Maternal and infant prediction of the child BMI trajectories; studies across two generations of Northern Finland birth cohorts

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Abstract:

Background/objective: Children BMI is a longitudinal phenotype, developing through interplays between genetic and environmental factors. Whilst childhood obesity is escalating, we require a better understanding of its early origins and variation across generations to prevent it.

Subjects/Methods: We designed a cross-cohort study including 12,040 Finnish children from the Northern Finland Birth Cohorts 1966 and 1986 (NFBC1966 and NFBC1986) born before or at the start of the obesity epidemic. We used group-based trajectory modelling to identify BMI trajectories from 2 to 20 years. We subsequently tested their associations with early determinants (mother and child) and the possible difference between generations, adjusted for relevant biological and socioeconomic confounders.

Results: We identified four BMI trajectories, 'stable-low' (34.8%), 'normal' (44.0%), 'stable-high' (17.5%) and 'early-increase' (3.7%). The 'early-increase' trajectory represented the highest risk for obesity. We analysed a dose-response association of maternal pre-pregnancy BMI and smoking with BMI trajectories. The directions of effect were consistent across generations and the effect sizes tended to increase from earlier generation to later. Respectively for NFBC1966 and NFBC1986, the adjusted risk ratios of being in the early-increase group were 1.08 (1.06-1.10) and 1.12 (1.09-1.15) per unit of pre-pregnancy BMI and 1.44 (1.05-1.96) and 1.48 (1.17-1.87) in offspring of smoking mothers compared to non-smokers. We observed similar relations with infant factors including birthweight for gestational age and peak weight velocity. In contrast, the age at adiposity peak in infancy was associated with the BMI trajectories in NFBC1966 but did not replicate in NFBC1986.

Conclusion: Exposures to adverse maternal predictors were associated with a higher risk obesity trajectory and were consistent across generations. However, we found a discordant association for the timing of adiposity peak over a 20-year period. This suggest the role of residual environmental factors, such as nutrition, and warrants additional research to understand the underlying gene-environment interplay.

Key words: Epidemiology, life-course, BMI trajectories, adiposity peak, obesity

INTRODUCTION

In 2016, the World Health Organisation (WHO) reported a global prevalence of 41 million children under the age of five and 340 million between 5 and 19 years old with overweight or obesity [1]. Over the last four decades, obesity in the latter age category has increased tenfold [2]. Obesity, including during childhood, is currently being explained by interplays between a polygenetic build-up [3,4] and interrelated environmental risk factors acting upon body composition (epidemiologically proxied from BMI). Whilst the polygenetic structure has remained stable over the last four decades, including in the population studied in the current research [5], we are observing major changes in the set of environmental risk factors affecting the risk of obesity, with growing evidence to support the role of the environment in the early years of life. At the population level, BMI and changes in BMI during childhood are therefore highly heterogeneous and different paths to obesity may coexist throughout the life-course, some of them starting very early and influencing child's growth patterns [6-8].

So far, a vast majority of studies have considered childhood BMI from a cross-sectional manner without accounting for the longitudinal effect such as changes over time. Various analytical strategies have been proposed to study child BMI development. Conventional growth modelling methods assume that a single growth trajectory approximates the entire population and that covariates influence each individual in the same manner [9]. However, these models cannot account for the heterogeneity of BMI development over longer periods [10,11]. In contrast, in growth mixture models (GMM), the attention is put on relationships among individuals and the longitudinal characteristics of the measures. They assume that the population is made of latent groups, sharing the same pattern over time. GMM is a flexible modelling approach that can provide quantitative insights in the longitudinal aspect of BMI changes throughout the life course.

Previous longitudinal studies have described multiple BMI trajectories defined from latent growth trajectory analysis supporting more than one BMI trajectories in childhood [12-15]. As to whether early biological and/or psychosocial factors, classically associated with the child BMI [16], influenced each BMI trajectory in a comparative manner and whether the strength of such association is affected from one generation to another remains a debatable area of research. In the current study, we hypothesized that maternal and early childhood factors are determinants of the BMI trajectory a child embarks. We further hypothesized that the strength (*i.e.* effect size) of the associations linking a risk factor to the child BMI trajectory could be modified from one generation to another. Testing such hypotheses might help identify potential shared and generation specific risk factors and further advance the understanding of child BMI development.

To study the association of early risk factors with childhood BMI trajectories and its evolution over time, we performed a BMI trajectory analysis in two birth cohorts about one generation apart, using GBTM (Group Based Trajectory Modelling) in SAS PROC TRAJ [10]. Importantly, we studied the Northern Finland Birth Cohort

(NFBC)1966, pre-dating the obesity epidemic and the NFBC1986, born 20 years later, with prospective recruitment at the start of the obesity epidemic in Finland. While consistent evidence supports replicability of effects of early life factors on the child BMI and the risk of obesity [17], we may anticipate important generational effects depending on contextual differences in terms of feeding and nurturing practices and changes in the environmental exposures.

METHODS

Study population

The study was based on the two Northern Finland Birth Cohorts initiated 20 years apart from the same region (the two northernmost provinces of Finland: Oulu and Lapland) and founder population. NFBC1966 recruited pregnant women with a due date between the 1st of January and the 31st of December 1966 (12 055 mothers, 12 231 babies, 96.3% of all births from this period in the region). NFBC1986 included pregnant women with an expected delivery date between 1st of July 1985 and 30th of June 1986 (9362 mothers, 9479 babies, 99% of all births from this period in the region). A total of 12 058 and 9432 babies were born alive in the NFBC1966 and 1986 respectively.

Data collection of the child BMI measures

The mothers entered the study around the 16th gestational week for NBC1966 and the 10th to 12th gestational weeks for NFBC1986. Pregnant mothers were followed throughout pregnancy. Children's height and weight measures were collected by linking data from questionnaires, Health and Welfare records, clinical examination and national registers. Briefly, in Finland, a child welfare nurse checks up on infants every month during the first few months and then once a year, usually around their birthday. When they start school at seven years of age, the school nurse takes over the yearly check-ups. Children's measurements data were completed by self-reported measurements at 14 years for NFBC1966 and 7-8 years for NFBC1986. At 16 years old, NFBC1986 members were invited to a clinical examination with a trained nurse.

Exclusion criteria

We excluded preterm babies (<37 gestational weeks) and multiple births (N=2 199) (Supplementary Figure S1). We calculated BMI (kg/m^2) from height and weight. It is recommended and customary to use weight-for-length rather than BMI to measure growth during the first two years of life [18]. Therefore, we chose to model BMI in 16 age-windows, one per year from two to 16.9 years-old and, due to the scarcity of the data in late adolescence, the last group comprised ages from 17 to 20. Individuals with less than three repeated BMI measurements, required for model stability, were excluded (N=7 159 altogether in NFBCs). Attrition in the data could be due either to non-attendance to check-ups or to non-retrieved or lost records. There were

117 little differences between the children included from the model and those excluded: the mothers of the
118 excluded children were more often single and less educated than the mothers of the included children
119 (Supplementary table S1).

120 The study comprised 12 040 individuals (51.9% male), 6864 from NFBC1966 (53.7% male) and 5176 from
121 NFBC1986 (49.4% male).

122 **Maternal data**

123 In the pregnancy questionnaire, mothers were asked to report their pre-pregnancy weight. The
124 corresponding BMI was calculated using height measurement from the first prenatal visit. Maternal
125 education was categorised as elementary, vocational or secondary, matriculation level, matriculation and
126 beyond. Maternal smoking status at eight weeks of pregnancy was categorized as smokers and no smokers
127 and their marital status as married or cohabitating, single, widowed or divorced.

128 **Infant and child data**

129 The first rise in the BMI curve called adiposity peak (AP), around nine months of age and the nadir of the
130 curve called adiposity rebound (AR) around six years were obtained from random effects models fitted from
131 0 to 18 months and from 18 months to 13 years as described elsewhere [19]. The peak height velocity (PHV)
132 and peak weight velocity (PWV) in infancy were derived from parametric growth curves [20,21]. These methods
133 are developed in the supplementary materials. Gestational age at birth was calculated from the mother's last
134 menstrual period in NFBC1966, and ultrasound in priority before the last menstrual period in NFBC1986.
135 Birthweight was adjusted for gestational age, sex and cohort. BMI measures were sex and cohort
136 standardized, for each age-windows as described previously [3,4]. Briefly, the z-scores were calculated
137 internally, derived from NFBC1966 and NFBC1986, comprising respectively 96% and 99% of all children born
138 in the north of Finland at the time.

139 **Statistical analysis**

140 **Developmental Growth trajectories**

141 We used GBTM from the PROC TRAJ procedure in SAS software, based on Nagin's approach to group-based
142 modelling [22], to determine BMI growth trajectories. This approach consists in fitting a mixture of parametric
143 models to the data, using the maximum likelihood method, handling missing data under the missing at
144 random assumption. PROC TRAJ fits longitudinal data to discern rather than assume two or more distinctive
145 trajectories or latent groups of individuals and estimate their prevalence in the population. Group-based
146 trajectory modelling has been successfully applied to BMI in large cohort studies [13,14,23].

147 We used PROC TRAJ with BMI modelled as censored normal to identify subgroups which share a similar BMI
148 growth from two to 20 years in both cohorts modelled together. We started by fitting a quartic polynomial

to the models, increasing one by one the number of groups up to 7. The first step of the modelling consisted in choosing the optimal model. Bayesian Information Criterions (BIC) values are compared and the model with the smallest absolute value is chosen. The second step consisted in determining the shape of each trajectory by identifying the best polynomial order. Model adequacy was evaluated by calculating the average posterior probabilities of belonging to each group, they should be at least 0.7 with the closest to 1 reflecting the best discrimination between groups. We also calculated the Odds of Correct Classification, they should be over 5, and sought for a close correspondence between the estimated and actual percentages for each group and a reasonably tight confidence intervals of each trajectory [10]. A group should represent at least 1% of the population [9]. Parsimony and a priori knowledge of the topic combined with an evaluation of the graphical shape of the trajectories should be taken into account.

Descriptive and association analysis

All analyses were performed using SAS software 9.4 (SAS Institute Inc, Cary, North Carolina). Characteristics of participants were presented as frequencies for categorical variables and means and SD for continuous variables. We used non-parametric tests for comparisons between groups and χ^2 test for categorical variables. Multivariate models were applied to calculate risk ratios (RR) and their 95% confidence intervals in associations between maternal, infancy and childhood predictors and BMI trajectories, trajectory two being the reference. The confounders for the models were selected according to existing literature and previous analyses [19]. We tested three models for the maternal parameters: unadjusted, adjusted for maternal education and adjusted for parity, maternal education, maternal age and smoking (Fig. 2a)/pre-pregnancy BMI (Fig. 2b). Birthweight was not included in model 2a-b as it might be in the causal pathway between prenatal factors and the BMI trajectories. For birthweight, we tested three models: unadjusted, adjusted for pre-pregnancy BMI and adjusted for parity, pre-pregnancy BMI, maternal age, maternal education, smoking. For childhood predictors, we tested four models: unadjusted, adjusted for birthweight z-scores, adjusted for pre-pregnancy BMI and the last model adjusted for parity, pre-pregnancy BMI, maternal age, maternal education, smoking and birthweight z-scores.

RESULTS

Characteristics of the study population

On average, mothers enrolled in the NFBC1986 cohort were 3 cm taller, 2 months younger and had a 0.9 BMI smaller in comparison to NFBC1966 mothers (Supplementary Table S2). In addition, they also had fewer children, were more often smoker and better educated. Furthermore, offspring born to the NFBC1986 mothers were 86 grams heavier, had a 3.7% increase in PHV and a 2.3% decrease in PWV compared to their

NFBC1966 counterparts. They were also younger at the time of AP by 3.6 weeks and AR by 7.7 months suggesting distinct early growth patterns.

BMI trajectories

In an exploratory analysis, we modelled the trajectories separately by cohort (Supplementary Fig. S2 and table S3). To compare the cohort effect, we modelled the pooled cohorts, controlling for sex in the modelling process. The model converged well using the default starting values (codes in Supplementary material). During the modelling of the trajectories, we could not identify the best number of trajectories based on the Bayesian Index Criterion (BIC), i.e. BIC continued decreasing through all seven tested models. In this situation Nagin advised to use more subjective criteria [10]. Between the visual analysis of the trajectory graphs, the objective of the study and the knowledge of the other goodness of fit criteria (Supplementary Fig. S3 and table S4), we were able to identify four trajectories (polynomials 4, 3, 4, 3) as the optimal model for the studied population (Fig. 1). The trajectories were named according to their position in the graph (low to high) as 1: 'stable-low' (34.8% of total population, 34.4% of NFBC1966 and 35.4% of NFBC1986), 2: 'normal' (44.0%, 44.9% of NFBC1966 and 42.9% of NFBC1986), 3: 'stable-high' (17.5%, 13.3% of NFBC1966 and 17.7% of NFBC1986), 4: 'early-increase' (3.7%, 3.4% of NFBC1966 and 4.0% of NFBC1986). We observed that, compared to the other trajectories, the early-increase trajectory started already at a higher point, with a steeper curve. The cohort and sex prevalence per group are presented in Supplementary table S5.

In both cohorts, from trajectory one to four, we observed a stepwise increase in pre-pregnancy BMI and smoking during pregnancy (Table 1). The effect was consistent between cohorts both in terms of direction and magnitude. Parity and maternal marital status were associated to trajectories in a stepwise manner in NFBC1966 only. We also noted a decrease in the proportion of non-instrumental vaginal deliveries from group one to four in both cohorts.

The early life determinants followed the same stepwise pattern described earlier (Table 2). Birthweight was on average higher in NFBC1986 for each group trajectory and increased gradually by 245 and 270g between trajectory one to four in NFBC1966 and NFBC1986 respectively. We observed the same trend in PHV with higher PHV in NFBC1986 and an increase of 1.1 cm/year from group one to four in NFBC1966 only. PWV increased by 2.13 and 1.99 kg/year, for NFBC1966 and NFBC1986 respectively. At AP, we observed a stepwise increase in BMI between trajectory one and four, 1.2 and 0.8 kg/m^2 in NFBC1966 and NFBC1986 respectively. Changes in age at AP showed the same trend with only one week increase for NFBC1966. AR occurred earlier in NFBC1986 than in NFBC1966 and we observed a dramatic stepwise decrease of 2.6 and 2.9 years between the low stable and the early increase trajectory for NFBC1966 and NFBC1986 respectively. It is interesting to notice that in trajectory four, BMI at AP and AR are high, above 18 kg/m^2 in both cohorts.

Associations between maternal factors and BMI trajectories

We observed differences between trajectories, showing positive associations of pre-pregnancy BMI and maternal smoking with stable high and early increase trajectories (Fig. 2). In Figure 2a, in the fully adjusted model compared to the normal trajectory, pre-pregnancy BMI was associated to a lower risk of belonging to the stable-low trajectory in both NFBC1966 and NFBC1986. From high-stable to early-increase trajectories, the risk steadily increased up to a RR of 1.08 (95% CI 1.06-1.10) for NFBC1966 and 1.12 (95% CI 1.09-1.15) for NFBC1986. Maternal smoking was associated to a 34% (adjusted-RR (aRR): 1.34, 95% CI 1.14-1.59) and 42% (aRR: 1.42, 95% CI 1.22-1.64) higher risk of being in the high-stable trajectory for NFBC1966 and NFBC1986 respectively (Fig. 2b). The risk increased up to 44% (aRR: 1.44, 95% CI 1.05-1.96) and 48% (aRR: 1.48, 95% CI 1.17-1.87) in the early-increase trajectory for NFBC1966 and NFBC1986 respectively.

Associations between early life factors and BMI trajectories

The association between BW z-score and BMI trajectories (Fig. 3a) showed, in both cohorts, the stepwise pattern described in Fig. 2. A higher BW z-score was associated to a higher risk of belonging to the highest trajectory, with an aRR of 1.18 (95% CI 1.05-1.33) in NFBC1966 and 1.28 (95% CI: 1.12-1.46) in NFBC1986 (Fig. 3a). PWV (Fig. 3b) was associated with a decreased risk of belonging to the low-stable trajectory (aRR: 0.92, 95% CI 0.92-0.93 in NFBC1966 and aRR: 0.89, 95% CI: 0.88-0.90 in NFBC1986). High PWV was associated with an 8% and 7% higher risk of being in the early-increase trajectory, for NFBC1966 and NFBC1986 respectively. Regarding PHV, the pattern was divergent between the cohorts (Fig. 3c). PHV was positively associated with trajectory four (aRR:1.014, 95% CI: 1.002-1.026) in NFBC1966, but no association was found in NFBC1986. The stepwise pattern described earlier was maintained in the association between age at AP and the four trajectories in NFBC1966. The adjusted RR were ranging from 0.989 (95% CI: 0.986-0-991) in the lowest trajectory to 1.015 (95% CI: 1.008-1.022) in the early-increase trajectory (Fig. 3d). However, there was no association in NFBC1986.

DISCUSSION

To our knowledge, this is the first time that BMI latent growth trajectories were modelled in two birth cohorts set 20 years apart. The specific study design relied on using two separate prospective birth cohorts from the same founder population born 20 years apart. Whilst the causal genomic factors affecting BMI development are highly likely to be stable from one generation to another, we have observed important changes in the environmental risk factors associated to BMI development from the mid 60's and mid 80's in Europe. We identified four BMI z-scores trajectories from 2 to 20 years in the combined NFBC studies. Our findings suggested that, in both cohorts, offspring of high pre-pregnancy BMI or smoking mothers had more chances of belonging to the more adverse childhood BMI trajectory. Conversely, children of low pre-pregnancy BMI or non-smoking mothers had better chances in following more favourable trajectories. Our results also

suggested that the child's faster weight and height gains in infancy associated with adverse trajectories in both cohorts. Furthermore, we uncovered that age at AP was associated with every BMI trajectory in NFBC1966, but the association was lost in NFBC1986, suggesting that adiposity measured around 9 months of age might not be a stable determinant of later adiposity during childhood.

Our findings about the association of adverse maternal factors and BMI trajectories were in line with others [15,25]. The age of adiposity rebound decreased in a stepwise manner from group trajectories one to four, consistent with a higher risk of obesity. We observed the same pattern between the two cohorts which suggests that the effect associated to the variation of pre-pregnancy BMI and smoking remained over 20 years. They are important factors to consider in future generations and cohort studies. Interestingly, we observed that the amplitude of the effect differed. Although the average pre-pregnancy BMI was lower in NFBC1986 than in NFBC1966, its effect on the trajectories appeared stronger in the early increase trajectory. The association of birthweight with the trajectories was reflecting the strong link shown with pre-pregnancy BMI, unchanged over a 20-year period. A Danish study showed a stable association between birthweight and childhood overweight across almost 50 years [26], those results were supported by a study comparing both NFBC studies [27]. Infancy peak velocities occurred around the first month of life and were associated with BMI trajectories in both cohorts. Birthweight as an indicator of foetal growth and the peak velocities as indicators of early postnatal growth could be expected to be associated with the trajectories. However, there are still some important areas of debate pertained by mismatched findings between epidemiological observations and the causal inference made by Mendelian randomisation [28,29] or the measures of genetic overlap between these early adiposity phenotypes [30]. The relationship between these early growth phenotypes (BW, PWV and PHV) and the child BMI trajectory from 2 years onwards may still need clarifications as highlighted by our present observations. Possible inter-individuals and -generational differences in childcare and early nutrition may be important sources of moderation of the above relationships. These inter-individual and generational factors might explain the large confidence intervals and differential effect size or the lack of replication as these observed for PHV.

One of the main findings of this study was that the age at AP followed a different pattern of association between the two cohorts with a stepwise association observed between the age at AP and BMI trajectories in NFBC1966 only. The current literature in the field shows contrasting findings. Evidence from Swedish and Dutch birth cohorts supported a positive association between the BMI at adiposity peak and the later risk of obesity [31,32]. However, the generalisation of such association is currently being debated by two recent GWAS supporting distinct molecular factors regulating infant and child BMI [30,33]. Furthermore, in western populations, it was reported that BMI at adiposity peak is getting lower in more contemporary cohorts. This may seem counterintuitive with the increasing prevalence of childhood obesity during the last decades but it aligned with a study based on European cohorts establishing that children from contemporary cohorts had

a lower BMI at two years, a greater BMI growth velocity and earlier age at AR than children from older cohorts [34]. Altogether, these findings warrant a better understanding of the nature of the association linking the BMI of a child in infancy and during childhood to support evidence-based recommendations for parents and health care professionals. The present observation for an inconsistent effect between two generations of birth cohort from the same founder population may allow us to speculate about an indirect (confounded), association between the timing of the adiposity peak and the risk of being in an adverse BMI trajectory.

Although, we are lacking quantitative or qualitative indicators to explain this generational difference in the age at AP and PHV in infancy, it was meaningful, and it might highlight important moderating factors. The Finnish society underwent a massive change between 1966 and 1986, from agricultural to high-tech society. This transformation was accompanied with better pre- and post-natal care, but it also brought convenient energy-dense food affecting both adult and children nutrition. We might speculate that the differences in PHV and AP between cohorts, observed so soon after birth, might be due to early nutrition. Although, breastfeeding data in NFBC was incomplete, when included in the model (data not shown), it did not alter the results. The changes in PHV and AP between the cohorts might also indicate some residual confounding that we were unable to analyse. Historically, breastfeeding in Finland, like in other European countries, decreased from the second World War to its record low in the 1960s and 1970s until it started to increase again [35,36]. Following this trend, it is likely that NFBC1966 infants were less often breastfed than the NFBC1986. Exclusive breastfeeding for five months has been shown to modulate the timing of AP and AR and BMI velocities in Avon Longitudinal Study of Parents And Children study [37]. Exclusive breastfeeding for six months reduced the associations of birthweight and early weight gain on fat mass in three year old children in a Danish cohort [38].

Strengths and limitations

One of the great strengths of this study was the richness of data, we were able to closely follow any variation in childhood BMI through 16 age-windows. Another highly valuable strength resided in the use of two birth cohorts, born before and at the start of the obesity epidemic, originating from the same geographic area of Finland and characterised by a genetically homogeneous population. Nevertheless, limitations should be considered. One limitation of this study would reside in the harmonization of variables between cohorts, such as paternal data, type of infant feeding or maternal weight gain during pregnancy which could not be reciprocated in both cohorts. Due to model requirements, many individuals from both cohorts were excluded. In addition, we should acknowledge that BMI measures the ratio between weight and height. Each of these two measures are susceptible to describe their own trajectories during childhood which might affect the BMI trajectories described in this report. One of the future steps to undertake, to grow our understanding of the biological and environmental mechanisms being at play would be the development of analytical strategy modelling child height and weight trajectory simultaneously.

There are few statistical methods available to model children BMI. Modelling approaches using mixed-effect models, latent curve analysis, hierarchical modelling or growth-curve modelling are offering measures of individual growth profiles against the mean and may provide a health professional with derived phenotypes such as the age at adiposity rebound. In contrast, the GBTM used in this study, is a person-centred data-driven process and assumes that the population is composed of latent groups, they do not assume the one-size-fits-all approach. These subgroups are homogeneous within their trajectory but distinct from other trajectories, each following the same behaviour over time. This latent approach captures more information, especially the longitudinal relationships at the child level but, is specific to the modelled population. Unlike growth models, GBTM are limited in the obtention of distinct phenotypes that could be directly translated as clinical measures. Nonetheless, they seem to present a new set of tools to study individual variation in response to clinical interventions and randomized trials [39].

Conclusion

Our results add new insights to the study of childhood obesity by using two generations of Finnish birth cohorts, initiated before and at the start of the obesity epidemic. In both cohorts, detrimental maternal factors were associated to adverse BMI trajectories, independent of time. However, we were observing a larger amplitude of the effects in the younger cohort suggesting moderation by a more obesogenic environment. Our findings support evidence for very early mechanisms in the first months of life linked to childhood obesity and affected over the course of a generation. Finally, the cross-cohort design exemplified by this research might be a powerful way to detect indirect associations such as the one linking early variation at the time of the adiposity peak and later BMI trajectories. Further research, and methodological development are warranted to identify the intergenerational changes that might help revealing gene-environment interplays.

Data Availability Statement: Data is available from the Northern Finland Birth Cohort (NFBC) for researchers who meet the criteria for accessing confidential data. Please, contact NFBC project center (NFBCprojectcenter@oulu.fi) and visit the cohort website (www.oulu.fi/nfbc) for more information.

Ethical approval: All procedures performed were in accordance with the 1964 Helsinki declaration. The Ethics Committee of the Northern Ostrobothnia Hospital District has approved the NFBC1966 and NFBC1986 studies.

Informed consent: Mothers gave their informed consent in the beginning of the NFBC1966 and 1986 data collections. Written informed consent has been obtained from the cohort participants in the 31- and 46-year data collections.

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Conflict of Interest

The authors, RN, JM, MM, MRJ and SS declare that they have no competing interest.

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462 **LEGENDS**.

463

464 **Table 1**. Characteristic of maternal variables according to the group trajectories. BMI: Body Mass Index.
465 Statistical tests performed between trajectories by cohorts and between cohorts by trajectories.

466 **Table 2**. Characteristics of infancy and childhood variables according to the group trajectories. PHV: Peak
467 Height Velocity, PWV: Peak Weight Velocity, AP: Adiposity Peak, AR: Adiposity Rebound. Statistical tests
468 performed between trajectories by cohorts and between cohorts by trajectories.

469 **Fig. 1**: BMI z-scores trajectories of NFBC studies from 2 to 20 years. Solid lines represent the trajectories and
470 dashed lines the 95% confidence intervals. Group trajectories, 1: Stable-low (34.8%, N=4195), 2: Normal
471 (44.0%, N=5299), 3: Stable-high (17.5%, N=2106) ND 4: Early-increase (3.7%, N=440).

472 **Fig. 2**: Forest-plot of unadjusted and adjusted Risk Ratios (RR) between maternal parameters and BMI z-
473 scores trajectory classes. Fig. 2a: pre-pregnancy BMI (kg/m^2), Fig. 2b: maternal smoking during pregnancy.
474 RR with 95% confidence intervals. ●: unadjusted; ▲: adjusted for maternal education; ■: adjusted for pre-
475 pregnancy BMI (Fig. 2b); ▼: adjusted for parity, maternal age, maternal education, maternal smoking (Fig.
476 2a) / maternal age, parity, maternal education and pre-pregnancy BMI (Fig. 2b). G1: Stable Low group
477 trajectory; G2: Normal group trajectory (reference); G3; Stable high group trajectory; G4; Early Increase group
478 trajectory.

479 **Fig. 3**: Forest-plot of unadjusted and adjusted Risk Ratios (RR) between early growth parameters and BMI z-
480 scores trajectory classes. Fig. 3a: birthweight z-scores, Fig. 3b: peak weight velocity in infancy (kg/year), Fig.
481 3c: peak height velocity in infancy (cm/year), Fig. 3d: age at adiposity peak (years). RR with 95% confidence
482 intervals. ●: unadjusted; ▲: adjusted for birthweight z-score (Fig. 3b, 3c and 3d); ■: adjusted for pre-
483 pregnancy BMI; ▼: adjusted for parity, pre-pregnancy BMI, maternal age, maternal education, maternal
484 smoking (Fig. 3a) / birthweight z-score, parity, pre-pregnancy BMI, maternal age, maternal education,
485 maternal smoking (Fig. 3b, 3c and 3d). G1: Stable Low group trajectory; G2: Normal group trajectory
486 (reference); G3; Stable high group trajectory; G4; Early Increase group trajectory.

Table 1

	Trajectories								
	1: Stable-low		2: Normal		3: Stable-high		4: Early-increase		
	N=4195		N=5299		N=2106		N=440		
	N	mean±SD	N	mean±SD	N	mean±SD	N	mean±SD	***p* value**
Maternal pre-pregnancy weight (kg)									
NFBC1966	2250	57.8 ± 8.2	2933	59.9 ± 8.9	1136	61.4 ± 9.8	223	63.6 ± 10.1	**<0.0001**
NFBC1986	1801	57.2 ± 8.5	2187	59.5 ± 9.1	895	62.4 ± 10.3	201	66.6 ± 14.0	**<0.0001**
***p* value**		**0.0187**		**0.0440**		0.775		0.325	
Maternal pre-pregnancy BMI (kg/m^2)									
NFBC1966	2171	22.5 ± 3.0	2814	23.3 ± 3.2	1091	24.2 ± 3.5	215	25.1 ± 3.8	**<0.0001**
NFBC1986	1795	21.5 ± 3.0	2175	22.3 ± 3.2	891	23.3 ± 3.6	201	25.1 ± 5.1	**<0.0001**
***p* value**		**<0.0001**		**<0.0001**		**<0.0001**		0.295	
Parity									
NFBC1966	2358	3.0 ± 2.2	3078	3.0 ± 2.2	1188	2.8 ± 2.1	234	2.6 ± 2.1	**0.0006**
NFBC1986	1828	1.6 ± 2.0	2212	1.5 ± 1.9	914	1.3 ± 1.7	206	1.4 ± 1.7	0.1
***p* value**		**<0.0001**		**<0.0001**		**<0.0001**		**<0.0001**	
	N	%	N	%	N	%	N	%	***p* value**
Maternal Smoking									
NFBC1966	2321		3008		1167		230		**0.0038**
Smoker	309	13.3	388	12.9	194	16.6	41	17.8	
No smoker	2012	86.7	2620	87.1	973	83.4	189	82.2	
NFBC1986	1827		2208		912		205		**<0.0001**
Smoker	302	16.5	400	18.1	236	25.9	62	30.2	
No smoker	1525	83.5	1808	81.9	676	74.1	143	69.8	
***p* value**		**0.0037**		**<0.0001**		**<0.0001**		**0.0024**	
Maternal marital status									
NFBC1966	2358		3078		1185		234		**0.0419**
Married/Cohabiting	2291	97.1	2995	97.3	1139	96.1	222	94.9	
Single	56	2.4	71	2.3	35	3.0	8	3.4	
Widowed /Divorced	11	0.5	12	0.4	11	0.9	4	1.7	
NFBC1986	1831		2213		917		206		0.13
Married/Cohabiting	1750	95.6	2124	96.0	881	96.1	194	94.2	
Single	56	3.0	73	3.3	32	3.5	8	3.9	
Widowed /Divorced	25	1.4	16	0.7	4	0.4	4	1.9	

***p* value**		**0.0028**		**0.0225**		0.33		0.95	
Operative delivery									
NFBC1966	839		1087		441		97		**0.0009**
Non-instrumental vaginal deliveries	642	76.5	822	75.6	323	73.2	59	60.8	
Caesarian Section	90	10.7	131	12.1	54	12.3	26	26.8	
Others (vacuum extraction, forceps)	107	12.8	134	12.3	64	14.5	12	12.4	
NFBC1986	1834		2218		918		206		**<0.0001**
Non-instrumental vaginal deliveries	1545	84.2	1828	82.4	714	77.8	158	76.7	
Caesarian Section	177	9.7	278	12.5	133	14.5	31	15.1	
Others (vacuum extraction, forceps)	112	6.1	112	5.1	71	7.7	17	8.3	
***p* value**		**<0.0001**		**<0.0001**		**0.0004**		**0.0155**	

Table 2

	Trajectories								
	1 Stable-low		**2 Normal**		**3 Stable-high**		**4 Early-increase**		
	N=4195		**N=5299**		**N=2106**		**N=440**		
	N	**%**	**N**	**%**	**N**	**%**	**N**	**%**	***p* value**
Sex (%male)									
NFBC1966	2361	51.8	3081	56.2	1188	50.6	234	54.7	**0.0010**
NFBC1986	1834	48.7	2218	51.4	918	45.7	206	50.5	**0.0286**
p value		**0.0458**		**0.0005**		**0.0276**		0.38	
	N	**mean±SD**	**N**	**mean±SD**	**N**	**mean±SD**	**N**	**mean±SD**	***p* value**
Birthweight (grams)									
NFBC1966	2361	3450 ± 467	3081	3568 ± 481	1188	3642 ± 520	234	3695 ± 465	**<0.0001**
NFBC1986	1834	3519 ± 440	2218	3662 ± 460	918	3739 ± 479	206	3789 ± 517	**<0.0001**
p value		**0.0001**		**<0.0001**		**<0.0001**		**0.0369**	
Birthweight z-score									
NFBC1966	2361	-0.14 ± 0.94	3081	0.08 ± 0.95	1188	0.25 ± 1.03	234	0.35 ± 0.94	**<0.0001**
NFBC1986	1834	-0.19 ± 0.93	2218	0.10 ± 0.96	918	0.27 ± 1.00	206	0.36 ± 1.11	**<0.0001**
p value		0.063		0.49		0.46		0.93	
PHV in Infancy (cm/year)									
NFBC1966	2081	50.31 ± 3.72	2726	50.67 ± 3.71	1069	50.92 ± 3.90	209	51.41 ± 4.06	**<0.0001**
NFBC1986	1785	52.42 ± 6.72	2150	52.49 ± 6.74	893	52.61 ± 6.83	199	52.28 ± 6.54	0.95
p value		**<0.0001**		**<0.0001**		**<0.0001**		0.2705	
PWV in infancy (kg/year)									
NFBC1966	2145	12.03 ± 1.43	2806	13.07 ± 1.56	1096	13.65 ± 1.89	213	14.16 ± 2.07	**<0.0001**
NFBC1986	1798	11.65 ± 2.39	2167	13.01 ± 2.85	898	13.42 ± 3.05	200	13.64 ± 3.40	**<0.0001**
p value		**<0.0001**		**<0.0001**		**<0.0001**		**0.0029**	
Age AP (years)									
NFBC1966	1817	0.75 ± 0.03	2427	0.76 ± 0.03	959	0.77 ± 0.04	188	0.77 ± 0.04	**<0.0001**
NFBC1986	1753	0.70 ± 0.02	2114	0.69 ± 0.02	882	0.69 ± 0.02	195	0.69 ± 0.02	**<0.0001**
p value		**<0.0001**		**<0.0001**		**<0.0001**		**<0.0001**	
BMI AP (kg/m^2)									
NFBC1966	1817	17.5 ± 0.7	2427	18.1 ± 0.7	959	18.4 ± 0.8	188	18.7 ± 0.9	**<0.0001**
NFBC1986	1753	17.2 ± 0.6	2114	17.7 ± 0.6	882	17.9 ± 0.7	195	18.0 ± 0.8	**<0.0001**

p value		**<0.0001**		**<0.0001**		**<0.0001**		**<0.0001**	
Age AR (years)									
NFBC1966	2323	6.20 ± 0.59	3033	5.67 ± 0.60	1168	4.79 ± 0.71	231	3.59 ± 0.71	**<0.0001**
NFBC1986	1822	5.72 ± 0.72	2197	5.02 ± 0.73	911	3.92 ± 0.71	200	2.83 ± 0.42	**<0.0001**
p value		**<0.0001**		**<0.0001**		**<0.0001**		**<0.0001**	
BMI AR (kg/m^2)									
NFBC1966	2323	14.4 ± 0.5	3033	15.5 ± 0.4	1168	16.6 ± 0.6	231	18.1 ± 1.1	**<0.0001**
NFBC1986	1822	14.6 ± 0.5	2197	15.8 ± 0.4	911	16.95 ± 0.6	200	18.3 ± 1.1	**<0.0001**
p value		**<0.0001**		**<0.0001**		**<0.0001**		**0.0503**	

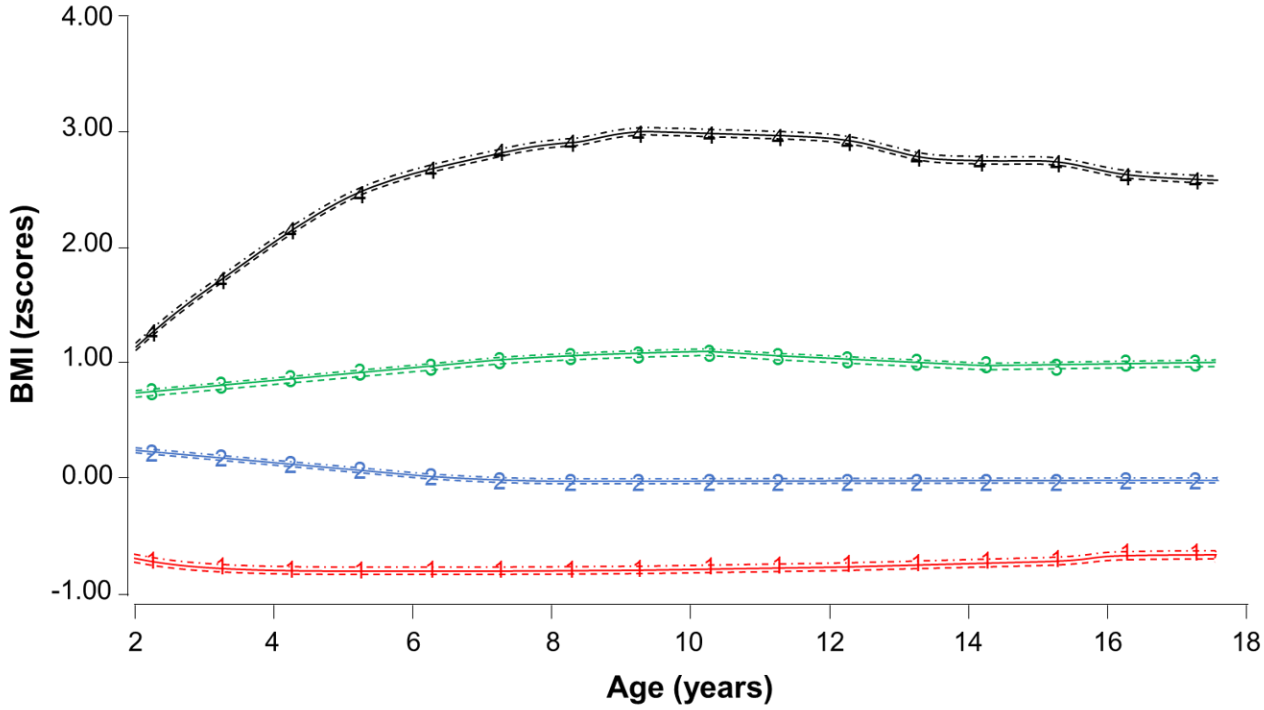

Figure 1

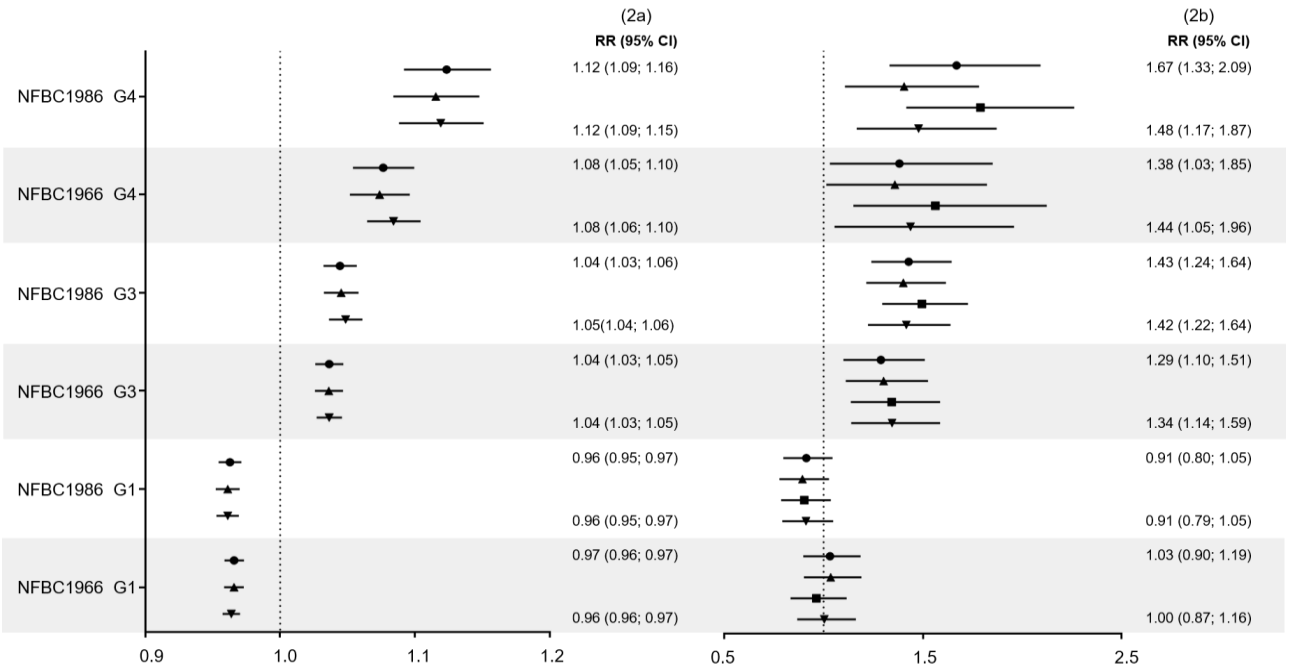
(2a)
RR (95% CI)
(2b)
RR (95% CI)
NFBC1986 G4
1.12 (1.09; 1.16)
1.12 (1.09; 1.15)
1.67 (1.33; 2.09)
1.48 (1.17; 1.87)
NFBC1966 G4
1.08 (1.05; 1.10)
1.08 (1.06; 1.10)
1.38 (1.03; 1.85)
1.44 (1.05; 1.96)
NFBC1986 G3
1.04 (1.03; 1.06)
1.05(1.04; 1.06)
1.43 (1.24; 1.64)
1.42 (1.22; 1.64)
NFBC1966 G3
1.04 (1.03; 1.05)
1.04 (1.03; 1.05)
1.29 (1.10; 1.51)
1.34 (1.14; 1.59)
NFBC1986 G1
0.96 (0.95; 0.97)
0.96 (0.95; 0.97)
0.91 (0.80; 1.05)
0.91 (0.79; 1.05)
NFBC1966 G1
0.97 (0.96; 0.97)
0.96 (0.96; 0.97)
1.03 (0.90; 1.19)
1.00 (0.87; 1.16)
0.9
1.0
1.1
1.2
0.5
1.5
2.5

Figure 2

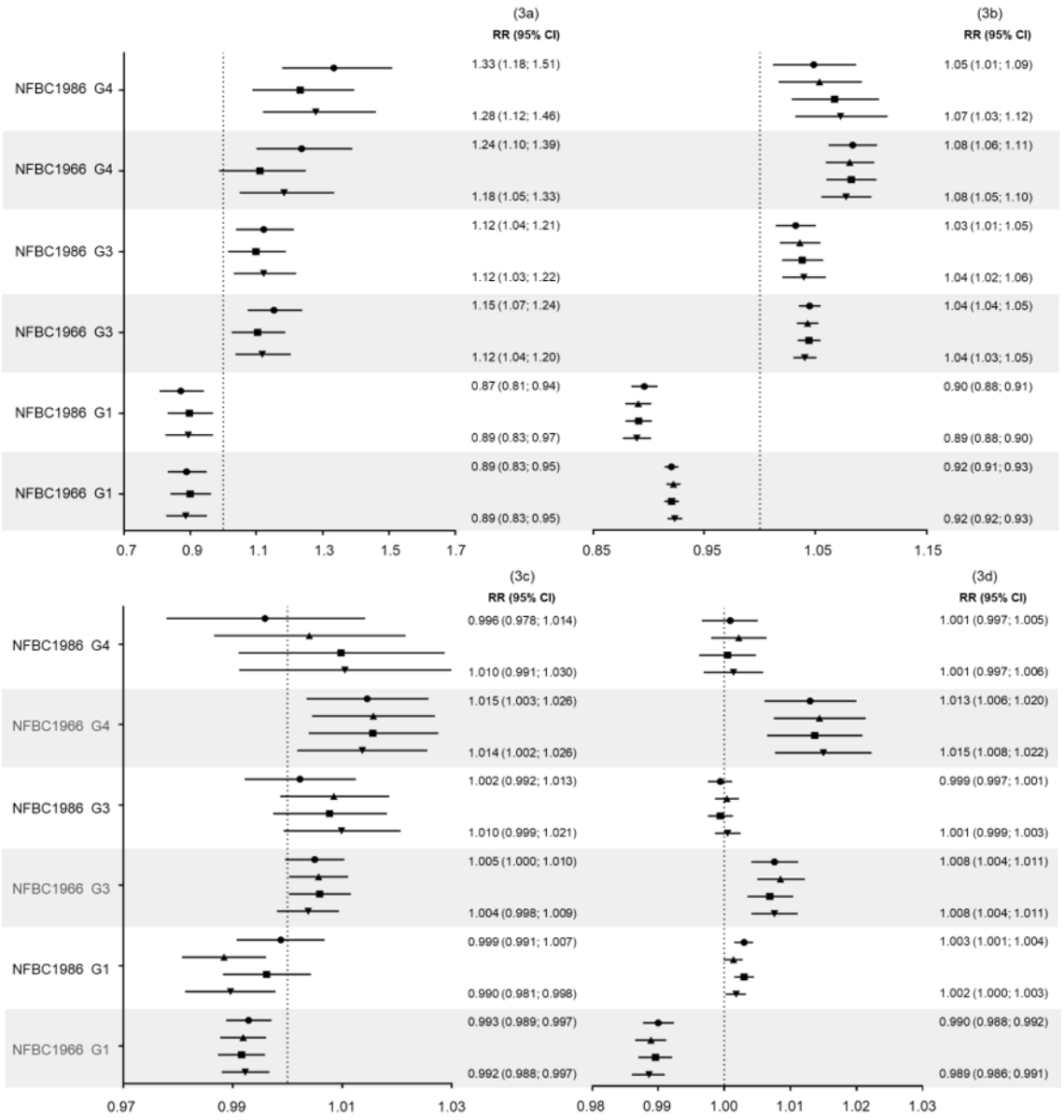
(3a)
RR (95% CI)
NFBC1986 G4
1.33 (1.18; 1.51)
1.28 (1.12; 1.46)
NFBC1966 G4
1.24 (1.10; 1.39)
1.18 (1.05; 1.33)
NFBC1986 G3
1.12 (1.04; 1.21)
1.12 (1.03; 1.22)
NFBC1966 G3
1.15 (1.07; 1.24)
1.12 (1.04; 1.20)
NFBC1986 G1
0.87 (0.81; 0.94)
0.89 (0.83; 0.97)
NFBC1966 G1
0.89 (0.83; 0.95)
0.89 (0.83; 0.95)
0.7
0.9
1.1
1.3
1.5
1.7
(3b)
RR (95% CI)
1.05 (1.01; 1.09)
1.07 (1.03; 1.12)
1.08 (1.06; 1.11)
1.08 (1.05; 1.10)
1.03 (1.01; 1.05)
1.04 (1.02; 1.06)
1.04 (1.04; 1.05)
1.04 (1.03; 1.05)
0.90 (0.88; 0.91)
0.89 (0.88; 0.90)
0.92 (0.91; 0.93)
0.92 (0.92; 0.93)
0.85
0.95
1.05
1.15
(3c)
RR (95% CI)
NFBC1986 G4
0.996 (0.978; 1.014)
1.010 (0.991; 1.030)
NFBC1966 G4
1.015 (1.003; 1.026)
1.014 (1.002; 1.026)
NFBC1986 G3
1.002 (0.992; 1.013)
1.010 (0.999; 1.021)
NFBC1966 G3
1.005 (1.000; 1.010)
1.004 (0.998; 1.009)
NFBC1986 G1
0.999 (0.991; 1.007)
0.990 (0.981; 0.998)
NFBC1966 G1
0.993 (0.989; 0.997)
0.992 (0.988; 0.997)
0.97
0.99
1.01
1.03
(3d)
RR (95% CI)
1.001 (0.997; 1.005)
1.001 (0.997; 1.006)
1.013 (1.006; 1.020)
1.015 (1.008; 1.022)
0.999 (0.997; 1.001)
1.001 (0.999; 1.003)
1.008 (1.004; 1.011)
1.008 (1.004; 1.011)
1.003 (1.001; 1.004)
1.002 (1.000; 1.003)
0.990 (0.988; 0.992)
0.989 (0.986; 0.991)
0.98
0.99
1.00
1.01
1.02
1.03

Figure 3

Supplementary Material

Maternal and infant prediction of the child BMI trajectories; studies across two generations of Northern Finland Birth Cohorts

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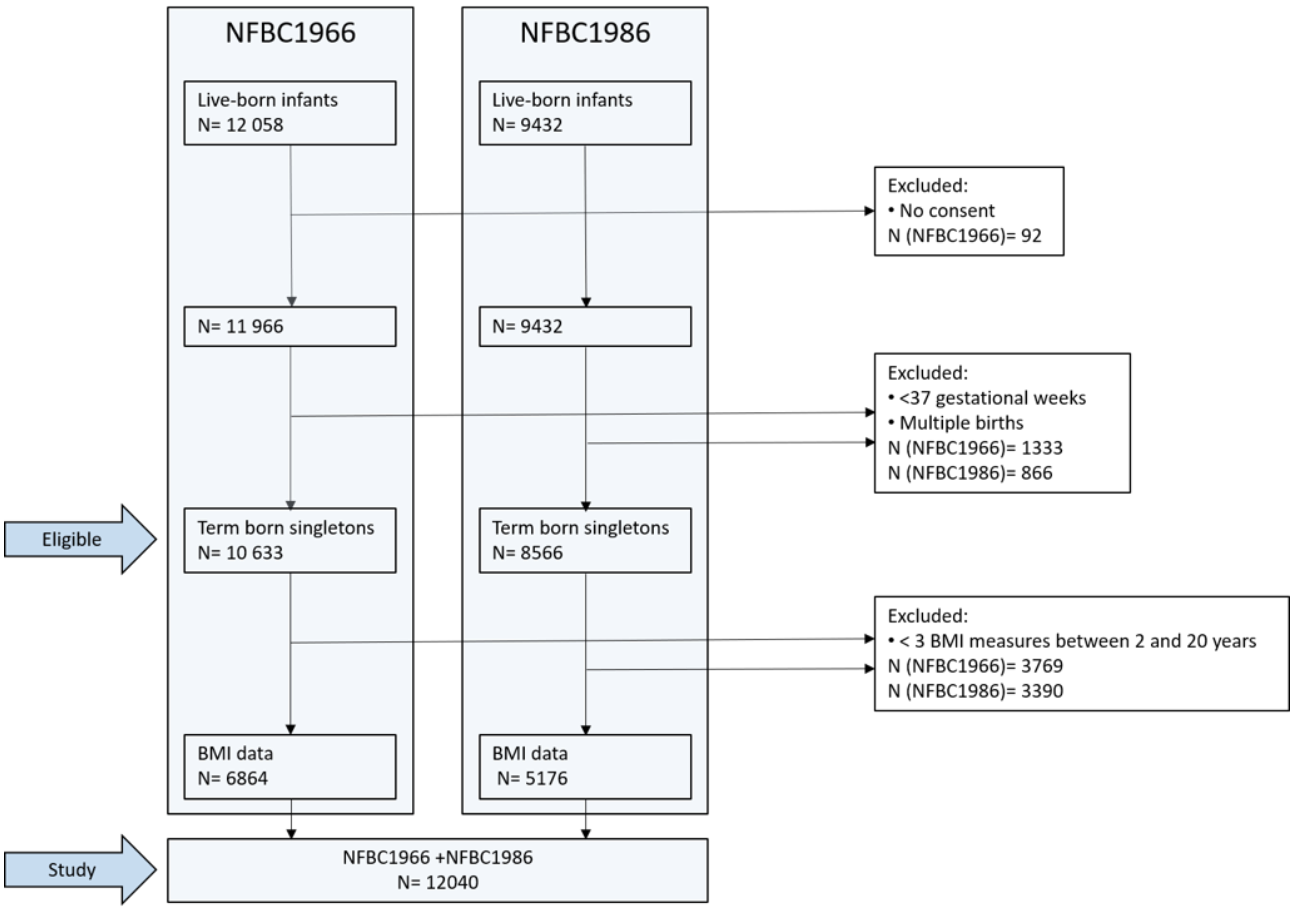
Included in the Online Supplementary Material:

Table S5: Characteristics of the group trajectories according to cohort and sex.



Supplementary Figure S1: Flow chart of the study.

Supplementary table S1: Differences between the study participants included in the trajectory modelling and the study participants excluded of the modelling due to insufficiency of repeated BMI measures.

	Inclusion in the model		Exclusion from the model	
	N	**mean ± SD**	**N**	**mean ± SD**
Mother's age (years)	12004	28.1 ± 6.2	7144	27.5 ± 6.0
Parity	12018	2.3 ± 2.2	7139	2.1 ± 2.1
Birth lenght (cm)	11966	50.6 ± 2.0	7093	50.4 ± 2.2
Birthweight (grams)	12040	3581 ± 482	7158	3525 ± 533
GA	12040	40.2 ± 1.4	7159	40.2 ± 1.4
	N	**%**	**N**	**%**
Sex	12040		7159	
Male	6243	51.8	3574	49.9
Female	5797	48.2	3585	50.1
Maternal marital status	12022		3765	
Married/cohabiting	11596	96.5	3583	95.2
Single	339	2.8	156	4.1
widowed/Divorced	87	0.7	26	0.7
Maternal education	11330		3709	
Elementary	5664	50.0	2371	63.9
Vocational or secondary	4003	35.3	1122	30.2
Matriculation	315	2.8	21	0.6
Matriculation and more	1348	11.9	195	5.3

Supporting methods for assessing early growth indicators.

Peak height velocity (PHV) and peak weight velocity (PWV) in infancy

PHV and PWV were derived from the postnatal data using the Reed1 model for boys and girls separately, using the previously described procedure [1,2,3]. Reed1 was chosen because it showed a better fit to the early growth data than the Kouchi, Carlberg and Count models, and an equally good fit to the Reed2 model which has one more parameter than the Reed1 model [4]. Reed1 model allows the velocity to peak after birth, whereas other models force it to peak at birth. In normal individuals, weight may drop up to 10% in the first couple of weeks after birth, the PWV is thus usually not in the first weeks after birth but slightly later. Therefore, the Reed1 model is more realistic (especially for weight) and more flexible. The Reed1 model was fitted by sex on all weight and height measurements taken at 0–3 years of age, including birth weight and length. We assumed both a fixed and a random component for all four parameters in the model. For each person, the first derivative of the fitted distance curve was taken to get the weight or height velocity curve. Subsequently, the maximum of this curve was taken to obtain the PWV or PHV in infancy. This is a 4-parameter extension of the 3-parameter Count model [9] and since this model is not defined at birth (t=0), it was modified for this study in the same way as in Simondon et al [5]:

$Y = A + Bt + C\ln(t+1) + D/(t+1)$

where t = postnatal age, Y = height reached at age t and A, B, C and D the function parameters. Of the function parameters, A is related to the baseline height at birth, B to the linear component of the growth velocity, C to the decrease in the growth velocity over time, and D to the inflection point that allows growth velocity to peak after birth rather than exactly at birth. All subjects with at least one height measurement from birth to 24 months at least 0.1 month (~3 days) apart were included in the Reed1 model fitting. Although the model converged for the whole group, random effects for parameters b and c were estimated to be zero for those with only one measurement (typically birth length). Even having two measurements was inadequate to capture the shape of the growth curve and therefore we included those with a minimum of three measurements per person.

Adiposity peak and rebound

The BMI growth pattern is nonlinear as part of the normal growth and development of a child. Two periods are considered: infancy from 2 weeks to 18 months and childhood from 18 months to 13 years. Age and BMI at adiposity peak (AP) and rebound (AR) were derived from cubic models from the two age groups separately as described previously [2,6]. In addition to fixed effects, random effects for the constant and the slope were included in the model. Individuals with fewer than tree measurements per period were excluded. The models are written as:

Infancy model: $\log(BMI) = \beta0 + \beta1\ Age + \beta2\ Age2 + \beta3\ Age3 + \beta4\ Sex + u0 + u1\ (Age) + \varepsilon$

Childhood model: $\log(BMI) = \beta0 + \beta1\ Age + \beta2\ Age2 + \beta3\ Age3 + \beta4\ Sex + \beta5\ Age * Sex + \beta6\ Age2 * Sex + u0 + u1\ (Age) + \varepsilon$

An autoregressive within person correlation structure between measurements was assumed.

For each participant, predicted BMI at AP and AR were calculated using the estimated fixed and random coefficients. Age at AP was defined as the age for a maximum BMI between 0.25 and 1.25 years and age at AR as the age for a minimum BMI between 2.5 and 8.5 years.

Z-cores

Z-scores are routinely used in clinical practices to monitor child growth but also in epidemiological studies to interpret growth measurements. Z-scores are statistical transformations, allowing to compare scores from different normal distributions They are calculated by the formula:

$z=(x - \mu)/\sigma)$

where x is value of the observation, μ is the population mean and σ is the population standard deviation. The Z-score system is used to compare a group to a reference population, it expresses a value as a number of standard deviations, also called z-scores or standard score, below or above the reference mean/median. BMI z-scores are measures of BMI adjusted for sex and the age of the child at the time of the measure and birthweight z-scores are measures of birthweight adjusted for sex and gestational age.

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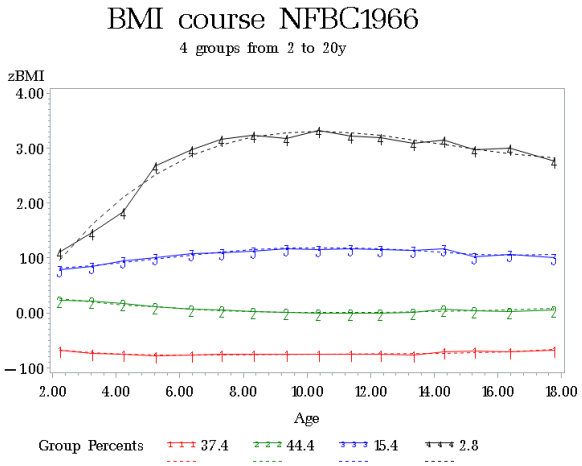
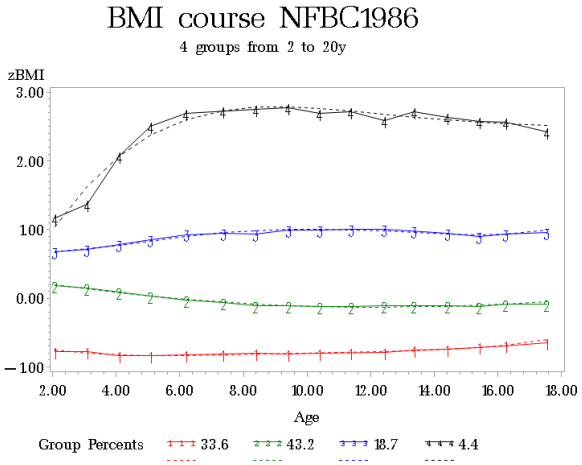
Supplementary Table S2. Characteristics of the study by cohort.

	NFBC1966		NFBC1986		
	N	**mean ± SD**	**N**	**mean ± SD**	***p* value**
Mother's height (cm)	6539	160.2 ± 5.4	5133	163.2 ± 5.5	**<0.0001**
Mother's weight (kg)	6542	59.7 ± 9.1	5084	59.5 ± 9.6	**0.006**
Mother's BMI (kg/m^2)	6291	23.2 ± 3.3	5062	22.3 ± 3.4	**<0.0001**
Mother's age (years)	6828	28.2 ± 6.6	5176	28.0 ± 5.5	0.2
Parity	6858	2.9 ± 2.2	5160	1.5 ± 1.9	**<0.0001**
Birth lenght (cm)	6809	50.5 ± 2.0	5157	50.8 ± 1.9	**<0.0001**
Birthweight (grams)	6864	3544 ± 489	5176	3630 ± 468	**<0.0001**
Birthweight z-score	6894	0.04 ± 0.97	5173	0.04 ± 0.98	0.7
Peak Height Velocity Infancy (cm/year)	6085	50.6 ± 3.8	5027	52.5 ± 6.7	**<0.0001**
Peak Weight Velocity Infancy (kg/year)	6260	12.9 ± 1.7	5063	12.6 ± 2.9	**<0.0001**
Age at Adiposity Peak (year)	5391	0.76 ± 0.03	4944	0.69 ± 0.02	**<0.0001**
BMI at Adiposity Peak (kg/m^2)	5391	18.0 ± 0.8	4944	17.6 ± 0.7	**<0.0001**
Age at Adiposity Rebound (year)	6755	5.63 ± 0.87	5130	4.99 ± 1.04	**<0.0001**
BMI at Adiposity Rebound (kg/m^2)	6755	15.4 ± 1.0	5130	15.6 ± 1.1	**<0.0001**
	N	**%**	**N**	**%**	***p* value**
Sex	6864		5176		**<0.0001**
Male	3685	53.7	2558	49.4	
Female	3179	46.3	2618	50.6	
Maternal smoking (2 months pregnancy)	6726		5152		**<0.0001**
Smoker	932	13.9	1000	19.4	
No smoker	5794	86.1	4152	80.6	
Maternal marital status	6855		5167		**0.0013**
Married/Cohabiting	6647	97.0	4949	95.8	
Single	170	2.5	169	3.3	
Widowed/Divorced	38	0.5	49	0.9	
Maternal education	6762		4568		**<0.0001**
Elementary	4535	67.1	1129	24.7	
Vocational or secondary	1935	28.6	2068	45.3	
Matriculation	49	0.7	266	5.8	
Matriculation and more	243	3.6	1105	24.2	
Operative delivery	2464		5176		**<0.0001**
Non-instrumental vaginal deliveries	1846	74.9	4245	82.0	
Caesarian Section	301	12.2	619	12.0	
Others (vacuum extraction, forceps)	317	12.9	312	6.0	





Supplementary Figure S2: Plots illustrating trajectory models for NFBC1966 and NFBC1986.

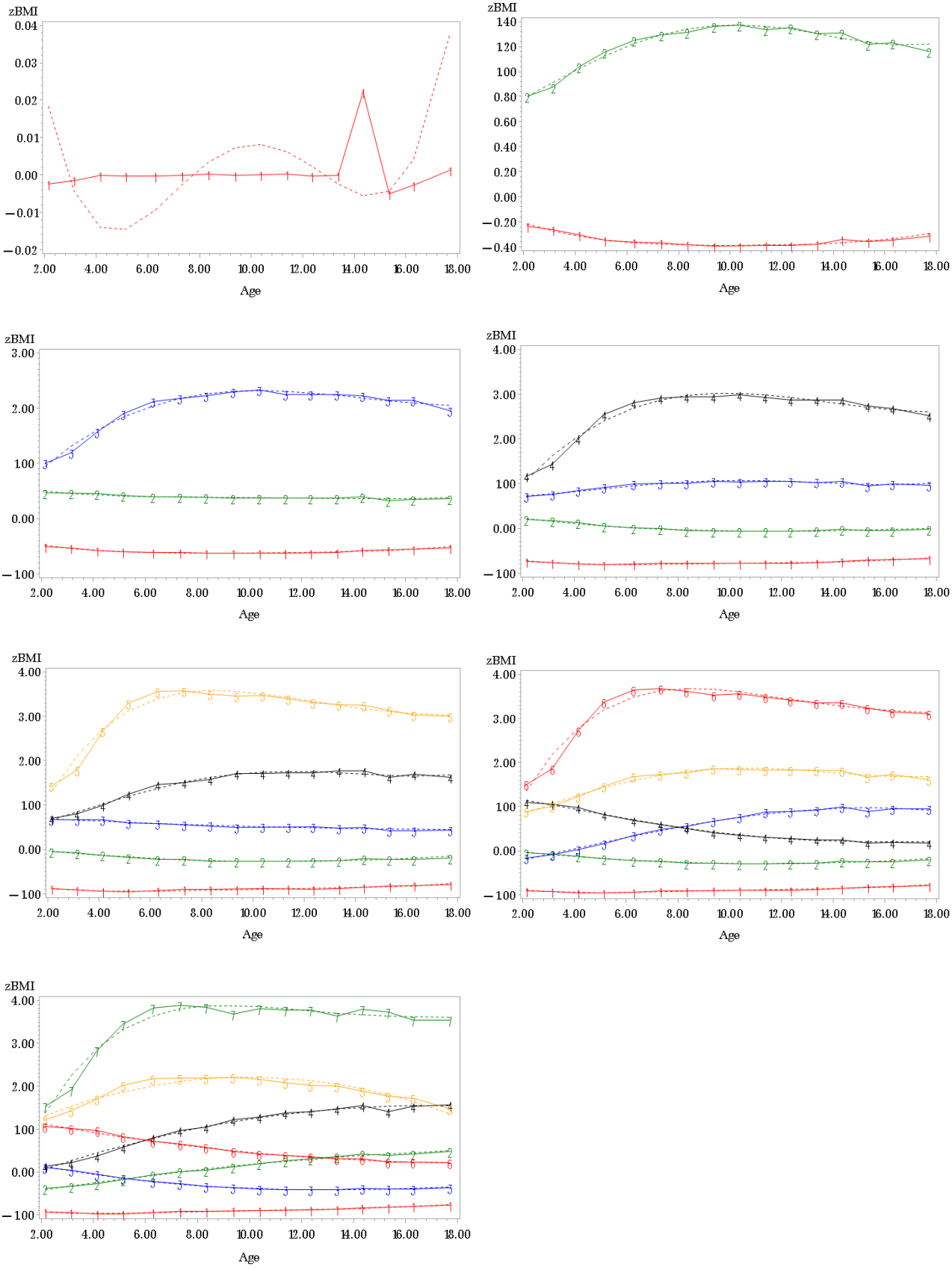
Supplementary Table S3: Sensitivity analysis. Association between maternal and early growth parameters in NFBC1966 and NFBC1986 distinct group trajectories models. Model 1: unadjusted, Model 2: adjusted for maternal age, maternal BMI, birthweight z-score, maternal education, parity, maternal smoking (according to the independent variable).

			Groups						
			1		2	3		4	
Variables	Cohort	Model	RR	95% CI		RR	95% CI	RR	95% CI
Maternal BMI	NFBC1966	1	0.96	0.96 ; 0.97	Ref	1.04	1.03 ; 1.05	1.07	1.05 ; 1.10
		2	0.97	0.96 ; 0.97	Ref	1.04	1.03 ; 1.05	1.08	1.06 ; 1.10
	NFBC1986	1	0.97	0.90 ; 1.18	Ref	1.26	1.07 ; 1.49	1.47	1.08 ; 1.99
		2	0.94	0.81 ; 1.08	Ref	1.33	1.12 ; 1.58	1.53	1.11 ; 2.12
Maternal smoking	NFBC1966	1	0.97	0.90 ; 1.18	Ref	1.26	1.07 ; 1.49	1.47	1.08 ; 1.99
		2	0.94	0.81 ; 1.08	Ref	1.33	1.12 ; 1.58	1.53	1.11 ; 2.12
	NFBC1986	1	0.93	0.81 ; 1.07	Ref	1.41	1.22 ; 1.62	1.62	1.30 ; 2.02
		2	0.87	0.76 ; 1.01	Ref	1.46	1.26 ; 1.69	1.47	1.15 ; 1.88
BW z-score	NFBC1966	1	0.87	0.82 ; 0.93	Ref	1.15	1.07 ; 1.24	1.18	1.04 ; 1.34
		2	0.88	0.82 ; 0.94	Ref	1.12	1.04 ; 1.21	1.13	0.99 ; 1.29
	NFBC1986	1	0.87	0.80 ; 0.94	Ref	1.11	1.03 ; 1.20	1.30	1.15 ; 1.48
		2	0.89	0.82 ; 0.97	Ref	1.12	1.03 ; 1.21	1.24	1.08 ; 1.42
Age at Adiposity Peak	NFBC1966	1	0.989	0.987 ; 0.991	Ref	1.008	1.004 ; 1.011	1.012	1.004 ; 1.020
		2	0.987	0.985 ; 0.990	Ref	1.008	1.004 ; 1.011	1.014	1.006 ; 1.022
	NFBC1986	1	1.003	1.001 ; 1.004	Ref	0.999	0.997 ; 1.001	1.001	0.997 ; 1.005
		2	1.002	1.000 ; 1.003	Ref	1.000	0.998 ; 1.002	1.002	0.998 ; 1.006
Peak Weight Velocity in infancy	NFBC1966	1	0.92	0.91 ; 0.93	Ref	1.04	1.03 ; 1.05	1.08	1.06 ; 1.10
		2	0.92	0.92 ; 0.93	Ref	1.04	1.03 ; 1.05	1.07	1.05 ; 1.10
	NFBC1986	1	0.89	0.88 ; 0.91	Ref	1.03	1.02 ; 1.05	1.05	1.02 ; 1.09
		2	0.89	0.87 ; 0.90	Ref	1.04	1.02 ; 1.06	1.08	1.04 ; 1.11
Peak Height Velocity in infancy	NFBC1966	1	0.992	0.988 ; 0.996	Ref	1.004	0.998 ; 1.009	1.017	1.006 ; 1.028
		2	0.992	0.987 ; 0.996	Ref	1.004	0.998 ; 1.010	1.017	1.005 ; 1.029
	NFBC1986	1	0.996	0.988 ; 1.004	Ref	1.002	0.992 ; 1.012	0.995	0.979 ; 1.012
		2	0.985	0.976 ; 0.993	Ref	1.010	1.000 ; 1.021	1.012	0.994 ; 1.031

RR: Risk Ratios, CI: Confidence Interval, BMI: Body Mass Index, BW z-core: Birthweight z-score.

Proc Traj Codes for 4 groups model :

```
proc traj data=trajNFBC out=of4 outplot=op4 outstat=os4; id project_id; var
zBMI1-zBMI16; indep windage1-windage16; model CNORM; min -30; max 30; ngroups 4;
risk gender; order 4 3 4 3; run;
%trajplot (OP4, OS4,'BMIzscore course NFBC1966-NFBC1986', '4 groups from 2 to
20y', 'zBMI', 'Age');
```



Supplementary Figure S3: Plots illustrating 1 to 7 trajectories models in the pooled Northern Finland Birth Cohort Studies.

Supplementary Table S4: Fit Statistics for the trajectory groups in the group-based trajectory models. Bold numbers indicate the chosen model.

Number of groups	BIC	AvPP	OCC	Estimated Percentage	Observed Percentage	Sample size
1	-176237			100	100	12040
2	-147593	0.99	28	77.7	77.8	9368
		0.97	113	22.3	22.2	2672
3	-134036	0.96	22	52.7	52.8	6364
		0.95	29	39.6	39.5	4752
		0.97	388	7.7	7.7	924
4	**-127135**	**0.94**	**29**	**35.0**	**34.8**	**4195**
		0.93	**17**	**43.9**	**44.0**	**5299**
		0.95	**90**	**17.5**	**17.5**	**2106**
		0.98	**1275**	**3.7**	**3.7**	**440**
5	-123438	0.93	41	24.5	24.2	2909
		0.92	16	42.4	42.9	5168
		0.93	44	23.0	22.9	2755
		0.96	269	8.2	8.1	978
		0.98	2530	1.9	1.9	230
6	-120217	0.93	42	24.0	23.8	2860
		0.92	17	41.0	41.6	5014
		0.9	71	11.3	11.1	1333
		0.89	45	15.3	15.1	1820
		0.96	334	6.7	6.7	810
		0.99	5725	1.7	1.7	203
7	-117987	0.93	43	23.4	23.3	2802
		0.84	29	15.4	14.9	1796
		0.88	15	33.0	33.6	4051
		0.92	146	7.3	7.3	876
		0.96	547	4.2	4.2	508
		0.90	49	15.6	15.5	1863
		0.99	8151	1.2	1.2	144

BIC: Bayesian Information Criterion; AvPP: Average Posterior Probabilities; OCC: Odds of Correct Classification

Supplementary table S5. Characteristics of the group trajectories according to cohort and sex.

		Stable-low Group		Normal Group		Stable-high group		Early-increase group	
		N	%	N	%	N	%	N	%
Sex	Male	2116	50.4	2874	54.2	1021	48.5	232	52.7
	Female	2079	49.6	2425	45.8	1085	51.5	208	47.3
NFBC1966			56.3		58.1		56.4		53.2
	Male	1223	51.8	1733	56.3	601	50.6	128	54.7
	Female	1138	48.2	1348	43.7	587	49.4	106	45.3
NFBC1986			43.7		41.9		43.6		46.8
	Male	893	48.7	1141	51.4	420	45.7	104	50.5
	Female	941	51.3	1077	48.6	498	54.3	102	49.5