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FAMILY-RELATED OBESITY RISK FACTORS AND DIETARY BEHAVIOURS IN HIGH-RISK POPULATIONS: ASSOCIATIONS WITH CHILD WEIGHT DEVELOPMENT

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ABSTRACT

Background

Obesity rates in Swedish children are currently not increasing, however socioeconomic disparities are widening. Many children become obese as early as their preschool years. Hereditary and environmental family-related risk factors are the dominating determinants of child obesity, with parental obesity as the most important. Prevention is a high priority, and increased knowledge on risk factors specifically in high-risk populations is of vital importance for the development of efficient preventive interventions.

Aims

The primary aim was to analyse the impact of parental adiposity and parental educational level on child relative weight from infancy to adolescence, in high-risk populations. Further, to assess the associations between infant relative weight and early life factors, infant dietary intake, infant eating behaviours and parental food intake. Also, to validate a questionnaire measuring obesity-related eating behaviours in Swedish preschool children. Finally, the aim was to validate the dietary intake in infants and parents using a biomarker for fat intake.

Material and methods

Four child-parent populations were studied: 231 obese children followed longitudinally, from the Swedish National Childhood Obesity Centre in Stockholm (Study I); 197 (Study II) and 193 (Study IV) one-year old infants in high- and low-risk families (determined by parental weight status), participating in Early STOPP (Stockholm Obesity Prevention Project) and recruited from child healthcare in Stockholm County; 174 children 1-6 years old recruited from kindergartens in Stockholm (Study III). Study I: Associations between severity of obesity at age 7 and 15, age at onset of obesity and parental BMI were analysed in obese children, using data from BORIS, the Swedish quality registry for childhood obesity. Study II: Infant relative weight at 3, 6 and 12 months and rapid weight gain 0-6 months were analysed in relation to parental adiposity, parental educational level and early life factors. Study III: A factorial validation of the Swedish translation of an eating behaviour questionnaire (CEBQ) was performed on children 1-6 years old, and associations with child age, gender, relative weight and parental weight status were explored. Study IV: Infant dietary intake, infant eating behaviours and parental food intake were compared between high- and low-risk families. Associations between child and parental diet quality as well as between child weight, dietary intake and eating behaviours were assessed. The reported intake of fat from selected foods was correlated with the fatty acid composition in plasma.

Results
Study I: Maternal BMI was associated with degree of obesity at age 7, and both parents' BMI was associated with degree of obesity at age 15. The relationships were stronger in adolescence. High parental educational level was associated with a lower degree of obesity in adolescence. Parental BMI was not associated with obesity onset. Study II: Child relative weight during the first year was associated with parental education but not with parental adiposity. Birth weight was the most important predictor of growth during the first year. Study III: The factor analysis of CEBQ revealed a seven-factor solution with good reliability. Several eating behaviour factors varied by child age. Study IV: Dietary intake and eating behaviours at age one did not differ between high- and low risk infants, but parents in high-risk families had a higher intake of obesogenic foods. Infant and paternal intake of vegetables and fish were related, but no parent-child associations were found for obesogenic foods. Relative weight at age one was associated with obesity-related eating behaviours but not with dietary intake. Overall, fat from selected foods correlated with the corresponding fatty acids in plasma, indicating satisfactory validity of reported dietary habits.

Conclusions
Parental adiposity and educational level are both important independent determinants of child weight development and degree of obesity, and can be used to identify children at high risk of obesity. However the timing of their influence differs. Parental adiposity does not affect the relative weight of infants, nor the obesity onset, but the impact of both maternal and paternal BMI becomes stronger with child age and affects the degree of obesity later in childhood and in adolescence. Low parental educational level is associated with higher infant weight as early as their first year, and a protective effect of high educational level may be long-term. Infant relative weight is also independently associated with birth weight and eating behaviours, but not with dietary intake, which is not influenced by parental adiposity or parental obesogenic food intake as early as at age one. This thesis indicates that preventive efforts targeting clearly identified high-risk families should be initiated as early as in infancy.

SAMMANFATTNING

Bakgrund

Fetma hos svenska barn ökar för närvarande inte, men de sociodemografiska klyftorna växer. Många barn utvecklar fetma redan i förskoleåldern. Familjerelaterade riskfaktorer, där både arv och miljö spelar in, dominerar, och av dessa är fetma hos föräldrar den allra viktigaste. Prevention är ett prioriterat område, och att öka kunskapen om riskfaktorer specifikt i högrisk-populationer är av stor betydelse för att möjliggöra effektiva preventiva insatser.

Syfte

Det primära syftet var att studera inverkan av föräldrars viktstatus och utbildningsnivå på barns relativa vikt, från spädbarnsåldern till tonåren, i högrisk-populationer. Vidare att undersöka samband mellan spädbarns viktutveckling och tidiga riskfaktorer, kostintag, ätbeteende och föräldrars matvanor. Ytterligare ett syfte var att validera en enkät för mätning av fetmarelaterade ätbeteenden hos svenska förskolebarn. Slutligen, att validera kostintag hos spädbarn och föräldrar med en biomarkör för fettintag.

Metod

Fyra olika barn-föräldrapopulationer har studerats: 231 barn/ungdomar med fetma från Rikscentrum Barnobesitas i Stockholm, som följts longitudinellt (Studie I); 197 (Studie II) respektive 193 (Studie IV) barn 1 år i hög- och lågriskgrupper (baserat på föräldrarnas viktstatus) som deltar i Early STOPP, en fetmapreventiv intervention, och rekryterats från barnhälsovården i Stockholms län; 174 barn 1-6 år, rekryterade från förskolor i Stockholm (Studie III). <u>Studie I:</u> Samband mellan grad av fetma vid 7 och 15 år, debutålder för fetma och föräldrars BMI studerades baserat på data från BORIS, nationellt kvalitetsregister för barnfetma. <u>Studie II:</u> Spädbarns relativa vikt vid 3, 6 och 12 månader, samt snabb viktökning 0-6 månader, studerades i relation till föräldrars viktstatus och utbildningsnivå samt tidiga riskfaktorer. <u>Studie III:</u> Faktoriell validering av den svenska översättningen av CEBQ (Children's Eating Behaviour Questionnaire) genomfördes på barn 1-6 år, och samband med ålder, kön, vikt och föräldrars viktstatus undersöktes. <u>Studie IV:</u> Spädbarns kostintag, ätbeteende och föräldrars livsmedelsintag jämfördes mellan hög- och lågriskgrupper. Samband mellan spädbarns och föräldrars kostkvalité, samt mellan spädbarns vikt, kostintag och ätbeteende studerades. Rapporterat intag av fett från utvalda livsmedelsgrupper jämfördes med fettsyremönster i plasma.

Resultat

<u>Studie 1</u>: Vid 7 år var barnens grad av fetma relaterat till mors BMI och vid 15 år sågs samband till båda föräldrars BMI. Sambanden var starkare i tonåren. Hög utbildningsnivå hos föräldrarna var relaterat till en lägre grad av fetma vid 15 år. Föräldrars BMI hade ingen inverkan på debutålder för fetma. <u>Studie II</u>: En högre vikt hos spädbarn under det första året var kopplat till låg utbildningsnivå hos föräldrar, men inte till föräldrars viktstatus. Födelsevikt var den mest betydelsefulla faktorn för viktutveckling under första året. <u>Studie III:</u> Faktoranalysen av CEBQ identifierade sju faktorer, med god intern reliabilitet. Flera ätbeteendefaktorer varierade med ålder. <u>Studie IV:</u> Det var ingen skillnad på spädbarns kostintag och ätbeteende mellan högrisk- och lågriskgrupp, men föräldrarna i högriskfamiljer hade ett högre intag av onyttiga livsmedel. Samband sågs mellan kvalitativa mått på barns och pappors intag av grönsaker och fisk, men inga samband kunde identifieras till föräldrarnas intag av onyttiga livsmedel. Spädbarns relativa vikt var associerat till ätbeteende, men inte till kostintag. Fettintag korrelerade med motsvarande fettsyror i plasma, vilket indikerade en godtagbar validitet för rapporterat kostintag.

Slutsatser

Fetma och utbildningsnivå hos föräldrar är oberoende faktorer av betydelse för barns viktutveckling och grad av fetma, och kan användas för att identifiera högriskpopulationer. Dock verkar de tidsmässigt olika. Fetma hos föräldrar har ingen effekt på spädbarns viktutveckling och inte heller på åldern då fetma utvecklas, men sambandet blir starkare ju äldre barnen blir och BMI hos båda föräldrar påverkar graden av fetma hos barn och ungdomar. Låg utbildningsnivå hos föräldrar är kopplat till en högre vikt hos spädbarn redan under första året, och en skyddande effekt av hög utbildningsnivå sågs även i tonåren. Spädbarns vikt är också tydligt kopplat till födelsevikt och ätbeteende, men inte till deras kostintag, som vid 1 år inte har något samband med föräldrars viktstatus eller ohälsosamma matvanor. Denna avhandling indikerar att preventiva insatser riktade till tydligt identifierade högriskfamiljer bör starta redan i spädbarnsåldern.

LIST OF SCIENTIFIC PAPERS

I. **Associations between severity of obesity in childhood and adolescence, obesity onset and parental BMI: a longitudinal cohort study**
Svensson V, Jacobsson JA, Fredriksson R, Danielsson P, Sobko T, Schiöth HB*, Marcus C*.
International Journal of Obesity 2011; 35:46–52

II. **Infant growth is associated with parental education but not with parental adiposity – Early Stockholm Obesity Prevention Project**
Svensson V*, Ek A*, Forssén M, Ekbom K, Cao Y, Ebrahim M, Johansson E, Nero H, Hagströmer M, Ekstedt M, Nowicka P, Marcus C.
Acta Paediatrica 2014; doi:10.1111/apa.12551

III. **Obesity related eating behaviour patterns in Swedish preschool children and association with age, gender, relative weight and parental weight - factorial validation of the Children's Eating Behaviour Questionnaire**
Svensson V, Lundborg L, Cao Y, Nowicka P, Marcus C, Sobko T.
International Journal of Behavioral Nutrition and Physical Activity 2011; 8:134

IV. **Dietary behaviours in families with infants at high and low obesity risk - Early Stockholm Obesity Prevention Project**
Svensson V, Sobko T, Ek A, Forssén M, Ekbom K, Johansson E, Nowicka P, Westerståhl M, Risérus U, Marcus C.
Manuscript

* Equal contribution

CONTENTS

ABBREVIATIONS AND DEFINITIONS

ABBREVIATIONS

BMI	Body mass index
BMI SDS	Body mass index standard deviation score
BMR	Basal metabolic rate
BORIS	Barn Obesitas Register i Sverige; the Swedish National Quality Register for Childhood Obesity
CE	Cholesterol esters; lipid fraction in plasma
CEBQ	Children's Eating Behaviour Questionnaire
CHC	Child healthcare
CI	Confidence interval
DHA	Docosahexaenoic acid; marine polyunsaturated omega-3 fatty acid
E%	Energy percent; percent of total energy intake
Early STOPP	Early Stockholm Obesity Prevention Project
EPA	Eicosapentaenoic acid; marine polyunsaturated omega-3 fatty acid
FFQ	Food frequency questionnaire
FTO	Fat mass and obesity associated gene
GWG	Gestational weight gain
kJ	Kilojoule; standard unit of energy intake
MJ	Megajoule; 1000 kJ
MUFA	Monounsaturated fatty acids
NNR	Nordic Nutrition Recommendations
OR	Odds ratio
p	Significance level
PL	Phospholipids; lipid fraction in plasma
PUFA	Polyunsaturated fatty acids
r	Pearson correlation coefficient

RCT	Randomized controlled trial
SCB	Statistiska centralbyrån (Statistics Sweden)
SD	Standard deviation
SES	Socio-economic status
SFA	Saturated fatty acids

DEFINITIONS

Adiposity	Adiposity refers to excess of body fat. In this thesis the term reflects 'degree of adiposity', i.e. low or high levels of body fat.
Adiposity rebound	Age at the second rise of a child's BMI curve, i.e. the age in early childhood when body fat begins to increase (normally between age 5 and 7).
Degree of obesity	Synonymous with relative weight or BMI SDS in an obese child/adolescent, and with severity of obesity.
Diet quality	Dietary intake or food intake assessed using predefined diet quality indicators
Dietary behaviours	Dietary intake and eating behaviours.
Dietary intake	Intake of energy and macronutrients and diet quality indicators.
Eating behaviours	Appetite traits, e.g. enjoyment of food, food responsiveness, satiety responsiveness and slowness in eating
Food intake	Intake of different food items of food groups, in frequencies per day or week.
Infant	A child 0-2 years old.
Macronutrients	Energy yielding nutrients: protein, fat, carbohydrate.
Obesity risk	Primarily determined by both parents' weight status. High risk = two overweight or at least one obese parent; low risk = two normal weight parents. Alternatively determined by both parents' educational level. High risk = neither parent >12 years of school; low risk = at least one parent >12 years of school
Obesogenic	A factor known or suggested to be associated with obesity.
Preschool child	A child 2-5 years old.
Relative weight	BMI SDS in children, BMI in parents.

BACKGROUND

INTRODUCTION

This thesis focuses on family obesity-related risk factors and their effect on child weight development and adiposity in high-risk populations, and the implications for early obesity prevention. The body of research on obesity risk factors is almost overwhelmingly comprehensive. However, the specific focus of this thesis on high-risk populations is a sub-discipline of obesity research that is, surprisingly, much more limited. So why is it important to study risk factors explicitly in high-risk individuals? The identification of risk factors is the key to prevention, and high-risk individuals are often the targets of prevention. Thus enhancing knowledge about the effect of suggested risk factors in high-risk populations may increase the chances of successful and more efficient preventive efforts. This could be accomplished by increasing the precision of identifying the high-risk individuals, by targeting the right modifiable behaviours and through knowledge of when prevention should be initiated. Two of the studies of this thesis are based on baseline data from a preventive obesity intervention in high-risk preschool children, and the implications of the results for targeted prevention will be discussed.

Family-related factors may encompass a comprehensive range of aspects - hereditary, socio-demographic and behavioural. Not all have been studied in this thesis. The focus has specifically been on parental adiposity, parental educational level, other socio-demographic factors and early life factors, such as birth weight and infant feeding. Both hereditary and environmental family aspects are studied, however it is not the aim to distinguish between them. Additionally, this thesis has a specific focus on dietary behaviours, which is recognised as one of several components of the family lifestyle that may affect child weight development. Some other important family-related behavioural risk factors will be briefly described in the background section.

Outside the family there are additional areas of potential importance for children's weight development, such as community and neighbourhood surroundings, accessibility of recreational facilities, preschool and school environment and accessibility of foods and restaurants [1-3] (Figure 1). These are likely to interact with the family-level factors, such as physical activity and dietary behaviours. However, in young children the familial heritance and environment dominates and interactions within the family, between child and parental characteristics, is the focus of this thesis.

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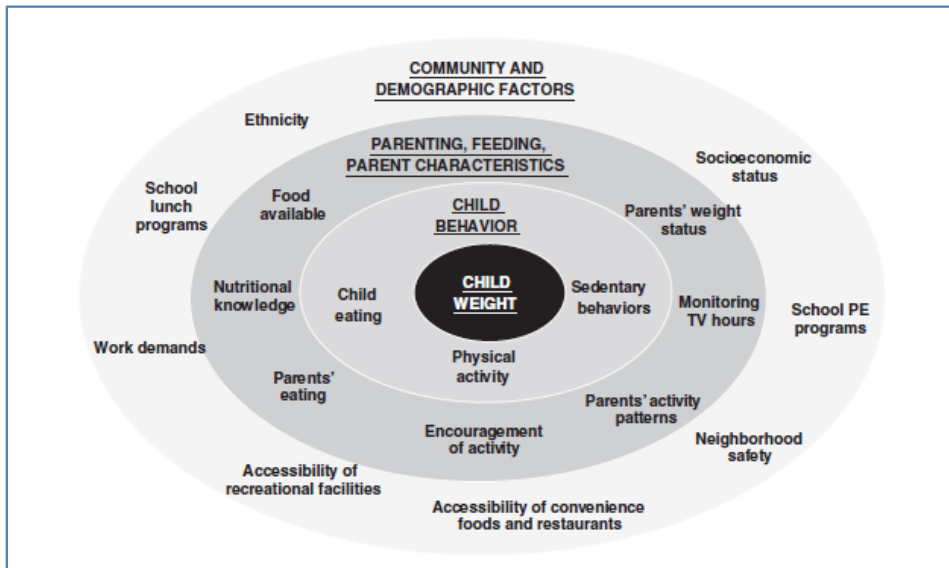
Figure 1. Obesity risk factors on child, parental/family and community level (from Skelton et al. Pediatr Clin North Am; 2011. '*Etiologies of obesity in children: Nature and nurture*') [2].

Since *risk factor* is a key concept of this thesis, awareness of the meaning of this term is important in interpreting the results. A risk factor is a type of correlate associated with the increased probability of a specific undesirable outcome. Also, a risk factor must occur before the outcome. If a risk factor can be modified, and if it is it changes the probability of the outcome, then the risk factor may be causal. Further, a risk factor can be used to divide a population into high-risk and low-risk groups, where the probability of the outcome is greater in the high-risk compared with the low-risk population [4]. Other related terms are risk marker, determinant and protective factor [5]. A risk marker is also a factor associated with the outcome, but changing a risk marker does not affect the probability of the outcome. A determinant is a variable that that is associated with either increased or decreased risk of the outcome, and a protective factor increases the probability of welcome outcomes.

With that explained - in this thesis the term risk factor is used in its general meaning denoting an association between an exposure and the outcome of interest. It is not within the scope of this thesis to provide evidence of causality. This would require experimental research, i.e. studying whether alterations of the factors analysed actually change the outcome – child weight development and adiposity - which has not been performed. Finally, it is important to keep in mind that risk factors for a particular outcome cannot be assumed to be the same, or to be of the same strength, in different populations [4].

OBESITY IN CHILDREN AND ADULTS

Definition of obesity

Obesity is defined as a condition of excess body fat and is the result of an imbalance between energy intake and energy expenditure over a prolonged period [6]. Overweight and obesity in children and adults is determined by body mass index (BMI), a proxy measure of adiposity calculated as weight/height^2 (kg/m$^{2)}$). BMI is not a precise measure of adiposity, for example it does not distinguish between fat mass and fat-free mass, however it is a simple, widely-used tool for defining obesity. The normal development of children's BMI and adiposity over time is a rapid increase over the first year, thereafter a decline until approximately the age of 5-6 years, whereby it gradually increases again until adulthood (Figure 2). Therefore, the BMI cut-offs for obesity in children vary with age and gender. For children from two years of age, age- and gender-specific international cut-off values for both overweight and obesity as defined by the International Obesity Task Force are commonly used [7]. These cut-offs follow the BMI curve and decrease between the ages of 2 and 4 and then gradually increase from age 5 to 18. At age 18 the cut-offs for adults is used; overweight 25-29.9 kgm^{-2} and obesity $\geq$ 30 kgm^{-2} [8].
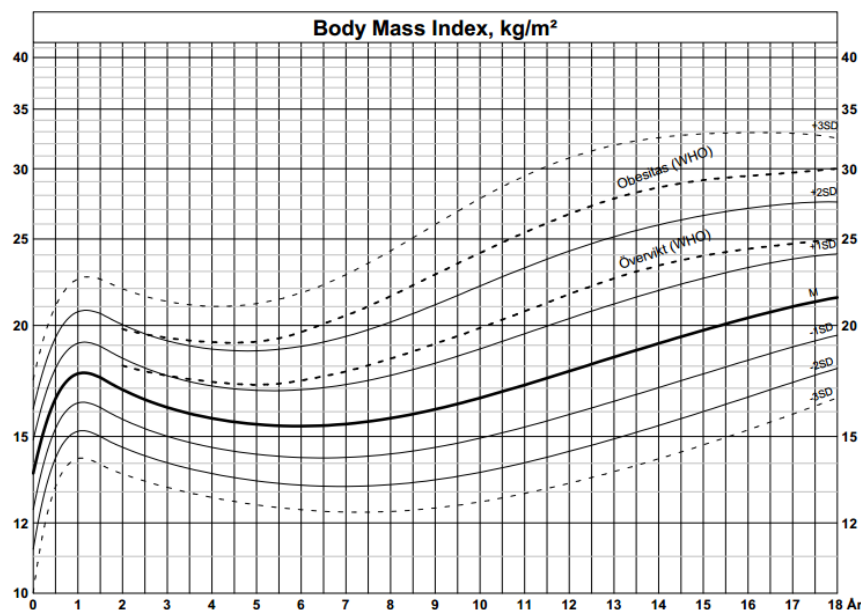
Figure 2. BMI curve for girls according to Swedish reference data [9].
The age when the BMI curve begins to increase is referred to as the adiposity rebound.

BMI can additionally be used to compare the relative weight and degree of obesity in adults. However, for children BMI cannot be compared directly across different child age groups and genders. Instead, BMI SDS (body mass index standard deviation score),

a measure of relative weight in children that accounts for differences in BMI by age and gender, can be used. BMI SDS is calculated based on weight, height, age and gender using a reference population [9]. The term 'relative weight' is used throughout this thesis referring to BMI SDS in children and BMI in adults.

Prevalence of obesity

Children

The prevalence of overweight and obesity in children increased dramatically between the 1980ies and 2000 [10]. Overweight more than doubled, from less than 10% in the 1980ies to about 20% in 2000 and obesity increased 4-5 times to approximately 3-5 % in 10-year old children [10]. During the last decade the prevalence of overweight and obesity in children has stabilized on this high level in Sweden, with some indications of a levelling-off [11]. In a national representative sample of Swedish children 7-9 years old measured in 2008 the prevalence of overweight and obesity was approximately 20%, including 3% obesity [12]. However, the socio-demographic disparities seem to be widening [13]. The risk for overweight and obesity are higher in low-SES areas compared to high-SES areas as well as in rural compared to urban areas [12].

Similar trends have been observed for Swedish preschool children. There are no Swedish national data for this group, but child healthcare services in different regions in Sweden have reported a declining prevalence of obesity in 4-year old children born 2000 - 2007. However, the overweight and obesity rates differ substantially between different regions, from 11% in Stockholm to near 20% in Västernorrland for children born in 2003 [14]. In Stockholm a slight decline has been observed over the last years and 11% of the 4-year old children born in 2007 are overweight or obese. However, also within Stockholm County there are substantial differences in prevalence numbers between municipalities, reflecting considerable area-related socio-demographic determinants [15] (Figure 3).

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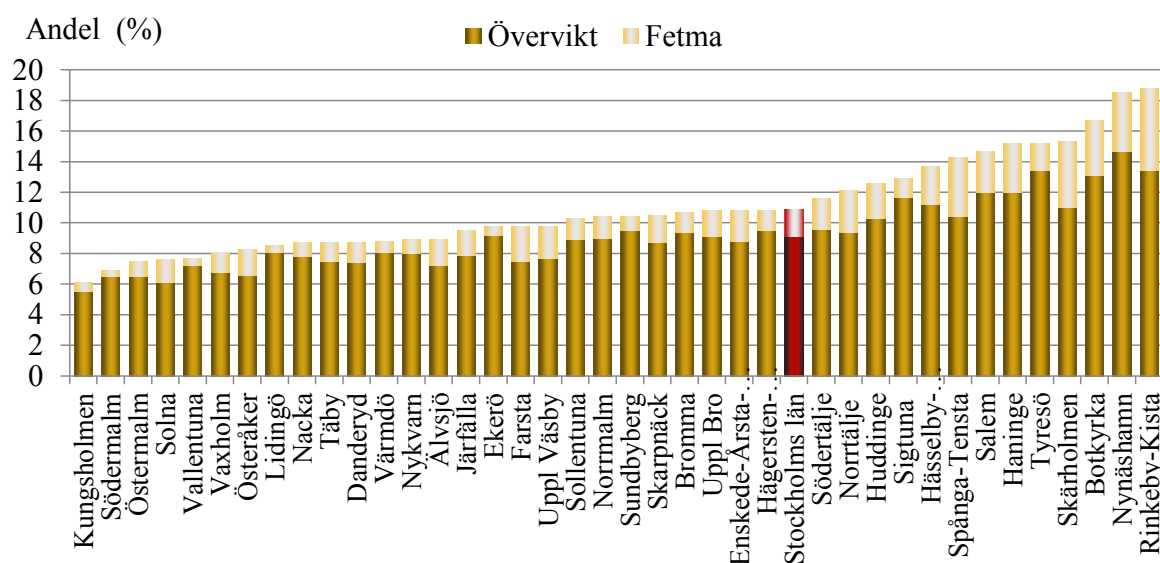
Figure 3. Prevalence of overweight and obesity in 4-year old children born 2007 in different municipalities of Stockholm County (from 'Barnhälsovård Årsrapport. Stockholms läns landsting; 2012) [15].

In comparison to other European countries Sweden does not have the highest child obesity numbers. The countries that top the childhood obesity list are several southern-European countries such as Italy, Greece and Spain, as well as the UK [16-18]. In the United States, 8% of children <5 years of age have been estimated to be obese [19] and it has even been suggested that obesity should be diagnosed as early as during infancy [20]. However, there is evidence for a stabilization in several parts of the world, including the US [21, 22].

Adults

Similar trends as in children have been observed for adults. Obesity rates in Swedish adults more than doubled between 1980 and 2000, however during the last decade the increase has slowed down [23]. In the national survey on living conditions conducted by Statistics Sweden (SCB) in 2011 over half of Swedish men and about 4 of 10 Swedish women were overweight or obese. About 11% were obese. As these numbers are based on self-reported weight and height, they are likely to be underestimates, which comparisons with studies that have included measured BMI data show. In different regional studies where BMI has been measured, a prevalence of obesity of 15-20% in men and 10-15% in women has been identified [23]. In 2009 12% of pregnant Swedish women were obese at their first antenatal care visit and 25% were overweight [24]. Recently prevalence of overweight and obesity among Swedish expectant parents was

reported, and the odds of being overweight or obese increased relative to the partner's overweight or obesity [25].

Consequences of childhood obesity

Childhood obesity has important negative consequences for health and quality of life both during childhood and also in later adult life, including physical and psychosocial effects [26-32]. Obesity acquired already during the preschool years is likely to be persistent [33] and obese children are likely to become obese adults [34].

FAMILY-RELATED OBESITY RISK FACTORS

There are many family-related factors associated with the increased risk for a child to develop obesity operating through genetic, environmental, social and behavioural mechanisms.

Parental obesity

Parental obesity has been established as the predominant risk factor for child obesity, likely owing to a combination of genetic, social and environmental factors [35-37]. The increased risk of overweight or obesity in the offspring of two obese parents, compared to two non-obese parents, has been estimated to over 6 times at age 4 (overweight) [38], 10 times at age 7 [39] and 14 times in 7-9 year children [13]. Having obese parents also increases the risk of childhood obesity persisting into adulthood [34, 37].

Associations between parental and offspring weight are likely to be determined by both hereditary and environmental factors, the latter including the intrauterine foetal environment. There is evidence for the mother-child associations being stronger compared to father-child associations [38-41]. This is suggested as support to an additional maternal impact through the intrauterine environment. However these associations depend on child age, and several other studies have found the impact of both parents to be of equal importance from 2-3 years of age [42-45] whereas at birth and during the infant years maternal BMI seem to have a clearly stronger influence on the childrens' growth than the paternal BMI [38, 43, 46]. There is some indication of the associations gradually becoming stronger as the child grows older [37, 38, 41, 43]. However, there are few longitudinal studies from childhood until adolescence presenting how parental-child associations in relative weight change over time [37, 47]. Also, the evidence of these associations in high-risk populations is limited [48]. There is no strong or consistent evidence concerning different parental effects by offspring gender, i.e. the mother-daughter and mother-son associations are similar in magnitude, and likewise paternal

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associations are similar for both offspring genders [45, 46], although contradictory evidence does also exist [47, 49, 50].

Genetics

It is well known that obesity is a hereditary disease and that genetic factors play a significant role for individual differences in relative body weight [51, 52]. From twin, adoption and family studies it has been estimated that the genetics contributes between 40 and 90 percent to obesity in both children and adults [52, 53]. Smaller but significant effects of genetics on weight have been seen in infancy [54, 55], and these effects then become gradually stronger with age [56]. Common obesity is polygenic, in other words it involves the additive effect of numerous genes and complex gene-gene, as well as gene-environment, interactions [57, 58].

Several individual gene variants have been identified and linked to an increased risk of obesity and obesity-related phenotypes (observable physical traits). The most important is FTO, the fat mass and obesity associated gene, first identified in 2008 [59]. Variants in the FTO gene predispose to both childhood and adult obesity and linked metabolic disorders, possibly through the regulation of energy intake and appetite [60-64]. Genetic risk can also be assessed with genetic risk scores, combining multiple gene variants associated with obesity. Such genetic risk scores have been associated with early rapid growth in infancy, early adiposity rebound, BMI throughout childhood and an increased risk of obesity [65-67]. However, the obesity genes identified have a modest effect on body weight, only 1-2% of the variance in BMI is explained by known obesity genes. Their predictive ability is poor, i.e. they do not accurately discriminate between obese and non-obese individuals [68]. The 'missing link' between the high heritability estimates from quantitative genetics and the impact of the identified gene variants, is referred to as the 'missing heritability [69], and may possibly be explained by epigenetic mechanisms.

Epigenetics

In addition to genetics, epigenetic mechanisms are likely to be involved in obesity development [70]. Epigenetic modifications are heritable changes in gene expression that do not involve alteration of the DNA, but can occur in response to environmental exposure. Epigenetic mechanisms are thus examples of gene-environment interactions. Epigenetic inheritance can be trans-generational, in other words the effects of epigenetic changes can be observed in later generations. For example, Swedish studies on subjects from Överkalix have shown that grandsons of Swedish men who were exposed to famine during childhood were less likely to die of cardiovascular disease [71], and that granddaughters of paternal grandmothers who had experienced sharp changes in food supply showed an increased risk of cardiovascular mortality [72]. A potential epigenetic

effect involves the effect of the foetus uterine environment on the subsequent health of the offspring. It has been shown that children born after their mothers had lost a substantial amount of weight due to obesity surgery experienced a decreased risk of obesity, compared to children born before surgery [73]. Even parents' diet before the intrauterine development stage may have epigenetic effects on offspring adiposity [74]. The links between the child's early nutritional environment and long term health may also involve epigenetic mechanisms [75].

Parental obesity co-morbidities

Family history of obesity-related co-morbidities - such as diabetes, gestational diabetes, cardio-vascular disease, hypertension - may in addition to parental obesity further increase the obesity risk for the child, most likely through heritable mechanisms [76-78].

Parental socio-economic status

Associations between socio-economic status (SES), often measured using parental education, and adiposity in children are predominately inverse in high-income countries [79, 80]. The effect of low parental SES is likely to be independent of parental obesity [13, 80], but may also interact with parental obesity contributing to an increased risk for overweight in children [81]. Low parental SES has been independently associated with high offspring growth already in infancy and higher rates of overweight and obesity during the preschool years [82-84]. The associations have partly been explained by infant feeding practices (breastfeeding), maternal smoking during pregnancy and maternal age [83, 84]. Level of urbanization of the residential area is another way of measuring the impact of socio-economic status. In Sweden childhood obesity is higher in rural compared to urban areas [13], however this may also be explained, to a considerable extent, by area level education [12].

Ethnicity

Ethnic background also affects obesity risk. In a large Swedish cohort of children 5 years old, the obesity risk were 2-3 times increased for children with a foreign-born mother, compared to children of Swedish ethnicity [85]. Similar results were seen in another study, where children of parents of non-Nordic origin showed a more than doubled risk of obesity [13]. Differences in obesity risk by race or ethnicity has recently been linked to a higher frequency of early life risk factors in these groups, which may contribute to the higher prevalence of obesity [86].

Family structure

A small number of household members, single-parenthood, living with grand-parents rather than parents and being the only or last-born child have been related to increased

risk of obesity [36, 87-89]. Having many siblings may be protective [87], even though paradoxically having siblings also is associated with more unhealthy dietary patterns early in life [90].

Early life factors

A large volume of research has focused on identifying early determinants of obesity, in the prenatal and early postnatal period [91]. Some of these identified or proposed early risk factors, in addition to parental adiposity and sociodemographic factors, include high maternal gestational weight gain, smoking during pregnancy, cesarean section, maternal age, single parenthood, high birth weight, rapid weight gain, no or short duration of breastfeeding and early introduction of solid foods [36, 39, 92, 93]. Synergic effects have been identified between the presence of parental obesity and unfavourable early life factors [94]. Together with parental factors, early life factors may be used to identify infants at highest risk of subsequent obesity [36, 93, 95, 96]. However, compared to parental obesity, these factors have much smaller effect on the child obesity risk [36].

Maternal gestational weight gain

A high maternal gestational weight gain (GWG) has been associated with an increased risk of obesity in children and later in life, partly mediated by birth weight [97, 98]. However, the effect on offspring weight and obesity rates is minor [97]. Children of non-obese mothers with high gestational weight gain have the highest risk for accelerated infant growth and subsequent obesity [99]. In a recent Swedish study, a higher GWG was associated with a higher birth weight, but not with preschool child BMI [100].

Parental smoking

Maternal smoking during pregnancy has been independently associated with a moderately increased risk for later overweight and obesity in childhood [101]. One suggested mechanism is the effect of nicotine exposure, via the placenta, on fetal growth and appetite control [101]. The impact of postnatal exposure of parental smoking on obesity risk is far less studied [102]. Observed associations with parental smoking, and especially postnatal exposure, may be affected by residual confounding by other factors that is common to both parental smoking and obesity [102, 103] even though most studies have taken some of these factors into account, such as parental age and socio-economic status[101].

Birth weight

Evidence supports an effect of the prenatal environment on obesity risk later in life, and birth weight is often used as an indicator of the conditions during foetal life [104]. A high birth weight has independently been associated with a higher BMI both in childhood and

adulthood [39, 105-107]. The risk of obesity may be doubled by a high birth weight, i.e. more than 4 kg, compared to a normal birth weight [107, 108]. However the relationship between birth weight and obesity is complex, as both high and low birth weight have been associated with increased adiposity in children [106, 107]. A higher birth weight has been associated with subsequent higher lean mass (fat free mass), whereas a lower birth weight has been linked to a higher proportion of fat mass [106]. A low birth weight has been associated with a postnatal rapid weight gain, which may mediate the increased obesity risk for children with low birth weight [106]. The effect of birth weight on obesity risk appears to be independent of parental BMI [107].

Early high or rapid growth
The association between infant growth and subsequent obesity has been extensively studied and the evidence from longitudinal studies of a modest effect is convincing [109-112]. Both high early weight [39, 109, 113] and rapid growth [93, 110-112] in infancy have consistently been identified as risk factors for obesity in children. Weight gain in infancy and early childhood have also been linked to an increased metabolic risk in young adults [114].

The effect of rapid weight gain on obesity risk decreases by age when obesity is measured and increases by a longer period for the weight gain measure [111]. A standard definition of rapid weight gain has been proposed by Ong and Loos: a change in weight SD score >0.67, which represents an upward crossing through at least one centile band on infant growth charts [111]. However, several other definitions have been used [109, 110]. The period between birth and 6 months have been suggested the most critical, even though rapid weight gain over other periods in infancy have also been studied in relation to obesity risk [111]. Regarding high infant weight, there has been no standard preferred measure; some measures used include BMI at 6 and 12 months, weight at 1 year, 'infant obesity' defined as weight centile > 90% at 3 and 6 months, or weight SD score at 8 months [109].

Breastfeeding
The proposed protective role of prolonged exclusive breastfeeding on child overweight has been extensively examined in observational studies [115]. Several meta-reviews of observational studies have reported a weak protective effect as concerns child overweight and obesity [116-118], however the risk of publication bias and residual confounding is likely [115]. Factors supporting the hypothesis that breast-feeding protects against obesity relate to breast-feeding behaviour, appetite regulation and to the biological component of breast-milk, such as a lower protein content. Breastfed babies have been seen to have a slower weight development during infancy [119]. However, there

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are many potential parental and child confounders of the association between breastfeeding and obesity risk, such as parental adiposity, socio-economic status, smoking and age and child birth weight and early weight gain [115, 120]. The experimental evidence is limited; one cluster-randomized controlled trial involving breastfeeding promotion showed no effect on child weight development [121]. However, this study may have lacked the statistical power to detect the slight effects on children's adiposity that have been reported in observational studies [115]. Nevertheless, if breast-feeding plays a role in preventing obesity, the magnitude of its influence is very limited [122].

Introduction of complementary foods
The timing of introduction of complementary and solid foods has also been studied in relation to obesity and early weaning has been suggested to increase the risk of obesity. However, the evidence is limited and inconsistent [123, 124].

DIETARY INTAKE AND EATING BEHAVIOUR

Dietary intake and obesity
The role of dietary intake in obesity development is obvious, as a positive energy balance, i.e. an energy intake exceeding energy expenditure, is required. However, the scientific evidence for associations between specific dietary components or dietary patterns and obesity has proven hard to identify [125, 126]. One major problem is the difficulties related to correctly measuring dietary intake. Additionally, it is not easy to distinguish the effects of individual dietary components from each other and from the potential confounding effects of related life-style aspects [127].

Several aspects of dietary intake have been proposed as obesogenic, such as energy-dense and nutrient-poor foods, large portion sizes, high snacking/meal frequency and eating while watching TV [128-130]. In reality there are few conclusive associations between energy intake, diet composition or intake of individual obesogenic (high-sugar, high-fat or energy dense) foods and subsequent overweight development in children [131]. Regarding individual foods, only one clear and positive association to obesity in children has been identified, for sugar-sweetened beverage consumption [132]. Regarding diet composition, a high protein intake in infancy has been linked to a higher relative weight and increased risk of obesity [133-135].

Analysing dietary patterns of the entire food intake in relation to obesity is receiving increasing attention, since examining multiple dietary factors in combination may better explain obesity risk than individual nutrients or foods [136]. The evidence from a recent

systematic review indicates that dietary patterns that are high in energy-dense, high-fat and low-fibre foods may predispose for later overweight and obesity in children [136]. However, most of this research has focused on children older than 5 years.

Determinants of children's dietary habits

Shaping children's dietary habits and food preferences starts very early in life [137]. Children's dietary patterns can be tracked through infancy and childhood [138, 139]. Thus the early establishment of healthy dietary habits may have important long term health consequences. Parents' dietary habits are likely to have an impact on children's. Preschool children's dietary habits and food preferences are associated with their parents', or at least their mothers regarding intake of fruit and vegetables, snacks, sweetened beverages, high-sugar foods, overall quality [140-144]. The parents' weight status may also be associated with children's dietary intake. Differences in dietary intake and food preferences between preschool children with lean and obese parents have been identified in a few studies, regarding the intake of vegetables, fat and beverages [145-147]. Other studies have not seen any differences in energy or fat intake, energy density or eating behaviour of pre-schoolers in relation to their parents' weight status [148-151]. In a large Swedish birth cohort, maternal overweight was associated with the early introduction of sweets and sugar-sweetened beverages as well as a higher intake of high-sugar foods at 12 months of age [140]. Also, parents (mothers) with lower levels of education, lower age, being smokers and having older siblings have all been associated with poorer quality in the child diet [140, 152-156].

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Dietary intake in Sweden

Dietary recommendations

A new edition of the Nordic Nutrition Recommendations was recently published [157], which replaces the previous Swedish Nutrition Recommendations from 2005. NNR 2012 is based on the latest scientific evidence available regarding associations between dietary patterns, foods, and nutrients and specific health outcomes. The new recommendations have an increased focus on the whole diet and emphasize the role that healthy and high-quality dietary patterns can have in the prevention of common, diet-related chronic diseases, such as cardiovascular disease, type-2 diabetes, cancer and obesity. NNR 2012 focuses more on diet quality, such as type of fats and carbohydrates, rather than amounts of foods.

Regarding prevention of obesity, NNR 2012 concludes that '*there is clear evidence to conclude that fibre-rich foods [...] and perhaps also dairy products, are associated with reduced weight gain. In contrast, refined cereals, sugar-rich foods and drinks, red meat, and processed meat are associated with increased weight gain in long-term studies*.' In Figure 4, the NNR 2012 recommendations regarding 'Food consumption changes for promoting health in Nordic populations' are summarized.

Increase	Exchange		Limit
Vegetables Pulses	Refined cereals	➡ Wholegrain cereals	Processed meat Red meat
Fruits and berries	Butter Butter based spreads	➡ Vegetable oils vegetable oil based fat spreads	Beverages and foods with added sugar
Fish and seafood	High-fat dairy ➡ Low-fat dairy		Salt
Nuts and seeds			Alcohol

Figure 4. Food consumption changes for promoting health in Nordic populations, NNR 2012 [157].

NNR 2012 covers nutrition recommendations for children and adults. Recommendations regarding the relative intake of macronutrients (fat, protein and carbohydrates) and different types of fat differ for infants and children from 2 years of age and adults. For infants 11-23 months old, the lower limit for fat intake is higher and the upper limit for protein intake is lower compared to older children and adults (Table 1).

In addition, the Swedish National Food Agency (Livsmedelsverket) has developed dietary guidelines for infants, children above 2 years of age and adults. The guidelines for infants were published in 2012 ('Good food for infants under one year'; 'Good food

for children between one and two years') and includes advice on what types of foods to serve and meal frequency.

Table 1. Recommended intake of macronutrients, NNR 2012 [157].

Macronutrient	Infants 11-23 months old	Children > 2 years and Adults
Fat	30 - 40 E%	25 - 40 E%
Protein	10 - 15 E%	10 - 20 E%
Carbohydrates	45 - 60 E%	45 - 60 E%
Saturated fat	< 10 E%	< 10 E%
Added sugars		< 10 E%

E% - Energy percent; % of the total energy intake.

Dietary intake in children

Swedisch preschool children have a too-high intake of sugar and saturated fat and their intake of polyunsaturated fat, including omega-3 fat, is too low as compared to recommendations [158-160]. Additionally, the quality of young children's food habits has implications for markers of metabolic health [160, 161]. A Swedish thesis from 2008, that studied the health implications of dietary intake in infancy and early childhood, concluded that dietary fat in infancy should be more focused on quality rather than quantity [160, 161].

Dietary intake in adults

Surveys of the dietary intake of Swedish adults have shown that the intake of sugar, saturated fat and salt is too high and that the intake of fruits, vegetables, dietary fibre and wholegrain is too low, compared with recommendations [162, 163]. Less than one of ten adults consumes five portions of fruits and vegetables per day and only three of ten eat fish and shellfish at least twice a week. Also, three of ten eat unhealthy foods such as candy, soft drinks and pastries, every day.

Obesity related eating behaviour patterns

Behavioural aspects of food intake are also important in relation to weight and obesity development. Specific obesity-related eating behaviours may explain part of the individual variation in weight in response to the obesogenic environment [164], and there is evidence that obesity-promoting eating behaviours are higher in obese than normal weight children [165-167]. Eating behaviour patterns develop as early as in infancy, as children's genetic predispositions and natural food responses are influenced by exposure to foods and by parental feeding practices [168]. Children have innate preferences for fat and sweet tastes and also an innate reluctance to try new foods (food neophobia), which

begins to develop at 18-24 months. Parents are advised to use repeated food exposures to help their children acquire broad taste preferences [169, 170].

Specific eating behaviours that have been associated with obesity include under-responsiveness to internal satiety cues, such as a low satiety responsiveness and a high speed of eating, and also an over-responsiveness to external food cues such as taste, smell and availability [164, 171]. On the other hand, fussy or picky eating, a lack of interest in food and unwillingness to taste new foods, may lead to a reduced intake of food. Also, appetite may be reduced or increased under the influence of negative feelings, such as anger and anxiety. Individual differences in children's eating behaviours can be measured using validated questionnaires [172-174], where the Children's Eating Behaviour Questionnare (CEBQ) is one of the most widely used [174].

Eating behaviours have been seen to vary by child age. Normally, the ability to self-regulate food intake decreases with age, whereas the interest for food and responsiveness to taste and availability normally increases with age [175]. Also food fussiness normally decreases after the age of 3 years, as food neophobia diminishes [175]. Problematic eating behaviours are quite common and consistent among preschool children, approximately 20% in children 2-4 years old may be overeating [176]. Appetite traits being evident very early in life is plausible as eating behaviours have been shown to be highly heritable [177-181].

OTHER LIFESTYLE AND BEHAVIOURAL RISK FACTORS

There are several other lifestyle and behavioural factors of importance to obesity development that have not been studied in this thesis; these will be briefly described.

Physical activity and sedentary behaviours

Physical activity and inactivity are balanced against dietary behaviours to determine whether or not a positive energy balance and possibly weight gain is experienced [125, 182]. The available evidence suggests that increased physical activity and decreased sedentary behaviours, such as screen time, are protective against adiposity and weight gain, even though the effects may be modest [183, 184]. However, as a physically active lifestyle may develop already early in childhood and track from youth to adulthood, early promotion of physical activity is important [185]. Energy-balance related behaviours – diet, physical activity and inactivity - have been seen to cluster, leading to increased risk of obesity [125, 182, 186, 187]. Just to give one example: TV viewing, which may be the screen activity with the strongest effect on weight in young children, is associated with a higher consumption of unhealthy foods, such as snacks and sweet beverages [128, 182, 188]. Thus interventions to prevent obesity need to focus on all these lifestyle aspects to be efficient [189, 190].

Sleep duration

Short sleep duration has consistently been associated with an increased obesity risk in children [191, 192]. Sleep processes are involved in the regulation of hormones related to growth and energy homeostasis, which may explain the association with obesity [191]. Also, sleep patterns are closely linked to the other energy-balance behaviours. Sleep loss increases appetite, affect food approach eating behaviours and is associated with a higher intake of obesogenic foods [193, 194]. Children that are short of sleep may be less likely to engage in active play and more likely to spend time in sedentary activities [187]. A good sleep quality is promoted by physical activity during the day [195]. Sleep duration should therefore be considered as a modifiable behavioural target for prevention [190-192].

Child temperament and behavioural problems

Child temperament and behavioural problems may affect child weight development and obesity risk. Associations between psychological problems, such as ADHD and other neuropsychiatric disorders, and obesity have been mostly studied and identified in school-aged children [196-198]. In preschool children the evidence is limited and less clear [199, 200], but child temperament may affect weight gain in infants [201] and have been linked to eating behavior in young children [202, 203].

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Parenting practices

Parental practices, both general parenting style and specific parental feeding-related behaviours, are also potential determinants of children's dietary behaviours and weight development [204, 205]. Specific feeding-related behaviours include rules around child food intake (control, restriction), pressure to eat, encouragement, emotional feeding (offering food to soothe, comfort or distract the child) and instrumental feeding (offer food as a reward). Parental practices and behaviours may affect child eating behaviour and food intake [206-208], however parental behaviour may also be in response to child behaviour and weight status [209]. Evidence to prove the impact of parental practices on children's weight development is not conclusive [209, 210].

PREVENTION OF OBESITY

Due to high obesity rates, negative consequences of childhood obesity and lack of efficient treatment effects [211, 212], prevention should be given a high priority. Behaviours that are likely to contribute to obesity - unhealthy food habits, frequent sedentary behaviour and low physical activity levels – are prevalent already during early childhood, and are likely to persist throughout childhood [139, 185]. Early intervention to positively impact on weight and obesity-promoting behaviours is therefore vital.

Primary prevention

There is a general agreement that childhood obesity must be addressed by means of primary prevention, in other words directed at healthy, normal weight children. Either through general prevention directed to all children of a population or through targeted prevention directed to a risk group, such as parents with obesity or low socio-economic status or low SES areas. A number of different settings or arenas are available for the prevention of childhood obesity: school, child care, child healthcare, family/home and maternal antenatal care. Especially for young children there are multiple options for intervention settings, however the involvement of parents has been identified as one key success factor [213].

Prevention effects and success factors

The evidence on the effects of obesity prevention initiatives is rapidly increasing and extended to new settings and age groups. The first Cochrane review of controlled preventive intervention studies in children was published in 2005 and included 22 studies, of which most were school interventions. It concluded that less than 15% of the interventions had been effective on weight outcomes and that high-quality studies were lacking [214]. An updated Cochrane report on the same subject was published in late 2011,

now including 55 studies [213]. The evidence for beneficial effects of prevention programs targeting children 6 to 12 years of age in school settings had increased considerably [213, 215]. There have been far fewer high-quality studies in preschool-aged children, although the limited evidence suggests that larger intervention effects may be achieved in this age group [213]. Additional reviews of prevention programs in preschool children [216-218] have shown that behaviours that contribute to obesity can be positively impacted in different settings. However, not all interventions have been proven efficient in affecting children's relative weight or weight status [216, 217]. Some studies have focused specifically on parental factors in the role of obesity prevention [218].

Important conclusions drawn from available evidence on obesity prevention in young children are that [213, 216-219]:
- a healthy lifestyle should be promoted from an early age
- parents should be involved
- parents need support from professionals
- long-term follow up is necessary
- programs should be thoroughly evaluated
- in order to achieve long term sustainable impacts it is necessary to identify how effective intervention components can be embedded within existing health, education and care systems

In a systematic review focusing on home-based prevention beneficial effects on the children's dietary and sedentary behaviours were reported, but without any significant effect on weight outcomes [220]. The review concluded that the strength of evidence is so far low to support the effectiveness of home-based child obesity prevention programs, and that additional research is needed. So not surprisingly, more evidence on what works is required to implement efficient interventions, most importantly regarding relevant methods of identifying at-risk children in early childhood and which key behavioural measures to target.

Behaviours to target
Important modifiable behavioural targets proposed for inclusion in interventions in early childhood, based on current evidence, include food intake, eating behavior patterns, parental practices and family interaction, physical activity, sedentary behaviours and sleep habits [189, 221]. Some specific examples of proposed preventive messages are [221]:
- avoiding sugar-sweetened beverages, drinking water instead
- replacing high-sugar, energy-dense and empty-calorie foods with fruits and vegetables at all meals and snacks

- providing opportunities for children to participate in physical activity at least 1 hour per day
- reducing screen-time
- promoting sufficient and high-quality sleep

ASSESSING DIETARY INTAKE

Challenges in diet assessment

Measuring and analyzing the dietary intake of individuals is a challenging task. There are several different diet assessment methods for reported dietary intake, prospective and retrospective, suitable for different settings and purposes [222, 223]. However no method lacks shortcomings or is capable of perfectly capturing the true intake of foods, energy and nutrients. In order to assess the validity of a dietary assessment, it needs to be compared with one or several objective measures that reflect, but are independent of, food intake [223]. Biomarkers provide objective data on specific aspects of dietary intake and can be used to evaluate the validity of dietary assessments. However, biomarkers for the intake of many nutrients are lacking, limiting the ability to fully estimate the errors associated with reported dietary intake [222].

Misreporting

The major challenge common to all dietary assessment methods is mis- and underreporting, which is especially apparent in obesity-related research, as it has been shown that obese individuals, both adults and children, are more prone to underreport in general and unhealthy foods in specific [224-226]. Other common problems in diet assessment are difficulties in estimation of portion sizes, that retrospective methods rely on memory and that the food databases necessary for nutrient calculation provides a finite amount of food items. For young children, parents and other caregivers are responsible for reporting food intake. Parental reports of young children's intake may be accurate when the parent is present to observe the child's intake, but parents are not reliable reporters of their child's out-of-home intake [227]. Food records of toddlers reported by parents have been shown to be reasonably accurate [228]. However, the parents' own weight status, relationship to food and concern for the child may affect the quality and degree of underreporting of the child's intake [143, 150].

Under-reporting of energy intake

Under-/misreporting of energy intake is common in children as in adults [229]. A method for identifying plausible under-reporters of energy intake, developed by Goldberg and Black, is commonly used in diet research [230, 231]. For a reported energy intake to be

realistic it must meet, at a minimum, basal metabolic requirements. The ratio of reported energy intake and estimated basal metabolic rate (BMR) is calculated and compared to an interval of plausible values, where the lower cut-off represents a level of energy intake regarded to be implausible. Individuals below this cut-off are classified as under-reporters. Often under-reporters are not excluded from analyses but instead the analyses are repeated to see if the results are affected [232]. It is important to note that this method can only identify underreporting in individuals with an apparent deficient energy intake. Since misreporting is likely to occur along the whole range of energy intake, this method is unlikely to capture all mis- and underreporting.

Diet assessment methods

Two different diet assessment methods have been used in this thesis: a food frequency questionnaire for parents and a food record for infants, registered by parents. A general description of these methods is provided [222, 223]. Additionally some other common methods are briefly mentioned.

Food frequency questionnaire

Food frequency questionnaires (FFQ) assess habitual diet by asking questions on how often different food items or food groups are eaten, e.g. per day or week, over a certain period (e.g. the last 6 months). The number and types of food items and groups included depend on the purpose of the questionnaire, but the foods selected should be major sources of the nutrients of interest, contribute to the variability in intake between individuals and be commonly consumed by the study population. To be able to capture energy intake and most nutrients, a FFQ needs to be very comprehensive with hundreds of items. A more limited FFQ (~20 items) may be used to describe specific diet quality aspects. A FFQ may also include estimates of portion sizes, what is termed semi-quantitative FFQ. A FFQ needs to be tailored to the specific population to include foods or food groups commonly eaten. FFQs are often used in large-scale epidemiological studies as they are easy to fill in, collect and analyze. Over-estimation of food intake is a problem, particular for foods eaten less often or for foods perceived as healthy. It has also been suggested that measurement errors of FFQs have produced false negative results in studies of diet-disease associations [233].

Food record

In a food record (also called food diary) all food items and drinks are registered prospectively at the time of consumption, along with detailed information about portion sizes, brands, energy and nutrient content of foods and cooking methods. In order to capture the usual food intake for an individual at least 3 days are required, and both weekdays and weekend days should be represented. Portion sizes and amounts can be

estimated or weighed. Detailed instructions, and for estimated food records additionally booklets with pictures of portion sizes, must be provided. The 7-day weighed food diary is referred to as 'gold standard' even though this method is also prone to underreporting [234]. The advantage of the food diary is that it does not rely on memory and that both quantitative and qualitative aspects of dietary intake can be analyzed. A specific drawback is that the process of completing the food record may affect the food intake. Food records are also burdensome to fill in and require motivated participants. However, it is the recommended method for assessing dietary intake in preschool children [235]. In order to calculate energy and nutrient content of a food record, all food and drink items of the records need to be entered into a software package using an underlying food database.

Other diet assessment methods
Dietary recall is another diet assessment method commonly used in research. This is a retrospective method where an individual is asked to describe everything he/she ate or drank during the previous day or the preceding 24 hours. Multiple food recalls are required to capture the usual food intake of an individual, but single recalls are adequate for describing the dietary intake on the group level. Diet history is a retrospective method often used in clinical settings rather than in research. A diet history describes the usual food intake over a longer period of time, e.g. 6 months or a year. It is carried out through a structured interview performed by an educated health professional. Lately, new promising diet assessment methods involving digital camera and mobile telephone technology have emerged [236, 237].

Biomarkers
The ultimate goal of a biomarker is to measure the 'true diet intake'. Biomarkers can be used to validate reported intake, to assess exposure, to control compliance in dietary interventions and to directly measure risk-disease associations [238]. A biomarker can be defined as a molecule that is associated with the exposure of a specific food or a nutrient, and can be measured in the body, for example in blood, saliva or urine. An ideal biomarker is easy to collect and measure, sensitive to small differences in dietary intake and correctly reflects the dietary intake over a specific period, long or short-term. There are different types of biomarkers. Recovery biomarkers are gold standard and offer very accurate estimates of energy and protein intake using the DLW (doubled-labelled-water) method and measures of urinary nitrogen respectively. The DLW method is relatively expensive and technically complicated and the measurement of urinary nitrogen requires samples of urine collected for at least 24 hours. Another type of biomarker is known as concentration biomarkers that can estimate the relative intake of specific nutrients, i.e. they correlate to the intake but absolute amounts cannot be

estimated. Examples of concentration biomarkers are fatty acids and carotenoids in the blood.

Biomarkers for fat intake

Biomarkers of fat intake are particularly valuable, since the effect of fat intake on health and diseases is often of interest but challenging to study with traditional diet assessment methods, for several reasons. A specific under-reporting of dietary fat among obese subjects [239] makes it difficult to investigate the 'true' associations between dietary fat intakes and obesity. Also, the between-subject variation of both amount and type of fat in the diet is quite large, compared to other macronutrients such as protein, and many fats are 'hidden' in foods. Individuals are also sensitive to questions about fat intake in their diets [240].

There is no biomarker for total fat intake available [238]. However, the relative intake of dietary fatty acids (FA) can be estimated by measuring fatty acid composition in different body tissues, such as plasma or serum, cholesterol esters (CE), phospholipids (PL), erythrocytes, whole blood and adipose tissue [238]. There is a great variation in turnover rates of dietary fatty acids in the different tissues, and thus they reflect fat intake over different periods of time. FA in adipose tissue reflect long-term fat intake (years), whereas FA in erythrocytes and in serum or plasma correspond to more short-term intake (months and weeks respectively). However, adipose tissue is rarely used in epidemiologic studies because of the difficulty in obtaining samples [241].

The FA composition in plasma or serum has been identified as an indicator of usual dietary fat quality in both adults and children [228, 242]. One common analysis technique for FA composition in serum/plasma is gas liquid chromatography [243]. The fatty acid pattern analysed is expressed in percent of the total amount of identified fatty acids and can be related to the relative intake of dietary fatty acids. Fatty acids that are not synthesized in the body are those best suited as biomarkers. These include essential polyunsaturated omega-3 and omega-6 fatty acids (linoleic acid and a-linolenic acid), saturated fatty acids found in milk fat, but also polyunsaturated (omega-3) fatty acids in fish fat (EPA, DHA) are good biomarkers [238, 244, 245]. The major saturated (except odd-chain FA) and mono-unsaturated fatty acids both reflect dietary intake and metabolism (i.e. synthesis and desaturation), and are thus generally weaker biomarkers to be used in observational studies.

Whole diet analyses

The diet assessment methods described above provide data on intake of energy, specific nutrients and food items or groups, which can be analysed for traditional nutrient- or food-based associations with obesity. However, daily diet is composed of numerous food items with many relationships between nutrients and foods, and associations between diet and obesity may more efficiently be studied using a measure of the whole diet. The advantages of using whole-of-diet measures include the opportunity to assess the overall diet quality, which in turn can be related to parental, child and socio-demographic characteristics. Additionally the combination of food factors may improve the power to detect diet-disease associations [246]. There are two types of overall dietary measures, a-priori defined dietary indexes and posteriori data-driven dietary patterns [247, 248]. The evidence base for applicability to child obesity research is still limited [136], but several recent reviews show that the use of whole-of-diet measures in young children is increasing [127, 246]. However more research is needed to establish the predictive validity of these methods as concerns health outcomes such as obesity in childhood [127].

Dietary index

A dietary index usually reflects dietary guidelines or current knowledge about dietary aspects of importance for a specific outcome, such as obesity [127]. A dietary index is determined a priori based on a set of dietary components such as nutrients, foods or food groups. The dietary components may be weighed to reflect each component's relative importance [246]. Each component provides points to a total score, which ranks individuals having more or less healthy dietary habits. Dietary indices may be applied to both small and large samples. In this thesis a previously-developed food index was applied to the parent's food intake data. Additionally, diet quality indicators were defined and applied to the child diet data, although these were not summarized into an overall score.

Dietary patterns

In dietary pattern analysis food intake is examined using cluster or factor analysis to group together individuals who eat similar types of foods or to identify patterns of foods often consumed together. Examples of dietary patterns that may emerge are 'Healthy', 'Unhealthy', 'Western' and 'Traditional'. In infancy, examples of typical dietary patterns are 'Infant guidelines' and 'Adult pattern' [90]. Dietary pattern analysis requires large samples and was not applicable for the studies in this thesis [249].

AIMS

The overall aim of this thesis was to measure the impact of family hereditary, environmental and dietary obesity risk factors on children's relative weight in high-risk populations.

Specific aims were:
To analyse the degree of obesity at ages 7 and 15 in relation to parental BMI, exploring the impact of gender, birth weight, parental obesity-related co-morbidities, parental educational level and treatment in a cohort of obese children. An additional aim was to analyse whether age at onset of obesity was associated with parental BMI. (Study I)

To compare infant growth during the first year between children at high and low risk of developing obesity, based on both parents' weight status and educational level, and to examine which early-life factors may mediate the effects of parental obesity risk on infant growth. (Study II)

To examine the factor structure and reliability of the Swedish version of the Children's Eating Behaviour Questionnaire in a population of preschool children 1-6 years old, and to examine associations between eating behaviours and child age, gender, relative weight and parental weight. (Study III)

To compare infant dietary behaviours (dietary intake and eating behaviours) and parental food intake in families of high and low obesity risk based on both parents' weight status. Additional aims were to study associations between child and parental dietary intake and between children's relative weight, dietary intake and eating behaviours. (Study IV)

To compare the reported food intake in infants and parents with an objectively measured biomarker for fat quality. (Study IV)

Hypotheses were:
High parental BMI would be associated with higher degree of obesity in childhood and adolescence and lower age at onset of obesity. (Study I)

High parental BMI and low parental educational level would interact to an increased infant weight and weight gain during the first year. (Study II)

Obesity related eating behaviours would vary by age and would be associated with weight in preschool children. (Study III)

Dietary intake in one-year old infants would not be associated with parental adiposity, however differences in food intake between normal weight and overweight/obese parents were expected. (Study IV)

METHODS

STUDY DESIGN AND POPULATION

An overview of the design and population for each of the studies is presented in Table 2.

Table 2. Design and population in each study.

Study	Design	Population	Recruitment of population
Study I	Longitudinal cohort	213 obese children and their parents Longitudinal weight data 2-15 years	Patients enrolled at National Childhood Obesity Centre between 1997 and 2010. Registered in the BORIS database 2005-2006
Study II	Longitudinal cohort (Baseline of RCT)	197 children and their parents Longitudinal weight data 0-1 year - 144 high-risk - 53 low-risk	Families recruited to Early STOPP mainly via child healthcare centres in Stockholm County 2010-2012
Study III	Cross-sectional	174 children and their parents Children 1-6 years old	Via five kindergartens in Stockholm County in 2010
Study IV	Cross-sectional (Baseline of RCT)	193 children and their parents Children 1 year old - 143 high-risk - 50 low-risk	Families recruited to Early STOPP mainly via child healthcare centres in Stockholm County 2010-2013

In Study I, longitudinal data on weight and height for a cohort of obese children, treated at the National Childhood Obesity Centre ('Rikscentrum Barnobesitas') at Karolinska University Hospital were studied. The data were retrieved from the Swedish national healthcare quality registry for childhood obesity (BORIS, Barn Obesitas Register i Sverige), where data on weight development and obesity treatment is registered for paediatric patients.

Studies II and IV were based on baseline data from the longitudinal randomized controlled trial Early STOPP (Early Stockholm Obesity Prevention Project). Families with one-year old children at high and low risk of developing obesity based on parental weight status were recruited mainly via CHC centres in the Stockholm county between 2010 and 2013.

In Study II, longitudinal data on weight and height during the first year of life were studied in infants at high and low risk of obesity. Data on weight and height measured at

child healthcare centres during the first year were reported by the parents as part of the baseline measurement of Early STOPP.

Study III used cross-sectional data on eating behavior patterns and relative weight for children 1-6 years old, recruited through five kindergartens in two areas of Stockholm County.

In Study IV, cross-sectional data on child and parental dietary behaviours – dietary intake and eating behaviours - reported by parents, and measured child relative weight at age one were studied. The population consisted of high- and low-risk families.

Early STOPP

Early STOPP is an ongoing randomized controlled (RCT) obesity intervention with the primary aim of studying if obesity can be prevented in high-risk preschool children up to 6 years of age. The five-year intervention targets overweight and obese parents with infants recruited before age one from child healthcare (CHC) centers within Stockholm County. A reference group of families where both parents are normal weight is followed during the same period (low risk group). The high-risk families are randomized to intervention and control groups through cluster randomization of CHC centres. The intervention is delivered by trained coaches in regular (two to four times per year) individual coaching sessions with the parents in their home, regarding the child's dietary, physical activity, sedentary and sleeping behaviours. Early STOPP was initiated in 2009, and families were included into the project on a continuous basis during 2010-2013. In total, 242 families have been at baseline measurements, of these 182 high-risk families participate in the intervention and 60 families are low-risk families. In this thesis baseline data from the Early STOPP high-risk and low-risk families are used (Studies II and IV).

Sample sizes

Study I. This was an explorative study. The sample size was given by registered data in the BORIS database and was further reduced substantially due to missing data in the outcome and primary predictor variables.

Studies II and IV. The size of the high-risk population was given by the power calculation for the Early STOPP RCT. The intervention was planned to include 200 families, 100 in each group, providing 80% power at the 5% significance level (double-sided test), considering a 15-20% dropout rate (at least 168 high-risk families were required). The power calculation was based on detecting a 50% lower prevalence of child overweight and obesity in the intervention group, 20% in the intervention group

compared to 40% in the control group, at age 6 years. The size of the low-risk population in Early STOPP was planned to 50 families.

Study III. Sample sizes of similar validation studies on the same questionnaire was used as the basis for the number of questionnaires distributed taking into account an estimated response rate of 50%.

Population characteristics

In Table 3 detailed characteristics of the populations in each study are presented. Studies I, II and IV include high-risk populations whereas Study III is performed on a mix-risk population. A low-risk population is also included in Studies II and IV enabling comparisons of outcomes with the high-risk population.

Obesity risk was primarily determined by the prevalence of parental obesity. In Study I, the clinical sample of obese children, 34% of the mothers and 31% of the fathers were obese. The study populations in Studies II and IV both originate from the Early STOPP study, which specifically targets both high-risk and low-risk populations. In the high-risk populations in Studies II and IV, the prevalence of maternal obesity was 62% and 57% respectively and in fathers 44% (these figures were not reported in the studies), whereas no parents were obese among the low-risk families. The proportion of high-risk families with two obese parents was 15% in Study I and 24% in Studies II and IV. In the low-risk populations, all parents were reported to be normal weight at the time of recruitment, however at baseline a small proportion of the low-risk parents had increased their BMI and were classified as overweight. Study III was classified as a mix-risk population, including some obese parents (3%).

Regarding other parental obesity risk factors, the prevalence of low parental education level (defined as only elementary or secondary education, i.e. a maximum of 12 years of school, see below) and foreign ethnic background was higher in the high-risk populations compared with the low-risk groups. Based on both parents' educational level (see definition below), 37%, 35% and 29% respectively of the high-risk families in Studies I, II and IV showed a low educational level. The corresponding numbers in the low-risk families were 6% and 10% in Studies II and IV respectively. In Study II the populations were additionally divided into high and low risk by family education (see Table 1 of Study II).

Table 3. Study populations, divided into high and low risk on basis of parental BMI/weight status.

	Study I	Study II		Study III	Study IV	
	High risk	High risk	Low risk	Mixed risk	High risk	Low risk
N	231	144	53	174	143	50
Child gender (% boys)	49	51		50	48	
Child age	7-15	0-1		1-6 (m 3.8)	1	
Child BMI SDS [1], mean (SD)	4.9 (1.9) age 7 4.5 (1.5) age 15	-0.37 (1.2)	-0.49 (0.9)	-0.41 (1.1) (n = 47)	-0.46 (1.1)	-0.40 (0.9)
Child weight status (%) [2]	76 OB age 7 81 OB age 15	-	-	100 NW (n = 47)	-	-
Maternal BMI, mean (SD)	28.5 (5.8)	32.6 (6.3)	22.0 (1.9)	22.6 (3.4)	31.7 (6.3)	22.5 (2.2)
Paternal BMI, mean (SD)	28.5 (4.6)	29.9 (4.9)	23.0 (1.5)	24.9 (2.5)	29.9 (4.7)	23.0 (1.5)
Maternal weight status (%)	34 OB 34 OW	62 OB 22 OW	0 OB 11 OW	3 OB 11 OW	57 OB 25 OW	0 OB 12 OW
Paternal weight status (%)	31 OB 48 OW	44 OB 35 OW	0 OB 9 OW	3 OB 37 OW	44 OB 35 OW	0 OB 6 OW
High risk - Parental weight status (%) [3]	69	100	0	11	100	0
Two obese parents (%)	15	24	0	0	24	0
Parental education (%) [4]	20 high 28 medium	-	-	-	-	-
Maternal education (%) [5]	-	46 low	26 low	28 low	40 low	26 low
Paternal education (%) [6]	-	51 low	25 low	31 low	52 low	36 low
High risk - Parental education (%) [6]	37	35	6	18	29	10
Parental foreign ethnic background (%) [7]	-	19	13	24	19	12

Shaded cells: results not reported in the original studies

NW: normal weight; OW: overweight; OB: obese

[1] Studies I and III: Calculated using the French reference [250]; Study II and IV: calculated using the Swedish reference [9]

[2] Calculated according to IOTF/Cole [7]; not determined for one-year old children in Studies II and IV.

[3] Two overweight or at least one obese parent.

[4] Study I: High: at least one parent with tertiary education (academic degree); Medium: at least one parent with post-secondary education.

[5] Studies II, III and IV: Low: ≤ 12 years of school. High: > 12 years of school.

[6] Studies II, III and IV: Neither parent > 12 years of school.

[7] One or two parents of foreign origin; in Studies II and IV of non-Nordic origin; in Study III of non-Swedish origin.

Inclusion and exclusion criteria

Study I: Children registered in the BORIS database and enrolled at 'Rikscentrum Barnobesitas' between 1997 and 2010 were reviewed for inclusion. Only children having complete data for all three outcome variables (age at obesity onset and relative weight at age 7 and 15) as well as for parental BMI were included. Children with diagnoses that can cause secondary obesity were excluded (Prader-Willi, Laurence-

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Moon-Bardet-Biedl, Fragile-X, Morbus Down, melanocortin-4 receptor deficiency). Additionally preterm children (born before week 37) and children with an unknown gestational age were excluded in analyses including birth weight as a covariate.

Early STOPP – common to Studies II and IV: Obesity risk was assessed by reported maternal pre-pregnancy BMI and current paternal BMI. Families were eligible for the high-risk group if both parents were overweight (BMI ≥ 25) or at least one parent was obese (BMI ≥ 30) and for the low-risk group if both parents were normal weight (BMI < 25). Parents had to be able to communicate in Swedish. Infants with chronic health problems likely to influence growth or lifestyle habits were excluded.

Study II – additional criteria: Early STOPP baseline data collected until May 2012 were used. Pre-term children (born before week 37) were excluded.

Study III: Children 1-6 years old for whom parents had completed the questionnaire on eating behaviours and additional background questions on children's age and parental BMI were included. Children with a disease with a potential impact on eating behaviours were excluded (such as diabetes, lactose intolerance, acid refluxe disease). Reported child weight and height data was only used if measured within two months prior to collection of data.

Study IV – additional criteria: Children for whom the parents had registered a food record for at least three days at the baseline visit to Early STOPP were included.

DATA COLLECTION AND DEFINITIONS

An overview of data collected or derived in each of the studies is presented in Table 4.

Data collection procedures
In Study I, all data were retrieved from the BORIS database, previously collected at clinical visits to the treatment center. In the following data definitions details of the origin of each variable are described.

In Studies II and IV, measurements (anthropometrics, blood samples) were collected by trained staff members at the research centre at Karolinska University Hospital Huddinge, using standard operating procedures and calibrated instruments. Questionnaires, one for each parent and one for the child, were mailed to the parents prior to their visit to the research centre. Parents were also instructed to complete a 4-

day food record for their child before the visit. Questionnaires were checked for completeness during the visit.

In Study III, questionnaires and a covering letter were distributed at five kindergartens, after having obtained approval for participation from the kindergarten management. One reminder notice to respond to the questionnaire was distributed at the kindergartens to all children contacted. The parents completed the questionnaire at home and mailed it back to the research team.

Table 4. Data collected/derived in each study.

Data	Study I	Study II	Study III	Study IV
Child anthropometrics (weight, height, BMI SDS) [1]	M	M + M/R	M/R	M
Child gender	X	X	X	X
Child age	X	X	X	X
Child age at onset of obesity	X			
Child first-born				X
Child birth weight	X	X		X
Child gestational age	X	X		
Child basal metabolic rate (BMR)				X
Child diagnoses for exclusion	X	X	X	
Child early feeding:				
Duration of exclusive breastfeeding		X		X
Age at introduction of solid foods		X		X
Child eating behaviours (CEBQ)			X	X
Child dietary intake				X
Child obesity treatment >1 year	X			
Parental anthropometrics (weight, height, BMI) [1]	R	M	R	M
Parental education	X	X	X	X
Parental co-morbidities	X			
Maternal gestational weight gain		X		
Parental age		X		X
Parental ethnicity		X	X	X
Parental smoking habits		X		X
Parental food intake				X
Fatty acid composition in plasma (child and parents)				X

[1] M: measured. R: reported.
M/R: In Study II and III measured weight and height records from child healthcare were reported by parents.

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Data processing and definitions

Child data

Weigh, height, BMI and weight status

In Study I children's weight and height had been measured wearing light clothing during clinical visits at the treatment centre and was available in BORIS for annual visits. In Study II the children's weight and height records measured at CHC centres between birth and 12 months were used to calculate the outcome variables 'BMI SDS at 3 months', 'BMI SDS at 6 months' and 'rapid weight gain 0-6 months'. At 12 months, weight was measured to the nearest 0.1 kg without clothing using a baby scale (Seca 376, Hamburg, Germany) and height was measured horizontally to the nearest 0.1 cm (Seca 712, Seca, Hamburg, Germany). The mean of three measurements was used. BMI (body mass index) was calculated as weight/height^2. In Study III the parents reported their child's most current weight and height record measured at the CHC centre. In Study IV weight and height at age one year were measured as described in Study II, see above. Children in Studies I and III were classified as normal weight, overweight or obese according to international age- and gender-specific BMI cut-off points, defined by the International Obesity Task Force [7]. Weight status according to this definition can only be determined in children from the age of 2 years and was not used in Studies II and IV.

BMI SDS

Two different reference populations were used to calculate BMI SDS, the children's relative weight, in this thesis: one older French material by Rolland-Cachera collected in 1953 [250] and a Swedish population of children born 1973-75 published by Karlberg [9]. In Studies I and III, BMI SDS according to the French reference was used. In Studies II and IV, BMI SDS was determined using the Swedish reference. More details are provided below in the section *Outcome and independent variables*.

Age at onset of obesity

See the description in the section *Outcome and independent variables* below.

Treatment

In Study I, data on treatment was used as an independent variable in the analyses between child and parental relative weight. The dichotomous variable 'treatment over at least one year' was created based on whether child had been in treatment for at least 12 months before the age of 15.

Infant rapid weight gain
See the description in the section *Outcome and independent variables* below.

Basal Metabolic Rate
Basal metabolic rate (BMR) is the energy expended daily for a person in rest. In Study IV the children's BMR was calculated according to the Shofield equation, using gender, weight and height [251]. BMR was used in to identify potential under-reporters of energy intake.

First-born
In Study IV data on 'first-born' was used. This variable was derived from questions on number and age of siblings of the child. First-born twins without older siblings were defined as first-born.

Infant early feeding
Data on infant early feeding was used in Studies II and IV. A 'short period' of exclusive breast-feeding was defined as less than 2 months. Age at introduction of solid foods was measured in months. In Study IV breastfeeding status at age one was additionally used (breastfed/not breastfed).

Dietary intake at age one
Data on the children's dietary intake were measured in Study IV using a three- or four-day estimated food record. Detailed information about all food and drink consumed was registered. The parents were instructed to complete a food record over four consecutive days, including two weekend days. Only records kept for at least three full days were used. Detailed instructions and booklets with pictures of portion sizes of typical meals and sizes of common foods were provided. The quality of the food records was assessed by the research team. Amounts of breast-milk were approximated using the time noted for breast-feeding meals and an estimation of the amount per minute at age 12 months [252]. Energy and nutrient content was calculated using the Dietist XP software (version 3.2, Kost- och näringsdata, Bromma, Sweden). Dietary supplements were not included in the calculations.

Dietary intake variables used in analyses were total energy intake (kJ), the proportion of the energy intake (E%) from protein, carbohydrates, fat, saturated fat (SFA), monounsaturated fat (MUFA) and polyunsaturated fat (PUFA) and additionally the energy adjusted intake of dietary fibre (g/MJ). Dietary intake was compared with the Nordic Nutrition Recommendations [157]. Potential underreporting of the children's energy intake was estimated by comparing the ratio of reported mean energy intake and

basal metabolic rate (EI:BMR) to the adapted Goldberg lower confidence interval cut-off [231]. In this calculation references for physical activity levels, inter-subject variation in energy intake, BMR and physical activity for young children were taken from Black [230].

The food records were also used to define diet quality indicators, representing potentially obesogenic or obesity-protective habits and the degree of introduction to family meals. The indicators were chosen based on 1) being included in dietary indices or patterns that have been used to study links between whole diet and health in young children [127] and 2) representing dietary intake components of the Early STOPP intervention [190]. The indicators were determined based on whether the children were consumer of predefined food items, that is if the food item occurred one or several times in the food record. Obesogenic indicators were 'high-sugar foods', 'soft drinks' and 'salty snacks'. Obesity-protective indicators were 'wholegrain bread or grains', 'fish', 'at least two different types of separate vegetables' (=in all days; vegetables as part of mixed dishes not included), 'fruits daily' (=at 3 days) and 'water at main meals' (=at all main meals).

Eating behaviours
The children's eating behaviours were measured in Studies III and IV using the Children's Eating Behaviour Questionnaire, originally developed and validated in the UK [174, 253]. The CEBQ is a multi-dimensional, parent-reported questionnaire measuring children's eating behaviours related to obesity risk. The original questionnaire consists of 35 items, covering eight dimensions of eating behaviours which can be grouped into 'food-approach' and food-avoidant' behaviours, see Table 5. The CEBQ has been used extensively to measure associations between eating behaviours and relative weight in different child populations 1-13 years old [254-260].The questionnaire was translated into Swedish using two independent authorized translators. In Study IV, two aggregated scores were additionally determined by calculating the sum scores for the food-approach and food-avoidant measures respectively.

Table 5. Example items of the eight eating behaviour dimensions of CEBQ, Children's Eating Behaviour Questionniare.

Eating behaviour factor	Example item
Food approach behaviours	
Enjoyment of food	'My child looks forward to mealtimes'
Food responsiveness	'Even if my child is full up, he/she finds room to eat his/her favourite food'
Emotional overeating	'My child eats more when anxious'
Desire to drink	'My child is always asking for a drink'
Food avoidant behaviours	
Satiety responsiveness	'My child gets full before his/her meal is finished'
Slowness in eating	'My child eats slowly'
Emotional undereating	'My child eats less when he/she is angry'
Food fussiness	'My child decides that he/she doesn't like a food, even without tasting it'

Parental data
Weight, height, BMI and weight status
In Studies I and III parental weight and height were reported through questionnaires. In Study I the parents reported their weight and height at the first clinical visit to the treatment centre. In Studies II and IV, parental weight and height were measured. Height was measured to the nearest 0.1 cm using a fixed stadiometer (Ulmer, Busse Design Engineering, Elchinge, Germany). Weight was measured to 0.1 kg with light clothing using a portable scale (HD-216, Tanita Corp, Tokyo, Japan). The mean of three measurements was used. For pregnant mothers, the reported weight before pregnancy was used. BMI was calculated as $weight/height^2$. Based on BMI the parents were classified as normal weight (BMI 18-24.9 kgm^{-2}), overweight (BMI 25-29.9 kgm^{-2}) or obese (BMI $\geq$ 30 kgm^{-2}), according to international cut-off points [8]. In Studies II, III and IV the weight status of both parents was combined to define the obesity risk for each family: in high-risk families both parents were overweight or at least one parent was obese and in low-risk families both parents were normal weight (Study III additionally included families with one normal weight and one overweight parent in the low-risk population).

Educational level
In Study 1, both parents' occupation was used to define parental (family) education into one of three categories based on official Swedish socio-economic categories and the Swedish standard classification of occupations: 1) at least one parent with an academic degree (>12 years of education); 2) at least one parent with post-secondary education (= 12 years of education); and 3) others (both parents <12 years of education, unemployed, early disability retired, long-term sick-listed, house-wives and participants in Study programs). In Studies II and IV the educational level for both parents was combined and dichotomized into 'low parental educational level' if neither parent had >12 years of school versus 'high parental educational level' if at least one parent had >12 years of

school. In Study III the educational level of each parent was described as one of three categories: 'Elementary school' (9 years of school),'High school' (secondary education, 12 years of school) and 'College/University' (tertiary education, >12 years of school).

Ethnicity

Ethnic origin was described for the parents in Studies III and IV. The definition of a non-Swedish (Study III) or non-Nordic (Study IV) ethnic background was having at least one parent of foreign origin, or origin outside the Nordic countries, respectively.

Co-morbidities

In Study I, data on parental cardio-metabolic co-morbidities – cardiovascular disease, hypertension, hyperlipidaemia, type 2 diabetes mellitus and gestational diabetes mellitus – were used to define independent variables for 'number of co-morbidities' for each parent.

Smoking habits

Parents were defined as 'smoker' or 'non-smoker' based on their current smoking status. The mother's smoking status was used in Study II and both parents' smoking status was included in Study IV.

Food intake

In Study IV, the parents' food intake was measured using a 17-item food frequency questionnaire, which had previously been developed and validated by the Swedish National Food Agency [163]. Frequencies per day or week were calculated for fruit and vegetables; whole grain bread; fish; french fries; sausages; full fat cheese; sweets and chocolates; buns, biscuits and cakes and soft drinks. Type of spread was defined as low fat (< 40% fat) or high fat (> 60 %).The selected food items had previously been associated with diet quality indicators for fat, saturated fat, sugar and dietary [163]. A food index was calculated based on these indicators, representing healthy food habits according to the Swedish dietary guidelines [261] (Study IV).

Plasma fatty acid composition – children and parents

In Study IV, fatty acid composition was measured in plasma in order to validate the reported intake of fat from selected foods. Blood samples were drawn from both parents and children (fasting for parents, non-fasting for the children). Plasma samples were stored in -80 C before analysis. The fatty acid composition of plasma phospholipids and cholesterol esters was measured using gas liquid chromatography [243]. The relative amount of fatty acids was expressed as the percentage of the total amount of identified fatty acids. Selected fatty acids in plasma were correlated to the reported intake of fat in

selected foods, previously found to be valid biomarkers: dairy products (cow's milk, sour milk, yoghurt, cream) [245, 262], infant formula [228] and fish [244].

Outcome and independent variables

In Table 6 the outcome and independent variables in each study are presented.

Study I

In Study I, three different outcomes were studied: age at onset of obesity and BMI SDS (degree of obesity) at age 7 and 15. 'Age at onset of obesity' was retrieved directly from BORIS. Age at onset of obesity had previously been derived from growth charts collected at referral to the treatment centre, plotting weight and height records measured at CHC centres, in school health care and by referral units. It was defined as the age at which the BMI of the child for the first time exceeded the BMI for the specific age and gender corresponding to BMI 30 kgm^{-2}, the adult cutoff for obesity [7]. BMI SDS at age 7 was extracted directly from BORIS and had been determined by interpolating weight and height measurements using the children's growth charts. BMI SDS at age 15 was determined using BMI SDS data for all annual clinical visits in BORIS, identifying visits as close as possible to age 15 (records between 14.5 and 15.9 years were included).

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Table 6. The outcome and independent variables in each study.

Study	Outcome variables	Primary independent variables	Other independent variables
Study I	Age at onset of obesity BMI SDS at 7 years BMI SDS at 15 years	Parental BMI	Gender Birth weight Parental co-morbidities Parental education Treatment for at least one year

Study II	BMI SDS at 3, 6 and 12 months
	Rapid weight gain 0-6 months
		Parental weight status -
		  high/low obesity risk
		Parental education -
		  high/low obesity risk
			Gender
			Birth weight
			Maternal age
			Maternal gestational weight gain
			Maternal smoking habits
			Gestational age
			Short exclusive breast-feeding
			Age at introduction of solid foods
			Antibiotics during first year

Study III	Child eating behaviours
	Child BMI SDS at 1-6 years
		Child age and gender
		Child eating behaviours
			Parental weight status -
			  high/low obesity risk
			Parental educational level –
			  …high/low obesity risk

Study IV	Child dietary intake Child eating behaviours Child BMI SDS at 1 year	Parental weight status - high/low obesity risk	Parental educational level Parental ethnicity Parental smoking status Parental age Parental food intake Gender First-born Infant early feeding Child basal metabolic rate (BMR) Child dietary intake Child eating behaviour pattern

Study II

In Study II, BMI SDS at 3, 6 and 12 months were based on weight and height records as close as possible to these ages. Records were excluded if outside ± 2 weeks at 3 months, ± 4 weeks at 6 months and ± 2 months at 12 months. 'Rapid weight gain 0-6 months' was defined as the weight SD gain between birth and 6 months of age > 0.67 SD [111]. Weight SD was calculated using the Swedish growth reference [263] and the formula: (individual mean – reference mean) / reference SD.

Study III

In Study III, the mean scores of the eating behaviour factors identified in the factor analysis were determined and used as dependent variables in relation to age and gender. BMI SDS was an additional outcome variable.

Study IV
Main outcome variables in Study IV were the child dietary behaviours and the children's relative weight. Child dietary behaviours refer to dietary intake, diet quality and eating behaviour variables, see definitions above.

STATISTICAL ANALYSES

Statistical methods
In Table 7 the statistical methods used in each study are listed.

Table 7. Statistical methods in each study.

Method	Study I	Study II	Study III	Study IV
Descriptive statistics	X	X	X	X
Pearson correlation	X	X	X	X
Linear regression	X	X	X	X
Logistic regression		X		X
Chi-2 test	X	X		X
T-test independent samples		X	X	X
Mann Whitney-U test				X
ANOVA, one-way			X	
Principal component analysis			X	X
Reliability coefficient (Cronbach's alpha)			X	

Main analyses
Study I
Associations between the BMI SDS at age 7 and 15 and age at onset of obesity and parental BMI were analysed. Potential confounding effects of gender, birth weight, parental education, parental co-morbidities and treatment were tested (birth weight and parental co-morbidities not included in the final models). In the analysis of BMI SDS at age 15, the BMI SDS at age 7 was also included.

Study II
Associations between BMI SDS at 3, 6 and 12 months and rapid weight gain 0-6 months and obesity risk (high versus low) as determined by both parental weight status and by parental educational level were analysed. The associations were adjusted for gender, birth weight, short exclusive breastfeeding, maternal gestational weight gain and maternal smoking, exploring the potential mediating effects of these factors on the

association between infant growth and parental obesity risk. Additional independent factors tested, but not included in the final models, were gestational age, maternal age, introduction of solid foods and number of days of antibiotics during the first year (as a proxy for the level of illness).

Study III
Factor analysis of the CEBQ and examination of internal consistency and inter-correlations between the resultant eating behavior scales (Cronbach's alpha) was carried out. Age and gender differences in eating behaviours were analysed. The children's BMI SDS was analysed in relation to eating behaviours, adjusting for gender, age, parental weight status (obesity risk) and educational level.

Study IV
Child dietary behaviours and parental food intake were compared between families at low and high risk of obesity determined by parental weight status, adjusting for child and parental demographics. Reported intake of fat was validated using fatty acid composition in plasma. The odds for high infant diet quality in relation to parental diet quality were analysed. Associations between the children's BMI SDS, dietary intake and eating behaviours were analysed. The results were adjusted for obesity risk, parental education, early infant feeding, breastfeeding status at age one and birth weight.

Common statistical procedures
Outcome variables were tested for normality, through visual inspection of histograms. All tests were two-sided, and p-values < 0.05 were regarded as statistically significant. In Study IV, the chance of random significant results was accounted for by comparing the number of significant results in proportion to the total number of tests. Statistical analyses were performed with STATISTICA, version 9.1 (Study I), version 10 (Study III) and version 11 (Studies II and Study IV) (StatSoft, Inc., Tulsa, OK, USA, http://www.statsoft.com). The logistic regression analysis in Study II was performed with SPSS Statistics 20 (IBM, Armonk, NY, USA, www.ibm.com).

ETHICAL APPROVAL

Ethical approval was granted by the Stockholm Regional Ethical Review Board: 2005/1231-31/2 (Study I), 2009/217-31 (Studies II and IV), 2009/754-32 (Studies II and IV) and 2011/1147-32 (Study III).

RESULTS

THE STUDY POPULATIONS

In Study I, the relative weight of the excluded subjects (due to missing data) was not significantly different compared to the study population at either age.

In Study II, maternal and paternal low education was significantly more common in the study population, compared with the ES population not included in the study. A difference in family low education was indicated (p = 0.09). There were no differences in anthropometrics or ethnicity.
The differences in early life factors in high- and low-risk families, as determined by parental weight status and parental education, are summarized in Table 10. Gestational weight gain was higher in mothers of low-educated families (p = 0.02), and short exclusive breastfeeding was more common in infants with overweight or obese parents (p < 0.001).

In Study III, the response rate for the eating behaviour questionnaire was 46%. The number of individuals excluded due to missing data was small (n = 19), and no comparisons between the excluded subjects and the study population were made.

In Study IV the families excluded (due to missing diet records) did not differ significantly compared to the study population with regard to child and parental anthropometry, parental weight status or parental education.

CHILD AND PARENTAL RELATIVE WEIGHT (STUDIES I, II, III)

In this thesis associations between parental adiposity and children's BMI SDS in different age intervals have been analysed. Infancy (0-1 year) was studied in Study II, childhood (1-6 years) in Study III and 7 years in Study I and adolescence (15 years) in Study I. Additionally the association between age at onset of obesity and parental BMI was analysed (Study I). These results are summarized in Table 6, including results from new analyses (associations to parental BMI were not originally reported in Study II and III; instead associations to obesity risk based on parental weight status were reported).

In infancy

Children's BMI SDS during the first year, at 3, 6 and 12 months, as well as rapid weight gain during the first 6 months was not significantly associated with parental BMI or obesity risk as determined by parental weight status ($p > 0.05$; Study II).

In childhood and adolescence

In children 1-6 years old, the BMI SDS was significantly higher in children with overweight or obese parents (high risk), compared to the low risk children (unadjusted $p = 0.002$, not reported in study; adjusted $p = 0.01 – 0.02$; adjusted for age, gender, parental education and eating behaviours) (Study III). In Study I, BMI SDS at age 7 was significantly associated with maternal BMI when adjusting for gender, parental education and age at onset of obesity ($\beta = 0.09$; $p = 0.05$). The associations at age 15 were stronger and significant with both parents' BMI ($\beta = 0.17$; $p = 0.01$ maternal BMI; $\beta = 0.16$; $p < 0.01$ paternal BMI). The associations at age 15 were adjusted for gender, parental education, age at onset of obesity, BMI SDS at age 7 and treatment for at least one year (Table 8).

Age at onset of obesity

The mean age at onset of obesity was 4.9 years, 58% of the children became obese at age 4 or younger and 77% were obese at age 6 or younger. Parental BMI did not have a clinically relevant impact on the age at obesity onset (Study I). A significant negative correlation between paternal BMI and age at onset was identified but this association was very weak explaining only 1% of the variation in age at obesity onset.

Associations by child gender

The associations between child and parental relative weight were of similar magnitude for boys/girls and mothers/fathers at age 7 and 15 in Study I (Table 9).

Table 8. Associations between child BMI SDS and age at onset of obesity and parental BMI/obesity risk as determined by both parents' weight status.

	Maternal BMI	Paternal BMI	Obesity risk High / Low	Population High-/ Low-/ Mixed-risk	n	Study
Unadjusted associations	r	r				
Child BMI SDS						
3 months	0.02	0.15		High + Low	166 mother 159 father	II
6 months	0.03	0.15		High + Low	166 mother 159 father	II
12 months	0.02	0.05		High + Low	166 mother 159 father	II
1-6 years	0.40 **	0.24		Mixed	47	III
7 years	0.11	0.17 *		High	231	I
15 years	0.29 **	0.27 **		High	231	I
Age at onset of obesity	0	-0.14 *		High	231	I
Adjusted associations	β	β	β			
Child BMI SDS						
3 months	-0.03	0.04	-0.05	High + Low	160	II
6 months	0.04	0.05	0.02	High + Low	165	II
12 months	0.02	0.04	-0.00	High + Low	174	II
1-6 years			0.37 - 0.41 *	Mixed	47	III
7 years	0.09 *	0.04	-	High	231	I
15 years	0.17 **	0.16 *	-	High	231	I
Age at onset of obesity	0.04	-0.14 *	-	High	231	I

Shaded cells: results not reported in the original studies.
Obesity risk High vs Low; based on both parents' weight status
* $p < 0.05$, ** $p < 0.01$

Table 9. Pearson correlation coefficients between child and parental relative weight, by gender.

Child BMI SDS	Maternal BMI	Paternal BMI
7 years		
Girls	0.14	0.20 *
Boys	0.07	0.14
15 years		
Girls	0.28 **	0.24 *
Boys	0.32 **	0.31 **

* $p < 0.05$, ** $p < 0.01$.

Child BMI SDS in relation to number of obese parents

Children with non-obese, one obese and two obese parents were compared by dividing the children into tertiles of the BMI SDS range (Study I). A higher proportion of the children within the highest tertile of the BMI SDS range had two obese parents compared to children with more moderate obesity, indicated at 7 years (23%, 12% and 9% respectively; p = 0.06) and significant at 15 years (25%, 14% and 5% respectively; p < 0.001). See Figure 5.
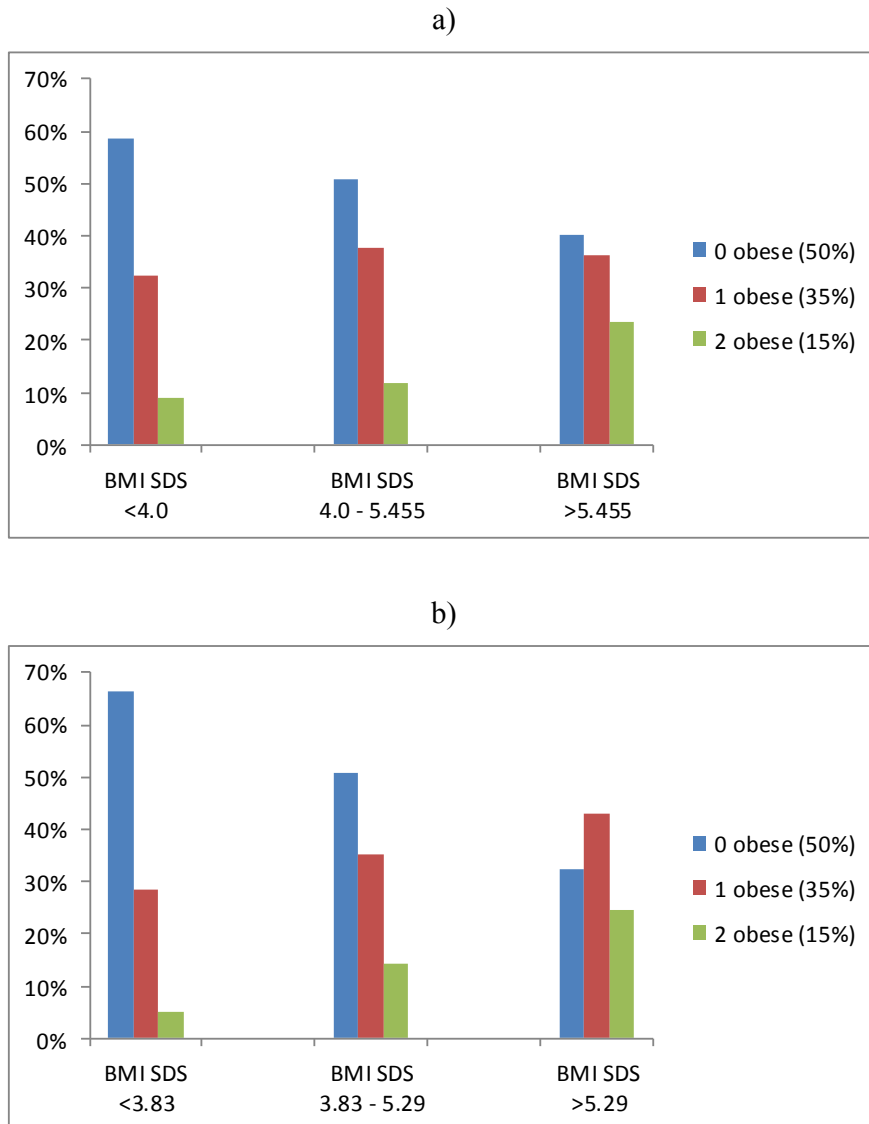
a)

b)

Figure 5. The proportion of children in each tertile of the BMI SDS range at age 7 and 15 having 0, 1 or 2 obese parents. a) At age 7. b) At age 15.

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CHILD RELATIVE WEIGHT AND PARENTAL EDUCATION (STUDIES I AND II)

In Study I parental education level was included as a potential confounder to the associations between child and parental relative weight. In Study II parental education was used to define obesity risk and to analyse its association with infant growth in conjunction with the risk as determined by parental BMI. (Parental educational level was also used as a covariate in Study III and IV; not reported here).

In infancy (Study II)
BMI SDS at 3 and 6 months were significantly positively associated with low parental educational level, independent of obesity risk as determined by parental BMI, birth weight, infant feeding and gestational weight gain ($\beta = 0.18$; $p = 0.02$ at 3 months; $\beta = 0.16$; $p = 0.04$ at 6 months). This association was statistically indicated at 12 months ($\beta = 0.15$; $p = 0.06$). No association was seen between parental educational level and rapid weight gain.

In childhood and adolescence (Study I)
In Study I, a high parental educational level was negatively associated with BMI SDS at age 15, independently of parental BMI, BMI SDS at age 7 and treatment ($\beta = -0.11$; $p = 0.05$). Parental education did not impact on age at onset of obesity ($p = 0.31$) and BMI SDS at age 7 ($p = 0.43$).

CHILD RELATIVE WEIGHT AND EARLY LIFE FACTORS (STUDIES I AND II)

In Study II the associations between infant growth and early life factors were analysed with the aim of exploring potential mediating effects of these factors on the associations between infant growth and obesity risk. In Study I birth weight was included as a potential confounder of the associations between child and parental relative weight and age at obesity onset. Here these associations are presented separately from the main findings, including unadjusted associations not reported in the original studies, see Table 10.

Birth weight
In Study II, birth weight was strongly and independently associated with infant growth during the first year, positively with relative weight at 3, 6 and 12 months ($\beta = 0.40$, 0.31 and 0.25 respectively; $p < 0.01$) and negatively with rapid weight gain (OR 0.86, 95 %

CI 0.80 – 0.93). In Study I only weak and non-significant correlations between birth weight and degree of obesity were identified (and between birth weight and age at obesity onset; not reported in Study I).

Gestational weight gain
Maternal gestational weight gain correlated weakly to relative weight at 6 and 12 months in unadjusted analyses (r = 0.20 and 0.17 respectively; p < 0.05), and this association was additionally indicated at 6 months in multivariate analyses (p = 0.06-0.08).

Infant feeding
Exclusive breastfeeding for less than 2 months and age at introduction of solid foods were not associated with infant growth.

Maternal smoking
BMI SDS at 12 months was significantly higher in infants with smoking mothers (β = 0.18; p = 0.01 adjusted analysis).

Maternal age
A low maternal age correlated to a high BMI SDS at 12 months (r = -0.23, p < 0.01), however this association became non-significant in adjusted analyses.

Mediating effects of early life factors on the association between parental education and growth
The association between parental education and growth reported above could not be explained by the studied early life factors, with the exception for maternal smoking that partly mediated some of the impact between parental education and child relative weight at 12 months.

Table 10. Early life factors; difference between high- and low-risk children and associations with infant growth, unadjusted and adjusted (Study II).

Early life factor	Parental BMI HR vs LR	Parental education HR vs LR	BMI SDS 3 months		BMI SDS 6 months		BMI SDS 12 months		Rapid weight gain 0-6 months	
			r	β	r	β	r / Chi-2	β	r / Chi-2	OR
Maternal age							-0.23 **			
Maternal smoking							Chi-2 *	0.18 *	Chi-2 ***	
Birth weight			0.40 ***	0.40 ***	0.32 ***	0.31 ***	0.24 **	0.25 **	***	0.86 ***
Gestational weight gain		HR > LR *			0.20 *		0.17 *			
Short exclusive breastfeeding	HR > LR ***									
Introduction of solid foods										

Shaded cells: results not reported in original study
HR: High risk, LR: Low risk
* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$
r: Pearson correlation coefficient; β: estimate from linear regression; Chi-2: results of Chi-2 test
Only significant results are reported; empty cells = no significant associations.

VALIDATION OF AN EATING BEHAVIOUR QUESTIONNAIRE (STUDIES III AND IV)

The factorial validation of the Swedish version of the CEBQ was performed in Study III on children 1-6 years old. A new factor analysis was performed in Study IV on children one-year old, since the number of one-year old children included in Study III was very small (n=25), and the CEBQ was originally developed for children from the age of two years.

The factor analysis in Study III identified seven distinct eating behaviour factors. Two of the original factors ('Food responsiveness' and 'Emotional over-eating') loaded onto the same factor and was thus combined into one scale entitled 'Overeating'. Most items (questions) loaded onto the factors as expected according to the original factor structure, with some exceptions (see Study III). Internal reliability (Cronbach's alpha coefficients) for the seven eating behaviour factors were all acceptable (0.71-0.90), comparable to previous CEBQ validation studies [174, 257, 260]. The three food-approach scales (behaviours that promote eating) and four food-avoidant scales (behaviours with a hampering impact on food intake) were overall significantly inter-correlated and negatively correlated between the two groups of scales (Table 11).

Table 11. Pearson correlation coefficients between the CEBQ subscales, seven-factor solution.

CEBQ scales	EOE/FR	EF	DD	SR	SE	EUE	FF
Overeating (EOE/FR)	-						
Enjoment of food (EF)	**0.26 ****	-					
Desire to drink (DD)	**0.39 *****	-0.09	-				
Satiety responsiveness (SR)	-0.16 *	-0.38 ***	0.07	-			
Slowness in eating (SE)	-0.23 **	-0.49 ***	0.18 *	**0.38 *****	-		
Emotional undereating (EUE)	0.07	-0.01	0.17 *	**0.33 *****	-0.03	-	
Food fussiness (FF)	-0.02	-0.58 ***	0.14	**0.33 *****	**0.28 *****	0.12	-

* p < 0.05   ** p < 0.01   *** p < 0.001

Bold area upper-left corner: significant inter-correlations between 'food approach' subscales.

Bold area bottom-right corner: significant inter-correlations between 'food avoidant' subscales.

In Study IV, the factor analysis resulted in the original eight-factor solution, with only two items not loading as expected (see Study IV). Therefore the original solution was used in Study IV.

CHILD EATING BEHAVIOURS AND AGE (STUDIES III AND IV)

The mean eating behaviour scores by child age are presented in Table 12, including results for both Study III and Study IV.

Four of the eating behaviour factors varied significantly by child age in the population of children 1-6 years (Study III). The scores for 'Enjoyment of food', 'Overeating' and 'Emotional under-eating' decreased gradually in older children (p<0.05). The 'Food fussiness' scale was least present in the youngest children (p < 0.05) (Figure 6).

Table 12. Mean eating behaviour scores by child age, in Study III and Study IV

	Study III						Study IV
	1 year (n = 25)	2 years (n = 30)	3 years (n = 34)	4 years (n = 39)	5-6 years (n = 46)	p [1]	1 year (n = 188)
Food approach behaviours							
Overeating	1.8 (0.6)	1.5 (0.5)	1.6 (0.5)	1.5 (0.4)	1.5 (0.4)	0.04 *	
Food responsiveness							1.8 (0.7)
Emotional overeating							1.9 (0.5)
Enjoment of food	3.8 (0.7)	3.6 (0.6)	3.4 (0.6)	3.5 (0.5)	3.2 (0.7)	0.01 *	3.8 (0.6)
Desire to drink	2.1 (0.8)	2.0 (0.9)	2.1 (0.9)	1.9 (0.6)	2.0 (0.7)	0.76	1.8 (0.7)
Food avoidant behaviours							
Satiety responsiveness	3.1 (0.7)	3.1 (0.6)	3.1 (0.6)	3.0 (0.5)	3.1 (0.6)	0.91	2.8 (0.6)
Slowness in eating	2.4 (0.7)	2.8 (0.6)	2.8 (0.6)	2.7 (0.7)	2.8 (0.8)	0.14	2.5 (0.8)
Emotional undereating	3.6 (0.8)	3.4 (0.9)	3.5 (0.9)	3.0 (1.0)	3.0 (1.0)	0.01 *	3.4 (1.0)
Food fussiness	2.3 (0.7)	2.7 (0.8)	2.9 (0.7)	2.9 (0.7)	3.0 (0.9)	0.01 *	2.0 (0.6)

[1] P-value from one-way ANOVA, testing age variation in the eating behaviour factors in Study III.
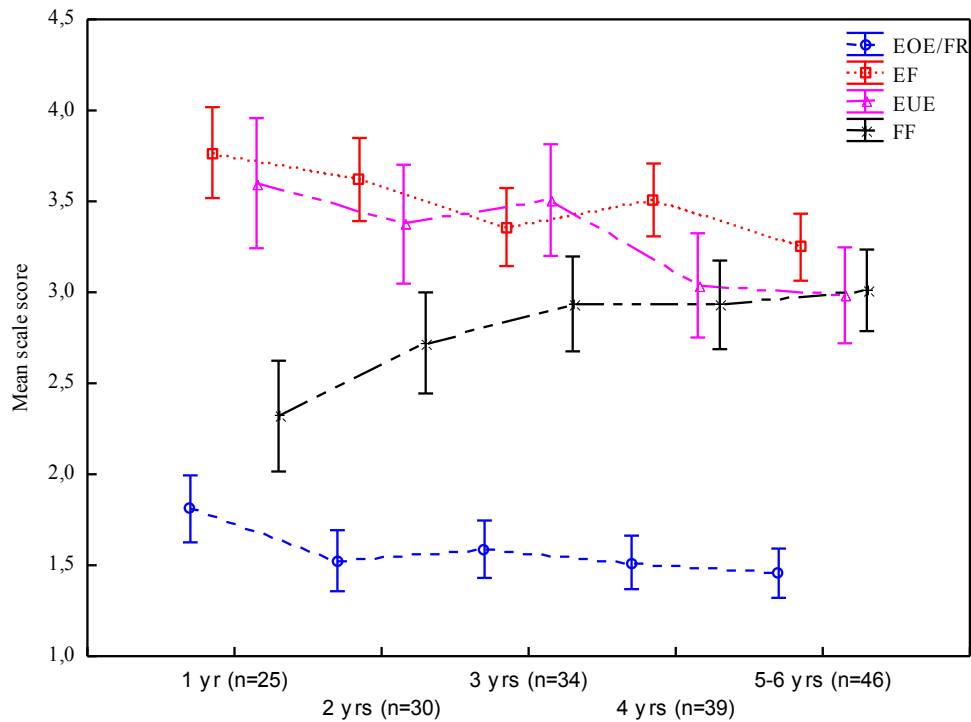
Figure 6. Mean eating behavior scores by child age (Study III).
EOE/FR: Emotional overeating / Food responsiveness ('Overeating')
EF: Enjoyment of food
EUE: Emotional undereating
FF: Food fussiness

VALIDATION OF FOOD INTAKE WITH A BIOMARKER FOR FAT (STUDY IV)

In Study IV, the food intake of infants and parents were correlated with an objectively measured biomarker for fat quality, fatty acid composition in plasma (Table 13).

In children the intake of fat from milk products (milk, sour milk, yoghurt and cream) was correlated with the saturated fatty acids 14:0, 15:0 and 17:0 ($r = 0.31 - 0.44$; $p < 0.05$). The children's intake of formula correlated negatively with 14:0, 15:0, 17:0 and 18:3 n-6 ($r = -0.20$ to -0.71) and positively with 18:2 n-6 ($r = 0.30$). The parent's intake of fish correlated with the 'fish' fatty acids EPA and DHA ($r = 0.55$ and 0.41 for mothers, $p < 0.01$; $r = 0.44$ and 0.21 for fathers; $p < 0.05$).

Table 13. Correlations between fat from selected foods and fatty acids in plasma, in children and parents.

| Fatty acids in serum | Children [1] | | Parents [2] |
| | Milk products [3] | Formula | Fish |
	r	r	r
Children			
14:0 PL	0.44 **	-0.49 ***	
15:0 PL	0.31 *	-0.33 *	
17:0 PL	0.34 *	-0.71 ***	
18:2 n-6 PL		0.30 *	
18:3 n-3 PL		-0.20	
Mothers			
20:5 n-3 CE (EPA)			0.55 ***
22:6 n-3 CE (DHA)			0.41 **
Fathers			
20:5 n-3 CE (EPA)			0.44 **
22:6 n-3 CE (DHA)			0.20 *

[1] Food intake in children is expressed as fat intake from the selected foods in percent of total fat per day.
[2] Food intake in parents is expressed as intake frequencies per week.
[3] Milk products: milk, cream, yoghurt, sour milk
* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$
PL: phospholipids; CE: cholesterol esters

CHILD RELATIVE WEIGHT AND DIETARY BEHAVIOURS (STUDIES III AND IV)

Associations between child BMI SDS and dietary behaviours were presented in Study III (eating behaviours) and Study IV (dietary intake, eating behaviours).

Dietary intake
At age one, BMI SDS was not associated with the intake of energy, macronutrients, fat quality or dietary fibre, nor with diet quality indicators. The results were adjusted for obesity risk (parental weight status), parental educational level, infant feeding and birth weight (Study IV).

Eating behaviours
At age one, BMI SDS was positively associated with food-approach eating behaviours ($\beta = 0.34$; $p < 0.001$) and negatively with food-avoidant behaviours ($\beta = -0.24$; $p < 0.01$) in the entire population including both high- and low-risk infants (Study IV). The results were adjusted for obesity risk (parental weight status), parental educational level, infant feeding, dietary intake and birth weight (Study IV). In the children 1-6 years old, BMI SDS was not associated with eating behaviours, when adjusted for child age, gender, obesity risk (parental weight status) and parental educational level (Study III).

INFANT DIETARY BEHAVIOURS AND PARENTAL WEIGHT STATUS (STUDIES III AND IV)

Dietary intake
At age one, the infants' intake of energy, macronutrients, fat quality or dietary fibre was not associated with parental weight status (obesity risk), i.e. no differences in the intake of these nutrients could be detected between high- and low-risk infants (Figure 7). Similarly, no difference in the proportion of infants with high diet quality could be identified between high- and low risk infants. The proportion of infants adhering to nutritional recommendations was the same in high- and low-risk groups, except for the protein intake - here it was more common among high-risk children not to adhere to recommendations ($p < 0.05$). Of all infants, only a third adhered to recommendations for saturated fat, and one in five had a protein intake exceeding the recommended level (Study IV).
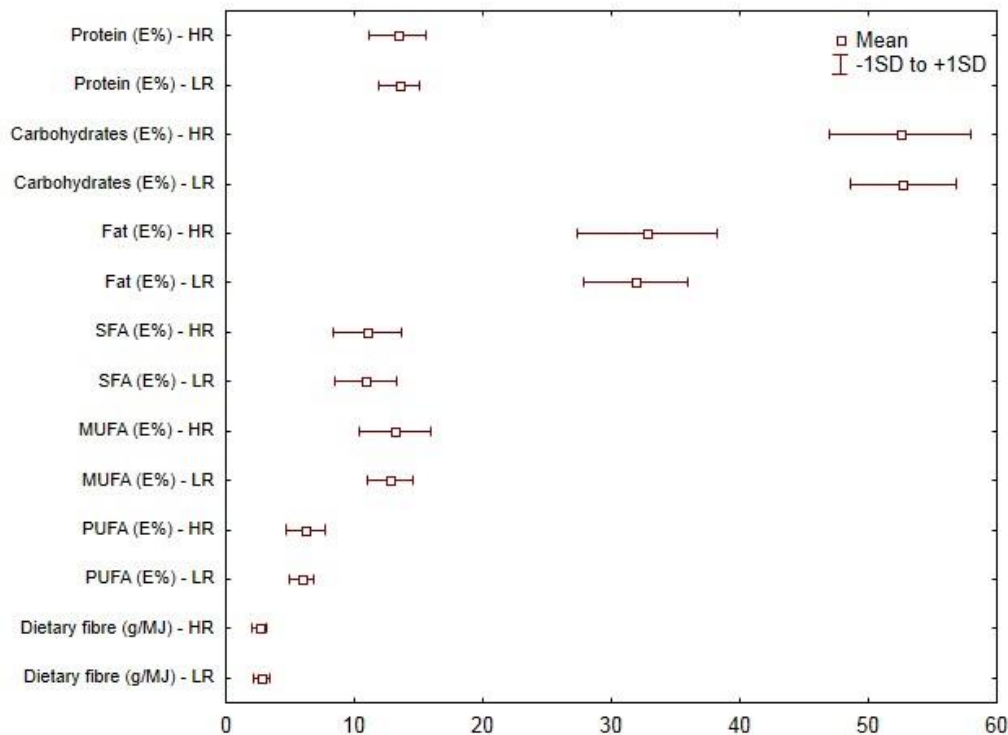
Figure 7. Mean and SD of macronutrients (E%) and dietary fibre (g/MJ) in high- (HR) and low-risk (LR) infants (Study IV).

Eating behaviours

At age one, the eating behaviour factors were not associated with obesity risk, i.e. no differences could be detected between high- and low-risk infants in Study IV. Similarly, in the mixed-risk population in Study III (11% high-risk families), the eating behaviours did not differ in high- and low-risk children (not reported in Study III).

INFANT AND PARENTAL FOOD INTAKE (STUDY IV)

Parental food frequencies differed between high- and low risk families in several obesogenic indicators. Mothers in high-risk families consumed fruit less often and soft-drinks, french fries, and low-fat spread more often ($p < 0.05$). Fathers in high-risk families consumed fruit and fish less often and french fries more often ($p = 0.05$). There were no significant differences between the high- and low-risk parents in the intake of healthy foods, nor in the total diet index score (Figure 8). The results were independent of parental adiposity, socio-demographics, firstborn and breastfeeding status at age one.
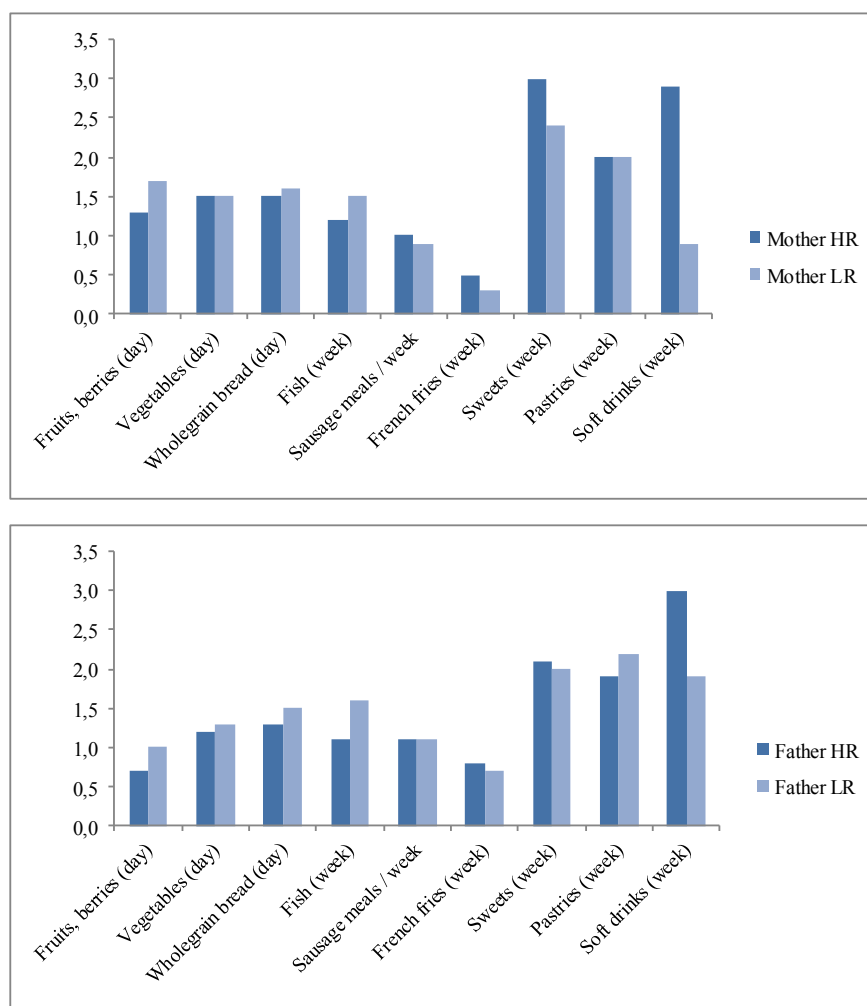
Figure 8. Food frequencies in mothers and fathers of high- (HR) and low-risk (LR) families.

The odds for high diet quality indicators in infants in relation to maternal and paternal diet indicators were assessed in Study IV. A high intake level of vegetables and fish in fathers increased the odds for infants being consumers of several vegetables (OR=1.7; 95% CI 1.0-2.9) and fish meals respectively (OR=2.1; 95% CI 1.2-3.5). No associations between maternal food intake and infants' diet quality could be identified, nor between parental intake of obesogenic foods and the corresponding infant diet indicators.

INFANT DIETARY INTAKE AND EATING BEHAVIOURS (STUDY IV)

Associations between dietary intake and eating behaviours in infants were analysed in Study IV. The aggregated food-approach and food-avoidant scores were correlated with the relative intake of macronutrients and dietary fibre (Table 14). The food-approach

behaviour score correlated positively with the protein intake (r = 0.20 / β = 0.21; p < 0.01), whereas the food-avoidant behaviour score correlated negatively with the intake of dietary fibre (r = -0.20 / β = -0.22; p < 0.01) and positively with fat intake in unadjusted analysis (r = 0.16; p < 0.05).

Table 14. Associations between dietary intake and eating behaviours in infants.

Infant dietary intake	Food approach behaviour score		Food avoidant behaviour score	
	Unadjusted, r	*Adjusted ^{a}, β*	*Unadjusted, r*	*Adjusted ^{1}, β*
Energy (kJ)	-0.01	-0.03	-0.11	-0.13
Protein (E%)	0.20 **	0.21 **	-0.12	-0.13
Carbohydrate (E%)	-0.05	-0.07	-0.07	-0.04
Fat (E%)	-0.05	-0.05	0.16 *	0.13
Dietary fibre (g/MJ)	0.06	0.06	-0.23 **	-0.22 **

** p < 0.01; * p < 0.05
[1] Adjusted for obesiy risk, parental educational level, early infant feeding and breastfeeding status at age one.

DISCUSSION

MAIN FINDINGS

This thesis has shown that both parents' adiposity and educational level are important independent determinants of child weight development in high-risk populations, however the timing of their influence differs. Parental adiposity does not have a distinct effect on the relative weight of infants, nor on age at obesity onset, however the impact of both maternal and paternal BMI becomes stronger with child age and affects the degree of obesity later in childhood and adolescence. Parental educational level affects infant growth as early as their first year, and an effect is still present in relation to degree of obesity in adolescence. Infant relative weight is also independently associated with birth weight and obesity-related eating behaviours, but not with dietary intake, which is unrelated to parental adiposity and parental obesogenic food intake at age one.

WHAT CHARACTERISES THE HIGH-RISK POPULATIONS?

As this thesis focus on high-risk populations, it is of interest to assess the *degree* of increased risk in our populations, compared with the general population. Also, to consider the implications of studying specifically high risk populations, separately and in comparison with low risk populations.

Definition of high risk
The study populations included in this thesis were classified as high-, mixed- and low-risk, primarily determined on the basis of the most important risk factor for childhood obesity, the prevalence of parental overweight and obesity. Parental educational level was additionally used to define high and low risk in Study II.

The weight status and educational level of *both* parents were used to define obesity risk. Many studies have used only maternal adiposity or education to define obesity risk [79, 151, 264]. Even though maternal and paternal obesity risk may not affect offspring weight development similarly or via the same mechanisms, it has been shown that both parents matter [25, 37, 39]. Also, in Sweden where gender equality is very developed it would not make sense to use only the mother's educational level to define obesity risk. As the aim of two of the studies (Studies II and IV) was to compare the impact of high versus low obesity risk on child outcomes, using one distinctly defined risk variable to distinguish

populations was prudent. Additionally, the Early STOPP populations were recruited based on inclusion criteria including both parents' weight status. By combining the obesity risk conferred from both parents, the difference in obesity risk level between the high- and low-risk populations became more extreme. Interaction effects of the mother's and the father's obesity risk would be possible or even probable, but this was statistically tested only in Study I where no significant interaction could be identified.

Characteristics of the high-risk populations
Early STOPP was specifically targeting a high-risk population and families were recruited based on parental BMI, so naturally the obesity risk was increased. The population of obese children in Study I was also a selected group, although not recruited based on parental BMI. So how much was the obesity risk increased compared to the general Swedish population, where approximately 15-20% of the men and 10-15% of the women are obese [24]? In Study I, the parental obesity rates were two to three times higher. In the Early STOPP population, obesity was about four times more common among mothers and twice as common among fathers. Also, in nearly one of four of the Early STOPP high-risk families both parents were obese, and this was true for 15% of the families in the clinical sample (but bear in mind that parental BMI in that study was self-reported, known to be underestimates [265]. In comparison, as reported from a recent population-based Swedish study of expectant parents, in only 2% of the couples both partners were obese [25].

Parental socio-economic status can also be used to define obesity risk and divide populations into high and low risk, and this was carried out in Study II, using the combination of both parents' educational level (equivalent to applying the highest educational level of the household). In the other studies parental education was used as a covariate. Compared to the general Swedish population, where 65-70% has only secondary-education or below (equivalent to low educational level in this thesis; SCB), our study populations as a whole cannot be considered to be high risk as measured by parental education. However when splitting the study sample into high and low risk by parental educational level, obviously the difference in obesity risk was very pronounced: all mothers and fathers of the high-risk families had a low educational level, whereas this was true for only one of five parents of the low-risk, i.e. well-educated, families.

Overall, the study populations cannot be considered high-risk in terms of ethnicity. Compared to the general population of Stockholm County where 27% have a foreign background (SCB), the prevalence of foreign ethnic background was considerably lower in the study populations. Of note, the available data on ethnic origin in Studies II, III and IV was not based on the definition used by SCB ('utländsk härkomst': born abroad or

both parents born abroad) and thus a direct comparison with the prevalence in our studies is not applicable. A lower prevalence of families of foreign background in the Early STOPP study was partly a consequence of the inclusion criteria requiring parents to speak and understand Swedish. Despite efforts to recruit more families of foreign origin, cultural obstacles regarding the view on necessity for prevention may have affected parental interest for participating in an obesity prevention study [266, 267].

Interaction between parental adiposity and low educational level
In the Early STOPP population, low parental educational level was more common in the families with overweight and obese parents compared to families with normal weight parents, which also has been seen in other studies [25, 81]. This implicates a potential interaction between parental adiposity and low educational level regarding the obesity risk, i.e. an additional increased obesity risk for children whose parents are both overweight/obese and not well-educated. However, such an interaction effect in relation to infant relative weight could not be identified in Study II (not tested in the other studies), possibly due to the lack of impact of parental adiposity or the early age of the children. It is possible that such an additive effect will develop later in childhood.

Implications of high-risk population studies
The effect of important obesity risk factors on children's BMI SDS may be stronger in children with higher BMI SDS than in normal weight children [268, 269], which emphasise the need for more research on high-risk populations. Populations of high-risk individuals, where the risk is determined by parental BMI, may permit a more efficient study of the determinants of obesity than a study of individuals with a normal distribution of body weight, because individuals are likely to have a strong genetic potential [48]. Also, comparing weight development between high-risk and low-risk children is proposed as an efficient way of detecting clinically distinct differences regarding the impact of obesity risk. Findings from population-based studies may not be comparable with our studies, but comparisons will nevertheless be made in this thesis in lack of other high-risk population studies.

HOW DOES PARENTAL ADIPOSITY AFFECT CHILD WEIGHT DEVELOPMENT?

In this thesis associations between both parents' adiposity and child relative weight have been reported at different child ages, from infancy to adolescence, in high-risk populations. These associations have been described in terms of correlations between continuous measures (BMI and BMI SDS) as well as through the impact of an obesity

risk variable represented by the combination of both parents' adiposity. Additionally the impact of parental BMI on children's age at onset of obesity has been reported. Even though the findings of each study cannot be compared directly, as they were carried out in different populations and results were adjusted for different factors, they will be discussed together in the light of when and how the impact of parental adiposity may be manifested on children's relative weight and whether both parents are of equal importance. The studies have shown that parental adiposity does not seem to exert a clinically distinct impact on children's growth during the first year, nor on the age at obesity onset. Parental and child relative weight become more closely related as the child grow older, and this seems especially evident for the father-child associations. Parental adiposity is likely to operate through a combination of hereditary, social and behavioural mechanisms; this is further discussed in the section on *Nature and nurture* below.

Timing and strength
Studying weight development as early as infancy is of importance because BMI can be tracked from infancy to childhood [135, 270] and a rapid growth early in life have been independently associated with an increased obesity risk later in childhood [109, 111]. We did not identify any significant associations with parental BMI /obesity risk during the first year, at 3, 6 and 12 months. Our results confirm the findings of a previous study of similar design, comparing growth from birth until 6 years of age between high- and low-risk children [48]. That study identified significant and clinically distinct differences in child weight only at age 4, however it may be of importance that the obesity risk was based on maternal BMI only. On the other hand, very large community-based studies have identified statistically significant associations between parental and child relative weight as early as infancy, even though the relationships were quite weak during the first year [38, 43]. The power to detect statistically significant associations has been high in these studies due to large sample sizes, however the clinical relevance of the findings has not been discussed. Our study design possibly allows clinically distinct differences regarding the impact of parental adiposity to be identified. The impact of potential confounding factors must also be taken into account, and in Study II the impact of parental adiposity was adjusted for several other important risk factors, such as birth weight, infant feeding and parental education. Thus the results of Study II provide additional evidence that the impact of parental adiposity is not of clinically relevance for the growth of infants as early as during the first year of life.

In Study III, in a mixed-risk small sample of children (n = 47), the association between parental adiposity and child relative weight was very distinct. The children were older which may explain the stronger association with parental adiposity. However, as

stronger associations were observed in this study compared with Study I and other studies, the risk of random effects due to the small sample size should be taken into consideration.

In Study I longitudinal associations between both parents' BMI and the degree of obesity in childhood and adolescence were reported. At age 7, a significant association between maternal BMI and children's degree of obesity was identified. At age 15, the associations to both parent's BMI were significant and stronger than at age 7. A strengthened association was particularly pronounced for the paternal impact, which was comparable to maternal impact at age 15. No similar longitudinal study on parent-child resemblance in relative weight within a high-risk population has been identified. However, population-based longitudinal studies have reported similar results, showing that associations with parental BMI grow stronger from childhood to adolescence and that associations with both parents are of similar strength [37, 47, 271]. Also very large population-based cross-sectional studies including children of all ages have reported similar degree of parent-child resemblance in relative weight [41, 44, 272]. The identified degree of associations in relative weight of our and most other studies (r ~ 0.2-0.3) may be considered fairly weak [272]. In our study the obese children appear to be no more similar to their parents in body weight than other children. However it has to be considered that the associations is found within a group of obese children, and not in comparison with children in general, which strengthen the specificity of the results.

The number of obese parents

Children with the most severe obesity were more likely to have two obese parents, compared to children with more moderate obesity (Study I). As the risk for childhood obesity persisting into adulthood is higher in children with two obese parents and additional persistence is increased by the degree of obesity, the prognosis for the most severely obese children with obese parents is poor [34]. In the Early STOPP high-risk populations as many as 25% of the infants had two obese parents (Studies II and IV). These infants may be ten times more likely to develop obesity by age 7 compared to the low-risk infants [39]. But even though having none obese parent is protective, it does not prevent obesity in all cases; half of the obese children in Study I were in this situation. However, children with no obese parent were more likely to have a moderate degree of obesity.

There is evidence that parents' relative weight is inter-correlated ('assortative mating'), implying that partner selection is affected by similarity in body fatness [273]. Since assortative mating appears to be more common in couples where both individuals are obese, this may confer a higher risk of obesity in the offspring generation [273]. An

increased rate of assortative mating has been suggested as contributing to the increase of severe obesity in children [274].

Maternal and paternal impact

The question of whether the impact of maternal and paternal BMI was of similar magnitude was addressed in Study I. At age 7 the association with maternal BMI was stronger, when adjusted for obesity onset, whereas at age 15, adjusted associations with both parents were of similar strength, stronger than at age 7. We have not identified any comparable longitudinal studies in high-risk populations, however the findings of several large population-based studies are somewhat conflicting. According to most studies the impact of both parents is equally strong from 2-3 years of age, whereas the mother appears to exert a stronger influence at birth and during the infant years [37, 42-45, 275]. However, evidence for a significantly stronger maternal influence has also been demonstrated [38, 41, 46], and a few studies have identified stronger impact of paternal BMI or obesity [135, 276]. However, our finding is in line with the studies concluding that both parents have a similar long-term impact [42, 44, 45].

Gender differences in parental-child associations was also analysed in Study I, but no differences between mother-daughter and mother-son, and between father-daughter and father-son associations were observed. The evidence for different parental effects by offspring gender is conflicting; some studies have not reported such an effect [45, 46, 277], whereas others have [47, 49, 50].

Obesity onset

In Study I, parental BMI did not have a clinically relevant impact on the age at onset of obesity (even though a higher paternal BMI correlated significantly to an earlier obesity onset, this association only explained 2% of the variance in obesity onset). Our sample of obese children developed obesity early, almost 60% of the children were obese by age 4 or younger. This is comparable to other clinical samples of obese children [278, 279].

Our finding is interesting, suggesting that heredity, in terms of parental obesity, is not important for *when* the offspring develop obesity (although parental adiposity may not only reflect heredity; see the section on *Nature and nurture* below). Previously, an early age at onset in childhood was associated with monogenetic forms of obesity [280]. More recently, common genetic markers have been associated with increased weight gain very early in infancy [65, 66]. However, the genetic impact conferred from parental adiposity has been shown to be independent of known genetic markers [65], and may influence children's weight development differently from identified obesity genes (see further the section on *Nature and nurture* below), which can explain why no impact of parental

BMI on obesity onset was identified. Surprisingly, there are few other studies that have studied age at obesity onset as the outcome, in relation to parental adiposity. Instead, adiposity rebound, the age when the child's BMI curve start to rise, has been in focus, identified as one of several critical periods for obesity development [281]. An early adiposity rebound has been associated with an increased obesity risk, independent of parental adiposity, both later in childhood and in adulthood [34, 39, 282]. It is likely that an early adiposity rebound is linked to early obesity onset, even though no reports of this association have been identified. An earlier adiposity rebound has been linked to parental adiposity [282-284], and these findings may be considered inconsistent with our result. However, the findings of Study II and other studies [48, 285] regarding a lack of an early impact of parental adiposity on children's adiposity are in line with the hypothesis that parental adiposity would not influence early obesity onset.

HOW DOES PARENTAL EDUCATIONAL LEVEL AFFECT CHILD WEIGHT DEVELOPMENT?

The impact of parental educational level, as a proxy for family socio-economic status, on child relative weight has been taken into consideration in all the studies of this thesis. The associations between child weight and parental BMI were adjusted for parental education in Studies I, III and IV. In Study II, the hypothesis that low parental educational level would interact with high parental adiposity to increase the risk of accelerated growth was tested. Our results support that an impact of parental educational level is present already in infancy, but also that it influences degree of obesity in adolescence.

In Study II, associations between low parental educational level as an obesity risk factor and infant relative weight at 3, 6 and 12 months were identified. Some previous studies have reported similar associations between low parental SES and infant growth [83, 84]. In contrast, in a large British longitudinal study socio-economic differences in children's BMI did not become apparent until age 4 [286]. Again, it is possible that our study design, comparing two populations with a very pronounced difference in parental educational levels, may optimise the chance of detecting clinically distinct differences between the groups. Our results correspond to absolute differences in mean weight of approximately 0.5 kg at 6 and 12 months, which is not a negligible effect size at these early ages. It is important to note that the associations identified were independent of birth weight, which was the strongest predictor of child relative weight during the first year.

No association between parental education and rapid weight gain could be identified. Results from previous similar studies are conflicting [83, 287]. Why our results regarding associations to parental education differ for the two different infant growth outcomes, high relative weight and rapid weight gain, is not clear to us. Rapid weight gain was associated with a lower birth weight, just as expected since early postnatal rapid weight gain may occur as a catch-up effect of prenatal growth restriction [284]. Follow-up analyses on the Early STOPP cohort will disentangle the impact of both infant growth outcomes on future weight development in relation to parental factors.

In Study I, parental education was not associated with obesity onset or the degree of obesity at age 7. However, at age 15 a protective effect of high level of parental education on degree of obesity was indicated. These findings suggest that the influence of parental educational level may become stronger with age. Evidence from other longitudinal studies showing that SES differences in child weight increase with age further confirms our finding [81, 286, 288]. For example it has been reported that socio-economic differences in relative weight present at age 4–5 more than doubled by age 10–11, independent of parental BMI [288]. Increasing differences between healthy and unhealthy lifestyles may contribute to these growing socio-economic inequalities as the child becomes older [289]. This is further demonstrated by evidence from population-based studies that the widening socio-economic disparities reflect both decreasing mean BMI in the more advantaged children, coupled with simultaneously worsening rates of overweight in the more disadvantaged [288].

The somewhat conflicting results regarding the timing of the impact of parental education - association identified in infancy, no association seen later in childhood and finally an association observed in adolescence - may be explained by differences in the populations and different measures of parental education in the two studies. Nevertheless, our findings support a very early influence as well as an effect of parental educational level that is still present in adolescence. However, in comparison with parental adiposity, the long-term impact of parental educational level is weaker.
So which underlying mechanisms can then explain the impact of SES factors on child weight? These mechanisms are likely to differ early on in infancy compared to later in childhood. In infancy, potential mediating factors include infant feeding methods, maternal smoking during pregnancy and parental age. These factors have previously been seen to partially explain SES differences in infants' weight [83, 84]. The mediating effect of these factors was tested in Study II, as well as the impact of gestational weight gain and birth weight. Only maternal smoking was seen to partially contribute to the association between education and child growth and we could not confirm the mediating effect of infant feeding reported by previous studies [83, 84] (see below the section on *How*

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do early life factors…). One hypothesis is that short sleep duration could possibly mediate the association between SES and weight in infants, however this has not been observed in older children [289]. Other potential mechanisms by which the association to parental education could operate are parental feeding practices, such as responsive feeding, and child eating behaviours, which both have been related to SES factors [176, 290]. Later in childhood the association with parental education may be explained by parental and child lifestyle [289, 291, 292].

HOW DO EARLY LIFE FACTORS AFFECT CHILD WEIGHT DEVELOPMENT?

In addition to the impact of parental adiposity and educational level, other early life factors – such as maternal gestational weight gain, birth weight and parental smoking – may further increase the risk of obesity [36, 94]. Associations between early life factors and infant growth were primarily studied in Study II, but the effect of birth weight and infant feeding on child relative weight was also tested in Study IV. Furthermore, the influence of birth weight on degree of obesity and obesity onset was reported in Study I. These factors were included to control for confounding effects between child weight/growth and parental adiposity/educational level. The independent associations with early life factors are discussed here, separately from the main outcome of these studies. The only distinct association observed was between birth weight and growth in infancy.

Birth weight
The findings of Study I and II have shown that birth weight clearly affects weight development in infancy, however the impact diminishes with age and most of its long-term effects may be attributable to parental adiposity. In Study II, birth weight was the dominating predictive factor for both relative weight and rapid weight gain during the first year; a high birth weight was associated with a higher relative weight and lower probability of rapid weight gain. These results confirm previous findings [106, 293-295], and reflect the complex relationship between birth weight and obesity, where both high and low birth weight has been linked to an increased obesity risk [106]. The strength of the associations between birth weight and infant weight was not surprising, given the close distance in time/age, seen also in other studies of infants [295]. In Study I birth weight was not significantly associated with the degree of obesity at age 7 and 15. The associations between birth weight and relative weight may be attenuated by age and by adjusting for obesity risk factors with greater effect, such as parental adiposity [293, 296]. Also, birth weight was not associated with obesity onset in Study I, which was more unexpected, especially in the light of the strong associations identified in Study II. Weak but

independent associations between birth weight and obesity status at age 7 [39, 297] and body composition measures at age 15 [293] have been demonstrated in other studies. Of note, associations between birth weight and obesity risk have often been analysed using dichotomised data for birth weight (high vs low) rather than continuous measures [107], as in our studies, which is important to consider when comparing our results with other studies.

Maternal gestational weight gain

We could not see any distinct effect of maternal gestational weight gain (GWG) on infant growth in the multivariate analyses where birth weight was identified as the strongest predictor, although weak unadjusted correlations to child relative weight at 6 and 12 months were found. This demonstrates that the influence of GWG on child weight development predominately is mediated by birth weight, as has been shown before [97, 98, 100].

Infant feeding

A short period of exclusive breastfeeding was not associated with high infant weight or rapid growth, in contrast to several previous studies [83, 84, 294, 298, 299]. In Study II about 25% of the infants were breastfed for less than two months, and this was more common in infants with overweight or obese parents. Even though the long-term protective effect of breastfeeding on childhood obesity is negligible, the associations between short duration of breastfeeding and early introduction of formula feeding on growth in infancy may be stronger [83, 84]. However, stopping breastfeeding and starting complementary feeding may also be a response to rapid early weight gain rather than a cause [300, 301]. A higher protein content of formula compared to breast milk may contribute to increased infant weight gain, and a higher intake of protein has been linked to infant weight gain and higher adiposity [302-304]. However, in Study IV no cross-sectional association between protein intake and infant weight could be identified. The age at introduction of solid foods showed no association with infant growth. Previous research has provided inconsistent findings regarding the impact of an early introduction of solid foods on obesity risk [124].

Maternal smoking

Infants of smoking mothers had a higher relative weight at 12 months. In Study II maternal smoking status when the child was one year was used. However, it is the *prenatal* effect of maternal smoking during pregnancy that has been the primary focus with regard to obesity risk later in childhood, through prenatal growth restriction, a lower birth weight and an early postnatal catch-up growth [101]. Unfortunately, data on smoking during pregnancy was not available Still, negative effects of *postnatal* parental

smoking on child growth have also been reported [94, 102], although it has been argued that the effect is likely to be explained by other factors not measured and adjusted for, such as parental psychological health [102]. Residual confounding may explain the association between maternal smoking and infant weight also in our study.

ARE DIETARY HABITS AT AGE ONE OBESOGENIC?

This question will be discussed in the light of the findings of Study IV regarding the potential obesogenic dietary components in infants at age one, regarding the impact of parental food intake on the diet quality of their infants, and finally regarding the impact of the infants' dietary intake on their weight.

Our main hypotheses about potential obesogenic components of food habits in children at age one, based on previous evidence, included a too-high intake of protein, an unhealthy balance in fat quality and early introduction to unhealthy foods, where these latter aspects possibly would be associated with parental food habits. Additionally we initially aimed to include analyses of the children's meal frequency, but this aspect was not retained in the study. We had hypothesised that we would not identify any significant discrepancies in dietary intake between children at high and low risk of obesity as determined by parental adiposity, and that the potential influence of parental food habits would not yet be substantial due to young age. These hypotheses were confirmed.

The infant's food habits were found to be very homogeneous, regarding nutritional content, diet quality measures and food choices, and no differences between infants at high and low risk were observed (Figure 9). Most children had been introduced to family meals, but typical infant foods such as formula, porridge and ready-made baby dishes dominated. Most children drank water at main meals, four of five children ate fruit daily, about half of the children had been introduced to sweets, but only one in ten to sugar-sweetened beverages and only 5% to salted snacks. Thus the infants showed a fairly good overall diet quality using these measures. However, the children did not adhere fully to nutritional recommendations; specifically the intake of saturated fat was too high in the majority of the infants compared to recommendations. This confirms a previous study of Swedish infants, concluding that the quality of dietary fat was not within recommendations [160]. Regarding protein intake, most of the infants had an intake according to recommendations, although one in five had a too high intake and a tendency that this was more common among the high risk children was observed. This may increase the risk for subsequent adiposity, because a too-high protein intake during

infancy have been associated with an increased risk of higher relative weight and obesity later in childhood [133, 135, 305]. It has been shown that one-year-old children have a higher diet quality compared to children 2-6 years old [306, 307]. This is consistent with our finding that the overall diet quality of one-year-old infants is fairly good.
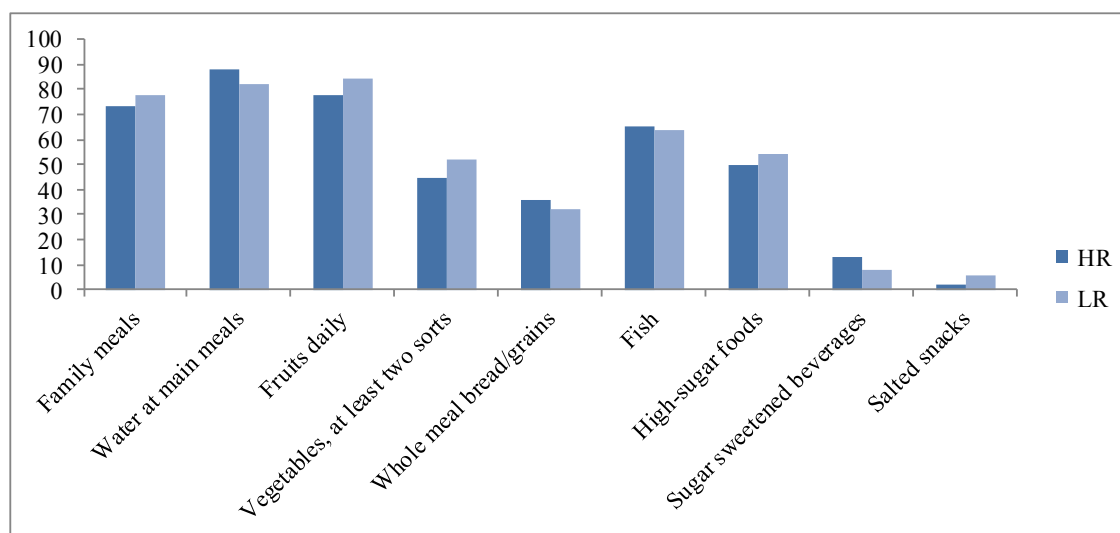

Figure 9. Proportions (%) of children fulfilling the dietary quality indicators in high- (HR) and low-risk (LR) infants (Study IV).

The children's dietary intake was not associated with obesity risk, i.e. no differences in energy intake or diet composition between high and low-risk children were observed, confirming a previous study of similar design [151, 308]. Furthermore, no associations between parental and child unhealthy diet indicators (high-sugar foods, sugar-sweetened beverages) were observed. So even though an unhealthy dietary pattern was evident among the high-risk parents, their intake of unhealthy foods had apparently not been carried over to the children. On the other hand, regarding some healthy foods (fruits and fish) significant associations between the child's and the father's intake were identified. The evidence for associations between child and parental food habits mostly relies on studies in older children [145-147]. However, in line with our results, parent-child resemblance in unhealthy aspects of dietary intake has been shown to be stronger among older children, whereas resemblance in healthy dietary aspects may be strongest among younger children [309]. In contrast, early influences of parental food habits have been reported from a large Swedish birth cohort, where the intake of high-sugar foods in one-year-old children was associated with the mother's intake of high-sugar foods (during pregnancy) and with an overall more unhealthy dietary pattern [140]. Nevertheless, a reasonable conclusion is that one-year-old children not yet have been heavily exposed to obesogenic food habits.

No associations between child dietary intake and child relative weight (BMI SDS) were identified. However, energy intake correlated to both weight and BMR which support accurate reporting of food intake (see below the section on *Validity of dietary intake*). The lack of association between dietary intake and *relative weight* indicate that the homogenous dietary intake at age one does not impact on the children's adiposity or may be due to variations in physical activity. A lack of concurrent association between child dietary intake and relative weight at age one has been reported previously [151, 310]. However, evidence for a time-lagged association between energy intake at 3 and 6 months and weight at 12 months has been identified [151]. In future studies of the Early STOPP infants, the impact of their dietary habits at age one on subsequent weight development can be studied using a prospective longitudinal design, contributing to increased knowledge about their potential obesogenic effects.

Most Swedish parents have frequent contacts with their CHC centre during the first year and are well informed about recommended weaning practices, appropriate meal patterns and what foods to serve the child. This may contribute to the very coherent pattern of dietary intake in Swedish children at this age, additionally demonstrated through the lack of consistent associations with socio-demographic factors, in contrast to previous research [140, 153, 155, 156]. Further, considering that the parents have chosen to participate in the Early STOPP study, they are likely to be conscious of their own habits, both healthy and unhealthy, and interested in and possibly knowledgeable about what constitutes healthy habits for their child. Also, many of the overweight and obese parents have expressed the wish to avoid their child inheriting their unhealthy habits/life style and becoming overweight.

When a child adopts the family food, he/she is likely to be exposed to a more varied diet and more new flavours, compared to eating only typical infant food. It has been shown that flavours that children have been exposed to early in life, even prenatally, have a long-lasting positive effect for their food preferences later in childhood [311, 312]. Thus it is likely that an early introduction to family meals, with repeated exposures to an increased variety of flavours, will impact positively on the child's taste preferences and food habits later in life [313]. In Study IV three in four infants had been introduced to family foods, but very few had completed the transition to family foods. However, eating the same food as the other members of the family also increases the likelihood that the child is introduced to unhealthy foods. For example, having older siblings is associated with a higher intake of high-sugar foods [156, 314], which also was indicated in our study (not reported in Study IV). On the other hand, independent of this negative impact on food habits, having siblings is also associated with a decreased risk of obesity [89]. Thus, positive effects of having siblings appear to dominate, possibly through the impact of

higher levels of physical activity or less amounts of food available per child [315]. Whether early introduction of high-sugar and energy-dense foods is obesogenic needs to be further studied in prospective studies.

ARE EATING BEHAVIOURS IN PRESCHOOL CHILDREN OBESOGENIC?

Associations between eating behaviours, measured using the previously developed and validated instrument Child Eating Behaviour Questionnaire (CEBQ), and child relative weight were reported in two of the studies in this thesis – with opposite results. In the validation study (Study III) no significant associations were identified, whereas in the Early STOPP study (Study IV) eating behaviours were clearly related to child relative weight. The results of both studies were independent of parental adiposity and education. It should be recognised that our studies are cross-sectional and based on our findings no inference on causality can be made. However our findings will be discussed in the light of additional evidence from longitudinal studies.

How should the conflicting findings of the two studies be interpreted? Firstly, the two study populations differed in several ways, regarding child age, obesity risk profile and sample size, characteristics that are likely to affect results. The small sample size in the validation study, with data on weight only available for a small sub-population, limited opportunities of detecting significant associations, recognised as a limitation of that study. The Early STOPP cohort included approximately four times more children. The relationship between eating behaviours and weight in infants has been seen to be moderated by parental obesity, observing associations only in high-risk infants with obese parents [316]. This may also explain the different results, as Study IV included high-risk infants, whereas Study III mainly included low-risk children. Also, as several of the eating behaviours were shown to vary considerably with child age in the age bracket 1-6 years, comparisons of associations between one-year-olds only and a mix of children 1-6 years old may not be appropriate. The identified associations in Study IV were also independent of birth weight, which further strengthened the results.

Concurrent associations between eating behaviours and child weight have been identified in different populations of children, using different instruments [164, 172, 173]. Only few studies have been conducted as early as during infancy, but some evidence support very early links, as early as at 3 months, between child appetite traits and weight [151, 180]. Later in childhood it has been demonstrated that obese children have higher levels of obesity-promoting behaviours, such as lower satiety responsiveness, higher food cue

responsiveness, faster eating rate and not slowing down their eating rate towards the end of the meal, compared with normal weight children [165-167].

How infant eating behaviours are related to subsequent adiposity in children has been studied in a few longitudinal studies [151, 176, 317, 318]. In one longitudinal study from 3 to 15 months it was demonstrated that the associations between appetitive traits and subsequent weight were stronger than between weight and subsequent appetite, supporting that differences in appetitive traits influence weight gain in early childhood [317]. Additionally, picky eating and overeating at ages 2, 3 and 4 have been related to body weight at age 4 [176]. In contrast, an eating avidity score measured at age one was not associated with child adiposity measures at age 7 [318]. These results may indicate that the strength of the associations between infant appetite traits and subsequent weight become weaker the older the child is when the outcome weight is measured.

Eating behaviours measured by psychometric questionnaires, such as CEBQ, are likely to be closely related to appetite regulation, which is one mechanism through which obesity-associated genetic markers operate [60, 319, 320]. For example, evidence support that the FTO gene exerts its effect through appetite control [61, 63, 321] and FTO has also been associated with satiety responsiveness and food cue responsiveness in children [64]. Thus a genetically determined up-regulated appetite, involving the 'appetite hormone' ghrelin, may lead to early rapid growth and subsequently increased risk of obesity [66, 319]. This is consistent with the early associations between eating behaviours and child weight identified in Study IV.

NATURE AND NURTURE IN CHILD WEIGHT DEVELOPMENT

As has been reported throughout this thesis, both genetic/biological (nature) and environmental/social/behavioural (nurture) factors contribute to weight development and subsequent obesity in children. There are many potential and suggested interactions between nature and nurture in the development of obesity. Even though it is outside the scope of this thesis to distinguish between the influence of nature and nurture, our results provide insights about their timing and interrelations regarding the impact of parental adiposity, parental educational level and child eating behaviours.

Nature and nurture interactions
Both nature and nurture are involved in the development of childhood obesity [53]. Regardless of genes, unless an individual is exposed to an obesogenic environment and to a positive energy balance over time, obesity does not develop. On the whole, the

increase in obesity prevalence over the past decades must be attributed to changes in the environment, whereas individual differences in susceptibility most likely are attributed to genetic differences between individuals [52]. It has been shown that the increase in childhood adiposity can only partly be explained by the increase in parental adiposity, which supports a major contribution of environmental factors [44, 297]. Evidence of gene-environment interactions is increasing [57, 322]. The shift of the BMI distribution, where the greatest increases in BMI have been observed at the highest BMI, which indicates that overweight and obese children are more strongly affected by the obesogenic environment than normal weight children, also confirms a strong gene-environment interaction [268, 269, 323].

Timing of impact

The effect of both genetic and environmental influences on body weight changes over time. Large twin studies have shown that the contribution of genetics is low at birth and in early infancy, but it increases gradually during childhood, whereas the influence of common environmental factors on body weight is strongest at birth and then reduces over time [51, 56, 324, 325]. The results of Study II aligns with these findings, as infant weight over the first year was associated parental educational level but not with parental adiposity. The findings of Study I are also in line with an increasingly stronger hereditary influence, as the associations with parental BMI grew stronger from childhood to adolescence.

Parental adiposity

The impact of parental adiposity on child weight development most likely operates through both hereditary and environmental mechanisms. The results of this thesis primarily support a genetic or epigenetic effect of parental adiposity on offspring weight development. This has been demonstrated by 1) lack of impact of parental adiposity on growth in infancy, when the children have not yet adopted the lifestyle of their parents and parental adiposity therefore is likely to represent genetics rather than environment (Study II and IV) and 2) increasing influence of parental BMI on degree of obesity from childhood to adolescence when the parental interference with the lifestyle of their children declines (Study 1). Adoption studies, reporting stronger correlations in relative weight between parents and biological children than between parents and adopted children, provide evidence for a strong genetic impact of parental adiposity [53]. However, the impact of parental adiposity on child growth and obesity risk may be independent of genetic risk as measured through a multilocus genetic risk score [65]. This indicates that if parental BMI primarily operates through genetics, the mechanism is not explained by known genetic markers but possibly through epigenetic mechanisms [70, 326], or the "missing heritability" [69]. Of note, even though parental adiposity and known genetic

variants both independently affect child weight development, the effect size of a genetic risk score appears to be negligible compared to that of parental adiposity [36, 65, 68].

On the other hand, adoption studies have also shown that parents' BMI may influence common environment in childhood, as correlations in relative weight have been observed between adopted children and their adoptive parents, although considerably weaker than between parents and biological offspring [53] (in contrast, adoption studies show no impact of environment on adult obesity). Suggested environmental impact conferred through parental adiposity includes many of the obesity risk factors discussed in this thesis, because parental obesity is related to, and may mediate, many environmental factors. Parental obesity can affect the prenatal environment through maternal obesity and diabetes, overnutrition, gestational weight gain and caesarian section. In the postnatal environment parental adiposity can mediate the influence of parental practices, infant feeding, food preferences and parental lifestyle habits on child weight. However, the relatively weak resemblance in weight status between parents and offspring may be explained by relatively weak parent-child resemblance in dietary and physical activity behaviours [272, 309, 327]. Also, in adolescence an environmental effect of parental adiposity is likely to be considerably reduced.

Most studies on associations between child and parental BMI are based on parents' BMI in adulthood, and very few studies have considered associations with parental BMI in childhood. In one intergenerational study offspring BMI was independently associated with both adult parental BMI and parental BMI in childhood [328]. It is possible that the effects of parental BMI in adulthood and in childhood operate through different mechanisms. Evidence of associations with parental BMI in childhood is likely to reflect a stronger genetic influence and may increase the risk of an earlier development of obesity in the offspring [328]. Even though associations with parental BMI in adulthood also reflect a genetic impact, an additional impact of the shared environment is possible, as discussed above [53].

Parental adiposity and low socio-economic status
Parental adiposity and low SES have been seen to interact to increased child adiposity [81, 329]. However, in Study II no such interaction effect between parental adiposity and education on infant relative weight was demonstrated, even though low parental education was much more common among overweight and obese parents. If parental adiposity mainly represents genetics, as discussed above, this suggests a stronger genetic/epigenetic-environmental interaction later in childhood, which possibly is an effect of the associations to both parental adiposity and parental education becoming stronger in older children.

Eating behaviours

The impact of eating behaviours on weight also appears to operate through both genetic and environmental mechanisms. There is evidence of a strong genetic influence on appetite traits in children, but environmental factors, such as parental food habits and feeding practices, play an important role in modelling children's eating behaviours [207]. Twin studies have shown that differences in weight/growth in infancy and later in childhood may be due partly to genetically determined differences in eating behaviours [177, 179, 180]. Particularly high heritability estimates have been identified for speed of eating and satiety responsiveness [179]. Also, the FTO gene has been associated with eating behaviours, such as diminished satiety, in children [64]. A genetic influence is consistent with the early independent associations between eating behaviours and child weight identified in Study IV and by previous research [151, 180]. Combined with the growing evidence of the genetic influence on weight and growth in early life [54, 66], appetite traits are likely to explain the genetically determined growth in early infancy [179]. In Study IV the associations between eating behaviours and infant relative weight were independent of parental adiposity. In contrast, parental obesity has also been seen to moderate an early association between eating behaviour and weight, which was evident only among children with obese parents [316]. However, even though parental adiposity and eating behaviours both represent genetically-determined obesity risk factors in infancy, these may not necessarily be related.

For other eating behaviours, such as food responsiveness and enjoyment of food, the shared environment has a moderate effect, indicating that infants' appetitive responses to food and food cues are affected by environmental factors, such as such as over-nutrition in utero and parental feeding practices in early childhood [179]. As children get older, eating behaviours become more sensitive to environmental influences both within the family and outside the home [178]. The environmental impact on eating behaviours may also influence on their effect on child weight.

WHEN SHOULD PREVENTION BE INITIATED AND WHO SHOULD BE TARGETED?

With the current high obesity prevalence there is no dispute over the need for preventive initiatives. However it is less obvious at what age it is most efficient to begin interventions and whether interventions should be directed at all children or target specific risk groups. The cost of prevention versus the benefits as well as potential negative consequences of prevention also needs to be considered.

When to start

Several critical periods in childhood for the development of obesity have been proposed: the prenatal and early post-natal period, the period of adiposity rebound (age 5-7) and adolescence [281]. It has been suggested that obesity that begins at these critical periods may increase the risk of persistent obesity and therefore should be considered for preventive efforts [281]. The need for preventive initiatives must also take into account that obesity today is common at younger ages.

The sooner the better? Indeed, the arguments for initiating prevention early in childhood are several. The early childhood years is a changing period in many ways for both children and parents. It is under a substantial amount of control by parents and other care-givers yet sensitive to environmental changes. Additionally early childhood offer multiple settings for prevention, such as family/home environment, child healthcare and child care [221]. Also, as has been presented, many obesity risk factors are present very early in life, even prenatally, and have long-term impact [39, 93, 330]. Several of these early risk factors are modifiable, such as early infant feeding and maternal smoking, and could be targeted in interventions. As demonstrated, infant weight as early as their first year is higher in families with low education. Even though the underlying mechanisms and consequences are not yet fully comprehended, this provides an indication that the early post-natal environment can be targeted for obesity prevention. Also, while infant feeding and infant dietary intake were not related to early weight development in our populations, future studies will reveal their long-term effect. Furthermore, in order to prevent obesity, efforts naturally need to be initiated before the onset of obesity. In the US where the obesity prevalence in preschool children is high and the age of obesity onset is alarmingly low, the critical period for preventing childhood has been suggested to be during the first 2 years of life and thus infants are suggested to be the target of prevention [278, 331]. In our clinical sample of severely obese children in Study I, many became obese already by age two and could potentially have benefitted from preventive efforts very early in life. Targeting infants naturally involves the parents, which has been identified as one key success factor of obesity prevention [213]. Parents of newborns may be particularly sensitive to information given about their child's health, which offers additional support for initiating prevention during infancy [36]. Also, it is easier to establish healthy habits from the beginning than changing behaviours later on.

The Early STOPP intervention is an example of early obesity prevention initiated during the child's first year, when the families were recruited through child healthcare centres [190]. The age of one appears suitable for the initiation of a preventive intervention for many reasons, besides those mentioned already. At this age the child's daily habits are rapidly changing, for example the transition to family foods is ongoing, opportunities to

physical activity increase, sleep habits are becoming more regular and new daily routines are introduced as many children start kindergarten.

The optimal duration of preventive interventions depends on the intervention, but from existing evidence a follow-up period of at least one year is recommended [213]. Short-term interventions may not be efficient in producing long-lasting effects [213]. The Early STOPP intervention is five year long, following children until 6 years of age [190]. As reported, the risk is high that children of obese parents develop obesity by school age [39]. The aim of the Early STOPP intervention is therefore to help parents establishing healthy habits for their child at an early age and to continuously support them as they are facing new challenges regarding their child's daily habits and development phases as well as a gradually increasing exposure to the obesogenic environment.

Or perhaps obesity prevention should be initiated even earlier, before birth, directed to pregnant women [332, 333]? Several prenatal risk factors emerge already during pregnancy and women may be especially motivated to modify their behaviour during this period. Interventions targeting pregnant women would focus on a healthy gestational weight gain and a healthy foetus environment [332]. The idea is to prevent foetal over- or under-nutrition, leading to a non-optimal birth weight (too high or too low) which in turn increases the risk of future obesity [108].

On the other hand, even though increasing attention regarding obesity preventive efforts are directed at younger children, school-age children should not be disregarded. In mid-childhood, between 7 and 9 years of age, a substantial excess weight gain may occur [334]. Therefore it has been suggested that prevention should focus on school-aged children as well as the preschool years

Who to target
The next question is whether obesity prevention should be directed at all children or target specific risk groups? Which is the most efficient, general prevention to many or targeted prevention to a selected high risk population? More evidence for both types are needed, and both targeted and general randomised intervention projects are currently ongoing in Sweden [190, 335].

It has been argued that due to the high prevalence of obesity in parents and children, population based prevention is required [329]. On the other hand, the efficiency of targeted prevention largely depends on how precise the high risk population can be identified. The 'prevention paradox', first described in 1981 by the epidemiologist Geoffrey Rose, stipulates that a small preventive effort to many often is more efficient than a

comprehensive intervention to a targeted risk group [336, 337]. This is explained by the fact that the majority of cases of a disease often come from a population at low or moderate risk of that disease, and only a minority of cases come from the high-risk population. This is because the number of people at high risk is small (the example studied was cardio-vascular disease). Further, misclassification of individuals may limit the effectiveness of an intervention targeting a subpopulation at high risk. The prevention paradox has been demonstrated also in obesity prevention; in a large sample of children, the subgroup with the highest risk of obesity, based on risk factors present early in childhood, represented less than 10% of the overweight cases [338]. This indicates that even highly effective prevention programs for selected high-risk subgroups may not considerably reduce childhood overweight on a population level [338].

However, if all individuals that will develop obesity could be correctly identified beforehand, the efficiency of targeted prevention would be considerably enhanced. This could be accomplished if consistent, high-quality evidence for important obesity risk factors can be presented. What if a simple formula could be applied, using a set of factors known to affect obesity risk, to calculate the individual obesity risk very early in life? Well, such formulas have recently been developed [36, 95]. In one such model, British researchers used data from three different cohorts of more than 6 000 children from Finland, Italy and the U.S. to develop and validate predictive equations for childhood and adolescent obesity in newborns [36]. Independent predictors of obesity included in the equations were parental BMI, birth weight, maternal gestational weight gain, number of household members, maternal occupation and maternal smoking during pregnancy. The accuracy of the models was very good, identifying approximately 80% of all children becoming obese later in childhood or adolescence. The models were applicable, with some modifications, to different populations with different culture and obesity prevalence. Severe and persistent obesity was better predicted than mild obesity. In comparison, most of the factors included in the model have been studied in this thesis, but an influence on obesity risk have not be confirmed for all of them (it should be acknowledged that we have not measured the longitudinal impact of all factors and also other outcome measures have been used). However, the clinical applicability of such a predictive tool is potentially very high, as a large proportion of infants could be excluded from preventive interventions and consequently the cost-effectiveness of prevention could be improved. However, the relevance of such a formula must be confirmed for the population of interest.

Obesity prevention is likely to be costly [339] and to fully estimate the cost-effectiveness of prevention efforts the long-term costs of childhood obesity needs to be taken into account [340]. Also, potential adverse effects of prevention must be assessed to ensure that

interventions are safe and appropriate [213]. This is particularly important in early childhood, as this is an important growth period. Prevention in young children may also possibly disturb parental-child interactions. Targeted prevention could be stigmatising for the families being identified at risk. In older children, potentially negative effects of prevention that should be evaluated include unhealthy eating behaviours (eating disorders), body image perception, teasing and stigmatization. However, there is no evidence of any adverse effects, but only few studies have reported that negative consequences have been assessed [161, 213, 215].

METHODOLOGICAL CONSIDERATIONS

In addition to methodological issues already mentioned in the preceding sections, the following aspects should also be considered in the interpretation of the results.

External validity

Generalisation of the results must take the characteristics of the study populations into account. The main research questions were specifically formulated for high-risk populations. As have been demonstrated the populations were indeed high risk on the basis of parental adiposity and thus the results would be valid for similar high-risk samples and for selected populations with an extreme difference in obesity risk. Generalization of our findings may additionally be limited to ethnic homogeneous groups.

In Study I, the population of obese children was clearly a selected group as all children were severely obese undergoing treatment at a clinical tertiary referral centre. The associations identified between the parents' and children's relative weight may only be generalisable to populations with obese children. Still, comparisons of our results with populations of similar risk level in terms of parental adiposity may also be applicable. Children with the most severe obesity were more likely to have two obese parents. Possibly self-selection bias could contribute to this finding if obese parents are more 'tolerant' as concerns moderate obesity in their child and only seek health care for a child with severe obesity.

Regarding the findings of the Early STOPP studies (Studies II and IV) it should be acknowledged that the high- and low-risk groups were not randomised and thus there may be unknown differences between the groups that were not be adjusted for. In general, the Early STOPP parents are likely to be more interested in healthy habits and/or have a higher level of concern for their child's risk of developing obesity,

compared to the source population. This may have affected the findings related to environmental or modifiable factors, such as parental educational level and family food habits. Thus the differences identified in infants' relative weight by high and low parental educational level in Study II may have been underestimated. Still these results may only be generalized to groups of infants where parental educational level or possibly other SES indicators differ substantially and comparing infant growth between families with less socio-economic disparity may result in less distinct differences. Even though the study population had a higher prevalence of low parental educational level compared to the whole ES population, there is no reason to believe that our findings of Study II (the associations between parental educational level and infant growth), would have been different in the whole population. Concerning the lack of impact of parental adiposity on infants' weight despite the extreme discrepancy in obesity risk, which probably reflects heredity rather than environment at this early age, it is likely that such an impact is even weaker in the general population due to a smaller variation in parental adiposity. The self-selection bias mentioned above could also have contributed to the non-significant results in Study IV, where the infant's dietary intake and eating behaviour did not differ between the high- and low-risk families. Early STOPP parents may be more anxious to serve their child healthy foods than the source populations of high and low risk families.

In Study III, the absence of association between eating behaviours and relative weight may be possibly be explained by self-selection bias in the recruitment of the subjects. The parents that agreed to respond to the questionnaire may have been more interested in healthy habits and behaviours than non-responders and possibly therefore answered the questions more homogeneously.

Different measures of child relative weight

As reported, two different measures of child relative weight, BMI SDS, have been used in this thesis. The older French reference was used in Studies I and III [250], and the Swedish, more contemporary reference was used in Studies II and IV [9]. The measures differ mainly due to the reference population being collected before and after the obesity epidemic.

Could the use of the different BMI SDS measures have affected the results, and if so, how? The relationship between the two measures have been analysed using data from children 6-10 years old and estimated at: BMI SDS Karlberg = -0.17+ 0.89 * BMI SDS Rolland-Cachera – 0.05 x BMI SDS Rolland-Cachera^2 (Figure 10) [341]. Values between -2 and 2 are relatively similar for the two measures, but below -2 and above 2 values cannot be compared straight forward with no adjustment (the measure using the French

reference has higher absolute values). In Study I most of the children had a BMI SDS outside this range, thus associations to parental BMI could have been slightly affected if the measure based on the Swedish reference had been used instead. Because of the strong correlation between the two measures of BMISDS, there is no reason to believe that the associations to other factors will vary very much. However, comparison of absolute levels of BMI SDS between the two measures should be avoided outside the range of -2 to 2. In Studies II, III and IV, most children had BMI SDS values within the -2 to 2 interval, and thus it is less likely that the choice of measure would have affected the results.
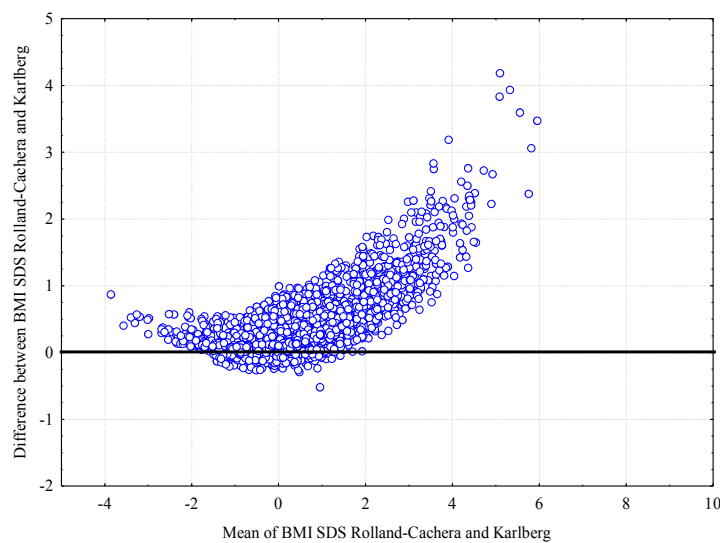
Figure 10. Estimation of the relationship between BMI SDS Rolland-Cachera and BMI SDS Karlberg.BMI SDS Karlberg = -0.17+ 0.89 * BMI SDS Rolland-Cachera − 0.05 x BMI SDS Rolland-Cachera^2 [341].

Different measures of socio-economic status

It should be recognised that parental education is only a proxy for the socio-economic environment, which may be measured in relation to obesity using a range of different indicators, both on the family level and on the living area and country level [13, 291, 342]. Living area measures, such as degree of urbanisation or area-level income, have been found to be more weakly associated with obesity compared to family-level SES-indicators [13, 288]. In addition to parental education, parental occupation and income are two other common SES indicators on the family level. Of these three, parental education is considered of particular importance regarding child obesity. Additionally, data on parental educational level is easy to collect and to compare between different studies and countries [342].

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Validity of eating behaviours

The children's obesity-related eating behaviours have been assessed using the Children's Eating Behaviour Questionnaire (CEBQ), previously developed and validated against behavioural measures in UK child populations 2-7 years old [174, 253]. Since the CEBQ had not previously been used on Swedish children, exploring the factor structure of the Swedish translation of the questionnaire was performed in Study III (and repeated in Study IV). The factor analysis tested if the individual questions of the questionnaire were inter-correlated and correlated to the overlying factors (eating behaviour traits) as expected, compared to the structure of the original questionnaire. Besides factorial validity, this section further addresses the validity of the eating behaviours estimates in terms of variation in age and associations with child weight and dietary intake.

The aim of Study III was to validate the factor structure of CEBQ in a population of preschool children similar to the Early STOPP populations. Thus the children recruited were between one and six years of age, corresponding to a cross-section of the child ages in the Early STOPP follow-up period. The factor analysis identified seven distinct factors with an acceptable internal reliability and correlations between sub-scales, similar to the original eight factor solution [174]. An identical seven-factor solution had previously been identified on a Dutch sample [257]. The Swedish version of the CEBQ was thus considered to have good factorial validity and reliability. However, the population in the validation study did not correspond to the high risk population of Early STOPP and this is a limitation of Study III. Only a small proportion of the parents were obese and all children were normal weight. In this population no associations between eating behaviour factors and child weight could be identified, possibly due to the weight homogeneous sample or self-selection bias. Hence the identified factor structure for children 1-6 years of age may not be applicable to a high-risk population. Therefore a new factor analysis was performed on the Early Stopp infants in Study IV, resulting in the original eight-factor structure, which was used for further analyses in Study IV.

The CEBQ capability of identifying associations between eating behaviours and infant weight was demonstrated in Study IV, where a very distinct pattern of associations was identified. The 'food-approach' behaviours, which promote eating, were all positively associated with the infants' relative weight, whereas the 'food-avoidant' behaviours, which reduce eating, were negatively associated, when controlled for obesity risk (parental adiposity), parental education and infant feeding. Only associations with the individual dimensions of eating behaviors have been reported previously, however in our study additionally associations with the two aggregated measures were identified

and reported. This may be an applicable method for categorising children into overall appetite traits.

As the CEBQ was originally developed and validated for children 2 years and older [174, 253], it is possible that the validity of the eating behaviour estimates was lower for the infants of Study IV. Some questions may have been less applicable for one-year-old children, which could have affected the resulting factor structure, the eating behavior estimates and the associations to child weight. However, as the factor structures identified were similar to the original structure in both studies, it is plausible that this did not have a significant effect on the results. After our study was performed, the CEBQ has been used in other populations including one-year old children [254, 256].

Study III showed that some of the eating behaviour factors varied with child age in an opposite way compared to what has been demonstrated previously. For example enjoyment of food and overeating (food responsiveness/emotional overeating) were less present in older children of our population, whereas these behaviours are thought to increase with age. However the stability of appetite traits have been estimated in children from age 4 to 11 [175], and thus the age variation reported for our population is not comparable, because infants and toddlers were included. This is clearly illustrated with our findings for food fussiness. Food fussiness is related to food neophobia, which is known to emerge by 18-24 months, peak at age 3, and then gradually decrease by age. However, in our study food fussiness was least present in the youngest, one-year old children - just as expected since food neophobia has not yet developed at age one.

The link between eating behaviours and weight would logically be dietary intake, and evidence for such associations would further support the validity of the eating behaviour estimates. However, these associations have not been satisfactory explored previously [206, 343, 344]. In Study IV several reasonable associations between eating behaviours and dietary intake was identified: positive associations between food-approach behaviours and protein intake, and between food-avoidant behaviours and fat intake as well as a negative association between food-avoidant behaviours and dietary fibre. A plausible interpretation is that children with a 'high appetite' (high scores on food-approach behaviours) eat higher amounts of foods rich in protein, such as meat, fish, milk and egg, and children with a 'poor appetite' (high scores on food-avoidant behaviours) are served a diet with more fat and eat less vegetables, fruits and high-fibre foods. In one comparable study in children 2-6 years old, food neophobia, the reluctance to taste new foods, was related to a lower intake of vegetables, fruit and meat [343] – a result very similar to ours. Thus the identified link between eating behaviours and dietary intake additionally supports the validity of the eating behaviour measures.

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Validity of dietary intake

In order to determine the validity of a dietary assessment, comparisons with another independent measure must be carried out [223]. Several ways to evaluate the validity of the reported dietary intake of the infants and parents in Study IV were performed, including assessing plausible under-reporting of the infants' energy intake, comparing dietary intake with the findings from other studies and, most importantly, comparing fat intake of selected food groups with an objectively measured biomarker for fat quality, fatty acid composition in plasma. The choice of dietary assessment methods, different for infants and parents, are also discussed with regard to the validity of the reported intake.

Infants

For the infants an estimated 4-day food record was chosen as the diet assessment method, mainly as it offers flexibility in the ways the diet data can be analysed. A food record can provide output regarding energy, diet composition, nutrient intake, intake of food items/groups and meal frequency. Also, a dietary index or diet quality indicators can be applied using food record data. It was considered too burdensome for the parents to record a weighed food record. When parents register the food records of their infants the dietary intake is possibly less influenced by the process of recording, normally a drawback of using food records [222]. The diet quality indicators, that were defined based on the intake of some proposed obesogenic or obesity-protective foods included in previously defined diet indexes, had not been applied or validated elsewhere. This reduces the validity of the parental-child associations in diet quality.

Several limitations regarding the quality of the food records and the nutrient calculations were considered, possibly affecting the results. Firstly, due to a limited amount of resources during the data collection, missing or unclear information in the diet records could not be verified with the parents. However, the quality of all the diet records were assessed and only a small number were considered of low quality in terms of missing information about food products or portion sizes. Secondly, in cases where the food database did not include specified food items, alternative products as similar as possible in nutrient content were selected. Thirdly, several research assistants were involved in the work with the nutrient calculations of the food records, which possibly could have introduced bias due to different processing of food records. To overcome this, the work was documented in detail and frequently discussed between the research assistants. Even though the data quality problems were likely to be randomly distributed among the children, it is conceivable that the way they were handled resulted in a 'regression-toward the mean' effect, i.e. that the food records became more similar to each other. Consequently this could have contributed to the non-significant differences in dietary intake between high- and low-risk infants. However other circumstances may have

counteracted these issues and contributed to enhancing the quality of the food records. Firstly, as only a few children had begun at kindergarten, the parents had control over their child's intake in almost all families, facilitating the reporting of all meals and food items in a consistent manner. Secondly, a large proportion of the children's intake constituted typical 'infant's foods' (infant formula and porridge, ready-made infant dishes) which were easy to record.

To assess if the reported energy intake was plausible, the adapted Goldberg equation for estimating individual misreporters was applied using the ratio of energy intake to basal metabolic rate, EI:BMR [230, 231]. None of the children was judged either an under-reporter or over-reporter of energy intake. The mean EI:BMR ratio for the population was 1.67, which is above the common cut-off on group-level of 1.55, according to Black [230]. This is in line with reports of under-reporting being less common in young children than in older children and adults [345]. (A remark: as it is known that obese individuals are more prone to under-report, our original intention was to analyse whether the obese parents were more prone to underreport their child's intake, compared to the normal weight parents. These analyses have not been completed and are not included in this thesis.) Additionally, the energy intake and the absolute intake of macronutrients and dietary fibre correlated to child weight and BMR, which indicates a plausible dietary intake in relation to the child's nutrient requirements. Further, the dietary intake variables were adjusted for energy intake to account for confounding effects of nutrients by total energy intake [346]. The reported energy and fat intake in our study was comparable to other studies in infants [160, 161].

The relative intake of fat from milk products and infant formula were compared with the fatty acid (FA) pattern in plasma, in a sub-population. Although the sub-population was not randomly selected (selected families had sufficient amounts of blood collected for the child and at least one parent), the sub-population did not differ in important characteristics compared to the study population, with the exception of paternal BMI. The chosen food groups were selected because the fatty acids in these foods (odd-numbered saturated FA and essential polyunsaturated FA) are known to be valid biomarkers [228, 262]. The correlations between the reported amount of fat from these foods and the corresponding fatty acids in plasma were significant and of moderate strength, even though the sample was small (n = 56; Figure 11). Of note, although both 15:0 and 17:0 are formed in the gut of ruminants and thus often regarded as dairy-fat specific biomarkers, both these fatty acids are also found in fish [347], which possibly may dilute
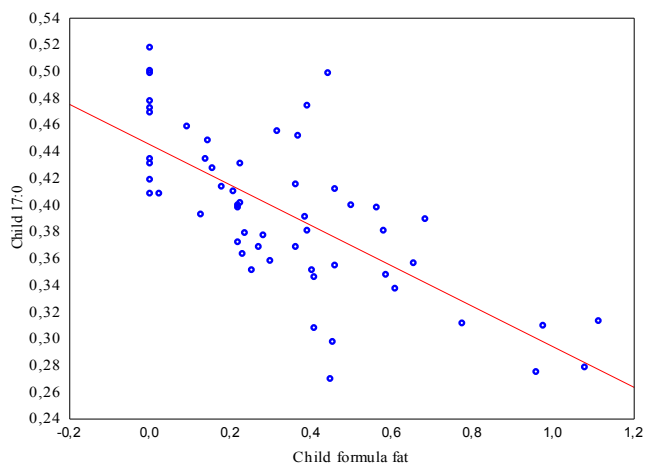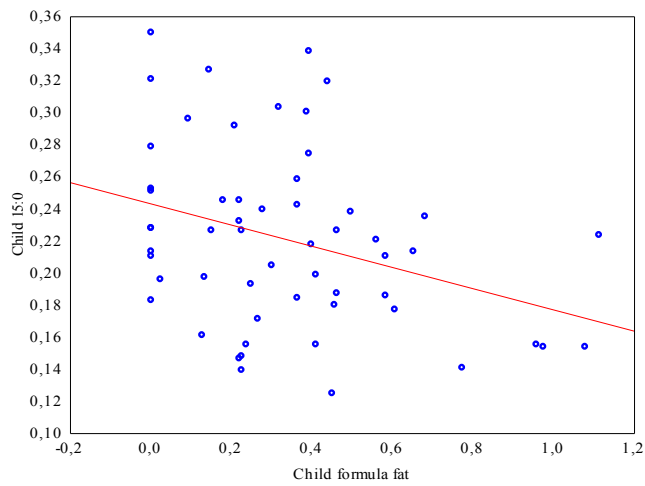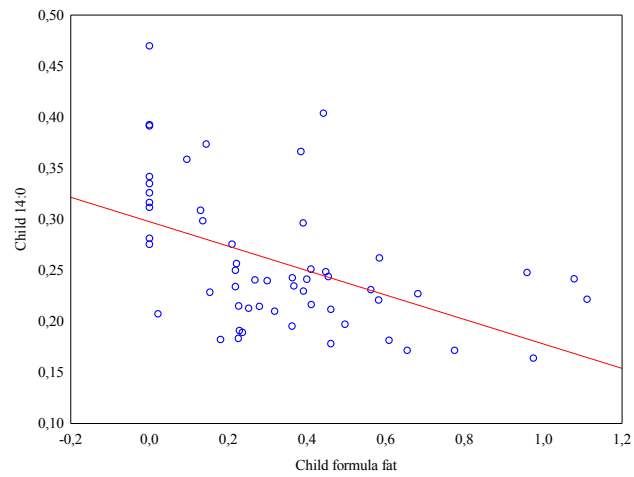
Figure 11. Correlations (Pearson correlation coefficient) between reported fat from formula (% of total fat/day) and saturated fatty acids 14:0, 15:0 and 17:0 (% of total FA in plasma phospholipid fraction).14:0; r = -0.49, 15:0; r = -0.33; 17:0 r = -0.71.

the relationships to milk/formula products. However, the fact that similar and even stronger associations were found for 14:0 and these foods support our findings, since 14:0 also has been shown to be a good marker for dairy fat intake. It was not possible to correlate the plasma FAs directly with the corresponding intake of the same FAs, due to limited data on FAs in the food database for many of the typical infant foods (formula, porridge, ready-made infant meals). Our results were similar to the findings on Finnish infants, reporting results of a comprehensive validation of the dietary intake using fatty acid composition [228]. A strength of our study was that fatty acid composition was assessed in specific lipid fractions rather than in whole plasma which have mainly been used in previous studies in children [228]. Whole plasma is not as informative as lipid fractions since the interpretation of the data is more difficult.

Based on these assessments we judge that the validity of the infant's dietary intake were fairly good. However, as described, the poor quality of some food records may have contributed to the null findings of the study.

Parents

The parents reported their food intake through a previously validated short FFQ, specifically developed to measure some key quality components of the Swedish dietary guidelines [163]. This method was chosen to reduce the burden for the parents as the total amount of Early STOPP questionnaire data was quite substantial, and parental food habits are not even secondary outcomes of the Early STOPP project. As the chosen FFQ included only a small number of selected food items, energy and nutrient intake calculations were not applicable. This limited the type of analyses possible, e.g. with regard to comparisons of reported food intake with the fatty acid composition in plasma. In the analyses, only those food items previously shown to be associated with the total amount of fat, saturated fat, dietary fibre and sugar were used [163].

Our population scored lower on the total diet index compared to another large sample of Swedish adults [261]. It has been indicated that parents may have more unhealthy food habits than adults without children [348], but it is likely that the more unhealthy diet pattern of our population was related to the high obesity risk profile. The mothers scored better than the fathers, which are in line with other studies consistently showing that women report healthier food habits than men [349, 350]. Further, compared to the normal weight parents the overweight and obese parents reported a higher intake of unhealthy foods, which may reflect true unhealthier food habits in these families. However, the scores for the total diet index did not differ between the groups, most probably since the overweight/obese parents scored higher for one of the indicators, reflecting intake of low-fat spread. This attenuated the differences between the groups in the aggregated

index. The fact that it was more common among the overweight and obese parents to use low fat spread seems reasonable, suggesting that some food choices may be influenced by the concern for weight.

In correlating parental food intake with FA in plasma, only one measurement was reported, as the FFQ data limited more sophisticated analyses. The intake of fish, in frequencies per week, was correlated with the relative amount of the fatty acids EPA and DHA in plasma, as omega-3 fatty acids in fish are known to be valid biomarkers [244]. The resulting correlations, significant in both mothers and fathers, were convincing, considering the crude measure of fish intake that was used. Optimally, fatty acids in plasma should be correlated to the reported relative intake of the same fatty acids. When evaluating the resulting correlations, the intake level of the food/FA needs to be taken into account. For example correlations between measured and reported fish FA (EPA and DHA) has been seen to be very strong in a Japanese population where the intake of fish is very high [244]. In populations with a lower fish intake, the reported correlations have been much lower [238, 351]. As the Early STOPP parents were not big fish consumers, these results supported a fairly valid reporting of the parents' fish intake, considering the above mentioned circumstances. However, as misreporting is known to be more common for unhealthy foods [352], the parents may well have reported their fish intake accurately while not been equally accurate in their reporting of unhealthy foods. Still, since the overweight and obese parents indeed did report higher intakes of unhealthy foods, the level of misreporting was possibly not very high.

Another problem possibly affecting the correlation between reported and measured food intake concerns the measurement period. The parents were instructed to keep the food intake during the last three months in mind when answering the FFQ. However, the FA composition in plasma reflects short-term intake of fat. This could have attenuated the reported correlations. However, the assumption often made in epidemiological studies is that people are not likely to make very drastic short-term diet changes, and thus FA patterns in plasma/serum is still widely used [238]. On the other hand, a substantial share of the parents reported that they were trying to lose weight and had tried to change their food habits or had started on a diet. This is important to take into account when evaluating the parental food intake.

It should be acknowledged that the ability of the FA biomarker to reflect dietary intake can be affected by non-dietary factors such as genetic background, obesity, smoking, physical activity and metabolism [351] and these factors may have had an effect on the reported correlations between FA and food intake in our study. Comparisons of the fatty

acid patterns between the high- and low-risk groups were limited by the small sample size and were not reported in Study IV.

Overall, considering the shortcomings and crude output of the chosen FFQ, the parental food intake may have been fairly valid.

STRENGTHS AND LIMITATIONS

A particular strength of this thesis is that it is based on well-characterised, high-risk populations. It is of great importance to specifically study high-risk populations in order to increase knowledge about factors potentially contributing to obesity in individuals being most susceptible to obesogenic environments. Another strength is the study designs where outcomes in high- and low risk populations were compared, expected to efficiently distinguish clinical relevant differences in the outcomes. Also, the longitudinal design of Study I, allowing child-parent associations of adiposity to be followed from childhood to adolescence in a unique cohort of severely obese children. Similar relationships between obesity risk exposures and outcomes were studied in several of the studies, enabling comparisons of findings across studies and enhancing the awareness of how population characteristics may have influenced results. Furthermore, anthropometry was measured for the children in all studies, and for parents in the Early STOPP studies, limiting reporting bias. Also, the use of an objectively measured biomarker for fat intake strengthened the assessment of the dietary intake validity. Measurements of fatty acid composition have not previously been performed in Swedish infants. Finally, the Early STOPP baseline studies will enable the tracking of multiple potential causal risk factors for the development of obesity during the preschool years in future research on the Early STOPP cohort.

Some limitations should be acknowledged. All studies were observational and even though a large number of potential confounding effects were tested, residual confounding is likely to be present. The study samples were relatively small, affecting the power to detect statistical significant results. Overall, the populations cannot be considered high risk in terms of family socio-economic status and ethnic background, thus limiting the external validity to populations of similar socio-demographic profiles. Also, recall bias may have affected the quality of data that were retrospectively collected from the parents in the Early STOPP studies, such as gestational weight gain and history of breastfeeding, and may have masked the potential mediating effect of these variables on infant growth. One additional limitation is that estimates of undeclared non-paternity were not taken into account, which may have underestimated the paternal-child weight

associations. However, several large studies that have analysed the potential effect of undeclared non-paternity, have not seen such an effect [40-44]. Also, rates of undisclosed non-paternity are believed to be low in Sweden, as have been seen in studies were undeclared non-paternity has been verified with DNA testing [353]. Furthermore, a potential impact of non-paternity is likely to be attenuated in three of four of our studies where the results were not based on direct associations to parental BMI. Also, information about parents not living with their children was not taken into consideration in the analyses, which could have affected the parental-child associations for behavioural factors, i.e. dietary habits in Study IV. However few of the Early STOPP children lived with only one parent. In two of the studies self-reported (or partner-reported) data for parental weight and height were used, which are known to underestimate BMI [265]. However, reported BMI may be reliable for estimating associations [37], but associations could possibly have been underestimated. Lastly, the definition of low parental educational level was different in Study I compared to the other studies, as it was derived using parental occupation, and furthermore, due to lack of quality in the occupational data, parental educational level was missing for many children. However, the highest level of education was used as the reference in the analyses, ensuring reasonably robust estimates.

FURTHER RESEARCH

More research on the impact of obesity risk factors specifically in high-risk populations are needed, to enable the development of more efficient targeted preventive interventions. This includes factors that may be used to accurately identifying high-risk individuals, but also the identification of modifiable behaviours that may contribute to obesity development. Specifically the need for more evidence of which factors that predict age at obesity onset are warranted, as this is of importance for when obesity prevention should be initiated.

It is of importance to follow the concurrent impact of both parental adiposity and educational level, as well as other family-related obesity risk factors on children's weight development in additional studies using longitudinal prospective designs. Also, the mechanisms underlying the impact of parental educational level on child weight development need to be further explored. Future Early STOPP studies will enable causal relationships to obesity to be studied through its longitudinal, randomised and interventional design.

Genetic and epigenetic impact on child weight development and obesity should be evaluated further, and their associations with other family-related factors. In future studies of the Early STOPP population, both genetic and epigenetic effects will be analysed, e.g. in relation to appetite measures and dietary intake.

Clear evidence on how and when dietary habits contribute to obesity development in young children is lacking, and should preferably be achieved through longitudinal studies starting very early in life. In future studies of the Early STOPP children the impact of their dietary habits in infancy on subsequent weight development can be studied.

Relationships between dietary intake and other life-style behaviours, such as physical activity, sedentary behaviours and sleep habits, in young children need to be further evaluated. Additional evidence for how the clustering of these behaviours develops over time and affects child weight development is important.

In order to increase the validity of obesity and diet associations, more research is needed that includes additional, objectively-measured biomarkers, e.g. biomarkers for carotenoids and whole-grain. Also, further development and validation of whole diet measures or diet quality indicators of importance to child obesity would be useful. Possibly dietary intake and eating behaviours could be combined into new, more comprehensive measures reflecting both hereditary and environmental aspects of dietary behaviours of importance to child weight development.

Efficiency and cost-effectiveness of both targeted and general early childhood obesity prevention interventions need to be further evaluated, including assessment of the child age period when preventive efforts are most likely to provide long-term sustainable effects on childhood obesity.

CONCLUSIONS

This thesis has shown that

- Parental adiposity and educational level are both important, independent determinants of child weight development and can be used to identify children at high risk of obesity, however the strength and timing of their influence differs.

- Parental adiposity does not have a distinct effect on the relative weight of infants, nor on age at obesity onset. However, the influence of both maternal and paternal BMI is strengthened by child age and affects the degree of obesity in childhood and adolescence.

- Low parental educational level is associated with higher infant weight as early as their first year, however the underlying mechanisms are not clear. The effect of parental educational level is long term; it is still present in relation to the degree of obesity in adolescence, but its effect is weak in relation to parental adiposity.

- Birth weight is the most important predictor of infant growth during the first year, but is not related to the degree of obesity in childhood and adolescence. Other early life factors show no or very weak associations with infant growth in our populations.

- Dietary intake and eating behaviours do not differ between high- and low-risk infants at age one, who are not heavily exposed to their parents' unhealthy food intake at this early age. However, healthy aspects of paternal and child diet quality may be associated as early as at age one.

- Infants' relative weight at age one is not related to their dietary intake, but it is independently associated with obesity-related eating behaviours.

- The assessment of the validity of the reported dietary intake in both infants and parents is strengthened by an objectively measured biomarker for fat quality.

IMPLICATIONS FOR PREVENTION

With enhanced knowledge of obesity risk factors, where the family-related factors studied in this thesis are some of the most important, obesity prevention can become more efficient. Evidence for the impact of risk factors specifically in high-risk populations is of importance in order to identify the right high-risk children for targeted prevention as well as the most important modifiable behaviours.

Based on the conclusions of this thesis, both parental BMI and educational level should be considered when identifying high-risk children for early, targeted prevention. The early impact of parental educational level on infant growth supports the proposal that prevention should be initiated as early as in infancy. However, more knowledge concerning which modifiable behaviours to target in infancy is required.

Even though parental adiposity does not affect the growth of infants or the age of obesity onset, it is unarguably the strongest predictor of obesity later in childhood. Therefore parental obesity should be used to identify high-risk children also when prevention is initiated very early. Furthermore, our results support that the mother's and the father's weight status are both important in assessing the child's obesity risk.

Monitoring children's appetite traits may be valuable to identify children who are particularly vulnerable to an obesogenic food environment. Attention should be paid to parenting practices and parental food habits that may influence children's eating behaviours. Parents should also be encouraged in their function as positive role models regarding the family food environment. This may be of particular importance during children's second year in life, when the transition to family foods is likely to be carried out.

This thesis does not support that early modifiable risk factors such as maternal gestational weight gain, maternal smoking and infant feeding should be specifically targeted in obesity prevention. Neither appears birth weight useful in predicting long term impact on child weight, even though it determines growth during the first year. Previous research have indicated that these factors, together with parental obesity and socio-economic status, may additionally increase the child's obesity risk to some extent, however this is not supported by this thesis.

In identifying high-risk children for targeted prevention, the risk of stigmatisation of the parents must be considered and handled through clear, but non-offensive, messages. Still, childhood obesity is a very serious health issue with a long-term

impact and different types of preventive efforts, both targeted prevention to high-risk groups and general prevention to all children, must be evaluated. Early STOPP (www.earlystopp.se) and Primrose (https://primroseprojektet.se/info) are two preventive research projects initiated by Karolinska Institutet and carried out in collaboration with child healthcare. These projects, along with other initiatives, will increase the evidence on the efficiency of obesity prevention in preschool children.

Child healthcare maintains regular contact with almost all Swedish children in the period from infancy until school age, and has an important role to play in early obesity prevention. In several Swedish counties, guidelines on how work with obesity prevention should be organised and carried out, where child healthcare is one of several actors, have been introduced. Structured programmes and tools for the work with obesity prevention are essential. Several surveys have shown that many child healthcare nurses, even though they are trained and experienced in communicating with parents about child health issues, still experience that obesity and obesity-related life style behaviours are especially difficult to bring up and talk about with parents [267, 354, 355]. Many parents struggle to give their children a healthy lifestyle in an environment fraught with daily temptations to make unhealthy choices, and more active support from professionals is warranted [356].

BETYDELSE FÖR PREVENTION

Genom ökad kunskap om riskfaktorer som bidrar till fetma hos barn, där de familjerelaterade faktorer som studerats i denna avhandling tillhör de viktigaste, kan preventiva insatser bli mer effektiva. Evidens för hur riskfaktorer påverkar barn i högriskgrupper är särskilt viktigt, dels för att bättre kunna identifiera de barn som har högst risk att utveckla fetma och som riktad prevention ska vända sig till, men också för att rikta in prevention på de beteenden som orsakar fetma och som går att påverka.

Baserat på slutsatserna i denna avhandling så kan både fetma och låg utbildningsnivå hos föräldrar användas för att identifiera barn för tidiga riktade preventiva insatser. Sambandet mellan låg utbildningsnivå hos föräldrar och en högre vikt hos spädbarn redan under första året stödjer att prevention bör initieras tidigt. Dock behövs mer kunskap om vilka faktorer som ligger bakom detta samband, och som preventiva insatser i denna tidiga ålder ska rikta in sig på.

Även om fetma hos föräldrar inte förefaller ha någon inverkan på spädbarns viktutveckling och inte heller på vilken ålder då barn utvecklar fetma, så är fetma hos föräldrar tveklöst den starkaste riskfaktorn för senare utveckling av fetma hos barn. Fetma hos föräldrar bör därför användas för att identifiera hög-risk barn även då preventiva insatser påbörjas mycket tidigt. Våra resultat tyder dessutom på att både mammas och pappas viktstatus är viktiga för att bedöma barnets risk.

Att mäta och följa upp barns aptitrelaterade ätbeteenden kan vara viktigt för att tidigt identifiera barn som har en ökad sårbarhet för ohälsosamma matvanor. Föräldrar bör av denna anledning bli uppmärksammade på hur deras egna beteenden och vanor kan påverka barnets ätbeteenden. Föräldrar bör även uppmuntras i rollen som positiva förebilder för sina barn när det gäller familjens matvanor. Detta kan vara särskilt viktigt under barnets andra levnadsår, då många barn helt går över till att äta samma mat som föräldrarna och resten av familjen.

Våra resultat ger inget stöd för att prevention bör rikta in sig på tidiga riskfaktorer som moderns viktuppgång under graviditet, rökning hos modern, kort exklusiv amningsperiod eller tidig introduktion av fast föda. Födelsevikt förefaller inte heller användbart för att förutse långsiktig viktutveckling hos barn, även om födelsevikt styr barnets tillväxt under det första året. Tidigare forskning har indikerat att dessa faktorer, i kombination med föräldrafetma och socioekonomisk status, kan bidra till en något ytterligare ökad risk för fetma hos barn, men denna avhandling bidrar inte med evidens för detta.

Det finns en risk för stigmatisering av föräldrar till barn som "pekas ut" för riktade preventiva insatser på grund av egen fetma eller låg utbildningsnivå. Detta bör hanteras genom tydligt formulerade budskap utan "pekpinnar". Fetma hos barn är dock ett mycket allvarligt hälsoproblem med långvariga negativa konsekvenser, och det är viktigt att olika typer av preventiva insatser prövas, både riktad prevention till riskgrupper och generell prevention till alla barn. Early STOPP (www.earlystopp.se) och Primrose (https://primroseprojektet.se/info) är två preventiva forskningsprojekt som drivs vid Karolinska Institutet i samarbete med barnhälsovården. Dessa och andra preventiva initiativ kommer att öka evidensen för betydelsen av prevention av fetma till barn i förskoleåldern.

Barnhälsovården, som har en regelbunden kontakt med nästan alla svenska barn från spädbarnsåldern till skolåldern, har en viktig roll i det tidiga förebyggande arbetet. I flera landsting har vårdprogram utarbetats för hur det fetmaförebyggande arbetet skall organiseras och genomföras, och barnhälsovården är en av flera aktörer. Strukturerade program och verktyg för att arbeta med fetmaprevention är viktigt. Flera undersökningar har visat att många som arbetar i barnhälsovården tycker att det är extra känsligt och svårt att prata med föräldrar om övervikt och fetma och de livsstilsrelaterade vanor som är kopplade till fetma [267, 354, 355], trots utbildning och erfarenhet i att kommunicera med föräldrar om barns hälsorelaterade problem. Många föräldrar kämpar med att ge sina barn hälsosamma vanor, i en miljö som innebär dagliga frestelser till ohälsosamma val, och efterfrågar mer stöd från bl.a. barnhälsovården [356].

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REFERENCES

1.	Lobstein T. The prevention of obesity in children. *Pediatr Endocrinol Rev* 2004; 1 Suppl 3: 471-5.
2.	Skelton JA, Irby MB, Grzywacz JG, et al. Etiologies of obesity in children: nature and nurture. *Pediatr Clin North Am* 2011; 58(6): 1333-54, ix.
3.	Pate RR, O'Neill JR, Liese AD, et al. Factors associated with development of excessive fatness in children and adolescents: a review of prospective studies. *Obes Rev* 2013; 14(8): 645-58.
4.	Offord DR, Kraemer HC. Risk factors and prevention. *Evid Based Mental Health* 2000; 3: 70-1.
5.	Burt BA. Definitions of risk. *J Dent Educ* 2001; 65(10): 1007-8.
6.	Lakshman R, Elks CE, Ong KK. Childhood obesity. *Circulation* 2012; 126(14): 1770-9.
7.	Cole TJ, Bellizzi MC, Flegal KM, et al. Establishing a standard definition for child overweight and obesity worldwide: international survey. *BMJ* 2000; 320(7244): 1240-3.
8.	WHO. Preventing and Managing the Global Epidemic of Obesity. Report of the World Health Organization Consultation of Obesity. *Geneva* 1997.
9.	Karlberg J, Luo ZC, Albertsson-Wikland K. Body mass index reference values (mean and SD) for Swedish children. *Acta Paediatr* 2001; 90(12): 1427-34.
10.	Marild S, Bondestam M, Bergstrom R, et al. Prevalence trends of obesity and overweight among 10-year-old children in western Sweden and relationship with parental body mass index. *Acta Paediatr* 2004; 93(12): 1588-95.
11.	Lissner L, Sohlstrom A, Sundblom E, et al. Trends in overweight and obesity in Swedish schoolchildren 1999-2005: has the epidemic reached a plateau? *Obes Rev* 2010; 11(8): 553-9.
12.	Sjoberg A, Lissner L, Albertsson-Wikland K, et al. Recent anthropometric trends among Swedish school children: evidence for decreasing prevalence of overweight in girls. *Acta Paediatr* 2008; 97(1): 118-23.
13.	Moraeus L, Lissner L, Yngve A, et al. Multi-level influences on childhood obesity in Sweden: societal factors, parental determinants and child's lifestyle. *Int J Obes (Lond)* 2012; 36(7): 969-76.
14.	Braback L, Gunnel B, Ekholm L. [No further increase of obesity among Swedish 4-year old children. Large regional differences indicate the significance of socioeconomic factors]. *Lakartidningen* 2009; 106(43): 2758-61.
15.	Barnhälsovården. Barnhälsovård Årsrapport. 29. Stockholms läns landsting, 2012.
16.	Cattaneo A, Monasta L, Stamatakis E, et al. Overweight and obesity in infants and pre-school children in the European Union: a review of existing data. *Obes Rev* 2010; 11(5): 389-98.
17.	Jackson-Leach R, Lobstein T. Estimated burden of paediatric obesity and co-morbidities in Europe. Part 1. The increase in the prevalence of child obesity in Europe is itself increasing. *Int J Pediatr Obes* 2006; 1(1): 26-32.
18.	Pigeot I, Barba G, Chadjigeorgiou C, et al. Prevalence and determinants of childhood overweight and obesity in European countries: pooled analysis of the existing surveys within the IDEFICS Consortium. *Int J Obes (Lond)* 2009; 33(10): 1103-10.

19. Mei Z, Ogden CL, Flegal KM, et al. Comparison of the prevalence of shortness, underweight, and overweight among US children aged 0 to 59 months by using the CDC 2000 and the WHO 2006 growth charts. *J Pediatr* 2008; 153(5): 622-8.

20. McCormick DP, Sarpong K, Jordan L, et al. Infant obesity: are we ready to make this diagnosis? *J Pediatr* 2010; 157(1): 15-9.

21. Olds T, Maher C, Zumin S, et al. Evidence that the prevalence of childhood overweight is plateauing: data from nine countries. *Int J Pediatr Obes* 2011; 6(5-6): 342-60.

22. Wen X, Gillman MW, Rifas-Shiman SL, et al. Decreasing prevalence of obesity among young children in Massachusetts from 2004 to 2008. *Pediatrics* 2012; 129(5): 823-31.

23. Neovius M, Janson A, Rossner S. Prevalence of obesity in Sweden. *Obes Rev* 2006; 7(1): 1-3.

24. Neovius M, Rasmussen F. [Alarming overweight and obesity figures in Sweden and in the world]. *Lakartidningen* 2011; 108(49): 2566-8.

25. Edvardsson K, Lindkvist M, Eurenius E, et al. A population-based study of overweight and obesity in expectant parents: socio-demographic patterns and within-couple associations. *BMC Public Health* 2013; 13: 923.

26. Cote AT, Harris KC, Panagiotopoulos C, et al. Childhood obesity and cardiovascular dysfunction. *J Am Coll Cardiol* 2013; 62(15): 1309-19.

27. De Niet JE, Naiman DI. Psychosocial aspects of childhood obesity. *Minerva Pediatr* 2011; 63(6): 491-505.

28. Franks PW. Body weight and risk of early death. *Obesity (Silver Spring)* 2013; 21(9): 1743.

29. Franks PW, Hanson RL, Knowler WC, et al. Childhood obesity, other cardiovascular risk factors, and premature death. *N Engl J Med* 2010; 362(6): 485-93.

30. Reilly JJ, Methven E, McDowell ZC, et al. Health consequences of obesity. *Arch Dis Child* 2003; 88(9): 748-52.

31. Larsson C, Hernell O, Lind T. Moderately elevated body mass index is associated with metabolic variables and cardiovascular risk factors in Swedish children. *Acta Paediatr* 2011; 100(1): 102-8.

32. Dietz WH. Health consequences of obesity in youth: childhood predictors of adult disease. *Pediatrics* 1998; 101(3 Pt 2): 518-25.

33. Gardner DS, Hosking J, Metcalf BS, et al. Contribution of early weight gain to childhood overweight and metabolic health: a longitudinal study (EarlyBird 36). *Pediatrics* 2009; 123(1): e67-73.

34. Whitaker RC, Wright JA, Pepe MS, et al. Predicting obesity in young adulthood from childhood and parental obesity. *N Engl J Med* 1997; 337(13): 869-73.

35. Maffeis C. Aetiology of overweight and obesity in children and adolescents. *Eur J Pediatr* 2000; 159 Suppl 1: S35-44.

36. Morandi A, Meyre D, Lobbens S, et al. Estimation of newborn risk for child or adolescent obesity: lessons from longitudinal birth cohorts. *PLoS One* 2012; 7(11): e49919.

37. Lake JK, Power C, Cole TJ. Child to adult body mass index in the 1958 British birth cohort: associations with parental obesity. *Arch Dis Child* 1997; 77(5): 376-81.

38. Durmus B, Arends LR, Ay L, et al. Parental anthropometrics, early growth and the risk of overweight in pre-school children: the Generation R Study. *Pediatr Obes* 2013; 8(5): 339-50.

39. Reilly JJ, Armstrong J, Dorosty AR, et al. Early life risk factors for obesity in childhood: cohort study. *BMJ* 2005; 330(7504): 1357.

40. Lawlor DA, Smith GD, O'Callaghan M, et al. Epidemiologic evidence for the fetal overnutrition hypothesis: findings from the mater-university study of pregnancy and its outcomes. *Am J Epidemiol* 2007; 165(4): 418-24.

41. Whitaker KL, Jarvis MJ, Beeken RJ, et al. Comparing maternal and paternal intergenerational transmission of obesity risk in a large population-based sample. *Am J Clin Nutr* 2010; 91(6): 1560-7.

42. Davey Smith G, Steer C, Leary S, et al. Is there an intrauterine influence on obesity? Evidence from parent child associations in the Avon Longitudinal Study of Parents and Children (ALSPAC). *Arch Dis Child* 2007; 92(10): 876-80.

43. Fleten C, Nystad W, Stigum H, et al. Parent-offspring body mass index associations in the Norwegian Mother and Child Cohort Study: a family-based approach to studying the role of the intrauterine environment in childhood adiposity. *Am J Epidemiol* 2012; 176(2): 83-92.

44. Kivimaki M, Lawlor DA, Smith GD, et al. Substantial intergenerational increases in body mass index are not explained by the fetal overnutrition hypothesis: the Cardiovascular Risk in Young Finns Study. *Am J Clin Nutr* 2007; 86(5): 1509-14.

45. Patel R, Martin RM, Kramer MS, et al. Familial associations of adiposity: findings from a cross-sectional study of 12,181 parental-offspring trios from Belarus. *PLoS One* 2011; 6(1): e14607.

46. Linabery AM, Nahhas RW, Johnson W, et al. Stronger influence of maternal than paternal obesity on infant and early childhood body mass index: the Fels Longitudinal Study. *Pediatr Obes* 2012.

47. Magarey AM, Daniels LA, Boulton TJ, et al. Predicting obesity in early adulthood from childhood and parental obesity. *Int J Obes Relat Metab Disord* 2003; 27(4): 505-13.

48. Berkowitz RI, Stallings VA, Maislin G, et al. Growth of children at high risk of obesity during the first 6 y of life: implications for prevention. *Am J Clin Nutr* 2005; 81(1): 140-6.

49. Botton J, Heude B, Maccario J, et al. Parental body size and early weight and height growth velocities in their offspring. *Early Hum Dev* 2010; 86(7): 445-50.

50. Perez-Pastor EM, Metcalf BS, Hosking J, et al. Assortative weight gain in mother-daughter and father-son pairs: an emerging source of childhood obesity. Longitudinal study of trios (EarlyBird 43). *Int J Obes (Lond)* 2009; 33(7): 727-35.

51. Dubois L, Ohm Kyvik K, Girard M, et al. Genetic and environmental contributions to weight, height, and BMI from birth to 19 years of age: an international study of over 12,000 twin pairs. *PLoS One* 2012; 7(2): e30153.

52. Maes HH, Neale MC, Eaves LJ. Genetic and environmental factors in relative body weight and human adiposity. *Behav Genet* 1997; 27(4): 325-51.

53. Silventoinen K, Rokholm B, Kaprio J, et al. The genetic and environmental influences on childhood obesity: a systematic review of twin and adoption studies. *Int J Obes (Lond)* 2010; 34(1): 29-40.

54. Demerath EW, Choh AC, Czerwinski SA, et al. Genetic and environmental influences on infant weight and weight change: the Fels Longitudinal Study. *Am J Hum Biol* 2007; 19(5): 692-702.

55. Levine RS, Hennekens CH, Jesse MJ. Genetic variance of weight and length in infant twins. *Am J Epidemiol* 1987; 126(5): 929-35.

56. Haworth CM, Carnell S, Meaburn EL, et al. Increasing heritability of BMI and stronger associations with the FTO gene over childhood. *Obesity (Silver Spring)* 2008; 16(12): 2663-8.

57. Hetherington MM, Cecil JE. Gene-environment interactions in obesity. *Forum Nutr* 2010; 63: 195-203.

58. Yang W, Kelly T, He J. Genetic epidemiology of obesity. *Epidemiol Rev* 2007; 29: 49-61.

59. Frayling TM, Timpson NJ, Weedon MN, et al. A common variant in the FTO gene is associated with body mass index and predisposes to childhood and adult obesity. *Science* 2007; 316(5826): 889-94.

60. Cecil J, Dalton M, Finlayson G, et al. Obesity and eating behaviour in children and adolescents: contribution of common gene polymorphisms. *Int Rev Psychiatry* 2012; 24(3): 200-10.

61. Cecil JE, Tavendale R, Watt P, et al. An obesity-associated FTO gene variant and increased energy intake in children. *N Engl J Med* 2008; 359(24): 2558-66.

62. Jacobsson JA, Klovins J, Kapa I, et al. Novel genetic variant in FTO influences insulin levels and insulin resistance in severely obese children and adolescents. *Int J Obes (Lond)* 2008; 32(11): 1730-5.

63. Timpson NJ, Emmett PM, Frayling TM, et al. The fat mass- and obesity-associated locus and dietary intake in children. *Am J Clin Nutr* 2008; 88(4): 971-8.

64. Wardle J, Carnell S, Haworth CM, et al. Obesity associated genetic variation in FTO is associated with diminished satiety. *J Clin Endocrinol Metab* 2008; 93(9): 3640-3.

65. Belsky DW, Moffitt TE, Houts R, et al. Polygenic risk, rapid childhood growth, and the development of obesity: evidence from a 4-decade longitudinal study. *Arch Pediatr Adolesc Med* 2012; 166(6): 515-21.

66. Elks CE, Loos RJ, Sharp SJ, et al. Genetic markers of adult obesity risk are associated with greater early infancy weight gain and growth. *PLoS Med* 2010; 7(5): e1000284.

67. Warrington NM, Howe LD, Wu YY, et al. Association of a Body Mass Index Genetic Risk Score with Growth throughout Childhood and Adolescence. *PLoS One* 2013; 8(11): e79547.

68. Loos RJ. Genetic determinants of common obesity and their value in prediction. *Best Pract Res Clin Endocrinol Metab* 2012; 26(2): 211-26.

69. Hebebrand J, Volckmar AL, Knoll N, et al. Chipping away the 'missing heritability': GIANT steps forward in the molecular elucidation of obesity - but still lots to go. *Obes Facts* 2010; 3(5): 294-303.

70. Waterland RA. Epigenetic epidemiology of obesity: application of epigenomic technology. *Nutr Rev* 2008; 66 Suppl 1: S21-3.

71. Kaati G, Bygren LO, Edvinsson S. Cardiovascular and diabetes mortality determined by nutrition during parents' and grandparents' slow growth period. *Eur J Hum Genet* 2002; 10(11): 682-8.

72. Bygren LO, Tinghog P, Carstensen J, et al. Change in paternal grandmothers early food supply influenced cardiovascular mortality of the female grandchildren. *BMC Genet* 2014; 15(1): 12.

73. Kral JG, Biron S, Simard S, et al. Large maternal weight loss from obesity surgery prevents transmission of obesity to children who were followed for 2 to 18 years. *Pediatrics* 2006; 118(6): e1644-9.

74. Wu Q, Suzuki M. Parental obesity and overweight affect the body-fat accumulation in the offspring: the possible effect of a high-fat diet through epigenetic inheritance. *Obes Rev* 2006; 7(2): 201-8.

75.   Lillycrop KA, Burdge GC. Epigenetic mechanisms linking early nutrition to long term health. *Best Pract Res Clin Endocrinol Metab* 2012; 26(5): 667-76.

76.   Bao W, Srinivasan SR, Valdez R, et al. Longitudinal changes in cardiovascular risk from childhood to young adulthood in offspring of parents with coronary artery disease: the Bogalusa Heart Study. *JAMA* 1997; 278(21): 1749-54.

77.   Huus K, Ludvigsson JF, Enskar K, et al. Risk factors in childhood obesity-findings from the All Babies In Southeast Sweden (ABIS) cohort. *Acta Paediatr* 2007; 96(9): 1321-5.

78.   Kim SY, England JL, Sharma JA, et al. Gestational diabetes mellitus and risk of childhood overweight and obesity in offspring: a systematic review. *Exp Diabetes Res* 2011; 2011: 541308.

79.   Lakshman R, Zhang J, Koch FS, et al. Higher maternal education is associated with favourable growth of young children in different countries. *J Epidemiol Community Health* 2013.

80.   Shrewsbury V, Wardle J. Socioeconomic status and adiposity in childhood: a systematic review of cross-sectional studies 1990-2005. *Obesity (Silver Spring)* 2008; 16(2): 275-84.

81.   Semmler C, Ashcroft J, van Jaarsveld CH, et al. Development of overweight in children in relation to parental weight and socioeconomic status. *Obesity (Silver Spring)* 2009; 17(4): 814-20.

82.   Thorn J, Waller M, Johansson M, et al. Overweight among Four-Year-Old Children in Relation to Early Growth Characteristics and Socioeconomic Factors. *J Obes* 2010; 2010.

83.   Van Den Berg G, Van Eijsden M, Galindo-Garre F, et al. Low maternal education is associated with increased growth velocity in the first year of life and in early childhood: the ABCD study. *Eur J Pediatr* 2013; 172(11): 1451-7.

84.   Wijlaars LP, Johnson L, van Jaarsveld CH, et al. Socioeconomic status and weight gain in early infancy. *Int J Obes (Lond)* 2011; 35(7): 963-70.

85.   Khanolkar AR, Sovio U, Bartlett JW, et al. Socioeconomic and early-life factors and risk of being overweight or obese in children of Swedish- and foreign-born parents. *Pediatr Res* 2013; 74(3): 356-63.

86.   Dixon B, Pena MM, Taveras EM. Lifecourse approach to racial/ethnic disparities in childhood obesity. *Adv Nutr* 2012; 3(1): 73-82.

87.   Formisano A, Hunsberger M, Bammann K, et al. Family structure and childhood obesity: results of the IDEFICS Project. *Public Health Nutr* 2013: 1-9.

88.   Haugaard LK, Ajslev TA, Zimmermann E, et al. Being an only or last-born child increases later risk of obesity. *PLoS One* 2013; 8(2): e56357.

89.   Hunsberger M, Formisano A, Reisch LA, et al. Overweight in singletons compared to children with siblings: the IDEFICS study. *Nutr Diabetes* 2012; 2: e56.

90.   Robinson S, Marriott L, Poole J, et al. Dietary patterns in infancy: the importance of maternal and family influences on feeding practice. *Br J Nutr* 2007; 98(5): 1029-37.

91.   Brisbois TD, Farmer AP, McCargar LJ. Early markers of adult obesity: a review. *Obes Rev* 2012; 13(4): 347-67.

92.   Li HT, Zhou YB, Liu JM. The impact of cesarean section on offspring overweight and obesity: a systematic review and meta-analysis. *Int J Obes (Lond)* 2012.

93.   Weng SF, Redsell SA, Swift JA, et al. Systematic review and meta-analyses of risk factors for childhood overweight identifiable during infancy. *Arch Dis Child* 2012.

94.   Mangrio E, Lindstrom M, Rosvall M. Early life factors and being overweight at 4 years of age among children in Malmo, Sweden. *BMC Public Health* 2010; 10: 764.

95.	Manios Y, Birbilis M, Moschonis G, et al. Childhood Obesity Risk Evaluation based on perinatal factors and family sociodemographic characteristics: CORE Index. *Eur J Pediatr* 2013.

96.	Steur M, Smit HA, Schipper CM, et al. Predicting the risk of newborn children to become overweight later in childhood: the PIAMA birth cohort study. *Int J Pediatr Obes* 2011; 6(2-2): e170-8.

97.	Ludwig DS, Rouse HL, Currie J. Pregnancy Weight Gain and Childhood Body Weight: A Within-Family Comparison. *PLoS Med* 2013; 10(10): e1001521.

98.	Monte S, Valenti O, Giorgio E, et al. Maternal weight gain during pregnancy and neonatal birth weight: a review of the literature. *J Prenat Med* 2011; 5(2): 27-30.

99.	Beyerlein A, Nehring I, Rzehak P, et al. Gestational weight gain and body mass index in children: results from three german cohort studies. *PLoS One* 2012; 7(3): e33205.

100.	Berglind D, Willmer M, Naslund E, et al. Differences in gestational weight gain between pregnancies before and after maternal bariatric surgery correlate with differences in birth weight but not with scores on the body mass index in early childhood. *Pediatr Obes* 2013.

101.	Oken E, Levitan EB, Gillman MW. Maternal smoking during pregnancy and child overweight: systematic review and meta-analysis. *Int J Obes (Lond)* 2008; 32(2): 201-10.

102.	Yang S, Decker A, Kramer MS. Exposure to parental smoking and child growth and development: a cohort study. *BMC Pediatr* 2013; 13: 104.

103.	Cnattingius S, Haglund B. Decreasing smoking prevalence during pregnancy in Sweden: the effect on small-for-gestational-age births. *Am J Public Health* 1997; 87(3): 410-3.

104.	Fallucca S, Vasta M, Sciullo E, et al. Birth weight: genetic and intrauterine environment in normal pregnancy. *Diabetes Care* 2009; 32(12): e149.

105.	Dubois L, Girard M. Early determinants of overweight at 4.5 years in a population-based longitudinal study. *Int J Obes (Lond)* 2006; 30(4): 610-7.

106.	Ong KK. Size at birth, postnatal growth and risk of obesity. *Horm Res* 2006; 65 Suppl 3: 65-9.

107.	Yu ZB, Han SP, Zhu GZ, et al. Birth weight and subsequent risk of obesity: a systematic review and meta-analysis. *Obes Rev* 2011; 12(7): 525-42.

108.	Schellong K, Schulz S, Harder T, et al. Birth weight and long-term overweight risk: systematic review and a meta-analysis including 643,902 persons from 66 studies and 26 countries globally. *PLoS One* 2012; 7(10): e47776.

109.	Baird J, Fisher D, Lucas P, et al. Being big or growing fast: systematic review of size and growth in infancy and later obesity. *BMJ* 2005; 331(7522): 929.

110.	Monteiro PO, Victora CG. Rapid growth in infancy and childhood and obesity in later life--a systematic review. *Obes Rev* 2005; 6(2): 143-54.

111.	Ong KK, Loos RJ. Rapid infancy weight gain and subsequent obesity: systematic reviews and hopeful suggestions. *Acta Paediatr* 2006; 95(8): 904-8.

112.	Druet C, Stettler N, Sharp S, et al. Prediction of childhood obesity by infancy weight gain: an individual-level meta-analysis. *Paediatr Perinat Epidemiol* 2012; 26(1): 19-26.

113.	Andersen LG, Holst C, Michaelsen KF, et al. Weight and weight gain during early infancy predict childhood obesity: a case-cohort study. *Int J Obes (Lond)* 2012; 36(10): 1306-11.

114.	Ekelund U, Ong K, Linne Y, et al. Upward weight percentile crossing in infancy and early childhood independently predicts fat mass in young adults: the Stockholm Weight Development Study (SWEDES). *Am J Clin Nutr* 2006; 83(2): 324-30.

115.	Beyerlein A, von Kries R. Breastfeeding and body composition in children: will there ever be conclusive empirical evidence for a protective effect against overweight? *Am J Clin Nutr* 2011; 94(6 Suppl): 1772S-5S.

116.	Arenz S, Von Kries R. Protective effect of breast-feeding against obesity in childhood: can a meta-analysis of published observational studies help to validate the hypothesis? *Adv Exp Med Biol* 2009; 639: 145-52.

117.	Harder T, Bergmann R, Kallischnigg G, et al. Duration of breastfeeding and risk of overweight: a meta-analysis. *Am J Epidemiol* 2005; 162(5): 397-403.

118.	Owen CG, Martin RM, Whincup PH, et al. The effect of breastfeeding on mean body mass index throughout life: a quantitative review of published and unpublished observational evidence. *Am J Clin Nutr* 2005; 82(6): 1298-307.

119.	Oddy WH. Infant feeding and obesity risk in the child. *Breastfeed Rev* 2012; 20(2): 7-12.

120.	Ludvigsson JF, Ludvigsson J. Socio-economic determinants, maternal smoking and coffee consumption, and exclusive breastfeeding in 10205 children. *Acta Paediatr* 2005; 94(9): 1310-9.

121.	Kramer MS, Matush L, Vanilovich I, et al. A randomized breast-feeding promotion intervention did not reduce child obesity in Belarus. *J Nutr* 2009; 139(2): 417S-21S.

122.	Casazza K, Fontaine KR, Astrup A, et al. Myths, presumptions, and facts about obesity. *N Engl J Med* 2013; 368(5): 446-54.

123.	Grote V, Theurich M, Koletzko B. Do complementary feeding practices predict the later risk of obesity? *Curr Opin Clin Nutr Metab Care* 2012; 15(3): 293-7.

124.	Moorcroft KE, Marshall JL, McCormick FM. Association between timing of introducing solid foods and obesity in infancy and childhood: a systematic review. *Maternal & child nutrition* 2011; 7(1): 3-26.

125.	te Velde SJ, van Nassau F, Uijtdewilligen L, et al. Energy balance-related behaviours associated with overweight and obesity in preschool children: a systematic review of prospective studies. *Obes Rev* 2012; 13 Suppl 1: 56-74.

126.	van Stralen MM, te Velde SJ, van Nassau F, et al. Weight status of European preschool children and associations with family demographics and energy balance-related behaviours: a pooled analysis of six European studies. *Obes Rev* 2012; 13 Suppl 1: 29-41.

127.	Smithers LG, Golley RK, Brazionis L, et al. Characterizing whole diets of young children from developed countries and the association between diet and health: a systematic review. *Nutr Rev* 2011; 69(8): 449-67.

128.	Ford C, Ward D, White M. Television viewing associated with adverse dietary outcomes in children ages 2-6. *Obes Rev* 2012; 13(12): 1139-47.

129.	Perez-Escamilla R, Obbagy JE, Altman JM, et al. Dietary energy density and body weight in adults and children: a systematic review. *J Acad Nutr Diet* 2012; 112(5): 671-84.

130.	Newby PK. Are dietary intakes and eating behaviors related to childhood obesity? A comprehensive review of the evidence. *J Law Med Ethics* 2007; 35(1): 35-60.

131.	Moreno LA, Rodriguez G. Dietary risk factors for development of childhood obesity. *Curr Opin Clin Nutr Metab Care* 2007; 10(3): 336-41.

132. Ludwig DS, Peterson KE, Gortmaker SL. Relation between consumption of sugar-sweetened drinks and childhood obesity: a prospective, observational analysis. *Lancet* 2001; 357(9255): 505-8.

133. Rolland-Cachera MF, Deheeger M, Akrout M, et al. Influence of macronutrients on adiposity development: a follow up study of nutrition and growth from 10 months to 8 years of age. *Int J Obes Relat Metab Disord* 1995; 19(8): 573-8.

134. Scaglioni S, Agostoni C, Notaris RD, et al. Early macronutrient intake and overweight at five years of age. *Int J Obes Relat Metab Disord* 2000; 24(6): 777-81.

135. Ohlund I, Hernell O, Hornell A, et al. BMI at 4 years of age is associated with previous and current protein intake and with paternal BMI. *Eur J Clin Nutr* 2010; 64(2): 138-45.

136. Ambrosini GL. Childhood dietary patterns and later obesity: a review of the evidence. *Proc Nutr Soc* 2013: 1-10.

137. Harris G. Development of taste and food preferences in children. *Curr Opin Clin Nutr Metab Care* 2008; 11(3): 315-9.

138. Lioret S, McNaughton SA, Spence AC, et al. Tracking of dietary intakes in early childhood: the Melbourne InFANT Program. *Eur J Clin Nutr* 2013; 67(3): 275-81.

139. Northstone K, Emmett PM. Are dietary patterns stable throughout early and mid-childhood? A birth cohort study. *Br J Nutr* 2008; 100(5): 1069-76.

140. Brekke HK, van Odijk J, Ludvigsson J. Predictors and dietary consequences of frequent intake of high-sugar, low-nutrient foods in 1-year-old children participating in the ABIS study. *Br J Nutr* 2007; 97(1): 176-81.

141. Greenberg RS, Ariza AJ, Binns HJ. Activity and dietary habits of mothers and children: close ties. *Clin Pediatr (Phila)* 2010; 49(11): 1026-32.

142. Lee SY, Hoerr SL, Schiffman RF. Screening for infants' and toddlers' dietary quality through maternal diet. *MCN Am J Matern Child Nurs* 2005; 30(1): 60-6.

143. McGowan L, Croker H, Wardle J, et al. Environmental and individual determinants of core and non-core food and drink intake in preschool-aged children in the United Kingdom. *Eur J Clin Nutr* 2012; 66(3): 322-8.

144. Johnson L, van Jaarsveld CH, Wardle J. Individual and family environment correlates differ for consumption of core and non-core foods in children. *Br J Nutr* 2011; 105(6): 950-9.

145. Kral TV, Stunkard AJ, Berkowitz RI, et al. Beverage consumption patterns of children born at different risk of obesity. *Obesity (Silver Spring)* 2008; 16(8): 1802-8.

146. Nguyen VT, Larson DE, Johnson RK, et al. Fat intake and adiposity in children of lean and obese parents. *Am J Clin Nutr* 1996; 63(4): 507-13.

147. Wardle J, Guthrie C, Sanderson S, et al. Food and activity preferences in children of lean and obese parents. *Int J Obes Relat Metab Disord* 2001; 25(7): 971-7.

148. Berkowitz RI, Moore RH, Faith MS, et al. Identification of an obese eating style in 4-year-old children born at high and low risk for obesity. *Obesity (Silver Spring)* 2010; 18(3): 505-12.

149. Kral TV, Stunkard AJ, Berkowitz RI, et al. Daily food intake in relation to dietary energy density in the free-living environment: a prospective analysis of children born at different risk of obesity. *Am J Clin Nutr* 2007; 86(1): 41-7.

150. McGloin AF, Livingstone MB, Greene LC, et al. Energy and fat intake in obese and lean children at varying risk of obesity. *Int J Obes Relat Metab Disord* 2002; 26(2): 200-7.

151.   Stunkard AJ, Berkowitz RI, Schoeller D, et al. Predictors of body size in the first 2 y of life: a high-risk study of human obesity. *Int J Obes Relat Metab Disord* 2004; 28(4): 503-13.

152.   Cameron AJ, Ball K, Pearson N, et al. Socioeconomic variation in diet and activity-related behaviours of Australian children and adolescents aged 2-16 years. *Pediatr Obes* 2012; 7(4): 329-42.

153.   Fernandez-Alvira JM, Mouratidou T, Bammann K, et al. Parental education and frequency of food consumption in European children: the IDEFICS study. *Public Health Nutr* 2013; 16(3): 487-98.

154.   Manios Y, Kourlaba G, Kondaki K, et al. Diet quality of preschoolers in Greece based on the Healthy Eating Index: the GENESIS study. *J Am Diet Assoc* 2009; 109(4): 616-23.

155.   Rogers I, Emmett P, Team AS. The effect of maternal smoking status, educational level and age on food and nutrient intakes in preschool children: results from the Avon Longitudinal Study of Parents and Children. *Eur J Clin Nutr* 2003; 57(7): 854-64.

156.   Smithers LG, Brazionis L, Golley RK, et al. Associations between dietary patterns at 6 and 15 months of age and sociodemographic factors. *Eur J Clin Nutr* 2012; 66(6): 658-66.

157.   NNR 2012. Nordic Nutrition Recommendations 2012. Part 1 Summary, principles and use. *Nordic council of ministers* 2013.

158.   Garemo M, Lenner RA, Strandvik B. Swedish pre-school children eat too much junk food and sucrose. *Acta Paediatr* 2007; 96(2): 266-72.

159.   Livsmedelsverket. Riksmaten – barn 2003. Livsmedels- och näringsintag bland barn i Sverige. 2003.

160.   Ohlund I, Hornell A, Lind T, et al. Dietary fat in infancy should be more focused on quality than on quantity. *Eur J Clin Nutr* 2008; 62(9): 1058-64.

161.   Simell O, Niinikoski H, Ronnemaa T, et al. Special Turku Coronary Risk Factor Intervention Project for Babies (STRIP). *Am J Clin Nutr* 2000; 72(5 Suppl): 1316S-31S.

162.   Amcoff E, Edberg A, Enghardt Barbieri H, et al. Riksmaten – vuxna 2010–11 Livsmedels- och näringsintag bland vuxna i Sverige. *Livsmedelsverket* 2012.

163.   Sepp H, Ekelund U, Becker W. Enkätfrågor om kost och fysisk aktivitet bland vuxna. Underlag till urval av frågor i befolkningsinriktade enkäter. SLV Rapport 21. *Livsmedelsverket* 2004.

164.   Carnell S, Wardle J. Appetitive traits and child obesity: measurement, origins and implications for intervention. *Proc Nutr Soc* 2008; 67(04): 343.

165.   Barkeling B, Ekman S, Rossner S. Eating behaviour in obese and normal weight 11-year-old children. *Int J Obes Relat Metab Disord* 1992; 16(5): 355-60.

166.   Carnell S, Wardle J. Appetite and adiposity in children: evidence for a behavioral susceptibility theory of obesity. *Am J Clin Nutr* 2008; 88(1): 22-9.

167.   Lindgren AC, Barkeling B, Hagg A, et al. Eating behavior in Prader-Willi syndrome, normal weight, and obese control groups. *J Pediatr* 2000; 137(1): 50-5.

168.   Birch LL, Fisher JO. Development of eating behaviors among children and adolescents. *Pediatrics* 1998; 101(3 Pt 2): 539-49.

169.   Birch LL. Development of food preferences. *Annu Rev Nutr* 1999; 19: 41-62.

170.   Birch LL, Doub AE. Learning to eat: birth to age 2 y. *Am J Clin Nutr* 2014.

171.   Schachter S. Obesity and eating. Internal and external cues differentially affect the eating behavior of obese and normal subjects. *Science* 1968; 161(843): 751-6.

172.   Archer LA, Rosenbaum PL, Streiner DL. The children's eating behavior inventory: reliability and validity results. *J Pediatr Psychol* 1991; 16(5): 629-42.

173.   van Strien T, Oosterveld P. The children's DEBQ for assessment of restrained, emotional, and external eating in 7- to 12-year-old children. *Int J Eat Disord* 2008; 41(1): 72-81.

174.   Wardle J, Guthrie CA, Sanderson S, et al. Development of the Children's Eating Behaviour Questionnaire. *J Child Psychol Psychiatry* 2001; 42(7): 963-70.

175.   Ashcroft J, Semmler C, Carnell S, et al. Continuity and stability of eating behaviour traits in children. *Eur J Clin Nutr* 2008; 62(8): 985-90.

176.   Dubois L, Farmer A, Girard M, et al. Problem eating behaviors related to social factors and body weight in preschool children: A longitudinal study. *Int J Behav Nutr Phys Act* 2007; 4: 9.

177.   Carnell S, Haworth CMA, Plomin R, et al. Genetic influence on appetite in children. *Int J Obes* 2008; 32(10): 1468-73.

178.   Dubois L, Diasparra M, Bedard B, et al. Genetic and environmental influences on eating behaviors in 2.5- and 9-year-old children: a longitudinal twin study. *Int J Behav Nutr Phys Act* 2013; 10: 134.

179.   Llewellyn CH, van Jaarsveld CH, Johnson L, et al. Nature and nurture in infant appetite: analysis of the Gemini twin birth cohort. *Am J Clin Nutr* 2010; 91(5): 1172-9.

180.   Llewellyn CH, van Jaarsveld CH, Plomin R, et al. Inherited behavioral susceptibility to adiposity in infancy: a multivariate genetic analysis of appetite and weight in the Gemini birth cohort. *Am J Clin Nutr* 2012; 95(3): 633-9.

181.   Tholin S, Rasmussen F, Tynelius P, et al. Genetic and environmental influences on eating behavior: the Swedish Young Male Twins Study. *Am J Clin Nutr* 2005; 81(3): 564-9.

182.   De Craemer M, De Decker E, De Bourdeaudhuij I, et al. Correlates of energy balance-related behaviours in preschool children: a systematic review. *Obes Rev* 2012; 13 Suppl 1: 13-28.

183.   Must A, Tybor DJ. Physical activity and sedentary behavior: a review of longitudinal studies of weight and adiposity in youth. *Int J Obes (Lond)* 2005; 29 Suppl 2: S84-96.

184.   Jimenez-Pavon D, Kelly J, Reilly JJ. Associations between objectively measured habitual physical activity and adiposity in children and adolescents: Systematic review. *Int J Pediatr Obes* 2010; 5(1): 3-18.

185.   Telama R, Yang X, Leskinen E, et al. Tracking of Physical Activity from Early Childhood through Youth into Adulthood. *Med Sci Sports Exerc* 2013.

186.   Gubbels JS, Kremers SP, Stafleu A, et al. Clustering of energy balance-related behaviors in 5-year-old children: lifestyle patterns and their longitudinal association with weight status development in early childhood. *Int J Behav Nutr Phys Act* 2012; 9: 77.

187.   Must A, Barish EE, Bandini LG. Modifiable risk factors in relation to changes in BMI and fatness: what have we learned from prospective studies of school-aged children? *Int J Obes (Lond)* 2009; 33(7): 705-15.

188.   Olafsdottir S, Berg C, Eiben G, et al. Young children's screen activities, sweet drink consumption and anthropometry: results from a prospective European study. *Eur J Clin Nutr* 2013.

189.   Davis MM, Gance-Cleveland B, Hassink S, et al. Recommendations for prevention of childhood obesity. *Pediatrics* 2007; 120 Suppl 4: S229-53.

190.   Sobko T, Svensson V, Ek A, et al. A randomised controlled trial for overweight and obese parents to prevent childhood obesity - Early STOPP (STockholm Obesity Prevention Program). *BMC Public Health* 2011; 11(1): 336.

191.   Chen X, Beydoun MA, Wang Y. Is sleep duration associated with childhood obesity? A systematic review and meta-analysis. *Obesity (Silver Spring)* 2008; 16(2): 265-74.

192.   Liu J, Zhang A, Li L. Sleep duration and overweight/obesity in children: review and implications for pediatric nursing. *J Spec Pediatr Nurs* 2012; 17(3): 193-204.

193.   Burt J, Dube L, Thibault L, et al. Sleep and eating in childhood: a potential behavioral mechanism underlying the relationship between poor sleep and obesity. *Sleep Med* 2014; 15(1): 71-5.

194.   Kjeldsen JS, Hjorth MF, Andersen R, et al. Short sleep duration and large variability in sleep duration are independently associated with dietary risk factors for obesity in Danish school children. *Int J Obes (Lond)* 2014; 38(1): 32-9.

195.   Ekstedt M, Nyberg G, Ingre M, et al. Sleep, physical activity and BMI in six to ten-year-old children measured by accelerometry: a cross-sectional study. *Int J Behav Nutr Phys Act* 2013; 10: 82.

196.   Holcke M, Marcus C, Gillberg C, et al. Paediatric obesity: a neurodevelopmental perspective. *Acta Paediatr* 2008; 97(6): 819-21.

197.   Pitrou I, Shojaei T, Wazana A, et al. Child overweight, associated psychopathology, and social functioning: a French school-based survey in 6- to 11-year-old children. *Obesity (Silver Spring)* 2010; 18(4): 809-17.

198.   van Egmond-Frohlich AW, Weghuber D, de Zwaan M. Association of symptoms of attention-deficit/hyperactivity disorder with physical activity, media time, and food intake in children and adolescents. *PLoS One* 2012; 7(11): e49781.

199.   Garthus-Niegel S, Hagtvet KA, Vollrath ME. A prospective study of weight development and behavior problems in toddlers: the Norwegian Mother and Child Cohort Study. *BMC Public Health* 2010; 10: 626.

200.   Olsen NJ, Pedersen J, Handel MN, et al. Child behavioural problems and body size among 2-6 year old children predisposed to overweight. results from the "healthy start" study. *PloS one* 2013; 8(11): e78974.

201.   Bergmeier H, Skouteris H, Horwood S, et al. Associations between child temperament, maternal feeding practices and child body mass index during the preschool years: a systematic review of the literature. *Obes Rev* 2014; 15(1): 9-18.

202.   Haycraft E, Farrow C, Meyer C, et al. Relationships between temperament and eating behaviours in young children. *Appetite* 2011; 56(3): 689-92.

203.   Mackenbach JD, Tiemeier H, Ende J, et al. Relation of emotional and behavioral problems with body mass index in preschool children: the Generation R study. *J Dev Behav Pediatr* 2012; 33(8): 641-8.

204.   Sleddens EF, Gerards SM, Thijs C, et al. General parenting, childhood overweight and obesity-inducing behaviors: a review. *Int J Pediatr Obes* 2011; 6(2-2): e12-27.

205.   Kiefner-Burmeister AE, Hoffmann DA, Meers MR, et al. Food consumption by young children: A function of parental feeding goals and practices. *Appetite* 2014; 74: 6-11.

206.   Rodenburg G, Kremers SP, Oenema A, et al. Associations of children's appetitive traits with weight and dietary behaviours in the context of general parenting. *PLoS One* 2012; 7(12): e50642.

207.   Scaglioni S, Arrizza C, Vecchi F, et al. Determinants of children's eating behavior. *Am J Clin Nutr* 2011; 94(6 Suppl): 2006S-11S.

208. Topham GL, Hubbs-Tait L, Rutledge JM, et al. Parenting styles, parental response to child emotion, and family emotional responsiveness are related to child emotional eating. *Appetite* 2011; 56(2): 261-4.
209. Webber L, Cooke L, Hill C, et al. Child adiposity and maternal feeding practices: a longitudinal analysis. *Am J Clin Nutr* 2010; 92(6): 1423-8.
210. Ventura AK, Birch LL. Does parenting affect children's eating and weight status? *Int J Behav Nutr Phys Act* 2008; 5: 15.
211. Danielsson P, Kowalski J, Ekblom O, et al. Response of Severely Obese Children and Adolescents to Behavioral Treatment. *Arch Pediatr Adolesc Med* 2012: 1-6.
212. Danielsson P, Svensson V, Kowalski J, et al. Importance of age for 3-year continuous behavioral obesity treatment success and dropout rate. *Obes Facts* 2012; 5(1): 34-44.
213. Waters E, de Silva-Sanigorski A, Hall BJ, et al. Interventions for preventing obesity in children. *Cochrane Database Syst Rev* 2011; (12): CD001871.
214. Summerbell CD, Waters E, Edmunds LD, et al. Interventions for preventing obesity in children. *Cochrane Database Syst Rev* 2005; (3): CD001871.
215. Marcus C, Nyberg G, Nordenfelt A, et al. A 4-year, cluster-randomized, controlled childhood obesity prevention study: STOPP. *Int J Obes (Lond)* 2009; 33(4): 408-17.
216. Bluford DA, Sherry B, Scanlon KS. Interventions to prevent or treat obesity in preschool children: a review of evaluated programs. *Obesity (Silver Spring)* 2007; 15(6): 1356-72.
217. Hesketh KD, Campbell KJ. Interventions to prevent obesity in 0-5 year olds: an updated systematic review of the literature. *Obesity (Silver Spring)* 2010; 18 Suppl 1: S27-35.
218. Skouteris H, McCabe M, Swinburn B, et al. Parental influence and obesity prevention in pre-schoolers: a systematic review of interventions. *Obes Rev* 2011; 12(5): 315-28.
219. Care) SSbfmuTSCoTAiH. Förebyggande åtgärder mot fetma. 2004.
220. Showell NN, Fawole O, Segal J, et al. A systematic review of home-based childhood obesity prevention studies. *Pediatrics* 2013; 132(1): e193-200.
221. Baidal JA, Taveras EM. Childhood obesity: shifting the focus to early prevention. *Arch Pediatr Adolesc Med* 2012; 166(12): 1179-81.
222. Collins CE, Watson J, Burrows T. Measuring dietary intake in children and adolescents in the context of overweight and obesity. *Int J Obes (Lond)* 2010; 34(7): 1103-15.
223. Rutishauser IH. Dietary intake measurements. *Public Health Nutr* 2005; 8(7A): 1100-7.
224. Lissner L. Measuring food intake in studies of obesity. *Public Health Nutr* 2002; 5(6A): 889-92.
225. Rennie KL, Coward A, Jebb SA. Estimating under-reporting of energy intake in dietary surveys using an individualised method. *Br J Nutr* 2007; 97(6): 1169-76.
226. Waling MU, Larsson CL. Energy intake of Swedish overweight and obese children is underestimated using a diet history interview. *J Nutr* 2009; 139(3): 522-7.
227. Baranowski T, Sprague D, Baranowski JH, et al. Accuracy of maternal dietary recall for preschool children. *J Am Diet Assoc* 1991; 91(6): 669-74.
228. Uusitalo L, Nevalainen J, Salminen I, et al. Fatty acids in serum and diet--a canonical correlation analysis among toddlers. *Maternal & child nutrition* 2013; 9(3): 381-95.
229. Forrestal SG. Energy intake misreporting among children and adolescents: a literature review. *Maternal & child nutrition* 2011; 7(2): 112-27.

230. Black AE. Critical evaluation of energy intake using the Goldberg cut-off for energy intake:basal metabolic rate. A practical guide to its calculation, use and limitations. *Int J Obes Relat Metab Disord* 2000; 24(9): 1119-30.

231. Goldberg GR, Black AE, Jebb SA, et al. Critical evaluation of energy intake data using fundamental principles of energy physiology: 1. Derivation of cut-off limits to identify under-recording. *Eur J Clin Nutr* 1991; 45(12): 569-81.

232. Bornhorst C, Huybrechts I, Hebestreit A, et al. Diet-obesity associations in children: approaches to counteract attenuation caused by misreporting. *Public Health Nutr* 2013; 16(2): 256-66.

233. Bingham SA, Luben R, Welch A, et al. Are imprecise methods obscuring a relation between fat and breast cancer? *Lancet* 2003; 362(9379): 212-4.

234. Livingstone MB, Robson PJ, Wallace JM. Issues in dietary intake assessment of children and adolescents. *Br J Nutr* 2004; 92 Suppl 2: S213-22.

235. Mouratidou T, Mesana MI, Manios Y, et al. Assessment tools of energy balance-related behaviours used in European obesity prevention strategies: review of studies during preschool. *Obes Rev* 2012; 13 Suppl 1: 42-55.

236. Stumbo PJ. New technology in dietary assessment: a review of digital methods in improving food record accuracy. *Proc Nutr Soc* 2013; 72(1): 70-6.

237. Svensson A, Waling M, Backlund C, et al. Overweight and Obese Children's Ability to Report Energy Intake Using Digital Camera Food Records during a 2-Year Study. *J Nutr Metab* 2012; 2012: 247389.

238. Baylin A, Campos H. The use of fatty acid biomarkers to reflect dietary intake. *Curr Opin Lipidol* 2006; 17(1): 22-7.

239. Goris AH, Westerterp-Plantenga MS, Westerterp KR. Undereating and underrecording of habitual food intake in obese men: selective underreporting of fat intake. *Am J Clin Nutr* 2000; 71(1): 130-4.

240. Arab L. Biomarkers of fat and fatty acid intake. *J Nutr* 2003; 133 Suppl 3: 925S-32S.

241. Beynen AC, Katan MB. Rapid sampling and long-term storage of subcutaneous adipose-tissue biopsies for determination of fatty acid composition. *Am J Clin Nutr* 1985; 42(2): 317-22.

242. Ma J, Folsom AR, Shahar E, et al. Plasma fatty acid composition as an indicator of habitual dietary fat intake in middle-aged adults. The Atherosclerosis Risk in Communities (ARIC) Study Investigators. *Am J Clin Nutr* 1995; 62(3): 564-71.

243. Boberg M, Croon LB, Gustafsson IB, et al. Platelet fatty acid composition in relation to fatty acid composition in plasma and to serum lipoprotein lipids in healthy subjects with special reference to the linoleic acid pathway. *Clin Sci (Lond)* 1985; 68(5): 581-7.

244. Kuriki K, Nagaya T, Tokudome Y, et al. Plasma concentrations of (n-3) highly unsaturated fatty acids are good biomarkers of relative dietary fatty acid intakes: a cross-sectional study. *J Nutr* 2003; 133(11): 3643-50.

245. Wolk A, Vessby B, Ljung H, et al. Evaluation of a biological marker of dairy fat intake. *Am J Clin Nutr* 1998; 68(2): 291-5.

246. Lazarou C, Newby PK. Use of dietary indexes among children in developed countries. *Adv Nutr* 2011; 2(4): 295-303.

247. Kant AK. Indexes of overall diet quality: a review. *J Am Diet Assoc* 1996; 96(8): 785-91.

248. Kant AK. Dietary patterns and health outcomes. *J Am Diet Assoc* 2004; 104(4): 615-35.

249. Pala V, Lissner L, Hebestreit A, et al. Dietary patterns and longitudinal change in body mass in European children: a follow-up study on the IDEFICS multicenter cohort. *Eur J Clin Nutr* 2013; 67(10): 1042-9.

250. Rolland-Cachera MF, Sempe M, Guilloud-Bataille M, et al. Adiposity indices in children. *Am J Clin Nutr* 1982; 36(1): 178-84.

251. Schofield WN. Predicting basal metabolic rate, new standards and review of previous work. *Hum Nutr Clin Nutr* 1985; 39 Suppl 1: 5-41.

252. Paul AA BA, Evans J, Cole TJ, Whitehead RG. Breastmilk intake and growth in infants from two to ten months. *J Hum Nutr Dietet* 1988; 1: 437-50.

253. Carnell S, Wardle J. Measuring behavioural susceptibility to obesity: Validation of the child eating behaviour questionnaire. *Appetite* 2007; 48(1): 104-13.

254. Cao YT, Svensson V, Marcus C, et al. Eating behaviour patterns in Chinese children aged 12-18 months and association with relative weight--factorial validation of the Children's Eating Behaviour Questionnaire. *Int J Behav Nutr Phys Act* 2012; 9: 5.

255. Loh DA, Moy FM, Zaharan NL, et al. Eating Behaviour among Multi-Ethnic Adolescents in a Middle-Income Country as Measured by the Self-Reported Children's Eating Behaviour Questionnaire. *PLoS One* 2013; 8(12): e82885.

256. Mallan KM, Liu WH, Mehta RJ, et al. Maternal report of young children's eating styles. Validation of the Children's Eating Behaviour Questionnaire in three ethnically diverse Australian samples. *Appetite* 2013; 64: 48-55.

257. Sleddens EFC, Kremers SPJ, Thijs C. The Children's Eating Behaviour Questionnaire: factorial validity and association with Body Mass Index in Dutch children aged 6-7. *International Journal of Behavioral Nutrition and Physical Activity* 2008; 5(1): 49.

258. Spence JC, Carson V, Casey L, et al. Examining behavioural susceptibility to obesity among Canadian pre-school children: The role of eating behaviours. *Int J Pediatr Obes* 2010.

259. Webber L, Hill C, Saxton J, et al. Eating behaviour and weight in children. *Int J Obes (Lond)* 2009; 33(1): 21-8.

260. Viana V, Sinde S, Saxton JC. Children's Eating Behaviour Questionnaire: associations with BMI in Portuguese children. *Br J Nutr* 2008; 100(02).

261. Becker W. Indikatorer för bra matvanor. Resultat från intervjuundersökningar 2008. SLV Rapport 22. *Livsmedelsverket* 2009.

262. Wolk A, Furuheim M, Vessby B. Fatty acid composition of adipose tissue and serum lipids are valid biological markers of dairy fat intake in men. *J Nutr* 2001; 131(3): 828-33.

263. Albertsson-Wikland K, Karlberg J. Natural growth in children born small for gestational age with and without catch-up growth. *Acta Paediatr Suppl* 1994; 399: 64-70; discussion 1.

264. Olson CM, Demment MM, Carling SJ, et al. Associations Between Mothers' and Their Children's Weights at 4 Years of Age. *Child Obes* 2010; 6(4): 201-7.

265. Connor Gorber S, Tremblay M, Moher D, et al. A comparison of direct vs. self-report measures for assessing height, weight and body mass index: a systematic review. *Obes Rev* 2007; 8(4): 307-26.

266. Berlin A, Johansson SE, Tornkvist L. Working conditions and cultural competence when interacting with children and parents of foreign origin--Primary Child Health Nurses' opinions. *Scand J Caring Sci* 2006; 20(2): 160-8.

267. Isma GE, Bramhagen AC, Ahlstrom G, et al. Swedish Child Health Care nurses conceptions of overweight in children: a qualitative study. *BMC Fam Pract* 2012; 13: 57.

268. Beyerlein A, Toschke AM, Schaffrath Rosario A, et al. Risk factors for obesity: further evidence for stronger effects on overweight children and adolescents compared to normal-weight subjects. *PLoS One* 2011; 6(1): e15739.

269. Beyerlein A, Toschke AM, von Kries R. Risk factors for childhood overweight: shift of the mean body mass index and shift of the upper percentiles: results from a cross-sectional study. *Int J Obes (Lond)* 2010; 34(4): 642-8.

270. Fuentes RM, Notkola IL, Shemeikka S, et al. Tracking of body mass index during childhood: a 15-year prospective population-based family study in eastern Finland. *Int J Obes Relat Metab Disord* 2003; 27(6): 716-21.

271. Maffeis C, Talamini G, Tato L. Influence of diet, physical activity and parents' obesity on children's adiposity: a four-year longitudinal study. *Int J Obes Relat Metab Disord* 1998; 22(8): 758-64.

272. Liu Y, Chen HJ, Liang L, et al. Parent-child resemblance in weight status and its correlates in the United States. *PLoS One* 2013; 8(6): e65361.

273. Jacobson P, Torgerson JS, Sjostrom L, et al. Spouse resemblance in body mass index: effects on adult obesity prevalence in the offspring generation. *Am J Epidemiol* 2007; 165(1): 101-8.

274. Hebebrand J, Wulftange H, Goerg T, et al. Epidemic obesity: are genetic factors involved via increased rates of assortative mating? *Int J Obes Relat Metab Disord* 2000; 24(3): 345-53.

275. Parsons TJ, Power C, Logan S, et al. Childhood predictors of adult obesity: a systematic review. *Int J Obes Relat Metab Disord* 1999; 23 Suppl 8: S1-107.

276. Freeman E, Fletcher R, Collins CE, et al. Preventing and treating childhood obesity: time to target fathers. *Int J Obes (Lond)* 2012; 36(1): 12-5.

277. Leary S, Davey Smith G, Ness A. No evidence of large differences in mother-daughter and father-son body mass index concordance in a large UK birth cohort. *Int J Obes (Lond)* 2010; 34(7): 1191-2.

278. Harrington JW, Nguyen VQ, Paulson JF, et al. Identifying the "tipping point" age for overweight pediatric patients. *Clin Pediatr (Phila)* 2010; 49(7): 638-43.

279. Quattrin T, Liu E, Shaw N, et al. Obese children who are referred to the pediatric endocrinologist: characteristics and outcome. *Pediatrics* 2005; 115(2): 348-51.

280. Farooqi IS, O'Rahilly S. New advances in the genetics of early onset obesity. *Int J Obes (Lond)* 2005; 29(10): 1149-52.

281. Dietz WH. Critical periods in childhood for the development of obesity. *Am J Clin Nutr* 1994; 59(5): 955-9.

282. Taylor RW, Grant AM, Goulding A, et al. Early adiposity rebound: review of papers linking this to subsequent obesity in children and adults. *Curr Opin Clin Nutr Metab Care* 2005; 8(6): 607-12.

283. Dorosty AR, Emmett PM, Cowin S, et al. Factors associated with early adiposity rebound. ALSPAC Study Team. *Pediatrics* 2000; 105(5): 1115-8.

284. Ong KK, Ahmed ML, Emmett PM, et al. Association between postnatal catch-up growth and obesity in childhood: prospective cohort study. *BMJ* 2000; 320(7240): 967-71.

285. Chandler-Laney PC, Gower BA, Fields DA. Gestational and early life influences on infant body composition at 1 year. *Obesity (Silver Spring)* 2013; 21(1): 144-8.

286. Howe LD, Tilling K, Galobardes B, et al. Socioeconomic disparities in trajectories of adiposity across childhood. *Int J Pediatr Obes* 2011; 6(2-2): e144-53.

287. Wright CM, Parkinson KN, Drewett RF. The influence of maternal socioeconomic and emotional factors on infant weight gain and weight faltering (failure to thrive): data from a prospective birth cohort. *Arch Dis Child* 2006; 91(4): 312-7.

288. Jansen PW, Mensah FK, Nicholson JM, et al. Family and neighbourhood socioeconomic inequalities in childhood trajectories of BMI and overweight: longitudinal study of Australian children. *PLoS One* 2013; 8(7): e69676.

289. Fernandez-Alvira JM, te Velde SJ, De Bourdeaudhuij I, et al. Parental education associations with children's body composition: mediation effects of energy balance-related behaviors within the ENERGY-project. *Int J Behav Nutr Phys Act* 2013; 10: 80.

290. Saxton J, Carnell S, van Jaarsveld CH, et al. Maternal education is associated with feeding style. *J Am Diet Assoc* 2009; 109(5): 894-8.

291. Magnusson MB, Sjoberg A, Kjellgren KI, et al. Childhood obesity and prevention in different socio-economic contexts. *Prev Med* 2011; 53(6): 402-7.

292. Veldhuis L, Vogel I, Renders CM, et al. Behavioral risk factors for overweight in early childhood; the 'Be active, eat right' study. *Int J Behav Nutr Phys Act* 2012; 9: 74.

293. Eriksson M, Tynelius P, Rasmussen F. Associations of birthweight and infant growth with body composition at age 15--the COMPASS study. *Paediatr Perinat Epidemiol* 2008; 22(4): 379-88.

294. Mihrshahi S, Battistutta D, Magarey A, et al. Determinants of rapid weight gain during infancy: baseline results from the NOURISH randomised controlled trial. *BMC Pediatr* 2011; 11: 99.

295. Touwslager RN, Gielen M, Derom C, et al. Determinants of infant growth in four age windows: a twin study. *J Pediatr* 2011; 158(4): 566-72 e2.

296. Parsons TJ, Power C, Manor O. Fetal and early life growth and body mass index from birth to early adulthood in 1958 British cohort: longitudinal study. *BMJ* 2001; 323(7325): 1331-5.

297. Williams SM, Taylor RW, Taylor BJ. Secular changes in BMI and the associations between risk factors and BMI in children born 29 years apart. *Pediatr Obes* 2013; 8(1): 21-30.

298. Gunnarsdottir I, Schack-Nielsen L, Michaelsen KF, et al. Infant weight gain, duration of exclusive breast-feeding and childhood BMI - two similar follow-up cohorts. *Public Health Nutr* 2010; 13(2): 201-7.

299. Gaffney KF, Kitsantas P, Cheema J. Clinical practice guidelines for feeding behaviors and weight-for-age at 12 months: a secondary analysis of the Infant Feeding Practices Study II. *Worldviews Evid Based Nurs* 2012; 9(4): 234-42.

300. Wright CM, Cox KM, Le Couteur A. How does infant behaviour relate to weight gain and adiposity? *Proc Nutr Soc* 2011; 70(4): 485-93.

301. Wright CM, Parkinson K, Scott J. Breast-feeding in a UK urban context: who breast-feeds, for how long and does it matter? *Public Health Nutr* 2006; 9(6): 686-91.

302. Escribano J, Luque V, Ferre N, et al. Effect of protein intake and weight gain velocity on body fat mass at 6 months of age: the EU Childhood Obesity Programme. *Int J Obes (Lond)* 2012; 36(4): 548-53.

303. Heinig MJ, Nommsen LA, Peerson JM, et al. Energy and protein intakes of breast-fed and formula-fed infants during the first year of life and their association with growth velocity: the DARLING Study. *Am J Clin Nutr* 1993; 58(2): 152-61.

304. Koletzko B, von Kries R, Closa R, et al. Lower protein in infant formula is associated with lower weight up to age 2 y: a randomized clinical trial. *Am J Clin Nutr* 2009; 89(6): 1836-45.

305.   Gunnarsdottir I, Thorsdottir I. Relationship between growth and feeding in infancy and body mass index at the age of 6 years. *Int J Obes Relat Metab Disord* 2003; 27(12): 1523-7.

306.   Kudlova E, Schneidrova D. Dietary patterns and their changes in early childhood. *Cent Eur J Public Health* 2012; 20(2): 126-34.

307.   Kyttala P, Erkkola M, Kronberg-Kippila C, et al. Food consumption and nutrient intake in Finnish 1-6-year-old children. *Public Health Nutr* 2010; 13(6A): 947-56.

308.   Stunkard AJ, Berkowitz RI, Stallings VA, et al. Energy intake, not energy output, is a determinant of body size in infants. *Am J Clin Nutr* 1999; 69(3): 524-30.

309.   Beydoun MA, Wang Y. Parent-child dietary intake resemblance in the United States: evidence from a large representative survey. *Soc Sci Med* 2009; 68(12): 2137-44.

310.   Zhou SJ, Gibson RA, Gibson RS, et al. Nutrient intakes and status of preschool children in Adelaide, South Australia. *Med J Aust* 2012; 196(11): 696-700.

311.   Mennella JA, Jagnow CP, Beauchamp GK. Prenatal and postnatal flavor learning by human infants. *Pediatrics* 2001; 107(6): E88.

312.   Trout KK, Wetzel-Effinger L. Flavor learning in utero and its implications for future obesity and diabetes. *Curr Diab Rep* 2012; 12(1): 60-6.

313.   Mennella JA, Trabulsi JC. Complementary foods and flavor experiences: setting the foundation. *Ann Nutr Metab* 2012; 60 Suppl 2: 40-50.

314.   Schrempft S, van Jaarsveld CH, Fisher A, et al. Family and infant characteristics associated with timing of core and non-core food introduction in early childhood. *Eur J Clin Nutr* 2013; 67(6): 652-7.

315.   Ochiai H, Shirasawa T, Ohtsu T, et al. Number of siblings, birth order, and childhood overweight: a population-based cross-sectional study in Japan. *BMC Public Health* 2012; 12: 766.

316.   Fuemmeler BF, Lovelady CA, Zucker NL, et al. Parental obesity moderates the relationship between childhood appetitive traits and weight. *Obesity (Silver Spring)* 2013; 21(4): 815-23.

317.   van Jaarsveld CH, Llewellyn CH, Johnson L, et al. Prospective associations between appetitive traits and weight gain in infancy. *Am J Clin Nutr* 2011; 94(6): 1562-7.

318.   Wright CM, Cox KM, Sherriff A, et al. To what extent do weight gain and eating avidity during infancy predict later adiposity? *Public Health Nutr* 2012; 15(4): 656-62.

319.   Cole TJ. Early causes of child obesity and implications for prevention. *Acta Paediatr Suppl* 2007; 96(454): 2-4.

320.   Wang Y, Wang A, Donovan SM, et al. Individual genetic variations related to satiety and appetite control increase risk of obesity in preschool-age children in the STRONG kids program. *Hum Hered* 2013; 75(2-4): 152-9.

321.   Karra E, O'Daly OG, Choudhury AI, et al. A link between FTO, ghrelin, and impaired brain food-cue responsivity. *J Clin Invest* 2013; 123(8): 3539-51.

322.   Riedel C, von Kries R, Fenske N, et al. Interactions of genetic and environmental risk factors with respect to body fat mass in children: results from the ALSPAC study. *Obesity (Silver Spring)* 2013; 21(6): 1238-42.

323.   Flegal KM, Troiano RP. Changes in the distribution of body mass index of adults and children in the US population. *Int J Obes Relat Metab Disord* 2000; 24(7): 807-18.

324.   Johnson L, Llewellyn CH, van Jaarsveld CH, et al. Genetic and environmental influences on infant growth: prospective analysis of the Gemini twin birth cohort. *PLoS One* 2011; 6(5): e19918.

325. Touwslager RN, Gielen M, Mulder AL, et al. Changes in genetic and environmental effects on growth during infancy. *Am J Clin Nutr* 2011; 94(6): 1568-74.

326. Gluckman PD, Hanson MA. Developmental and epigenetic pathways to obesity: an evolutionary-developmental perspective. *Int J Obes (Lond)* 2008; 32 Suppl 7: S62-71.

327. Simonen RL, Perusse L, Rankinen T, et al. Familial aggregation of physical activity levels in the Quebec Family Study. *Med Sci Sports Exerc* 2002; 34(7): 1137-42.

328. Li L, Law C, Lo Conte R, et al. Intergenerational influences on childhood body mass index: the effect of parental body mass index trajectories. *Am J Clin Nutr* 2009; 89(2): 551-7.

329. Keane E, Layte R, Harrington J, et al. Measured parental weight status and familial socio-economic status correlates with childhood overweight and obesity at age 9. *PLoS One* 2012; 7(8): e43503.

330. Monasta L, Batty GD, Cattaneo A, et al. Early-life determinants of overweight and obesity: a review of systematic reviews. *Obes Rev* 2010; 11(10): 695-708.

331. Wojcicki JM, Heyman MB. Let's Move--childhood obesity prevention from pregnancy and infancy onward. *N Engl J Med* 2010; 362(16): 1457-9.

332. Gillman MW, Ludwig DS. How early should obesity prevention start? *N Engl J Med* 2013; 369(23): 2173-5.

333. Mustila T, Raitanen J, Keskinen P, et al. Pragmatic controlled trial to prevent childhood obesity in maternity and child health care clinics: pregnancy and infant weight outcomes (the VACOPP Study). *BMC Pediatr* 2013; 13: 80.

334. Hughes AR, Sherriff A, Lawlor DA, et al. Timing of excess weight gain in the Avon Longitudinal Study of Parents and Children (ALSPAC). *Pediatrics* 2011; 127(3): e730-6.

335. Bohman B, Ghaderi A, Rasmussen F. Training in Methods of Preventing Childhood Obesity Increases Self-efficacy in Nurses in Child Health Services: A Randomized, Controlled Trial. *J Nutr Educ Behav* 2013.

336. Rose G. Strategy of prevention: lessons from cardiovascular disease. *Br Med J (Clin Res Ed)* 1981; 282(6279): 1847-51.

337. Strachan D, Rose G. Strategies of prevention revisited: effects of imprecise measurement of risk factors on the evaluation of "high-risk" and "population-based" approaches to prevention of cardiovascular disease. *J Clin Epidemiol* 1991; 44(11): 1187-96.

338. Beyerlein A, Kusian D, Ziegler AG, et al. Classification tree analyses reveal limited potential for early targeted prevention against childhood overweight. *Obesity (Silver Spring)* 2014; 22(2): 512-7.

339. Wright DR, Taveras EM, Gillman MW, et al. The cost of a primary care-based childhood obesity prevention intervention. *BMC Health Serv Res* 2014; 14(1): 44.

340. John J, Wenig CM, Wolfenstetter SB. Recent economic findings on childhood obesity: cost-of-illness and cost-effectiveness of interventions. *Curr Opin Clin Nutr Metab Care* 2010; 13(3): 305-13.

341. Kowalski J, Nyberg G, Danielsson P, et al. How severe childhood obesity shall be defined: relation and agreement between two commonly used body mass index standard deviation scores. *Obesity Facts 2009;2(suppl 2):1-256 (Abstract 17th ECO 2009 Amsterdam)* 2009.

342. Bammann K, Gwozdz W, Lanfer A, et al. Socioeconomic factors and childhood overweight in Europe: results from the multi-centre IDEFICS study. *Pediatr Obes* 2013; 8(1): 1-12.

343. Cooke L, Wardle J, Gibson EL. Relationship between parental report of food neophobia and everyday food consumption in 2-6-year-old children. *Appetite* 2003; 41(2): 205-6.

344. French SA, Epstein LH, Jeffery RW, et al. Eating behavior dimensions. Associations with energy intake and body weight. A review. *Appetite* 2012; 59(2): 541-9.

345. Sichert-Hellert W, Kersting M, Schoch G. Underreporting of energy intake in 1 to 18 year old German children and adolescents. *Z Ernahrungswiss* 1998; 37(3): 242-51.

346. Willett WC, Howe GR, Kushi LH. Adjustment for total energy intake in epidemiologic studies. *Am J Clin Nutr* 1997; 65(4 Suppl): 1220S-8S; discussion 9S-31S.

347. Saadatian-Elahi M, Slimani N, Chajes V, et al. Plasma phospholipid fatty acid profiles and their association with food intakes: results from a cross-sectional study within the European Prospective Investigation into Cancer and Nutrition. *Am J Clin Nutr* 2009; 89(1): 331-46.

348. Laroche HH, Wallace RB, Snetselaar L, et al. Changes in diet behavior when adults become parents. *J Acad Nutr Diet* 2012; 112(6): 832-9.

349. Fiala J, Brazdova Z. A comparison between the lifestyles of men and women--parents of school age children. *Cent Eur J Public Health* 2000; 8(2): 94-100.

350. Johansson L, Thelle DS, Solvoll K, et al. Healthy dietary habits in relation to social determinants and lifestyle factors. *Br J Nutr* 1999; 81(3): 211-20.

351. Baylin A, Kim MK, Donovan-Palmer A, et al. Fasting whole blood as a biomarker of essential fatty acid intake in epidemiologic studies: comparison with adipose tissue and plasma. *Am J Epidemiol* 2005; 162(4): 373-81.

352. Heitmann BL, Lissner L. Dietary underreporting by obese individuals--is it specific or non-specific? *BMJ* 1995; 311(7011): 986-9.

353. Voracek M, Haubner T, Fisher M. Recent decline in non-paternity rates: a cross-temporal meta-analysis. *Psychol Rep* 2008; 103: 799-811.

354. Isma GE, Bramhagen AC, Ahlstrom G, et al. Obstacles to the prevention of overweight and obesity in the context of child health care in Sweden. *BMC Fam Pract* 2013; 14: 143.

355. Thafvelin M. Mat och rörelse på BVC i Stockholms läns landsting. Rapport 26. *Stockholms läns landsting Centrum för folkhälsa* 2006.

356. Stenhammar C, Wells M, Ahman A, et al. 'Children are exposed to temptation all the time'- parents' lifestyle-related discussions in focus groups. *Acta Paediatr* 2012; 101(2): 208-15.