Relationship between the rate of gestational weight gain and overweight in offspring at the age of 3 years

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Abstract

Objective: To assess the relationship between maternal weight gain during pregnancy and overweight including obesity in 3-year-old offspring.

Methods: The present study comprised 3916 children born between 1997-2004 in Pirkanmaa, southern Finland, with increased HLA-conferred susceptibility to type 1 diabetes. Information on both maternal anthropometries at first and last antenatal visit and BMI (body mass index) in the offspring at 3 years of age was available for 2143 mother-singleton child pairs. Rate of gestational weight gain was calculated as [(weight at last – weight at first antenatal visit) /number of weeks between the visits] and divided into quarters. Childhood overweight (obesity included) was defined according to IOTF (International Obesity Task Force) criteria for BMI. Logistic regression was used to study the relationship of rate of gestational weight gain and potential confounders to child overweight.

Results: Prevalence of overweight was higher in girls (14.6%) than in boys (7.8%), p= <0.001. Risk of child overweight was increased for both the highest [unadjusted OR 2.11 (95% CI 1.50-2.98)] and the lowest [unadjusted OR 1.47 (95% CI 1.01-2.15)] quarter of rate of gestational weight gain, compared to the middle two quarters. After adjustment for maternal BMI, level of education, smoking during pregnancy and gestational diabetes; sex, birth weight and gestational age of the child; duration of exclusive breast feeding; location of residence and paternal diabetes, the risk was statistically significantly increased in the lowest quarter [OR 1.73 (1.17-2.55)] of gestational weight gain. We did not observe any effect modification of the association by maternal BMI (interaction p=0.22).

Conclusion: Compared to the average rate of gestational weight gain, the lowest rate of weight gain placed the offspring at increased risk of overweight at 3 years of age.
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### List of Abbreviation

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<th>Description</th>
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<tr>
<td>BMI</td>
<td>Body mass index</td>
</tr>
<tr>
<td>CDC</td>
<td>Center for Disease Control</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence interval</td>
</tr>
<tr>
<td>DEXA</td>
<td>Dual-energy x-ray absorptiometry</td>
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<tr>
<td>DIPP</td>
<td>Diabetes Prediction and Prevention Project</td>
</tr>
<tr>
<td>HLA</td>
<td>Human leucocyte antigen</td>
</tr>
<tr>
<td>IOM</td>
<td>Institute of Medicine</td>
</tr>
<tr>
<td>IOTF</td>
<td>International Obesity Task Force</td>
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<tr>
<td>kg</td>
<td>kilogram</td>
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<td>OR</td>
<td>Odds Ratio</td>
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1. INTRODUCTION

Overweight and obesity among children has increased worldwide. For instance, rising trends in child overweight/obesity were observed in 12 year old Finnish children between 1986 and 2006. The rise was 1.8 fold in boys and 1.5 fold in girls with more prevalence in rural areas (Vuorela et al., 2009). American children and adolescents also showed increasing trends in overweight and obesity. The increase was from 13.8% in boys and 14% in girls to 16% and 18.2% in 1992-2000 and 2000-2004 respectively (Ogden et al., 2006). Taking into consideration the increasing trends in child overweight and obesity, a further rise is expected in the future. The predictable rise is from 43 million obese children in 2010 to 60 million in 2020 (de Onis et al., 2010).

Overweight and obesity can endanger the health of a child. The likelihood of obese children to become obese adults and suffer the consequences is more than normal weight children (Serdula et al., 1993). These consequences are evident in the form of chronic illness, such as type 2 diabetes and cardiovascular diseases. Obese children are at risk of developing adverse health outcomes in childhood and are prone to carry the risk with them to their adulthood (Young et al., 2010; Freedman et al., 1998). Therefore it is vital to investigate the risk factors for overweight/obesity early in life.

Risk factors for overweight and obesity are multifarious. They are the product of a complex interaction of antenatal and postnatal environments (Oken et al., 2003). The antenatal period is a critical period in the development of fetal health in vivo and is a forerunner of potential life events. Regarding intrauterine life, both maternal undernutrition and overnutrition during pregnancy are important predictors of child obesity (Dietz, 1994). Research (Sebire et al., 2001) suggests that increased gestational weight gain is a predictor of short-and longer-term maternal and child health outcomes. These outcomes include gestational diabetes mellitus, postpartum hemorrhage, urinary and genital tract infections, pre-eclampsia, caesarian section, intrauterine death and high birth weight babies. On the other hand decreased weight gain during pregnancy (undernutrition) is associated with low birth weight of the baby, which is related to chronic diseases and obesity later in life (Barker, 2004).

Further research has been done to discover the effect of gestational weight gain on the weight of the children and adolescents. However, studies investigating the association between gestational weight
gain and child overweight are limited. In addition, these studies have drawn different conclusions. Most of them provide positive results for the association, showing that weight gain during pregnancy does affect weight of the offspring (Moreira et al., 2007; Oken et al., 2007; Olson et al., 2008; Wrotnick et al., 2008; Kleiser et al., 2009; Kries et al., 2010). Others (Whitaker et al., 2004; Gale et al., 2007) prove no association, showing that gestational weight gain has no effect on the weight of the offspring, while still others have given controversial results (Crozier et al., 2010).

Among studies examining the association, a few shortcomings have been noticed; some have not taken the relationship between gestational weight gain and child overweight as their primary focus (Oken et al., 2009; Kleiser et al., 2009) whereas others have given their results for a relatively small sample (Olson et al., 2008).

Various studies have examined the effect of maternal BMI (body mass index) on the association between gestational weight gain and child overweight. The results among studies vary. Some studies have shown that the association was affected by maternal BMI (Wrotniak et al., 2008; Olson et al., 2008) while others have not found any effect modification of the association by maternal BMI (Oken et al., 2007 and 2008; Andersen et al., 2010; Croizer et al., 2010). The inconsistent results of the previous research merits further analysis of the relationship of gestational weight gain with child overweight and maternal BMI.

The aim of the present study is to investigate the effect of weight gain in pregnancy on offspring’s weight when the child is 3 years old. The study included data from the Diabetes Prediction and Prevention Project (DIPP) and consisted of 2143 mother-singleton child pairs. Child overweight and obesity was defined according to IOTF (International Obesity Task Force ) criteria for BMI and maternal weight gain during pregnancy was calculated as rate of gestational weight gain and divided into quarters. None of the previous studies have taken categorized rate of gestational weight gain for discovering the association for children overweight at 3 years. Nor have they discovered the association for rate of gestational weight gain and child overweight for such a large sample.

Our study is targeted to study the relationship between maternal pregnancy weight gain and offspring overweight after adjusting for potential confounding factors and to identify possible interaction of maternal BMI for the association. The results provided by our study would help to further understand the relationship.
2. LITERATURE REVIEW

A thorough search was made for the literature review through Ovid Medline, Pubmed and Google scholar. University of Tampere online search facilities were utilized for electronic collection of journals. National academic press website was sourced for the relevant pregnancy weight gain guidelines. For further search, references of the relevant studies were accessed. Both reviews and empirical studies were included. Besides main key words such as childhood obesity/overweight and pregnancy weight gain, other key words used were adolescent obesity/overweight, trends, factors and consequences of weight gain. Search was only restricted to articles in English. Abstracts of only those articles were used which were comprehensive enough to understand the study and could not be accessed through the library portal. However the study includes very few abstracts and most of the articles included are full text articles. Search continued till November 2011.

2.1. Assessment of overweight and obesity

Body fatness is assessed through various techniques, a few of which are defined in this thesis.

Body fat is either measured directly or is estimated as relative fatness. Direct measures include bioelectrical impedance analysis (BIA), magnetic resonance imaging (MRI), computerized tomography (CT), under water weighing (hydro-densitometry), dual-energy X-ray absorptiometry (DEXA) and air-displacement plethysmography. Anthropometric measures for relative fatness include BMI, weight and weight-for-height, skin fold thickness and waist circumference. (Lobstein T et al., 2004)

2.1.1. Direct methods for assessing body composition

Bioelectrical impedance analysis

It uses experimentally derived equation for the relation between the volume of the conductor (the body), the length of the conductor (height) and impedance to electric flow (Lobstein et al., 2004). This method estimates fat mass of the body and is based on the principle that electric conduction is
greater in fat free mass (water and conducting electrolytes in the body) than in fat mass (Lukaski et al., 1985).

**Dual-Energy X-ray Absorptiometry (DEXA)**

It is based on the principle that two x-rays beams when pass through the body achieve a certain degree of attenuation, which depend on its passage through bone and soft tissue. The attenuation through the bone tissue is constant, whereas it varies linearly with the fatty fraction of the soft tissue. A calibrated equation is then used to estimates the fat percentage of the soft tissue. (Svendsen et al., 1992)

**MRI and computerize tomography**

These procedures use x-rays for providing images that show fatty tissue in the body. (Lobstein et al., 2004)

2.1.2. Indirect methods for assessing body composition

**Skin fold thickness**

Skin fold thickness comprises measurements at different sites in the body. For instance, triceps skin-fold is measured between the olecranon and acromion process of the arm. It is measured by grabbing the skin and subcutaneous tissue and then applying skin-fold caliper to it. Fat mass is estimated and measurements are then compared to the percentile curves (5<sup>th</sup>, 10<sup>th</sup>, 25<sup>th</sup>, 50<sup>th</sup>, 75<sup>th</sup>, 90<sup>th</sup>, 95<sup>th</sup>) of the reference data. (Owen, 1982)

**Waist circumference**

It consists of a measurement taken at the midpoint between iliac crest and 10<sup>th</sup> rib with an anthropometric tape. These measurements are then applied to the age and sex specific percentile curves for the 5<sup>th</sup>, 10<sup>th</sup>, 25<sup>th</sup>, 50<sup>th</sup>, 75<sup>th</sup>, 90<sup>th</sup> and 95<sup>th</sup> percentile. (McCarthy et al., 2001)
**Body mass index (BMI)**

There are various methods for defining overweight and obesity based on BMI. Frequently used criteria are BMI percentiles, BMI for age z-score and BMI cut-off points.

**BMI for percentiles**

Depending on the reference population, cut-off for overweight and obesity varies among studies. Widely used CDC growth charts define overweight children as those with BMI above 95\textsuperscript{th} percentile and ‘at risk of overweight’ as those with BMI $\geq$85\textsuperscript{th} and $< 95\textsuperscript{th}$ percentile for age specific reference population (Kuczmarski RJ et al., 200). In one of the studies obesity in American children is defined as BMI $\geq$ 85\textsuperscript{th} percentile (Whitaker et al., 19997) and others define overweight in adolescents as BMI $\geq$ 95\textsuperscript{th} percentile of reference population (Himes and Dietz, 1994).

**BMI for age z-score**

Overweight and obesity can be reported as BMI for age z-scores when they are compared to reference data set. A score of +1.00 equals approximately to the value of 84\textsuperscript{th} centile, a z score of 0 equals 50\textsuperscript{th} centile and a z score of 2 refers to approximately 98\textsuperscript{th} centile. (Lobstein et al., 2004)

**BMI for adult cut-off points**

Another frequently used criterion for defining overweight and obesity is the IOTF BMI limits. It provides a series of age and gender specific BMI cut-offs that are equivalent to widely used adult BMI cut-offs for overweight (25kg/m\textsuperscript{2}) and obesity (30kg/m\textsuperscript{2}). (Cole et al., 2000)

**2.2. Worldwide trends in children and adolescents overweight and obesity**

Prevalence of child obesity or overweight has been increasing worldwide. From 1970s to 1990s it has almost doubled or tripled in countries such as Japan, United States, UK, Spain, Greece, Germany, Canada and Brazil (Wang and Lobstein, 2005). Prevalence of overweight increased from
0.5 to 1 percentage points per annum in 1980s and 1990s respectively whereas annual percentage points for obesity rose from below 0.1 in 1980 to 0.3 in 1990s. Among 71 million children in the European region in 2006, approximately 22 million were reported to be overweight or obese. (Leach and Lobstein, 2006).

In addition to a rise in the worldwide prevalence of overweight and obesity among children, studies from individual countries have also shown an increase. Increasing trend in obesity and overweight among American children and adolescent from 1992-2000 to 2003-04 has been reported. The increase was from 13.8% in boys and 14% in girls to 16% and 18.2% in 1992-2000 and 2003-04 respectively (Ogden et al., 2006). Tends in overweight (including obesity) have also been analyzed in Danish children by Pearson et al. (2000). An increase for adolescent overweight was reported between 2002-2007. The increase was from 22.7% to 25.4% for girls and from 15.8% to 18.9% for boys. Studies regarding Chinese children and adolescents between 7 and 18 years of age reported increasing trends in overweight/obesity. This prevalence grew from 14% and 7.4% in 1985 to 34.2% and 30.3% in 2005 in boys and girls respectively (Ji and Cheng, 2009).

Examining prevalence of obesity between 1995 and 2004 in a European country, such as England, showed slight instability. Obesity increased from 3.1% among boys and 5.2% among girls to 6.9% in boys and 7.4% in girls from 1995 to 2004 respectively. It showed a downward projection in 2006 to 6.3% in boys and 6.1% in girls. However, trends rose again to 6.4% in boys and 7.4% in girls in 2007 (Stamatakis et al., 2010).

In another European study of 64147 Finnish adolescents of age 12-18 years, a steady increase in the prevalence of overweight and obesity was observed in late 1990s. The study examined trends over a period of 22 years and found a rise in obesity from 1.1% for boys and 0.4% for girls to 2.7% for boys and 1.4% for girls between 1977 and 1999 respectively (Kautiainen et al., 2001). Recent trends in Finland show some fluctuation for the prevalence of overweight/obesity in 5 and 12 year old children. Increasing trends were noticed among 12 year old children between 1986 and 2006. The increase in overweight was 1.8 fold in boys and 1.5 in girls with more prevalence in rural areas. However, increasing trends between 1986 and 2006 were not significant among 5-year old Finnish children (Vuorela et al., 2009).

Upward projection in overweight/obesity is not evident in all the countries. For instance, trends in overweight and obesity among Swedish adolescents found stability between 2001 and 2007
Furthermore, decreasing prevalence of overweight/obesity have been reported among of Australian children (under 5 years old) between 1999 and 2007. The decrease was from 18.5% to 15.4% among 3.5 years old children and from 13.5% to 12.4% among 2 years old children in 1999 and 2007 respectively (Nicholas et al., 2011).

Studies from underdeveloped countries show increasing trends in children and adolescents overweight and obesity. A Vietnamese study reported increasing obesity trends among pre-school children in urban areas between 2002-2005. This 3 year trend showed a rise in the prevalence of overweight/obesity from 21.4% to 36.8% (Dieu et al., 2008). Trends from South Africa show an increase in children’s overweight and obesity in ten year period (1994-2004). The increase was from 1.2% to 13.0% in overweight and 0.2% to 3.3% in obesity (Armstrong et al., 2011). Prevalence of obesity also increased in Indian children of 14-17 years of age. The prevalence rose from 9.8% in 2006 to 11.7% in 2009 (Gupta et al., 2011).

Taking into consideration the increasing trends in obesity and overweight among children and adolescents, a further rise is expected in the future. The expected rise is from 43 million children in 2010 to 60 million in 2020 (de Onis et al., 2010).

2.3. Consequences of children and adults overweight and obesity

2.3.1. Physical consequences

Consequences of obesity are obvious both in adults and children. Child obesity is chained to adult obesity. Children who are overweight at 2, 8 or 11 years are more at risk of developing adult obesity than normal weight children of the same age (Magarey et al., 2002). Research shows that 32.2% of obese boys and 41.0% of obese girls grow as obese adults (Kotani et al., 1997). The likelihood of these obese children to become obese adults and suffer the consequences is more than normal weight children (Serdula et al., 1993; Charney et al., 1976).

Obesity is responsible for causing chronic illnesses, such as cardiovascular diseases and diabetes. Overweight children are 2.5 times more at risk of increase in plasma cholesterol levels (Freedman et
al., 1998). Children who are overweight and have high waist circumference have high probability of antherogenic lipoprotein, high systolic and mean arterial pressure (Craig et al., 2008). In a Chinese study of 7.5-13-year-old children, risk factors for cardiovascular diseases, for instance increased serum triglycerides, increased low density lipoproteins and decreased high density lipoprotein were positively associated with overweight and obesity (Zhang et al., 2008). In another study of 2-19 year old Brazilian children obesity was directly linked to dyslipidemia and hypertension (Periera et al., 2008).

Recently reported problem of type 2 diabetes in obese children is demanding the attention of public health personnel for controlling obesity in childhood (Ehtisham et al., 2000; Drake et al., 2002). Obese children and adults represent a high proportion of population with impaired glucose tolerance (Sinha et al., 2002). Risk of type 2 diabetes is higher in those individuals who were obese at childhood and grow as obese adults (Yeung et al., 2010). Obese adults with history of obesity at childhood have a greater risk of developing metabolic syndrome than obese adults with no history of childhood obesity (Vanhala et al., 1998, 1999).

In addition to the chronic diseases, obesity is positively associated with respiratory and neurological illnesses and mortality. Excessively obese children with obstructive sleep apnea are prone to neurocognitive deficits such as memory and learning disabilities (Susan et al., 1995). Obesity in children is positively associated with asthma (Figueroa-Muñoz et al., 2001). Furthermore, the risk of mortality from cardiovascular disease and cancer is high with greater BMI (Calle et al., 1999).

2.3.2. Psychosocial and economic consequences

In addition to the unfavourable health outcomes, obesity is linked to psychosocial and economic problems. The economic burden from obesity has grown 3-fold in America. It was $35 million during 1979-81 and rose to $127 million during 1997-99 (Wang and Dietz, 2002). Compared to the non-overweight women, overweight women have less qualification, lower job status, are poorer and less likely to get married. When compared to the normal weight children, overweight children are a greater victim of social marginalization (Struss and Pollack, 2003). In a study of 9-12 year old children, obese children reported lower self-esteem and higher behaviour problems (Braet et al., 1996).
2.4. Determinants of children and adolescents overweight and obesity

2.4.1. Familial, life style and environmental factors

Determinants of obesity are broad spectrum, presenting either at individual or at a wider environmental level. These determinants include consumption of energy dense food and sweetened drinks, living a sedentary life, the insecure development processes of build environment (Maziak et al., 2008) and finally familial predisposition (Lake et al., 1997; Maffeis et al., 1998).

Sedentary life style is a known factor for causing obesity. Dietz et al. (1985) reports positive relationship for obesity among children and adolescents with time spent in front of TV. In a Finnish study of adolescents aged 14-18 years, television watching has been positively associated with overweight in girls and 16 year old boys (Kautiainen et al., 2005). After following non-overweight 8-12 years old girls for 4 years, Must et al. (2006) found inverse and direct relationship of body fat percentage with activity and inactivity respectively.

Parental overweight has been proved to be responsible for causing obesity in children and adolescents. According to Lake et al. (1997) and Maffeis et al. (1998) children whose parents were obese had a greater risk of becoming obese children and later obese adults. Maternal pre-pregnancy BMI is associated with child obesity (Lawlor et al., 2007). Negal et al. (2009) examined a sample of 6-9 year old children and found that obesity was positively related to parental obesity, watching television, consuming sweetened drinks, low level of parental education, smoking during pregnancy and skipping a breakfast.

Prolonged breast feeding is proved to provide protection against overweight and obesity in children. An inverse association between overweight and prolonged duration of breast feeding (3 months or less versus 7 months) at 9-14 years of age is detected by Gillman et al.(2001). Other studies have also emphasized prolonged duration of breast feeding for better health outcomes (von Kries et al.,1993; Kalies et al., 2005).

Regarding sweetened drinks Ludwig et al. (2001) reported risk of obesity in 11.7 years old children consuming sugar sweetened drinks.
### 2.4.2. Intrauterine factors

Besides lifestyle and environmental factors, intrauterine setting plays a crucial role for detecting future risk of obesity. Antenatal period is a critical period in the development of child health in vivo and is a forerunner of potential life events (Dietz, 1994). Therefore, relationship between the perinatal factors and later health outcomes is being studied. For instance, smoking during pregnancy and child obesity has been examined and positive association is indicated in the studies (Tosche et al., 2002; von Kris et al., 2002).

Maternal obesity during pregnancy and gestational weight gain is being analysed for maternal and child health outcomes. Maternal obesity during pregnancy has been found to confer threat to the mother and the baby. These threats include gestational diabetes mellitus, postpartum haemorrhage, urinary and genital tract infections, pre-eclampsia, caesarean section, intrauterine death and high birth weight babies (Sebire et al., 2001). In addition to obesity of the mother during pregnancy, gestational weight gain has been related to both neonatal (Fraser et al., 2010) and child obesity (Olson et al., 2008).

### 2.5. Gestational weight gain and child overweight and obesity

Association of gestational weight gain with child obesity is the primary point of interest of the present study. Previous research speculates either none or positive or mixed results for the association. Most of the studies are based on either the old or new guidelines by IOM, mentioned in the table 1 and 2. Summary of the studies on the association between gestational weight gain and child obesity is given in table 3.

#### Table 1

**Old recommendation by Institute of Medicine for gestational weight gain according to pre-pregnancy BMI (1990).**

<table>
<thead>
<tr>
<th>Pre-pregnancy BMI</th>
<th>Recommended gestational weight gain (kg)</th>
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<tr>
<td>Underweight (&lt; 19.8 kg/m²)</td>
<td>12.5–18</td>
</tr>
<tr>
<td>Normal weight (19.8–26.0 kg/m²)</td>
<td>11.5–16</td>
</tr>
<tr>
<td>Overweight (&gt;26.0–29.0 kg/m²)</td>
<td>7–11.5</td>
</tr>
<tr>
<td>Obese (&gt; 29.0 kg/m²)</td>
<td>≥ 6.8</td>
</tr>
</tbody>
</table>
The first study analysed in the literature review is a prospective cohort study by Whitaker CR. (2004). The study recruited 8494 children from Ohio, USA. For calculating child obesity 2000 CDC growth charts were used. Overweight in children was defined as BMI ≥ 95th percentile for age and sex specific reference population. Net rate of pregnancy weight gain [(maternal weight gain - birth weight) / length of gestation] was divided into quartiles; quartile one being the lowest and four being the highest. Odds of obesity in quartile four at 2, 3 and 4 years of age, when compared to first quartile were 0.92 (95% CI: 0.72-1.16), 1.07 (95% CI: 0.86-1.34) and 1.09 (95% CI: 0.87-1.37) respectively. Hence the study reported non-significant relation between gestational weight gain and child overweight. Although the author has found a positive association between first trimester maternal obesity and child weight gain, but weight in early pregnancy might serve as a proxy for the preconception BMI rather than maternal weight gain during pregnancy.

Oken et al. (2007) reported positive association between gestational weight gain and child overweight at 3 years of age. They included 1044 mother-child pairs from project Viva. For child BMI, 2000 CDC reference data was used. Overweight was defined as BMI ≥ 95th percentile for age and sex specific reference population. Total gestational weight gain was defined as the difference between the last weight recorded before delivery and self-reported pre-pregnancy weight. Total gestational weight gain was also analysed as a continuous variable. Institute of Medicine, 1990 pregnancy weight gain recommendations were used for categorizing gestational weight gain. The results were in favour of child obesity for women gaining adequate or excessive weight during pregnancy. Mothers gaining adequate and excessive weight gain had greater odds for child obesity compared to the mothers who gained inadequately. Final results were controlled for Maternal age, education, household income, ethnicity, parental weight and height, pre-pregnancy weight and height, mode of delivery, parity, smoking, marital status and glucose tolerance test. The odds of obesity with comparison to inadequate weight gain mothers were 3.77 (95% CI: 1.38-10.27) for adequate weight gain mothers and 4.35 (95% CI: 1.69-11.24) for mothers who gained excessively.

### Table 2
New recommendation by Institute of Medicine for gestational weight gain according to pre-pregnancy BMI (2009).

<table>
<thead>
<tr>
<th>Pre-pregnancy BMI</th>
<th>Total weight gain Range (kg)</th>
<th>Rates of weight gain 2nd and 3rd trimester Mean (range) in kg/week</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight (&lt; 18.5kg/m²)</td>
<td>12.5-18</td>
<td>0.51 (0.44-0.58)</td>
</tr>
<tr>
<td>Normal weight (18.5–24.9kg/m²)</td>
<td>11.5-16</td>
<td>0.42 (0.35-0.50)</td>
</tr>
<tr>
<td>Overweight (25.0–29.9kg/m²)</td>
<td>7-11.5</td>
<td>0.28 (0.23-0.33)</td>
</tr>
<tr>
<td>Obese (≥ 30.0 kg/m²)</td>
<td>5-9</td>
<td>0.22 (0.17-0.27)</td>
</tr>
</tbody>
</table>
When total gestational weight gain was taken as a continuous measure, OR for obesity was 1.52 (95% CI: 1.19-1.94) for a 5kg increment of total gestational weight gain. Results showed that the risk of obesity was even for children whose mother gained weight within the recommended range.

In another study by Oken et al. (2009), five outcomes of gestational weight gain have been examined. These outcomes were preterm delivery, small for gestational age infant, large for gestational age infant, maternal postpartum weight retention and child obesity at age 3 years, in a sample of 1205 mother-child pairs from the same project Viva. Results were based on rate of gestational weight gain which was determined by dividing total weight gained (kg) by the length of gestation in weeks. For 0.1 kg/week of gestational weight gain, the odds ratio for child obesity was 1.16 (95% CI: 0.88-1.51) for normal weight mothers (18.5-24.9 kg/m²), 1.35 (95% CI: 1.01-1.81) for overweight women (25.0-29.9 kg/m²), and 1.22 (95% CI: 0.96-1.56) for obese mothers (≥ 30.0 kg/m²). Interestingly, for healthy outcome of pregnancy, a loss rather than any gain of gestational weight has been suggested for overweight and obese mothers. The recommended loss of weight was 0.03 kg/week and 0.19 kg/week for overweight and obese women respectively. In the above study Oken et al. (2007) challenge the weight gain recommendation and later they (Oken et al., 2009) suggest new guidelines for healthy outcome of pregnancy.

Moreira et al. (2007) randomly selected a sample of 4845 Portuguese children of 6-12 years of age. Overweight in children was defined according to IOTF criteria (Cole et al., 2000). After controlling for confounding factors they found greater odds for overweight children whose mothers gained ≥ 16kg during gestation [OR, 1.27 (CI 95%: 1.01-1.61)] compared to those with < 9kg of weight gain. The study presents increase in maternal weight gain during pregnancy as a risk factor for child overweight irrespective of maternal pre-pregnancy BMI categories.

Croizer et al. (2010) analysed a longitudinal cohort of 948 mother child pairs. Child body composition was assessed by dual energy X-ray absorptiometry (DEXA) at birth, 4 and 6 years of age. Gestational weight gain was calculated as the difference between pre-pregnancy weight and weight at 34 weeks gestation. Maternal weight gain during pregnancy was analysed both as categorical and continuous variable. Total gestational weight gain was categorized as women gaining inadequate, adequate and excessive weight according to IOM (2009) guidelines. The study found mixed results. After controlling for maternal smoking during pregnancy, height, parity, educational attainment, breast feeding duration and birth weight, the researchers found a positive association between excessive weight gain during pregnancy and child fat mass at birth. U-shaped
association was found between weight gain during pregnancy and child fat mass at 4 and 6 years of age. This U-shaped association was only significant for 6 years old children. However when pregnancy weight gain was analysed as a continuous variable, analysis per 5 kg increase showed no, weak and positive association with offspring fat mass at 4 years, 6 years and at birth respectively. In addition, the study showed that there was no effect of maternal pre-pregnancy BMI on the relationship between gestational weight gain and offspring fat mass.

Other studies showed maternal pre-pregnancy BMI as a factor modifying the association of gestational weight gain with child obesity. Wrotniak et al. (2008) examined 10226 participants in a retrospective cohort study in USA. Child obesity for this cohort of 7-year old children was defined as BMI ≥ 95th percentile of a reference population (Himes and Dietz, 1994). Maternal weight gain during pregnancy was categorized into recommended, excess and insufficient gestational weight gain according to IOM 1990 weight gain categories. Final results were adjusted for maternal race, age, pre-pregnancy BMI, cigarette smoking, gestational age, child sex, first born status and study city. Greater odds of 1.48 (95% CI: 1.06-2.06) for child obesity (BMI ≥ 95th versus 95th percentile), at 7 years of age were reported for mothers who gained excessively as compared to women who gained inadequately. In addition, stratified analysis for maternal pre-pregnancy BMI (<19.8 kg/m² versus ≥ 19.8 kg/m²) revealed that underweight mothers gaining excessive gestational weight gain confer highest risk of obesity to their children.

Olson et al. (2009) recruited 208 mother child pairs from Bassetts Health Care Network in USA. Obesity in children was defined as BMI ≥ 85th for the reference population. IOM 1990 weight gain categories were considered for maternal pregnancy weight gain. Although the study had small sample size, positive relationship between gestational weight gain and child obesity at 3 years of age was found. Analysis was stratified by maternal pre-pregnancy BMI. For overweight (including obese) and normal weight (including underweight) mothers gaining excessive gestational weight, percentages of overweight children were 47.5% and 23.7% respectively. In contrast to the above study (Wrotniak et al., 2008), association of excessive gestational weight gain with child obesity is strongest for obese women.
Table 3: Summary of the studies examining association between gestational weight gain (GWG) and child obesity. Studies presented in chronological order.

<table>
<thead>
<tr>
<th>Reference</th>
<th>Study design and place</th>
<th>Child Overweight Defined</th>
<th>GWG&lt;sup&gt;1&lt;/sup&gt; and maternal BMI Categories</th>
<th>Factors Controlled</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Whitaker CR, 2004.</td>
<td>Retrospective cohort study</td>
<td>Using 2000 CDC growth charts overweight defined as BMI ≥ 95th percentiles for age and sex specific reference.</td>
<td>Net rate of pregnancy weight gain divided into quartiles. Maternal first trimester BMI level categorized according to 5 levels established by WHO.</td>
<td>Maternal education, parity, weight gain, race/ethnicity, age, smoking during pregnancy, marital status, birth year, birth weight and gender.</td>
<td>No association was found between pregnancy weight gain and child obesity at 2, 3 and 4 years of age. Though positive association of first trimester maternal obesity and child obesity was indicated.</td>
</tr>
<tr>
<td>Moreira et al., 2007.</td>
<td>Cross-sectional analysis</td>
<td>IOTF cut off points for defining overweight and obesity in children. Weight gain divided into study group quartiles. Lowest was &lt; 9kg and highest was ≥ 19kg.</td>
<td>Parental education and BMI, smoking during pregnancy, breast feeding, child gender, age, energy intake, calcium to protein ratio, electronic games, computer use, television viewing, birth weight and order of birth.</td>
<td>Women gaining ≥ 16kg during pregnancy had greater odds for child obesity as compared to women gaining &lt; 9kg.</td>
<td></td>
</tr>
<tr>
<td>Oken et al., 2007.</td>
<td>Prospective cohort study</td>
<td>Child overweight defined as a BMI ≥ 95&lt;sup&gt;th&lt;/sup&gt; percentile by CDC growth charts.</td>
<td>IOM, 1990 Total GWG&lt;sup&gt;1&lt;/sup&gt; guidelines. Total GWG&lt;sup&gt;1&lt;/sup&gt; also analyzed as a continuous variable.</td>
<td>Maternal age, education, household income, ethnicity, parental weight and height, pre-pregnancy weight and height, mode of delivery, parity, smoking, marital status and glucose tolerance test.</td>
<td>Women with excessive and adequate GWG&lt;sup&gt;1&lt;/sup&gt; had higher risk of child overweight than women who gained inadequately. For continuous total GWG&lt;sup&gt;1&lt;/sup&gt; there was an increase OR for child obesity for 5kg increment in total GWG&lt;sup&gt;1&lt;/sup&gt;.</td>
</tr>
</tbody>
</table>

Table continued
## Table 3 continued

<table>
<thead>
<tr>
<th>Study</th>
<th>Participants</th>
<th>BMI Definition</th>
<th>GWG Categories</th>
<th>Maternal Factors</th>
<th>GWG1 of ≥ 20.43 kg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Li et al., 2007</td>
<td>1739</td>
<td>BMI ≥ 95th percentile</td>
<td>Divided into 5 categories</td>
<td>Maternal smoking, male gender, birth order, birth weight, breastfeeding and black ethnicity.</td>
<td>Early onset overweight but no association with late onset overweight.</td>
</tr>
<tr>
<td>USA</td>
<td></td>
<td>Reference data used.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gale et al., 2007.</td>
<td>Prospective cohort study of 216, 9 year old children</td>
<td>Dual-energy X-ray absorptiometry (DEXA)</td>
<td>Categorized according to IOM, 1990 categories and also analysed as a continuous variable.</td>
<td>Maternal height, weight gain, age, birth weight, smoking in pregnancy and duration of breastfeeding.</td>
<td>No association was found between maternal weight gain during pregnancy and child BMI at 9 years of age.</td>
</tr>
<tr>
<td>UK</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wrotniak et al., 2008</td>
<td>Retrospective cohort study.</td>
<td>Overweight defined as BMI ≥ 95th percentile for age and sex specific reference population (Himes and Dietz, 1994)</td>
<td>IOM, 1990 GWG1 categories</td>
<td>Child age, first born status, sex, maternal pre-pregnancy BMI, age, race, gestational age, study city.</td>
<td>Women gaining excessive weight during pregnancy had greater risk for child obesity as compared to women gaining inadequately. In addition, risk of offspring obesity was highest for underweight women.</td>
</tr>
<tr>
<td>USA</td>
<td>10226 7-year old participants</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Olson et al., 2009.</td>
<td>Prospective cohort study.</td>
<td>Overweight defined as BMI&gt; 85th percentile for sex and age specific percentile by CDC growth charts.</td>
<td>IOM 1990, GWG1 categories</td>
<td>Exclusive breastfeeding for at least 6 months, infant birth weight, parity and smoking during pregnancy.</td>
<td>Positive relationship of GWG1 with child obesity was found. The association was strongest for obese women.</td>
</tr>
<tr>
<td>USA</td>
<td>208 mother child pairs. Children at 3 years of age.</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table continued
<table>
<thead>
<tr>
<th>Study</th>
<th>Design</th>
<th>Population</th>
<th>Methods</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oken et al., 2009</td>
<td>Longitudinal pre-birth cohort study.</td>
<td>2012 mother-child pairs recruited. BMI of 1205 children was available at age 3 years of age. USA</td>
<td>Obesity defined as BMI &gt; 95th percentile. Maternal BMI divided in tertiles. Rate of GWG(^1) analysed as continuous variable. Maternal smoking status, ethnicity, parity, age.</td>
<td>Relationship between child obesity and rate of gestational weight gain was found per 0.1kg/week of gain for all the three BMI categories. However the association was only significant for overweight women.</td>
</tr>
<tr>
<td>Kleiser et al., 2009</td>
<td>Cross-sectional study.</td>
<td>13450 non-underweight children and adolescents age 3-17 years of age. Germany</td>
<td>IOTF cut-off points used for defining overweight and obesity. Weight gain in pregnancy categorized as gaining &lt; 20kg and ≥ 20kg.</td>
<td>Age, gender, maternal weight status. Association of GWG(^1) with obesity was found only for normal weight mother. GWG(^1) was not the primary focus of the study.</td>
</tr>
<tr>
<td>Kries et al., 2010</td>
<td>Longitudinal cohort study.</td>
<td>10784 children age 3-17 years. Germany</td>
<td>IOTF cut-off points used for defining overweight and obesity. Maternal GWG(^1) categorized into quartiles. Lowest included less than 10 kg gain and highest included greater than 17 kg.</td>
<td>Child sex, low physical activity, high TV consumption, age, smoking in pregnancy and low socioeconomic conditions. Stratified analysis of maternal pre-pregnancy BMI(^2) gave positive association between excessive GWG(^1) and child overweight only for normal weight mothers.</td>
</tr>
<tr>
<td>Crozier et al. 2010</td>
<td>Longitudinal cohort study.</td>
<td>948 mother child pairs. UK</td>
<td>DEXA for assessing child body composition. Greater GWG(^1) also analysed as a continuous variable.</td>
<td>Maternal height, educational attainment, smoking during pregnancy, parity, birth weight and feeding duration. Compared to adequate weight gain women, mothers gaining excessively had children with increase in fat mass of 7%, 4% and 10% at birth, 4y and 6 y of age respectively. As a continuous measure GWG(^1) had, no, week and positive association at 4 y, 6 y and neonate respectively.</td>
</tr>
</tbody>
</table>

\(^1\) GWG= gestational weight gain
Other studies have found positive association between excessive gestational weight gain and child overweight only for normal weight women. Kries et al. (2010) recruited 10784 children of age 3-17 years. Overweight was defined according to IOTF age and sex specific BMI cut off points. Maternal weight gain during pregnancy was calculated as total gestational weight gain and was divided into quartiles. These included lowest quartile (0-10kg), middle two quartiles combined and referred to as average gestational weight gain (11-17kg) and highest quartile (> 17kg). Odds ratio was calculated in reference to average maternal pregnancy weight gain. For high gestational gain (>17kg), odds ratio was 1.16 (95% CI: 1.02-1.32) and for the low gestational weight gain it was 1.01 (95% CI: 0.89-1.15). However when the analysis was stratified by pre-pregnancy BMI, odds were 1.39 (95% CI: 0.54-3.35) for underweight, 1.20 (95% CI: 1.01-1.43) for normal weight, 1.02 (95% CI: 0.79-1.32) for overweight and 1.24 (95% CI: 0.88-1.76) for obese mothers. Results showed significant relationship only for normal weight mothers. Association of low gestational weight gain with child overweight found no significant results for all the maternal BMI categories. Klieser et al. (2009) examined the potential determinants of obesity among 13450 children and adolescents of 3-17 years of age. Association of child obesity and maternal weight gain during pregnancy was not the primary point of interest of the study. The authors gave a positive relationship between high pregnancy weight gain and child obesity only for normal weight mothers. Odds ratio for normal weight mothers gaining >20kg was 2.82 (95% CI: 1.6-5.0) and overweight mothers gaining >20kg was 0.71 (0.3-1.6) when compared to the women gaining ≤20kg.

Li et al. (2007) examined the relationship of weight gain in pregnancy with development of early and late onset child overweight. They recruited 1739 participants below 2 years of age and followed them to 12-years of age. Overweight in children was defined as BMI ≥95th percentile using CDC reference data. Early onset overweight “represented children in early onset of overweight and persisted throughout childhood”. Late onset overweight “represented children who had a moderately high probability of overweight at 2 years of age, low probability at 4 and 6 years but growing probability of overweight age 8 years”. Results of the study found, that gestational weight gain of ≥ 20.43 kg was associated with early onset child overweight with odds ratio of 1.7 (95% CI: 1.0-2.9) but had no association with late onset overweight which had odds ratio of 0.8 (95% CI: 0.3-2.1).

In a British cohort study of 9 years old children, association of maternal weight gain and child body composition was examined. Although the sample was relatively small consisting of 216 children,
the authors did not find association between gestational weight gain and fat mass index at 9 years of age. (Gale et al, 2007)

In summary, the above studies give either positive, none or mixed results for the association between gestational weight gain and child obesity or overweight. Two of the studies present a small sample size (Gale et al., 2007, Olson et al., 2009). Another two have not considered the association between maternal weight gain and child obesity as their primary point of interest (Kleiser et al., 2009, Oken et al., 2009). One of the studies analyses the association irrespective of maternal pre-pregnancy BMI (Moreira et al., 2007). Among those who gave positive association, two of them proved it only for normal weight women gaining excessive gestational weight gain (Kries et al., 2010, Klieser et al., 2000). Another one showed strongest relationship of excessive gestational weight gain with child obesity for underweight mothers (Wrotniak et al., 2008). In contrast, Olson et al. (2008) found strongest association for overweight (including obese) women. However, not every study found influence of maternal BMI on the association of gestational weight gain with offspring overweight/obesity. Croizer et al. (2010) found no effect of maternal BMI on the association. Nor was the effect of maternal BMI on the association between gestational weight gain and offspring overweight shown by Oken et al. (2007).

Furthermore Oken et al. (2007) challenge the IOM 1990 guidelines by proving an association between gestational weight gain and child obesity even for women who gain within the recommended range. Therefore, new pregnancy weight guidelines are suggested, according to which, for getting lowest predicted health outcomes, a loss rather than any rate of gestational weight gain is recommended for overweight and obese women (Oken et al., 2009).

Besides the above mentioned articles other studies related to the study topic were searched but not mentioned in the discussion. They were either of poor quality (Sowan and stember, 2000) or did not mention the results for pregnancy weight gain and child overweight (Ong et al., 2000).
3. AIMS OF THE STUDY

3.1. General aim

The aim of the study is to explore the relationship between gestational weight gain and child overweight.

3.2. Specific aims

Specific aims of the study are to examine:

1) The association of rate of gestational weight gain with child overweight at 3 years of age.

2) Possible effect of maternal BMI on the association between gestational weight gain and child overweight.
4. SUBJECTS AND METHODS

4.1. Subjects

Type 1 Diabetes Prediction and Prevention Project (DIPP) started in 1994, is a Finnish population based cohort study. It comprises children with HLA-conferred susceptibility to type 1 diabetes. This genetic susceptibility was evaluated at birth from umbilical cord blood sample. Children born at Turku, Oulu and Tampere University Hospitals were screened after obtaining written informed consent from their parents. Those who were positive for HLA-DQB1 *02/*0302 and *0302/x were invited to participate in DIPP study. These genetically predisposed children are monitored for signs of autoimmunity and diabetogenic antibodies. DIPP study aims at predicting and preventing diabetes at early stages. The project also monitors these children for growth, viral infections, diet and allergies at 3-12 months interval. (Kupila et al., 2001)

DIPP Nutrition study is a part of DIPP study comprising of at-risk children for type 1 diabetes from Oulu and Tampere University Hospitals. It focuses on the development of beta cell autoimmunity in these children by monitoring the type of food intake, age at introduction of supplementary food and breast feeding duration. DIPP Nutrition study monitors children for their feeding patterns at 3, 6, 12 and 24 month of age. Information about children’s diet is collected from food frequency questionnaires and food diaries and is checked by trained nurses. Information obtained comprises:

- duration of exclusive breast feeding (defined as the time period during which the child received breast milk plus vitamin and/or mineral supplement and drops of water)
- duration of total breast feeding (defined as the time period during which the child received complementary feeding in addition to milk)
- age at introduction of infant formula
- type of infant formula
- age at introduction of supplementary food
- type of supplementary food such as, berries, roots, cereals, mild products, fish and meat. (Virtanen et al., 2006)

In addition, information is collected retrospectively from questionnaires filled by mothers after delivery and from Pikanmaa Medical Birth Registries. Questionnaires included the following information:

- child’s date of birth
- child’s sex
- maternal weight, height and gestational week at first antenatal visit to maternity center
- maternal weight, height and gestational week at last visit to maternity center
- maternal and paternal basic and high education status
- maternal and paternal diabetes
- gestational diabetes (referred to intake of special diet during pregnancy because of impaired glucose metabolism)
- maternal age
- paternal height and weight
- urbanization level of place of residence at birth

Following additional information was collected from birth registries:

- number of previous deliveries
- smoking during pregnancy
- mode of deliver
- duration of gestation
- child’s birth weight
Total of 3916 mother-child pairs born between 1997 and 2004 in Pirkanmaa Hospital District were enrolled in the study. The sample was then restricted to singletons, mothers with weight and height measurements at first and last antenatal visit and children with BMI measurements at 3-years of age. This reduction resulted in a final sample of 2143 participants for the analysis (Figure 1).

Participation in the study was voluntary and written informed consent was taken from the parents according to ethical board statement of DIPP study.

**4.2. Measurements used in the study**

**4.2.1. Measures of maternal pre-pregnancy BMI and rate of gestational weight gain**

Depending on the weight and height of mothers at first antenatal visit, maternal BMI was calculated by dividing weight in kg by height in meters squared (kg/m$^2$). Our study used first antenatal visit BMI as a proxy for maternal pre-pregnancy BMI.
However, a number of women attended the antenatal clinic for their first antenatal visit in their second trimester and a few in their third trimester of pregnancy. Considering the first visit weight and height measurements as a substitute for pre-pregnancy BMI has put forward a dilemma of misclassifying normal weight women as obese, if they have come for their first visit during later stages of pregnancy. For instance, a woman with a BMI of 23 kg/m$^2$ would be classified as normal weight if she consults antenatal clinic for her first visit in the beginning of pregnancy. However the same woman could be misclassified as obese if she comes for her first antenatal visit during the end of pregnancy with a BMI of 32 kg/m$^2$. The increased BMI for the same woman corresponds to weight gain during pregnancy rather than her true pre-pregnancy BMI.

Data lacking maternal weight measurements before conception can use various techniques for estimating pre-pregnancy BMI. One of the methods is by means of using weight and height measurements taken during pregnancy. These pregnancy weight measurements can be extrapolated retrospectively to an estimate of maternal weight at conception (Harris and Ellison, 1998). In the present study, the same extrapolation technique was applied for assessing maternal pre-pregnancy BMI. Therefore, weight of mothers who came after 10 weeks of their pregnancy for their first antenatal visit was extrapolated back to 10th week of gestation. The reason for taking 10th week of gestation as the cut-off was due to the fact that a linear weight gain is observed from approximately 10th week of gestation until term (Pitkin, 1977).

Maternal BMI was used both as a continuous and categorized variable in the analysis. These BMI categories were defined according to IOM (2009); underweight (< 18.5 kg/m$^2$), normal weight (18.5-24.9 kg/m$^2$), overweight (25.0-29.9 kg/m$^2$) and obese (≥ 30.0 kg/m$^2$). As few women were present in underweight category, it was therefore grouped with normal weight women. Final categories included normal, overweight and obese women.
Rate of gestational weight gain is the main exposure variable of the study. It was calculated as \[((\text{weight at last} - \text{weight at first antenatal visit})/\text{number of weeks between the visits})\] and divided into quarters. Lowest quarter included weight gain of less than $0.3250$ kg/week, Second quarter ranged from $0.3250-0.4193$ kg/week, third included $0.4194-0.5172$ kg/week and the highest quarter included weight gain of greater than $0.5172$ kg/week.

4.2.2. Assessment of child overweight and obesity

Height and weight of children were measured at regular clinical visits. BMI for children was calculated as, weight (kilograms)/ height$^2$ (meters)$^2$. Overweight and obesity in children was defined according to IOTF criteria for BMI. IOTF provides a series of age and gender specific BMI cut-off points for 2-18 years of age which are equivalent to widely used adult BMI of $25$ kg/m$^2$ for overweight and $30$ kg/m$^2$ for obesity (Cole et al, 2000). Overweight in our study includes the definition of obesity.

4.2.3. Assessment of potential confounders

In addition to the primary exposure variable (rate of gestational weight gain) and outcome variable (overweight at age of 3-years) other variables analyzed were parental BMI, educational status and diabetes, maternal smoking during pregnancy, duration of gestation, birth weight, location of residence, breastfeeding duration, way and mode of delivery and gestational diabetes. Some of the categorized variables had more than two categories. These were re-categorized into study group categories as shown in table 4. Additional variables were created from already existing variables, which included, exclusive breast feeding where hospital feeding is included (less than 3 months and 3 or more months) and total breast feeding (less than 6 months and 6 or more months). A few continuous variables such as maternal age in years was categorized into the following four categories; $<25$, $25-29.9$, $30-34.9$ and $\geq 35$. 24
4.3. Analysis

In order to get familiar with the data frequency distribution tables were drawn and baseline characteristics of the subjects were determined. For the quarters of rate of gestational weight gain, middle two quarters were combined into a single category, finally presenting three categories of lowest, middle two and highest quarter. Middle two quarters were then used as a reference category in logistic regression.

Chi-Square test was done to see the statistical significance of rate of gestational weight gain and child overweight with categorized study variables. Likewise, appropriate tests were done for finding relationship of the exposure and outcome variable with the continuous variables. For an association with skewed continuous variables (maternal and paternal BMI, birth weight and duration of gestation) Mann-Whitney test was done for child overweight and Kruskal-Wallis test for categorized rate of gestational weight gain. The respective parametric tests for the normally distributed variables were t-test and One-Way Anova, investigated for child overweight and categorized rate of gestational weight gain respectively.

Dummy variable was created to check whether association of rate of gestational weight gain with child overweight varied between women who were present for first antenatal visit before and after 10th week of gestation. This variable was generated before extrapolation of the maternal first antenatal visit weight to 10th week of gestation. Dummy variable was created for first antenatal visit for mothers presenting at less and greater than ten weeks of gestation. Analysis was investigated by creating an interaction term for quartiles of gestational weight gain and first visit dummy variable. Statistical significance was checked after regressing the variable separately for overweight at 3-years of age and when adjusted for other confounders. Analysis revealed no statistically significant interaction, therefore first visit dummy variable was excluded from further analysis.
Table 4: Original categories of study variables and their re-categorization.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Original category</th>
<th>Re-categorization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smoking during pregnancy</td>
<td>1= no smoking&lt;br&gt;2= gave up smoking during the first trimester of pregnancy&lt;br&gt;3= Smoked during the first trimester of pregnancy&lt;br&gt;4= no information</td>
<td>0= no&lt;br&gt;1= yes</td>
</tr>
<tr>
<td>Maternal basic education</td>
<td>1= less than elementary school&lt;br&gt;2= elementary school&lt;br&gt;3= part of high school&lt;br&gt;4= high school graduate</td>
<td>1=less than high school&lt;br&gt;2= high school graduate</td>
</tr>
<tr>
<td>Paternal basic education</td>
<td>1= less than elementary school&lt;br&gt;2= elementary school&lt;br&gt;3= part of high school&lt;br&gt;4= high school graduate</td>
<td>1= less than high school&lt;br&gt;2= high school graduate</td>
</tr>
<tr>
<td>Maternal vocational education</td>
<td>1= none&lt;br&gt;2= vocational education or course&lt;br&gt;3= secondary vocational education&lt;br&gt;4= university studies or degree</td>
<td>1= none or vocational school or course&lt;br&gt;2= secondary vocational education&lt;br&gt;3= university studies or degree</td>
</tr>
<tr>
<td>Paternal vocational education</td>
<td>1= none&lt;br&gt;2= vocational education or course&lt;br&gt;3= secondary vocational education&lt;br&gt;4= university studies or degree</td>
<td>1= none or vocational school or course&lt;br&gt;2= secondary vocational education&lt;br&gt;3= university studies or degree</td>
</tr>
<tr>
<td>Number of previous deliveries</td>
<td>1= 0&lt;br&gt;2=1&lt;br&gt;3=2&lt;br&gt;4= ≥ 3</td>
<td>0= none&lt;br&gt;1= 1&lt;br&gt;2= ≥ 2</td>
</tr>
</tbody>
</table>

Table continued
Association of child overweight and birth weight was investigated after taking birth weight both as a continuous and categorized variable (quintiles). -2 log likelihood for these two models were compared and no statistically significant difference was found (0.25 < P < 0.05). It was concluded that birth weight was associated with child BMI in a linear way and could be analyzed as a continuous variable in the study. Same analyses were repeated for maternal and paternal BMI and similar conclusion was drawn.

Binary logistic regression was chosen for the analysis because of the binominal nature of the outcome variable. Univariate logistic regression model was applied to understand the association of rate of gestational weight gain and covariates with offspring overweight separately. Next, multivariate logistic regression model was used to regress offspring overweight on quarters of rate of gestational weight gain after adjusting for potential confounders. Final step was addition of birth weight and duration of gestation to the model. The reason for adding birth weight at the end was that it might affect the association of rate of gestational weight gain with child overweight and might be a potential mediator of the association.

To explore the influence of maternal BMI on the association of the rate of gestational weight gain with child overweight, an interaction term for maternal BMI and rate of gestational weight gain
(maternal BMI*rate of gestational weight gain) was created and added to the model. The purpose of this calculation was to investigate whether the association between rate of gestational weight gain and child overweight was different for normal, overweight and obese women.

In this study two sided p-value of <0.05 was considered as significant. SPSS version 19 was used for the purpose of analysis.
5. RESULTS

5.1. Characteristics of the mothers and children in relation to the rate of gestational weight gain

Rate of gestational weight gain was normally distributed among the subjects. Mean rate of gain was 0.42 kg/week (SD 0.15). Among obese women, more than 50% lied in the lowest quarter of rate of gestational weight gain. Higher percentage of women with less basic education (43.8) and less vocational education (45.8%) fell in the lowest quarter of rate of gestational weight gain compared to the women with high level of basic and vocational education. Likewise was observed for fathers with less vocational education. Lowest quarter of rate of gestational weight gain constituted high percentage of diabetic mothers and mothers with history of two or more previous deliveries. Lowest quarter also consisted of high percentage of mothers with gestational diabetes, who exclusively breast fed their children for more than 3 months or totally breast fed their children for more than 6 months and who belonged to rural areas (Table 5). Mean for maternal BMI (25.36 kg/m$^2$) lying in the lowest quarter of gestational weight gain was higher than the middle two and highest quarter (Table 6).

5.2. Characteristics of the mothers and children in relation to the prevalence of offspring overweight

Among total 2143 subjects, 237 (11.1%) were overweight. More girls were overweight than boys. Socio-demographic and perinatal factors influenced were associated with prevalence of obesity. Results showed high prevalence of overweight for children whose mothers smoked during pregnancy (20.9%), had less basic education (13.6%), had less vocational education (13.4%) and who had two or more previous deliveries. High risk of overweight was observed in children resident in rural municipality (18.4 %) and in children who were either exclusively breastfed for less than 3 months (12.8%) or totally breastfed (16.4%) for less than 6 months (Table 5). Regarding maternal BMI, mothers of overweight children had a higher BMI than those of non-overweight children. The same was true for paternal BMI (Table 6).
Table 5. Characteristics of the participants and their association with child overweight and rate of gestational weight gain.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Subjects (n=3719)</th>
<th>Overweight at 3 years of age (n=2143)</th>
<th>Quarters of rate of gestational weight gain (n=2544)</th>
<th>p-value&lt;sup&gt;3&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%) 2&lt;sup&gt;nd&lt;/sup&gt; quartile of gestational weight gain (%)</td>
<td>p-value&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boys</td>
<td>1921 (51.7)</td>
<td>86 (7.8)</td>
<td>326 (24.6)</td>
<td>0.815</td>
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<td>Girls</td>
<td>1798 (48.3)</td>
<td>151 (14.6)</td>
<td>312 (25.6)</td>
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</tr>
<tr>
<td>Maternal basic education</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Less than high school</td>
<td>1624 (44.8)</td>
<td>114 (13.6)</td>
<td>275 (27.1)</td>
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<td>High school graduate</td>
<td>1997 (55.2)</td>
<td>115 (9.1)</td>
<td>354 (23.8)</td>
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<tr>
<td>Paternal basic education</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Less than high school</td>
<td>2145 (61.3)</td>
<td>142 (11.9)</td>
<td>376 (25.9)</td>
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<td>High school graduate</td>
<td>1355 (38.7)</td>
<td>84 (9.7)</td>
<td>239 (24.3)</td>
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<tr>
<td>Maternal vocational education</td>
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<td>99 (13.4)</td>
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<td>University studies or degree</td>
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<td>48 (9.7)</td>
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<td>Paternal vocational education</td>
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<td></td>
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<td></td>
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<tr>
<td>None or vocational school or course</td>
<td>1841 (51.9)</td>
<td>125 (12.4)</td>
<td>324 (26.2)</td>
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<td>Secondary vocational education</td>
<td>960 (27.1)</td>
<td>60 (9.9)</td>
<td>171 (24.8)</td>
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</table>

Table continued
### Table 5 continued

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Subjects (n=3719) n (%)</th>
<th>Overweight at 3 years of age (n=2143) n (%)</th>
<th>Quarters of rate of gestational weight gain (n=2544) n (%)</th>
<th>p-value</th>
<th>p-value</th>
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<tbody>
<tr>
<td>Maternal diabetes</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>No</td>
<td>3595 (96.7)</td>
<td>225 (10.9)</td>
<td>605 (24.5)</td>
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<td>Yes</td>
<td>124 (3.3)</td>
<td>12 (15.0)</td>
<td>33 (42.3)</td>
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<td>0.001</td>
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<td></td>
<td></td>
<td></td>
<td>0.017</td>
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<td>220 (10.7)</td>
<td>612 (25.1)</td>
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<td>0.507</td>
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<td>81 (2.2)</td>
<td>11 (21.2)</td>
<td>18 (31.6)</td>
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<td></td>
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<tr>
<td>Location of residence</td>
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<td>0.007</td>
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<td>38 (18.4)</td>
<td>75 (31.4)</td>
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<td>Semi-urban</td>
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<tr>
<td>Urban</td>
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<td>476 (23.5)</td>
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<td></td>
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<td>&lt;25</td>
<td>673 (18.1)</td>
<td>38 (12.70)</td>
<td>87 (20.9)</td>
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<tr>
<td>25-29.9</td>
<td>1271 (34.2)</td>
<td>75 (10.0)</td>
<td>184 (20.2)</td>
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<tr>
<td>30-34.9</td>
<td>1102 (29.6)</td>
<td>72 (10.7)</td>
<td>210 (27.1)</td>
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<tr>
<td>≥ 35</td>
<td>673 (18.1)</td>
<td>52 (12.3)</td>
<td>153 (34.1)</td>
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<tr>
<td>Mode of delivery</td>
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<td>0.190</td>
<td>0.886</td>
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<td>Vaginal</td>
<td>3290 (88.5)</td>
<td>203 (10.7)</td>
<td>564 (25.0)</td>
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<tr>
<td>Non Vaginal</td>
<td>429 (11.5)</td>
<td>34 (13.5)</td>
<td>74 (25.9)</td>
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</table>

Table continued
### Table 5 continued

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Subjects (n=3719) n (%)</th>
<th>Overweight at 3 years of age (n=2143) n (%)</th>
<th>Quarters of rate of gestational weight gain (n=2544) n (%)</th>
<th>p-value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal smoking during pregnancy</td>
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<td></td>
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<td>&lt;0.001</td>
<td>0.350</td>
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<td>No</td>
<td>3303 (90.0)</td>
<td>199 (10.3)</td>
<td>563 (24.6)</td>
<td>1154 (50.3)</td>
<td>576 (25.1)</td>
</tr>
<tr>
<td>Yes</td>
<td>329 (9.1)</td>
<td>32 (20.9)</td>
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<td>89 (46.2)</td>
<td>47 (24.5)</td>
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<tr>
<td>Length of exclusive breastfeeding&lt;sup&gt;4&lt;/sup&gt;</td>
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<td></td>
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<td>0.002</td>
<td>0.002</td>
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<tr>
<td>Less than 3 months</td>
<td>1838 (63.3)</td>
<td>165 (12.8)</td>
<td>421 (27.0)</td>
<td>732 (47.0)</td>
<td>405 (26.0)</td>
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<td>3 or more months</td>
<td>1064 (36.7)</td>
<td>71 (8.6)</td>
<td>208 (22.3)</td>
<td>505 (54.2)</td>
<td>218 (23.4)</td>
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<tr>
<td>Length of total breastfeeding</td>
<td></td>
<td></td>
<td></td>
<td>0.001</td>
<td>0.006</td>
</tr>
<tr>
<td>Less than 3 months</td>
<td>570 (20.8)</td>
<td>60 (16.4)</td>
<td>139 (30.2)</td>
<td>200 (43.4)</td>
<td>122 (26.5)</td>
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<tr>
<td>3 or more months</td>
<td>2173 (79.2)</td>
<td>77 (10.1)</td>
<td>463 (24.2)</td>
<td>981 (51.2)</td>
<td>473 (24.7)</td>
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<td>Gestational diabetes&lt;sup&gt;5&lt;/sup&gt;</td>
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<td></td>
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<td>0.018</td>
<td>&lt;0.001</td>
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<td>No</td>
<td>2616 (94.8)</td>
<td>204 (10.8)</td>
<td>562 (23.3)</td>
<td>1228 (51.0)</td>
<td>618 (25.7)</td>
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<tr>
<td>Yes</td>
<td>144 (5.2)</td>
<td>19 (18.3)</td>
<td>76 (55.9)</td>
<td>43 (31.6)</td>
<td>17 (12.5)</td>
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<tr>
<td>Maternal BMI</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
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<tr>
<td>Normal weight</td>
<td>1674 (65.3)</td>
<td>100 (8.2)</td>
<td>306 (18.4)</td>
<td>935 (56.3)</td>
<td>421 (25.3)</td>
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<tr>
<td>Overweight</td>
<td>1628 (24.5)</td>
<td>59 (12.4)</td>
<td>199 (31.9)</td>
<td>255 (40.9)</td>
<td>170 (27.2)</td>
</tr>
<tr>
<td>Obese</td>
<td>263 (10.3)</td>
<td>46 (24.2)</td>
<td>133 (51.6)</td>
<td>81 (31.4)</td>
<td>44 (17.1)</td>
</tr>
</tbody>
</table>

Table continued
Table 5 continued

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Subjects (n=3719)</th>
<th>Overweight at 3 years of age (n=2143)</th>
<th>Quarters of rate of gestational weight gain (n=2544) n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td>p-value</td>
</tr>
<tr>
<td>Number of previous deliveries</td>
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<td></td>
<td>0.493</td>
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<tr>
<td>No previous delivery</td>
<td>1673 (45.2)</td>
<td>111 (11.2)</td>
<td></td>
</tr>
<tr>
<td>One previous delivery</td>
<td>1227 (33.2)</td>
<td>70 (10.1)</td>
<td></td>
</tr>
<tr>
<td>Two or more previous deliveries</td>
<td>799 (21.6)</td>
<td>55 (12.3)</td>
<td></td>
</tr>
</tbody>
</table>

1 Overweight defined according to International Obesity Task Force (IOTF) criteria for body mass index (BMI) and includes the definition of obesity.
2 Rate of gestational weight gain calculated as [(weight at last – weight at first antenatal visit) /number of weeks between the visits] and divided in quarters. It was calculated after extrapolating maternal weight to 10th week of gestation for women presenting for antenatal clinic visit later in pregnancy.
3 P-value based on chi square test.
4 Exclusive breast feeding defined as intake of vitamin/ or mineral supplement in addition to breast milk.
5 Gestational diabetes referred to consumption of special diet during pregnancy due to impaired glucose metabolism.
Table 6. Characteristics of the participants and their association with overweight and rate of gestational weight gain quarters.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Subjects</th>
<th>Overweight1 at 3 years of age(^1), median (Range)</th>
<th>Quarters of rate of gestational weight gain(^2), median (Range)</th>
<th>(p)-value(^3)</th>
<th>Lower</th>
<th>middle two</th>
<th>upper</th>
<th>(p)-value(^4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal BMI(^5)</td>
<td>2565</td>
<td>23.4 (15.6-43.6)</td>
<td>25.1 (17.3-49.5)</td>
<td>&lt;0.001</td>
<td>25.3</td>
<td>22.8</td>
<td>23.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Paternal BMI</td>
<td>1766</td>
<td>25.4 (16.6-44.9)</td>
<td>26.8 (19.6-47.7)</td>
<td>&lt;0.001</td>
<td>25.6</td>
<td>25.5</td>
<td>25.5</td>
<td>0.432</td>
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<tr>
<td>Birth weight</td>
<td>3718</td>
<td>3.6 (0.9-5.5)</td>
<td>3.8 (0.6-5.5)</td>
<td>&lt;0.001</td>
<td>3.5</td>
<td>3.59</td>
<td>3.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Duration of gestation</td>
<td>3701</td>
<td>40.0 (27.5-42.8)</td>
<td>40.1 (25.0-42.5)</td>
<td>0.457</td>
<td>40.0</td>
<td>40.4</td>
<td>40.0</td>
<td>0.070</td>
</tr>
</tbody>
</table>

1 Overweight defined according to International Obesity Task Force (IOTF) criteria for body mass index (BMI) and includes the definition of obesity.
2 Rate of gestational weight gain calculated as \([(weight at last – weight at first antenatal visit) / number of weeks between the visits]\) and divided in quarters. It was calculated after extrapolating maternal visit to 10\(^{th}\) week of gestation for women presenting for antenatal clinic visit later in pregnancy.
3 \(p\)-value based Mann-Whitney test
4 \(p\)-value based on Kruskal-Wallis test
5 Maternal BMI calculated using the first antenatal visit weight and height measurement after extrapolating maternal weight to 10\(^{th}\) week for women presenting for antenatal clinic visit later in pregnancy.
5.3. Prevalence of offspring overweight in relation to the rate of gestational weight gain

The association between quarters of rate of gestational weight gain and offspring overweight at the age of 3 years was statistically significant, p=<0.001. Figure 2 illustrates that higher percentage of overweight children (15.5%) belonged to the lowest quarter, second highest percentage of overweight children (11.5%) in the highest quarter and lowest percentage (8.0%) of overweight children belonged to the middle two quarter of rate of gestational weight gain.

Figure. 2

5.4. Unadjusted results for association of the rate of gestational weight gain with offspring overweight

Univariate analysis was done to understand the association of rate of gestational weight gain and potential confounders with child overweight independently. Analysis for the relationship of the quarters of rate of gestational weight gain with child overweight, discovered significant association between the independent and dependent variables of the study. There were increased odds ratios for overweight at both the lowest (Unadjusted OR 2.11, 95% CI: 1.50-2.98) and the highest extremes
(Unadjusted OR 1.47, 95% CI: 1.01-2.15), as compared to the average rate of gestational weight gain (Table 7).

In addition, significant association with overweight was found for child sex, maternal smoking, maternal basic and vocational education, paternal diabetes, location of residence, paternal and maternal BMI, duration of exclusive and total breast feeding, gestational diabetes and birth weight. Higher odds for overweight were found among girls (versus boys), mothers who smoked during pregnancy (versus mothers who did not smoke during pregnancy), mothers with basic education less than high school (versus high school graduate), mothers with no or vocational school education (versus university studies), paternal diabetes (versus no diabetes), rural location of residence (versus urban). Higher odds ratio for overweight included the following continuous variables, maternal BMI, paternal BMI and birth weight.

5.5. Adjusted results for association of the rate of gestational weight gain with offspring overweight

Variables taken into consideration in multivariate logistic regression model were based on having a significant association with overweight. The variables considered consisted of sex of the child, maternal basic and vocational education, paternal diabetes, location of residence, maternal smoking during pregnancy, duration of exclusive and total breast feeding, location of residence and gestational diabetes (Table 5), maternal and paternal BMI, and birth weight (Table 6).

Nevertheless, the model was restricted to inclusion of the following variables: sex, smoking during pregnancy, maternal basic education, paternal diabetes, location of residence, gestational diabetes, maternal BMI, exclusive breast feeding, duration of gestation and birth weight (Table 7). Covariates having a positive association with overweight but excluded from the model were paternal BMI (for large number of missing values), maternal vocational education (as both basic and vocational education variables cannot be included in the same model) and total breast feeding (the analysis repeated after inclusion and exclusion to the model and no big effect was found).

When the logistic regression model was adjusted for the respective covariates, the OR for the association between lowest rate of gestational weight gain and child overweight at the age of 3 years was still significant. However the odds for high weight gain were no longer significant and crossed one (Table 7).
Table 7. Unadjusted and adjusted logistic regression model for the relationship between the rate of gestational weight gain and overweight in the offspring at the age of 3 years.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Unadjusted</th>
<th>1</th>
<th>Adjusted for confounders 2,4</th>
<th>2</th>
<th>Adjusted for additional confounders 3</th>
<th>3</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>OR 95%CI</td>
<td>P-value</td>
<td>OR 95%CI</td>
<td>P-value</td>
<td>OR 95%CI</td>
<td>P-value</td>
</tr>
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<td>Rate of gestational weight gain quarters</td>
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<td></td>
<td></td>
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<tr>
<td>Lowest quarter</td>
<td>2.11 1.50-2.98</td>
<td>&lt;0.001</td>
<td>1.53 1.05-2.26</td>
<td>0.051</td>
<td>1.73 1.17-2.55</td>
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<td>Middle two quarters</td>
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<td>1</td>
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<td>1</td>
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<td>Highest quarters</td>
<td>1.47 1.01-2.15</td>
<td>&lt;0.001</td>
<td>1.45 0.97-2.15</td>
<td>&lt;0.001</td>
<td>1.20 0.80-1.81</td>
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<td></td>
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<tr>
<td>Boys</td>
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<tr>
<td>Girls</td>
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<td>1.87 1.34-2.57</td>
<td>0.005</td>
<td>2.45 1.45-4.12</td>
<td>0.001</td>
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<td>1</td>
<td>1</td>
<td>1</td>
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<tr>
<td>Yes</td>
<td>2.31 1.52-3.51</td>
<td>&lt;0.001</td>
<td>2.06 1.24-3.44</td>
<td>&lt;0.001</td>
<td>2.45 1.45-4.12</td>
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<td>Less than high school</td>
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<td>1.23 0.88-1.72</td>
<td>0.220</td>
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<td>1</td>
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<tr>
<td>Paternal Diabetes</td>
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<td></td>
<td></td>
<td></td>
</tr>
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<td>1</td>
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<tr>
<td>Yes</td>
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<td>1.55 0.64-3.73</td>
<td>&lt;0.001</td>
<td>1.67 0.69-4.02</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Place of residence</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Rural</td>
<td>2.03 1.38-2.99</td>
<td>&lt;0.001</td>
<td>1.69 1.08-2.64</td>
<td>0.058</td>
<td>1.63 1.03-2.58</td>
<td>0.089</td>
</tr>
<tr>
<td>Semi-urban</td>
<td>1.24 0.82-1.88</td>
<td>1.26 0.80-2.04</td>
<td>0.003</td>
<td>0.289</td>
<td>0.003</td>
<td>0.289</td>
</tr>
<tr>
<td>Urban</td>
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<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Gestational diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Yes</td>
<td>1.85 1.10-3.10</td>
<td>&lt;0.001</td>
<td>1.11 0.61-2.03</td>
<td>0.713</td>
<td>1.04 0.56-1.92</td>
<td>0.885</td>
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<tr>
<td>Maternal BMI</td>
<td>1.11 1.08-1.14</td>
<td>&lt;0.001</td>
<td>1.08 1.05-1.12</td>
<td>&lt;0.001</td>
<td>1.06 1.03-1.10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Exclusive Breast feeding</td>
<td>0.003</td>
<td>0.289</td>
<td>0.80 0.57-1.13</td>
<td>0.221</td>
<td>0.80 0.57-1.13</td>
<td>0.221</td>
</tr>
<tr>
<td>Less than 3 months</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>3 months or more</td>
<td>0.63 0.47-0.85</td>
<td>0.003</td>
<td>0.83 0.59-1.16</td>
<td>0.85</td>
<td>0.80 0.57-1.13</td>
<td>0.221</td>
</tr>
<tr>
<td>Birth weight</td>
<td>2.44 1.85-3.22</td>
<td>&lt;0.001</td>
<td>3.12 2.14-4.56</td>
<td>0.057</td>
<td>2.14-4.56</td>
<td>0.001</td>
</tr>
<tr>
<td>Duration of gestation</td>
<td>1.03 0.95-1.11</td>
<td>0.457</td>
<td>0.85 0.75-0.97</td>
<td>0.016</td>
<td>0.75-0.97</td>
<td>0.016</td>
</tr>
</tbody>
</table>

BMI=body mass index, OR= odds ratio, CI=confidence interval
OR of 1 indicates the reference category of each variable
1 Univariate analysis for the association between child overweight and potential confounders.
2 Results are adjusted for child’s sex, maternal smoking during pregnancy, maternal basic education, paternal diabetes, place of residence, gestational diabetes, maternal BMI, exclusive breast feeding.
3 Additional adjustments for birth weight and duration of gestation (adjusted + birth weight and duration of gestation).
Finally the model was adjusted for birth weight and duration of gestation. The reason for adding birth weight at the end was that it could be a mediator for the association between rate of gestational weight gain and child overweight and might lie in the causal pathway. However addition of birth weight and duration of gestation to the model made the association stronger (table 5).

5.6. Results for maternal BMI interaction

Further analysis for finding an effect of maternal BMI on the association between rate of gestational weight gain and child overweight revealed non-significant interaction (interaction p=0.22). It revealed that the association between the lowest quarter of rate of gestational weight gain and offspring overweight at the age of 3 years was independent of maternal BMI.
6. DISCUSSION

6.1. Main findings of the study

The aim of this study was to explore an association between maternal weight gain in pregnancy and child weight. To evaluate this effect, gestational weight gain was analyzed as a categorized variable because of the non-linear association of the rate of gestational weight gain with child BMI. This primary exposure variable was taken as the quarters of rate of gestational weight gain and child overweight was assessed at 3 years according to IOTF criteria for BMI. For the purpose of analysis, the middle two quarters were combined as one category and used as a reference. Unadjusted results for the relationship of child overweight revealed a positive association both for the lowest and highest quarters of categorized rate of gestational weight gain. The association discovered was somewhat U-shaped with overweight children lying at both the upper and lower extremes of rate of gestational weight gain. Adjusting the association for the child’s sex, maternal smoking during pregnancy, maternal basic education, paternal diabetes mellitus, location of residence, gestational diabetes mellitus, maternal BMI and exclusive breast feeding, attenuated the results. Statistically significant results for overweight were discovered only for the lowest quarter. Odds ratio for the highest quarter was no more significant after controlling for covariates.

The results were further investigated by adding birth weight and duration of gestation to the final model. The reason for investigating the final model with birth weight was that it might be a mediator for the association and may lie in the causal pathway. This additional adjustment for birth weight shifted the association and made it stronger. This implies a suppression effect of birth weight on the association between categorized rate of gestational weight gain and child overweight. This effect could be explained as “a situation in which the magnitude of the relationship between an independent variable and a dependent variable becomes larger when a third variable is included would indicate suppression” (MacKinnon et al., 2000).

Another important feature of the present analysis was to explore the effect of maternal BMI on the association between rate of gestational weight gain and child overweight. Our results showed that obese women were gaining less weight during pregnancy and therefore maternal BMI may possibly modify the association of rate of gestational weight gain with offspring overweight. To analyze this
effect, an interaction term for maternal BMI and categorized rate of gestational weight gain was added to the final model. The results revealed no effect modification of the association by maternal BMI therefore, concluding that the association between rate of gestational weight gain and child overweight is independent of maternal BMI.

The study found that, compared to women gaining average weight during pregnancy, women who gain less weight make their children prone to obesity later in life.

The results also revealed socio-demographic, perinatal and antenatal factors to be predictors of overweight in children. Overweight was more prevalent in girls, in children resident in a rural municipality and whose mothers had smoked during pregnancy. Other factors included low maternal basic and vocational education, paternal diabetes, gestational diabetes, maternal and paternal BMI, children who are exclusively breast fed for less than 3 months or totally breast fed for less than 6 months and in children with high birth weight.

6.2. Strengths of the study

To evaluate the strengths of our study I analyzed the statistical procedure used in the study, estimates of measurements (child’s BMI), the extent of controlling for covariates and generalizability of the results to the population.

Firstly, binary logistic regression was used for the analysis. This statistical method provided a good basis for our analysis and effectively verified the relationship between rate of gestational weight gain and child overweight after controlling for various confounding factors.

Secondly, the study included 2143 mother-child pairs from the Tampere region. The inclusion of such a big cohort decreased the chances of random error. Furthermore, it is the largest sample to date for investigating an association between rate of gestational weight gain and child overweight.

Thirdly, the study included participants from various socio-demographic backgrounds with different parental age levels, health conditions and educational status. This wide range of variables allowed us to study the association after controlling for various confounding factors.
Fourthly, good estimates of child measurements were important for accurate application and interpretation of the results. In our study, children’s weight and height measurements were assessed at regular clinical visits by trained nurses in the clinics. Provision of these anthropometries by trained nurses was the basis for increased internal validity of the study.

Fifthly, selecting rate of gestational weight gain as the primary exposure variable strengthened our results since rate of gestational weight gain, calculates weight gain between two points and unlike total gestational weight gain does not require pre-pregnancy weight measurements (Amorim et al., 2008).

Finally I analyzed the concept of external validity that is to check whether the results can be generalized from the sample to the entire population. The criterion for inclusion in our study was HLA-conferred susceptibility to Type 1 diabetes at birth. Although, the study included children who were vulnerable to developing type 1 diabetes, yet they represent a large part of Finnish children. Taking this scenario in consideration, the concept of external validity can be achieved and it is likely that the results could be generalized to the population.

6.3. Limitations of the study

Just as in any research work this study comprises some limitations. To assess these limitations I analyzed maternal BMI measurements. Our study did not include data on maternal pre-pregnancy BMI, rather the mothers’ weight and height measurements at first antenatal visit were used as a proxy for maternal pre-pregnancy BMI. Only using maternal first visit BMI as a substitute for maternal pre-pregnancy BMI may have greatly biased our results as normal weight women could be misclassified as overweight if they have presented for their first antenatal visit at the end of pregnancy. However, this situation was dealt with by extrapolating the maternal BMI to the tenth week of gestation for women who presented after the tenth week of their pregnancy. Nevertheless, there are chances of slight bias in our study, as there may be a gain of 1-2 kg in weight in the first trimester of pregnancy (Pitkin et al., 1976).

Most of the previous research had investigated the association of total gestational weight gain with child overweight. Due to lack of pre-pregnancy BMI in our study it was not possible to calculate
total gestational weight gain correctly. Lack of this variable limited the comparability of our results with other research.

Another shortcoming in the study was the number of subjects with missing values. Considering the wide range of missing values, it is possible that information is different for those included in the study and those excluded from the study. This difference in information might bias our results because the association might be different between subjects with missing values and subjects with complete data. For instance, because of the large missing value for paternal BMI it was excluded from our analysis.

6.4. Relation to previous studies

Few studies have examined the association of gestational weight gain with child overweight and obesity. Studies which examine this association have used different measurement criteria for assessing gestational weight gain. The most common measurement used is total gestational weight gain. Total gestational weight gain is most frequently used as a categorized variable. It is categorized either according to IOM (2009) guidelines or the study group’s own categories. Very few have considered rate of gestational weight gain as their exposure variable.

6.4.1. Association between the rate of gestational weight gain and offspring overweight

The unadjusted results of our study bring an insight into understanding the relationship of rate of gestational weight gain with child overweight. These unadjusted results show that, compared to average weight gain both high and low rate of gestational weight gain are associated with child overweight, therefore discovering somewhat U-shaped association between the exposure and outcome variables. The results are in accordance with the study by Stuebe Am et al. (2009), who investigated the association between maternal weight gain during pregnancy and daughter’s weight at 18 years of age. They found a U-shaped association of total gestational weight gain with daughters’ overweight. Finding by Croizer et al. (2010) are also in correspondence with the results of the current study. They showed a U-shaped association of maternal total weight gain during pregnancy with child fat mass at 4 and 6 years of age. However the association was significant only for 6 years old children. In addition, our unadjusted results correlates to the unadjusted results by
Oken et al. (2008), who found a U-shaped association for total gestational weight gain and offspring overweight. Our study differs from the above three studies in the context of gestational weight gain variable. Unlike our study, which examined pregnancy weight gain as rate of gestational weight gain, these three studies have analyzed it as total gestational weight gain. Furthermore, two of the studies (Croizer et al., 2010; Oken et al., 2008) have investigated the association between pregnancy weight gain and child obesity according to IOM guidelines.

Rate of gestational weight gain, the main exposure variable of the study provides an intricate insight into discovering the earliest exposures to potential life events. Certainly, intrauterine period reflects a critical period in the development of life (William H Dietz., 1994). However, risk factors for an individual health are not just limited to the in utero setting but comprise a complex interaction of intrauterine and postnatal environment. (Oken et al., 2003). Therefore, an association of decreased weight gain during pregnancy and child obesity can possibly be explained by a complex relation of antenatal and postnatal factors. For instance, Barker (2004) associates maternal undernutrition during pregnancy with low birth weight which is then linked to catch up growth and finally to chronic diseases later in life (Barker, 2004). Our study found positive association of decreased rate of gestational weight gain both with child obesity (Table 7) and low birth weight (Table 6). Scrutinizing this finding in the context of our study suggest that decreased weight gain during pregnancy can lead to low birth weight babies, who then might be exposed to catch up growth and later obesity. Similarly, Stube et al. (2009) correlates their finding, for the U-shaped association between total gestational weight gain and offspring overweight, with that of Barker’s (2004) phenomenon.

Not all of the studies show a positive association between maternal weight gain during pregnancy and child obesity later in life. Whitaker et al. (2004) found no association between net gestational weight gain and child obesity at 2, 3 and 4 years of age. In addition, Gale et al. (2007) found no association of total gestational weight gain with child body fat composition at the age of 9 years.

Most of the studies, unlike our results, established a direct association of increased gestational weight gain with child overweight (Moreira et al., 2007; Oken et al., 2007; Olson et al., 2008; Wrotnick et al., 2008; Kleiser et al., 2009; Kries et al., 2010).
6.4.2. Rate of gestational weight gain as the primary exposure variable

Very few studies have taken rate of gestational weight gain as their exposure variable. Oken et al. (2009) found an association for child obesity per 0.1kg/week of gain for normal, overweight and obese women. The association in their study was only significant for normal weight women. However, our study differs from this study in the context of rate of gestational weight gain taken as categorized rather than a continuous variable. Andersen et al. (2010) analyses the association of rate of gestational weight gain and child BMI at 7 years of age. They have taken the rate of gestational weight gain in three phases during pregnancy and suggests that rate of gestational weight gain in the last phase has a positive association with that of child obesity.

6.4.3. Interaction of maternal BMI

An interesting feature of our study was to explore the potential modifying effect of maternal BMI on the association between rate of gestational weight gain and child overweight. For instance, to check that although obese women may gain less weight during pregnancy, they may expose their children to subsequent obesity through an effect of higher maternal BMI. When the study was investigated for maternal BMI interaction, we found no effect modification of the association by maternal BMI. This may implicate that the association between maternal pregnancy weight gain and child overweight is independent of maternal pre-pregnancy BMI, however we cannot exclude lack of power in the interaction analysis as a potential explanation for not finding a modifying effect of maternal BMI on the association between rate of gestational weight gain and offspring overweight.

Our results correspond to those by Oken et al. (2007 and 2008), Andersen et al. (2010) and Croizer et al. (2010). Oken et al. (2007) studied a sample of 1044 mother-child pairs and reported a positive association between total gestational weight gain and child overweight at the age of 3 years, giving no effect modification by maternal BMI (Oken et al., 2007). In another study, Andersen et al. (2010) examined the association between rate of gestational weight gain and offspring BMI at 7 years of age. They found no effect modification of the association by maternal BMI. In still another study of 11,994 adolescents aged 9-14 years, maternal gestational weight gain was associated with adolescent overweight and obesity, which was also not modified by maternal BMI (Oken et al., 2008). Furthermore, Croizer et al. (2010), who found a U-shaped association between total
gestational weight gain and child fat mass at 6 years, did not report any effect modification of the association by maternal BMI.

However, our results are not in accordance with all the previous studies. Wrotniak et al. (2008) reported a positive association for the relationship between excessive gestational weight gain and child obesity in 7 year old children and found that the risk was highest for underweight mothers. In a relatively small sample of 208 mother child pairs, Olson et al. (2008) found a positive association for excessive weight during gestation and child overweight at 3 years. The association was strongest for overweight (including obese) women.

6.4.4. Association of the covariates with child overweight

The results of the association of the covariates with child overweight are similar to many but not all studies. For instance, in our study prolonged duration of exclusive (less or 3 months versus more than 3 months) and total breast feeding (less or 6 months versus more than 6 months) provided protection against obesity in childhood. Gillman et al. (2001) discovered a negative association between duration of breast feeding and child overweight at 9-14 years of age. Similarly studies by von Kries et al. (1999) and Kalies et al. (2005) encouraged prolonged duration of breast feeding for good health outcomes. In contrast, Huus et al. (2008) did not support the protective effect of breast feeding against obesity in 5 year old children. Nor did Araújo et al. (2006) find that breast feeding gave a protective effect against overweight in 4 years old children.

Intrauterine exposure to cigarette smoke is a risk factor for overweight in childhood (Tosche et al., 2002; von Kries et al., 2002). Our study found that smoking during pregnancy was associated with child overweight in 3 year old children. Similar results are reported by Tosche et al. (2002) and von Kries et al. (2002), who discovered a positive association between child overweight and smoking during pregnancy. However, our results are not in accordance with a study by Sharma et al. (2008). Their study included data from nine American and two tribal nations and examined the association for child overweight and maternal smoking during pregnancy after stratifying it by maternal race/ethnicity. The study did not find an association between cigarette smoking and overweight in 2-4 year old children among Hispanics, American Indians or Alaska Natives, and Asian or Pacific Islanders (Sharma et al., 2008).
Birth weight in our study is associated with obesity. This is in accordance with Seidman et al. (1991), who found positive association of birth weight with obesity at 17 years of age. In contrast, Curhan et al. (1996), discovered low birth weight as a risk factor for diabetes and hypertension.

6.5. Public health implementation

The outcomes of this study are not totally at odds with previous literature. These results are in accordance with the conclusion drawn from a number of prior studies (Stuebe Am et al., 2009; Oken et al., 2007; 2008; Andersen et al., 2010). Therefore previous work underpins the importance of the present results and confirms the fact that the findings of this study are applicable to public health implementation.

However, some previous studies differed from the present study and discovered a positive association between increased gestational weight gain and child overweight. This shift of association in a positive direction may provide diverging interventions which would involve only those women who gain more weight during pregnancy. In the light of our study, women who gain less weight during pregnancy have a high risk for child obesity. Therefore, appropriate gestational weight gain guidelines endeavoring to promote healthy outcome of pregnancy must be provided for all pregnant women.

Public health implications rely on the slogan “prevention is better than cure”. To accomplish their goal public health personnel need to identify the earliest predictors of child overweight and obesity, namely intrauterine environment. Therefore, guidelines for healthy weight gain during pregnancy should be made a part of maternal and child health care interventions.

In addition, health promotion programs need to focus on the factors which served as the main confounding variables of the study. Therefore, interventions aiming at promoting education, breast feeding and discouraging smoking during pregnancy are recommended for health improving polices.
6.6. Further research proposals

The inconsistent association of rate of gestational weight gain with offspring overweight demands further examination for an explanation of this variation. I would encourage further research for evaluating the effect of maternal BMI on the association between pregnancy weight gain and child overweight. Another suggestion would be to explore other aspects of obesity, such as child nutritional behavior and physical activity, in the context of investigating maternal weight gain during pregnancy in the etiology of child overweight.
7. CONCLUSION

Our study aimed to investigate the association of rate of gestational weight gain with child overweight at 3 years of age. Compared to average rate of gestational weight gain, lower and higher rates of gestational weight gain were associated with increased risk of offspring overweight. However, adjusting for confounders attenuated the results; the association between higher rate of gestational weight gain and child overweight (compared to the average rate of gestational weight gain) was no longer statistically significant, whereas decreased rate of gestational weight gain was still statistically significantly associated with a higher risk of offspring overweight. We did not observe a modifying effect of maternal BMI on this association.

The inconsistent results for the association of the rate of gestational weight gain with child overweight and maternal BMI demand further examination of the association. We further recommend that nutrition and physical activity of the child is included in any further studies of the relationship.

Even if the study leaves open questions for further research, it presents a goal to policy makers, which is aimed at detecting earliest predictor of child overweight and obesity. Policy makers need to promote maternal and child health care through appropriate knowledge, attitude and tools aimed at promoting optimal gestational weight gain. In addition, health promotion activities need to focus on promoting parental education, breastfeeding and discouraging smoking during pregnancy.
8. ACKNOWLEDGEMENTS

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9. REFERENCES


Andersen CS, Gmborg M, Sørensen TIA, Nohr EA. Weight gain in different periods of pregnancy and offspring’s body mass index at 7 years of age. Int J Pediatr obes 2011;6(2-2): e179-86.


de Onis M, Blössner M, Borghi E. Global prevalence and trends in overweight and obesity among preschool children. Am J Clin Nutr 2010;92.1257-64.


Gillman MW, Rifas-Shiman SL, Camargo CA, Berkey CS, Frazier AL, Rockett HRH, Field AE, Colditz GA. Risk of overweight among adolescents who were breastfed as infants. JAMA 2001;285: 2461-2467.


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