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# Potential selection effects when estimating associations between the infancy peak or adiposity rebound and later body mass index in children

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**Key words:** cohort of European children, growth velocity, fractional polynomial mixed effects model, IDEFICS study, I.Family study

**Running title:** BMI growth measures as predictors for later obesity

## **Conflict of interest**

All the authors declare that there are no conflicts of interest.

## Abstract

## Introduction

This study aims to evaluate a potential selection effect caused by exclusion of children with non-identifiable infancy peak (IP) and adiposity rebound (AR) when estimating associations between age and BMI at IP and AR and later weight status.

## Subjects and Methods

In 4 744 children with at least 4 repeated measurements of height and weight in the age interval from 0 to 8 years (37 998 measurements) participating in the IDEFICS/I.Family cohort study, fractional polynomial multi-level models were used to derive individual BMI trajectories. Based on these trajectories, age and BMI at IP and AR, BMI values and growth velocities at selected ages as well as the area under the BMI curve were estimated. The BMI growth measures were standardized and related to later BMI z-scores (mean age at outcome assessment: 9.2 years).

## Results

Age and BMI at IP and AR were not identifiable in 5.4% and 7.8% of the children, respectively. These groups of children showed a significantly higher BMI growth during infancy and childhood. In the remaining sample, BMI at IP correlated almost perfectly ( $r \ge 0.99$ ) with BMI at ages 0.5, 1 and 1.5 years whereas BMI at AR correlated perfectly with BMI at ages 4 to 6 ( $r \ge 0.98$ ). In the total study group, BMI values in infancy and childhood were positively associated with later BMI z-scores where associations increased with age. Associations between BMI velocities and later BMI z-scores were largest at ages 5 and 6. Results differed for children with non-identifiable IP and AR demonstrating a selection effect.

## Conclusions

IP and AR may not be estimable in children with higher-than-average BMI growth. Excluding these children from analyses may result in a selection bias that distorts effect estimates. BMI values at age 1 and age 5 might be more appropriate to use as predictors for later weight status instead.

Word count: 300/300

#### 1 Introduction

The obesity epidemic is of growing concern, especially in children<sup>1, 2</sup>. Lots of 2 3 research has been conducted to identify early life factors and weight, height or body 4 mass index (BMI) growth characteristics in infancy and childhood related to an unfavorable weight development<sup>3-11</sup>. For instance, a late age at infancy peak (IP), an 5 6 early age at adiposity rebound (AR) as well as BMI at IP and AR were shown to be 7 positively associated with later adiposity status<sup>12-19</sup>. The IP describes the maximum of 8 a BMI growth curve occurring at an age of about 9 months, whereas the AR denotes 9 the nadir at an age of about 6 years that occurs before the BMI curve increases once 10 again. However, the BMI is just a function of weight (kg) divided by height (m) 11 squared such that the minimum and maximum of a BMI trajectory may not have a 12 biological meaning. From a public health perspective, the usefulness of these 13 measures has also been guestioned because age and BMI (in the following: 14 age/BMI) at infancy peak and adiposity rebound can only be determined retrospectively. Hence, the potential use for intervention purposes is limited. Dietz 15 suggested the AR to be mainly an epiphenomenon<sup>20</sup>. As discussed by Cole<sup>13</sup>, early 16 17 AR may be a risk factor for later obesity only as it identifies children whose BMI centile is high and/or crossing upwards. Also rapid growth<sup>3</sup> and catch-up growth<sup>21</sup> 18 19 predict later obesity status and may be strongly related to age/BMI at IP and AR. 20 These measures provide more direct indicators of later obesity risk and amongst 21 others biological programming of obesity during fetal and early postnatal life has been suggested as an underlying mechanism<sup>21-24</sup>. 22

BMI growth characteristics are typically determined based on growth curve modeling
because approaches based on visual inspection are not feasible in large cohort
studies with a limited number of repeated BMI measurements<sup>25, 26</sup>. Fractional

26 polynomial multi-level models (FPMLM) provide a flexible tool for this purpose as 27 these models can handle unbalanced data, i.e. a varying number of measurements per individual at irregular time points, under a missing at random assumption<sup>26, 27</sup>. 28 29 The improvement of multi-level models over conventional general linear regression for estimating growth curves has been demonstrated by Johnson et al.<sup>28</sup>. 30 31 However, there is an additional problem with the use of the IP and AR as exposures. 32 The IP and AR are not always identifiable, e.g. as observed by Wen et al.: "this 33 occurs when the individual-specific curves lack a local maximum (infancy peak) or minimum (adiposity rebound)"<sup>26</sup>. Typically, children with non-identifiable IP or AR are 34 35 excluded from the subsequent analysis. But not observing a minimum or maximum 36 could be a result of a BMI trajectory that is continuously increasing during infancy 37 and childhood. This might especially be likely in overweight/obese children. Exclusion 38 of children with non-identifiable IP or AR could thus result in under-representation of 39 overweight children, a bias that may also affect effect estimates of later disease risk. 40 The present study aims to investigate the usefulness of the IP and AR in comparison 41 to other measures of BMI growth as indicators of later weight status. For the first 42 time, the selection effect possibly occurring when excluding children with nonidentifiable IP or AR will be explored. For this purpose, associations between various 43 44 BMI growth measures and later weight status will be estimated based on a sample of 45 European children from a multi-center cohort study.

46

#### 47 Subjects and methods

48 Description of the study population

49 The IDEFICS (Identification and Prevention of Dietary- and Lifestyle-Induced Health

50 Effects in Children and Infants) cohort is a multi-center population-based study

51 aiming to investigate the causes of diet- and lifestyle-related diseases in 2.0 to 9.9 52 year old children. The baseline survey (T0) was conducted from September 2007 to 53 May 2008 in eight European countries (Belgium, Cyprus, Estonia, Germany, 54 Hungary, Italy, Sweden, Spain) where 16 228 children participated. Children were 55 approached via schools and kindergartens to facilitate equal enrolment of all social 56 groups. The survey included interviews with parents concerning lifestyle habits and 57 dietary intakes as well as anthropometric measurements and examinations of the 58 children. All measurements were taken using standardized procedures in all eight countries. Details on the design and objectives of the study can be found in Ahrens et 59 al.<sup>29-31</sup>. A first follow-up examination (T1) was conducted in 2009/2010 applying the 60 61 same standardized assessments where 13 596 children aged 4.0-11.9 years were 62 enrolled (2 555 newcomers; 11 041 children who participated already in T0). A 63 second follow-up examination (T3<sup>\*</sup>; I.Family) took place in 2013/2014 during which 7 64 105 out of the children already participating at T0 or T1 were examined. 65 Parents and children aged 12 years and over gave written informed consent while 66 younger children gave oral consent prior to the examinations. Each study center 67 obtained ethical approval by the local institutional review board.

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69

#### 70 Anthropometric measurements

71 Height [cm] of the children was measured to the nearest 0.1 cm with a calibrated

72 stadiometer (Seca 225 stadiometer, Birmingham, UK), body weight [kg] was

73 measured in fasting state in light underwear on a calibrated scale accurate to 0.1 kg

74 (adapted Tanita BC 420 MA for children ≤6 years, BC 418 MA for children >6 years,

<sup>&</sup>lt;sup>\*</sup> In 2010/2011, an additional postal survey was conducted (T2). As no physical examinations took place, the T2 data are not considered here.

Tanita Europe GmbH, Sindelfingen, Germany). BMI was calculated as weight [kg] 75 76 divided by height [m] squared. The BMI at last follow-up examination was converted 77 to an age- and sex-specific z-score using the extended criteria of the International Obesity Task Force (IOTF)<sup>32</sup>. Apart from the heights and weights measured at the 78 79 T0, T1 and T3, additional height/weight measurements from records of routine child 80 visits or registry data (part of birth data in Sweden) were collected in Belgium, 81 Cyprus, Germany, Hungary, Italy, Spain and Sweden and linked to the survey data 82 (up to 33 measurements per child). Information was supplemented by parentally 83 reported birth weights and lengths (questionnaire data) if measurements of birth 84 length/weight were missing in the records of routine child visits. Good repeatability 85 was previously shown for maternally reported birth characteristics and pregnancyrelated events in IDEFICS<sup>33</sup>. Good agreement was also observed between measured 86 87 and reported birth lengths and weights (unpublished data). 88 89 Analysis dataset 90 The flow chart in Fig 1 visualizes the numbers of height and weight measurements 91 available from the different sources and summarizes the exclusion process leading to 92 the final analysis dataset. 93 (Please insert Fig 1 here) 94

Because data from records of routine child visits were not available from Estonia,
only seven countries were included in the analysis. In total, 75 787 height/weight
measurements of 14 509 children were available with numbers of measurements as
well as time points of measurements varying among children. As described in detail
elsewhere<sup>34</sup>, duplicate observations (30 obs), implausible height/weight
measurements or combinations (4 131 obs), heights decreasing by more than 20%

101 (38 obs) as well as weights decreasing by more than 50% (14 obs) over time were 102 excluded. To achieve sufficient model stability, only measurements in the age interval 103 from 0 to 8 years were considered as well as only children with a minimum of four 104 repeated measurements (45 417 observations of 5 026 children). To account for 105 collinearity of measurements taken closely in time, a minimum time lag of 1 month 106 (for measurements taken below 6 months of age), 2 months (measurements between 107 6 months to 1.5 years) or 3 months (measurements > 1.5 years), respectively, was 108 imposed by random deletion of 6 353 measurements taken closer in time. Other 109 inclusion criteria were that for each child at least one measurement should lie in the 110 potential age range of the IP (>0.25 to  $\leq$ 4 years) and of the AR (>2.5 to  $\leq$ 8 years), 111 and that information on birth term (pre-term vs. in time) was available. The final 112 analysis group consisted of 4 744 children with 37 998 height and weight 113 measurements. The average number of repeated measurements per child was 8 114 (median: 8, interguartile range: 6-9); numbers of BMI measurements by age group 115 and sex are given in Table S1 as supplementary material. Comparing the final 116 analysis sample with the original IDEFICS cohort, distributions of sex and weight 117 status were almost identical.

118

#### 119 Statistical analysis

Growth trajectories were modelled using fractional polynomial multi-level models with two levels (measurement occasion and individual) allowing individuals to have different intercepts and age-effects, i.e. their own trajectory<sup>27</sup>. As described previously<sup>34</sup>, in a first step all fractional polynomials with up to three powers of age out of the following powers (-2, -1, -0.5, log, square root, 1, 2, 3) were estimated to identify the best-fitting model for BMI growth. As age must be strictly positive when using fractional polynomials<sup>35</sup>, this was achieved by adding a constant of 0.001 to

age at birth. The best-fitting fractional polynomial according to both, the Bayesian
information criterion (BIC; value: 108709) as well as the Akaike information criterion
(AIC; value: 108576), reads as follows:

 $BMI_{i,j} = (\beta_0 + u_{i,0} + \varepsilon_{i,j}) + (\beta_1 + u_{i,1})age_{i,j}^1 + (\beta_2 + u_{i,2})age_{i,j}^2 + (\beta_3 + u_{i,3})\log(age_{i,j})$ 130 where  $\beta_0, \beta_1, \beta_2, \beta_3$  denote the fixed intercept and slopes,  $u_{i,0}, u_{i,1}, u_{i,2}, u_{i,3}$  denote the
131 random intercept and slopes and  $\varepsilon_{i,j}$  denotes the error term with *i*=1,...*n* and *j*=1,...*n<sub>i</sub>*132 (*n*: number of subjects; *n<sub>i</sub>*: number of measurements of subject *i*).

birth term (born in time vs. pre-term) including respective interactions with the age
terms, as well as for measured vs. reported BMI at birth to adjust for differential
measurement error.

Using SAS PROC MIXED the BMI growth model was estimated adjusting for sex and

137 Based on the estimated individual BMI trajectories, 29 measures of BMI growth were

138 derived as described in Wen et al.<sup>26</sup>: age at IP and AR, BMI at IP and AR, BMI values

139 and growth velocities (kg/m<sup>2</sup>/year) at defined ages (0.5, 0.75, 1, 1.5, 2, 3, 4, 5, 6, 7

140 and 8 years) and cumulated BMI growth measures (area under the curve (AUC):

141 birth to 2 years, birth to 5 years, birth to 8 years).

133

Applying the classifications most commonly used in previous studies, age at IP was categorized into 'Early: age at IP < 8 months', 'Medium: 8 months  $\leq$  age at IP < 1.0 years', 'Late: age at IP  $\geq$  1.0 years' and 'Not estimable'. Analogously, age at AR was categorized as 'Early: age at AR < 5 years', 'Medium: 5  $\leq$  age at AR < 7 years', 'Late:

146 age at IP  $\geq$  7 years' and 'Not estimable'.

For each IP and AR category, pairwise Pearson correlation coefficients between the derived BMI growth measures were calculated. In addition, associations between the BMI growth measures and later BMI z-score (last available BMI measurement; mean age: 9.2 years) were estimated using linear regression models adjusting for sex and

151 study center. For this purpose, the BMI growth measures were standardized to allow 152 direct comparability of the effect estimates. All models were estimated for the whole 153 study group, for children with non-estimable vs. estimable IP as well as for children 154 with non-estimable vs. estimable AR to assess possible differences in effect 155 estimates between these groups, i.e. to assess a potential selection effect when 156 ignoring children with non-identifiable IP or AR. Effect estimates were compared 157 based on (non-)overlapping 95% confidence intervals.

All analyses were performed using SAS® statistical software version 9.3 (SAS
Institute, Inc., Cary, NC).

160

#### 161 **Results**

162 The average age at IP was 0.9 and age at AR 5.2 years. The IP or AR were not 163 identifiable in 5.4% (N=257) and 7.8% (N=371) of the children, respectively. Table 1 164 displays distributions of sex, weight status at last follow-up and birth term (born in 165 time vs. pre-term) by IP and AR categories (early, medium, late, not estimable). As 166 expected, percentages of overweight/obese children were higher in the groups of 167 children with late IP (30.6%) and early AR (33.0%) compared to children in the other 168 IP and AR categories and compared to the total study group (18.2%). Even more of 169 the children with non-estimable IP or AR, 76.2% and 55.2%, respectively, were 170 classified as overweight/obese. 171 From an age of 1.5 years onwards, BMI values of children with non-estimable IP and

172 AR were significantly higher than average BMI values in the total group (see Table 2

and Figure 2). Also BMI growth velocities were higher at all ages in the groups of

174 children with non-estimable IP and AR compared to the total study group.

As displayed in Table 3, BMI at IP showed almost perfect correlation with BMI values at ages 0.5, 1, and 1.5 years and very high correlations (r>0.9) with BMI up to age 3. BMI at AR showed the highest correlation with BMI at age 5 (r=0.99) and very high correlations with BMI at ages 3 to 7 (r>0.9). Both, BMI at IP and AR were most strongly correlated with BMI growth velocities in early infancy. Age and BMI at AR were also strongly positively correlated with the AUC measures; correlations of age and BMI at IP with the AUC were moderate to low.

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- 183

#### (Please insert Fig 2 here)

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185 Table 4 presents the results of the regression models relating the standardized BMI 186 growth measures to later BMI z-scores for children with estimable vs. non-estimable 187 IP and AR as well as for the total study group. For children with estimable IP or AR, 188 in addition associations between standardized BMI/age at IP/AR and later BMI z-189 score are displayed. At all ages and in all subgroups, standardized BMI values, 190 velocities and the AUC measures were positively associated with later BMI z-score. 191 With regard to BMI values, associations increased from infancy to childhood and 192 were largest for BMI at age 7 and 8. BMI velocities at age 5 and 6 showed the 193 strongest association with later BMI z-score; in children with non-estimable IP or AR 194 associations were stronger at younger ages. For AUC measures, associations were 195 largest when accumulating BMI values from birth to 8 years in all groups. Later BMI 196 z-score was similarly associated with (a) BMI at IP and BMI at age 1, and (b) BMI at 197 AR and BMI at age 3 and 4 years. Effect estimates for BMI values, velocities and 198 AUC measures with later BMI z-score were in general markedly smaller in the group 199 of children with non-estimable IP compared to the total study group. From an age of

5 years onwards, associations between BMI values in childhood and later BMI zscore were significantly higher in children with identifiable IP and AR compared to the total study group demonstrating a distortion of effect estimates caused by a selection effect. In general, later BMI z-score in children with an identifiable IP was significantly smaller (1.54 SD) compared to children with non-identifiable IP. Analogously, later BMI z-score in children with an identifiable AR was significantly smaller (0.86 SD) compared to children with a non-identifiable AR.

207

#### 208 Discussion

209 This is the first study documenting the selection effect that occurs – as is usually 210 done – if children with non-identifiable IP or AR are excluded when estimating 211 associations of age and BMI at IP/AR with later weight status. In this context, the 212 usefulness of age and BMI at IP and AR in comparison to other BMI growth 213 measures as predictors for later weight status has also been evaluated. Consistent with the literature<sup>15-18, 20</sup>, in the present study age and BMI at IP as well as 214 215 BMI at AR were found to be positively associated and age at AR was negatively 216 associated with later BMI z-score. In our sample, age/BMI at IP and AR were not 217 identifiable in 5.4% and 7.8% of the children respectively, which is in line with 218 previous studies that reported numbers of up to 17% of non-identifiable peak values<sup>15, 26, 36</sup>. Our results revealed that both groups markedly differ from the overall 219 220 study population with regard not only to later weight status but also BMI development 221 during infancy and childhood. The observed differences in effect estimates 222 comparing children with identifiable/non-identifiable IP/AR further suggest that 223 associations between age/BMI at IP/AR and later weight status reported in previous 224 studies may be biased due to the exclusion of children with non-identifiable IP/AR.

225 BMI at IP and AR correlated almost perfectly with BMI values at certain ages. The 226 effect sizes of associations with later BMI z-score were also similar when using BMI 227 values at fixed ages instead of BMI at IP or AR. This is in line with other studies that 228 reported e.g. BMI at AR not to provide additional information in predicting adult weight status if the BMI at age 7 years (or 8 years) was known<sup>37</sup>. Hof et al.<sup>15</sup> found 229 230 that BMI at age 9 months showed a similar association with body composition at 5 to 231 6 years as does the BMI at IP. A late IP or early AR may thus be just an indicator of 232 children with higher-than average BMI values and/or higher-than-average BMI velocities<sup>13</sup>. BMI values at fixed ages provide more direct measures of later weight 233 234 status and can be obtained in all children, i.e. their use avoids selection effects due 235 to non-identifiability. Also for pediatricians who monitor children's growth it may be 236 easier to identify children with higher-than-average BMI values (as typically 237 determined based on percentile curves) than children with late IP or early AR or 238 children that do not show an IP or AR.

239 When assessing associations between different BMI growth measures and later 240 weight status, the use of non-standardized (raw) BMI measures may be problematic 241 as effect estimates cannot be directly compared between exposures with different 242 units, mean values and standard deviations. For example, raw BMI values are 243 typically lowest from approximately age 3 to 6 years (time period of AR) such that a 244 one unit increase in this period can be expected to show a higher effect estimate 245 compared to BMI values at other ages when using raw values. The use of 246 standardized exposure measures solved this problem. Consequently, estimation of 247 associations using raw BMI growth measures led to somewhat differing results (see 248 Table S2 in the supplementary material): For instance, the largest association for the 249 raw BMI values with later weight status was observed at 4 years in the total study 250 group with effect estimates being similar at 3 and 5 years whereas associations

between standardized BMI values with later weight status increased with age and
were largest for BMI values at 7 and 8 years. Analogously, the raw AUC from birth to
2 years but the standardized AUC from birth to 8 years showed the largest
associations with later weight status.

255 As associations with later weight status were stronger for BMI values at older ages 256 compared to BMI at IP or AR, our results do not support the conclusion that the IP or 257 AR are critical periods for later weight status as discussed earlier<sup>13, 20, 38</sup>. Growth 258 velocities were most predictive for later weight status at ages 5 and 6 which 259 corresponds to the period of school entry that is typically accompanied by lifestyle changes including reduced physical activity<sup>39, 40</sup>. Furthermore, observing the highest 260 261 effect estimate for the AUC covering the largest time span, i.e. the from birth to 8 262 years, is in line with the accumulation of risk model (which is the notion that life 263 course exposures may lead to cumulative damage as the severity, duration, and number of exposures increases)<sup>41, 42</sup>. 264

265 Estimation of age and BMI at IP and AR is likely to depend on the numbers of 266 repeated BMI measurements available, on the sample size as well as on the 267 approach chosen for determining the IP and AR. Multi-level models offer several advantages over other growth modeling techniques<sup>25, 27, 28, 36, 43</sup>. However, there are 268 269 various choices of more complex multi-level models compared to our model (like 270 higher degree fractional polynomials or penalized spline models with random 271 coefficients). But also these models face the problem of non-identifiability of the IP or 272 AR in certain children as has been reported e.g. using higher-order fractional polynomial models in Wen et al.<sup>26</sup> as well as applying the penalized spline approach 273 for identification of age/BMI at IP<sup>18</sup>. In line with our study, Silverwood et al.<sup>18</sup> 274

275 mentioned as a main reason for subjects not having an identified BMI peak that their276 BMI observations continued to increase over the first few years of life.

277 As the number of BMI measurements strongly differed between children in our 278 sample (range: 4 up to 22 measurements), sensitivity analyses were conducted to 279 check whether the number of available BMI measurements per child affects 280 identifiability of the IP and AR. Comparing children with identifiable vs. non-281 identifiable IP and AR, mean numbers of available BMI measurements per child were 282 almost equal. Also when limiting our dataset to children with at least 6 or at least 8 283 repeated measurements, respectively, the percentage of children with non-284 identifiable IP and AR remained almost unchanged compared to the full analysis 285 group. Numbers of available measurements and corresponding inclusion criteria strongly differ between studies ranging from  $3^{15}$  up to  $\ge 18^{26}$  available BMI 286 287 measurements per child. Nevertheless, also the latter study reported the problem of 288 non-identifiable IP and AR. As a guidance, Cole suggested to have at least three BMI measurements spread over several years to identify the AR<sup>13</sup>. 289

290

#### 291 Limitations and strengths

292 As discussed above, the choice of the growth modeling approach may affect the 293 estimation of the BMI trajectory and hence of the IP and AR. In large epidemiological 294 studies with few repeated measurements, multi-level models offer a powerful tool for 295 growth modeling and enable handling of unbalanced data under a missing at random 296 assumption. This assumption is less strict compared to the missing completely at 297 random assumption that is e.g. required for complete cases analyses. In our sample, 298 the assumption seemed justified as missing BMI values may mainly result from the 299 differing schedules of the routine child visits in the single countries. However, it has

300 to be acknowledged that the assumption cannot be proven formally. Deriving 301 exposure measures based on trajectories and then relating the derived exposures to a certain outcome is commonly referred to as two-step approach<sup>44</sup>. In the present 302 303 analysis, the uncertainty in the estimates of the exposures derived in step one has 304 not been taken into account which is certainly a limitation. However, this limitation 305 applies to all of the derived exposures and models and is hence unlikely to alter our 306 conclusions. Furthermore, our regression models were adjusted only for sex and 307 study center. The main purpose of the models was to derive comparable effect 308 estimates and to illustrate a potential selection effect when excluding children with 309 non-identifiable IP or AR but not to assess fully adjusted effect estimates for the 310 single exposures. As (time-varying) confounders like physical activity or diet differ 311 depending on the age at exposure assessment (e.g. energy intake at 5 years may be 312 related to subsequent but not previous BMI values), consideration of further 313 confounders would have limited comparability of effect estimates and also reduced 314 the size of the analysis sample (due to incomplete covariate information). 315 Our mean age at outcome assessment was 9.2 years, different results may be 316 observed for other ages at outcome assessment limiting also the comparability 317 between studies. 318 To our knowledge, this is the first study that discusses a potential selection effect that

320 age/BMI at IP or AR to a later health outcome. We hope that we were able to raise
321 the awareness of researchers for potential selection effects and would like to
322 encourage researchers to carefully check subgroups of children being excluded.

may result from the exclusion of children with non-identifiable IP or AR when relating

323

319

#### 324 Conclusions

325 Associations between BMI growth characteristics in infancy and childhood and later 326 BMI z-scores were largest for the most recent BMI values whereas BMI growth 327 velocities at 5 and 6 years showed the strongest associations. Age and BMI at IP and 328 AR may not be estimable in children with markedly higher-than-average BMI growth. 329 Excluding these children from subsequent analyses may thus result in a selection 330 bias. BMI values at age 1 and 5 years perfectly correlated with BMI at IP and AR, 331 respectively, are easier to interpret and might hence be more appropriate predictors 332 for later weight status or disease risk.

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335 Supplementary information is available at International Journal of Obesity's website
336 (supplementary material file S1 including Table S1 and Table S2).

## Acknowledgement

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#### **Contributor's statement**

Each author has seen and approved the contents of the submitted manuscript. All authors contributed to conception and design, acquisition of data, analysis or interpretation of data. Final approval of the version published was given by all the authors. All the authors revised the article critically for important intellectual content.

#### **Ethics statement**

We certify that all applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research, and that the IDEFICS/I.Family projects passed the Ethics Review process of the Sixth Framework Programme (FP6) and Seventh Framework Programme (FP7) of the European Commission. Ethical approval was obtained from the relevant local or national ethics committees by each of the eight study centers, namely from the Ethics Committee of the University Hospital Ghent (Belgium), the National Bioethics Committee of Cyprus (Cyprus), the Tallinn Medical Research Ethics Committee of the National Institutes for Health Development (Estonia), the Ethics Committee of the University Bremen (Germany), the Scientific and Research Ethics Committee of the Medical Research Council Budapest (Hungary), the Ethics Committee of the Health Office Avellino (Italy), the Ethics Committee for Clinical Research of Aragon (Spain), and the Regional Ethics Review Board of Gothenburg (Sweden). All children aged 12 years or older and parents or legal guardians of younger children gave written informed consent to data collection, examinations, collection of samples, subsequent analysis and storage of personal data and collected samples. Additionally, children younger than 12 years child gave oral consent after being orally informed about the modules by a study nurse immediately before every examination using a simplified text. The oral consenting process was not further documented, but it was subject to central

and local training and quality control procedures of the study. Study participants and their parents/legal guardians could consent to single components of the study while abstaining from others. All procedures were approved by the above-mentioned Ethics Committees.

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Figure 1: Data flow chart describing the exclusion process leading to the final analysis sample

**Figure 2:** Mean estimated BMI values at selected ages in children with early, medium, late or non-estimable infancy peak (top) and early, medium, late or non-estimable adiposity rebound (buttom)





	Age at infancy peak (mean: 0.9 years)									Age at adiposity rebound (mean: 5.2 years)								
	Not est	Not estimable		mths	8 mths-<	8 mths-< 1.0 yr		≥ 1.0 yr		imable	<5 yrs		5-<7 yrs		≥ 7 yrs		A	11
	N	%	Ν	%	Ν	%	Ν	%	N	%	Ν	%	Ν	%	Ν	%	N	%
Sex	-		-	-			-	-			-	-	-	-	-	-		
Boys	154	59.9	177	37.2	1 490	50.5	639	60.2	221	59.6	931	57.2	1 247	48.2	61	38.6	2 460	51.9
Girls	103	40.1	299	62.8	1 460	49.5	422	39.8	150	40.4	697	42.8	1 340	51.8	97	61.4	2 284	48.1
Weight status at last follow-up*																		
Thin	3	1.2	151	31.7	292	9.9	26	2.5	33	8.9	37	2.3	354	13.7	48	30.4	472	9.9
Normal weight	58	22.6	299	62.8	2 339	79.3	710	66.9	133	35.8	1 054	64.7	2 111	81.6	108	68.4	3406	71.8
Overweight	99	38.5	25	5.3	289	9.8	262	24.7	107	28.8	452	27.8	114	4.4	2	1.3	675	14.2
Obese	97	37.7	1	0.2	30	1.0	63	5.9	98	26.4	85	5.2	8	0.3	-	-	191	4.0
Birth term																		
Born in time	192	74.7	387	81.3	1 938	65.7	668	63.0	277	74.7	1 050	64.5	1 749	67.6	109	69.0	3 185	67.1
Pre-term birth	65	25.3	89	18.7	1 012	34.3	393	37.0	94	25.3	578	35.5	838	32.4	49	31.0	1 559	32.9
All	257	5.4	476	10.0	2 950	62.2	1 061	22.4	371	7.8	1 628	34.3	2 587	54.5	158	3.3	4 744	100

**Table 1:** Description of the study population: Distributions of sex, weight status at last available follow-up measurement (mean age: 9.2 years) and birth term (< vs.  $\geq$  37<sup>th</sup> gestational week) by categories of the infancy peak and adiposity rebound (mths=months, yrs=years)

\*BMI classification according to Cole & Lobstein<sup>32</sup> Percentages may not add up to 100% due to rounding.

	Age at infancy peak (mean: 0.9 years)									Age at adiposity rebound (mean: 5.2 years)																	
	Not	t estima	able	<	8 mont	hs	8 mon	ths-< 1	.0 year	· ≥ 1.0 year		Not	estima	able		<5 yea	ars		5-<7	years	rs ≥7 yea		ars		All		
	Mean	LCL	UCL	Mean	LCL	UCL	Mean	LCL	UCL	Mean	LCL	UCL	Mean	LCL	UCL	Mean	LCL	UCL	Mean	LCL	UCL	Mean	LCL	UCL	Mean	LCL	UCL
BMI at age		-	-	-	-	-	-	-	-	-	-	-		-	-	-	-	-	-	-	-	-	-	-			-
0.5	16.5	16.3	16.7	16.4	16.3	16.5	16.8	16.8	16.9	16.7	16.7	16.8	16.5	16.3	16.6	16.6	16.5	16.7	16.9	16.8	16.9	16.9	16.7	17.0	16.7	16.7	16.8
0.75	16.8	16.6	16.9	16.4	16.3	16.5	16.9	16.9	17.0	16.9	16.8	17.0	16.7	16.6	16.8	16.7	16.7	16.8	16.9	16.9	17.0	17.0	16.8	17.2	16.9	16.8	16.9
1	16.9	16.8	17.1	16.3	16.2	16.4	16.9	16.8	16.9	17.0	16.9	17.1	16.8	16.7	17.0	16.7	16.7	16.8	16.9	16.9	17.0	17.0	16.8	17.2	16.9	16.8	16.9
1.5	17.1	17.0	17.3	16.0	15.9	16.0	16.7	16.7	16.7	17.0	16.9	17.1	17.0	16.8	17.1	16.6	16.6	16.7	16.7	16.7	16.8	16.8	16.7	17.0	16.7	16.7	16.7
2	17.3	17.1	17.5	15.6	15.5	15.7	16.4	16.4	16.5	16.9	16.8	17.0	17.0	16.9	17.2	16.5	16.4	16.5	16.4	16.4	16.5	16.6	16.4	16.7	16.5	16.5	16.5
3	17.6	17.4	17.8	14.9	14.9	15.0	15.9	15.9	16.0	16.7	16.6	16.7	17.1	16.9	17.3	16.2	16.1	16.2	15.9	15.8	15.9	16.0	15.9	16.2	16.1	16.0	16.1
4	17.9	17.7	18.2	14.5	14.4	14.5	15.6	15.5	15.6	16.5	16.5	16.6	17.3	17.1	17.5	16.0	16.0	16.1	15.4	15.4	15.5	15.5	15.3	15.7	15.8	15.8	15.8
5	18.5	18.2	18.7	14.2	14.2	14.3	15.4	15.3	15.4	16.5	16.4	16.6	17.5	17.3	17.8	16.1	16.0	16.2	15.2	15.2	15.2	15.1	14.9	15.3	15.7	15.6	15.7
6	19.2	18.9	19.4	14.3	14.2	14.4	15.4	15.4	15.5	16.7	16.6	16.8	17.9	17.7	18.2	16.4	16.3	16.5	15.1	15.1	15.2	14.8	14.6	15.0	15.8	15.7	15.8
7	20.1	19.8	20.4	14.6	14.5	14.7	15.7	15.6	15.7	17.0	16.9	17.1	18.5	18.2	18.8	17.0	16.9	17.0	15.3	15.3	15.4	14.7	14.5	14.9	16.1	16.1	16.2
8	21.1	20.8	21.5	15.2	15.1	15.3	16.2	16.2	16.3	17.6	17.5	17.7	19.2	18.8	19.6	17.8	17.7	17.9	15.7	15.7	15.8	14.7	14.5	14.9	16.7	16.6	16.7
Velocity (kg/m²/year) at		-	-	-	-	-	-	-	-	-	-	-		-	-	-	-	-	-	-	-	-	-	-		-	-
age	1 4	1 1	1 5	0.2	0.2	0.2	0.0	0.0	0.0	10	1 1	10	1 0	1 0	1 1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
0.5	1.4	1.4	1.5	0.3	0.3	0.3	0.0	0.0	0.0	1.2	0.5	1.2	1.3	1.3	1.4	0.9	0.9	0.9	0.0	0.0	0.0	0.9	0.0	0.9	0.9	0.0	0.9
0.75	0.0	0.0	0.9	-0.5	-0.3	-0.5	0.1	0.1	0.1	0.5	0.5	0.5	0.7	0.0	0.7	0.2	0.2	0.2	0.1	0.1	0.1	0.2	0.1	0.2	0.2	0.2	0.2
1.5	0.5	0.5	0.0	-0.5	-0.0	-0.5	-0.2	-0.2	-0.2	0.1	0.1	0.1	0.4	0.4	0.4	-0.1	-0.1	-0.1	-0.5	-0.5	-0.2	-0.2	-0.2	-0.1	-0.1	-0.1	-0.1
1.5	0.3	0.3	0.4	-0.7	-0.7	-0.7	-0.5	-0.5	-0.5	-0.1	-0.1	-0.1	0.2	0.1	0.2	-0.3	-0.3	-0.3	-0.5	-0.5	-0.5	-0.4	-0.5	-0.4	-0.4	-0.4	-0.4
2	0.3	0.2	0.3	-0.7	-0.6	-0.6	-0.5	-0.5	-0.5	-0.2	-0.2	-0.2	0.1	0.0	0.1	-0.3	-0.3	-0.3	-0.0	-0.0	-0.0	-0.5	-0.0	-0.5	-0.4	-0.4	-0.4
3	0.0	0.0	0.5	-0.0	-0.0	-0.0	-0.3	-0.3	-0.3	-0.2	-0.2	-0.2	0.1	0.1	0.1	0.2	-0.2	0.2	-0.5	-0.0	-0.3	-0.5	-0.0	-0.5	-0.7	-0.4	-0.4
	0.4	0.4	0.0	-0.4	-0.4	-0.0	-0.0	-0.0	-0.0	0.1	0.1	0.1	0.2	0.2	0.2	0.0	0.1	0.0	-0.4	-0.4	-0.0	-0.3	-0.5	-0.4	0.2	0.2	0.2
6	0.8	0.7	0.8	0.1	0.1	0.2	0.1	0.1	0.1	0.3	0.1	0.3	0.5	0.0	0.5	0.4	0.4	0.4	0.2	0.1	0.1	-0.2	-0.2	-0.2	0.0	0.0	0.0
7	1.0	0.9	1.0	0.5	0.4	0.5	0.4	0.4	0.4	0.4	0.4	0.5	0.6	0.6	0.7	0.7	0.7	0.7	0.3	0.3	0.3	-0.1	-0.1	0.0	0.4	0.4	0.5
8	1.2	1.1	1.3	0.8	0.7	0.8	0.6	0.6	0.7	0.6	0.6	0.7	0.8	0.7	0.9	1.0	0.9	1.0	0.5	0.5	0.5	0.1	0.1	0.1	0.7	0.7	0.7
AUC																											
0.01 to 2 yrs	33.2	32.9	33.6	31.9	31.8	32.1	33.0	33.0	33.1	33.2	33.1	33.4	33.0	32.8	33.3	32.8	32.7	32.9	33.1	33.0	33.2	33.2	32.9	33.6	33.0	32.9	33.1
0.01 to 5 yrs	86.6	85.7	87.6	76.2	75.8	76.6	80.4	80.2	80.6	83.1	82.8	83.5	84.7	83.9	85.5	81.3	81.0	81.6	80.2	80.0	80.4	80.6	79.8	81.3	80.9	80.8	81.1
0.01 to 8 yrs	145.7	143.9	147.5	119.7	119.1	120.3	127.3	127.0	127.5	133.9	133.3	134.5	139.5	137.8	141.1	131.5	131.1	132.0	126.1	125.8	126.4	124.9	123.7	126.2	129.0	128.7	129.3
Age at last follow-up	9.1	8.8	9.5	9.3	9.1	9.6	9.2	9.1	9.3	9.2	9.0	9.4	9.3	9.0	9.6	9.0	8.9	9.2	9.2	9.1	9.3	9.9	9.6	10.3	9.2	9.1	9.3
BMI z-score at last follow-up	1.9	1.8	2.0	-0.5	-0.6	-0.4	0.1	0.1	0.1	0.8	0.7	0.8	1.2	1.0	1.3	0.8	0.8	0.9	-0.1	-0.1	-0.1	-0.6	-0.7	-0.5	0.3	0.3	0.3

**Table 2:** Estimated BMI values and BMI velocities (kg/m<sup>2</sup>/year) at selected ages, AUC measures as well as mean age and BMI at last follow-up in children with early, medium and late infancy peak or adiposity rebound as well as for children with non-estimable infancy peak or adiposity rebound and for the total study group AUC: area under the BMI growth curve, LCL: lower 95% confidence interval, UCL: upper 95% confidence interval

	Age	e at IP	BM	ll at IP	Age	at AR	BMI at AR			
BMI at age	r	p-value	r	p-value	r	p-value	r	p-value		
0.5	0.03	0.075	1.00	<.0001	0.11	<.0001	0.71	<.0001		
0.75	0.08	<.0001	1.00	<.0001	0.09	<.0001	0.74	<.0001		
1	0.13	<.0001	1.00	<.0001	0.07	<.0001	0.77	<.0001		
1.5	0.22	<.0001	0.99	<.0001	0.03	0.0427	0.82	<.0001		
2	0.30	<.0001	0.97	<.0001	-0.02	0.2009	0.87	<.0001		
3	0.43	<.0001	0.91	<.0001	-0.14	<.0001	0.94	<.0001		
4	0.52	<.0001	0.84	<.0001	-0.28	<.0001	0.98	<.0001		
5	0.55	<.0001	0.75	<.0001	-0.42	<.0001	0.99	<.0001		
6	0.54	<.0001	0.68	<.0001	-0.54	<.0001	0.98	<.0001		
7	0.48	<.0001	0.61	<.0001	-0.64	<.0001	0.94	<.0001		
8	0.40	<.0001	0.56	<.0001	-0.71	<.0001	0.88	<.0001		
Velocity at age										
0.5	0.69	<.0001	0.58	<.0001	-0.13	<.0001	0.75	<.0001		
0.75	0.87	<.0001	0.28	<.0001	-0.27	<.0001	0.70	<.0001		
1	0.89	<.0001	0.03	0.0349	-0.35	<.0001	0.58	<.0001		
1.5	0.82	<.0001	-0.20	<.0001	-0.45	<.0001	0.43	<.0001		
2	0.75	<.0001	-0.29	<.0001	-0.54	<.0001	0.38	<.0001		
3	0.64	<.0001	-0.31	<.0001	-0.72	<.0001	0.38	<.0001		
4	0.47	<.0001	-0.23	<.0001	-0.87	<.0001	0.41	<.0001		
5	0.28	<.0001	-0.10	<.0001	-0.93	<.0001	0.43	<.0001		
6	0.11	<.0001	0.03	0.0896	-0.90	<.0001	0.41	<.0001		
7	-0.01	0.464	0.12	<.0001	-0.83	<.0001	0.39	<.0001		
8	-0.09	<.0001	0.18	<.0001	-0.77	<.0001	0.36	<.0001		
AUC										
0.01 to 2 years	0.13	<.0001	0.06	<.0001	1.00	<.0001	0.77	<.0001		
0.01 to 5 years	0.35	<.0001	-0.11	<.0001	0.95	<.0001	0.91	<.0001		
0.01 to 8 years	0.44	<.0001	-0.34	<.0001	0.85	<.0001	0.97	<.0001		

**Table 3:** Pearson correlations between estimated ages and BMI at infancy peak (IP) and adiposity rebound (AR) with estimated BMI values and BMI velocities at selected ages and areas under the curve (AUC); only children with estimable age/BMI at IP (N=4 487) and AR (N=4 373) were considered, respectively (p-values are added for exploratory purposes, only)

	IP no	not estimable			IP estimable			ot estir	nable	AR	estima	ble			
	β	LCL	UCL	β	LCL	UCL	β	LCL	UCL	β	LCL	UCL	β	LCL	UCL
BMI z-score at age (years)															
0.5	0.42	0.34	0.50	0.49	0.46	0.51	0.48	0.36	0.59	0.48	0.46	0.51	0.47	0.44	0.50
0.75	0.42	0.34	0.50	0.50	0.48	0.53	0.50	0.39	0.62	0.50	0.48	0.53	0.50	0.47	0.52
1	0.42	0.34	0.50	0.52	0.50	0.55	0.53	0.42	0.64	0.52	0.49	0.55	0.52	0.50	0.55
1.5	0.42	0.34	0.49	0.56	0.54	0.59	0.58	0.48	0.68	0.56	0.54	0.59	0.58	0.55	0.60
2	0.42	0.35	0.49	0.60	0.58	0.63	0.63	0.54	0.72	0.61	0.58	0.63	0.63	0.61	0.65
3	0.43	0.37	0.50	0.70	0.67	0.72	0.70	0.63	0.78	0.70	0.68	0.73	0.72	0.69	0.74
4	0.46	0.40	0.52	0.80	0.77	0.82	0.75	0.68	0.81	0.80	0.78	0.82	0.78	0.76	0.80
5	0.49	0.43	0.55	0.89	0.87	0.91	0.76	0.70	0.81	0.89	0.86	0.91	0.83	0.81	0.84
6	0.51	0.45	0.57	0.95	0.93	0.97	0.74	0.70	0.79	0.95	0.92	0.97	0.85	0.84	0.87
7	0.52	0.46	0.58	0.98	0.96	1.00	0.72	0.68	0.76	0.97	0.95	0.99	0.87	0.85	0.88
8	0.51	0.45	0.57	0.96	0.94	0.98	0.69	0.65	0.73	0.97	0.94	0.99	0.86	0.85	0.88
BMI velocity z-score at age (years)															
0.5	0.36	0.28	0.43	0.52	0.49	0.55	0.59	0.50	0.68	0.54	0.52	0.57	0.57	0.54	0.59
0.75	0.37	0.29	0.46	0.53	0.49	0.56	0.69	0.60	0.78	0.56	0.53	0.60	0.56	0.54	0.59
1	0.39	0.29	0.48	0.47	0.43	0.5	0.75	0.66	0.84	0.51	0.47	0.54	0.52	0.49	0.55
1.5	0.41	0.30	0.52	0.39	0.36	0.43	0.79	0.71	0.88	0.42	0.39	0.46	0.47	0.44	0.50
2	0.45	0.33	0.57	0.40	0.37	0.44	0.79	0.71	0.88	0.42	0.39	0.46	0.48	0.45	0.51
3	0.53	0.42	0.64	0.53	0.49	0.56	0.70	0.63	0.78	0.53	0.50	0.57	0.55	0.53	0.58
4	0.51	0.42	0.60	0.66	0.63	0.69	0.66	0.60	0.71	0.66	0.63	0.70	0.64	0.61	0.66
5	0.44	0.36	0.52	0.70	0.67	0.73	0.60	0.55	0.65	0.72	0.69	0.75	0.68	0.65	0.70
6	0.39	0.32	0.47	0.67	0.64	0.69	0.57	0.52	0.62	0.70	0.67	0.73	0.67	0.65	0.69
7	0.36	0.29	0.43	0.62	0.59	0.64	0.56	0.51	0.61	0.65	0.62	0.68	0.64	0.61	0.66
8	0.34	0.27	0.41	0.57	0.55	0.60	0.56	0.50	0.61	0.61	0.58	0.63	0.60	0.57	0.62
AUC: 0.01 to 2 years (z-score)	0.42	0.34	0.50	0.53	0.50	0.56	0.55	0.44	0.65	0.53	0.50	0.55	0.53	0.51	0.56
AUC: 0.01 to 5 years (z-score)	0.44	0.37	0.51	0.67	0.65	0.70	0.70	0.62	0.78	0.67	0.65	0.70	0.70	0.68	0.72
AUC: 0.01 to 8 years (z-score)	0.48	0.42	0.54	0.83	0.81	0.85	0.75	0.70	0.81	0.83	0.81	0.85	0.81	0.79	0.83
BMI z-score at IP/AR <sup>§</sup>				0.51	0.48	0.53				0.75	0.73	0.77			
Age z-score at IP/AR <sup>§</sup>				0.36	0.33	0.39				-0.55	-0.58	-0.53			
IP estimable vs. non-estimable <sup>#</sup>													-1.54	-1.67	-1.42
AR estimable vs. non-estimable <sup>#</sup>													-0.86	-0.96	-0.75

**Table 4:** Effect estimates and 95% confidence intervals for the associations of standardized BMI values and velocities at selected ages, AUC measures and ages/BMI at IP and AR with BMI z-score at last follow-up in groups of children with (non)estimable infancy peak and adiposity rebound as well as for the total study group. All models were adjusted for sex and study center.

<sup>§</sup>The estimated age and BMI at infancy peak was related to later BMI z-score in the group of children with calculable infancy peak; the age and BMI at adiposity was related to later BMI z-score in the group of children with calculable adiposity rebound

<sup>#</sup>Dummy variables indicating whether the infancy peak or adiposity rebound were identifiable were related to later BMI z-score AUC: area under the BMI growth curve LCL: lower 95% confidence interval UCL: upper 95% confidence interval

	Boys				Girls		All				
	Ν	Mean	SD	Ν	Mean	SD	Ν	Mean	SD		
0 to <0.5 years	6070	3.6	1.4	5058	3.5	1.3	11128	3.5	1.4		
0.5 to <1 year	2298	3.4	1.2	2454	3.4	1.2	4752	3.4	1.2		
1 to <2 years	3359	3.5	1.1	3103	3.5	1.0	6462	3.5	1.1		
2 to <3 years	1670	2.1	1.1	1520	2.0	1.1	3190	2.1	1.1		
3 to <4 years	1031	2.5	1.1	965	2.4	1.1	1996	2.5	1.1		
4 to <5 years	1645	2.6	1.0	1475	2.7	1.0	3120	2.7	1.0		
5 to <6 years	1714	2.5	1.1	1700	2.5	1.1	3414	2.5	1.1		
6 to <7 years	973	1.7	1.1	869	1.7	1.0	1842	1.7	1.1		
7 to ≤8 years	1089	1.7	1.0	1005	1.6	1.0	2094	1.7	1.0		
All	19849			18149			37998				

**Table S1:** Total number of BMI measurements and mean number of BMI measurements per child in the analysis group by age category and sexSD: Standard deviation

	IP not estimable			IP	estima	ble	AR no	ot estir	nable	AR	estima	ble			
	β	LCL	UCL	β	LCL	UCL	β	LCL	UCL	β	LCL	UCL	β	LCL	UCL
BMI at age															
0.5	0.38	0.31	0.46	0.44	0.42	0.46	0.43	0.33	0.54	0.44	0.41	0.46	0.42	0.40	0.45
0.75	0.37	0.30	0.44	0.44	0.42	0.47	0.44	0.35	0.54	0.44	0.42	0.46	0.44	0.41	0.46
1	0.37	0.30	0.43	0.46	0.43	0.48	0.46	0.37	0.56	0.45	0.43	0.48	0.46	0.43	0.48
1.5	0.36	0.30	0.43	0.49	0.46	0.51	0.50	0.42	0.59	0.49	0.46	0.51	0.50	0.48	0.52
2	0.36	0.30	0.42	0.52	0.50	0.54	0.54	0.46	0.62	0.52	0.50	0.54	0.54	0.52	0.56
3	0.36	0.30	0.41	0.58	0.56	0.60	0.58	0.52	0.65	0.58	0.56	0.60	0.59	0.58	0.61
4	0.35	0.30	0.40	0.61	0.60	0.63	0.57	0.53	0.62	0.62	0.60	0.63	0.60	0.58	0.62
5	0.34	0.30	0.38	0.62	0.60	0.63	0.53	0.49	0.56	0.61	0.60	0.63	0.57	0.56	0.59
6	0.31	0.28	0.35	0.58	0.57	0.60	0.46	0.43	0.49	0.58	0.57	0.59	0.52	0.51	0.54
7	0.28	0.25	0.31	0.52	0.51	0.54	0.39	0.36	0.41	0.52	0.51	0.53	0.47	0.46	0.47
8	0.24	0.21	0.26	0.45	0.44	0.46	0.32	0.30	0.34	0.45	0.44	0.46	0.40	0.39	0.41
BMI velocity at age															
0.5	0.91	0.72	1.10	1.34	1.27	1.41	1.51	1.28	1.74	1.39	1.32	1.47	1.45	1.39	1.52
0.75	1.21	0.93	1.48	1.71	1.61	1.81	2.24	1.96	2.52	1.83	1.73	1.94	1.83	1.74	1.91
1	1.32	0.99	1.65	1.59	1.48	1.71	2.57	2.27	2.87	1.73	1.61	1.85	1.77	1.68	1.86
1.5	1.42	1.03	1.81	1.37	1.25	1.49	2.76	2.45	3.06	1.47	1.35	1.59	1.64	1.54	1.73
2	1.60	1.18	2.01	1.43	1.30	1.55	2.82	2.53	3.10	1.50	1.37	1.62	1.69	1.60	1.79
3	1.97	1.56	2.38	1.97	1.84	2.10	2.76	2.52	3.01	1.99	1.86	2.12	2.07	1.97	2.17
4	1.94	1.59	2.29	2.51	2.39	2.64	2.50	2.29	2.71	2.53	2.40	2.65	2.42	2.33	2.52
5	1.60	1.31	1.89	2.52	2.42	2.63	2.15	1.97	2.33	2.59	2.48	2.70	2.44	2.35	2.52
6	1.25	1.01	1.49	2.13	2.04	2.22	1.82	1.66	1.98	2.23	2.13	2.32	2.14	2.06	2.22
7	0.99	0.79	1.19	1.70	1.62	1.77	1.54	1.39	1.68	1.79	1.71	1.87	1.75	1.69	1.82
8	0.80	0.63	0.97	1.35	1.29	1.41	1.31	1.18	1.44	1.43	1.36	1.49	1.41	1.35	1.47
AUC: 0.01 to 2 years	0.19	0.16	0.23	0.24	0.23	0.26	0.25	0.20	0.30	0.24	0.23	0.26	0.25	0.23	0.26
AUC: 0.01 to 5 years	0.08	0.07	0.09	0.12	0.11	0.12	0.12	0.11	0.14	0.12	0.11	0.12	0.12	0.12	0.13
AUC: 0.01 to 8 years	0.05	0.04	0.05	0.08	0.08	0.08	0.07	0.07	0.08	0.08	0.08	0.08	0.08	0.08	0.08
BMI at IP/AR <sup>§</sup>				0.45	0.43	0.47				0.62	0.61	0.64			_
Age at IP/AR <sup>§</sup>				1.42	1.31	1.52				-0.55	-0.58	-0.53			
IP estimable vs. non-estimable <sup>#</sup>													-1.54	-1.67	-1.42
AR estimable vs. non-estimable <sup>#</sup>													-0.86	-0.96	-0.75

**Table S2:** Effect estimates and 95% confidence intervals for the associations of raw BMI values and velocities (kg/m<sup>2</sup>/year) at selected ages, AUC measures and ages/BMI at IP and AR with later BMI z-score in groups of children with (non)estimable infancy peak and adiposity rebound as well as for the total study group. All models were adjusted for sex and study center.

<sup>§</sup>The estimated age and BMI at infancy peak was related to later BMI z-score in the group of children with calculable infancy peak; the age and BMI at adiposity was related to later BMI z-score in the group of children with calculable adiposity rebound

<sup>#</sup>Dummy variables indicating whether the infancy peak or adiposity rebound were identifiable were related to later BMI z-score AUC: area under the BMI growth curve LCL: lower 95% confidence interval UCL: upper 95% confidence interval