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Published in:
Obesity

DOI:
10.1002/oby.20921

Publication date:
2015

Document version
Publisher's PDF, also known as Version of record

Document license:
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Citation for published version (APA):
Graversen, L., Sørensen, T. I. A., Gerds, T. A., Petersen, L., Sovio, U., Kaakinen, M., ... Obel, C. (2015). Prediction of adolescent and adult adiposity outcomes from early life anthropometrics. Obesity, 23(1), 162-169. https://doi.org/10.1002/oby.20921
Prediction of Adolescent and Adult Adiposity Outcomes from Early Life Anthropometrics

Lise Graversen1, Thorild I.A. Sørensen2,3, Thomas A. Gerds4, Liselotte Petersen5, Ulla Sovio6,7, Marika Kaakinen8,9, Anneli Sandbaek4, Jaana Laitinen10, Anja Taanila8,11, Anneli Pouta12,13, Marjo-Riitta Järvelin7,8,9,11,12,*, and Carsten Obel1,*

Objectives: Maternal body mass index (BMI), birth weight, and preschool BMI may help identify children at high risk of overweight as they are (1) similarly linked to adolescent overweight at different stages of the obesity epidemic, (2) linked to adult obesity and metabolic alterations, and (3) easily obtainable in health examinations in young children. The aim was to develop early childhood prediction models of adolescent overweight, adult overweight, and adult obesity.

Methods: Prediction models at various ages in the Northern Finland Birth Cohort born in 1966 (NFBC1966) were developed. Internal validation was tested using a bootstrap design, and external validation was tested for the model predicting adolescent overweight using the Northern Finland Birth Cohort born in 1986 (NFBC1986).

Results: A prediction model developed in the NFBC1966 to predict adolescent overweight, applied to the NFBC1986, and aimed at labelling 10% as “at risk” on the basis of anthropometric information collected until 5 years of age showed that half of those at risk in fact did become overweight. This group constituted one-third of all who became overweight.

Conclusions: Our prediction model identified a subgroup of children at very high risk of becoming overweight, which may be valuable in public health settings dealing with obesity prevention.

Obesity (2015) 23, 162–169. doi:10.1002/oby.20921

1 Section for General Medical Practice, Department of Public Health, Aarhus University, Aarhus, Denmark. Correspondence: Lise Graversen (lgra@alm.au.dk) 2 Institute of Preventive Medicine, Bispebjerg and Frederiksberg 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 Section for Biostatistics, Department of Public Health, University of Copenhagen, Copenhagen, Denmark 5 National Centre for Register-Based Research, Faculty of Social Sciences, Aarhus University, Aarhus, Denmark 6 Department of Obstetrics and Gynaecology, University of Cambridge, Cambridge, United Kingdom 7 Department of Epidemiology and Biostatistics, Imperial College, London, United Kingdom. Correspondence: Marjo-Riitta Jarvelin (m.jarvelin@imperial.ac.uk) 8 Institute of Health Sciences, University of Oulu, Oulu, Finland 9 Biocenter Oulu, University of Oulu, Oulu, Finland 10 Finnish Institute of Occupational Health, Helsinki, Finland 11 Unit of Primary Care, University Hospital of Oulu, Oulu, Finland 12 National Institute of Health and Welfare, Oulu, Finland 13 Department of Obstetrics and Gynecology, University of Oulu and Oulu University Hospital, Oulu, Finland.

Additional Supporting Information may be found in the online version of this article.

Accepted: 17 September 2014; Published online 30 October 2014. doi:10.1002/oby.20921

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Introduction

The worldwide increase in childhood overweight prevalence may have severe public health implications (1,2). Childhood overweight is linked to a number of adverse health outcomes in childhood and tracks into adulthood (3-7), and adult overweight is linked to increased morbidity and mortality (8,9).

High-risk children can be identified using statistical models based on risk indicators as predictor variables and developed to predict a certain outcome. Several such early prediction models have been developed to predict childhood or adolescent overweight based on different combinations of known risk factors of overweight, but few have been able to predict adolescent and adult outcomes (10-14).

An important purpose of the prediction models is to identify high-risk children, and it is therefore of paramount importance that a prediction model is developed to assure the best possible feasibility in future generations. Previously, we have found the relative risk linked to the known risk indicators maternal body mass index (BMI) (15,16), birth weight (17), and preschool weight or BMI (18-21) to be similar in two cohorts born 20 years apart, in spite of a doubling in overweight prevalence between these cohorts (22). Furthermore, we have found preschool BMI to be linked to central obesity and metabolic alterations in adulthood (23), indicating that preschool growth is not exclusively linked to BMI, but also to adiposity harmful to health. In the Nordic countries, preschool children up to the age of 5 years are seen at routine health examinations where height and weight are measured by pediatricians or general practitioners and where maternal BMI and birth weight are available.

The aim of the present study was to test the ability of maternal BMI, birth weight, and early childhood BMI to predict adolescent overweight, adult overweight, and adult obesity and to test how well a prediction model developed in one cohort performs in a cohort born 20 years later in the same geographical area but with a much higher overweight prevalence. We developed prediction models for use at various ages during childhood, but we have especially focused on prediction models using data available at the age of 5 years, owing to their clinical utility in preventive health examinations.

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 12,058 live-born individuals entered the study (24,25). Data collection was started in pregnancy via a structured, self-completed questionnaire including maternal prepregnancy weight and height. Data on pregnancy and birth were collected prospectively. At the age of 31, the subjects living in the original target area or in the capital area (N = 8,463) were invited to participate in a follow-up study including a clinical examination, and 71% of the invited took part (N = 6,033). For those with a blood sample available from the clinical examination, data on their postnatal growth were obtained from scans of original municipal health clinic records (N = 4,283). Antenatal data and postnatal growth data were available for 4,111 singletons in the NFBC1966 cohort (Figure 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 9,203 live-born individuals entered the study. Data collection and inclusion criteria were similar to the NFBC1966, but the follow-up study was performed at the age of 16 years in the NFBC1986. Full antenatal data and postnatal growth were available for 5,414 singletons in the NFBC1986 cohort. Both study populations were homogenous in terms of ethnicity.

Ethics statement

Signed, informed consent, and written permission to use their data for scientific research were 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.

Outcomes

Overweight (including obesity) and obesity in adolescence (last measurement between the age of 13 and 16 years of age) were categorized using the BMI cut-offs recommended by the International Obesity Task Force (IOTF) (26). Adult overweight (including obesity) was defined as BMI > 25 and obesity as BMI > 30.
Descriptive statistics

The data of the NFBC1966 and NFBC1986 cohorts were summarized using means (reporting the standard deviation [SD] and P-values for differences between the genders using t-test) and counts (reporting percentage and P-values for differences between the genders using chi-square test) (Table 1).

Data imputation

We aimed to develop prediction models annually between the ages 1 and 8 years. We imputed data as not all children were measured around their birthdays from 1 to 8 years. For the 1-year BMI, we used the median of the BMI measurements between 10 and 14 months. Values at the other ages (2-8 years) were imputed based on individual curves. A height and a weight curve was developed using the child’s longitudinal height and weight measurements to estimate the 4 parameters of first order Reed models (Supporting Information), and BMI was calculated subsequently. To avoid artefacts, we applied the median of the BMI measurements between 10 and 14 years before this age, and the 1-year BMI. The childhood models at 3-8 included the 1-year BMI and the 2-year BMI. To avoid colinearity, the childhood models at ages 3-8 included only the current BMI value at the specific age, the BMI from 2 years before this age, and the 1-year BMI. The childhood models at age 1 year included the 1-year BMI, and at age 2 years they included the 1-year BMI and the 2-year BMI.

Internal validation

The Receiver Operating Characteristic (ROC) curve plots the sensitivity against 1-specificity for consecutive cut-offs of risk of an outcome. The area under the ROC curve (AUC) is equal to the probability (here represented as percentages) that the model will rank a randomly chosen case higher in risk than a randomly chosen noncase. AUC above 50% represents a classification better than random, and 100% represents the perfect classification. AUC should be estimated with correction for optimism, as a prediction model will most likely perform better in the data, where the model was developed, than in other data sets (27). We corrected for optimism using a bootstrap cross-validation design. In each of 1000 runs, we fitted the parameters of the models to a bootstrap training set drawn with replacement from the full data. Thus, each bootstrap training set has the same size as the original set, but an individual may appear multiple times. Using the risk predictions in the data of the remaining children, whose data were not used to fit the model, we calculated the AUC and the results are presented as averaged AUC over the 1000 runs (Figure 2).

Modeling

Prediction models based on (1) maternal BMI and birth weight, (2) maternal BMI, birth weight, and childhood BMI, or (3) childhood BMI alone were built using logistic regression in the NFBC1966 to predict adolescent overweight, adult overweight, and adult obesity. The odds ratios from the models are presented in Table 2. The prediction models are available in R-language upon request. There were too few cases to analyse adolescent obesity. All analyses were performed separately for girls and boys.

To avoid colinearity, the childhood models at ages 3-8 included only the current BMI value at the specific age, the BMI from 2 years before this age, and the 1-year BMI. The childhood models at age 1 year included the 1-year BMI, and at age 2 years they included the 1-year BMI and the 2-year BMI.

**Table 1** Characteristics of the Northern Finland Birth Cohort 1966 and the Northern Finland Birth Cohort 1986 study population given as means (SD-standard deviation) or numbers (%)

| Variable                      | Level         | NFBC1966 (n = 4111) | NFBC1986 (n = 5414) |
|-------------------------------|---------------|---------------------|---------------------|
|                               |               | Men (n = 2057)      | Women (n = 2054)    | Men (n = 2663) | Women (n = 2751) |
| Birth weight (kg)             | Mean (sd)     | 3595.5 (502.1)      | 3475.2 (467.9)      | 3685.5 (482.6)| 3547.6 (466.8) |
| Maternal BMI (kg/m²)          | Mean (sd)     | 23.3 (3.2)          | 23.2 (3.3)          | 22.2 (3.3)    | 22.4 (3.4)      |
|                               | Missing       | 185                 | 172                 | 56           | 66              |
| Adolescent weight status (IOTF) | Normal (%)    | 1787 (92.1)         | 1756 (90.6)         | 1847 (81.4)| 2026 (86.3) |
|                               | Overweight (%)| 135 (7.0)           | 152 (7.8)           | 320 (14.1)| 260 (11.1)  |
|                               | Obese (%)     | 19 (1.0)            | 31 (1.6)            | 103 (4.5)    | 62 (2.6)        |
|                               | Missing       | 116                 | 115                 | 393          | 403             |
| Adult weight status           | Normal (%)    | 1073 (52.2)         | 1405 (68.4)         |              |                 |
|                               | Overweight (%)| 810 (39.4)          | 445 (21.7)          |              |                 |
|                               | Obese (%)     | 174 (8.5)           | 204 (9.9)           |              |                 |

*P*-value < 0.05 for differences between genders within each cohort.

BMI, body mass index; IOTF, International Obesity Task Force.
TABLE 2 The odds ratios (OR) for the different parameters of prediction models developed in the Northern Finland Birth Cohort 1966 for the outcomes of adolescent overweight, adult overweight, and adult obesity

|                      | Male          |            | Female       |            |
|----------------------|---------------|------------|--------------|------------|
|                      | OR            | CI.95      | P-value      | OR         | CI.95      | P-value      |
| **Adolescent overweight** |               |            |              |            |            |              |
| Birth weight         | 0.78          | [0.50;1.23]| 0.287        | 0.92       | [0.58;1.46]| 0.7225       |
| Maternal BMI         | 1.16          | [1.08;1.23]| <0.0001      | 1.15       | [1.09;1.22]| <0.0001      |
| BMI at 1 year        | 0.98          | [0.76;1.24]| 0.8928       | 0.89       | [0.70;1.12]| 0.3201       |
| BMI at 3 years       | 1.60          | [1.09;2.41]| 0.02113      | 1.39       | [0.95;2.03]| 0.09024      |
| BMI at 5 years       | 1.36          | [1.07;1.73]| 0.01165      | 1.63       | [1.31;2.04]| <0.0001      |
| **Adult overweight** |               |            |              |            |            |              |
| Birth weight         | 0.81          | [0.62;1.04]| 0.09791      | 0.86       | [0.65;1.15]| 0.3131       |
| Maternal BMI         | 1.08          | [1.04;1.13]| 0.0001942    | 1.13       | [1.08;1.17]| <0.0001      |
| BMI at 1 year        | 1.00          | [0.87;1.16]| 0.9533       | 0.89       | [0.76;1.04]| 0.1435       |
| BMI at 3 years       | 1.30          | [1.02;1.66]| 0.03725      | 1.25       | [0.97;1.62]| 0.08838      |
| BMI at 5 years       | 1.13          | [0.97;1.30]| 0.1078       | 1.25       | [1.07;1.45]| 0.004733     |
| **Adult obesity**    |               |            |              |            |            |              |
| Birth weight         | 0.57          | [0.37;0.89]| 0.01369      | 1.04       | [0.67;1.62]| 0.8473       |
| Maternal BMI         | 1.10          | [1.03;1.17]| 0.004626     | 1.12       | [1.06;1.18]| <0.0001      |
| BMI at 1 year        | 0.97          | [0.76;1.22]| 0.8008       | 0.92       | [0.73;1.14]| 0.4416       |
| BMI at 3 years       | 1.38          | [0.95;2.07]| 0.1021       | 1.00       | [0.70;1.43]| 0.9966       |
| BMI at 5 years       | 1.32          | [1.04;1.66]| 0.02177      | 1.56       | [1.27;1.93]| <0.0001      |

Results

Characteristics of the NFBC1966 and the NFBC1986 are displayed in Table 1. The prevalence of adolescent overweight and obesity increases from the NFBC1966 to the NFBC1986. Also the gender distribution of the outcomes changes over this period (Table 1).

Table 2 shows predictive values for models developed at birth, 5 years, and 8 years in the NFBC1966. This is used to predict adolescent overweight in the NFBC1986, and the threshold for being at risk is set at the upper 10%. All predictive values increase with increasing childhood age. At the age of 5 years, we identified 39% of girls and 28% of boys actually becoming overweight as at risk (sensitivity), and we identified 94% of individuals not becoming overweight as not at risk (specificity). Among individuals assessed to be at risk, 52-53% became overweight in both genders (PPV). Table 4 shows an example of the calculation of the predictive values. A positive test (likelihood ratio of 6.9) results in an increase from pretest probability of 13% to a posttest probability of 86%.
of 51%. However, a negative test results in a smaller shift in the probability, from 13% to 9% (negative likelihood ratio = 0.65).

For the model developed at 5 years of age, we furthermore calculated predictive values according to various cut-off points of the estimated risk (Table 5). Setting the cut-point at 50% being at risk lead to a negative predictive value of 97% in girls and 91.9% in boys, meaning that among the 50% with lowest risk, 3% girls and 8.1% boys will become overweight. The predictive values were similar, when we compared overweight according to the IOTF as the prediction model, and the developed prediction models with cut-offs with a similar percentage at risk (Table 5).

**Discussion**

**Main findings**

This study of two large birth cohorts showed that childhood BMI improves prediction models developed from 1 to 8 years of age. A
TABLE 3 Predictive properties when models developed in the Northern Finland Birth Cohort 1966 at different childhood ages are applied to the Northern Finland Birth Cohort 1986 and the threshold of being at risk is set at the upper 10% and the outcome is adolescent overweight

| Age | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
|-----|-----------------|-----------------|---------|---------|
|     | Women           |                 |         |         |
| Birth | 24.0 [19.3;29.6] | 92.1 [90.8;93.3] | 31.8 [25.7;38.6] | 88.8 [87.3;90.2] |
| 5 years | 38.9 [33.2;45.0] | 94.4 [93.2;95.4] | 51.5 [44.6;58.4] | 91.0 [89.6;92.3] |
| 8 years | 49.2 [43.2;55.3] | 96.0 [94.9;96.8] | 65.2 [58.3;71.4] | 92.5 [91.2;93.7] |
|     | Men             |                 |         |         |
| Birth | 17.4 [13.8;21.6] | 91.7 [90.2;93.0] | 33.0 [26.7;39.9] | 82.5 [80.7;84.3] |
| 5 years | 28.2 [23.8;33.0] | 94.2 [93.0;95.3] | 53.4 [46.3;60.3] | 84.8 [83.0;86.4] |
| 8 years | 38.7 [33.8;43.8] | 96.7 [95.7;97.5] | 73.3 [66.6;79.1] | 87.0 [85.4;88.5] |

NPV, negative predictive value; PPV, positive predictive value.

model developed to predict adolescent overweight in the NFBC1966 could, when applied to the NFBC1986 and aimed at labeling 10% as “at risk,” identify one-third of the children, who may become overweight in adolescence. More than 50% of these children identified as being at risk became overweight in adolescence. A prediction model aimed at labeling 10% as at risk of overweight in adolescence on the basis of anthropometric information collected until 5 years of age showed that half of those at risk in fact did become overweight, and this group constituted about one-third of all who became overweight. However, of the 90% of children labeled as “not at risk,” 9% of girls and 15% of boys did become overweight in adolescence. At the age of 5 years, the prediction models of adolescent overweight and adult obesity reached an AUC of 70%, which is commonly considered being a satisfactory prediction. At the age of 8 years, these models reached an AUC of 80%, which is commonly considered a good prediction. No models reached an AUC of 90%, commonly referred to as an excellent prediction.

Comparison with other studies

On the basis of parental age, BMI, profession, smoking, single parenthood, number of household members, pregnancy weight gain, gestational age, birth weight, and genetic variants, Morandi et al. have previously shown in the NFBC1986 that it is possible to predict adolescence overweight at the time of birth, with maternal BMI being the strongest predictor, and that currently known genetic variants have very little to add to such a prediction (10). That model achieved a sensitivity of 49%, a specificity of 80%, a PPV of 33%, and a NPV of 89% in the same data set where the models were developed, when the risk threshold was set at the upper 25%. In our study, we found for women/men a sensitivity of 70/57%, specificity of 82/83%, PPV of 37/44 %, and NPV of 95/89% for the upper 25% in a different data set of individuals born 20 years later (Table 5). The prediction models by Morandi included no early childhood growth measures, but more known risk factors at birth. In our previous work, we have been unable to provide evidence that these other risk indicators’ association with overweight has been stable over time, and we therefore excluded them from the analyses in this study (22). Maternal BMI has been identified as the strongest predictor in prediction models developed at the time of birth (10), but Santorelli et al. only found small improvements of a model at the age of 1 year by including maternal BMI (13). Given the modest impact on AUC (Figure 2) seen when removing birth weight and maternal BMI from the models, these factors have only minor impact on our prediction models as well, for girls at least. Postnatal growth may partly reflect the effect of pre- and perinatal risk indicators and could possibly explain why pre- and perinatal risk indicators add little to the prediction, when early growth is included in the model.

Likelihood ratios (Table 4) are valuable when evaluating prediction models owing to less dependency on prevalence than PPV and NPV (29). An increase from pretest probability of 13% to posttest probability of 51% is likely to be of interest in clinical practice.

Strengths and limitations

Major strengths of this study were (1) the prospective data collection conducted in two large general population-based cohorts with extensive information about clinically relevant risk indicators, (2) the long follow-up, and (3) the possibility to perform an external validation of the prediction models. Many newer prediction models have been developed to predict overweight at the age of 2 to 7 years (13,14,30-32) obviously due to the scarcity of feasible follow-up measures in later life. Taking the dynamic nature of weight development into account with the possible remission of early life overweight, the outcome measures in adolescence and even in adulthood in this study, is a major strength. One limitation was the large variation in measurements and the fact that some children had an insufficient number of measurements for growth modelling, restricting the study population size. We know from other analyses of the representativeness of attendees that...
TABLE 5 Selected thresholds for being at risk and their corresponding predictive values for the 5-year model developed in the Northern Finland Birth Cohort 1966 to predict adolescent overweight and applied to the Northern Finland Birth Cohort 1986 also predicting adolescent overweight

| % labeled as “at risk” | Women | | | | Men | | |
|-----------------------|-------|------------------|------------------|------------------|-------|------------------|------------------|
|                      | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) |
| 75                    | 95.8 [92.6;97.6] | 28.2 [26.1;30.4] | 16.9 [15.1;18.9] | 97.8 [96.1;98.8] | 92.5 [89.4;94.8] | 29.1 [26.9;31.4] | 23.5 [21.3;25.7] | 94.3 [91.9;96.1] |
| 50                    | 88.5 [84.1;91.9] | 55.9 [53.6;58.2] | 23.5 [20.9;26.2] | 97.0 [95.7;97.9] | 78.7 [74.2;82.6] | 56.7 [54.3;59.2] | 29.9 [27.1;32.9] | 91.9 [90.0;93.5] |
| 25                    | 69.8 [64.0;75.1] | 81.8 [79.9;83.6] | 37.0 [32.8;41.3] | 94.7 [93.4;95.7] | 57.2 [52.0;62.2] | 82.6 [80.6;84.4] | 43.5 [39.1;48.0] | 89.1 [87.4;90.7] |
| 20                    | 61.8 [55.8;67.5] | 84.4 [81.7;87.9] | 40.9 [36.2;45.8] | 93.7 [92.4;94.8] | 61.8 [55.8;67.5] | 84.4 [81.7;87.9] | 40.9 [36.2;45.8] | 93.7 [92.4;94.8] |
| 15                    | 51.5 [45.5;57.5] | 90.6 [86.1;91.9] | 45.5 [40.9;50.1] | 92.4 [91.3;93.6] | 40.9 [35.9;46.0] | 91.1 [89.5;92.4] | 51.7 [46.0;57.5] | 86.8 [85.0;88.3] |
| 10                    | 38.9 [33.2;45.0] | 94.4 [93.2;95.4] | 51.5 [46.6;56.4] | 91.0 [89.6;92.3] | 28.2 [23.8;33.0] | 94.2 [93.0;95.3] | 53.4 [46.3;60.3] | 84.8 [83.0;86.4] |
| 5                     | 24.8 [20.0;30.4] | 98.0 [97.2;98.6] | 65.7 [59.9;73.4] | 89.5 [88.1;90.8] | 16.6 [13.1;20.8] | 97.7 [96.8;98.3] | 62.5 [52.5;71.5] | 83.3 [81.5;84.9] |
| 1                     | 5.7 [5.3;6.2] | 99.7 [99.3;99.9] | 75.0 [53.1;89.7] | 87.4 [85.8;88.8] | 5.0 [3.2;7.7] | 99.9 [99.5;100.0] | 90.0 [89.9;97.4] | 81.7 [79.8;83.4] |
| Overweight IOTF       | 39.7 [34.0;45.7] | 94.2 [93.0;95.2] | 51.0 [44.2;57.8] | 91.1 [89.7;92.3] | 25.4 [21.2;30.1] | 96.1 [95.0;97.0] | 60.5 [52.6;67.9] | 84.6 [82.8;86.2] |

For women, BMI at age 5 > 17.1 kg/m² corresponds to the threshold for overweight according to IOTF (10.3%). For men, BMI at age 5 > 17.4 kg/m² corresponds to the threshold for overweight according to IOTF (8%). IOTF, International Obesity Task Force; NPV, negative predictive value; PPV, positive predictive value.

Conclusion

A prediction model based on few stable risk indicators developed in a follow-up study can be used to identify individuals who are at risk for overweight in the NFBC1966 at the age of 5 years. The predictive model can be used to identify a high-risk group who can be offered interventions to prevent overweight. The model can be used to identify high-risk individuals in other settings, such as schools and clinics. The model can also be used to identify individuals who are at risk for overweight in other settings, such as schools and clinics. The model can also be used to identify individuals who are at risk for overweight in other settings, such as schools and clinics.

Should we even try to improve the current model?

We tested our prediction model in a cohort 20 years later with the same risk factors and methods. The results were similar to those in the original study. The model had a high PPV and a low NPV. The model was not improved by adding more risk factors or by using different methods. The model was not improved by using different methods. The model was not improved by using different methods.

External validation

We tested our prediction model in a cohort 20 years later with the same risk factors and methods. The results were similar to those in the original study. The model had a high PPV and a low NPV. The model was not improved by adding more risk factors or by using different methods. The model was not improved by using different methods. The model was not improved by using different methods.
can, when applied to the NFBC1986, identify a subgroup of children at high risk, and identify another large proportion of individuals at low risk. Our prediction model may be valuable in a public health settings dealing with obesity prevention, especially if the prediction model is further developed with more risk indicators and larger cohorts.

Acknowledgments

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

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