Stability of the Associations between Early Life Risk Indicators and Adolescent Overweight over the Evolving Obesity Epidemic

Lise Graversen1*, Thorkild I. A. Sørensen2,3, Liselotte Petersen4, Ulla Sovio5,6, Marika Kaakinen6,7,8, Anneli Sandbæk1, Jaana Laitinen9, Anja Taanila10, Anneli Pouta11,12, Marjo-Riitta Järvelin6,7,8,10,11,9, Carsten Obel1

1 Section for General Medical Practice, Department of Public Health, Aarhus University, Aarhus, Denmark, 2 Institute of Preventive Medicine, Bispebjerg and Frederiksberg University Hospital, The Capital Region, Copenhagen, Denmark, 3 Novo Nordisk Foundation Center for Basic Metabolic Research, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark, 4 National Centre for Register-Based Research, Faculty of Social Sciences, Aarhus University, Aarhus, Denmark, 5 Department of Obstetrics and Gynaecology, University of Cambridge, Cambridge, United Kingdom, 6 Department of Epidemiology and Biostatistics, Imperial College, London, United Kingdom, 7 Institute of Health Sciences, University of Oulu, Oulu, Finland, 8 Biocenter Oulu, University of Oulu, Oulu, Finland, 9 Finnish Institute of Occupational Health, Oulu, Finland, 10 Primary Health Care Unit, University Hospital of Oulu, Oulu, Finland, 11 National Institute of Health and Welfare, Oulu, Finland, 12 Department of Obstetrics and Gynecology, University of Oulu and Oulu University Hospital, Oulu, Finland

Abstract

Background: Pre- and perinatal factors and preschool body size may help identify children developing overweight, but these factors might have changed during the development of the obesity epidemic.

Objective: We aimed to assess the associations between early life risk indicators and overweight at the age of 9 and 15 years at different stages of the obesity epidemic.

Methods: We used two population-based Northern Finland Birth Cohorts including 4111 children born in 1966 (NFBC1966) and 5414 children born in 1985–1986 (NFBC1986). In both cohorts, we used the same a priori defined prenatal factors, maternal body mass index (BMI), birth weight, infant weight (age 5 months and 1 year), and preschool BMI (age 2–5 years). We used internal references in early childhood to define percentiles of body size (<50, 50–75, 75–90 and >90) and generalized linear models to study the association with overweight, according to the International Obesity Taskforce (IOTF) definitions, at the ages of 9 and 15 years.

Results: The prevalence of overweight at the age of 15 was 9% for children born in 1966 and 16% for children born in 1986. However, medians of infant weight and preschool BMI changed little between the cohorts, and we found similar associations between maternal BMI, infant weight, preschool BMI, and later overweight in the two cohorts. At 5 years, children above the 90th percentile had approximately a 12 times higher risk of being overweight at the age of 15 years compared to children below the 50th percentile in both cohorts.

Conclusions: The associations between early body size and adolescent overweight showed remarkable stability, despite the increase in prevalence of overweight over the 20 years between the cohorts. Using consequently defined internal percentiles may be a valuable tool in clinical practice.

Introduction

The prevalence of overweight especially among children in the developed countries has been increasing for decades [1,2]. Childhood overweight and obesity have serious public health implications, as they are linked to adverse health outcomes in childhood, and they track into adulthood [3–7]. However, the prevention of weight gain and the management of established overweight pose major challenges. Interventions to treat overweight in children have shown small effects [8,9] and only a few...
studies of interventions to prevent childhood overweight have been performed. However, recent reviews indicate that intervention in the preschool years involving the parents [9] may have larger effect than intervention in later childhood [10]. The identification of preschool children at risk of developing overweight followed by well-designed preventive interventions seems therefore highly warranted.

Pre- and perinatal risk indicators and preschool measures of body size have been studied in relation to later overweight [11–15], and the association with later overweight is confirmed for a number of risk indicators, such as high maternal body mass index (BMI) \( (\text{kg/m}^2) \) [16–19], parity [20], parental level of education [21], birth weight [22–25], different measures of infancy/ preschool weight, BMI or weight gain [13,26–30], and early BMI rebound (the age when BMI reaches its nadir) [31,32].

In many countries, data on these risk indicators is available, and height and weight are included in local health registries. In particular, the BMI of children born 20 years apart, i.e. at an as advanced age as possible (the age of 15 years), but as different stages of the obesity epidemic. The Northern Finland Birth Cohorts offer a unique opportunity of studying cohorts from different stages of the obesity epidemic including this broad range of risk indicators.

The aim of the present study was to test the associations between pre- and perinatal risk indicators, simple postnatal measures of body size up till the age of 5 years (infant weight (5 months and 1 year) and preschool BMI (2–5 years)) and later overweight. The study compares the associations in two large population-based cohorts of children born 20 years apart, i.e. at different stages of the obesity epidemic. We compared the cohorts at an as advanced age as possible (the age of 15 years), but as growth spurts in adolescence alter growth development and could confound the findings, we also compared the cohorts before adolescence (at the age of 9 years).

**Material and Methods**

**NFBC1966**

The Northern Finland Birth Cohort 1966 (NFBC1966) consists of 96.3% of all children who were due to be born in the provinces of Oulu and Lapland in Northern Finland in 1966, and 11 744 live-born singletons entered the study [33,34]. Data collection was started in pregnancy via a structured, self-completed questionnaire concerning health and the family’s social situation. Data on pregnancy and birth were collected prospectively. Data on postnatal growth up till adolescence was obtained from scanning the original health clinic records \( (N = 4310) \). Children born before the 36th gestational week were excluded from the present study. Full antenatal data and postnatal growth data were available for 4111 singletons in the NFBC1966 cohort. Sufficient data to estimate growth curves was available for 2120 children. BMI was available for 1399 children at the age of 9 years, and for 1911 children at the age of 15 years (Table 1).

**NFBC1986**

The Northern Finland Birth Cohort 1986 (NFBC1986) consists of 99% of all children who were due to be born in the provinces of Oulu and Lapland in Northern Finland between 1 July 1985 and 30 June 1986, and 9203 live-born singletons entered the study. Data collection and inclusion criteria were similar to the NFBC1966. Data on postnatal growth were available for 5674 children. Full antenatal data and data on postnatal growth were available for 5414 singletons in the NFBC1986 cohort. Sufficient data to estimate growth curves was available for 4581 children. BMI was available for 4064 at the age of 9 years, and for 3709 at the age of 15 years (Table 1).

Both study populations were homogenous in terms of ethnicity.

**Ethics statement**

Signed, informed consent and written permission to use their data for scientific research was obtained from the study participants at the age of 31 in the NFBC1966. In the NFBC1986, the adolescents and their parents gave informed consent and written permission to use their data for scientific research. The University of Oulu Ethics Committee approved the study.

**Measures of growth**

Birth weight was obtained from medical records. Birth weight was divided into percentile groups according to week of gestation from the 36th to the 43rd week. From birth until the age of 5.5 years, individual growth curves were fitted (File S1), and weight and height at specific time points were extracted from these fitted growth curves. From birth until 1 year of age, we used weight, and from the age of 2 to 5 years, we used BMI, as these measures of body size are generally used in clinical practice. We subdivided children at these specific time points into 4 groups according to weight or BMI percentiles \( (<50, 50–75, 75–90 \text{ and } >90) \) in the study population. Participants were categorized at the age of 9 and 15 years as normal weight or overweight (including obese) using the BMI cut-offs recommended by the Childhood Obesity Working Group of the International Obesity Taskforce (IOTF) [35].

**Statistical analyses**

Differences in the examined weight and BMI medians and distributions between the cohorts were tested using Wilcoxon rank-sum test. A 5% significance level was used.

The relative risk of overweight at the age of 15 years (defined as the latest measurement between the age of 14 and 16 years) by different risk indicators were analyzed using a generalized linear regression model with log link. In adolescence, sexual maturation causes a growth spurt. We tested the associations with overweight just before adolescence, i.e. at the age of 9 years (latest measurement between the age of 8 and 10 years) to account for differences in pubertal development between the cohorts. Moreover, we tested for interactions with gender; in the NFBC1986, BMI at the age of 2 years was more strongly associated with overweight at the age of 9 years in females than in males. At the age of 15 years, this was the case for BMI from 2 to 4 years. As this was not the case in general, and because differences in associations between the genders decreased, when overweight was examined at the age of 16 years, the associations shown are not stratified, but adjusted for gender.

To explore whether slightly preterm babies or babies with fetal growth retardation had an impact on the results, we also performed the analysis excluding infants with birth weight \(<2500 \text{ g} \), infants small for gestational age (the lowest 5% for each gestational week) and infants born in the 36th week of gestation. We calculated predictive values of the strongest risk indicators. The predictive values are presented as sensitivity, specificity,
positive predictive value (PPV) and negative predictive value (NPV).

Stata version 10 SE was used for all statistical analyses. The results are reported as medians (with the 5–95% percentiles), percentages and relative risks (with their 95% confidence intervals (CI)).

Results

The descriptive data of the two cohorts are displayed in Table 1. The prevalence of overweight, measured at the age of 9 and 15 years, was 9% for both ages in the NFBC1966, and 17% at the age of 9, and 16% at the age of 15 in the NFBC1986. Medians of infant weight (5 months and 1 year) and preschool BMI (2–5 years) in the two cohorts were overall similar, but small differences were detected.

Surprisingly, the median maternal BMI fell slightly from the NFBC1966 to the NFBC1986. Further analysis revealed an equal median weight, but an increased median height in the NFBC1986 compared with the NFBC1966.

In Tables 2 and 3, we present infant weight and preschool BMI and the corresponding risk of overweight at the age of 9 and 15 years. We tested for differences between the cohorts using a 5% significance level. Very few differences were found, and we therefore also calculated common estimates for the two cohorts by pooling all the data. Excluding slightly preterm babies and babies with fetal growth retardation did not change the results.

Infant weight and preschool BMI were strongly associated with overweight at the age of 9 and 15 years in both cohorts. As expected, the strength of the associations weakened with increasing time between exposure and outcome.

In Tables 4 and 5, we present pre- and perinatal risk indicators and the corresponding risk of overweight at the age of 9 and 15 years. High and low maternal age only seemed to be associated with offspring overweight in the NFBC1966. Female gender was associated with a higher risk of overweight than male gender in the NFBC1966 at the age of 9 years and 15 years. However, in the NFBC1986, there was no difference at the age of 9 years, but at the age of 15 years, we found that males were more likely to be overweight than females. All other factors were similarly associated in the two cohorts. Maternal BMI was associated with overweight at both ages in both cohorts with similar strength. Birth weight, maternal smoking, and single motherhood all seemed to be associated with overweight, but the associations were not consistently statistically significant.

Positive predictive values for all risk indicators can be seen in the tables 2–5 (n(%)) and full predictive values of being among the top 10% in BMI at the age of 5 years or being exposed to maternal pre-pregnancy overweight (incl. obesity) are shown in table 6. The PPV of being overweight at the age of 15 years linked to being among the top 10% in preschool growth increased with age (table 2 and 3). Furthermore, the PPV increases from the NFBC1966 to the NFBC1986 due to increasing overweight prevalence. The PPV reached 53% at the age of 5 years in the
NFBC1986 meaning that half of all children in the top 10% of BMI at the age of 5 years are overweight at the age of 15 years.

Discussion

Main findings

In this study, we examined how predefined pre- and perinatal risk indicators, infant weight, and preschool BMI were associated with overweight at the age of 9 and 15 years. We studied this in two large longitudinal birth cohorts born in 1966 and 1986. We found that maternal BMI, infant weight, and preschool BMI were strongly associated with overweight just before and during adolescence in both cohorts. We found no substantial differences between the two cohorts in terms of changes in median infant weight or preschool BMI, and the relative risk associated with the percentile division of these were very similar in the two cohorts. A third of all children in the top 10% of 5 year BMI were overweight at the age of 15 years in the NFBC1966, and this was the case for more than half of children in the top 10% of 5 year BMI in the NFBC1986.

Comparison with other studies

The associations between overweight in later life and early life risk indicators, such as parity [36], education level [36], maternal

Table 2. Relative risk of overweight at the age of 9 years according to the IOTF associated with early weight and BMI measures in the NFBC1966 and the NFBC1986.

| Weight at 5 months (kg) | NFBC1966 (N = 1399) | NFBC1986 (N = 4064) | Total (N = 5463) |
|------------------------|----------------------|----------------------|------------------|
| N                      | n(%)                 | RR(95%CI)            | N                | n(%)     | RR(95%CI) | N                | n(%)     | RR(95%CI) |
| <=50 percentile        | 685 55(8)            | 1                    | 2038 227(11)     | 1        | 2723 282(10) | 1 |
| 50<75                  | 355 29(8)            | 1.2(0.7–1.8)         | 1013 192(19)     | 1.9(1.6–2.2) | 1368 221(16) | 1.7(1.5–2.0) |
| 75<90                  | 215 20(9)            | 1.4(0.9–2.4)         | 610 129(21)      | 2.2(1.8–2.6) | 825 149(18)  | 2.0(1.7–2.4) |
| =90                    | 144 23(16)           | 2.6(1.6–4.1)         | 403 125(31)      | 3.2(2.6–4.0) | 547 148(27)  | 3.1(2.6–3.7) |
| Weight at 1 year (kg)  |                      |                      |                  |          |          |                  |          |          |
| <=50 percentile        | 699 52(7)            | 1                    | 2031 210(10)     | 1        | 2730 262(10) | 1 |
| 50<75                  | 345 27(8)            | 1.2(0.7–1.8)         | 1016 188(19)     | 1.9(1.6–2.3) | 1361 215(16) | 1.8(1.5–2.1) |
| 75<90                  | 210 21(10)           | 1.6(1.0–2.6)         | 608 143(24)      | 2.5(2.1–3.0) | 818 164(20)  | 2.3(1.9–2.8) |
| =90                    | 145 27(19)           | 3.0(2.0–4.6)         | 409 132(32)      | 3.5(2.9–4.3) | 554 159(29)  | 3.4(2.8–4.0) |
| BMI at 2 years (kg/m²) |                      |                      |                  |          |          |                  |          |          |
| <=50 percentile        | 701 39(6)            | 1                    | 2036 196(10)     | 1        | 2737 235(9)  | 1 |
| 50<75                  | 353 31(9)            | 1.6(1.0–2.6)         | 1007 161(16)     | 1.7(1.4–2.0) | 1360 192(14) | 1.7(1.4–2.0) |
| 75<90                  | 202 23(11)           | 2.1(1.3–3.5)         | 617 147(24)      | 2.5(2.1–3.0) | 819 170(21)  | 2.5(2.1–3.0) |
| =90                    | 143 34(24)           | 4.5(3.0–6.9)         | 404 169(42)      | 4.4(3.7–5.3) | 547 203(37)  | 4.4(3.8–5.2) |
| BMI at 3 years (kg/m²) |                      |                      |                  |          |          |                  |          |          |
| <=50 percentile        | 715 25(4)            | 1                    | 2028 141(7)      | 1        | 2738 166(6)  | 1 |
| 50<75                  | 345 32(9)            | 2.7(1.7–4.5)         | 1024 171(17)     | 2.4(2.0–3.0) | 1369 203(15) | 2.5(2.0–3.0) |
| 75<90                  | 206 28(14)           | 4.0(2.4–6.7)         | 615 152(25)      | 3.6(2.9–4.5) | 821 180(22)  | 3.7(3.0–4.5) |
| =90                    | 138 42(30)           | 8.9(5.6–14.0)        | 397 209(53)      | 7.6(6.3–9.2) | 535 251(47)  | 7.8(6.6–9.3) |
| BMI at 4 years (kg/m²) |                      |                      |                  |          |          |                  |          |          |
| <=50 percentile        | 706 18(3)            | 1                    | 2030 83(4)       | 1        | 2736 101(4)  | 1 |
| 50<75                  | 341 19(6)            | 2.3(1.2–4.3)         | 1024 153(15)     | 3.7(2.8–4.7) | 1365 172(13) | 3.4(2.7–4.4) |
| 75<90                  | 217 32(15)           | 5.9(3.4–10.2)        | 607 178(29)      | 7.2(5.7–9.2) | 824 210(25)  | 7.0(5.6–8.7) |
| =90                    | 135 58(43)           | 17.1(10.4–27.9)      | 403 259(64)      | 15.7(12.6–19.7) | 538 317(59) | 16.0(13.1–19.6) |
| BMI at 5 years (kg/m²) |                      |                      |                  |          |          |                  |          |          |
| <=50 percentile        | 697 14(2)            | 1                    | 2038 62(3)       | 1        | 2735 76(3)  | 1* |
| 50<75                  | 348 24(7)            | 3.5(1.9–6.7)         | 1010 135(13)     | 4.4(3.2–5.9) | 1358 159(12) | 4.2(3.2–5.5) |
| 75<90                  | 205 25(12)           | 6.2(3.3–11.8)        | 603 195(32)      | 10.6(8.1–14.0) | 808 220(27) | 9.9(7.7–12.6) |
| =90                    | 149 64(43)           | 21.0(12.1–36.4)      | 413 281(68)      | 22.3(17.3–28.8) | 562 345(61) | 22.0(17.5–27.8) |

*Statistically significant difference between genders. No statistically significant differences between the cohorts found. BMI – Body mass index. IOTF – overweight/obese according to the International Obesity Task Force. NFBC1966 and NFBC1986 – Northern Finnish Birth Cohorts born in 1966 and 1986.

doi:10.1371/journal.pone.0095314.t002
smoking during pregnancy [36–38], maternal pre-pregnancy BMI [36,38,39], and birth weight [37,38] in the Northern Finnish Birth Cohorts have previously been reported with more statistical power owing to larger sample sizes, but a comparison of the association with adolescence overweight in the two cohorts has not previously been reported. Few studies have the opportunity to examine the development of risk indicators over time. Rugholm et al [24] found that mean birth weight and the link between birth weight and school age overweight were stable over a 20-year period. We found a small increase in median birth weight from 1966 to 1986, but also failed to prove differences in the associations between birth weight and school age overweight between the cohorts. We confirmed the strong associations between weight and BMI measures early in life and school age BMI found in a number of studies [11–15,26–30].

### Growth spurt in adolescence

We examined early life risk indicators in relation to overweight at the age of 9 years, as the growth spurt in adolescence could alter weight class at the age of 15 years. Age at growth spurt has decreased over time, and since heavier children are known to enter growth spurt earlier than other children [40,41], this could influence our results. Hence, more children in the NFBC1986 than in the NFBC1966 were expected to have entered height or

---

**Table 3. Relative risk of overweight at the age of 15 years according to the IOTF associated with early weight and BMI measures in the NFBC1966 and the NFBC1986.**

| BMI at 2 years (kg/m²) | NFBC66 (N = 1911) | NFBC86 (N = 3709) | Total (N = 5620) |
|------------------------|-------------------|-------------------|-----------------|
| N n(%) RR(95%CI) | N n(%) RR(95%CI) | N n(%) RR(95%CI) |
| 50 percentile | 955 48(5%) 1 | 1872 174(9%) 1 | 2827 222(8%) 1 |
| 50–75 | 477 42(9%) 2.5(1.6–3.8) 918 141(15) 1.6(1.3–2.0) 1395 178(13) 1.6(1.3–1.9) |
| 75–90 | 279 39(14) 3.9(2.5–6.0) 565 144(25) 3.5(2.9–4.4) 844 183(22) 3.6(3.0–4.4) |
| 90 | 199 36(18) 7.0(4.7–10.4) 355 127(36) 6.0(4.9–7.3) 554 203(37) 6.2(5.1–7.4) |
| *Statistically significant difference between genders. No statistically significant differences between the cohorts found. BMI – Body mass index. IOTF – overweight/obese according to the International Obesity Task Force. NFBC1966 and NFBC1986 – Northern Finnish Birth Cohorts born in 1966 and 1986. doi:10.1371/journal.pone.0095314.t003**
both height and weight spurt at the age of 15 years, because the proportion of heavy children was larger in 1986 than in 1966; these children could appear with a lower BMI due to this growth spurt. Girls are known to enter growth spurt earlier than boys [41] and in this study, we found girls to be more often normal weight than boys at the age of 15 years in the NFBC1986 (Table 5). Furthermore, the prevalence of overweight decreases slightly in the NFBC1986 from the age of 9 years to the age of 15 years. These findings could indicate that a lower BMI at the age of 15 years due to growth spurt could hide overweight children, especially girls, because they have entered growth spurt more frequently than their normal weight peers.

BMI rebound

BMI rebound has been shown to be a strong indicator of adult overweight [32], but the clinical relevance of BMI rebound has been subject to doubt. Early BMI rebound may be an indicator of later obesity alone, because it identifies children, whose BMI percentile is high and/or crossing upwards [42]. Furthermore, weight and height measurements at the age of 8–9 years are needed to estimate BMI rebound.

We explored the possibility of estimating BMI rebound at the age of 5 years, as children with early rebound and hence at higher risk of overweight, will have had their BMI rebound before this age. Two strategies were tested: First, we defined BMI rebound as the lowest measured BMI between the age of 2 and 6 followed by higher measurements. Second, we defined it as the nadir on fitted BMI curves up till the age of 5.5, if a nadir existed. Both strategies failed to demonstrate stronger associations with future overweight than just BMI at the age of 5 years, even though children with no estimated BMI rebound were included as a separate group.

Table 4. Relative risk of overweight at the age of 9 years according to the IOTF associated with pre- and perinatal risk indicators in the NFBC1966 and the NFBC1986.

|                        | NFBC1966 (N = 1399) | NFBC1986 (N = 4064) | Total (N = 5463) |
|------------------------|---------------------|---------------------|------------------|
|                        | N  n(%) RR(95%CI)   | N  n(%) RR(95%CI)   | N  n(%) RR(95%CI) |
| Maternal BMI (kg/m²)   |                     |                     |                  |
| <25                    | 1042 83(8) 1        | 3334 474(14) 1     | 4376 557(13) 1   |
| ≥25–<30                | 225 30(13) 1.6(1.1–2.4) | 512 132(26) 1.8(1.5–2.1) | 737 162(22) 1.7(1.5–2.0) |
| ≥30                    | 39 9(23) 2.9(1.6–3.3) | 133 51(38) 2.7(2.1–3.4) | 172 60(35) 2.7(2.2–3.4) |
| Maternal smoking       |                     |                     |                  |
| no                     | 1187 104(9) 1      | 3275 489(15) 1     | 4462 593(13) 1   |
| 1–10 cigarettes/day    | 159 16(10) 1.2(0.7–1.9) | 338 77(23) 1.5(1.2–1.9) | 497 93(19) 1.4(1.2–1.7) |
| >10 cigarettes/day     | 31 5(16) 2.0(0.9–4.4) | 371 97(26) 1.8(1.5–2.1) | 402 102(25) 1.9(1.6–2.3) |
| Maternal cohabiting    |                     |                     |                  |
| Cohabiting             | 1358 120(9) 1      | 3893 639(16) 1     | 5251 759(14) 1   |
| Single                 | 39 6(15) 1.6(0.8–3.5) | 165 34(21) 1.3(0.9–1.7) | 204 40(19) 1.3(1.0–1.8) |
| Maternal age           |                     |                     |                  |
| <25                    | 597 58(10) 1.3(0.9–1.8) | 1135 183(16) 1.0(0.8–1.1) | 1732 241(14) 0.9(0.8–1.1) |
| 25–35                  | 611 46(8) 1        | 2412 400(17) 1     | 3023 446(15) 1   |
| >35                    | 190 23(12) 1.6(1.0–2.6) | 517 90(17) 1.1(0.9–1.3) | 707 113(16) 1.1(0.9–1.3) |
| Long maternal education|                     |                     |                  |
| no                     | 858 76(9) 1        | 859 160(19) 1      | 1717 236(14) 1   |
| yes                    | 525 50(10) 1.1(0.8–1.5) | 2793 451(17) 0.9(0.8–1.0) | 3259 501(15) 1.1(1.0–1.3) |
| Offspring gender       |                     |                     |                  |
| Male                   | 670 46(7) 1        | 1999 325(16) 1     | 2669 371(14) 1** |
| Female                 | 729 81(11) 1.6(1.1–2.3) | 2065 348(17) 1.0(0.9–1.2) | 2794 429(15) 1.1(1.0–1.3) |
| Birth weight (kg)      |                     |                     |                  |
| <50 percentile         | 708 65(9) 1        | 2046 289(14) 1     | 2754 354(13) 1   |
| ≥50–<75                | 362 22(6) 0.7(0.4–1.1) | 1002 154(15) 1.1(0.9–1.3) | 1364 176(13) 1.0(0.9–1.2) |
| ≥75–<90                | 187 24(13) 1.5(0.9–2.3) | 620 124(20) 1.4(1.2–1.7) | 807 148(18) 1.5(1.2–1.7) |
| ≥90                    | 142 16(11) 1.3(0.8–2.2) | 396 106(27) 1.9(1.6–2.4) | 538 122(23) 1.8(1.5–2.2) |
| Offspring first born   |                     |                     |                  |
| yes                    | 576 56(10) 1       | 1341 246(18) 1     | 1917 302(16) 1   |
| no                     | 820 71(9) 0.9(0.6–1.2) | 2712 425(16) 0.9(0.9–1.0) | 3532 496(14) 0.9(0.8–1.0) |

No statistically significant differences between genders found.
**Statistically significant difference between cohorts. BMI – body mass index. IOTF – overweight/obese according to the International Obesity Task Force. NFBC1966 and NFBC1986 – Northern Finnish Birth Cohorts born in 1966 and 1986.
doi:10.1371/journal.pone.0095314.t004
Reference material and percentile division of risk indicators

Body size measures are most often defined according to one of various external reference materials [43,44]. External references, if clearly defined, are an important epidemiological tool that may be used to follow the obesity epidemic. However, BMI distributions differ between countries and over time, and this has given rise to many different reference materials that are not necessarily the most adequate or clinically relevant reference materials for a given population [45–47].

In view of this, internal reference poses a valid alternative. The technical development of electronic patient files and central registration can today provide up-to-date reference material for a given population over a short period of time. Reference materials can be created by automated collection of growth measurements on all children attending e.g. preventive health examinations through childhood in a whole population. Of particular interest in

### Table 5. Relative risk of overweight at the age of 15 years according to the IOTF associated with pre-and perinatal risk indicators in the NFBC1966 and the NFBC1986.

| Maternal BMI (kg/m²) | NFBC1966 (N = 1911) | NFBC1986 (N = 3709) | Total (N = 5620) |
|----------------------|---------------------|---------------------|------------------|
| <25                  | 1456 104(7)         | 3054 392(13)        | 4510 496(11)     |
| ≥25–<30              | 297 45(15)          | 454 115(25)         | 751 160(21)      |
| ≥30                  | 44 12(27)           | 120 52(43)          | 164 64(39)       |

| Maternal smoking | NFBC1966 (N = 1911) | NFBC1986 (N = 3709) | Total (N = 5620) |
|------------------|---------------------|---------------------|------------------|
| no               | 1629 138(8)         | 2205 439(15)        | 4634 577(12)     |
| 1–10 cigarettes/day | 210 24(11)        | 303 61(20)          | 513 85(17)       |
| >10 cigarettes/day | 35 2(6)            | 328 66(20)          | 363 68(19)       |

| Maternal cohabiting | NFBC1966 (N = 1911) | NFBC1986 (N = 3709) | Total (N = 5620) |
|---------------------|---------------------|---------------------|------------------|
| Cohabiting         | 1857 161(9)         | 3548 551(16)        | 5405 712(13)     |
| Single             | 52 6(12)            | 156 26(17)          | 208 32(15)       |

| Maternal age | NFBC1966 (N = 1911) | NFBC1986 (N = 3709) | Total (N = 5620) |
|--------------|---------------------|---------------------|------------------|
| <25          | 832 74(9)           | 1046 162(15)        | 1878 236(13)     |
| 25–35        | 848 60(7)           | 2190 340(16)        | 3038 400(13)     |
| >35          | 228 32(14)          | 473 75(16)          | 701 107(15)      |

| Long maternal education | NFBC1966 (N = 1911) | NFBC1986 (N = 3709) | Total (N = 5620) |
|-------------------------|---------------------|---------------------|------------------|
| no                      | 1158 112(10)        | 788 136(17)         | 1946 248(13)     |
| yes                     | 725 53(7)           | 2504 390(16)        | 3229 443(14)     |

| Offspring gender | NFBC1966 (N = 1911) | NFBC1986 (N = 3709) | Total (N = 5620) |
|------------------|---------------------|---------------------|------------------|
| Male             | 920 70(8)           | 1815 332(18)        | 2735 420(15)     |
| Female           | 991 97(10)          | 1894 245(13)        | 2885 342(12)     |

| Birth weight (g) | NFBC1966 (N = 1911) | NFBC1986 (N = 3709) | Total (N = 5620) |
|------------------|---------------------|---------------------|------------------|
| <50 percentile  | 973 85(9)           | 1872 236(13)        | 2845 321(11)     |
| ≥50–<75         | 491 38(8)           | 932 153(16)         | 1423 191(13)     |
| ≥75–<90         | 266 25(9)           | 556 104(19)         | 822 129(16)      |
| ≥90             | 181 19(11)          | 349 84(24)          | 530 103(19)      |

| Offspring first born | NFBC1966 (N = 1911) | NFBC1986 (N = 3709) | Total (N = 5620) |
|----------------------|---------------------|---------------------|------------------|
| yes                  | 789 71(9)           | 1229 198(16)        | 2018 269(13)     |
| no                   | 1119 96(9)          | 2468 377(15)        | 3587 473(13)     |

No statistically significant differences between genders found.

**Statistically significant difference between cohorts. BMI – body mass index. IOTF – overweight/obese according to the International Obesity Task Force. NFBC1966 and NFBC1986 – Northern Finnish Birth Cohorts born in 1966 and 1986.

doi:10.1371/journal.pone.0095314.t005

### Table 6. Predictive values of 5 year BMI in the top 10% and maternal overweight (incl. obesity).

| Predicting overweight at 15 years | Sensitivity | Specificity | PPV | NPV |
|-----------------------------------|-------------|-------------|-----|-----|
| 5 year BMI in the top 10%, NFBC1966 | 40.1        | 92.7        | 34.5 | 94.2 |
| 5 year BMI in the top 10%, NFBC1986 | 33.6        | 94.6        | 35.3 | 88.6 |
| Maternal overweight (incl. obesity), NFBC1966 | 35.4        | 82.6        | 16.7 | 92.9 |
| Maternal overweight (incl. obesity), NFBC1986 | 29.9        | 86.7        | 29.1 | 87.2 |

BMI- Body mass index. PPV- positive predictive value. NPV - negative predictive value. NFBC1966 and NFBC1986 – Northern Finnish Birth Cohorts born in 1966 and 1986.

doi:10.1371/journal.pone.0095314.t006
Strengths and limitations

The obesity epidemic, manifested in the rise in prevalence at the age of 9 and 15 years seen in the NFBC1986, does not seem to have much affected the median weight at 5 months and 1 year, and BMI from 2 to 5 years. However, the distribution of BMI is right-skewed, and a predisposition to later overweight may have been established in some children with only small, or without changes in early life weight and BMI measures. As overweight is a slowly developing condition, we cannot reject that small changes seen in early childhood could reflect crucial changes in a child’s growth trajectory. Alternatively, causes of the rising prevalence are to be found among factors affecting later childhood.

Many no major differences in the risk associated with percentile division of risk indicators were found between the two cohorts. This implies that the rise in overweight prevalence later in life is a general phenomenon that affects the entire population, throughout the broad range of risk indicators. Thus, the rise in prevalence of overweight cannot be attributed to a rise in levels of risk indicators or a greater effect of the upper levels of the risk indicators.

Stability of risk indicators

The strength of this study was the prospective data collection conducted in two large general population-based cohorts with extensive information about clinically relevant risk indicators. The children were followed prospectively from pregnancy until adolescence. Numerous height and weight measurements made it possible to fit growth curves and to estimate the size of the child at any point of time in early childhood. Moreover, the two cohorts, with individuals born 20 years apart, offered the unique possibility for studying risk indicators over time. One limitation was that some children had an insufficient number of measurements for growth modelling, restricting the study population size especially in the NFBC1966. The difference between the cohorts in the proportion with sufficient measurements is due to changes over the years in the timing of routine measurements. We know from other analyses of the representativeness of attendees that individuals with only basic education and individuals with unemployment history are slightly underrepresented among attendees [48], and that individuals with sufficient measurements to fit growth curves in the NFBC1966 have slightly lower adult BMI than individuals with insufficient numbers of measurements [49]. If this has impact on the results, we will, most likely, have underestimated the associations as the population studied is thought to be somewhat healthier than the total population. A more similar proportion with growth curves would most likely result in more similar associations between the cohorts rather than larger differences. Moreover, the lack of data on diet and physical activity collected at the same age in childhood could be seen as a limitation. Diet and physical activity patterns are likely to have changed over this 20-year period, but the evidence of these factors’ association with overweight development in observational studies is inconsistent [50] and the probability that data on these factors would have changed the conclusion is minor. Finally, separate analysis of preterm infants was not possible due to the limited number of preterm infants.

Conclusions

Infant weight and preschool BMI were strongly associated with overweight in later childhood and adolescence in both NFBC1966 and NFBC1986. Despite the substantial increase in the prevalence of overweight, the relative risk of overweight linked to the percentile division of early weight and BMI measures appeared to be stable in two cohorts born 20 years apart and, hence, at very different stages of the obesity epidemic. Infant weight and preschool BMI have great potential for clinical use in the prediction of a child’s risk of developing overweight, as the relative risk linked to them remains stable over time. A child’s risk of future overweight can be determined on the basis of its weight and BMI measures from early infancy, and throughout early childhood with even greater certainty. We may assume that this will also apply to future children and thus be beneficial as a component in early life prevention of overweight.

Perspective

Providing physicians with knowledge about a specific child’s risk of later overweight at routine health examinations could provide a unique opportunity for overweight prevention. However, in spite of good evidence of the tracking of overweight from adolescence to adulthood, some overweight adolescents become normal weight adults [51]. In order to make sure that we target individuals at risk of clinically relevant outcomes, further analyses of the associations between these preschool weight and BMI measures and adult outcomes linked to morbidity and mortality would be highly interesting.

Supporting Information

File S1 Description of the growth modelling.

Acknowledgments

We thank the late Professor Paula Rautakallio (launch of NFBC1966 and initial data collection), Ms Sarianna Vaara (data collection), Ms Taula Viltalo (administration) and Mr Markku Koiranen (data management).

Author Contributions

Conceived and designed the experiments: LG CO TIAS. Performed the experiments: LG. Analyzed the data: LG. Contributed reagents/materials/analysis tools: US. Wrote the paper: LG CO TIAS. Supervision of the analyses, reviewed and revised the manuscript, and approved the final manuscript as submitted: LP MK. Revision of the manuscript and approved the final manuscript as submitted: AS JL. Participation in data collection, revised the manuscript, and approved the final manuscript as submitted: AP AT.

References

1. Wang Y, Lobstein T (2006) Worldwide trends in childhood overweight and obesity. Int J Pediatr Obes 1: 11–25.
2. Han JC, Lavelle DA, Kimm SY (2010) Childhood obesity. Lancet 375: 1737–1748.
3. Lloyd LJ, Langley-Evans SC, McMullen S (2012) Childhood obesity and risk of the adult metabolic syndrome: A systematic review. Int J Obes (Lond) 36: 1–11.
4. Freedman DS, Khan LK, Dietz WH, Srinivasan SR, Berenson GS (2001) Relationship of childhood obesity to coronary heart disease risk factors in adulthood: The Bogalusa heart study. Pediatrics 108: 712–718.
5. Reilly JJ, Methven E, McDowell ZC, Hacking B, Alexander D, et al. (2003) Health consequences of obesity. Arch Dis Child 88: 748–752.

6. Serdula MK, Ivery D, Coates RJ, Freedman DS, Williamson DF, et al. (1995) Do obese children become obese adults? A review of the literature. Prev Med 22: 499–508.

7. Singh AS, Mulder C, Twick JW, van Mechelen W, Chinapaw MJ (2008) Tracking of childhood overweight into adulthood: A systematic review of the literature. Obes Rev 9: 474–480.

8. Oude Luttikhuisk H, Baur L, Janssen H, Shrewsbury VA, O’Malley C, et al. (2009) Interventions for treating obesity in children. Cochrane Database Syst Rev (1): CD001872.

9. Bluford DA, Sherry B, Scanlon KS (2007) Interventions to prevent or treat obesity in preschool children: A review of evaluated programs. Obesity (Silver Spring) 15: 1356–1372.

10. Waters E, de Silva-Sanigorski A, Hall BJ, Brown T, Campbell KJ, et al. (2011) Interventions for preventing obesity in children. Cochrane Database Syst Rev (4): CD001871.

11. Monteiro PO, Victora CG (2005) Rapid growth in infancy and childhood and obesity in later life—a systematic review. Obes Rev 6: 143–154.

12. Monasta L, Batty GD, Cattaneo A, Ferrari A, Ronfani L, et al. (2010) Early-life determinants of overweight and obesity: A review of systematic reviews. Obes Rev 11: 399–407.

13. Baird J, Fisher D, Lucas P, Kleijnen J, Roberts H, et al. (2005) Being big or growing fast: Systematic review of size and growth in infancy and later obesity. BMJ 330: 929–930.

14. Reilly JJ, Armstrong J, Dorothy AR, Emmett PM, Ness A, et al. (2005) Early life risk factors for obesity in childhood. Cohort study. BMJ 330: 1357.

15. Weng SF, Redell SA, Scott JA, Yang M, Glazebrook CP (2012) Systematic review and meta-analyses of risk factors for childhood overweight identifiable during infancy. Arch Dis Child 97: 1019–1026.

16. Whitaker RC (2004) Predicting preschooler obesity at birth: The role of maternal overweight in early pregnancy. Pediatrics 114: e29–36.

17. Whitaker RC, Wright JA, Pepe MS, Seidel KD, Dietz WH (1997) Predicting obesity in young adulthood from childhood and parental obesity. N Engl J Med 337: 869–873.

18. Kral JG, Biron S, Simard S, Hould FS, Lebel S, et al. (2006) Large maternal weight gain during the first half of pregnancy and offspring obesity at 6 years. A prospective cohort study. BMJ 331: 929–932.

19. Laitinen J, Power C, Jarvelin MR (2001) Family social class, maternal body mass index, and age at menarche as predictors of adult body composition in young adult men–a prospective twin study. Int J Obes Relat Metab Disord 25: 193–201.

20. Reynolds RM, Osmond C, Phillips DI, Godfrey KM (2010) Maternal BMI, childhood body mass index, and age at menarche as predictors of adult weight loss from obesity surgery prevents transmission of obesity to children who were followed for 2 to 18 years. Pediatrics 118: e1644–9.

21. Laitinen J, Jaakelainen A, Poosinen J, Nautinen O, Schwab U, Pirkola J, et al. (2011) Intergenerational transmission of overweight among finnish adolescents and their parents: A 16-year follow-up study. Int J Obes (Lond) 35: 1289–1294.

22. Aksglaede L, Juul A, Olsen LW, Sørensen TI (2009) Age at puberty and the emerging obesity epidemic. PLoS One 4: e4050.

23. Jaakelainen A, Poosinen J, Nautinen O, Schwab U, Pirkola J, et al. (2011) Intergenerational transmission of overweight among finnish adolescents and their parents: A 16-year follow-up study. Int J Obes (Lond) 35: 1289–1294.

24. Nader PR, O’Brien M, Houts R, Bradley R, Belsky J, et al. (2006) Identifying young children without overweight at high risk for adult overweight: A systematic review of the evidence. Int J Obes (Lond) 33 Suppl 3: S1–92.

25. Singh AS, Mulder C, Twick JW, van Mechelen W, Chinapaw MJ (2008) Tracking of childhood overweight into adulthood: A systematic review of the literature. Obes Rev 9: 474–480.