Prediction of Childhood Obesity from Nationwide Health Records

Hagai Rossman, MSc1,2,*, Smadar Shilo, MD1,2,3,*, Shiri Barbash-Hazan, MD4,5,*, Nitzan Shalom Artzi, MSc1,2, Eran Hadar, MD1,5, Ran D. Balicer, MD, PhD, MPH1,7, Becca Feldman, ScD7, Arnon Wiznitzer, MD4,5, and Eran Segal, PhD1,2

Objective To evaluate body mass index (BMI) acceleration patterns in children and to develop a prediction model targeted to identify children at high risk for obesity before the critical time window in which the largest increase in BMI percentile occurs.

Study design We analyzed electronic health records of children from Israel’s largest healthcare provider from 2002 to 2018. Data included demographics, anthropometric measurements, medications, diagnoses, and laboratory tests of children and their families. Obesity was defined as BMI ≥95th percentile for age and sex. To identify the time window in which the largest annual increases in BMI z score occurs during early childhood, we first analyzed childhood BMI acceleration patterns among 417 915 adolescents. Next, we devised a model targeted to identify children at high risk before this time window, predicting obesity at 5-6 years of age based on data from the first 2 years of life of 132 262 children.

Results Retrospective BMI analysis revealed that among adolescents with obesity, the greatest acceleration in BMI z score occurred between 2 and 4 years of age. Our model, validated temporally and geographically, accurately predicted obesity at 5-6 years old (area under the receiver operating characteristic curve of 0.803). Discrimination results on subpopulations demonstrated its robustness across the pediatric population. The model’s most influential predictors included anthropometric measurements of the child and family. Other impactful predictors included ancestry and pregnancy glucose.


A global analysis demonstrated that in 2016, 50 million girls and 74 million boys worldwide had obesity,1 making it a global public health crisis.2,3 Predicting excess weight gain in children is important because pediatric obesity is a multisystem disease that can greatly impact a child’s physical and mental health.4 It is associated with a greater risk for premature mortality5 and earlier onset of chronic disorders such as hypertension, dyslipidemia, ischemic heart disease, and type 2 diabetes, with insulin resistance identified in children with obesity as young as 5 years of age.6,7 Previous studies demonstrated an underestimation of obesity by both parents and physicians,8-11 and there is currently little guidance for healthcare professionals to identify infants at risk.12 There is evidence supporting young age as a critical time period for intervention, which includes promoting healthy eating habits and physical activity and reducing sedentary behaviors, which are associated with more beneficial long-term outcomes.13 Few studies have analyzed the effectiveness of family-level interventions designed to prevent obesity in children younger than 5 years of age; however, current evidence suggests that behaviors that contribute to obesity can be positively impacted at an early age.14 Although clinical prediction models are becoming increasingly prevalent in medicine,15 very few studies have focused on childhood overweight or obesity prediction.16,17 Here we analyzed electronic health records (EHR) of children from Israel’s largest healthcare provider to identify the most critical time window in which the largest annual increases in body mass index (BMI) percentile occurs during early childhood and to devise a model targeted to identify high-risk children before this critical time window.

From the 1Department of Computer Science and Applied Mathematics and 2Department of Molecular Cell Biology, Weizmann Institute of Science, Rehovot; 3Pediatric Diabetes Unit, Ruth Rappaport Children’s Hospital of Hadas, Rambam Healthcare Campus, Haifa; 4Heleen Schneider Hospital for Women, Rabin Medical Center, Petach Tikvo; 5Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv; 6Clalit Health Services, Clalit Research Institute, Tel Aviv; and 7Department of Public Health, Faculty of Health Sciences, Ben Gurion University, Beer Sheva, Israel.

*Contributed equally.

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auPR Area under the precision-recall curve
auROC Area under the receiver operating characteristic curve
BMI Body mass index
CDC Centers for Disease Control and Prevention
EHR Electronic health record
WFL Weight-for-length
SHAP Shapley additive explanation
The model was based on a population of children from birth to 2 years of age and predicted their future obesity risk at 5-6 years of age. We extracted predictors and outcomes from a nationwide dataset encompassing more than 10 years of full administrative and clinical data from EHRs of an integrated health care system in Israel, Clalit Health Services. Clalit serves as a nonprofit integrated care organization including more than 4 million individuals from all socioeconomic groups in Israel, encompassing more than one-half of the country’s population, and has a membership turnover of less than 2% annually.¹⁸ The dataset included demographic data, weight and height measurements, clinic and hospital diagnoses, medication dispensation, and laboratory tests from 2002 to 2018 (Section 1 in the Appendix; available at www.jpeds.com).

First, to assess the dynamics of BMI changes in early childhood, we analyzed historical data from children who had a BMI measurement at 13-14 years of age, which is a routine weight checkup in Israel, and had at least 2 BMI measurements within a 1-year interval up to 13 years of age. There were 417,915 children with 1,551,869 measurements who met both criteria.

To construct a prediction model for childhood obesity, a separate cohort was extracted that contained 883,205 children who were born between 2003 and 2013 (Appendix Figure 1; available at www.jpeds.com). Of them, 132,262 children had weight and height measurements during at least 2 routine infant checkups, which are scheduled for all Israeli infants at ages 1, 2, 4, 6, 9, 12, and 18 months and a BMI outcome measurement between the ages of 5-6 years old. These children were further divided according to date of birth: data of 112,038 children who were born between January 1, 2003, and January 1, 2012, were included as training set (data used to fit the parameters of the model) and data of 20,224 children born between January 1, 2012, to January 1, 2013, were included in the temporal validation set (data used to provide an unbiased evaluation of the model), respectively. Extracted predictors included maternal, paternal and siblings’ data. Overall, 130,001 (98.3%) children included in the cohort had maternal data, 107,733 (81.4%) had paternal data, and 83,190 (62.9%) had data of at least 1 sibling. The characteristics of the study cohort are presented in Table I.

All EHR data available were divided by time periods and statistical measures (eg, median, maximum, slope between 2 time points) were taken as predictors for each period. Dispensed medications and clinical diagnoses were categorized by the Anatomical Therapeutic Chemical classification system codes and the International Classification of Diseases, Ninth Revision diagnosis codes, respectively, and counts in different time periods were taken as predictors. Weight, height, weight-for-length (WFL), and BMI data were converted to reference z scores provided by the Centers for Disease Control and Prevention (CDC) ²⁰ Implausible anthropometric measurements were identified by a valid automated method and were excluded from the analyses.²¹ Predictors from maternal pregnancy were divided into time categories in alignment with the routine pregnancy test schedule in Israel. Specific predictors of interest such as ancestry and socioeconomic status surrogates were formulated manually. Predictor generation methods are described in Section 3 in the Appendix. Altogether, 1556 predictors were devised for each child.

The outcome for our models was the obesity status of children at 5-6 years of age. We defined obesity status in accordance with healthcare professionals in Israel, using the CDC BMI reference percentiles. Cutoffs for normal weight, overweight, and obesity were determined using the CDC’s standard thresholds of the 85th percentile for overweight and 95th percentile for obesity. A previous study showed that using other percentile curves, such as the World Health Organization WFL and World Health Organization BMI, provided similar estimates of obesity risk as the CDC percentiles at 5 years of age.²² Distribution of weight status at the target age is described in Section 4 in the Appendix.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Train set (n = 112 038)</th>
<th>Temporal validation set (n = 20 224)</th>
<th>All (n = 132 262)</th>
</tr>
</thead>
<tbody>
<tr>
<td>WFL z score at last infant routine checkup (before 2 y of age), mean (SD)</td>
<td>-0.06 (1.19)</td>
<td>-0.05 (1.17)</td>
<td>-0.06 (1.19)</td>
</tr>
<tr>
<td>Obesity status at last infant routine checkup (before 2 y of age)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Underweight, %</td>
<td>10.085 (9.0%)</td>
<td>1729 (8.5%)</td>
<td>11 814 (8.91%)</td>
</tr>
<tr>
<td>Normal weight, %</td>
<td>82.933 (74.0%)</td>
<td>15 098 (74.7%)</td>
<td>98 031 (74.1%)</td>
</tr>
<tr>
<td>Overweight, %</td>
<td>11.647 (10.4%)</td>
<td>2077 (10.3%)</td>
<td>13 724 (104.3%)</td>
</tr>
<tr>
<td>Obese, %</td>
<td>7.373 (6.6%)</td>
<td>1320 (6.5%)</td>
<td>8693 (6.6%)</td>
</tr>
<tr>
<td>Number of available infant routine checkup measurements, mean (SD)</td>
<td>4.5 (1.8)</td>
<td>5.1 (1.7)</td>
<td>4.6 (1.8)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female, %</td>
<td>54.618 (48.7%)</td>
<td>9694 (47.9%)</td>
<td>64 312 (48.6%)</td>
</tr>
<tr>
<td>Male, %</td>
<td>45.382 (51.3%)</td>
<td>10 550 (52.1%)</td>
<td>67 850 (51.4%)</td>
</tr>
<tr>
<td>Number of children with maternal data, count (%)</td>
<td>103 989 (98.3%)</td>
<td>26 012 (98.2%)</td>
<td>130 001 (98.3%)</td>
</tr>
<tr>
<td>Maternal age at childbirth, y, mean (SD)</td>
<td>30.1 (5.2)</td>
<td>30.5 (5.2)</td>
<td>30.2 (5.2)</td>
</tr>
<tr>
<td>Maternal prepregnancy BMI, m/kg², mean (SD)</td>
<td>23.5 (4.7)</td>
<td>23.3 (4.5)</td>
<td>23.5 (4.6)</td>
</tr>
<tr>
<td>Number of children with paternal data, count (%)</td>
<td>86 393 (81.7%)</td>
<td>21 340 (80.6%)</td>
<td>107 733 (81.4%)</td>
</tr>
<tr>
<td>Paternal age, y, mean (SD)</td>
<td>33.1 (5.9)</td>
<td>33.3 (5.7)</td>
<td>33.2 (5.9)</td>
</tr>
<tr>
<td>Paternal BMI, m/kg², mean (SD)</td>
<td>25.9 (4.3)</td>
<td>25.5 (4.2)</td>
<td>25.9 (4.3)</td>
</tr>
<tr>
<td>Number of children with sibling data, count (%)</td>
<td>69 437 (62.0%)</td>
<td>13 753 (68.0%)</td>
<td>83 190 (62.9%)</td>
</tr>
<tr>
<td>Number of siblings per child, mean (SD)</td>
<td>1.1 (1.2)</td>
<td>1.3 (1.4)</td>
<td>1.1 (1.3)</td>
</tr>
<tr>
<td>Sibling BMI CDC z score, mean (SD)</td>
<td>-0.01 (1.04)</td>
<td>-0.03 (1.01)</td>
<td>-0.02 (1.04)</td>
</tr>
</tbody>
</table>
For our prediction task, we trained Gradient Boosting trees (Section 5 in the Appendix). The model was initially fit on a training dataset, which is a portion of the data used to fit the parameters of the model, and then tested on a separate validation dataset in order to provide an unbiased evaluation of the model. As stringent tests, we used both temporal and geographic validations, thus testing the performance of our model for distribution shifts over time and geographic location. The temporal validation set contained children born between 2012 and 2013. The geographic validation set contained all the clinics in the most populated and multiethnic city in Israel, Jerusalem. Unless stated otherwise, the reported results are on the temporal validation sets. Full results are available in Table II (available at www.jpeds.com).

To compare the computational model with current practice, we considered the last WFL z-score routine checkup measurement available before 2 years of age as a baseline model. This is in line with current guidelines that recommend clinicians to assess a child’s current nutritional and obesity status by calculating WFL percentile or BMI percentile in children 0-2 years of age, or older than 2 years of age, respectively. The WFL z-score thus emulates the information a caregiver has today to assess the current obesity status and future obesity risk of children younger than 2 years of age. This variable also contains information of sex and age, as it standardizes by them.

We analyzed the discrimination results of the model using the areas under the receiver operating characteristic (auROC) and the area under the precision-recall curves (auPR) analyses. Although the auROC curve represents the probability that a randomly chosen diseased individual is ranked greater than a randomly chosen healthy individual, the auPR curve provides the precision (positive predictive value) of the model for corresponding recall (sensitivity) values. As only auPR curve changes with the ratio of positives and negatives in the data, it is more suitable in cases of imbalanced datasets in which the number of negatives outweighs the number of positives significantly. These analyses also were performed across different subgroups including sex; obesity status at baseline as defined by the last available WFL z-score before 2 years of age; and the presence of at least one chronic disease defined as at least one diagnosis from a previously defined classification system.

Calibration refers to the accuracy of risk estimates of the model relating to the agreement between the estimated and observed number of events. As poorly calibrated models can potentially lead to erroneous clinical decision-making, we assessed the calibration of the model. Applying a clinical decision thereafter will vary and depend on the costs and benefits of the action, often assessed both clinically and economically. Decision curves offer a graphical tool to analyze clinical utility of adopting a new risk prediction model. The curves contain information that can guide clinicians to make decisions based on the risk thresholds and tradeoffs (costs and benefits) of their decision to treat. The costs and benefits can be translated into a function of the optimal threshold probability (Section 9 in the Appendix).

Finally, we investigated risk factors from the model by analyzing which predictors most attribute to the model’s prediction. We used the SHapley Additive exPlanation (SHAP) method, which aims to interpret the output of a machine learning model. A predictor’s Shapley value represents the average change in the model’s output by conditioning on that predictor when introducing predictors one at a time over all predictor orderings. Shapley values are calculated individually for every child’s predictor. An important property of Shapley values is that they are additive, meaning that the Shapley values of a child’s predictors add up to the predicted log-odds of obesity for that child. We transformed this value for each predictor and obtained a relative risk score. We can therefore analyze predictor contributions at the individual level, by examining plots of the Shapley value as a function of the predictor value for all individuals (Section 8 in the Appendix). This method enables us to capture nonlinear and continuous relations between a predictor’s impact on the prediction and the predictor’s value. A vertical spread in such a plot implies interaction with other predictors in the model, which would not have been attainable using a linear model, without explicitly modelling the interaction.

Building a model with many correlated predictors (e.g., a child’s weight measurement at adjacent timepoints) is bound to suffer from severe collinearity of the predictors, and consequently the predictor contributions will be spread across these related predictors in a non-trivial way. To tackle this, we made use of the additive property of Shapley values. By adding up the Shapley values of related predictors, grouped together according to domain knowledge, we could report an analysis on this group of predictors (Section 8 in the Appendix). This gives better estimates of relevant risk scores. Another use of the additive property allows adding predictors according to groups and analyzes the model globally by taking the mean over absolute Shapley values of all children in each group of predictors. This gives insight on the impact of a predictor group as a whole.

**Results**

Retrospective BMI and WFL z-score values in early childhood were analyzed initially to construct a model targeting the most critical time window in which maximal acceleration of weight occurs. We divided 417 915 adolescents into 2 groups: obese and nonobese at 13-14 years of age (Figure 1, A and B; available at www.jpeds.com). Among those who did not have obesity, the mean change in BMI z-score of children who did not have obesity between 1 and 14 years of age remained close to 0, with an annual mean change of less than 0.1 z scores. However, for children with obesity at 13-14 years of age, the BMI z-score incremented throughout infancy and early childhood, with the largest annual increase in BMI z-score observed at 2-4 years of age. This result motivated us to construct a model aimed at identifying children before the age of 2 years who will be at high risk for obesity within the subsequent 3-4 years of age.

Next, to further understand the BMI z-score transition over the first 6 years of life, we analyzed the transition of
obesity status in the 132,262 children that were included in our cohort. Obesity status was defined for each child at 2 time points: the last available routine checkup before 2 years of age and at 5-6 years of age. This analysis revealed that more than one-half of children with obesity at 5-6 years of age had normal weight before 2 years of age (50.5%).

We next constructed a model among 132,262 eligible children aged 0-2 years for prediction of childhood obesity at 5-6 years of age and evaluated the discrimination performance of the model using the auROC and auPR curves (see Methods) (Figure 2, A and C). Notably, our model outperforms the baseline model based on the child’s last WFL z score with an auPR of 0.312 (0.263-0.370) compared with 0.243 (0.189-0.312). Both temporal and geographic validation results are summarized in Table II. We analyzed clinical utility by constructing decision curves (Figure 2, D). Notably, our model dominates over other strategies in net benefit over all threshold probabilities, with significant margins in the lower threshold probability regime.

We further analyzed the discrimination results (auPR) of our model on different subpopulations of children (Section 6 in the Appendix). First, we evaluated the effect of sex on the model’s performance and found similar results for boys and girls. We then evaluated children who had at least one diagnosis of a complex chronic condition using a previously defined classification system. The discrimination of the model was similar for children with chronic medical conditions, demonstrating the robustness of the model across a clinically heterogeneous pediatric population. Finally, discrimination performance was evaluated in subpopulation defined by obesity status as defined by the last available WFL z score before 2 years of age. Our model had the greatest auPR in children with obesity, followed by overweight and normal weight before 2 years of age. It outperformed the baseline model in predicting future obesity in all infants, regardless of obesity status at baseline. Expectedly, an increase in the number of documented anthropometric measurements during routine checkups improved the discrimination performance of the model.

We next assessed the performance of multiple prediction models for childhood obesity at 5-6 years of age at the following time points: birth (up to the time of delivery, without birth weight, and mode of delivery), 6 months, 1 year, and 1.5 years of age. The effect of the child’s age at prediction and the model discrimination performance are presented in Figure 3, A, and in Section 7 of the Appendix Table II (available at www.jpeds.com). As expected, the model performance improved when the prediction is done at an older age, which is closer to the age at the defined outcome. However, a prediction model based on predictors available up to day of birth has an auROC of 0.715 and auPR of 0.181, slightly better than the baseline model based on the child’s WFL at 1 year of age, which has an auROC of 0.709 and auPR of 0.176 (Appendix). Our model outperformed the baseline model at every age point assessed.

An analysis of predictor attribution was performed using Shapley values (see Methods). Figure 3, A presents a global analysis of the model’s predictor attributions. The mean of absolute summation of Shapley values for different groups of predictors is presented for the entire cohort. We also examined predictor importance dependence plots of the Shapley value as a function of the predictor value for all individuals (Section 8 in the Appendix). As expected, most of the influential predictors were previous anthropometric measurements of the child and their family, with the child’s last measured WFL z score being the most impactful predictor (Figures 4, A and B). We next evaluated the dependence plots for several clinical variables that have been previously associated with childhood obesity: Familial BMI, ethnicity, and maternal pregnancy glucose levels. Anthropometric measurements of the child, his parents and siblings (Figures 4, A, B, and E) and North African Jewish descendants (Figure 4, H) had a considerable impact on the prediction. Maternal blood glucose measured in pregnancy as part of a 50-g glucose challenge test also was influential for the prediction of obesity, with relative risk increasing monotonically across the entire maternal glucose spectrum and reaching above 1 in values greater than 120 mg/dL (Figure 4, F).

An analysis of the relative importance of different groups of predictors at different ages revealed that the most influential predictors at birth are anthropometric measurements of the siblings, mother, and father. Following these, the influence of the child’s own anthropometrics measurements becomes more substantial and is roughly equal to the contribution of all other predictors at 1 year of age. Laboratory tests, medication dispensing, and medical diagnoses have relatively little influence, which decreases as the data on the child’s anthropometrics accumulates (Figure 3, B). Using information on pharmaceutical prescriptions, we next analyzed the effect of in utero and early life antibiotic exposure and revealed that neither the duration of antibiotic exposure nor the age of first exposure impact the prediction of obesity risk at 5-6 years of age.

Discussion

The target age of our prediction model is supported by our findings on BMI acceleration patterns as well as a study on the German population that revealed very similar patterns, marking 2-6 years of age as the maximal BMI acceleration time period. Our model is therefore timed to identify children at risk before this critical time window, in which mature eating patterns become more developed as children reduce breast milk or formula consumption. In addition, our analysis of the transition in obesity status in the first 6 years of life revealed that most children with obesity had normal weight during the first 2 years of life, underscoring the importance of building a tool that allows clinicians to identify high-risk infants that are considered to have a normal weight at infancy but will develop obesity, as they will constitute the majority of children with obesity in the future.

Our model achieved an auROC of 0.803 and auPR of 0.312. Further analysis of prediction performance on subpopulations of the cohort demonstrated robustness in
discrimination performance across the entire pediatric population, including children with complex chronic diseases. Unlike previous studies, our results were similar for boys and girls (Appendix). The model aimed at predicting obesity before 2 years of age and demonstrated family anthropometric measurements as top predictors in determining future obesity risk of the child. We have shown that a prediction model constructed prebirth, which is mainly based on family anthropometric measurements has very similar performance of predicting at 1 year of age based on the child’s last available weight and length measurements (Figure 3, A). These results highlight the importance of family-wide interventions to prevent childhood obesity. Preventive strategies that include nutritional and physical activity education, and parent skills training can therefore be targeted toward these known risk factors. Although the effect of prevention interventions in early childhood varies across trials, partially resulting from a wide range of interventions tested, some studies show promising results.
The mechanisms involved in the development of obesity in children are complex and include genetic, developmental, and environmental factors. Our large cohort of Israeli children represents a diverse and multiethnic population with genetic heterogeneity. Many of the variables found to be important in our model were directly related to the child’s previous anthropometric measurements. Familial anthropometric measurements, including paternal, maternal, and sibling’s BMI, were also important, in line with previous studies showing associations between these variables and childhood obesity. Among familial data, sibling’s BMI had the greatest impact on the prediction model, most likely due to shared genetic and environmental influences.

There is evidence that the uterine environment may cause a permanent influence on fetus’ future health, and may lead to enhanced susceptibility to diseases later in life. This concept is defined as “gestational programming” and is thought to be mediated by epigenetic mechanisms. Data on maternal pregnancy allow a unique opportunity to analyze associations of these predictors to the future obesity status of the offspring. One of the influential predictors in pregnancy was maternal blood glucose values (Figure 4, F). An increase in glucose challenge test during pregnancy, adjusted for all other predictors incorporated in the model (such as maternal BMI), was associated with a greater risk for childhood obesity. This association, which was apparent even in glucose values that are considered in the normal range, is in line with recent studies, demonstrating that exposure to greater glucose levels in utero throughout the entire maternal glucose spectrum is significantly associated with childhood obesity and insulin resistance of the offspring and is independently associated with childhood adiposity. Ethnicity as a risk factor has previously been studied in the United Kingdom and US populations, in which a greater prevalence of obesity was found among children of African descent. In the Israeli population, our analysis revealed North African Jewish descendancy as a contributor for predicting obesity.

Our study has several limitations. First, the majority of children in our dataset were excluded due to inadequate data on routine anthropometric measurements prior to 2 years of age (Appendix). The dataset does not contain information on nutrition or lifestyle habits, parental education, and socioeconomic status. Data on mode of delivery, gestational age, and birth weight were available for only a portion of the children included in the cohort. In addition, we did not have genetic information. Although currently known genetic variants have a relatively small contribution in childhood obesity prediction, a genome-wide polygenic risk score for obesity was associated with a gradient in weight that started to emerge in early childhood, and predicted differences in weight during early childhood. Thus, the incorporation of genetic information to the model may further enhance its predictive performance. Second, our data are retrospective in nature and thus may suffer from potential biases and be affected by a variety of healthcare processes. We tried to minimize sampling bias by choosing children based on the schedule of routine measurements of weight and height. Third, the prediction model is based solely on data of Israeli children. However, our validation process, including a geographic validation, the well-known universal risk factors for childhood obesity emerging from our analysis of the model, and the similarity of our analysis on BMI acceleration patterns to an independent, German cohort, all indicate that our results may be generalized to other populations as well. Finally, one study to explore the use of obesity risk tools in clinical practice demonstrated that identification of future risk during infancy was viewed positively by parents, no studies have examined the clinical impact of using these tools for intervention. Our study paves the way for future trials of focused intervention addressing the real-life efficacy of this approach.
Figure 4. Interpretation of the model. **A**, Shapley values (in absolute log-odds scale) of different groups of predictors. Note that the scale of the y-axis in **B-H** varies between panels. **B**, Predictor importance (Shapley values in log-odds scale) of the top 15 contributing predictors **C-H**, Plots showing in the lower part a histogram of the distribution of a predictor in the data and in the upper part a dependence plot of the predicted relative risk for obesity at 5-6 years of age vs the value of the predictor for **C**, child last WFL z score; **D**, siblings mean BMI z score; **E**, parental mean BMI: maternal (pink) and paternal (green); **F**, maternal 50-g GCT results during pregnancy; **H**, Child North African Ancestry index. GCT, glucose challenge test.

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Reprint requests: Prof Eran Segal, PhD, Department of Molecular Cell Biology and Department of Computer Science and Applied Mathematics, Weizmann Institute of Science, Rehovot, Israel. E-mail: eran.segal@weizmann.ac.il

Data Statement

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Intermittent Phenobarbital Treatment to Prevent Recurrent Febrile Seizures


This pioneering and cleverly designed study assessed the efficacy of intermittent phenobarbital dosing in preventing recurrent febrile seizures after the initial febrile convulsion. The authors performed an observational study of a cohort of 18,700 children born between 1960 and 1967 in the Kaiser Foundation Hospital. Records of children seen by network pediatrician clinics were reviewed, and 257 children who had a first febrile seizure before 3 years of age were identified. The authors compared a group of children with phenobarbital prophylaxis prescribed within 30 days of the seizure with the rest of the children (those who were prescribed phenobarbital after more than 30 days or were not prescribed at all). Recurrence rates between children treated and untreated also were compared. The decision for phenobarbital prophylaxis, including treatment regimen and dose, was up to the individual pediatrician and was not standardized. The authors found that the cumulative probability of a having a second seizure was significantly lower in the early prophylaxis group at 6 and 7 months (although it increased from 3.28% to 8%, respectively) compared with the non-early prophylaxis group (15.17% and 18.9%, respectively). The authors concluded that intermittent prophylactic phenobarbital administration was effective in decreasing the risk of recurrent febrile seizures and the efficacy was most significant in the first 6 months after the initial febrile seizure.

Since that report was published, there have been many discussions of whether treatment is necessary, given the benign nature of most febrile seizures. When antiseizure medication is considered, there is the question of whether intermittent administration at the onset of the fever is preferable. However, there are challenges: the seizure may be the first sign of a febrile illness, it is not clear whether therapeutic levels of the antiseizure medication are required to be efficacious, and there is the risk of masking an underlying severe infection. A meticulous approach to address the latter, as well as compliance, was described by Rosman et al in a double-blind randomized placebo-controlled trial of oral diazepam. Detailed instructions were given to the parents regarding administration and duration of treatment. The study staff called families daily during the febrile illness to monitor symptoms, treatment, and side effects.

Lessons learned from these studies should help design future studies of when and how to treat febrile seizures, taking into account various risk factors, including genetic susceptibility, that may play a role for the development of recurrent febrile seizures and other long-term consequences.

Aparna Polavarapu, MD
Solomon L. Mosché, MD
Isabelle Rapin Division of Child Neurology of the Saul R. Korey Department of Neurology
Montefiore Medical Center
Albert Einstein College of Medicine
Bronx, NY

Reference

Figure 1. BMI dynamics in early childhood. A, Mean WFL/BMI z score for children aged 0-2 and 2-18 years of age, respectively, with obesity (red) vs without obesity (blue) at 13 years of age. B, Mean change in annual BMI scores for the same groups of children. Shaded areas are 95% bootstrapped CIs.

Table II. Prediction results

<table>
<thead>
<tr>
<th>Baseline/Model</th>
<th>Discrimination on validation sets</th>
<th></th>
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<tr>
<td></td>
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<td>0.748 (0.706-0.790)</td>
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<td>Model</td>
<td>0.312 (0.263-0.370)</td>
<td>0.803 (0.781-0.825)</td>
<td>0.199 (0.016-0.470)</td>
</tr>
</tbody>
</table>

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