EARLY LIFE RISK FACTORS IN THE DEVELOPMENT OF SOCIAL INEQUALITIES IN PRE-SCHOOL-AGE OVERWEIGHT

THE GENERATION R STUDY

LENIE VAN ROSSEM

COLOFON

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THE GENERATION R STUDY

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CONTENTS

LIST OF ABBREVIATIONS

ANOVA	Analysis of Variance
BMI	Body Mass Index
BF	Breastfeeding
CI	Confidence Interval
FAD	Family Assessment Device
WFA	Weight-for-Age
WFH	Weight-for-Height
WHO	World Health Organization
IOTF	International Obesity Task Force
LN	Logaritmus Naturalis
MABS	Mother and Baby Scales
N.A.	Not applicable
NI	Not investigated
(A)OR	(adjusted) Odds Ratio
REF	Reference
SAS	Statistical Analysis Software
SES	Socioeconomic Status
SD(S)	Standard Deviation (Score)
SPSS	Statistical Package for Social Sciences
SQRT	Square Root
SS + TR	Sum of subscapular and triceps skinfold thicknesses
SS / TR	Ratio of subscapular and triceps skinfold thicknesses

CHAPTER 1
INTRO-
DUCTION

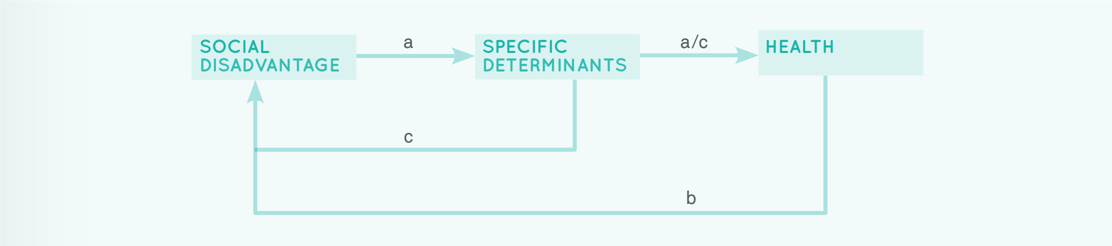
1.1 DESCRIPTION AND UNDERSTANDING OF THE ASSOCIATION BETWEEN SOCIAL DISADVANTAGE AND MORTALITY AND MORBIDITY

Social disadvantage, a collective term which may (among others) refer to low socioeconomic status (i.e. low educational level, low income, low job status) or non-native ethnicity, is a strong determinant of health.[1,2] Socioeconomic status and ethnicity (the latter being strongly associated with socioeconomic status) are of particular interest in the context of the subject of this thesis, i.e. overweight. These items are addressed in this introductory chapter.

People with a low socioeconomic status often have poor health compared with those with a high socioeconomic status.[3] In addition, not only the poorest people have worse health, health tends to gradually increase with increasing socioeconomic status.[4,5] Differences in health between subgroups in a population can be evaluated by comparing differences in life expectancy. In the Netherlands, for example, lower-educated men have a life expectancy at birth of 72.2 years, whereas higher-educated men have a life expectancy at birth of 79.1 years. For lower-educated women, life expectancy at birth is 78.1 years compared to 83.3 years for higher-educated women.[6] Another indicator of health in populations is *healthy* life expectancy: this is defined by the World Health Organization (WHO) as the average number of years that a person can expect to live in "full health" by taking into account the years lived in less than full health due to disease and/or injury. Lower-educated people have a lower healthy life expectancy at birth than higher-educated people: the difference is 19.2 years for men and 20.6 years for women.[7]

Until now, two perspectives have been proposed to understand socioeconomic inequalities in health (Figure 1.1). Socioeconomic inequalities in health may arise because people change their socioeconomic status (e.g. upwards). This is called social mobility and can refer to intergenerational (compared to a person's parents) or intragenerational (compared to that person earlier in time) mobility. This mechanism is called the *selection perspective*. Selection can be either direct or indirect.[8] Direct selection is the phenomenon that people in (ill) health are less likely to move (upward) in socioeconomic status. Indirect selection is the phenomenon that determinants of health are associated with social mobility and later health. One example of these determinants may be *coping styles*: better coping styles may be associated with higher socioeconomic status, and

Figure 1.1 Causation and selection mechanism explaining the association between social disadvantage and health.



a = Causation b = Direct selection c = Indirect selection

people with better coping styles are likely to be in better health. Another mechanism that applies most on how the data are described in this thesis, is called the *causation perspective*, which assumes that socioeconomic inequalities in health emerge because risk factors are unequally distributed among social subgroups. The main group of risk factors (with all factors interrelated) are material, psychosocial and behavioral factors, that in turn lead to biological characteristics and subsequently to disease.[9] These determinants may explain 40-70% of socioeconomic inequalities in health.[9] A third, relatively new perspective, integrates these two latter perspectives by taking the *life course* into account.[9,10]

Apart from the fact that socioeconomic inequalities in health are perceived to be unfair in many cases, decreasing socioeconomic inequalities in health can improve the health status of the population as a whole.[11] Therefore, the Dutch cabinet policy 'Choosing a healthy life 2007-2010' includes the aim to decrease socioeconomic inequalities in health.[12] One possibility to decrease socioeconomic inequalities in health is to decrease socioeconomic inequalities in the most prevalent diseases. For example, in the Netherlands, cardiovascular diseases are a main cause of death and disability,[13] and contribute to the higher death and disability rate among socially disadvantaged groups.[14-17]

1.2 OVERWEIGHT AND OBESITY AS EXPLANATORY FACTORS IN THE ASSOCIATION BETWEEN SOCIAL DISADVANTAGE AND CARDIOVASCULAR DISEASES

A strong determinant of cardiovascular disease is overweight,[18] illustrated by the fact that one in seven cases of cardiovascular diseases can be attributed to being overweight or obese.[19]

Overweight and obesity are the result of a distorted energy balance. In other words, the body accumulates fat because there is too much energy supply and/or too low energy expenditure.[20, 21] Fat storage in the body used to have an important function, because in periods of food scarcity fat was released to meet energy needs. In our developed society, however, food scarcity no longer occurs. [20, 21] A permanent accumulation of fat results in some biochemical processes that may lead to cardiovascular diseases.[22] In addition, as with cardiovascular diseases, both genes and the environment play an important role in the development of overweight and obesity. [23, 24] Although it is difficult to disentangle the effects of genetic factors from environmental ones (especially because genes and environment may interact), it is estimated that about 40-70% of individual variation in overweight is heritable. [25] The remaining part is environmental, or expresses in certain environments in obesity-prone people. [26] Therefore, overweight and obesity are probably to a large extent preventable.

In the Netherlands, overweight is estimated to be present in about 50% of the adult population, and obesity occurs in about 10% of adults. [27] Overweight is not only a problem of adulthood, but is increasingly prevalent in childhood. For example, among 4 to 16-year-old children, 14.5% of boys and 17.5% of girls is overweight, and 2.6% of boys and 3.3% of girls is obese. [28] Health consequences are already visible during childhood, and are similar to those among adults, i.e. hypertension, insulin resistance, and an unfavorable blood lipid profile. [29-31] Apart from cardiovascular problems, pulmonary complications like sleep apnea, asthma, and exercise intolerance also occur. [29] Finally , psychosocial problems caused by stigmatization have been reported in children from the age of 5 years onwards. [29] Childhood overweight tends to track into adulthood from an early age onwards. [32-36] Tracking tends to be stronger for shorter time intervals, with higher age, and among children with obese parents. [32-35] Moreover, it is estimated that about one third of obese preschool children will become obese adults.[32]

Overweight and obesity appear to make a considerable contribution to the association between socioeconomic status and cardiovascular diseases, although no exact estimates are known. [37-39] Therefore, studying the association between social disadvantage and overweight is an important step to decrease social inequalities in morbidity and mortality.

1.3 ASSOCIATION BETWEEN SOCIAL DISADVANTAGE AND OVERWEIGHT AND OBESITY

The first review on the association between socioeconomic status and overweight appeared in 1989. [40] There was ample evidence to allow to conclude that, in developed countries, an inverse association existed between socioeconomic status and overweight in women. The association was inconsistent for men and children in developed countries, but there was a positive association between socioeconomic status and overweight in men, women and children in developing countries.[40] Since the appearance of that review, interest in the association between socioeconomic status and overweight has increased. An updated review on the association between socioeconomic status and obesity for adults that focused on developing countries was published in 2004, [41] a review on adults in both developed and developing countries was published in 2007, [42] and a separate review on the association between socioeconomic status and obesity in children was published in 2008. [43] From these reviews it can be concluded that the associations between socioeconomic status and obesity have changed over time. The number of reported inverse associations between socioeconomic status and overweight has increased. Differences in the direction of the association between socioeconomic status and overweight between developed and developing countries are no longer so pronounced, but the inverse association between socioeconomic status and overweight is still most prevalent in women.

In children, the association has also changed. While the review by Sobal and Stunkard in 1989 reported positive, inverse and null associations for socioeconomic status (of the parents) with childhood obesity from age 5 years onwards,[40] the updated review by Shrewsbury and Wardle in 2007 reported only inverse and null associations.[43] The final conclusion of the latter review was that children from parents with a lower socioeconomic status already have a higher prevalence of overweight.[43] In addition, early childhood circumstances and adult overweight has also been examined. There is evidence that childhood socioeconomic status determines later health, including overweight and obesity, independent of the acquired adult socioeconomic status.[44-47]

1.4 EXPLAINING THE ASSOCIATION BETWEEN SOCIAL DISADVANTAGE AND CHILDHOOD OVERWEIGHT

As stated earlier, decreasing social inequalities in health is a public health priority. Because overweight is already highly prevalent in childhood and tracks into adulthood, overweight prevention targeted at socially-disadvantaged children may play an important role in decreasing socioeconomic inequalities in health. Determinants for developing overweight in either childhood or adulthood occur from fetal life, [48-51] infancy, [52-58] through to early childhood.[59-62] In infancy, for example, breastfeeding seems to have a small but consistent protective effect on the development of overweight. [52, 54, 57] However, it remains unknown which risk factors contribute most to the socio-economic gradient in childhood overweight. Also, very few studies report on the association between social disadvantage and relative overweight in preschool children (i.e. before the age of 5 years) and the results of these few studies are inconsistent. [63-65]

Thus, there is a clear socioeconomic gradient in overweight from the age of 5 year onwards, but it is unknown when this gradient develops. Also, risk factors for overweight are highly prevalent before that age.

This thesis aims to reveal some of the pathways that explain the association between social disadvantage and overweight by examining at what age this gradient develops, and what risk factors that occur from birth to preschool age are associated with social disadvantage or overweight in children.

The aims of this thesis are to study the association between:
1 early life risk factors for overweight and overweight at preschool age.
2 social disadvantage and early life risk factors for overweight.
3 social disadvantage and overweight at preschool age.

1.5 METHODS

The above-mentioned aims have been explored within two large population-based birth cohort studies: mainly Generation R (Rotterdam, the Netherlands)[66] and (for one study only): Project Viva (Boston, USA)[67].

The Generation R study was designed to identify early environmental and genetic determinants of growth, development and health. All pregnant women with an expected delivery date between April 2002 and January 2006, and expected to be resident of Rotterdam at time of delivery, were asked to participate in the study. Enrollment was aimed in early pregnancy (<18 weeks of gestation), but was possible until the birth of the child. The offspring of these pregnant women form a prenatally-recruited birth cohort. Measurements were obtained at regular time intervals by hands-on measurements and self-reported questionnaires. In addition, the child health centers provided information, including anthropometric measurements.

Project Viva was designed to find ways to improve the health of mothers and their children by looking at the effects of the mother's diet (and other factors) during pregnancy, on her health and the health of her child. Participants in Project Viva were recruited women who were attending their initial prenatal visit (between April 1999 and July 2002) at one of 8 urban and suburban obstetrical offices of a multi-specialty group practice located in eastern Massachusetts. Mothers completed regular interviews and questionnaires. Mothers and children visited the research centers where anthropometric measurements were taken.

Both studies provide ample information to study the current research questions regarding social inequalities in childhood overweight. Where appropriate, several indicators of social disadvantage were used. Although non-native ethnicity is highly associated with a low socioeconomic status, ethnic differences in overweight cannot be fully explained by socioeconomic status and will, therefore, be treated as a separate indicator of social disadvantage.[68]

Also, several methods exist to define weight status in children. Each method has its specific advantages, therefore for each chapter the most appropriate method for defining weight status for that study question was considered and applied.

1.6 OUTLINE

Following this introduction, Chapter 2 concerns the first study aim, and focuses on early life risk factors that occur in infancy and are reported as risk factors for later overweight. Chapter 2.1 explores the growth patterns of breastfed versus formula-fed children. Chapter 2.2 extends this subject by examining whether growth differences between breastfed and formula-fed children lead to differences in overweight status: this latter study was performed in a different birth cohort. Chapter 2.3 covers a third element of infant feeding that may be a risk factor for overweight: i.e. the association between early introduction of solids and growth. Chapter 3 concerns the second study aim, and focuses on the association between indicators of social disadvantage and risk factors for overweight. Chapter 3.1 describes the association between educational level as an indicator of social (dis)advantage, and breastfeeding initiation and continuation. Chapter 3.2 has the same interest, but then for ethnicity as an indicator of social (dis)advantage. Chapter 3.3 focuses on the association between social disadvantage and sedentary behaviors/physical activity that occur early in childhood, such as watching television and playing outside. Chapter 4 concerns the last study aim. Chapter 4.1 studies the association between socioeconomic status and growth and overweight during the first years of life. Chapter 4.2 addresses the same study question for ethnicity. Chapter 5 provides an overall discussion, including recommendations for future research, and for policy and practice. Table 1.1 presents an overview of the chapters in this thesis.

Table 1.1 Overview of the different studies presented in this thesis.

CHAPTER	SAMPLE (RESTRICTION)	POPULATION FOR ANALYSES	DETERMINANT	MAIN OUTCOMES
2.1	Generation R cohort	n=5074	Breastfeeding	Growth / Overweight
2.2	Project Viva	n=884	Breastfeeding	BMI / Skinfold thicknesses / Overweight
2.3	Generation R cohort	n=3184	Introduction of solids	Growth
3.1	Generation R cohort (Dutch only)	n=2914	Maternal educational level	Breastfeeding
3.2	Generation R cohort	n=3848	Maternal ethnicity	Breastfeeding
3.3	Generation R cohort	n=4688	Maternal educational level / Child's ethnicity	Physical activity / Sedentary behaviors
4.1	Generation R cohort (Dutch only)	n=2954	Maternal educational level / Household income	BMI / Overweight
4.2	Generation R cohort	n=4267	Child's ethnicity	BMI / Overweight

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CHAPTER 2
EARLY RISK FACTORS FOR RAPID INFANT WEIGHT GAIN AND CHILDHOOD OVERWEIGHT

ABSTRACT

Background
Breastfeeding has been suggested to be associated with the risks of obesity in children and adults. We assessed whether the duration and exclusiveness of breastfeeding is also associated with early postnatal growth rates and the risks of overweight and obesity until the age of 3 years.

Methods
This study was embedded in a population-based prospective cohort study from early fetal life onwards, among 5047 children and their mothers in the Netherlands.

Results
As compared to children who were breastfed, those who were never breastfed had a shorter gestational age (difference 0.40 weeks (95% confidence interval (CI) -0.57, -0.23) and lower weight at birth (difference 134 grams (95% CI -190, -77). Breastfeeding duration in the first 6 months was inversely associated with the change in age- and sex-adjusted standard deviation score for length, weight and body mass index (all P for trend < 0.05) between 3 and 6 months. Similar results were observed for breastfeeding exclusivity. No associations of breastfeeding duration and exclusivity were observed with growth rates before the age of 3 months and in the age window of 6 to 12 months. Shorter breastfeeding duration was associated with an increased gain in age- and sex-adjusted standard deviation scores for length, weight and body mass index (P for trend < 0.05) between the age interval from 3 to 6 months. Similar tendencies were observed for the associations of breastfeeding exclusivity with change in length, weight and body mass index. Breastfeeding duration and exclusivity were not consistently associated with the risks of overweight and obesity at the ages of 1, 2 and 3 years.

Conclusion
We conclude that breastfeeding duration and exclusivity during the first 6 months were inversely associated with growth rates for length, weight and body mass index until the age of 6 months but not with the risks of overweight and obesity until the age of 3 years.

2.1 BREASTFEEDING AND GROWTH IN CHILDREN UNTIL THE AGE OF 3 YEARS

BASED ON

Durmus B / van Rossem L / Arends LR / Duijts L / Van der Heijden AJ / Hofman A / Steegers EA / Raat H / Jaddoe VW
Breastfeeding, early growth and the risk of obesity in preschool children: The Generation R Study
Submitted

INTRODUCTION

Current recommendations advise initiation and continuation of breastfeeding for more than 6 months to promote child health.[1-4] Previous studies suggested that breastfeeding has protective effects on the risks of cardiovascular diseases in adulthood.[5, 6] Also, several studies suggested that breastfeeding leads to a lower risk of obesity in later life.[1-5] These associations have been shown in several studies and meta- analyses, also after adjustment for several potential confounders.[7] Furthermore, a dose-dependent association has been shown, suggesting that longer duration of breastfeeding is associated with a lower body mass index in older children and adulthood.[8]

Studies on the associations of breastfeeding with the risks of overweight and obesity in early childhood are scarce and showed inconsistent results.[9-11] This inconsistency may be due to differences in study designs, indicators of overweight or obesity, and assessment of breastfeeding.[12] Also, not all studies had data available about the exclusivity of breastfeeding. Assessing the associations of breastfeeding and childhood obesity at young ages is important since the risk of developing obesity may be partly explained by early postnatal growth patterns.[12] These growth patterns in early childhood might be intermediates in the associations of breastfeeding with obesity in later life.[13] Especially high growth rates during first months of life are associated with metabolic syndrome outcomes. [14, 15]

We hypothesized that prolonged duration and exclusivity of breastfeeding lead to lower growth rates during the first year of life, and subsequently to lower risks of overweight and obesity in preschool children. We examined, in a population-based prospective cohort study among 5047 children, the associations of breastfeeding duration and exclusivity with growth rates in infancy and the risks of overweight and obesity until the age of 3 years.

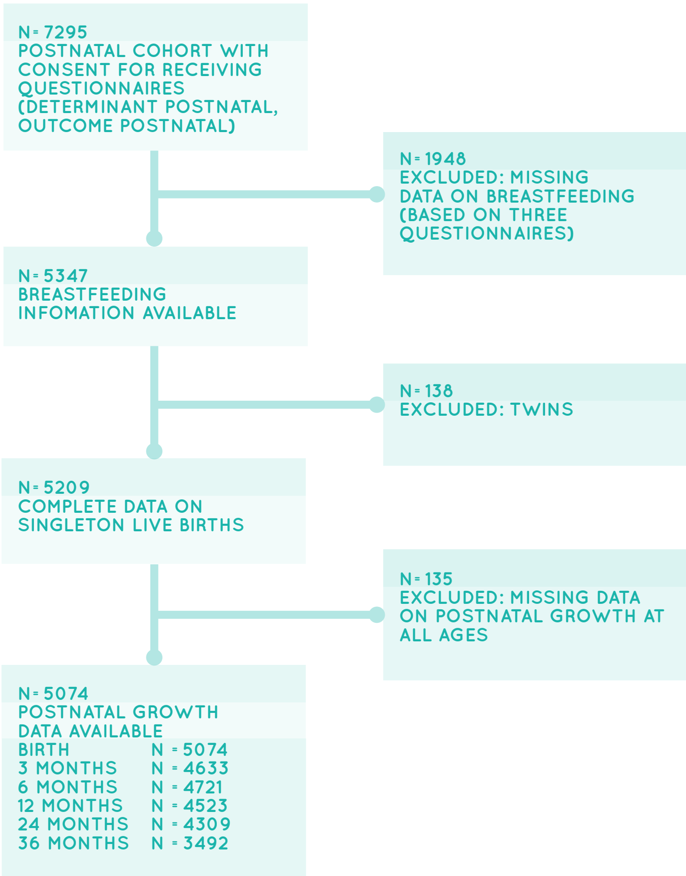
METHODS

Study design and population

This study was embedded in the Generation R Study, a population-based prospective cohort study of pregnant women and their children from fetal life onwards in Rotterdam, the Netherlands.[16, 17] Enrollment in the study was aimed at early pregnancy (gestational age <18 weeks) but was possible until birth of the child. Assessments during pregnancy included physical examinations, fetal ultrasound examinations, and administration of questionnaires.[17] All children were born between April 2002 and January 2006, and form a prenatally enrolled birth-cohort with a planned follow-up until young adulthood.

Postnatal growth data for the present study were available until the age of 3 years. Of all eligible children in the study area, 61% were participating in the study at birth. This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all

Figure 1 Flow chart of participants in this study



procedures involving human subjects were approved by the Medical Ethical Committee of the Erasmus Medical Center, Rotterdam. Written informed consent was obtained from all participants.

In total, 7295 children and their parents participated in the postnatal phase of the study and gave consent for participating in the questionnaire studies (Figure 1). Children without complete information on breastfeeding and twins were excluded from the analyses. Of the remaining singleton live births with complete data on breastfeeding, information about postnatal growth characteristics measures on at least one age was available in 5074 children.

Measurements

Duration and exclusiveness of breastfeeding

Information about breastfeeding initiation and continuation was obtained from delivery reports and postal questionnaires at the ages of 2, 6 and 12 months after birth. Mothers were asked whether they ever breastfed their child (yes/no) and at what age they quitted breastfeeding. Subsequently, breastfeeding duration was categorized into four groups: 1) never; 2) less than 3 months; 3) 3 to 6 months; and 4) 6 months or longer.

Duration of exclusive breastfeeding was defined by using information about at what age other types of milk and/or solids were introduced in the first 6 months of life, according to a short food frequency questionnaire. The information about duration and exclusiveness of breastfeeding was combined and categorized into the following three categories: 1) never; 2) partial breastfeeding until 4 months; and 3) exclusive breastfeeding until 4 months.

Never indicates infants who were never breastfed. Partial indicates infants receiving breastfeeding, formula feeding and/or solids in the first four months. Exclusive indicates infants who have been breastfed, without any other milk, solids or fluids during the first four months.

Postnatal growth characteristics

Postnatal growth was repeatedly measured at the Community Health Centers according to a standard schedule and procedures by a well-trained staff at the median ages of 3.1 months (95% range 1.1 – 4.5), 6.6 months (95% range 5.2 – 10.7), 13.0 months (95% range 11.1 – 15.9), 24.3 months (95% range 18.2 – 28.3) and 36.4 months (95% range 30.4 – 39.9) months. Length was measured in supine position to the nearest millimeter until the age of 14 months using a neonatometer, after which height was measured in standing position by a Harpenden stadiometer (Holtain Limited, Dyfed, U.K.). Weight was measured using a mechanical personal scale (SECA). Body mass index (kg/m^2) was calculated. Relative overweight (body mass index > 1.1 – 2.3 SDS) and obesity (body mass index > 2.3 SDS) were defined based on the age-and sex adjusted body mass index distributions based on the criteria of Cole.[18, 19] For this purpose, Fredriks et al transformed these international criteria for overweight and obesity to SDs to identify the pediatric centiles. They showed that an adult BMI of 25 kg/m^2 (overweight) corresponds to +1.1 SD and that an adult BMI of 30 kg/m^2 (obesity) corresponds to +2.3 SD in the reference growth diagrams based on the 1997 Dutch Growth Study. They suggested that the +1.1 and +2.3 SD lines in the 1997 BMI charts correspond to the recommended limits for overweight and obesity, respectively, which Cole also uses.

Standard deviation scores (SDS) for postnatal growth characteristics were obtained using Dutch reference growth curves (Growth Analyzer 3.0, Dutch Growth Research Foundation). Growth rates in age intervals were defined as the change in SDS in the age intervals between 0 to 3 months; 3 to 6 months; and 6 to 12 months.

Covariates

Gestational age, sex and birth weight were obtained from midwife and hospital registries at birth. Information about highest attained maternal educational level (low, moderate and higher), maternal ethnicity (European, non-European) and parity (primiparity, multiparity) were obtained at enrollment in the study. Ethnicity and educational level of the parents were defined according to the classification of Statistics Netherlands.[20, 21] Information on maternal smoking (yes, no) and alcohol consumption during pregnancy (yes, no) was retrieved from prenatal questionnaires. Maternal height and weight were measured at enrollment while the mother stood without shoes and heavy clothing, and body mass index was calculated (kg/m^2). Maternal age was registered at enrollment.

Statistical analysis

Differences in baseline characteristics between the breastfeeding duration categories were compared with ANOVA for continuous variables and Chi-square tests for categorical variables. The associations of breastfeeding (never/ever), breastfeeding duration (never; 0 to 3 months; 3 to 6 months; and 6 to 12 months), and breastfeeding exclusivity (never; partial until 4 months; and exclusive until 4 months) with the change in postnatal growth characteristics (length, weight and body mass index) in SD scores for different age periods (0 to 3; 3 to 6; and 6 to 12 months), were assessed using multiple linear regression models. The models were adjusted for potential confounders including child's age at visit, sex, birth weight, gestational age, maternal ethnicity, maternal education, maternal body mass index, parity and smoking. Gestational age at enrollment was not included in the models since it did not materially change the results. Confounders were included in the models based on literature, or a change in effect estimates of more than 10%.

For the analyses focused on the associations of breastfeeding duration with growth characteristics until the age of 3 months, we combined the breastfeeding groups into never and ever (0-3; 3-6; and > 6 months). For the analyses focused on growth characteristics at the age of 3-6 months we combined the breastfeeding duration groups into never; 0-3 months; 3-6 months (3-6 months and > 6 months). Furthermore, we examined the associations of breastfeeding, duration and exclusivity with differences in body mass index at the ages of 1, 2 and 3 years, and the risks of overweight and obesity at the same ages, using linear regression and logistic regression models, respectively. Finally, we assessed the associations of breastfeeding duration and exclusivity with the risk of a combined outcome (overweight and obesity, body mass index > 1.1 SDS). Tests for trends were performed by treating each categorized variable as a continuous term and by entering the variable into the fully adjusted linear regression model. To handle missing values in covariates, we performed multiple imputations by generating 5 independent datasets for all analyses. Imputations were based on the relationships between all covariates included in this study. All measures of association are presented with their 95% confidence intervals (CI). Cross-sectional analyses were performed using the Statistical Package of Social Sciences version 17.0 for Windows (SPSS Inc., Chicago, IL, USA).

RESULTS

Of the total group of 5074 children, 89.8% had ever been breastfed (Table 1). As compared to mothers who breastfed their children for more than 6 months, those who never breastfed their children tended to have a younger age, higher body mass index, higher rate of obesity, lower educational level, Dutch or European background and were more likely to smoke during pregnancy. Also, children who were never breastfed had a lower weight at birth and a higher prevalence of small size for gestational age and preterm birth (all P-values <0.05). The median duration of breastfeeding was 4.4 (95% range 0.5 – 12.0) months. In total, 65.7% of all children were breastfed partially until the age of 4 months, and 24.1% of all children were breastfed exclusively until the age of 4 months.

Table 2 shows the associations of breastfeeding, breastfeeding duration and breastfeeding exclusivity with postnatal growth rates (length, weight and body mass index) in different time periods presented as changes in SD scores. Breastfeeding duration and exclusivity were not associated with growth rates before the age of 3 months. As compared to children who were ever breastfed, those never breastfed had a higher gain in length and weight between the age of 3 and 6 months (difference 0.07 (95% CI 0.01, 0.14) SDS) and

(0.06 (95% CI 0.01, 0.12) SDS), respectively. As compared to children who were breastfed for more than 3 months, children who were breastfed shorter than 3 months had also a higher gain in length and weight between the ages of 3 to 6 months (all P-value for trend < 0.01). The highest gain in length was observed in children who were breastfed for only 0 to 3 months. We observed similar tendencies for the associations between breastfeeding exclusivity and gain in length, weight and body mass index between the age of 3 and 6 months. Children, who were never breastfed or breastfed partially until 4 months, show a higher increase in length, weight and body mass index. The highest effects were seen for children who are never breastfed. Breastfeeding duration and exclusivity were not associated with growth between the age of 6 and 12 months.

Table 1 Subject characteristics according to duration of breastfeeding (n=5074) * †

		TOTAL	NEVER BFD	0-3 MONTHS	3-6 MONTHS	>6 MONTHS
MATERNAL CHARACTERISTICS						
Age (years)		30.9 (21.9 – 38.5)	30.6 (21.3 – 38.5)	29.9 ** (20.9 – 37.8)	31.5 ** (23.0 – 38.3)	32.1 (24.2 – 39.2) **
Gestational weight change per week (kg)		0.45 (0.2)	0.45 (0.2)	0.44 (0.2)	0.45 (0.2)	0.45 (0.2)
Height (cm)		168.2 (7.3)	168.3 (6.9)	167.6 (7.4)	168.9 (7.1)	168.7 (7.3)
Weight (kg)		69.5 (12.8)	72.1 (15.4)	70.2 (13.7)*	68.9 (11.4) **	68.1 (11.2) **
Body Mass Index (kg/m^2)		24.6 (4.3)	25.4 (5.0)	25.0 (4.8)	24.2 (3.8) **	23.9 (3.7) **
Overweight (%) ‡		23.0	26.7	27.2	24.1	23.8
Obesity (%) ‡		11.0	17.1	13.9	8.7**	6.8**
Highest educational level (%)	Low	7.5	7.4	9.4**	3.8**	6.0**
	Moderate	41.1	62.4	50.0**	33.3**	26.5**
	Higher	51.4	30.2	40.6**	62.9**	67.5**
Ethnicity (%)	Dutch and other Europeans	67.6	79.7	62.2**	71.6**	71.1**
	Non-European	32.4	20.3	37.8**	28.4**	28.9**
Smoking during pregnancy (%)	Ever	25.4	40.1	31.1**	20.3**	17.1**
	Never	74.6	59.9	68.9**	79.7**	82.9**
Alcohol consumption during pregnancy (%)	Ever	59.9	49.2	55.7	69.2**	63.8**
	Never	40.1	50.8	44.3	30.8**	36.2**
Parity (%)	0	57.5	47.3	62.0**	60.1**	53.8*
	>=1	42.5	52.7	38.0**	39.9**	46.2*
BIRTH CHARACTERISTICS						
Sex	Males (%)	50	52	50	50	47
Gestational age (weeks)		39.9 (37.1 – 42.1)	39.7 (37.0 – 42.0)	39.9 (36.9 – 42.0)	39.9 (37.1 – 42.1) *	40.1 (37.7 – 42.1) **
Weight (grams)		3 449 (546)	3 391 (582)	3 409 (548)	3 456 (554)*	3 525 (506) **
Small for gestational age	(<5%) ‡	5.0	6.5	5.8	5.0	3.9*
Low birth weight	(<2500 g) %	4.1	5.8	5.2	4.1	2.0**
Preterm birth (%)		4.8	5.6	5.5	4.6	3.4*

* Values are means (SD), percentages or medians (90% range) for variables with skewed distribution.
† * P < 0.05 and ** P < 0.01. Differences in maternal and child characteristics for the breastfeeding duration groups were evaluated using ANOVA for continuous variables and chisquared tests for categorical variables. ‡ Overweight is defined as body mass index > 25 – 29.9 kg/m^2. Obesity is defined as body mass index > 30 kg/m^2. Small for gestational age is defined as the lowest 5% of gestational age adjusted birth weight.

Figure 2 shows that we did not observe any consistent associations of breastfeeding duration or exclusivity with the risk of overweight and obesity (BMI > 1.1 SDS) at the ages of 1, 2 and 3 years. Also, the associations of breastfeeding duration and exclusivity with the difference in body mass index and the risks of overweight (BMI > 1.1-2.3 SDS) and obesity (BMI > 2.3 SDS) at the ages of 1, 2 and 3 years did not show consistent relations (Appendix 1).

DISCUSSION

Main findings

Breastfeeding duration and exclusivity were inversely associated with growth rates in length, weight and body mass index between the age of 3 and 6 months. We did not observe associations between breastfeeding duration and exclusivity and the risk of overweight and obese in the first three years of life.

Strengths and weaknesses

An important strength of this study was the population-based cohort, with a large number of subjects being studied from early pregnancy onwards and information about a large number of potential confounders available. Information was available about duration and exclusivity of breastfeeding. Some methodological issues need to be considered. Of all children of this study, questionnaires with breastfeeding information were available in 68%. This non-response would lead to biased effect estimates if the associations of breastfeeding duration and exclusivity with postnatal growth characteristics would be different between those included and not included in the analyses. However, this seems unlikely because biased estimates in large cohort studies mainly arise from loss to follow-up rather than from non-response at baseline.[22] In the present analysis, loss to follow up was < 10%. However, the number of follow-up measurements was smaller with increasing age. Information about breastfeeding was prospectively collected by questionnaires without direct reference to any growth characteristic. Although assessing breastfeeding by questionnaires seems to be a valid method, misclassification may occur.[23, 24] We estimated breastfeeding exclusivity according to whether the child received breastfeeding without any other infant formula, milk or solids according to the short food frequency questionnaire. This definition does not cover the strict criteria used by the World Health Organization, which suggest that even the use of water in combination with breastfeeding does not fulfill the definition of exclusivity. However, we did ask for the most commonly introduced solids and fluids. Furthermore, in The Netherlands it is not common that children receive breastfeeding in combination with the use of water to prevent dehydration. Therefore, we think that our measurement of exclusive breastfeeding is a good proxy for exclusive breastfeeding according to the World Health Organization (WHO) criteria. Finally, we used body mass index for defining overweight and

Table 2 Breastfeeding duration and exclusivity and growth rates in different intervals during the first year of infancy (n=5074)* † ‡

	LENGTH (CHANGE IN SD SCORE)			WEIGHT (CHANGE IN SD SCORE)			BODY MASS INDEX (CHANGE IN SD SCORE)	
	0-3 months	3-6 months	6-12 months	0-3 months	3-6 months	6-12 months	3-6 months	6-12 months
EVER BREASTFEEDING								
Never	-0.01 (-0.14, 0.12)	0.07 (0.01, 0.14)*	-0.03 (-0.09, 0.03)	0.01(-0.08, 0.09)	0.06 (0.01, 0.12)*	-0.03 (-0.09, 0.03)	0.02 (-0.06, 0.11)	-0.03 (-0.11, 0.06)
Ever	Ref (0)	Ref (0)	Ref (0)	Ref (0)	Ref (0)	Ref (0)	Ref (0)	Ref (0)
DURATION								
Never	-0.02 (-0.15, 0.12)	0.17 (0.10, 0.24)**	-0.04 (-0.11, 0.03)	0.01 (-0.08, 0.09)	0.14 (0.08, 0.20)**	-0.03 (-0.10, 0.03)	0.03 (-0.06, 0.12)	-0.01 (-0.10, 0.08)
0-3 months	Ref (0)	0.19 (0.15, 0.24)**	-0.03 (-0.08, 0.02)	Ref (0)	0.14 (0.10, 0.18)**	-0.01 (-0.05, 0.04)	0.02 (-0.03, 0.08)	0.02 (-0.04, 0.08)
3-6 months	n.a.	Ref (0)	0.01 (-0.05, 0.06)	n.a.	Ref (0)	0.02 (-0.03, 0.07)	Ref (0)	0.03 (-0.04, 0.10)
> 6 months	n.a.	n.a.	Ref (0)	n.a.	n.a.	Ref (0)	n.a.	Ref (0)
P for trend	P = 0.48	P < 0.01	P = 0.15	P = 0.98	P < 0.01	P = 0.28	P = 0.03	P = 0.96
EXCLUSIVE BREASTFEEDING								
Never	-0.05 (-0.20, 0.10)	0.24 (0.17, 0.32)**	-0.05 (-0.12, 0.02)	0.01 (-0.09, 0.11)	0.22 (0.16, 0.29)**	-0.02 (-0.08, 0.05)	0.09 (-0.01, 0.18)	0.01 (-0.08, 0.10)
Partial until 4 months	-0.05 (-0.15, 0.04)	0.23 (0.18, 0.27)**	-0.02 (-0.07, 0.02)	0.01 (-0.05, 0.07)	0.21 (0.17, 0.25)**	0.02 (-0.02, 0.06)	0.08 (0.02, 0.14)**	0.05 (-0.01, 0.11)
Exclusive until 4 months	Ref (0)	Ref (0)	Ref (0)	Ref (0)	Ref (0)	Ref (0)	Ref (0)	Ref (0)
P for trend	P = 0.33	P < 0.01	P = 0.17	P = 0.82	P < 0.01	P = 0.96	P = 0.01	P = 0.37

* Values are standardized regression coefficients (95% confidence interval). † * P < 0.05 and ** P < 0.01 using multiple linear regression models. ‡ Models are adjusted for child's age at visit, sex, birth weight, gestational age, maternal ethnicity, maternal education, maternal body mass index, smoking and parity. For the analyses focused on growth characteristics at the age of 0-3 months we combined the breastfeeding duration groups into never and ever (0-3 months; 3-6 months; and > 6 months).
For the analyses focused on growth characteristics at the age of 3-6 months we combined the breastfeeding duration groups into never; 0-3 months; and 3-6 months (3-6 months and > 6 months).

Appendix 1 Breastfeeding duration and exclusivity and risks of overweight and obesity in the first three years of infancy (n=5074) * † ‡

	AGE 1 YEAR			AGE 2 YEARS			AGE 3 YEARS		
	Δ BMI kg/m² (95% CI)	Overweight OR (95% CI)‡	Obesity OR (95% CI)‡	Δ BMI kg/m² (95% CI)	Overweight OR (95% CI)‡	Obesity OR (95% CI)‡	Δ BMI kg/m² (95% CI)	Overweight OR (95% CI)‡	Obesity OR (95% CI)‡
BREASTFEEDING INITIATION									
Never	-0.03 (-0.16, 0.10)	0.81 (0.61, 1.08)	1.26 (0.60, 2.62)	0.02 (-0.12, 0.16)	0.77 (0.58, 1.04)	2.03 (0.66, 1.84)	-0.01 (-0.16, 0.14)	0.90 (0.63, 1.27)	1.44 (0.73, 1.83)
Ever	Ref (0)	Ref (1)	Ref (1)	Ref (0)	Ref (1)	Ref (1)	Ref (0)	Ref (1)	Ref (1)
BREASTFEEDING DURATION									
Never	0.10 (-0.05, 0.25)	0.92 (0.66, 1.27)	2.25 (0.83, 6.02)	0.03 (-0.12, 0.20)	0.86 (0.61, 1.19)	1.76 (0.92, 3.41)	0.02 (-0.15, 0.20)	1.03 (0.69, 1.53)	1.08 (0.48, 2.44)
0-3 months	0.19 (0.08, 0.29)**	1.27 (1.02, 1.58)*	1.96 (0.88, 4.37)	0.02 (-0.09, 0.14)	1.19 (0.95, 1.48)	0.94 (0.55, 1.61)	0.04 (-0.09, 0.16)	1.17 (0.88, 1.55)	0.73 (0.38, 1.39)
3-6 months	0.10 (-0.01, 0.22)	1.07 (0.84, 1.36)	1.75 (0.72, 4.25)	0 (-0.13, 0.12)	1.19 (0.94, 1.52)	0.68 (0.35, 1.31)	0.06 (-0.08, 0.20)	1.20 (0.88, 1.64)	0.71 (0.33, 1.55)
> 6 months	Ref (0)	Ref (1)	Ref (1)	Ref (0)	Ref (1)	Ref (1)	Ref (0)	Ref (1)	Ref (1)
P for trend	P < 0.01	P = 0.96	P = 0.09	P = 0.61	P = 0.92	P = 0.17	P = 0.72	P = 0.61	P = 0.87
EXCLUSIVE BREASTFEEDING									
Never	0.11 (-0.04, 0.26)	1.09 (0.78, 1.50)	1.60 (0.64, 3.95)	0.06 (-0.09, 0.22)	0.89 (0.64, 1.24)	2.32 (1.18, 4.55)*	-0.02 (-0.19, 0.15)	1.02 (0.68, 1.52)	1.12 (0.49, 2.54)
Partial until 4 months	0.18 (0.09, 0.27) **	1.46 (1.20, 1.79)**	1.36 (0.71, 2.60)	0.07 (-0.03, 0.16)	1.20 (0.98, 1.47)	1.19 (0.71, 1.99)	-0.01 (-0.12, 0.10)	1.19 (0.92, 1.52)	0.73 (0.40, 1.32)
Exclusive until 4 months	Ref (0)	Ref (1)	Ref (1)	Ref (0)	Ref (1)	Ref (1)	Ref (0)	Ref (1)	Ref (1)
P for trend	P = 0.01	P = 0.07	P = 0.79	P = 0.26	P = 0.83	P = 0.03	P = 0.77	P = 0.59	P = 0.99

* Values are unstandardized regression coefficients and odds ratios (95% confidence interval).
†* P < 0.05 and ** P < 0.01 using multiple linear and logistic regression models. Models are adjusted for child's age at visit, sex, birth weight, gestational age, maternal ethnicity, maternal education, maternal body mass index, smoking and parity.
‡ Overweight is defined as age- and sex adjusted body mass index > 1.1 – 2.3; obesity is defined as age- and sex body mass index > 2.3 SDS.

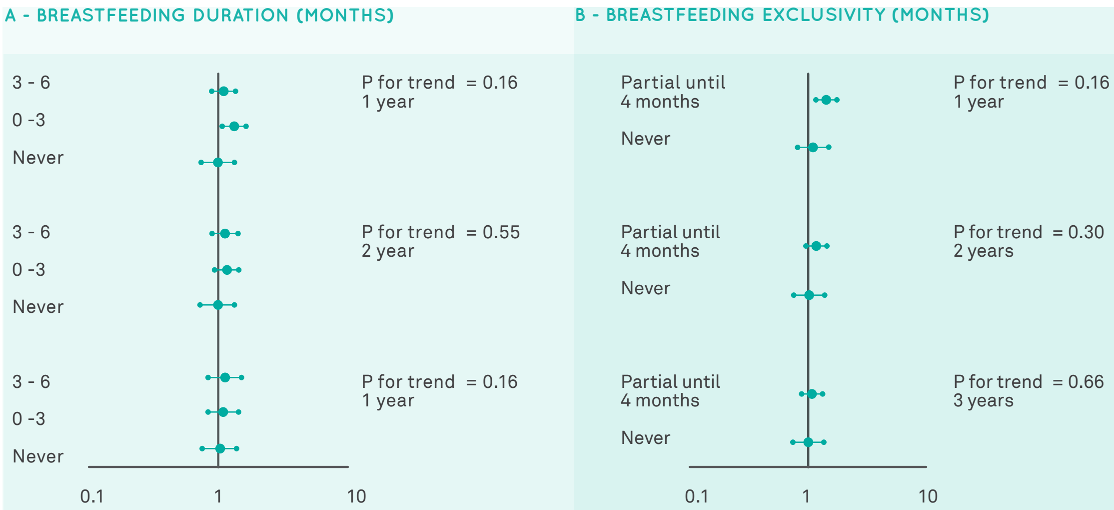
obesity in early childhood. We should be careful with these definitions, as at this young age there is no clear cut- off point to define obesity and body mass index cannot differentiate between fat and lean mass.

Comparison of main findings with other studies

In line with previous studies,[25-27] we observed differences in maternal characteristics between breastfeeding duration groups. We previously showed socioeconomic and ethnic differences in breastfeeding duration.[28, 29] In this study group, mothers who never breastfed their children were also more likely to have a younger age, higher body mass index, Dutch or European background and were more likely to smoke during pregnancy. We additionally observed that children who were never breastfed had a shorter gestational age, lower weight at birth and a higher risk of small size for gestational age and preterm birth. The associations of maternal and birth characteristics with breastfeeding initiation and duration, show that these characteristics should be considered as potential confounders when studying the associations between breastfeeding and childhood growth.

It has been shown that after the first week of life, growth patterns appear to be similar between breastfed and formula-fed children for the first 2 to 3 months.[30] However, thereafter the growth rates between breastfed and formula- fed children diverges with less distinct differences in length gain than weight gain. Previous studies

Figure 2 Breastfeeding and the risks of overweight in the first 3 years of life *†‡



* Values are odds ratios (95% confidence interval). Breastfeeding duration for more than 6 months and breastfeeding exclusivity until 4 months, are considered as the reference groups in A and B, respectively. m = months.
† * $P < 0.05$ using multiple logistic regression models. Models are adjusted for child's age at visit, sex, birth weight, gestational age, maternal ethnicity, maternal education, maternal body mass index, smoking and parity.
‡ Outcome is defined as age- and sex adjusted body mass index > 1.1 SDS.

suggested that breastfed children have a slower growth between 3 and 12 months of life.[31-34] Our results are in line with the findings but we showed that children who were never breastfed have higher growth rates in length and weight only between the ages of 3 and 6 months. After the age of 6 months, it is very likely that complementary foods like fruit and vegetable snacks are introduced. This may explain why we did not observe any effects in growth after the age of 6 months. We also showed that exclusive breastfeeding for 4 months was associated with a lower gain in length, weight and body mass index during the first 3 to 6 months. This is in line with a previous study in randomly selected healthy newborns from Denmark and Iceland, which showed that exclusive breastfeeding influenced growth rates during infancy.[34] The authors suggested that exclusive breastfeeding until 2 months is related to lower weight gain from 2 to 6 months as well as from 6 to 12 months.

The biological mechanisms by which breastfeeding might protect against high growth rates are not well understood. One suggested mechanism is that high protein intake in formulafeeding stimulates the secretion of insulin-like growth factor I (IGF-I) which accelerates growth and increases muscle mass and adipose tissue.[35] Prolonged breastfeeding duration might also reduce plasma levels of appetite-related peptide and ghrelin.[35, 36] Furthermore, formula- fed infants have higher plasma- insulin concentrations which might result in increased insulin resistance.[36]

Studies that focused on the associations between breastfeeding and the risks of overweight and obesity in early childhood showed inconsistent results.[9-11] In our study, breastfeeding duration and exclusivity were not consistently associated with the risks of overweight and obesity in the first 3 years of life. We observed that partial feeding until 4 months may increase risk of overweight and obesity. However, this association was not consistent with the other results. We cannot explain this specific association, which might also be a chance finding. Similar results in this age range were observed in previous studies.[37-39] Furthermore, high postnatal growth rates in the first 6 months of life are independently associated with the risk of overweight and obesity in later life.[40] Therefore, the associations between shorter duration of breastfeeding and the risks of overweight and obesity might appear at older ages.

Conclusion

Our results suggest that shorter breastfeeding duration and exclusivity are associated with increased postnatal growth rates for height, weight and body mass in the first 3 to 6 months of life. Breastfeeding duration and exclusivity are not associated with the risks of overweight and obesity in the first 3 years. Further research is needed to assess whether and from which age breastfeeding duration and exclusiveness are associated with childhood obesity.

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ABSTRACT

Background
Breastfeeding and infant weight change may be both associated with adiposity. We examined these associations at age 3 years.

Methods
We studied 884 children in a prospective cohort study. We determined breastfeeding status at 6 months. We defined infant weight change as change in weight-for-age z score between birth and 6 months. Our primary outcomes at 3 years were body mass index (BMI) z score and the sum of subscapular and triceps skinfold thicknesses (SS + TR); we also assessed obesity. We performed multivariable regression analyses.

Results
At age 6 months, 25.0% of infants were fully breastfed. At age 3 years, mean (SD) BMI z score was 0.45 (1.03). In linear regression analyses adjusted for mother's educational level, race/ethnicity, smoking, BMI, pregnancy weight gain and birth weight (adjusted for gestational age), the BMI z score of fully breastfed children was 0.17 (95% CI:-0.43, 0.09) units lower than never breastfed children. After additional adjustment for infant weight change, the estimate was attenuated (-0.03, 95% CI: -0.27, 0.20). Adjustment for infant weight change only modestly attenuated estimates for SS + TR (from -1.48 (95% CI: -2.52, -0.44) to -1.16 mm (95% CI: -2.18, - 0.14)), and for the odds of being obese (from 0.21 (95% CI: 0.07, 0.68) to 0.29 (95% CI: 0.08, 1.05)).

Conclusion
Infant weight change between birth and 6 months is strongly associated with adiposity at age 3, but does not mediate associations of breastfeeding with BMI.

2.2 BREASTFEEDING, INFANT WEIGHT CHANGE, AND WEIGHT STATUS AT AGE 3

BASED ON

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INTRODUCTION

Several reviews and meta-analyses of observational studies have concluded that breastfeeding protects against the development of overweight and obesity.[1-4] However, the mechanisms underlying the protective effect of breastfeeding on obesity are unclear. One of the proposed mechanisms is behavioral. Breastfed children may have learned better to self-regulate their energy-intake than formula-fed children.[5,6] However, in a previous study we did not find a strong mediating effect of maternal feeding restriction on the association between breastfeeding and adiposity.[7]

Another proposed mechanism involves infant growth rate: infants who gain weight more rapidly have a higher risk for developing obesity, an association that has been reported in a number of observational studies over the past 4 decades and summarized in recent metaanalyses.[8-11] Breastfed children generally grow slower during infancy.[12] Many studies have looked at infant feeding or infant growth in relation to adiposity, but few have been able to separate the two effects. The aim of the present study was to examine the extent to which infant weight change mediates the association between breastfeeding and adiposity. We hypothesized that the association of breastfeeding with adiposity at age 3 years would be attenuated by adjusting for infant weight change in the first 6 months after birth.

METHODS

Study design and population
Study subjects were participants in Project Viva, a prospective, observational cohort study of perinatal factors and maternal and child health.[13] We recruited women who were attending their initial prenatal visit at one of 8 urban and suburban obstetrical offices of a multi-specialty group practice located in eastern Massachusetts between April 1999 and July 2002. Details of recruitment and retention procedures are available elsewhere.[13]

Of the 2128 women who delivered a live infant, 1579 were eligible for 3-year follow up by virtue of having completed prenatal nutritional assessments and consenting for their children to be followed up. We collected follow-up information on 1405 children (66% of 2128), including in-person examinations on 1294 (61%). For this analysis, we excluded 36 participants who were missing the main outcome (child body mass index [BMI] at age 3 years) and 325 participants who were missing the main exposure (breastfeeding status at six months) or mediator (change in weight-for-age z score between birth and 6 months). We excluded 15 infants whose gestational age at birth was <34 weeks, as well as those with missing information on maternal BMI (n=4), smoking status (n=19), education (n=1), and pregnancy weight gain (n=10). Thus, our study population consisted of 884 mother-infant pairs.

Compared with 1244 lost to follow-up, included mothers were slightly older at study enrollment (32.7 years vs. 31.2 years), had higher educational attainment (74% vs. 58% completed college), and had a slightly lower pre-pregnancy BMI (24.4 kg/m^2 vs. 25.2 kg/m^2). More included than excluded children received full breastfeeding for 6 months (25% vs. 17%).

The human subjects committees of participating institutes approved the study protocols and all mothers provided written informed consent. All procedures were in accordance with the ethical standards for human experimentation established by the Declaration of Helsinki.

Measurements

Main exposures

Our main exposure was type of infant feeding during the first 6 months of life, which we assessed by interview at 6 months postpartum. We grouped women into 4 categories: 'never breastfed' (mothers who had fed their infants only formula since birth), 'any breastfeeding for less than 6 months' (mothers who had initiated breastfeeding, but discontinued it completely before 6 months), 'partial breastfeeding for 6 months' (mothers who had fed both breastmilk and formula at 6 months after birth), and 'full breastfeeding for 6 months' (mothers who fed their infant only breastmilk during the first six months after birth: this category includes both exclusive breastfeeding as well as infants who received food or fluids other than breast milk, but does not include infants who received formula[14]). We did not consider solids or liquids other than breastmilk and formula when defining these categories.

A secondary exposure was a continuous measure of breastfeeding duration. At 1 year postpartum, we asked the women who reported that they had breastfed their infants the following: "How old was your child when you stopped breastfeeding?". We truncated breastfeeding duration at 6 months to correspond to our hypothesized mediator, infant weight change between birth and 6 months of age.

Outcome measures

Trained Project Viva research assistants weighed children at 3 years with a digital scale (model 881; Seca, Hamburg, Germany) and measured height with a Shorr measuring board (Shorr Productions, Olney, MD). They measured skinfold thicknesses by using Holtain calipers (Holtain, Crosswell, United Kingdom). Research assistants performing all measurements followed standardized techniques and participated in bi-annual in-service training to ensure measurement validity. We calculated BMI z scores using US national reference data (www.cdc.gov/nccdphp/dnpa/growthcharts).[15]

Our main outcomes at 3 years of age were age- and sex-specific BMI z score, and the sum of subscapular and triceps skinfold thicknesses, a measure of subcutaneous adiposity (SS + TR).[16] We used obesity, defined as BMI for age and sex $\geq 95^{th}$ percentile, as a secondary outcome in the analyses. We used BMI 5^{th} – 85^{th} percentile as the comparison. We also showed obesity prevalence according to the classification of the International Obesity Task Force.[17] We considered the ratio of subscapular to triceps skinfold thicknesses (SS/TR) as a measure of central adiposity.[18, 19]

Mediator

We used the change in weight-for-age z score from birth to 6 months as an indicator of infant weight change. We used z scores because these measures can be interpreted independently of sex and age. We abstracted birth weight from hospital medical records. Project staff members weighed infants at 6 months and, on a subset, measured length at birth and 6 months of age as described above. We calculated weight-for-age z scores at birth and 6 months by using US national reference data.[15]

Other measures

Through a combination of questionnaires and interviews, we obtained information on mother's age, educational level, race/ethnicity, and smoking status during pregnancy. Mothers reported their pre-pregnancy body weight and height which we used to calculate BMI. We calculated total pregnancy weight gain by subtracting self-reported pre-pregnancy weight from the last clinically-measured prenatal weight. We determined birth weight for gestational age z score using a US national reference.[20]

Statistical Analyses
In bivariate analyses, we assessed characteristics of participants by infant feeding status at 6 months. To calculate unadjusted trend P values across infant feeding categories, we used Mantel-Haenszel Chi-Square for categorical characteristics and linear regression for continuous characteristics, with infant feeding categories coded as 1 to 4.

Using multivariable linear and logistic regression, we assessed the effect of breastfeeding on child adiposity measures at age 3 years independent of covariates. In our model building strategy, we first included variables of a priori interest based on previously identified associations with early childhood obesity[21, 22] namely maternal smoking, pre-pregnancy BMI, gestational weight gain, and educational level, which we used as an indicator of socioeconomic status, and birth weight adjusted for gestational age. We also included mother's race/ethnicity as it is associated with both breastfeeding and adiposity. Then we added each other possible confounder separately to that model. We considered country of birth, marital status, and maternal age at enrollment, but none of these covariates changed the estimates, and therefore we did not include them in the analyses. We entered covariates as continuous variables in the models, except for sex (male, female), educational level (less than high school, some college, BA/BS, graduate school), smoking status (never, former, during pregnancy), race/ethnicity (white, black, Hispanic, other). We report 3 models in this paper. In model 1 we report the association between breastfeeding and adiposity adjusted for child's sex and age at outcome assessment. Model 2 is additionally adjusted for maternal educational level, race/ethnicity, smoking status during pregnancy, prepregnancy BMI, and pregnancy weight gain, and birth weight adjusted for gestational age. In model 3 we added the mediator infant weight change. We report regression estimates (ß) or odds ratios (OR) and 95% confidence intervals (CI) for the main predictors. We conducted all analyses with SAS 9.1 (SAS Institute, Cary, NC).

RESULTS

Sample characteristics
Participant characteristics are summarized in Table 1. At 6 months postpartum, 9.2% of mothers had never breastfed fed their infants, whereas 25.0% had fed their infants breastmilk with no formula (Table 1). Mean (SD) duration of any breastfeeding was 4.3 (2.3) months. At age 3 years, mean (SD) child BMI z score was 0.45 (1.03) units, sum of subscapular plus triceps skinfold thicknesses was 16.7 (4.0) mm, and SS:TR ratio was 0.64 (0.15); 3.4% of children were obese according to the definition of the IOTF, this was 9.2% according to the criteria of the CDC (Table 1).

Associations of breastfeeding and infant weight change with adiposity measures
Whereas weight-for-age z score increased between birth and 6 months for both never breastfed infants (mean increase 0.43 [SD 0.94] units) and infants that were breastfed for less than 6 months (0.49 [SD 1.03]), fully breastfed infants hardly changed in weight-for-age z score (-0.03 [SD 1.07]), suggesting that they were growing as expected (Table 1). On unadjusted analyses, for each unit increase in weight-for-age z score between birth and 6 months, age 3 year BMI z score increased by 0.24 units (95% CI 0.18 , 0.30), SS + TR increased by 0.57 mm (95% CI 0.32 , 0.81), and the odds ratio for obesity was 2.05 (95% CI 1.62 , 2.60).

There was no association between breastfeeding status and the ratio of subscapular to triceps skinfold (Table 1). Compared to never breastfed children, mean BMI z score at 3 years was lower in fully breastfed children (ß = -0.27, [95% CI -0.53 , -0.01]) and children that were given any breastfeeding for 6 months (ß = -0.31, [95% CI -0.57, -0.05]), but did not differ for children that were given breastfeeding for less than 6 months (ß = 0.03, [95% CI -0.22 , 0.27]). Compared with never breastfed children, the prevalence of obesity was lower in the fully breastfed children group (OR = 0.14, [95% CI 0.04 , 0.41]), but not in the children that were breastfed for less than 6 months or were partially breastfed for 6 months. (Table 2, model 1). SS + TR showed a similar pattern as BMI z score (Table 2, model 1).

Multivariable estimates were attenuated slightly after adjustment for confounders: BMI z score (ß = -0.17 units, [95% CI -0.43 , 0.09]); SS + TR (ß = -1.48 mm, [95% CI -2.52 , -0.44]). Children who received any breastfeeding for 6 months also had somewhat lower BMI z score and lower SS + TR than never breastfed infants (Table 2, model 2). When we considered breastfeeding duration as a continuous measure, for each month that a child was breastfed until age 6 months, the decrement in BMI z score was 0.04 units (95% CI -0.07 , -0.01) and the decrement in SS + TR was 0.19 mm (95% CI -0.31 , -0.07) (Table 3, Figure 1). For each month that a child was breastfed, odds of being obese was reduced by 8% (95% CI -2 to 18%).

We repeated our analyses with age of introduction of solids as a confounder, but results were similar (data not shown).

Mediating effect of Infant Weight Change
After we added infant weight change to the multivariable model, effect estimates for BMI z score were attenuated among fully breastfed children (from ß= -0.17, [95% CI -0.43 , 0.09] to ß= -0.03, [95% CI -0.27 , 0.20]) and children that were given any breastfeeding for 6 months (from ß= - 0.20, [95% CI -0.46 , 0.05] to ß= -0.06, [95% CI -0.29 , 0.17] (Table 2, model 3), each compared with never breastfed

children. The odds ratio for obesity among fully breastfed children was modestly attenuated after we added infant weight change to the model (from OR = 0.21, [95% CI 0.07 , 0.68] to OR = 0.29, [95% CI 0.08 , 1.05]), as was the estimate for SS + TR (from ß= -1.48, [95% CI -2.52 , -0.44] to ß= -1.16, [95% CI -2.18 , -0.14]). Infant weight change was an independent predictor of all adiposity measures (Table 2).

Considering breastfeeding duration, estimates for BMI z score for each month that a child was breastfed were attenuated (from ß= -0.04, [95% CI -0.07 , -0.01] to ß= -0.01, [95% CI - 0.04 , 0.02]) after we added infant weight change to the multivariate model (Table 3, Figure 1). Estimates for SS + TR attenuated from ß= -0.19 (95% CI -0.31,-0.07) to ß= -0.13 (95% CI -0.25, - 0.01) (Table 3, Figure 1), and adiposity attenuated from OR=0.92 (95% CI 0.82-1.02) to OR=0.98 (95% CI 0.87-1.11) (Table 3). We saw similar results when we adjusted for change in weight for length (data not shown).

DISCUSSION

In this longitudinal study of over 800 infants in the US, we found that breastfeeding until 6 months of age was associated with a lower BMI z score, lower skinfold thicknesses, and lower odds of obesity at age 3 years. Infant weight gain was a strong independent predictor of these outcomes and fully mediated the associations of breastfeeding with BMI z score, but only partially with sum of skinfold thicknesses and odds of being obese.

Our finding that breastfeeding in the first 6 months of life is associated with lower adiposity at age 3 years is consistent with a large body of epidemiologic evidence summarized in recent systematic reviews and meta-analyses.[1,3,4] However, one review[23] concluded that the association between breastfeeding and mean BMI is likely to be confounded by socioeconomic status, maternal smoking and maternal BMI. Also, a large breastfeeding promotion intervention trial did not find a protective effect of breastfeeding on obesity.[24] It should be noted that this trial included only mothers that initiated breastfeeding and thus evaluated the consequences of longer breastfeeding duration, not the effects of breastfeeding relative to formula feeding. Residual confounding by lifestyle-related factors may explain the association between breastfeeding and obesity.

However, several behavioral and biological mechanisms have been proposed to explain the observed protective effect of breastfeeding on future obesity.[5,6,25] There is some support for the mechanisms in animal data, but there is a lack of experimental data in humans to support mechanistic hypotheses.[26] First, whereas formula fed children may be encouraged to take in more or less volume than they would otherwise, breastfed children may better learn to selfregulate their energy intake by internal satiety cues. This enhanced

Table 1 Characteristics of 884 mother-infant pairs in Project Viva according to infant feeding status at 6 months after birth

		N	%	INFANT FEEDING STATUS AT 6 MONTHS (%)				P FOR TREND
				Never bf N=81 (9%)	Any bf <6 months N=341 (39%)	Partial bf for 6 months N=241 (27%)	Full bf for 6 months N=221 (25%)	
MATERNAL CHARACTERISTICS								
Age at enrollment (years)	<25	56	6	9	11	4	1	0.001
	25-35	550	62	63	60	63	64	
	≥ 35	278	31	28	29	33	35	
Educational level	High school or less	52	6	10	8	5	2	<0.0001
	Some college	177	20	40	25	13	12	
	BA/BS	328	37	35	40	37	33	
	Graduate school	327	37	16	26	45	52	
Race /ethnicity	Black	89	10	7	13	10	6	0.02
	Hispanic	49	5	5	6	7	2	
	Other	77	9	2	11	8	9	
	White	627	76	85	69	76	83	
Smoking during pregnancy	Smoker	82	9	14	15	6	3	0.04
	Former smoker	180	20	23	19	23	19	
	Never	622	70	63	66	71	68	
Prepregnancy BMI, kg/m^2	< 25	580	66	51	62	71	71	<0.0001
	25-30	195	22	31	23	18	22	
	≥ 30	109	12	19	16	11	6	
Excessive pregnancy weight gain (2009 Institute of Medicine category)		527	60	65	60	59	57	0.22
CHILD CHARACTERISTICS								
Male		442	50	49	50	51	50	0.83
Birth weight-for-gestational age z score, mean (SD)		0.25 (0.93)		0.20 (0.95)	0.20 (0.93)	0.21 (0.93)	0.38 (0.91)	0.04
Change in weight-for-age z score between birth and 6 months, mean (SD)		0.24 (1.09)		0.43 (0.94)	0.49 (1.03)	0.05 (1.16)	-0.03 (1.07)	<0.0001
AGE 3 ANTHROPOMETRIC CHARACTERISTICS								
BMI z score, mean (SD)		0.45 (1.03)		0.58 (1.19)	0.61(1.01)	0.28 (1.10)	0.33 (0.86)	0.0003
BMI categories IOTF	normal	749	85	83	85	85	91	0.0008
	overweight	105	12	11	13	13	9	
	obese	30	3	6	5	2	1	
BMI percentiles	< 5th	20	2	2	1	4	2	<0.0001
	5th-85th	632	71	63	69	74	76	
	85th-95th	151	17	21	18	12	19	
	≥ 95th	81	9	14	12	10	2	
Skinfold thicknesses (mm, mean (SD))	Sum of subscapular and triceps	16.7 (4.0)		17.8 (4.5)	17.2 (4.2)	16.1 (3.9)	16.1 (3.5)	<0.0001
	Ratio of subscapular and triceps	0.64 (0.15)		0.63 (0.12)	0.65 (0.17)	0.65 (0.16)	0.61 (0.14)	0.09

self-regulation may persist beyond the breastfeeding period. Second, breastfed children may consume less protein than formula fed children. High protein intake in formula fed children may lead to higher insulin levels which subsequently stimulate greater adipose tissue deposition.[27] Third, breastfed children may be differently exposed to leptin, a hormone contained in breastmilk but not formula.[6] Breastmilk leptin may influence growth in infants.[25]

Few studies[28] have examined whether early infant weight change may mediate the observed relationship between breastfeeding and obesity. Breastfeeding may lead to less infant weight gain which in turn may lead to lower adiposity. Scholtens et al.[28] found that mean BMI and overweight prevalence at 7 years of age were lower among breastfed children. However, adjustment for BMI at 1 year of age attenuated the observed associations (from ß= -0.12, 95% CI: [-0.34, 0.10] to ß= -0.01, 95% CI [-0.22, 0.19] for children who were breastfed for at least 16 weeks compared to never breastfed children).[28] In our study, breastfeeding was still associated with SS + TR and obesity with confidence limits that excluded the null value for SS + TR even after adjustment for infant weight gain from birth to 6 months. A first possible explanation is that obesity and SS + TR may reflect body fatness better than BMI, which incorporates both fat and lean mass.[29, 30] This is in line with other studies that found breastfeeding associated with fat mass, but not with BMI.[31, 32] Another possible explanation may be that infant weight change in the first 6 months after birth is more associated with lean mass than fat mass[33] and therefore mediates the association between breastfeeding and BMI, but not fully between breastfeeding and obesity. However, other studies have reported rapid infant weight gain to be mainly associated with fat mass.[34]

We did not find an effect of breastfeeding or infant weight change on central adiposity, measured as the subscapular to triceps skinfold ratio.[18, 19] Rapid infant weight gain has been found to be positively associated with central obesity among older children.[34, 35]

Strengths of this study included research standard measures of growth at ages 6 months and 3 years. We were able to use several indicators of adiposity including measurement of skinfold thicknesses. We assessed breastfeeding during infancy, before outcomes were assessed, minimizing the likelihood of bias, and we were able to account for a wide variety of important confounders. Self-reported information on breastfeeding duration is valid and reliable when recalled within 3 years.[36]

However, some limitations should be considered when interpreting the results. Although we accounted for measured confounders, residual confounding may remain. Thus, the protective effect of

Table 2

Multivariable-adjusted adiposity estimates at 3 years of age according to type of infant feeding during 6 months, among 884 mother-child pairs in Project Viva

	BMI Z SCORE (N= 884)		SS + TR (N= 843)		BMI >95TH PERCENTILE* (N= 713)	
	ß	95% CI	ß	95% CI	OR	95% CI
MODEL 1: ADJUSTED FOR CHILD'S AGE AND SEX						
Never breastfed	ref (0)	ref	ref (0)	ref	ref (1)	ref
Any breastfeeding for less than 6 months	0.03	-0.22, 0.27	-0.56	-1.53, 0.40	0.80	0.39, 1.67
Partial breastfeeding for 6 months	-0.31	-0.57, -0.05	-1.68	-2.67, -0.68	0.61	0.28, 1.33
Full breastfeeding for 6 months	-0.27	-0.53, -0.01	-1.61	-2.62, -0.59	0.14	0.04, 0.41
MODEL 2: MODEL 1 + MOTHER'S EDUCATIONAL LEVEL/ ETHNICITY / SMOKING STATUS DURING PREGNANCY / BMI / AND PREGNANCY WEIGHT GAIN AND BIRTH WEIGHT ADJUSTED FOR GESTATIONAL AGE						
Never breastfed	ref (0)	ref	ref (0)	ref	ref (1)	ref
Any breastfeeding for less than 6 months	0.08	-0.16, 0.32	-0.33	-1.30, 0.63	0.90	0.40, 2.03
Partial breastfeeding for 6 months	-0.20	-0.46, 0.05	-1.50	-2.52, -0.48	0.88	0.37, 2.10
Full breastfeeding for 6 months	-0.17	-0.43, 0.09	-1.48	-2.52, -0.44	0.21	0.07, 0.68
MODEL 3: MODEL 2 + CHANGE IN INFANT WEIGHT -FOR-AGE Z SCORE BETWEEN BIRTH AND 6 MONTHS						
Never breastfed	ref (0)	ref	ref (0)	ref	ref (1)	ref
Any breastfeeding for less than 6 months	0.05	-0.17, 0.27	-0.32	-1.27, 0.62	0.85	0.33, 2.18
Partial breastfeeding for 6 months	-0.06	-0.29, 0.17	-1.18	-2.18, -0.18	1.44	0.53, 3.96
Full breastfeeding for 6 months	-0.03	-0.27, 0.20	-1.16	-2.18, -0.14	0.29	0.08, 1.05
Change in infant weight-for-age z score	0.44	0.38, 0.51	0.89	0.60, 1.17	4.30	3.02, 6.14

* The odds on which the odds ratios are based, is a comparison between obese and normal weight children, overweight children were not included.

Table 3

Multivariable-adjusted adiposity estimates at 3 years of age according to breastfeeding duration until 6 months among 877 mother-child pairs in Project Viva

	BMI Z SCORE (N = 877)		SS + TR (N = 837)		BMI >95TH PERCENTILE (N = 708)	
	ß	95% CI	ß	95% CI	OR	95% CI
Model 1: adjusted for child's age and sex	-0.06	-0.09, -0.03	-0.22	-0.33, -0.11	0.86	0.78, 0.94
Model 2: adjusted for confounders*	-0.04	-0.07, -0.01	-0.19	-0.31, -0.07	0.92	0.82, 1.02
Model 3: model 2 + change in infant weight-for-age z score between birth and 6 months	-0.01	-0.04, 0.02	-0.13	-0.25, -0.01	0.98	0.87, 1.11
Change in infant weight-for-age z score	0.45	0.38, 0.51	0.91	0.63, 1.19	4.21	2.97, 5.96

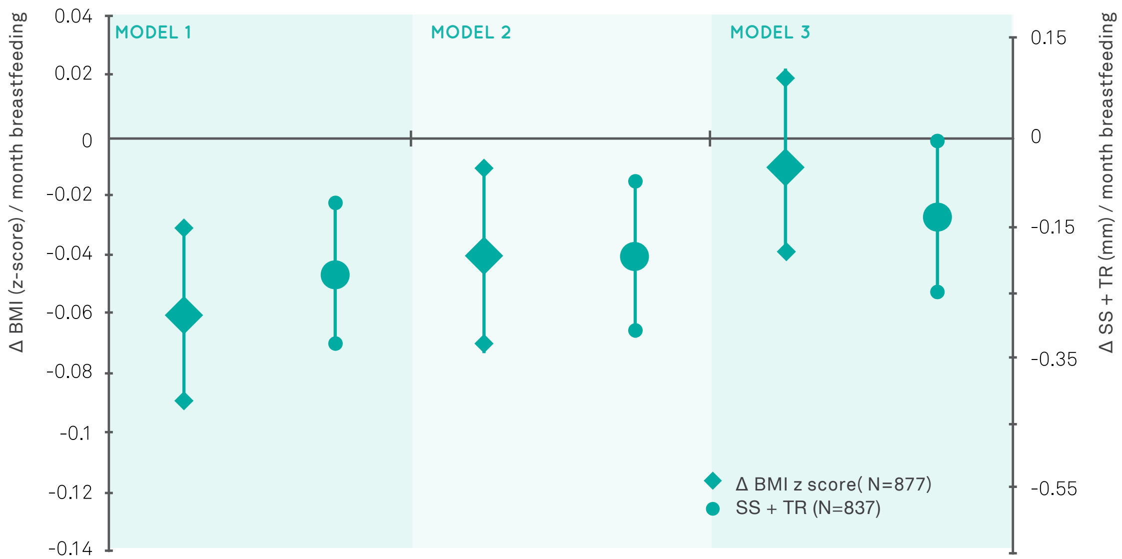
* model 2 was adjusted for all variables in model 1 + mother's educational level, race/ethnicity, smoking status during pregnancy, BMI, and pregnancy weight gain and birth weight adjusted for gestational age

breastfeeding on overweight may be due to confounding or selection bias.[2, 23,27] Also, the association between breastfeeding and infant weight change may be subject to reverse causality; mothers may choose to switch from breastfeeding to formula feeding if their infant is growing quickly and seems very hungry. Thus, those infants who grow slower were able to be exclusively breastfed for 6 months. On the other hand, it is also possible that mothers whose infants grow slower may discontinue breastfeeding, because they feel not confident that the baby is satisfied with breastfeeding only.[37] Furthermore, most of the measures were selfreported. However, we expect that any misclassification would have been nondifferential, and may therefore have attenuated the results. Lastly, adiposity is more accurately measured by methods such as dual-energy X-ray absorptiometry (DXA) or densitometry than by using BMI.[29]

We performed an in-person study visit during infancy only at age 6 months, and therefore we were not able to directly compare our results with other studies such as Stettler et al.[38] It may be that another time period for infant weight change has a more relevant critical window. However, it should be noted that four months was also an arbitrary timepoint, as that was the age at which Stettler et al had data available. Further research with multiple research quality assessments of infant growth will be helpful in ascertaining the periods of growth during infancy that have the greatest influence of obesity risk. Also, it may be that weight-for-age is not the best measure of adiposity gain.

Fully breastfed children in our study may already have received complementary feeding before 6 months of age. Complementary feeding before 4 months of age may have an effect on developing adiposity.[39] We did not measure body composition at birth, which may be a stronger confounder than birth weight adjusted for gestational age. Loss to follow-up might have introduced selection bias, for example if non-participants fully breastfed their infants and these infants were more often overweight at age 3. Although children lost to follow-up were more often formula-fed, we have no evidence that they differ in weight status. Lastly, the mothers in this study may not fully represent the general population as they were generally well educated and all resided in Massachusetts.

Figure 1 Multivariable-adjusted adiposity estimates at 3 years of age according to breastfeeding duration until 6 months among 877 children in Project Viva



model 1 = breastfeeding duration (months), adjusted for child's age and sex. model 2 = model 1 + mother's educational level, race/ethnicity, smoking status during pregnancy, BMI, and pregnancy weight gain and birth weight adjusted for gestational age. model 3 = model 2 + change in infant weight-for-age z score between birth and 6 months

Conclusion

Our findings suggest that infant weight change may be in the intermediate pathway between breastfeeding and later size. Because the attenuation of effect was only modest for indicators of adiposity, infant weight change does not appear to be the only mechanism by which breastfeeding protects against adiposity. Future research may search for additional pathways that explain the association between breastfeeding and obesity.

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ABSTRACT

Background
The effect of early introduction of solids on infant weight gain and later overweight remains debatable. We examined the association between the introduction of solids and weight gain between birth and 45 months, taking into account weight development in several periods.

Methods
Data from 3184 children were used. Timing of introduction of solids was obtained from a questionnaire at 12 months postpartum. Anthropometric data were collected maximally 12 times over 45 months during standardized child health center visits. Weight-for-height (wfh) was converted into a z score. Multivariable linear regression and repeated measurements analyses with splines were used to obtain estimates for wfh.

Results
In adjusted cross-sectional analyses, relative to infants introduced to solids after 6 months, wfh z scores were higher in children introduced to solids between 3-6 months at 11 months (z=0.10, 95% CI: 0.01, 0.18), while wfh z scores did not differ for children that were introduced to solids between 0-3 months at any time point. Increase in wfh z score was higher before the introduction of solids in children introduced to solids between 3-6 months (z=0.65, 95% CI: 0.34-0.95) than in children introduced to solids after 6 months (z= -0.04, 95% CI: -0.05, -0.03), but this was followed by a relative decrease in wfh z score. After the introduction of solids, wfh gain was similar in all groups.

Conclusion
These results imply that early introduction of solids has no long-term effect on weight-for-height, and therefore probably neither for later obesity.

2.3 GROWTH PATTERNS BEFORE, DURING, AND AFTER THE INTRODUCTION OF SOLIDS

BASED ON

Van Rossem L / Kiefte-de Jong JC / Looman CN / Jaddoe VW / Hofman A / Hokken-Koelega AC / Mackenbach JP / Moll HA / Raat H.
Weight gain before, during, and after the introduction of solids: results from a longitudinal birth cohort.
Submitted

INTRODUCTION

The importance of infant feeding for later disease risk has often been studied.[1] One focus of these studies is the association between infant feeding and obesity risk. There is small but consistent evidence that breastfeeding has a protective effect on the development of overweight and obesity.[2-4] A proposed mechanism to explain the association between breastfeeding and obesity concerns infant weight gain.[5] Breastfed and formula-fed infants differ in weight gain throughout the first year of life, resulting in breastfed infants being relatively leaner at 12 months compared to formula-fed infants.[6] Rapid infant weight gain is, in turn, associated with overweight.[7] However, infant feeding does not only include milk feeding, and the contribution of solids in the infant's diet increases throughout the first year of life. The association between introduction of solids and weight gain is less well studied and results are conflicting.[8-10] Some report that early introduction of solids, independent of breastfeeding or other confounding factors, results in rapid infant weight gain and higher obesity risk in childhood,[8-10] whereas others show no independent association between timing of introduction of solids and childhood obesity.[11-14]

Determinants of early introduction of solids are young maternal age, smoking during pregnancy, and early cessation of breastfeeding.[15] The latter two are also associated with weight gain and may therefore confound the association. It is also reported that mothers start introducing solids when they perceive their infant as being hungry.[15] However, most studies do not take into account that introduction of solids may be related to weight gain before, during, and after introduction of solids to the infant's diet. In addition, it is plausible that any effect of the introduction of solids on weight gain will not be linear over time.

Therefore, the present study examines the association between the introduction of solids and weight gain between birth and 45 months, taking into account weight development in several periods. We hypothesized that infants introduced to solids at an early age will have faster weight gain in infancy before and after the introduction of solids.

METHODS

Study design and population

This study was embedded in The Generation R study, a population-based prospective cohort study from fetal life onwards. Details of the study are described elsewhere.[16] In short, the Generation R study was designed to identify early determinants of growth, development and health. Invitations to participate in the study were made to all pregnant mothers who had an expected delivery date between April 2002 and January 2006 and who lived in the study area (Rotterdam, the Netherlands) at time of delivery. The study was conducted in accordance with the guidelines proposed in the World Medical Association Declaration of Helsinki, and was approved by the Medical Ethical Committee at Erasmus MC, University Medical Center Rotterdam. Written consent was obtained from all participants.

Of the 7295 children who were followed from birth 5088 received the 12-months food frequency questionnaire, because data collection on food started from 2003 onwards. Of these, 3643 (72%) completed the 12-months food frequency questionnaire. Excluded were twins (n=82) and children born before 37 weeks of gestation (n=158), because of their different growth pattern. Also excluded were all children with less than four measurements on weight and height (n=219). Finally, data of 3184 children were analyzed, with a median number of observations of 9 and a total of 38208 anthropometric observations.

Compared to those with missing information on the introduction of solids and those having less than four weight and height observations, mothers included in the present study were more often breastfeeding at 6 months (32.9% vs. 26.9%), higher educated (33.4% vs. 21.8%), more often had infants with a normal birth weight (85.0% vs. 81.8%), were more often native Dutch (67.7% vs. 44.2%), less often smoked during pregnancy (7.7% vs. 12.5%) ($p<0.001$ for all), and more often had a normal weight, defined as a body mass index (BMI) ≤ 25 kg/m^2 (75.9% vs. 72.0%) ($p<0.01$).

Measurements

Infant feeding

At the child's age of 12 months, parents were asked at what age they had first introduced the following solids in the infant's diet: (full or semi-skimmed) dairy products, porridge, bread, biscuits, crackers, baby cookies, pasta, (breaded) meat products, vegetarian meat substitutes, fish, shellfish, vegetables, fruit, peanuts and nuts. These food products were included in a Dutch food consumption survey among infants.[17] Answer categories included 'never given', 'between 0-3 months', 'between 3-6 months', 'between 6-9 months', and 'older than 9 months', which we recoded into 3 categories: '0-3 months', '3-6 months', and '6 months or later'. The latter group is the group that adheres best to the feeding recommendations of the WHO and is therefore used as the reference group.[18]

Anthropometrics

Height and weight were measured with standardized methods at each visit to the child health center. Standard visits at the child health center take place at 1, 2, 3, 4, 6, 11, 14, 18, 24, 30, 36, and 45 months of age. Weight-for-height (wfh) z score was calculated from a national reference using the Growth Analyzer program (http://www.growth-analyser.org).[19] Z-scores reflect differences from the population mean. The population mean is 0, and 95% of children will be in the range from -2 SD to +2 SD.

Covariates

Through a combination of data collected from measurements, questionnaires and medical records, information was obtained on educational level of the mother, ethnicity, parental BMI, birth weight, gestational age, breastfeeding, history of food allergy in the infant's first year of life, and hospital admission during the first year after birth.

Statistical analyses

The characteristics of mothers introducing solids before 6 months were compared with those of mothers introducing solids after 6 months. Differences were tested with the Chi-square test for categorical variables and by ANOVA for continuous variables.

First, the association between timing of introduction of solids and wfh z score was analyzed by means of linear regression, for which betas and their 95% confidence intervals (95% CI) are reported for each feeding group. These cross-sectional analyses were performed at four time points: at birth, 3 months, 6 months, 11 months, and 36 months of age. These time points were chosen to reflect the effect of weight gain before, around, shortly after and some time after the introduction of solids. For each linear regression model, three models are shown: model 1 is unadjusted, model 2 is adjusted for the previous measure of wfh to give insight into conditional wfh gain, and model 3 is adjusted for the following covariates: mother's educational level, mother's ethnicity, continued smoking during pregnancy, BMI, history of (any) food allergy in the first year of life, hospital admission in the first year of life, and duration of breastfeeding.

Then, multilevel analyses (mixed procedure in SAS) were performed with the wfh z score as an outcome. This longitudinal method adjusts for the within-subject dependency associated with the repeated observations on weight by allowing the regression coefficients to be random.[20] For this analysis linear splines were created, which can be used when different estimates are needed for different time periods. The knots for the splines were set shortly after the start of the introduction of solids (because no immediate effect of introduction is expected), shortly after the end of the category, and after 12 months. Thus, estimates for wfh gain are given for the following periods: birth until the start of introduction of solids (i.e. until 1.5, 4.5, or 7.5 months), wfh gain during the period of introduction of solids (i.e. 1.5-4.5 months, 4.5-7.5 months, 7.5-11.5 months), wfh gain after the period of introduction of solids (i.e. after 4.5, 7.5 and 11.5 months), and wfh gain after 12 months (similar for all groups). To confirm our choice for these periods, we compared our model with linear splines with the best model for wfh as a function of age by using fractional polynomials.[21] The best model for wfh was predicted by age and √age. The predicted values of wfh for the two methods had a mean difference of 0.11% (SD 2.65). Linear splines were put in the model as time variables, and we tested the fit of the model with and without interaction terms for introduction of solids with all spline variables by using the -2 Log-likelihood ratio test. The model with interaction terms was significantly better (Chi^2=133.8, df=8, p<0.001). Interactions were significant (cut-off point: p<0.10) for the period until the start of introduction of solids (p<0.001), during the period of introduction of solids (p<0.001), but not after the introduction of solids until 12 months (p=0.32), and after 12 months (p=0.93). Stratified analyses are presented for each group of introduction of solids.

Because there were no differences between boys and girls in the association between the introduction of solids and wfh, analyses include both sexes.

Analyses were conducted using the Statistical Package for Social Sciences (SPSS) version 17.0 for Windows (SPSS Inc, Chicago, IL, USA). For the multilevel analyses, Statistical Analysis Software (SAS) version 9.1.3 for Windows (SAS Institute, Cary, NC, USA) was used.

RESULTS

Overall, 38% of mothers introduced solids after 6 months. Relative to mothers that introduced solids before 6 months, mothers that introduced solids after 6 months were more often higher educated, native Dutch, non-smokers, gave breastfeeding until 6 months, and more often had an infant with a history of food allergy in the first year of life (p<0.001). Hospital admission in the first year of life and mother's BMI (both categorical and continuous) were not significantly associated with timing of the introduction of solids. The number of children with either a low or high birth weight did not differ between groups, but the mean birth weight of children that were introduced to solids before 3 months was slightly lower (Table 1).
In unadjusted cross-sectional analyses, children that were introduced to solids between 3-6 months of age had a higher wfh z score at 3 months (b=0.09, 95% CI: 0.002, 0.17), and at 11 months (b=0.11, 95% CI: 0.04, 0.18) compared to children that were introduced to solids after 6 months. After adjustment for the previous measurement, children that were introduced to solids between 3-6 months had a higher wfh z score at 11 months compared to children that were introduced to solids after 6 months. After adjustment for all covariates, children that were introduced to solids between 3-6 months of age, had a significantly higher wfh z score at 11 months (Table 2).

Table 3 presents data on multilevel analyses. Wfh gain was estimated for each group of solid introduction per predefined period. Until the start of introduction of solids, infants introduced to solids between 3-6 months had significantly higher wfh (z=0.65, 95% CI: 0.34-0.95) compared to those introduced to solids after 6 months (z= -0.04, 95% CI: -0.05, -0.03). Significantly lower wfh was found after introducing solids until the endpoint category for infants introduced to solids

Table 1 Subject characteristics according to the timing of introduction of solids (n=3184)*

		TOTAL	INTRODUCTION OF SOLIDS			P-VALUE
			0-3 months (n=171)	3-6 months (n=1808)	≥ 6 months (n=1205)	
SOCIO-DEMOGRAPHIC FACTORS						
Educational level	Low	14.1	21.1	15.9	10.5	<0.001
	Mid-low	26.8	36.0	28.1	23.6	
	Mid-high	25.7	23.6	24.8	27.5	
	High	33.4	19.3	31.2	38.5	
Mother's ethnicity	Native Dutch	67.6	53.7	67.5	69.6	<0.001
	Other western	11.5	12.3	10.1	13.3	
	Non-western	20.9	34.0	22.3	17.0	
PARENTAL CHARACTERISTICS						
Maternal smoking during pregnancy		7.8	13.8	9.5	4.3	<0.001
Mother's BMI (kg/m^2)	Normal	75.9	74.3	75.2	77.1	0.47
	Overweight	16.9	17.1	16.8	16.8	
	Obese	7.2	8.6	7.9	6.0	
PERINATAL CHARACTERISTICS						
Birth weight (grams)	Low (<2500)	1.4	1.2	1.2	1.7	0.41
	Normal (2500-4000)	81.9	86.5	82.0	81.0	
	High (>4000)	16.8	12.3	16.8	17.3	
Birth weight (grams)	Mean (SD)	3521 (497)	3422 (476)	3528 (494)	3525 (503)	<0.05
POSTNATAL CHARACTERISTICS						
Breastfeeding at 2 months		69.2	56.3	66.9	74.4	<0.001
Breastfeeding at 6 months		32.8	22.2	27.3	42.6	<0.001
History of food allergy		6.4	5.6	5.1	8.6	<0.001
Hospital admission in first year of life		6.1	7.0	5.4	7.0	0.20
Overweight at age 3 years according to IOTF criteria		9.1	8.3	9.4	8.6	0.78

* Missing data were: 99 (3.1%) for educational level, 58 (1.8%) for ethnicity, 532 (16.7%) for maternal smoking, 698 (21.9%) for mother's BMI, 3 (0.1%) for birth weight, 87 (2.7%) for breastfeeding at 2 months, 56 (1.8%) for breastfeeding at 6 months, 172 (5.4%) for history of allergy, 199 (6.3%) for hospital admission, and 990 (31.1%) for overweight at age 3 years.

between 0-3 months (z=-0.13, 95% CI: -0.23, -0.04) and 3-6 months (z=-0.13, 95% CI: -0.18, -0.08). After the endpoint category and the age of 12 months, all children had a similar wfh gain, and wfh gain was as expected, i.e. around a z score of 0. Figure 1 is a graphic presentation of the results in Table 3.

DISCUSSION

This study shows that timing of the introduction of solids is independently associated with anthropometric measures in the first year of life. Wfh gain was higher before any solids were introduced in infants introduced to solids between 3-6 months compared to those introduced to solids after 6 months. However, there seems to be no long-term effect of the introduction of solids on later weight or obesity.

Studying the association between early introduction of solids and weight gain presents a methodological challenge. First, the association between early introduction of solids and weight gain may be subject to reverse causality, i.e. infants experiencing rapid weight gain may be introduced to solids earlier, or later. Therefore, some studies adjusted the analyses for birth weight. However, this does not take into account the rate of weight gain shortly after birth. The present results reveal no significant differences in birth weight z score among subgroups, but show that infants that were introduced early to solids were already heavier prior to the introduction of solids. Second, the association between early introduction of solids and weight gain may be confounded by several factors. Although we were able to adjust for the most important confounders, we had no detailed information on breastfeeding exclusivity according to the WHO definition, i.e. breastfeeding with no other fluids or solids at all, not even water. Also, because we lacked information on the exact amount of formula feeding intake, we also lacked details on exact calorie and protein intake. When adjusting for any breastfeeding, children could have received mixed feeding and may have a high caloric intake due to the infant formula. This may obscure the effect of breastfeeding on slower infant weight gain, and give an overestimation of our adjusted results. Also, our questionnaire only covered the foods commonly eaten by infants and did not include items such as confectionary. Therefore, some subjects may be misclassified concerning their timing of introduction of solids. As this is unlikely to be related to weight status, this misclassification is not likely to bias our results.

Our finding that early introduction of solids is associated with weight measures in the first year of life is consistent with the findings of others,[8, 9, 11] although one randomized trial found no association between early introduction of solids and infant's growth in the first year of life.[14] Similarly, our finding that early introduction of solids is not associated with weight measures after the first year of life, was confirmed by others with weight measures between 3 and 5 years of age.[12, 13, 22] Wilson et al. found an association between early introduction of solids and weight in 7-year-olds,[10] and Schack-Nielsen et al. reported an association between early introduction of solids and weight in adults.[23] The two latter studies reported an association between introduction of solids and weight, independent of weight before the introduction of solids. The authors suggest that the mechanism underlying the association between early introduction of solids, growth and later obesity may be environmental. We propose that infants that were already on a fast weight gain track, may continue on that path. Indeed, the introduction of solids may further enhance rapid weight gain but may not be the direct cause, and other obesity-inducing behaviors may be related to early introduction of solids. In addition, our results show that after the introduction of solids, wfh z score was not necessarily higher in children introduced to solids before the age of 6 months. After an initial increase in wfh z score, there will be a tendency to revert to the mean (regression to the mean), which may explain the decrease in weight for age z score in our results.

Table 2

Associations between timing of introduction of solids and weight-for-height (wfh) z score at 3, 6, 11 and 36 months

		MODEL 1	MODEL 2*	MODEL 3††
		unadjusted	adjusted for previous measurement	adjusted for covariates
WFH Z SCORE AT 3 MONTHS (N= 2259)				
Introduction solids	0-3 months	0.12 (-0.08, 0.31)	0.03 (-0.15, 0.26)	-0.01 (-0.24, 0.22)
	3-6 months	0.09 (0.002, 0.17)	0.04 (-0.04, 0.11)	0.07 (-0.03, 0.18)
	≥ 6 months	0 (ref)	0 (ref)	0 (ref)
WFH Z SCORE AT 6 MONTHS (N= 2781)				
Introduction solids	0-3 months	-0.02 (-0.19, 0.15)	-0.10 (-0.25, 0.06)	-0.15 (-0.34, 0.05)
	3-6 months	0.03 (-0.05, 0.10)	0.03 (-0.04, 0.09)	-0.01 (-0.10, 0.08)
	≥ 6 months	0 (ref)	0 (ref)	0 (ref)
WFH Z SCORE AT 11 MONTHS (N= 2768)				
Introduction solids	0-3 months	-0.05 (-0.20, 0.11)	-0.02 (-0.14, 0.11)	-0.05 (-0.24, 0.13)
	3-6 months	0.11 (0.04, 0.18)	0.09 (0.04, 0.15)	0.10 (0.01, 0.18)
	≥ 6 months	0 (ref)	0 (ref)	0 (ref)
WFH Z SCORE AT 36 MONTHS (N= 2288)				
Introduction solids	0-3 months	-0.04 (-0.23, 0.14)	-0.02 (-0.22, 0.18)	-0.08 (-0.29, 0.13)
	3-6 months	0.05 (-0.03, 0.13)	0.07 (-0.02, 0.15)	0.07 (-0.03, 0.16)
	≥ 6 months	0 (ref)	0 (ref)	0 (ref)

*Model 2: previous measurement was at 2 months for wfh z score at 3 months, at 4 months for wfh z score at 6 months, at 6 months for wfh z score at 11 months, and at 24 months for wfh z score at 36 months.†Model 3: adjusted for mother's ethnicity, mother's educational level, continued maternal smoking during pregnancy, mother's BMI, history of allergy, hospital admission during first year of life, for breastfeeding initiation for wfh z score at birth, adjusted for breastfeeding at 2 months for wfh z score at 3 months, adjusted for breastfeeding at 6 months for wfh z score at 6, 11, and 36 months.

Table 3

Data on longitudinal analyses of the association between timing of introduction of solids and weight-for-height z score (n=3184)

		TIMING OF INTRODUCTION TO SOLIDS		
		0-3 months	3-6 months	≥ 6 months
Intercept for unadjusted analyses		0.30 (0.11, 0.48)	-0.40 (-0.71, -0.08)	0.43 (0.37, 0.49)
Weight gain (z score) until start of introduction of solids*	unadjusted	0.02 (-0.02, 0.07)	0.67 (0.42, 0.92)‡	-0.04 (-0.05, -0.03)
	adjusted†	0.02 (-0.03, 0.08)	0.65 (0.34, 0.95) ‡	-0.04 (-0.05, -0.03)
Weight gain (z score) between start point of introduction of solids and endpoint category§	unadjusted	-0.12 (-0.20, -0.05)‡	-0.13 (-0.17, -0.08)‡	0.02 (0.001, 0.05)
	adjusted†	-0.13 (-0.23, -0.04)‡	-0.13 (-0.18, -0.08)‡	0.02 (-0.01, 0.05)
Weight gain (z score) between endpoint category** and 12 months	unadjusted	0.01 (-0.03, 0.06)	-0.01 (-0.02, 0.01)	-0.06 (-0.11, -0.02)
	adjusted†	0.02 (-0.03, 0.08)	0.005 (-0.01, 0.02)	-0.05 (-0.10, 0.002)
Weight gain (z score) after 12 months of age	unadjusted	-0.003 (-0.009, 0.003)	-0.003 (-0.006, -0.001)	-0.003 (-0.005, -0.001)
	adjusted†	-0.01 (-0.01, 0.002)	-0.004 (-0.01, -0.001)	-0.003 (-0.01, -0.001)

Note: Analyses were stratified for each group of solid introduction. Numbers represent weight gain in z score for each specified period. Time periods in the rows represent different periods for each introduction of solids group. Therefore, comparisons across columns should be made with caution. * Starting point was 1.5 months, 4.5 months and 7.5 months, respectively † Adjustments were made for mother's educational level, ethnicity, smoking during pregnancy, mother's BMI, breastfeeding, history of allergy, and hospital admission in the first year ‡ Before stratification; significant different interaction term compared to reference group (≥ 6 months) § Weight gain between 1.5-4.5 months, 4.5-7.5 months and 7.5-11.5 months, respectively ** End point was 4.5, 7.5, and 11.5 months, respectively

Appendix 1

Associations between timing of introduction of protein rich solids and weight-for-height (wfh) z score at 3 months, 6 months, 11 months, and 36 months

		MODEL 1	MODEL 2 *	MODEL 3 †
		unadjusted	adjusted for previous measurement	adjusted for covariates
WFH Z SCORE AT 3 MONTHS (N= 2259)				
Introduction solids	0-3 months	0.12 (-0.20, 0.43)	-0.03 (-0.35, 0.29)	0.06 (-0.33, 0.45)
	3-6 months	0.06 (-0.04, 0.15)	0.03 (-0.06, 0.12)	0.03 (-0.09, 0.15)
	≥ 6 months	0 (ref)	0 (ref)	0 (ref)
WFH Z SCORE AT 6 MONTHS (N= 2781)				
Introduction solids	0-3 months	0.03 (-0.25, 0.31)	-0.07 (-0.32, 0.19)	-0.11 (-0.46, 0.23)
	3-6 months	0.02 (-0.07, 0.10)	0.01 (-0.07, 0.09)	-0.01 (-0.11, 0.09)
	≥ 6 months	0 (ref)	0 (ref)	0 (ref)
WFH Z SCORE AT 11 MONTHS (N= 2768)				
Introduction solids	0-3 months	-0.29 (-0.55, -0.04)	-0.22 (-0.44, -0.01)	-0.28 (-0.60, 0.04)
	3-6 months	0.001 (-0.08, 0.08)	-0.01 (-0.07, 0.06)	0.01 (-0.09, 0.10)
	≥ 6 months	0 (ref)	0 (ref)	0 (ref)
WFH Z SCORE AT 36 MONTHS (N= 2288)				
Introduction solids	0-3 months	-0.02 (-0.29, 0.33)	0.05 (-0.29, 0.38)	-0.03 (-0.45, 0.39)
	3-6 months	-0.04 (-0.13, 0.05)	-0.03 (-0.12, 0.07)	0.002 (-0.10, 0.11)
	≥ 6 months	0 (ref)	0 (ref)	0 (ref)

*Model 2: previous measurement was at 2 months for wfh z score at 3 months, at 4 months for wfh z score at 6 months, at 6 months for wfh z score at 11 months, and at 24 months for wfh z score at 36 months.
† Model 3: adjusted for mother's ethnicity, mother's educational level, continued maternal smoking during pregnancy, mother's BMI, history of allergy, hospital admission during first year of life, for breastfeeding at 2 months for wfh z score at 3 months, adjusted for breastfeeding at 6 months for wfh z score at 6, 11, and 36 months.

Recently, faster weight gain in formula-fed children was suggested to be caused by a large protein intake.[24] We separately analyzed protein-rich (i.e. dairy products, meat, fish, poultry, and meat substitutes) complementary feeding, but found no effect of the introduction of protein-rich solids and weight (Appendix 1). However, these results need to be confirmed taking into account the amount of protein consumption from infant feeding.

Conclusion

Infant weight gain may stimulate parents to introduce solids at an early stage. Child health centers should be aware that parents might think that their infants need more energy as a result of the fast gain in weight. However, we recommend performing a qualitative study to explore why mothers introduce solids at a certain moment. This will provide more insight into the causality of the association between introduction of solids and infant weight.

Figure 1

Estimated weight-for-height z score for each age group of introduction to solids (this figure is a graphic presentation of the data in Table 3).

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CHAPTER 3 SOCIAL DISADVANTAGE AND EARLY RISK FACTORS FOR CHILDHOOD OVERWEIGHT

ABSTRACT

Background
Given the health benefits of breastfeeding, we assessed the association between mother's educational level with starting and continuing breast-feeding. We also assessed the mediating role of socio-demographic, life-style related, psycho-social, and birth characteristics in this association.

Methods
We used the data of 2914 participants in the Generation R study, a population-based prospective cohort study. Information on educational level, breast-feeding, socio-demographic (maternal age, single parenthood, parity, job status), life-style related (body mass index, smoking, alcohol use), psycho-social (whether the pregnancy was planned or not, stress), and birth characteristics (gestational age, birth weight, Cesarean section, place and type of delivery) were obtained between pregnancy and twelve months after birth. Odds ratios and 95% confidence intervals of starting and continuing breast-feeding for educational level were obtained by logistic regression, adjusted for each group of covariates separately and for all covariates simultaneously.

Results
95.5% (985/1031) of highest-educated mothers started breast-feeding; this was 73.1% (255/349) in the lowest-educated mothers. At six months, 39.3% (405/1031) of highest-educated mothers and 15.2% (53/349) of lowest-educated mothers were still breast-feeding. Educationally-related differences were present in starting breast-feeding and the continuation of breast-feeding until two months, but not in breast-feeding continuation between two and six months. Life-style related and birth characteristics attenuated the association between educational level and breast-feeding, but the association was hardly affected by sociodemographic and psycho-social characteristics.

Conclusion
Decisions to start breast-feeding, or to continue it for the first two months after birth, differed substantially with mother's educational background. The underlying pathways require further research. For the time being, interventions on promoting breast-feeding should start early in pregnancy, and should increase their focus on low-educated women.

3.1 ARE STARTING AND CONTINUING BREASTFEEDING RELATED TO EDUCATIONAL BACKGROUND?

BASED ON

van Rossem L / Oenema A / Steegers EA / Moll HA / Jaddoe VW / Hofman A / Mackenbach JP / Raat H.
Are starting and continuing breastfeeding related to educational background? The generation R study.
Pediatrics 2009 / 123(6):e1017-27.

INTRODUCTION

Breastfeeding has convincingly been established as the best type of feeding for a child, bringing short-term health benefits such as a lower risk for otitis media[1], gastroenteritis[2], and respiratory infections[3]. In the long term, breastfeeding may also reduce the risk for obesity[4] and diabetes mellitus[5]. To benefit from these health effects, the World Health Organization (WHO) recommends six months of exclusive breastfeeding.[6]

Various studies have found that socially disadvantaged mothers start breastfeeding less often, and also breast-feed for a shorter period.[7-11] Though none of these studies explained such social inequalities in breast-feeding, the implication is clear: at the start of their lives, children from socially disadvantaged families may already run a higher risk of several diseases.

The literature on the determinants of breast-feeding[12-18] has consistently identified maternal smoking and lower maternal age as predictors of lower breastfeeding rates.[17] To establish the role of these and other characteristics in explaining the social inequalities relative to breastfeeding, we used the Generation R study, a birth cohort study, to collect data on breastfeeding and on relevant demographic, psycho-social, life-style related, and birth characteristics.

Our study had two objectives. The first was to establish whether there were any differences between high-educated and low-educated mothers with regard to (1) starting breastfeeding, (2) continuing it for two months after birth, and (3) to continuing it for between two and six months after birth. The second objective was to establish how the known determinants of breast-feeding affected the association between mother's educational level and starting and continuing breastfeeding. For the second objective, we conceptualized that educational level is the most distal factor determining breastfeeding behavior, and sociodemographic, life-style related, psycho-social and birth characteristics are more proximal factors for breast-feeding initiation or continuation.

Maternal education was used as an indicator of socioeconomic status because it reflects not only material resources but also non-economic characteristics such as general and health related knowledge, which in turn influence health behavior, and problem-solving skills.[19, 20] The association between socioeconomic status and infant feeding practice may vary by ethnic group.[21-25] For example, Griffiths et al.[21] found that socioeconomic status is not associated with breast-feeding continuation in non-white women.[21] This study was restricted to women with a Dutch ethnicity to eliminate the effect of ethnicity from the effect of educational level on breastfeeding.

METHODS

Study design and population

This study was embedded in the Generation R study, a population-based prospective cohort study from fetal life until young adulthood. The Generation R study was designed to identify early determinants of growth, development and health.[26] Enrollment ideally took place in early pregnancy (gestational age < 18 weeks), which was the case in 69%, but was possible until the birth of the child. The study was conducted in accordance with the guidelines proposed in the World Medical Association Declaration of Helsinki, and was approved by the Medical Ethical Committee at Erasmus MC, University Medical Center Rotterdam. Written consent was obtained from all participants.

The Generation R study is conducted in Rotterdam, the Netherlands. The study area is defined by postal codes and covers more than half of the city's inhabitants (about 600,000). Collaboration was established with all eight midwifery practices, three hospitals and sixteen child health centers located in this area. Invitations to participate in the study were made to all pregnant mothers who had an expected delivery date between April 2002 and January 2006 and who lived in the study area.

This study was restricted to Dutch participants. A woman was classified as being of Dutch ethnicity when she reported that both her parents had been born in the Netherlands.[27] Consent for postnatal follow-up was given by a total of 3787 Dutch women with live-born children. Because of the different circumstances regarding breast-feeding and delivery, twin pregnancies (115) were excluded. To avoid clustering, our analyses excluded data on the second (n=365) or third pregnancy (n=8) of the women who were participating in the Generation R study with more than one child (10.2%). Our analyses also excluded participants with missing data on any of the following: educational level (n=14), starting breast-feeding (n=130), breastfeeding at two months after birth (n=186), or breast-feeding at six months after birth (n=55). Eventually, 2914 subjects were available for analyses. Thus, after exclusion of the data of mothers who gave birth to twins, and of mothers regarding their second or third pregnancy in the study, complete data on determinant and outcome was available for 88.3% of Dutch mothers that gave postnatal consent.

Measurements

Educational level

Level of maternal education was established at enrollment and categorized as follows: 1 (low : no education; primary school; three years or less general secondary school; 2 (mid-low : >3 years general secondary school); 3 (mid-high: higher vocational training; undergraduate programs or Bachelor's degree); and 4 (high: higher academic education) (Appendix 1).[28]

Breast-feeding

Three indicators of breast-feeding were constructed: starting breast-feeding[23], the continuation of any breast-feeding for two months after birth, and the continuation of breast-feeding between two months and six months after birth. Data on starting breast-feeding were collected from delivery reports and data on breast-feeding initiation and continuation were derived from postal questionnaires at two, six, and twelve months after birth. Information on exclusive breastfeeding was available for two months. Questionnaire items are included in appendix 2.

Covariates

Literature on determinants of breast-feeding[12-18, 29] was used to select potential mediators for the association between maternal educational level and breast-feeding (categories in parentheses):

Socio-demographic characteristics.

Parity (primiparity, multiparity) and maternal age (<30, 30- 35, and ≥ 35) were measured at intake. Single parenting (no partner, partner) and job status after birth (not employed, employed) was established using a questionnaire.

Psycho-social characteristics.

Prenatal stress was measured using the Family Assessment Device (FAD), a 12-item questionnaire on general family function (pathological score: ≥ 2.17, nonpathological score: <2.17).[30] Postnatal stress was measured using the 13-item subscale 'lack of confidence in caretaking' from the Mother and Baby Scales (MABS), which was administered two months after birth (cut-off point at mean + one standard deviation).[31, 32] Planned pregnancy (yes, no) was assessed using a prenatal questionnaire.

Life-style related characteristics.
Maternal height was assessed at the research center at enrollment; pre-pregnancy weight was self-reported. Body mass index (BMI) was calculated (normal weight (BMI<25), overweight (BMI=25-30), obesity (BMI ≥30)).[33] Information on maternal smoking (non-smoking during pregnancy, smoking during pregnancy) and alcohol use (non-user during pregnancy, user during pregnancy) was retrieved from the prenatal questionnaire.

Birth characteristics.
These were obtained from delivery records and included birth weight (<2500 grams, ≥ 2500 grams), Cesarean section (yes, no), and gestational age (<37 weeks, ≥ 37 weeks). In the Netherlands, delivery by women who are not at increased risk of obstetric and medical complications are conducted under the responsibility of a community midwife, either at home or in hospital. Delivery by women with an increased risk (e.g. twin pregnancy, gestational hypertension) takes place in hospital under the responsibility of an obstetrician. Place and type of delivery was obtained from delivery reports (home birth, hospital delivery-low risk, hospital delivery-high risk).

Statistical analyses
We established the frequency-distributions of breast-feeding and covariates for breast-feeding according to educational level. Chi-square tests were used to test the differences in mother's educational level for covariates for breast-feeding.

Multivariable logistic regression was used to test the association between educational level, breast-feeding indicators, and mediators. Model 1 was the association between educational level and breast-feeding indicators. Then, we added successively to model 1 all socio-demographic characteristics (model 2), all life-style-related characteristics (model 3), all psycho-social characteristics (model 4), and all birth characteristics (model 5). In model 6, all covariates were simultaneously added to model 1. All covariates were treated as categorical variables.

If the percentage of missing values of covariates in the study population did not exceed five percent, subjects with missing values on that covariate were assigned to the most prevalent category for that variable (single parenting, place and type of delivery, parity). If more than five percent was missing on a particular covariate, a separate 'missing' category was included in the analyses (job status, maternal BMI, maternal smoking, alcohol use, method of delivery, planned pregnancy, maternal stress).[34] The maximum percentage of missing values was 25.0%.

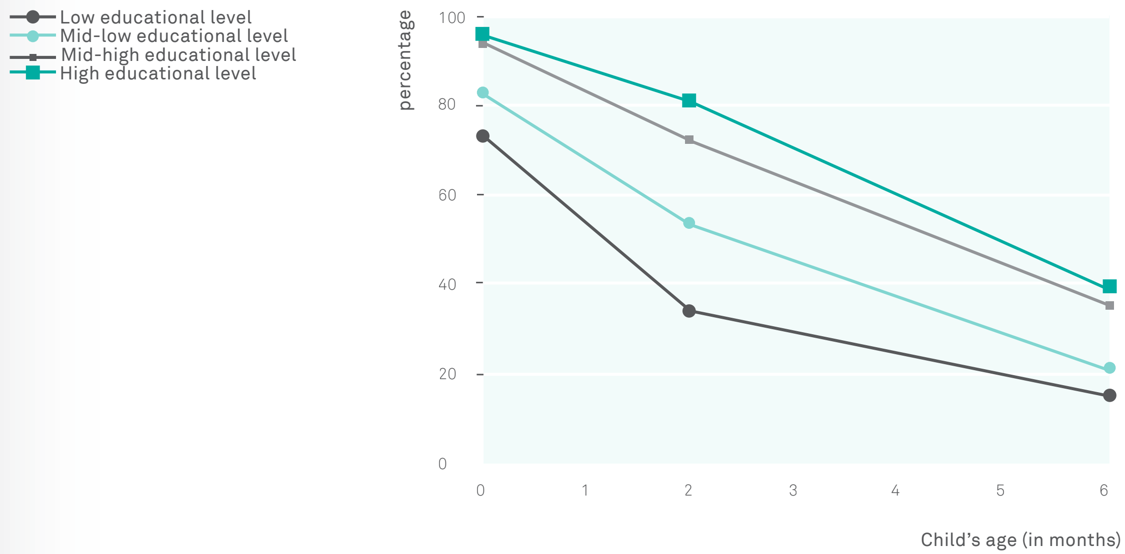
All statistical analyses were performed using the Statistical Package for Social Sciences version 15.0 for Windows (SPSS Inc, Chicago, IL, USA).

RESULTS

The mothers' mean age was 31.7 (Standard Deviation (SD) 4.22). The babies' mean birth weight was 3490 grams (SD 551), and lay below 2500 grams for 4.1%. Mean gestational age was 40.0 weeks (range 27.1-43.4 weeks); 4.5% of babies were born before 37 weeks of gestation (Table 1). All covariates in Table 1, except Cesarean section and gestational age, were significantly associated with educational level. Overall, 89.1% (2596/2914) of women started breast-feeding, which was lower for mothers in education category 1 (73.1% (255/349)) than for mothers in education category 4 (95.5% (985/1031)) (p<0.001) (Figure 1, Table 2). Of the 2596 mothers who started breastfeeding, 1.923 (74.1%) were still breast-feeding when their babies were aged two months (Figure 1); 1042 (40.1%) of babies were exclusively breast-fed. During this period, more mothers in education category 4 than mothers in education category 1 continued breast-feeding (OR: 6.36, 95%CI: 4.71-8.60) (Table 3), and more continued exclusive breast-feeding (OR: 2.78, 95%CI: 2.04-3.80). Of the 1923 mothers who were still breast-feeding when their babies were aged two months, 904 (47%) continued breast-feeding until six months (Figure 1). The continuation of breast-feeding between two and six months did not differ between mothers in education category 4 and education

Figure 1

Percentage of mothers who breast-fed during their children's first six months of life; by mother's educational level (n=2914)



category 1 (OR: 1.17; 95%CI: 0.79-1.72) (data not shown). At six months, 39.3% (405/1031) of highest-educated mothers and 15.2% (53/349) of lowest-educated mothers were still breast-feeding. All covariates, except prenatal stress and preterm birth, were associated with at least one of three breast-feeding indicators (Appendix 3).

The association between educational level and starting breast-feeding was attenuated most by the addition of the life-style related characteristics followed by the birth characteristics. Socio-demographic and psycho-social characteristics had no appreciable effect on the odds ratios for starting breast-feeding (Table 2). A similar effect was seen in the association between educational level and continuing breast-feeding for two months (Table 3).

Table 1 Subject characteristics for total study population and by educational level (n=2914)

		TOTAL	MOTHER'S EDUCATIONAL LEVEL (%)*				*P* VALUE †
		%	1 (n=349)	2 (n=747)	3 (n=787)	4 (n=1031)	
MATERNAL CHARACTERISTICS							
Age (years)	<30	30.3	53.3	41.0	28.5	16.1	<0.001
	30-35	49.8	30.7	42.4	50.1	61.3	
	≥ 35	20.0	16.0	16.6	21.5	22.6	
Single parenting	yes	6.1	15.2	7.0	4.4	3.6	<0.001
	no	93.9	84.8	93.0	95.6	96.4	
Parity	primiparae	67.0	60.5	68.8	69.5	66.0	<0.05
	multiparae	33.0	39.5	31.2	30.5	34.0	
Prepregnant BMI (kg/m^2)	<25	67.4	53.9	61.8	70.1	73.8	<0.001
	25-30	14.1	18.6	16.5	12.8	11.9	
	≥ 30	5.4	11.7	9.2	3.7	1.8	
	missing	13.1	15.8	12.4	13.3	12.4	
Continued smoking in pregnancy	yes	8.1	28.1	10.4	4.7	2.2	<0.001
	missing	13.2	10.6	14.6	13.2	13.0	
Alcohol use in pregnancy	yes	21.4	8.6	14.1	23.0	29.9	<0.001
	missing	13.0	10.3	14.5	12.7	13.0	
Planned pregnancy	yes	78.5	66.5	75.1	79.7	84.1	<0.001
	missing	5.8	5.4	5.4	6.7	5.6	
Prenatal stress (FAD‡)	yes	3.9	6.9	4.3	4.2	2.3	<0.001
	missing	9.8	12.9	11.6	7.1	9.4	
Postnatal stress (MABS§)	yes	16.2	12.0	13.4	17.0	18.9	<0.01
	missing	12.9	16.0	14.1	10.5	12.9	
Job status after delivery	employed	62.1	40.7	56.5	65.9	70.4	<0.001
	missing	25.0	31.8	26.6	23.3	22.9	
BIRTH CHARACTERISTICS							
Gestational age (weeks)	<37	4.5	6.9	4.7	4.1	4.0	0.13
	≥ 37	95.5	93.1	95.3	95.9	96.0	
Birth weight (grams)	<2500	4.1	7.2	4.4	3.9	2.9	<0.01
	≥ 2500	95.9	92.8	95.6	96.1	97.1	
Cesarean section	yes	12.9	14.0	14.1	13.2	11.4	0.62
	missing	7.6	6.6	8.2	7.8	7.4	
Place and type of delivery	home	20.5	10.6	15.5	24.5	24.2	<0.001
	hospital low-risk	16.2	22.9	17.3	13.9	14.9	
	hospital high-risk	63.3	66.5	67.2	61.6	60.8	

*1=lowest, 4=highest; †p-value for Chi-square tests; ‡FAD=Family Assessment Device, yes=score above 2.17 (clinical cut-off score); § MABS=Mother and Baby Scales; subscale=lack of confidence in caretaking, yes=score one standard deviation above mean

DISCUSSION

This cohort study shows that while there was a graded inverse gradient between educational level and starting breast-feeding and to continuing it until two months after birth, there was no such gradient for continuing breast-feeding between two and six months after birth. These associations are partly explained by life-style related and birth characteristics. Nonetheless, associations between breast-feeding practices and a woman's educational background remained largely unexplained.

Methodological considerations

This study used maternal educational level as single indicator of maternal socioeconomic status.[35] Socioeconomic status is a multifactor construct, whose commonest indicators are educational level, income level, and occupational class.[20,35] As a socioeconomic indicator, level of education can also be applied to teenage and unemployed mothers – unlike occupational class, for example. However, educational level does not entirely capture the material and financial aspects of socioeconomic status.[19,20] Although fathers also influence breast-feeding decisions, [8] father's educational level was not taken into account. We chose to study the association between mother's educational level and breast-feeding, because she is the main caregiver for the child, and the only person that actually can give breast-feeding. However, father's educational level was associated with all breast-feeding indicators, but less strong than mother's educational level. In addition, father's educational level did not differ much from mother's educational level within one family (data not shown).

There was some selection towards a study population that was relatively highly educated and somewhat healthier.[26] For selective participation to explain our results, nonresponders would have been more often of low socioeconomic status and more often give breast-feeding. This is unlikely, although we cannot ascertain this.

This study was restricted to Dutch women. In accordance with the Dutch Standard Classification[27], we assigned a Dutch ethnicity to a participant if both her parents had been born in the Netherlands. However, when identifying immigrant descent in Dutch residents, this classification goes no further than the second generation. The number of third-generation immigrants is nonetheless likely to have been very small and not to have affected our conclusions. Non-Dutch women in the Generation R study had a substantially different distribution on educational level, and some categories were not represented, which makes it difficult to distinguish between the effect of ethnicity and educational level. However, ethnicity may also be an important marker of social disadvantage and its association with breast-feeding should be further investigated.

Table 2 Logistic regression for starting breast-feeding (n=2914)

		MODEL 1*	MODEL 2*	MODEL 3*	MODEL 4*	MODEL 5*	MODEL 6*
Mother's educational level†	1 (reference)	1.00	1.00	1.00	1.00	1.00	1.00
	2	1.77 (1.30-2.39)	1.73 (1.27-2.37)	1.54 (1.12-2.11)	1.75 (1.29-2.38)	1.70 (1.25-2.31)	1.47 (1.06-2.04)
	3	5.55 (3.82-8.07)	5.39 (3.65-7.96)	4.38 (2.96-6.46)	5.40 (3.70-7.89)	5.16 (3.54-7.52)	4.03 (2.68-6.06)
	4	7.89 (5.41-11.53)	7.85 (5.24-11.75)	5.93 (3.98-8.85)	7.86 (5.34-11.55)	7.31 (4.99-10.71)	5.51 (3.59-8.45)
SOCIO-DEMOGRAPHIC FACTORS							
Maternal age	< 30 years		1.00				1.00
	30-35 years		1.00 (0.75-1.32)				1.04 (0.78-1.38)
	≥ 35 years		1.46 (1.00-2.15)				1.56 (1.06-2.32)
Single Parenting	no		1.00				1.00
	yes		0.91 (0.58-1.43)				0.89 (0.55-1.45)
Parity	primiparae		1.00				1.00
	multiparae		0.63 (0.49-0.82)				0.58 (0.44-0.77)
Job Status	not employed		1.00				1.00
	employed		0.73 (0.50-1.06)				0.74 (0.50-1.09)
	missing		0.57 (0.38-0.84)				0.55 (0.37-0.82)
LIFE-STYLE RELATED FACTORS							
Prepregnant BMI	normal weight			1.00			1.00
	overweight			0.86 (0.61-1.21)			0.91(0.64-1.29)
	obese			0.46 (0.31-0.70)			0.50 (0.33-0.77)
	missing			0.91 (0.63-1.32)			0.81 (0.53-1.26)
Smoking	never			1.00			1.00
	in pregnancy			0.47 (0.33-0.66)			0.45 (0.31-0.64)
	missing			0.62 (0.44-0.87)			0.52 (0.36-0.75)
PSYCHO-SOCIAL FACTORS							
Planned pregnancy	planned				1.00		1.00
	unplanned				1.03 (0.76-1.41)		1.03 (0.73-1.44)
	missing				1.08 (0.60-1.94)		1.51 (0.73-3.12)
Prenatal stress (FAD)‡	no				1.00		1.00
	yes				0.87 (0.61-1.23)		1.67 (0.87-3.20)
	missing				0.51 (0.37-0.70)		1.66 (1.05-2.64)
BIRTH CHARACTERISTICS							
Gestational age	≥ 37 weeks					1.00	1.00
	< 37 weeks					1.07 (0.55-2.09)	0.97 (0.50-1.90)
Birth weight	≥ 2500 grams					1.00	1.00
	< 2500 grams					0.68 (0.35-1.30)	0.74 (0.38-1.44)
Cesarean section	no					1.00	1.00
	yes					0.79 (0.55-1.13)	0.78 (0.54-1.13)
	missing					0.73 (0.47-1.15)	0.71 (0.44-1.13)
Place and type of delivery	home					1.00	1.00
	hospital, low-risk					0.49 (0.32-0.75)	0.45 (0.29-0.69)
	hospital, high-risk					0.75 (0.51-1.11)	0.67 (0.45-1.00)

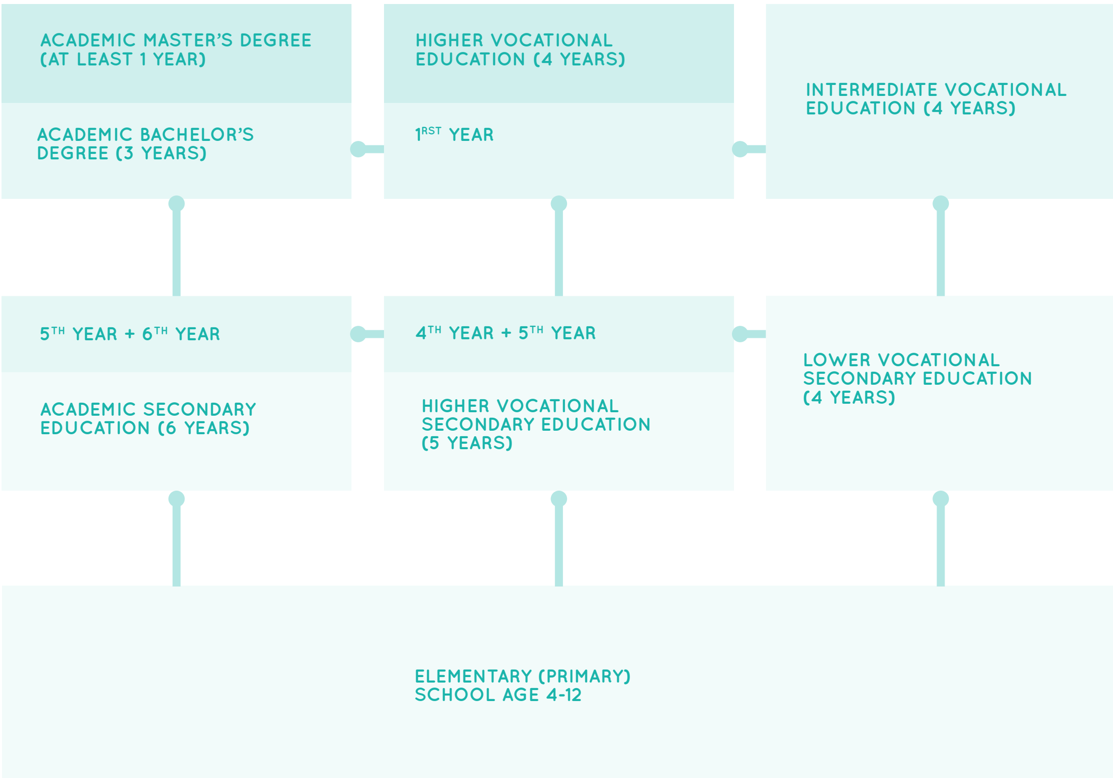
* values are odds ratios (95% confidence intervals) model 1: basic model= association between educational level and breast-feeding, model 2: basic model + socio-demographic factors simultaneously, model 3: basic model + life-style related factors simultaneously, model 4: basic model + psycho-social factors simultaneously, model 5: basic model + birth characteristics simultaneously , model 6: basic model + model 2,3,4,5 ; † 1=lowest, 4=highest; ‡ FAD=Family Assessment Device, yes=score above 2.17 (clinical cut-off score)

Table 3 Logistic regression for continuing breast-feeding until baby's age of two months (n=2596)

		MODEL 1*	MODEL 2*	MODEL 3*	MODEL 4*	MODEL 5*	MODEL 6*
Mother's educational level†	1 (reference)	1.00	1.00	1.00	1.00	1.00	1.00
	2	2.11 (1.57-2.84)	2.16 (1.60-2.92)	1.84 (1.35-2.49)	2.12 (1.58-2.85)	2.07 (1.54-2.80)	1.84 (1.34-2.52)
	3	3.82 (2.83-5.15)	3.85 (2.81-5.26)	3.01 (2.20-4.12)	3.87 (2.86-5.24)	3.68 (2.71-4.98)	2.94 (2.11-4.10)
	4	6.36 (4.71-8.60)	6.33 (4.59-8.73)	4.81 (3.49-6.62)	6.44 (4.75-8.74)	6.14 (4.52-8.33)	4.70 (3.33-6.64)
SOCIO-DEMOGRAPHIC FACTORS							
Maternal age	< 30 years		1.00				1.00
	30-35 years		1.19 (0.96-1.47)				1.26 (1.01-1.57)
	≥ 35 years		1.72 (1.29-2.28)				1.85 (1.38-2.49)
Single Parenting	no		1.00				1.00
	yes		0.93 (0.64-1.36)				0.94 (0.63-1.41)
Parity	primiparae		1.00				1.00
	multiparae		1.05 (0.85-1.30)				0.96 (0.77-1.21)
Job Status	not employed		1.00				1.00
	employed		0.79 (0.59-1.05)				0.78 (0.58-1.04)
	missing		0.90 (0.66-1.24)				0.95 (0.68-1.31)
LIFE-STYLE RELATED FACTORS							
Prepregnant BMI	normal weight			1.00			1.00
	overweight			0.64 (0.49-0.82)			0.66 (0.51-0.86)
	obese			0.37 (0.25-0.55)			0.39 (0.26-0.58)
	missing			0.86 (0.64-1.14)			0.87 (0.62-1.23)
Smoking	never			1.00			1.00
	in pregnancy			0.52 (0.37-0.74)			0.47 (0.33-0.67)
	missing			0.57 (0.12-2.71)			0.55 (0.11-2.69)
Alcohol use	no alcohol use			1.00			1.00
	alcohol use			1.12 (0.88-1.42)			1.01 (0.79-1.28)
	missing			2.14 (0.44-10.30)			1.94 (0.38-9.78)
PSYCHO-SOCIAL FACTORS							
Planned pregnancy	planned				1.00		1.00
	unplanned				1.03 (0.80-1.32)		1.24 (0.92-1.68)
	missing				1.15 (0.73-1.80)		1.24 (0.92-1.68)
Postnatal stress (MABS)‡	no				1.00		1.00
	yes				0.85 (0.66-1.09)		0.82 (0.63-1.06)
	missing				1.24 (0.92-1.68)		1.26 (0.92-1.72)
BIRTH CHARACTERISTICS							
Gestational age	≥ 37 weeks					1.00	1.00
	< 37 weeks					1.07 (0.63-1.83)	1.13 (0.66-1.93)
Birth weight	≥ 2500 grams					1.00	1.00
	< 2500 grams					1.06 (0.60-1.88)	1.00 (0.56-1.79)
Cesarean section	no					1.00	1.00
	yes					0.72 (0.55-0.94)	0.71 (0.54-0.94)
	missing					1.57 (1.02-2.42)	1.44 (0.92-2.23)
Place and type of delivery	home					1.00	1.00
	hospital, low-risk					0.72 (0.52-1.01)	0.71 (0.50-0.99)
	hospital, high-risk					0.63 (0.48-0.82)	0.62 (0.47-0.82)

* values are odds ratios (95% confidence intervals) model 1: basic model= association between educational level and breast-feeding, model 2: basic model + socio-demographic factors simultaneously, model 3: basic model + life-style related factors simultaneously, model 4: basic model + psycho-social factors simultaneously, model 5: basic model + birth characteristics simultaneously , model 6: basic model + model 2,3,4,5 ; † 1=lowest, 4=highest; ‡ MABS=mother and baby scales, yes=score 1 SD above mean

Appendix 1 Dutch educational system and categories used in this study.



When women recall breast-feeding only shortly after it has finished, as in our study, selfreported information on breast-feeding has shown itself to be valid and reliable.[36] However, because we lacked information on postnatal smoking behavior, we used smoking during pregnancy as a proxy for postnatal smoking. Consequently, non-smoking mothers during pregnancy who re-started smoking after delivery were misclassified as 'non smoking'. In addition, smoking during pregnancy is likely to be underreported, which was slightly the case in our population.[37] Misclassification or underreporting of the determinants of breast-feeding, and in particular smoking status, may have led to residual confounding resulting in a lack of an explanation for the association we observed between maternal education and breast-feeding.

Health gain from breast-feeding is optimal when a baby is exclusively breast-fed for six months.[38] Data on exclusive breast-feeding were available for the first two months after birth. Educationally-related differences were seen in both breast-feeding and exclusive breast-feeding. However, health benefits are also reported for breast-feeding initiation and several durations of (partly) breast-feeding compared to never breast-fed.[39]

Comparison with other studies
While the breastfeeding rates in our study were fairly high relative to those in earlier reports,[16,40] they were consistent with the upward trend towards breastfeeding that has been taking place in Western countries since the 1990s.[41]

Our study is also consistent with earlier reports stating that rates of breast-feeding are higher in women with a higher socioeconomic status than in those with a lower socioeconomic status.[7-11] However, the educationally-related differences were greater than those reported in earlier studies. [7-11] For example, when comparing mothers who had at least a high school diploma with those who had no such diploma, Dubois and Girard[7] found an odds ratio of 3.54 (95% CI: 2.56-4.89) for starting breast-feeding. When we repeated our analyses, categorizing maternal education into three levels similar to those of Dubois and Girard[7], the odds ratio for the highest versus the lowest educated mothers was 5.99 (95% CI: 3.40-10.58). A recent study that found no socioeconomic differences in breast-feeding claimed that when overall breast-feeding prevalence exceeds 80%, there will no longer be any socioeconomic differences.[42] Our results would tend to refute this: despite a very high overall breast-feeding initiation rate, we found substantial educationally related differences in breast-feeding rates.

Appendix 2

Breast-feeding questions used to define starting breast-feeding, breast-feeding continuation for two months and breast-feeding continuation between 2 and 6 months.

2-MONTHS QUESTIONNAIRE PART 1 (CHILD)	1. How many weeks in total did you breast-feed your child up until now? (also in addition to the bottle)	____ Weeks
	2. In what way do you feed your child at the moment? (one answer only)	☐ Breast feeding only ☐ Bottle feeding only ☐ As much breast as bottle feeding ☐ More than half breast feeding ☐ More than half bottle feeding
2-MONTHS QUESTIONNAIRE PART 2 (MOTHER)	1. Have you ever breastfed your child? (this refers to the child participating in this survey)	☐ No ☐ Yes
6-MONTHS QUESTIONNAIRE	1. Have you ever breastfed your child?	☐ No ☐ Yes
	2. How many months of age was your child when you stopped beastfeeding? (one answer only)	☐ I am still breastfeeding ☐ Younger than 1 month ☐ Between 1 and 2 months ☐ Between 2 and 3 months ☐ Between 3 and 4 months ☐ Older than 4 months
	3. How often do you breastfeed your child at the moment? (one answer only)	☐ I no longer breastfeed ☐ 1 to 2 times a day ☐ 2 to 3 times a day ☐ 3 to 5 times a day ☐ 5 to 7 times a day ☐ More than 7 times a day
12-MONTHS QUESTIONNAIRE	1. Have you breast-fed your child in the last 6 months?	☐ No, proceed to A4 ☐ Yes
	2. How often do you breast-feed your child at the moment. (one answer only)	☐ I no longer breast-feed my child ☐ 1 to 2 times a day, go to A4 ☐ 2 to 3 times a day, go to A4 ☐ 3 times or more a day, go to A4
	3. How many months old was your child when you comple tely stopped breast-feeding it? (one answer only)	☐ Between 6 and 7 months ☐ Between 8 and 9 months ☐ Between 10 and 11 months ☐ Older than 11 months

Explaining the educational level-breast-feeding association

We considered four groups, including 13 covariates in total, of potential mediators. Life-style related and birth characteristics can be considered as mediators because they considerably attenuated the association between educational level and breast-feeding.[43] Below, we discuss the role of potential mediating covariates in the association between educational level and breast-feeding. However, since the causal mechanisms regarding the effects on breast-feeding are unknown, the covariates in our study might also be considered as additional markers of social disadvantage.

The role of obesity

It is unclear why obese mothers breast-feed less than non-obese mothers. Four possible mechanisms have been described.[44] First, obese women more often have medical complications. However, this is probably not the underlying mechanism in our study, as we adjusted for several perinatal characteristics. Second, psychological factors may play a role; obese mothers are more often depressed and depressed mothers are less likely to breast-feed. From our data, prenatal and postnatal stress did not influence the association between educational level and breast-feeding. A third mechanism may be anatomically/physiologically. A delayed lactogenesis has been found in obese women. [44, 45] Also, obese women often have large breasts, which can give difficulties in attaching the baby to the breast. Finally, obese women more often belong to environments with different health beliefs. These last two mechanisms could also be interrelated; the delay in lactogenesis can be due to a lower intention to breastfeed.[44]

The role of smoking

Alterations in babies' sleep-patterns have been found after they had ingested nicotine from breast-feeding. It is hypothesized that decreased (quality of) sleep results in dissatisfied babies, which is then thought by the mothers to be due to lack of breast-feeding.[46] Indeed, smoking mothers are more likely to perceive their milk supply as insufficient, and are less likely to seek help with breast-feeding difficulties than non-smokers.[46-49] However, this does not fully explain the association we found of smoking on starting breast-feeding. Literature describes that smokers also have a lower intention to breast-feed.[47] This suggests that smoking in our study may be a proxy for other, more motivational factors, rather than for chemical factors.

The role of place and type of delivery

Relative to those who had delivered at home, fewer women who delivered in hospital started breast-feeding. More research is needed to elucidate this finding. But, in any case, hospitals should give optimal guidance to mothers on breast-feeding.

Appendix 3

Percentages of mothers starting breast-feeding (n=2914), and continuing breastfeeding until baby's age of two months (n=2596), and continuing breast-feeding between baby's age of two and six months (n=1923) within categories for each covariate.

		STARTING BF (%)	CONTINUATION OF BF 0-2 MONTHS (%)	CONTINUATION OF BF 2-6 MONTHS (%)
Age (years)	<30	85.9	65.6	43.9
	30-35	89.9	76.2	46.0
	≥ 35	91.9	80.9	52.9
	p-value*	< 0.001	< 0.001	< 0.05
Single parenting	no	89.4	74.5	46.3
	yes	84.2	67.1	60.0
	p-value	<0.05	<0.05	<0.01
Parity	primiparae	90.6	73.1	44.5
	multiparae	86.1	76.1	52.1
	p-value	< 0.001	0.11	<0.01
Prepregnant BMI (kg/m²)	< 25	90.8	77.4	47.1
	25-30	87.4	66.1	48.3
	≥ 30	74.1	47.9	50.0
	missing	88.2	74.1	44.6
	p-value	< 0.001	< 0.001	0.81
Continued smoking in pregnancy	no	91.2	75.5	46.3
	yes	73.3	50.9	45.5
	missing	85.9	77.3	51.8
	p-value	< 0.001	< 0.001	0.26
Alcohol use in pregnancy	yes	93.3	78.2	43.7
	no	88.4	72.0	47.2
	missing	85.4	77.7	52.2
	p-value	< 0.001	<0.01	0.10
Planned pregnancy	yes	89.7	74.8	46.8
	no	85.6	69.3	50.6
	missing	90.0	76.5	41.0
	p-value	< 0.05	0.06	0.22
Prenatal stress (FAD†)	yes	88.5	-	-
	no	88.9	-	-
	missing	91.2	-	-
	p-value	0.47	-	-
Postnatal stress (MABS‡)	yes	-	72.9	38.7
	no	-	73.8	47.6
	missing	-	77.3	54.4
	p-value	-	0.35	< 0.01
Job status after delivery	employed	90.8	74.7	44.9
	not employed	88.6	70.9	60.6
	missing	85.2	74.2	45.6
	p-value	< 0.001	0.35	< 0.001
Gestational age (weeks)	< 37	86.4	70.2	37.5
	≥ 37	89.2	74.3	47.4
	p-value	0.30	0.33	0.08
Birth weight (grams)	< 2500	83.2	68.7	38.2
	≥ 2500	89.3	74.3	47.3
	p-value	<0.05	0.21	0.14
Cesarean section	yes	87.0	65.1	40.4
	no	89.7	74.5	47.3
	missing	86.4	84.3	53.4
	p-value	0.12	< 0.001	<0.05
Place and type of delivery	home	93.3	83.3	51.8
	hospital, low- risk	83.7	74.9	43.9
	hospital, high-risk	89.1	70.8	45.9
	p-value	< 0.001	< 0.001	< 0.05

* p-values are for chi-square tests; †FAD=Family Assessment Device, yes=score above 2.17 (clinical cut-off score);
‡ MABS=Mother and Baby Scales; subscale=lack of confidence in caretaking, yes=score one standard deviation above mean

The role of motivational determinants of breast-feeding

We had no information on the motivational determinants of breast-feeding. From the literature, it is known that breast-feeding behavior can be predicted by attitudes, perceived control and social support, including social norms, peer influence and intergenerational factors (elements of the theory of planned behavior).[50-52] The effects of smoking behavior and maternal obesity on the association between educational level and breast-feeding may be partly explained by motivational factors.[53]

Conclusion

Compared to their less-educated counterparts, more mothers with a higher level of education started breast-feeding, and more continued for the first two months after birth. Because breastfeeding benefits health both in childhood and adulthood, increasing breast-feeding by less educated mothers would help reduce socially based health inequalities, potentially achieving a broad public health impact.

However, more research is needed on obesity and smoking behavior, and their association with motivational factors that underlie social inequalities in breast-feeding.

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ABSTRACT

Background
Because breastfeeding is the best method of infant feeding, groups at risk of low breastfeeding rates should be identified. Therefore, this study compared breastfeeding patterns of ethnic minority groups in the Netherlands with those of native mothers, and established how they were influenced by generational status and socio-demographic determinants of breastfeeding.

Methods
We used data on 2914 Dutch, 366 Mediterranean first generation, 143 Mediterranean second generation, 285 Caribbean first generation and 140 Caribbean second generation mothers. Information on starting breastfeeding and breastfeeding at 2 and 6 months after birth were obtained from questionnaires during the first year after birth.

Results
Overall, 90.6% of women started breastfeeding after delivery. This percentage was lowest among the native Dutch (89.1%) and highest among the Mediterranean second generation women (98.6%) ($p<0.001$). At 6 months postpartum, 30.6% of mothers were still breastfeeding, ranging from 19.3% in the Caribbean second generation mothers to 42.6% in first generation Mediterranean mothers. After adjustment for covariates, more non-native mothers started breastfeeding than native Dutch mothers. While Mediterranean first generation mothers had higher breastfeeding rates at 6 months (OR: 2.71, 95% CI: 2.09-3.51), there were no differences in Mediterranean second generation and Caribbean mothers compared to native Dutch mothers.

Conclusion
More non-native mothers started breastfeeding than native mothers, but relatively fewer continued. Although both native Dutch and non-native mothers had low continuation rates, ethnic minorities may face other difficulties in continuing breastfeeding than native women.

3.2 BREASTFEEDING PATTERNS AMONG ETHNIC MINORITIES

BASED ON

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INTRODUCTION

Breastfeeding is the most optimal feeding for a child and health effects of breastfeeding compared to formula-feeding are well-established for both mother and child.[1] Therefore, the World Health Organization (WHO) recommends at least 6 months of exclusive breastfeeding for children in developed countries.[2]

Many studies have shown that breastfeeding patterns can differ profoundly between ethnic subgroups in society. For example, studies conducted in the US have shown that fewer black mothers start breastfeeding, and also breast-feed for a shorter duration than US-born white mothers.[3-5] In contrast, breastfeeding rates in the UK are higher in Black and Asian mothers than in native British mothers.[6-8] In Australia, while Mediterranean-Turkish mothers have high breastfeeding initiation rates, Vietnamese mothers have relatively low breastfeeding initiation rates compared to Australian native mothers.[9] Thus, breastfeeding patterns vary between ethnic minority groups, but also depend on the countries where specific ethnic groups live. In specific countries, fewer children from some ethnic minority groups receive breastfeeding than their native counterparts, which may contribute to the general health disadvantage that has been described for ethnic-minority child populations.[10-12] Despite the increase in the number of children born to non-native parents, in mainland Europe, there is very little information on breastfeeding patterns in ethnic minorities.[13]

Irrespective of ethnicity, it has been shown that educational level is strongly associated with breastfeeding.[14] Since ethnic minority groups relatively often are socially disadvantaged, it may be that, in specific ethnic minorities, low breastfeeding rates can be explained by social disadvantage.[15-17] However, there may be also other factors, e.g. related to specific cultural contexts, which explain ethnic differences in breastfeeding behaviors. For example, various studies have reported that health behaviors are more similar between natives and ethnic minorities with increasing acculturation.[7, 15, 17, 18] Many of the

available studies did not take acculturation into account.[3-5]
Within the Generation R study, a large multi-ethnic prospective birth cohort in the Netherlands, we collected information on breastfeeding patterns, generational status, socioeconomic status, psychosocial, demographic, perinatal and lifestyle-related characteristics.

The objective of our study was to study ethnic differences in starting breastfeeding and breastfeeding frequency at 2 and 6 months; before and after taking into account important covariates. In this way, ethnic disparities in breastfeeding and explanations for these disparities may be found, providing clues for preventive interventions. The study focused on two major ethnic groups, i.e. Mediterranean and Caribbean. These groups were compared to the native Dutch population.

METHODS

Study design and population

This study was embedded in the Generation R study, a population-based prospective cohort study of individuals from fetal life until young adulthood.[19, 20] Although enrollment ideally took place in early pregnancy (gestational age < 18 weeks), it was possible until the birth of the child. Invitations to participate in the study were made to all pregnant mothers who had an expected delivery date between April 2002 and January 2006 and who lived in the study area (Rotterdam, the Netherlands). At birth, 61% of eligible women were included in the study. The study was conducted in accordance with the guidelines proposed in the World Medical Association Declaration of Helsinki, and was approved by the Medical Ethical Committee at Erasmus MC, University Medical Center Rotterdam. Written consent was obtained from all participants.

Consent for postnatal follow-up was given by a total of 7295 women with live-born children (92.0% of pregnant women). Because of the different circumstances regarding breastfeeding and delivery, twin pregnancies (n=179) were excluded. To avoid clustering, our analyses excluded data on the second (n=530) or third pregnancy (n=12) of any woman who was participating in the Generation R study with more than one child (7.6%). Our analyses also excluded participants with missing data on starting breastfeeding (n=476), on breastfeeding at 2 months after birth (n=699), and at 6 months after birth (n=247). We also excluded mothers with missing data on their generational status (n=2) and educational background (n=55). Analyses were carried out in mothers with a Dutch (n=2914), Mediterranean (n=509), and Caribbean (n=425) background. Mediterranean participants included mothers from Moroccan and Turkish descent, and Caribbean participants included mothers from Surinam and Dutch Antilles. The results of 1247 mothers with another ethnic background are not presented, because of the mixed composition of these populations. In total, our population for analyses consisted of 3848 subjects.

Non-response
Relative to mothers with missing information on breastfeeding, fewer mothers with information on breastfeeding were in the lowest educational level (18.0% versus 29.7%), and more mothers were native Dutch (59.2% versus 32.8%).

Measurements

Data were collected by medical records, by hands-on measurements and by postal questionnaires. Questionnaires were available in Dutch, English, and Turkish. Furthermore, staff from different ethnic minorities was available for assistance in completing the questionnaires, by phone or by home visits. They were able to verbally translate materials into Arabic and French. With this, the study staff could communicate to all participants.

Ethnicity
Each mother's ethnic background was assessed on the basis of her parent's country of birth. Information about countries of birth was obtained by questionnaire. A participating mother was of non-native ethnic origin if at least one of her parents was born abroad.[21] If both parents were born abroad, the country of birth of the mother's mother decided on the ethnicity. Generational status was established only for non-native mothers using a questionnaire. First generation included mothers who were born abroad; second generation included mothers who were born in the Netherlands. Because breastfeeding behaviour may vary according to generational status, we stratified the ethnic groups according to their generational status.

Breastfeeding
Breastfeeding prevalence was available for starting breastfeeding (any amount or duration of breastfeeding),[17] full and any breastfeeding at 2 months, and (any) breastfeeding at 6 months.[22] Data on breastfeeding were collected from postal questionnaires. Medical records were used to establish breastfeeding initiation for mothers with missing information on breastfeeding initiation in the questionnaires. Information for breastfeeding initiation from medical records was similar in 98.7% of mothers with complete follow-up on both the questionnaires and medical records when comparing the questionnaires to the medical records.

Covariates
The following covariates were considered to influence the association between maternal ethnic background and breastfeeding. These were selected on current literature on determinants of breastfeeding.[23-29] Categories are indicated in parentheses.

Socio-demographic characteristics. We used level of maternal education as a single indicator of socioeconomic status. Level of maternal education was established at enrollment on the basis of a questionnaire: low (no education; primary school; lower vocational training; intermediate general school; or three years general secondary school); middle (>3 years general secondary school; intermediate vocational training); high (higher vocational training; Bachelor's degree, higher academic education).[30] Maternal age (<20, 20-25, 25-30, 30-35, and ≥ 35), and parity (nulliparity, any parity) were measured at intake. Single parenting (no partner, partner) and job status (not employed, employed) were established from the prenatal questionnaire.

Lifestyle-related characteristics. Maternal height was assessed at the research center at enrollment; maternal pre-pregnancy weight was self-reported. Body mass index (BMI) was calculated (normal weight (BMI<25), overweight (BMI=25-30), obesity (BMI ≥ 30)), according to the definition of the WHO.[31] Information on maternal smoking (non-smoking during pregnancy, smoking during pregnancy) was retrieved from all prenatal questionnaires.

Psycho-social characteristics. Planned pregnancy (yes, no) was assessed using a prenatal questionnaire.

Birth characteristics. In the Netherlands, delivery by women who are not at increased risk of obstetric and medical complications takes place under the responsibility of a community midwife, either at home or in hospital. Delivery by women with an increased risk, such as diabetes or hypertension, takes place in hospital under the responsibility of an obstetrician.[32] Information on birth characteristics was obtained from delivery records, and included place and type of delivery (home birth, low-risk hospital delivery, high-risk hospital delivery), birth weight (<2500 grams, ≥ 2500 grams), Cesarean section (yes, no), and gestational age (<37 weeks, ≥ 37 weeks).

Statistical analyses

Frequency tables were used to explore associations between mother's ethnicity and sociodemographic, psycho-social, lifestyle-related and birth characteristics. Chi-square tests were used to test for differences in these characteristics among ethnic groups.

We used logistic regression to obtain odds ratios (OR) and 95% confidence intervals (CI) for the associations between mother's ethnicity and breastfeeding (reference group: native Dutch). This is referred to as model 1. In model 2, we added educational level to the model to show the effect of the covariate that was expected to have the largest influence on the association. Finally, we adjusted the association between mother's ethnicity and breastfeeding for educational level and other covariates (model 3). For breastfeeding initiation, the covariates included in model 3 were parity, smoking status, place and type of delivery, and planned pregnancy. For breastfeeding at 2 months, the covariates were age and parity. For breastfeeding at 6 months, the covariates were age, parity, smoking status, Cesarean section and place and type of delivery. To be selected for model 3, a bootstrap analysis was conducted to examine whether the strength of the association between ethnicity and breastfeeding changed significantly after adding a covariate to model 2. This was tested for each covariate separately. Bootstrapping uses the study sample as the population. By drawing random samples with replacement from the study population, 1000 replications were formed to estimate confidence intervals around the beta-differences (i.e., the regression coefficient of ethnicity).

Missing values in the covariates were treated in accordance with Harrell.[33] If the percentage of missing values in the study population did not exceed five percent, subjects with missing values on that covariate were assigned to the most prevalent category for that variable (place and type of delivery, parity). If more than five percent were missing on a particular covariate, a separate 'missing' category was included in the regression analyses. This was done for 478 (12.4%) missing values on maternal smoking and for 254 (6.6%) missing values for planned pregnancy.

Statistical analyses were performed using the Statistical Package for Social Sciences version 15.0 for Windows (SPSS Inc, Chicago, IL, USA). S-plus 6.0 Professional Release 1 (Insightful Corp., Seattle, WA, USA) was used for the Bootstrap procedure.

RESULTS

Characteristics of the mothers are described in Table 1. Ethnic differences were present in all variables from Table 1, except for gestational age.

Overall, 90.6% of women started breastfeeding after delivery. This percentage was lowest among the Dutch native (89.1%) and highest among the Mediterranean 2nd generation women (98.6%) ($p<.001$) (Figure 1, Table 2). Of the 3848 mothers, 2491 (64.7%) were still breastfeeding when their babies were aged 2 months and 1179 (30.6%) continued until 6 months. Ethnic differences in breastfeeding were seen at all three time points ($p<.001$) (Figure 1).

Relative to Dutch native mothers, starting breastfeeding was significantly higher in all non native groups (Table 2). Adjustment for educational level strengthened the associations.

In unadjusted analyses, breastfeeding frequency at 2 months was lower in Mediterranean 2nd generation mothers and Caribbean mothers (Table 3, model 1). However, after adjustment for educational level, these differences disappeared. More Mediterranean 1st generation mothers breastfed at 2 months than native Dutch

Figure 1 Percentage of breast-feeding mothers per ethnicity (n=3848)

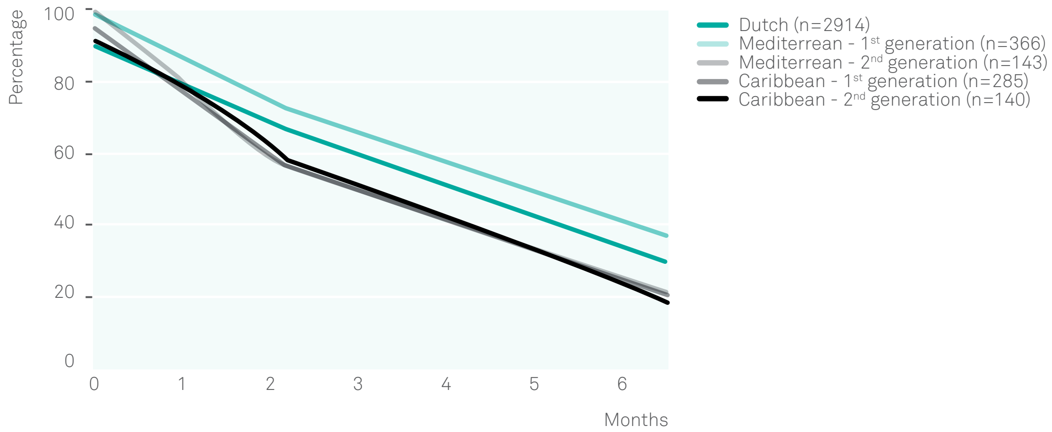

Table 1 Characteristics of 3848 mothers in the Generation R study, total and per ethnicity*

		TOTAL	NATIVE DUTCH	MEDITER-RANEAN	MEDITER-RANEAN	CARIB-BEAN	CARIB-BEAN	P-VALUE
		n=3848	1st gen n=2914	2nd gen n=366	2nd gen n=143	1st gen n=285	2nd gen n=140	
SOCIO-DEMOGRAPHIC FACTORS								
Educational level	low	19.4	12.0	53.8	40.6	33.0	35.7	<0.0001
	middle	28.9	25.6	30.1	45.5	44.2	45.7	
	high	51.7	62.4	16.1	14.0	2.8	18.6	
Age (years)	<20	1.9	1.0	2.2	5.6	4.2	11.4	<0.0001
	20-25	10.8	5.7	19.7	48.3	19.6	35.7	
	25-30	25.5	23.6	35.8	33.6	25.6	31.4	
	30-35	43.9	49.8	28.4	10.5	34.7	15.7	
	> 35	17.9	20.0	14.0	2.1	15.8	5.7	
Parity at enrollment	nulliparae	64.0	67.0	38.5	69.9	56.1	77.9	<0.0001
Single parenthood		9.3	6.1	3.8	7.0	34.4	42.9	<0.0001
Job status	employed	76.3	84.5	35.4	56.1	58.2	54.1	<0.0001
LIFE-STYLE RELATED CHARACTERISTICS								
Prepregnant BMI	normal	73.9	78.2	52.3	63.7	64.8	73.1	<0.0001
	overweight	17.9	15.8	31.7	18.5	21.5	16.0	
	obese	8.2	6.1	16.0	17.7	13.7	10.9	
Smoking in pregnancy		10.0	9.3	9.9	20.7	8.2	15.6	<0.0001
PSYCHO-SOCIAL CHARACTERISTICS								
Planned pregnancy		78.6	83.3	74.9	72.8	54.4	42.4	<0.0001
BIRTH CHARACTERISTICS								
Gestational age	<37 weeks	4.7	4.5	4.9	5.6	4.6	7.9	0.47
Birth weight	< 2500 grams	4.3	4.1	2.7	4.2	7.7	7.1	0.01
Cesarean section		13.1	14.0	7.0	9.7	14.1	11.9	0.007
Place/type of delivery	home	16.6	20.5	2.2	2.1	6.7	8.6	<0.0001
	hospital low-risk	20.8	16.2	40.7	37.8	29.8	30.0	
	hospital high-risk	62.6	63.3	57.1	60.1	63.5	61.4	

* Values are expressed as percentage of subjects; p-values are for Chi-Square tests. Gen = generation.

mothers. Additional analyses of full breastfeeding at 2 months showed that fewer non-native mothers gave full breastfeeding at 2 months in the unadjusted analyses. These differences disappeared after adjustment for covariates, with the exception of Caribbean 1st generation mothers (Appendix 1).

Breastfeeding at 6 months showed a similar pattern as breastfeeding at 2 months: breastfeeding was lower for all, but Mediterranean 1st generation mothers, compared with native Dutch mothers. In fully adjusted analyses, more Mediterranean 1st generation mothers breastfed at 6 months than native Dutch mothers. There were no differences between the other ethnic groups compared to native Dutch mothers (Table 4).

DISCUSSION

Ethnic differences in breastfeeding patterns exist. This study shows that while more non native mothers start breastfeeding, fewer Caribbean and Mediterranean 2nd generation mothers continue breastfeeding in the first 2 months after birth than native mothers, resulting in no differences in breastfeeding frequency at 2 and 6 months after birth between these mothers and native Dutch mothers. However, more Mediterranean 1st generation mothers continued breastfeeding than native Dutch mothers.

Bulk-Bunschoten et al.[13] found that more mothers from ethnic minorities start breastfeeding than native Dutch mothers do, and, that in contrast to our study, they all do so for longer.[13] Our results are in line with the finding of an Australian study that found that Mediterranean-Turkish mothers have high breastfeeding rates.[9] American and British studies showed a similar effect of generational status on breastfeeding: second-generation non-native mothers, although in our study only those of Mediterranean descent, are less favorable towards breastfeeding frequency than their first-generation counterparts.[15, 17, 18]

This is the first study that showed opposing results for ethnic differences in starting breastfeeding and for ethnic differences in breastfeeding frequency at 2 and 6 months after birth. The higher percentage of people from ethnic minorities who start breastfeeding seems to have a cultural basis: The Koran recommends two years of breastfeeding, which may underlie the high starting rates of Mediterranean women in our study.[13] Given the fact that more non native mothers start breastfeeding, we had not expected to find no differences in breastfeeding frequency at 2 and 6 months for Caribbean and Mediterranean 2nd generation subgroups. Non native mothers may experience barriers to continuing breastfeeding, such as inadequate breastfeeding counseling by health care providers, due among other factors to language difficulties.[9] A US study reported that African-American mothers were more likely to report that they had stopped breastfeeding in order to return to work.[34] Working conditions may mean that non-native mothers face greater difficulties in continuing breastfeeding than their native peers. Qualitative studies are needed to elucidate why relatively fewer non-native mothers continue breastfeeding than native mothers despite their better starting rates, especially because no studies have examined factors such as mother's resolution of solving breastfeeding difficulties, or their attitudes to feeding in public.

When interpreting our results, some methodological considerations should be taken into account. In accordance with the Dutch Standard Classification[21], we assigned a Dutch ethnicity to a participant if both her parents had been born in the Netherlands. However, when identifying immigrant descent in Dutch residents, this classification goes no further than the second generation. The number of third-generation immigrants is nonetheless likely to have been very small and not to have affected our conclusions. Also, self-assigned ethnicity may differ from interview-assigned ethnicity. We compared self-assigned ethnicity with interview-assigned ethnicity, and agreement ranged from 86% in the Caribbean mothers to 99% in native Dutch mothers.

We assumed that a mother's ethnicity played a greater role in the decision to breastfeed than a father's, although father's ethnicity has shown to be associated with breastfeeding.[18] We repeated the analyses with father's ethnicity and saw that results were quite similar (Appendix 2).

When women are asked to recall breastfeeding only shortly after it has finished, as in our study, self-reported information on breastfeeding has shown itself to be valid and reliable,[35] although misclassification of the determinants of breastfeeding may have led to residual confounding for the association we observed between mother's ethnicity and breastfeeding indicators. For example, smoking may have led to socially desired answers. Also, determinants like educational level, job status and single parenting may change over time. Non-differential misclassification may be the result. This may also have resulted in residual confounding. However, it is not likely that this has affected the associations.

Covariates were entered simultaneously in model 3; some of them may have opposite effects on the association between ethnicity and breastfeeding, herewith balancing out the effect on the effect estimates. E.g. Caribbean 1st generation mothers smoke less than native Dutch mothers, but have more often an unplanned pregnancy. The first is a determinant for increasing breastfeeding frequency, the latter a determinant for decreasing breastfeeding frequency. We performed the analyses entering each covariate separately, but effects on the association between ethnicity and breastfeeding were small (data not shown).

Table 2 Regression models for starting breastfeeding (yes/no) (n=3848)*

	N	%	MODEL 1	MODEL 2 †	MODEL 3 ‡
		Starting bf	(unadjusted)		
Native Dutch	2914	89.1	1	1	1
Mediterranean-1st generation	366	97.3	4.36 (2.30-8.26)	9.22 (4.80-17.70)	10.96 (5.64-21.31)
Mediterranean-2nd generation	143	98.6	8.64 (2.13-35.04)	17.24 (4.23-70.32)	19.71 (4.81-80.79)
Caribbean-1st generation	285	93.7	1.82 (1.11-2.97)	3.23 (1.96-5.34)	3.49 (2.08-5.83)
Caribbean-2nd generation	140	90.0	1.10 (0.63-1.94)	2.04 (1.15-3.63)	1.98 (1.09-3.59)

*values are odds ratios (95% confidence intervals †model 2 = model 1 + mother's educational level, ‡ fully adjusted model = model 2 + parity at enrollment, smoking during pregnancy, place type of delivery, and planned pregnancy.

Table 3 Regression models for breastfeeding at 2 months (n=3848)*

	N	%	MODEL 1	MODEL 2 †	MODEL 3 ‡
		bf at 2 months	(unadjusted)		
Native Dutch	2914	66.0	1	1	1
Mediterranean-1st generation	366	71.6	1.30 (1.02-1.65)	2.77 (2.13-3.61)	2.91 (2.22-3.82)
Mediterranean-2nd generation	143	53.1	0.59 (0.42-0.82)	1.11 (0.78-1.58)	1.36 (0.94-1.98)
Caribbean-1st generation	285	54.7	0.62 (0.49-0.80)	1.04 (0.80-1.35)	1.09 (0.84-1.43)
Caribbean-2nd generation	140	52.9	0.58 (0.41-0.81)	1.02 (0.71-1.46)	1.20 (0.83-1.74)

*values are odds ratios (95% confidence intervals) †model 2 = model 1 + mother's educational level, ‡ fully adjusted model = model 2 + mother's age, and parity at enrollment

Table 4 Regression models for breastfeeding at 6 months (n=3848)*

	N	%	MODEL 1	MODEL 2 †	MODEL 3 ‡
†		bf at 6 months	(unadjusted)		
Native Dutch	2914	31.0	1	1	1
Mediterranean-1st generation	366	42.6	1.65 (1.32-2.06)	2.57 (2.01-3.29)	2.71 (2.09-3.51)
Mediterranean-2nd generation	143	22.4	0.64 (0.43-0.96)	0.97 (0.64-1.46)	1.28 (0.83-1.98)
Caribbean-1st generation	285	21.1	0.59 (0.44-0.80)	0.82 (0.60-1.11)	0.87 (0.63-1.18)
Caribbean-2nd generation	140	19.3	0.53 (0.35-0.81)	0.76 (0.49-1.18)	0.96 (0.61-1.51)

*values are odds ratios (95% confidence intervals), †model 2 = model 1 + mother's educational level, ‡model 2 + maternal age, parity at enrollment, smoking, Cesarean section, place and type of delivery.

Appendix 1

Regression models for full breastfeeding (yes/no) until the baby was aged 2 months (n=3483)*

	N	%	MODEL 1	MODEL 2†	MODEL 3‡
		Exclusive bf at 2 months	(unadjusted)		
Native Dutch	2686	38.8	1	1	1
Mediterranean 1st generation	290	29.3	0.65 (0.50-0.85)	1.12 (0.84-1.49)	1.12 (0.84-1.50)
Mediterranean 2nd generation	128	25.0	0.53 (0.35-0.79)	0.86 (0.56-1.31)	1.04 (0.67-1.61)
Caribbean 1st generation	247	17.8	0.34 (0.25-0.48)	0.50 (0.35-0.70)	0.52 (0.37-0.73)
Caribbean 2nd generation	132	21.2	0.43 (0.28-0.65)	0.65 (0.42-1.01)	0.78 (0.49-1.22)

*values are odds ratios (95% confidence intervals), †model 1 + mother's educational level, ‡model 2 + mother's age, and parity at enrollment.

Appendix 2

Tables 2, 3, and 4 from main text repeated for father's ethnicity

Table 2: Regression models for starting breastfeeding (yes/no) (n=2897)*

	N	%	MODEL 1	MODEL 2†	MODEL 3‡
		Starting bf	(unadjusted)		
Native Dutch	2412	90.5	1	1	1
Mediterranean-1st generation	197	95.9	2.49 (1.21-5.12)	3.89 (1.84-8.20)	4.64 (2.19-9.86)
Mediterranean-2nd generation	52	96.2	2.64 (0.64-10.90)	4.25 (1.02-17.68)	4.58 (1.09-19.26)
Caribbean-1st generation	165	93.3	1.48 (0.79-2.76)	2.37 (1.26-4.49)	2.48 (1.30-4.75)
Caribbean-2nd generation	71	94.4	1.77 (0.64-4.89)	2.62 (0.94-7.31)	2.48 (0.89-6.96)

*values are odds ratios (95% confidence intervals), †model 1 + father's educational level, ‡model 2 + parity at enrollment, smoking during pregnancy, place and type of delivery and planned pregnancy.

Table 3: Regression models for breastfeeding until the baby was aged 2 months (n=2897)*

	N	%	MODEL 1	MODEL 2†	MODEL 3‡
		Bf at 2 months	(unadjusted)		
Native Dutch	2412	67.5	1	1	1
Mediterranean-1st generation	197	62.4	0.80 (0.59-1.08)	1.14 (0.82-1.57)	1.28 (0.92-1.78)
Mediterranean-2nd generation	52	55.8	0.61 (0.35-1.06)	0.92 (0.52-1.61)	1.17 (0.66-2.09)
Caribbean-1st generation	165	56.4	0.62 (0.45-0.86)	0.93 (0.67-1.30)	0.98 (0.70-1.37)
Caribbean-2nd generation	71	64.8	0.89 (0.54-1.45)	1.24 (0.75-2.06)	1.50 (0.89-2.52)

*values are odds ratios (95% confidence intervals), †model 1 + father's educational level, ‡model 2 + father's age, and parity at enrollment.

Table 4: Regression models for breastfeeding until the baby was aged 6 months (n=2897)*

	N	%	MODEL 1	MODEL 2†	MODEL 3‡
		Bf at 6 months	(unadjusted)		
Native Dutch	2412	29.9	1	1	1
Mediterranean-1st generation	197	33.5	1.18 (0.87-1.61)	1.46 (1.05-2.02)	1.78 (1.26-2.50)
Mediterranean-2nd generation	52	25.0	0.78 (0.42-1.47)	1.00 (0.53-1.91)	1.34 (0.70-2.59)
Caribbean-1st generation	165	20.6	0.61 (0.41-0.90)	0.78 (0.52-1.15)	0.85 (0.57-1.27)
Caribbean-2nd generation	71	29.6	0.99 (0.59-1.65)	1.20 (0.71-2.03)	1.38 (0.81-2.36)

*values are OR (95% CI), †model 1 + father's educational level, ‡model 2 + paternal age, parity at enrollment, smoking, Cesarean section, place and type of delivery.

Socioeconomic status is an important covariate in the association between mother's ethnicity and breastfeeding.[15-17] In this study, it was established on the basis of a single indicator: mother's educational level.[36] However, socioeconomic status is a complex and multifactor construct, whose commonest indicators are educational level, income level, and occupational class.[36, 37] Here we used level of education because it can also be applied to teenage and unemployed mothers – unlike indicators such as occupational class. But it does not fully capture the material and financial aspects of socioeconomic status.[37, 38] We repeated all analyses with income as the indicator of socioeconomic status. Results were similar, although effect estimates were somewhat smaller (data not shown). This may have been the result of more missing data for income, or the fact that educational level reflects health consciousness and problem-solving knowledge, which are probably more important factors for breastfeeding behaviour than factors associated with income.

The response rate at birth in the Generation R Study was 61%,[20] but there was some selection towards a relatively high educated and somewhat healthier study population. Also, breastfeeding initiation rates were fairly high.[39] The mothers in this study do therefore not fully represent the source population and results cannot be generalised to the general population. It is difficult to ascertain whether the association between ethnicity and breastfeeding would be different in non-responders. Our non response analyses showed that non native Dutch mothers were underrepresented, as were mothers with a lower educational level. Non-response is often associated with adverse health outcomes or adverse health behaviours. If the non-participating mothers were indeed less favourable towards breastfeeding than participating mothers, the association between ethnicity and breastfeeding continuation might be somewhat underestimated.

Conclusion

Generally, although more mothers from ethnic minorities in the Netherlands start breastfeeding than native mothers do, they are less likely to continue. Although breastfeeding continuation until 2 months is generally low among both Dutch native and non-native mothers, health workers should realize that ethnic minorities may face other difficulties in continuing breastfeeding than native women as a consequence of their socio-cultural background, and therefore adapt healthcare advice. Future research should concentrate on such women's difficulties in continuing breastfeeding. Interventions for native and non-native mothers should focus on breastfeeding continuation and duration.

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ABSTRACT

Background
To describe ethnic and socioeconomic differences in indicators of sedentary behaviors and physical activity in an urban multi-ethnic prospective birth cohort study.

Methods
We analyzed data from 4688 children. Indicators of sedentary behavior (watching television and sitting in a buggy) and physical activity (playing outside) were measured by a parent-reported questionnaire at age 3. We adjusted for mother's social circumstances and indicators of health behaviors. Logistic regression was used to obtain odds ratios (OR) and 95% confidence intervals (CI).

Results
There were significant socioeconomic and ethnic differences in sedentary behaviors, indicated by watching television and time spent in a buggy. Children from mothers with a midlow educational level and non-Western children less often played outside than native Dutch children with a high educated mother. Mother's unemployment was indepedently associated with watching television, but not with time spent in a buggy or playing outside. Indicators of mother's health behaviors did not predict sedentary behaviors and physical activity. Mother's social circumstances slightly reduced the association between socioeconomic status, ethnicity, and sedentary behaviors. Mother's health behaviors did not affect these associations.

Conclusion
Socioeconomic status and ethnicity have an independent association with sedentary lifestyles of preschool children. Further research should search underlying mechanisms that could contribute to reducing these differences.

3.3 SOCIOECONOMIC AND ETHNIC DIFFERENCES IN PHYSICAL ACTIVITY AND SEDENTARY BEHAVIOR IN PRESCHOOL CHILDREN

BASED ON

van Rossem L / Vogel I / Moll HA / Jaddoe VW / Hofman A / Mackenbach JP / Raat H.
Socioeconomic and ethnic differences in physical activity and sedentary behavior in preschool children. The generation R study.
Submitted.

INTRODUCTION

Childhood overweight is a worldwide problem with severe consequences for morbidity and mortality.[1] Overweight prevalence is unequally distributed among social subgroups: socially disadvantaged subgroups have a higher prevalence of overweight compared to socially advantaged subgroups.[2] This gradient has been shown in children from the age of 5 years onwards.[3]

Overweight is the result of a distorted energy-balance: too much food intake, too low energy expenditure or a combination of both.[4, 5] Literature has consistently shown that sedentary behaviors and lack of physical activity are associated with the development of overweight in childhood.[6-11] These lifestyle-related behaviors are established early in life.[12] Although some studies indeed reported an association between social disadvantage and sedentary behaviors in children,[13-15] which may precede the social gradient in overweight, few did this in preschool age.[16, 17]

The aim of this study was to describe socioeconomic and ethnic differences (as indicators of social disadvantage) in indicators of sedentary behaviors and physical activity at preschool age. We also studied the contribution of mother's social circumstances and mother's health-related behavior in the association between socioeconomic status, ethnicity, and indicators of sedentary behavior and physical activity. This was done in an urban multi-ethnic prospective birth cohort study.

METHODS

Study design and population
This study was embedded in The Generation R study, a population-based prospective cohort study from fetal life onwards. Invitations to participate in the study were made to all pregnant mothers who

had an expected delivery date between April 2002 and January 2006 and who lived in the study area (Rotterdam, the Netherlands) at time of delivery. Details of the study are described elsewhere.[18] The study was conducted in accordance with the guidelines proposed in the World Medical Association Declaration of Helsinki, and was approved by the Medical Ethical Committee at Erasmus MC, University Medical Center Rotterdam. Written consent was obtained from all participants.

Postnatal consent was given by 7295 mothers. Of these 2383 (32.7%) did not provide information on watching television or playing outside at age 3 and were therefore excluded. We also excluded participants whose ethnicity was unknown, as well as those who provided no information on educational level (n=224). We analyzed data on 4688 children (64.3%).

Measurements

Social disadvantage

We used the following indicators of social disadvantage: mother's educational level to represent socioeconomic status, and non-native ethnicity. Level of maternal education was established at enrollment. The Dutch Standard Classification of Education[19] was used to categorize 4 levels of education: low (less than 4 years of high school), mid-low (college), midhigh (Bachelor's degree), and high (Master's degree). Ethnicity was defined according to country of birth of parents and grandparents, and grouped into 'native Dutch', 'other western', and 'non-western'. [20]

Indicators of sedentary behavior and physical activity

The following indicators of sedentary behavior and physical activity at age 3 were included in this study: watching television, time spent in a buggy, and playing outside. For all behaviors, the question was 'How much time has your child been occupied with the following in the last month'. This question was asked two times; for weekenddays and weekdays. Answer categories were: none or less than 30 minutes/day, 30 minutes to 1 hour /day, 1-2 hours/day, 2- 3 hours/day, >3 hours/day. We calculated the mean time spent for each behavior. First, we took the middle number of minutes per category (for example, 1-2 hours/day is 1.5 hours/day), and multiplied this number by 5 for weekdays, and by 2 for weekenddays. This number was divided by 7 to obtain the mean number of minutes spent on that behavior. According to the recommendation of the American Academy of Pediatrics, we dichotomized watching television in <2 hours/day and $\geq$ 2 hours/day.[21] Time spent in a buggy and playing outside were dichotomized in $\geq$ 1 hour/day and <1 hour/day.

Covariates

We adjusted in the analyses for general confounders: child's sex and age, and the season (summer, i.e april until october, and winter, i.e. november until march) during which the questionnaire was completed by the parents.

Mother's social circumstances: These included mother's job status, financial difficulties, single motherhood, and number of days that the child was cared for by others. Mother's job status was asked when her child was aged 2 years as 'Which description applies most to you at the moment?' Answer categories included 'paid job', 'self employed', 'looking for work', 'disabled', 'social benefits', 'housewife', 'student', 'other'. We categorized 'paid job' and 'self employed' into one category and recoded the other answer categories into 'no paid job'. The following question was asked during pregnancy to determine financial difficulties (yes, no): 'Do you have any difficulty in paying food, rent, electricity bill and suchlike?' Answer categories included 'no' (no), 'some' (yes), and 'great' (yes) difficulties. Single motherhood (yes, no) was asked during pregnancy. Number of days that the child is cared for by others was asked as follows: How many hours a week is your child cared for by: babysitter, aupair, childminder, family, creche, playgroup or other. Answer categories were: 'never', 'less than 8 hours a week', '8-16 hours/week' , '16-24 hours/week', '24-32 hours/week', and 'more than 32 hours/week'. The midpoints of these categories were counted for each type of child care to calculate the total number of days that a child is not cared for by the mother.

Indicators of mother's health behavior: These included maternal body mass index (BMI), maternal smoking, and breastfeeding status at 6 months. Maternal BMI (kg/m^2) was obtained from self-reported pre-pregnancy weight and measured height at intake, information on maternal smoking (never, until pregnancy known, during pregnancy) was obtained from several questionnaires during pregnancy, and breastfeeding status at 6 months (breastfeeding, no breastfeeding) was derived from questionnaires during the first 12 months after birth.

Statistical analyses

Multiple logistic regressions were used to obtain odds ratios (OR) and their 95% confidence intervals (CI). We tested the association between social disadvantage and sedentary behaviors/physical activity in three steps. In the basic model (model 1) we included mother's educational level and child's ethnic background, adjusted for general confounders: child's age, sex, and season. Second, we assessed the independent contribution of two groups of covariates: model 2A) mother's social circumstances (financial difficulties, job status, single motherhood, and number of days that the child is cared by others), and model 2B) the influence of health related behavior (breastfeeding, smoking status, and maternal BMI). Third, model 3 is the fully adjusted model.

The interaction term for educational level*ethnicity was p=0.25 for watching television, p=0.04 for playing outside, and p=0.18 for time spent in a buggy. When stratifying the analyses for each ethnicity, associations were in the same direction. Therefore, we do not show stratified analyses.

Because covariates were derived from measurements at different time-points, total number of missing values in the covariates was relatively high (up to 22.5% for smoking). We therefore applied multiple imputation. Five imputed datasets were generated using a fully conditional specified model to handle missing values. Imputations were based on the relations between all covariates in the study.[22] Analyses were conducted with Statistical Package for Social Sciences (SPSS) version 17.0 for Windows (SPSS Inc, Chicago, IL, USA).

RESULTS

Of all participants, 14.7% were in the lowest educational level. The sample consisted of 9.5% children of other Western ethnicities, and 23.1% of non-Western ethnicities. Nearly 10% of children watched at least 2 hours television per day, and more than one third played less than 1 hour per day outside (Table 1).

Table 2 shows the association between indicators of social disadvantage and watching television. The lower educated the mother; the more likely it was that children watched at least 2 hours television per day. Also all non-native Dutch children were more likely to watch television at least 2 hours a day compared to native Dutch children. Of indicators of mother's social circumstances, having no paid job was independently associated with watching television for at least 2 hours a day. None of the indicators of mother's health behaviors was an independent predictor of watching television for at least 2 hours a day. Inclusion of mother's social circumstances slightly attenuated the association between indicators of social disadvantage and watching television, but inclusion of mother's health behaviors hardly affected the association.

The other indicator of sedentary behavior, time spent in a buggy, showed similar results for indicators of social disadvantage as watching television. Mother's social circumstances were not independently associated with time spent in a buggy, but did reduce the association between social disadvantage and time spent in a buggy (Appendix 1).

Table 3 shows the association between indicators of social disadvantage and playing outside. Children from mothers with a mid-low educational level (OR: 1.34, 95% CI: 1.13-1.59) and children with a

non-Western ethnicity (OR: 1.46, 95% CI: 1.24-1.73) less often played outside compared to their counterparts. Mother's social circumstances and mother's health indicators were not independently associated with playing outside, and they hardly affected the association between social disadvantage and playing outside.

DISCUSSION

This study showed large socioeconomic and ethnic differences in indicators of sedentary behaviors and, to a lesser extent, physical activity in preschool children. Significant determinants of watching television were mother's job status, but this only slightly attenuated associations between socioeconomic status, ethnicity, and watching television.

To our knowledge, only two studies have assessed the association between social disadvantage and sedentary behavior in preschool children as the main interest.[17, 23] Other studies report the association between social disadvantage and sedentary behavior as secondary analyses,[16] or have studied the association in older children or adolescents.[13]

These studies confirm our findings that socially disadvantaged children are more likely to engage in sedentary behaviors.[13, 16, 17] In addition, the association between social disadvantage and sedentary behaviors was found to be stronger than for physical activity.[16, 17] However, one study did not find an association between socioeconomic status and physical acticity in preschool children, as measured with accelerometers.[23] An explanation might be that accelerometers distinguish between moderate to vigorous physical activity and sedentary behavior and do therefore not distinguish between types of activity, such as sleeping (which may be protective in the development of overweight) and watching television.[23]

Mother's job status seemed to be an important contributing factor in the association between educational level and ethnicity with watching television. We hypothesize that this may be a mediator in the association between social disadvantage and sedentary behaviors. Our results showed more television watching in children from unemployed mothers. This was independent of the number of days that the child is cared for by others. Literature is conflicting on the association between maternal employment and watching television by their children. One study reported more television watching in children whose mothers worked fulltime or were not employed (compared to parttime),[24] whereas another study reported more television watching in children from employed mothers.[25] Unemployment may be associated with underlying stress-related factors, which were not studied. Stress-related factors may cluster in socially disadvantaged families and give mothers less space for undertaking activities with their children. Another study found that family conflict, which may

Table 1 Characteristics of 4688 mother-child pairs in the Generation R Study

		N	%
GENERAL CHARACTERISTICS			
Child's gender	Boy	2337	49.9
Child's age at measurement	Mean months (SD)	36.65 (1.39)	
INDICATORS OF SOCIAL DISADVANTAGE			
Mother's educational level	Low	687	14.7
	Mid-low	1287	27.4
	Mid-high	1168	24.9
	High	1546	33.0
Child's ethnicity	Dutch	3158	67.4
	Other western	447	9.5
	Non-western	1083	23.1
MOTHER'S SOCIAL CIRCUMSTANCES			
Mother's job status	Paid job	3216	81.5
Single motherhood	Yes	370	8.0
Financial difficulties	Yes	528	13.7
Number of days per week that the child is cared by others	<1 day	243	6.5
	1-2 days	531	14.3
	2-3 days	967	26.0
	3-4 days	1025	27.6
	4-5 days	666	17.9
	≥ 5 days	282	7.6
INDICATORS OF MOTHER'S HEALTH BEHAVIORS			
Maternal smoking during pregnancy	Never	2912	77.7
	Until pregnancy known	461	12.3
	During pregnancy	374	10.0
Mother's pre-pregnancy BMI	Normal weight	2779	76.5
	Overweight	614	16.9
	Obesity	241	6.6
Breastfeeding at 6 months	Yes	1426	32.9
INDICATORS OF CHILD'S SEDENTARY BEHAVIOR/PHYSICAL ACTIVITY AT AGE 3			
Watching television	< 0.5 hours/day	1086	23.5
	0.5-1 hours/day	1882	40.8
	1-2 hours/day	1285	27.9
	≥ 2 hours/day	359	7.8
Playing outside	< 0.5 hours/day	160	3.5
	0.5-1 hours/day	1509	32.9
	≥ 1 hour/day	2911	63.6
Sitting in a buggy	< 0.5 hours/day	3844	84.0
	0.5-1 hours/day	565	12.3
	≥ 1 hour/day	170	3.7

Missings were 941 (20.1%) for smoking, 1054 (22.5%) for mother's BMI, 356 (7.6%) for breastfeeding, 744 (15.9%) for job status, 90 (1.9%) for single motherhood, 834 (17.8%) for financial difficulties, 974 (20.8%) for number of days cared for by others, 76 (1.6%) for watching television, 108 (2.3%) for playing outside, 109 (2.3%) for sitting in a buggy at age 3.

Table 2 Associations between indicators of social disadvantage and watching television at age 3 for at least 2 hours/day (n=4612)*

		MODEL 1	MODEL 2A	MODEL 2B	MODEL 3
		Basic model†	Adjusted for mother's social circumstances	Adjusted for indicators of mother's health behaviors	Fully adjusted
SOCIAL DISADVANTAGE					
Mother's educational level	high	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	mid-high	1.86 (1.25-2.78)	1.78 (1.19-2.67)	1.85 (1.24-2.77)	1.76 (1.17-2.64)
	mid-low	3.38 (2.39-4.79)	2.87 (1.98-4.17)	3.31 (2.30-4.76)	2.75 (1.89-4.02)
	low	4.61 (3.14-6.78)	3.42 (2.24-5.22)	4.55 (3.07-6.72)	3.27 (2.12-5.05)
Child's ethnicity	Dutch	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	other western	2.22 (1.52-3.23)	2.03 (1.38-2.97)	2.27 (1.55-3.32)	2.09 (1.42-3.08)
	non western	3.16 (2.45-4.06)	2.64 (2.01-3.45)	3.18 (2.47-4.10)	2.67 (2.04-3.49)
MOTHER'S SOCIAL CIRCUMSTANCES					
Mother's job status	paid job		1 (ref)		1 (ref)
	no paid job		1.82 (1.41-2.36)		1.87 (1.44-2.43)
Single motherhood	no		1 (ref)		1 (ref)
	yes		1.33 (0.95-1.86)		1.30 (0.93-1.84)
Financial difficulties	no		1 (ref)		1 (ref)
	yes		1.35 (0.97-1.87)		1.39 (1.00-1.93)
Number of days that the child is cared for by others	<2		1 (ref)		1 (ref)
	2-4		0.97 (0.62-1.51)		1.00 (0.63-1.59)
	≥ 4		0.92 (0.63-1.34)		0.94 (0.64-1.38)
INDICATORS OF MOTHER'S HEALTH BEHAVIORS					
Mother's BMI	Normal weight			1 (ref)	1 (ref)
	Overweight			0.86 (0.63-1.16)	0.84 (0.62-1.15)
	Obese			1.35 (0.93-1.97)	1.37 (0.93-2.01)
Smoking during pregnancy	Never			1 (ref)	1 (ref)
	Until pregnancy known			0.86 (0.60-1.24)	0.87 (0.61-1.24)
	During pregnancy			0.75 (0.50-1.14)	0.74 (0.48-1.13)
Breastfeeding	≥ 6 months			1 (ref)	1 (ref)
	< 6 months			0.85 (0.65-1.10)	0.78 (0.60-1.02)

* values are odds ratios (95% confidence intervals) †adjusted for child's sex, child's age at measurement, and season at measurement

also be an indicator of stress, was predictive of watching television.[26]

We did not find evidence that watching television by the child clustered with other health-related behaviors of the mother, because child's sedentary behaviors were not predicted by mother's health behaviors. Mother's BMI was not associated with watching television, which was confirmed in another study.[27]

Mother's social circumstances and mother's health behaviors were not independently associated with time spent in a buggy or playing outside. Determinants for specific indicators of sedentary behavior and physical activity probably differ.

When interpreting the results, some methodological considerations should be taken into account. We used mother's educational level

Table 3 Associations between indicators of social disadvantage and playing outside for less than 1 hour/day (n=4580)

		MODEL 1	MODEL 2A	MODEL 2B	MODEL 3
		Basic model†	Adjusted for mother's social circumstances	Adjusted for indicators of mother's health behaviors	Fully adjusted
SOCIAL DISADVANTAGE					
Mother's educational level	high	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	mid-high	1.09 (0.92-1.29)	1.11 (0.94-1.31)	1.11 (0.94-1.31)	1.12 (0.95-1.33)
	mid-low	1.30 (1.10-1.53)	1.31 (1.10-1.55)	1.33 (1.12-1.57)	1.34 (1.13-1.59)
	low	1.13 (0.92-1.40)	1.13 (0.90-1.41)	1.16 (0.94-1.44)	1.17 (0.93-1.47)
Child's ethnicity	Dutch	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	other western	1.03 (0.83-1.29)	1.02 (0.82-1.27)	1.03 (0.83-1.29)	1.02 (0.82-1.28)
	non western	1.50 (1.28-1.76)	1.48 (1.26-1.75)	1.48 (1.25-1.73)	1.46 (1.24-1.73)
MOTHER'S SOCIAL CIRCUMSTANCES					
Mother's job status	paid job		1 (ref)		1 (ref)
	no paid job		1.18 (0.97-1.43)		1.17 (0.97-1.42)
Single motherhood	no		1 (ref)		1 (ref)
	yes		0.82 (0.65-1.05)		0.83 (0.65-1.05)
Financial difficulties	no		1 (ref)		1 (ref)
	yes		1.05 (0.86-1.29)		1.05 (0.86-1.29)
Number of days that the child is cared for by others	<2		1 (ref)		1 (ref)
	2-4		0.87 (0.70-1.07)		0.85 (0.69-1.06)
	≥ 4		0.91 (0.78-1.07)		0.91 (0.77-1.07)
INDICATORS OF MOTHER'S HEALTH BEHAVIORS					
Mother's BMI	Normal weight			1 (ref)	1 (ref)
	Overweight			1.06 (0.88-1.28)	1.05 (0.87-1.27)
	Obese			1.01 (0.77-1.31)	1.00 (0.77-1.31)
Smoking during pregnancy	Never			1 (ref)	1 (ref)
	Until pregnancy known			1.00 (0.82-1.22)	1.00 (0.82-1.22)
	During pregnancy			0.79 (0.63-1.00)	0.79 (0.63-1.00)
Breastfeeding	≥ 6 months			1 (ref)	1(ref)
	< 6 months			1.10 (0.96-1.27)	1.10 (0.96-1.26)

* values are odds ratios (95% confidence intervals) †adjusted for child's sex, child's age at measurement, and season at measurement

as an indicator of socioeconomic status. Socioeconomic status is a complex and multifactor construct, whose commonest indicators are educational level, income level, and occupational class. Educational level was used as the main indicator because it reflects not only economical factors, but also problem-solving skills, and general and health-related knowledge which may be more important for overweight related behaviour than income or occupational class. Similarly, ethnicity may refer to people belonging to the same nation, religion, language, country of birth, or culture. We used country of birth because it is the most objective and stable measure that can be used in young children. Nevertheless, country of birth does not cover all aspects of ethnicity, such as culture and ethnic identity. Our indicators of sedentary behaviour and physical activity were based on parental reports. Observations may have been better. Some covariates, for example single motherhood and financial difficulties were asked during pregnancy. These variables may have changed over time and therefore some (non-differential) misclassification may occur, resulting in an attenuation of results. Also, we did not take father-related variables into account, because we assume that mother is the main caregiver. When repeating the basic models with father's educational level instead of mother's educational level, associations were – although less strong – similar. Missing values in the covariates were relatively high. We therefore applied multiple imputation. Multiple imputation is currently the best method to deal with missing at random, which means that the association between those included in the study should be similar as those not included in the study.[22] We have no evidence that this assumption is violated.

Conclusion

Large social inequalities in watching television and other indicators of sedentary behaviors require action, as they may precede social inequalities in overweight. Future studies should replicate socio-economic and ethnic differences in (different types of) sedentary behaviors and physical activity at preschool age in other populations. The underlying pathways are yet unclear and should be unraveled. We recommend in depth studying of family social circumstances, including the role of family stress in the association between social disadvantage and indicators of sedentary behaviors. Second, the role of these behaviors in the development of social inequalities in overweight should be further studied. For now, interventions to reduce social inequalities in sedentary behavior should not focus on healthy behavior in general, as this seem not to be related.

Appendix 1

Associations between indicators of social disadvantage and sitting in a buggy for at least 1 hour/day at age 3 (n=4579)*

		MODEL 1	MODEL 2A	MODEL 2B	MODEL 3
		Basic model†	Adjusted for mother's social circumstances	Adjusted for indicators of mother's health behaviors	Fully adjusted
SOCIAL DISADVANTAGE					
Mother's educational level	High	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	Mid-high	1.66 (0.91-3.04)	1.68 (0.91-3.08)	1.64 (0.89-3.00)	1.65 (0.90-3.03)
	Mid-low	3.23 (1.90-5.49)	3.12 (1.81-5.37)	3.12 (1.83-5.33)	2.98 (1.72-5.17)
	Low	5.14 (2.96-8.92)	4.72 (2.61-8.53)	4.97 (2.84-8.70)	4.48 (2.45-8.19)
Child's ethnicity	Dutch	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	Other western	2.24 (1.29-3.90)	2.16 (1.24-3.78)	2.27 (1.30-3.96)	2.19 (1.25-3.84)
	Non western	3.62 (2.53-5.18)	3.35 (2.30-4.88)	3.72 (2.59-5.35)	3.44 (2.35-5.03)
MOTHER'S SOCIAL CIRCUMSTANCES					
Mother's job status	Paid job		1 (ref)		1 (ref)
	No paid job		1.32 (0.83-2.09)		1.35 (0.85-2.16)
Single motherhood	No		1 (ref)		1 (ref)
	Yes		1.20 (0.76-1.91)		1.18 (0.74-1.88)
Financial difficulties	No		1 (ref)		1 (ref)
	Yes		1.03 (0.68-1.56)		1.03 (0.68-1.57)
Number of days that x level child is cared for by others	< 2		1 (ref)		1 (ref)
	2-4		0.81 (0.46-1.45)		0.84 (0.47-1.49)
	≥ 4		0.72 (0.44-1.17)		0.73 (0.45-1.18)
INDICATORS OF MOTHER'S HEALTH BEHAVIORS					
Mother's BMI	Normal weight			1 (ref)	1 (ref)
	Overweight			0.95 (0.59-1.53)	0.94 (0.59-1.52)
	Obese			1.05 (0.59-1.84)	1.05 (0.59-1.86)
Smoking during pregnancy	Never			1 (ref)	1 (ref)
	Until pregnancy known			1.13 (0.69-1.86)	1.14 (0.69-1.88)
	During pregnancy			1.14 (0.67-1.96)	1.14 (0.67-1.95)
Breastfeeding	≥ 6 months			1 (ref)	1 (ref)
	< 6 months			0.83 (0.58-1.18)	0.81 (0.57-1.17)

* values are odds ratios (95% confidence intervals) †adjusted for child's sex, child's age at measurement, and season at measurement

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CHAPTER 4 SOCIAL DISADVANTAGE AND OVERWEIGHT IN PRESCHOOL CHILDREN

ABSTRACT

Background
We assessed whether socioeconomic inequalities in overweight were already present in preschool children.

Methods
We used data from 2954 Dutch children participating in a longitudinal birth cohort study. Indicators of socioeconomic status were mother's educational level and household income. Body mass index (BMI)-for-age z- scores were derived from a national reference. Overweight was defined at 24 and 36 months according to age and sex-specific cut-off points for BMI. Multiple regression analyses were performed.

Results
Relative to children from mothers with the highest educational level, mean BMI z-score was lower at age 24 months in children from mothers with the low, mid-low, and mid-high educational level, and in the mid-low group at 36 months (p<0.001). Prevalence of overweight was lower in children from mothers with the mid-low educational level at age 24 and 36 months (aOR24 months: 0.61; 95% CI: 0.43-0.87 and aOR36 months: 0.65; 95% CI: 0.44-0.96), but was not significantly different for the other educational levels. There were no significant differences in childhood overweight by income level.

Conclusion
The inverse association between socioeconomic status and childhood overweight presumably emerges after the age of 3 years. Before this age, the gradient may even be the reverse.

4.1 SOCIOECONOMIC STATUS IS NOT INVERSELY ASSOCIATED WITH OVERWEIGHT IN PRESCHOOL CHILDREN

BASED ON

van Rossem L / Silva LM / Hokken-Koelega AC / Arends LR / Moll HA / Jaddoe VW / Hofman A / Mackenbach JP / Raat H.
Socioeconomic Status is not Inversely Associated with Overweight in Preschool Children.
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INTRODUCTION

Overweight and obesity are a major public health problem worldwide, and associated cardiovascular and psychosocial problems are well documented.[1, 2] Although overweight and obesity may affect all people in society, it disproportionally affects the socially disadvantaged.[3] Moreover, the latter group also experience the largest increase in prevalence of overweight and obesity over time.[3, 4] Socioeconomic inequalities in overweight have been extensively described for adults, adolescents, and children.[5, 6] In adults, there is a clear inverse association between socioeconomic status and overweight, and it is suggested that socioeconomic inequalities in adult obesity have their origins in childhood. [7] Indeed, this association in children is often reported [4, 6, 8-12] whereas others found no association between social disadvantage and childhood overweight.[13] Only a few studies have explored socioeconomic inequalities in overweight in preschool children.[4, 8, 11]

Given the presence of a clear socioeconomic gradient in overweight in adults (with a relatively high prevalence of overweight in disadvantaged subgroups) it is important to know at what age this socioeconomic gradient emerges. This will help elucidate the underlying pathways and subsequently enable preventive interventions.

Therefore, the present study evaluates socioeconomic differences in overweight in children at the age of 24 and 36 months, and assesses the contribution of known risk factors for childhood obesity in this association. In addition, body mass index (BMI) curves were constructed between 1 and 36 months of age to see whether these curves differed for educational subgroups. This was done in a longitudinal birth cohort study with multiple weight and height measurements in the first years after birth. The main hypothesis is that socially disadvantaged children are more often overweight, even at this young age.

METHODS

Study design and population

This study was embedded in The Generation R study, a population-based prospective cohort study from fetal life onwards. The Generation R study was designed to identify early determinants of growth, development and health. Invitations to participate in the study were made to all pregnant mothers who had an expected delivery date between April 2002 and January 2006 and who lived in the study area (Rotterdam, the Netherlands) at time of delivery. Details of the study are described elsewhere.[14] The study was conducted in accordance with the guidelines proposed in the World Medical Association Declaration of Helsinki, and was approved by the Medical Ethical Committee at Erasmus MC, University Medical Center Rotterdam. Written consent was obtained from all participants.
We restricted our analyses to children with a native Dutch mother, because the association between socioeconomic status and overweight may differ in and between certain ethnic subpopulations.[15-17] Consent for postnatal follow-up was available for 3877 children with a native Dutch mother. Twins (n=116) were excluded from the analyses. To avoid clustering, the analyses excluded data on the second or third pregnancy of any woman who was participating in The Generation R study with more than one child (n=389). Also excluded were data of participants with no information on educational level (n=16), as well as children without height or weight measures between 24 and 36 months of age (n=402). Finally, data of 2954 subjects were available for analyses.

Measurements

Socioeconomic status

Our primary determinant was the educational level of the mother as an indicator of socioeconomic status. Level of maternal education was established at enrollment. The Dutch Standard Classification of Education[18] was used to categorize 4 subsequent levels of education: low (less than 4 years of high school), mid-low (college), mid-high (Bachelor's degree), and high (Master's degree). Household income was included as a second indicator of socioeconomic status. Data on household income was obtained at enrollment and was dichotomized, using the 2005 monthly general labour income as the cut-off point (< € 1600, ≥ € 1600). Households that earn below € 1600 per month are considered as low-income groups.[19]

BMI and overweight

BMI: Height and weight were measured with standardized methods at each visit to the Child Health Centers. Standard visits at the Child Health Centers take place at 1, 2, 3, 4, 6, 11, 18, 24 and 36 months of age. BMI was calculated as weight/height^2. We calculated BMI-for-age standard deviation scores (SDS), which were calculated from a national reference[20] using the Growth Analyzer program (http://www.growthanalyser.org). SDS (or z-scores) reflect differences from the population mean. The population mean is 0, and 95% of children will be in the range from -2 SD to +2 SD.

Overweight: The main outcomes were overweight at age 24 and 36 months. International age and sex-specific cut-off points for BMI were used to define overweight (including obesity).[21] These cut-off points are extrapolated from the adult cut-off point (which is at 25 kg/m^2) to age and sex-specific cut-off points for children. The advantage of using this measure compared to weight-for-height SDS from population-based growth studies is that it is internationally comparable, and cut-off points are based on health risk instead of time-dependent cut-off points.[22]

Confounders and mediators

Selection of covariates was based on reports of early determinants of childhood overweight and obesity.[10, 13] Child's sex and exact age at measurement were treated as confounders. The effect of socioeconomic status on the development of overweight is likely to act through more proximal determinants, so-called mediators. To elucidate possible mechanisms on how socioeconomic status is associated with childhood overweight, the following covariates were considered as mediators (categorized in prenatal, perinatal, and postnatal mediators):

Prenatal mediators were parental BMI and maternal smoking during pregnancy. Mothers reported their pre-pregnancy weight. Height was measured at enrollment. Mother's BMI was calculated as weight/height^2. Father's BMI was calculated from measured weight and height at enrollment. Smoking during pregnancy (yes, no) was derived from prenatal questionnaires.

Perinatal mediators were birth weight (grams) and gestational age (weeks). Both were obtained from medical records.

Postnatal mediators were breastfeeding and change in BMI SDS between 1 and 6 months after birth. Information on breastfeeding was obtained by a combination of questionnaires administered at 2, 6 and 12 months after birth. We considered breastfeeding duration in months, and exclusive breastfeeding for 2 months. BMI SDS change was calculated as the difference in BMI-for-age SDS between 1 month after birth and 6 months after birth.

Statistical analyses

Associations between educational level and subject characteristics were explored. Chi-square tests were used to test for differences in categorical variables, analysis of variance (ANOVA) was used to test for differences in continuous variables, and the Kruskal-Wallis test was used to test for differences in non-normally distributed continuous variables.

The association between mother's educational level and child's BMI SDS was assessed at 24 and 36 months using multiple linear regression. Unstandardized beta coefficients and 95% confidence intervals (CI) are reported for each educational level compared to the reference category (highest educational level). The association between mother's educational level and child's overweight status at 24 and

Tabel 1

Characteristics of the 2954 participants in the Generation R cohort, by mother's educational level

			MOTHER'S EDUCATIONAL LEVEL				
		Total	low (n=387)	mid-low (n=738)	mid-high (n=811)	high (n=1018)	p-value*
SOCIODEMOGRAPHIC FACTORS							
Low household income	% < €1600/month	10.1	33.3	13.4	8.5	2.2	<0.001
MATERNAL LIFESTYLE FACTORS							
Smoking during pregnancy	% yes	10.4	20.3	12.0	11.3	4.8	<0.001
PARENTAL OVERWEIGHT †							
Mother	% normal weight	78.0	64.4	72.4	80.9	84.7	<0.001
	% overweight	15.6	19.7	18.0	14.7	13.1	
	% obese	6.4	15.9	9.7	4.4	2.2	
Father	% normal weight	53.3	43.5	50.0	54.9	57.5	<0.001
	% overweight	39.6	41.7	41.4	39.6	37.7	
	% obese	7.1	14.8	8.6	5.5	4.8	
CHILD'S BIRTH CHARACTERISTICS							
Birth weight	% low (<2500 g)	3.8	6.7	4.1	3.9	2.3	<0.001
	% normal (2500-4000 g)	79.2	80.4	81.3	78.7	77.7	
	% high (>4000 g)	17.0	12.9	14.6	17.4	20.0	
Gestational age	weeks (mean, SD)	40.0 (1.7)	39.6 (1.7)	39.9 (1.8)	40.0 (1.6)	40.2 (1.5)	<0.001
OTHER CHILD CHARACTERISTICS							
Sex % boy		50.5	53.7	49.7	48.6	51.3	0.36
Breastfeeding % (exclusive)	at least 2 months	40.0	19.7	29.2	46.7	49.6	<0.001
Breastfeeding (any)	duration (median, 100% range)	5.0 [0-12]	1.0 [0-12]	2.5 [0-12]	5.0 [0-12]	5.0 [0-12]	<0.001
BMI SD score at 1 months of age‡	mean, SD	0.37 (0.98)	0.31 (0.97)	0.29 (1.01)	0.42 (0.99)	0.40 (0.96)	0.13
BMI SD score at 6 months of age‡	mean, SD	0.03 (0.96)	0.06 (0.95)	0.05 (1.02)	0.03 (0.95)	0.01 (0.94)	0.87
Height SD score at 24 months‡	mean, SD	0.04 (0.97)	0.11 (1.05)	0.07 (0.99)	-0.01 (0.94)	0.03 (0.95)	0.21
Height SD score at 36 months‡	mean, SD	0.04 (0.97)	0.06 (1.07)	0.07 (0.96)	-0.02 (0.98)	0.04 (0.93)	0.42
Weight SD score at 24 months‡	mean, SD	-0.02 (0.94)	-0.01 (1.06)	-0.07 (0.95)	-0.06 (0.90)	0.06 (0.92)	0.03
Weight SD score at 36 months‡	mean, SD	-0.03 (0.93)	0.04 (1.09)	-0.05 (0.95)	-0.08 (0.96)	0.00 (0.83)	0.22

Missing values were 491 (16.6%) for household income, 571 (19.3%) for maternal smoking during pregnancy, 650 (22.0%) for mother's BMI, 563 (19.1%) for father's BMI, 497 (16.8%) for exclusive breastfeeding at 2 months, 900 (30.5%) for (any) breastfeeding duration, 934 (31.6%) for BMI SDS at 1 month of age, and 580 (19.6%) at 6 months.
* p-values for Chi-square tests for categorical variables, ANOVA for continuous variables, Kruskal-Wallis test for non-normally distributed continuous variables † According to the World Health Organization definition, BMI<25= normal weight, BMI 25-30=overweight, BMI >30=obesity. ‡ BMI-for-age standard deviation scores were derived from a national reference (Fredriks et al. 2000).

36 months was assessed by multiple logistic regression. Odds ratios (OR) and 95% CIs were obtained for each educational level compared to the reference category (highest educational level). Analyses for BMI SDS and overweight were not stratified for sex, as results were similar for boys and girls and the interaction term was not significant (p>0.30). In model 1, we adjusted for exact age at measurement and sex. Then, the mediators were added according to a hierarchical structure. In model 2, we adjusted for model 1 + the prenatal risk factors for overweight (smoking during pregnancy, parental BMI). In model 3, we adjusted for model 2 + the perinatal risk factors (birth weight, gestational age). In model 4, we adjusted for model 3 + postnatal risk factors (breastfeeding, infant BMI SDS change between 1 to 6 months after birth).

Repeated measurements analysis ('PROC MIXED' procedure in SAS) was performed to calculate whether BMI curves differ per educational level throughout the first 3 years of life. The best fitting model for BMI as a function of age was built using fractional polynomials.[23] The best fitting model for BMI was: $BMI = \beta_0 + \beta_1 * \ln(age) + \beta_2 * \sqrt{age}$. To this model, educational level was added as a main determinant (reference: high education), and an interaction term of educational level with both data transformations (ln and sqrt) of age. The -2 log likelihood of this model was compared to the -2 log likelihood of the model without interaction terms for educational level by means of the Chi-square test, to see whether the model fit was significantly better. The repeated measurement analyses were stratified for sex, to enhance comparison with existing BMI-for-age curves.

Percentage of missing values in the covariates ranged from 0% (birth weight) to 41.1% (change in BMI SDS between 1 and 6 months). Because the missing values were not completely at random, the multiple imputation procedure in SPSS 17.0 was used.[24] Five imputed datasets were generated using a fully conditional specified model to handle missing values. Imputations were based on the relations between all covariates in the study. Pooled estimates from these five imputed datasets were used to report betas, ORs and their 95% CIs.

Analyses were conducted using the Statistical Package for Social Sciences (SPSS) version 17.0 for Windows (SPSS Inc, Chicago, IL, USA) and Statistical Analysis Software (SAS) version 9.1.3 for Windows (SAS Institute, Cary, NC, USA).

RESULTS

Sample characteristics

Overall, 13% of mothers were in the lowest educational level and 35% were in the highest educational level. Lower-educated mothers more often smoked during pregnancy, were more often overweight, more often had overweight partners, more often had a child with a low birth

Table 2

Multiple linear regression analyses for associations between mother's educational level and child's BMI SDS* (n=2954)

		MEAN (SE)	MODEL 1	MODEL 2	MODEL 3	MODEL 4
			(adjusted for exact age and sex)	(model 1 + adjusted for prenatal factors)	(model 2 + adjusted for perinatal factors)	(model 3 + adjusted for postnatal factors)
BMI SDS AT 24 MONTHS †						
Educational level	low	0.09 (0.06)	-0.22 (-0.34, -0.10)	-0.31 (-0.43, -0.19)	-0.25 (-0.36, -0.13)	-0.25 (-0.36, -0.13)
	mid-low	0.08 (0.04)	-0.22 (-0.32, -0.13)	-0.27 (-0.36, -0.17)	-0.27 (-0.36, -0.17)	-0.23 (-0.33, -0.14)
	mid-high	0.18 (0.04)	-0.13 (-0.22, -0.04)	-0.14 (-0.23, -0.04)	-0.14 (-0.23, -0.04)	-0.12 (-0.21, -0.03)
	high	0.31 (0.03)	0 (ref)	0 (ref)	0 (ref)	0 (ref)
BMI SDS AT 36 MONTHS †						
Educational level	low	0.13 (0.05)	-0.03 (-0.14, 0.08)	-0.14 (-0.26, -0.03)	-0.09 (-0.20, 0.02)	-0.09 (-0.20, 0.03)
	mid-low	0.03 (0.04)	-0.12 (-0.21, -0.03)	-0.17 (-0.26, -0.08)	-0.14 (-0.23, -0.05)	-0.14 (-0.23, -0.06)
	mid-high	0.06 (0.04)	-0.09 (-0.18, 0.00)	-0.10 (-0.19, -0.01)	-0.09 (-0.17, 0.00)	-0.09 (-0.17, 0.00)
	high	0.15 (0.03)	0 (ref)	0 (ref)	0 (ref)	0 (ref)

* Values are unstandardized betas (95% confidence interval). Prenatal factors were maternal smoking during pregnancy, father's BMI, and mother's BMI. Perinatal factors were birth weight and gestational age. Postnatal factors were exclusive breastfeeding for 2 months, and BMI-for-age standard deviation scores difference between 1-6 months after birth. † BMI-for-age standard deviation scores were derived from a national reference (Fredriks et al. 2000). Note: Adjusted R^2 for model 1-4 respectively was 0.007, 0.023, 0.079, 0.180 (24 months), and 0.002, 0.036, 0.086, 0.161 (36 months)

Table 3

Multiple logistic regression analyses for associations between mother's educational level and children's overweight* (n=2954)

		%	MODEL 1	MODEL 2	MODEL 3	MODEL 4
		overweight children	(adjusted for exact age and sex)	(model 1 + adjusted for prenatal factors)	(model 2 + adjusted for perinatal factors)	(model 3 + adjusted for postnatal factors)
OVERWEIGHT AT 24 MONTHS †						
Educational level	low	9.8	0.91 (0.61-1.35)	0.72 (0.47-1.09)	0.82 (0.54-1.25)	0.82 (0.53-1.27)
	mid-low	7.5	0.67 (0.47-0.94)	0.60 (0.42-0.85)	0.64 (0.45-0.91)	0.61 (0.43-0.87)
	mid-high	8.8	0.80 (0.57-1.11)	0.77 (0.54-1.08)	0.80 (0.57-1.13)	0.80 (0.57-1.13)
	high	10.7	1 (ref)	1 (ref)	1 (ref)	1 (ref)
OVERWEIGHT AT 36 MONTHS †						
Educational level	low	9.1	1.06 (0.69-1.63)	0.73 (0.46-1.15)	0.85 (0.54-1.34)	0.86 (0.54-1.37)
	mid-low	6.8	0.75 (0.51-1.09)	0.62 (0.42-0.91)	0.66 (0.45-0.97)	0.65 (0.44-0.96)
	mid-high	7.7	0.85 (0.59-1.21)	0.80 (0.56-1.14)	0.84 (0.59-1.20)	0.85 (0.59-1.22)
	high	8.8	1 (ref)	1 (ref)	1 (ref)	1 (ref)

* Values are odds ratios (95% confidence intervals).
Prenatal factors were smoking during pregnancy, father's BMI, and mother's BMI. Perinatal factors were birth weight and gestational age. Postnatal factors were exclusive breastfeeding for 2 months, and BMI-for-age standard deviation scores difference between 1-6 months after birth. Note: R^2 (Nagelkerke) for models 1 to 4, respectively, was 0.012, 0.029, 0.065, 0.162 (24 months), and 0.013, 0.079, 0.111, 0.197 (36 months).
† Overweight was defined according to the sex- and age-specific cut-off points of the International Obesity Taskforce.

weight, had a shorter gestational duration, and less often started and continued breastfeeding ($p<0.001$).

There were no significant differences between educational subgroups for BMI SDS difference at 1 or 6 months after birth, or for height SDS at 24 and 36 months. Weight SDS at 24 months was highest in children from the highest educated mothers ($p<0.05$), but there were no significant differences for weight SDS at 36 months between the educational subgroups (Table 1). However, change in weight SDS between 24 and 36 months was significantly higher in children from lower-educated mothers (SDSchange = 0.07, SD 0.46) than in children from higher-educated mothers (SDSchange = -0.03, SD 0.49) ($p<0.05$).

Associations between socioeconomic status and indicators of child's overweight

BMI SDS

Mean BMI SDS at 24 months was lower in children from mothers with the low (B= -0.22, 95% CI: -0.34, -0.10), mid-low (B= -0.22, 95% CI: -0.32, -0.13), and mid-high (B= -0.13, 95% CI: -0.22, -0.04) educational levels compared to children from mothers with the highest educational level (Table 2, model 1). Although adjustment for prenatal factors slightly strengthened the associations, after full adjustment estimates were similar to those estimated from the crude model (Table 2). Results were similar at 36 months, but mean BMI SDS at 36 months was only lower in children from mothers with the mid-low educational level (B= -0.12, 95% CI -0.21, -0.03), and did not differ for children from mothers with the low and mid-high educational level (Table 2).

Overweight

At age 24 months, 9.3% of the children were overweight. Compared to children from mothers in the highest educational level, children from mothers in the mid-low educational level were less often overweight (OR: 0.61; 95% CI: 0.43-0.87). This was also the case at 36 months after full adjustment (OR: 0.65; 95% CI: 0.44-0.96) (Table 3, model 4). Adjustment for mediators showed a similar pattern as described for BMI SDS. Children from mothers in the low or mid-high educational level did not differ in their prevalence of overweight compared to children from mothers in the highest educational level at any age (Table 3).

The secondary determinant (income as an indicator of socioeconomic status) showed no association with being overweight at 24 and 36 months, in both the unadjusted and adjusted analyses (Table 4).

Role of covariates

The strongest and most consistent predictors for both BMI SDS and overweight at both ages were infant gain in BMI and birth weight ($p<0.001$). Parental BMI was also an important predictor ($p<0.01$).

Repeated measurement analysis

BMI curves differed from 1 to 36 months for the educational subgroups. For boys (Figure 1a) the model fit was significantly better after adding interaction terms for educational level to the model (Chi^2= 13.1, df=6, p<0.05). This was also the case for girls (Chi^2=24.2, df=6, p<0.01) (Figure 1b). Estimated BMI was highest in children from mothers with the highest educational level from 12 months of age onwards.

DISCUSSION

In the present study among preschool children, no evidence was found that a low socioeconomic status is associated with a higher risk of being overweight. In contrast, the results show that mean BMI SDS is lower in children from mothers with a low, mid-low, or mid-high educational level compared to children from mothers in the highest educational level at age 24 months; however, at 36 months these differences were only present for children from mothers in the mid-low educational level. Relative to children from mothers in the highest educational level, children from mothers in the mid-low educational level had a lower prevalence of overweight at 24 and 36 months. No association was found between household income, lowest or mid-high educational level, and being overweight.

In a review based on 54 studies, Shrewsbury and Wardle conclude that children from families with a lower socioeconomic status are more often obese; however, they only included children older than 5 years.[25] Only one study reported an inverse socioeconomic gradient in overweight in 3-year-old children.[8] Another (cohort) study found no socioeconomic gradient in overweight at age 2 years, but reported more overweight in the lower socioeconomic class at age 6 years; it was concluded that the socioeconomic gradient in overweight emerges between those ages.[11] Also Herngreen et al. found no socio-economic differences in weight, height and weight gain between 1 and 24 months.[26] We expect that, due to the ongoing social patterning of obesity, the social gradient in childhood overweight will shift to an earlier age in the coming years. In an earlier review on socioeconomic status and overweight (published in 1989), studies on the association between socioeconomic status and childhood overweight reported direct, inverse and no associations.[6] A systematic review by Parsons et al. (published in 1999) found that early childhood social circumstances are associated with adult overweight status, while a consistent association with childhood overweight status was not found.[27] In the updated review from Shrewsbury and Wardle (published in 2008) only inverse and no associations between socio-economic status and childhood overweight were reported.[25]

Children from mothers with a lower educational level are reported to be more exposed to several risk factors for developing overweight, such as parental obesity and not receiving breastfeeding.[13, 28-31] Our multiple regression analyses showed that children with an overweight parent had a higher BMI and that breastfed children had a lower BMI at age 3 years (data not shown), although the latter was not significant in the analyses. These factors, and subsequently other obesity-inducing behaviors, may accumulate or track over time and lead to socioeconomic differences in (childhood) obesity. Because children from families with a lower socioeconomic status have a lower birth weight, which was also found in the Generation R study,[32] it may take more than 3 years to catch-up after this initial lower weight and reverse the gradient between socioeconomic status and weight, and subsequently BMI.

This study used mother's educational level as an indicator of socio-economic status.[33] Socioeconomic status is a multifactor construct, whose commonest indicators are educational level, income level, and occupational class. As a socioeconomic indicator, educational level influences knowledge and beliefs; these are considered important for healthy lifestyles and the development of overweight. Moreover, the review by Shrewsbury and Wardle on socioeconomic status and overweight revealed that education was more consistently inversely associated with obesity than other indicators.[25] However, educational level does not entirely capture the material and financial aspects of socioeconomic status. Access to resources (e.g. healthy food is generally more expensive), may also be important in the development of socioeconomic inequalities in childhood obesity. Therefore income was explored as a secondary indicator of socioeconomic status. Lastly, neighborhood socioeconomic status may be more important than individual socioeconomic status for health outcomes.[34] However, we found

Table 4

Multiple logistic regression analyses for associations between household income and children's overweight* (n=2954)

		%	MODEL 1	MODEL 2	MODEL 3	MODEL 4
		overweight children	(adjusted for exact age and sex)	(model 1 + adjusted for prenatal factors)	(model 2 + adjusted for perinatal factors)	(model 3 + adjusted for postnatal factors)
OVERWEIGHT AT 24 MONTHS †						
Low income (< € 1600/month)	Yes	7.8	0.81 (0.49-1.34)	0.81 (0.49-1.35)	0.90 (0.54-1.50)	0.90 (0.54-1.49)
	No	9.5	1(ref)	1(ref)	1 ref)	1 (ref)
OVERWEIGHT AT 36 MONTHS †						
Low income (<€ 1600/month)	Yes	6.8	0.83 (0.45-1.53)	0.83 (0.45-1.54)	0.92 (0.48-1.76)	0.94 (0.49-1.79)
	No	8.2	1(ref)	1(ref)	1 ref)	1 (ref)

* Values are odds ratios (95% confidence intervals). Prenatal factors were smoking during pregnancy, father's BMI, and mother's BMI. Perinatal factors were birth weight and gestational age. Postnatal factors were exclusive breastfeeding for 2 months, and BMI-for-age standard deviation scores difference between 1-6 months after birth. † Overweight was defined according to the sex and age-specific cut-off points of the International Obesity Taskforce (Cole et al. 2000).

Figure 1a

Repeated measurement analyses for estimated BMI in boys. Each line represents a maternal educational level. Model fit was significantly better after adding interaction terms for educational level to the model ($Chi^2 = 13.1$, df = 6, $p<0.05$)

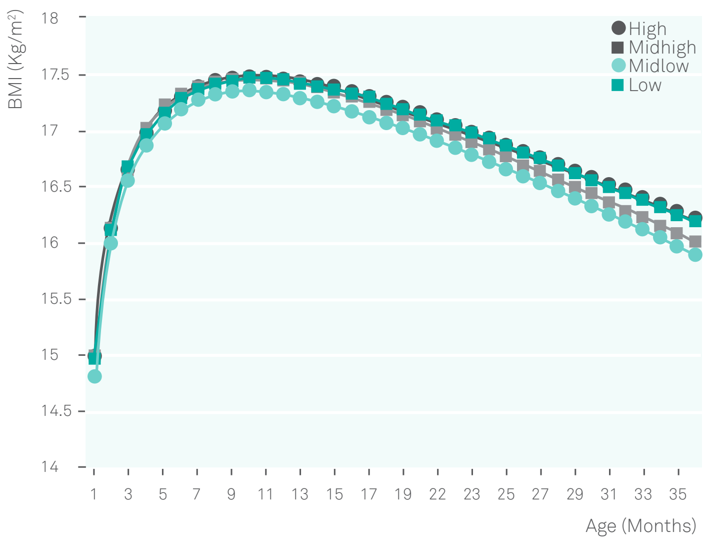
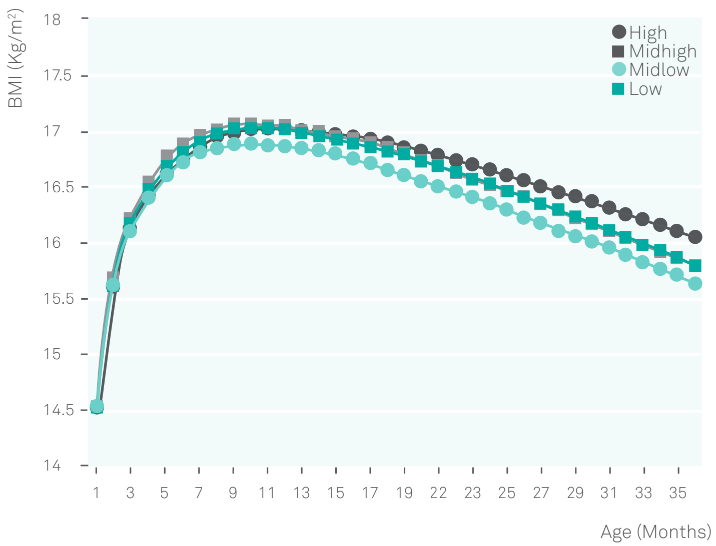


Figure 1b

Repeated measurement analyses for estimated BMI in girls. Each line represents a maternal educational level. Model fit was significantly better after adding interaction terms for educational level to the model ($Chi^2 = 24.2$, df = 6, $p<0.01$)



no effect of living in a deprived area on risk of overweight. An effect was absent when deprived area was taken as a separate indicator of socioeconomic status, and also when this variable was added to the individual measures of socioeconomic status (data not shown). Strengths of this study include the longitudinal design with repeated measurements of weight and height in the first years of life, as well as adjustment for a number of important covariates. However, some limitations should be taken into account. BMI was used as a measure of overweight, and is a measure of excess weight rather than of excess fat mass. BMI in childhood correlates with both fat mass and fat-free mass.

The response rate among pregnant Dutch women in The Generation R Study was relatively high (68%), but there was some selection towards a study population that was somewhat healthier and relatively highly educated.[14] This might result in a reduced lower risk if the lower-educated families that were not in our study more often had children with overweight. Although we were unable to confirm this, we think this is unlikely because prevalences of risk factors for developing overweight were in the expected direction (i.e. higher) in lower-educated families.

Some children were missing height and weight measurements during follow-up. Children from families with a lower socioeconomic status more often had missing values on weight and height. We imputed the missing values according to the multiple imputation procedure. This procedure is valid, even if a specific group of people more often has missing values, as long as the association between determinant and outcome in subjects lost to follow-up is the same as in subjects that are still in the study (missing at random).[35] Accordingly, we assume that our multiple imputation procedure was valid since there were no significant differences in important covariates for overweight, i.e. birth weight, mother's BMI, and infant BMI gain between those with and without measurements of weight and height (data not shown).

Replication of our results in other (ethnic) populations is needed, as development of socioeconomic differences in childhood overweight may differ between populations.

Conclusion

The inverse association between socioeconomic status and childhood overweight presumably emerges after the age of 3 years. Before this age, the gradient may even be the reverse. Follow-up is needed to establish during which phase in child development (at which age) socioeconomic differences in childhood overweight emerge. Further studies are needed to explore the role of early manifestation of socio-economic differences in risk factors for developing overweight.

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ABSTRACT

Background
We assessed the association between ethnicity and overweight in preschoolers, and evaluated to what extent socio-demographic factors, lifestyle-related factors, birth characteristics, and postnatal factors contribute to this association.

Methods
We used data on 4267 children enrolled in a prospective birth cohort study. Child's ethnicity was defined according to country of birth of parents and grandparents. Body mass index (BMI) was calculated at 1, 2, 3, 4, 6, 11, 14, 18, 24, and 36 months of age. Overweight was defined according to cut-off points for BMI from the international obesity task force.

Results
Relative to native Dutch children, risk of developing overweight was significantly higher in Turkish (aOR: 2.53, 95% CI: 1.80-3.57) and Moroccan (aOR: 2.22, 95% CI: 1.49-3.30) children at 24 months of age, but did not differ in Cape Verdean, Antillean/Surinamese-Creole, and Surinamese-Hindustani children. Parental BMI and infant gain in BMI explained most of the associations. Compared with native Dutch children, BMI from age 1-36 months was higher in Turkish (b=0.60, 95% CI: 0.45-0.75) and Moroccan (b=0.55, 95% CI: 0.38-0.73) children, but lower in Surinamese-Hindustani children (b= -0.79, 95% CI: -1.08, -0.51).

Conclusion
Ethnic differences in overweight are already present at 24 months of age. These associations are partly explained by the mediating effect of parental BMI and infant gain in BMI. Future studies should focus on prenatal and postnatal determinants of infant weight gain, such as infant feeding behavior, to search for explanatory mechanisms of ethnic disparities in overweight.

4.2 ETHNICITY AND OVERWEIGHT IN PRESCHOOL CHILDREN

BASED ON

Van Rossem L / Hafkamp-de Groen E / Jaddoe VW / Hofman A / Mackenback JP / Raat H.
Ethnic differences in growth and overweight in early life: results from a prospective multi-ethnic birth cohort.
Submitted

INTRODUCTION

The high prevalence of childhood overweight and obesity is a major public health problem.[1] Health consequences of childhood overweight and obesity can arise during childhood.[1] Moreover, childhood overweight and obesity tends to track into adulthood.[2] Although the causes of overweight and obesity are not yet fully clarified, they are probably environmental because genetic causes could not have resulted in such increases in a relatively short period.[3]

Some groups are at high risk of developing overweight and obesity. For example, children from families with a low socioeconomic status are consistently described as being at increased risk to develop overweight and obesity.[4] Studies have also focused on describing ethnic differences in prevalence of childhood overweight, both between and within countries. In Europe, a comparison between countries reported the highest prevalence of childhood overweight in Mediterranean countries and the British Isles.[5] In the USA, childhood overweight prevalence is higher among Blacks and Hispanics than among Caucasians;[6] and in the UK, overweight prevalence is higher among South-Asian and African-Caribbean children, although inconsistencies arise when different definitions of overweight are used.[7] Studies from Australia, Germany and the Netherlands also report that certain ethnic groups have a higher prevalence of childhood overweight.[8-10]

It is important to elucidate these ethnic differences in childhood overweight in order to take measures to prevent overweight in these groups. Although it is clear that ethnic minorities or immigrant groups are often socially disadvantaged, which may partly explain their higher prevalence of overweight, the extent to which socio-cultural, environmental or biological differences (or a combination of these factors) explain the ethnic differences in the prevalence of childhood overweight is less clear. In addition, few studies have focused on preschool children or on body mass index (BMI) development from birth.

The present study compares the prevalence of overweight between ethnic groups in preschool children in the Netherlands. In addition, we studied the contribution of sociodemographic, other parental factors, birth characteristics, and postnatal factors on ethnic differences in early childhood overweight.

METHODS

Study design and population

This study was embedded in the Generation R study, a population-based multi-ethnic prospective cohort study from fetal life onwards. Invitations to participate in the study were made to all pregnant mothers who had an expected delivery date between 2002 and 2006 and who lived in the study area (Rotterdam, the Netherlands). Details of the study are described elsewhere.[11, 12] The study was conducted in accordance with the guidelines proposed in the World Medical Association Declaration of Helsinki, and was approved by the Medical Ethical Committee at Erasmus MC, University Medical Center Rotterdam. Written consent was obtained from all participants.

Consent for postnatal follow-up was available for 7893 children. We excluded twins from the analyses (n=197). To avoid clustering, our analyses excluded data on the second or third pregnancy of any woman who was participating in the Generation R study with more than one child (n=580). We also excluded participants of whom we missed the following information: ethnicity (n=657), and children who did not have any measures concerning their height or weight between 2 and 3 years of age (n=1148). In total, data of 5311 subjects were available for analyses. Children with a European, Asian western, Asian non-Western, American Western, American non-Western and Surinamese-other ethnicity were excluded from the analyses because of their small sample size and heterogeneity (n=1035).

Measurements

Child's ethnicity

Ethnicity was assigned according to country of birth of the parents.[13] A child is considered as having an immigrant background if one of both parents is born abroad. Deviations from this definition were made for third generation immigrants and children with one parent born abroad, but four grandparents born in the Netherlands. All possible combinations and their consequences for assignment of child's ethnicity are described in Appendix 1.

We initially distinguished six ethnic groups according to country of birth. Surinamese children were further subdivided according to self-assigned ethnicity of the mother because different ethnicities live in that country. We performed analyses on 2936 native Dutch, 450 Turkish, 331 Moroccan, 186 Cape Verdean, 249 Antillean/Surinamese-Creole, and 124 Surinamese-Hindustani children (n=4276).

BMI and overweight

Birth weight and height was retrieved from medical records. Height and weight were measured at the child health centers. A child usually visits the child health center that is assigned according to postal code. Routine visits at the child health centers take place at 1, 2, 3, 4, 6, 11, 14, 18, 24, and 36 months of age. BMI was calculated as weight/height^2.

Our main outcomes were overweight at age 24 and 36 months. We used the international age and sex specific cut-off points for BMI to define overweight.[14]

Covariates

Although ethnicity may have an effect on the risk of developing overweight, because of a genetic predisposition, at least part of an association between ethnicity and overweight can be expected to be caused by environmental factors. Known risk factors for developing childhood overweight and obesity may be unequally distributed among ethnic subgroups. We consider the following risk factors (in italics) in the association between ethnicity and overweight:

Socio-demographic variables: *Household income* was asked at enrollment and was dichotomized (< € 1600 per month, ≥ € 1600 per month). Households that earn below this cutoff point are considered as low-income groups.[15] *Level of maternal education* was established at enrollment.[16] The following question was asked to determine material hardship: 'Do you have any difficulty in paying food, rent, electricity bill and such like?'

Other parental variables: *Mother's BMI* was calculated from self-reported pre-pregnancy weight and measured height at intake. Father's BMI was calculated from measured weight and height at enrollment. *Smoking during pregnancy* (yes, no) was derived from the prenatal questionnaires.

Birth characteristics: *Birth weight* (grams) and *gestational age* (weeks) were obtained from medical records.

Postnatal factors: Information on *breastfeeding* was obtained by a combination of questionnaires administered at 2, 6 and 12 months after birth. *Infant gain in BMI* was calculated by subtracting birth BMI from BMI at 6 months.

Statistical analyses

We assessed characteristics of participants for the total population and for each ethnicity separately. P-values for differences between ethnic groups were calculated by means of the Chisquare test for categorical variables and ANOVA for continuous variables.
We performed logistic regression to obtain independent estimates

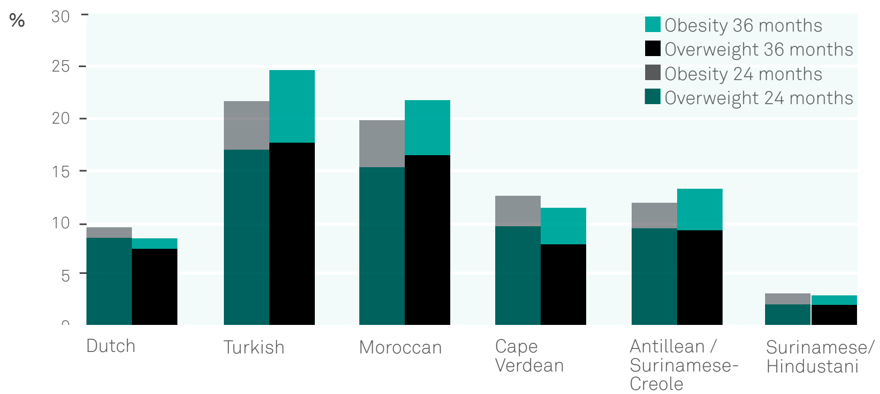
of the association between ethnicity and childhood overweight. We built our models in three steps. First, we assessed the association between ethnicity and childhood overweight, adjusted for exact age and sex at outcome assessment (model 1). Then, we adjusted separately for the socio-demographic variables (model 2), other parental variables (model 3), birth characteristics (model 4), and postnatal risk factors (model 5) to show the contribution of each of these groups on the association between ethnicity and overweight. Lastly, we adjusted for all variables simultaneously (model 6).

We performed repeated measurement analyses to assess the association between ethnicity and BMI between 1 and 36 months after birth. The best fitting model for BMI as a function of age was built using fractional polynomials.[17] The best fitting model for BMI was: BMI = ß0 + ß1*(ln)age + ß2*√age, where ß0 = 16.5271 (95% CI: 16.4787-16.5755), ß1 = 2.6300 (95% CI: 2.5936-2.6663), and ß2 = -1.6526 (95% CI: -1.6802 – -1.6249). To this model we added ethnicity as a main determinant (reference: native Dutch), and an interaction term of ethnicity with both transformations of age. The deviance was used to test whether the model with or without interaction terms had the best model fit.

Missing values in the study variables ranged from 0% (birth weight) to 36% (length at birth). Because the missing values were not completely at random, the multiple imputation procedure in SPSS 17.0 was used. Five imputed datasets were generated using a fully conditional specified model to handle missing values. Imputations were based on the relations between all covariates in the study. Pooled estimates

Figure 1

Prevalence of overweight and obesity per ethnicity at 24 (n=3619) and 36 (n=3148) months.



from these five imputed datasets were used to report odds ratios (OR) and their 95% confidence intervals (CI).

Analyses were conducted with the Statistical Package for Social Sciences (SPSS) version 17.0 for Windows (SPSS Inc, Chicago, IL, USA). We used procedure 'PROC MIXED' of the Statistical Analysis Software (SAS) version 9.1.3 for Windows (SAS Institute, Cary, NC, US) for the repeated measurement analysis.

RESULTS

Sample characteristics

Ethnic differences were present in all covariates (Table 1). Generally, non-Dutch mothers were lower educated, had a lower household income, suffered more often from material hardship, and were more often single ($p<0.001$) compared to native Dutch mothers. The direction of differences in parental BMI, smoking during pregnancy, breastfeeding, birth weight and gestational age varied according to ethnic subgroup.

Associations between ethnicity and overweight and contribution of covariates

Prevalence of overweight and obesity was highest in Turkish and Moroccan children and lowest in Surinamese-Hindustani children at ages 24 (Table 2, Figure 1) and 36 months (Figure 1) (see Appendix 2 for sex-specific data). Because prevalence differed from 24 months onwards, contributing factors were described only for 24 months, and not for 36 months in Table 2. Adjustment for socio-demographic factors and birth characteristics did not explain the association for Turkish and Moroccan children, but adjustment for parental characteristics and postnatal factors attenuated the estimates. This was mainly due to the variables parental BMI and infant gain in BMI. However, after full adjustment Turkish (OR: 2.53, 95% CI: 1.80-3.57) and Moroccan (OR: 2.22, 95% CI: 1.49-3.30) children were more likely to develop overweight at 24 months of age (Table 2). The lower odds for being overweight in Surinamese-Hindustani children compared to native Dutch children at 24 months changed from 0.31 (95% CI 0.10-0.92) to 0.46 (95% CI 0.16-1.37) by adding birth weight and gestational age to the model (Table 2).

Associations between ethnicity and repeated measures of BMI

Relative to Dutch children, mean BMI over 36 months was 0.52 units (95% CI: 0.36-0.68) higher in Turkish, 0.49 units (95% CI: 0.31-0.68) higher in Moroccan children, 0.37 units (95% CI 0.14- 0.59) higher in Surinamese-Creole/Antillean children, and 0.31 units (95% CI 0.10-0.52) higher in Cape Verdean children, but 0.65 units (95% CI: -0.94, -0.37) lower in Surinamese-Hindustani children in unadjusted repeated measurements analyses. Because the age by ethnicity interaction was not significant, the best fitting model for the (unadjusted)

Table 1 Subject characteristics for 4276 children of different ethnicities in the Generation R study.

		TOTAL	DUTCH	TURKISH	MOROCCAN	CAPE VERDEAN	ANTILLEAN/ SURINAMESE CREOLE	SURINAMESE-HINDU	P-VALUE
		(n=4276)	(n=2936)	(n=450)	(n=331)	(n=186)	(n=249)	(n=124)	
SOCIO-DEMOGRAPHIC VARIABLES									
Mothers educational level	% low	8.9	2.2	33.5	27.8	22.5	11.5	11.4	<0.001
	% middle	43.1	35.0	54.3	57.3	65.2	71.2	73.2	
	% high	48.0	62.8	12.2	14.9	12.4	17.3	15.4	
Household income	% low	23.5	8.0	64.9	68.4	64.7	66.1	50.0	<0.001
Material hardship	% yes	17.6	8.9	45.7	36.2	39.2	45.6	34.1	<0.001
Single motherhood	% yes	10.7	5.1	7.5	7.6	47.5	52.4	24.2	<0.001
OTHER PARENTAL CHARACTERISTICS									
BMI mother	in kg/m²	23.7 (4.3)	23.2 (3.8)	25.3 (5.1)	25.5 (4.7)	23.7 (4.0)	24.8 (5.4)	23.6 (5.3)	<0.001
BMI father	in kg/m²	25.3 (3.4)	25.1 (3.3)	26.4 (4.1)	26.1 (3.9)	24.7 (3.3)	25.2 (3.4)	25.0 (3.6)	<0.001
Smoking during pregnancy	% yes	11.1	10.2	17.6	7.8	1.7	13.4	9.6	<0.001
BIRTH CHARACTERISTICS									
Birth weight	in grams	3455 (553)	3510 (553)	3408 (508)	3485 (482)	3264 (532)	3191 (566)	3046 (513)	<0.001
Gestational age	in weeks	40.0 (1.7)	40.0 (1.7)	39.8 (1.7)	40.2 (1.7)	39.8 (1.5)	39.5 (1.9)	39.4 (1.6)	<0.001
POSTNATAL RISK FACTORS									
BMI gain from 0-6 months	in kg/m²	3.4 (1.9)	3.2 (1.8)	3.9 (1.9)	3.5 (2.1)	4.1 (1.9)	4.2 (2.1)	3.9 (1.3)	<0.001
Breastfeeding at 6 months	% yes	29.1	29.7	39.5	26.5	16.4	18.3	19.8	<0.001

Values are percentages or mean (SD). P-values are for Chi-square test for categorical variables, and ANOVA for continuous variables.
Missing values were 90 (2.1%) for educational level, 907 (21.2%) for income, 961 (22.5%) for material hardship, 73 (1.7%) for single motherhood, 907 (21.1%) for BMI mother, 1164 (27.2%) for BMI father, 785 (18.4%) for smoking during pregnancy, 691 (16.2%) for breastfeeding at 6 months, 1540 (36.0%) for BMI at birth, and 958 (22.4%) for BMI at 6 months.

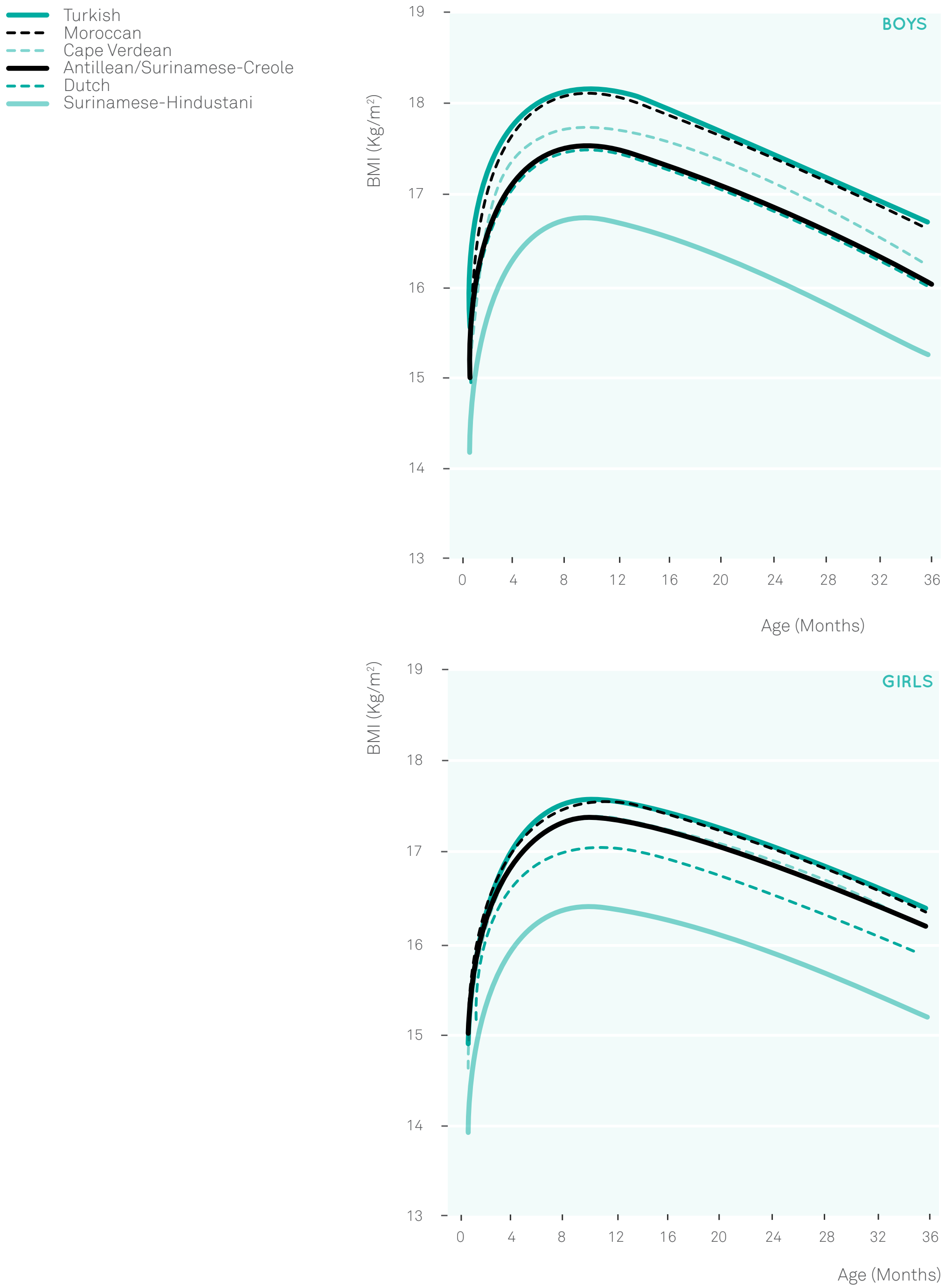
Table 2 Association between ethnicity and overweight at 24 months, and contribution of covariates (n=4276)*

		MODEL 1*	MODEL 2*	MODEL 3*	MODEL 4*	MODEL 5*	MODEL 6*
Child's ethnicity	native Dutch	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)	1 (ref)
	Turkish	2.65 (2.04-3.45)	2.77 (2.03-3.78)	2.22 (1.68-2.93)	2.99 (2.28-3.92)	2.22 (1.69-2.91)	2.53 (1.80-3.57)
	Moroccan	2.42 (1.75-3.34)	2.54 (1.79-3.61)	2.03 (1.45-2.84)	2.63 (1.89-3.66)	2.10 (1.50-2.93)	2.22 (1.49-3.30)
	Cape Verdean	1.39 (0.87-2.22)	1.48 (0.91-2.41)	1.37 (0.85-2.20)	1.76 (1.09-2.83)	1.08 (0.67-1.73)	1.60 (0.95-2.69)
	Antillean/ Surinamese-Creole	1.29 (0.85-1.96)	1.41 (0.88-2.26)	1.20 (0.78-1.85)	1.67 (1.08-2.57)	0.98 (0.63-1.52)	1.56 (0.92-2.65)
	Surinamese-Hindu	0.31 (0.10-0.92)	0.34 (0.11-1.02)	0.30 (0.10-0.89)	0.46 (0.16-1.37)	0.26 (0.09-0.78)	0.45 (0.14-1.45)
Household§ income	low		0.93 (0.63-1.37)				0.93 (0.65-1.33)
	above average		1 (ref)				1 (ref)
Mother's educational level	low		0.78 (0.56-1.08)				0.86 (0.59-1.25)
	middle		0.91 (0.63-1.32)				1.18 (0.77-1.80)
	high		1 (ref)				1 (ref)
Material hardship	no		1 (ref)				1 (ref)
	yes		0.97 (0.68-1.38)				0.88 (0.62-1.24)
Mother's BMI	(per unit)			1.05 (1.03-1.07)			1.03 (1.00-1.06)
Father's BMI	(per unit)			1.08 (1.04-1.12)			1.06 (1.02-1.10)
Smoking during pregnancy	no			1 (ref)			1 (ref)
	until pregnancy known			0.93 (0.66-1.31)			0.87 (0.59-1.27)
	yes			0.89 (0.59-1.33)			1.07 (0.72-1.60)
Birth weight	(per kg)				2.66 (2.11-3.35)		6.71 (4.99-9.02)
Gestational age	(per week)				0.90 (0.83-0.98)		0.91 (0.83-1.00)
Breastfeeding at 6 months	no					1 (ref)	1 (ref)
	yes					0.95 (0.76-1.19)	0.88 (0.68-1.13)
Difference in BMI between birth and 6 months	(per unit)					1.31 (1.24-1.38)	1.67 (1.56-1.79)

*values are odds ratios (95% confidence intervals); model 1=adjusted for sex and exact age at measurement, model 2=adjusted for socio-demographic variables, model 3=adjusted for other parental factors, model 4=adjusted for birth characteristics, model 5=adjusted for postnatal risk factors, model 6=full adjustment

Figure 2

Best fitting model for repeated measurement analyses for the association between ethnicity and BMI for boys and girls.



association between ethnicity and BMI was the model without interaction terms for ethnicity and is shown in Figure 2. After adjustment, the associations were reduced to 0.39 (95% CI: 0.06-0.72) for Turkish children, to 0.34 (95% CI: -0.16-0.85) for Moroccan children, to 0.00 (95% CI: -0.56, 0.56) for Surinamese-Creole/Antillean children, to 0.04 (95% CI -0.45, 0.52) for Cape Verdean children, and to -0.69 (95% CI: -1.40, 0.01) for Surinamese-Hindustani children.

DISCUSSION

Main findings

This study shows that relative to native Dutch children, Turkish and Moroccan children are more likely to develop overweight and obesity at a very young age, while Surinamese-Hindustani children are less likely to develop overweight. Higher parental BMI and a higher infant BMI gain between birth and 6 months of age were important contributors in explaining the higher prevalence of overweight in Turkish and Moroccan children, while birth characteristics were important for explaining a lower prevalence of overweight in Surinamese-Hindustani children compared to native Dutch children. However, most of the higher prevalence of overweight in Turkish and Moroccan children remains unexplained.

Overweight prevalence

The results of our study are consistent with the findings of a study that reported a higher prevalence of overweight in Turkish and Moroccan children from the age of 3 years onwards.[8, 18] Similar findings were also reported in Australia for Mediterranean white children from the age of 5 years onwards.[10]

Explanatory factors

Maternal education, household income and material hardship hardly affected our estimates for the association between ethnicity and overweight. This is in line with Whitaker and Orzol, who studied whether socioeconomic factors could explain the higher prevalence of overweight in Hispanic children in the USA. The authors concluded that the higher prevalence of overweight could not be explained by maternal education, household income or food security.[19]

In our study, parental BMI explained about a quarter of the association between ethnicity and childhood overweight. This is in line with a large body of evidence that linked parental BMI to offspring BMI. However, in contrast to the literature, we found a somewhat stronger effect for paternal BMI than maternal BMI, which we cannot explain.[20] Parental obesity may be associated with childhood obesity because risk of developing obesity is partly heritable.[21] Parental obesity may also be associated with childhood obesity by a shared obesogenic environment. There is evidence that children from obese mothers are more engaged in sedentary behaviors.[22] Lastly, there may be an interaction term between genetic susceptibility with shared environmental family factors, such as sedentary behavior or food intake.[23]

Postnatal factors (i.e. faster gain in infant BMI) also explained about a quarter of the association between ethnicity and childhood overweight in our study. Rapid infant weight gain is a well-established risk factor for later overweight.[24] Gain in infant BMI between birth and 6 months might be driven by infant feeding practices. Woo et al. reported that breastfeeding mediates the association between ethnicity and overweight in adolescents.[25] We did not see a mediating effect of breastfeeding on the association between ethnicity and overweight until age 3 years, but the protective effect of breastfeeding on overweight may express at a later age. Also, we did not study complementary feeding. It has been reported that some ethnic groups do not adhere to the feeding recommendations, which may result in overfeeding.[26, 27] Cultural differences may play an important role in overfeeding, as a 'chubby' baby is often seen as the most healthy baby in some ethnic groups.[28] Thus, part of the association may be due to feeding practices other than breastfeeding that is reflected in faster infant weight gain. However, determinants of infant weight gain can also be genetic or based on developmental factors during pregnancy.[29, 30]

Methodological considerations

Ethnicity is not a standardized, well-defined concept. It refers to people belonging to the same nation, religion, language, country of birth, or culture.[31] We used country of birth because it is the most objective and stable measure that can be used in young children. Nevertheless, country of birth does not cover all aspects of ethnicity, such as culture and ethnic identity.[32] Also, we categorized the children of mixed ethnicity according to ethnic background of the mother's family, which may have attenuated our results. Future studies could give the associations between several aspects of ethnicity and overweight.

We used BMI as an indicator of overweight and obesity. BMI is a measure of excess weight rather than of excess fat. Fat percentage may differ for BMI levels among ethnic subgroups: this is especially the case in Asians.[7] However, there are no specific cut-off points available for Asians to define overweight and obesity according to the BMI.[33] DXA measures for this cohort will become available in the future.

A substantial number of values in the covariates – especially birth length - were missing; however, on the assumption that these are missing at random (i.e. missings may be correlated with variables in the model, but may not be correlated with variables not in the model) they are unlikely to affect our estimates. Also, self-reported weight is likely to be underreported. However, mother's weight was also measured at the research centres in early, mid, and late pregnancy and these measurements explained 94% of the variance in pre-pregnancy weight. Lastly, the percentages of mothers from ethnic minorities are lower among the participants than expected from the population data in Rotterdam.[12]

Conclusion

Ethnic differences in overweight emerge at a very young age, but can only be partly explained. Parental BMI and infant gain in BMI are important contributors in explaining the higher risk of developing overweight in certain ethnic groups, but the underlying mechanisms are not yet completely understood. We recommend that future studies focus on infant feeding behaviors in ethnic subgroups. Because ethnic differences in overweight seem to originate at least partly from birth, suboptimal conditions that affect obesity risk may be created during pregnancy, or even before. Therefore, we also recommend to study ethnic differences in fetal growth and their effect on the risk of overweight and obesity. For the time being, healthcare practitioners should be aware of the higher risk of developing overweight in children with rapid infant weight gain, as well as in children with overweight parents.

Appendix 1

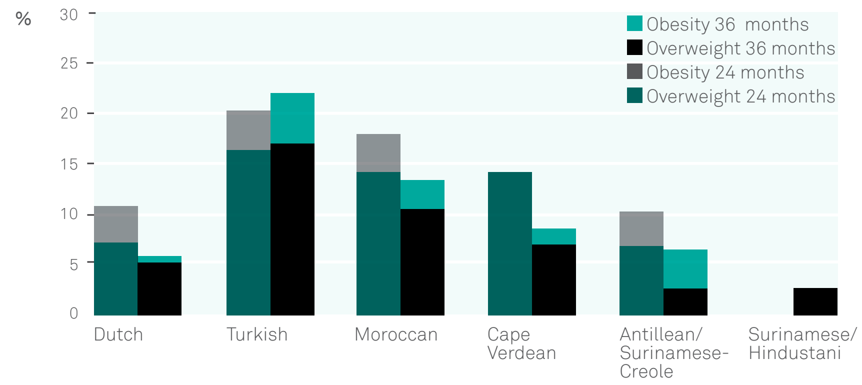
Assignment of child's ethnicity according to country of birth parents and grandparents

CHILD'S ETHNICITY	COUNTRY OF BIRTH OF					
	Mother	Father	Mother's mother (grandmother)	Mother's father (grandfather)	Father's mother (grandmother)	Father's father (grandfather)
DUTCH						
	Netherlands	Netherlands	Netherlands	Netherlands	Netherlands	Netherlands
	Netherlands	Netherlands	Abroad	Netherlands	Netherlands	Netherlands
	Netherlands	Netherlands	Netherlands	Abroad	Netherlands	Netherlands
	Netherlands	Netherlands	Netherlands	Netherlands	Abroad	Netherlands
	Netherlands	Netherlands	Netherlands	Netherlands	Netherlands	Abroad
	Netherlands	Netherlands	Abroad	Netherlands	Abroad	Netherlands
	Netherlands	Netherlands	Abroad	Netherlands	Netherlands	Abroad
	Netherlands	Netherlands	Netherlands	Abroad	Abroad	Netherlands
	Netherlands	Netherlands	Netherlands	Abroad	Netherlands	Abroad
	Netherlands	Abroad	Netherlands	Netherlands	Netherlands	Netherlands
	Abroad	Netherlands	Netherlands	Netherlands	Netherlands	Netherlands
NON-DUTCH						
Second generation	Netherlands	Abroad	n.a.*	n.a.*	n.a.*	n.a.*
	Abroad	Netherlands	n.a.*	n.a.*	n.a.*	n.a.*
	Abroad	Abroad	n.a.*	n.a.*	n.a.*	n.a.*
Third generation	Netherlands	Netherlands	**Abroad**	Abroad	Abroad	Abroad
	Netherlands	Netherlands	Abroad	Abroad	Netherlands	Netherlands
	Netherlands	Netherlands	Netherlands	Netherlands	Abroad	Abroad
	Netherlands	Netherlands	**Abroad**	Abroad	Abroad	Netherlands
	Netherlands	Netherlands	Abroad	Abroad	Netherlands	Abroad
	Netherlands	Netherlands	Netherlands	Abroad	**Abroad**	Abroad
	Netherlands	Netherlands	Abroad	Netherlands	**Abroad**	Abroad

In case of different birth countries, the bold one decides on child's ethnicity.
* At least one of the grandparents is born abroad.

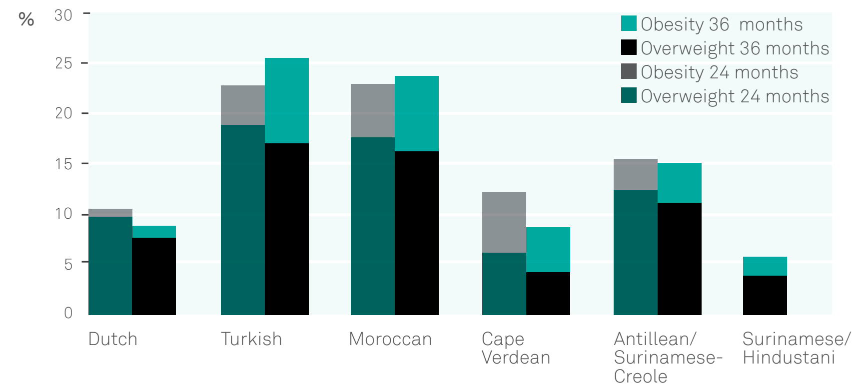
Appendix 2
Figure A2a / boys

Ethnic specific prevalence of overweight and obesity stratified by sex



Appendix 2
Figure A2b / girls

Ethnic specific prevalence of overweight and obesity stratified by sex



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CHAPTER 5
DISCUSSION

THE AIM OF THIS THESIS WAS THREEFOLD.

First, to study the association between risk factors for overweight and overweight. Second, to assess the association between social disadvantage and risk factors for overweight. Third, to assess the association between social disadvantage and overweight at preschool age.

In this chapter, a summary of findings will be given (paragraph 5.1) and these results will be discussed in a broader context (paragraph 5.2). Then, some methodological issues will be highlighted (paragraph 5.3). This chapter will conclude with recommendations for policy and practice (paragraph 5.4) and future study (paragraph 5.5), and a final conclusion (paragraph 5.6).

5.1 SUMMARY OF MAIN FINDINGS

IN CHAPTER 2 RISK FACTORS FOR OVERWEIGHT AND OBESITY WERE ASSESSED.

Chapter 2.1 describes the association between breastfeeding and overweight. Breastfeeding was not associated with overweight at preschool age in the Generation R Study. Chapter 2.2 describes the association between breastfeeding, infant weight change, and overweight at age 3 years within Project Viva. Breastfeeding was not associated with overweight after adjustment for covariates, but rapid infant weight gain between birth and six months of age was a strong predictor of overweight. Chapter 2.3 describes the association between early introduction of solids and growth/overweight. No association was found between early introduction of solids and overweight at preschool age in the Generation R Study.

IN CHAPTER 3 THE ASSOCIATION BETWEEN SOCIAL DISADVANTAGE AND RISK FACTORS FOR OVERWEIGHT WAS ASSESSED.

Chapter 3.1 describes the association between mother's educational level and breastfeeding. Lower-educated mothers less often initiated and continued breastfeeding than higher-educated mothers. This was partly due to the fact that lower-educated mothers more often smoked during pregnancy and because they were more often obese. Chapter 3.2 describes the association between ethnicity and breastfeeding. All non-native Dutch mothers more often initiated breastfeeding but less often continued breastfeeding, compared to native Dutch mothers. Therefore, no differences in breastfeeding prevalence were found at 2 and 6 months of age between native Dutch and non-native Dutch mothers. An exception were the Mediterranean mothers of the first generation: they more often initiated and continued breastfeeding. Chapter 3.3 describes the association between socioeconomic status, ethnicity and indicators of physical activity and sedentary behavior. Children from mothers with a low educational level and children with a non-native Dutch ethnicity more often watched television for at least two hours/day than their counterparts. Children with a non-western ethnicity less often played outside for at least 1 hour/day than native Dutch children.

IN CHAPTER 4 THE ASSOCIATION BETWEEN SOCIAL DISADVANTAGE AND OVERWEIGHT WAS ASSESSED.

Chapter 4.1 describes the association between mother's educational level and overweight of the children until age 3 years. Lower educational level of the mother was not associated with a higher risk of overweight. On the contrary, the association tended to be the reverse, because children from mothers with a mid-low educational level had an even somewhat lower risk of developing overweight compared to children from mothers with a high educational level.
Chapter 4.2 describes the association between ethnic background

and overweight of the child until age 3 years. Relative to native Dutch children, Turkish and Moroccan children had a higher risk of overweight from age 2 years onwards, while Surinamese-Hindustani children had a lower risk of overweight. There were no differences in overweight prevalence between Cape Verdean and Surinamese-Creole/Antillean children and native Dutch children. The higher risk of Turkish and Moroccan children compared to native Dutch children could be explained (in part) by the higher body mass index of their parents, and their rapid weight gain in infancy.

In summary, while infant feeding was not associated with overweight, high birth weight, rapid infant weight gain, and high parental BMI were strong predictors of overweight at preschool age. Large socioeconomic and ethnic differences were found in many early life risk factors for overweight. However, there was no association between socioeconomic status and overweight at preschool age. Although ethnic differences in overweight were present, they could not be fully explained by these risk factors.

5.2 INTERPRETATION OF FINDINGS

STUDY AIM 1 EARLY RISK FACTORS FOR OVERWEIGHT

Our first study aim addressed early life risk factors for overweight. Overweight is a complex problem with no single cause. Besides a disturbance of the energy-balance, evidence accumulates that certain characteristics in pregnancy and infancy result in metabolic imprinting.[1, 2] Thus, besides looking at indicators of high caloric intake or low physical activity, mother's pregnancy characteristics should also be taken into account. An overview of risk factors for overweight occurring between the preconception period and early childhood is provided in Table 5.1. These risk factors are based on five reviews addressing risk factors for childhood overweight,[3-7] and on a review addressing childhood predictors of adult obesity.[8] Some reviews included only a specific type of risk factors, like dietary risk factors,[6] or modifiable risk factors.[5] The risk factors are grouped in their chronological occurrence, because one risk factor may influence another risk factor that occurs later in life. The dependency between these risks is not taken into account in the reviews. This was the aim of four western birth cohort studies that included a large number of risk factors for overweight: the identification of the most important risk factors for childhood overweight.[9-12] In all four studies, parental overweight was indicated as the strongest independent risk factor for overweight. In three of four studies, high birth weight was indicated as a strong and independent risk factor for overweight in later life.[9, 11, 12] Below, each group of risk factors from Table 5.1 will be consecutively addressed. Exceptions are the risk factors 'ethnicity' and 'socioeconomic status'. These are addressed under study aim 3.

Risk factors for offspring overweight present before conception
As mentioned above, parental overweight and maternal pre-pregnancy overweight are the strongest and most independent mentioned risk factors for offspring overweight. This is in line with our results (Chapter 4), and other results from the Generation R Study, where parental overweight was a strong and independent risk factor for childhood overweight. It is not exactly known how maternal overweight affects childhood overweight, but it is probably multifactorial.[13] One possible mechanism is related to the fetal programming theory:[14, 15] in obese women having a normal glucose tolerance, impaired insulin sensitivity was reported. This results in an abundance of available nutrients for the fetus.[13,16] This is also in line with findings from the Generation R Study, where higher maternal BMI gave higher estimated fetal weight from mid-pregnancy onwards, and the effect became larger with increasing gestational age.[17] Offspring of obese mothers more often have a higher birth weight, [18] a risk factor for overweight that is discussed later in this chapter. Fetal programming expresses after birth: evidence from animal studies shows that overnutrition of the fetus results in a higher intake of milk and fat after birth.[19] Besides fetal programming, maternal obesity may have an effect after the prenatal period via other, later mentioned, behavioral mechanisms.[14] Obese mothers tend to less often start and continue breastfeeding.[20] Also, mothers and children tend to share the same diet quality, and sedentary behaviors.[14]

Risk factors for offspring overweight in pregnancy
Two meta-analyses and reviews reported a consistent association between smoking and childhood overweight.[21, 22] Two main hypotheses may explain this association. First, smoking during pregnancy is probably not directly related to childhood overweight, but smoking is known to lead to fetal growth restriction. This is compensated after birth, by a catch-up growth. Catch-up growth has been linked to obesity in later life. Our results showed no independent effect of smoking on overweight at preschool age (Chapter 4). However, smoking still seems to have a direct effect on childhood obesity, independent of infant weight gain. A second mechanism may include altered fat cells, because despite children from smoking mothers are born with a smaller size for gestational age, they have proportionally more fat mass.[21, 22] It may be that we did not detect this effect, because overweight was measured with the BMI.

Risk factors for overweight that occur in the perinatal period
Birth weight is a crude marker of intra-uterine circumstances. Literature describes that the association between birth weight and overweight is J-shaped or U-shaped, thus both those infants at the

lower and higher ends of the distribution are at higher risk. However, those studies reporting higher risk at the lower end of the distribution are probably for a large part confounded by smoking during pregnancy that leads to lower birth weight and subsequent catch-up growth. Also, if body composition at birth is taken into account, the association between low birth weight and later overweight is much stronger. Especially those at the low end of the distribution tend to have relatively more fat mass.[23] On the contrary, high birth weight is clearly associated with high BMI, as reported in chapter 4, but the exact association between birth weight and lean body mass or fat mass is unclear.[18]

Risk factors for overweight in infancy
Our finding that infant weight gain is a strong predictor of overweight is consistent with a large body of evidence showing an association between rapid infant weight gain and obesity in later life, as summarized by two systematic reviews.[24, 25] Breastfeeding is associated with infant growth.[26] Several mechanisms have been proposed to explain the protective effect of breastfeeding on developing overweight. First, breastfed children may have learned to selfregulate their energy

Table 5.1 Risk factors for childhood overweight identified in reviews[3-8], and the association between each risk factor and overweight at preschool age established in the Generation R Study

RISK FACTORS IDENTIFIED IN REVIEWS	ASSOCIATION IN THE GENERATION R STUDY AT PRESCHOOL AGE
FACTORS PRESENT BEFORE CONCEPTION	
Ethnicity	+ (for specific ethnicities)*
Low socioeconomic status	0*
Parental overweight/Maternal pre-pregnancy overweight	+*†
FACTORS PRESENT DURING PREGNANCY	
Smoking during pregnancy	0*
High gestational weight gain	NI
PERINATAL FACTORS	
High and low birth weight	+ (high) /0 (low)*
FACTORS PRESENT IN INFANCY	
Lack of breastfeeding/ formula feeding	0*
Rapid growth in infancy and childhood	+*
Early introduction of solids	0*
FACTORS PRESENT IN EARLY CHILDHOOD	
Bottle use beyond infancy	NI
Early feeding experiences	NI
Watching television by the child	0‡
High early energy intake by the child	NI
High intake of sugar-sweetened beverages by the child	0‡
Low physical activity by the child	0‡
Short sleep duration by the child	NI

NI = not investigated (yet) += positive association -=inverse association 0=no association
* = this thesis, † = published results from the Generation R Study Group, ‡ = secondary analyses/unpublished results from the Generation R Study

intake by internal satiety cues, while formula fed children may be encouraged to take in more or less volume than they would otherwise. This enhanced selfregulation may persist beyond the breastfeeding period. Second, breastfed children consume less protein than formula fed children. High protein intake in formula fed children may lead to higher insulin levels which subsequently stimulate greater adipose tissue deposition.[27] Third, breastfed children may be differently programmed by leptin, a hormone contained in breastmilk. The mechanism behind the association between early introduction of solids and overweight would be the high energy-intake, and the fact that early introduction of solids goes at the cost of breastfeeding. The discrepancy between findings from the Generation R Study and the literature on the association between infant feeding and overweight may be that the above described mechanisms express at a later age.

Risk factors for later overweight in early childhood
The literature is fairly consistent in reporting an association between soft drinks and overweight,[28-30] and in reporting an association between sedentary behavior and physical activity with overweight.[31-37] Although reported associations are relatively small, they have been reported across all age ranges. Of behaviours of sedentary behaviour and physical activity, watching television is probably the strongest predictor of overweight, as this influences overweight in different ways. It is not only that energy expenditure is reduced, resting metabolism also decreases.[38] Furthermore, watching television often goes together with unconscious eating, and children may be exposed to snack advertisements.[37] In secondary analyses, we found that indicators of physical activity and food intake, for which we had data available from the age of 2 years onwards, were not associated with childhood overweight. Three explanations may cause the discrepancy between our findings and the literature. First, the time lag between measurement of these behaviors and measurement of overweight may be too short (< 2 years). Second, the measurement may be not accurate for several reasons. In the Generation R Study at ages 2, 3, and 4 years, the answer categories for time spent watching television ended at 2 hours a day, while associations for watching television and overweight in literature were reported for at least 4 hours of daily watching.[31] Also, we do not know whether television was just on, or that children were actively watching it. A review concluded that watching television is critical in the risk for developing overweight from the age of 6 onwards.[32] At the age of 6, children can better understand what they are watching and this may enhance attention. Duration of television viewing tracks from preschool age,[39] which may explain that associations were found between watching television at preschool age and later overweight. Lastly, indicators of sedentary behavior and physical activity reported in chapter 3.3 may represent only part of an obesogenic lifestyle.

STUDY AIM 2 SOCIAL DISADVANTAGE AND RISK FACTORS FOR OVERWEIGHT

An overview of the earlier mentioned risk factors and their association with low socioeconomic status in the Generation R Study is given in Table 5.2. The association between socioeconomic status and overweight is consistently described for women from the 1980s onwards,[40] and is still present.[41] The association between socioeconomic status and smoking (during pregnancy) is also quite persistent.[42-44] Although the overall prevalence of smoking has decreased over the past decades due to recognized health concerns, and subsequently campaigns to reduce smoking rates, these campaigns seem to have less effect on people with a low socioeconomic status. Consequently, disparities in smoking prevalence have even increased.[42-44] Probably associated with socioeconomic differences in smoking prevalence, is the large body of evidence on socioeconomic differences in birth weight. Indeed, literature, including results from the Generation R Study, found that maternal smoking explained much of the association between low socioeconomic status and low birth weight.[45]

Maternal smoking and maternal overweight also played an important role in the association between socioeconomic status and breastfeeding. However, in line with several studies, an independent association between socioeconomic status and infant feeding

Table 5.2 Association between socioeconomic status and risk factors for childhood overweight in the Generation R Study

	LOW SOCIOECONOMIC STATUS
FACTORS PRESENT BEFORE CONCEPTION	
Ethnicity (non native Dutch)	+*
Parental overweight/ Maternal pre-pregnancy overweight	+*
FACTORS PRESENT DURING PREGNANCY	
Smoking during pregnancy	+*
High gestational weight gain	NI
PERINATAL FACTORS	
Birth weight (high/low)	-†/+*
FACTORS PRESENT IN INFANCY	
Lack of breastfeeding/ formula feeding	+*
Rapid growth in infancy and childhood	+ (depends on growth indicator) *‡
Early introduction of solids	+*
FACTORS IN EARLY CHILDHOOD	
Bottle use beyond infancy	NI
Early feeding experiences	NI
Watching television by the child	+*
High early energy intake by the child	NI
High intake of sugar-sweetened beverages by the child	+‡
Low physical activity by the child	0*
Short sleep duration by the child	NI

NI = not investigated, + = more prevalent than in high socioeconomic status, - = less prevalent than in high socioeconomic status, 0 = no difference compared to high socioeconomic status.
* = this thesis, † = published results from the Generation R Study Group, ‡ = secondary analyses/unpublished results from the Generation R Study

remained.[46-49] Not much literature is available on the association between socioeconomic status and anthropometrics in infancy. Two studies were indentified, both reported no association between socioeconomic status and weight, length, or weight gain until the age of 2.[50, 51] This is in line with the results of Chapter 4.1, where BMI z score did not differ at 1 and 6 months for socioeconomic groups. However, one other Generation R Study reported socioeconomic differences in length gain in infancy. As birth weight is also lower, it is logical that BMI is similar across groups. However, more research, and especially on change in body composition during infancy among socioeconomic groups would be of interest. Socioeconomic differences in sedentary behaviors and indicators of food intake are reported in literature.[52]

An overview of the association between risk factors for ethnicity and overweight is given in Table 5.3. Low socioeconomic status has been often reported in studies on ethnic differences in health, and is usually considered the main confounder for the association under study.[53] The finding that some ethnic groups more often smoke during pregnancy may be attributed to the several stages of the 'tobacco epidemic', while the finding that Moroccan mothers less often smoke may be attributed to their traditional lifestyle.[54]

The lower birth weight in some of the ethnic groups was found to be attributable to shorter gestational weight gain and parental height, two factors that are not easy to modify.[55]

As described in chapter 3.2, breastfeeding patterns vary between ethnic minority groups, but also depend on the countries where specific ethnic groups live. However, there are no studies that have reported opposing effects between starting and continuing breastfeeding. The higher percentage of people from ethnic minorities who start breastfeeding seems to have a cultural basis: The Koran recommends two years of breastfeeding, which may underlie the high starting rates of Mediterranean women in our study.[56] Non-native mothers may experience barriers to continuing breastfeeding, such as inadequate breastfeeding counseling by health care providers, due among other factors to language difficulties.[57] A US study reported that African-American mothers were more likely to report that they had stopped breastfeeding in order to return to work.[58] Working conditions may mean that non-native mothers face greater difficulties in continuing breastfeeding than their native peers. There is not much literature on weight gain in infancy among ethnic groups. However, one earlier Dutch study confirmed our results that infant weight gain is higher in Moroccan and Turkish mothers.[56] Ethnic differences in sedentary behaviors and indicators of food intake are reported in literature.[52]

STUDY AIM 3 SOCIAL DISADVANTAGE AND CHILDHOOD OVERWEIGHT

An extensive review, based on 54 studies, on the association between socioeconomic status and childhood overweight that included children from the age of 5 years onwards, concluded that low socioeconomic status is associated with higher risk on overweight.[59] Few studies have assessed the association between socioeconomic status and overweight at an earlier age.[51, 60, 61] One study reported an inverse socioeconomic gradient in overweight in 3-year-old children.[60] Another (cohort) study found no socioeconomic gradient in overweight at age 2 years, but reported more overweight in the lower socioeconomic class at age 6 years; it was concluded that the socio-economic gradient in overweight emerges between those ages.[61] Herngreen et al. found no socioeconomic differences in weight, height and weight gain between 1 and 24 months, but this study did not consider BMI or overweight as an outcome.[51] We did not find an association between mother's socioeconomic status, measured with either educational level or income, with child's overweight. On the contrary, the association seemed rather to be the reverse. A potential explanation for this phenomenon is that children from families with a lower socioeconomic status are born with a lower birth weight. It might take some years before this initial lower relative weight has been caught-up, and for the trend between socioeconomic status and (over)weight to reverse (Figure 5.1). Also, the association between socioeconomic status and overweight may be different when evaluating body composition instead of body mass index. In addition, the initial lower birth weight in children from mother with a low socioeconomic status may be even the cause of later overweight. This is in line with the literature that reports more overweight in adults who were socially disadvantaged during childhood, irrespective of adulthood socioeconomic status.[8] Finally, risk factors may accumulate over time, both in number and in intensity.

Two studies were found that attempted to study a pathway between socioeconomic status and overweight, both among adolescents. One study found that the higher body mass index of adolescents with a low socioeconomic status was for 35% explained by higher levels of watching television.[62] Another study reported that breastfeeding explained about 25% of the association between parental education and adolescent BMI.[63] For both breastfeeding and watching television, we reported substantial socioeconomic differences. Although we did not find a significant association between breastfeeding and watching television with overweight at preschool age, adverse effects of these risk behaviors may manifest themselves in later life, e.g. in adolescence.

Our finding that Moroccan and Turkish children have a higher prevalence of overweight at preschool age was confirmed in two other Dutch studies.[64, 65] Other studies have reported a higher prevalence of overweight among non-western adolescents.[66, 67] As all studied ethnicities are non-western, a comparison cannot be made. One other study reported the association between ethnicity and overweight in adults and included Turkish, Moroccan, and Surinamese/Antillean participants.[68] Prevalence of overweight was higher in all non-Dutch groups compared to Dutch adults. Also, whereas birth weight of Turkish and Moroccan children differed little from native Dutch children, children of other non native Dutch backgrounds had a lower birth weight. Therefore, similarly as in children from families with a low socioeconomic status, it is important to evaluate whether Surinamese/Antillean subgroups develop a higher prevalence of overweight at a later age compared to native Dutch children.

In the Netherlands, no studies were identified that attempted to explain the association between ethnicity and overweight. There are some directions from literature from other countries: one German study reported that the higher prevalence of overweight in 5/6 year old Turkish children could be explained by maternal educational level

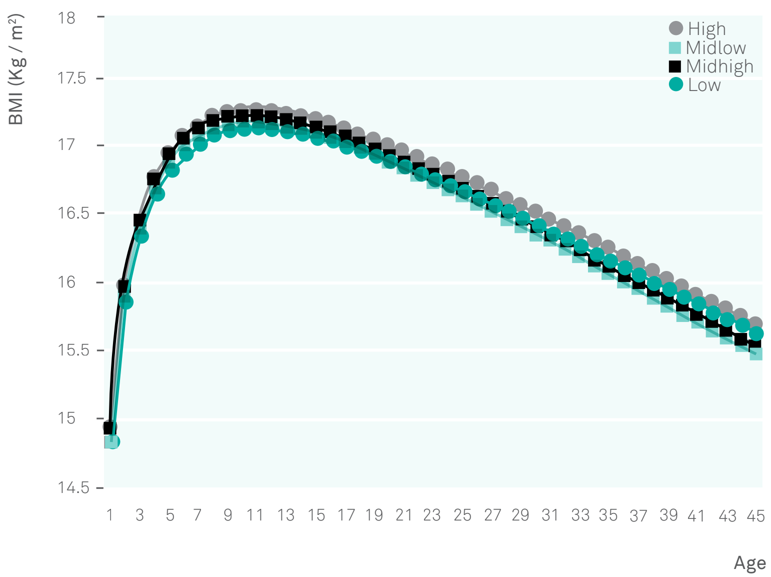
Table 5.3 Risk factors for childhood overweight for each ethnicity in the Generation R Study

	TURKISH	MOROCCAN	CAPE VERDEAN	ANTILLEAN/ SURINAMESE CREOLE	SURINAMESE -HINDUSTANI
FACTORS PRESENT BEFORE CONCEPTION					
Low socioeconomic status*	+	+	+	+	+
Parental overweight/ Maternal pre-pregnancy overweight*	+	+	0	+	0
FACTORS PRESENT DURING PREGNANCY					
Smoking during pregnancy*†	+	-	0	+	0
High gestational weight gain	NI	NI	NI	NI	NI
PERINATAL FACTORS					
Birth weight (high/low) *†	-/0	+/-	-/+	-/+	-/+
FACTORS PRESENT IN INFANCY					
Lack of breastfeeding/ formula feeding*	-	-	0	0	0
Rapid growth in infancy and childhood*	+	+	+	+	+
Early introduction of solids	NI	NI	NI	NI	NI
FACTORS IN EARLY CHILDHOOD					
Bottle use beyond infancy	NI	NI	NI	NI	NI
Early feeding experiences	NI	NI	NI	NI	NI
Watching television*‡	+	+	+	+	+
High early energy intake	NI	NI	NI	NI	NI
High intake of sugarsweetened beverages‡	+	+	+	+	+
Low physical activity*‡	+	+	+	+	+
Short sleep duration	NI	NI	NI	NI	NI

NI = not investigated, + = more prevalent than in native Dutch group, - = less prevalent than in native Dutch group, 0 = no difference compared to native Dutch group. * = this thesis, †= published results from the Generation R Study Group, ‡ = secondary analyses/unpublished results from the Generation R Study and watching television by the child.[69] Woo et al. reported that ethnic differences in adolescent body mass index were explained by breastfeeding for less than four months.[63] A comparison is difficult to make, because Woo et al. had different ethnicities in their sample than the ethnicities that are represented in the Generation R Study. Our results are not quite in line with the findings of Woo et al.: although Turkish children in our sample were more often overweight at preschool age, they were breastfed the longest. However, we did not measure exclusivity of the breastfeeding. Indeed, in secondary analyses, we noticed that among Turkish children, those with the heaviest weight received mixed feeding at 2 months (both breastfeeding and formula feeding). Among Dutch children, those with the heaviest weight received only formula feeding at 2 months. Thus, Turkish children may be overfed during infancy, but these feeding patterns were not elaborately measured in the Generation R Study. Also, Turkish mothers smoked more often during pregnancy than Dutch mothers, but this was not the case in Moroccan mothers, while both Turkish and Moroccan children had a higher prevalence of overweight at preschool age. Pathways from ethnicity to overweight may therefore be ethnicity-specific.

Figure 5.1

Body Mass Index curves between 1 and 48 months after birth per educational level (Dutch only) in the Generation R Study



In addition to the above-mentioned mechanisms, there may be alternative explanations or undiscovered pathways in the association between social disadvantage and overweight. From the Generation R Study, it is known that children from lower SES families score higher on activity level on an infant temperament scale.[70] This could also explain the tendency to have a relatively low prevalence of overweight in their preschool years. There is some evidence from literature that a more difficult infant temperament increases the risk on childhood overweight in later life.[3] In secondary analyses of our own data, infant temperament at 6 months was not yet associated with overweight at preschool age (data not shown). Still, it is relevant to further investigate infant temperament with parental control of feeding behavior, as this may contribute to later overweight.

SUMMARY

Large socioeconomic inequalities were found in all risk factors for later overweight. Some of these risk factors (high birth weight, rapid infant weight gain, and parental overweight) were associated with overweight at preschool age. No association was found between socioeconomic status and overweight at preschool age. We hypothesize that the association between socioeconomic status and overweight will occur at a later age in our cohort due to longer and/or increased exposure to risk factors in subgroups with a low socioeconomic status. Because especially children from families with a low socioeconomic status start with a relatively low birth weight, some time may be needed before they have recovered this initial lower birth weight, and can reverse the trend.

Similarly, large ethnic inequalities were found in all risk factors for later overweight. A higher prevalence of overweight was already present in Turkish and Moroccan preschool-aged children compared to native Dutch preschool-aged children. The higher prevalence of overweight in Turkish and Moroccan children compared to native Dutch children could be partly explained by the higher prevalence of parental overweight and rapid infant weight gain in Turkish and Moroccan children compared to native Dutch children. The birth weight of Turkish and Moroccan children differed very little from native Dutch children, whereas the birth weight of other ethnic groups was lower. We recommend follow-up of this cohort to evaluate whether other non-native Dutch groups also develop a higher prevalence of overweight due to prolonged exposure to risk factors.

5.3 METHODOLOGICAL CONSIDERATIONS

STUDY DESIGN

All studies described in this thesis are based on a population-based closed cohort study. The advantage of such a design is that many determinants and several outcomes can be studied over time. A disadvantage may be a long waiting time before certain outcomes, such as overweight, occurs. Also, causation cannot be inferred from this type of study.[71] Causality is mainly inferred from experimental studies, but this is not feasible and unethical for many if not all of the topics in this thesis. Breastfeeding for example, has been convincingly proven to have many health effects,[72] and it is therefore unethical to randomize mothers in either a breastfeeding or formula feeding group, as in the latter case, mothers and children will be withhold from well-established health benefits. At the best, randomizations can be done for breastfeeding advice to create a group that probably more often breastfeed.[73] When performing a cohort study, validity of the results may be threatened. Below, the most relevant types of errors that may occur to all the associations studied in this thesis will be discussed.

INTERNAL VALIDITY

Internal validity refers to the extent that the design and conduct of the study are likely to have prevented bias. In other words, it is the degree to which a study measures what it is supposed to measure. There are three types of bias that may occur in epidemiological studies: selection bias, information bias, and confounding. These will be discussed first. Then, specific measurements for this thesis will be discussed. This paragraph on internal validity will conclude with a discussion on statistical methods.

Bias in epidemiological studies

Selection bias

Participation rate in the Generation R Study is estimated to be around 61% for the whole sample, and 68% for the native Dutch subsample.[74] Selection bias occurs when there is selective participation, either at the start of the study or during follow-up. It harms the validity of the study when the association between determinant and outcome differs between those included in the study and those not participating (anymore) in the study. As in many follow-up studies,[75, 76] participants in the Generation R Study are generally more often higher educated, native Dutch, and healthier compared to the figures from the source population (pregnant women with an expected delivery data between 2002-2006, and living in Rotterdam).[74] In non response analyses in the separate studies of this thesis we compared those lost to follow-up compared to those included in the analyses. This consistently showed a similar pattern: those lost to follow-up were relatively more often lower educated, more often non native Dutch, and showed more unhealthy behavior. However, this selective non response only harms the validity of the study when the association between determinant and outcome differs between those included in the study and those not participating (anymore) in the study. This is difficult to ascertain, because we do not know the association between determinant and outcome from those not included in the study. One can argue that selection bias will be small, because the outcome is unknown at the start of the study, but this is not always true, because the outcome under study may be associated with social, educational and health related characteristics of those not participating in the study. Two similar pregnancy-recruited birth cohorts from Scandinavia were able to compare some well-established associations between those included in the study and those not participating in the study.[76, 77] Similar associations were found.[76, 77] We therefore assume that selection bias may not be a major threat to the validity of our results.

Information bias

There are two main types of information bias: recall bias and misclassification. As most information in the Generation R Study was prospectively collected, recall bias will hardly be an issue in our studies. Misclassification can be non-differential and differential. Non-differential misclassification refers to independent misclassification: misclassification of the outcome does not depend on exposure status and vice versa, while in differential misclassification, this is the case. Non-differential misclassification occurs to some extent in every study, and includes for example typing errors in data entry. The result for dichotomous outcomes is an attenuation of results. For continuous outcomes, non-differential misclassification can either exaggerate orattenuate a result.[71] However, in nearly all chapters in this thesis, we reported at least one dichotomous outcome. Dichotomous outcomes were in line with the continuous outcome from which they were derived. We therefore assume that due to non-differential misclassification, our results may be somewhat attenuated.

Many of the variables of interest in this thesis were obtained by self report via postal questionnaires. Although anonymity was assured, participants may have given socially desirable answers. This may especially be true for lifestyle-related characteristics. Mother's BMI for example, was calculated from self-reported pre-pregnancy weight, and is likely to be underreported.[78] Underreporting of weight is associated with socioeconomic status: underreporting occurs more often in women with a lower socioeconomic status.[79] However, mother's weight was also measured at the research centres in early, mid, and late pregnancy and these measurements explained 94% of the variance in pre-pregnancy weight. Therefore, we assume that differential misclassification did not occur to a large extent.

Confounding

Confounding results in a spurious association between determinant and outcome. It occurs when the determinant is associated with the outcome, and the confounding variable is also a predictor of the outcome. The choice for which variable to include as a confounder in this thesis was generally based on two considerations. First, all variables that are described in the literature as confounding variables were included. Then, we considered additional variables based on conceptual grounds. Because we were able to adjust for many potentially confounding variables, we restricted the number of variables to maintain precise estimates. This was done by testing whether the variable changed the association measures with at least 10%. Because of this, and the above described non-differential misclassification, residual confounding may result in an overestimation of adjusted results.

Measurements

Above mentioned sources of bias are specific for epidemiological studies. Biases regarding the specific measures in this thesis are discussed in the Discussion section of the specific chapters.
However, there are two other issues on internal validity that are discussed below, because they apply to all chapters in this thesis. This concerns the measurement of social disadvantage and definition of overweight, because all chapters include one of those measurements.

Social disadvantage

Several measures of social disadvantage have been used in this thesis; it was the main focus of chapters 3 and 4. For this part of the discussion, we will distinguish between measures of socioeconomic status and ethnicity. Socioeconomic status refers to the 'social and economic factors that influence what positions individuals or groups hold within the structure of society'.[80] Socioeconomic status is a complex and multifactor construct, whose commonest indicators are educational level, income level, and occupational class. In many sub studies in this thesis, educational level was used as the main indicator of socioeconomic status for several reasons. First, level of education reflect not only economical factors, but also problem-solving skills, and general and health-related knowledge which may be more important for overweight and overweight related behaviour than income or occupational class. Indeed, educational level has been shown to be most associated with cardiovascular disease risk among other indicators.[81] Second, level of education can also be applied to teenage and unemployed mothers – unlike occupational class, for example. However, educational level does not entirely capture the material and financial aspects of socioeconomic status. We therefore repeated our analyses on educational level with income as an indicator of socioeconomic status, which yielded similar results.

Ethnicity refers to people belonging to the same nation, religion, language, country of birth, or culture. It is not a standardized, well-defined concept.[82,83] In this thesis, according to the definition of Statistic Netherlands,[84] ethnicity was based on country of birth. Country of birth is objective and stable. Nevertheless, country of birth does not cover all aspects of ethnicity, such as culture and ethnic identity.[82,83] In chapter 3.2, we stratified non-Dutch participants in first generation and second generation in addition to country of birth. There were large differences according to generational status within ethnic groups. For future studies, it is recommended to include several aspects of ethnicity in the analyses.

Overweight

Chapters 2.1, 2.2, 4.1, and 4.2 report associations for overweight in preschool children. Body fatness can be most accurately measured by techniques as under water weighing, dual energy Xray absorptiometry, or computed tomography.[85] However, these techniques are invasive or expensive, and therefore unpractical in research and clinical settings. Widely used indicators of body fatness are skinfold thicknesses measurements, waist circumference and indexes like weight relative to height: weight-for-height, BMI, or the Rohrer index. However, as can be seen from the formulas: weight-for-height (weight/height), BMI (weight/height^2) and Rohrer index (weight/height^3) are measures of excess weight rather than measures of excess fat. Their use in children have been reviewed: both weight-for-height and BMI are good predictors of body fatness in children from the age of 2 years onwards, while the Rohrer index performs less well.[86] BMI is a continuous measure. Therefore, cut-off points are used to define overweight and obese children. Two different methods of defining overweight and obese children can be distinguished. The first is a cut-off point based on population studies. Those in the highest percentiles are defined as being overweight or obese. These cut-offs depend on the BMI distribution in the population, and sensitivity and specificity are high.[87] The second one is a cutoff point based on the recommendations of the International Obesity Task Force (IOTF).[88] These cut-off points are derived from the cut-off points for adult overweight and obesity, and are based on their association with disease risk. Another advantage of this method is that overweight prevalence is comparable between populations. Some discussion has arisen whether the cut-off points of the international obesity task force can be attributed to all ethnic populations, especially Asian populations, given that they have generally higher fat mass with lower BMI, but studies have shown that the cut-off points are still valid in these populations.[89] A limitation of the IOTF criteria is that the sensitivity for defining overweight is lower than population-based references, leading to a lower prevalence of overweight and less power.[87] This is in line with our findings: in chapter 3.2, associations were reported for cut-offs based on population references. In this paper, we also report on overweight prevalence according to IOTF. Indeed, overweight prevalence was lower when using IOTF criteria. However, associations between breastfeeding and overweight were similar.

Statistical analyses

In several chapters, for example 2.2, 3.1, and 3.2, the focus was on mediating mechanisms. Several methods can be used to assess mediation, and each method has strengths and limitations.[90, 91] In this thesis, mediation was calculated as the percentage change between two effect estimates. The use of regression adjustment to assess the level of degree of mediation has been criticized, since the required assumptions on causality are difficult to verify and the percentage change can be similar for different absolute changes in effect estimates.[92] This problem is especially prevalent in studying mediation mechanisms between ethnicity and health outcomes, as estimates for each ethnicity may differ substantively. We therefore applied bootstrap analyses to assess mediation in chapter 3.2, where the significance of the change in estimates is tested rather than the percentage change.

Missing data frequently occur in follow-up studies. All kind of reasons are imaginable: people do not have time to fill in a questionnaire, people may not want to answer questions on delicate topics, or anthropometric measurements fail because the equipment did not work properly. Missing values in a dataset are most often handled with one of the following methods: complete case analysis, imputation by the mean, adding a missing category, and more recently: multiple imputation.[93] The proper method to handle missing values is dependent on the type of missings. An impropriate method to handle missing values can threat the validity of the study. There are three types of missingness: missing completely at random (MCAR), missing at random (MAR), and missing not at random (MNAR). Missing completely at random means that missing data is completely due to coincidence, for example when due to logistic problems, i.e. questionnaires were not sent in a certain period. Missing at random is present when missingness is related to variables in the study, i.e. a specific group of people has more often missing values, but this is not related to the outcome under study. Missing not at random occurs when missingness is associated with both determinant and outcome, for example children from low-income families having more overweight do not show up at the child health centers. Each type requires specific approaches for adequately handle missing values and obtaining valid results. However, there is no statistical analysis that can test what kind of missingness one is dealing with. This has to be based on assumptions. For most studies in this thesis, we considered missing to be random (MAR). The best way to deal with missing at random is multiple imputation.[94] This method has therefore been applied in chapters 2.1, 3.3, 4.1, and 4.2.

EXTERNAL VALIDITY

Prevalence estimates that were mentioned in the studies included in this thesis reflect the inclusion of a population that is generally healthier and more health minded than those in the source population. For example, our breastfeeding rates were higher than reported from national figures. Therefore, prevalence estimates cannot be generalized to the population. However, prevalence of low socioeconomic status, non native Dutch ethnicity, risk factors, or overweight is not the most important issue for external validity. External validity in the context of this thesis refers to the extent that an association found in the study can be generalized to populations that were not in the source population.

In chapters 3.1 and 4.1, we restricted our population to those with a native Dutch ethnicity to be able to separate the effect of socioeconomic status from ethnicity. These findings may therefore be generalized to the Dutch population, considered that the health care system is similar across the country. However, generalization to all Caucasian populations should be done with care. A comparison of socioeconomic differences in health between North and South Europe revealed that the socioeconomic gradient in health was in the same direction for all countries, but that the magnitude varied considerably.[74] This may be associated with health care access, or educational opportunities. Our findings are not generalisable to developing countries, and in particular those with a low gross national product, where socioeconomic status is often reported to be also positively associated with obesity.[40, 95] However, due to social patterning that is reported to be ongoing,[95] these findings may be relevant for developing countries to adopt early strategies to prevent arising social inequalities in overweight.

In chapters 3.2 and 4.2, associations for ethnic subgroups were described. The results may apply to the general non native Dutch population, because all ethnicities in the Netherlands are represented in the study, and reasons and time frame for migration is similar within ethnic groups across the country. However, it is difficult to compare our results with those in other countries, and especially the US. Migration patterns differ strongly within and between countries, as well as the acquired socioeconomic status. Also, the results are not generalisable to the host country, because people that migrate from that country are probably a different, e.g. a healthier group.[96]

5.4 IMPLICATIONS FOR POLICY AND PRACTICE

We found abundant evidence that risk factors for overweight are unequally distributed from a very young age onwards. This unequal distribution of risk factors precedes the development of a social gradient in overweight at school age and in adolescence.[59] As socio-economic status is not easy to change, and ethnicity is impossible to change, interventions can focus on amendable factors that underlie the association between social disadvantage in early childhood and (later) overweight.

The most proximal factors that may lead to later overweight are behavioral factors related to a disturbed energy balance. Establishing healthy behaviors in early childhood is important, because food intake in early childhood is predictive for adult food intake.[97, 98] In addition, it may be good to focus on healthy behaviors instead of focusing on weight status, as willingness and ability of parents to perceive their children as overweight may be limited, especially in some cultural or socioeconomic environments.[99] There is not much evidence for interventions to prevent overweight that focus on preschool children.[100] An example of a successful intervention combined dietary and physical activity interventions and included a behavior theoretical framework.[101] For now, it seems that interventions are only useful if multiple strategies are used. This also means that not only parents should change their behavior, but it should also be made possible by their environment. For example, during the last decades, food marketing has increased, and the environment is built to stimulate sedentary behaviors.[100]

In addition to focusing on indicators of a healthy energy balance in childhood, preventive interventions in infancy are also recommended, because infancy seems to be a period where obesity susceptibility is established, probably among others due to differentiation and development of fat cells. Although evidence for an association between breastfeeding and obesity was not consistently found in this thesis, the effect of breastfeeding on overweight still may become prevalent at a later age. Given well-established other health benefits of breastfeeding,[102, 103] interventions to promote breastfeeding will benefit the population. Successful interventions to promote (exclusive) breastfeeding are widely applied, and still ongoing. However, interventions to promote breastfeeding can be further encouraged in the work environment, as this is mentioned as the most frequent reason to stop breastfeeding in the Netherlands.[104] Infant weight change was an independent predictor of overweight in preschool children. Child health centers have the opportunity to educate parents about healthy behavior. Growth is intensively monitored, and clear information should be provided on how to interpret growth curves.[105]

Prevention of childhood overweight should already start before conception. Maternal BMI was the strongest risk factor for offspring overweight. Prepregnancy counseling, as currently widely available throughout the country, could address overweight of the mother. During pregnancy, mothers should be encouraged to quit smoking, which will yield a broad range of health benefits.[106]

Most importantly, all interventions should also be suitably geared for use among socially disadvantaged families.

5.5 DIRECTIONS FOR FURTHER RESEARCH

Some further research is recommended for the following topics:

First, it is necessary to establish at what age the inverse association between social disadvantage and overweight, which has been described in many studies, occurs. Replication of the results in other studies and populations is highly relevant, because results on the association between social disadvantage and overweight at preschool age are currently conflicting. [51,60,61]

Second, maternal overweight was the strongest risk factor for childhood overweight, and only one of few factors that was associated with overweight at preschool age. Further research in disentangling pathways from parental overweight to offspring overweight would be of great importance. Other risk factors for overweight were not associated with overweight at preschool age, i.e. breastfeeding or watching television. The association between infant feeding and overweight in ethnic subgroups should be further explored, as many other factors besides breastfeeding seem to play a role. It is necessary to follow-up this cohort to establish whether these factors will be associated with overweight at later age.

Generally, many of the pathways from social disadvantage to overweight are not yet revealed. It is necessary to follow-up this cohort to contribute to the understanding of the mechanisms behind the association between social disadvantage and health, and in particular overweight. The life course approach is very suitable for future study.[107]

Concerning methodology, measurements that give more insight in fat mass and lean mass in addition to BMI would be helpful to understand associations between for example birth weight and overweight. Objective measurements of physical acticity would enhance interpretation of the association between physical acticity and overweight in young children. Lastly, loss to follow-up should be minimized, or at least some basic measurements in those lost to follow-up would be helpful to consider selection bias.

5.6 CONCLUSION

Strong risk factors for overweight in preschool children are high birth weight, rapid infant weight gain, and high parental BMI. No evidence was found for infant feeding to predict overweight in preschool children.

Evidence was found for an association between several indicators of social disadvantage and various early life risk factors for overweight, such as child being breastfed and watching television by the child. Mother's educational level and ethnicity were the indicators of social disadvantage that were strongest associated with early life risk factors.

An association between socioeconomic status and overweight at preschool age was absent, but large ethnic inequalities were found in overweight at preschool age. Specifically children with a Moroccan and Turkish ethnicity had a relatively high risk to develop overweight at preschool age. The ethnic inequalities in overweight could not fully be explained and should be further investigated. Children of Moroccan and Turkish descent should be carefully monitored concerning their weight change from birth onwards.

A wide-ranged program of preventive interventions is needed from the preconception stage onwards, including pregnancy, infancy, and early childhood, focused on ethnic minorities and families with a low socioeconomic status to establish healthy behaviors to prevent later chronic diseases.

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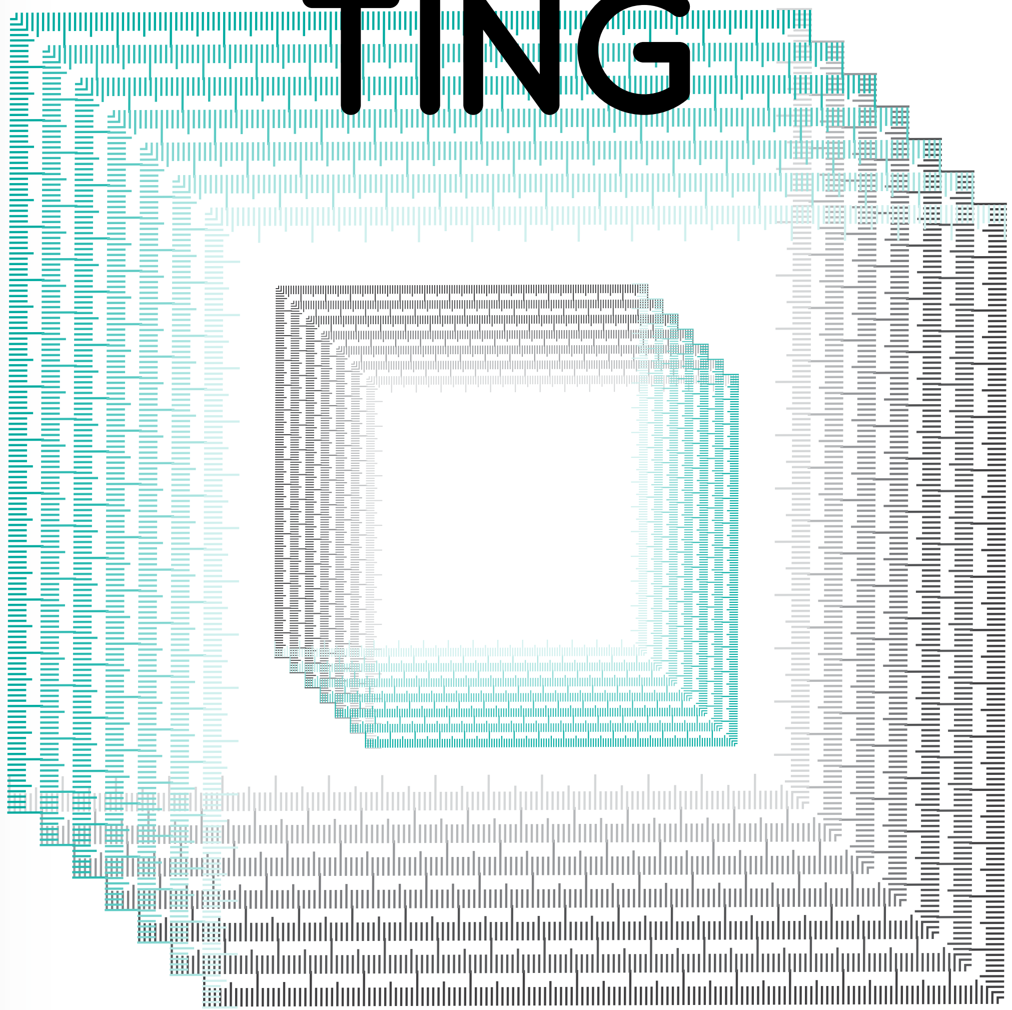
CHAPTER 6 SUMMARY / SAMENVAT-TING



SUMMARY

CHAPTER 1
ADDRESSES THE BACKGROUND AND RATIONALE FOR THE WORK PRESENTED IN THIS THESIS

Overweight and obesity are major public health problems worldwide, mainly because they increase the risk of morbidity and mortality. Overweight and obesity are also highly prevalent among children. Moreover, obese children can suffer from health-related problems during their childhood, and overweight and obesity in childhood tends to track into adulthood.

Some socially disadvantaged groups (which in this thesis refers to those with a low socioeconomic status or non-native ethnicity) are disproportionately affected with regard to their risk of developing overweight and, consequently, their risk of morbidity and mortality. Social inequalities in overweight are often already present in children: this has been consistently reported from the age of 5 years onwards. In addition to the fact that social inequalities in health are perceived to be unfair in many cases, decreasing social inequalities in health can improve the health status of the general population as a whole. Therefore, decreasing social inequalities in (childhood) overweight/obesity is a public health priority.

Reports on social inequalities in overweight in preschool-aged children are scarce and inconsistent. Risk factors for overweight are highly prevalent even before that age, and can arise during the entire period covering preconception (e.g. parental overweight), pregnancy (e.g. smoking), infancy (e.g. breastfeeding) through to preschool age (e.g. sedentary behaviours). However, it remains unknown at what age this social gradient in overweight develops, and what the contribution of these risk factors is to this social gradient in overweight.

This thesis aims to reveal some of the pathways that explain the association between social disadvantage and overweight by examining at what age this gradient develops, and what risk factors are associated with social disadvantage or overweight at preschool age.

The aims of this thesis are to study the association between:
1. early life risk factors for overweight, and overweight at preschool age.
2. social disadvantage and early life risk factors for overweight.
3. social disadvantage and overweight at preschool age.

This study was performed within the Generation R Study (Rotterdam, the Netherlands) and (for one sub-study) within Project Viva (Boston, USA). Both are prospective birth cohort studies using data collected via self-reported questionnaires and hands-on measurements.

CHAPTER 2
EXPLORES THE ASSOCIATION BETWEEN RISK FACTORS FOR OVERWEIGHT THAT OCCURRED IN INFANCY AND OVERWEIGHT.

Chapter 2.1 describes the association between breastfeeding and overweight. Breastfeeding was not associated with overweight at preschool age in the Generation R Study. Chapter 2.2 describes the association between breastfeeding, infant weight change, and overweight at age 3 years within Project Viva. Breastfeeding was not associated with overweight after adjustment for covariates, but rapid infant weight gain was a strong predictor of overweight. Chapter 2.3 describes the association between early introduction of solids and growth/overweight. No association was found between early introduction of solids and overweight at preschool age in the Generation R Study.

CHAPTER 3
INVESTIGATES THE ASSOCIATION BETWEEN INDICATORS OF SOCIAL DISADVANTAGE AND RISK FACTORS FOR OVERWEIGHT.

Chapter 3.1 describes the association between the mother's educational level and breastfeeding. Lower-educated mothers less often initiated and continued breastfeeding than higher-educated mothers. This was partly due to the fact that lower-educated mothers more often smoked during pregnancy and because they were more often obese. Chapter 3.2 describes the association between ethnicity and breastfeeding. All non-native Dutch mothers more often initiated breastfeeding but less often continued breastfeeding, compared to native Dutch mothers. Therefore, no differences in breastfeeding prevalence were found at 2 and 6 months of age between native Dutch and non-native Dutch mothers. An exception were the Mediterranean mothers of the first generation: they more often initiated and continued breastfeeding. Chapter 3.3 describes the association between socioeconomic status, ethnicity and indicators of physical activity and sedentary behavior. Children from mothers with a low educational level and children with a non-native Dutch ethnicity more often watched television for at least 2 hours/day than their counterparts. Children with a non-Western ethnicity less often played outside for at least 1 hour/day than native Dutch children.

CHAPTER 4
EXAMINES THE ASSOCIATION BETWEEN INDICATORS OF SOCIAL DISADVANTAGE AND THE DEVELOPMENT OF OVERWEIGHT AT PRESCHOOL AGE.

Chapter 4.1 describes the association between mother's educational level and overweight of the children until age 3 years. Lower educational level of the mother was not associated with a higher risk of overweight. On the contrary, the association tended to be the reverse, because children from mothers with a mid-low educational level had an even somewhat lower risk of developing overweight compared to children from mothers with a high educational level. Chapter 4.2 describes the association between ethnic background and overweight of the child until age 3 years. Relative to native Dutch children, Turkish and Moroccan children had a higher risk of overweight from age 2 years onwards, while Surinamese-Hindustani children had a lower risk of overweight. The higher risk of Turkish and Moroccan children compared to native Dutch children could be explained (in part) by the higher body mass index of their parents, and their rapid weight gain in infancy.

CHAPTER 5 DISCUSSES THE FINDINGS OF CHAPTERS 2 THROUGH 4 IN A BROADER CONTEXT.

Large socioeconomic inequalities were found in all risk factors for overweight. Some of these risk factors (high birth weight, rapid infant weight gain, and parental overweight) were associated with overweight at preschool age. No association was found between socioeconomic status (indicated by mother's educational level and household income) and overweight at preschool age. We hypothesize that the association between socioeconomic status and overweight will occur at a later age in our cohort due to longer and/or increased exposure to risk factors in subgroups with a low socioeconomic status. Because especially children from families with a low socioeconomic status start with a relatively low birth weight, some time may be needed before they have recovered this initial lower birth weight, and can reverse the trend.

Large ethnic inequalities were found in all risk factors for overweight. A higher prevalence of overweight was already present in Turkish and Moroccan preschool-aged children compared to native Dutch preschool-aged children. The higher prevalence of overweight in Turkish and Moroccan children compared to native Dutch children could be partly explained by the higher prevalence of parental overweight and rapid infant weight gain in Turkish and Moroccan children compared to native Dutch children. The birth weight of Turkish and Moroccan children differed very little from native Dutch children, whereas the birth weight of other ethnic groups was lower.

Further follow-up of this cohort is recommended to establish whether associations will emerge between risk factors for overweight, and actual overweight. Also, further follow-up of this cohort is recommended to evaluate when the social gradient in overweight emerges, and to evaluate whether other non-native Dutch groups also develop a higher prevalence of overweight due to prolonged exposure to risk factors.

To conclude, because large social inequalities in risk factors for overweight have been found, interventions should now focus on establishing healthy behavior in families from the preconception period onwards. These interventions should also be suitably geared for use among socially-disadvantaged families.

SAMENVATTING

IN HOOFDSTUK 1 WORDT DE ACHTERGROND VAN EN DE RATIONELE VOOR HET WERK IN DEZE THESIS BESCHREVEN.

Overgewicht en obesitas vormen wereldwijd een groot volksgezondheidsprobleem, omdat deze leiden tot het vaker voorkomen van hart- en vaatziekten en sterfte hieraan. Overgewicht en obesitas komen ook bij kinderen al vaak voor. Behalve dat gezondheidsproblemen bij obese kinderen al tijdens de kindertijd kunnen ontstaan, leiden overgewicht en obesitas in de kinderjaren vaak ook tot overgewicht en obesitas in de volwassenheid.

Sommige groepen met een lage sociale positie (wat in deze thesis verwijst naar mensen met een laag sociaal-economische status en niet-Nederlandse etniciteit) hebben een onevenredig grote kans om overgewicht te ontwikkelen, en daarmee meer kans op morbiditeit en mortaliteit. Sociale verschillen in overgewicht worden al consequent in de literatuur gerapporteerd bij kinderen vanaf 5 jaar oud. Buiten het feit dat het vaak maatschappelijk gezien als onrechtvaardig wordt beschouwd dat deze groepen dergelijke verhoogde kansen hebben, levert het verkleinen van sociale gezondheidsverschillen gezondheidswinst op voor de populatie als geheel. Daarom is het verkleinen van deze verschillen een belangrijk doel voor het beleid in de volksgezondheid.

Literatuur over sociale verschillen in overgewicht op de peuterleeftijd is schaars en inconsequent. Risicofactoren voor overgewicht, zoals roken tijdens de zwangerschap of het geven van borstvoeding, zijn al sterk aanwezig voor aanvang van deze leeftijd en komen voor vanaf de preconceptie tot de peutertijd. Desondanks is het 1) niet bekend op welke leeftijd deze sociale verschillen in overgewicht precies ontstaan en 2) wat de bijdrage is van risicofactoren op deze sociale verschillen in overgewicht.

Deze thesis heeft het doel te ontrafelen via welke wegen de associatie tussen sociale positie en overgewicht ontstaat door te onderzoeken a) op welke leeftijd deze verschillen ontstaan en b) te onderzoeken welke factoren gerelateerd zijn aan sociale positie of overgewicht. Hiervoor werden de volgende onderzoeksdoelen geformuleerd:

1. Het bestuderen van de associatie tussen vroege risicofactoren voor overgewicht en overgewicht in de peuterleeftijd.
2. Het bestuderen van de associatie tussen sociale positie en vroege risicofactoren voor overgewicht.
3. Het bestuderen van de associatie tussen sociale positie en overgewicht bij kinderen in de peuterleeftijd.

Deze studie is uitgevoerd binnen de Generation R Studie (Rotterdam, Nederland), en één substudie (hoofdstuk 2.2) is uitgevoerd binnen Project Viva (Boston, VS). Beide studies zijn prospectieve geboortecohorten waarbij gegevens zijn verzameld door vragenlijsten en metingen.

IN HOOFDSTUK 2 WORDT DE ASSOCIATIE TUSSEN RISICOFACTOREN VAN OVERGEWICHT EN OVERGEWICHT BESTUDEERD.

Hoofdstuk 2.1 beschrijft de associatie tussen borstvoeding en overgewicht. Borstvoeding was niet geassocieerd met overgewicht op de peuterleeftijd in het Generation R onderzoek. Hoofdstuk 2.2 beschrijft de associatie tussen borstvoeding, verandering in gewichtstoename in de babytijd, en overgewicht op de leeftijd van 3 jaar in Project Viva. Borstvoeding was niet duidelijk geassocieerd met overgewicht, maar snelle gewichtstoename in de eerste 6 maanden na de geboorte was wel een sterke voorspeller voor overgewicht op 3 jaar. Hoofdstuk 2.3 beschrijft de associatie tussen vroege introductie van bijvoeding en groei/overgewicht. Er werd geen associatie gevonden tussen vroege introductie van bijvoeding en overgewicht in het Generation R onderzoek.

IN HOOFDSTUK 3 WORDT DE ASSOCIATIE TUSSEN SOCIALE POSITIE EN RISICOFACTOREN VOOR OVERGEWICHT BESTUDEERD.

Hoofdstuk 3.1 beschrijft de associatie tussen opleidingsniveau van de moeder en borstvoeding. Lager opgeleide moeders startten minder vaak met borstvoeding geven en stopten sneller dan hoog opgeleide moeders. Dit kwam gedeeltelijk doordat lager opgeleide moeders vaker rookten tijdens de zwangerschap en doordat zij vaker obesitas hadden. Hoofdstuk 3.2 beschrijft de associatie tussen etniciteit en borstvoeding. Niet-Nederlandse moeders startten minder vaak met het geven van borstvoeding dan Nederlandse moeders, maar stopten eerder met het geven van borstvoeding. Hierdoor werden geen verschillen in borstvoeding prevalentie gevonden op 2 en 6 maanden tussen Nederlandse en niet-Nederlandse moeders. Een uitzondering vormt de eerste generatie mediterrane (Turkse en Marokkaanse) moeders; zij startten vaker met het geven van borstvoeding en gingen ook langer door. Hoofdstuk 3.3 beschrijft de associatie tussen sociaal-economische status, etniciteit, en indicatoren van lichamelijke activiteit en inactief gedrag van het kind. Kinderen met een laag sociaal-economische status en kinderen met een niet-Nederlandse etniciteit keken vaker meer dan 2 uur per dag televisie in vergelijking met Nederlandse kinderen met een hoge sociaal-economische status. Kinderen met een niet-westerse etnische achtergrond speelden minder vaak minimaal 1 uur per dag buiten in vergelijking met Nederlandse kinderen.

IN HOOFDSTUK 4 WORDT DE ASSOCIATIE TUSSEN SOCIALE POSITIE EN DE ONTWIKKELING VAN OVERGEWICHT BIJ PEUTERS BESTUDEERD.

Hoofdstuk 4.1 beschrijft de associatie tussen opleidingsniveau van de moeder (als indicator voor sociaal-economische status) en overgewicht van het kind tot de leeftijd van 3 jaar. Overgewicht was niet geassocieerd met laag sociaal-economische status. De associatie leek juist het tegenovergestelde, omdat kinderen van moeders met een middellaag opleidingscategorie zelfs een iets lager risico hadden op het ontwikkelen van overgewicht vergeleken met kinderen van moeders met het hoogste opleidingsniveau. Hoofdstuk 4.2 beschrijft de associatie tussen etnische achtergrond en overgewicht bij peuters tot de leeftijd van 3 jaar. In vergelijking met Nederlandse kinderen hadden Turkse en Marokkaanse kinderen een hoger risico op het ontwikkelen van overgewicht vanaf 2-jarige leeftijd, terwijl Surinaams- Hindoestaanse kinderen juist een lager risico op overgewicht hadden ten opzichte van Nederlandse kinderen. Het hogere risico bij Turkse en Marokkaanse kinderen kon slechts gedeeltelijk worden verklaard door de hogere body mass index (BMI) van de ouders en de snelle gewichtstoename in de babytijd.

IN HOOFDSTUK 5 WORDEN DE BEVINDINGEN UIT HOOFDSTUK 2, 3, EN 4 IN EEN BREDERE CONTEXT BEDISCUSSIEERD.

Grote sociaal-economische verschillen werden gevonden in alle risicofactoren voor overgewicht. Enkele van deze risicofactoren (hoog geboortegewicht, snelle gewichtstoename in de babytijd en overgewicht van de ouders) waren geassocieerd met overgewicht op de peuterleeftijd. Een associatie tussen laag sociaal-economische status en overgewicht op de peuterleeftijd was niet aanwezig. Onze hypothese is dat de associatie tussen laag sociaal-economische status en overgewicht op een latere leeftijd zal ontstaan door langere en intensievere blootstelling aan risicofactoren. Vooral omdat kinderen uit families met een laag sociaal-economische status met een lager geboortegewicht starten, kost het tijd voordat zij dit oorspronkelijk lager gewicht hebben ingehaald, en hiermee de trend te keren.

Ook werden etnische verschillen gevonden in alle risicofactoren voor overgewicht. Een hogere prevalentie van overgewicht was al aanwezig bij Turkse en Marokkaanse kinderen vergeleken met Nederlandse kinderen. Overgewicht van de ouders en snelle gewichtstoename na de geboorte waren belangrijke risicofactoren, maar konden de hogere prevalentie van overgewicht bij Turkse en Marokkaanse kinderen ten opzichte van Nederlandse kinderen slechts gedeeltelijk verklaren. Het geboortegewicht van Turkse en Marokkaanse kinderen verschilde niet veel van Nederlandse kinderen, maar het geboortegewicht van kinderen uit de andere niet-Nederlandse groepen was lager in vergelijking met de Nederlandse kinderen.

Het verder volgen van de kinderen in deze studie wordt aanbevolen om vast te stellen of er op latere leeftijd associaties zullen ontstaan tussen risicofactoren van overgewicht die op de peuterleeftijd nog niet geassocieerd waren met overwicht en overgewicht. Ook wordt het verder volgen van de kinderen in deze studie aanbevolen om te bestuderen wanneer de sociale gradiënt in overgewicht ontstaat, en of kinderen uit de andere niet-Nederlandse groepen vaker overgewicht ontwikkelen door langere blootstelling aan risicofactoren. Tot slot zouden interventies zich moeten richten op het bewerkstelligen van gezonde gedragingen in de familie vanaf de preconceptie periode tot de kindertijd. Deze interventies moeten speciaal geschikt zijn voor families met een lage sociale positie.

CHAPTER 7 MANUSCRIPTS / AUTHORS AND AFFILIATIONS / CV / PHD PORTFOLIO / DANKWOORD

MANUSCRIPTS BASED ON THIS THESIS

CHAPTER 2.1

Durmuş B / van Rossem L / Arends LR / Duijts L / Hofman A / Steegers EA / Raat H / Jaddoe VW.
Breastfeeding and growth in children until the age of 3 years: The Generation R Study
Submitted

CHAPTER 2.2

Van Rossem L / Taveras EM / Gillman MW / Kleinman KP / Rifas-Shiman SL / Raat H / Oken E.
Is the association of breastfeeding with child obesity explained by infant weight change?
International Journal of Pediatric Obesity / in press / Oct 28 2010 / [Epub ahead of print]

CHAPTER 2.3

Van Rossem L / Kiefte-de Jong JC / Looman CN / Jaddoe VW / Hofman A / Hokken-Koelega AC / Mackenbach JP / Moll HA / Raat H.
Weight gain before, during, and after the introduction of solids: results from a longitudinal birth cohort
Submitted

CHAPTER 3.1

van Rossem L / Oenema A / Steegers EA / Moll HA / Jaddoe VW / Hofman A / Mackenbach JP / Raat H.
Are starting and continuing breastfeeding related to educational background? The generation R study.
Pediatrics 2009 / 123(6):e1017-27.

CHAPTER 3.2

van Rossem L / Vogel I / Steegers EA / Moll HA / Jaddoe VW / Hofman A / Mackenbach JP / Raat H.
Breastfeeding patterns among ethnic minorities: the Generation R Study
Journal of epidemiology and community health 2010 / Aug 15 / [Epub ahead of print]

CHAPTER 3.3

Van Rossem L / Vogel I / Jaddoe VW / Moll HA / Hofman A / Mackenbach JP / Raat H.
Socio-economic and ethnic differences in indicators of sedentary behavior and physical activity at preschool age: The Generation R Study
Submitted

CHAPTER 4.1

van Rossem L / Silva LM / Hokken-Koelega AC / Arends LR / Moll HA / Jaddoe VW / Hofman A / Mackenbach JP / Raat H.
Socioeconomic Status is not Inversely Associated with Overweight in Preschool Children
J Pediatr 2010 / Jul 13 / [Epub ahead of print]

CHAPTER 4.2

Van Rossem L / Hafkamp-de Groen E / Jaddoe VW / Hofman A / Mackenback JP / Raat H.
Ethnic differences in growth and overweight in early life: results from a prospective multi-ethnic birth cohort
Submitted

AUTHORS AND AFFILIATIONS

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From the Department of Paediatrics, Erasmus MC, Rotterdam, the Netherlands: *L. Duijts / B. Durmuş B / J.C. Kiefte-de Jong / H.A. Moll / V.W.V. Jaddoe*

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CURRICULUM VITAE

Lenie van Rossem was born in Woensdrecht, the Netherlands, on 18th August 1982. In 2000 she finished pre-university education and started her study ‘Nutrition and Dietetics’ at HAN University of Applied Sciences (Hogeschool van Arnhem en Nijmegen). In 2004 she obtained her diploma and continued studying ‘Nutrition and Health’ at Wageningen University. For her specialization she chose the subject ‘Epidemiology and Public Health’. The work for her Master’s thesis was performed within the PIAMA study, a large birth cohort study. In September 2006 she graduated (cum laude) and started her PhD project at the Generation R Study Group and the Department of Public Health at Erasmus MC, University Medical Center Rotterdam: the results of this research are presented in this thesis. In 2008 she obtained a second Master of Science degree in Health Sciences, specialization Public Health, from the Netherlands Institute of Health Sciences. In spring 2009, she spent time working with another birth cohort (Project Viva) at Harvard Medical School in Boston, USA. From September 2010 onwards, she works as a postdoctoral researcher at the Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht.

PHD PORTFOLIO

SUMMARY OF PHD TRAINING AND TEACHING

Name PhD student	Lenie van Rossem
Erasmus MC Department	Public Health
Research School	NIHES
PhD period	2006-2011
Promotor	Prof. dr. JP Mackenbach
Supervisor	dr. H Raat

YEAR	WORKLOAD HOURS	ECTS	
			PhD training
			GENERAL COURSES
2008-2009		4.0	Biomedical English Writing and Communication
2009	16.0		CITI course on Human Research: basic course and responsible conduct of research
2009		0.5	Didactic skills ' Didactiek op Maat'
			SPECIFIC COURSES / NIHES PUBLIC HEALTH
2007		0.7	Principles of Research in Medicine and Epidemiology
2007		0.7	Methods of Public Health Research
2007		0.7	Health Economics
2007		0.7	Introduction to Public Health in the Changing Global Context
2007		0.7	Methods of Health Services Research
2007		0.7	Prevention Research
2008		1.4	Genome Wide Association Studies
2008		0.7	Conceptual Foundation of Epidemiologic Study Design
2008		0.7	Principles of Genetic Epidemiology
2008		1.4	Genomics in Molecular Medicine
2008		0.4	Large-scale Multicenter Studies
2007		4.3	Study Design
2007		1.4	Public Health Research: Analysis of Population Health
2007		1.4	Public Health Research: Analysis of Determinants
2007		1.4	Public Health Research: Intervention Development and Evaluation
2007		4.3	Modern Statistical Methods
2007		1.4	International Comparison of Health Care Systems
2008		1.4	Repeated Measurements in Clinical Studies
2008		0.7	Missing Values in Clinical Research
2008		1.4	Medical Demography
2008		0.9	Health Status Measurement
2008		1.1	Ethnicity, Health, and Health Care
2009		1.4	Advanced Genome Wide Association Studies
			SEMINARS AND WORKSHOPS
2006-2010	100.0		Attending seminars at the Department of Public Health
2006-2010	50.0		Attending Generation R research meetings/symposia
2006-2010	25.0		Attending seminars at Department of Epidemiology
2007	6.0		PhD day, Erasmus MC (workshop Time Management, Creative Thinking)
2008	6.0		Symposium 'Een gezonde start voor een gezond leven' (Amsterdam Born Children and their Development – ABCD study), AMC, Amsterdam
2009	6.0		Symposium 40 jaar epidemiologie, Erasmus MC,Rotterdam
			PRESENTATIONS
2007		0.6	Pathways from social disadvantage to relative overweight in 2-5 year old children: the role of individual and environmental factors (Retraite van de Werkgemeenschap Jeugd en Gezondheid)
2007		0.6	Pathways from social disadvantage to relative overweight in 2-5 year old children: the role of individual and environmental factors (Generation R seminar)
2007		0.6	Sociaal-economische verschillen in overgewicht bij 2-5 jaar oude kinderen Opleidingverschillen in start en duur borstvoeding (CEPHIR seminar)
2007		0.6	Educational differences in breastfeeding initiation: the Generation R study (Department of Public Health seminar)
2007		0.6	Educational differences in breastfeeding initiation, and continuation of breastfeeding: the Generation R study (Generation R seminar)
2009		0.6	Opleidingsverschillen in de start en duur van borstvoeding (flits- en posterpresentatie Nederlands Congres Volksgezondheid)
2009		0.6	Social Disadvantage and Overweight in Early Childhood (Generation R seminar)
2010		1.3	Early introduction of solids and growth (oral at conference Power of Programming)
2010		1.3	Socioeconomic differences in Physical and Sedentary Behavior in Preschool Children (poster presentation at ISBNPA)
			(INTER)NATIONAL CONFERENCES
2007		0.6	Retraite van de Werkgemeenschap Jeugd en Gezondheid, Soesterberg, the Netherlands
2008	8.0		Nederlands Congres Volksgezondheid (NCVGZ), Groningen, the Netherlands
2010	24.0		Power of Programming, Munich, Germany
2010	24.0		International Society of Behavioral Nutrition and Physical Activity (ISBNPA), Minneapolis, USA
			Teaching
			LECTURING
2009	2.0		Introduction lecture: Youth Health Care Assignment
			TUTORING
2009		0.2	Teacher Assistant: Principles of Research in Medicine
2007-2009	8.0		Supervising medical students in writing assignments, 4th year, Erasmus MC Rotterdam, Thema 4.2 The population as a patient
			SUPERVISING MASTER'S THESES
2009	8.0		Supervised Sanne Abel, medical student. Thesis topic: Home environment and
overweight			
	283	**41.6**	**TOTAL**

DANKWOORD

Het meest gelezen hoofdstuk, maar het minst wetenschappelijk onderbouwd, en ook nog eens niet zo goed in woord en getal uit te drukken. Toch maar een poging om de meest significante mensen te bedanken.

Allereerst zou er geen proefschrift bestaan zonder promotor en copromotor.

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Zonder de waardevolle bijdrage van co-auteurs zouden de artikelen die de basis voor dit proefschrift vormen er toch wat anders uitzien. Met een tweede auteur wordt intensief samengewerkt en deze wil ik dan ook specifiek noemen: Anke Oenema (zeer grondig en kritisch), Ineke Vogel (snel, recht voor zijn raap en geen verkeerd getalletje meer in het artikel), Lindsay Silva (om het paper van een duidelijke boodschap te voorzien), Jessica Kiefte-de Jong (zeer vernieuwend – we doen alleen geen nieuwe analyses meer op vrijdagmiddag) en Esther Hafkamp-de Groen (snel, enthousiast en ontzettend behulpzaam). Dank ook aan alle andere co-auteurs: Caspar Looman en Lidia Arends (het is zo fijn om er zeker van te zijn dat de optimale statistische kennis is gebruikt voor een artikel), Henriëtte Moll, Eric Steegers, Vincent Jaddoe, Albert Hofman, Anita Hokken-Koelega: door jullie suggesties zijn de artikelen nog mooier geworden! For one article, I spent some time in Boston. Thanks to prof. dr. Matthew Gillman for giving me the opportunity to work on the Project Viva data. A special word of thanks to dr. Emily Oken, thank you for supervising this paper, our effective and efficient meetings, and the quick responses to my emails after my stay. Thanks to dr. Elsie Taveras, dr. Ken Kleinman, dr. Sheryl Rifas-Shiman for their help during my stay and for the paper.

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De artikelen die de basis voor dit proefschrift vormen zouden ook niet bestaan zonder gegevens om te kunnen onderzoeken. Een onderzoek waarbij gegevens worden verzameld van duizenden kinderen draait niet vanzelf. De gegevens zouden er sowieso niet zijn zonder deelnemers. Dank aan alle deelnemers voor het invullen van de vragenlijsten en het komen naar de onderzoekscentra. In dit proefschrift zijn ook gegevens gebruikt van kinderen met een Turkse en Marokkaanse afkomst. Zonder de consulentes Rukiye en Sabah zouden er veel minder gegevens zijn over deze kinderen. Maar ook: zonder Claudia geen data, zonder Alwin geen werkende computer en zonder Patricia geen werkende fax (onder andere).

Het oog wil ook wat. De resultaten in dit proefschrift komen veel beter tot hun recht dankzij een optimale vormgeving. Clara, ontzettend bedankt voor het mooie ontwerp.

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In de epidemiologie heb je wel eens te maken met antecedenten. Dat geldt ook voor het beginnen aan een (epidemiologisch) promotietraject. Een goed begeleide stage (door Alet) bij de PIAMA studie was een enorme trigger om voor de wetenschap te gaan. Salome, je hebt me erg geholpen met het bewandelen van het pad naar de wetenschap.

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Joost, er is niemand die dit promotietraject zo intensief gevolgd heeft als jij, waarbij gevolgd een understatement is. Buiten het installeren van onïnstalleerbare statistische programma's, het omtoveren van een logeerkamer in een 'proefschriftafmaak' kantoor en het helpen met tabellen maken, ben je altijd lief, geduldig en ondersteunend geweest. Mijn dank is niet in aantal kusjes uit te drukken.