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Prenatal Influences on Childhood Overweight: Impact and Prediction of Gestational Weight Gain and Potential Benefits of Early Alteration

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Abbreviations:

BMI = Body mass index

CI = Confidence interval

DLR+ = Positive diagnostic likelihood ratio

GWG = Gestational weight gain

IOM = Institute of Medicine

IOTF = International Obesity Task Force

KiGGS = Kinder- und Jugend-Gesundheitssurvey

NRC = National Research Council

NPV = Negative predictive value

OR = Odds ratio

PPV = Positive predictive value

RCT = Randomised controlled trial

SES = Socioeconomic status

WHO = World Health Organisation

Abstract

Background: Childhood overweight has become a growing public health challenge. It has been suggested that inadequate or excessive gestational weight gain (GWG) may result in permanent metabolic and neuronal changes in the developing fetus. Although effects of GWG on birth weight are established, less is known about its effects on the long-term weight status of the child. In 2009, the Institute of Medicine (IOM) and the National Research Council (NRC) published recommendations for trimester-specific and total GWG depending on maternal pre-pregnancy body mass index (BMI). It is unknown, however, how well the trimester-specific IOM/NRC recommendations for GWG identify women at risk of total GWG outside those recommendations. It is also unknown, whether a reverse from excessive GWG in early or mid-pregnancy reduces the risk of childhood overweight.

Aims: Contribute to the existing knowledge on the association between GWG and childhood overweight (study 1). Examine whether and to what extent inadequate or excessive total GWG can be predicted in the first, second and third trimester, based on trimester-specific GWG cut-off values (study 2). Investigate whether a reverse from excessive GWG before the third trimester is associated with a risk reduction of childhood overweight (study 3).

Methods: A retrospective cohort study was conducted. The sample was recruited prior to the school entry health examinations in 2009 and 2010. Data on maternal weight was derived from medical records and child's anthropometric data were measured. From 11,730 mother-child pairs available, 6,837 were included in study 1, 7,962 in study 2 and 6,767 in study 3. To investigate the effect of total GWG, overall and stratified by maternal pre-pregnancy BMI, and reverse from excessive GWG in early or mid-pregnancy, multivariate logistic regression analyses were conducted including a large number of potential confounders. Odds ratios (OR) and 95% confidence intervals (CI) were calculated. The prognostic values of lower and upper trimester-specific GWG cut-off values were examined by calculating sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and positive diagnostic likelihood ratio (DLR+).

Results: 1) Overall, the risk of childhood overweight increased by 4% per additional kg GWG (OR: 1.04, 95% CI: 1.02, 1.05). Excessive total GWG was associated with a 57 % higher risk of childhood overweight (OR: 1.57, 95% CI: 1.30, 1.91). Stratified by maternal pre-pregnancy BMI, significant associations between excessive GWG and childhood overweight found among normal weight mothers (OR: 1.29, 95% CI: 1.01, 1.66) and overweight mothers (OR: 1.64, 95% CI: 1.06, 2.63).

2) Prediction of total GWG within the IOM/NRC recommendations increased with gestational age and was related to the maternal BMI category and outcome. In trimester two, inadequate total GWG could be predicted with a sensitivity of 49% and 60.2% and a PPV of 72.1% and 68.3% in underweight and normal-weight mothers, respectively. Excessive GWG could be predicted with a sensitivity of 72.7% and 70.4% and a PPV of 94.3% and 93.3% in overweight and obese mothers, respectively.

3) Compared to mothers who always gained below the excessive GWG cut-off values (reference category), children of mothers with excessive GWG in the third and any previous trimester had a 42% higher risk of overweight at school entry (OR: 1.42, 95% CI: 1.17, 1.72). There was a 39% higher risk if mothers gained excessively in the third trimester only (OR: 1.39, 95% CI: 1.06, 1.82). No higher risk was observed for mothers who reversed from excessive GWG before the third trimester compared to reference category.

Conclusions: Excessive total GWG appears to be a risk factor for childhood overweight. It can be well predicted from the second trimester on, in particular in overweight and obese women. Reverse from excessive GWG before the third trimester may reduce the risk of childhood overweight. More research is required to further establish the strength of association between GWG and childhood overweight. It appears possible to identify women at risk of gaining outside the recommendations as early as the second trimester. Those women should be allocated to appropriate weight modifying measures. The long-term benefit of GWG modifying measures on childhood overweight, especially a reverse from excessive GWG in the first or second trimester, should be investigated in randomised controlled studies.

Zusammenfassung

Hintergrund: Kindliches Übergewicht stellt eine wachsende Herausforderung an das Gesundheitssystem dar. Es wird angenommen, dass eine inadäquate oder exzessive mütterliche gestationale Gewichtszunahme (GGZ) zu dauerhaften metabolischen und neuronalen Veränderungen im heranwachsenden Fötus führen kann. Zusammenhänge zwischen der GGZ und dem Geburtsgewicht des Kindes wurden umfassend belegt. Weniger erforscht ist der Einfluss der GGZ auf die langfristige Gewichtsentwicklung des Kindes. Im Jahre 2009 veröffentlichten das Institute of Medicine (IOM) und das National Research Council (NRC) Grenzwerte für die trimester-spezifische und totale GGZ in Abhängigkeit des mütterlichen Body Mass Index (BMI). Bisher unbekannt ist, in wie weit sich diese trimester-spezifischen Grenzwerte dazu eigenen, um eine Abweichung von den Grenzwerten am Ende der Schwangerschaft vorherzusagen und somit gefährdete Mütter frühzeitig zu identifizieren. Zudem ist ungeklärt, ob eine Umkehr von der exzessiven GGZ vor dem dritten Trimester mit einer Risikoreduktion für kindliches Übergewicht einhergeht.

Ziele: Beitrag zur existierenden Literatur über den Zusammenhang zwischen GGZ und kindlichem Übergewicht (Studie 1). Analyse, ob und in welchem Ausmaß inadäquate oder exzessive GGZ am Ende der Schwangerschaft durch trimester-spezifische IOM/NRC GGZ Grenzwerte vorhergesagt werden kann (Studie 2). Analyse, ob eine Umkehr von exzessiver GGZ in der frühen oder mittleren Schwangerschaft das Risiko von späteren kindlichen Übergewichts reduziert (Studie 3).

Methoden: In einer retrospektiven Kohortenstudie wurden Daten von 11.730 Mutter-Kind Paaren erhoben. Die Stichprobenrekrutierung erfolgte im Rahmen der Schuleingangsuntersuchungen in den Jahren 2009 und 2010. Angaben zum mütterlichen Gewicht wurden dem Mutterpass entnommen und die anthropometrischen Daten des Kindes gemessen. Von 11.730 verfügbaren Mutter-Kind Paaren, wurden 6.837 in Studie 1, 7.962 in Studie 2 und 6.767 in Studie 3 eingeschlossen. Multivariate logistische Regressionsanalysen wurden herangezogen, um den Effekt von totaler GGZ während der Schwangerschaft, über alle Mütter hinweg und stratifiziert nach präkonzeptionellen BMI, und der Umkehr von exzessiver GGZ vor dem dritten Trimester zu analysieren. Odds Ratios (OR) und 95% Konfidenzintervalle (CI) wurden berechnet und eine große Anzahl an potenziellen Störvariablen eingeschlossen. Die Vorhersagekraft der trimester-spezifischen Grenzwerte wurde mittels der Berechnung von Sensitivität, Spezifität, positiver prädiktiver Wert (PPV), negativer prädiktiver Wert (NPV) und der positive diagnostische Likelihood Ratio (DLR+) analysiert.

Ergebnisse: 1) Insgesamt war jedes zusätzliche kg GGZ mit einer 4%igen Risikoerhöhung für kindliches Übergewicht assoziiert (OR: 1.04, 95% CI: 1.02, 1.05). Eine exzessive totale GGZ war mit einer 57%igen Risikosteigerung verbunden (OR: 1.57, 95% CI: 1.30, 1.91). Die stratifizierte Analyse ergab signifikante Effekte für exzessive totale GGZ innerhalb der normalgewichtigen (OR: 1.29, 95% CI: 1.01, 1.66) und übergewichtigen Mütter (OR: 1.64, 95% CI: 1.06, 2.63).

2) Die Vorhersage der totalen GGZ innerhalb der IOM/NRC Empfehlungen verbesserte sich mit fortschreitendem Gestationsalter und war abhängig von der mütterlichen BMI Kategorie und der Zielgröße. Bei den untergewichtigen bzw. normalgewichtigen Müttern konnte mit den trimester-spezifischen GGZ Grenzwerten des zweiten Trimesters eine inadäquate totale GGZ mit einer Sensitivität von 49% bzw. 60.2% und einem PPV von

72.1% bzw. 68.3% vorhergesagt werden. Bei den übergewichtigen und adipösen Müttern konnte mit den trimester-spezifschen GGZ Grenzwerten des zweiten Trimesters eine totale exzessive GGZ mit einer Sensitivität von 72.7% bzw. 70.4% und einem PPV von 94.3% bzw. 93.3% vorhergesagt werden.

3) Im Vergleich zu Müttern die während der gesamten Schwangerschaft unterhalb des Grenzwertes für exzessives GGZ lagen (Referenzkategorie), war eine exzessive Gewichtszunahme im dritten und mindestens einem vorhergehenden Trimester mit einer 42%igen Risikoerhöhung assoziiert (OR: 1.42, 95% CI: 1.17, 1.72). Nahmen die Mütter nur im letzten Trimester exzessiv zu, lag die Risikoerhöhung bei 39% (OR: 1.39, 95% CI: 1.06, 1.82). Kein erhöhtes Risiko für kindliches Übergewicht zeigte sich bei den Müttern die ausschließlich in den ersten zwei Trimestern exzessiv zugenommen hatten.

Diskussion: Exzessive GGZ scheint ein Risikofaktor für kindliches Übergewicht zu sein. Insbesondere bei übergewichtigen und adipösen Müttern kann eine exzessive GGZ außerhalb der IOM/NRC Empfehlungen ab dem zweiten Trimester vorhergesagt werden. Die Umkehr einer exzessiven GGZ vor dem dritten Trimester scheint das Risiko für kindliches Übergewicht zu reduzieren. Weitere Forschung über Stärke des Zusammenhangs zwischen GGZ und kindlichem Übergewicht ist notwendig. Es scheint möglich, Frauen deren totale GGZ potenziell außerhalb der Empfehlungen liegt ab dem zweiten Trimester zu identifizieren. Diese Frauen sollten wirkungsvollen gewichtsmodifizierenden Maßnahmen zugeführt werden. Die langfristige positive Auswirkung dieser Maßnahmen, insbesondere eine Umkehr von exzessiver GGZ vor dem dritten Trimester, auf die Prävention von kindlichem Übergewicht, sollte in randomisiert-kontrollierten Studien untersucht werden.

1 Background

1.1 Childhood Overweight

1.1.1 Prevalence

Over the past decade, childhood overweight and obesity have become a major public health challenge. In developed countries, the estimated prevalence of childhood overweight including obesity is 11.7%. It increased from 7.9% to 11.7% between 1990 and 2010 and is projected to exceed 14% in 2020 (1).

A representative survey on health of children and adolescents in Germany, including a sample of more than 14,000 participants between age 3 and 17 years, found an overall overweight prevalence of 15% for overweight (including obesity) (2). With regard to age group, the corresponding prevalence differs between 9.1% (age 3-6), 15.4% (age 7-10), 18.6% (age 11-13) and 17.1% (age 14-17). Although cross-sectional, those figures indicate an increase of overweight with age. No gender-related differences were reported (2).

The first four years in school appear to be a critical period. An increase of overweight after school entry was reported (3). According to von Kries et al. (4), a possible explanation is a lower overweight remission rate combined with a growing incidence during school-age.

There is evidence that overweight in youth persists into adulthood and that overweight children are therefore at a higher risk of remaining overweight (5). Early intervention measures are urgently needed and it is therefore essential to identify modifiable early risk factors for childhood overweight.

1.1.2 Definition

In epidemiological research, the body mass index (BMI) is widely used to classify underweight, normal-weight, overweight and obesity. The BMI is calculated as body weight (kg) divided by body height (metres) squared:

$$\text{BMI} = \frac{\text{body weight (kg)}}{\text{body height (metres)}^2}$$

According to World Health Organisation (WHO) definitions, overweight in adult populations is defined as BMI between >= 25 and <= 29.9 kg/m² and obesity as BMI >= 30 kg/m² (6). However, that classification is not applicable to children and adolescents, since BMI is substantially influenced by age and gender during that developmental period (7). In order to account for those influences, age- and gender-specific reference values were developed by the International Obesity Task Force (IOTF) which correspond to the BMI cut-off values used in the adult population (8,9). Those reference values are based on percentile curves with the 90^{th} percentile corresponding to BMI >= 25 kg/m² (overweight) and the 97^{th} percentile corresponding to BMI >= 30 kg/m² (obesity).

1.1.3 Individual and Economic Consequences

Childhood overweight and obesity are associated with consequences for health and psychological well-being of the child. Associations were found with metabolic complications, such as early-onset type II diabetes mellitus or glucose intolerance, and mechanical complications, such as obstructive sleep apnoea or orthopaedic disorders (10,11). Several social and psychological consequences may affect the emotional development of the child. It was reported that overweight in childhood is associated with anxiety, depression, low global self-esteem, impaired social functioning and peer relationship problems (12–15).

Besides negative individual consequences, increasing rates of overweight and obesity are a growing economic burden. Breitfelder et al. (16) analysed data of a German sample of children and adolescents and found that the economic impact of overweight and obesity is already visible in childhood. The authors report increased expenses of direct costs, which refer to the utilisation of healthcare, and indirect costs, which include the productivity loss of parents, for overweight and obese children. Compared to 468 € for underweight and 402 € for normal weight children, the estimated direct costs per child are 468 € for overweight and 680 € for obese children. A similar trend was found for indirect costs.

1.1.4 Prenatal Origins

Based on findings of cross-sectional, adoptee and cohort studies, there is strong evidence on the association of maternal and paternal overweight and childhood overweight (17–20). It was found that maternal overweight has a significantly higher effect on childhood overweight than paternal overweight with an odds ratio (OR) of 2.81 (95% confidence interval [CI]: 2.39, 3.32) or 2.01 (95% CI: 1.71, 2.37), respectively (21). A possible explanation for these findings is that overweight mothers may be more likely than overweight fathers to prime the child to a lifestyle that is characterised by high calorie intake and low levels of physical activity (often referred to as 'obesogenic lifestyle'). An alternative explanation for the higher impact of maternal weight status may be that priming occurs during pregnancy. The concept of priming influences during pregnancy is referred to as fetal programming.

The theory behind fetal programming suggests that prenatal or early postnatal factors determine long-term effects on health outcomes in the offspring (22). The concept is based on the work of Anders Forsdal (23) and David Baker and colleagues (24–26) who examined the impact of poor living conditions, poverty and maternal health on the offspring's risk of coronary heart disease. In the context of childhood overweight, it was suggested that some events occurring *in utero* result in permanent changes in the metabolic system of the developing fetus (27). There is evidence from epidemiological and animal studies that babies subjected to under- or overnutrition *in utero* are at risk of overweight and obesity in child- and adulthood (28). Maternal weight gain during pregnancy, also referred to as gestational weight gain (GWG), may reflect the mother's nutritional condition and is therefore associated with under- or overnutrition of the growing fetus. The following chapter provides details about potential underlying mechanisms and an overview of the recent literature on GWG and childhood overweight.

1.2 Gestational Weight Gain and Childhood Overweight

1.2.1 Recommendations for Gestational Weight Gain

In 1990, the Institute of Medicine (IOM) and the National Research Council (NRC) published recommendations for GWG including specific recommendations for maternal BMI categories derived from the Metropolitan Life Insurance tables (29). Those guidelines were revised in 2009 (30). They are based on the most recent evidence available regarding consequences for short- or long-term health of mother and child, which are related to pregnancy weight gain (31). Similar to the 1990 guidelines, maternal weight status before conception is taken into account to give recommendations on GWG for every BMI category with the ranges becoming narrower as the BMI category increases. The revised guidelines differ from the 1990 version in two ways: first, they include a relatively narrow range of recommended GWG for obese women; second, they are based on the WHO (6) BMI cut-off points. Table 1 gives an overview of the BMI specific recommendations for GWG at the end of pregnancy.

Table 1: Institute of Medicine/National Research Council (30) recommendations for total gestational weight gain (GWG) and rate of GWG

Pre-pregnancy body mass index	**Total gestational weight gain (Range in kg)**
Underweight (< 18.5 kg/m²)	12.5 - 18
Normal weight (18.5 - 24.9 kg/m²)	11.5 - 16
Overweight (25.0 - 29.9 kg/m²)	7 - 11.5
Obese (>= 30 kg/m²)	5 - 9

(Source: Institute of Medicine (30), pg. S-2)

In addition to GWG recommendations, the guidelines include reviews on several topics, such as determinants of GWG and health consequences for mother and child. Although the recommendations are widely used in research, they appear to be less regarded in the primary care context (30,32).

1.2.2 Impact of Inadequate or Excessive Gestational Weight Gain

The energy intake of the mother is positively associated with GWG (33). Inadequate or excessive GWG may therefore be an indicator for under- or overnutrition *in utero*. It was reported that babies subjected to under- or overnutrition *in utero* are at risk of overweight and obesity in later life (28).

There is evidence from animal studies that maternal undernutrition during pregnancy may have an impact on the adipocyte metabolism and child fat mass (28). For example, Vickers et al. (34) found an increased fat disposition of adult offspring from rat mothers that were on severe restricted diet during pregnancy.

In the context of overnutrition *in utero*, fetal programming and childhood overweight, it was suggested that pregnant women with a greater amount of body fat provide the developing fetus with more glucose and fatty acids (27,28). The increased concentration of glucose and fatty acids leads to a higher fetal secretion of insulin which may result in increased growth, permanent changes to the islet cells of the pancreas, hypothalamus and adipose tissue and thus providing conditions for overweight and obesity throughout life (28,35). While the causal link between maternal pre-pregnancy obesity and greater BMI in the offspring seems fairly established (36), less is known about the long-term effects of excessive GWG on childhood overweight.

Associations between GWG and childhood overweight have been investigated in a number of studies. However, the studies differ in reference values used for the classification of childhood overweight or adequate GWG, respectively. In most studies, either the former GWG recommendations (29) were applied (37–40), or adequate GWG was determined by percentile curves of the study population or other classification (41–44).

There is only a small number of studies on GWG and childhood overweight where the revised IOM/NRC GWG recommendations (30) were applied (45–48). A detailed description of the main study characteristics and findings is included in the appendix section (Table 14 and Table 15).

In sum, the studies examined the effect of pre-pregnancy BMI and GWG on anthropometric outcomes in the offspring at different age groups. While Deierlein et al. (46) focussed on infants, Crozier et al. (45) examined pre-school aged children, Fraser et al. (47) children at age 9 and Margerison-Zilko et al. (48) at age 2 to 20. The studies differ in exposure and outcome measurement. In only one study pre-pregnancy weight was measured; the other studies relied on self-reported data or estimations of pre-pregnancy weight. In two of the studies child BMI was used as surrogate outcome measure (47,48), Crozier et al. (45) used X-ray absorptiometry to analyse the impact of GWG on the offspring's body composition. Except from Deierlein et al. (46), the studies did not account for any type of diabetes (gestational or pregestational diabetes mellitus). None of the three studies investigating children at pre-school age, included child's physical activity or screen-based behaviour.

Across all studies, harmful effects of greater or excessive GWG on offspring's anthropometric outcomes were found, although some effects attenuated in the fully adjusted models. There are inconsistent findings with regard to inadequate GWG. While Fraser et al. (47) reported a protective effect of inadequate GWG on greater childhood BMI, Crozier et al (45) tested for an U-shaped relationship between GWG and childhood overweight and found a significant association. Although pre-pregnancy BMI was accounted for in each of the studies, only Margerison-Zilko et al. (48) conducted stratified analyses. They found a harmful effect per additional kg GWG on childhood overweight in the strata of normal weight mothers only. Fraser et al. (47) reported a higher risk of childhood overweight per additional kg pre-pregnancy weight. The findings of the studies may be limited to children of women who are older at birth and of higher socioeconomic status, since women who refused to participate or dropped out from the studies tended to be younger, were less educated and had lower income.

The findings of the studies provide evidence on the harmful influence of excessive GWG on childhood overweight. The results on the effect of inadequate GWG on childhood overweight, however, are conflicting. The impact of pre-pregnancy BMI and excessive or inadequate GWG needs further investigation. Besides the study by Margerison-Zilko et al. (48), other studies examining the effect in the BMI strata used either the former IOM/NRC GWG recommendations (29) or applied a different classification system. For example, von Kries et al. (44) analysed data from the German Health Interview and Examination Survey for Children and Adolescents and determined total GWG of < 11 kg as inadequate, 11-17 kg as adequate and > 17 kg as excessive across all maternal BMI strata. After adjustment for potential confounders, they found that excessive GWG was associated with a 16% higher risk of childhood overweight (OR: 1.16, 95% CI: 1.02, 1.32). In the stratified analyses, excessive GWG was significantly associated with a higher risk of childhood overweight in the strata of normal-weight mothers only. Inadequate GWG was not associated with childhood overweight in the overall and the stratified analyses.

The aim of this dissertation is to contribute to the existing knowledge and further disentangle the effects of pre-pregnancy BMI and GWG on childhood overweight by examining the effect of inadequate or excessive GWG in the four BMI strata.

1.2.3 Prediction of Gestational Weight Gain

The IOM/NRC guidelines (30) provide trimester-specific cut-off values for inadequate or excessive GWG. It is unclear, however, how accurately these cut-off values predict whether women will gain weight within the recommended range or deviating from it. So far, there are no publications on the prognostic value of trimester-specific cut-off values and on total GWG.

Prediction of inadequate or excessive GWG in early or mid-pregnancy would allow for early identification of women at risk of deviating from the recommended GWG ranges and provide an opportunity for timely interventions. With respect to inadequate GWG, there is evidence that a balanced protein-energy supplementation may be useful in achieving adequate GWG (49). With regard to excessive GWG, it was shown in recent meta-analyses that interventions increasing physical activity can reduce excessive GWG (50,51). For example, Streuling et al. (51) reported a mean difference of -0.61 kg (95% CI: -1.17, -0.06) between intervention and control group, indicating lower total GWG in the exercise group compared to the control group. Dietary interventions were shown to significantly reduce total GWG: Tanentsapf, Heitmann and Adegboye (52) combined data of ten intervention trials and found a mean difference of – 1.92 kg (95% CI: - 3.65, - 0.19). A combination of physical activity, nutritional counselling and supplementary weight monitoring was also found to be effective in reducing total GWG (53).

The aim of this dissertation is to assess whether and to what extent GWG below or above the recommended trimester-specific cut-off values predicts inadequate or excessive total GWG.

1.2.4 Benefit of Early Alteration of Excessive Gestational Weight Gain

Evidence on the potential benefits of early alteration of excessive GWG comes mainly from intervention studies (52). So far, however, studies investigating the beneficial effects of weight reducing interventions in pregnancy have primarily focussed on pregnancy outcomes or short-term health outcomes for the child. With respect to excessive GWG, significantly reduced weight postpartum retention after six months and incidence of caesarean section were reported (52). However, there are no studies investigating to what extent the reduction of excessive GWG in early or mid-pregnancy reduces the long-term risk of childhood overweight.

In general, the definite proof of the benefit of GWG modifying interventions on long-term child outcomes would have to come from randomised controlled trials with long-term follow-up periods. Initialising and conducting such trails however, requires a large amount of resources. Prior to planning such trials, it is therefore important to investigate whether the suspected effects can be found using other study designs. Longitudinal observational studies provide the opportunity to investigate long-term effects of exposures and are therefore useful in examining potential effects (54).

This dissertation aims to contribute to the lacking knowledge on the benefit of GWG alteration on the long-term effects for the child. By analysing natural course GWG data, it will be investigated whether reversing from excessive GWG in early or mid-pregnancy is associated with reduced risk of childhood overweight at school entry.

2 Research Questions and Hypotheses

In this dissertation three principal research objectives will be addressed: first, to disentangle the impact of inadequate or excessive GWG on the development of childhood overweight and to examine the role of pre-pregnancy BMI (Analysis 1); second, it will be examined whether and to what extent trimester-specific cut-off values for inadequate or excessive GWG provided by the IOM/NRC (30) predict total inadequate or excessive GWG (Analysis 2); third, it will be analysed whether a reverse from excessive GWG in the first or second trimester is associated with risk reduction for childhood overweight (Analysis 3). Table 2 and table 3 provide an overview of the research questions and hypotheses.

Table 2: Research questions and hypotheses (Analysis 1)

1a. Total Gestational weight gain (GWG) and the prevalence of childhood overweight at school entry (Analysis 1)	
Question 1.1	Is inadequate total GWG compared to adequate total GWG a risk factor for childhood overweight?
Hypothesis 1.1	Compared to adequate total GWG, inadequate total GWG is a risk factorfor childhood overweight.
Question 1. 2	Is excessive total GWG compared to adequate total GWG a risk factor for childhood overweight?
Hypothesis 1.2	Compared to adequate total GWG, excessive total GWG is a risk factor for childhood overweight.
1b. Influence of maternal pre-pregnancy body mass index (BMI) on the association between total GWG and the prevalence of childhood overweight at school entry (Analysis 1)	
Question 1.3	Is inadequate total GWG compared to adequate total GWG a risk factor for childhood overweight across the four maternal BMI strata?
Hypothesis 1.3	Compared to adequate total GWG, inadequate total GWG is a risk factor for childhood overweight across the four maternal BMI strata.
Question 1.4	Is excessive total GWG compared to adequate total GWG a risk factor for childhood overweight across the four maternal BMI strata?
Hypothesis 1.4	Compared to adequate total GWG, excessive total GWG is a risk factor for childhood overweight across the four maternal BMI strata.

Table 3: Research questions and hypotheses (Analysis 2 and 3)

2. Prediction of inadequate or excessive total gestational weight gain (GWG) by trimester-specific GWG cut-off values (Analysis 2)	
Question 2.1	Whether and to what exent do trimester-specific GWG cut-off values for inadequate GWG predict inadequate total GWG?
Hypothesis 2.1	Trimester-specific GWG cut-off values for inadequate GWG predict inadequate total GWG.
Question 2.2	Whether and to what exent do trimester-specific GWG cut-off values for excessive GWG predict excessive total GWG.
Hypothesis 2.2	Trimester-specific GWG cut-off values for excessive GWG predict excessive total GWG.
3. Association between reverse from excessive GWG in the first or second trimester and childhood overweight at school entry (Analysis 3)	
Question 3	Does a reverse from excessive GWG in the first or second trimester reduce the risk of childhood overweight?
Hypothesis 3	A reverse from excessive GWG in the first or second trimester reduce the risk of childhood overweight.

3 Methods

3.1 Sample

The sample was recruited during the Bavarian school entry health examinations. Data collection centres were distributed in a wide geographical area and included the towns Augsburg, Ansbach, Dachau, Passau, Landshut and Rosenheim.

Prior to the school entry health examinations, information leaflets and a questionnaire (see appendix), including a large number of questions on potential confounders, were sent to the parents. Mothers and their children were invited to take part in the study. Signed informed consent was obtained and the study protocol was approved by the local ethics committee.

3.1.1 Data Collection

Data were collected by trained study nurses from October 2009 to June 2011. On the day of the school entry health examination, completed questionnaires were returned by the parents and children's anthropometric data were measured.

The questionnaire consisted of standardised questions obtained from already validated questionnaires and newly developed questions. Child lifestyle and parental SES was assessed by questions derived from the German Health Interview and Examination Survey for Children and Adolescents (55) and breastfeeding by using questions from the Bavarian Breastfeeding Study (56). All other questions were designed for the purposes of this study.

Data on maternal pre-pregnancy weight and weight gain during pregnancy were obtained from the "maternity pass". In Germany, a "maternity pass" is issued to every pregnant woman at her first antenatal visit to the gynaecologist. The "maternity pass" includes complete documentation of health-care visits during pregnancy. It provides comprehensive prenatal data on ultrasound check-ups, laboratory assessments and the “gravidogram”, which includes several weight measurements at different times during pregnancy. The study nurses abstracted information on maternal height, pre-pregnancy weight, maternal weight during pregnancy at several measurement points, diabetes mellitus before pregnancy, gestational diabetes mellitus and gestational age at delivery from the “maternity pass”.

Children’s weight was measured, wearing underwear, using a calibrated electronic balance scale (SECA, Birmingham, UK) with an accuracy of 0.1 kg. Height was measured, without wearing shoes, with an accuracy of 0.1 cm using a stadiometer (Seca, Birmingham, UK).

3.1.2 Response Rate

Of 21,454 examinations conducted in the study period, 11,730 mother-child pairs participated in the study, accounting for a response rate of 54.7%. Table 4 gives an overview of the response rates per collection centre.

Table 4: Response rates per data collection centre

	Location of data collection centres						
	Ansbach	Augsburg	Dachau	Landshut	Passau	Rosenheim	**Total**
Mother-child pairs invited to participate in study	4,131	4,537	2,494	4,003	3,472	2,817	**21,454**
Mother-child pairs participating in study	2,708	2,928	1,151	1,654	2,106	1,183	**11,730**
Response rates (%)	**65.55**	**64.54**	**46.15**	**41.32**	**60.66**	**42.00**	**54.68**

3.1.3 Overview: Data and Methods Used in Analysis 1, 2 and 3

Research questions 1, 2 and 3 were examined in three separate analyses. Table 5 provides an overview of explanatory and outcome variables investigated in each analysis, the corresponding statistical tests and the included study population.

Table 5: Overview of explanatory and outcome variables, statistical tests used and study population examined in analysis 1, 2 and 3

Analysis	Explanatory variable	Outcome	Statistical tests	Study population
1	Overall total GWG: per kg and categorical according to IOM/NRC (30) Total GWG stratified by maternal pre-pregnancy BMI: per kg and categorical according to IOM/NRC (30)	Child overweight at school entry health examination (categorical)	**Sample characteristics:** t-test, chi²-test, Mann-Whitney-U-test **Analysis question 1:** univariate and multivariate binary logistic regression	Mother-child pairs
2	Inadequate GWG at trimester 1, 2 and 3 (categorical) Excessive GWG at trimester 1, 2 and 3 (categorical)	Inadequate total GWG (categorical) Excessive total GWG (categorical)	**Sample characteristics:** t-test, chi²-test, Mann-Whitney-U-test **Analysis question 2:** Prognostic values: Sensitivity, specificity, positive predictive value, negative predictive value, positive likelihood ratio	Mothers
3	Never excessive (reference category) Excessive GWG in trimester 1 or trimester 2 only Excessive GWG in trimester 3 only Excessive GWG in trimester 3 and any previous	Child overweight at school entry health examination (categorical)	**Sample characteristics:** t-test, chi²-test **Analysis question 3:** univariate and multivariate binary logistic regression	Mother-child pairs

Abbreviations: GWG = Gestational weight gain; IOM = Institute of Medicine; NRC = National Research Council

Details on inclusion criteria, definition of outcome and explanatory variables, included confounders and statistical analyses are provided in the following subchapters.

3.2 Analysis 1

3.2.1 Inclusion Criteria

Only singleton, term-birth children were included whose mothers did not have a history of diabetes mellitus or gestational diabetes prior or during pregnancy, respectively. For analysis of the overall and stratified effect of GWG on childhood overweight, the sample was further confined to children with full information on height, weight, maternal GWG and potential confounding variables (chapter 3.2.3). Total GWG values below the 0.1% percentile or above the 99.9% percentile were defined as implausible and subjects excluded from the analysis.

A total of 6,837 mother-child pairs were included in the final analysis on the impact of GWG on childhood overweight. Figure 1 provides an overview of the subjects included.

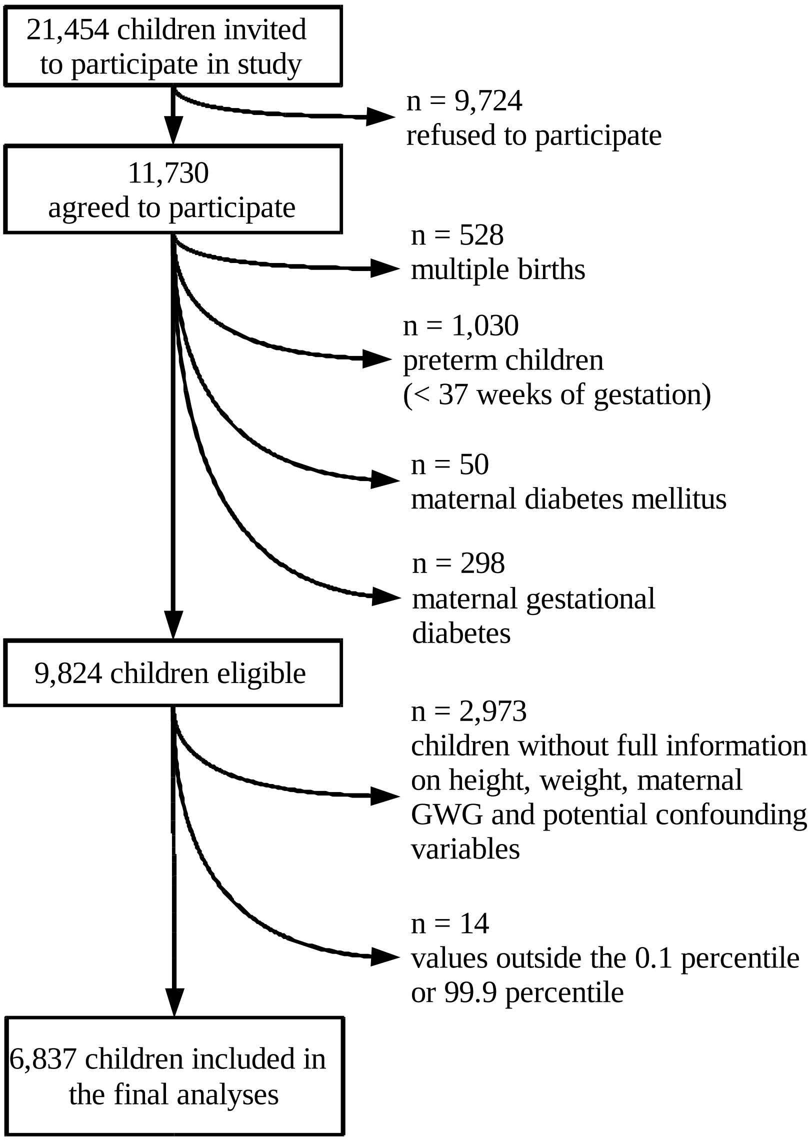

Figure 1: Study flow diagram (Analysis 1)

3.2.2 Explanatory and Outcome Variables

Maternal pre-pregnancy BMI was calculated as weight before pregnancy in kilograms divided by squared height before pregnancy in meters. Body mass index categories were defined according to WHO definitions (underweight: <18.5 kg/m², normal weight: 18.5 – 24.9 kg/m², overweight: 25 – 29.9 kg/m², obese: >= 30 kg/m²) (6).

Total maternal GWG was defined as difference between maternal pre-pregnancy body weight and last weight measurement before delivery. Week specific GWG cut-off values

(30) were used to determine inadequate or excessive GWG at the week the last measurement was conducted (30). On average, the last GWG measurement (mean: 38.1, median: 38) was taken about one week before the child was born (mean: 39.4, median: 39). The IOM/NRC recommendations (30) classify adequate weight gain at the end of week 40 as total weight gain within 12.5 – 18 kg for underweight women, 11.5 – 16 kg for normal weight women, 7 – 11.5 kg for overweight women and 5 – 9 kg for obese women. If the last measurement was taken at the end of week 36, for example, adequate weight gain was classified as total weight gain within 10.8 – 15.8 kg for underweight, 9.9 – 14.1 kg for normal weight, 6.1 – 10.2 kg for overweight and 4.3 – 8.0 kg for obese women. A table with the week-specific IOM/NRC GWG cut-off values can be found in the appendix section.

The main outcome parameter was children's overweight. The IOTF (8) age- and sex-specific reference values were applied to classify whether a child was overweight (>= 90^{th} percentile) at school entry health examination. In this dissertation, the term "childhood overweight" includes overweight and obesity.

3.2.3 Confounders

Besides pre-pregnancy weight and GWG, other risk factors for the development of childhood overweight and obesity, related to the parents and the offspring's lifestyle, have been identified and included in analysis 1. Maternal pre-pregnancy BMI was not included as confounder. The IOM/NRC recommendations (30) provide BMI specific ranges. An additional adjustment for maternal pre-pregnancy BMI would have resulted in over-adjustment. The following potential confounders were included in analysis 1:

Parental socioeconomic status (SES): Low parental SES is associated with increased risk of childhood overweight (18,57,58).

Maternal smoking (prior or during pregnancy): Maternal smoking in pregnancy appears to increase the risk of childhood overweight (57,59–63).

Maternal age: Adverse metabolic processes during pregnancy and GWG appear to increase with maternal age (30).

Breast feeding: Breast-feeding may have a protective effect against the development of childhood overweight (64–67).

Birth weight: High birth weight is associated with increasing risk of childhood obesity. The findings related to low birth are conflicting (68–71).

Child's television viewing: Positive associations between time spent with television viewing and childhood overweight were reported (72–75).

Child's physical activity: Increased physical activity a protective factor against childhood overweight (73,76–78).

In this dissertation, parental SES was defined using an additive index as suggested by Böhm et al. (79). It includes maternal and paternal educational background and current type of employment. Educational background was categorised as "low" (< ten years of formal education) (score: 1), "medium" (ten years of formal education) (score: 2) and "high" (> ten years of formal education) (score: 3). Type of employment was categorised as "not employed" (score: 1) and "at least part-time employed" (score: 2). Maternal and paternal educational background or type of employment, respectively, was added. If one parent did not provide information on educational background or type of employment, the status of the other parent was considered two times to calculate the score. Socioeconomic status was categorised as “low” (total parental score: <= 6), “medium” (total parental score: 7-8) and “high” (total parental score: >= 9). Maternal smoking during pregnancy was dichotomised as “at no times during pregnancy” or “any time during pregnancy”. Maternal age in years was included as continuous variable. Breastfeeding was dichotomised as “at least one month full-time without interruption” and “less than one month full-time”. Child’s birth weight in grams was included as continuous variable. Television consumption of the child at the time of the school entry examination was categorised as “less than one hour daily” and “more than one hour daily”. Child’s physical activity included outdoor physical activity in winter and summer and sports related or not related to sports clubs. The four variables were dichotomised on the point where they distinguished best between frequent and rare in our sample (physical activity summer: frequent= almost every day; physical activity winter: frequent ≥ 3-5 times per week; sports in sports clubs: frequent ≥ 1-2 times per week; sports not related to sports clubs: frequent ≥ 1-2 times per week). The dichotomous variables where then combined to define the variable “outdoor activity” (high: frequent in outdoor summer and outdoor winter; medium: at least frequent in outdoor summer or outdoor winter; low: rare in outdoor summer and outdoor winter) and “sports” (high: frequent in sports related and not related to sports clubs; medium: at least frequent in one of both; low: rare in sports related and not related to sports clubs). The variables “outdoor activity” and “sports” were combined to categorise in “high physical activity” (at least outdoor activity or sports high, the other medium), “medium physical activity” (at least outdoor activity or sports high, the other low or both categories medium) or “low physical activity” (either one or both of the categories low, the other medium).

3.2.4 Statistical Analysis

Only subjects with complete measurement data for outcome, exposure and potential confounders were included. T-tests, U-tests and chi²-tests (as appropriate) were used to compare whether participants included in the study differed from participants excluded.

Univariate and multivariate logistic regression models were conducted to examine the effects of GWG per kg and inadequate or excessive total GWG on childhood overweight at school entry. Odds ratios for the impact of GWG per kg and inadequate or excessive total GWG on childhood overweight at school entry were calculated. Average GWG was used as reference category. Binominal 95% CIs were calculated. All potential confounders were included in the final analyses.

Statistical significance of effects was determined by p-values of <.05 or by 95% CIs. All statistical analyses were conducted using the software package R 2.12.1 (http://cran.r-project.org).

3.3 Analysis 2

3.3.1 Inclusion Criteria

Inclusion criteria were similar to those described in analysis 1 (chapter 3.2.1). For analysis of the prediction of inadequate or excessive total GWG based on trimester-specific GWG cut-off values, the sample was confined to pregnancies with plausible and complete weight data for all three trimesters. For 1,840 pregnancies, weight data were missing in at least one trimester. For each trimester, weight gains below the 0.1% percentile or above the 99.9% percentile were defined as implausible and subjects excluded.

The trimesters were defined as: first trimester between week 1 and week 13, second trimester between week 14 and week 26 and third trimester between week 27 and week 40. The definition of non-overlapping ranges prevented from potential statistical problems resulting from multiple measurements within a trimester. Figure 2 provides an overview of the subjects included in the analyses on the prediction of inadequate or excessive total GWG.

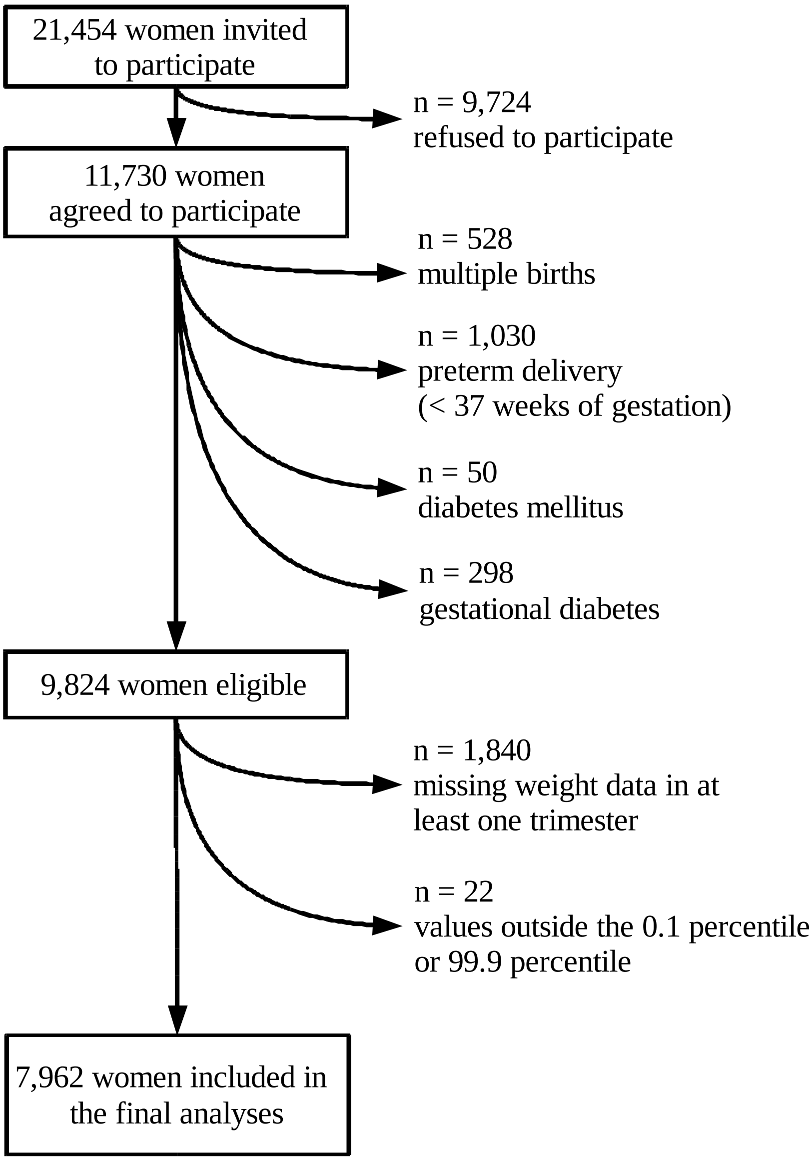

Figure 2: Study flow diagram (Analysis 2)

3.3.2 Explanatory and Outcome Variables

Maternal pre-pregnancy BMI was calculated and defined as described in chapter 3.2.2. The week-specific cut-off points in trimester 1, 2 and 3 for inadequate and excessive GWG according to IOM/NRC guidelines (30) were calculated. In the IOM/NRC guidelines, a linear progression of GWG during pregnancy is assumed with different slopes in the first trimester and the following two trimesters: There is a slower rate of GWG in the first trimester, followed by a faster rate of gain in the second and third trimester. For example, for normal-weight women, the upper cut-off point of adequate GWG at the end of the first trimester is 3 kg. Subtracted from the corresponding upper cut-off point of total GWG (16 kg) at the end of pregnancy, the upper limit in the remaining 27 weeks (trimester 2 and 3) is a total of 13 kg. This results in a weekly gain of 0.23 kg (3 kg/ 13 weeks) in the first trimester and 0.48 kg in the second and third trimester (13 kg/ 27 weeks). Similarly, the lower cut-off point of adequate GWG in the first trimester for normal-weight women is 1 kg. Subtracted from the corresponding lower cut-off point of total GWG (11.5 kg), the lower limit in the remaining 27 weeks is a total of 10.5 kg. This results in a weekly gain of 0.39 kg (10.5 kg/ 27 weeks) in the second and third trimesters. That weekly gain was accumulated to obtain the lower and the upper limit of weight gain for week 1 to 40 according to IOM/NRC guidelines (30). For example, in week 24 the lower limit was 5.28 kg (1 kg in the first trimester plus 11 weeks x 0.39 kg/week) and the upper limit was 8.3 kg (3 kg in the first trimester plus 11 weeks x 0.48 kg/week). A similar procedure was conducted for each BMI category. To determine whether the actual GWG in a specific week deviated from the recommended ranges of adequate GWG in that week, for each woman, her actual GWG in the particular week was compared with these limits to ascertain whether her gain was below or above the week specific cut-off point. A table of the week specific cut-off values per maternal BMI group can be found in the appendix (Table 16, table 17 and table 18)

The main outcome parameter was inadequate or excessive total GWG as described in chapter 3.2.2.

3.3.3 Confounders

Due to the nature of the analysis, no confounders were included.

3.3.4 Statistical Analysis

Only subjects with complete measurement data for explanatory and outcome variables were included in the analyses. T-tests, U-tests and chi²-tests (as appropriate) were used to compare whether women included in the study differed from women excluded from the study.

To assess the prediction of inadequate or excessive total GWG based on trimester-specific GWG cut-off values in the first, second or the third trimester, prognostic values for each of the three measurement periods were calculated: Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV). In general, sensitivity and specificity are measures of the validity of a test: sensitivity refers to the probability of a positive test given that the person has the disease; specificity refers to the probability of a negative test given that the disease is truly absent (80). To give an example in the context of the study question, sensitivity refers to the proportion of women with total excessive GWG ("disease present"), who have exceeded the trimester-specific GWG cut-off value in a given trimester ("positive test"). The PPV is the probability that an individual actually has the disease given that the test result is positive (80). With regard to the study question, it, for example, refers to the proportion of women who exceeded the trimester-specific cut-off value in a given trimester ("positive test"), and had excessive total GWG ("disease present"). The NPV refers to the probability that a person does not have the disease given a negative test result (80). Positive diagnostic likelihood ratios (DLR+) defined as DLR+ = sensitivity/(1-specificity) were calculated (81). The DLR+ indicates to what extent a positive diagnostic test result (i. e. deviating from the week-specific GWG cut-off values) will increase the pretest probability of the target disease (i. e. deviating from the recommended GWG ranges at the end of pregnancy) (81). The 95% CIs of the DLR+ were calculated as suggested by Simel (82).

3.4 Analysis 3

3.4.1 Inclusion Criteria

Inclusion criteria were similar to those applied in analysis 1 and 2 (chapter 3.2.1). For analysis of the association between reverse from excessive GWG in early or mid-pregnancy and childhood overweight, the sample was confined to pregnancies with plausible GWG data for all three trimesters. Due to missing data on weight measurements or potential confounders, 3,001 subjects were excluded from the analyses. For each trimester, weight gains below the 0.1% percentile or above the 99.9% percentile were defined as implausible and subjects excluded. The trimesters were defined as described in analysis 2 (chapter 3.3.1).

This resulted in 6,767 subjects included in the final analyses. Figure 3 provides an overview of the subjects included in the analyses on the association between excessive GWG patterns and childhood overweight.

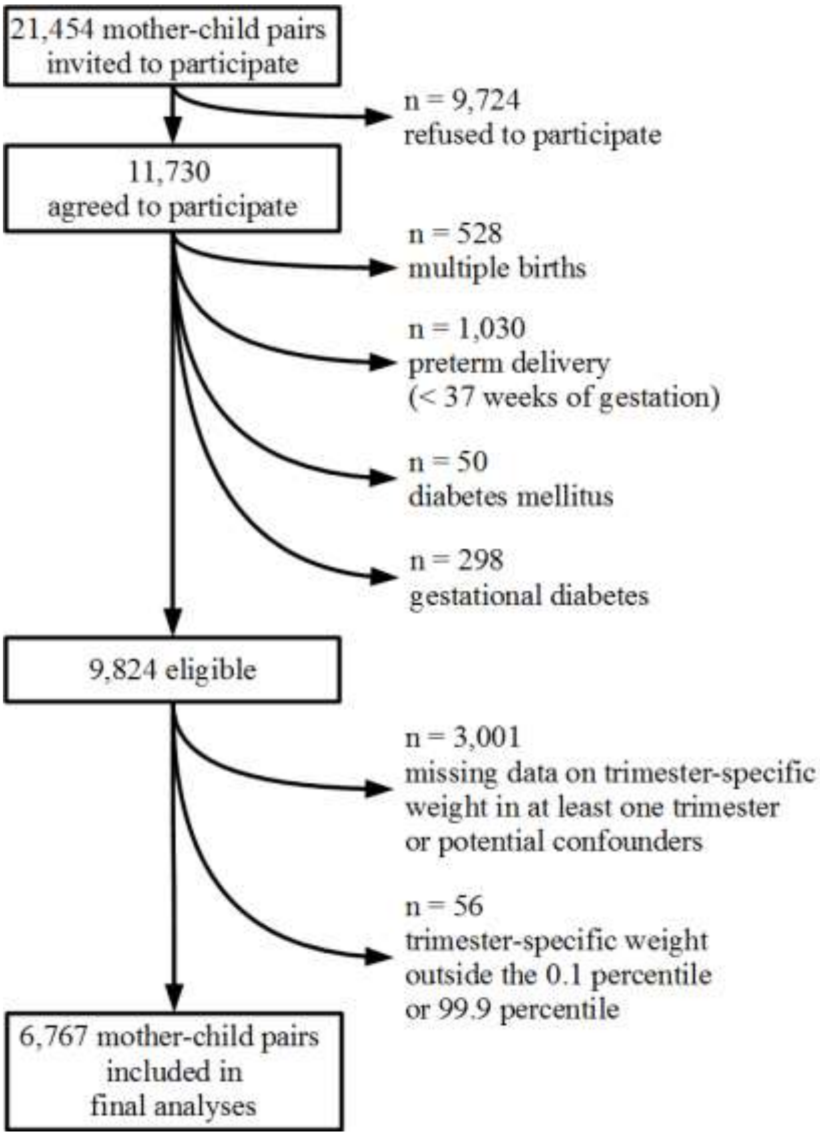

Figure 3: Study flow diagram (Analysis 3)

3.4.2 Explanatory and Outcome Variables

The main outcome parameter was child overweight as defined in chapter 3.2.2. The main exposures were patterns of excessive GWG as described subsequently. Trimester specific GWG was defined as described in chapter 3.2.2. Excessive GWG at each trimester was determined based on the week-specific GWG cut-off values provided by the IOM/NRC guidelines (30) (as described in chapter 1.2.1).

To assess whether reversing from excessive GWG in the first or second trimester, i.e. before the third trimester, was associated with lower risk of childhood overweight, three categories were defined: “excessive GWG in the first or second trimester only”, “excessive GWG in the third trimester only” and “excessive GWG in the third and any previous trimester”. Those categories were then compared with the reference category that includes mothers who did not exceed the GWG recommendations at any trimester. Figure 4 provides an overview on the categories and number of subjects in each category.

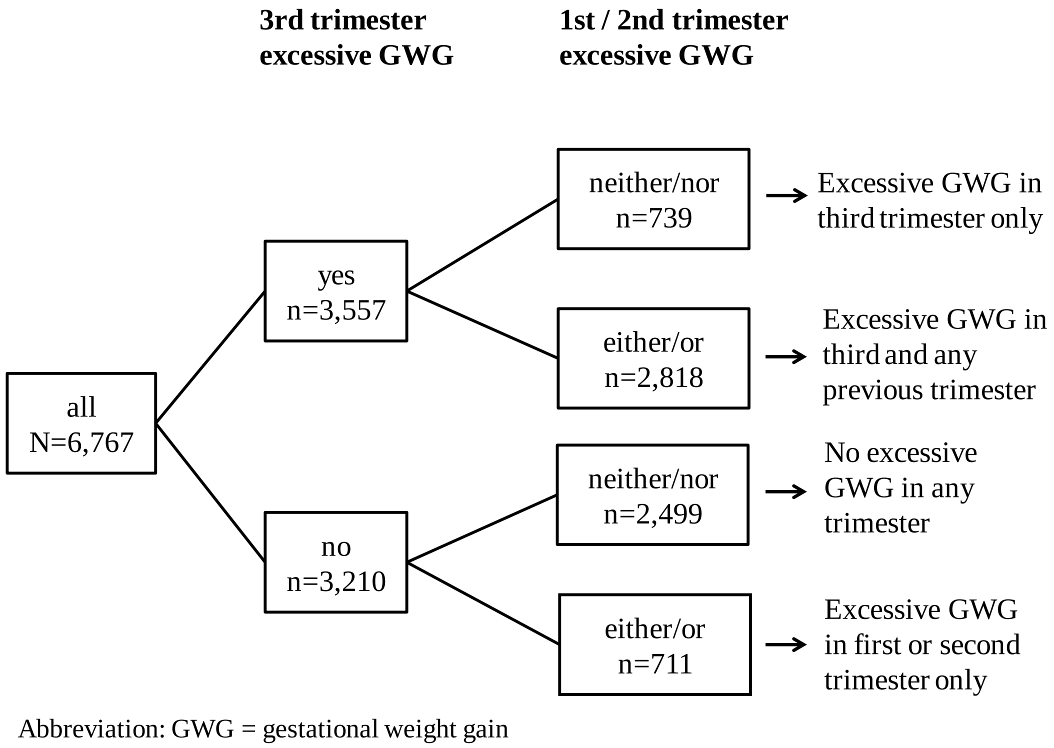

Figure 4: Distribution of individuals in the exposure categories and groups considered

3.4.3 Confounders

Similar to analysis 1 (chapter 3.2.3), several confounders were included in the analyses: Birth weight, maternal age, maternal smoking during pregnancy, SES, breastfeeding and physical activity. Child’s TV watching was not significantly associated with the exposure and therefore not included in the analysis.

3.4.4 Statistical Analysis

Only children with complete measurement data on exposure, outcome and potential confounders were analysed. T-tests, U-tests and chi^2-tests (as appropriate) were used to compare subjects included and excluded.

Univariate and multivariate logistic regression models were used to analyse the association between the three excessive GWG patterns on childhood overweight compared to the reference category. Crude and adjusted analyses were conducted. Model 1 includes potential prenatal confounders and model 2 additionally includes potential confounders related to early nutrition and behavioural aspects of the child. Odds ratios were calculated and binominal 95% CIs determined.

4 Results

4.1 Analysis 1

4.1.1 Sample Characteristics

Table 6 shows characteristics of the study population with regard to the main explanatory variable, outcome and potential confounders. Overall, 14.6% of mothers gained below and 53.5% above the range recommended by IOM/NRC (30). Prior to pregnancy, more than two third of the mothers were normal weight and about 20% were overweight. Almost two third of the overweight children were exposed to excessive GWG.

Mothers of children included in the analyses were slightly older, had fewer children, a lower prevalence of smoking during pregnancy and were less likely to have low socioeconomic status compared mothers of children excluded. Children included in the final analyses had a slightly lower BMI, were less likely to be overweight, watched less TV and were less likely to be physically inactive compared to children excluded from the analyses (Table 6).

Table 6: Sample characteristics (Analysis 1)

Characteristic	All (n= 9,824) Mean/ median/ proportion	All 95% CI	Eligible and excluded (n= 2,987) Mean/ median/ proportion	Eligible and excluded 95% CI	Eligible and included (n= 6,837) Mean/ median/ proportion	Eligible and included 95% CI
Mother:						
Maternal age (years)	28.9	[28.8, 29.0]	**28.7**	**[28.6, 28.8]**	**29.0**	**[28.9, 29.1]**[1)]*****
Parity	1	[1, 3]	**2**	**[1, 3]**	**1**	**[1, 3]**[3)]*****
Pre-pregnancy BMI (kg/m²)	23.4	[23.3, 23.5]	23.4	[23.3, 23.5]	23.4	[23.3, 23.5][1)]
Underweight	5.1%	[4.6, 5.5]	5.9 %	[4.9, 6.8]	4.8 %	[4.3, 5.3][2)]
Normal weight	69.1%	[68.2, 70.0]	67.1%	[65.2, 69.0]	69.6%	[68.6, 70.7][2)]
Overweight	18.1%	[17.3, 18.8]	18.6%	[17.0, 20.2]	17.9%	[17.0, 18.8][2)]
Obese	7.7%	[7.2, 8.3]	8.4%	[7.3, 9.5]	7.7%	[7.0, 8.3][2)]
Total GWG (kg)	14.9	[14.8, 15.0]	14.9	[14.8, 15.0]	14.9	[14.8, 15.1][1)]
Inadequate GWG	14.6%	[14.0, 15.5]	15.2%	[13.6, 16.8]	14.6%	[13.8, 15.4][2)]
Adequate GWG	31.9%	[30.8, 32.8]	31.6%	[29.5, 33.6]	31.8%	[30.7, 32.9][2)]
Excessive GWG	53.5%	[52.5, 54.5]	53.2%	[51.1, 55.5]	53.6%	[52.4, 54.7][2)]
Smoking in pregnancy	12%	[11.4, 12.7]	**14.1%**	**[12.8, 15.4]**	**11.2 %**	**[10.4, 11.9]**[2)]*****
Low parental SES	33.2%	[32.2, 34.1]	**39.5%**	**[37.6, 41.3]**	**30.8 %**	**[29.7, 31.9]**[2)]*****
Child:						
BMI (kg/m²)	15.5	[15.5, 15.6]	**15.6**	**[15.6, 15.7]**	**15.5**	**[15.5, 15.5]**[1)]*****
Overweight children	11.0%	[10.4, 11.7]	**12.4%**	**[11.1, 13.6]**	**10.5%**	**[9.8, 11.2]**[2)]*****
Exposed to:						
inadequate GWG	11.9%	[9.8, 13.9]	10.0%	[6.0, 14.0]	12.4%	[10.0, 14.8][2)]
adequate GWG	23.1%	[20.5, 25.9]	24.1%	[18.4, 29.7]	22.9%	[19.8, 26.0][2)]
excessive GWG	65.0%	[61.9, 68.0]	65.9%	[59.6, 72.2]	64.7%	[61.2, 68.2][2)]
Child's age (years)	5.8	[5.8, 5.8]	5.8	[5.8, 5.8]	5.8	[5.8, 5.8][1)]
Birth weight (g)	3413	[3403, 3422]	3413	[3404, 3422]	3413	[3404, 3422][1)]
Female sex	48.6%	[47.6, 49.6]	49.4%	[47.6, 51.2]	48.3%	[47.1, 49.4][2)]
Breastfeeding (>= 1 month full)	73.2%	[72.3, 74.1]	73.8%	[72.0, 75.6]	73.0%	[71.9, 74.0][2)]
TV consumption (> 1 hour daily)	33.6%	[32.6, 34.5]	**36.1%**	**[34.1, 38.1]**	**32.8%**	**[31.6, 33.9]**[2)]*****
Low physical activity	5.6%	[5.1, 6.0]	**7.4%**	**[6.4, 8.5]**	**4.9%**	**[4.3, 5.4]**[2)]*****

* Significantly ($p < 0.05$) different from subjects included in the study

[1)] t-test, [2)] Chi²-test, [3)] Mann-Whitney U-test

Abbreviations: BMI= Body mass index; GWG= Gestational weight gain; CI= Confidence interval ; SES= Socioeconomic status

4.1.2 Overall Effect of Total Gestational Weight Gain on Childhood Overweight

Each additional kg of GWG was associated with a 4% higher risk of childhood overweight (OR: 1.04, 95% CI: 1.02, 1.05) indicates a 4% higher risk of childhood overweight per additional kg GWG (Table 7).

Excessive GWG compared to adequate GWG was associated with a 57% higher risk of childhood overweight (OR: 1.57, 95% CI: 1.30, 1.91). No significant association was found for inadequate GWG on childhood overweight.

Table 7: Odds ratios and 95% confidence intervals for the association between gestational weight gain and childhood overweight at school entry health examination

		OR [95% CI]	
		Crude	Adjusted (2)
GWG continuous (kg)		**1.02 [1.01, 1.04]**	**1.04 [1.02, 1.05]**
GWG categorical	Inadequate (1) (n= 996)	1.20 [0.92, 1.57]	1.20 [0.91, 1.57]
	Excessive (1) (n= 3,657)	**1.78 [1.48, 2.15]**	**1.57 [1.30, 1.91]**

(1) Odds ratio relativ to reference category 'adequate GWG'
(2) Adjusted for: birth weight, maternal age, maternal smoking during pregnancy, breastfeeding, TV consumption, physical activity, socioeconomic status
Abbreviations: CI= Confidence intervall; GWG= Gestational weight gain; OR= Odds ratio

4.1.3 Effect of Total Gestational Weight Gain Stratified by Maternal Pre-Pregnancy Body Mass Index

Stratified analyses by maternal pre-pregnancy BMI category revealed inconsistent associations between GWG and childhood overweight (Table 8). In the subgroups of normal weight and obese mothers, each additional kg of GWG was associated with a 4% higher risk of childhood overweight (normal weight OR: 1.04, 95% CI: 1.02, 1.07; obese OR: 1.04, 95% CI: 1.01, 1.07). Compared to adequate total GWG, excessive total GWG was associated with a higher risk of childhood overweight in the strata of normal-weight mothers (OR: 1.29, 95% CI: 1.01, 1.66) and the overweight mothers (OR: 1.64, 95% CI: 1.06, 2.63).

In the strata of overweight mothers, inadequate GWG was related to a more than two times higher risk of childhood overweight (OR: 2.52, 95% CI: 1.28, 4.91).

Table 8: Odds ratios and 95% confidence intervals for the association between gestational weight gain and child's overweight stratified by maternal pre-pregnancy body mass index

	GWG	OR [95% CI] Crude	OR [95% CI] Adjusted (2)
Underweight mothers [BMI: < 18.5 kg/m²] (n= 326)	Continuous (kg)	1.02 [0.90, 1.14]	1.03 [0.90, 1.16]
	Inadequate (< 12.5 kg) (1) (n= 66)	1.38 [0.28, 5.80]	1.74 [0.30, 8.97]
	Excessive (> 18 kg) (1) (n= 109)	1.10 [0.27, 4.27]	1.50 [0.34, 6.39]
Normal-weight mothers [BMI: 18.5 - 24.9 kg/m²] (n= 4,769)	Continuous (kg)	**1.06 [1.04, 1.08]**	**1.04 [1.02, 1.07]**
	Inadequate (< 11.5 kg) (1) (n= 760)	1.04 [0.73, 1.46]	1.02 [0.71, 1.43]
	Excessive (> 16 kg) (1) (n= 2,313)	**1.43 [1.13, 1.83]**	**1.29 [1.01, 1.66]**
Overweight mothers [BMI:25.0-29.9 kg/m²] (n= 1,224)	Continuous (kg)	1.02 [1.00, 1.05]	1.01 [0.98, 1.04]
	Inadequate (< 7 kg) (1) (n= 84)	**2.43 [1.25, 4.69]**	**2.52 [1.28, 4.91]**
	Excessive (> 11.5 kg) (1) (n= 904)	**1.75 [1.14, 2.80]**	**1.64 [1.06, 2.63]**
Obese mothers [BMI: >= 30.0 kg/m²] (n= 518)	Continuous (kg)	**1.04 [1.01, 1.07]**	**1.04 [1.01, 1.07]**
	Inadequate (< 5 kg) (1) (n= 86)	0.69 [0.34, 1.40]	0.63 [0.30,1.30]
	Excessive (> 9 kg) (1) (n= 331)	1.21 [0.73, 2.04]	1.17 [0.70, 2.01]

(1) Odds ratio relativ to reference category 'adequate GWG'
(2) Adjusted for: birth weight, maternal age, maternal smoking during pregnancy, breastfeeding, TV consumption, physical activity, socioeconomic status
Abbreviations: BMI= Body mass index; CI= Confidence intervall; GWG= Gestational weight gain; OR= Odds ratio

4.2 Analysis 2

4.2.1 Sample Characteristics

On average, women included had significantly fewer children, had higher total GWG and their children had a higher mean birth weight compared to women excluded (Table 9). Among the women excluded, those with normal weight were more likely to have inadequate total GWG and those with overweight and obesity were less likely to have excessive total GWG.

Underweight mothers were most likely to experience adequate or inadequate total GWG. In normal-weight mothers, adequate or excessive total GWG were about equally common, observed in about 40% each. Excessive total GWG was observed in more than two thirds of overweight and obese mothers, while inadequate total GWG was rarely detected.

Table 9: Sample characteristics (Analysis 2)

	All (n=9,824)		**Eligible and excluded (n= 1,862)**		**Eligible and included (n=7,962)**	
Characteristic	Mean/ median/ proportion	95% CI	Mean/ median/ proportion	95% CI	Mean/ median/ proportion	95% CI
Mother:						
Maternal age (years)	28.9	[28.8, 29.0]	**28.6**	**[28.5, 28.7]**	**29.0**	**[28.9, 29.1][1)]***
Parity	1	[1, 2]	**2**	**[1, 2]**	**1.0**	**[1, 2][3)]***
Pre-pregnancy BMI (kg/m²)	23.4	[23.3, 23.5]	23.4	[23.3, 23.5]	23.4	[23.3, 23.5][1)]
Total GWG (kg)	14.9	[14.8, 15.0]	**14.4**	**[14.2, 14.5]**	**15.0**	**[14.9, 15.1][1)]***
Underweight mothers						
Inadequate total GWG	28.2%	[24.0, 32.5]	34.3%	[23.0, 45.7]	27.2%	[22.6, 31.7][2)]
Adequate total GWG	47.4%	[42.7, 52.0]	41.8%	[30.0, 53.6]	48.4%	[43.3, 53.5][2)]
Excessive total GWG	24.4%	[20.3, 28.4]	23.9%	[13.7, 34.1]	24.4%	[20.1, 28.8][2)]
Normal weight mothers						
Inadequate total GWG	20.8%	[19.8, 21.8]	**27.6%**	**[24.2, 31.1]**	**20.0%**	**[18.9, 21.1][2)]***
Adequate total GWG	39.0%	[37.7, 40.2]	36.2%	[32.5, 39.5]	39.3%	[38.0, 40.6][2)]
Excessive total GWG	40.2%	[39.0, 41.5]	36.2%	[32.9, 39.5]	40.7%	[39.4, 42.0][2)]
Overweight mothers						
Inadequate total GWG	7.4%	[6.2, 8.7]	8.4%	[4.3, 12.4]	7.3%	[6.0, 8.7][2)]
Adequate total GWG	23.7%	[21.6, 25.7]	31.3%	[24.5, 38.1]	22.7%	[20.5, 24.9][2)]
Excessive total GWG	68.9%	[66.6, 71.2]	**60.3%**	**[53.2, 67.5]**	**70.0%**	**[67.6, 72.4][2)]***
Obese mothers						
Inadequate total GWG	16.7%	[13.9, 19.6]	24.5%	[15.8, 33.2]	15.5%	[12.5, 18.4][2)]
Adequate total GWG	20.9%	[17.8, 24.0]	29.8%	[20.5, 39.0]	19.4%	[16.2, 22.7][2)]
Excessive total GWG	62.4%	[58.7, 66.0]	**45.7%**	**[25.7, 55.8]**	**65.1%**	**[61.2, 68.9][2)]***
Child:						
Birth weight (g)	3410	[3400, 3420]	**3380**	**[3370, 3390]**	**3420**	**[3410, 3430][1)]***
Week of delivery	39.4	[30.5, 48.3]	39.4	[39.3, 39.4]	39.4	[39.4, 39.4][1)]

* Significantly ($p < 0.05$) different from women included in the study

[1)] t-test, [2)] Chi²-test, [3)] Mann-Whitney-U-test

Abbreviations: BMI= Body mass index; GWG= Gestational weight gain; CI= Confidence interval; SES= socioeconomic status

The distribution of weight measurements varies by trimester (Figure 5). The time points of weight measurement in trimester one were evenly distributed between week 1 and 13 (Median= 7; 1% Percentile= 3; 99% Percentile= 13). In trimesters two and three, most weight measurements were taken in the second half of the trimester, between week 20 and week 27 in trimester two (Median= 24; 1% Percentile= 21; 99% Percentile= 26), and week 33 to 40 in trimester three (Median= 36; 1% Percentile= 34; 99% Percentile= 38).

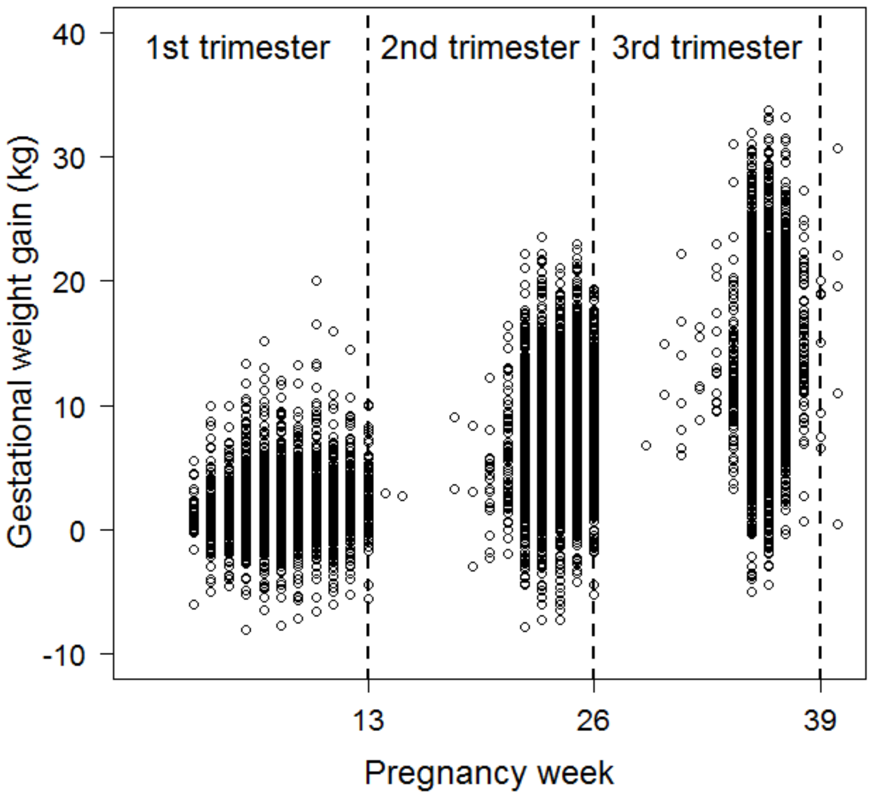

Figure 5: Distribution of weight measurement per pregnancy week

4.2.2 Prediction of Gestational Weight Gain

Prognostic Value of the Lower Cut-off Values at the First, Second and Third Trimester

In all BMI categories, the sensitivity, specificity and hence the DLR+ to predict inadequate total GWG from the lower gestational week-specific cut-off values increased from the first to the third trimester (Table 10). Sensitivity to predict inadequate weight gain in the second trimester was higher in obese and overweight mothers than in underweight and normal-weight mothers. In contrast, the specificity was considerably lower in obese and overweight than in underweight and normal weight mothers. This resulted in DLR+ above 4 in underweight and normal-weight mothers compared to 2.4 in overweight and 2.0 in obese mothers. This is also reflected in PPVs of about 70% in underweight and normal-weight mothers compared to lower PPVs in overweight and obese mothers (Table 10).

Table 10: Prognostic values of the lower gestational weight gain (GWG) cut-offs at trimester 1, 2 and 3 for inadequate total GWG

BMI category	Trimester	Prognostic values for inadequate total GWG				
		Sensitivity (%) [95% CI]	Specificity (%) [95% CI]	PPV (%) [95% CI]	NPV (%) [95% CI]	DLR+ [95% CI]
Underweight (n= 373)	1st	66.0 [55.9, 75.2]	51.1 [43.5, 58.7]	43.1 [35.2, 51.4]	72.8 [64.2, 80.4]	1.4 [1.1, 1.7]
	2nd	49.0 [38.9, 59.2]	89.3 [83.8, 93.5]	72.1 [59.9, 82.3]	75.7 [69.3, 81.4]	4.6 [2.8, 7.1]
	3rd	73.0 [63.2, 81.4]	98.3 [95.2, 99.7]	96.1 [88.9, 99.2]	86.6 [81.2, 91.0]	43.3 [11.8, 112.6]
Normal-weight (n=5,545)	1st	69.1 [66.3, 71.8]	46.5 [44.3, 48.6]	39.7 [37.4, 41.9]	74.7 [72.3, 77.0]	1.3 [1.2, 1.4]
	2nd	60.2 [57.2, 63.1]	85.8 [84.3, 87.3]	68.3 [65.3, 71.3]	80.9 [79.2, 82.5]	4.2 [3.8, 4.8]
	3rd	72.5 [69.7, 75.1]	95.9 [94.9, 96.7]	90.0 [87.8, 91.9]	87.3 [85.8, 88.6]	17.6 [14.8, 22.5]
Overweight (n=1,448)	1st	80.8 [71.9, 87.8]	32.9 [27.8, 38.3]	28.0 [23.0, 33.4]	84.1 [76.6, 90.0]	1.2 [1.1, 1.4]
	2nd	82.7 [74.0, 89.4]	65.8 [60.4, 71.0]	43.9 [36.8, 51.1]	92.2 [87.9, 95.3]	2.4 [2.1, 2.9]
	3rd	81.7 [73.0, 88.6]	95.3 [92.4, 97.4]	85.0 [76.5, 91.4]	94.2 [91.1, 96.5]	17.5 [9.9, 27.1]
Obese (n=596)	1st	68.9 [58.3, 78.2]	36.3 [27.4, 45.9]	46.3 [37.6, 55.1]	59.4 [46.9, 71.1]	1.1 [0.9, 1.3]
	2nd	86.7 [77.9, 92.9]	57.5 [47.9, 66.8]	61.9 [52.8, 70.4]	84.4 [74.4, 91.7]	2.0 [1.7, 2.6]
	3rd	87.8 [79.2, 93.7]	84.1 [76.0, 90.3]	81.4 [72.3, 88.6]	89.6 [82.2, 94.7]	5.5 [3.6, 8.5]

Abbreviations: BMI= Body mass index; DLR+= Positive diagnostic likelihood ratio; GWG= Gestational weight gain; NPV= Negative predictive value; PPV= Positive predictive value

Prognostic Value of the Upper Cut-off Values at the First, Second and Third Trimester

In all four BMI categories, the sensitivity to predict excessive total GWG from upper trimester-specific cut-off values increased from the first to the third trimester, while the relation to specificity was not consistent (Table 11). Increasing DLRs+ by trimester are mainly a reflection of increasing sensitivity. Sensitivity to predict total excessive GWG based on second trimester GWG cut-offs was similar (above 70%) in all maternal BMI categories. The specificity was higher in obese and overweight compared to underweight and normal-weight mothers, which resulted in DLRs+ above 4 in overweight and obese mothers compared to 2.8 in normal and underweight mothers, respectively. This is also reflected in PPVs of 94.3 in overweight and 93.3 in obese mothers.

Table 11: Prognostic values of the upper gestational weight gain (GWG) cut-offs at trimester 1, 2 and 3 for excessive total GWG

		Prognostic values for excessive total GWG				
		Sensitivity (%) [95% CI]	Specificity (%) [95% CI]	PPV (%) [95% CI]	NPV (%) [95% CI]	DLR+ [95% CI]
BMI category	**Trimester**					
Underweight (n= 373)	**1st**	58.9 [48.0, 69.2]	71.3 [64.1, 77.9]	51.0 [41.0, 60.9]	77.4 [70.3, 83.6]	2.1 [1.05, 2.7]
	2nd	75.6 [65.4, 84.0]	73.0 [65.9, 79.4]	58.6 [49.1, 67.7]	85.5 [78.9, 90.7]	2.8 [2.1, 3.6]
	3rd	94.4 [87.5, 98.2]	82.6 [76.2, 87.9]	73.3 [64.3, 81.1]	96.7 [92.5, 98.9]	5.4 [4.0, 7.7]
Normal-weight (n=5,545)	**1st**	42.7 [40.7, 44.8]	79.3 [77.5, 81.0]	68.1 [65.6, 70.6]	57.2 [55.4, 59.0]	2.1 [1.9, 2.3]
	2nd	79.6 [77.8, 81.2]	71.4 [69.4, 73.3]	74.2 [72.4, 76.0]	77.1 [75.2, 79.0]	2.8 [2.6, 3.0]
	3rd	94.8 [93.8, 95.7]	75.8 [74.0, 77.6]	80.3 [78.7, 81.8]	93.3 [92.0, 94.4]	3.9 [3.7, 4.3]
Overweight (n=1,448)	**1st**	30.6 [27.8, 33.6]	86.3 [82.1, 90.0]	87.4 [83.4, 90.7]	28.7 [25.9, 31.7]	2.2 [1.7, 3.0]
	2nd	72.7 [69.8, 75.5]	86.3 [82.1, 89.9]	94.3 [92.4, 95.8]	50.6 [46.4, 54.9]	5.3 [4.0, 6.9]
	3rd	96.2 [94.8, 97.3]	80.7 [76.0, 84.9]	93.9 [92.3, 95.3]	87.2 [82.9, 90.8]	5.0 [4.0, 6.3]
Obese (n=596)	**1st**	35.1 [30.4, 40.2]	83.2 [75.0, 89.6]	87.5 [81.2, 92.3]	27.7 [23.0, 32.8]	2.1 [1.3, 3.2]
	2nd	70.4 [65.5, 74.9]	83.2 [75.0, 89.6]	93.3 [89.8, 95.9]	45.6 [39.7, 52.7]	4.2 [2.7, 6.2]
	3rd	94.4 [91.6, 96.5]	81.4 [73.0, 88.1]	94.4 [91.6, 96.5]	81.4 [73.0, 88.1]	5.1 [3.4, 7.3]

Abbreviations: BMI= Body mass index; DLR+= Positive diagnostic likelihood ratio; GWG= Gestational weight gain; NPV= Negative predictive value; PPV= Positive predictive value

4.3 Analysis 3

4.3.1 Sample Characteristics

At the end of pregnancy, more than half of the mothers gained excessively according to IOM/NRC (30), with increasing proportions of the course of pregnancy (Table 12). The prevalence of overweight (including obesity) was 10.3%.

On average, women excluded from the analysis were younger, had more children, a higher pre-pregnancy BMI and higher GWG in the first trimester. They were less likely to have excessive total GWG, more likely to have smoked during pregnancy and more likely to have lower SES than women included. Children excluded had slightly higher BMI, were more likely to be overweight, watched TV for more than one hour daily and were less physically active than children included.

Weight measurements in the first, second and third trimesters were around the 7^{th}, the 24^{th} and the 36^{th} week (trimester 1: median= 7, 1% percentile= 3, 99% percentile=13; trimester 2: median= 24, 1% percentile= 21, 99% percentile= 26; trimester 3: median= 36, 1% percentile= 34, 99% percentile= 37).

Table 12: Sample characteristics (Analysis 3)

Characteristic	**All (n=9,824)** Mean/ median/ proportion	95% CI	**Eligible and excluded (n= 3,057)** Mean/ median/ proportion	95% CI	**Eligible and included (n=6,767)** Mean/ median/ proportion	95% CI
Mother:						
Maternal age (years)	28.9	[28.8, 29.0]	**28.6**	**[28.5, 28.7]**	**29.1**	**[29, 29.2][1)]***
Parity	1	[1, 3]	**2**	**[1, 3]**	**1**	**[1, 3][3)]***
Pre-pregnancy BMI (kg/m²)	23.4	[23.3, 23.5]	**23.6**	**[23.5, 23.7]**	**23.3**	**[23.2, 23.4][1)]**
GWG (kg)						
Total (kg)	14.9	[14.8, 15.0]	14.8	[14.6, 14.9]	15.0	[14.9, 15.1][1)]
Trimester 1 (kg)	1.2	[1.2, 1.3]	**1.6**	**[1.5, 1.7]**	**1.1**	**[1.1, 1.1][1)]***
Trimester 2 (kg)	7.5	[7.4, 7.6]	7.5	[7.4, 7.6]	7.5	[7.5, 7.6][1)]
Trimester 3 (kg)	13.6	[13.5, 13.7]	13.4	[13.3, 13.5]	13.6	[13.5, 13.7][1)]
Excessive GWG						
Total	53.5%	[52.5, 54.5]	52.0%	[49.9, 54.2]	54.0%	[52.8, 55.2][2)]
Trimester 1	27.1%	[26.2, 28.0]	27.0%	[25.1, 28.9]	27.1%	[26.1, 28.2][2)]
Trimester 2	45.4%	[44.3, 46.4]	44.3%	[42.2, 46.4]	45.7%	[44.5, 46.9][2)]
Trimester 3	52.1%	[51.1, 53.1]	50.8%	[48.7, 52.9]	52.6%	[51.4, 53.8][2)]
Smoking in pregnancy	12.0%	[11.4, 12.7]	**15.1%**	**[13.8, 16.4]**	**10.7%**	**[10.0, 11.5][2)]***
Low parental SES	33.2%	[32.2, 34.1]	**40.5%**	**[38.6, 42.4]**	**30.3%**	**[29.2, 31.4][2)]***
Child:						
BMI (kg/m²)	15.5	[15.5, 15.6]	**15.7**	**[15.6, 15.7]**	**15.5**	**[15.5, 15.5][1)]***
Overweight children	11.0%	[10.4, 11.7]	**12.7%**	**[11.5, 13.9]**	**10.3%**	**[9.5, 11.03][2)]***
Child age (years)	5.8	[5.8, 5.8]	5.8	[5.8, 5.8]	5.8	[5.8, 5.8][1)]
Female sex	48.6%	[47.6, 49.6]	49.0%	[47.2, 50.8]	48.5%	[47.3, 49.7][2)]
Birth weight (g)	3413	[3404, 3422]	3404	[3395; 3413]	3417	[3408; 3425][1)]
Breastfeeding (>= 1 month full)	73.2%	[72.3, 74.1]	72.3%	[70.5, 74.1]	73.5%	[72.5, 74.6][2)]
Low physical activity	5.6%	[5.1, 6.0]	**7.8%**	**[6.8, 8.8]**	**4.7%**	**[4.2, 5.2][2)]***

* Significantly ($p < 0.05$) different from subjects included in the study

[1)] t-test, [2)] Chi²-test, [3)] Mann-Whitney-U-test

Abbreviations: BMI= Body mass index; CI= Confidence interval, GWG= Gestational weight gain; SES= Socioeconomic status

4.3.2 Impact of Reverse from Excessive Gestational Weight Gain in the First or Second Trimester on Childhood Overweight

A significant association between excessive GWG pattern and childhood overweight was observed for mothers with excessive GWG in the third trimester, irrespective of excessive GWG in previous trimesters (Table 13). Compared to reference category, excessive GWG in the third and any previous trimester was associated with a 42% higher risk of childhood overweight in the fully adjusted model (OR: 1.42, 95% CI: 1.17, 1.72). Likewise, there was a 39% higher risk if mothers gained excessively in the third trimester only (OR: 1.39, 95% CI: 1.06, 1.82). No association with childhood overweight was observed in children of mothers with excessive GWG in the first or second trimester only compared to reference category.

Table 13: Odds ratios and 95% confidence intervals for the association between excessive gestational weight gain patterns compared to reference category and childhood overweight at school entry health examination

		Crude		**Model 1**		**Model 2**	
Excessive GWG:	**n**	OR	[95% CI]	OR	[95% CI]	OR	[95% CI]
No excessive GWG in any trimester (reference category)	2,499	1.00		1.00		1.00	
1st or 2nd trimester only	711	1.00	[0.73 ; 1.36]	1.00	[0.72 ; 1.36]	0.99	[0.71 ; 1.34]
3rd and any previous trimester	2,818	**1.64**	**[1.36 ; 1.97]**	**1.43**	**[1.18 ; 1.73]**	**1.42**	**[1.17 ; 1.72]**
3rd trimester only	739	**1.55**	**[1.18 ; 2.02]**	**1.40**	**[1.06 ; 1.83]**	**1.39**	**[1.06 ; 1,82]**

Model 1: adjusted for birth weight, maternal age, maternal smoking during pregnancy, socioeconomic status
Model 2: adjusted for birth weight, maternal age, maternal smoking during pregnancy, socioeconomic status breastfeeding, physical activity
Abbreviations: CI= Confidence intervall; GWG= Gestational weight gain, OR= Odds ratio

5 Discussion

5.1 Gestational Weight Gain and Childhood Overweight

The aim of this dissertation is to examine, first, whether inadequate or excessive total GWG have an effect on childhood overweight, second, whether inadequate or excessive total GWG can be predicted early in pregnancy and, third, whether alteration of excessive GWG in early or mid-pregnancy reduces the risk of childhood overweight.

The findings indicate a positive association between GWG and the risk of childhood overweight (Analysis 1). In the overall analyses, each additional kg of GWG was associated with a 4% higher risk of childhood overweight. Excessive GWG was associated with a more than 50% higher risk of childhood overweight. The findings of the overall analysis are in accordance with those reported elsewhere (45–48). After stratification by maternal pre-pregnancy BMI, significant effects of excessive total GWG were only found among normal-weight and overweight mothers. The effect of excessive total GWG in underweight and obese mothers followed the same direction, but was not statistically significant. Associations of excessive GWG with a higher risk of childhood overweight in the strata of normal weight mothers were also reported elsewhere (44,48).

In the overall analysis, no association between inadequate total GWG and childhood overweight was detected. In the strata of overweight mothers, it was found that inadequate total GWG was associated with a higher risk of childhood overweight. These findings are conflicting with some of the results reported in previous studies, where associations of adequate total GWG with a lower risk of childhood overweight, irrespective of maternal BMI (47), or no associations were found (44,48).

Prediction of inadequate total GWG based on second trimester GWG cut-offs was highest in underweight and normal-weight mothers, due to a high specificity of the second trimester GWG cut-offs (Analysis 2). The GWG cut-offs are fairly good in identifying women not at risk of inadequate total GWG. With regard to sensitivity, only about 50% of the pregnancies with inadequate total GWG could be identified among those mothers based the second trimester GWG cut-offs. Particularly among underweight mothers, inadequate GWG is associated with increasing risk of intrauterine growth retardation (83). The corresponding PPV was about 70% for underweight and normal-weight women, which indicates that about 70% of women with inadequate second trimester GWG had inadequate total GWG at the end of pregnancy.

Prediction of excessive total GWG based on second trimester cut-offs was highest in overweight and obese women, also due to a high specificity. With respect to sensitivity, about 70% of pregnancies with excessive total GWG could be identified based on the second trimester cut-offs. In these mothers the corresponding PPV was about 94%, indicating that more than 90% of the mothers exceeding second trimester GWG cut-offs had excessive total GWG. The relatively high prevalence of excessive total GWG of 70% and 65.1% in overweight and obese women in the sample had an impact on the high PPV of the second-trimester week-specific GWG cut-off values. In general, a higher prevalence of the condition in a population increases the probability that a person with a positive test result will have that particular condition. However, similar prevalence values have been reported elsewhere (45,48). The corresponding NPVs of 50.6 and 45.6 imply that only about half of the women with GWG below the week-specific upper cut-off will eventually have an adequate total GWG. This indicates that adequate total GWG cannot be predicted well for the second-trimester, week-specific cut-off values. Overall, the DLRs+ found in analysis 2 varied between 2.0 and 5.3 for second trimester GWG cut-offs. Those are comparable to DLRs+ reported in a study on screening for childhood overweight (21). In this study, weight gain between birth and 24 months was the best predictor of childhood overweight with a DLR+ of 2.4.

The exploratory analysis of life course GWG data (Analysis 3) indicates that reversing excessive GWG in the first or second trimester may be associated with a reduced risk of childhood overweight. The strength of this association was almost identical for women who had not experienced excessive GWG at any trimester and those with excessive GWG in the first or second trimester or both only. Interventions aiming to reduce excessive GWG in the first or second trimester may therefore useful for the prevention of childhood overweight.

Three recently published studies investigated the effect of absolute week-specific GWG (in kg) in different periods of pregnancy (47,84,85). The findings of those studies suggest that absolute week-specific GWG in the first and second trimester was more relevant for the risk of later overweight in the offspring than absolute week-specific GWG in the third trimester (47,84,85) suggesting that most of the effect of GWG on overweight in the offspring is determined in the first two trimesters. High absolute GWG in any of these time periods, however, may account for excessive third trimester GWG relative to the IOM/NRC recommendations (30). However, in two of the studies (47,84), measurement periods were not trimester-specific and differed in length: In the paper of Fraser et al. (47), the first two periods include the first 36 weeks of pregnancy and thus almost the entire pregnancy period; the periods defined in Andersen et al. (84) were data driven and overlapping. For example, they categorised the second period from week 13 to 21 until week 25 to 32 and the third period from week 26 to 33 until the end of pregnancy. Based on those definitions, the impact of GWG in the third trimester is not detectable.

The findings of the exploratory analysis indicate a risk reduction of childhood overweight if mothers reverse from excessive GWG before the third trimester. As shown in analysis 2, trimester-specific GWG cut-off values allow for early prediction of excessive GWG, particularly in the high risk groups of overweight and obese women. Early identification and allocation to interventions may also reduce the long-term risk of the child to become overweight.

5.2 Strengths

The findings of this dissertation are based on a large non-US sample of preschool-age children. The sample size is higher than sample sizes used in the most recent studies on GWG and childhood overweight (45–48).

Maternal weight data prior or during pregnancy and maternal health were ascertained from medical records by trained stuff, as recommended by IOM/NRC (30). All maternal weight data, apart from pre-pregnancy weight, which was based on self-report, were measured by the physician consulted at the day of the antenatal visit. Inadequate and excessive GWG was determined based on the latest IOM/NRC recommendations (30). The findings of analysis 1 are therefore comparable to the results reported in the most recent literature. Anthropometric data of the child was collected by trained stuff, using standardised stadiometers and balance scales. The objective measurement of outcome and exposure data reduces the risk of systematic errors caused by subjectively reported or recalled data.

The high sample size allows for stratified analyses of the effect and prediction of inadequate or excessive GWG by maternal pre-pregnancy BMI and exploratory analysis of the impact of different excessive GWG patterns.

A large number of prenatal and lifestyle related confounders were included. Unlike most other recent studies (45,47,48), women with gestational diabetes or diabetes mellitus II could be identified and excluded from the analyses. There is evidence that diabetes in pregnancy has an influence on GWG (86) which may distort the findings and affect external validity.

5.3 Limitations

The results of this dissertation should be interpreted in the context of three limitations.

First, similar to previous studies (46,48), self-reported pre-pregnancy weight was used to calculate maternal pre-preganancy BMI and total GWG. The findings may be therefore affected by under- or overestimation of pre-pregnancy weight by the mother. However, there is evidence that using self-reported pre-pregnancy weight data leads to valid estimates of maternal weight (87,88).

Second, the findings may be affected by selection bias, because the excluded subjects were more likely to be exposed to several risk factors related to explanatory variables or outcome (maternal age, maternal smoking, low SES, TV consumption, physical activity) compared to those included in the final analyses. Although this might be of some importance for the external validity of the findings, it is unlikely that it had an influence on the main findings. Similar differences between the sample included and excluded were also reported elsewhere (45–48). Some differences related to explanatory and outcome variables between subjects included and subjects excluded, may have caused under- or overestimation of the effects. In analysis 1, children included had a slightly lower BMI and were less likely to be overweight. The power of the study to detect a truly present difference may be therefore reduced due to the lower prevalence of childhood overweight in the study sample. In analysis 2, the prevalence of inadequate GWG in normal weight mothers was significantly lower than in mothers excluded. This may have resulted in underestimation of the prognostic values. The prevalence of excessive GWG was significantly higher in the included overweight and obese mothers, which may have caused some overestimation of the prognostic values in those subgroups. In analysis 3, first trimester gain was lower among the women included which may have had an effect on the number of subjects per pattern. What is more, the lower prevalence of childhood overweight in the study sample may have reduced the power.

Third, due to missing values in outcome, exposure or confounder data, a relatively high number of subjects had to be excluded from the analyses. This may have affected the power of this study, particularly in analysis 1 and 3 were 30.4% and 31.1% had to be excluded. It was necessary to include a large number of confounders, however, to account for the complex web of potential determinants of childhood overweight (89). Based on findings of other studies, a small effect of GWG on childhood overweight was expected. Detecting a small effect required large sample sizes (54). By excluding about one third of the subjects, the sample sizes may not have been sufficient to detect a small but truly present effect.

5.4 Methodical Evaluation

5.4.1 Study Design and Participation

The findings of this dissertation are based on data collected in a large retrospective cohort study. One of the major advantages was the availability of pre-existing clinical records for the collection of exposure data. Data on GWG was recorded in the "maternity pass" prior to any knowledge of the study which allows for objective and unbiased classification of the exposure status. Compared to a prospective cohort approach, acquisition of exposure data was relatively inexpensive and problems related to drop-outs could be avoided. The outcome was measured by trained stuff using standardised measurements. Data on potential confounders were collected by questionnaire. Some of the answers, however, such as child’s TV watching or physical activity, may have been affected by social desirability response resulting in underestimation of its influence.

The generalisability of results may be influenced by effects of non-participation. Overall, 54.7% of the population available agreed to take part in the study. The response rates varied between the study centres. Although non-participation concerns the generalisability of the study findings to the general population, it does not have an impact on the internal validity of the results (80). It is unlikely that the non-response is directly related to GWG, confounders and the outcome variables. It is more likely that the rate of non-response is related to either the exposure or the outcome which results in under- or overestimation of the association (80).

5.4.2 Representativeness of the Study Sample

The study was conducted in six towns located in different parts of Bavaria. The mean pre-pregnancy BMI of women eligible was 23.4, it was slightly lower in the included sample. Total GWG was on average 14.9 kg. Those figures are comparable to data collected in the regional evaluations of the Bavarian working group on quality assessment (Bayerische Arbeitsgemeinschaft für Qualitätssicherung), where an average pre-pregnancy BMI of 23.9 and an average total GWG of 14.0 kg were reported (90). With regard to the distribution of pre-pregnancy BMI categories, of the sample eligible, 5.1% of mothers were underweight, 69.1% normal weight, 18.1% overweight and 7.7% obese. In a comparable sample of German participants, the proportion of underweight, overweight and obese mothers was only slightly higher (5.8 %, 20.0% and 9.5%, respectively) and the proportion of normal weight slightly lower (64.7%) (44).

Children eligible for this study were on average 5.8 years and the prevalence of overweight was 11% among the children eligible and slightly lower among the children included. Reference values of the IOTF (8) were used to categorise children as overweight. A similar prevalence (10.7%) was reported in a study conducted in Germany, including more than 7,000 children with a mean age of 6.0 years (4).

In conclusion, the exposure data and outcome analysed in this dissertation is comparable to representative data sets from the same geographical region. Similar proportions of pre-pregnancy BMI categories and prevalence of childhood overweight were reported in other studies conducted in Germany.

5.4.3 Classification of Explanatory and Outcome Variable

The accuracy of total GWG may have been influenced by underestimation of self-reported pre-pregnancy weight (see also chapter 5.3). Inadequate and excessive GWG were categorised based latest IOM/NRC recommendations (30). The IOM/NRC guidelines are based on the most recent evidence available regarding consequences of GWG for short- or long-term health of mother and child and they are applicable to women in the US and other developed countries (30).

It has been questioned whether child BMI is a valid indicator for childhood overweight. Child BMI does not distinguish between fat and lean body-mass which may in turn have very different effects on health (35). The BMI is widely used in epidemiological research and is inexpensive and relatively easy to determine compared to more precise measures of body fatness (91). There is evidence that children with a higher BMI relative to gender and age group are likely to have higher body fat and that the validity of BMI as an indicator of body fat increases for children in the upper age-and gender-specific BMI percentiles (92). Childhood BMI appears therefore a valid indicator for childhood overweight.

A related issue is the classification of childhood overweight. The findings of this dissertation are based on the IOTF classification (8), where data from six countries were pooled and linked to the adult overweight and obesity cut-off points. Cole et al. (8) aimed to provide cut-off values that were less arbitrary defined than other cut-off values which, for example, determined childhood overweight between the 85th and 95th percentile (93,94) or between the 90th to 97th percentile (9). Most of the data analysed by Cole et al. (8) was derived from high income countries and allows therefore for direct comparisons of trends in industrialised countries.

5.4.4 Data Analysis

In the stratified analyses, excessive total GWG was associated with a 29% (OR: 1.29, 95% CI: 1.01, 1.66) higher risk of childhood overweight among normal weight mothers; 64% among overweight mothers (OR: 1.64, 95% CI: 1.06, 2.63) (Table 8). Although statistically significant, the confidence intervals are relatively wide, indicating that with a probability of 95% the true population value may lie between 1% to 66% for normal weight mothers and 6% to 163% for overweight mothers. Future research could address this issue by including larger sample sizes to narrow the width of the confidence intervals. This could be achieved by pooling data of cohort studies or conducting meta-analysis.

The temporal distribution of GWG measurements in the first, second and third trimester varied (Figure 5). In the first trimester, weight measurements were almost equally distributed across time. In the second and third trimesters, in contrast, weight measurements were predominantly performed in the second half of the trimesters. Therefore, the observed DLRs+ may not be equally valid at each time during the respective trimester but reflect rather late time points in the respective trimesters. This may have created some overestimation of these DLRs+. In the future, analysis 2 and analysis 3 should be replicated in a data set that includes data from early in the second trimester.

With regard to the analysis of different patterns of excessive GWG and the association of childhood overweight (Analysis 3), the numbers for some patterns were not high enough to yield significant estimates for each possible pattern after consideration of all possible confounders. Some patterns where therefore combined. However, this does not invalidate the findings, since the overall effect was consistent in the subgroups considered. Future research could disentangle the effects of each pattern on childhood overweight and investigate potential dose effects regarding excessive GWG in the first and second or both trimesters.

5.5 Implications for Clinical Research and Practice

Excessive total GWG appears to be associated with a higher risk of childhood overweight. In context of the contemporary state of research, there are some indicators for a causal relationship, as postulated in the Bradford Hill criteria for causation (95), between excessive total GWG and childhood overweight. The Bradford Hill criteria are neither sufficient nor absolutely necessary; the more criteria are present, the more likely it is that an association is causal. Although the underlying pathophysiological mechanisms are not completely understood yet, the association appears biological plausible and was found in human- and animal-studies (coherence) as well as in different study populations and geographical areas (consistency). The criteria of temporality is also met, since the cause (excessive GWG) naturally precedes the effect (childhood overweight). With regard to the strength of association, most of the findings are based on cohort studies which, after meta-analysis and randomised controlled trials (RCT), hold a high position in the hierarchy of evidence of study designs (96). The quantitative strength of association of 57% higher risk of childhood overweight in the overall sample and 29% for normal weight and 64% for overweight mothers may appear relatively low, compared to effects found in other epidemiological research, such as smoking and lung cancer. In the context of prenatal risk factors for childhood overweight however, it is comparable to findings reported for other risk factors, such as smoking during pregnancy (OR: 1.50, 95% CI: 1.36, 1.65) (61). Since most of the Bradford Hill criteria are met, a causal association between excessive GWG and childhood overweight appears likely.

Excessive GWG has a relatively high impact on the population level. In the study population, more than 50% of the mothers gained excessively during pregnancy and the harmful effect of excessive GWG was between 29% and 64% (overall: OR: 1.57, 95% CI: 1.30, 1.91; stratified normal weight: OR: 1.29, 95% CI: 1.01, 1.66; stratified overweight: OR: 1.64, 95% CI: 1.06, 2.63). Future research could contribute to the research on the strength of association by conducting study designs with even stronger evidence. Since RCTs with random allocation of mothers to gain excessively or not and follow their children for several years are unethical and hardly feasible, data of cohort studied applying similar reference values and the latest IOM/NRC recommendations (30) should be combined in a meta-analysis.

The week-specific GWG cut-offs allow for a fairly good prediction of inadequate total GWG from the second trimester on in underweight and normal weight women and a good prediction of excessive total GWG in overweight and obese women. This observation is useful for gynaecologists advising women in early or intermediate stages of pregnancy to achieve adequate total GWG. By applying the week-specific GWG cut-offs, women at risk of deviating from the IOM/NRC recommendations (30) can be identified early in pregnancy and allocated to weight modifying interventions. Those interventions should be initiated as early as possible during pregnancy to allow for sufficient time for the intervention to become effective. As mentioned in chapter 1.2.3, a number of effective approaches to achieve adequate GWG have been reported: among women gaining inadequately, a balanced protein-energy supplementation may be useful in achieving adequate GWG (49). Women gaining excessively may benefit from interventions that aim to increase physical activity (50,51), dietary interventions (52) or a combination of physical activity, nutritional counselling and supplementary weight monitoring (53).

Despite the risk of raising unjustified concerns about weight gain in mothers (97), routine weighing in pregnancy is an effective and relatively inexpensive measure to identify women at risk of deviating from the IOM/NRC recommendations (30) at the end of pregnancy. However, there is evidence that the IOM/NRC recommendations (30) are not sufficiently implemented in primary care. Moore Simas et al. (32) reviewed 477 medical records from clinics in Massachusetts and found that advice on GWG was documented for less than 15% of the study sample; advice on pre-pregnancy specific GWG recommendations was documented for less than 10%. There is evidence that woman provided with advice on GWG according to the IOM/NRC recommendations (30) in primary care, were more than five times more likely to have a concordant GWG goal, which, in turn, is a predictor for actual total GWG within the recommended ranges (98). A possible explanation for the insufficient implementation of the IOM/NRC recommendations (30) may be concerns about the sensitivity of the topic and insufficient training on weight counselling (99). However, most of the studies on the implementation of IOM/NRC recommendations (30) were conducted in the US. Systematic research on the implementation of the IOM/NRC recommendations (30) in Germany is missing. Recently published articles in German journals for further training of obstetricians and gynaecologists indicate a raising awareness of the topic (100,101). Further efforts should focus on systematic research on the current awareness of, and the barriers to implementation of IOM/NRC GWG recommendations (30) in primary care in Germany.

The results of this dissertation (Analysis 3) provide evidence that reversing from excessive GWG in the early or mid-pregnancy may result in a reduced risk of childhood overweight. This question has not been addressed yet by other studies investigating the effect of trimester-specific relative GWG. Therefore, more research on the question whether a reverse from excessive GWG before the third trimester decreases the risk of childhood overweight is required. However, the analysis of life course data can only provide indicators. The proof of the beneficial effect of weight modification towards adequate GWG according to IOM/NRC (30) could only come from well-designed RCTs. By randomly allocating pregnant women to an effective intervention, long-term effects of GWG modification on the development of childhood overweight could be investigated.

6 Conclusions and Recommendations

Gestational weight gain is associated childhood overweight. Excessive total GWG is associated with an increased risk of childhood overweight, in particular among normal weight and overweight mothers. A deviation from IOM/NRC recommendations (30) in either direction can be predicted from the second trimester on. A fairly good prediction inadequate total GWG based on second trimester GWG cut-off values was observed in underweight and normal weight woman; a good prediction of excessive total GWG based on second trimester GWG cut-off values was observed in overweight and obese women. The reverse from excessive GWG before the third trimester may reduce the risk of childhood overweight.

Further research could address the following topics:

- Meta-analysis of studies investigating the effect of total GWG, overall and stratified by maternal pre-pregnancy BMI, on childhood overweight. The analysis should include results from studies based on similar reference values for childhood overweight and the latest IOM/NRC recommendations (30).

- Replication of analysis 2 and 3 in a data set that includes trimester-specific data from early in the second trimester.

- Disentangle the effects of each excessive GWG pattern on childhood overweight and investigate potential dose effects regarding excessive GWG in the first and second or both trimesters.

- Randomised controlled trials on the long-term effects of successful GWG modification towards adequate GWG on childhood overweight: Random allocation of pregnant woman at risk of excessive total GWG to an effective intervention and examine the long-term benefits of GWG modification on the development of childhood overweight.

- Systematic research on the current awareness of IOM/NRC recommendations (30) and the barriers for its implementation in primary care in Germany.

The development of childhood overweight is multi-factorial and weight gain in pregnancy is only one potential determinant. Compared to hereditary or demographic risk factors, however, GWG can be monitored and modified with relatively small efforts. Besides other parameters for maternal and child health, GWG monitoring and counselling should be therefore included in routine medical check-ups during pregnancy. Since excessive total GWG, which is in turn associated with a higher risk of childhood overweight, was observed in a large proportion of pregnancies, preventive and interventive measures against excessive GWG may have significant impact on the population level and effectively contribute the reduction of childhood overweight.

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B Appendix

B.1 Questionnaire

Fragebogen „Beitrag pränataler (vorgeburtlicher) Einflussfaktoren an der Entstehung von kindlichem Übergewicht“

1. Angaben zur Mutter ***(Bitte dem Mutterpass entnehmen)***

Bitte geben Sie Ihr Alter bei Beginn der Schwangerschaft an: (in Jahren)

Wie schwer waren Sie vor Schwangerschaftsbeginn (Mutterpass Seite 5 oder 21)? kg

Wie groß sind Sie? cm

Bitte geben Sie die Anzahl Ihrer Schwangerschaften (Gravida) incl. dieser an:

Bitte geben Sie die Anzahl Ihrer ausgetragenen Schwangerschaften (Para) an:

Bitte geben Sie die Anzahl Ihrer Fehlgeburten nach der 12. Schwangerschaftswoche (SSW) an:

War diese Geburt eine Mehrlingsgeburt (z.B. Zwillinge)? ☐ Ja ☐ Nein

Lag bei Ihnen vor Eintritt dieser Schwangerschaft ein Diabetes mellitus vor? ☐ Ja ☐ Nein

Ist bei Ihnen während dieser Schwangerschaft ein Schwangerschafts-diabetes festgestellt worden (Diätpflicht und/oder Insulingabe)? ☐ Ja ☐ Nein

Bitte entnehmen Sie die folgenden Angaben dem Mutterpass Seite 7 oder 23:

Bitte geben Sie das Datum der ersten Vorsorgeuntersuchung an: Tag Monat Jahr

Bitte geben Sie die Schwangerschaftswoche dieser Vorsorgeuntersuchung an *(wenn vorhanden: „SSW ggf. Korr.“)*:

Wie schwer waren Sie bei dieser Vorsorgeuntersuchung? kg

Bitte geben Sie das Datum der Vorsorgeuntersuchung am Ende der 22.-26. SSW an: Tag Monat Jahr

Bitte geben Sie die Schwangerschaftswoche dieser Vorsorgeuntersuchung an *(wenn vorhanden „SSW ggf. Korr.“)*:

Wie schwer waren Sie bei dieser Vorsorgeuntersuchung? kg

Bitte geben Sie das Datum der Vorsorgeuntersuchung am Ende der 35.-37. SSW an: Tag Monat Jahr

Bitte geben Sie die Schwangerschaftswoche dieser Vorsorgeuntersuchung an *(wenn vorhanden „SSW ggf. Korr.“)*:

Wie schwer waren Sie bei dieser Vorsorgeuntersuchung? kg

Bitte entnehmen Sie die folgenden Angaben aus der letzten ausgefüllten Zeile des Gravidogramms (Mutterpass Seite 7 oder 23):

Bitte geben Sie das Datum der letzten Vorsorgeuntersuchung vor der Geburt an: ☐☐ ☐☐ ☐☐☐☐ (Tag / Monat / Jahr)

Bitte geben Sie die Schwangerschaftswoche dieser Vorsorgeuntersuchung an *(wenn vorhanden „SSW ggf. Korr."):* ☐☐

Wie schwer waren Sie bei dieser Vorsorgeuntersuchung? ☐☐☐,☐ kg

2. Angaben zum Kind *(Bitte dem Kinder-Untersuchungsheft (gelbes Heft) entnehmen)*

Ist Ihr Kind ein Junge oder Mädchen? ☐ Junge ☐ Mädchen

Nach welcher vollendeten Schwangerschaftswoche wurde Ihr Kind geboren (gelbes Heft, U1)? ☐☐

Bitte geben Sie das Datum der U1 an: ☐☐ ☐☐ ☐☐☐☐ (Tag / Monat / Jahr)

Bei der Geburt: Wie schwer war Ihr Kind? ☐☐☐☐ Gramm Wie groß war Ihr Kind? ☐☐ cm

Bitte geben Sie das Datum der U6-Früherkennungsuntersuchung an: ☐☐ ☐☐ ☐☐☐☐ (Tag / Monat / Jahr)

Gewicht bei der U6? ☐☐☐☐☐ Gramm Größe bei der U6? ☐☐☐ cm

Bitte geben Sie das Datum der U7-Früherkennungsuntersuchung an: ☐☐ ☐☐ ☐☐☐☐ (Tag / Monat / Jahr)

Gewicht bei der U7? ☐☐☐☐☐ Gramm Größe bei der U7? ☐☐☐ cm

Ernährung

Wie haben Sie Ihr Kind in den ersten 6 Lebensmonaten ernährt? Bitte antworten Sie für jeden Monat. Falls sich die Ernährung im Laufe eines Monats geändert hat, dann kreuzen Sie an, wie Sie das Kind in diesem Monat überwiegend ernährt haben.

MONAT nach der Geburt	1.	2.	3.	4.	5.	6.
voll gestillt (ohne Säuglingsmilch, aber mit Getränken wie z.B. Wasser, Tee)	☐	☐	☐	☐	☐	☐
teilweise gestillt (mit zusätzlicher Säuglingsmilch oder anderer Nahrung wie z.B. Brei, Gläschenkost)	☐	☐	☐	☐	☐	☐
Gar nicht gestillt	☐	☐	☐	☐	☐	☐

Freizeitverhalten

Wie häufig spielt Ihr Kind im Sommer im Freien?

☐ Fast jeden Tag ☐ Etwa 3-5 mal pro Woche ☐ Etwa 1-2 mal pro Woche ☐ Seltener ☐ Nie

Wie häufig spielt Ihr Kind im Winter im Freien?

☐ Fast jeden Tag ☐ Etwa 3-5 mal pro Woche ☐ Etwa 1-2 mal pro Woche ☐ Seltener ☐ Nie

Wie häufig treibt Ihr Kind Sport in einem Verein?

☐ Fast jeden Tag ☐ Etwa 3-5 mal pro Woche ☐ Etwa 1-2 mal pro Woche ☐ Seltener ☐ Nie

Wie häufig treibt Ihr Kind Sport außerhalb eines Vereins (z.B. Schwimmen, Radtour)?

☐ Fast jeden Tag ☐ Etwa 3-5 mal pro Woche ☐ Etwa 1-2 mal pro Woche ☐ Seltener ☐ Nie

Wie lange sieht Ihr Kind durchschnittlich pro Tag Fernsehsendungen oder Videofilme (Bitte kreuzen Sie an, was am ehesten zutrifft.)	an einem Wochentag?	an einem Samstag/Sonntag?
Gar nicht	☐	☐
Nicht täglich	☐	☐
Weniger als 30 Min. pro Tag	☐	☐
Ca. 30 Min. pro Tag	☐	☐
1-2 Std. pro Tag	☐	☐
3-4 Std. pro Tag	☐	☐
Mehr als 4 Std. pro Tag	☐	☐

Wie lange spielt Ihr Kind durchschnittlich pro Tag mit elektronischen Spielgeräten (Gameboy, Playstation, XBox, PC-Spiele, etc.) (Bitte kreuzen Sie an, was am ehesten zutrifft.)	an einem Wochentag?	an einem Samstag/Sonntag?
Gar nicht	☐	☐
Nicht täglich	☐	☐
Weniger als 30 Min. pro Tag	☐	☐
Ca. 30 Min. pro Tag	☐	☐
1-2 Std. pro Tag	☐	☐
3-4 Std. pro Tag	☐	☐
Mehr als 4 Std. pro Tag	☐	☐

3. Allgemeine Angaben

Was meinen Sie, ist Ihr Kind:

☐ viel zu dünn ☐ ein bisschen zu dünn ☐ genau richtig vom Gewicht ☐ ein bisschen zu dick ☐ viel zu dick

Rauchte die Mutter vor oder während der Schwangerschaft (jeweils mindestens 1 Zigarette täglich)?
Bitte kreuzen Sie an, wann die Mutter geraucht hat.
(Mehrfachantworten sind möglich)

☐ Vor Beginn der Schwangerschaft
☐ In den ersten 3 Monaten der Schwangerschaft
☐ Bis zum Ende der Schwangerschaft
☐ Nein, nie

Welchen Schul-/Hochschulabschluss haben Sie? (Nennen Sie bitte nur den höchsten Abschluss. Bitte für beide Elternteile angeben)

	Mutter	*Vater*
Hauptschulabschluss/Volksschulabschluss	☐	☐
Realschulabschluss (Mittlere Reife) oder Abschluss der Polytechnischen Oberschule (POS, 10. Klasse)	☐	☐
Fachhochschulreife (Abschluss einer Fachoberschule) oder Abitur (Gymnasium bzw. Erweiterte Oberschule)	☐	☐
Abschluss eines Studiums an einer Fachhochschule oder Universität	☐	☐
Anderer Schulabschluss	☐	☐
Schule beendet ohne Schulabschluss	☐	☐
(Noch) keinen Schulabschluss	☐	☐

Welche der folgenden Angaben zur Erwerbstätigkeit trifft auf Sie zu?
(Bitte für beide Elternteile angeben)

	Mutter	*Vater*
Nicht berufstätig (Hausfrau, Rentner, Student, usw.)	☐	☐
Arbeitslos	☐	☐
Vorübergehende Freistellung (z.B. Erziehungsurlaub)	☐	☐
Teilzeit oder stundenweise berufstätig	☐	☐
Voll berufstätig	☐	☐
Auszubildender (z.B. Lehrling)	☐	☐

Welche Muttersprache haben Sie?	*Mutter*	*Vater*
Deutsch	☐	☐
Türkisch	☐	☐
Serbokroatisch	☐	☐
Italienisch	☐	☐
Russisch	☐	☐
Andere	☐	☐
Wenn andere, *welche*:	______________	______________

4. Angaben aus der Schuleingangsuntersuchung (Wird vom Gesundheitsamt ausgefüllt)

Bitte geben Sie das Untersuchungsdatum an: [|] [|] [| | |] Tag Monat Jahr

Gewicht des Kindes bei Untersuchung: [| |],[ ] kg

Größe des Kindes bei Untersuchung: [| |],[ ] cm

Taillenumfang des Kindes bei Untersuchung: [| |],[ ] cm [| |],[ ] cm [| |],[ ] cm

Mittelgradig-schwere Ödeme (48) ☐ Gestationsdiabetes (50) ☐ Letzte Periode [|] [|] [| | |] Tag Monat Jahr

B.2 Overview of Most Recent Studies on Gestational Weight Gain and Childhood Overweight

Table 14: Overview of studies on gestational weight gain according to Institute of Medicine/ National Research Council and childhood overweight

Study:	Exposure measurement:	Outcome measurement:	Factors adjusted for:	Results:
Crozier et al., 2010 (45), Southampton Women's Survey (N= 948)	**Pre-pregnancy BMI:** height and weight measured at baseline (Median 1.1 ys before concenption). Regression adjustment to account for weight increases between baseline and conception. **GWG:** measured weight at 34 wk gestation - adjusted pre-pregnancy weight	**Child body composition at birth, age 4, age 6:** - fat mass - fat free mass	**GWG categorical:** **Model 1**: maternal smoking in pregnancy, maternal age, maternal height, parity, maternal educational attainment, breastfeeding duration **Model 2**: additionally adjusted for birth weight	**GWG categorical:** **Model 1**: Compared to children of mothers with adequate GWG, children of mothers with **excessive GWG had greater fat mass at birth (ß: 0.17, 95% CI: 0.02, 0.32; p= 0.03) at age 4 (ß: 0.17, 95% CI: 0.00, 0.35; p= 0.05) and at age 6 (ß: 0.30, 95% CI: 0.11, 0.49; p= 0.002)**. **Model 2**: After adjustment for birth weight, a significant association between **excessive GWG** compared to adequate GWG and child fat mass was found at **age 6 (ß: 0.26, 95% CI: 0.07, 0.45; p= 0.007)**.
			GWG continuous (per 5 kg GWG increase): **Model 3:** pre-pregnancy BMI, maternal smoking in pregnancy, maternal age, maternal height, parity, maternal educational attainment, breastfeeding duration **Model 4:** additionally adjusted for birth weight	**GWG continuous (per 5 kg GWG increase):** **Model 3**: **Greater GWG** was associated with **greater fat mass at birth (ß: 0.10, 95% CI: 0.04, 0.15; p= 0.0004) and age 6 (ß: 0.07, 95% CI: 0.00, 0.14; p= 0.05)**. At age 4 greater GWG was associated with greater fat-free mass (ß: 0.04, 95% CI: 0.00, 0.09; p= 0.04). **Model 4**: After adjustment for birth weight no significant associations were found between GWG and fat mass or fat-free mass at any measurement points.
Deierlein et al., 2010 (46), Pregnancy, Infection and Nutrition (PIN) study (N=363)	**Pre-pregnancy BMI:** self-reported pre-pregnancy weight and measured height **GWG:** last weight measurement before delivery - self-reported pre-pregnancy weight	**Child weight and length measurements at approximately 6 months:** - weight for age - length for age - weight-for-length z-scores	**Model 1:** gestational age, maternal height, maternal race/ethnicity, marital status, prenatal smoking, household income, education, pre-pregnancy BMI, pre-existing diabetes mellitus **Model 2:** additionally adjusted for birthweight z-score	**Model 1:** Compared to children born to mothers with adequate GWG, children with mothers with **excessive GWG had higher weight for age (ß: 0.39, 95% CI: 0.15, 0.62) and higher length for age (ß: 0.34, 95% CI: 0.12, 0.56)**. **Model 2:** After adjusting for birthweight z-score, children born to mothers with **excessive GWG had higher lenght for age (ß: 0.22, 95% CI: 0.004, 0.43)** compared to children with mothers who gained adequately.

Table 15: Overview of studies on gestational weight gain according to Institute of Medicine/ National Research Council and childhood overweight

Study:	Exposure measurment	Outcome measurement:	Factors adjusted for:	Results:
Fraser et al., 2010 (47), Avon Longitudinal Study of Parents and Children (ALSPAC) (N= 5,154)	**Pre-pregnancy BMI:** predicted pre-pregnancy weight, reported height **GWG:** last measurement before delivery - first measurement in pregnancy (both derived from obstetric notes)	**Child anthropometric data at age 9:** - weight - height - BMI - overweight (>= 90th percentile[1]) - obesity (>= 97 percentile[1])	**Model 1**: maternal age, child gender, child fat mass, maternal height, maternal height squared **Model 2**: additionally adjusted for pre-pregnancy weight, head of household social class, parity, maternal smoking in pregnancy, age at birth, mode of delivery	**Model 1**: Women with **inadequate GWG were less likely to have children with greater BMI (ß: -0.29, 95% CI: -0.47, -0.12)** than women with adequate GWG. Compared to adequate GWG, women with **excessive GWG were more likely to have children with greater BMI (ß: 0.78, 95% CI: 0.59, 0.97)**. **The risk of childhood overweight increased by 4% per 1 kg increase in pre-pregnancy weight (OR: 1.04, 95% CI: 1.03, 1.05).** **Model 2**: The effects attenuated slightly after adjustment for additional counfounders. Women who gained **inadequately were less likely (ß: -0.33, 95% CI: -0.50, -0.15), women who gained excessively were more likely (ß: 0.74, 95% CI: 0.55, 0.94) to have offspring with greater BMI**, compared to mothers with adequate GWG. Compared to adequate GWG, **inadequate GWG was a protective factor against childhood overweight (OR: 0.80, 95% CI: 0.67, 0.96)**. **Excessive GWG increased the risk of childhood overweight by more than 70% (OR: 1.73, 95% CI: 1.45, 2.05)**. **The risk of childhood overweight increased by 4% per 1 kg increase in pre-pregnancy weight (OR: 1.04, 95% CI: 1.03, 1.05).**
Margerison-Zilko et al., 2010 (48), National Longitudinal Survey of Youth 1979 (NLSY79) (N= 4,496)	**Pre-pregnancy BMI:** self-reported pre-pregnancy weight and height in the first survey after pregnancy [3)] **GWG:** self-reported weight at delivery - self-reported pre-pregnancy weight [3)]	**Child anthropometric data (age 2-20 ys.):** - weight - height - BMI - overweight (>= 85th percentile [2])	Maternal age at birth, maternal height, maternal race/ethnicity, poverty status, maternal educational attainment, martial status, parity, smoking during pregnancy, maternal pre-pregnancy BMI, year of birth, length of gestation	In the subgroup of **normal weight mothers, the risk of childhood overweight increased by 3% (OR: 1.03, 95% CI: 1.02, 1.04) per 1 kg GWG increase**. No significant associations were found in the other pre-pregnancy BMI strata. Compared to adequate GWG, **excessive GWG increased the risk of childhood overweight by 27% (OR: 1.27, 95% CI: 1.10, 1.48)**. No significant effect was found for inadequate GWG compared to adequate GWG.

[1] = International Obesity Task Force (Cole et al. 2000, [8])
[2] = Centers for Disease Control (2009) (92)
[3] = Adjusted by regression calibration

B.3 Lower and Upper Week-specific Gestational Weight Gain Cut-Off Values

Table 16: Lower and Upper Gestational weight gain cut-off values trimester 1

Maternal body mass index (BMI) category:	Gestational weight gain cut-off (kg):	Gestational week trimester 1:												
		1	2	3	4	5	6	7	8	9	10	11	12	13
Underweight (BMI < 18.5 kg/m²)	lower	0.08	0.15	0.23	0.31	0.38	0.46	0.54	0.62	0.69	0.77	0.85	0.92	1.00
	upper	0.23	0.46	0.69	0.92	1.15	1.38	1.62	1.85	2.08	2.31	2.54	2.77	3.00
Normal-weight (BMI 18.5 - 24.9 kg/m²)	lower	0.08	0.15	0.23	0.31	0.38	0.46	0.54	0.62	0.69	0.77	0.85	0.92	1.00
	upper	0.23	0.46	0.69	0.92	1.15	1.38	1.62	1.85	2.08	2.31	2.54	2.77	3.00
Overweight (BMI 25.5 - 29.9 kg/m²)	lower	0.08	0.15	0.23	0.31	0.38	0.46	0.54	0.62	0.69	0.77	0.85	0.92	1.00
	upper	0.23	0.46	0.69	0.92	1.15	1.38	1.62	1.85	2.08	2.31	2.54	2.77	3.00
Obesity (BMI >= 30 kg/m²)	lower	0.02	0.04	0.05	0.07	0.09	0.11	0.12	0.14	0.16	0.18	0.19	0.21	0.23
	upper	0.15	0.31	0.46	0.62	0.77	0.92	1.08	1.23	1.38	1.54	1.69	1.85	2.00

Table 17: Lower and Upper Gestational weight gain cut-off values trimester 2

Maternal body mass index (BMI) category:	Gestational weight gain cut-off (kg):	Gestational week trimester 2:												
		14	15	16	17	18	19	20	21	22	23	24	25	26
Underweight (BMI < 18.5 kg/m²)	lower	1.43	1.85	2.28	2.70	3.13	3.56	3.98	4.41	4.83	5.26	5.69	6.11	6.54
	upper	3.56	4.11	4.67	5.22	5.78	6.33	6.89	7.44	8.00	8.56	9.11	9.67	10.22
Normal-weight (BMI 18.5 - 24.9 kg/m²)	lower	1.39	1.78	2.17	1.56	2.94	3.33	1.00	4.11	4.50	4.89	5.28	5.67	6.06
	upper	3.48	3.96	4.44	4.93	5.41	5.89	6.37	6.85	7.33	7.81	8.30	8.78	9.26
Overweight (BMI 25.5 - 29.9 kg/m²)	lower	1.22	1.44	1.67	1.89	2.11	2.33	2.56	2.78	3.00	3.22	3.44	3.67	3.89
	upper	3.31	3.63	3.94	4.26	4.57	4.89	5.20	5.52	5.83	6.15	6.46	6.78	7.09
Obesity (BMI >= 30 kg/m²)	lower	0.41	0.58	0.76	0.94	1.11	1.29	1.47	1.64	1.82	2.00	2.17	2.35	2.53
	upper	2.26	2.52	2.78	3.04	3.30	3.56	3.81	4.07	4.33	4.59	4.85	5.11	5.37

Table 18: Lower and Upper Gestational weight gain cut-off values trimester 3

Maternal body mass index (BMI) category:	Gestational weight gain cut-off (kg):	Gestational week trimester 3:													
		27	28	29	30	31	32	33	34	35	36	37	38	39	40
Underweight (BMI < 18.5 kg/m²)	lower	6.96	7.39	7.81	8.24	8.67	9.09	9.52	9.94	10.37	10.80	11.22	11.65	12.07	12.50
	upper	10.78	11.33	11.89	12.44	13.00	13.56	14.11	14.67	15.22	15.78	16.33	16.89	17.44	18.00
Normal-weight (BMI 18.5 - 24.9 kg/m²)	lower	6.44	6.83	7.22	7.61	8.00	8.39	8.78	9.17	9.56	9.94	10.33	10.72	11.11	11.50
	upper	9.74	10.22	10.70	11.19	11.67	12.15	12.63	13.11	13.59	14.07	14.56	15.04	15.52	16.00
Overweight (BMI 25.5 - 29.9 kg/m²)	lower	4.11	4.33	4.56	4.78	5.00	5.22	5.44	5.67	5.89	6.11	6.33	6.56	6.78	7.00
	upper	7.41	7.72	8.04	8.35	8.67	8.98	9.30	9.61	9.93	10.24	10.56	10.87	11.19	11.50
Obesity (BMI >= 30 kg/m²)	lower	2.70	2.88	3.06	3.23	3.41	3.59	3.76	3.94	4.12	4.29	4.47	4.65	4.82	5.00
	upper	5.63	5.89	6.15	6.41	6.67	6.93	7.19	7.44	7.70	7.96	8.22	8.48	8.74	9.00

B.4 Regression Tables

Analysis 1: Overall

Table 19: Crude odds ratios and 95% confidence intervals for the association between gestational weight gain (GWG) in kg / inadequate or excessive GWG and childhood overweight (see Table 7)

	OR	95% CI lower	95% CI upper
(Intercept)	0.08	0.06	0.10
GWG (kg)	1.02	1.01	1.04
(Intercept)	0.08	0.07	0.10
GWG inadequate	1.20	0.92	1.57
GWG adequate	1.00		
GWG excessive	1.78	1.48	2.15

Abbreviations: CI = Confidence intervall;
GWG = Gestational weight gain; OR = Odds ratio

Table 20: Adjusted odds ratios and 95% confidence intervals for the association between gestational weight gain (kg) and childhood overweight (see Table 7)

	OR	95% CI lower	95% CI upper
(Intercept)	0.00	0.00	0.00
GWG (kg)	1.04	1.02	1.05
Birth weight (g)	1.27	1.06	1.53
Maternal age (years)	0.99	0.97	1.00
Smoking in pregnancy (no)	1.00		
Smoking in pregnancy (yes)	1.39	1.09	1.74
Maternal BMI	1.13	1.11	1.15
Breastfeeding (>= 1 month)	1.00		
Breastfeeding (< 1 month)	1.23	1.03	1.46
TV (<= 1 hour daily)	1.00		
TV (> 1 hour daily)	1.38	1.16	1.63
Physical activity (high)	1.00		
Physical activity (medium)	1.17	0.93	1.45
Physical activity (low)	1.30	0.92	1.81
SES (high)	1.00		
SES (medium)	1.12	0.90	1.39
SES (low)	1.24	0.98	1.57

Abbreviations: BMI = Body mass index; CI = Confidence intervall; GWG = Gestational weight gain; OR = Odds ratio; SES = Socioeconomic status

Table 21: Adjusted odds ratios and 95% confidence intervals for the association between inadequate or excessive gestational weight gain and childhood overweight (see Table 7)

	OR	95% CI lower	95% CI upper
(Intercept)	0.01	0.01	0.03
GWG inadequate	1.20	0.91	1.57
GWG adequate	1.00		
GWG excessive	1.57	1.30	1.91
Birth weight (g)	1.63	1.36	1.95
Maternal age (years)	0.99	0.98	1.01
Smoking in pregnancy (no)	1.00		
Smoking in pregnancy (yes)	1.43	1.13	1.78
Breastfeeding (>= 1 month)	1.00		
Breastfeeding (< 1 month)	1.38	1.16	1.64
TV (<= 1 hour daily)	1.00		
TV (> 1 hour daily)	1.43	1.22	1.69
Physical activity (high)	1.00		
Physical activity (medium)	1.19	0.96	1.47
Physical activity (low)	1.24	0.88	1.72
SES (high)	1.00		
SES (medium)	1.24	1.00	1.54
SES (low)	1.54	1.22	1.93

Abbreviations: CI = Confidence intervall;
GWG = Gestational weight gain; OR = Odds ratio;
SES = Socioeconomic status

Analysis 1: Stratified by Maternal Pre-Pregnancy Body Mass Index

Table 22: Crude odds ratios and 95% confidence intervals for the association between gestational weight gain (GWG) in kg / inadequate or excessive GWG and childhood overweight stratified by maternal pre-pregnancy body mass index (see Table 8)

		OR	95% CI lower	95% CI upper
Underweight mothers	(Intercept)	0.03	0.00	0.18
	GWG (kg)	1.02	0.90	1.14
Normal-weight mothers	(Intercept)	0.03	0.02	0.05
	GWG (kg)	1.06	1.04	1.08
Overweight mothers	(Intercept)	0.14	0.09	0.21
	GWG (kg)	1.02	1.00	1.05
Obese mothers	(Intercept)	0.22	0.15	0.33
	GWG (kg)	1.04	1.01	1.07
Underweight mothers	(Intercept)	0.03	0.01	0.08
	GWG inadequate	1.38	0.28	5.80
	GWG adequate	1.00		
	GWG excessive	1.10	0.27	4.27
Normal-weight mothers	(Intercept)	0.07	0.06	0.08
	GWG inadequate	1.04	0.73	1.46
	GWG adequate	1.00		
	GWG excessive	1.43	1.13	1.83
Overweight mothers	(Intercept)	0.12	0.08	0.18
	GWG inadequate	2.43	1.25	4.69
	GWG adequate	1.00		
	GWG excessive	1.75	1.14	2.80
Obese mothers	(Intercept)	0.33	0.21	0.51
	GWG inadequate	0.69	0.34	1.40
	GWG adequate	1.00		
	GWG excessive	1.21	0.73	2.04

Abbreviations: CI = Confidence intervall; GWG = Gestational weight gain; OR = Odds ratio

Table 23: Adjusted odds ratios and 95% confidence intervals for the association between gestational weight gain (kg) and childhood overweight stratified by maternal pre-pregnancy body mass index (see Table 8)

	Underweight mothers			Normal-weight mothers			Overweight mothers			Obese mothers		
	OR	95% CI lower	95% CI upper	OR	95% CI lower	95% CI upper	OR	95% CI lower	95% CI upper	OR	95% CI lower	95% CI upper
(Intercept)	0.04	0.00	15.45	0.01	0.00	0.05	0.05	0.01	0.24	0.15	0.02	1.23
GWG (kg)	1.03	0.90	1.16	1.04	1.02	1.07	1.01	0.98	1.04	1.04	1.01	1.07
Birth weight (g)	1.52	0.37	6.10	1.32	1.01	1.71	1.59	1.13	2.25	0.91	0.58	1.41
Maternal age (years)	0.94	0.81	1.06	0.99	0.97	1.01	0.98	0.95	1.01	1.00	0.96	1.04
Smoking in pregnancy (no)	1.00			1.00			1.00			1.00		
Smoking in pregnancy (yes)	NA	NA	NA	1.48	1.08	2.01	1.63	1.03	2.54	1.10	0.63	1.90
Breastfeeding (>= 1 month)	1.00			1.00			1.00			1.00		
Breastfeeding (< 1 month)	0.66	0.14	2.46	1.28	1.01	1.63	1.39	1.00	1.94	1.01	0.66	1.55
TV (<= 1 hour daily)	1.00			1.00			1.00			1.00		
TV (> 1 hour daily)	0.27	0.04	1.15	1.54	1.23	1.93	1.06	0.76	1.46	1.94	1.28	2.94
Physical activity (high)	1.00			1.00			1.00			1.00		
Physical activity (medium)	NA	NA	NA	1.33	0.98	1.77	1.06	0.68	1.60	0.98	0.56	1.66
Physical activity (low)	NA	NA	NA	1.74	1.14	2.58	0.84	0.34	1.83	0.97	0.38	2.28
SES (high)	1.00			1.00			1.00			1.00		
SES (medium)	0.28	0.01	2.38	1.15	0.87	1.52	1.03	0.68	1.58	1.34	0.66	2.88
SES (low)	2.60	0.58	14.31	1.18	0.86	1.61	1.10	0.71	1.72	1.85	0.94	3.90

NA= not available, cell not occupied

Abbreviations: CI = Confidence intervall; GWG = Gestational weight gain; OR = Odds ratio; SES = Socioeconomic status

Table 24: Adjusted odds ratios and 95% confidence intervals for the association between inadequate or excessive gestational weight gain and childhood overweight stratified by maternal pre-pregnancy body mass index (see Table 8)

	Underweight mothers			Normal-weight mothers			Overweight mothers			Obese mothers		
	OR	95% CI lower	95% CI upper	OR	95% CI lower	95% CI upper	OR	95% CI lower	95% CI upper	OR	95% CI lower	95% CI upper
(Intercept)	0.03	0.00	13.43	0.02	0.01	0.06	0.03	0.01	0.17	0.18	0.02	1.54
GWG inadequate	1.74	0.30	8.97	1.02	0.71	1.43	2.52	1.28	4.91	0.63	0.30	1.30
GWG adequate	1.00			1.00			1.00			1.00		
GWG excessive	1.50	0.34	6.39	1.29	1.01	1.66	1.64	1.06	2.63	1.17	0.70	2.01
Birth weight (g)	1.87	0.46	7.81	1.44	1.11	1.85	1.67	1.19	2.36	0.98	0.63	1.52
Maternal age (years)	0.94	0.82	1.06	0.98	0.96	1.01	0.98	0.95	1.01	1.00	0.96	1.04
Smoking in pregnancy (no)	1.00			1.00			1.00			1.00		
Smoking in pregnancy (yes)	NA	NA	NA	1.55	1.12	2.10	1.64	1.03	2.56	1.16	0.66	1.99
Breastfeeding (>= 1 month)	1.00			1.00			1.00			1.00		
Breastfeeding (< 1 month)	0.74	0.15	2.84	1.30	1.02	1.65	1.41	1.01	1.96	1.03	0.67	1.57
TV (<= 1 hour daily)	1.00			1.00			1.00			1.00		
TV (> 1 hour daily)	0.28	0.04	1.21	1.54	1.23	1.93	1.03	0.74	1.43	1.95	1.29	2.96
Physical activity (high)	1.00			1.00			1.00			1.00		
Physical activity (medium)	NA	NA	NA	1.32	0.97	1.77	1.06	0.68	1.60	0.97	0.56	1.64
Physical activity (low)	NA	NA	NA	1.73	1.14	2.57	0.83	0.33	1.81	0.89	0.35	2.07
SES (high)	1.00			1.00			1.00			1.00		
SES (medium)	0.30	0.01	2.53	1.15	0.87	1.53	1.01	0.66	1.54	1.43	0.71	3.07
SES (low)	2.64	0.58	14.84	1.19	0.87	1.62	1.07	0.69	1.68	1.94	0.98	4.09

NA= not available, cell not occupied

Abbreviations: CI = Confidence intervall; GWG = Gestational weight gain; OR = Odds ratio; SES = Socioeconomic status

Analysis 3:

Table 25: Crude odds ratios and 95% confidence intervals for the association between excessive gestational weight gain patterns compared to reference and childhood overweight (see Table 13)

	OR	95% CI lower	95% CI upper
(Intercept)	0.09	0.07	0.10
No excessive GWG in any trimester (reference category)	1.00		
Excessive GWG in 1st or 2nd trimester only	1.00	0.73	1.36
Excessive GWG in 3rd and any previous trimester	1.64	1.36	1.97
Excessive GWG in the 3rd trimester only	1.55	1.18	2.02

Abbreviations: CI = Confidence intervall;
GWG = Gestational weight gain; OR = Odds ratio;
SES = Socioeconomic status

Table 26: Adjusted odds ratios and 95% confidence intervals for the association between excessive gestational weight gain patterns compared to reference and childhood overweight (see Table 13)

	Model 1			Model 2		
	OR	95% CI lower	95% CI upper	OR	95% CI lower	95% CI upper
(Intercept)	0.01	0.01	0.03	0.01	0.00	0.02
No excessive GWG in any trimester	1.00			1.00		
Excessive GWG in 1st or 2nd trimester only	1.00	0.72	1.36	0.99	0.71	1.34
Excessive GWG in 3rd and any previous trimesters	1.43	1.18	1.73	1.42	1.17	1.72
Excessive GWG in the 3rd trimester only	1.40	1.06	1.83	1.39	1.06	1.82
Birth weight (g)	1.00	1.00	1.00	1.00	1.00	1.00
Maternal age (years)	0.99	0.97	1.01	0.99	0.98	1.01
SES (high)	1.00			1.00		
SES (medium)	1.45	1.17	1.82	1.41	1.13	1.76
SES (low)	1.94	1.55	2.44	1.78	1.42	2.26
Smoking in pregnacy (no)	1.00			1.00		
Smoking in pregnacy (yes)	1.65	1.31	2.08	1.52	1.20	1.92
Breastfeeding (>= 1 month)	--	--	--	1.00		
Breastfeeding (< 1 month)	--	--	--	1.40	1.17	1.66
Physical activity (high)	--	--	--	1.00		
Physical activity (medium)	--	--	--	1.17	0.93	1.47
Physical activity (low)	--	--	--	1.42	1.00	1.97

Abbreviations: CI = Confidence intervall; GWG = Gestational weight gain;
OR = Odds ratio; SES = Socioeconomic status

C Orginalitätserklärung

Ich erkläre, dass ich diese Arbeit selbstständig verfasst, nicht anderweitig für Prüfungszwecke vorgelegt, keine anderen als die angegebenen Quellen und Hilfsmittel verwendet, sowie wörtliche und sinngemäße Zitate gekennzeichnet habe

München, 03.Oktober 2012

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Ort, Datum	Andrea Chmitorz