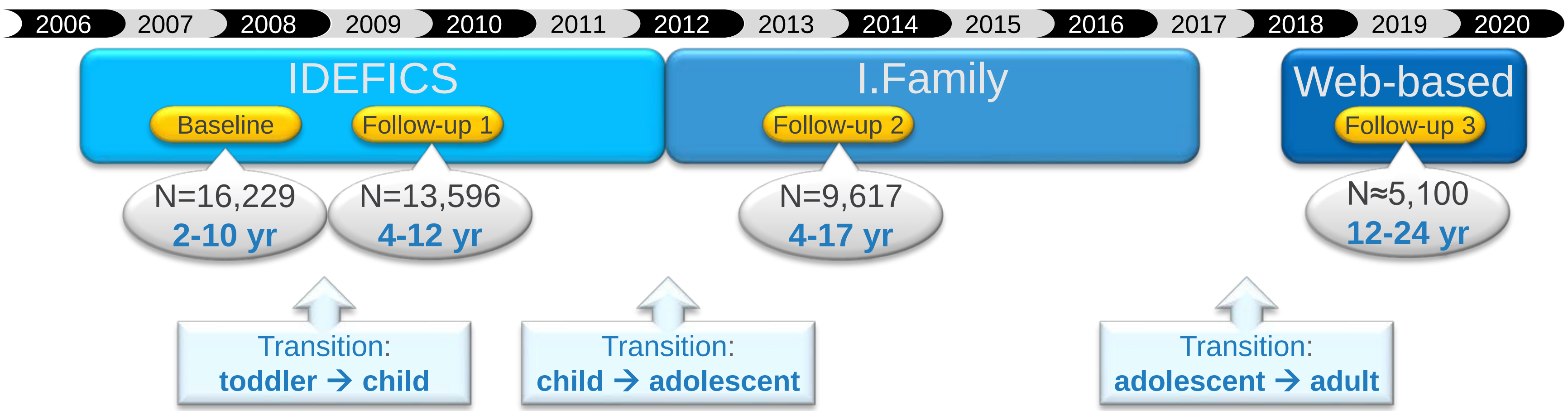
Basic design: IDEFICS study

- **8 European countries** from South to North & East to West
  - One intervention/one control region (not randomized)
  - Pre-school/primary school children in each region
- Power/sample size
  - 80% to detect a true reduction in overweight/obesity prevalence from 15% to 12% stratified by country and school level, α=0.05: 1,000 children (500 pre-school, 500 primary school) in intervention/ control regions in each country
- **Common manual of operations, highly standardized**
  - Central and local trainings in SOPs
  - Side visits
- **Baseline** and **follow-up survey** after intervention

Partners

1. Strovolos, Cyprus
2. Ghent, Belgium
3. Copenhagen, Denmark
4. Tallin, Estonia
5. Helsinki, Finland
6. Bremen, Germany
7. Pécs, Hungary
8. Avellino, Italy
9. Milan, Italy
10. Utrecht, Netherlands
11. Palma de Mallorca, Spain
12. Zaragoza, Spain
13. Gothenburg, Sweden
14. Bristol, United Kingdom
15. Lancaster, United Kingdom
16. Andover, United Kingdom

Timeline of recruitment and follow-up of the IDEFICS – I.Family cohort



Exposures/ behaviours and endpoints assessed at each examination:

- Food choice, eating behaviour, sensory taste preference, screen time, physical activity, sleep, well-being, family/ social/ built environment
- Sub-clinical changes & health outcomes (body composition, blood pressure, metabolic profile, bone health)

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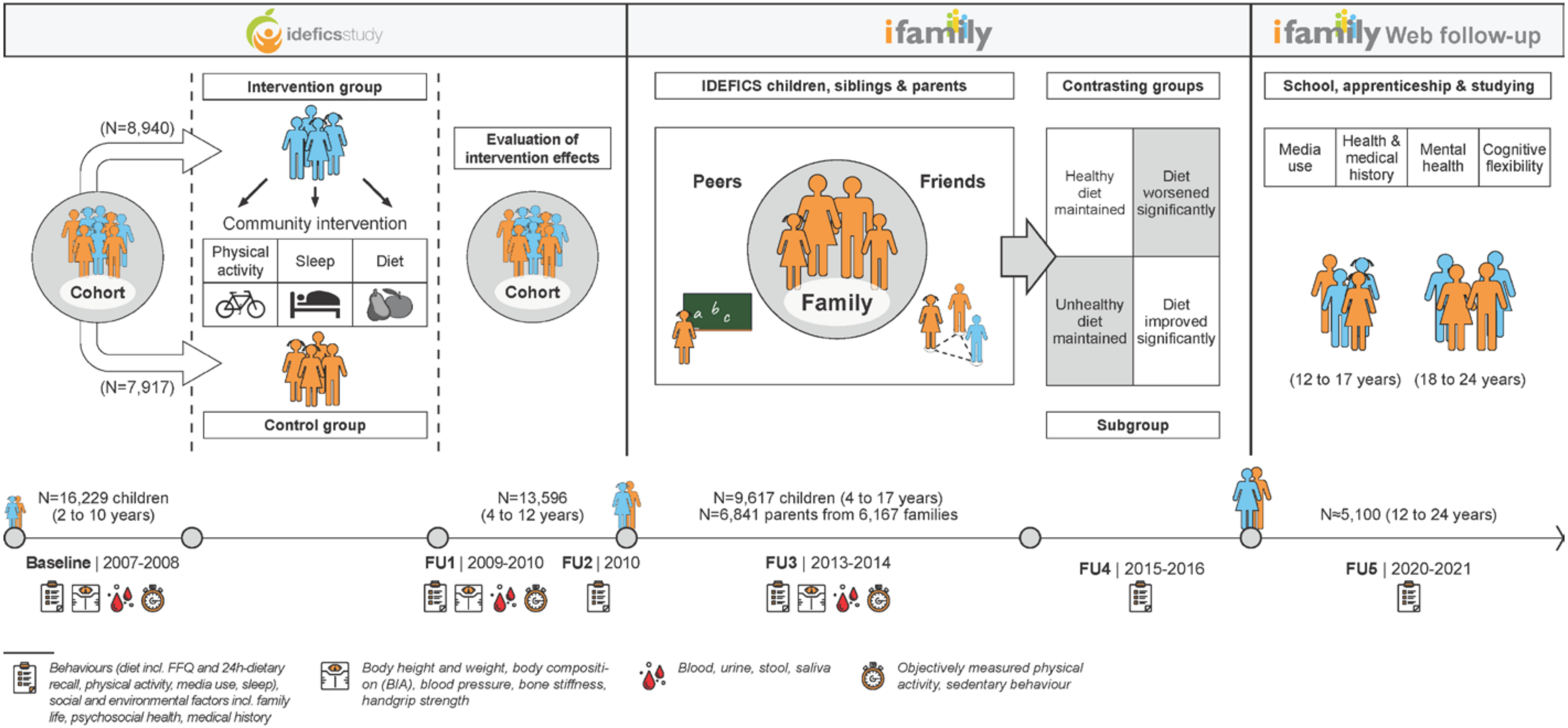

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Questionnaires & examinations 1

- Questionnaires (parent + child)
  - **Social factors, lifestyle, peers + physical activity**
  - **Food frequency, preference, eating behaviour**
  - **Medical history**
  - **Family members + household**
- 24-hour dietary recall
  - Web-based **dietary recall**
- Physical activity
  - **Accelerometer:** 7 days
  - **Built environment:** GIS + GPS

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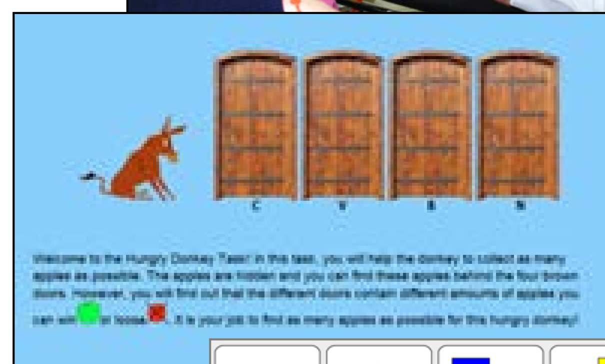
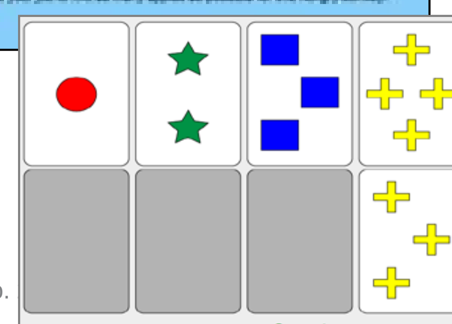
Questionnaires & examinations 2

- Physical examinations
  - ➢ **Anthropometry + blood pressure**
  - ➢ **Bone health:** ultrasound
- Biological markers
  - ➢ **Blood, saliva + urine**
- Specific tests in subgroups
  - ➢ **Sensory taste perception**
  - ➢ **Neuropsychological tests:** impulsivity
  - ➢ **Brain mechanisms of food choice:** fMRI





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Challenges

- **Pre-test** of all instruments
  - Adaption necessary
  - Validation studies
- **Data cleaning** and **documentation**
  - Data sharing via data portal at BIPS
  - Data provenance: all instruments provided
- **Loss to follow-up**
- **Technical developments**
  - Change of instruments ➢ calibration studies
- **Renewal of informed consent**
  - Study participants now adults

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Statistical Analyses…

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…at Baseline

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Type of analyses

- **Descriptive statistics**, in particular prevalences

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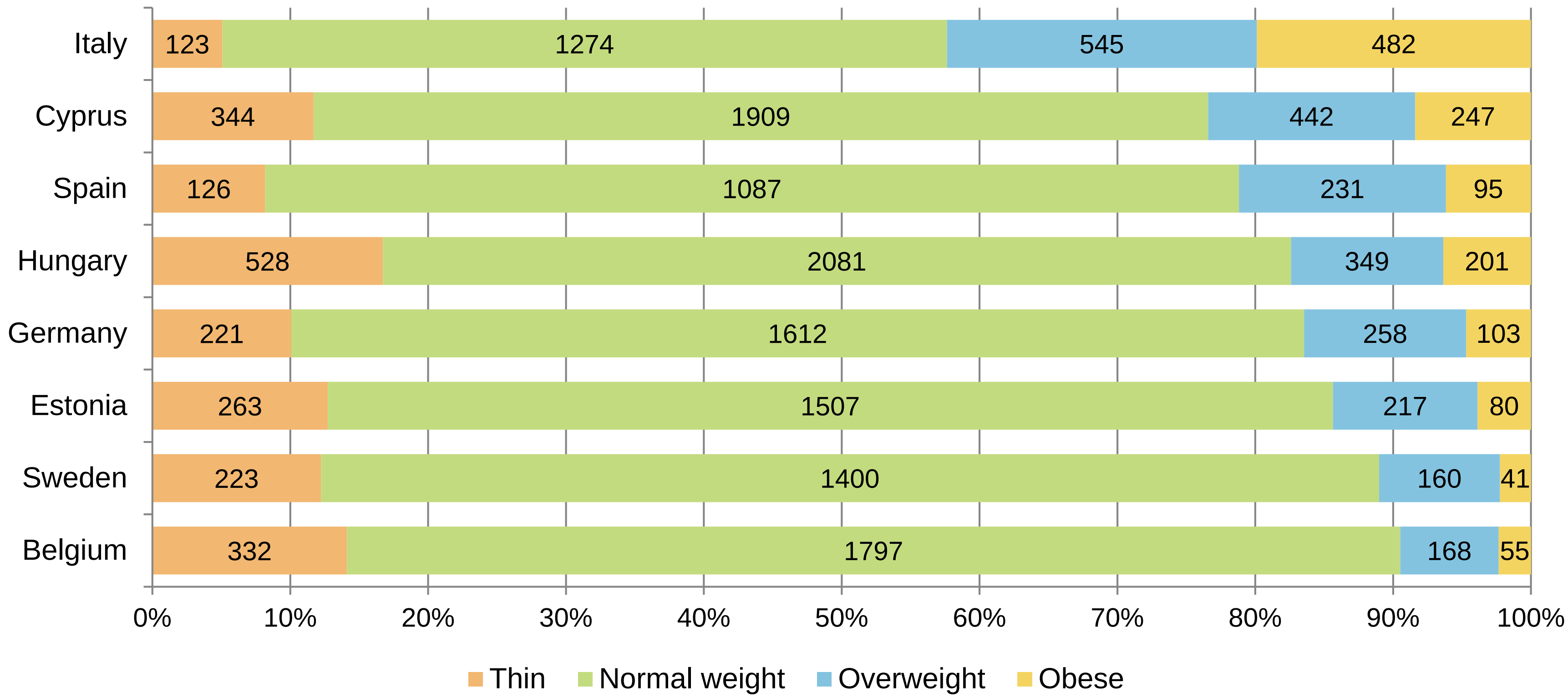
Prevalence of childhood overweight/obesity (2-10 yr)



Ahrens W, Pigeot I et al.; IDEFICS Consortium. Prevalence of overweight and obesity in European children below the age of 10. Int J Obes (Lond) 2014; 38(Suppl 2): S99-107

Type of analyses

- **Descriptive statistics**, in particular prevalences
- **Stratified analyses**, in particular by socioeconomic status and country

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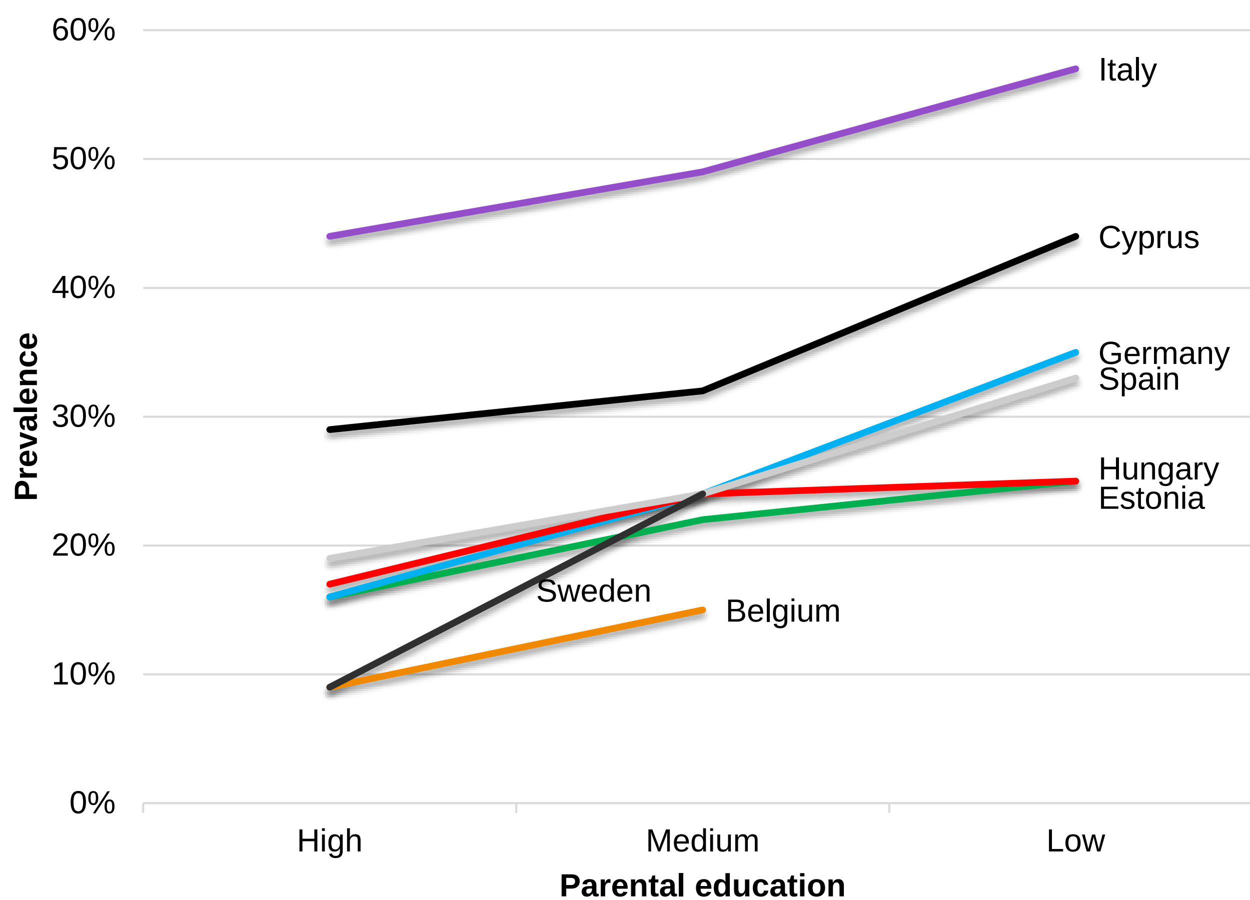
Prevalence of overweight/obesity by parental education



Ahrens W, Pigeot I et al.; IDEFICS Consortium. Prevalence of overweight and obesity in European children below the age of 10. Int J Obes (Lond) 2014; 38(Suppl 2): S99-107

Type of analyses

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- **Stratified analyses**, in particular by socioeconomic status and country
- **Regression analyses**, in particular to estimate associations

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Sleep and weight status

- **Short sleep duration**
  - **being overweight** – particularly in primary school children
- Inverse relationship between sleep duration and BMI
  - mainly explained by inverse association between sleep duration & fat mass
- Insulin may explain part of this association, in particular in heavier children

Hense S et al. Factors that influence weekday sleep duration in European children. Sleep 2011; 34: 633-9
Hense S et al. Sleep duration and overweight in European children: is the association modified by geographic region. Sleep 2011; 34: 885-90

Type of analyses

- **Descriptive statistics**, in particular prevalences
- **Stratified analyses**, in particular by socioeconomic status and country
- **Regression analyses**, in particular to estimate associations
- **Measurement error analysis**, in particular to assess dietary behaviour
  - Under-/overreporting

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Dietary behaviour

- Prevalence of under-/overreporting
  - Based on age-/sex-specific Goldberg cut-offs: 8.0%, 3.4% (24-hdr data)
  - Increased with BMI z-score, household size, higher in low income groups
  - Affected by social desirability and parental perception of their child's weight status
- Diet-obesity associations
  - Affected/even masked by measurement errors
  - Attenuation counteracted by accounting for reporting status and inclusion of propensity score for misreporting

Börnhorst et al. Prevalence and determinants of misreporting among European children in proxy-reported 24 h dietary recalls. Br J Nutr 2013; 109: 1257-65

Börnhorst et al.. Diet-obesity associations in children: approaches to counteract attenuation caused by misreporting. Public Health Nutr 2013;16: 256-66

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- **Stratified analyses**, in particular by socioeconomic status and country
- **Regression analyses**, in particular to estimate associations
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  - Under-/overreporting
- **Kernel density estimation**

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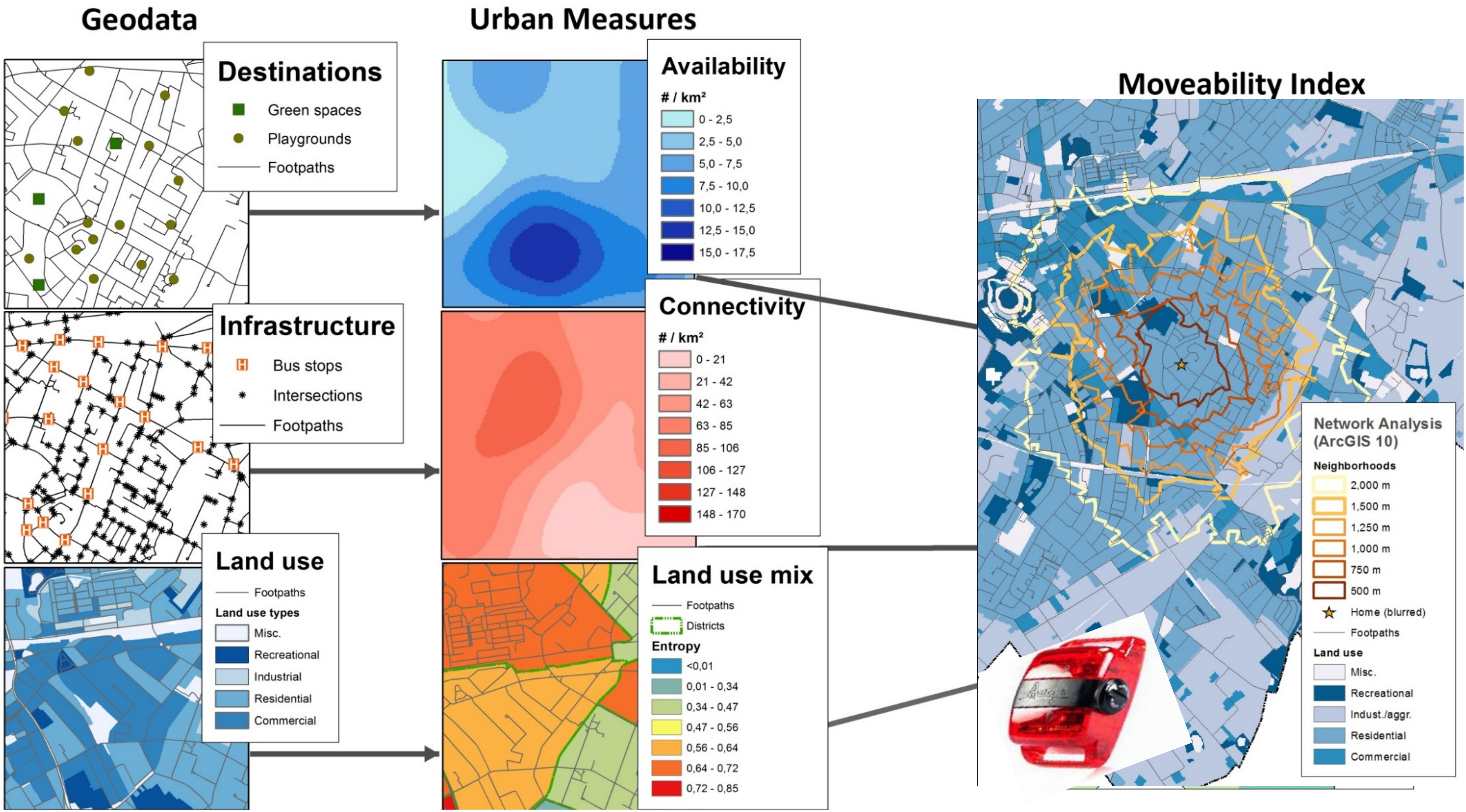
Built environment and physical activity



Buck et al. Development and application of a moveability index to quantify possibilities for physical activity in the built environment of children. Health Place 2011, 17: 1191-201

Type of analyses

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- **Regression analyses**, in particular to estimate associations
- **Measurement error analysis**, in particular to assess dietary behaviour
  - Under-/overreporting
- **Kernel density estimation**
- **GAMLSS** (Rigby and Stasinopoulos 2005), in particular to calculate reference values

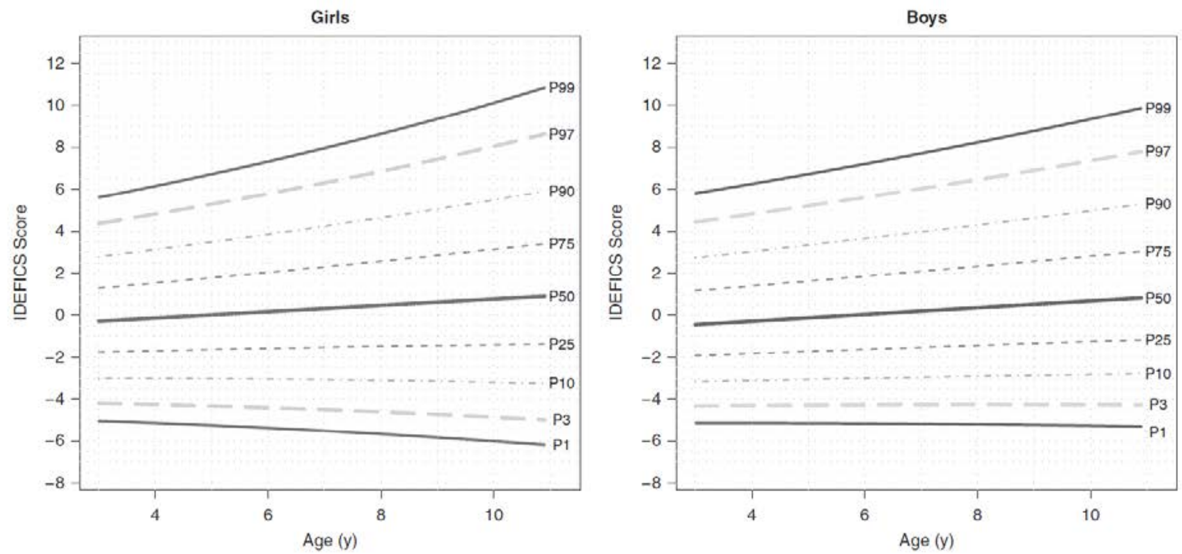
Rigby, Stasinopoulos Generalized additive models for location, scale and shape. JRSS Series C (Applied Statistics) 2005; 54:507-54

Metabolic syndrome (MS)

- Reference values for biomarkers
  - Age-/sex- [for blood pressure (BP) also height-] specific
- New definition of MS based on
  - Percentile curves for waist circumference (WC), HOMA index (HOMA), systolic (SBP) & diastolic BP (DBP), triglycerides (TRG) & cholesterol (HDL):

Recommended for worldwide use in paediatrics

IDEFICS MetS-Score: $z_{WC} + z_{HOMA} + (z_{SBP}+z_{DBP})/2 + (z_{TRG} - z_{HDL})/2$



Ahrens et al. Metabolic syndrome in young children: definitions and results of the IDEFICS study. Int J Obes 2014; 38 S2: S4-14
Chiarelli & Mohn Early diagnosis of metabolic syndrome in children. Lancet Child Adolesc Health 2017; 1(2):86-88

…of Intervention Study

Nutrition	Physical activity	Stress
Daily water → **Less soft drinks**	Reduce TV-viewing	Spend more time together →**Family time**
Daily fruit & vegetables	Daily PA →**Safe bicycle lanes** →**Outdoor playing**	Adequate sleep duration

Type of analyses

- **Mixed models** adjusting for age and socio-economic status of parents, with additional random effect for study centre to account for clustered study design
  - effect estimates for quantitative outcome variables: difference between mean change in intervention group and mean change in control group
  - not adjusted for multiple testing

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Results

- Children **adhering to more key messages** at start of IDEFICS **less likely to develop overweight**
- Effects of intervention on behaviour (physical activity, diet and sleep), body composition and markers of healthy aging were **overall very weak**
- Parents and families **often did not notice or remember messages** from intervention

Type of analyses

- **Mixed models** adjusting for age and socio-economic status of parents, with additional random effect for study centre to account for clustered study design
  - effect estimates for quantitative outcome variables: difference between mean change in intervention group and mean change in control group
  - not adjusted for multiple testing
- **Hypothetical interventions**
  - Parametric g-formula: generalisation of standardisation for time-varying exposures and confounders
    - appropriately adjusts for time-varying confounding by prior exposure
    - provides estimates of absolute risks under critical assumptions.

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- Used to estimate 13-year overweight/obesity risks under hypothetical interventions compared to risk under no intervention
- Population intervention effects when intervening only in vulnerable groups
  - children of parents with low/medium ISCED level
  - children of mothers with BMI > 25 kg/m^2

Results:

- 13-year risk of developing overweight/obesity was 30.7% under no intervention and 25.4% when adhering to 6 behavioural intervention messages
  - Following recommendations to limit screen time most effective approach, followed by enforcing physical activity
- For some behaviours: already small behavioural changes similar effect as compared to strictly meeting the related recommendations
  - membership in sports club particularly promising intervention target for vulnerable children

Börnhorst, Pigeot The effects of hypothetical behavioral interventions on the 13-year incidence of overweight/obesity in children and adolescents. Int J Behav Nutr Phys Act 2023; 20: 100

…of Follow-up (Longitudinally)

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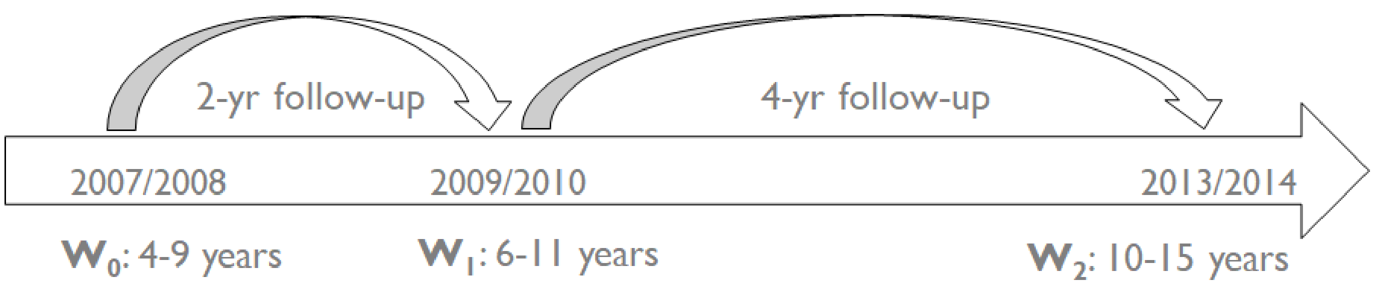
Type of analyses

➢ Latent Transition Analysis

- Identifies **latent groups** of children with similar metabolic profiles ("dimension reduction")
- Estimation based on 4 MetS components
(3 levels: normal, > 90th percentile (P90), > 90th percentile (P95))
- Estimates transition probabilities over time



Börnhorst et al. Metabolic status in children and its transitions during childhood and adolescence-the IDEFICS/I.Family study. Int J Epidemiol 2019; 48:1673-1683

- **Analysis group (N=6.768)**, 4 ≤ age ≤ 15
  - ≥ 2 measurements of all 4 MetS components
  - Exclusions: non-fasting status, current medication use
- **Best fit (BIC): 5-group model**
  - Percentages = estimated probabilities of a child having elevated values
- No group identified being characterised by elevated fasting glucose

Metabolically healthy	
WAIST+	3.6%
LIPIDS+	6.4%
GLU+	12.8%
BP+	8.5%

Abdominal obesity	
WAIST+	**94.2%**
LIPIDS+	12.0%
GLU+	25.3%
BP+	17.7%

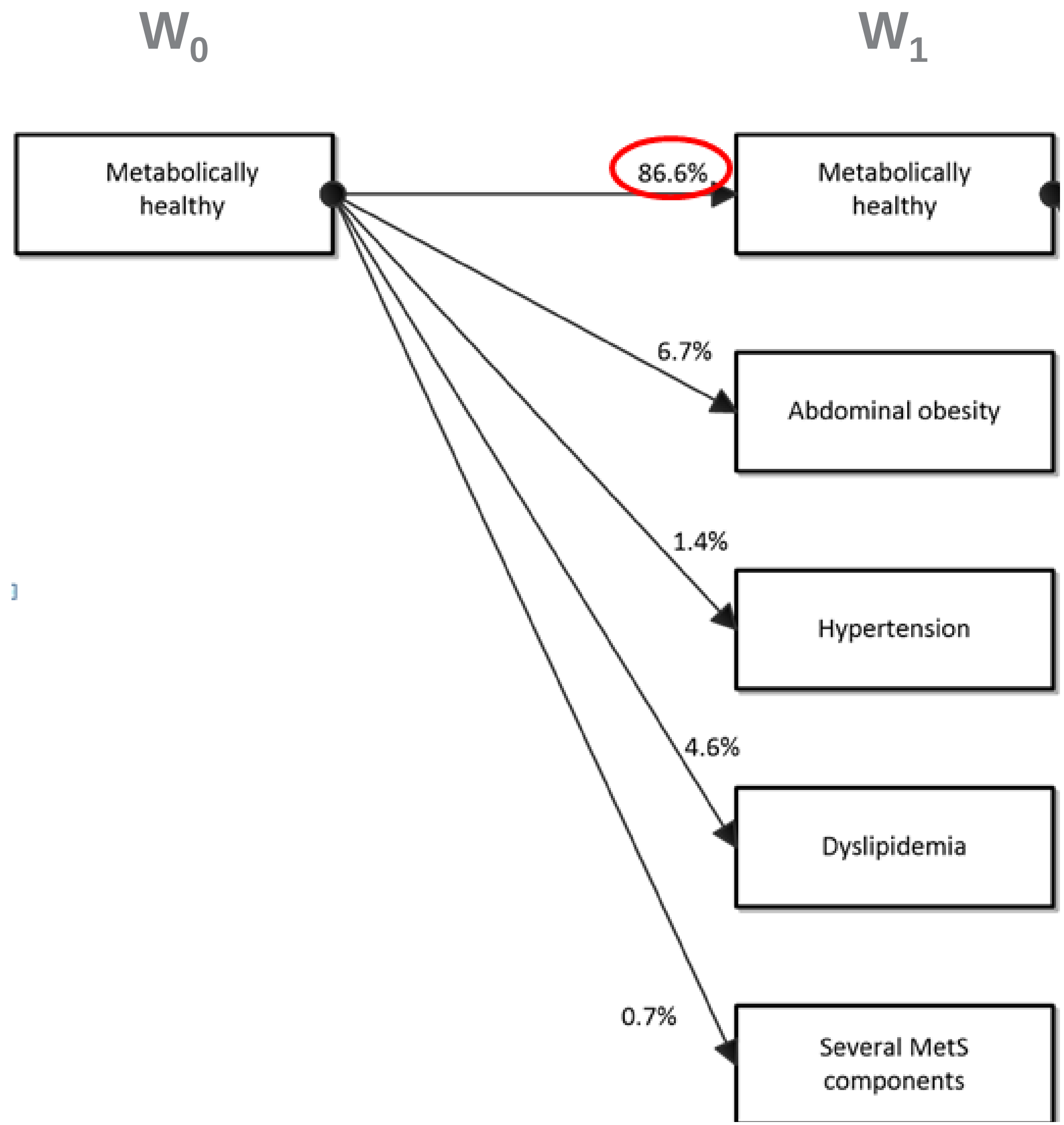
Hypertension	
WAIST+	12.6%
LIPIDS+	9.4%
GLU+	22.2%
BP+	**82.2%**

Dyslipidemia	
WAIST+	13.0%
LIPIDS+	**75.4%**
GLU+	22.3%
BP+	14.6%

Several MetS comp.	
WAIST+	**99.3%**
LIPIDS+	**60.4%**
GLU+	**51.7%**
BP+	**44.8%**

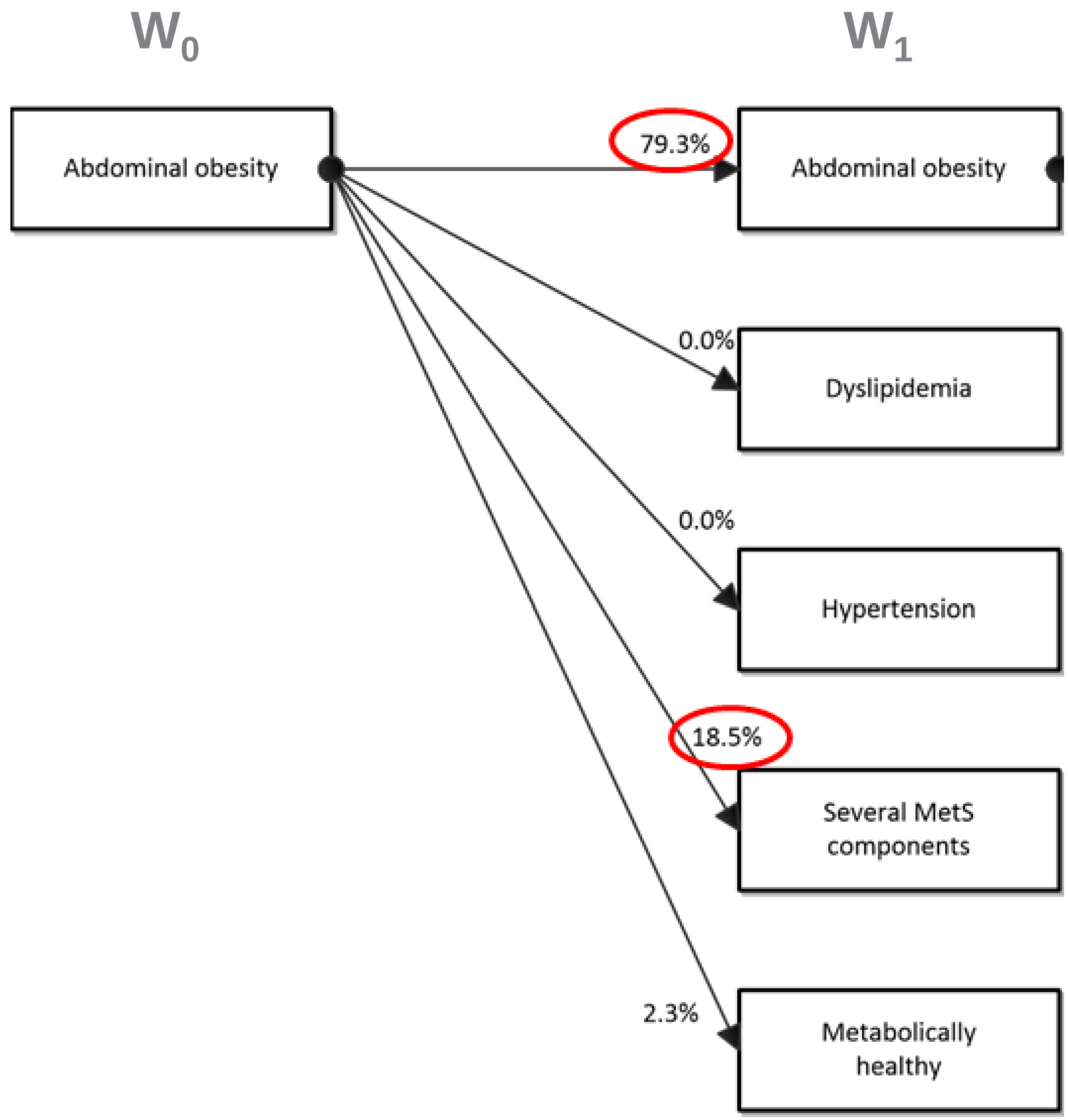
Börnhorst et al. Metabolic status in children and its transitions during childhood and adolescence-the IDEFICS/I.Family study. Int J Epidemiol 2019; 48:1673-83

Transitions: metabolically healthy



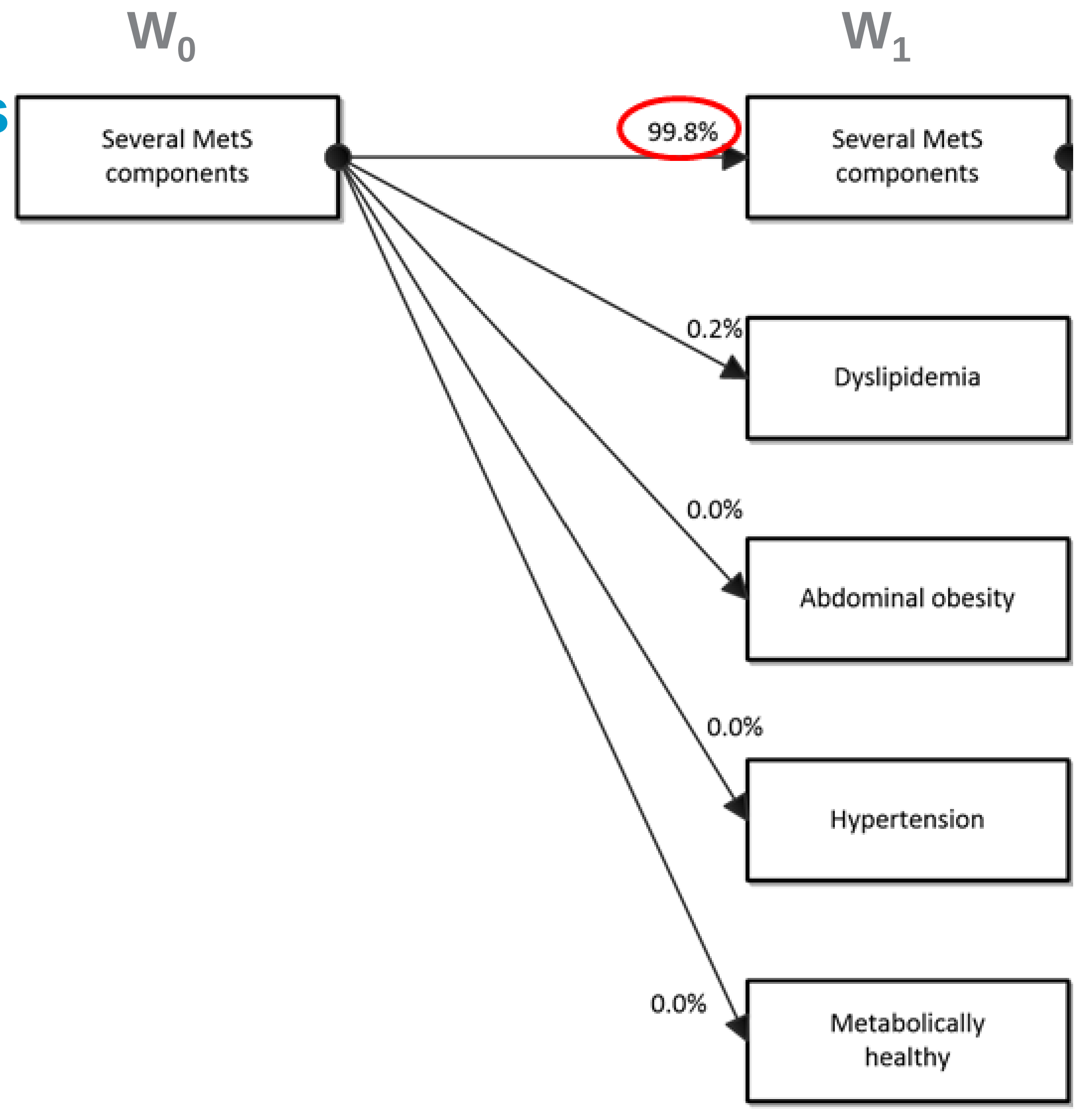
Börnhorst et al. Metabolic status in children and its transitions during childhood and adolescence-the IDEFICS/I.Family study. Int J Epidemiol 2019; 48:1673-83

Transitions: abdominal obesity



Börnhorst et al. Metabolic status in children and its transitions during childhood and adolescence-the IDEFICS/I.Family study. Int J Epidemiol 2019; 48:1673-83

Transitions: multiple MetS components



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Discussion

Challenges

- Central cleaning
- Central server for data access
- Multiple testing
- Missing values
- Loss to follow-up

Further methods

- Cluster analysis, principal component analysis to assess dietary behaviour
- Specific methods to analyse fMRI data to assess brain correlates of food cues and choice
- Genetic analyses
- ….

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Thank you!

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