

Rheinische Friedrich-Wilhelms-Universität
Landwirtschaftliche Fakultät
Institut für Ernährungs- und Lebensmittelwissenschaft
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**Determinants and health risks of overweight and obesity
among children and adolescents in Germany**

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Christina Kleiser

aus Löffingen

Referent: PD Dr. Reinhild Prinz-Langenohl
Korreferenten: Prof. Dr. Thomas Remer
Dr. Gert B.M. Mensink
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Determinants and health risks of overweight and obesity among children and adolescents in Germany

The worldwide growing prevalence of overweight and obesity is becoming an important public health concern, also among children and adolescents. To establish effective prevention strategies, it is important to identify potential determinants and health related consequences in an early stage of life. In the present study, major determinants of overweight and obesity as well as the association between overweight and cardiovascular disease (CVD) risk factors were analysed using data from the large nationally representative German Health Interview and Examination Survey for Children and Adolescents (KiGGS). Furthermore, the relevance of different anthropometric overweight measures for assessing health risk was evaluated.

From the obtained information, parental overweight was identified as a major determinant of overweight and obesity among children and adolescents. A positive independent association with obesity was also seen for low socio-economic status (SES), migration background (only significant among 3-13 year olds), high weight gain during pregnancy (only significant for normal weight mothers), maternal smoking during pregnancy, high birth weight, short sleep duration (only significant among 3-10 year olds), and high media consumption. A low SES was also associated with a higher occurrence of unfavourable behaviour and conditions.

All observed overweight measures, showed a consistent positive association with adverse CVD risk factors, even in children younger than 11 years of age. Depending on the overweight measure chosen, the highest differences in the adjusted mean values of CVD risk factors between overweight and non-overweight were 14 mg/dl for total cholesterol, 12 mg/dl for LDL cholesterol, -10 mg/dl for HDL cholesterol, 9 mm Hg for systolic blood pressure, 4 mm Hg for diastolic blood pressure, and 1.2 mg/l for C-reactive protein. Among adolescents, body mass index (BMI), waist circumference and waist-to-height ratio showed a stronger association with CVD risk factors than waist-to-hip ratio and skinfold thickness.

Children and adolescents from families with overweight parents and low SES have a higher risk for overweight and obesity and are therefore important target groups for prevention. BMI, waist circumference and waist-to-height ratio are good predictors for adverse CVD risk factors. Combining BMI and waist circumference or BMI and waist-to-height ratio may be even more useful for risk assessment in large-scale epidemiologic studies.

Determinanten und gesundheitliche Risiken von Übergewicht und Adipositas bei Kindern und Jugendlichen in Deutschland

Die weltweit steigende Prävalenz von Übergewicht und Adipositas ist von zunehmender Public Health Relevanz, auch bei Kindern und Jugendlichen. Um effektive Präventionsstrategien auszuarbeiten, ist es wichtig Determinanten und gesundheitliche Konsequenzen frühzeitig zu identifizieren. In der vorliegenden Arbeit wurden die bedeutendsten Determinanten von Übergewicht und Adipositas sowie der Zusammenhang zwischen Übergewicht und kardiovaskulären Risikofaktoren analysiert. Hierzu wurden Daten des national repräsentativen Kinder- und Jugendgesundheits surveys (KiGGS) herangezogen. Darüber hinaus wurden unterschiedliche anthropometrische Maße zur Bestimmung von Übergewicht hinsichtlich ihrer Relevanz für die Risikobewertung beurteilt.

Elterliches Übergewicht wurde anhand der erhobenen Daten als wichtigste Determinante von Übergewicht und Adipositas bei Kindern und Jugendlichen identifiziert. Es zeigte sich zudem ein positiver unabhängiger Zusammenhang zwischen Adipositas und niedrigem Sozialstatus, Migrationshintergrund (nur bei 3- bis 13-Jährigen signifikant), hoher Gewichtszunahme in der Schwangerschaft (nur bei normalgewichtigen Müttern signifikant), mütterlichem Rauchen in der Schwangerschaft, hohem Geburtsgewicht, geringer Schlafdauer (nur bei 3- bis 10-Jährigen signifikant) sowie hohem Medienkonsum. Ein niedriger Sozialstatus war darüber hinaus mit einem höheren Auftreten ungünstiger Verhaltensweisen und Lebensbedingungen assoziiert. Bei allen erfassten Übergewichtsmaßen zeigte sich bereits bei Kindern unter 11 Jahren ein durchgehend positiver Zusammenhang mit ungünstigen kardiovaskulären Risikofaktoren. Abhängig vom gewählten Maß zur Bestimmung von Übergewicht zeigten sich die höchsten Unterschiede zwischen Übergewichtigen und nicht Übergewichtigen in den adjustierten Mittelwerten der kardiovaskulären Risikofaktoren mit 14 mg/dl für Gesamtcholesterin, 12 mg/dl für LDL-Cholesterin, -10 mg/dl für HDL-Cholesterin, 9 mm Hg für systolischen Blutdruck, 4 mm Hg für diastolischen Blutdruck und 1,2 mg/l für C-reaktives Protein. Bei Jugendlichen war der Zusammenhang von kardiovaskulären Risikofaktoren mit Body Mass Index (BMI), Taillenumfang und Taille-Größe-Quotient stärker ausgeprägt als der mit Taille-Hüft-Quotient und Hautfaltendicken.

Kinder und Jugendliche aus Familien mit übergewichtigen Eltern und niedrigem Sozialstatus sind bedeutende Zielgruppen für die Prävention. BMI, Taillenumfang und Taille-Größe-Quotient sind gute Prädiktoren für ein ungünstiges kardiovaskuläres Risikoprofil. Eine Kombination von BMI und Taillenumfang oder BMI und Taille-Größe-Quotient kann für die Risikobewertung in großangelegten epidemiologischen Studien sinnvoll sein.

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LIST OF ABBREVIATIONS

AGA	Arbeitsgemeinschaft Adipositas im Kindes- und Jugendalter (Working Group Obesity in Childhood and Adolescence)
AUC	Area under the curve
BMI	Body mass index
CVD	Cardiovascular disease
CDC	Centers for Disease Control
CI	Confidence interval
DBP	Diastolic blood pressure
ECOG	European Childhood Obesity Group
FFQ	Food frequency questionnaire
FKE	Forschungsinstitut für Kinderernährung (Research Institute of Child Nutrition)
HbA1c	Glycosylated haemoglobin
HC	Hip circumference
HDL-C	High density lipoprotein cholesterol
HEI	Healthy eating index
Hs-CRP	High sensitivity C-reactive protein
HuSKY	Healthy nutrition score for kids and youth
IL-6	Interleukin-6
IOTF	International Obesity Task Force
KiGGS	Kinder- und Jugendgesundheitsurvey (German Health Interview and Examination Survey for Children and Adolescents)
LDL-C	Low density lipoprotein cholesterol
NCEP	National Cholesterol Education Program
NHANES	National Health and Nutrition Examination Survey
NHBPEP	National High Blood Pressure Education Program
OR	Odds ratio
ROC	Receiver operating characteristic
SAS	Statistical Analysis System
SBP	Systolic blood pressure
SCOFF	Acronym reflecting the five questions addressing core features of eating disorders
SE	Standard error

Sens	Sensitivity
SES	Socio-economic status
SFT	Skinfold thickness
Spec	Specificity
TC	Total cholesterol
TNF- α	Tumor necrosis factor alpha
US	United States
WC	Waist circumference
WHO	World Health Organization
WHR	Waist-to-hip ratio
WHtR	Waist-to-height ratio

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1 INTRODUCTION

"Corpulence is not only a disease itself, but the harbinger of others."

Hippocrates

1.1 Background

“We are all aware that obesity is one of the most serious public health challenges facing the WHO European Region today. It is a particular danger for the young and socially disadvantaged. [...] Not only is obesity itself a health risk, it also contributes to so many other serious medical conditions”.

These were the introductory words of Marc Danzon, World Health Organization (WHO) Regional Director for Europe, within the scope of the WHO European Ministerial Conference on Counteracting Obesity held in Istanbul, Turkey, 15-17 November 2006. This statement is related to the fact that overweight and obesity, in particular among children and adolescents, is becoming a major public health concern. The prevalence of overweight and obesity increased dramatically during the past decades, in particular in Western countries. Furthermore, overweight and obesity affect quality of life as well as social, mental and physical health. For instance, obesity is one of the most important risk factors for cardiovascular disease (CVD)¹⁻³. However, aetiology as well as health consequences of overweight and obesity underlie complex associations which are not totally clarified.

Currently, the proportion of overweight and obese persons in Western countries is alarming. A recent systematic review focussing on obesity among European adults showed that the prevalence of obesity ranged from 4% to 28% in men and from 6% to almost 37% in women⁴. Prevalences of obesity were higher in Eastern Europe and the Mediterranean countries compared to those in Western and Northern Europe. Considering data from 2003 for German adults, the prevalence of overweight was 49% in men and 34% in women; the prevalence of obesity was 17% in men and 20% in women⁵. Data from the United States (US) showed that the prevalence of overweight and obesity among both adults and children had dramatically increased since the 1960s⁶.

Furthermore, representative cross-sectional school-based surveys conducted in several European countries, Israel and the US estimated the highest prevalence of overweight among US children ranging from 11% to 15%⁷. Nationally representative data from the recent German Health Interview and Examination Survey for Children and Adolescents (KiGGS) showed that in Germany 15% of the 3-17 year olds were considered overweight or obese according to national reference values. The prevalence of obesity was 6.3%⁸. This implies an increase of 50% in the prevalence of overweight compared to the early 1990s, while the prevalence of obesity has doubled.

Under evolutionary aspects, our genes are predisposed to accumulate as much energy as possible in the body to assure survival. However, environmental and behavioural circumstances have considerably changed during the last centuries resulting in an affluent society or so called “obesogenic environment”. For example, motorisation and “mediasation” have led to less physical activity. The unlimited availability of food in industrialised countries encourages the overall drift for overeating. Physiologically, overweight and obesity are consequences of a long-term imbalance between energy intake and energy expenditure. Energy balance is determined by food intake and physical activity and further influenced by a large set of biological and environmental factors. These factors affect energy balance to different (individually conditioned) extents, at different stages and may interact (Figure 1). Therefore, the particular causal pathways leading to overweight and obesity remain unclear to a certain extent. In general, any factor that influences energy balance, even to a small extent, may cause overweight and obesity.

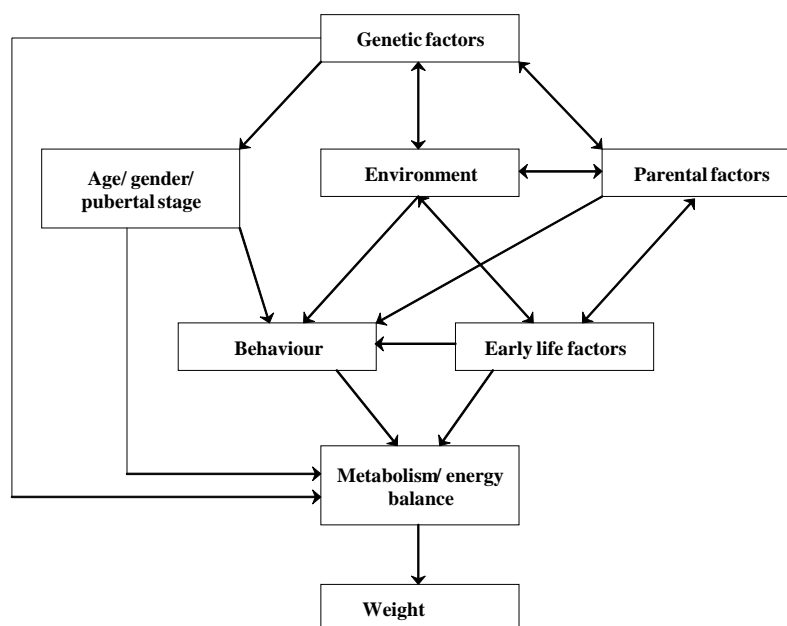


Figure 1: Overview of potential risk factors for overweight and obesity and possible pathways

Source: own illustration

The consequences of overweight and obesity are multifaceted, including physical, psychological, social, and economic impairments. On the physical level a range of health related effects may occur, affecting different body parts. Obesity may have several short-term consequences (for example social discrimination, lower quality of life, suffering of chronic diseases)⁹ and long-term consequences (for example persistence of obesity, increased morbidity, a higher prevalence of elevated CVD risk factors in adulthood)^{9, 10}. Among adults, over-

weight and obesity have a strong impact on the development of CVD and obesity is the most important risk factor for type 2 diabetes mellitus, which is also associated with CVD. Beside cancer, CVD is the most important cause of mortality in Western societies¹. Among children and adolescents clinical consequences of overweight and obesity may not appear yet and are therefore less evident at this age. However, elevated levels of CVD risk factors have also been documented in obese children¹¹. In addition, since obesity is associated with increasing costs for therapy and medication related to chronic diseases such as diabetes mellitus or CVD it may cause a large economic burden¹². Furthermore, obesity and its health consequences may lead to an inability to undertake work. These numerous consequences of overweight and obesity pose a tremendous challenge on the individual and public health level as well as on the health system.

1.2 Terminology

Clinically, overweight and obesity imply different conditions where obesity is a severe form of overweight. However, in the scientific literature, the two terms are often used synonymously or may vary in its specific meanings. In particular when focussing on children and adolescents, some methodological issues have to be considered. There are no consistently used criteria for defining overweight and obesity among children and adolescents in the literature, whereas different statistical approaches, reference populations and threshold values were used. Furthermore, different anthropometric measures for overweight and obesity exist and it is still under discussion which measure of overweight and obesity has the highest relevance for health consequences.

Throughout this work, when results of previous studies are presented, the terms overweight and obesity are used in the same way as in the corresponding study. For example, if obesity was explicitly analysed, only the term obesity was mentioned in the text. If results apply to both conditions the phrase overweight and obesity was used. For the analyses presented in the following chapters, depending on the purpose of the respective analysis, different criteria for defining overweight and obesity were used. For the evaluation of potential determinants of overweight and obesity, the definitions established by the International Obesity Task Force (IOTF) were used to allow an international comparison¹³. For the analysis of the association between CVD risk factors and overweight a sample based definition was used to ensure a systematic comparison of different measures of overweight. For the latter purpose, there was no distinction between overweight and obesity. In order to facilitate readability of the corre-

sponding chapter only the term overweight was used. Thereby, the measures of overweight include body mass index, skinfold thickness, waist circumference, waist-to-hip ratio, and waist-to-height ratio. The specific purposes and the definitions are described in more detail in the corresponding chapters.

Overweight and obesity are CVD risk factors as well. However, since the focus here is the association between overweight and other CVD risk factors, in Chapter 5, the term CVD risk factors include blood pressure, serum lipoproteins, high sensitivity C-reactive protein, and glycosylated haemoglobin.

1.3 Objectives and outline

Overweight and obesity should be prevented as early in life as possible. For establishing effective interventions, it is also important to identify risk factors and health consequences at an early stage of life. Health related behaviour and preferences will be developed in childhood and mostly persist until adulthood. Furthermore, overweight and obese persons are often stigmatised, which can affect mental health as well as quality of life. Early and carefully planned prevention may reduce the risk for health related and psycho-social consequences.

Previous studies mainly were clinical or included rather small, non-representative population samples. For Germany, until recently, data was predominantly derived from school entrance health examinations or local studies and therefore included only a small age range or limited information. With the KiGGS study, for the first time, comprehensive and nationally representative data for the entire group of children and adolescents living in Germany is now available. It is therefore possible to analyse potential risk factors for overweight and obesity on the one side as well as potential consequences of overweight and obesity on the other side.

The aim of this thesis is to identify major determinants of overweight and obesity as well as adverse risk factors associated with CVD as potential health consequences among children and adolescents in Germany. Furthermore, the measures of overweight with the most important health relevance among young people should be identified. Therefore, the following research questions will be considered:

- What are major potential determinants of overweight and obesity in children and adolescents?

- Is there a consistent association between overweight and other CVD risk factors among children and adolescents in Germany?
- Which measure of overweight shows the strongest association with CVD risk factors and may therefore be preferably used for risk assessment and prevention?
- Which cutoff points of anthropometric measures should be used to identify children and adolescents with higher CVD risk?

This thesis is divided into eight chapters. Chapter 2 is concerned with the criteria for defining overweight and obesity, in particular among children and adolescents, and describes the principles of the assessment of overweight and obesity applied in the present analyses. Furthermore, determinants of overweight and obesity discussed in the scientific literature are described as well as the relationship with CVD risk factors. The subjects and methods used in the KiGGS study are presented in Chapter 3. In Chapter 4, major determinants of overweight and obesity are identified. The association between overweight and CVD risk factors as well as the predictive values of different overweight measures are presented in Chapter 5. Cutoff points of anthropometric measures in relation to adverse CVD outcomes are described in Chapter 6. Each Chapter 4 to 6 includes the operationalisations of study variables, the statistical analyses adopted, the empirical results as well as a discussion of the respective chapter. The main findings of the analyses are discussed in Chapter 7, including methodological considerations and implications for public health and further research. Finally, Chapter 8 summarises the most important findings and provides some conclusions.

2 STATE OF RESEARCH

2.1 Defining overweight and obesity

Overweight exists when body weight exceeds a defined threshold value related to body height. Obesity is defined as an abnormal or excess body fat accumulation to an extent that health may be impaired. Such an accumulation of body fat occurs either due to hypertrophy of existing fat cells or due to a combination of hypertrophy and hyperplasia of fat cells¹⁴. Excess fat mass can lead to metabolic and endocrine complications, for example to a malfunctioning carbohydrate metabolism, dyslipidemia as well as to several diseases such as hypertension or coronary artery disease. However, the extent of fat accumulation, its distribution within the body, and the associated consequences vary considerably between individuals¹⁵. The definition of overweight and obesity should therefore be based on an increased risk of morbidity and mortality. According to Reilly¹⁶, such definitions should achieve two criteria: to be diagnostic of high body fat content and to be an indicator of the increased risk of adverse health outcomes.

Among adults, the WHO definitions of overweight and obesity are commonly used. These definitions are based on the body mass index (BMI) specifying thresholds from which the risk of comorbidity is increased (Table 1).

Table 1: WHO BMI classification for adults

Classification	BMI (kg/m ²)	Risk of comorbidities
Underweight	< 18.5	Low (but risk of other clinical problems increased)
Normal range	18.5 - < 25	Average
Overweight	≥ 25	
Preobese	25 - < 30	Increased
Obese class I	30 - < 35	Moderate
Obese class II	35 - < 40	Severe
Obese class III	≥ 40	Very severe

Source: adapted from WHO 2000¹⁵

Due to physiological and maturational changes in the body composition during the growth phase, the BMI changes considerably among children and adolescents¹⁷. Therefore, it is not applicable to use consistent absolute thresholds among children and adolescents. However, no widely (internationally) used standard definitions exist.

2.2 *Assessment of overweight and obesity*

2.2.1 General aspects

Definitions of overweight and obesity require an assessment of body fat as well as specified thresholds for excess body fat mass. For the precise assessment of body fat extensive methods are needed. Multi-component measurements such as dual energy x-ray absorption, densitometry or a four-component model (assessment of total body mineral, total body water, body weight, and body density) provide the best estimates of body fat^{18, 19}. Since these techniques are mostly too expensive and extensive for epidemiological research, simple anthropometric measures, including weight, height, skinfold thickness (SFT), waist circumference (WC) and hip circumference (HC) are often used in population based studies. In the following chapters, several indicators of body fat used in large-scale studies will be discussed. It will be focussed on studies conducted among children and adolescents as well as on such parameters which are used in the presented analyses.

2.2.2 Body mass index (BMI)

The BMI is a simple index of weight-for-height and the most commonly used indicator of body fat. It is calculated as body weight in kilogram divided by the squared body height in meter.

$$BMI = \frac{\text{Body weight [kg]}}{\text{Body height}^2 [m^2]}$$

Although the BMI does not directly measure the amount of body fat it was found to be an appropriate indicator as it highly correlates with body fat^{17, 20, 21}. However, the BMI is not able to distinguish between fat and lean body mass. Therefore, it does not completely take into account the variability of the body stature (for example an ectomorphic body is characterised by long and thin limbs). The BMI is often used in large-scale epidemiologic studies since it is a stable measure, easy to obtain, inexpensive and non-invasive¹⁵. But, numerous disadvantages and limitations have been described previously. For instance, the relationship between BMI and body fat is dependent on age, ethnicity, body constitution (muscle mass), and pubertal stage²²⁻²⁴. Many BMI validation studies have been conducted to evaluate whether BMI is an appropriate measure of body fat. Different age groups and reference methods have been used, which makes a definite statement difficult^{21, 23-28}. One of the most striking obser-

vation was that there may be a large range in body fat percentage within a given BMI^{21, 23, 25}. That means that some individuals who are classified as being overweight by using the BMI do not necessarily have a high percentage of body fat whereas others may have a BMI within the normal range but a high percentage of body fat. Hence, not all subjects with the same BMI also have the same body fat composition. This shows that although the BMI is the indicator mostly used for the definition of overweight and obesity, it is of limited validity on the individual level to assess body fat. Further anthropometric data such as waist circumference, skinfold thickness as well as metabolic indicators (blood pressure, lipoprotein profile) are important and helpful parameters to assess the individual health risk^{29, 30}.

2.2.3 Skinfold thickness (SFT)

As an alternative to the BMI, several researchers prefer the measurement of SFT for estimating body fat. The subcutaneous fat tissue correlates with total body fat³¹. The measurement of SFT is also relatively simple and quickly to perform. However, it is more difficult to ensure standardised SFT measurements compared to the measurements of weight and height. Tanner and Whitehouse³² described in detail how to measure two skinfolds (triceps and subscapular) in a standardised way. They recommended, for example, using the left body side and gave exact instructions for the location of skinfold measurement. Not all researchers apply these recommendations, for instance, Johnson and Scholz³³ recommended using the right body side for measurement. They stated that the highest correlation with body fat is reached when as much skinfolds as possible are measured, at least three or four skinfolds. In addition, different equations for estimating total body fat from SFT exist, which give inconsistent results. For example, Slaughter et al.³⁴ noted that measuring two skinfolds on the right hand side is adequate. They established equations considering gender, pubertal stage and race. Deurenberg and colleagues³⁵ measured four skinfolds on the left body side to estimate total body fat. The prediction of total body fat using four skinfolds was only slightly better than the prediction using only two skinfolds. Both authors considered gender and pubertal stage and emphasised that these are important determinants of body fatness and in turn of the skinfold thickness. Another way to look at skinfold data is the calculation of the triceps-subscapular-ratio which is negatively associated with BMI³⁶. This index also varies with gender and age and no adequate reference values have been determined so far. In general, a major problem using SFT is that the results essentially depend on trained investigators and highly standardised measurements. Furthermore, considerably inter- and intra-individual measurement errors may occur^{37, 38}. Validation studies concluded that neither the equations of Slaughter et al. nor those

from Deurenberg et al. allow robust estimates of total body fat^{39, 40}. Often, the sum of skinfold thickness was used in epidemiologic studies⁴¹⁻⁴³.

2.2.4 Waist circumference (WC)

In particular abdominal fat accumulation is a risk factor for type 2 diabetes mellitus, dyslipidemia, hypertension and therefore for CVD⁴⁴⁻⁴⁶. It is increasingly evident that WC is an appropriate measure for abdominal fat mass, even among children^{47, 48}. Furthermore, WC is a measure that can be obtained quickly, easily and in a standardised way. Several validation studies showed that WC may be the most useful measure of body fatness and fat distribution for children and adolescents compared to other anthropometric indicators such as BMI, SFT and waist-to-hip ratio (WHR)^{47, 49, 50}. In contrast, among Spanish males 7-16.9 years of age it was observed that BMI, triceps skinfold as well as WC predicted total body fat percentage well. It was concluded that WC may be preferred in terms of clinical practice²⁶. In another Spanish study conducted in a clinical setting WC seemed to be the best predictor for CVD risk factors in children. However, there was no statistically significant difference between BMI, WC, triceps and subscapular skinfold⁵¹. McCarthy⁴⁸ stated that WC should routinely be measured in health examinations, since it adds more information on risks of the metabolic syndrome and CVD in later life than BMI. Likewise, WC is a surrogate measure and does not quantify body fat directly.

2.2.5 Waist-to-hip ratio (WHR)

Metaphorically, one can distinguish between apple-shaped individuals with fat accumulation around the abdomen and pear-shaped persons showing a larger accumulation of fat in the lower body. The ratio of waist circumference to hip circumference has been used as an indicator for abdominal fat accumulation and fat distribution among adults¹⁵. However, there are only few studies among children and adolescents using WHR to identify the fat distribution as a diversification indicator of overweight. Different validation studies using different reference methods showed that WHR is a less appropriate indicator of body fatness, fat distribution or central obesity in young people, in particular when compared with BMI or WC^{35, 47, 52}. Most likely this is explained by the fact that children still undergo developmental changes of body fat distribution. As pointed out in a Spanish study, there was a high variability in WHR with sex and age so that it may not be an appropriate measure without any reference values³⁶. Since body fat distribution is less influenced by developmental changes among post-pubertal

adolescents, WHR may be more meaningful in this age group³⁵. Among adults, WHR was associated with cardiovascular events and diabetes mellitus^{53, 54}. Studies among children found that WHR is not strongly correlated with CVD risk factors^{55, 56}.

2.2.6 Waist-to-height ratio (WHtR)

The ratio of waist circumference to body height was first used in the Framingham Study⁵⁷. WHtR is another simple index for body fat distribution and only weakly associated with age⁵⁸. WHtR is highly correlated with visceral fat mass among adults⁵⁹. Several studies among children and adolescents showed that WHtR is stronger associated with CVD risk factors than other anthropometric measures^{60, 61}. For instance, a study among Japanese schoolchildren showed that WHtR is a better predictor for adverse CVD risk factors than BMI, percentage body fat, WHR, and WC⁶¹. Li et al.⁶² concluded that WHtR may be a precise tracking indicator of fat distribution and accumulation by age, since it accounts for both the increase in height and the increase in WC. Whether WHtR is a better measure of overweight than WC remains unclear. Like all other measure mentioned above, WHtR is a simple and surrogate measure of body fatness.

2.2.7 Reference systems and cutoff points

Among adults, the WHO definitions of overweight and obesity and thresholds related to BMI are commonly used. In contrast, there is no widely applied (international) standard definition for overweight and obesity in childhood and adolescence⁶³. There is an ongoing debate as to which measure of childhood overweight and obesity is the best predictor for adverse health outcomes and which threshold values and reference systems should be used. Due to the physiological changes in BMI with increasing age, there is a consensus to use BMI in combination with age and sex specific percentile curves of a reference population. To calculate BMI reference percentiles, usually the LMS method established by Cole⁶⁴ is used. This method summarises the data concerning three smoothed age specific curves: L (lambda, skewness), M (mu, median) and S (sigma, coefficient of variation). The respective BMI percentile provides the information about the percentage of individuals in the reference population showing BMI values below the corresponding percentile. For example, 90% of the individuals have values below the 90th percentile. An individual value can then be compared with the reference value. Different cutoff points as well as different reference populations have been applied^{13, 29, 65, 66}. For instance, the German 'Arbeitsgemeinschaft Adipositas im Kindes- und Jugendalter'

(AGA) ⁶⁷ recommends a German reference population described by Kromeyer-Hauschild et al. ⁶⁵ and used the 90th and 97th age and sex specific percentile as cutoff for overweight and obesity, respectively. These percentile curves are presented in Figure A-1 in the appendix. The European Childhood Obesity Group (ECOG) also recommends using the 90th and 97th age and sex specific percentile ³⁸. They used a French reference population described by Rolland-Cachera and colleagues ²⁹. In contrast, the US Centers for Disease Control and Prevention (CDC) currently recommend the 85th and 95th age and sex specific percentile curve to define overweight and obesity using data from five nationally representative health examination surveys ⁶⁸. All these reference values are based on different reference populations in different countries and used data from different periods of time. Therefore, their comparison is limited.

An expert group of the International Obesity Task Force (IOTF) criticised the principle of the mentioned cutoff points as arbitrary ¹³. Therefore, they established international BMI cutoff points based on data from six large nationally representative cross-sectional studies conducted in Brazil, Great Britain, Hong Kong, the Netherlands, Singapore, and the United States. Percentile curves of BMI were constructed for each dataset by sex using the LMS method described by Cole ⁶⁴. The BMI percentile curves were then adapted in such a way that they fit to the cutoff points of 25 kg/m² and 30 kg/m² for adults at the age of 18 years (Table A-1 in the appendix) ¹³. For this procedure, BMI values were converted to exact z-scores. Each z-score provides the formula for a percentile curve passing through the specified point of 25 kg/m² or 30 kg/m². This was repeated for all six datasets by sex and then the curves were averaged to provide a single smoothed curve passing through the adult cutoff points ¹³.

For all other anthropometric indicators less data is available. There are only few national reference values on skinfold thickness among children and adolescents ^{26, 69} and it seems that they are not appropriate to use as an international standard. In 2006, the IOTF published reference curves for body fat measured by bio-impedance in Caucasian children and adolescents aged 5-18 years ⁷⁰. To use them as reference data, exactly the same method for estimating body fat has to be applied.

For adults, the WHO defined elevated WC values related to an increased risk of metabolic complications. The cutoff points are ≥ 94 cm for men and ≥ 80 cm for women. A substantially increased metabolic risk is estimated for men with WC ≥ 102 cm and for women with WC

≥ 88 cm¹⁵. For children and adolescents no widely applied definition for elevated WC exists. However, Fredriks et al.⁷¹ presented age references for waist circumference in 14500 Dutch children and adolescents aged 0-20 years. They concluded that WC can be used to screen for increased abdominal fat mass. A cutoff point determined by 1.3 standard deviations seemed to be most appropriate.

A high WHR is defined as > 1 in men and > 0.85 in women¹⁵. Cutoff points for children and adolescents do not exist.

For WHtR it is suggested that the same cutoff value of 0.5 may be used for children, adolescents and adults. Suggested by the authors this leads to a simple message for all individuals: 'Keep your waist circumference to less than half your height'⁷².

As Guillaume⁷³ demonstrated, small differences in the reference values used can result in meaningful differences in prevalence estimates. Therefore, a comparison of studies using different reference systems is difficult. Prentice and Jebb²² recommended adopting the reference standard from the IOTF as a single international definition for childhood overweight and obesity. Reilly⁷⁴ concluded to use national reference data for clinical and epidemiological purposes since they are reliable, feasible and evidence-based. For an international comparison the international reference data should be used. Furthermore, it is discussed using not only the BMI for classifying overweight and obesity but also direct measurements of body fat or alternative measures like WC or SFT^{16, 22}. Among adults, in particular measurements of general and abdominal fat mass appear to be predictive of health outcomes⁷⁵. Thus, some researchers suggested that WC and/or WHtR alone or in combination with BMI may be more useful for risk assessment in children and adolescents than only using BMI^{58, 60, 76}.

2.3 Determinants of overweight and obesity

The aetiology of overweight and obesity is complex and multifactorial. There are a tremendous numbers of potential risk factors for overweight and obesity covering genetic, biological, physical, lifestyle, and environmental conditions. Examples for those risk factors are parental overweight, prenatal malnutrition, high or low birth weight, breastfeeding behaviour, rapid growth in infancy, early adiposity rebound, low level of physical activity, high level of sedentary behaviour, unfavourable dietary behaviour, and an "obesogenic" (home) environment^{10, 77-85}. Furthermore, biological or endocrine disorders, eating disorders (for example

binge-eating disorder), chronic stress or the use of several drugs can also cause overweight and obesity. The latter aspects are not presented and further discussed in this thesis. In the following, the most important potential risk factors and for those data are available in the KiGGS study are described in more detail.

2.3.1 Social factors

Social factors such as education and income are discussed as being determinants of overweight and obesity. It was shown that in developing countries overweight and obesity more often occur in higher socio-economic status (SES) groups, while in industrialised countries people with low SES are more often overweight and obese than those with high SES^{15, 86, 87}. These observations may have several possible explanations. For example, the studies were conducted in different countries with different social structures and life circumstances. Furthermore, different attitudes in beauty and health between developed and developing countries may play an important role. While in industrialised countries currently a slim body is seen as the ideal of beauty and health, in many developing countries a well-fed (overweight) person stands for wealth and health.

Beyond, the association between overweight, obesity and SES seems to be more pronounced among women than men. As two comprehensive reviews concluded, there was a consistently inverse association among women in developed countries, with a higher likelihood of obesity in lower SES groups^{86, 87}. This relation was inconsistent among men.

Among children, the inverse association between weight status and SES was weaker and less consistent than among adult women⁸⁶. However, in most studies no sex specific differences were observed in children. Stamatakis et al.⁸⁸ observed an association of borderline significance between parental social class and obesity in the offspring. Analyses of the KiGGS study also showed a higher occurrence of obesity among children and adolescents with low SES compared to those with high SES⁸.

Ethnic and migrant specific differences in the prevalence of overweight and obesity have been observed as well. Several US studies showed that the inverse association between SES and obesity did not occur among African American or Hispanic children and adolescents⁶. There were considerable ethnic and racial differences, even in homogenous SES groups. In Germany, it was observed that migrants were more often overweight and more often obese than

non-migrants^{8, 89-91}. However, the magnitude and characteristics of the differences were not consistent. While in one study no difference according to the country of origin was observed⁹⁰, two other studies showed that children from Turkey had the highest prevalence of overweight^{89, 91}. Both social and ethnic factors can contribute to differences in attitudes, lifestyle, and health. Ethnic aspects may account for differences in the genetic predisposition. These aspects are discussed in the following.

2.3.2 Genetic factors

Genetic factors have important effects on physical constitutions, regulation of energy intake, energy expenditure, and behaviour and may play an important role on the onset of overweight and obesity. However, the absolute extent of genetically caused overweight is not clear. Twin and adoption studies suggested a considerable impact of heritability on body weight, height and therefore on BMI⁹²⁻⁹⁵. For example, in a twin study there was large intrapair correlation of BMI among monozygotic twins (intrapair correlation coefficient = 0.77)⁹². Therefore, the authors estimated the heritability of BMI to be almost 80%. An adoption study showed a strong association between the weight status of adopted children and the BMI of their biological parents but no relation between the weight status of adopted children and the BMI of their adoptive parents⁹³. It was observed that the risk of overweight was higher among children with a family history of overweight. Several recent studies showed a higher risk of overweight for the offspring, even if just one parent was overweight^{79, 96, 97}. Environmental aspects (in particular the intrauterine environment) as well as (inherited) lifestyle also contribute to the development of overweight and obesity. For example, a study among surrogate mothers showed that the intrauterine environment provided by the bearing mother was more important for the child's birth weight than the genetic contribution of the biological mother⁹⁸.

Bouchard⁹⁹ estimated that about 25-40% of the individual differences in BMI or body fat are predicted by heritability. In his opinion, the current epidemic of obesity in developed countries is not caused primarily by genetic factors but is caused by a lifestyle that favours positive energy balance. As mentioned before, evolutionary we are predisposed to accumulate fat to ensure survival. Since the genetic constitution has not changed essentially in the last centuries¹⁵ the secular increase in obesity rates can not exclusively be explained by genetic variation. Rather, it is an example for gene-environment interactions and in a broader sense an example for interactions of genetic factors with lifestyle, environmental, socio-demographic,

and socio-economic conditions. Above all, some people may be more susceptible to becoming overweight than others even with similar behaviour and environmental conditions.

2.3.3 Early life factors

Potential risk factors occurring in prenatal and early life are multifaceted. For example, the intrauterine environment, the behaviour and physical constitution of pregnant women, as well as circumstances and physical development during the first year(s) of life have an important influence on later weight status of the offspring.

There is increasing evidence that the intrauterine environment is of particular importance for the (physical) development of the child and therefore, it may be an important condition for later overweight. Of particular importance is the so called “thrifty phenotype hypothesis” described by Hales and Barker¹⁰⁰. This hypothesis proposes that the associations between poor foetal/infant growth and the development of symptoms of metabolic syndrome in later life (for example obesity, type 2 diabetes mellitus) result from prenatal malnutrition, which is related to permanent metabolic changes¹⁰⁰. Another issue is the perinatal programming which is defined as the process that environmental factors (and not primarily genetic factors) affect the metabolic and hormonal system in such a way that the development of diseases in later life is more likely¹⁰¹. In this field of early epigenetic conditioning, it is supposed that environmental influences during specific periods of life affect developmental processes inducing ongoing changes in organ structures, metabolism, gene expression and therefore, in the risk of disease¹⁰².

Beside a prenatal (mal-)nutrition, maternal smoking during pregnancy is discussed as being one potential risk factor for later obesity^{79, 97, 103}. In particular, smoking during the first trimester of pregnancy seemed to have negative consequences for the child. A dose response relation was observed. Among women who smoked during pregnancy a higher prevalence of obesity in the offspring occurred with increasing cigarette consumption¹⁰³. Recently, it has been suggested that paternal smoking is also a risk factor for childhood obesity almost similar in magnitude as maternal smoking¹⁰⁴. This is an indication that questions the causality of the association between maternal smoking in pregnancy and obesity in the offspring. However, von Kries and colleagues¹⁰⁵ have shown that there still remained an effect for smoking in pregnancy when smoking of the father was accounted for.

Weight gain in pregnancy is another factor that influences the intrauterine environment. It was observed that excessive weight gain during pregnancy is a risk factor for overweight in the offspring at age 3 years^{106, 107}. It was also shown that the association between weight gain during pregnancy and overweight in the offspring was strongest for women who were underweight before pregnancy¹⁰⁸. No statistically significant effect of a high weight gain in pregnancy was found when the mother was overweight, in contrast to normal weight or underweight mothers¹⁰⁹. A potential explanation for this interaction could be that changes in the intrauterine environment in overweight mothers are similar to the changes occurring with high weight gain during pregnancy. In a recent study of Voigt et al.¹¹⁰ it was observed that weight gain during pregnancy is determined by body height and weight. For instance, relatively heavy and short women gain less weight during pregnancy than relatively tall and thin women. As shown in a Finnish birth cohort study, children whose mother had a higher BMI in pregnancy had a more rapid growth in childhood and an increased risk of becoming obese¹¹¹.

Birth weight is a common indicator for prenatal growth. Several studies showed a positive association between high birth weight and obesity in later life^{79, 97, 111} and a recent review confirmed this association¹¹². Sex specific differences were observed in the study of Danielzik and colleagues⁹⁷. While there was a positive association in girls, boys with low birth weight were at higher risk for later obesity. Birth weight is also associated with height at birth, the weight status of the mother and weight gain during pregnancy. Therefore, it is not fully independent parameter for predicting overweight or obesity in later life. The metabolic programming during pregnancy as well as the foetal environment may play an important role for the association between birth weight and obesity in later life¹¹¹.

Recent studies addressed the role of growth and weight gain during infancy as a predictor of obesity in later life. Excess weight gain in early life (until the age 2 years) was as strong predictor for both body fat and lean mass in later life^{113, 114}. Recent systematic reviews confirmed the positive association between rapid weight gain and growth in the first years of life and the occurrence of overweight, obesity, or higher fat mass in later life^{85, 115}. The occurrence of rapid weight gain between birth and 2 years of age and its effect on body fat in children whose birth weight was appropriate for gestational age was influenced by both intrauterine and postnatal factors such as tobacco in utero, being firstborn, having been bottle fed, or having an overweight mother, as determined in a recent multicenter study¹¹⁶. In a longitudinal study of young adults in the United Kingdom the most important predictors of BMI and

WC in adulthood were either height at the age of 5 years or high weight velocity in childhood (from 1 year and 9 month to 5 years)¹¹⁷. There was no association with accelerated growth in the first few months and birth weight once weight gain in childhood was taken into account.

Another risk factor for overweight and obesity in early life is the so called “adiposity rebound”. Body fat mass, as estimated by BMI for example, increases during the first year of life and then decreases. About the age of 6 years BMI rises again. This raise is called the adiposity rebound. A study by Rolland-Cachera and colleagues¹¹⁸ showed that an early adiposity rebound (before the age of 5.5 years) is associated with higher BMI levels in later life compared to those with a later rebound (after the age of 7 years). In a retrospective cohort study it was shown that adult obesity rates were higher in those with early adiposity rebound than in those with late rebound. The association was independent of parental obesity and BMI at the time of the adiposity rebound¹¹⁹. A recent review concluded that a considerable body of literature confirmed that early adiposity rebound increased the risk of obesity in later life⁸¹.

Breastfeeding has been discussed to be a protective factor concerning obesity in later. It was observed that children who were breastfed are less often obese in later life^{79, 97, 120}. A recent meta-analysis estimated that breastfeeding reduced the risk for overweight by 25% compared to non-breastfed children¹²¹. A review concluded that breastfeeding seems to have a small but consistent protective effect against obesity in later life⁷⁷. Von Kries and colleagues¹²⁰ observed that not only breastfeeding in general had a protective effect, but also the duration of breastfeeding. The longer a child was breastfed the less likely was obesity. This observation was confirmed in a meta-analysis which supports the dose dependent association¹²². There may also be an interaction with other parameters, for example with early protein intake. It has been shown that a higher protein intake during the period of complementary feeding was associated with higher BMI and body fat mass of children at the age of 7 years¹²³. This “early protein hypothesis” is currently being tested in a large European intervention trial¹²⁴.

In conclusion, early childhood is increasingly seen as a critical period for the development of obesity^{82, 125}. Many different risk factors may be involved and it is evident that they do not interact independently. It is suggested that a combination of certain early life risk factors accounts for an important proportion of obese children¹²⁶. An outstanding role seems to be played by the metabolic programming during gestation and the prenatal environment.

2.3.4 Life style factors

An inactive lifestyle has been discussed to be another risk factor for overweight and obesity. Dietary intake influences energy balance and therefore the development of overweight and obesity. As concluded in a recent review there is a convincing positive association between obesity, sedentary lifestyle, and high intake of energy dense food and a convincing negative relationship with a high intake of non-starch polysaccharides ¹²⁷. However, results from epidemiological studies, especially those from cross-sectional studies are often inconsistent. In the following, a brief overview of studies concerning physical activity, electronic media consumption, sleep duration, and dietary behaviour is given.

Physical activity

Physical activity is one of the most important factors that influence energy balance. However, the prospective association between overweight and physical activity among children and adolescents is still a subject of controversial discussions. For example, a systematic review from the late 1990s indicated that there was almost no evidence for an influence of physical activity in infancy on obesity in later life and inconsistent but suggestive evidence for a predictive effect of physical activity in childhood on obesity in later life ¹²⁸. Two recent reviews about the association between physical activity and body weight/fatness also reported inconsistent results. While several studies (mostly cross-sectional) showed an inverse association between physical activity and weight status, a substantial number of studies did not find such an association ^{80, 129}. Even the results from prospective cohort studies are inconsistent showing rather no or just a weak association or a relationship with an unexpected direction. However, changes in physical activity in late childhood and adolescence were related to changes in measures of body fatness in a large multicentre longitudinal study among US girls ¹³⁰. Increasing aerobic physical activity has been found to be effective in preventing childhood overweight and obesity ¹³¹. Although there are inconsistent results, this does not imply that physical activity has no or only a weak impact on the development of overweight. In particular large-scale epidemiologic studies have to deal with methodological issues, which may result in inaccurate measurement of physical activity, uncontrolled confounding, or reverse causality ⁸⁰. Physical activity is difficult to assess accurately, controlling for energy intake is even harder. The association between energy balance and overweight is discussed in more detail in Chapter 7.2. Indeed, any kind of physical activity contributes to energy expenditure.

Electronic media consumption

Due to technical advances during the last decade and the widespread and easy access to electronic media (television, video games, and internet), leisure time activity has changed essentially with an increased time spent on electronic media consumption. Even pre-school children have a remarkable consumption of electronic media. For instance, 82% of children aged 3-4 years watched television on a typical day for approximately 90 minutes in average¹³². Several studies showed a consistent positive association between time of electronic media consumption and risk for overweight or obesity, even after controlling for potential confounders¹³³⁻¹³⁵. For example, in a cross-sectional study based on school entry health examinations in six Bavarian public health offices, children who spent two or more hours per day consuming electronic media had a significant 70% higher risk for obesity compared to those who never or sometimes used electronic media¹³⁴. Furthermore, a positive linear relationship between hours of television viewing and obesity has been observed in a cohort study⁷⁹. An important confounder in this context may be the consumption of energy-dense foods while watching television^{96, 136, 137}. This could lead to an unnoticed increased energy intake by reducing satiety signals. A causal relationship between electronic media consumption and overweight has not been confirmed definitely. Thus, it may be that overweight children in general spend more time on electronic media consumption but in turn not all children with high electronic media consumption may have a higher risk for becoming overweight.

Duration of sleep

Several studies showed that an inadequate duration of sleep is associated with a higher prevalence of obesity among children and adolescents^{79, 138, 139}. Metabolic changes (for example changes in carbohydrate metabolism) and endocrine changes (for example in the secretion of leptin, a hormone that regulates appetite) have been discussed as possible explanations^{138, 139}. It is possible that the duration of sleep also reflects a certain lifestyle. So, the extent of physical activity could influence tiredness and therefore the duration of sleep⁷⁹. Several reviews have found a stronger association between obesity and sleep duration in younger children, at least when compared to adults¹⁴⁰⁻¹⁴². However, the causal relationship remains unclear, since all these studies are cross-sectional. It may also be possible that a shorter duration of sleep is a consequence of obesity.

Dietary behaviour

Food intake is the factor that determines energy intake and therefore substantially influences energy balance. Food intake and overall dietary behaviour as well as its assessment and metabolism are very complex. Fundamental food preferences and choices as well as certain behaviours are established in early childhood¹⁴³⁻¹⁴⁵. As summarised in a recent review, a range of physical, social, family and environmental factors influence children's eating habits¹⁴⁶. Different ingredients or characteristics of foods (like taste, smell, texture, and palatability), certain food habits as well as circumstances of food intake may have different consequences related to overweight and obesity (for example on satiety). In the following, a brief overview of several aspects of dietary behaviour will be given that are discussed in the literature.

Fat intake and energy dense foods

Dietary fat is the macronutrient with the highest energy density. Experimental animal studies showed, that fat and total energy intake was strongly positively related to weight gain¹⁵. In Western populations, it was observed that energy intake increased during the last decades but fat intake decreased. Since the prevalence of overweight and obesity substantially increased during the same period this led to controversial and still unresolved discussions about the impact of fat intake on overweight¹⁴⁷⁻¹⁵².

There seems to be an association between intake of energy dense foods and obesity^{150, 153, 154}. It was further shown that a high consumption of energy dense foods in combination with low physical activity can easily lead to a positive energy balance¹⁵³. A higher consumption of energy dense snacks was related to duration and frequency of television viewing among 5-year old girls, and predicted their increase in BMI from age 5 to 9⁹⁶. Moreover, other signals of satiety are supposed for energy-dense foods compared to foods rich in dietary fibre. For example, since foods rich in fat are palatable, signals of satiety may be disregarded. As reported by the WHO, experimental studies showed a negative association between the consumption of energy dense food and satiety which could lead to a "passive overconsumption"¹⁵.

In this context, the increasing consumption of fast food and energy-rich snacks has been discussed. A recent review confirmed the positive association between fast food consumption and weight gain¹⁵⁵. However, studies among children and adolescents were less conclusive. Results from studies which analysed the association between the consumption of sugar-

sweetened beverages (another energy dense food group) and overweight are summarised in another review⁸³. The results supported the positive association between the consumption of sugar-sweetened beverages and obesity. A possible mechanism may be the low satiety signals of liquid carbohydrates and the incomplete compensation of energy intake. In a large representative health survey, a positive association between beverage consumption and total energy intake was observed but there was no statistically positive relationship between total beverage intake and BMI¹⁵⁶. Recent longitudinal studies observed no consistent long-term association (2 to 5 years of observation) between sugar-sweetened or energetic beverage consumption and fat mass among children and adolescents^{157, 158}.

Energy density may also play an important role with regard to the social class. For instance, there was an inverse relationship between energy density and energy costs¹⁵⁴. It was suggested that people with a low income preferentially purchase energy dense foods to constrain their costs. Yet, it is not clear if this observation can be generalised since relative food prices vary considerably between countries.

Overall dietary pattern

Overall dietary pattern is very difficult to define and to assess. There are different approaches such as using cluster or factor analysis to obtain a picture of specific food choice or using specifically constructed indexes¹⁵⁹. It is also difficult to analyse the association between overall dietary pattern and overweight. For example, an association between the healthy eating index (HEI) and weight status in adults was observed¹⁶⁰. This index reflects the overall diet quality and is based on 10 components (5 food groups, 4 nutrients, and a measure of variety)¹⁶¹. There was a significant increased likelihood of obesity with descending HEI indicating a worse dietary pattern¹⁶⁰. However, there was no association between overall diet quality measured with a dietary index and overweight among children⁹⁷. This association between dietary indexes and overweight is discussed in more detail in Chapter 4.5.3.

As hypothesised in a review, changes in eating patterns, such as higher soft drinks consumption, higher frequency in eating out, increased portion size, and skipping breakfast may have a more important impact on obesity than single foods or nutrients¹⁶². In this context, Schulz et al.¹⁶³ identified in a prospective cohort study that a food pattern characterised by high-fibre, low-fat and high-carbohydrate food choice is associated with weight change in adults and may help to prevent excess weight gain over time. A recent longitudinal study among children

5 and 7 years of age showed similar results¹⁶⁴. An energy-dense, low-fibre, and high-fat diet was associated with greater fat mass among children at the age of 9 years.

Despite the fact that breakfast consumers seemed to have a higher energy intake, regular breakfast consumption may be associated with lower BMI^{165, 166}. For instance, a recent prospective study showed that the frequency of having breakfast was inversely associated with BMI in a dose response manner¹⁶⁷. One possible link might be an overall healthier lifestyle including better dietary quality and higher physical activity. In this context general meal frequency is also discussed to have an impact on obesity. A protective effect of an increased daily meal frequency among children has been observed¹⁶⁸. A review concluded that inconsistent meal patterns could lead to obesity¹⁶². Currently, there is not enough evidence to give a definite conclusion which food pattern is most strongly related to overweight^{150, 166}.

In summary, different aspects and stages of life may be involved in the development of overweight and obesity. Most risk factors do not occur independently which means that there are interactions of potential determinants. Therefore, it is not possible to blame only one or few single risk factors for the onset of overweight and obesity. Rather, an accumulation of several risk factors, a specific combination of different risk factors, and/or unfavourable conditions may lead to weight gain. There are some factors which can be influenced by people itself (for example behaviour) and others which can not be influenced (for example genetic factors). Some people may (genetically) be more susceptible than other persons or belong to a specific risk group which needs specific attention. Furthermore, the development of overweight and obesity is a gradual process, often taking several years. This further complicates the identification of causal relationships. After all, as mentioned before, every factor or condition that leads to a positive energy balance can cause overweight or obesity.

2.4 Health risks of overweight and obesity

In this chapter, the focus will be on CVD risk factors since CVD is an important health consequence of overweight and obesity. CVD risk factors such as dyslipidemia, hypertension, and insulin resistance are strongly related to coronary heart disease in adults¹⁶⁹ as well as in young people¹⁷⁰. The extent of atherosclerotic lesions increases with the presence of multiple CVD risk factors and multiple risk factors have a synergistic effect on morbidity and mortality¹⁷⁰. There is increasing evidence that even among children and adolescents obesity is associated with several CVD risk factors such as high blood pressure, adverse lipid profile, and

insulin resistance^{11, 60, 171, 172}. Some of these studies reported a clustering of CVD risk factors among obese children and adolescents¹⁷² or a positive relationship between the level of overweight and the prevalence of the metabolic syndrome¹¹. A relationship between the metabolic syndrome in childhood and the risk of CVD in later life was observed¹⁷³.

Overweight and obesity are characterised by a state of chronic low-grade inflammation and there is increasing evidence that such an inflammation is associated with an increased risk of CVD¹⁷⁴. For European countries, only few large studies are available concerning the association between overweight, obesity and CVD risk factors among children and adolescents^{175, 176}. For Germany, mainly local or small studies on this topic exist^{177, 178}. The association between (abdominal) obesity and adverse CVD risk factors is evident among adults^{53, 54}. In the following sections, the focus will be on findings among children and adolescents and the CVD risk factors which will be analysed in Chapter 5 are described.

2.4.1 The role of body fat

Adipose tissue is an endocrine organ. White adipocytes produce and secrete several hormones (leptin, adiponectin) as well as several other proteins (adipokines such as tumor necrosis factor alpha (TNF- α) or interleukin-6 (IL-6))^{179, 180}. These hormones and proteins are important mediators related to insulin resistance, type 2 diabetes mellitus, and CVD¹⁸¹. For instance, increased levels of free fatty acids derived from adipocytes contribute to insulin resistance and circulating levels of cytokines are elevated in individuals with type 2 diabetes mellitus¹⁸². A significant positive correlation between adipokines and measures of obesity has been shown, except for adiponectin, which is inversely associated with total body fat¹⁸¹. TNF- α and IL-6 are proinflammatory cytokines increasing in response to acute and chronic inflammatory events. They stimulate the hepatic production of acute phase proteins including C-reactive protein (CRP). Therefore, white adipose tissue plays an important role in the circulation of CRP¹⁸⁰.

The location of body fat appears to be an important factor in explaining the link between obesity and health risk¹⁸². In this context, the “portal theory” blames visceral adipose tissue as a health risk whereby the “ectopic fat theory” blames the fat deposition outside the adipose tissue (for example in muscle or liver) as more important¹⁸¹. As described in Chapter 2.2, it is currently discussed which measure of childhood obesity is the best predictor for adverse health outcomes. Weight-height indices are of limited adequacy in assessing obesity and do

not measure adipose tissue directly. Since the abdominal fat mass is important in relation to health outcomes, measures taking fat distribution and location of body fat into account may be better predictors than BMI^{58,60}.

2.4.2 Chronic inflammation

Overweight and obesity are characterised by a state of chronic low-grade inflammation and there is increasing evidence that chronic low-grade inflammation has been associated with an increased risk of adverse CVD risk factors¹⁷⁴. One possibility for the origin of inflammatory markers in overweight and obesity is that white adipose tissue secretes substances that stimulate the production of inflammatory markers from the liver and other organs. For instance, the hepatic production of CRP is stimulated by increased IL-6 resulting from excessive fat mass¹⁸⁰. CRP is an acute-phase protein and a sensitive marker of inflammation, with the extent of an inflammation reflected by increasing levels of CRP¹⁸³. The circulation of serum levels of CRP increases with BMI and therefore elevated levels of CRP have been associated with obesity¹⁸⁰. Several studies reported that moderately elevated concentrations of CRP correlate with obesity and metabolic syndrome among children and adolescents¹⁸⁴⁻¹⁸⁸. There seems to be a strong association with abdominal obesity^{188,189}. Furthermore, a meta-analysis of seven prospective population based studies among adults observed a combined risk ratio of 1.7 for future coronary events in persons with elevated baseline CRP levels¹⁹⁰. An update of this meta-analysis with 22 prospective studies observed a combined odds ratio of 1.6¹⁹¹. A study of Turkish children observed higher CRP levels in children with adverse CVD risk factors compared to children without adverse CVD risk factors¹⁹². Thus, overweight and obesity during childhood and adolescence are already associated with low-grade inflammation which may be a risk factor for CVD in later life.

2.4.3 Dyslipidemia

Dyslipidemia is one of the most important risk factors for coronary heart disease. Research increasingly indicates that the atherosclerotic process begins in early life^{171,193-195}. For instance, increased cholesterol concentrations in childhood were associated with elevated cholesterol levels and increased risk of atherosclerosis in adulthood¹⁹³. Obesity and the distribution of body fat are factors that influence blood lipids and lipoproteins^{171,195}. Several studies among children and adolescents observed a positive association between relative excess of adipose tissue, in particular in the abdominal region, and adverse concentrations of blood lip-

ids^{45, 172, 196}. In particular, low density lipoprotein cholesterol (LDL-C) particles account for the accumulation of atherosclerotic plaque and the LDL-C level is causally associated with the development of atherosclerosis. Furthermore, a low high density lipoprotein cholesterol (HDL-C) level is an independent risk factor for CVD¹⁹⁷.

2.4.4 High blood pressure

The positive relationship between blood pressure and overweight and obesity is well documented. However, the association between overweight, obesity and elevated blood pressure in children seems to be a function of an increased heart rate rather than a rise in the systemic vascular resistance as it was observed in adults¹⁹⁸. Several studies conducted among children and adolescents living in developed as well as in developing countries, showed that obese individuals had higher blood pressure levels than non-obese¹⁹⁹⁻²⁰³. In particular abdominal obesity was observed to play an important role in blood pressure levels^{202, 204}. A recent review based on data from the US, Canada, Italy, England, Ireland, Pakistan, and the Republic of the Seychelles concluded that the current prevalence of elevated blood pressure is relatively high among children and adolescents and strongly associated with overweight²⁰⁵. However, the data did not support the hypothesis that the worldwide epidemic of overweight and obesity in children and adolescents has resulted in a corresponding increase in blood pressure levels. A review on the current evidence regarding diet and its role in blood pressure stated that genetic, environmental, and lifestyle factors may be involved in the development of hypertension²⁰⁶. The relationship between dietary nutrients and blood pressure remains controversial. For instance, there is evidence, that weight loss through caloric restriction and increased physical activity lowers blood pressure, while the evidence for a direct relation between sodium and blood pressure is less conclusive^{198, 206}.

2.4.5 Hyperglycaemia/insulin resistance/diabetes mellitus

Hyperglycaemia is a result of an absolute or relative insulin deficiency or inadequate insulin efficiency²⁰⁷. An auto-immune caused destruction of the insulin secreting beta cells in the pancreas is responsible for type 1 diabetes mellitus. Type 2 diabetes mellitus is characterised by an inadequate secretion of insulin which leads to a decreased effect of insulin (insulin resistance). Both insulin resistance and diminished insulin secretion are independent predictors of the development of type 2 diabetes mellitus¹⁸¹. Obesity seems to be a primary risk factor for type 2 diabetes mellitus in children and adolescents as well as in adults. Even modest

weight gain in early (adult) life is associated with a substantial risk for developing type 2 diabetes mellitus²⁰⁸. As shown in a longitudinal study, obesity during childhood and adolescence was closely related to markers of insulin resistance in later life²⁰⁹. A recent cross-sectional study showed a significant relationship between higher amounts of body fat and insulin resistance. When comparing non-overweight to overweight or obese adolescents, markers of insulin resistance were almost tripled in the overweight/obese group²¹⁰. As shown in a multicenter randomised clinical trial, higher visceral fat and WC, BMI, WHR, and WHtR significantly predicted the onset of diabetes mellitus among adults²¹¹. However, none of these measures was significantly better in predicting the onset of diabetes mellitus than any other. In contrast, central obesity was one of the main predictors of insulin resistance among children²¹². Studies among adults showed that lifestyle intervention including the reduction of overweight could reduce the incidence of type 2 diabetes mellitus^{213, 214}. A study among adolescents showed that those with higher amounts of body fat might profit most from an increase of time spent undertaking vigorous physical activity and an overall increase of total physical activity²¹⁰.

2.4.6 Threshold values for elevated CVD risk factors

Similar to the definition of overweight and obesity, there are commonly applied definitions for adverse CVD risk factors among adults but not among children and adolescents. For example, there is no consensus about reference values for elevated blood lipids and lipoprotein levels among children and adolescents. The US National Cholesterol Education Program (NCEP) recommended the use of 200 mg/dl for total cholesterol (TC), 130 mg/dl for LDL-C, and < 40 mg/dl for HDL-C as absolute cutoff points for children and adolescents^{194, 195, 215}. However, it is now known that cholesterol concentrations vary by age and sex. For example, using data from two different US studies it was examined how age and sex specific variation in cholesterol concentrations contributed to the screening result among children and adolescents as having high cholesterol levels when fixed criteria were used²¹⁶. It was concluded that changes in blood lipid levels during growth make absolute values inappropriate as an indicator for a certain individual. Therefore, age and sex specific criteria are preferable for risk assessment. In 2006, new age and sex specific lipoprotein cutoff points have been developed for 12-20 year olds based on data from a large representative US survey (NHANES III)²¹⁷. The benefits the authors mentioned are that the age and sex specific thresholds reflect the natural variation in lipoprotein concentration that occur with growth and maturation in contrast to the absolute cutoff points supported by the NCEP²¹⁵. Furthermore, the age and sex specific cutoff

points are linked to the adult NCEP values which themselves are based on increased risk of CVD²¹⁷.

Magnussen and colleagues²¹⁸ compared the ability of the NCEP and the new NHANES lipoprotein classification to predict abnormal lipoprotein levels in adulthood. The results showed that a separate use of NHANES for HDL-C and NCEP for TC, LDL-C, and triglycerides yielded the most accurate classification. It seems that the predictive power of the cutoff points depend on the period when the cutoff points were developed as well as on the study population. For the first time for German children and adolescents, smoothed percentile distributions for serum TC, LDL-C, and HDL-C have recently been published²¹⁹.

Among adults, elevated blood pressure is defined for values greater or equal 140 mm Hg for systolic blood pressure (SBP) and greater or equal than 90 mm Hg for diastolic blood pressure (DBP)²²⁰. Blood pressure increases with age and taller children have higher blood pressure levels than smaller ones of the same age. Therefore, the National High Blood Pressure Education Program (NHBPEP) Working Group on Hypertension Control in Children and Adolescents developed age and height specific references for boys and girls to define elevated blood pressure levels for children and adolescents²²¹. Hypertension is defined by values greater or equal to the 95th percentile by gender, age, and height. For Germany, such definitions do not exist up to now. When defining elevated blood pressure levels, one must distinguish between an individual diagnosis (which implies a more extensive examination) and screening procedures in epidemiologic studies.

Casual glucose levels above 200 mg/dl and fasting glucose levels above of 126 mg/dl are diagnostic criteria for type 2 diabetes mellitus among adults, adolescents and children^{222, 223}. To assess blood glucose levels adequately, 12-hour-fasting blood samples are needed²⁰⁷. In large-scale studies it is often not possible to take fasting blood samples. Glycosylated haemoglobin (HbA1c) is a good indicator of long-standing blood glucose elevation, independently of food intake and short-term blood glucose levels²⁰⁷ and has also been reported to be a good predictor of later development of type 2 diabetes mellitus in children^{224, 225}. Therefore, HbA1c has been suggested as an acceptable measure for the diagnostic of type 2 diabetes mellitus and for the use as a screening tool in adults and children. In general, HbA1c levels above 6% are considered as elevated²²⁵.

There are no explicit definitions of elevated CRP levels for children and adults. Concerning elevated levels of CRP it has to be distinguished between CRP levels reflecting a low-grade chronic inflammation or those reflecting an acute inflammation. In general, serum CRP concentrations of 10 mg/l and higher are considered to reflect acute inflammatory processes²²⁶. In contrast, even a slightly increased CRP level may be an important indicator for chronic inflammation. Cutoffs to define elevated CRP levels used in previous studies are for example 2.1 mg/l^{187, 188} or 3 mg/l^{183, 189}.

3 METHODS: THE KiGGS STUDY

3.1 Design

The cross-sectional KiGGS study is the first comprehensive health examination survey, representative for the entire group of children and adolescents in Germany including a wide range of information about health status and health related behaviour. KiGGS provides important data for health policy, health reporting, epidemiological research, and intervention programs to highlight the most relevant health problems and risk groups. Furthermore, with this data it is possible to analyse complex associations between life circumstances, behaviour and health outcomes. Additionally, KiGGS provides reference data for health related indicators.

From May 2003 to May 2006, a total of 17641 children and adolescents 0-17 years of age, participated in the KiGGS study. Data was obtained using computer assisted personal interviews, physical examinations, self administered questionnaires as well as blood and urine samples. The large data set includes information about physical, social and mental health, chronic diseases, living conditions, lifestyle, health behaviour, health risks, and health care. Participants 14 years of age or older and all parents provided written informed consent prior to the interview and examination. The study was approved by the Federal Office for Data Protection and by the ethics committee of the Charité University Medicine, Berlin and financially supported by the Federal Ministry of Health, the Federal Ministry of Education and Research, and the Robert Koch Institute.

Several special modules were attached to the KiGGS study which allows more detailed analyses for several topics. The modules were mainly conducted in sub-samples of the main study population. Furthermore, there was a regional module carried out in Schleswig-Holstein. The additional modules are presented in Figure 2. All analyses in this thesis are based on data conducted in the main study.

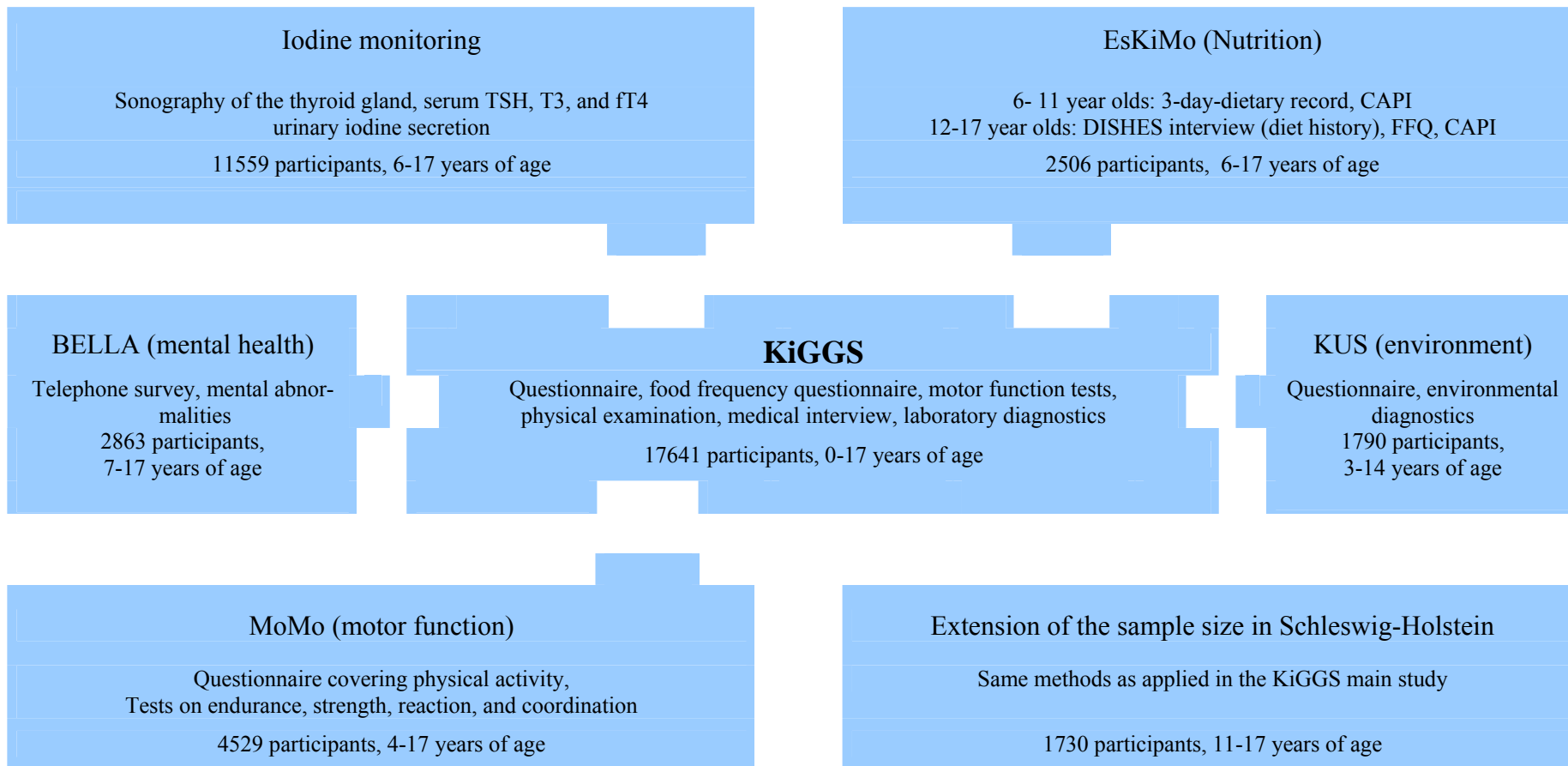


Figure 2: The modular structure of the KiGGS study

Source: adapted from Kurth 2007 ²²⁷

3.2 Sampling procedure

The sampling methods have been previously described in detail ^{228, 229}. In brief, the sample was drawn using a two-stage clustered and stratified sampling procedure. In the first stage, 167 sample points (communities) representative for Germany were selected with regard to community size and federal state. In order to ensure appropriate sample size for analyses differentiating between residence in the former East and West Germany, a disproportionate number of sample points were included (disproportionately higher number of sample points were included from the former East Germany). In the second stage, within each sample point, participants were selected at random from the official registers of local residents with stratification in one-year age bands. Since a higher proportion of unreachable contacts and non-respondents were expected among children and adolescents from migrant families, this group was oversampled. The overall response rate was 66.6%. In detail, the response rate was 65% for 0-2 year olds, 66% for 3-6 year olds, 70% for 7-10 year olds, 69% for 11-13 year olds and 63% for 14-17 year olds ²²⁹.

To enhance the representativeness of the sample, a weighting factor was constructed and applied correcting for the deviances of the KiGGS sample to the total population structure (at 31.12.2004) concerning age, gender, residence (West Germany, East Germany, Berlin) and nationality (German, non-German). Since participants were not selected absolutely at random but clustered within the sample points, conventionally calculated p-values and confidence intervals tend to be too small. Therefore, all analyses are based on specific statistical survey procedures which take into account the cluster design of the study. With these procedures the variance is not estimated between individuals but between the sample points. The stratification with regard to community size and federal state is not considered in these procedures. Therefore, the analysed p-values and confidence limits tend to be conservative ²²⁹.

3.3 Data collection

The examination took place at local examination centres in the 167 sample points. Four examination teams including trained medical staff followed a detailed route plan all across Germany, which assured a random spread over season and regions. A differentiated examination program according to physical development was constructed for five age groups: infants (0-2 years of age), preschoolers (3-6 years), schoolchildren (7-10 years), age of puberty (11-13 years), and teenagers (14-17 years). Parents of participants 0-13 years of age and partici-

pants 14 years of age and older underwent a computer assisted personal interview performed by a physician with topics covering disease history, vaccination, and use of pharmaceuticals. A physical examination including anthropometric and blood pressure measurements was conducted by specifically trained staff. Furthermore, casual blood and urine samples were collected. Information about socio-demographic characteristics, living conditions, health, and health related behaviour was obtained using age specific self-administered questionnaires. An overview of the spectrum of available data is given in Table 2. In the chapters 3.4 to 3.6, the collection of data used in the present analyses is described in more detail. The precise use of study variables is summarised in the corresponding result chapter.

3.4 Data obtained from the physical examination

Measurements of body height, body weight, triceps and subscapular skinfold thicknesses (among all participants) as well as waist and hip circumference (among participants 11 years of age and older) were obtained according to a highly standardised protocol. Body height was measured, without wearing shoes, to the nearest 0.1 cm using a portable Harpenden stadiometer (Holtain Ltd., Crymych, UK). Body weight was measured, wearing underwear, to the nearest 0.1 kg with a calibrated electronic scale (SECA, Birmingham, UK). Waist circumference was measured with a flexible non-elastic tape at the smallest abdominal position between the lower rib margin and the iliac crest. Hip circumference measurement was taken at the point yielding the maximum circumference over the buttocks. A Harpenden-Caliper was used to measure one set of triceps and subscapular skinfold thickness on the right body side with an accuracy of 0.2 mm. Two readings of systolic and diastolic blood pressure were obtained among participants 3 years of age and older using an automated oscillometric device at two minutes interval. The measurement took place in a sedentary position on the right arm after a five minute rest. Participants 10 years of age and older were asked to assess their pubic hair status based on showcards displaying pubertal hair growth patterns according to Tanner stages 1-6²³⁰. They were classified into three groups: pre-pubertal (Tanner stage 1), pubertal (Tanner stage 2 or 3) and post-pubertal (Tanner stage 4 to 6).

Table 2: Methods used in the KiGGS study - overview

Method	Contents	Age group	Remarks
Self-administered questionnaires	Physical health and diseases	0-17 years	5 different parent versions related to age (0-2 years, 3-6 years, 7-10 years, 11-13years, 14-17 years) 2 different children versions related to age (11-13 years, 14-17 years) 7 different languages (German, English, Turkish, Russian, Arabic, Vietnamese, Serbo-Croatian)
	Mental health and problems	3-17 years	
	Social health, living conditions	0-17 years	
	Lifestyle and health related behaviour	0-17 years	
	Health care utilisation	0-17 years	
Food frequency questionnaire	Food intake	1-17 years	54 food items 2 different versions identical in content (for parents of 1-10 year olds, for participants aged 11-17 years)
Physical examination	Anthropometry:		Conducted by trained medical staff
	Height, weight, skinfold thickness	0-17 years	
	Waist circumference	11-17 years	
	Blood pressure and heart rate	3-17 years	
	Motor activity, reaction and coordination	4-17 years	
	Sonography of the thyroid gland	6-17 years	
	Vision tests	3-17 years	
	Laboratory diagnostics (blood and urine samples)	1-17 years	
	Nutritional status (e.g. Vitamins, Ca, Na, Fe)		
	Blood lipids and lipoproteins		
HbA1c			
Hs-CRP			
Allergic sensitisation			
Immunity			
Computer-assisted personal interview	History of disease	0-17 years	Conducted by a trained physician (parents of children aged 0-13 years, participants aged 14-17 years)
	Vaccination	0-17 years	
	Use of pharmaceuticals	0-17 years	

Source: own illustration

3.5 Laboratory assay

Casual venous blood samples were obtained from participants 1 year of age and older, only if the accompanying parent or caregiver provided consent. Blood serum was separated and transported by car on dry ice to a central laboratory according to a highly standardized protocol²³¹. TC was analysed using an enzymatic assay (cholesterol-oxidase-PAP-method) (Roche, Mannheim, Germany). LDL-C and HDL-C were measured directly with a homogenous enzymatic colorimetric assay (Roche). High sensitivity CRP (hs-CRP) was measured by an immunoturbidimetric assay. The initially applied assay (SCIL Diagnostics, Martinsried, Germany) was withdrawn from the market in 2004 and was replaced by an equivalent assay from a different provider (Roche, Mannheim, Germany). A correction factor calculated with a Passing Bablok regression equation was used for the analysis²³¹. HbA1c was analysed using high performance liquid chromatography (HPLC, Diastat, Bio-Rad, Munich, Germany).

3.6 Data obtained from self-administered questionnaires

Health questionnaire

A wide range of health relevant information was obtained from self-administered questionnaires. Different versions of the questionnaire existed, which were aimed to the five age groups mentioned before. All parents as well as participants 11 years of age or older were asked to fill in a questionnaire. For migrants with only limited knowledge of the German language, a shortened version was available in six different languages (English, Turkish, Russian, Serbo-Croatian, Arabic, and Vietnamese)²³². Topics of the health questionnaire included, amongst others, socio-demographic characteristics (such as parental income, parental and offspring education, nationality), living conditions (such as living space, number of siblings), parental weight and height, parental smoking, maternal smoking during pregnancy, birth weight, breastfeeding behaviour, mental health (such as self-esteem, contact with family/friends), and health related behaviour (such as physical activity, electronic media consumption).

Information on physical activity, electronic media consumption, and sleep duration was obtained differently for participants 3-10 years of age and participants 11-17 years of age: among 3-10 year olds, physical activity was obtained as the frequency of doing sports (separately for with or outside a sports club) in categories of almost daily/3-5 times per week/1-2 times per week/seldom/never. Among 11-17 year olds, self-reported vigorous physical activ-

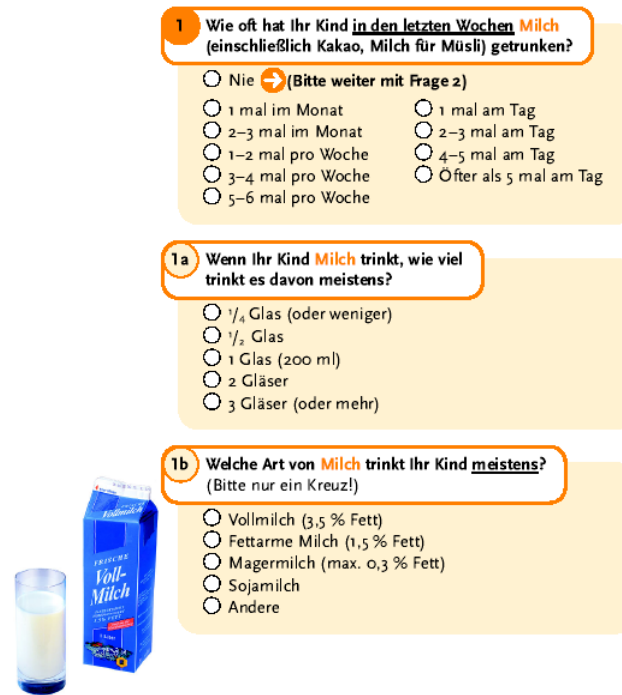
ity (“During leisure time, how often are you physically active in such a way that lets you come out of breath or makes you sweat?”) was assessed in categories of almost daily/3-5 times per week/1-2 times per week/seldom/never.

Among 3-10 year olds, electronic media consumption was assessed as the average time per day spent on watching television/video and using the computer in categories of not at all/about 30 minutes/1-2 hours/3-4 hours/more than 4 hours and was documented separately for weekdays and the weekend. Among 11-17 year olds, media consumption was asked in a similar way as for younger participants and additionally, playing videogames was asked. In contrast to 3-10 year olds, it was not distinguished between weekdays and weekends in the older age group. Sleep duration was reported as the average hours of sleep per day among 3-10 year olds and as hours of sleep during the last night among 11-17 year olds.

Some information was only obtained for participants 11-17 years of age, for example smoking behaviour and alcohol consumption. Furthermore, a rough screening on indications of possible eating disorders was performed with the SCOFF questionnaire (SCOFF is an acronym reflecting the five questions addressing core features of eating disorders)^{233, 234}.

Food frequency questionnaire

Food consumption was assessed with a self administered semi-quantitative food frequency questionnaire (FFQ) including 54 food items. A detailed description of the development and content of the FFQ is presented elsewhere²³⁵. There were two versions of the questionnaire, identical in content. Parents of children 1-10 years of age were asked to complete the FFQ for their children, children and adolescents 11-17 years of age completed the FFQ by themselves. The questionnaire was sent by postal mail prior to the interview and examination visit. During the survey period, a telephone hotline was offered for support in completing the questionnaire. In the study centre, the FFQs were checked for completeness. For 45 of the 54 food items covered, the FFQ asked the average food frequency in ‘the last few weeks’ as well as the average consumed portion size. An example is given in Figure 3.



1 Wie oft hat Ihr Kind in den letzten Wochen Milch (einschließlich Kakao, Milch für Müsli) getrunken?

Nie → (Bitte weiter mit Frage 2)

1 mal im Monat 1 mal am Tag

2–3 mal im Monat 2–3 mal am Tag

1–2 mal pro Woche 4–5 mal am Tag

3–4 mal pro Woche Öfter als 5 mal am Tag

5–6 mal pro Woche

1a Wenn Ihr Kind Milch trinkt, wie viel trinkt es davon meistens?

¼ Glas (oder weniger)

½ Glas

1 Glas (200 ml)

2 Gläser

3 Gläser (oder mehr)

1b Welche Art von Milch trinkt Ihr Kind meistens? (Bitte nur ein Kreuz!)

Vollmilch (3,5 % Fett)

Fettarme Milch (1,5 % Fett)

Magermilch (max. 0,3 % Fett)

Sojamilch

Andere

Figure 3: Example for a food item from the KiGGS food frequency questionnaire

Source: http://www.kiggs.de/questionnaires/pdfs/Eltern_.pdf

The remaining 9 food items cover habits like general consumption of supplements, fortified foods, light products, convenience food, and probiotic products. Categories for frequencies were identical for all food items: never, once per month, 2-3 times per month, 1-2 times per week, 3-4 times per week, 5-6 times per week, once per day, 2-3 times per day, 4-5 times per day, more than 5 times per day. Food specific portion sizes were often predefined with given standard household measures (cups, spoons, etc.). Furthermore, to ease the estimation of portions sizes, they were often illustrated with examples. There were always five categories which were equal for all ages (for example ¼ cup, ½ cup, 1 cup, 2 cups, 3 cups).

4 RESULTS: DETERMINANTS OF OVERWEIGHT AND OBESITY

This chapter is an adapted version of:

Kleiser C, Schaffrath Rosario A, Mensink GBM, Prinz-Langenohl R, Kurth BM: Potential determinants of obesity among children and adolescents in Germany: results from the cross-sectional KiGGS study. *BMC Public Health* 2009, 9:46

Overweight and obesity are consequences of a long-term imbalance between energy intake and energy expenditure, determined by food intake and physical activity and influenced by biological and environmental factors. As described in detail in Chapter 2.3, potential risk factors for overweight and obesity in early life include genetic, physical, lifestyle, and environmental conditions. These risk factors are often related to each other but their relationship is unknown at the individual as well as the population level. Although many factors are known, their confounding or cumulative effect on the development of overweight and obesity as well as their clustering and their effects over time on the causal pathway remain unclear to a certain extent. For an effective prevention of overweight and obesity, it is necessary to identify major determinants and their relationships early in life. For Germany, for the first time, comprehensive and nationally representative data for the entire group of children and adolescents living in Germany are available with the KiGGS study. The aim of this chapter is to identify major determinants of overweight and obesity and to evaluate risk groups among 3-17 year olds.

4.1 Sample

The analyses of determinants of overweight and obesity were conducted among children and adolescents aged 3-17 years (N = 14836). For children 0-2 years of age only limited information on potential determinants was available. Furthermore, 89 participants with no information on weight status and 1297 underweight participants (thinness grade 1, as defined by Cole et al. ²³⁶) were excluded. The reason for this exclusion is a presumed difference in the relationship of socio-economic and behavioural determinants with weight status among underweight and overweight people ²³⁷. Furthermore, the exclusion of underweight persons allowed a better comparison of normal weight with overweight and obese persons. A sensitivity analysis on the effect of this exclusion showed only marginally changes in the presented results. The sample thus comprised 13450 participants. For some analyses the number of participants was smaller due to missing data. For instance, food intake data was available for 12792 children and adolescents. The analyses concerning SES included 13102 participants. For the multivariable model presented in Table 7, 10021 children and adolescents with complete data were included.

4.2 Use of study variables

To allow an international comparison, BMI was classified according to age and sex specific IOTF cutoffs for children and adolescents (Table A-1)¹³. As described in more detail in Chapter 2.2.7, the IOTF cutoff points are defined to pass through BMI values of 25 kg/m² and 30 kg/m² at age 18, obtained by averaging data from Brazil, Great Britain, Hong Kong, the Netherlands, Singapore, and United States. In the present chapter, the term overweight includes obesity. The term obesity is restricted to exclusively obese children and adolescents as defined by the IOTF.

For all participants, information on parents' income, occupational status and education was used to quantify the SES which was categorised into low, medium, and high SES^{238, 239}. Information about nationality and country of birth was used to identify children and adolescents with a migration background. A participant was defined to have a one-sided (two-sided) migration background if one (both) of the parents was (were) not born in Germany and/or have no German citizenship²³². Self-reported height and weight of mothers and fathers were used to calculate parental BMI which was classified into overweight (including obesity) or non-overweight according to the WHO cutoff points of 25 kg/m²¹⁵. Only the weight status of the biological parents was considered in this thesis. To avoid excluding all single-parent families, a separate category "incomplete data" for the variable parental overweight was used in the analysis. Parental smoking at the time of interview (yes or no) was documented for mothers and fathers. Maternal smoking during pregnancy was classified into yes or no. Furthermore, reported birth weight (in grams) was defined as low when less than 2500 g²⁴⁰ and as high when more than 4000 g was reported. In addition, mothers were asked for weight gain during pregnancy (in kg), presence of maternal diabetes during pregnancy, and breastfeeding behaviour.

For all participants, physical activity was calculated as times per week and additionally categorised into approximate age specific tertiles (due to of the ordinal scale of the initial variables). Total electronic media consumption was calculated in hours per day for use as a continuous variable and additionally categorised into age specific tertiles. Reported hours of sleeping time was used to construct a sleeping score (expressed as midranks ranging from 0% to 100%), which can be interpreted as percentiles as described by Bayer et al.²⁴¹. This variable was used in tertiles as well as continuously (per 20% increase in midranks). Among 11-17 year olds, regular alcohol consumers were defined as those drinking at least one glass of

alcohol (beer, wine, liquor) per week. Smoking behaviour was differentiated into smokers and non-smokers.

For the analyses of food intake, frequencies were recoded into times of servings per month (where 1 month was set equal to 4 weeks, for example once per week = 4, once per day = 28, more than five times per day = 168). For frequency bands such as one or two times per day the arithmetic mean was used. Portion sizes were converted into gram amounts using the given standard portion sizes in the FFQ. The average food intake was calculated by multiplication of recorded frequency and portion size. Then, age and sex specific tertiles of food intake were calculated for defined food groups. The total intake of energy-providing food and beverages was used as an overall indicator of food intake.

Additionally, an overall dietary score, called HuSKY (Healthy nutrition score for kids and youth), based on the FFQ items was applied. The HuSKY has been described in detail elsewhere²⁴². In brief, for this score, the average food intake of eleven food groups (beverages, fruit, vegetables, bread and cereals, pasta/rice/potatoes, milk and dairy products, eggs, meat and sausage, fish, butter and margarine, sweets/snacks/sugared drinks) was compared with age and sex specific food based dietary guidelines for children and adolescents²⁴³ by calculating the ratio (food intake / recommended intake). Depending on the guidelines to eat plenty, moderate or small amounts of specific food, each of these food ratios then were valued with points. For each food group, a maximum of 100 points were given when the recommendation was totally met. Finally, these single scores were added together and standardised to a scale from zero to 100. A higher score value implies a better overall dietary quality relating to the recommendations.

4.3 Statistical analysis

All analyses used sampling weights, as described in brief in Chapter 3.2 and in more detail elsewhere²²⁸. The SAS survey procedures (SAS version 9.2)²⁴⁴ were applied in order to take into account the clustered sampling design. A p-value < 0.05 (in interaction analyses p < 0.10) was considered to be statistically significant based on two-sided tests.

First, frequencies of overweight (including obesity) as well as frequencies of obesity stratified by potential determinants were analysed. The corresponding odds ratios (OR), adjusted for age and gender, were calculated with binary logistic regression models (univariable analysis).

Second, frequencies of overweight as well as frequencies of obesity were compared across the tertiles of food intake of several food groups and the HuSKY. Binary logistic regression models were calculated, adjusted for age and gender, and the p-values for the comparison of the highest vs. the lowest tertile are reported. Third, a multivariable binary logistic regression analysis was performed with obesity as the dependent variable. All variables which showed a statistically significant association with obesity in the univariable analysis were included as well as statistically significant qualitative interactions with gender, age or parental overweight. An interaction was considered as qualitative when the interaction term was statistically significant in the univariable analysis, and when the interaction remained qualitative in the multivariable model in the sense that there was a statistically significant association with obesity in one group, but not in the other. In the multivariable model media consumption, physical activity, sleep duration, and food intake were included as continuous variables and all others as class variables. Total intake of energy-providing food and beverages (in units of 100 g per day) was used as an overall indicator for total food intake. Since intake of energy-providing food and beverages was far from significant ($p = 0.9$) and the estimators for all other variables changed only marginally, this variable was not included in the final model. Furthermore, pubertal stage (which is strongly associated with age) and SCOFF were not included in the multivariable model. These characteristics may be effects rather than causes of obesity and the respective data were only available for older participants.

Additionally, a descriptive analysis separately for the three SES groups was performed. First, the distribution of the potential determinants by SES group was described. Then, the frequency of obesity was tabulated in subgroups defined by SES and the potential determinants, for those variables showing a significant univariable interaction with SES.

4.4 Results

4.4.1 Main characteristics of the study population

The main characteristics of the study population for the analysis of determinants of overweight and obesity are shown in Table 3. The sample included 6885 boys (51.2%) and 6565 girls (48.8%) 3-17 years of age. Among the 10-17 year olds, 61.4% of the boys were post-pubertal, whereas 75.6% of the girls were post-pubertal. About 21% of the boys and girls were overweight, of which about 5% were obese according to definitions of the IOTF. Less than 30% of the boys and girls had a low or high SES, respectively. 17.8% of the boys and

17.1% of the girls had a two-parent migration background. Almost 17% of both boys and girls lived in the Eastern part of Germany and the proportion of boys and girls living in rural areas was 18%.

Table 3: Main characteristics of the study population used for the analysis of determinants [% (95% CI)], 3-17 years

	Boys (N = 6885)		Girls (N = 6565)	
Age group				
3-6 years	23.7	(23.2-24.2)	23.8	(23.2-24.4)
7-10 years	25.3	(24.8-25.8)	25.0	(24.5-25.5)
11-13 years	19.9	(19.4-20.4)	20.1	(19.6-20.6)
14-17 years	31.1	(30.4-31.9)	31.1	(30.3-31.9)
Pubertal stage (10-17 years)				
Pre-pubertal	12.3	(11.0-13.5)	9.6	(8.5-10.6)
Pubertal	26.4	(25.0-27.7)	14.8	(13.6-16.1)
Post-pubertal	61.4	(59.8-63.0)	75.6	(74.3-76.9)
BMI status (IOTF criteria)				
Normal weight	79.3	(78.0-80.6)	79.5	(78.3-80.8)
Overweight/obese	20.7	(19.4-22.0)	20.5	(19.2-21.7)
Obese	5.5	(4.9-6.1)	5.2	(4.5-5.8)
Socio-economic status				
Low	28.1	(26.3-29.8)	27.7	(26.2-29.1)
Medium	45.3	(43.7-47.0)	45.9	(44.2-47.6)
High	26.6	(24.7-28.5)	26.4	(24.5-28.3)
Migration background				
Two-parent	17.8	(15.7-20.0)	17.1	(14.9-19.2)
One-parent	7.9	(7.0-8.9)	7.6	(6.7-8.5)
Non-migrant	74.3	(71.7-76.8)	75.3	(72.7-78.0)
Residence				
Eastern Germany	16.5	(11.8-21.3)	16.7	(11.9-21.5)
Western Germany	83.5	(78.7-88.2)	83.3	(78.5-88.1)
Degree of urbanisation				
Rural	18.0	(11.9-24.0)	18.2	(12.1-24.3)
Small town	27.8	(20.4-35.2)	27.4	(20.0-34.7)
Middle-sized town	29.7	(22.2-37.2)	29.5	(22.0-37.0)
Urban	24.6	(17.5-31.6)	25.0	(17.9-32.1)

4.4.2 Univariable analysis

The statistically significant associations between both overweight and obesity and different social, environmental and behavioural determinants, adjusted for age and gender, are shown in Tables 4-6. A low SES was associated with higher frequencies of overweight (including obesity) as well as with obesity. Children and adolescents with a two-parent migration background were more often overweight and also more often obese than non-migrants. However, this was not true for children and adolescents with a one-parent migration background. Children and adolescents whose parents were overweight, whose parents smoke, whose mother smoked during pregnancy, whose mother gained more than 20 kg during pregnancy, who were never predominantly breastfed, who had high birth weight, who had a post-pubertal

status, a low level of physical activity, high media consumption, who ate most energy-providing food and beverages, and who showed indications of eating disorders were more often overweight and more often obese than their respective counterparts (Tables 4-6).

Table 4: Frequency of overweight (including obesity) and obesity according to potential determinants and odds ratio, personal and social factors, 3-17 years

	N ^{a)}	Overweight (including obesity) [%] ^{b)}	OR ^{c)} for Overweight (95% CI)	p-value	Obesity [%] ^{b)}	OR ^{c)} for Obesity (95% CI)	p-value
Personal and social factors							
Socio-economic status							
Low	3655	26.6	2.1 (1.8-2.4)	<0.001	8.9	3.8 (3.0-4.7)	<0.001
Medium	6121	20.3	1.5 (1.3-1.7)	<0.001	4.7	1.9 (1.4-2.5)	<0.001
High	3326	14.5	ref.		2.5	ref.	
Missing data	348						
p for trend			<0.001			<0.001	
Migration background							
One-parent	920	19.0	1.0 (0.8-1.2)	0.9922	4.7	1.0 (0.7-1.5)	0.9790
Two-parent	2031	25.2	1.4 (1.2-1.6)	<0.001	7.6	1.6 (1.3-2.0)	<0.001
Non-Migrant	10444	19.7	ref.		4.9	ref.	
Missing data	55						
p for trend			<0.001			<0.001	
Parental overweight at time of interview (biological parents)							
Both overweight/obese	2696	32.4	4.9 (4.1-6.0)	<0.001	10.6	10.2 (6.7-15.3)	<0.001
Mother overweight/obese	1056	18.5	2.4 (1.8-3.1)	<0.001	4.4	4.0 (2.4-6.7)	<0.001
Father overweight/obese	3435	17.5	2.2 (1.8-2.7)	<0.001	3.6	3.3 (2.1-5.1)	<0.001
None overweight/obese	2707	8.6	ref.		1.1	ref.	
Incomplete data ^{d)}	3556	24.4	3.2 (2.6-3.9)	<0.001	6.5	5.8 (3.7-8.9)	<0.001
p for trend			<0.001			<0.001	
Parental smoking at time of interview							
Father and mother smoke	2534	27.8	1.9 (1.7-2.2)	<0.001	8.8	2.5 (1.9-3.1)	<0.001
Only mother smokes ^{e)}	1788	24.3	1.5 (1.3-1.8)	<0.001	6.7	1.8 (1.3-2.4)	<0.001
Only father smoke	2474	19.7	1.2 (1.1-1.4)	0.0030	4.8	1.3 (1.0-1.7)	0.0500
No smoking parents	6340	17.0	ref.		3.8	ref.	
Missing data	314						
p for trend			<0.001			<0.001	
Pubertal stage (10-17 years)							
Pre-pubertal	904	23.0	ref.		3.9	ref.	
Pubertal	1633	23.7	1.2 (0.9-1.5)	0.2469	5.4	1.6 (0.9-2.8)	0.0874
Post-pubertal	4497	23.6	1.7 (1.3-2.3)	0.0006	6.6	2.4 (1.2-4.5)	0.0104
Not assessed/missing data	6416						
p for trend			<0.001			0.031	
SCOFF (11-17 years)							
Conspicuous	1436	40.7	3.4 (2.9-4.0)	<0.001	14.1	4.6 (3.6-5.8)	<0.001
Inconspicuous	4663	18.0	ref.		3.8	ref.	
Not assessed/missing data	7351						

N = 13450 participants, 3-17 year olds (after exclusion of underweight participants)

a) unweighted

b) Based on IOTF cutoff points.

c) Odds ratio, adjusted for age and gender

d) Children not living with both biological parents or for which information on the mother's and/or father's BMI is missing.

e) Father does not smoke or no information on the father available.

Table 5: Frequency of overweight (including obesity) and obesity according to potential determinants and odds ratio, early life factors, 3-17 years

	N ^{a)}	Overweight (including obesity) [%] ^{b)}	OR ^{c)} for Overweight (95% CI)	p- value	Obesity [%] ^{b)}	OR ^{c)} for Obesity (95% CI)	p- value
Early life factors							
Maternal smoking during pregnancy							
Yes	2273	27.8	1.7 (1.5-1.9)	<0.001	8.4	1.9 (1.6-2.4)	<0.001
No	10724	18.9	ref.		4.6	ref.	
Missing data	453						
Weight gain during pregnancy							
Up to 20 kg	10748	19.5	ref.		5.0	ref.	
21 kg and more	994	28.3	1.8 (1.5-2.1)	<0.001	8.5	1.9 (1.4-2.6)	<0.001
Missing data	1708						
High birth weight							
Yes (>4000 g)	1451	28.4	1.7 (1.5-2.0)	<0.001	8.4	1.8 (1.5-2.3)	<0.001
No	11342	19.3	ref.		4.9	ref.	
Missing data	657						
Ever predominantly breastfed							
Yes	7999	17.9	ref.		4.2	ref.	
No	3977	25.3	1.5 (1.3-1.7)	<0.001	7.3	1.7 (1.4-2.2)	<0.001
Missing data	1474						

N = 13450 participants, 3-17 year olds (after exclusion of underweight participants)

a) unweighted

b) Based on IOTF cutoff points.

c) Odds ratio, adjusted for age and gender

Non-consistent and non-significant results are shown in Table A-2 in the appendix. There was a significantly negative association between low birth weight and obesity, but not with overweight. Maternal diabetes during pregnancy, the presence of siblings and smoking of the adolescents (11-17 years) were associated with a higher proportion of overweight, but not with obesity. There were no statistically significant associations between overweight or obesity and gender, living in Eastern vs. Western Germany, degree of urbanisation, regular alcohol consumption of the adolescents, and HuSKY (Table A-2).

Table 6: Frequency of overweight (including obesity) and obesity according to potential determinants and odds ratio, behavioural factors, 3-17 years

	N ^{a)}	Overweight (including obesity) [%] ^{b)}	OR ^{c)} for Overweight (95% CI)	p- value	Obesity [%] ^{b)}	OR ^{c)} for Obesity (95% CI)	p- value
Behavioural factors							
Sleep duration							
Lowest tertile	4451	22.5	1.2 (1.1-1.4)	0.0018	5.9	1.2 (1.0-1.6)	0.0715
Middle tertile	4399	19.4	0.9 (0.8-1.1)	0.3847	5.0	0.9 (0.7-1.1)	0.3708
Highest tertile	4318	19.6	ref.		4.9	ref.	
Missing data	282						
p for trend			<0.001			0.010	
Media consumption							
Lowest tertile	4293	15.6	ref.		3.7	ref.	
Middle tertile	4076	20.0	1.3 (1.2-1.5)	<0.001	4.7	1.2 (1.0-1.6)	0.0744
Highest tertile	4326	26.1	2.0 (1.7-2.2)	<0.001	7.3	2.1 (1.6-2.6)	<0.001
Missing data	755						
p for trend			<0.001			<0.001	
Physical activity							
Lowest tertile	4479	23.1	1.4 (1.2-1.6)	<0.001	6.4	1.4 (1.1-1.8)	0.0100
Middle tertile	4364	20.0	1.2 (1.0-1.3)	0.0079	4.7	1.0 (0.8-1.3)	0.8035
Highest tertile	4035	18.2	ref.		4.7	ref.	
Missing data	572						
p for trend			<0.001			0.011	
Intake of energy-providing food and beverages							
Lowest tertile	3691	19.4	ref.		4.9	ref.	
Middle tertile	3773	20.5	1.1 (0.9-1.2)	0.2800	4.7	1.0 (0.7-1.2)	0.7083
Highest tertile	3791	22.5	1.2 (1.1-1.4)	0.0019	6.4	1.3 (1.1-1.7)	0.0190
Missing data	2195						
p for trend			0.006			0.011	

N = 13450 participants, 3-17 year olds (after exclusion of underweight participants)

a) unweighted

b) Based on IOTF cutoff points.

c) Odds ratio, adjusted for age and gender

4.4.3 Overweight and food intake

Results of the analysis on overweight and dietary intake (lowest vs. highest tertile of food intake of several food groups) are shown in Figures 4-6 as well as in Figure A-2 for non-significant results in the appendix. There was a statistically significant positive association between overweight as well as obesity and the total food and beverage intake, and the intake of energy-providing food and beverages (Figure 4). The total beverage intake and the consumption of water (including tea) were positively associated with both overweight and obesity. The consumption of soft drinks was positively associated with overweight but not with obesity. In contrast, there was a statistically significant negative association between intake of juice and both overweight and obesity (Figure 5).

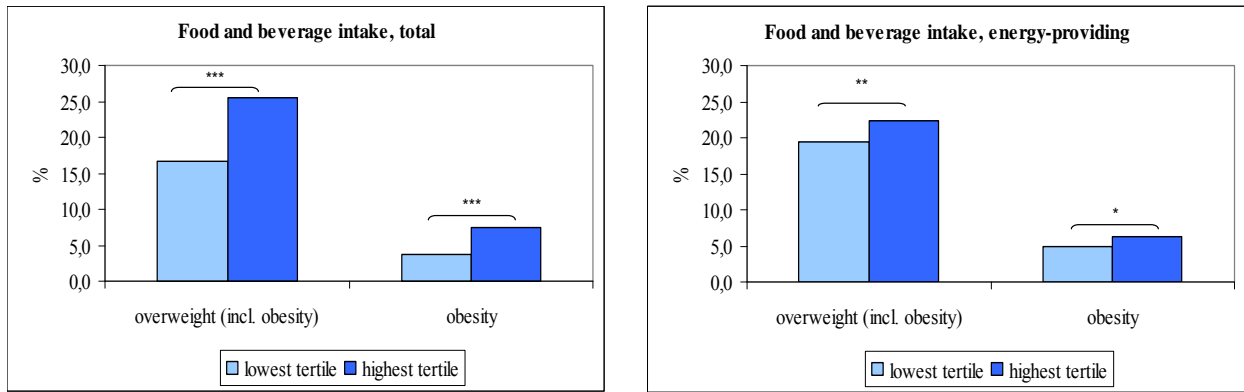


Figure 4: Frequency of overweight (including obesity) and obesity by lowest and highest tertiles of intake of total food and beverage [%]

N = 12792 participants, 3-17 year olds (underweight participants excluded)

p-value for lowest vs. highest tertile from univariable regression models with overweight or obesity as independent variable, adjusted for age and gender; * = $p < 0.05$; ** = $p < 0.01$; *** = $p < 0.01$

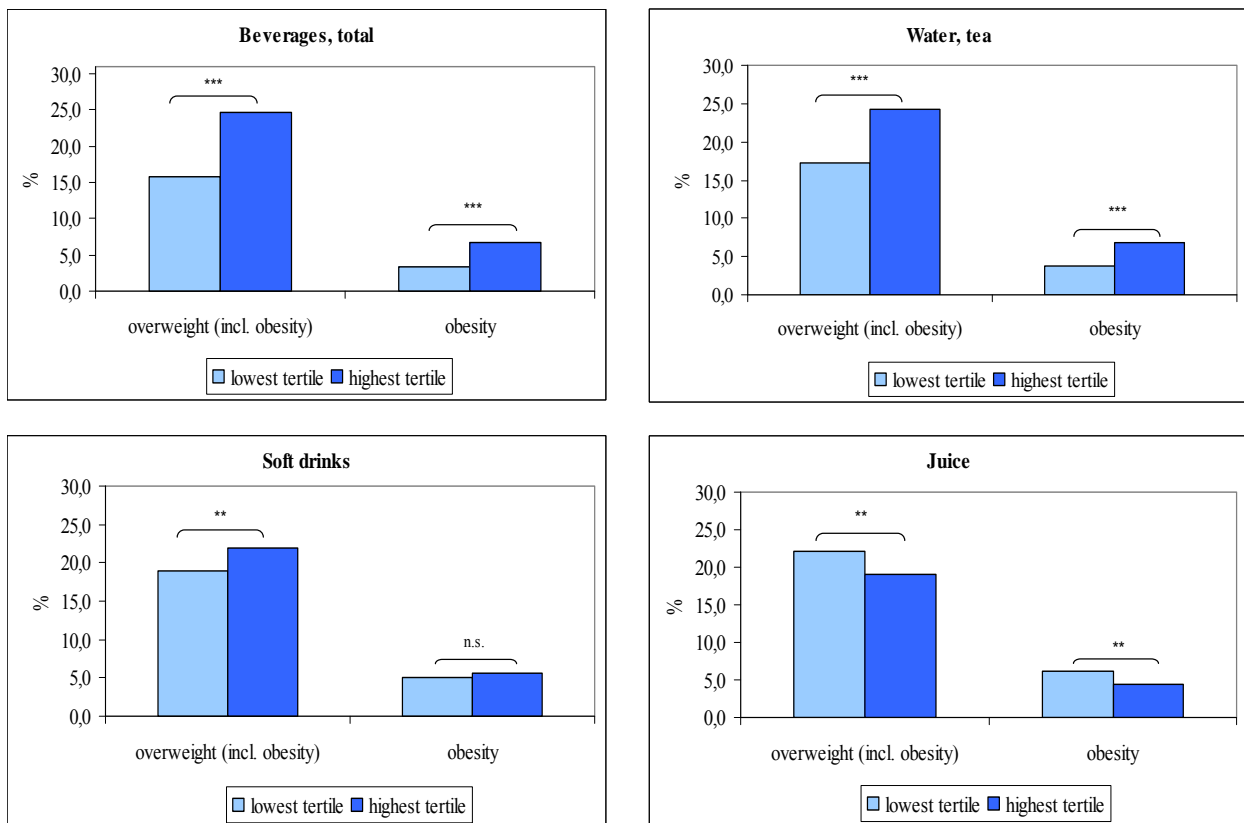


Figure 5: Frequency of overweight (including obesity) and obesity by lowest and highest tertiles of beverage intake [%]

N = 12792 participants, 3-17 year olds (underweight participants excluded)

p-value for lowest vs. highest tertile from univariable regression models with overweight or obesity as independent variable, adjusted for age and gender; * = $p < 0.05$; ** = $p < 0.01$; *** = $p < 0.01$

There was a statistically significant positive association between the intake of meat and sausages and both overweight and obesity. Furthermore, overweight was positively associated with the consumption fast food (fried sausage, curry sausage, hamburger, doner kebab) and

negatively associated with the intake of salty snacks (cracker, crisps, nuts) and butter/margarine (Figure 6). No significant association appeared between overweight and the consumption of vegetables and fresh fruit as well as for pasta/rice/potatoes, bread/cereals, milk/dairy products, fish, eggs, and sweets (Figure A-2 in the appendix).

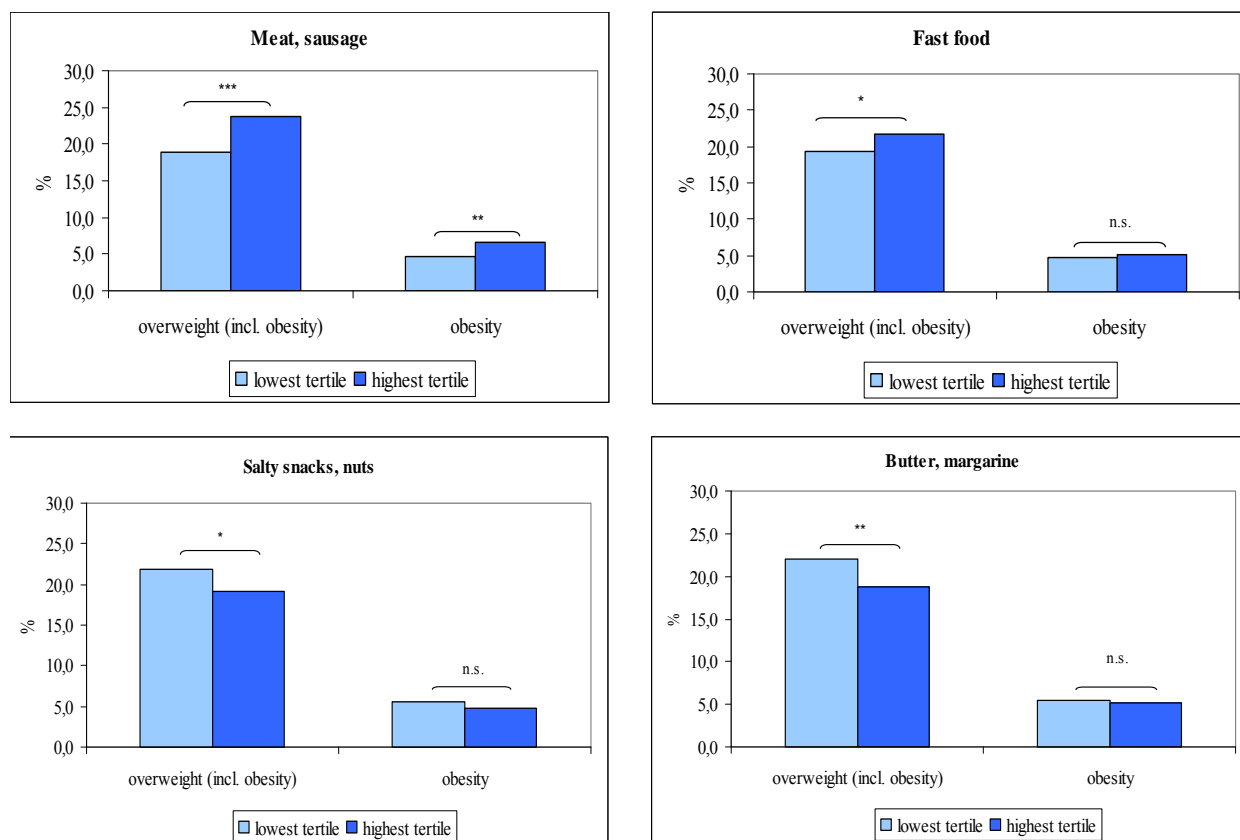


Figure 6: Frequency of overweight (including obesity) and obesity by lowest and highest tertiles of intake of meat/sausage, fast food, salty snacks/nuts, and butter/margarine [%]

N = 12792 participants, 3-17 year olds (underweight participants excluded)

p-value for lowest vs. highest tertile from univariable regression models with overweight or obesity as independent variable, adjusted for age and gender; * = $p < 0.05$; ** = $p < 0.01$; *** = $p < 0.001$

4.4.4 Multivariable analysis

The multivariable logistic regression model (Table 7) contains three significant qualitative interactions: the interaction of age with sleep duration, age with migration background, and the interaction of maternal weight status with high weight gain during pregnancy. The model showed a statistically significant independent positive association between obesity and the following variables: low SES, parental overweight, maternal smoking during pregnancy, high birth weight, and media consumption. Furthermore, migration background among 3-13 year olds and weight gain during pregnancy more than 20 kg (for normal weight mothers) were statistically significantly positively associated with obesity.

Table 7: Results of the multivariable logistic regression model with obesity as dependent variable, adjusted for age and gender, 3-17 years

	Odds ratio	95% CI	p-value
Socio-economic status			
Low	2.3	(1.6-3.2)	
Medium	1.5	(1.0-2.1)	
High	ref.	-	<0.001
Migration background (interaction with age)			
Migrant vs. Non-migrant ^{a)} , in 3-13 year olds	1.7	(1.1-2.4)	0.0105
Migrant vs. Non-migrant ^{a)} , in 14-17 year olds	0.7	(0.3-1.3)	0.2227
Parental overweight at time of interview (biological parents) (interaction with weight gain during pregnancy)			
<i>With weight gain during pregnancy ≤ 20 kg:</i>			
Both overweight/obese	11.2	(6.4-19.7)	
Mother overweight/obese	4.3	(2.2-8.6)	
Father overweight/obese	3.5	(2.0-6.3)	
None overweight/obese	ref.	-	
Incomplete data ^{b)}	4.7	(2.6-8.5)	<0.001
<i>With weight gain during pregnancy > 20 kg:</i>			
Both overweight/obese	2.8	(1.0-7.7)	
Mother overweight/obese	1.1	(0.4-3.1)	
Father overweight/obese	3.5	(2.0-6.3)	
None overweight/obese	ref.	-	
Incomplete data ^{b)}	2.2	(0.9-5.7)	<0.001
Parental smoking (at time of interview)			
Mother and/or father	1.3	(1.0-1.7)	0.0601
None	ref.	-	
Maternal smoking during pregnancy			
Yes	1.4	(1.0-1.8)	0.0267
No	ref.	-	
Weight gain during pregnancy (interaction with mother's current relative weight status)			
Mother normal weight: Weight gain during pregnancy >20 kg vs. ≤ 20 kg	2.8	(1.6-5.0)	0.0004
Mother overweight: Weight gain during pregnancy >20 kg vs. ≤20 kg	0.7	(0.3-1.6)	0.3971
Incomplete data ^{b)} : Weight gain during pregnancy >20 kg vs. ≤ 20 kg	1.3	(0.7-2.5)	0.4081
High birth weight			
Yes (> 4000 g)	1.9	(1.4-2.5)	<0.001
No	ref.	-	
Ever predominantly breastfed			
Yes	0.9	(0.7-1.1)	0.2970
No	ref.	-	
Sleep duration per 20 % increase in midranks (interaction with age)			
Sleep duration in 3-10 year olds	0.9	(0.8-1.0)	0.0461
Sleep duration in 11-17 year olds	1.0	(0.9-1.1)	0.8498
Media consumption (hours per day)	1.1	(1.0-1.2)	0.0107
Physical activity (times per week)	1.0	(0.9-1.0)	0.4514

N = 10021 participants, 3-17 year olds (after exclusion of underweight participants and those with missing data)

^{a)} Reference group, including children with a one-parent migration background.

^{b)} Children not living with both biological parents or for which information on the mother's and/or father's BMI is missing.

There was a negative association with obesity for sleep duration among 3-10 year olds. Parental overweight showed the strongest association with obesity. The OR for obesity was 11.2 for the offspring when both parents were overweight, compared to children with no overweight parents (with weight gain during pregnancy ≤ 20 kg). The OR for obesity when only the

mother (father) was overweight was 4.3 (3.5). Children and adolescents with low SES had a more than two times higher OR for obesity than those with high SES. No statistically significant association with obesity was seen for parental smoking at the time of interview, breastfeeding and physical activity. Furthermore, migration background among 14-17 year olds and sleep duration among 11-17 year olds were not statistically significantly associated with obesity.

4.4.5 Associations with SES

As shown in Table 8, the distribution of the presented determinants was less preferable among children and adolescents with low SES, compared to those with medium or high SES. The exceptions were a one-parent migration background and high birth weight, which showed a similar distribution in all SES groups. Parents of children and adolescents with low SES were more often overweight compared to parents of those with medium or high SES. This was also true when the participants with incomplete data on parental weight in the low SES group (which is mostly due to single-parent families) were excluded. Parents of children and adolescents with low SES smoked more often at time of interview and respective mothers smoked more often during pregnancy than those of children with higher SES. Furthermore, children and adolescents with low SES were less often predominantly breastfed, showed higher electronic media consumption, lower levels of physical activity, and a higher intake of energy-providing food and beverages.

Table 8: Distribution of potential determinants of obesity, differentiated by SES [% (95% CI)], 3-17 years

	Low SES N ^{a)} = 3655	Medium SES N ^{a)} = 6121	High SES N ^{a)} = 3326
Migration background			
One-parent	8.0 (6.8-9.2)	7.2 (6.3-8.1)	9.0 (7.6-10.4)
Two-parent	31.0 (27.3-34.7)	12.5 (10.7-14.3)	6.0 (4.8-7.2)
Non-Migrant	61.0 (56.8-65.2)	80.3 (78.0-82.5)	85.0 (82.9-87.1)
Parental overweight at time of interview (biological parents)			
Both overweight or obese	24.1 (22.4-25.9)	21.9 (20.5-23.3)	14.9 (13.4-16.3)
Mother overweight or obese	8.3 (7.3-9.4)	8.8 (7.8-9.7)	6.9 (6.0-7.9)
Father overweight or obese	19.2 (17.6-20.7)	27.5 (26.0-29.0)	31.3 (29.6-33.1)
None overweight or obese	11.3 (10.0-12.6)	20.0 (18.7-21.3)	32.4 (30.5-34.4)
Incomplete data ^{b)}	37.1 (34.8-39.3)	21.9 (20.3-23.4)	14.5 (13.0-16.0)
Parental smoking (at time of interview)			
Father and mother smoke	31.0 (28.8-33.3)	18.7 (17.5-19.9)	11.2 (9.9-12.6)
Only mother smokes ^{c)}	10.8 (9.6-12.1)	11.6 (10.7-12.6)	8.4 (7.3-9.6)
Only father smokes	23.5 (21.6-25.3)	20.2 (19.0-21.5)	15.1 (13.5-16.7)
Neither mother nor father smokes	34.6 (32.1-37.2)	49.4 (47.7-51.1)	65.2 (63.1-67.3)
Maternal smoking during pregnancy			
Yes	30.4 (28.4-32.4)	16.6 (15.4-17.9)	8.3 (7.1-9.5)
No	69.6 (67.5-71.6)	83.4 (82.1-84.6)	91.7 (90.5-92.9)
High birth weight			
Yes (> 4000 g)	10.6 (9.4-11.8)	11.3 (10.2-12.3)	11.8 (10.6-12.9)
No	89.4 (88.2-90.6)	88.7 (87.7-89.8)	88.2 (87.1-89.4)
Ever predominantly breastfed			
Yes	53.6 (51.0-56.2)	65.9 (64.0-67.9)	78.7 (76.9-80.6)
No	46.4 (43.8-49.0)	34.1 (32.1-36.0)	21.3 (19.4-23.1)
Media consumption			
Lowest tertile	24.0 (22.2-25.8)	33.3 (31.7-35.0)	48.2 (45.3-51.1)
Middle tertile	32.3 (30.3-34.3)	33.4 (31.9-34.9)	32.2 (29.9-34.6)
Highest tertile	43.7 (41.4-46.0)	33.3 (31.5-35.2)	19.6 (17.7-21.4)
Physical activity			
Lowest tertile	42.5 (40.6-44.3)	34.8 (33.2-36.4)	26.8 (24.8-28.7)
Middle tertile	29.7 (27.9-31.5)	34.2 (32.9-35.5)	37.6 (35.6-39.6)
Highest tertile	27.9 (26.0-29.7)	31.0 (29.5-32.6)	35.7 (33.6-37.8)
Intake of energy-providing food and beverages			
Lowest tertile	30.4 (28.2-32.5)	35.6 (33.8-37.3)	36.3 (34.3-38.3)
Middle tertile	28.6 (26.9-30.3)	34.2 (32.6-35.8)	37.8 (36.0-39.6)
Highest tertile	41.0 (38.9-43.2)	30.2 (28.5-32.0)	25.9 (24.0-27.8)

N = 13102 participants, 3-17 year olds (after exclusion of underweight participants and those with missing data in SES)

a) unweighted

b) Children not living with both biological parents or for which information on the mother's and/or father's BMI is missing.

c) Father doesn't smoke or no information on the father available.

Table 9 shows the frequency of obesity according to potential determinants, differentiated by SES groups. Included were only potential determinants which showed a statistically significant univariable interaction with SES. The highest frequency of obesity was found among children and adolescents with low SES of which both parents are overweight (12.4%). With the exception of parental overweight, the data showed that children and adolescents with low SES, although they had favourable levels of other potential determinants, were more often obese than those with medium or high SES, even if the latter had unfavourable levels of those determinants. As an example, the frequency of obesity among those with low SES but low

media consumption was higher than among those with medium or high SES and high media consumption.

Table 9: Frequency of obesity according to potential determinants, differentiated by SES [% (95% CI)]

	Low SES N ^{a)} = 3655		Medium SES N ^{a)} = 6121		High SES N ^{a)} = 3326	
Parental overweight at time of interview ^{b)}						
Both overweight or obese	12.4	(10.1-14.7)	10.6	(8.6-12.5)	7.3	(4.9-9.8)
Mother overweight or obese	8.9	(4.7-13.2)	2.6	(0.9-4.4)	2.7	(0.2-5.1)
Father overweight or obese	5.6	(3.4-7.8)	3.4	(2.4-4.5)	2.7	(1.7-3.6)
None overweight or obese	3.6	(1.7-5.5)	0.9	(0.3-1.4)	0.5	(0.1-0.9)
Incomplete data ^{c)}	10.0	(8.2-11.8)	4.8	(3.6-6.0)	1.9	(0.6-3.2)
Ever predominantly breastfed						
Yes	8.4	(7.0-9.9)	4.0	(3.2-4.7)	1.8	(1.2-2.4)
No	9.7	(7.9-11.5)	6.4	(4.9-8.0)	4.7	(3.0-6.3)
Media consumption						
Low	9.6	(7.2-12.1)	2.7	(1.9-3.4)	1.7	(1.1-2.4)
Middle	7.3	(5.6-9.1)	4.3	(3.3-5.4)	2.7	(1.7-3.8)
High	9.1	(7.4-10.9)	7.0	(5.7-8.3)	3.8	(2.2-5.5)

N = 13102 participants, 3-17 year olds (after exclusion of underweight participants and those with missing data in SES)

a) unweighted

b) biological parents

c) Children not living with both biological parents or for which information on the mother's and/or father's BMI is missing.

4.5 Discussion

4.5.1 Personal and social factors

Consistent with other studies^{79, 97}, the strongest determinant in the multivariable analysis was parental overweight. When both parents were overweight the risk of obesity for the offspring was increased 11-fold (in case of a low weight gain during pregnancy). If only one parent was overweight, the OR was still higher than that for any other determinant in the model. The ORs changed by approximately 10% when the analysis was extended to include all parents, biological as well as social ones. The strong association with parental overweight may be explained by genetic, as well as environmental and behavioural factors^{79, 94, 95}. A recent twin-study concluded that genetic factors play an important role in determining which children become obese in a changed environment⁹⁴. However, the secular increase in obesity rates cannot be explained by genetic variation alone. It is an example for gene-environment interactions. Furthermore, (inherited) behaviour plays an important role and the so called mere exposure effect provides a link between parental behaviour and those of the offspring. This effect describes the phenomenon that attitudes, for instance to a specific behaviour, will be positively influenced just because one gets familiar with them. For example, it has been shown

that the repeated experience of tasting and eating an unknown food reduces the tendency to dislike this food¹⁴⁵. Beside social influences, the mere exposure effect is supposed to be one of the major process that modifies (food) preferences.

SES was statistically significantly associated with overweight and obesity. Furthermore, almost all analysed potential determinants of obesity were more prevalent among children and adolescents with low SES. Obesity occurred significantly more often among the low SES group, even among those with favourable behaviours, compared to those with medium or high SES and unfavourable behaviours. The relationship between low SES and overweight is complicated. For example, a low SES can lead to overweight by unfavourable environmental factors, a certain lifestyle, lower education and knowledge, and financial constraints^{245, 246}. In turn, it may also be possible that overweight and in particular obesity lead to lower SES by, for example, social discrimination, physical impairment and inability to undertake work. However, among children, usually parents' data are used to quantify SES. Thus, the direction seems to be trivial, since an overweight or obese child would not affect the parents' socioeconomic situation. The complexity of the association between SES and overweight in the present analysis is illustrated by the fact that the group with incomplete data on parental overweight showed a higher obesity risk than those with none or just one overweight parent. Incomplete data in parental overweight mainly occurred due to single-parent families. These families more often have a low SES. This in turn might be due to less income and the difficulty to manage job and family, especially for single mothers.

Up to the age of 13, children with a two-parent migration background showed a higher obesity risk than those with a one-parent or no migration background. It may be that this difference disappeared at higher ages because adolescent migrants behave more similarly to native Germans than younger migrants. For example, it has been shown that acculturation, which in turn is related to duration of stay, changed dietary patterns among migrants^{247, 248}. Another explanation for this interaction may be different participation patterns among older adolescent migrants.

Migrants were more often obese than non-migrants within every SES group. Similar results have been found for some ethnic minorities in the US^{249, 250}. Although SES explained some of the impact of the migration background (and vice versa), migration background remained an independent determinant which also reflects culturally determined attitudes and behav-

iors^{90, 251}. For example, considerable differences in food intake between children and adolescents with and without a migration background have been shown. In particular, migrants of Turkish or Russian origin showed a less preferable diet compared to non-migrants²⁵². However, it remains unclear whether primarily cultural aspects contribute to the development of overweight or if migration is associated with lower SES for example by lower education and/or lower income. Furthermore, different genetic constitutions and behaviour among migrants and non-migrants is possible.

An association between pubertal stage and obesity was observed in this thesis only on the univariable level. The direction of the relationship between weight status and the onset of puberty remained unclear. An early onset of puberty might be more a consequence of obesity and there is no evidence on the other hand that an early onset of puberty is a risk factor for obesity. It is suggested that obesity is causally related to an earlier onset of puberty, at least among girls^{253, 254}. One explanation is that leptin provides the link between body fat and the onset of puberty by affecting gonadotropin secretion²⁵⁴.

Furthermore, a univariable association between obesity and indication of eating disorders has been found but the causal relationship is unclear. It was shown that both overweight and obese 11-17 year olds more often showed symptoms of eating disorders than non-overweight age-mates. This highlights the importance of taking psychological factors into account when tackling the obesity problem, and it reminds one that prevention and intervention measures must take care not to increase the psycho-social burden of overweight and obesity.

4.5.2 Early life factors

As discussed in detail in Chapter 2.3.3 early life is an essential period for the development of overweight in later life, comprising among other things the intrauterine environment, the behaviour of the pregnant women, and the physical development of the offspring. The importance of maternal smoking during pregnancy, high weight gain during pregnancy, and high birth weight observed in the present analyses was also seen in other studies^{79, 97, 103, 108}.

The present data showed a significant interaction between high weight gain during pregnancy and maternal overweight, as was noticed before in a simultaneously conducted analysis of this dataset²⁵⁵. For overweight mothers, high weight gain during pregnancy was not associated with obesity in the offspring, but was for normal weight mothers. The association between

weight gain in pregnancy and obesity in the offspring might be mediated by high birth weight, and the mediation effect might be different between normal weight and overweight mothers. An additional analysis without high birth weight was also run but the odds ratios changed by less than 10%, so this cannot be the main explanation for the interaction effect. Weight gain in pregnancy has been found to increase with maternal BMI. However, the variability was higher in overweight women and mean weight gain was less in obese as compared to overweight (but not obese) women²⁵⁶. A potential explanation for the interaction effect could be that changes in the intrauterine environment in overweight mothers are similar to the changes occurring with high weight gain during pregnancy. Therefore, the coexistence of both factors may confer no additional increase in obesity risk in the offspring.

High birth weight is an independent risk factor for obesity in the present analysis. The OR changed only marginally in the multivariable model compared to the OR calculated in the univariable analysis. Birth weight is an indicator of prenatal growth. As mentioned before, the metabolic programming during gestation as well as the intrauterine environment may also play an important role for the association between birth weight and obesity in later life¹¹¹.

The present results confirmed the observed association between maternal smoking during pregnancy and overweight in the offspring^{103, 104}, even after controlling for current parental smoking. The variable “mother or father smokes at the time of interview” was used in addition to smoking in pregnancy in the multivariable model. Parental smoking at the time of interview was only marginally significant. However, when restricted to daily smokers, it remained significant in the multivariable model. Hence, smoking of the parents is a marker for families with a higher obesity risk, especially when both parents smoke regularly. Additionally, smoking during pregnancy is associated with several other risk factors such as parental overweight, low birth weight, low physical activity and higher television viewing^{77, 79, 97, 126}. Therefore, maternal smoking can be interpreted as an indicator for suboptimal health behaviour in general and may be an indicator that explains part of the socio-economic differences in the prevalence of childhood obesity. Furthermore it is suggested that smoking during pregnancy influences the intrauterine environment, is involved in programming the appetite regulation¹⁰³ and is associated with low birth weight²⁵⁷. Often children with low birth weight have a high increase in weight and height during the first year of life (catch-up-growth) which is associated with later obesity^{85, 258}.

A recent meta-analysis as well as a recent review concluded that breastfeeding has a protective effect against overweight in later life ^{77, 121}. This association was not confirmed in the multivariable analysis of the present study. There may also be interactions with other parameters such as smoking during pregnancy. As Reilly et al. ⁷⁹ determined, the risk for obesity was decreased when the child was breastfed and the mother did not smoke during pregnancy. When the mother smoked during pregnancy, a decreased risk by breastfeeding was not observed any longer. These findings might also occur due to methodological weaknesses of the cited study, since the analysed groups were small. Furthermore, a large randomized intervention trial recently found no effect of breastfeeding on adiposity in 6-year olds ²⁵⁹. Thus, the positive effects of breastfeeding found in observational studies might be partly due to uncontrolled confounding or selection bias.

4.5.3 Life style factors

Previous findings focussing on the association between lifestyle factors and overweight (in particular those on dietary behaviour and physical activity) are inconsistent, as described in detail in Chapter 2.3.4. In the present study, for some food groups (for example total intake of energy-providing food, total beverage intake, consumption of meat and sausages), differences in consumption were found between children and adolescent with and without overweight and obesity. In contrast, there was no significant association between obesity and the total consumption of energy-providing food on the multivariable level. Furthermore, no association between overall dietary quality, assessed with the HuSKY, and overweight was observed in the present analysis. However, the HuSKY does not primarily aim to reflect an association between dietary behaviour and overweight but was constructed to capture “healthy eating habits” and to reflect the agreement with the current recommendations on dietary intake ²⁴². Preventing overweight is not the primary objective of those recommendations. Furthermore, the HuSKY provides no information about total energy intake. Therefore, an association between overweight and the HuSKY may be not expected.

Physical activity was associated with overweight and obesity in the univariable analysis. But, the observed association between physical activity and obesity disappeared after further adjustments. This may be mainly due to the fact that physical activity is only marginally assessed. A major problem in correlating weight status and physical activity as well as food intake is the inaccurate measurement of both behavioural aspects in large-scale epidemiologic studies. Instruments for measuring dietary intake and physical activity are often not precisely

enough to draw exact conclusions about energy intake and expenditure. This is also true for the instruments used in the KiGGS study. In addition, cross-sectional studies are of limited predictive ability. However, longitudinal studies may be able to show the association between energy imbalance and body fat mass²⁶⁰. For the development of overweight a long-term positive energy balance is crucial (rather than an unhealthy food pattern). The methodological problems in detecting the association between dietary behaviour, and in particular energy balance, and overweight are discussed in more detail in Chapter 7.2.

In the present analyses, children and adolescents with high electronic media consumption time were more often overweight and more often obese than those with lower media consumption time. Media consumption time, as an indicator of sedentary behaviour during leisure time, might be easier to assess than total physical activity, especially in children. Overall, the observed impact of media time per hour was small. When television watching in hours per day was considered independently from other media consumption in the multivariable model, the OR was slightly higher compared to the OR for total media consumption. This was also seen in a recent study among Spanish adolescents¹³⁵. This implies that television watching is currently the most important sedentary behaviour in relation to overweight and obesity.

The causal direction between media consumption, physical activity and overweight and obesity also remained unclear and a relationship in both directions is possible. On the one hand, overweight people may spend more time using electronic media and may be less motivated to take exercise because they are overweight. On the other hand, they may be overweight because they spent more time with sedentary behaviour which may contribute to a positive energy balance. However, a high level of electronic media consumption does not necessarily have to go together with a low level of physical activity. Nevertheless, a randomized controlled trial showed that children who reduced the use of television, videotape and videogame had a significant decrease in various overweight measures²⁶¹.

In the present analyses, there was only a negative association between duration of sleep and obesity among children 3-10 years of age. The association between a low sleeping time and higher prevalence of obesity was observed in several previous studies among children^{138, 139, 142}. In line with the present findings, recent reviews have reported a stronger association of obesity with sleep duration in younger children, at least when compared to adults¹⁴⁰⁻¹⁴². The differences in the findings with age in the present data could also be due to

methodological differences. Among 11-17 year olds, only sleep duration in the last night was documented, whereas average sleep duration was requested among children aged 3-10 years. The causality of sleep duration and obesity is still discussed ¹⁴¹.

In summary, the present results highlight the complex nature of overweight and obesity. Parental overweight was identified as the major determinant of childhood and adolescence overweight and obesity. Further independent potential determinants for obesity were low SES, maternal smoking during pregnancy, high birth weight, and high media consumption. There were interactions between migration background and age, weight gain during pregnancy and weight status of the mother as well as between sleep duration and age. Overweight and obesity occurred more often among children and adolescents with low SES and this group showed the most unfavourable conditions in general.

**5 RESULTS: ASSOCIATION BETWEEN OVERWEIGHT AND CVD
RISK FACTORS**

As described in detail in Chapter 2.4, there is increasing evidence that even among children and adolescents obesity is associated with several CVD risk factors such as high blood pressure, adverse lipid profile, and insulin resistance. The practical implications of these associations are less clear. In addition, it is still unclear which measure of childhood obesity is the best predictor for adverse health outcomes. If waist circumference and/or waist-to-height ratio alone or in combination with BMI may be more useful for risk assessment in children and adolescents than BMI itself, is a subject of the current research. Most previous studies were clinic-based or included rather small, non-representative population samples. With the present study, it will be possible to examine the relationship between major CVD risk factors and various measures of body weight and body fat distribution using a large representative dataset. The aim of this chapter is to analyse if there is a consistent and clinically relevant association between different measures of overweight and CVD risk factors among children and adolescents. Furthermore, the measures of overweight showing the strongest association with CVD risk factors will be identified.

5.1 Sample

For the present analysis, participants with chronic health problems or on current medication likely to affect one or more of the considered CVD risk factors have been excluded. These included children and adolescents with a history of type 1 diabetes mellitus (N = 20) or hypertension (N = 30), participants on lipid lowering drugs (N = 12), antidiabetic medication (N = 12), glucocorticosteroids (N = 22) or antihypertensives (N = 25) and girls taking oral contraceptives (N = 429). Furthermore, participants with CRP-levels of 10 mg/l and higher (N = 259) and participants for whom anthropometric (N = 365) or laboratory variables (N = 1951) were incomplete have been excluded. Overall, out of 14836 participants 3-17 years of age 3062 were excluded. Thus, the analyses are based on data of the net study sample of 11774 children and adolescents, with 6228 participants aged 3-10 years (3190 boys, 3038 girls) and 5546 participants aged 11-17 years (3031 boys, 2515 girls).

5.2 Use of study variables

In addition to BMI, as described before, the ratio of WC to HC (waist-to-hip ratio, WHR), the ratio of WC to body height (waist-to-height ratio, WHtR) and the sum of two skinfold thickness measures were calculated. To provide a systematic comparison of different overweight measures, overweight was defined as values exceeding the 90th age and sex

specific percentile ($> P90$) of the net study sample of at least one of the following anthropometric measurements: BMI, WC, WHR, WHtR, and skinfold thickness measures (triceps, subscapular and sum of skinfold thickness).

The arithmetic mean of the two measured values of SBP and DBP was used for the present analysis. The 90th age and sex specific percentile was used to define elevated levels of SBP and DBP (Table A-3 in the appendix). The respective percentiles are based on the KiGGS population with exclusion of children and adolescents suffering from chronic diseases and/or on medication that influences growth or height development (personal communication). The 90th age and sex specific percentile of the total KiGGS population was used to define elevated serum concentrations of TC, LDL-C, and HbA1c. The 10th age and sex specific percentile of HDL-C was taken as cutoff point for low serum HDL-C (Tables A-4 and A-5). Serum hs-CRP was dichotomised at 2.1 mg/l, as this cutoff value was previously applied in large epidemiological studies of children and adolescents^{187, 188}.

Furthermore, among 11-17 year olds a variable was constructed defining children and adolescents with high risk of CVD (yes/no), using the same percentile values as described above. A high CVD risk was defined when at least three of the following conditions were met:

- TC above the 90th age and sex specific percentile
- LDL-C above the 90th age and sex specific percentile
- HDL-C below the 10th age and sex specific percentile
- SBP above the 90th age and sex specific percentile
- DPB above the 90th age and sex specific percentile
- hs-CRP above 2.1 mg/l

5.3 Statistical analysis

All analyses of the association between cardiovascular disease risk factors and overweight were stratified by sex and age groups (3-10 years and 11-17 years) and used sampling weights as described in brief in Chapter 3.2 and in detail elsewhere²²⁸. The SAS survey procedures (SAS version 9.2)²⁴⁴ were applied in order to take the clustered sampling design into account. A p-value < 0.05 was considered to be statistically significant based on two-sided tests. Descriptive statistics were computed for all continuous study variables. Means and corresponding 95% confidence intervals are presented, stratified according to age group and

sex. Univariable regression models were conducted to evaluate statistically significant differences between boys and girls and age groups (3-6 years versus 7-10 years and 11-13 years versus 14-17 years). Means and corresponding confidence intervals of CVD risk factors according to age group, sex, and measure of overweight were calculated and graphically presented.

The prevalence of boys and girls with adverse CVD risk factors levels was assessed according to overweight ($> P90$ versus $\leq P90$). Separate analyses were calculated for each CVD risk factor and overweight measure. Corresponding p-values were calculated by modified chi square test.

Furthermore, separate linear regression models were calculated with individual CVD risk factors as dependent variables and the different measures of overweight as explanatory variable of main interest. Among 3-6 year olds regression models were adjusted for age in years and among 11-17 year olds additionally for pubertal stage as categorical variables. The coefficient of determination (R-squared) of the regression models was used to estimate the proportion of variability explained by the model. Additionally, among 11-17 year olds, the joint impact of BMI, WC and WHtR was tested, using combined variables of BMI, WC, and WHtR (for example, exceeding the 90th percentile of BMI and exceeding the 90th percentile of WC) and by entering BMI and WC as well as BMI and WHtR into the linear regression model, simultaneously. Among 11-17 year olds it was also tested if the association between overweight and CVD risk factors may occur due to uncontrolled confounding. Therefore, the regression models were adjusted for physical activity, smoking behaviour and regular alcohol consumption using the variables as described in Chapter 4.2.

Separate logistic regression models adjusted for age among 3-6 year olds and among 11-17 year olds additionally adjusted for pubertal stage were used to estimate odds ratios (OR) and 95% confidence intervals (CI) for exceeding the defined cutoffs for the various CVD risk factors in relation to the different overweight measures ($> P90$ versus $\leq P90$). Furthermore, among 11-17 year olds logistic regression models were calculated for boys and girls with the variable high CVD risk (yes/no) as dependent variable and different measures of overweight as independent variable, adjusted for age in years and pubertal stage.

Due to the differences in the obtained data, the following results are separately presented for children 3-10 years of age and children and adolescents aged 11-17 years. For example, for

children aged 3-10 years there is no information about WC, WHR, and WHtR. Therefore, only BMI and skinfold thickness have been compared and no combinations of anthropometric measures were calculated.

5.4 Results

As presented in Table 10, the study population for the analysis of the association between overweight and CVD risk factors included more boys than girls. The weighted proportion of the age groups ranged from 22% to almost 30%. About 65% of the 10-17 year olds were at post-pubertal stage. Pubertal stage was not assessed among children younger than 10 years of age. Almost 4% of the boys and 3% of the girls were defined to have a high CVD risk.

Table 10: Descriptive characteristics of the study population for the analysis of the association between overweight and CVD risk factors, 3-17 years

		N unweighted	Percentage (%) weighted
Gender	Boys	6221	53.2
	Girls	5553	46.8
Age group	3-6 years	2773	21.9
	7-10 years	3455	26.5
	11-13 years	2676	22.0
	14-17 years	2870	29.6
	Missing value or not assessed (3-9 years)	5497	
Pubertal stage (10-17 years)	Pre-pubertal	864	11.8
	Pubertal	1590	22.8
	Post-pubertal	3823	65.4
	Missing value or not assessed (3-9 years)	5497	
High CVD risk (11-17 years)	Boys		
	Yes	119	3.9
	No	2912	96.1
	Girls		
	Yes	75	3.0
	No	2440	97.0

5.4.1 Results for children 3-10 years of age

As shown in Table 11, mean body height, weight, BMI, and skinfold thickness, serum levels of TC, HDL-C as well as SBP and DBP increased significantly with age group in both sexes while levels of hs-CRP decreased ($p < 0.001$). LDL-C differs only slightly between age groups and there are no statistically significant differences in HbA1c according to age group and gender. Mean skinfold thickness as well as serum levels of TC and LDL-C were consistently higher for girls than for boys and levels of hs-CRP were significantly lower among girls ($p < 0.001$). There were no consistent gender differences in blood pressure levels.

Table 11: Means and 95% confidence intervals of anthropometric data and cardiovascular risk factors according to age group and gender, 3-10 years

	Boys		Girls	
	3-6 years (N = 1413)	7-10 years (N = 1777)	3-6 years (N = 1360)	7-10 years (N = 1678)
Height [cm]	112.3 (111.8-112.8)	136.1 (135.6-136.5)	111.6 (111.2-112.1)	135.3 (134.8-135.7)
Weight [kg]	20.1 (19.9-20.3)	32.3 (31.9-32.7)	19.8 (19.5-20.0)	31.9 (31.5-32.3)
BMI [kg/m ²]	15.8 (15.7-15.9)	17.3 (17.1-17.4)	15.7 (15.6-15.8)	17.2 (17.0-17.3)
Triceps skinfold thickness [mm]	10.1 (9.9-10.3)	12.2 (11.9-12.5)	11.6 (11.4-11.8)	14.0 (13.7-14.3)
Subscapular skinfold thickness [mm]	5.8 (5.7-5.9)	7.4 (7.2-7.7)	6.6 (6.4-6.7)	8.7 (8.4-9.0)
Sum of skinfold thickness [mm]	15.9 (15.7-16.2)	19.6 (19.1-20.1)	18.2 (17.8-18.5)	22.8 (22.2-23.3)
Total cholesterol [mg/dl]	164.0 (162.2-165.8)	166.3 (164.9-167.8)	167.5 (165.6-169.3)	171.0 (169.4-172.6)
LDL-cholesterol [mg/dl]	96.0 (94.3-97.6)	94.0 (92.8-95.3)	98.9 (97.2-100.6)	99.5 (98.1-101.0)
HDL-cholesterol [mg/dl]	55.8 (54.9-56.6)	60.3 (59.6-61.1)	55.0 (54.2-55.8)	58.8 (58.1-59.4)
Systolic blood pressure [mm Hg]	97.9 (97.4-98.5)	103.0 (102.4-103.4)	98.3 (97.8-98.8)	103.3 (102.8-103.8)
Diastolic blood pressure [mm Hg]	59.6 (59.1-60.0)	63.0 (62.6-63.4)	60.3 (59.9-60.7)	63.0 (62.6-63.4)
Glycosylated haemoglobin [%]	4.9 (4.8-4.9)	4.9 (4.9-4.9)	4.8 (4.8-4.9)	4.9 (4.8-4.9)
High sensitivity C-reactive protein [mg/l]	0.9 (0.7-1.0)	0.7 (0.6-0.7)	1.0 (0.9-1.1)	0.9 (0.8-1.0)

Figures 7 to 9 show mean values of CVD risk factors according to age group, gender, and overweight measure. Arithmetic means and corresponding confidence intervals were calculated differentiated by overweight ($> P90$, \times) and normal weight ($\leq P90$, $-$) children and separately presented for boys and girls as well as for age groups (3-6 years, 7-10 years). Non-overlapping confidence intervals indicate statistically significant differences. There was only a tendency of higher mean serum levels of TC and LDL-C among overweight boys compared to normal weight boys. Among girls, the results were inconsistent. Among 7-10 year old boys and girls, mean serum levels of HDL-C were significantly lower in overweight than in normal weight children (Figure 7).

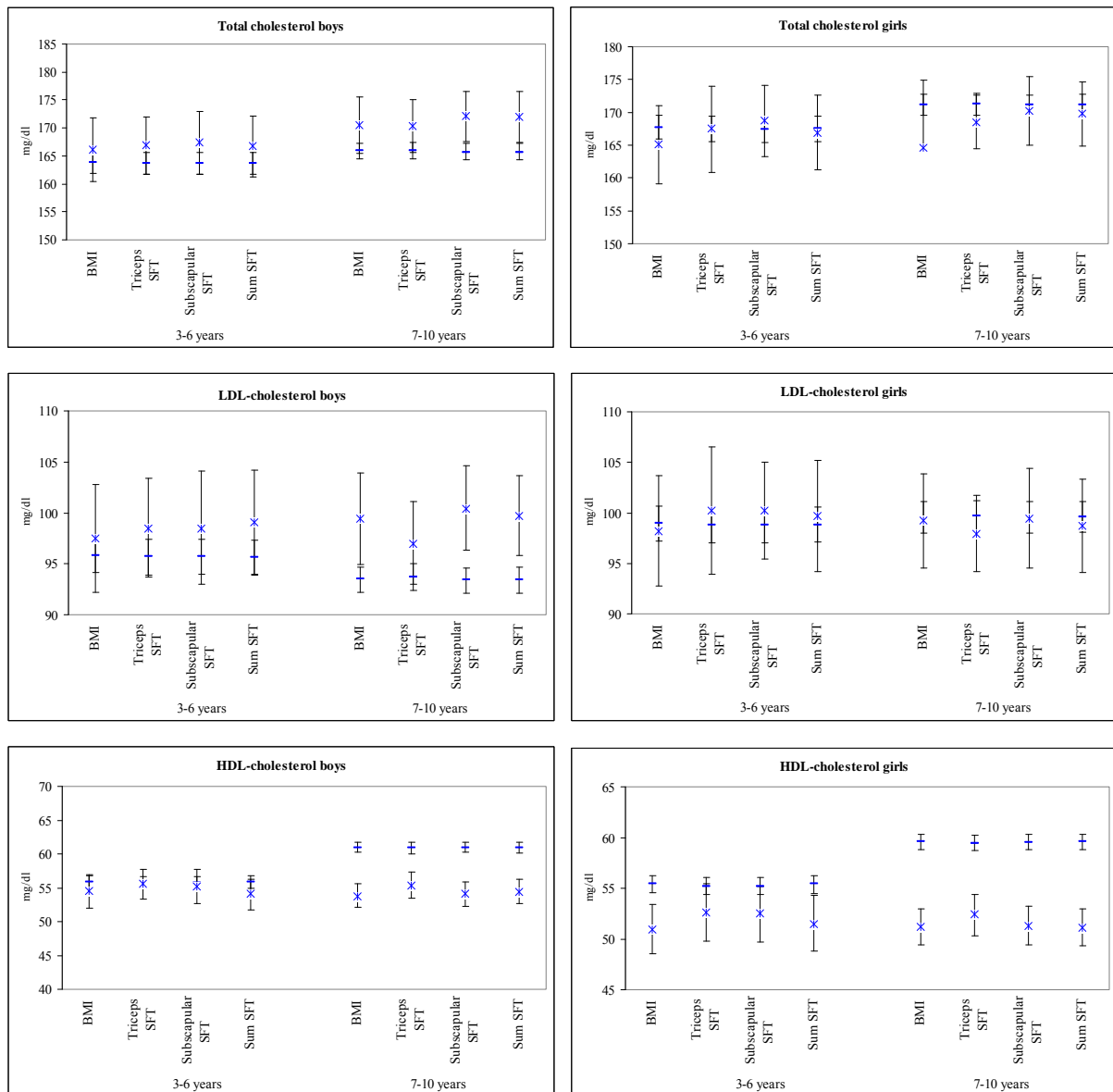


Figure 7: Means and 95% confidence intervals for serum lipoproteins according to age group, gender and different measures of overweight, dichotomised at the 90th age and sex specific percentile, 3-10 years

- normal weight ($\leq 90^{\text{th}}$ percentile)

x overweight ($> 90^{\text{th}}$ percentile)

BMI: body mass index, SFT: skinfold thickness

Consistently, among the age groups 3-6 years and 7-10 years, boys and girls with overweight had higher mean SBP and DBP (Figure 8). Among 7-10 year olds, mean hs-CRP were higher in overweight compared to normal weight children (Figure 9).

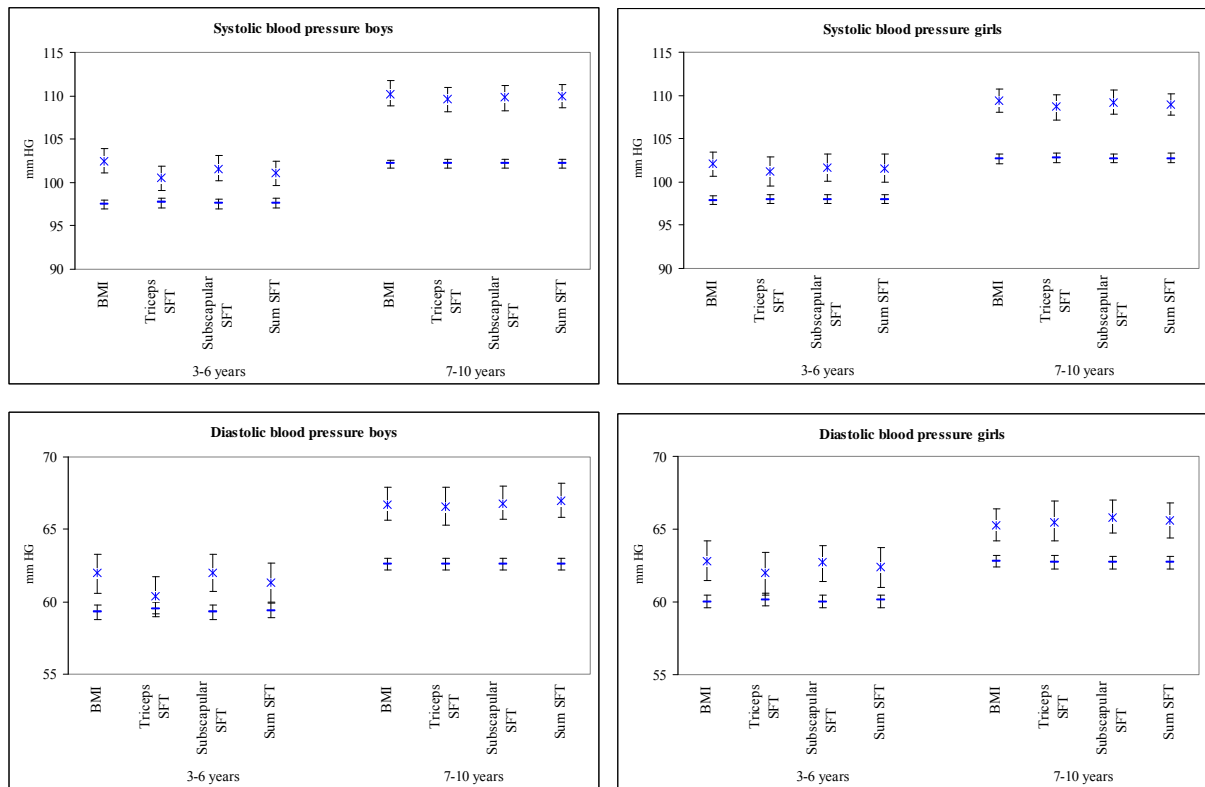


Figure 8: Means and 95% confidence intervals for blood pressure according to age group, gender and different measures of overweight, dichotomised at the 90th age and sex specific percentile, 3-10 years

- normal weight ($\leq 90^{\text{th}}$ percentile)
 × overweight ($> 90^{\text{th}}$ percentile)
 BMI: body mass index, SFT: skinfold thickness

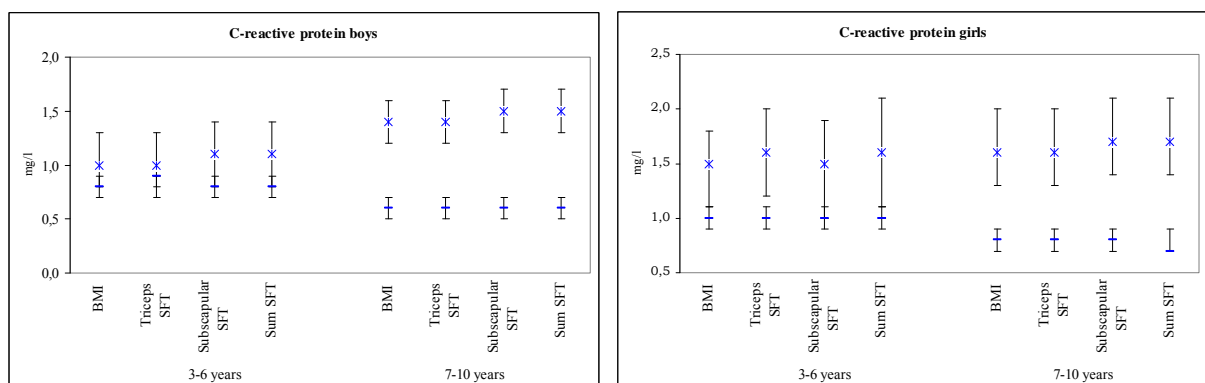


Figure 9: Means and 95% confidence intervals for hs-CRP according to age group, gender and different measures of overweight, dichotomised at the 90th age and sex specific percentile, 3-10 years

- normal weight ($\leq 90^{\text{th}}$ percentile)
 × overweight ($> 90^{\text{th}}$ percentile)
 BMI: body mass index, SFT: skinfold thickness

Prevalences of children exceeding the defined cutoffs for CVD risk factors were predominantly higher for overweight children ($> P90$) according to each different indicator of overweight compared to those with normal weight (Table 12). Statistically significantly higher prevalences are most pronounced for HDL-C, SBP, DBP, and hs-CRP. For example, 29.9% of boys and 22.3% of girls with BMI $> P90$ had elevated SBP compared to 8.8% of boys and 8.2% of girls with BMI $\leq P90$ ($p < 0.001$).

The results from the linear regression models in Table 13 showed that even among boys and girls 3-10 years of age there is a significant association between overweight and HDL-C, SBP, DBP, and hs-CRP. For example, age adjusted differences in mean CVD risk factors between those with and without overweight were up to 6.6 mm Hg for SBP, 3.5 mm Hg for DBP, -6.5 mg/dl for HDL-C, and 0.8 mg/l for hs-CRP. However, there was no or only a weak association with TC, LDL-C and HbA1c. Furthermore, no measure of overweight consistently showed the strongest association with adverse CVD risk factors. Among boys and girls, BMI showed the strongest association with HDL-C and SBP, the sum of skinfold thickness with hs-CRP and subscapular skinfold thickness with DBP. Except for hs-CRP, age explained more of the variability in the dependent CVD variables compared to the different measures of overweight. This is shown when the R-squared with only age included in the model is compared with those for the models additionally including overweight.

Odds ratios and 95% confidence intervals for exceeding cutoffs for the various CVD risk factors in relation to the different overweight measures ($> P90$ versus $\leq P90$) are shown in Table 14. For example, boys and girls with overweight according to any of the chosen measure showed significant age adjusted ORs between 1.7 and 3.2 for low serum HDL-C. Adjusted ORs for elevated serum SBP ranged from 2.8 to 4.5, those for DBP from 1.8 to 2.6, and those for serum hs-CRP above 2.1 mg/l from 2.4 to 3.2. There were no consistent associations between overweight and TC, LDL-C, and HbA1c. Furthermore, none of the indicators of overweight showed consistently higher ORs for adverse CVD risk factors than any other.

Table 12: Prevalence [% (95% CI)] of children exceeding defined cutoffs for individual CVD risk factors according to different measures of overweight dichotomised at the age and sex specific 90th percentile, 3-10 years

	BMI ≤ P90	BMI > P90	Triceps SFT ≤ P90	Triceps SFT > P90	Subscap SFT ≤ P90	Subscap SFT > P90	Sum of SFT ≤ P90	Sum of SFT > P90
Boys	N = 2862	N = 328	N = 2867	N = 323	N = 2864	N = 326	N = 2857	N = 333
Total cholesterol > P90 (N = 295)	8.8 (7.5-10.1)	15.0** (10.5-19.6)	9.1 (7.9-10.4)	11.8 ^{n.s.} (7.5-16.1)	8.8 (7.5-10.1)	15.4** (10.9-19.9)	8.8 (7.5-10.0)	15.1* (10.4-19.8)
LDL-cholesterol > P90 (N = 310)	9.6 (8.3-11.0)	14.7* (10.2-19.3)	9.9 (8.6-11.3)	12.1 ^{n.s.} (8.1-16.1)	9.5 (8.2-10.9)	16.2** (11.5-20.9)	9.7 (8.4-11.1)	14.0 ^{n.s.} (9.7-18.2)
HDL-cholesterol < P10 (N = 285)	8.6 (7.3-9.9)	15.7** (11.0-20.4)	8.8 (7.5-10.1)	14.3* (9.9-18.8)	8.6 (7.3-9.9)	16.6 (11.9-21.3)	8.6 (7.3-9.9)	15.8 (11.6-20.1)
Systolic BP > P90 (N = 367)	8.8 (7.4-10.1)	29.9 (25.1-35.8)	9.3 (7.8-10.8)	25.3 (19.7-30.8)	9.3 (7.8-10.7)	26.4 (20.9-31.9)	9.1 (7.7-10.6)	27.1 (21.7-32.6)
Diastolic BP > P90 (N = 317)	8.5 (7.4-9.6)	19.1 (13.7-24.5)	8.9 (7.7-10.1)	15.8** (11.0-20.5)	8.6 (7.4-9.8)	18.6 ^{n.s.} (13.5-23.6)	8.6 (7.5-9.8)	18.2 (13.3-23.0)
HbA1c > P90 (N = 256)	7.9 (6.2-9.6)	10.8 ^{n.s.} (7.0-14.6)	8.1 (6.4-9.7)	9.2 ^{n.s.} (5.3-13.2)	8.0 (6.4-9.7)	9.8 (6.0-13.6)	8.1 (6.5-9.8)	8.6 ^{n.s.} (5.2-12.0)
hs-CRP > 2.1 mg/l (N = 263)	7.7 (6.6-8.8)	17.6 (13.2-22.0)	7.6 (6.6-8.7)	18.1 (13.6-22.7)	7.5 (6.4-8.6)	20.1 (15.2-25.0)	7.6 (6.5-8.6)	19.0 (14.3-23.8)
Girls	N=2728	N=310	N=2737	N=301	N=2729	N=309	N=2717	N=321
Total cholesterol > P90 (N = 298)	9.6 (8.1-11.0)	10.0 ^{n.s.} (6.2-13.9)	9.6 (8.1-11.1)	9.7 ^{n.s.} (6.1-13.4)	9.3 (7.9-10.7)	12.9 ^{n.s.} (8.7-17.1)	9.5 (8.0-10.9)	11.2 ^{n.s.} (7.4-15.0)
LDL-cholesterol > P90 (N = 289)	9.4 (8.1-10.7)	13.0 ^{n.s.} (8.7-17.2)	9.6 (8.3-10.9)	11.1 ^{n.s.} (6.8-15.4)	9.4 (8.1-10.8)	12.5 (8.7-16.2)	9.4 (8.1-10.7)	12.5 ^{n.s.} (8.5-16.4)
HDL-cholesterol < P10 (N = 256)	7.6 (6.5-8.7)	20.7 (15.4-26.0)	7.8 (6.6-9.0)	18.8 (13.4-24.1)	7.7 (6.6-8.8)	19.7 (14.0-25.3)	7.5 (6.5-8.6)	20.8 (15.3-26.3)
Systolic BP > P90 (N = 306)	8.2 (6.7-9.7)	22.3 (17.0-27.6)	8.4 (6.9-9.9)	20.7 (14.7-26.6)	8.2 (6.7-9.6)	22.9 (16.9-28.9)	8.3 (6.9-9.8)	21.0 (15.5-26.6)
Diastolic BP > P90 (N = 291)	8.5 (7.1-10.0)	16.6** (11.7-21.6)	8.7 (7.3-10.2)	15.0* (10.3-19.6)	8.6 (7.2-10.0)	16.3** (11.6-20.9)	8.7 (7.3-10.2)	14.7* (10.2-19.2)
HbA1c > P90 (N = 272)	9.0 (7.1-10.9)	10.7 ^{n.s.} (6.1-15.4)	9.1 (7.2-11.1)	9.6 ^{n.s.} (5.6-13.7)	8.8 (7.0-10.7)	12.3 ^{n.s.} (7.5-17.2)	9.0 (7.1-10.9)	10.6 ^{n.s.} (6.2-15.0)
hs-CRP > 2.1 mg/l (N = 344)	10.5 (9.2-11.9)	21.5 (16.0-27.0)	10.3 (9.0-11.6)	23.8 (17.7-29.9)	10.3 (9.0-11.6)	24.3 (18.4-30.1)	10.3 (9.0-11.7)	23.4 (18.0-28.8)

CI: confidence interval, Subscap: subscapular, SFT: skinfold thickness, hs-CRP: high sensitivity C-reactive protein, HbA1c: glycosylated haemoglobin
Differences between ≤ P90 and >P90 were highly significant (p<0.001) unless explicitly mentioned (n.s. = not significant, ** = p <0.01, * = p < 0.05), chi-square test

Table 13: Separate linear regression of individual CVD risk factors on different measures of overweight (> P90), adjusted for age, 3-10 years

Independent variables:	Total chol. [mg/dl]			LDL-chol. [mg/dl]			HDL-chol. [mg/dl]			SBP [mm Hg]			DBP [mm Hg]			HbA1c [%]			hs-CRP [mg/l]		
	b	SE	R ²	b	SE	R ²	b	SE	R ²	b	SE	R ²	b	SE	R ²	b	SE	R ²	b	SE	R ²
Boys			0.005 [†]			0.002 [†]			0.05 [†]			0.14 [†]			0.08 [†]			0.006 [†]			0.01 [†]
BMI > P90	3.6 ^{n.s.}	2.0	0.006	4.0*	1.8	0.005	-4.6	0.8	0.06	6.6	0.5	0.19	3.4	0.5	0.10	0.05 ^{n.s.}	0.03	<0.01	0.5	0.1	0.03
Triceps SFT > P90	3.9*	1.8	0.007	3.1 ^{n.s.}	1.6	0.004	-3.1	0.8	0.06	5.3	0.5	0.17	2.6	0.4	0.09	0.02 ^{n.s.}	0.03	<0.01	0.5	0.1	0.03
Subscap. SFT > P90	5.2**	1.8	0.008	5.3**	1.7	0.006	-4.3	0.9	0.06	6.0	0.5	0.18	3.5	0.4	0.10	0.04 ^{n.s.}	0.03	<0.01	0.6	0.1	0.03
Sum of SFT > P90	4.8**	1.8	0.008	5.0**	1.7	0.006	-4.5	0.8	0.06	5.7	0.5	0.18	3.3	0.4	0.10	0.02 ^{n.s.}	0.03	<0.01	0.6	0.1	0.03
Girls			0.006 [†]			0.002 [†]			0.04 [†]			0.13 [†]			0.05 [†]			0.01 [†]			0.005 [†]
BMI > P90	-1.9 ^{n.s.}	2.1	0.009	-0.5 ^{n.s.}	1.9	0.002	-6.5	0.8	0.07	5.5	0.5	0.17	2.6	0.5	0.06	0.06*	0.02	0.01	0.7	0.1	0.02
Triceps SFT > P90	-1.6 ^{n.s.}	1.9	0.009	-0.3 ^{n.s.}	1.8	0.002	-5.0	1.0	0.06	4.6	0.5	0.16	2.3	0.5	0.06	0.05*	0.02	0.01	0.7	0.1	0.03
Subscap. SFT > P90	0.1 ^{n.s.}	1.9	0.009	0.5 ^{n.s.}	1.8	0.002	-5.8	0.8	0.06	5.3	0.5	0.16	2.9	0.5	0.07	0.06 ^{n.s.}	0.03	0.01	0.7	0.1	0.03
Sum of SFT > P90	-1.0 ^{n.s.}	1.8	0.009	-0.1 ^{n.s.}	1.7	0.002	-6.3	0.9	0.07	5.0	0.5	0.16	2.6	0.5	0.06	0.06*	0.02	0.01	0.8	0.1	0.03

[†]R² for the model with only age and pubertal stage as independent variables

Regression coefficients (b) were highly significant (p < 0.001), unless explicitly mentioned (n.s. = not significant, ** = p < 0.01, * = p < 0.05)

B: regression coefficient, adjusted for age

R²: explained variance for the model with overweight indicator as independent variable, adjusted for age

Chol: cholesterol, SBP: systolic blood pressure, DBP: diastolic blood pressure, HbA1c: glycosylated haemoglobin, hs-CRP: high sensitivity C-reactive Protein, Subscap: subscapular, SFT: skinfold thickness, SE: standard error; SFT: skinfold thickness, P90: 90th age and sex specific percentile

Table 14: Odds ratios and 95% confidence intervals for different measures of overweight (> P90) with elevated CVD risk factors as dependent variables, adjusted for age, 3-10 years

Dependent variables:	Total chol > P90	LDL-chol > P90	HDL-chol < P10	SBP > P90	DBP > P90	HbA1c > P90	hs-CRP > 2.1 mg/l
Independent variables:							
Boys (N = 295)	(N = 310)	(N = 285)	(N = 367)	(N = 317)	(N = 256)	(N = 263)	
BMI > P90	1.8** (1.2-2.7)	1.6* (1.1-2.4)	3.2 (2.3-4.5)	3.2 (2.3-4.5)	2.1 (1.4-3.3)	1.2 ^{n.s.} (0.8-2.0)	2.6 (1.8-3.7)
Triceps SFT > P90	1.3 ^{n.s.} (0.8-2.1)	1.3 ^{n.s.} (0.8-1.9)	2.7 (1.9-4.0)	2.8 (1.9-4.2)	1.8** (1.2-2.8)	1.1 ^{n.s.} (0.7-1.7)	2.7 (1.9-3.9)
Subscap SFT > P90	1.9** (1.3-2.8)	1.8** (1.2-2.7)	2.9 (2.0-4.3)	3.4 (2.4-4.8)	2.1 (1.4-3.0)	1.5 ^{n.s.} (0.9-2.3)	3.2 (2.2-4.7)
Sum of SFT > P90	1.8** (1.2-2.7)	1.5* (1.0-2.2)	3.2 (2.3-4.6)	2.9 (2.1-4.2)	1.8** (1.2-2.7)	1.2 ^{n.s.} (0.8-1.9)	2.9 (2.0-4.2)
Girls (N = 298)	(N = 289)	(N = 256)	(N = 306)	(N = 291)	(N = 272)	(N = 344)	
BMI > P90	1.0 ^{n.s.} (0.7-1.6)	1.4 ^{n.s.} (1.0-2.2)	2.0 (1.3-2.9)	4.5 (3.3-6.0)	2.6 (1.8-3.7)	1.4 ^{n.s.} (0.9-2.1)	2.4 (1.6-3.4)
Triceps SFT > P90	1.0 ^{n.s.} (0.6-1.6)	1.2 ^{n.s.} (0.7-1.9)	1.7** (1.2-2.6)	3.3 (2.4-4.6)	2.0 (1.3-2.9)	1.2 ^{n.s.} (0.7-1.9)	2.7 (1.9-3.9)
Subscap SFT > P90	1.4 ^{n.s.} (1.0-2.2)	1.4 ^{n.s.} (0.9-2.0)	2.2 (1.5-3.1)	3.5 (2.6-4.9)	2.5 (1.8-3.5)	1.3 ^{n.s.} (0.8-2.0)	2.9 (2.0-4.0)
Sum of SFT > P90	1.2 ^{n.s.} (0.8-1.8)	1.4 ^{n.s.} (0.9-2.0)	2.0 (1.4-2.9)	3.7 (2.7-5.1)	2.4 (1.7-3.4)	1.1 ^{n.s.} (0.7-1.6)	2.7 (1.9-3.7)

Chol: cholesterol, SBP: systolic blood pressure, DBP: diastolic blood pressure, HbA1c: glycosylated haemoglobin, hs-CRP: high sensitivity C-reactive protein, BMI: body mass index, SFT: skinfold thickness, Subscap: subscapular, P90: 90th age and sex specific percentile
 ORs were highly significant ($p < 0.001$) unless explicitly mentioned (n.s. = not significant, ** = $p < 0.01$, * = $p < 0.05$)

5.4.2 Results for children and adolescents 11-17 years of age

Means and 95% confidence intervals of anthropometric data and CVD risk factors are presented by gender and age group in Table 15. Mean body height and weight as well as BMI and WC increased with higher age group in both sexes ($p < 0.001$). Mean WHR was lower among 14-17 year olds as compared to younger children ($p < 0.001$). Although 14-17 year old boys were taller and heavier than girls in this age group ($p < 0.001$), the mean BMI did not statistically differ between the sexes. Among the entire group, mean skinfold thicknesses were consistently higher for girls than for boys ($p < 0.001$), whereas means of WC, WHR, and WHtR were higher among boys ($p < 0.001$). Among boys, mean serum TC and lipoprotein concentrations were lower in 14-17 year olds than in 11-13 year olds ($p < 0.001$). In contrast, blood lipids did not differ between age groups among girls. Mean SBP and DBP increased with age group in both sexes ($p < 0.001$). At ages 14-17 years, boys had significantly lower serum TC and lipoprotein concentrations and higher SBP and DBP than girls ($p < 0.001$). Mean hs-CRP concentrations were slightly higher among 14-17 year olds. There were no considerable differences according to age or gender in mean HbA1c levels.

Table 15: Means and 95% confidence intervals of anthropometric data and cardiovascular risk factors according to age group and gender, 11-17 years

	Boys		Girls	
	11-13 years (N = 1364)	14-17 years (N = 1667)	11-13 years (N = 1312)	14-17 years (N = 1203)
Height [cm]	156.2 (155.6-156.8)	175.4 (175.0-175.8)	156.7 (156.3-157.2)	164.9 (164.5-165.4)
Weight [kg]	48.4 (47.6-49.3)	66.9 (66.2-67.6)	49.3 (48.5-50.1)	59.2 (58.4-60.0)
BMI [kg/m ²]	19.6 (19.4-19.9)	21.7 (21.5-21.9)	19.9 (19.6-20.1)	21.7 (21.5-22.0)
Triceps skinfold thickness [mm]	14.7 (14.2-15.2)	12.7 (12.3-13.0)	16.6 (16.1-17.0)	19.5 (18.9-20.0)
Subscapular skinfold thickness [mm]	9.9 (9.5-10.4)	10.5 (10.2-10.8)	11.4 (11.0-11.9)	13.4 (13.0-13.9)
Sum of skinfold thickness [mm]	24.7 (23.8-25.6)	23.2 (22.5-23.8)	28.0 (27.2-28.9)	32.9 (32.0-33.8)
Waist circumference [cm]	68.4 (67.7-69.0)	75.0 (74.6-75.5)	66.3 (65.8-66.9)	69.6 (69.1-70.2)
Waist-to-hip ratio	0.83 (0.83-0.84)	0.81 (0.81-0.81)	0.78 (0.77-0.78)	0.74 (0.74-0.74)
Waist-to-height ratio	0.44 (0.43-0.44)	0.43 (0.43-0.43)	0.42 (0.42-0.43)	0.42 (0.42-0.43)
Total cholesterol [mg/dl]	163.3 (161.4-165.2)	152.2 (150.7-153.8)	163.2 (161.4-165.0)	162.2 (160.2-164.1)
LDL- cholesterol [mg/dl]	91.3 (89.7-92.8)	85.4 (84.1-86.8)	92.6 (91.0-94.3)	91.8 (90.0-93.5)
HDL- cholesterol [mg/dl]	58.2 (57.3-59.1)	51.6 (50.9-52.3)	57.5 (56.7-58.3)	58.2 (57.3-59.1)
Systolic blood pressure [mm Hg]	110.0 (109.3-110.7)	120.8 (120.0-121.6)	110.4 (109.7-111.1)	113.5 (112.8-114.2)
Diastolic blood pressure [mm Hg]	65.9 (65.4-66.4)	70.2 (69.7-70.7)	66.0 (65.4-66.5)	68.6 (68.1-69.1)
Glycosylated haemoglobin [%]	4.9 (4.9-5.0)	4.9 (4.9-4.9)	4.9 (4.8-4.9)	4.8 (4.8-4.9)
High sensitivity C-reactive protein [mg/l]	0.7 (0.7-0.8)	0.9 (0.8-0.9)	0.7 (0.6-0.7)	0.8 (0.7-0.8)

Figures 10-12 show mean values of individual CVD risk factors according to age group, gender, and overweight measure, dichotomised at the 90th age and sex specific percentile with overweight > P90 (×) and normal weight ≤ P90 (-). Non-overlapping confidence intervals indicate statistically significant differences. Irrespective of the measure of overweight chosen, boys and girls with overweight had consistently higher mean serum levels of TC and LDL-C and lower serum levels of HDL-C compared to children and adolescents with normal weight (Figure 10).

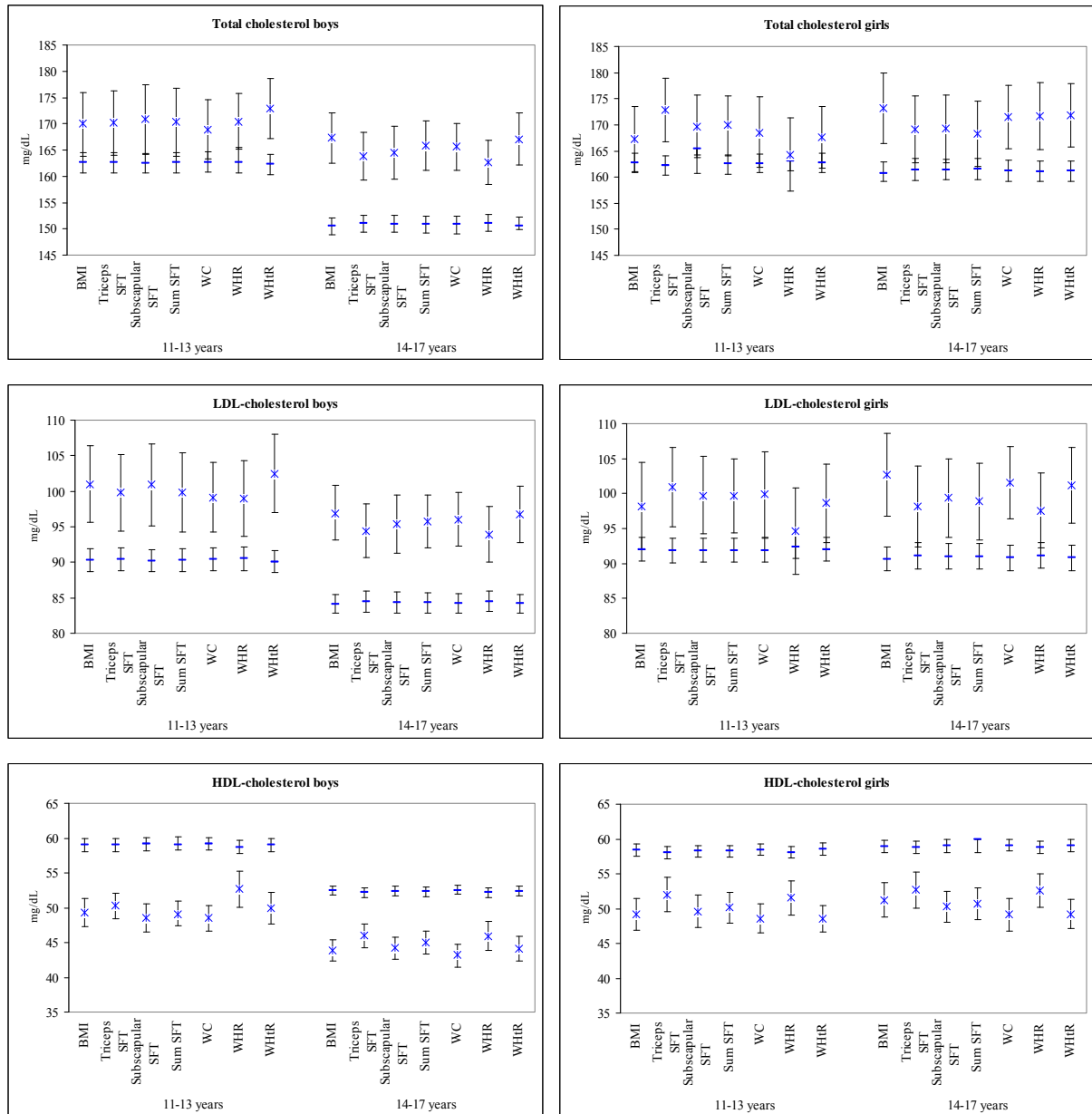


Figure 10: Means and 95% confidence intervals for serum lipoproteins according to age group, gender and different measures of overweight, dichotomised at the 90th age and sex specific percentile, 11-17 years

- normal weight ($\leq 90^{\text{th}}$ percentile)
- × overweight ($> 90^{\text{th}}$ percentile)

BMI: body mass index, SFT: skinfold thickness, WC: waist circumference, WHR: waist-to-hip ratio, WHtR: waist-to-height ratio

Mean SBP and DBP were significantly higher among overweight children and adolescents compared to those of normal weight, independently of age group, gender and measure of overweight (Figure 11). Consistently higher mean serum levels of hs-CRP in relation to overweight status were also observed (Figure 12), while there were no mean differences in HbA1c.

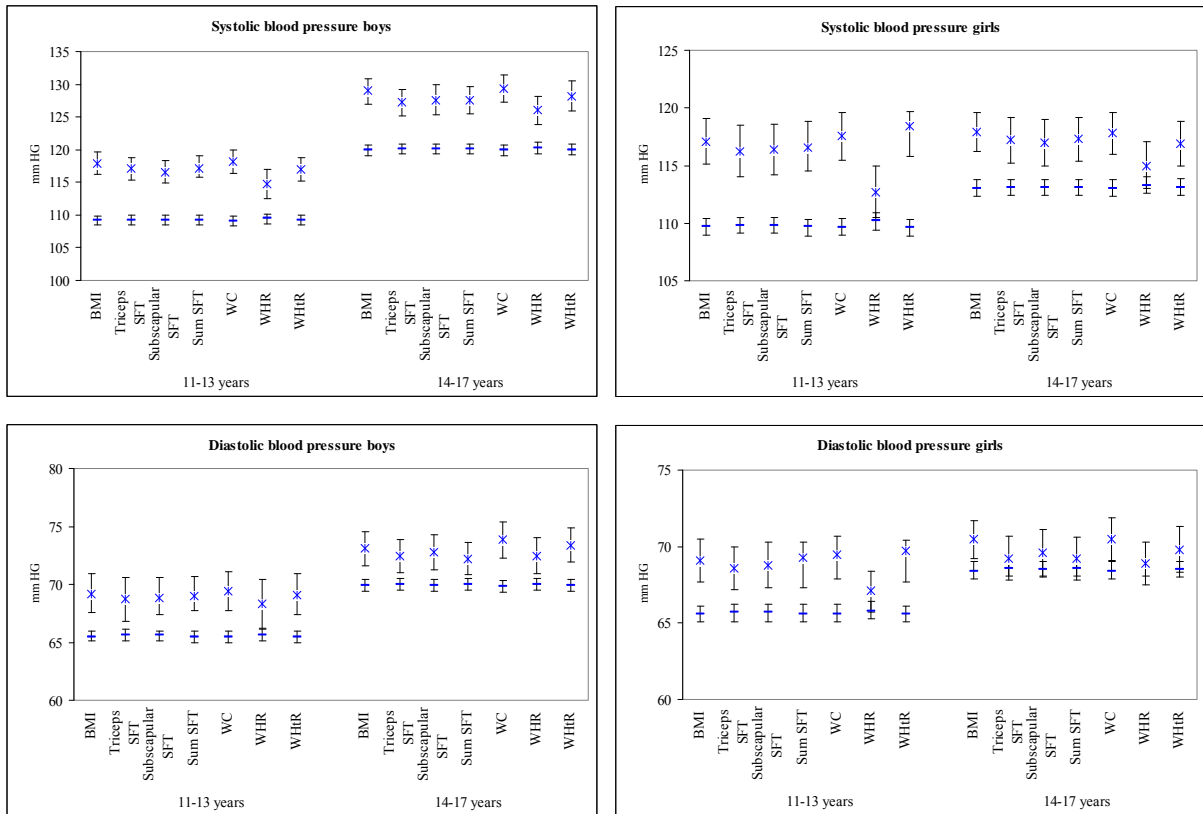


Figure 11: Means and 95% confidence intervals for blood pressure according to age group, gender and different measures of overweight, dichotomised at the 90th age and sex specific percentile, 11-17 years

- normal weight ($\leq 90^{\text{th}}$ percentile)

× overweight ($> 90^{\text{th}}$ percentile)

BMI: body mass index, SFT: skinfold thickness, WC: waist circumference, WHR: waist-to-hip ratio, WHtR: waist-to-height ratio

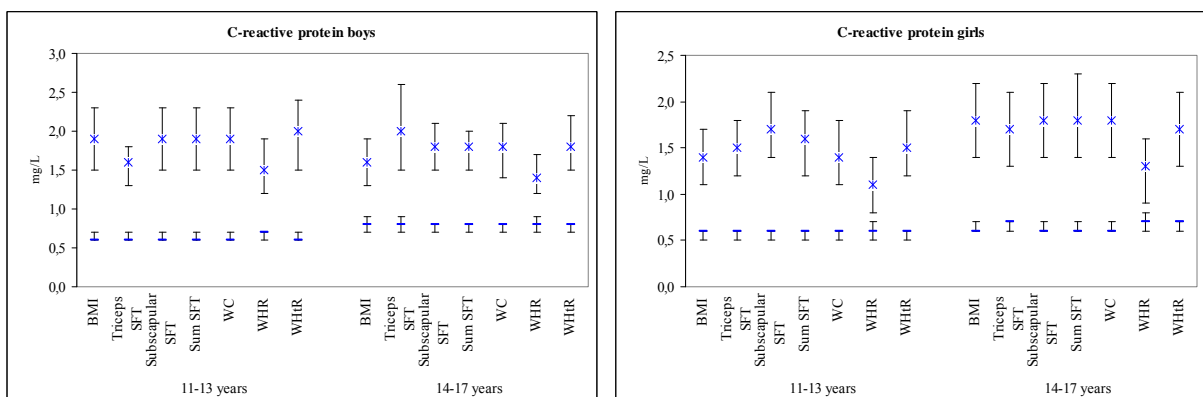


Figure 12: Means and 95% confidence intervals for hs-CRP according to age group, gender and different measures of overweight, dichotomised at the 90th age and sex specific percentile, 11-17 years

- normal weight ($\leq 90^{\text{th}}$ percentile)

× overweight ($> 90^{\text{th}}$ percentile)

BMI: body mass index, SFT: skinfold thickness, WC: waist circumference, WHR: waist-to-hip ratio, WHtR: waist-to-height ratio

For all CVD risk factors except for HbA1c and LDL-C among girls, the prevalence of boys and girls exceeding the defined risk factor cutoff was almost two- to fourfold higher if they were overweight as defined by BMI, WC or WHtR (Table 16). Among boys, all the differences in prevalence between overweight and non-overweight were highly statistically significant ($p < 0.001$). For example, 19.5% of boys and 14.4% of girls with BMI $> P90$ had elevated serum TC concentrations, compared to 8.0% of boys and 7.3% of girls with BMI $\leq P90$. The results for triceps and subscapular skinfold thickness as well as for WHR and body fat are similar, as shown in Table A-7 in the appendix.

Results from linear regression models for the various CVD risk factors and dichotomised measures of overweight ($> P90$ versus $\leq P90$), adjusted for age in years and pubertal stage, are shown in Table 17. All cardiovascular risk factors except HbA1c were consistently and highly significant related to the various measures of overweight among both sexes, independent of age and pubertal stage. There were some differences regarding the strength of the association between particular CVD risk factors and measures of overweight. As demonstrated by the regression coefficients as well as the R-squared of the regression models, overweight as defined by WC showed the strongest association with SBP and DBP among both sexes. Among boys, WHtR showed the highest correlation with serum TC and LDL-C as well as hs-CRP concentrations and BMI with LDL-C. Among girls, BMI and triceps skinfold thickness showed the highest correlation with serum TC, WC with LDL-C, WHtR with HDL-C, and subscapular skinfold thickness with hs-CRP. Age and puberty adjusted differences in mean CVD risk factors between those with and without overweight were substantial, for example up to 14 mg/dl for TC, 12 mg/dl for LDL-C, -10 mg/dl for HDL-C, 9 mm Hg for SBP, and 4 mm Hg for DBP. However, age and pubertal stage have a large impact on the variability in the dependent variables, except for hs-CRP, as shown by the R-squared for the models only including age and pubertal stage. Among girls, the explicitly impact of overweight on CVD risk factors is more pronounced for serum lipoproteins than among boys. As shown, age and pubertal stage explain most of the variability in SBP and DBP. Thus, among boys and girls, age and pubertal stage are important determinants for CVD risk factors.

Table 16: Prevalence [% (95% CI)] of children exceeding defined cutoffs for individual CVD risk factors according to different measures of overweight, dichotomised at the age and sex specific 90th percentile, 11-17 years

	BMI ≤ P90	BMI > P90	Sum of SFT ≤ P90	Sum of SFT > P90	WC ≤ P90	WC > P90	WHtR ≤ P90	WHtR > P90
Boys	N = 2741	N = 290	N = 2741	N = 290	N = 2746	N = 285	N = 2753	N = 278
Total cholesterol > P90 (N = 284)	8.0 (6.9-9.1)	19.5 (14.0-25.1)	8.1 (6.9-9.2)	19.2 (14.2-24.2)	8.3 (7.1-9.4)	17.3 (12.3-22.3)	8.0 (6.9-9.1)	19.4 (14.1-24.8)
LDL-cholesterol > P90 (N = 305)	9.1 (7.9-10.2)	19.7 (14.4-25.0)	9.3 (8.1-10.5)	17.5 (13.2-21.9)	9.3 (8.1-10.4)	17.9 (13.2-22.6)	9.1 (7.9-10.3)	19.7 (14.6-24.8)
HDL-cholesterol < P10 (N = 290)	7.9 (6.7-9.2)	26.4 (20.8-32.0)	8.2 (7.0-9.5)	23.9 (18.4-29.4)	7.6 (6.4-8.9)	29.1 (23.3-34.9)	7.9 (6.6-9.2)	27.0 (21.0-33.1)
Systolic blood pressure > P90 (N = 359)	9.2 (7.8-10.6)	34.3 (28.4-40.2)	9.5 (8.1-11.0)	31.5 (25.8-37.1)	8.9 (7.6-10.3)	36.8 (30.2-43.4)	9.5 (8.1-10.9)	31.7 (24.9-38.4)
Diastolic blood pressure > P90 (N = 265)	8.1 (6.8-9.3)	18.2 (13.0-23.4)	8.3 (7.1-9.6)	16.0 (11.1-20.9)	7.8 (6.5-9.0)	21.0 (15.7-26.3)	7.9 (6.6-9.1)	20.1 (14.6-25.5)
HbA1c > P90 (N = 282)	9.9 (7.9-11.9)	10.2 ^{n.s} (6.2-14.2)	9.8 (7.9-11.8)	11.3 ^{n.s} (6.8-15.9)	10.0 (8.0-12.0)	9.7 ^{n.s} (5.6-13.8)	9.9 (7.9-11.9)	10.2 ^{n.s} (5.6-14.7)
C-reactive protein > 2.1 mg/l (N = 262)	7.2 (6.0-8.4)	24.3 (18.7-29.9)	7.0 (5.8-8.1)	26.8 (21.3-32.4)	7.1 (5.8-8.3)	25.5 (20.1-30.9)	6.9 (5.7-8.1)	27.1 (21.3-33.0)
Girls	N = 2265	N = 250	N = 2279	N = 236	N = 2275	N = 240	N = 2271	N = 244
Total cholesterol > P90 (N = 207)	7.3 (5.9-8.6)	14.4** (9.1-19.7)	7.4 (6.1-8.8)	12.9* (8.0-17.9)	7.4 (6.0-8.8)	13.0* (7.8-18.1)	7.5 (6.1-8.8)	12.5 ^{n.s} (7.4-17.6)
LDL-cholesterol > P90 (N = 180)	6.9 (5.6-8.1)	12.7* (8.2-17.2)	7.0 (5.7-8.3)	11.8* (7.6-16.1)	7.0 (5.7-8.3)	11.2 ^{n.s} (6.9-15.5)	7.1 (5.8-8.4)	10.8 ^{n.s} (6.7-14.9)
HDL-cholesterol < P10 (N = 251)	7.8 (6.4-9.3)	27.9 (21.0-34.8)	8.1 (6.7-9.5)	25.4 (18.0-32.8)	7.7 (6.3-9.1)	29.5 (22.3-36.7)	7.7 (6.2-9.1)	29.6 (22.4-36.8)
Systolic blood pressure > P90 (N = 264)	8.7 (7.1-10.3)	28.3* (21.1-35.5)	8.9 (7.3-10.4)	26.8 (19.1-34.4)	8.8 (7.1-10.4)	27.9 (20.6-35.2)	8.6 (7.0-10.2)	29.1 (21.5-36.6)
Diastolic blood pressure > P90 (N = 226)	8.3 (6.8-9.8)	14.9 (10.1-19.7)	8.3 (6.9-9.8)	14.7* (9.6-19.9)	8.2 (6.7-9.8)	15.8** (10.9-20.6)	8.2 (6.7-9.7)	15.9** (10.9-20.8)
HbA1c > P90 (N = 266)	10.1 (8.0-12.3)	16.0 ^{n.s} (9.8-22.1)	10.3 (8.1-12.4)	14.8 ^{n.s} (8.8-20.9)	10.1 (7.9-12.3)	16.4 ^{n.s} (9.8-22.9)	10.2 (8.0-12.4)	15.3 ^{n.s} (9.0-21.6)
hs-CRP > 2.1 mg/l (N = 185)	5.7 (4.6-6.9)	23.6 (17.6-29.7)	5.7 (4.5-6.9)	24.1 (17.7-30.5)	5.8 (4.6-7.1)	23.2 (17.1-29.3)	6.0 (4.8-7.1)	21.8 (15.9-27.6)

CI: confidence interval, BMI: body mass index, SFT: skinfold thickness, WC: waist circumference, WHtR: waist-to-height ratio, HbA1c: glycosylated haemoglobin, hs-CRP: high sensitivity C-reactive protein;

Differences between ≤ P90 and >P90 were highly significant (p<0.001) unless explicitly mentioned (n.s. = not significant, ** = p <0.01, * = p < 0.05), chi-square test

Table 17: Separate linear regression of individual CVD risk factors on different measures of overweight (> P90), adjusted for age and pubertal stage, 11-17 years

Independent variables:	Total chol [mg/dl]			LDL-chol [mg/dl]			HDL-chol [mg/dl]			SBP [mm Hg]			DBP [mm Hg]			HbA1c [%]			hs-CRP [mg/l]		
	b	SE	R ²	b	SE	R ²	b	SE	R ²	b	SE	R ²	b	SE	R ²	b	SE	R ²	b	SE	R ²
Boys			0.07 [†]			0.03 [†]			0.09 [†]			0.27 [†]			0.10 [†]			0.006 [†]			0.004 [†]
BMI > P90	13.4	2.2	0.09	11.9	1.7	0.05	-9.2	0.7	0.13	9.1	0.7	0.32	3.6	0.6	0.12	-0.03 ^{n.s.}	0.03	<0.01	1.0	0.1	0.06
Triceps SFT > P90	10.3	1.9	0.08	9.2	1.6	0.05	-7.5	0.8	0.12	7.6	0.7	0.30	2.8	0.6	0.11	0.01 ^{n.s.}	0.03	<0.01	0.9	0.1	0.05
Subs. SFT > P90	11.5	2.1	0.09	10.8	1.7	0.05	-9.3	0.8	0.13	7.8	0.8	0.30	3.2	0.6	0.11	0.03 ^{n.s.}	0.03	<0.01	1.1	0.1	0.07
Sum of SFT > P90	11.8	2.0	0.09	10.3	1.6	0.05	-8.7	0.8	0.13	7.8	0.7	0.30	2.8	0.6	0.11	0.02 ^{n.s.}	0.03	<0.01	1.1	0.1	0.06
WC > P90	11.1	1.9	0.09	10.3	1.6	0.05	-10.2	0.7	0.14	9.3	0.7	0.32	4.1	0.6	0.12	-0.04 ^{n.s.}	0.03	<0.01	1.1	0.1	0.07
WHR > P90	9.5	1.7	0.08	8.5	1.6	0.04	-6.3	0.9	0.11	5.9	0.8	0.29	2.7	0.7	0.11	-0.01 ^{n.s.}	0.03	<0.01	0.7	0.1	0.03
WHtR > P90	13.8	2.1	0.09	11.9	1.7	0.05	-9.0	0.8	0.13	8.3	0.8	0.31	3.7	0.6	0.12	-0.02 ^{n.s.}	0.04	<0.01	1.2	0.1	0.08
Girls			0.01 [†]			0.006 [†]			0.009 [†]			0.06 [†]			0.05 [†]			0.01 [†]			0.01 [†]
BMI > P90	8.5	2.3	0.02	9.2	2.2	0.02	-8.3	0.9	0.05	5.9	0.7	0.09	2.7	0.5	0.06	0.07*	0.03	0.01	1.1	0.1	0.09
Triceps SFT > P90	8.5	2.2	0.02	7.8	2.1	0.01	-6.1	1.0	0.03	5.3	0.7	0.08	1.8	0.5	0.06	0.05 ^{n.s.}	0.03	0.01	1.0	0.1	0.08
Subs. SFT > P90	7.3**	2.2	0.02	8.1	2.0	0.02	-8.5	0.9	0.05	5.2	0.8	0.08	2.1	0.6	0.06	0.07*	0.03	0.01	1.2	0.1	0.11
Sum of SFT > P90	6.8**	2.1	0.02	7.7	1.9	0.01	-8.0	0.9	0.04	5.5	0.7	0.09	1.9	0.5	0.06	0.06*	0.03	0.01	1.1	0.1	0.10
WC > P90	8.2	2.2	0.02	9.6	2.1	0.02	-9.6	0.9	0.06	6.2	0.7	0.09	2.9	0.5	0.07	0.09*	0.03	0.01	1.1	0.1	0.09
WHR > P90	6.0**	2.2	0.01	4.3*	2.0	0.01	-6.4	0.9	0.03	2.3**	0.8	0.06	0.9 ^{n.s.}	0.5	0.05	0.03 ^{n.s.}	0.04	0.01	0.5	0.1	0.03
WHtR > P90	7.5	2.0	0.02	8.3	2.0	0.02	-9.7	0.9	0.06	5.9	0.7	0.09	2.5	0.5	0.06	0.08*	0.03	0.01	1.0	0.1	0.08

[†]R² for the model with only age and pubertal stage as independent variables

All regression coefficients (b) were highly significant (p < 0.001), unless explicitly mentioned (n.s. = not significant, ** = p < 0.01, * = p < 0.05)

b: regression coefficient, adjusted for age and pubertal stage

R²: explained variance for the model with overweight indicator as independent variable, adjusted for age and pubertal stage

Chol: cholesterol, SBP: systolic blood pressure, DBP: diastolic blood pressure, HbA1c: glycosylated haemoglobin, hs-CRP: high sensitivity C-reactive protein, Subs: subscapular, WC: waist circumference, WHR: waist-to-hip ratio, WHtR: waist-to-height ratio, SE: standard error; SFT: skinfold thickness, P90: 90th age and sex specific percentile

Every model in Table 17 was additionally adjusted for physical activity, smoking, and alcohol consumption since they may be potential confounders. However, none of these three factors had a consistent and substantial impact on the CVD risk factors (data not shown). There were only sporadic significant associations. For example, among boys a high level of physical activity lowered mean DBP by 1.6 mm Hg. Among girls, a high level of physical activity lowered TC and LDL-C by 5.5 mg/dl and 3.7 mg/dl, respectively. There was no impact of physical activity on SBP and DBP among boys and girls. Furthermore, none of the factors showed any significant association with SBP, hs-CRP, and HbA1c among both boys and girls and no association with TC and HDL-C only among boys.

Tables 18 and 19 show the results of the linear regression models with the use of combined variables of BMI, WC, and WHtR and the results of the regression models when BMI and WC or BMI and WHtR were entered simultaneously. As shown by the increased regression coefficient as well as by the R-squared, combined measures of BMI and WHtR led to slightly better results than single anthropometric measures among boys and the combined use of BMI and WC led to slightly better results among girls (Table 18). As shown in Table 19 when BMI and WC as well as BMI and WHtR were entered in the model simultaneously, in particular among boys this led to slightly higher regression coefficients and R-squared, except for DBP. Among girls, only for SBP and CRP, regression coefficients and R-squared were slightly higher with the simultaneous use of BMI and WC (Table 19).

Table 18: Separate linear regression of CVD risk factors of combined measures of overweight (>P90), adjusted for age and pubertal stage, 11-17 years

Independent variables:	Dependent variables:			Total chol [mg/dl]			LDL-chol [mg/dl]			HDL-chol [mg/dl]			SBP [mm Hg]			DBP [mm Hg]			hs-CRP [mg/l]		
	b	SE	R ²	b	SE	R ²	b	SE	R ²	b	SE	R ²	b	SE	R ²	b	SE	R ²			
Boys																					
BMI and WC > P90	13.3	2.4	0.09	12.0	1.8	0.05	-10.2	0.8	0.13	9.9	0.7	0.31	4.2	0.7	0.12	1.2	0.1	0.06			
BMI and WHtR > P90	16.3	2.6	0.09	14.3	2.0	0.06	-9.9	0.8	0.13	10.1	0.9	0.31	4.4	0.7	0.12	1.3	0.2	0.07			
Girls																					
BMI and WC > P90	9.1	2.7	0.02	10.5	2.5	0.02	-10.1	1.0	0.05	7.0	0.8	0.10	3.5	0.5	0.07	1.2	0.2	0.08			
BMI and WHtR > P90	8.1	2.6	0.02	9.0	2.5	0.02	-9.7	0.9	0.05	6.6	0.8	0.09	3.2	0.6	0.07	1.2	0.2	0.09			

Regression coefficients were highly significant ($p < 0.001$), b=regression coefficient, adjusted for age, R²=explained variance, adjusted for age

Chol: Cholesterol; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; hs-CRP: high sensitivity C-reactive protein, SE: standard error; BMI: Body mass index; WC: Waist circumference, WHtR: Waist-to-height ratio, P90: 90th age and sex specific percentile

Table 19: Separate multiple linear regression of CVD risk factors of combinations of single measures of overweight (>P90), adjusted for age and pubertal stage, 11-17 years

Independent variables:	Dependent variables:			Total chol [mg/dl]			LDL-chol [mg/dl]			HDL-chol [mg/dl]			SBP [mm Hg]			DBP [mm Hg]			hs-CRP [mg/l]		
	b	SE	R ²	b	SE	R ²	b	SE	R ²	b	SE	R ²	b	SE	R ²	b	SE	R ²	b	SE	R ²
Boys																					
BMI and WC			0.09			0.05			0.15			0.33			0.12						0.07
BMI > P90	11.8	3.5		9.8**	2.9		-3.3**	0.9		4.5	1.3		1.1 ^{n.s.}	0.9		0.4*	0.2				
WC > P90	2.1 ^{n.s.}	3.1		2.8 ^{n.s.}	2.8		-7.7	0.9		5.9	1.3		3.2	1.0		0.8	0.2				
BMI and WHtR			0.10			0.06			0.14			0.32			0.12						0.08
BMI > P90	7.4**	2.8		7.0**	2.3		-5.8	1.0		6.5	1.0		1.9*	0.8		0.3**	0.1				
WHtR > P90	8.6**	2.6		7.0**	2.3		-4.9	1.1		3.7**	1.2		2.4**	0.8		1.0	0.2				
Girls																					
BMI and WC			0.02			0.02			0.06			0.10			0.07						0.10
BMI > P90	5.5 ^{n.s.}	3.2		5.0 ^{n.s.}	2.9		-2.7 ^{n.s.}	1.4		3.0	0.9		1.2 ^{n.s.}	0.7		0.6	0.2				
WC > P90	4.0 ^{n.s.}	3.0		5.8*	2.7		-7.6	1.4		3.9	0.9		2.0**	0.7		0.6	0.2				
BMI and WHtR			0.02			0.02			0.06			0.10			0.06						0.10
BMI > P90	6.7*	3.4		7.0*	3.0		-2.2 ^{n.s.}	1.4		3.3	1.0		1.9**	0.6		0.6	0.2				
WHtR > P90	2.3 ^{n.s.}	3.0		2.9 ^{n.s.}	2.7		-8.0	1.3		3.4**	1.0		1.0 ^{n.s.}	0.7		0.6**	0.2				

Regression coefficients were highly significant ($p < 0.001$), unless explicitly mentioned (n.s. = not significant, ** = $p < 0.01$, * = $p < 0.05$)

b: regression coefficient, adjusted for age; R²: explained variance, adjusted for age, Chol: Cholesterol; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; hs-CRP: high sensitivity C-reactive protein, SE: standard error; BMI: Body mass index; WC: Waist circumference, WHtR: Waist-to-height ratio, P90: 90th age and sex specific percentile

Boys and girls with overweight showed adjusted ORs between 1.8 and 2.7 for elevated serum TC concentrations according to any of the chosen measures. Statistically significant ORs for elevated serum LDL-C ranged from 1.7 to 2.4, those for low serum HDL-C from 3.1 to 5.2, those for SBP from 2.2 to 6.1, those for DBP from 1.8 to 3.2, and those for serum hs-CRP above 2.1 mg/l from 3.0 to 6.1. The highest ORs for adverse CVD risk factors were observed for overweight measures according to BMI, WC and WHtR among boys, and for overweight as defined by BMI, subscapular skinfold thickness, WC and WHtR among girls.

Table 20: Odds ratios and 95% confidence intervals for different measures of overweight (> P90) with elevated CVD risk factors as dependent variables, adjusted for age and pubertal stage, 11-17 years

	TC > P90	LDL-C > P90	HDL-C < P10	SBP > P90	DBP > P90	HbA1c > P90	hs-CRP > 2.1 mg/l	High CVD risk
Boys	(N=284)	(N=305)	(N=290)	(N=359)	(N=265)	(N=282)	(N=262)	(N=119)
BMI	2.7	2.4	4.3	5.3	2.6	1.1 ^{n.s.}	4.2	10.0
> P90	(1.8-4.0)	(1.6-3.5)	(3.0-6.2)	(4.0-7.1)	(1.7-3.8)	(0.7-1.7)	(3.0-5.9)	(6.5-15.5)
Triceps	2.2	2.0	3.1	4.4	2.0**	1.0 ^{n.s.}	4.0	6.9
SFT > P90	(1.5-3.3)	(1.4-2.8)	(2.2-4.5)	(3.2-6.0)	(1.3-3.2)	(0.6-1.5)	(2.8-5.8)	(4.4-10.8)
Subscap	2.3	1.9**	4.6	4.7	2.3	1.4 ^{n.s.}	4.9	8.0
SFT > P90	(1.6-3.5)	(1.3-2.8)	(3.3-6.5)	(3.5-6.4)	(1.6-3.3)	(0.8-2.3)	(3.6-6.7)	(5.1-12.5)
Sum of	2.5	1.9	3.8	4.6	2.1	1.2 ^{n.s.}	4.9	8.0
SFT > P90	(1.7-3.6)	(1.4-2.7)	(2.6-5.4)	(3.5-6.2)	(1.4-3.1)	(0.8-1.9)	(3.5-6.8)	(5.3-12.0)
WC	2.1	2.0	5.2	6.1	3.2	1.0 ^{n.s.}	4.5	9.4
> P90	(1.4-3.1)	(1.4-2.9)	(3.7-7.4)	(4.5-8.2)	(2.2-4.6)	(0.6-1.6)	(3.3-6.3)	(6.1-14.3)
WHR	1.8	1.9**	3.2	3.0	2.3	1.2 ^{n.s.}	3.1	4.4
> P90	(1.2-2.8)	(1.3-2.8)	(2.2-4.8)	(2.1-4.3)	(1.5-3.5)	(0.8-1.8)	(2.2-4.3)	(2.7-7.2)
WHtR	2.5	2.3	4.8	4.8	2.9	1.1 ^{n.s.}	5.2	11.1
> P90	(1.7-3.7)	(1.6-3.4)	(3.2-7.0)	(3.4-6.6)	(2.0-4.3)	(0.6-1.8)	(3.7-7.2)	(7.1-17.4)
Girls	(N=207)	(N=180)	(N=251)	(N=264)	(N=226)	(N=266)	(N=185)	(N=75)
BMI	2.2**	2.0**	4.6	4.1	1.9**	1.7*	5.4	10.3
> P90	(1.4-3.5)	(1.2-3.3)	(3.1-6.9)	(3.0-5.8)	(1.3-2.9)	(1.0-2.8)	(3.5-8.3)	(6.2-17.2)
Triceps	2.0**	1.9**	3.1	4.1	1.8*	1.3 ^{n.s.}	5.0	11.8
SFT > P90	(1.3-3.2)	(1.2-3.1)	(2.0-4.7)	(2.9-5.7)	(1.1-2.9)	(0.8-2.2)	(3.2-7.7)	(7.0-19.7)
Subscap	2.0**	1.7*	3.9	3.6	2.2	1.7*	6.1	9.6
SFT > P90	(1.2-3.3)	(1.0-2.9)	(2.6-6.0)	(2.5-5.1)	(1.4-3.4)	(1.0-2.7)	(4.0-9.3)	(5.4-16.8)
Sum of	1.8*	1.8*	3.8	3.7	1.9**	1.5 ^{n.s.}	5.4	8.7
SFT > P90	(1.1-3.0)	(1.1-3.0)	(2.5-5.7)	(2.6-5.4)	(1.2-3.0)	(0.9-2.4)	(3.5-8.4)	(4.9-15.3)
WC	1.9*	1.7*	4.9	4.0	2.1	1.7*	5.1	8.7
> P90	(1.1-3.2)	(1.0-3.0)	(3.2-7.3)	(2.8-5.7)	(1.4-3.2)	(1.0-2.9)	(3.2-8.1)	(4.9-15.3)
WHR	1.8*	1.5 ^{n.s.}	3.3	2.2	1.2 ^{n.s.}	1.4 ^{n.s.}	3.0	4.7
> P90	(1.1-3.1)	(0.9-2.6)	(2.2-4.8)	(1.4-3.3)	(0.8-1.9)	(0.9-2.3)	(2.0-4.6)	(2.6-8.3)
WHtR	1.8*	1.5 ^{n.s.}	4.9	4.4	2.2	1.6 ^{n.s.}	4.6	9.4
> P90	(1.1-2.9)	(0.9-2.6)	(3.3-7.3)	(3.1-6.2)	(1.4-3.3)	(0.9-2.7)	(3.0-7.0)	(5.7-15.6)

TC: total cholesterol, C: cholesterol, SBP: systolic blood pressure, DBP: diastolic blood pressure, HbA1c: glycosylated haemoglobin, hs-CRP: high sensitivity C-reactive protein, CVD: cardiovascular disease, BMI: body mass index, SFT: skinfold thickness, Subscap: subscapular, WC: waist circumference, WHR: waist-to-hip ratio, WHtR: waist-to-height ratio, P90: 90th age and sex specific percentile
ORs were highly significant (p<0.001) unless explicitly mentioned (n.s. = not significant, ** = p < 0.01, * = p < 0.05)

Furthermore, ORs for high CVD risk ranged from 4.4 (for WHR) to 11.1 (for WHtR) among boys and from 4.7 (for WHR) and 11.8 (for triceps skinfold thickness) among girls. However, the group with high CVD risk is relatively small and therefore the confidence intervals are broad (Table 20).

Some additional analyses have been conducted. For this purpose among 3-17 year olds the percentage of body fat was calculated by using the skinfold equations of Slaughter et al.³⁴ and among 11-17 year olds the squared WHtR (WC divided by squared body height) have been used as additional overweight measures. Non-HDL-cholesterol (calculated by the difference between TC and HDL-C) and the ratio of LDL-C to HDL-C have been used as additional outcome variables (Tables A-7 to A-9 in the appendix). However, it was shown that percentage of body fat and the squared WHtR are not more useful than the other overweight measures. Precisely, percentage body fat led to results similar to those of sum of skinfold thickness and the results for the WHtR were clearly stronger than those for the squared WHtR (Table A-9).

5.5 Discussion

5.5.1 Association between overweight and CVD risk factors

The present results as well as those from previous studies showed a relationship between overweight and adverse levels of several CVD risk factors, even among pre-pubertal children^{11, 45, 60, 172, 175-177}. For example, in a German study of 4-18 year old overweight children and adolescents referred to obesity centers, the degree of overweight was significantly and positively associated with SBP and DBP. In addition, HDL-C and overweight were weakly and negatively associated, while no association between overweight and TC or LDL-C was observed¹⁷⁷. These observations are in line with the results among children 3-10 years of age. However, the latter observation of Reinehr and colleagues¹⁷⁷ is not in line with the findings among 11-17 year olds of the present study. This may at least partly be explained by methodological differences as the present study was population based assuring a much higher variability in weight status as compared to a study of overweight children seen in obesity centers. Furthermore, various overweight measures were used in the present analyses, and WC and WHtR rather than BMI were associated with lower serum HDL-C. Finally, it seems that a relationship between overweight and serum lipoproteins is evident only in higher age groups. Serum lipoproteins may be modulated by genetic or

developmental factors^{195, 262, 263}. In line with this reasoning, the variability explained by age and pubertal stage in the present results was higher than for any overweight measure. The variability explained by any overweight measure was higher for blood pressure and hs-CRP than for serum lipoproteins. Blood pressure seemed to be affected by overweight earlier in life than blood lipids.

In line with the present results, several previous studies consistently observed a strong association between elevated serum hs-CRP and obesity in children and adolescents^{11, 183, 187-189}. This was also true when a serum hs-CRP level of 3 mg/l was used as cutoff instead of 2.1 mg/l. This finding supports the view that chronic low-grade inflammation in the presence of overweight already plays a role in childhood and adolescence, independently of age.

There was only a weak association between overweight and HbA1c among girls. Overall, there was no large variation in HbA1c concentrations. The 90th age and sex specific percentile of HbA1c ranged between 5.3% and 5.4% which does not imply elevated levels. HbA1c is an indicator of long-standing blood glucose elevation, as it is not affected by food intake or short-term blood glucose variations. It has also been proposed to be a good predictor of later development of type 2 diabetes mellitus in children²²⁵. In a large representative US study, HbA1c was positively related to BMI²²⁴.

5.5.2 Choice of anthropometric variable

Only few studies systematically compared different measures of childhood overweight with respect to their association with CVD risk factors. Studies among pre-pubertal children are scarce. In the present study, even among pre-pubertal children, there was an association between overweight and adverse levels of several CVD risk factors. BMI and skinfold thickness as the obtained measures of overweight among 3-10 year olds showed similar associations. In the KiGGS study, there were no indicators of body fat distribution in children 10 years of age and younger. Therefore, in the following paragraphs the results from the analyses conducted among 11-17 year olds are interpreted in more detail and compared with previous studies.

In a study of Greek-Cypriot children aged 10-14 years, SBP, DBP, TC and LDL-C were significantly higher among children exceeding the 75th percentile for various overweight measures compared to the other children. The differences were most pronounced if WC or

WHtR were used to define overweight⁶⁰. WC also showed the most consistent and generally strongest association with adverse lipid concentrations in the Bogalusa Heart Study¹⁷². In the present study among both boys and girls the association with blood pressure was strongest for WC. Among boys, WHtR showed the strongest association with serum levels of TC, LDL-C, and hs-CRP and BMI with LDL-C. Among girls, BMI and triceps skinfold thickness showed the strongest association with TC, WC with LDL-C, and WHtR with HDL-C. In contrast, a recent regional study of 9-11 year old children and 13-16 year old adolescents in Germany found that various overweight measures (BMI, WC, triceps skinfold, percentage fat mass) were similarly associated with blood pressure and blood lipids concentrations⁷⁶. In agreement with the present results, among girls the strength of the association with blood pressure was higher for WC than for BMI. Overall, it was concluded that both WC and BMI were appropriate predictors of CVD risk factors⁷⁶. In a large US study, WHtR showed stronger associations with lipids and lipoproteins, whereas BMI was more closely related to blood pressure and insulin levels⁵⁸.

A weaker association between CVD risk factors and WHR as well as skinfold thickness was observed, as compared to WC, WHtR and BMI, in particular among boys. As shown among adults, WHR as a measure of body fat distribution was associated with cardiovascular events and diabetes mellitus^{53, 54}. However, some studies among children found that WHR was not strongly correlated with CVD risk factors among children^{55, 56, 196}. Most likely, this is explained by the fact that children still undergo developmental changes of body fat distribution. WHR also seems to be less helpful to predict CVD risk factors because it is a measure for body stature. For instance, there may be no difference in WHR between an obese and a lean person when both WC and HC are high in the obese person.

In line with the present results, a weaker association between skinfold thickness and CVD risk factors was found in previous studies^{41, 172}. As measurement of skinfold thickness is prone to observer bias, misclassification might mask the association with CVD risk factors. Besides, skinfold measurement taken at only two locations and without a replication, as done in the present study, may not be sufficiently reliable as a surrogate for body fat³⁹.

5.5.3 Use of combinations of anthropometric variables

Among 11-17 year olds, for all CVD risk factors, except for HbA1c, the impact of the combinations of BMI, WC, and WHtR was evaluated. In recent studies, the use of both BMI

and WC or BMI and WHtR resulted in a small improved identification of children and adolescents with adverse CVD risk factors^{58, 264, 265}. In accordance with this finding, it has been found in the present analyses that the proportion of variability in CVD risk factors explained by linear regression models improved slightly, when combinations of BMI and WC among girls and BMI and WHtR among boys were used. Janssen and colleagues²⁶⁴ observed that BMI and WC, when analysed as continuous variables, predicted CVD risk factors in a similar manner. However, when BMI and WC were used as categorical variables, the combination of WC and BMI provided information beyond that provided by BMI alone. Thus, there is some evidence that a combination of BMI and WC or BMI and WHtR may be useful for risk assessment. But, there is also a strong relationship between these measures.

In summary, even among children 3-10 years of age there was an association between overweight, as defined by BMI and skinfold thickness, and adverse CVD risk factors. In particular, SBP and DBP were significantly higher among overweight compared to non-overweight children, even in the youngest age group. However, none of the measures of overweight was consistently stronger associated with CVD risk factors than any of the others in the younger age group.

Among 11-17 year old boys and girls, overweight as defined by various anthropometric measures, including BMI, WC, WHR, WHtR, and skinfold thickness was consistently related to adverse levels of several CVD risk factors. In both sexes, the association with SBP and DBP was most pronounced for overweight defined by WC. Among boys, WHtR showed the strongest association with serum levels of TC, LDL-C, and hs-CRP and BMI with LDL-C. Among girls, the associations were less consistent. BMI and triceps skinfold thickness showed the strongest association with TC, WC with LDL-C, and WHtR with HDL-C. Age and puberty adjusted differences in mean CVD risk factors between those with and without overweight were substantial.

6 RESULTS: RECEIVER OPERATING CHARACTERISTIC (ROC) CURVES

Historically, the receiver operating characteristic (ROC) curve analysis was developed during World War II in the context of electronic radar detection²⁶⁶. In the late 1950s ROC plots were implemented for improving medical decision making, for example to describe the ability of an automated Pap smear analyser to distinguish between smears with and without malignant cells²⁶⁷. Meanwhile the methodology has been adapted to several medical areas, including epidemiology²⁶⁸.

As shown in Chapter 5, there is a strong association between overweight and adverse CVD risk factors among children and adolescents. However, the usefulness of the existing cutoffs for defining overweight and obesity^{29, 65, 68} as well as the cutoff used in the previous chapter for defining health related overweight is unclear and all cutoffs are chosen arbitrarily. In general, the development of standard definitions of overweight and obesity, in particular among children and adolescents, remains problematic. Often, surrogate measures of body fat mass such as BMI are used as described in Chapter 2. A large set of studies among children and adolescents used ROC curve analysis to determine the relationship of different anthropometric measures to body fatness with the aim of defining cutoffs with the highest predictive value for identifying childhood and adolescent obesity^{20, 27, 50, 269-271}. In comparison, fewer studies have used this concept for defining cutoffs for anthropometric measures with the highest predictive value in relation to the presence of adverse CVD risk factors among children and adolescents^{58, 272-274}. The latter approach is an example of the identification of health related cutoffs for defining overweight and obesity.

For the following analysis, the concept of ROC curve analysis has been applied to get indications for the optimal cutoff points of anthropometric measures for identifying children and adolescents 11-17 years of age with an adverse CVD risk profile. The discriminatory ability of each of the anthropometric measures BMI, triceps, subscapular, and sum of skinfold thickness, WC, WHR, and WHtR was analysed and the ideal cutoff percentiles to identify individuals with a high risk of adverse CVD risk factors was examined.

6.1 The principle of a diagnostic test - analysis of sensitivity and specificity

The easiest way of describing how well a test differentiates between subjects with and without a certain condition (for example diseased vs. non-diseased) is demonstrated by using a standard 2x2-table or so called contingency table to calculate the sensitivity and specificity of a diagnostic test (Table 21)²⁷⁵.

Table 21: Principle of a diagnostic test - Sensitivity and Specificity

		Condition/Disease		Total
		Yes	No	
Test result	Positive	True positive (TP)	False positive (FP)	All positive tests (TP+FP)
	Negative	False negative (FN)	True negative (TN)	All negative tests (FN+TN)
Total		All diseased (TP+FN)	All non-diseased (FP+TN)	Total sample (N)

Sensitivity is defined as the probability that a test correctly classifies people with the certain condition (disease). The sensitivity is estimated by the number of diseased persons with a positive test (TP) divided by the total number of diseased persons (TP+FN). The more sensitive a test, the larger is the detected prevalence in a given population. The specificity of a test is the probability that the test correctly classifies people that do not have the condition (disease). Specificity is estimated by the number of non-diseased persons with a negative screening test (TN) divided by the total number of non-diseased persons (FP+TN).

$$\text{Sensitivity} = \frac{TP}{TP + FN}; \quad \text{Specificity} = \frac{TN}{FP + TN}$$

The ROC curve provides a statistical method to assess the diagnostic accuracy of a test or (bio)marker that has a continuous spectrum of test results. Sensitivity and specificity for each possible value of the test variable is calculated. The ROC curve is a plot of the true positive rate (sensitivity) against the false positive rate (1 – specificity). Therefore, the ROC curve provides a visual demonstration of the trade-off between sensitivity and specificity (any increase in sensitivity will be accompanied by a decrease in specificity). The calculation of the area under the curve (AUC) is a way to quantify the discriminatory ability of a test. An AUC of 1.0 corresponds to a perfect test since it achieves both 100% sensitivity and 100% specificity. The aim of a diagnostic test (or biomarker) is to identify people with a certain condition with a maximum of accuracy. To evaluate the optimal cutoff point of the test, the Youden Index²⁷⁶ or “closest to 1.0 criterion” can be used.

On a ROC curve, the Youden Index demonstrates the point which results in the maximum vertical distance from the curve to the chance line (positive diagonal, 45° line). Therefore, the Youden Index can be interpreted as the point on the curve most distant from chance and is commonly used as an overall measure of test accuracy (+1 is perfect prediction)²⁷⁷.

$$\text{Youden Index} = (\text{sensitivity} + \text{specificity}) - 1$$

The closest to 1.0 criterion demonstrates the point closest to the upper left corner (intersection of sensitivity and specificity). That means any further increase in sensitivity will be accompanied by a decrease in specificity and vice versa. This point characterises the point on the curve closest to perfection²⁷⁷.

Perkins and Schisterman²⁷⁷ conclude that the Youden Index is the criterion which should be preferred because it shows a lower overall misclassification rate. However, in previous studies mostly the closest to 1.0 criterion has been used.

6.2 *Sample*

Since no consistent and sustainable association between overweight and serum lipoproteins was observed among children below the age of 11, and WC was not measured in this group, the current analysis was restricted to children and adolescent 11-17 years of age. The sample used is the same as described in Chapter 5 including data of 5546 participants (3031 boys, 2515 girls).

6.3 *Statistical analysis*

The outcome or diagnostic variable analysed here was the dichotomous variable ‘high CVD risk’ as defined in Chapter 5.2. A high CVD risk was therefore defined when at least three adverse individual CVD risk factors (as defined previously) were observed. The anthropometric measures BMI, skinfold thickness (triceps, subscapular, sum of skinfold thickness), WC, WHR, and WHtR were used as continuous test variables. Thereby, smoothed age and sex specific percentile values of the anthropometric measures based on the KiGGS reference population have been used by implementing the LMS method established by Cole⁶⁴. The KiGGS reference population and the construction of smoothed percentile curves are described in detail elsewhere²⁷⁸. In brief, for the reference population amongst others participants with chronic diseases and/or on medication that can influence growth and weight development were excluded. The LMS method is based on the assumption that anthropometric measure values can, for a given age, be transformed to a standard normal distribution^{64,278}.

Sensitivity and specificity were calculated for each percentile (in 1-percentile steps) for any of the anthropometric measures using logistic regression models. For each anthropometric measure, models were calculated for the total study population as well as for boys and girls separately, including high CVD risk as the dependent variable and the age and sex specific percentile value of the anthropometric measure as the independent variable. ROC curves (sensitivity plotted against $1 - \text{specificity}$) for all anthropometric measures have been plotted with high CVD risk as the diagnostic variable. The AUCs were calculated to identify the anthropometric measure with the highest discriminatory ability for identifying children and adolescents with high CVD risk. Furthermore, the percentiles yielding the maximum Youden Index as well as the percentiles reflecting the intersection of sensitivity and specificity (closest to 1.0 criterion) were analysed. These cutoff points may support the general definition of overweight among children and adolescents since a health related outcome has been considered in contrast to the pure statistical approach used until now. For the calculation of sensitivity and specificity as well as for plotting the ROC curves, a SAS macro established by Schneider²⁷⁹ has been used. For the calculation of AUC, Youden Index, and the intersection of sensitivity and specificity, a SAS macro established by Lambert et al.²⁸⁰ has been applied.

6.4 Results

The prevalence of boys and girls with high CVD risk was relatively low with 3.9% (N = 119) among boys and 3.0% (N = 75) among girls, as shown in Chapter 5.4.2 (Table 20). In Figures 13 and 14, the discriminatory ability of the different anthropometric measures based on percentiles in 1-percentile steps in relation to the presence of three or more adverse CVD risk factors was compared by using plots of ROC curves. With the exception of WHR, AUC values for each overweight measure were all in a similar range, for the total population as well as separately for boys and girls. In the total study population, the AUCs ranged from 0.67 for WHR to 0.78 for subscapular skinfold thickness (Table 22). Among boys, the lowest AUC value was observed for WHR with 0.67 and the highest for BMI, subscapular skinfold thickness, sum of skinfold thickness and waist circumference, simultaneously, with 0.79. Among girls, AUC was also lowest for WHR with 0.67 and highest for sum of skinfold thickness with 0.75.

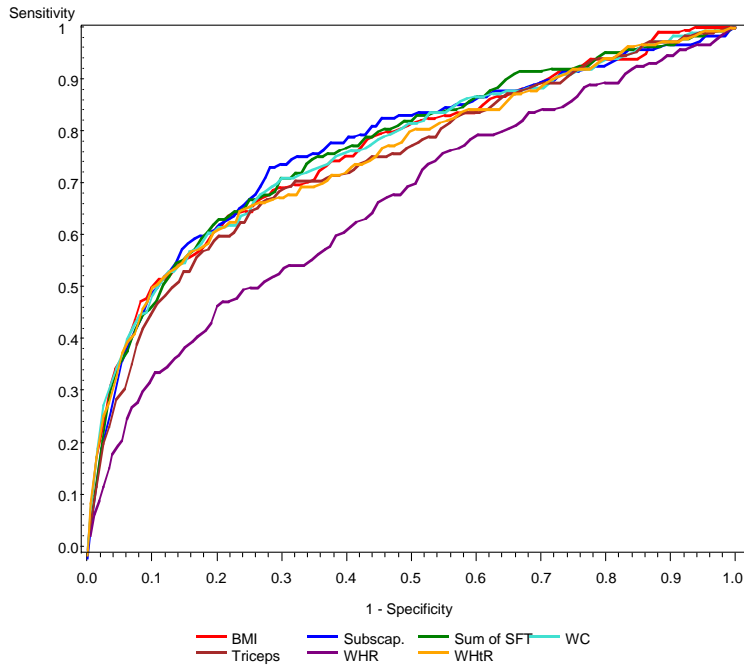


Figure 13: ROC curves for different anthropometric measures, 11-17 years

BMI: body mass index, Subscap: subscapular skinfold thickness, SFT: skinfold thickness, WC: waist circumference, WHR: waist-to-hip ratio, WHtR: waist-to-height ratio

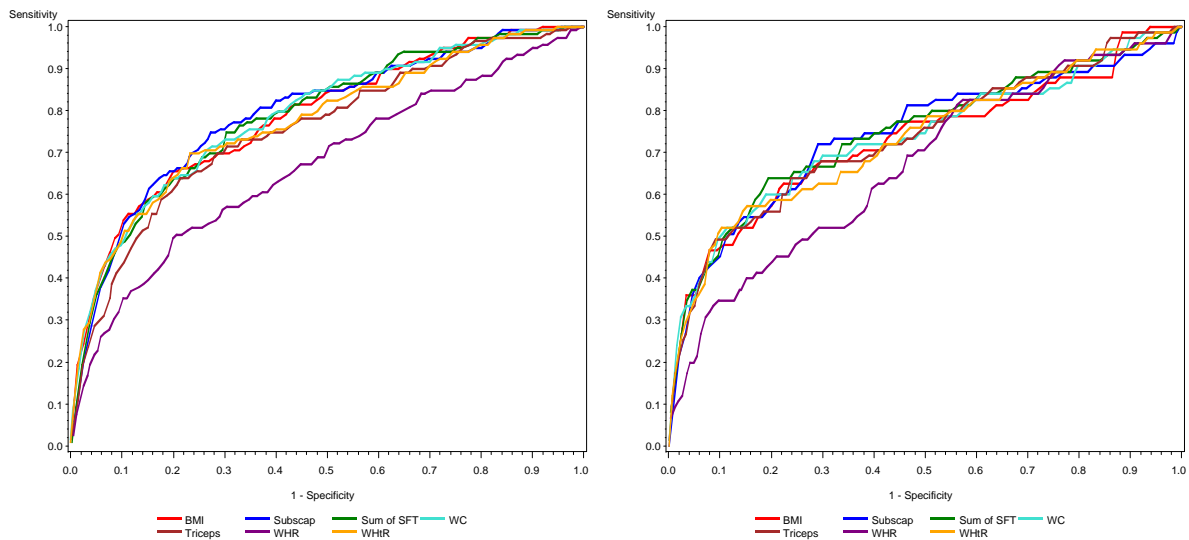


Figure 14: ROC curves for different anthropometric measures, boys (left) and girls (right), 11-17 years

BMI: Body Mass Index, Subscap: subscapular skinfold thickness, SFT: skinfold thickness, WC: waist circumference, WHR: waist-to-hip ratio, WHtR: waist-to-height ratio

Table 22: Areas under the ROC curves displayed in Figures 13 and 14

	Total	Boys	Girls
BMI	0.76	0.79	0.73
Triceps SFT	0.75	0.75	0.74
Subscapular SFT	0.78	0.79	0.74
Sum of SFT	0.77	0.79	0.75
Waist circumference	0.77	0.79	0.74
Waist-to-hip ratio	0.67	0.67	0.67
Waist-to-height ratio	0.76	0.77	0.73

The age and sex specific percentile values for which the Youden Index was highest (point most distant from chance) and those reflecting the intersection of sensitivity and specificity (point closest to perfection) are shown in Table 23.

In the total population, the Youden Index was highest for percentile values ranging from the 70th percentile for waist circumference and subscapular skinfold thickness to the 80th percentile for the sum of skinfold thickness. The intersection between sensitivity and specificity occurred for percentile values ranging from the 59th percentile for WHR to the 71st percentile for subscapular skinfold thickness. With exclusion of WHR, the optimal percentile values indicating the trade-off between sensitivity and specificity ranged from the 67th to the 71st percentile. Sensitivity for all measures ranged from 48% to 74%, and specificity ranged from 72% to 80% with regard to the Youden Index. Concerning the intersection, sensitivity ranged from 61% to 72% and specificity ranged from 62% to 73%. Sensitivity was consistently lowest for WHR compared all other anthropometric measures.

Among boys, percentile values for the Youden Index ranged between the 68th percentile for the sum of skinfold thickness and the 79th percentile for triceps skinfold thickness, while the percentile values for the trade-off between sensitivity and specificity ranged from the 58th percentile for WHR to the 71st percentile for subscapular skinfold thickness. Sensitivity and specificity with regard to the Youden Index ranged from 50% to 75% and from 73% to 80%, respectively. The values for sensitivity and specificity according to the intersection ranged from 61% to 73% and from 62% to 73%, respectively. Also among boys, sensitivity was lowest for WHR compared to all other anthropometric measures.

Among girls, percentile values for the Youden Index varied between the 43rd percentile for WHR and the 90th percentile for triceps skinfold thickness, while the percentile values for the trade-off between sensitivity and specificity ranged from the 59th percentile for WHR to the 70th percentile for subscapular skinfold thickness. With regard to the Youden Index, sensitiv-

ity ranged from 49% to 83%, and specificity ranged from 43% to 91%. Concerning the intersection, sensitivity ranged from 61% to 72% and specificity ranged from 60% to 71%. Among girls, specificity was lower for WHR than for all other anthropometric measures.

Overall, when the intersection of sensitivity and specificity was used, there was a tendency for lower optimal cutoffs among girls compared to boys. This was not true when the Youden Index was used, where there was no consistent difference in one direction in optimal cutoff points between girls and boys. When sensitivity and specificity of optimal Youden Index and intersection were compared, there was a tendency for lower sensitivity and higher specificity when the Youden Index is used. With the exception of WHR, the results were similar for all anthropometric measures.

Table 23: Percentile values (sensitivity; specificity) of maximum Youden Index and intercept of sensitivity and specificity

	Youden Index			Intersection of sensitivity and specificity		
	Total	Boys	Girls	Total	Boys	Girls
BMI	76 (0.64; 0.78)	78 (0.66; 0.80)	75 (0.63; 0.77)	66 (0.69; 0.69)	67 (0.70; 0.70)	65 (0.68; 0.68)
Triceps SFT	79 (0.68; 0.72)	79 (0.64; 0.78)	90 (0.49; 0.91)	67 (0.70; 0.70)	69 (0.70; 0.70)	64 (0.68; 0.68)
Subscapular SFT	70 (0.74; 0.72)	70 (0.75; 0.73)	70 (0.72; 0.71)	71 (0.72; 0.73)	71 (0.73; 0.73)	70 (0.72; 0.71)
Sum of SFT	80 (0.64; 0.80)	68 (0.75; 0.70)	80 (0.64; 0.81)	68 (0.72; 0.70)	69 (0.71; 0.70)	64 (0.67; 0.68)
Waist circumference	70 (0.69; 0.73)	77 (0.64; 0.80)	79 (0.60; 0.81)	67 (0.71; 0.71)	68 (0.71; 0.71)	65 (0.69; 0.69)
Waist-to-hip ratio	76 (0.48; 0.79)	76 (0.50; 0.79)	43 (0.83; 0.43)	59 (0.61; 0.62)	58 (0.61; 0.62)	59 (0.61; 0.60)
Waist-to-height ratio	73 (0.65; 0.76)	73 (0.70; 0.77)	83 (0.57; 0.85)	65 (0.69; 0.69)	67 (0.71; 0.71)	62 (0.65; 0.65)

6.5 Discussion

This chapter provides some indication for health related thresholds of anthropometric measures for identifying children and adolescents with adverse CVD risk factors. However, only few boys and girls 11-17 years of age were defined to have a high CVD risk (3.9% of boys, 3.0% of girls). Overall, the discriminatory ability, determined by the AUC, was in a similar range for all anthropometric measures, except for WHR. Thus, WHR appeared to be not appropriate as a measure of health related overweight among children and adolescents. Without considering WHR, the AUC ranged from 0.75 to 0.78 in the total study population, from 0.75 to 0.79 among boys, and from 0.73 to 0.75 among girls. When the Youden Index was chosen as the preferred criterion and WHR was not considered, the optimal percentile cutoff for the

different anthropometric measures ranged from the 70th to the 80th percentile in the total population, from the 68th to the 79th percentile among boys and from the 70th percentile to the 90th percentile among girls. The Youden Index may be preferred since it shows a lower overall misclassification rate ²⁷⁷.

The prevalence of children and adolescents with three or more adverse CVD risk factors was very low in the present study compared to previous studies observing between 16.5% and 19% children and adolescents with three or more elevated CVD risk factors ^{272, 273}. This may influence the predictive power of the present results. In comparison with previous studies, the AUCs identified here were somewhat higher than those examined in studies among adults ^{281, 282} and comparable to those examined in studies among children and adolescents ^{272, 273}. For example, a meta-analysis of 10 studies among adults with the aim to determine the measure of overweight and obesity (BMI, WC, WHR, WHtR) which is the best discriminator for hypertension, type 2 diabetes mellitus and dyslipidemia showed AUCs ranging from 0.67 to 0.73 in men and from 0.68 to 0.76 in women ²⁸². In contrast, in a study conducted among Portuguese children and adolescents aged 10-15 years each AUC for anthropometric variables discriminating for high percentage body fat were close to 1.0 ²⁶⁹. However, in this study obesity determined by percentage body fat was used as the outcome variable. When different studies are compared, one has to distinguish between studies using percentage body fat as the outcome and those using certain health risk factors. It is not surprising that results were more distinctive when body fat mass was used as the outcome variable since anthropometric measures are highly correlated with body fat mass.

In previous studies, different criteria for defining overweight as well as different thresholds for anthropometric overweight measures were used. For example, cutoffs based on age and sex specific BMI percentiles ranged between the 75th percentile and 95th percentile ^{60, 172}. Others used z-scores or the IOTF definitions ^{58, 264}. This makes a direct comparison difficult. In contrast to the present results, the optimal cutoffs to predict risk factor clustering were between the 50th and the 57th age and sex specific percentile of BMI and WC in two large-scale population based US studies among children and adolescents ^{272, 273}. A recent study among 12-19 year olds living in Hong Kong evaluated optimal BMI cutoffs at the 78th percentile for girls and the 72nd percentile for boys for predicting clustering of CVD risk factors ²⁷⁴. Optimal WC thresholds were at the 77th percentile for girls and the 76th percentile for boys. These cutoffs are more in line with the present results than those examined in the US studies mentioned

above. However, since the body statures of Chinese and German individuals differ in general, it is unclear how comparable those cutoffs are. Even among adults the discriminatory ability of different anthropometric measures for defining health related overweight is still under discussion^{283, 284}. This is discussed in more detail in Chapter 7.2. Since health consequences of overweight and obesity among children and adolescents are biologically not developed to a comparable extent as among adults, those definitions are even harder to assess for young individuals.

Consistent with previous studies, no anthropometric measure can be explicitly highlighted with regard to its predictive value for cardiovascular risk based on the ROC curve analysis^{272, 273, 281}. This is not surprising since these measures are highly correlated with each other. However, with respect to the results presented in Chapter 5 as well as due to their simplicity, BMI as well as the measures of abdominal obesity WC and WHtR should be preferred.

In summary, the optimal percentile cutoff points for different anthropometric measures varied, and percentile values between the 70th and the 90th age and sex specific percentile were associated with a higher risk for adverse CVD risk factors. Although the prevalence of the outcome variable was low in the present study, the AUCs for each anthropometric measure were comparable to previous studies. Compared to all other overweight measures, WHR seemed not to be an appropriate measure to identify children and adolescents with high CVD risk. There is no final conclusion as to which percentile value of anthropometric measures should be used in future for identifying overweight and obese children and adolescents with higher health risk. However, it was shown that adverse CVD risk factors are already present among children and adolescents with overweight measure values between the 70th and the 90th age and sex specific percentile.

7 GENERAL DISCUSSION

7.1 Main findings

7.1.1 Determinants of overweight and obesity

The present analyses confirm associations with overweight and obesity among children and adolescents for many of the supposed determinants. Independently of other factors, a positive association was observed between obesity and low SES, two-parent migration background (up to the age of 13), parental overweight, high weight gain during pregnancy (when the mother is of normal weight), maternal smoking during pregnancy, high birth weight, and high media consumption, as well as a negative association with sleep duration for 3-10 year olds. The variables parental smoking at the time of interview, breastfeeding, physical activity, and food intake all showed univariable associations with obesity, did not significantly contribute to the multiple logistic regression model. On the univariable level, there was a significant positive association between overweight and obesity and the total food intake, the intake of energy-providing food, the total beverage intake, the intake of water or tea, and the meat consumption. There was no relationship with the overall dietary quality, assessed by a healthy nutrition score. Of particular importance is the observation that parental overweight was most strongly associated with overweight in the offspring, independently from other variables. Furthermore, children and adolescents with low SES are significantly more affected by overweight and obesity and showed the most unfavourable overweight related behaviour and conditions.

Thus, the initial research question “What are major potential determinants of overweight and obesity in children and adolescents?” can be answered as followed: The most important determinant of overweight and obesity among children and adolescents aged 3-17 years living in Germany is parental overweight. Children and adolescents from families with low SES are of particular risk since low SES is associated with overweight and obesity as well as with a higher occurrence of other potential determinants, such as parental overweight, maternal smoking during pregnancy, and high electronic media consumption.

These results, in particular the observed relationships of single potential risk factors, underline the multifactorial nature of overweight and obesity. Overall, the results are in line with the current state of research as described in detail in Chapter 4.5. The strong association with parental overweight indicates an important genetic impact of the development of overweight and obesity in the offspring on the one hand. On the other hand, parental behaviour and attitudes play an essential role concerning the establishment of lifestyle pattern and preferences among

their children. For example, parents and the family environment influence the eating behaviour and the level of physical activity in the offspring^{285, 286}. Additionally, as shown in the present analysis as well as in previous studies, maternal constitution and behaviour during and after pregnancy influence their children's risk for overweight and obesity in later life^{77, 103, 106}. There is increasing evidence that children and adolescents from families with low SES are of particular health risk. As shown, they are not only more often overweight and more often obese but they also show unfavourable behaviour and conditions in general. It has been observed that children and adolescents from families with low SES showed a less favourable diet, were less often physical active and showed more often psychological problems compared to those from families with higher SES²⁸⁷. This picture was also shown for other health related areas²⁸⁸. Thus, this group can be seen as particularly vulnerable.

7.1.2 Association between overweight and CVD risk factors

Already among children 3-10 years of age, there was an association between overweight and adverse CVD risk factors. In particular, SBP and DBP were significantly higher among overweight compared to non-overweight children, even in the youngest age group (3-6 years). From age 7 years upwards, serum levels of HDL-C were significantly lower and serum levels of hs-CRP were significantly higher among overweight children. For example, adjusted differences in mean CVD risk factors between those with and without overweight were up to 6.6 mm Hg for SBP, 3.5 mm Hg for DBP, and -6.5 mg/dl for HDL-C. There was only a tendency for higher serum levels of TC and LDL-C among overweight children and the results were not statistically significant. Furthermore, there was no association between overweight and HbA1c among boys and only a weak association among girls. None of the measures of overweight was consistently more strongly associated with CVD risk factors than any of the others.

Among 11-17 year old boys and girls, overweight as defined by various anthropometric measures, including BMI, WC, WHR, WHtR, and skinfold thickness was consistently related to adverse levels of several CVD risk factors, except for HbA1c. Age and puberty adjusted differences in mean CVD risk factors between those with and without overweight were substantial, for example up to 9 mm Hg for SBP, and 12 mg/dl for LDL-C. Between 11% and 37% of overweight boys and girls exceeded the defined cutoffs for individual CVD risk factors. Age and puberty adjusted significant odds ratios (95% CI) for elevated CVD risk factors in overweight adolescents as compared to normal weight age mates ranged from 1.7 (1.0-3.0) to 6.1

(4.5-8.2). In both sexes, the association with SBP and DBP was most pronounced for overweight defined by WC. However, WHtR among boys showed the strongest association with serum levels of TC, LDL-C, and hs-CRP. Among girls, the associations were less consistent. BMI and triceps skinfold thickness showed the strongest association with TC, WC with LDL-C, and WHtR with HDL-C. The use of combinations of BMI, WC, and WHtR for identifying overweight boys and girls contributed to slightly better results. For example, regression coefficients and R-squared slightly increased when BMI and WHtR were used in combination among boys and when BMI and WC were used in combination among girls.

These results contribute to the answers of the research questions “Is there a consistent association between overweight and other CVD risk factors among children and adolescents in Germany?” and “Which measure of overweight shows the strongest association with CVD risk factors and may therefore be preferably used for risk assessment and prevention?”. The answer of the first of these two questions is that indeed there is a consistent association between the existence of overweight and adverse CVD risk factors with the exception of HbA1c. The positive association between major CVD risk factors and overweight is already seen among children younger than 11 years of age. To answer the second question, BMI, WC, and WHtR show a stronger association with CVD risk factors than WHR or skinfold thickness among 11-17 year olds. A combination of BMI and WC or BMI and WHtR may be even more useful for risk assessment than one single measure itself. Among 3-10 year olds, no final statement regarding which measure of overweight should preferably be used for risk assessment can be made, since none of the measures was consistently more strongly associated with CVD risk factors than any of the others.

These results confirm those from previous studies which examined the associations between overweight, obesity and CVD risk factors among children and adolescents^{45, 172, 175, 177}. This has been discussed in more detail in Chapter 5.5. There is evidence that obesity is an independent risk factor for CVD among adults and in line with the present study CVD risks have also been documented in obese children². A recent review and meta-analysis support strong associations between different measures of general and abdominal obesity and hypertension, type 2 diabetes mellitus and dyslipidemia among adults²⁸⁹. The authors summarised that there is some evidence that measures of abdominal obesity were more strongly related to diabetes risk than BMI, but this was not true for hypertension and dyslipidemia for which the relations with BMI, WC, and WHR were similar²⁸⁹. Although there is evidence for the demonstrated

associations further data from large-scale longitudinal studies are needed to get a deeper understanding of the biological mechanism and causal pathways. Up to now, there is no clear agreement whether measures of abdominal obesity are more strongly associated with overall CVD morbidity and mortality. In line with the present results a recent large-scale prospective study among adults supports the use of measures of fat distribution (such as WC) in addition to BMI for estimating health risk ⁷⁵.

7.1.3 ROC curve analyses

The ROC curve analyses gave some indications where threshold values for anthropometric measures could be set for identifying children and adolescents with adverse CVD risk profile. Only about 4% of the boys and 3% of the girls 11-17 years of age were defined to have an adverse CVD risk profile. The optimal percentile cutoff points for different anthropometric measures varied, depending on the criterion used (Youden Index versus intersection of sensitivity and specificity) as well as on the anthropometric measure chosen. When the results for WHR are not considered and the Youden Index was used as the preferred criterion, optimal percentile values ranged from the 68th percentile to the 79th percentile among boys and from the 70th percentile to the 90th percentile among girls. Thus, even percentile values below the 90th percentile were associated with a higher risk for elevated CVD. The discriminatory ability to identify children and adolescents at high CVD risk estimated by the areas under the ROC curves was comparable for all anthropometric measures, except for WHR and ranged from 0.75 to 0.79 among boys and from 0.73 to 0.75 among girls when WHR was not considered. WHR seemed not to be an appropriate measure to identify children and adolescents with high CVD risk.

The initial research question “Which cutoff points of anthropometric measures should be used to identify children and adolescents with higher CVD risk?” can not be definitively answered. An adverse CVD risk profile is already observed among children and adolescents with overweight measure values between the 70th and the 90th age and sex specific percentile.

Current data provide not enough evidence to formulate concrete recommendations for optimal cutoffs point defining health related overweight. This may be due to the low prevalence of the outcome variable. With increasing age, adverse consequences of overweight may cumulate and such an accumulation may be not yet visible among children and adolescents. Additionally, a more precise endpoint variable may be more useful for such an evaluation. This can be

achieved in the future by using longitudinal data with incident diseases as endpoints. Although there is no definite conclusion for the recommendation of optimal thresholds, the present results confirm those from previous studies among children and adolescents showing considerably lower optimal cutoffs compared to the current references. For example, results from the Bogalusa Heart Study as well as from NHANES showed that children and adolescents between the 50th and 57th age and sex specific percentile for different measures of overweight were at higher risk for elevated CVD risk factors^{272, 273}. This indicates that when current population based percentile values were used, adverse CVD risk factors occurred within percentile ranges considerably lower than several years before. One explanation for this observation may be that the prevalence of overweight and obesity is higher in the current population compared to the population used for the development of the reference values⁸. Thus, if the KiGGS population should be used as a new reference population, cutoffs for defining overweight and obesity may be defined as values considerably below the 90th and 97th percentile which are currently used as reference value for the German population of children and adolescents⁶⁵.

7.2 *Methodological considerations*

Causal inference

The KiGGS study provides representative data on health, living conditions, and behaviour among children and adolescents. Due to the cross-sectional design of the study no cause-effect inference but only associations can be evaluated. Hill²⁹⁰ proposed nine criteria to evaluate a causal relationship: strength, consistency, specificity, temporality, biological gradient, plausibility, coherence, experiment, and analogy. These criteria are commonly applied in epidemiologic research. However, according to Rothman and Greenland²⁷⁵ causal inference can not be evaluated by checking a list of criteria. They conclude that except temporality (the criteria that the cause precedes the effect) none of the criteria is necessary or sufficient for determining whether an association is causal. This temporal aspect is not available for all associations in the present study. Therefore, cause and effect can not be strictly delineated. Exceptions are early life factors such as weight gain during pregnancy, smoking during pregnancy, and high birth weight as well as migration background and SES since these factors temporally occur before the observed overweight or obesity at time of the KiGGS study.

In the complex field of the development of overweight and obesity, theoretical considerations also have to be made. More precisely, some potential risk factors may not be causally related

to overweight and obesity but rather act as parts of the causal chain. For example, parental overweight and in particular maternal overweight demonstrates a genetic element on the one hand but may also reflect a certain lifestyle which is adapted to the offspring on the other hand.

As observed in the KiGGS population, there is an interaction between maternal weight status and weight gain during pregnancy which in turn influences prenatal environment and therefore the development of overweight. Another example for the complex relationship is the association between overweight and low SES. As shown, a low SES is not only associated with higher occurrence of overweight and obesity but also with overall unfavourable conditions and behaviour. This implies that SES is linked to a certain lifestyle and environmental aspects which in turn are associated with overweight and obesity. Thus, due to the often interrelated synergy of a large range of potential risk factors, the single impact of those can not be explicitly separated. The following figure aims to illustrate these complex associations.

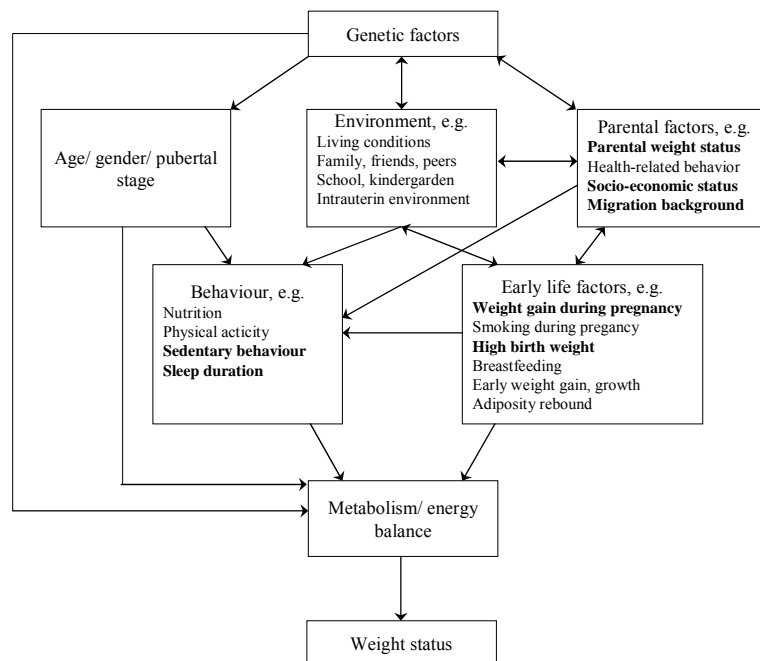


Figure 15: Potential determinants of overweight and obesity and possible pathways*

Source: own illustration

*Statistically significant independent determinants observed in the present analyses are highlighted (bold)

Different definitions of overweight, obesity and adverse CVD risk factors

As described in detail in Chapter 2 various definitions of overweight and obesity among children and adolescents exist and different approaches have been used in the scientific literature. Due to methodological considerations and depending on the purpose of the respective chapter, different definitions have been used in this thesis.

To allow an international across-study comparison of the prevalence of overweight and obesity and the occurrence of major determinants the international definitions established by the IOTF¹³ have been used in Chapter 4. Age and sex specific BMI cutoffs of the IOTF reference population were therefore applied to the KiGGS data. The choice of these cutoffs might have reduced the power to detect some associations since the number of obesity cases is rather small using this definition. For example, the prevalence of obesity was 5.5% among boys and 5.2% among girls using IOTF criteria in contrast to 6.8% and 7.0% using the criteria of Kromeyer-Hauschild⁶⁵, respectively. A sensitivity analysis with obesity using the criteria of Kromeyer-Hauschild as dependent variable led to only slightly lower ORs. Yet, the use of IOTF cut-points focuses more on the upper part of the distribution.

The aim of Chapter 4 was to conduct a systematic and population based comparison of different anthropometric measures and to evaluate which measure of overweight shows the strongest association with CVD risk. For this purpose, it was methodologically necessary that the number of children and adolescents defined to be overweight was similar for all anthropometric measures. Therefore, the definitions were consistently based on the 90th age and sex specific percentiles of the net study sample of 11774 children and adolescents of several anthropometric measures. Choosing the 90th age and sex specific percentiles as cutoff was somewhat arbitrary. However, the focus had to be on children and adolescent with percentile values within the upper margin of the distribution. For this purpose, using the 90th percentile as threshold is a common approach. Using a higher percentile (for example the 95th percentile) would have markedly reduced the numbers of observations in the upper groups and hence limited statistical comparisons.

A recent review among adults showed that overall mortality was lowest among men and women with BMI values about 22.5-25 kg/m²²⁸⁴. The authors concluded that BMI is a strong predictor of mortality, but other anthropometric measures may provide additional information. However, it was shown that the excess mortality associated with BMI did not significantly differ from the excess mortality with other anthropometric measures²⁹¹. In contrast, another

review stated that overweight patients (defined by BMI) with coronary artery disease had the lowest risk for total mortality and cardiovascular mortality²⁸³. These results question the ability of BMI to discriminate between individuals with increased health related risk or mortality risk. This suggests that even among adults, standard definitions of overweight and obesity should be based on thresholds from which adverse health impacts are likely. One possible approach to develop such definitions is using ROC curve analysis. For ensuring that the evaluated thresholds can be generalised for the entire population, representative data have to be available. Therefore, for the analyses in Chapter 5, smoothed and standardised age and sex specific percentile values for the anthropometric measures based on the KiGGS reference population have been used. To avoid uncontrolled confounding, the subsequent ROC analyses were conducted using the net study sample of N = 11774, for which children and adolescents with chronic diseases were excluded. The analyses showed that even with percentile values between the 70th and the 90th age and sex specific percentile, there was an association with adverse CVD risk factors. The definition of high CVD risk in the present analyses remains arbitrary. However, defining high CVD risk when only two single CVD factors are present did not change the overall results considerably. For a definite specification of optimal threshold a more diagnostic outcome variable (for example measuring intima media thickness as an indicator of early atherosclerotic changes) may be more useful.

There is no final evidence regarding the clinical and health relevant cutoffs for serum lipids^{195, 216-218} or blood pressure^{221, 292, 293} among children and adolescents. Thus, the cutoff levels chosen for CVD risk factors also remain arbitrary and their relevance for clinical and public health practice needs to be proven. However, they are appropriate for the present systematic analyses conducted on a population based level. For hs-CRP, threshold values as applied in a large US study were used¹⁸⁷. Cutoff levels for the other CVD risk factors were defined by the age and sex specific 90th percentiles (10th percentile for HDL-C) observed in the KiGGS population. In absolute terms, the chosen thresholds are comparable with those from previous studies^{195, 217, 221}. For example, data from the Lipid Research Clinic Pediatric Prevalence Study showed a 90th percentile for serum TC of 183 mg/dl for 15-19 year old males and 198 mg/dl for 15-19 year old females¹⁹⁵. In the KiGGS study population, the 90th percentile of serum TC was 185 mg/dl for 15 year old boys and 200 mg/dl for 15 year old girls. However, there were meaningful age dependent differences in serum lipoprotein levels in KiGGS (Table A-4 and A-5) as well as in NHANES²¹⁷. The thresholds for children aged 5-9 years from the Lipid Research Clinic Pediatric Prevalence Study were lower than those for KiGGS.

As shown in the present analyses age is an important determinant of CVD risk factors. Therefore, only age specific reference values seem to be appropriate in contrast to fixed cutoff values.

Aspects why the association between overweight and diet is often not visible

There was no consistent and independent association between food intake, physical activity and both overweight and obesity observed in the KiGGS population. As several recent reviews concluded, overall results concerning the association between dietary behaviour and overweight, particularly on causal relationships, are inconsistent and unclear, mainly because of methodological limitations and limited data^{84, 127, 150, 162}. It has also been shown that many factors further influence the association between dietary behaviour and overweight, for example the biological interdependency of nutrients and foods as well as genetic, metabolic and physical aspects^{127, 162, 294}. These factors are often not gathered. Furthermore, multiple aspects of diet have changed during the past decades, including food availability, food composition, and overall eating patterns¹⁵⁰.

In particular, methodological aspects may explain why the association between diet and overweight is often not visible, especially in large-scale observation studies. In fact, for long-term weight gain, a relatively small positive energy balance is sufficient. Willet²⁹⁵ estimated that an adult male with usual daily energy intake of 2500 kcal who increases his energy intake by 2% (50 kcal) will gain weight of 20 kg in a 10-year period, assuming that all other factors remain constant. However, this is a theoretical calculation. The weight gain will not be that large since increasing body mass is also associated with rising metabolic turnover. Hill et al.²⁹⁶ stated that of every excess 100 kcal consumed at least 50 kcal are stored in the body. A recent study based on a population of 963 children and adolescents 4-18 years of age claimed, that if this population would consume 10% less energy (187 kcal/d), their mean weight would be 4.5% (1.4 kg) lower²⁹⁷.

To draw exact conclusions about energy intake and energy expenditure extensive and cost-intensive methods are needed, which are usually not applied in large-scale studies. The common instruments used in epidemiological research are often too crude to detect the small energy imbalance. Furthermore, with cross-sectional studies it is not possible to measure long-term discrepancies in energy balance. Often conclusions are based on cross-sectional results, focussing on current dietary patterns. In KiGGS, the food intake of the last 4 weeks was ob-

tained. However, for the development of overweight the eating behaviour in the past is more important than the current food intake. Therefore, there is consensus that more longitudinal studies are needed^{84, 150, 166}.

Individual aspects influence energy intake and energy expenditure (genetic factors, basal metabolic rate, etc.). As described in detail by Willet²⁹⁵, energy expenditure and energy intake are mainly influenced by three factors: body size, metabolic efficiency, and physical activity. Body size affects the amount of energy needed to ensure resting metabolic as well as physical activities. Thus, a large person physically needs more energy than a small person. However, given the same BMI, body size may differ consistently. Physical activity plays an important role in determining the (individual) variation of energy expenditure. Even unconscious motor activity varies considerably between persons. For example, fidgety persons expend more energy than those who behave generally calmly. Therefore, residual confounding by physical activity may explain the often weak or not significant association between overweight and dietary behaviour. The metabolic efficiency and the ability to compensate energy imbalance also differs between individuals. Some people may store energy better and faster and may gain weight more rapidly than others even with similar energy intake.

Furthermore, it was reported that obese people tend to underreport their food intake more than lean people²⁹⁸. However, Huang et al.¹⁴⁹ determined an overreporting of energy intake by the parents/caregiver for young children in general and an underreporting in overweight adolescents. They further conclude that excluding implausible dietary records may play an important role in determining relationships between eating patterns and obesity, since the relationships were more consistent and stronger in the plausible sample compared to the total sample.

These aspects are often not adequately considered in studies evaluating the association between overweight and energy intake. Since we are a “free-living population” and do not live in a stable environment (not under laboratory conditions) it is hardly possible to accurately measure all these additional aspects. Therefore, the current body of literature on the relationship between diet and overweight should be interpreted with caution.

Strengths and weaknesses

For the first time in Germany, nationally representative data including comprehensive information about health status, living conditions, and behaviour of children and adolescents is

available in a large sample. The study was carried out carefully and provides excellent data including a large range of information. This allows conducting analyses broad in scope on potential determinants of overweight and obesity as well as on their associations with CVD risk factors. Since several indicators of overweight were available, it was possible to conduct a systematic comparison of their association with different CVD risk factors. In general, the analyses underlined the complexity of the aetiology of overweight as well as on potential health risks and provide important information for prevention and risk assessment. These baseline data provide an outstanding basis for further longitudinal analyses. For example, it will be possible to verify the established hypotheses, to analyse cause effect relations, and to evaluate optimal overweight thresholds.

Some methodological considerations, in particular concerning the assessment of physical activity and food consumption, have already been discussed in detail before. Some further limitations should be mentioned. Several potential risk factors, for example early adiposity rebound, catch-up growth, weight gain within the first year, and energy intake, were not considered in the analyses, since these data were not available. Furthermore, there was no information on waist circumference in children aged 3-10 years of age. Therefore, only BMI and measures of skinfold thickness were compared in this age group. Because of the cross-sectional design and the interdependency of many of the variables, no definite statement on causality or causal directions can be made.

7.3 Conclusions and implications

Major determinants of overweight and obesity have been identified in this thesis. On the population level, an association between overweight as defined with different anthropometric measures and major CVD risk factors was consistently observed, in particular among adolescents.

The main results can be summarised as follows:

- 1) The most important determinant of overweight and obesity is parental overweight.
- 2) Further independent determinants of obesity are maternal smoking during pregnancy, high birth weight, and high electronic media consumption.
- 3) Low SES is associated with higher prevalence of overweight and obesity as well as with higher occurrence of other potential determinants, such as parental overweight, maternal smoking during pregnancy, and high electronic media consumption.

- 4) There is a consistent association between overweight and adverse CVD risk factors, except for HbA1c. This association is already seen among children younger than 11 years of age.
- 5) BMI, WC, and WHtR show a stronger association with CVD risk factors than WHR or skinfold thickness.
- 6) WHR appears to be not appropriate to identify children and adolescents with an adverse CVD risk profile.
- 7) Adverse CVD risk factors are already seen among children and adolescents with values between the 70th and the 90th age and sex specific percentile of anthropometric variables.

These observations allow some implications for prevention, risk assessment and further research:

The observation that parental overweight and low SES were two of the most important independent determinants of obesity among children and adolescents in Germany implies that prevention of obesity has to start within families, focussing in particular on families with overweight history and low SES. The present results further indicate that prevention should start as early as possible since the intrauterine environment and early life factors have considerable consequences on later health outcomes. In general, beside genetic predisposition and behavioural aspects, social and environmental factors play an important role in the development of overweight and obesity. This has to be kept in mind for prevention strategies. Furthermore, it is of major importance to understand overweight and obesity as multifactorial problems with a large range of possible risk factors. Therefore, it is not appropriate to blame single factors. Moreover, there may be an unfavourable interaction of different factors, which may also interact differently on an individual level. There must be a separation of public health implications and individual prevention or therapy.

It is now known which factors may cause overweight and obesity and which population groups are of increased risk. A recent study among 6-14 year olds estimated that to prevent overweight the energy gap (the change in energy balance) should not exceed 46-72 kcal per day²⁶⁰. The energy gap reflects how much more energy expenditure and/or how much less energy intake is needed to avoid weight gain.

According to Hill ²⁹⁶, a daily reduction of 100 kcal may be necessary to close the energy gap. Such a reduction could be reached by for example an additional daily walk of 15-20 minutes. This implies that also small behavioural changes are important in the prevention and intervention of overweight and obesity. However, affecting people to change their individual behavioural is complicated. Recently, there is a large range of prevention and intervention efforts in Germany focussing on behavioural changes as well as on environmental changes. As an example, within the scope of the INFORM campaign initialised by the Federal Ministry of Food, Agriculture and Consumer Protection and the Federal Ministry of Health such efforts will be consolidated. In general, changes and rethinking are needed to make the healthy choice the easy one. However, such changes as well as social and environmental changes need time. Therefore, it is of particular importance for further research to evaluate which concrete strategies are effective in overweight prevention and which projects or efforts eventually have to be modified.

A consistent association between major CVD risk factors and overweight as defined by various indicators was demonstrated, even in young children. Differences in mean CVD risk factors in relation to overweight status were substantial and likely to be relevant with respect to clinical endpoints, given the fact that there is evidence for risk factors tracking from adolescence into adulthood ²⁹⁹⁻³⁰¹. This does not necessarily imply that every overweight child or adolescent will develop CVD in later life. For (individual) risk assessment, health professionals should not only examine weight status but additionally family history of diseases, health indicators such as blood pressure, blood lipid profile, indicators of diabetes mellitus, chronic inflammation and fat distribution. The fact, that an association between overweight and CVD risk factors is already seen among young children forces the need of early prevention.

There is consensus that for epidemiological studies simple, non-invasive, and practicable measurements are needed which can be obtained easily, quickly, and in a standardised way. The present results demonstrate that simple measures, namely BMI, WC, and WHtR, showed a stronger association with CVD risk factors than WHR or skinfold thickness measures. Each of the measures BMI, WC, and WHtR alone is a good predictor for adverse CVD risk profile. Therefore, when there are limited financial or temporal conditions in large-scale studies, the use of only one of these measures provide an appropriate indication on overweight and obesity. When the focus will be on blood pressure, it is supposed by the present results that WC is a more useful indicator than BMI. In general, since the fat distribution is a meaningful issue

regarding health related risks of overweight, for further epidemiologic research as well as for clinical practice, it is important calculating not only the BMI but also to measure WC as a simple indicator of fat distribution. The present results indicate that a combination of BMI and WC or BMI and WHtR may be even more useful than one single measure itself.

For (international) comparisons, it is necessary to establish clear definitions for overweight as well as for elevated CVD risk factors for children and adolescents. Up to now, such definitions do not exist. Using the KiGGS data, it has been shown that a clustering of single CVD risk factors already occurred in percentile ranges between the 70th and the 90th age and sex specific percentile of different anthropometric measures. If the KiGGS sample should be used as a standard population to define new reference values, the present results may be used as clues to establish cutoff values estimating a health related risk of overweight. However, no final conclusion can be made with respect to optimal thresholds of anthropometric measures to define overweight or obese children and adolescents with adverse health related risk. For this purpose and in order to give recommendations for risk assessment, longitudinal data including more severe and diagnostic consequences of overweight and obesity (for example chronic diseases like diabetes mellitus, early atherosclerotic changes assessed by intima media thickness) as well as family history on obesity related diseases would be helpful. How far risk profiles persist into adulthood also needs to be investigated in further cohort studies²¹⁸.

8 SUMMARY

During the last decades, prevalences of overweight and obesity among children and adolescents have increased, in particular in Western populations. Today, this is considered as one of the most important public health concerns. A substantial number of studies showed that overweight and obesity are associated with an adverse cardiovascular disease (CVD) risk profile, even among children. However, the long-term cardiovascular health consequences of overweight and obesity in young ages as well as the relevance of different anthropometric overweight measures for assessing health risk among children and adolescents are less clear. Health related behaviour and preferences, which are predominantly developed in childhood, will mostly persist until adulthood. Therefore, for establishing effective prevention and risk assessment it is important to identify risk factors for overweight and obesity as well as potential health related consequences in an early stage of life.

Previous studies on this subject predominantly included small, non-representative population samples or focussed mostly on a selected age range. Often, the spectrum of obtained information is very limited. An overview of the state of research is given in Chapter 2. Criteria for defining overweight and obesity, in particular among children and adolescents, determinants of overweight and obesity discussed in the scientific literature, as well as the relationship with CVD risk factors are described.

With the German Health Interview and Examination Survey for Children and Adolescents (KiGGS), conducted between 2003 and 2006, for the first time in Germany, comprehensive and nationally representative data for the group of children and adolescents is now available. This data allow analyses broad in scope. The subjects and methods used in the KiGGS study are presented in Chapter 3. The presented analyses were performed using different subsamples of the KiGGS study with a total sample of $N = 17641$.

Major determinants of overweight and obesity that were identified are presented in Chapter 4. For this purpose, frequencies of both overweight and obesity differentiated by potential determinants were analysed. Additionally, the distribution of the potential determinants as well as the frequency of obesity was analysed separately for three socio-economic status groups (low, medium, high). Furthermore, a multivariable logistic regression analysis was performed including obesity as the dependent variable. The analyses showed that parental overweight was the most important determinant of overweight and obesity. A positive independent association with obesity was shown for low socio-economic status, migration background (only

significant among 3-13 year olds), high weight gain during pregnancy (only significant for normal weight mothers), maternal smoking during pregnancy, high birth weight, short sleep duration (only significant among 3-10 year olds), and high media consumption. Several characteristics associated with increased risk for overweight and obesity were most prevailing among children and adolescents with low socio-economic status.

As shown in Chapter 5, the association between overweight and CVD risk factors (total cholesterol, LDL-cholesterol, HDL-cholesterol, systolic and diastolic blood pressure, C-reactive protein, and glycosylated haemoglobin) as indicators for cardiovascular health status was analysed using different anthropometric measures of overweight (body mass index, skinfold thickness, waist circumference, waist-to-hip ratio, and waist-to-height ratio). The measures of overweight with the strongest predictive value for adverse CVD risk factors were identified. For this purpose, overweight was defined for every value exceeding the 90th age and sex specific percentile of the net study sample (N = 11774) regarding the different anthropometric measures. The analyses showed a consistent positive association between CVD risk factors and overweight, even among children younger than 10 years of age. Means of CVD risk factors as well as prevalences of adverse CVD risk factors were consistently higher among overweight children and adolescents compared to non-overweight. For boys and girls, separate linear regression models with individual CVD risk factors as dependent variables and different measures of overweight as independent variables, adjusted for age in years (among 11-17 year olds additionally adjusted for pubertal stage) were calculated. Depending on the overweight measure chosen, the highest differences in adjusted means of CVD risk factors between those with and without overweight were 14 mg/dl for total cholesterol, 12 mg/dl for LDL-cholesterol, -10 mg/dl for HDL-cholesterol, 9 mm Hg for systolic blood pressure, 4 mm Hg for diastolic blood pressure, and 1.2 mg/l for C-reactive protein. Among 3-10 year old children, none of the measures of overweight (body mass index, triceps, subscapular and sum of skinfold thickness) was consistently more strongly related to CVD risk factors than any of the others. Among adolescents 11-17 years of age, body mass index, waist circumference, and waist-to-height ratio showed a stronger association with CVD risk factors than waist-to-hip ratio and skinfold thickness.

The analyses of receiver operating characteristic (ROC) curves in Chapter 6 indicate that adverse CVD risk factors among 11-17 year old boys and girls are already prevalent among those with age and sex specific percentile values between the 70th and the 90th percentile of

different measures of overweight. Waist-to-hip ratio appeared to be not appropriate to identify adolescents with adverse CVD risk profile.

Children and adolescents from families with overweight parents and low SES have a higher risk for overweight and obesity and are therefore important target groups for prevention. Since it was shown that overweight is strongly associated with adverse CVD risk factors, even among children younger than 11 years of age, it is important to initiate prevention and risk assessment in an early stage of life. Body mass index, waist circumference and waist-to-height ratio are good predictors for adverse CVD risk factors. Combining BMI and waist circumference or BMI and waist-to-height ratio may be even more useful for risk assessment in large-scale epidemiologic studies.

9 ZUSAMMENFASSUNG

Die Prävalenz von Übergewicht und Adipositas bei Kindern und Jugendlichen ist in den letzten Jahrzehnten, insbesondere in den westlichen Industrienationen, deutlich angestiegen. Derzeit wird diese Entwicklung als eines der wichtigsten Public Health Probleme angesehen. Eine Reihe von Studien hat gezeigt, dass Übergewicht und Adipositas bereits im Kindesalter mit ungünstigen kardiovaskulären Risikofaktoren assoziiert ist. Jedoch sind die kardiovaskulären Langzeitfolgen von Übergewicht und Adipositas in jungen Jahren sowie die Relevanz verschiedener anthropometrischer Übergewichtsmaße für die Risikobewertung bei Kindern und Jugendlichen noch weitgehend unklar. Gesundheitsrelevantes Verhalten und Vorlieben entwickeln sich jedoch vorwiegend in der Kindheit und bleiben meist bis ins Erwachsenenalter bestehen. Daher ist es für eine effektive Prävention und Risikobewertung wichtig, Risikofaktoren für Übergewicht und Adipositas sowie potenzielle Gesundheitsrisiken so früh wie möglich zu identifizieren.

Studien zu dieser Thematik umfassten bislang überwiegend kleine, nicht repräsentative Stichproben oder untersuchten eine bestimmte Altersgruppe. Häufig ist das Spektrum der erfragten Informationen sehr begrenzt. Kapitel 2 gibt einen Überblick über den aktuellen Stand der Forschung. Hierbei werden Kriterien zur Definition von Übergewicht und Adipositas, insbesondere bei Kindern und Jugendlichen, die in der wissenschaftlichen Literatur diskutierten Determinanten von Übergewicht und Adipositas sowie Zusammenhänge mit kardiovaskulären Risikofaktoren beschrieben.

Mit dem Kinder- und Jugendgesundheitsurvey (KiGGS), der zwischen 2003 und 2006 durchgeführt wurde, stehen erstmalig für Deutschland umfangreiche und national repräsentative Daten für die Gruppe der Kinder und Jugendlichen zur Verfügung. Die Daten erlauben breit angelegte Analysen. Die Studienpopulation und Methoden von KiGGS sind in Kapitel 3 beschrieben. Die hier dargestellten Analysen basieren auf unterschiedlichen Unterstichproben der KiGGS-Gesamtstichprobe von $N = 17641$.

Die wichtigsten identifizierten Determinanten von Übergewicht und Adipositas sind in Kapitel 4 dargestellt. Hierzu wurde die Häufigkeit von Übergewicht und Adipositas differenziert nach potenziellen Determinanten analysiert. Zudem wurden die Verteilung potenzieller Determinanten sowie das Auftreten von Adipositas getrennt nach drei Sozialstatusgruppen (niedrig, mittel, hoch) ausgewertet. Darüber hinaus wurde eine multivariate logistische Regressionsanalyse mit Adipositas als abhängiger Variable durchgeführt. Die Analysen zeigten, dass

elterliches Übergewicht die wichtigste Determinante für Übergewicht und Adipositas bei Kindern und Jugendlichen ist. Ein positiver, unabhängiger Zusammenhang zeigte sich zudem für niedrigen Sozialstatus, Migrationshintergrund (nur bei 3- bis 13-Jährigen signifikant), hohe Gewichtszunahme in der Schwangerschaft (nur bei normalgewichtigen Müttern signifikant), hohes Geburtsgewicht, kurze Schlafdauer (nur bei 3- bis 10-Jährigen signifikant) und hohen Medienkonsum. Bei Kindern und Jugendlichen mit niedrigem Sozialstatus traten verschiedene Merkmale, die mit einem höheren Risiko für Übergewicht und Adipositas assoziiert sind, häufiger auf.

In Kapitel 5 wurde der Zusammenhang zwischen Übergewicht und kardiovaskulären Risikofaktoren (Gesamtcholesterin, LDL-Cholesterin, HDL-Cholesterin, systolischer und diastolischer Blutdruck, C-reaktives Protein und glykiertes Hämoglobin) als Indikatoren für den kardiovaskulären Gesundheitsstatus untersucht. Dabei wurden verschiedene anthropometrische Übergewichtsmaße (Body Mass Index, Hautfaltendicken, Taillenumfang, Taille-Hüft-Quotient, und Taille-Größe-Quotient) verwendet. Die Übergewichtsmaße mit der größten Vorhersagekraft für ungünstige kardiovaskuläre Risikofaktoren wurden identifiziert. Hierfür wurden Kinder und Jugendliche als übergewichtig definiert, wenn das 90. alters- und geschlechtsspezifische Perzentil der Nettostichprobe (N = 11774) eines einzelnen Übergewichtsmaßes überschritten wurde. Die Analysen zeigten bereits bei Kindern unter 11 Jahren einen durchgehend positiven Zusammenhang zwischen kardiovaskulären Risikofaktoren und Übergewicht. Sowohl die Mittelwerte der kardiovaskulären Risikofaktoren als auch die Prävalenzen erhöhter kardiovaskulärer Risikofaktoren waren im Vergleich bei übergewichtigen Kindern und Jugendlichen durchgehend höher als bei nicht übergewichtigen. Für Jungen und Mädchen wurden separate lineare Regressionsmodelle mit den einzelnen kardiovaskulären Risikofaktoren als abhängige Variablen, adjustiert für Alter in Jahren (und für 11- bis 17-Jährige zusätzlich adjustiert für Pubertätsstatus), berechnet. Abhängig vom betrachteten Übergewichtsmaß zeigten sich die höchsten Unterschiede zwischen Übergewichtigen und nicht Übergewichtigen in den adjustierten Mittelwerten der kardiovaskulären Risikofaktoren mit 14 mg/dl für Gesamtcholesterin, 12 mg/dl für LDL-Cholesterin, -10 mg/dl für HDL-Cholesterin, 9 mm Hg für systolischen Blutdruck, 4 mm Hg für diastolischen Blutdruck und 1,2 mg/l für C-reaktives Protein. Beim Vergleich der Übergewichtsmaße (Body Mass Index, Trizeps, Rücken und Summe der Hautfaltendicken) hinsichtlich ihres Zusammenhangs mit kardiovaskulären Risikofaktoren zeigte bei 3- bis 10-Jährigen keines einen durchgehend stärkeren Zusammenhang als alle anderen. Bei den 11- bis 17-jährigen Jugendlichen waren Body

Mass Index, Taillenumfang und Taille-Größe-Quotient stärker mit kardiovaskulären Risikofaktoren assoziiert als der Taille-Hüft-Quotient und die Hautfaltendicken.

Die Analysen der Receiver Operating Characteristic (ROC) Kurven in Kapitel 6 zeigten, dass bei 11- bis 17-jährigen Jungen und Mädchen mit alters- und geschlechtsspezifischen Perzentilwerten zwischen dem 70. und dem 90. Perzentil bereits ein Zusammenhang mit einem ungünstigen kardiovaskulären Risikoprofil besteht. Der Taille-Hüft-Quotient erscheint hingegen nicht geeignet, um Jugendliche mit einem ungünstigen kardiovaskulären Risikoprofil zu identifizieren.

Kinder und Jugendliche aus Familien mit übergewichtigen Eltern und niedrigem Sozialstatus haben somit ein höheres Risiko für Übergewicht und Adipositas und sind deshalb wichtige Zielgruppen für die Prävention. Da ein Zusammenhang zwischen ungünstigen kardiovaskulären Risikofaktoren und Übergewicht bereits bei Kindern unter 11 Jahren beobachtet wurde, sind Prävention und Risikobewertung in frühen Jahren besonders wichtig. Body Mass Index, Taillenumfang und Taille-Größe-Quotient sind gute Prädiktoren für ungünstige kardiovaskuläre Risikofaktoren. Eine Kombination von Body Mass Index und Taillenumfang beziehungsweise Body Mass Index und Taille-Größe-Quotient kann darüber hinaus für die Risikobewertung in großangelegten epidemiologischen Studien hilfreich sein.

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11 APPENDIX

Additional Tables

Table A - 1: International cutoff points* for BMI for overweight and obesity by sex, 2-18 years

Age (years)	BMI 25 kg/m ²		BMI 30 kg/m ²	
	Males	Females	Males	Females
2	18.41	18.02	20.09	19.81
2.5	18.13	17.76	19.80	19.55
3	17.89	17.56	19.57	19.36
3.5	17.69	17.40	19.39	19.23
4	17.55	17.28	19.29	19.15
4.5	17.47	17.19	19.26	19.12
5	17.42	17.15	19.30	19.17
5.5	17.45	17.20	19.47	19.34
6	17.55	17.34	19.78	19.65
6.5	17.71	17.53	20.23	20.08
7	17.92	17.75	20.63	20.51
7.5	18.16	18.03	21.09	21.01
8	18.44	18.35	21.60	21.57
8.5	18.76	18.69	22.17	22.18
9	19.10	19.07	22.77	22.81
9.5	19.46	19.45	23.39	23.46
10	19.84	19.86	24.00	24.11
10.5	20.20	20.29	24.57	24.77
11	20.55	20.74	25.10	25.42
11.5	20.89	21.20	25.58	26.05
12	21.22	21.68	26.02	26.67
12.5	21.56	22.14	26.43	27.24
13	21.91	22.58	26.84	27.76
13.5	22.27	22.98	27.25	28.20
14	22.62	23.34	27.63	28.57
14.5	22.96	23.66	27.98	28.87
15	23.29	23.94	28.30	29.11
15.5	23.60	24.17	28.60	29.29
16	23.90	24.37	28.88	29.43
16.5	24.19	24.54	29.14	29.56
17	24.46	24.70	29.41	29.69
17.5	24.73	24.85	29.70	29.84
18	25.00	25.00	30.00	30.00

Source: Cole et al. 2000¹³

*Cutoff points are defined to pass through body mass index of 25 and 30 kg/m² at age 18, obtained by averaging data from Brazil, Great Britain, Hong Kong, Netherlands, Singapore, and United States

Table A - 2: Frequency of overweight (including obesity) and obesity according to potential determinants and odds ratio (non-consistent and non-significant results)

	N ^{a)}	Over-weight (including obesity) [%] ^{b)}	OR ^{c)} for Overweight (95% CI)	p-value	Obesity [%] ^{b)}	OR ^{c)} for Obesity (95% CI)	p-value
Residence							
Eastern Germany	4468	20.6	ref.		5.5	ref.	
Western Germany	8982	20.6	1.0 (0.9-1.1)	0.9186	5.3	1.0 (0.8-1.3)	0.9200
Degree of urbanisation							
Rural	3001	19.3	ref.		5.4	ref.	
Small town	3501	20.8	1.1 (0.9-1.3)	0.2864	5.3	1.0 (0.7-1.4)	0.9576
Middle-sized town	3904	20.1	1.1 (0.9-1.3)	0.5376	4.8	0.9 (0.6-1.2)	0.4869
Urban	3044	21.8	1.2 (1.0-1.4)	0.1086	6.0	1.1 (0.8-1.6)	0.4446
p for trend			0.4025			0.3957	
Presence of siblings							
Yes	10042	19.6	ref.		5.2	ref.	
No	2656	24.0	1.3 (1.2-1.5)	<0.001	5.4	1.1 (0.8-1.3)	0.7089
Missing data	752						
Maternal diabetes during pregnancy							
Yes	257	25.6	1.5 (1.0-2.0)	0.0283	7.0	1.5 (0.8-2.8)	0.1926
No	11325	19.7	ref.		5.0	ref.	
Missing data	1868						
Low birth weight							
Yes	658	18.4	0.9 (0.7-1.1)	0.3208	3.1	0.6 (0.4-0.9)	0.0181
No	12135	20.4	ref.		5.4	ref.	
Missing data	657						
Regular alcohol consumption (11-17 years)							
Yes	1123	22.5	1.0 (0.8-1.2)	0.9800	6.5	1.0 (0.7-1.5)	0.8251
No	5017	23.6	ref.		6.0	ref.	
Missing data/not assessed	7310						
Smoking (11-17 years)							
Yes	1229	25.9	1.4 (1.1-1.7)	0.0027	7.3	1.3 (0.9-1.8)	0.1128
No	4956	22.8	ref.		5.8	ref.	
Missing data/not assessed	7265						
HuSKY							
Lowest tertile	3604	19.5	0.9 (0.8-1.1)	0.9393	4.4	0.8 (0.6-1.0)	0.4842
Middle tertile	4280	20.4	1.0 (0.9-1.1)	0.9489	5.3	0.9 (0.8-1.2)	0.5633
Highest tertile	4309	20.3	ref.		5.6	ref.	
Missing data	599						
p for trend			0.6413			0.1616	

N = 13450 participants, 3-17 years (after exclusion of underweight participants)

a) unweighted

b) Based on IOTF cutoff points

c) Odds ratio, adjusted for age and gender

Table A - 3: Smoothed 90th percentile values of systolic and diastolic blood pressure

Age (years)	Boys		Girls	
	Systolic blood pressure [mm Hg]	Diastolic blood pressure [mm Hg]	Systolic blood pressure [mm Hg]	Diastolic blood pressure [mm Hg]
3	106	67	106	68
4	107	67	107	68
5	108	68	108	69
6	109	69	109	70
7	110	70	110	70
8	111	71	112	71
9	113	71	114	72
10	115	72	116	72
11	117	74	118	73
12	120	75	120	74
13	123	76	122	75
14	127	77	123	76
15	130	78	124	77
16	134	80	125	78
17	137	81	126	79

Table A - 4: Smoothed 90th percentile values of serum total cholesterol, LDL-cholesterol, and HbA1c and 10th percentile values for HDL-cholesterol, boys

Age (years)	Total cholesterol [mg/dl]	LDL-cholesterol [mg/dl]	HDL-cholesterol [mg/dl]	HbA1c [%]
3	194	127	36	5.4
4	198	129	38	5.4
5	200	129	40	5.4
6	200	127	41	5.4
7	199	125	42	5.4
8	199	124	43	5.4
9	200	125	44	5.4
10	202	126	44	5.4
11	204	126	44	5.4
12	202	125	43	5.4
13	196	122	41	5.4
14	189	118	40	5.4
15	185	115	38	5.4
16	185	116	37	5.4
17	190	118	37	5.4

Source: adapted from RKI 2009³⁰²

Table A - 5: Smoothed 90th percentile values of serum total cholesterol, LDL-cholesterol, and HbA1c and 10th percentile values for HDL-cholesterol, girls

Age (years)	Total cholesterol [mg/dl]	LDL-cholesterol [mg/dl]	HDL-cholesterol [mg/dl]	HbA1c [%]
3	197	129	35	5.3
4	200	131	37	5.3
5	203	132	39	5.3
6	205	133	41	5.3
7	205	133	42	5.3
8	206	133	43	5.4
9	206	133	43	5.4
10	205	132	43	5.4
11	203	130	42	5.4
12	200	127	42	5.4
13	198	126	42	5.4
14	198	125	42	5.3
15	200	127	42	5.3
16	206	131	43	5.3
17	213	136	43	5.3

Source: adapted from RKI 2009³⁰²**Table A - 6: Means and 95% confidence intervals of body fat, Non-HDL cholesterol, LDL-HDL-ratio**

	N	Body fat* [%]	Non-HDL-C [mg/dl]	LDL/HDL	
Boys	3-6 years	1413	15.3 (15.1-15.6)	108.2 (106.4-110.1)	1.8 (1.8-1.9)
	7-10 years	1777	18.3 (17.9-18.7)	106.0 (104.5-107.5)	1.6 (1.6-1.7)
	11-13 years	1364	20.9 (20.2-21.6)	105.1 (103.4-106.9)	1.7 (1.6-1.7)
	14-17 years	1667	17.9 (17.4-18.4)	100.6 (99.0-102.2)	1.7 (1.7-1.8)
Girls	3-6 years	1360	17.1 (16.8-17.3)	112.5 (110.7-114.3)	1.9 (1.9-1.9)
	7-10 years	1678	20.2 (19.8-20.6)	112.2 (110.7-113.8)	1.8 (1.7-1.8)
	11-13 years	1312	23.8 (23.3-24.3)	105.7 (103.9-107.5)	1.7 (1.7-1.7)
	14-17 years	1203	27.0 (26.5-27.5)	104.0 (101.8-106.1)	1.7 (1.6-1.7)

* according to Slaughter et al. 1988³⁴

C: cholesterol, LDL/HDL: LDL-HDL-ratio

Table A - 7: Prevalence [% (95% CI)] of children exceeding defined cutoffs for individual CVD risk factors according to different indicators of overweight status dichotomised at the age and sex specific 90th percentile, 11-17 years, triceps and subscapular skinfold, body fat, WHR

	Triceps SFT ≤ P90	Triceps SFT > P90	Subscap SFT ≤ P90	Subscap SFT > P90	Body fat ≤ P90	Body fat > P90	WHR ≤ P90	WHR > P90
Boys	N = 2744	N = 287	N = 2734	N = 297	N = 2741	N = 290	N = 2762	N = 269
Total cholesterol > P90 (N = 284)	8.2 (7.1-9.4)	17.7 (12.7-22.7)	8.2 (7.1-9.3)	17.8 (12.5-23.2)	8.1 (6.9-9.2)	19.2 (14.2-24.2)	8.5 (7.3-9.6)	15.4** (10.2-20.5)
LDL-cholesterol > P90 (N = 305)	9.3 (8.1-10.5)	17.8 (13.3-22.3)	9.4 (8.2-10.6)	16.9 (11.9-21.8)	9.3 (8.1-10.5)	17.5 (13.2-21.9)	9.4 (8.2-10.6)	16.9** (12.1-21.7)
HDL-cholesterol < P10 (N = 290)	8.5 (7.3-9.7)	21.6 (16.4-26.8)	7.9 (6.6-9.1)	27.3 (21.7-32.8)	8.2 (7.0-9.5)	23.9 (18.4-29.4)	8.4 (7.1-9.7)	22.5 (17.0-28.0)
Systolic blood pressure > P90 (N = 359)	9.6 (8.2-11.1)	30.8 (24.5-37.0)	9.5 (8.0-10.9)	32.0 (25.9-38.1)	9.5 (8.1-11.0)	31.5 (25.8-37.1)	10.3 (8.8-11.7)	24.4 (17.9-30.8)
Diastolic blood pressure > P90 (N = 265)	8.3 (7.1-9.6)	15.8** (10.5-21.2)	8.2 (6.9-9.4)	17.3 (12.5-22.1)	8.3 (7.1-9.6)	16.0 (11.1-20.9)	8.3 (7.0-9.5)	16.6** (10.8-22.4)
HbA1c > P90 (N = 282)	10.0 (8.0-12.0)	9.5 ^{n.s.} (5.8-13.2)	9.7 (7.7-11.7)	12.5 ^{n.s.} (7.4-17.6)	9.8 (7.9-11.8)	11.3 ^{n.s.} (6.8-15.9)	9.8 (7.8-11.8)	11.6 ^{n.s.} (7.2-15.9)
C-reactive protein > 2.1 mg/l (N = 262)	7.3 (6.1-8.5)	23.7 (18.2-29.3)	6.9 (5.7-8.1)	27.0 (21.5-32.4)	7.0 (5.8-8.1)	26.8 (21.3-32.4)	7.6 (6.4-8.9)	20.4 (15.5-25.4)
Girls	N = 2283	N = 232	N = 2287	N = 228	N = 2280	N = 235	N = 2272	N = 243
Total cholesterol > P90 (N = 207)	7.3 (6.0-8.7)	13.9** (9.0-18.8)	7.3 (6.0-8.7)	13.7* (8.5-19.0)	7.4 (6.0-8.8)	13.0* (8.0-18.0)	7.4 (6.0-8.8)	12.9* (7.8-18.1)
LDL-cholesterol > P90 (N = 180)	6.9 (5.6-8.2)	12.4* (8.2-16.7)	7.0 (5.7-8.3)	11.4 ^{n.s.} (7.1-15.7)	7.0 (5.6-8.3)	11.9* (7.6-16.2)	7.1 (5.8-8.4)	10.6 ^{n.s.} (6.3-15.0)
HDL-cholesterol < P10 (N = 251)	8.5 (7.0-10.0)	22.3 (15.2-29.5)	8.1 (6.7-9.5)	26.2 (18.7-33.7)	8.1 (6.7-9.5)	25.5 (18.1-32.9)	8.4 (6.9-9.8)	22.8 (16.6-29.1)
Systolic blood pressure > P90 (N = 264)	8.8 (7.2-10.4)	28.1 (21.0-35.2)	9.0 (7.4-10.6)	25.9 (18.4-33.4)	8.9 (7.3-10.4)	26.9 (19.3-34.6)	9.7 (7.9-11.6)	18.4** (12.1-24.6)
Diastolic blood pressure > P90 (N = 226)	8.4 (6.9-10.0)	14.0* (9.0-19.0)	8.2 (6.7-9.7)	16.1** (10.8-21.4)	8.3 (6.8-9.8)	14.8* (9.6-20.0)	8.8 (7.2-10.4)	10.2 ^{n.s.} (6.4-14.0)
HbA1c > P90 (N = 266)	10.4 (8.3-12.6)	13.3 ^{n.s.} (7.4-19.1)	10.2 (8.0-12.3)	15.9 ^{n.s.} (9.7-22.2)	10.3 (8.1-12.4)	14.9 ^{n.s.} (8.9-21.0)	10.3 (8.2-12.4)	14.8 ^{n.s.} (9.0-20.5)
C-reactive protein > 2.1 mg/l (N = 185)	5.9 (4.7-7.0)	23.0 (16.5-29.6)	5.6 (4.4-6.7)	25.8 (19.4-32.2)	5.7 (4.5-6.9)	24.3 (17.8-30.7)	6.4 (5.2-7.7)	17.1 (12.1-22.1)

CI: confidence interval, Subscap: Subscapular, SF: skinfold thickness, WHR: waist-to-hip ratio, HbA1c: glycosylated haemoglobin

Differences between ≤ P90 and >P90 were highly significant (p<0.001) unless explicitly mentioned (n.s. = not significant, ** = p <0.01, * = p < 0.05), chi-square test

Table A - 8: Separate linear regression of Non-HDL cholesterol and LDL-HDL-ratio on different measures of overweight (> P90), 3-17 years

Dependent variables:	3-10 year olds						11-17 year olds					
	Non-HDL cholesterol [mg/dl]			LDL-HDL-ratio			Non-HDL cholesterol [mg/dl]			LDL-HDL-ratio		
Independent variables:	b	SE	R ²	b	SE	R ²	b	SE	R ²	b	SE	R ²
Boys			0.004 [†]			0.04 [†]			0.02 [†]			0.006 [†]
BMI > P90	8.1	1.9	0.01	0.2	0.04	0.05	22.3	2.3	0.08	0.6	0.05	0.07
Triceps SFT > P90	7.0	1.9	0.01	0.1**	0.04	0.04	17.8	2.0	0.06	0.4	0.05	0.04
Subscap. SFT > P90	9.5	1.9	0.02	0.2	0.04	0.05	20.8	2.2	0.08	0.6	0.06	0.06
Sum of SFT > P90	9.3	1.8	0.01	0.2	0.04	0.05	20.6	2.0	0.07	0.5	0.05	0.05
Waist circumference > P90	-	-	-	-	-	-	21.3	2.0	0.08	0.6	0.05	0.07
Waist-to-hip ratio > P90	-	-	-	-	-	-	15.8	1.9	0.05	0.4	0.06	0.03
Waist-to-height ratio > P90	-	-	-	-	-	-	22.8	2.1	0.08	0.6	0.06	0.06
Girls			0.003 [†]			0.02 [†]			0.007 [†]			0.003 [†]
BMI > P90	4.6*	2.0	0.005	0.2	0.04	0.03	16.7	2.3	0.04	0.5	0.06	0.05
Triceps SFT > P90	3.4 ^{n.s.}	2.1	0.004	0.2**	0.06	0.02	14.6	2.3	0.03	0.4	0.06	0.03
Subscap. SFT > P90	5.9**	2.0	0.007	0.2	0.05	0.03	15.8	2.3	0.03	0.4	0.06	0.05
Sum of SFT > P90	5.3**	1.9	0.006	0.2	0.05	0.03	14.8	2.2	0.03	0.4	0.06	0.04
Waist circumference > P90	-	-	-	-	-	-	17.8	2.3	0.04	0.5	0.06	0.06
Waist-to-hip ratio > P90	-	-	-	-	-	-	12.3	2.4	0.02	0.3	0.05	0.02
Waist-to-height ratio > P90	-	-	-	-	-	-	17.2	2.2	0.04	0.5	0.06	0.06

[†]R² for the model with only age (among 3-10 year olds) and age and pubertal stage (among 11-17 year olds) as independent variables

Regression coefficients (b) were highly significant (p < 0.001), unless explicitly mentioned (n.s. = not significant, ** = p < 0.01, * = p < 0.05)

b: regression coefficient, adjusted for age among 3-10 year olds, adjusted for age and pubertal stage among 11-17 year olds

R²: explained variance for the model with overweight indicator as independent variable, adjusted for age (and pubertal stage)

Subscap: subscapular, SFT: skinfold thickness, SE: standard error; SFT: skinfold thickness, P90: 90th age and sex specific percentile

Table A - 9: Separate linear regression of individual CVD risk factors on total body fat and squared WHtR (> P90), 3-17 years

Dependent variables:	Total chol.			LDL-chol.			HDL-chol.			SBP			DBP			HbA1c			hs-CRP		
	[mg/dl]			[mg/dl]			[mg/dl]			[mm Hg]			[mm Hg]			[%]			[mg/l]		
Independent variables:	b	SE	R ²	b	SE	R ²	b	SE	R ²	b	SE	R ²	b	SE	R ²	b	SE	R ²	b	SE	R ²
Boys, 3-10 years			0.005 [†]			0.002 [†]			0.05 [†]			0.14 [†]			0.08 [†]			0.006 [†]			0.01 [†]
Total body fat > P90	4.7**	1.8	0.008	5.1**	1.7	0.006	-4.6	0.8	0.06	5.8	0.5	0.18	3.3	0.4	0.10	0.02 ^{n.s.}	0.03	0.006	0.6	0.09	0.03
Girls, 3-10 years			0.009 [†]			0.002 [†]			0.04 [†]			0.13 [†]			0.05 [†]			0.01 [†]			0.005 [†]
Total body fat > P90	-1.0 ^{n.s.}	1.8	0.009	-0.1 ^{n.s.}	1.7	0.002	-6.3	0.9	0.07	5.0	0.5	0.16	2.6	0.5	0.06	0.06*	0.02	0.01	0.8	0.1	0.03
Boys, 11-17 years			0.07 [†]			0.03 [†]			0.09 [†]			0.27 [†]			0.10 [†]			0.006 [†]			0.005 [†]
Total body fat > P90	11.8	2.0	0.09	10.3	1.6	0.05	-8.7	0.8	0.13	7.8	0.7	0.30	2.8	0.6	0.11	0.02 ^{n.s.}	0.03	0.006	1.1	0.1	0.06
WHtR ² > P90	11.4	1.8	0.09	9.8	1.6	0.05	-9.0	0.8	0.13	6.0	0.8	0.29	2.5	0.5	0.11	-0.01 ^{n.s.}	0.03	0.006	1.0	0.1	0.05
Girls, 11-17 years			0.01 [†]			0.006 [†]			0.009 [†]			0.06 [†]			0.05 [†]			0.01 [†]			0.01 [†]
Total body fat > P90	6.9**	2.1	0.02	7.8	2.0	0.01	-8.1	0.9	0.04	5.5	0.7	0.09	1.9	0.6	0.06	0.06 ^{n.s.}	0.03	0.01	1.1	0.1	0.10
WHtR ² > P90	6.1**	2.1	0.01	6.7	1.9	0.01	-8.8	0.9	0.05	4.7	0.8	0.08	2.2	0.5	0.06	0.08**	0.03	0.01	1.0	0.1	0.08

[†]R² for the model with only age (among 3-10 year olds) and age and pubertal stage (among 11-17 year olds) as independent variables

Regression coefficients (b) were highly significant (p < 0.001), unless explicitly mentioned (n.s. = not significant, ** = p < 0.01, * = p < 0.05)

b: regression coefficient, adjusted for age among 3-10 year olds and adjusted for age and pubertal stage among 11-17 year olds

R²: explained variance for the model with overweight indicator as independent variable, adjusted for age (and pubertal stage)

Chol: cholesterol, SBP: systolic blood pressure, DBP: diastolic blood pressure, HbA1c: glycosylated haemoglobin, hs-CRP: high sensitivity C-reactive Protein, Subscap: subscapular, SE: standard error; WHtR²: squared WHtR, P90: 90th age and sex specific percentile

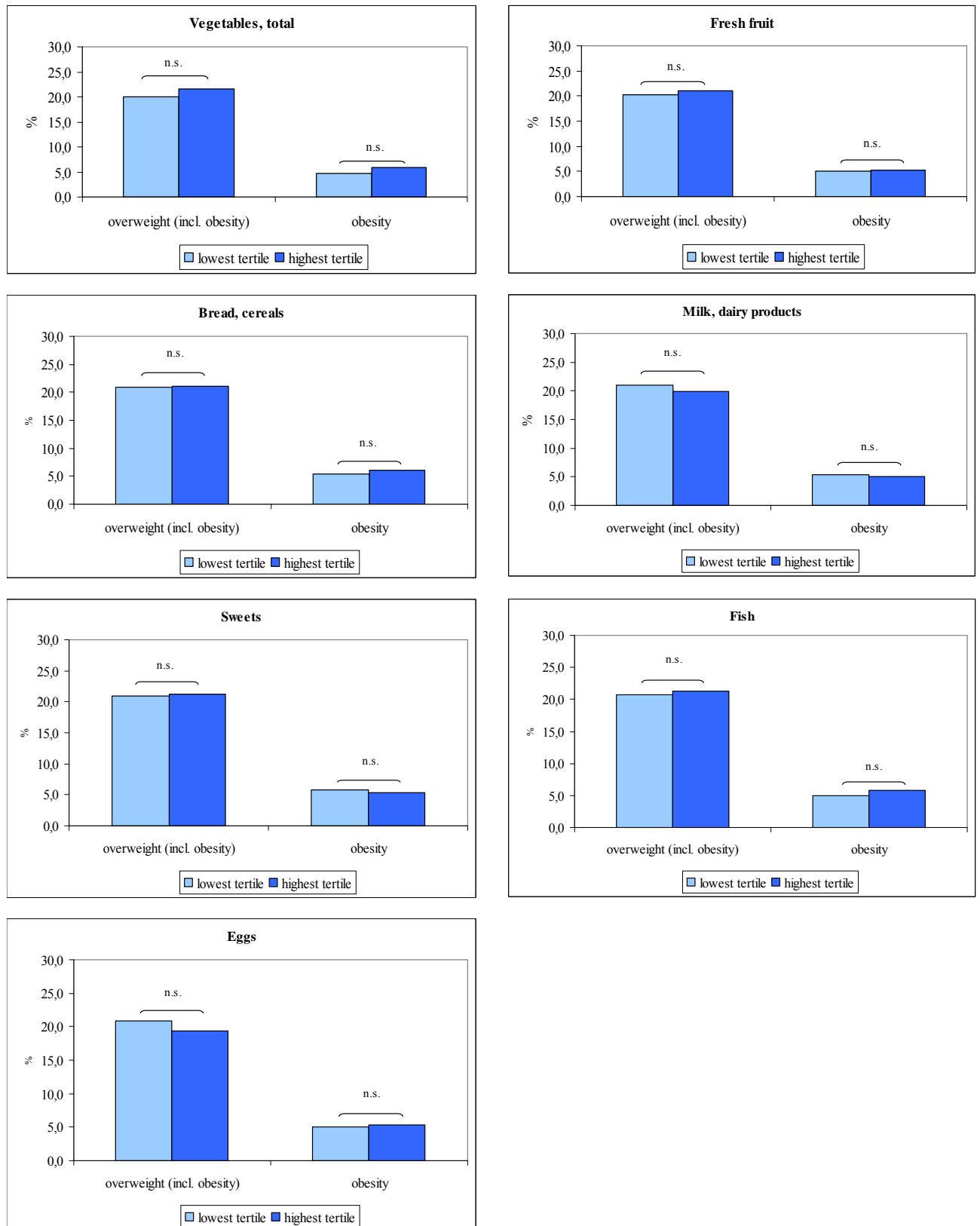


Figure A - 2: Frequency of overweight (including obesity) and obesity by lowest and highest tertiles of several food groups [%]

N = 12792 participants, 3-17 year olds (underweight participants excluded)

p-value for lowest vs. highest tertile from univariable regression models with overweight or obesity as independent variable, adjusted for age and gender; * = $p < 0.05$; ** = $p < 0.01$; *** = $p < 0.001$

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