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The first 1000 days and beyond

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CHAPTER 8

DIETARY HABITS IN TODDLERS PREDICT
ACCELERATED GROWTH
BETWEEN TWO AND SIX YEARS OF AGE

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ABSTRACT

Background: Growth between two and seven years of age is an important predictor for later life overweight. Numerous nutritional factors are known for their association with childhood growth.

Objective: To test the relation of toddler dietary habits with growth between two and six years and adiposity.

Design: 2495 children from the GECKO Drenthe birth cohort were measured for BMI and waist circumference at two and six years of age, we calculated the BMI Z-score change over that period. Toddler dietary habits were obtained by parent-reported questionnaires at 11 and 24 months. We classified 44 food items as beneficial or not and combined them into food scores at 11 and 24 months, and an overall score for sustained unhealthy or healthy dietary habits at 11 and 24 months. We tested the association of these food scores with accelerated growth, defined as $>0.67SD$ BMI Z-score change between two and six years of age, and with overweight and abdominal adiposity at two and six years of age, all adjusted for covariates.

Results: Higher food scores, thus unhealthier dietary habits at 11 or 24 months as well as the combined food score were associated with increased growth in BMI Z-score between two and six years of age (OR=1.09 [95%CI: 1.03-1.16], OR=1.10 [95%CI: 1.04-1.17], OR=1.08 [95%CI: 1.03-1.13], respectively). Additionally, unhealthier dietary habits at 24 months were associated with overweight (OR=1.07 [95%CI: 1.001-1.15]). We found no association with overweight at two years of age or abdominal adiposity at two or six years of age.

Conclusion: The importance of nutrition on growth is highlighted by the clear difference in early childhood growth between healthy and unhealthy dietary habits. The explanations for accelerated growth remain unknown but it likely represents a positive energy balance, which may predispose to obesity later in life.

INTRODUCTION

Childhood nutrition plays an important role in growth during infancy and it is, therefore, an important modifiable risk factor for childhood overweight¹⁻⁴. Early detection of the development of (childhood) overweight is important, because prevention and treatment are most effective at a younger age⁵⁻⁷. Furthermore, lifestyle patterns are often established during childhood with high risk of tracking into adult life⁸, which also holds for obesity: obese adolescents are at increased risk of becoming obese adults⁹. An important predictor of overweight later in life is growth between the ages of two and six or seven years^{10,11}. Additionally, this period is predictive of adult cardiometabolic risk¹². Both from a public health perspective as well as from a counseling setting it would be helpful to know which early dietary aspects are predictors for growth between two and six years of age.

Numerous single dietary aspects have been known for their association with growth, BMI and overweight in childhood, e.g. breastfeeding, complementary feeding and consumption of sugar-sweetened beverages^{2,13,14}. However, what is not yet known is which dietary habits during infancy are most important in explaining growth between two and six or seven years of age.

Furthermore, nutrition research has changed its focus from micro- and macronutrients towards a broader view on food groups and dietary habits¹⁵. Single nutrients are distant from the public's understanding but suitable for mechanistic research. Contrary, general dietary habits are close to daily food intake and part of a total healthy or unhealthy dietary pattern. These dietary habits can be regarded as "markers" instead of exact measurements. Dietary habits are better interpretable for public health compared to single nutrients and may improve translation to dietary guidelines¹⁶. Furthermore, objective quantification of exact nutritional intake is rather difficult in young children, because reliability of dietary assessment in infants and toddlers is often poor¹⁷, as the intake of single food items shows large day-to-day and/or week-to-week variation¹⁷. Therefore, we focused on general, easily obtainable dietary habits instead of detailed measurements of nutrient intake.

In the GECKO Drenthe birth cohort, we compared the contribution of multiple dietary habits at 11 and 24 months of life to the change in BMI Z-score between two and six years. We hypothesized that clustered dietary habits into two age-specific food scores

at 11 and 24 months, and one combined food score for dietary habits over the total age window of 11 to 24 months, would predict overweight and growth from two to six years of age.

METHODS

GECKO Drenthe

Data were derived from the GECKO Drenthe birth cohort, a population-based birth cohort to study the determinants of overweight in early life. All mothers from children born from April 2006 to April 2007 and living in Drenthe, a northern province of the Netherlands, were invited to participate during the third trimester of their pregnancy. Detailed information has been published elsewhere¹⁸. The study was approved by the Medical Ethics Committee of the University Medical Center Groningen and performed in accordance with the Declaration of Helsinki and all parents gave informed consent.

Data collection

Staff at Well Baby Clinics were explicitly trained to perform the anthropometric measurements. Body weight was assessed using an electronic scale with digital reading to the nearest 0.01 kg. Height was assessed using an infantometer to the nearest 0.1 cm. Waist circumference was measured with a standard tape measure at the midpoint between the lower costal margin and the anterior superior iliac crest. Birth weight was obtained from midwives' registries. For the current study, we focused on BMI and waist circumference at two and six years of age. For information on infant and toddler dietary habits we used data of parental questionnaires, filled in at 11 and 24 months after birth, the exact questions are shown in the **Supplementary Note**. For the information about breastfeeding versus formula feeding and introduction of solid foods we used questions at 0.5, 1, 2, 3, 4, 6, 7 and 9 months of age. A questionnaire during pregnancy contained questions about socioeconomic status, health and anthropometrics of the parents. The other questionnaires contained (repeated) questions about dietary habits and lifestyle of the child.

Parents of 2997 children intended to participate in the GECKO Drenthe cohort, of whom 2874 ever actively participated in the cohort. For the current analyses, we selected 2495 children with anthropometric data at two and six years of age. We interpolated missing data for weight and height at two years (due to loss to follow-up) using measurements

at 11, 14, 18, 36, 45 or 70 months, using the closest available measurements. All analyses were performed using complete cases for dietary habits and weight status (after this interpolation). Missing values on covariates (due to loss to follow-up) were imputed using five imputation datasets. **Figure 1** shows a flowchart with the numbers of children included in each of the analyses.

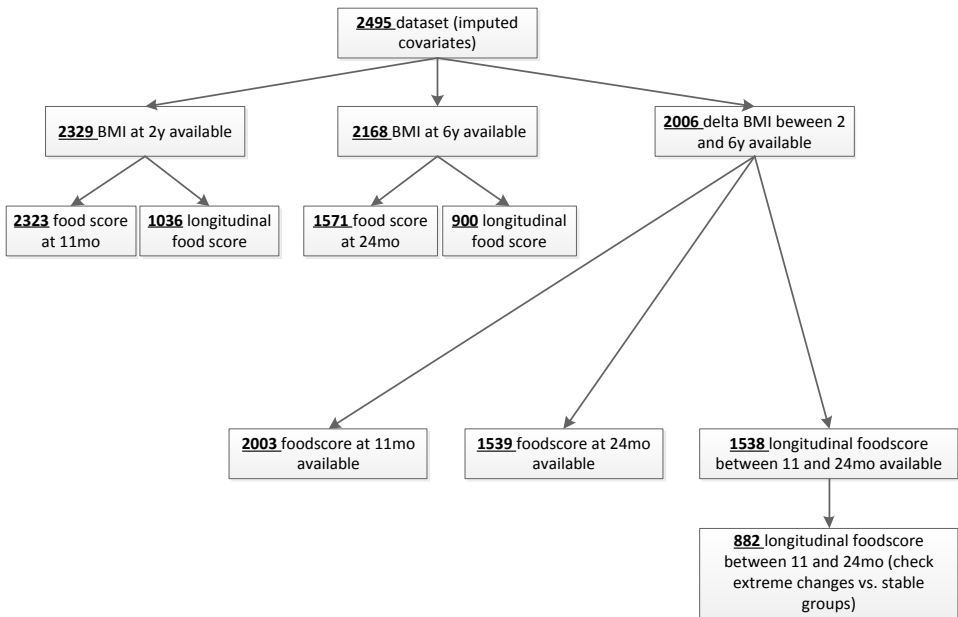


FIGURE 1. Flowchart for the selection of children for each sub-analysis.

For all children we used age- and gender-specific BMI Z-scores that were calculated using the 1997 Dutch growth references in the Growth Analyser software, version 3.5^{19,20}. These BMI Z-scores were calculated at two and six years of age. We calculated BMI Z-score change between two and six years and defined accelerated growth as >0.67 SD increase over a four year period, which corresponds to a quartile increase, a method that has been reported before²¹. Additionally, BMI was classified into normal (and underweight) versus overweight and obesity, based on the gender- and age-specific cut-off points given by Cole et al.²². Moreover we defined a dichotomous measure for abdominal adiposity as a waist circumference above the 90th percentile (**Table 1**).

TABLE 1. Basic characteristics of study participants.

| Child characteristics | N_{total} | Mean ± SE or N(%) |
|--|--------------------------|--------------------------|
| Birth weight (grams) | 2495 | 3541.44 ± 11.22 |
| Female gender | 2495 | 1224 (49.1%) |
| Gestational age at birth (weeks) | 2400 | 39.78 ± 0.033 |
| Child anthropometrics | N_{total} | Mean ± SE or N(%) |
| Age at 2 years measurement (years) | 2336 | 2.09 ± 0.002 |
| BMI (kg/m ² , 2 years) | 2329 | 16.51 ± 0.028 |
| Overweight or obese (kg/m ² , 2 years) | 2329 | 232 (10.0%) |
| Waist circumference (cm, 2 years) | 1664 | 47.51 ± 0.08 |
| High WC>90 th percentile (cm, 2 years) | 1664 | 177 (10.6%) |
| Age at 6 years measurement (years) | 2263 | 5.85 ± 0.007 |
| BMI (kg/m ² , 6 years) | 2168 | 16.05 ± 0.033 |
| Overweight or obese (kg/m ² , 6 years) | 2168 | 317 (14.6%) |
| Waist circumference (cm, 6 years) | 1995 | 54.76 ± 0.10 |
| High WC>90 th percentile (cm, 6 years) | 1995 | 216 (10.8%) |
| Delta BMI Z-score between 2 and 6 years | 2006 | 0.062 ± 0.019 |
| Accelerated growth (>0.67SD increase in BMI Z-score per 4 years, between 2 and 6 years) | 2006 | 418 (20.7%) |
| Parental characteristics | N_{total} | Mean ± SE or N(%) |
| Maternal smoking during pregnancy | 2495 | 354 (14.2%) |
| Age of the mother at date of birth of the child | 2485 | 30.79 ± 0.088 |
| Age of the father at date of birth of the child | 2273 | 33.49 ± 0.104 |
| Maternal prepregnancy BMI | 2495 | 24.75 ± 0.095 |
| Total gestational weight gain in kg | 2026 | 13.76 ± 0.121 |
| Paternal BMI before or during pregnancy | 2213 | 25.56 ± 0.071 |
| Net household income | 2099 | |
| < €1150 / month | | 88 (4.2%) |
| €1151-3050 | | 1367 (65.1%) |
| €3051-3500 | | 368 (17.5%) |
| €3501 or more | | 276 (13.2%) |
| Educational level mother ((applied) university) | 2340 | 859 (36.7%) |
| Educational level father ((applied) university) | 2495 | 791 (31.6%) |
| Maternal ethnicity (European) | 2495 | 2433 (97.6%) |
| Paternal ethnicity (European) | 2291 | 2234 (97.5%) |

Food items and food scores

All dietary habits were reported by the parents (mostly the mother) and reclassified into two or three categories, shown in **Table 2**. We focused on these dietary habits because these are structured habits covering the main elements of toddler dietary habits. First, we calculated the association of dietary habits (at 0.5, 1, 2, 3, 4, 6, 7, 9, 11, 14, 18 and 24 months) with BMI Z-score change between two and six years of age in univariate analyses. Among all these ages, the strongest relations of food items with BMI Z-score change were observed at 11 and 24 months. Therefore, we focused on dietary habits at those two ages. Individual food items are shown in **Table 2**. The first column lists the individual dietary markers, the second column lists the categories for the dietary markers, the third column represents the numbers (and percentage) of children in each category, the fourth and fifth columns show the delta BMI Z-score in each of the dietary categories, with their corresponding p-value for the association between the dietary marker and delta BMI Z-score, and finally in the sixth column we show the (increased or decreased) data-driven scoring for each dietary marker to be used in the food scores. A higher change in BMI Z-score was given a higher score. Sweetened beverages were defined as no sweetened beverages (>75% of all beverage consumption was water or tea without milk/sugar), a combination of beverages (satiating sugars, e.g. milk, and "empty" sugars, e.g. lemonade or soda, potentially combined with water), or >75% of all beverage consumption was "empty" sugars, potentially combined with water. Snacks were a combination of sweet (e.g. cookies), savory (e.g. potato chips) and neutral snacks (e.g. crackers) and these were defined as once per day or less, twice per day, or more than twice per day. The scores for the other food items are presented in **Table 2**.

Whereas individual food items may lack evidence due to their small individual contribution to the endpoint of interest, the combination of multiple food items may become meaningful. Therefore, we created food scores as combination of all dietary habits, described above and shown in **Table 2**. The food score at 11 months was a combination of 23 questions about the five dietary habits in **Table 2** (including 12 repeated questions about breastfeeding and 6 repeated questions about introduction of solid foods), this food score ranged from 0 to 9. The food score at 24 months was a combination of 24 questions about the eight dietary habits in **Table 2** and this food score ranged from 0 to 14. Subsequently, these two food scores were pooled into one combined food score representing stable versus changing dietary habits in the first two years of life (this combined sum score ranged from 0-8).

TABLE 2. Ranking and frequencies of individual eating habits and their association with change in BMI Z-score between 2 and 6 years of age.

| 11 months | Categories | N | Delta BMI-Z (2-6y) | P | Score |
|-----------------------------------|------------------------------------|--------------|---------------------------|----------|--------------|
| First introduction of solid foods | ≤4 months | 794 (33.0%) | 0.125 (0.058 ; 0.191) | | 2 |
| | 4-7 months | 1502 (62.3%) | 0.034 (-0.012 ; 0.080) | 0.080 | 0 |
| | 7-11 months | 113 (4.7%) | 0.053 (-0.106 ; 0.213) | | 1 |
| Breast feeding | Ever | 1952 (79.3%) | 0.052 (0.011 ; 0.092) | 0.257 | 0 |
| | Never | 508 (20.7%) | 0.105 (0.016 ; 0.194) | | 2 |
| Fruit (pieces per day) | 0 pieces per day | 105 (5.2%) | 0.213 (-0.003 ; 0.429) | | 2 |
| | 1 pieces per day | 1510 (75.4%) | 0.079 (0.033 ; 0.124) | 0.216 | 1 |
| | >1 piece per day | 387 (19.3%) | 0.035 (-0.054 ; 0.124) | | 0 |
| Vegetables (tablespoon per day) | 0 tablespoons per day | 135 (6.7%) | 0.111 (-0.090 ; 0.311) | | 2 |
| | 1 tablespoon per day | 1439 (71.8%) | 0.081 (0.035 ; 0.126) | 0.786 | 1 |
| | >1 tablespoons per day | 430 (21.5%) | 0.054 (-0.034 ; 0.143) | | 0 |
| Number of slices of bread | ≤1 per day | 1051 (52.3%) | 0.071 (0.016 ; 0.125) | | 0 |
| | 2 per day | 834 (41.5%) | 0.071 (0.008 ; 0.134) | 0.268 | 1 |
| | ≥3 per day | 125 (6.2%) | 0.212 (0.048 ; 0.377) | | 2 |
| 24 months | Categories | N | Delta BMI-Z (2-6y) | P | Score |
| Sweetened beverages | No sweetened beverages | 18 (1.0%) | -0.125 (-0.496 ; 0.246) | | 0 |
| | Combination of beverages | 1056 (57.9%) | 0.045 (-0.007 ; 0.097) | 0.009 | 1 |
| | Empty sugars (combined with water) | 751 (41.1%) | 0.167 (0.102 ; 0.233) | | 2 |
| Fruit (pieces per day) | ≤1 piece per day | 1234 (67.5%) | 0.073 (0.024 ; 0.122) | | 0 |
| | 2 pieces per day | 570 (31.1%) | 0.123 (0.049 ; 0.197) | 0.284 | 1 |
| | >2 pieces per day | 25 (1.4%) | 0.289 (-0.044 ; 0.622) | | 2 |

TABLE 2. Ranking and frequencies of individual eating habits and their association with change in BMI Z-score between 2 and 6 years of age. *Continued*

| 24 months | Categories | N | Delta BMI-Z (2-6y) | P | Score |
|---|-----------------------------|--------------|------------------------|-------|-------|
| Snacks (servings per day) | ≤1 time per day | 899 (49.2%) | 0.053 (-0.006 ; 0.111) | | 0 |
| | Twice per day | 661 (36.1%) | 0.117 (0.050 ; 0.184) | 0.155 | 1 |
| | ≥3 times per day | 269 (14.7%) | 0.156 (0.054 ; 0.258) | | 2 |
| Potatoes/rice/pasta (tablespoon per day) | <1 tablespoon per day | 421 (23.1%) | 0.113 (0.025 ; 0.200) | | 2 |
| | 1-2 tablespoons per day | 589 (32.3%) | 0.073 (0.003 ; 0.142) | 0.780 | 0 |
| | ≥2 tablespoons per day | 812 (44.7%) | 0.091 (0.030 ; 0.152) | | 1 |
| Vegetables (tablespoon per day) | 0 tablespoons per day | 460 (25.2%) | 0.148 (0.064 ; 0.232) | | 2 |
| | 1 tablespoon per day | 541 (29.7%) | 0.055 (-0.018 ; 0.128) | 0.235 | 0 |
| | >1 tablespoons per day | 821 (45.1%) | 0.081 (0.021 ; 0.141) | | 1 |
| Fries/pizza/pancakes | ≤1 time per month | 514 (28.2%) | 0.033 (-0.045 ; 0.111) | | 0 |
| | 2-4 times per month | 1222 (67.1%) | 0.114 (0.065 ; 0.162) | 0.195 | 1 |
| | >1 time per week | 85 (4.7%) | 0.134 (-0.082 ; 0.349) | | 2 |
| Number of slices of bread | ≤2 per day | 1100 (60.5%) | 0.079 (0.028 ; 0.131) | | 0 |
| | 3 per day | 513 (28.2%) | 0.080 (0.002 ; 0.157) | 0.324 | 1 |
| | ≥4 per day | 204 (11.3%) | 0.178 (0.056 ; 0.301) | | 2 |
| Type of bread | Brown | 1694 (95.7%) | 0.077 (0.119 ; -4.084) | 0.006 | 0 |
| | White (combined with brown) | 76 (4.3%) | 0.358 (0.546 ; -1.634) | | 2 |

P-values are based on ANOVA for the association with delta BMI Z-score.

For the food scores sweetened beverages were defined as no sweetened beverages (>75% of all beverage consumption was water or tea without milk/sugar), a combination of beverages (satiating sugars, e.g. milk, and "empty" sugars, e.g. lemonade or soda, potentially combined with water), or >75% of all beverage consumption was "empty" sugars, potentially combined with water. Snacks were a combination of sweet (e.g. cookies), savory (e.g. potato chips) and neutral snacks (e.g. crackers) and these were defined as once per day or less, twice per day, or more than twice per day.

TABLE 3. Associations of the food scores with anthropometric outcomes at two and six years of age.

| Food score at 11 months | 0-1 (18%) | 2 (27%) | 3 (19%) | 4 (17%) | 5-9 (18%) | P for trend | Sum score (score range 0-9) |
|--|---------------------------------|-------------------------|-----------------------------------|------------------------|--|------------------------|---|
| Accelerated growth between 2 and 6y* | 0.82 (0.56;1.21) | 0.95 (0.68;1.33) | 1.00 | 1.18 (0.83;1.67) | 1.28 (0.91;1.81) | 0.001 | 1.09 (1.03;1.16) |
| Overweight at 2y | 0.91 (0.59;1.42) | 1.28 (0.88;1.88) | 1.00 | 0.96 (0.63;1.46) | 1.30 (0.87;1.94) | 0.049 | 1.07 (0.99;1.15) |
| Abdominal adiposity at 2y (WC>90 th percentile) | 1.50 (0.89;2.51) | 1.55 (0.96;2.49) | 1.00 | 1.65 (1.00;2.72) | 1.67 (1.02;2.73) | 0.639 | 1.02 (0.93;1.12) |
| Food score at 24 months | 0-2 (6%) | 3-4 (27%) | 5-6 (37%) | 7-8 (22%) | 9-14 (8%) | P for trend | Sum score (score range 0-14) |
| Accelerated growth between 2 and 6y* | 0.93 (0.51;1.69) | 0.95 (0.69;1.32) | 1.00 | 1.38 (1.01;1.90) | 1.81 (1.17;2.80) | 0.002 | 1.10 (1.04;1.17) |
| Overweight at 6y | 0.85 (0.43;1.72) | 0.72 (0.48;1.06) | 1.00 | 1.00 (0.69;1.45) | 1.31 (0.79;2.17) | 0.014 | 1.07 (1.00;1.15) |
| Abdominal adiposity at 6y (WC>90 th percentile) | 0.93 (0.42;2.04) | 0.91 (0.58;1.41) | 1.00 | 1.09 (0.71;1.68) | 1.17 (0.63;2.18) | 0.272 | 1.03 (0.95;1.12) |
| Combined food score between 11 and 24 months | Stable healthy (29%) | Middle (43%) | Stable unhealthy (28%) | P for trend | Sum score (score range 0-8) | | |
| Accelerated growth between 2 and 6y* | 0.93 (0.67;1.30) | 1.00 | 1.58 (1.17;2.15) | 0.001 | 1.08 (1.03;1.13) | | |
| Overweight at 6y | 0.66 (0.44;0.996) | 1.00 | 1.09 (0.76;1.56) | 0.015 | 1.05 (0.99;1.11) | | |
| Abdominal adiposity at 6y (WC>90 th percentile) | 0.96 (0.62;1.50) | 1.00 | 1.26 (0.84;1.91) | 0.092 | 1.03 (0.96;1.09) | | |

Results are presented as odds ratios and corresponding 95% confidence intervals.

Analyses are adjusted for covariates birth weight, maternal pre-pregnancy BMI, maternal smoking during pregnancy and paternal education.

Overweight was calculated based on the gender- and age-specific cut-off points given by Cole et al.²².

* Accelerated growth is defined as >0.67SD per 4y.

Bold: P<0.05.

Table 3 shows multivariate logistic regression models for the association between the food scores and growth or weight status. The middle quintile was used as the reference category for calculating odds ratios in the other four quintiles. Additionally, tests for trend were conducted across quintiles using the median food score in each quintile as a continuous variable in the linear regression models

Statistical analysis

The statistical analyses were performed using IBM SPSS Statistics 22 for Windows (SPSS inc, Chicago, Illinois, USA). The significance level was set at 5%. The food scores were tested for their association with accelerated change in BMI Z-score between two and six years of age using logistic regression models. We also tested their association with overweight and abdominal adiposity at two and six years of age with logistic regression models. Based on literature and the association with child BMI in our dataset and to improve generalizability we adjusted the model for birth weight (kg), self-reported maternal pre-pregnancy BMI (kg/m²), smoking during pregnancy (yes vs. no) and paternal education (university vs. less than university). We calculated odds ratios for each food score category relative to the middle reference category.

RESULTS

We studied 2495 children within the GECKO Drenthe cohort with information on dietary habits from 11 to 24 months of age. The exact numbers of children included in the analyses varied by age, as can be seen in the flowchart in **Figure 1**. Basic characteristics are shown in **Table 1**. At two years of age 10% was overweight or obese, while at six years of age this prevalence increased to almost 15%.

Table 2 shows the scoring of the individual dietary habits for the food scores at 11 and 24 months. Additionally we show the frequencies per food item and ANOVA p-values to test the association with BMI Z-score change between two and six years of age. Sweetened beverages and type of bread at 24 months were significantly associated with change in BMI Z-score. No dietary habits at 11 months were individually associated with change in BMI Z-score.

Table 3 shows that these food scores most convincingly showed consistent trends with the risk of accelerated growth, showing a clear dose-response relationships. Thus a

higher food score, representing unhealthier dietary habits, showed an increased risk of accelerated growth velocity (Table 3). However, we also observed dose-response trends with overweight, but not consistently significant with abdominal adiposity. To explore the difference in prediction of overweight and growth further, data on the association between the combined food score and overweight at two and six years of age, as well as change in BMI Z-score are shown in Figures 2A, B and C.

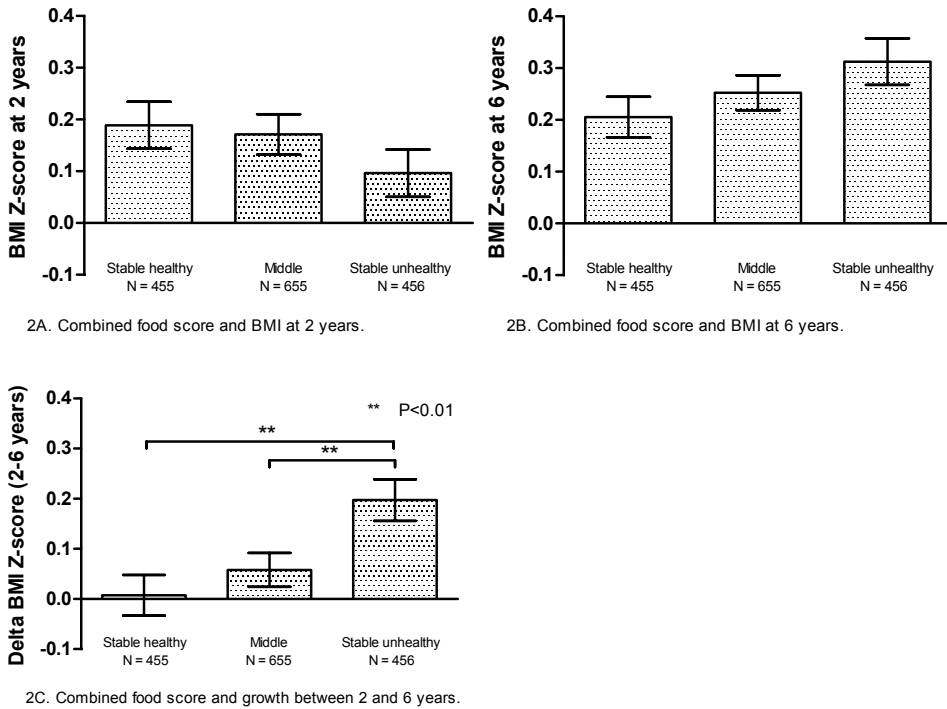


FIGURE 2. Associations between combined food score and BMI Z-score and growth.

DISCUSSION

In this study we showed that food scores, reflecting common dietary habits in toddlers, like eating more or less fruit or vegetables, type of beverage and frequency of snacks, were not consistently related to overweight or increased waist circumference at two or six years of age. However, these dietary habits were related to accelerated growth in terms of BMI. In other words, more unhealthy patterns were related to larger increase in BMI Z-score.

In the first half year of life, perinatal determinants are very predictive for growth velocity^{23,24} but thereafter, environmental aspects like diet become more important. With regard to the known determinants of BMI-related growth velocity of young age, birth weight, duration of breastfeeding, timing of introduction of complementary foods and parity have been identified^{23,25,26}. However, for future adiposity and metabolic health, the increase in BMI Z-score between two and six or seven years seems to be of special interest because of its consistent association with future development of adolescent overweight and metabolic syndrome^{10,12}. Possibly, the change in BMI Z-score best reflects the early environmental influence on development of adiposity. Several studies have examined the determinants of growth in this important age window between two and six years of age. Ong and colleagues showed that growth velocity in terms of weight between zero and five years of age was strongly predicted by parity, breast- or bottle feeding and maternal smoking²⁴. Karaolis-Danckert et al.²⁷ confirmed the relation of parity and breastfeeding, and they also showed gestational age to be an important predictor of growth. Yet another study showed ethnicity, infant BMI, parental overweight and smoking to be associated with growth between three to five years of age²⁸. However, not much evidence exists for early dietary predictors of growth in terms of weight or BMI between two and six years. In our study, the two most significant nutritional predictors of growth velocity were the consumption of sweetened beverages and a daily choice for white bread instead of brown or wholegrain bread. Sweetened beverages have previously been shown as the most important dietary factor to contribute to childhood overweight^{4,29}. Furthermore, in our study, both earlier and later introduction of solid foods seemed to be related to accelerated growth in BMI Z-score later on, however not significantly. Whereas many dietary habits were not individually significantly related to BMI change, many showed mild but consistent dose-response relationships. To investigate their combined effect, we combined the separate dietary habits into a food score at 11 and 24 months.

Mothers who consistently reported unhealthy dietary habits had a child with a relatively low BMI Z-score at two years of age (**Figure 2A**). We can only speculate what explains this inverse association, but it could be that mothers of low weight children either do not care about dietary intake, or actually may be worried about the low weight and give them 'something extra'. Especially the latter hypothesis seems to be supported by the data in **Figures 2A-C**. These figures show that those with unhealthier dietary habits had the lowest BMI Z-score at two years of age (**Figure 2A**) and the highest BMI Z-score at six years of age (**Figure 2B**), thus they gained the most between two and six years

(Figure 2C). It is less likely that mothers of high weight BMI children were selectively underreporting dietary habits, since most mothers are not aware of the adiposity status of their child at toddler age³⁰. Also the reported intake was not dependent on BMI of the mother ($P = 0.21$ for ANOVA of maternal pre-pregnancy BMI over the three combined food score categories). It seems likely that dietary habits are constantly adjusted to the current weight status of the toddler, which makes the cross-sectional data analysis a mixture of causal and reverse-causation relationships. Another possible reason is that despite the 'catch-up' growth, most children still did not reach the cutoff for overweight or obesity. As shown already a while ago in the NHANES data, the obesity epidemic is not only a question of obese becoming fatter, but also of lean individuals becoming less lean³¹.

With respect to the methods used, appropriately estimating food intake in toddlers is a challenge. Studies that have calculated food intake in toddlers before mostly used detailed food frequency questionnaires³². Although exact measurement of nutrient intake in toddlers is very important, reliability of dietary assessment in toddlers is often poor and the intake of single food items shows large day-to-day and/or week-to-week variation¹⁷. However, if the research interest is to investigate energy intake or macro or micronutrient intake, it is the best we have. In our study we presented a combined food score of dietary habits reported by the parents, mostly the mother. This has several advantages¹⁶. It may be a more realistic representation of the daily situation, especially when daily dietary habits are addressed, like the type of bread consumed. Furthermore, dietary patterns are easier to interpret or translate into diets. Therefore, analysis of dietary patterns can be helpful in making dietary recommendations in clinical practice¹⁶. As argued in an editorial by Jacques and Tucker: "we do not eat nutrients, but foods that are combined in certain patterns"³³. This also implicates some methodological issues. First, it means that dietary habits reported by parents cannot be directly translated into what it means for intake of energy or nutrients, since quantification is not exact but a proxy. Second, the dietary habits that we measured can be a proxy for another aspect of an unhealthy diet. For example, in the SPEEDY study, insufficient consumption of fruit or vegetables was related to high consumption of fat and non-milk extrinsic sugars, a cluster which also featured high screen time³⁴. Third, the external validity of the food score is uncertain. Some dietary habits may differ substantially from other countries. For example, in 2011-2012 in the US 34% of all children of 2-19 years old consumed fast food daily³⁵, while in our study only 5% reported intake of fast food once per week or more. Previously reported breakfast skipping in the same GECKO population at preschool age was rare³⁶,

on the other hand comparable to a low prevalence of breakfast skipping in Canadian children between 4 and 8 years of age³⁷. Fourth, we calculated 39 associations in **Table 3**, which may raise the question of correction for multiple testing. However, all food items in these food scores have previously been shown to be related to BMI, overweight and/or growth, therefore, this is not a hypothesis-free test that needs correction for multiple testing. However, after Bonferroni correction for 39 tests ($P < 0.0013$), the food score at 11 months and the combined food score between 11 and 24 months would still be significantly associated with accelerated growth between 2 and 6 years of age. Thus, this would not change the main conclusions of this study.

CONCLUSION

Finding the best predictors of future obesity at early age is important, now that it is acknowledged that early intervention or treatment is most effective. In conclusion, we highlighted the importance of nutrition on growth by the clear difference in early childhood growth between healthy and unhealthy dietary habits. The explanations for accelerated growth remain unknown but it likely represents a positive energy balance, which may predispose to obesity later in life.

REFERENCES

- 1 Michaelsen KF, Larnkjaer A, Molgaard C. Early diet, insulin-like growth factor-1, growth and later obesity. *World Rev Nutr Diet* 2013; 106: 113-8.
- 2 Pearce J, Langley-Evans SC. The types of food introduced during complementary feeding and risk of childhood obesity: a systematic review. *Int J Obes (Lond)* 2013; 37: 477-85.
- 3 Moreno LA, Rodriguez G. Dietary risk factors for development of childhood obesity. *Curr Opin Clin Nutr Metab Care* 2007; 10: 336-41.
- 4 Swinburn BA, Caterson I, Seidell JC, James WP. Diet, nutrition and the prevention of excess weight gain and obesity. *Public Health Nutr* 2004; 7: 123-46.
- 5 Bocca G, Corpeleijn E, Stolk RP, Sauer PJ. Results of a multidisciplinary treatment program in 3-year-old to 5-year-old overweight or obese children: a randomized controlled clinical trial. *Arch Pediatr Adolesc Med* 2012; 166: 1109-15.
- 6 Bocca G, Corpeleijn E, van den Heuvel ER, Stolk RP, Sauer PJ. Three-year follow-up of 3-year-old to 5-year-old children after participation in a multidisciplinary or a usual-care obesity treatment program. *Clin Nutr* 2014; 33: 1095-100.
- 7 Baidal JA, Taveras EM. Childhood obesity: shifting the focus to early prevention. *Arch Pediatr Adolesc Med* 2012; 166: 1179-81.
- 8 Craigie AM, Lake AA, Kelly SA, Adamson AJ, Mathers JC. Tracking of obesity-related behaviours from childhood to adulthood: A systematic review. *Maturitas* 2011; 70: 266-84.
- 9 Singh AS, Mulder C, Twisk JW, van Mechelen W, Chinapaw MJ. Tracking of childhood overweight into adulthood: a systematic review of the literature. *Obes Rev* 2008; 9: 474-88.
- 10 Liem ET, van Buuren S, Sauer PJ, Jaspers M, Stolk RP, Reijneveld SA. Growth during infancy and childhood, and adiposity at age 16 years: ages 2 to 7 years are pivotal. *J Pediatr* 2013; 162: 287.e2.
- 11 Baird J, Fisher D, Lucas P, Kleijnen J, Roberts H, Law C. Being big or growing fast: systematic review of size and growth in infancy and later obesity. *BMJ* 2005; 331: 929.
- 12 de Kroon ML, Renders CM, van Wouwe JP, van Buuren S, Hirasing RA. The Terneuzen Birth Cohort: BMI change between 2 and 6 years is most predictive of adult cardiometabolic risk. *PLoS One* 2010; 5: e13966.
- 13 Gunnarsdottir I, Schack-Nielsen L, Michaelsen KF, Sorensen TI, Thorsdottir I. Infant weight gain, duration of exclusive breast-feeding and childhood BMI - two similar follow-up cohorts. *Public Health Nutr* 2010; 13: 201-7.
- 14 Bachman CM, Baranowski T, Nicklas TA. Is there an association between sweetened beverages and adiposity? *Nutr Rev* 2006; 64: 153-74.
- 15 Ley SH, Hamdy O, Mohan V, Hu FB. Prevention and management of type 2 diabetes: dietary components and nutritional strategies. *Lancet* 2014; 383: 1999-2007.
- 16 Hu FB. Dietary pattern analysis: a new direction in nutritional epidemiology. *Curr Opin Lipidol* 2002; 13: 3-9.
- 17 Livingstone MB, Robson PJ. Measurement of dietary intake in children. *Proc Nutr Soc* 2000; 59: 279-93.
- 18 L'Abée C, Sauer PJ, Damen M, Rake JP, Cats H, Stolk RP. Cohort Profile: the GECKO Drenthe study, overweight programming during early childhood. *Int J Epidemiol* 2008; 37: 486-9.
- 19 DutchGrowthFoundation. Growth Analyzer. 2001-2007; 3.5.
- 20 Fredriks AM, van Buuren S, Burgmeijer RJ, et al. Continuing positive secular growth change in The Netherlands 1955-1997. *Pediatr Res* 2000; 47: 316-23.
- 21 Ong KK, Ahmed ML, Emmett PM, Preece MA, Dunger DB. Association between postnatal catch-up growth and obesity in childhood: prospective cohort study. *BMJ* 2000; 320: 967-71.
- 22 Cole TJ, Bellizzi MC, Flegal KM, Dietz WH. Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ* 2000; 320: 1240-3.
- 23 Kupers LK, L'Abée C, Bocca G, Stolk RP, Sauer PJ, Corpeleijn E. Determinants of Weight Gain during the First Two Years of Life-The GECKO Drenthe Birth Cohort. *PLoS One* 2015; 10: e0133326.

- 24 Ong KK, Preece MA, Emmett PM, Ahmed ML, Dunger DB, ALSPAC Study Team. Size at birth and early childhood growth in relation to maternal smoking, parity and infant breast-feeding: longitudinal birth cohort study and analysis. *Pediatr Res* 2002; 52: 863-7.
- 25 Griffiths LJ, Smeeth L, Hawkins SS, Cole TJ, Dezateux C. Effects of infant feeding practice on weight gain from birth to 3 years. *Arch Dis Child* 2009; 94: 577-82.
- 26 Baker JL, Michaelsen KF, Rasmussen KM, Sorensen TI. Maternal prepregnant body mass index, duration of breastfeeding, and timing of complementary food introduction are associated with infant weight gain. *Am J Clin Nutr* 2004; 80: 1579-88.
- 27 Karaolis-Danckert N, Buyken AE, Kulig M, et al. How pre- and postnatal risk factors modify the effect of rapid weight gain in infancy and early childhood on subsequent fat mass development: results from the Multicenter Allergy Study 90. *Am J Clin Nutr* 2008; 87: 1356-64.
- 28 Griffiths LJ, Hawkins SS, Cole TJ, Dezateux C. Risk factors for rapid weight gain in preschool children: findings from a UK-wide prospective study. *Int J Obes (Lond)* 2010; 34: 624-32.
- 29 de Ruyter JC, Olthof MR, Seidell JC, Katan MB. A trial of sugar-free or sugar-sweetened beverages and body weight in children. *N Engl J Med* 2012; 367: 1397-406.
- 30 Oude Luttikhuis HG, Stolk RP, Sauer PJ. How do parents of 4- to 5-year-old children perceive the weight of their children? *Acta Paediatr* 2010; 99: 263-7.
- 31 Ogden CL, Carroll MD, McDowell MA, Flegal KM. Obesity among adults in the United States--no statistically significant change since 2003-2004. *NCHS Data Brief* 2007; (1): 1-8.
- 32 Voortman T, Kieft-de Jong JC, Geelen A, et al. The development of a diet quality score for preschool children and its validation and determinants in the Generation R Study. *J Nutr* 2015; 145: 306-14.
- 33 Jacques PF, Tucker KL. Are dietary patterns useful for understanding the role of diet in chronic disease? *Am J Clin Nutr* 2001; 73: 1-2.
- 34 Elsenburg LK, Corpeleijn E, van Sluijs EM, Atkin AJ. Clustering and correlates of multiple health behaviours in 9-10 year old children. *PLoS One* 2014; 9: e99498.
- 35 Vikraman S, Fryar CD, Ogden CL. Caloric Intake From Fast Food Among Children and Adolescents in the United States, 2011-2012. *NCHS Data Brief* 2015; (213): 1-8.
- 36 Kupers LK, de Pijper JJ, Sauer PJ, Stolk RP, Corpeleijn E. Skipping breakfast and overweight in 2- and 5-year-old Dutch children--the GECKO Drenthe cohort. *Int J Obes (Lond)* 2014; 38: 569-71.
- 37 Barr SI, DiFrancesco L, Fulgoni VL, 3rd. Breakfast consumption is positively associated with nutrient adequacy in Canadian children and adolescents. *Br J Nutr* 2014; 112: 1373-83.

CHAPTER 8

SUPPLEMENTARY MATERIAL

SPECIFICATION OF ALL QUESTIONS USED IN THIS STUDY (TRANSLATED FROM DUTCH TO ENGLISH)

All 23 questions used for the food score at 11 months of age:

Does your child currently get breastfeeding? → this question was repeated 12 times between 0.5 until 24 months of age.

Have you started the introduction of solid foods? → this question was repeated 6 times between 3 until 11 months of age

If yes, which solid foods have been introduced?

Fruit / vegetables / porridge / bread / other, namely

If yes, how much does your child eat from these solid foods?

... bottles of porridge / bites / bowls / slices of bread

Does your child currently eat fruit (at 11 months of age)?

Does your child currently eat vegetables (at 11 months of age)?

... slices of bread, topping:..... (at 11 months of age)

... slices of bread, topping:..... (at 11 months of age)

... slices of bread, topping:..... (at 11 months of age)

All 24 questions used for the food score at 24 months of age:

... cups of whole milk (average) per day

... cups of reduced fat milk (average) per day

... cups of low fat milk (average) per day

... cups of sweetened milk beverages (average) per day

... cups of yoghurt drink (average) per day

Fruit

Fruit (1 portion is 1 snacks <1x per day / 1x per day / 2x per day / 3x per day / >3x per day

Hot meal

... tablespoons of potatoes / rice / pasta

... tablespoons of vegetables

Other

| | |
|--------------|--|
| French fries | 1x per month or less / 1x per 2 weeks / 1x per week / >1x per week |
| Pizza | 1x per month or less / 1x per 2 weeks / 1x per week / >1x per week |
| Pancakes | 1x per month or less / 1x per 2 weeks / 1x per week / >1x per week |

Bread

... slices of bread with cheese, meat or fish

... slices of bread with peanutbutter

... slices of bread with sweet toppings

... slices of bread with fruit (e.g. banana or strawberries)

... slices of bread without toppings

Type of bread mostly brown / mostly white / other, namely

Snacks

Neutral snacks
(e.g. (rice)cracker) <1x per day / 1x per day / 2x per day / 3x per day / >3x per day

Salty snacks
(e.g. crisps, cheese) <1x per day / 1x per day / 2x per day / 3x per day / >3x per day

Sweet snacks
(e.g. cookie, candy) <1x per day / 1x per day / 2x per day / 3x per day / >3x per day

Drinks

Water / tea <1x per day / 1x per day / 2x per day / 3x per day / >3x per day

Lemonade <1x per day / 1x per day / 2x per day / 3x per day / >3x per day

Fruit juice <1x per day / 1x per day / 2x per day / 3x per day / >3x per day

Soda (e.g. cola, sprite) <1x per day / 1x per day / 2x per day / 3x per day / >3x per day

