Gestational Weight Gain
Implications of an Antenatal Lifestyle Intervention
to Cornelis and Hampus
ANN-KRISTIN RÖNNBERG

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Implications of an Antenatal Lifestyle Intervention
Abstract


Background: Excessive gestational weight gain (GWG) is common in developed countries and is associated with an increased risk of maternal and offspring morbidity. Evidence regarding efficacy and safety of antenatal lifestyle intervention is limited in terms of both systematic reviews and original trials. This thesis is based on the need to further explore this research area.

Objectives: To assess and grade current evidence and evaluate short and long-term effects of an antenatal lifestyle intervention on women and their offspring

Materials: Controlled trials of intervention published before August 2009 were systematically searched and reviewed. A randomized controlled trial (RCT) including 445 healthy women aged >18 years with a body mass index (BMI) ≥19 and ≤16 weeks pregnant and their offspring was performed during 2007-2015 in Örebro Region, Sweden.

Methods: The Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system was used for review. Our RCT (called the VIGA trial) compared standard care with a composite intervention consisting of education, application of a personalized weight graph, prescription of exercise and more frequent monitoring of weight. Standardized measures of weight and height in offspring were analysed based on World Health Organization (WHO) Child Growth Standards.

Results: Quality of evidence across the studies published pre-August 2009 was concluded to be very low. Our intervention significantly reduced mean GWG (kg) but the proportion of women with excessive GWG, according to recommendations, was not significantly reduced. Short-term postpartum weight retention (PPWR) was significantly lower after the intervention but no significant difference remained 1 year after delivery. Offspring mean BMI z-scores or proportion of obesity did not differ between study groups at either birth or age 5.

Conclusions: The antenatal lifestyle intervention reduced mean GWG and short-term PPWR but no long-term effects on maternal weight retention or offspring obesity were seen. Alternative modes and timing of intervention should be considered in future research. Reducing the prevalence of pre-conception obesity must still be considered the primary means to improve maternal and fetal outcome.

Keywords: Gestational weight gain, maternal health, pregnancy, prevention of obesity, lifestyle intervention, childhood obesity.

Ann-Kristin Rönnberg, School of Health and Medical Sciences, Örebro University, SE-701 82 Örebro, Sweden, ann-kristin.ronnberg@regionorebrolan.se
Abstract


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LIST OF PUBLICATIONS


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ABBREVIATIONS

AGA  Appropriate for gestational age
BMI  Body mass index
CI   Confidence interval
CS   Caesarean section
FaR  Fysisk aktivitet på recept
     (Akronym for prescribed physical activity in Swedish)
FBW  Fetal birth weight
GDM  Gestational diabetes mellitus
GWG  Gestational weight gain
HT   Hypertension
IOM  Institute of Medicine
LGA  Large for gestational age
LMP  Last menstrual period
OR   Odds ratio
PE   Preeclampsia
PHT  Pregnancy induced hypertension
PP   Postpartum
PPWR Postpartum weight retention
SGA  Small for gestational age
SD   Standard deviation
VIGA Vikt Intervention under Graviditet (Trial akronym in Swedish)
WHO  World Health Organization
The first measured weight in pregnancy if first visit occurred at <16 weeks of pregnancy according to LMP or early ultrasound dating.

**DEFINITIONS**

Pre-pregnancy weight  
The first measured weight in pregnancy if first visit occurred at <16 weeks of pregnancy according to LMP or early ultrasound dating.

Gestational weight gain  
Bodyweight at delivery minus bodyweight at <16 w of pregnancy.

Postpartum weight retention  
Bodyweight at postpartum visit minus bodyweight at <16 w of pregnancy.

Preterm delivery  
Birth < 37 weeks’ gestation.

Perinatal mortality  
Stillbirths and deaths during the first seven days postpartum independent of gestational age.
INTRODUCTION

Excessive weight gain during pregnancy is common in developed countries and has been linked to an increased risk of complications during pregnancy, delivery and the postpartum period for both mother and child. High gestational weight gain (GWG) is primarily linked to morbidity associated with high fetal birth weight (FBW) (1) but women with excessive GWG are also more likely to have high postpartum weight retention (PPWR) (2) and their offspring have been reported to have an increased risk of becoming overweight or obese (3, 4). An effective intervention in maternal health care aimed at avoiding or limiting excessive GWG, could theoretically improve not only obstetric outcome but also long term-health in mother and child by reducing the risk of developing obesity.

The maternal and fetal risk associated with excessive weight gain however, has to be balanced against the risk associated with inadequate GWG. Low GWG or gestational weight loss (GWL) has been linked to negative obstetric outcome such as preterm birth, fetal growth restriction, and failure to initiate breast-feeding as well as increased infant mortality (5-7).

Maternal pre-pregnancy BMI modifies the association between GWG and many of these health outcomes (Figure 1) so that determining the optimal range of GWG for women in different BMI categories, balancing the risks associated with low and high gain for mother and child, has proved to be a challenge. In 1990 the Institute of Medicine (IOM) issued the first evidence-based guidelines for GWG in relation to maternal pre-pregnancy BMI. Primarily it was concern for women with pre-pregnancy underweight and low GWG that spurred the creation of the first IOM guidelines (8). Promted by an increased prevalence of overweight and obesity in women of reproductive age and the observation that an increasing number of women were gaining excessively during pregnancy, the IOM reconvened and revised their guidelines in 2009, adding an upper limit for GWG in women with pre-pregnancy obesity and at the same time adopting the World Health Organization (WHO) classifications for BMI (9) (Table 1).

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<th>BMI</th>
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<td>&gt;30</td>
<td>5-9</td>
<td>0.22</td>
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Table 1. Institute of Medicine (IOM) recommendations of 2009 for gestational weight gain (GWG) based on maternal pre-pregnancy body mass index (BMI).
Gestational weight gain (GWG) within IOM ranges was consistently associated with good maternal and fetal outcomes. Evidence at the time was judged inadequate to provide specific guidelines by grade of obesity or to support recommendations on GWG ≤ 5 kg or gestational weight loss (GWL) for obese women.

Observational studies have continued to provide ambiguous results on the subject. Several large population-based cohort studies published after the release of the IOM guidelines considered it safe to set more restrictive weight gain limitations for obese women (11-14). A systematic review published in 2010 states that overweight and obese women who gain less weight than the ranges recommended by the IOM do not have an increased risk of having a low birth weight infant (15). Other researchers have argued that even the present IOM recommendations may be too restrictive for severely obese women and may be associated with increased rates of preterm births, small-for-gestational-age (SGA) infants and perinatal mortality (7). Future studies may provide sufficient evidence to lead to customized recommendations on GWG in relation not only to grade of pre-pregnancy obesity but also to individual maternal metabolic status and genetic disposition for obesity.

An increasing awareness among obstetricians about the high prevalence of excessive GWG among Swedish women and the growing base of evidence regarding associations with negative short-term and long-term maternal and fetal outcome prompted this thesis which encompasses research in the field of antenatal lifestyle intervention with the aim to limit excessive GWG.

Figure 1. Gestational weight gain (GWG)-specific absolute risks for fetal and maternal outcome based on pre-pregnancy body mass index (BMI) (Weight gain during pregnancy: reexamining the guidelines. Washington, DC: National Academies Press; 2009, Appendix G, Reprinted with permission from publisher) (10).
Observational studies have continued to provide ambiguous results on the subject. Several large population-based cohort studies published after the release of the IOM guidelines considered it safe to set more restrictive weight gain limitations for obese women (11-14). A systematic review published in 2010 states that overweight and obese women who gain less weight than the ranges recommended by the IOM do not have an increased risk of having a low birth weight infant (15). Other researchers have argued that even the present IOM recommendations may be too restrictive for severely obese women and may be associated with increased rates of preterm births, small-for-gestational-age (SGA) infants and perinatal mortality (7). Future studies may provide sufficient evidence to lead to customized recommendations on GWG in relation not only to grade of pre-pregnancy obesity but also to individual maternal metabolic status and genetic disposition for obesity.

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BACKGROUND

Composition and timing of weight gain during pregnancy
A certain amount of weight gain is expected during pregnancy and considered essential to provide the nutritional support for fetal growth and also to prepare for lactation. The placenta, growing uterus and fetus, amniotic fluid, expansion of maternal blood volume, breast tissue as well as maternal adipose tissue and extracellular fluid all contribute to total maternal GWG (Figure 2) (16).

Excess weight that is not attributed to products of conception contributes to an increase in maternal energy stores (17). Knowledge about the degree to which pregnant women store excess energy in adipose tissue, and the sites where they do so, is still limited but excess GWG has primarily been associated with maternal fat mass accrual and not with lean mass accrual (18). Studies have so far focused mainly on women with pre-pregnancy overweight and obesity, but metabolic rate as well as the disposition to accumulate fat mass may however not be similar among normal or underweight women.

The maternal gain in adipose tissue can be deposited into visceral (central) or subcutaneous (peripheral) adipose tissue depots. Factors influencing site of fat deposition are likely to be similar with non-pregnant women but evidence here is also still lacking. Site of fat accrual is considered of importance because fat in visceral depots and around central organs such as the liver is associated with insulin resistance, risk

Figure 2. Composites of gestational weight gain (GWG) (kg).

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of cardiovascular disease, and the metabolic syndrome (19). Further understanding of the composition of excess weight gained during pregnancy is important since the potential metabolic impact and contribution to long-term risk is likely to vary depending on amount of fat mass accrued as well as the site of the fat depot (19).

During the first trimester of pregnancy approximately 0.5-2 kg weight gain is expected (20). The initial gain is mainly due to early placental development and expansion of maternal blood volume. Fetal weight does not contribute significantly to weight gain in the first trimester. The potential difference in fetal and maternal outcome depending on the timing of excessive weight gain is still unclear. Early excessive weight gain has been associated with impaired maternal glucose tolerance later in pregnancy (21, 22) and greater infant adiposity at birth (22, 23) independent of total maternal GWG. Early excessive weight gain has also been suggested to be predictive of total GWG. The predictive value differs however, depending on pre-pregnancy BMI, according to a recent study (22). In that study, women with a normal pre-pregnancy BMI had a 70% probability of excess total GWG if they gained excess weight already in first trimester, while overweight and obese women had a 90% probability of excess total GWG (22) if they gained excessively early in pregnancy. Further knowledge on the relevance of early GWG has implications for pre-conception counselling since very few women are admitted to maternal health care and advised on GWG in the first trimester of pregnancy.

**Gestational weight gain from a Swedish perspective**

The IOM guidelines have not been systematically implemented in Swedish maternal health care. Regional differences in addressing issues of maternal weight gain are reported and a variety of efforts are being made to help women achieve healthy weight goals before, during and after their pregnancies.

According to data from the Swedish Pregnancy Register, excessive GWG is mainly prevalent among women with pre-pregnancy overweight (BMI 25-29) or obesity Grade I (BMI 30-35). In 2013, mean GWG among women with pre-pregnancy BMI 25-29 was above IOM recommendations in all (21 out of 21) Swedish health care regions. In all but one region, mean GWG among obese (BMI >30) women was above IOM recommendations. Despite various efforts to limit excessive GWG there has been a tendency during 2013-2015 towards increasing GWG in all BMI groups except underweight women (24).
Among pregnant women with Grade II-III obesity (BMI >35) the majority of health care regions reported a mean GWG within recommended ranges (5-9 kg). Inadequate GWG was reported among underweight women in 9 out of 21 regions, setting focus on different issues needing to be addressed when discussing implementation of lifestyle intervention regarding GWG among underweight women.

Johansson et al recently published z-score charts of GWG for gestational age and maternal BMI using data from pregnancies in a geographically defined area in southern Sweden (Stockholm and Gotland) (25).
Figure 4. Smoothed percentiles and standard deviations (SDs), of gestational weight gain (GWG) among 141,767 women who gave birth in the Stockholm and Gotland regions of Sweden in 2008–2014. Reported by pre-pregnancy BMI group and with Institute of Medicine (IOM) recommendations on range of GWG in shaded areas (25). (Reprinted with permission from publisher)
Median weight gains in this Swedish population were higher than IOM recommendations for many BMI categories (from overweight to obesity Grade II). Median GWG among women with obesity Grade III (BMI >40) was however, within the IOM recommendations, but 10% of women in this group gained essentially no weight (0.5 kg) during pregnancy (Figure 4). Among women with normal BMI, the median GWG was within the IOM recommendations, whereas in underweight women, the median was at the lower limit. The observed distributions of GWG in this Swedish population were considerably broader than the range of the IOM recommendations.

The proportion of Swedish women with overweight or obesity (BMI>25) at admission to maternal health care has increased from 25.4% in 1992 to 38.1% in 2014. The study area for the VIGA trial, discussed in this thesis, had similar distribution of prepregnancy BMI at admission to maternal health care during the study period (Figure 5).

![Figure 5. Distribution of maternal pre-pregnancy body mass index (BMI) in the study area at the start of recruitment to the VIGA trial in 2008.](image-url)
Long-term maternal effects

Excessive GWG can affect the woman’s subsequent weight-related health. There are a number of observational studies linking excessive GWG to excessive PPWR (26) and increased risk of subsequent obesity (27). An extensive meta-analysis by Nehring et al concluded that excess weight gained in pregnancy was still retained >15 years postpartum (28). The degree of weight retention is, however, highly variable and women with pre-pregnancy overweight or obesity are considered more likely to experience a high degree of PPWR (15, 29).

Entering a potential subsequent pregnancy with a pre-pregnancy BMI >30 has implications for a number of maternal and fetal obstetric outcomes (30). Complications during pregnancy, delivery and postpartum, associated with maternal obesity will not be covered in this thesis other than to be mentioned here as a consequence of previous excessive GWG. The long-term impact of PPWR on subsequent pregnancies is, however, an important factor motivating intervention to reach GWG within recommended range among women entering first pregnancy with normal BMI.

Figure 6. Consequences of excessive gestational weight gain (GWG) in women of reproductive age over the course of multiple pregnancies.

Weight gain triggered by consecutive pregnancies contributes to the increased prevalence of overweight and obesity in reproductive age and postmenopausal women (27, 31, 32), and metabolic and/or behavioural changes that occur during the pregnancy
are likely to play a role in the weight status of mothers postpartum and in future life.

The risk of becoming overweight or obese seems to be even greater when excessive GWG and/or PPWR occurs in successive pregnancies and when combined with short inter-pregnancy intervals (33, 34). In recent data presented by Bogaerts et al, weight retention of ≥2 BMI units between first and second pregnancy was associated with an increased risk of gestational diabetes mellitus (GDM), pregnancy induced hypertension (PHT), caesarean section (CS) and large for gestational age (LGA) offspring. These findings were not dependent on the woman’s previous BMI but applied also to women still within normal BMI ranges. This is concurrent with earlier data by Villamor et al (2006) linking inter-pregnancy weight changes of >3 BMI units to similar negative obstetric outcomes (35).

The association between maternal inter-pregnancy weight gain and risk of stillbirth and infant mortality has been analysed in data from the Swedish Medical Birth Register where inter-pregnancy weight gain >4 BMI units was associated to an increased risk of stillbirth regardless of BMI status at first pregnancy. An increased risk of infant mortality was seen among offspring to women with normal weight at first pregnancy and inter-pregnancy gain >2 BMI units. Moreover, in overweight women, weight loss between pregnancies reduced the risk of neonatal mortality among second offspring. These findings further support that inter-pregnancy weight gain should be prevented and that weight loss should be promoted before second pregnancy in overweight women (36).

**Trans-generational effects**

The increasing prevalence of childhood obesity in developed countries is considered a major threat to future public health. Effective early preventive efforts are important as health consequences of obesity already begin during childhood and treatment of already established obesity has shown limited effect (37). Besides physical activity (PA), diet, parental BMI, environmental factors and genetics, the intrauterine environment is considered to influence the risk of developing childhood obesity. Excessive maternal GWG has been associated not only with significantly higher FBW, but also with childhood overweight/obesity (3, 4). Whether the association is explained by direct intra-uterine causal mechanisms or by environmental, lifestyle-related or genetic characteristics is still unclear.

Potential intra-uterine programming effects of excessive maternal GWG should be considered. The fetal overnutrition hypothesis suggests that increased placental transfer of nutrients to the developing fetus in women with excessive GWG may subsequently affect fetal development, fetal fat deposition and the development of the hypothalamic–endocrine system, which controls appetite and energy metabolism (38). This may theoretically predispose offspring to a greater risk of adverse obesity-related health outcomes in later life. Effective strategies to avoid or limit excessive
maternal GWG could therefore have a potential for positive long-term health effects for the offspring.

**Lifestyle intervention in relation to pregnancy**

Pregnancy has been proposed to be an optimal time for implementing positive changes in lifestyle behaviours. Multiple visits to maternal health care during pregnancy present many opportunities for different types of motivational intervention and information about the importance of healthy lifestyle for both mother and child. Positive results in achieving smoking cessation have spurred maternal health care staff to address other health-related factors such as diet and PA as well as screening for alcohol abuse and domestic violence during pregnancy. Diet and PA are the main elements of weight control during pregnancy since the option of pharmaceutical or surgical methods is limited due to issues of safety. An exception is Metformin, which has been tried among obese women without diabetes, with variable results: one study showed significant reduction of GWG compared with placebo among obese women, but no effect on FBW (39), and another concluded that there was no effect on GWG or FBW (40).

The optimal mode for effective intervention regarding GWG as well as the optimal timing is still unclear and this lack of evidence was also the rationale for this thesis. A review of antenatal interventions, published in 2009, will be presented as Paper I (41) in this thesis. A more recent meta-analysis has been published by the Cochrane Collaboration in 2015 (42), concluding that high-quality evidence indicates that diet or exercise, or both combined, during pregnancy can reduce the risk of excessive GWG. Relevant outcomes such as risk of CS, macrosomia, preterm delivery, pre-eclampsia and poor neonatal outcome were however, not significantly reduced by interventions included in the Cochrane review. No significant difference in effect on GWG between diet and PA intervention was detected.

Considering that pre-pregnancy maternal BMI is considered the most important factor determining risk of adverse events during pregnancy, delivery and postpartum, an effective pre-conception intervention would be preferable. The importance of entering pregnancy with a healthy weight cannot be overstated. No randomized controlled trials (RCTs) that assessed the effect of pre-conception health programmes and interventions in overweight and obese women with the aim of improving pregnancy outcomes was, however, found in a recently published Cochrane search (43). Until the effectiveness of pre-conception health programmes and interventions can be established, no strong recommendations can be made.
Figure 7. Alternative timing for lifestyle intervention in relation to gestation.

An alternative time for intervention is post-delivery/inter-pregnancy. The effect of PA strategies on weight loss in women postpartum was reviewed by Nascimento et al in 2014 (44) and their meta-analysis as well as results presented by Van der Pligt et al in 2013 (45) showed significant effects of lifestyle interventions initiated post-delivery on weight loss. Interventions during the postpartum period may have the additional benefit of focusing on a period when many women report high motivation for weight loss and when the potential risk of negative effects on intra-uterine fetal growth is no longer an issue. One Cochrane review on postpartum intervention concludes that both diet and exercise combined and diet alone helped women to lose weight after childbirth (46). However, improved maternal cardiorespiratory fitness and preservation of fat-free mass indicate that composite interventions including exercise are preferred. The postpartum interventions seemed not to affect breastfeeding performance but more evidence is needed to confirm whether diet and/or exercise, have negative effects on mother or child.

Reviewing scientific evidence – the GRADE system

Introducing new treatments, medical technology or interventions in healthcare is always characterized by some uncertainty. The base of evidence considered is often heterogenic in quality and provides results of varying coherence. The importance of methods for systematic evaluation of published results has been increasingly acknowledged in the research community and among decision makers during the last three decades. Several more or less complex systems for grading of evidence have been constructed and applied. The need for an internationally accepted system led to development of the GRADE system, originating from an informal international
collaboration of primarily methodologists, and introduced in 2004 (47). The GRADE working group has developed a common, sensible and transparent approach to grading quality (or certainty) of evidence and strength of recommendations. Many international organizations have provided input into the development of the GRADE system which is now considered an international standard in guideline development.

The system applies a systematic approach to judgments about the quality of evidence and the strength of recommendations (47, 48) taking into account study design, quality, consistency and directness. Strength of recommendation is determined by the balance between desirable and undesirable consequences of alternative management strategies, quality of evidence, variability in values and preferences and resource use. The strength of recommendations reflects the extent to which we can be confident that the desirable effects of an intervention outweigh the undesirable effects across the range of patients for whom the recommendations are intended.

<table>
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Figure 8. Grading quality of evidence and strength of recommendation, according to the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system.
ETHICAL CONSIDERATIONS

Before implementing an interventional programme potential unintended consequences on psychosocial wellbeing, equality, social and cultural values, informed choice, privacy and the attributions of personal responsibilities and liberty should be evaluated.

Ethical aspects involved in programmes to prevent excessive GWG largely overlap with ethical aspects of prevention of other types of unhealthy behaviour such as smoking. Attitudes as to whether, and to what extent, pregnant women have an extended duty to behave in a healthy manner should be addressed among health care providers, as should possible harmful effects of projecting a message of guilt to women not adherent to recommendations. That obesity is a social stigma is widely acknowledged in Sweden and an intervention specifically aimed at this population would require additional consideration of the interaction between health care providers and the obese pregnant woman.

The VIGA trial was approved by the Regional Board of Research Ethics in Uppsala, Sweden, under registration number 2007/031 on 21 February 2007. Written, informed consent was obtained from all participants.
AIMS

The overall aim of this thesis was to systematically review and grade current scientific evidence regarding lifestyle interventions aimed at reducing excessive GWG and to perform and analyse effects of an original RCT of an antenatal intervention on outcomes related to GWG, PPWR and offspring obesity at birth and at age 5.

Paper I  The primary objective was to determine whether published controlled trials of intervention aimed at reducing excessive GWG were of sufficient quality and provided sufficient data to enable evidence-based recommendations to be developed for clinical practice in antenatal care.

Paper II  The primary objective was to evaluate whether a feasible, low-cost antenatal lifestyle intervention could reduce the proportion of women gaining weight above the Institute of Medicine (IOM) recommendations on GWG, compared with standard maternity care. Mean GWG (kg) was also compared between groups and a sub-analysis regarding differences in outcome related to pre-pregnancy BMI and parity was performed as a secondary aim.

Paper III  The primary objective was to evaluate whether an antenatal lifestyle intervention could reduce short- and/or long-term maternal PPWR compared with standard maternity care. Risk estimates for excessive weight retention (>5 kg) 1 year after delivery were analysed as a secondary aim.

Paper IV  The primary objective was to evaluate whether an antenatal lifestyle intervention could affect offspring obesity at birth or age 5. Mean BMI z-scores and proportion (%) of over- and undernutrition (BMI z-score >±2 SD) in offspring was compared between groups at birth and age 5. Risk estimates for offspring obesity at age 5 were analysed with regard to maternal GWG and maternal pre-pregnancy BMI as a secondary aim.
MATERIALS AND METHODS

<table>
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<th>Study</th>
<th>Design</th>
<th>Method</th>
<th>Primary outcome</th>
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<td>Systematic review</td>
<td>Literature study using the GRADE method.</td>
<td>Grade of current quality of evidence and strength of recommendations.</td>
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<td>II</td>
<td>Randomized controlled trial of intervention</td>
<td>Prescribed PA, education on IOM recommendations, personalized weight-graph and increased body weight measurements.</td>
<td>Proportion of women with excessive GWG (%) in relation to study group. Mean GWG (kg) in relation to study group.</td>
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<td>III</td>
<td>Secondary analysis of a RCT of intervention</td>
<td>Prescribed PA, education on IOM recommendations, personalized weight-graph and increased body weight measurements.</td>
<td>Mean PPWR (kg) in relation to study group and time after delivery.</td>
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<td>IV</td>
<td>Secondary analysis of a RCT of intervention</td>
<td>Antenatal maternal lifestyle intervention. Standardized measure of weight and height in offspring within child health care.</td>
<td>Offspring mean BMI z-score at birth and age 5 in relation to study group. Proportion of overweight and undernutrition (%) at birth and age 5 in relation to study group.</td>
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BMI = body mass index; GRADE = Grading of Recommendations, Assessment, Development and Evaluation; GWG = gestational weight gain; IOM = Institute of Medicine; PPWR = postpartum weight retention; RCT = randomized controlled trial.

Paper I

A literature search was conducted in the scientific databases Pub-Med, Cochrane Library, CINAHL and PEDro, and the reference lists of relevant articles were reviewed. The literature search was concluded on 15 August 2009. All RCTs were considered for inclusion. As the number of published RCTs was limited, all non-randomized intervention studies that included a control group were also considered for inclusion. Systematic reviews were searched and examined in order to identify additional original studies.

Two reviewers independently assessed the quality of the design, methods and results of all included articles. Data were extracted from articles using a structured data collection form and classified using GRADE (47). The GRADE system offers four levels of evidence quality: high, moderate, low, and very low (Figure 8). Quality may be downgraded as a result of limitations in study design or implementation, imprecision of estimates (wide confidence interval (CI)), variability in results, indirectness of evidence or publication bias. Quality may be upgraded due to a very large magnitude of effect, or presence of a dose-response gradient. It may also be upgraded if all plausible biases would reduce an apparent treatment effect.
Papers II-IV

Women were included in the VIGA trial between 2007 and 2010. The research was performed as a RCT with no blinding to treatment. Consecutive randomization was applied after written, informed consent was obtained. Women, stratified by BMI category (normal, overweight, obese) were randomly assigned to the standard care control group or the lifestyle intervention. Eligible participants were all pregnant women aged ≥18 who signed in for maternity care in Orebro Region in Sweden at ≤16 weeks pregnancy according to last menstrual period (LMP) or an early ultrasound dating.

Women with a previous medical history including treatment of an eating disorder or with a history of having a growth-restricted infant were excluded from the study before randomization. We also excluded women with existing chronic illness, who required primarily specialized maternity care during pregnancy. Additional criteria for exclusion were inadequate knowledge of Swedish, BMI <19 at first antenatal visit, and multiple pregnancy. The first offspring was born in 2007 and the last offspring reached age 5 in 2015. All offspring to women analysed for GWG in the original study (Paper II) were included in the follow-up study of offspring obesity (Paper IV).

Intervention

The intervention programme consisted of individual education/information about the IOM guidelines for recommended GWG, according to pre-pregnancy BMI category at first antenatal visit. Since the study period started in 2007 the IOM guidelines from 1990 were applied throughout the study (Table 2).

<table>
<thead>
<tr>
<th>Pre-pregnancy BMI</th>
<th>Recommended GWG (kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Underweight: &lt;19.8</td>
<td>12.5–18.0</td>
</tr>
<tr>
<td>Normal weight: 19.8-26.0</td>
<td>11.5–16.0</td>
</tr>
<tr>
<td>Overweight: 26.1–29.0</td>
<td>7.0–11.5</td>
</tr>
<tr>
<td>Obese: &gt;29.0</td>
<td>&gt;6.8–11.5*</td>
</tr>
</tbody>
</table>

Table 2. Institute of Medicine (IOM) 1990 recommendations on gestational weight gain (GWG) depending on pre-pregnancy body mass index (BMI) (8).

*No upper limit for obese women was established in the 1990 guidelines. In the study protocol the same upper limit as for overweight women was applied.

The education was supplemented by a personalized graph showing the recommended interval of weight gain and allowing the woman, together with her midwife, to follow her own weight gain during pregnancy (Figure 9). Maternal weight was measured without shoes and outdoor clothing and discussed at each antenatal visit. Measured weights were recorded on the graph as well as in the study case record files.

The midwife issued written formalized prescriptions of PA (swedish acronym = FaR). The general recommendation for PA during pregnancy was a moderate level...
of exertion during a total of approximately 30 minutes per day. Activities should be chosen as to entail a minimal risk of falling. The activity chosen should be based on individual abilities/interests/skills and as physiological changes during pregnancy can influence and progressively alter conditions for the woman, the activity prescribed might also be adjusted during the pregnancy. The midwife was instructed to follow up and renew the prescription of exercise at every antenatal visit during the pregnancy. No extra antenatal visits were scheduled for this group and no additional funding was allocated to the care of women receiving intervention.

**Figure 9. Example of personalized weight graph applied in the trial.**

No recalled or self-reported measures of body weight were used in any of the studies in this thesis. Information on participating women’s height was, however, self-reported, which is routine in Swedish maternity care. The children were measured using the Swedish standards for child health care services at birth, 1, 4, 6, 8, 10, 12, 18 months, and 2 1/2, 3, 4 and 5 years of age. Scales were calibrated according to child health care routines. An infant scale was used up until age 2 and thereafter a standing paediatric scale was used. Small children were weighed without clothes and diapers while underwear was accepted when weighing the older children. Weight was registered in grams up to 9,999 g and thereafter in kilograms with one decimal. Length was measured in a standardized manner, with the child laying down until age 2 and thereafter standing up. Length was reported in centimetres with one decimal.
Maternal pre-pregnancy weight was defined as the first measured weight at admission to maternal health care before 16 weeks pregnancy and total GWG was defined as the difference between pre-pregnancy weight and weight at term pregnancy (>37 weeks). Data on breastfeeding status were collected at a visit to maternal health care <16 weeks after delivery.

Women randomized to the control group were given standard maternity care. In accordance with national guidelines in Sweden, maternal weight was registered three times during pregnancy: at the first visit, at 33 weeks of pregnancy, and when admitted to the delivery unit. Standard maternity care in Sweden includes recommendations on dietary intake during pregnancy according to guidelines from the Swedish National Food Administration (49). This advice was given at admission in early pregnancy, all study patients were given the same standardized written and oral information.

Randomization

Randomization was stratified for BMI group (normal weight, overweight, obese) in accordance with WHO standards and the sequence was computer-generated, in blocks of variable sizes between 4 and 8. The allocation sequence was concealed in opaque, sealed, sequentially numbered envelopes, and kept by administrative personnel not related to the study. When including a pregnant woman in the study, the recruiting midwife contacted the study administrator by telephone and she then opened the lowest numbered envelope in the relevant BMI category and gave information on the assigned study group to the midwife.

Statistical methods, Papers II-IV

All data analyses were carried out according to a modified intention to treat approach and the pre-established analysis plan. Statistical analysis was performed in IBM SPSS Statistics for Windows, version 21 and 22 (IBM Corp., Armonk, NY, USA). Chi-square test and independent samples t-test with 95% CIs were used to compare differences in proportions and means between groups. A two-sided significance test was used and a p-value of <0.05 was regarded as statistically significant. The correlation between GWG and PPWR in Paper III was analysed using Pearson product moment correlation.

In Paper IV, BMI z-scores, also called “BMI standard deviation (SD) scores”, were calculated using the World Health Organization (WHO) Child Growth Standards as external reference (50). Risk estimates were calculated by binary logistic regression and linear logistic regression, with adjustment for relevant confounding factors. Mixed model analysis of variance was used to analyse BMI z-scores in multiple measures during the study period (eleven measures, 0-5 years). A heterogeneous first-order autoregressive covariance structure was used for the mixed model analysis.
Sample size

The sample size for the VIGA trial was based on the anticipated effects of the intervention on GWG. An improvement where 60% of women, compared with 45% of women previously, had GWG within IOM recommendations was considered clinically relevant. With a two-sided 5% significance level, a power of 80%, and an anticipated dropout rate of 20%, a sample size of 210 women per group was estimated as adequate in the original study on GWG (Paper II). Sample size was not recalculated in the follow-up study of mean PPWR (Paper III).

To evaluate the statistical power to detect differences in our secondary analysis of offspring obesity, we performed an additional power calculation for the primary outcome, mean BMI z-scores. Given an α of 0.05, a β of 0.80, and a BMI z-score SD of 1.0, a difference between the intervention and the control group in offspring mean BMI z-score of 0.29 could be detected with a sample size of 187 children in each group. All offspring (374 children) to women included and analysed for GWG in the original study were included in the follow-up study.

Child Growth Standards applied in Paper IV

The WHO Child Growth Standards were used as an external reference in the assessment of BMI z-score in the offspring analysed in Paper IV (50). The WHO standards, issued in 2006, are based on the Multi-center Growth Reference Study (MGRS), which collected primary growth data and related information on approximately 8,500 children from widely different ethnic backgrounds and cultural settings (Brazil, Ghana, India, Norway, Oman and the USA) between 1997 and 2003. The gender-specific BMI for age standard is based on a total of 26,985 records. The data from MGRS provide a single international standard that represents the best description of physiological growth for all children from birth to age 5 and to establish the breastfed infant as the normative model for growth and development.

The WHO Child (0-5 years) Growth Standards are recommended by the International Paediatric Association as well as the European Childhood Obesity Group and were adapted, already in 2011, as an official standard in more than 125 countries (51), representing 75% of the world’s 0-5 years children. The scrutiny that the WHO standards have undergone is without precedent in the history of developing and applying growth assessment tools, whether national or international.
RESULTS

Paper I
Eleven trials of intervention were initially identified and considered for inclusion. After full text assessment, two studies were excluded because of a lack of a control group. One further study was excluded because of its primary focus on effects on blood pressure of a low-sodium diet in pregnancy. Three intervention studies with a randomized controlled design and one study with a quasi-randomized design qualified for inclusion in this review (306 patients). Three were conducted in the USA and one in Denmark (Table 3). Furthermore, four intervention studies with a non-randomized controlled design met the inclusion criteria and were therefore assessed (1,232 patients). The non-randomized studies included were conducted in Finland, Sweden, Canada and the USA (Table 4).
Results

Significant decrease in women with normal BMI exceeding IOM recommendations (58 vs 33%, p<0.05). Opposite trend among overweight women (32 vs. 59%, p=0.09).

Reduced GWG in the intervention group (p=0.002).

1st trimester; significantly less GWG with intervention (p<0.001)
2nd trimester; no difference; 3rd trimester; Significantly higher GWG with intervention (p<0.006)

Table 3. Details of randomized controlled trials (RCTs) of antenatal intervention.
### Results

Significant decrease in women with normal BMI exceeding IOM recommendations (58 vs 33%, p<0.05). Opposite trend among overweight women (32 vs. 59%, p=0.09).

Reduced GWG in the intervention group (p=0.002).

1st trimester: significantly less GWG with intervention (p<0.001).

2nd trimester: no difference.

3rd trimester: significantly higher GWG with intervention (p<0.006).

No significant difference in adherence to IOM recommendations (p=0.21).

### Outcome

<table>
<thead>
<tr>
<th>Proportion of women exceeding IOM recommendations.</th>
<th>Gestational weight gain (kg).</th>
<th>Weight gain (lb) per trimester.</th>
<th>Weight retention 6 weeks postpartum (lb).</th>
</tr>
</thead>
</table>

### Control

- Standard maternity care.
- Standard maternity care.
- Standard maternity care. Repeat nutrition assessment.

### Intervention

- Stepped-care behavioural intervention. Patient education by-mail. Personalized graph of weight gain.

### Population

- Low-income population in the USA. BMI > 19.8. Age > 18 yrs. n (Intervention) = 57. n (Control) = 53.
- Caucasian, non-smoking in Denmark. BMI > 30. Age > 18 yrs. n (Intervention) = 23. n (Control) = 27.
- African-American women in the USA. Age 13-18 yrs. n (Intervention) = 22. n (Control) = 24.
- USA. BMI < 40.5. Age 18-49 yrs. n (Intervention) = 57. n (Control) = 43.

### Design

- RCT
- Quasi-RCT
- RCT

### Study

- Polley et al 2002
- Wolff et al 2008
- Bechtel-Blackwell 2002
- Asbee et al 2009

### Table 3. Details of randomized controlled trials (RCTs) of antenatal intervention.

### Table 4. Details of non-randomized controlled trials of antenatal intervention.
<table>
<thead>
<tr>
<th>Studies (participants)</th>
<th>Limitations</th>
<th>Consistency</th>
<th>Directness</th>
<th>Precision</th>
<th>Publication bias</th>
<th>Quality of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>8 (1538)*</td>
<td>Serious limitations</td>
<td>Important inconsistency</td>
<td>Indirectness</td>
<td>No important imprecision</td>
<td>Unlikely</td>
<td>Very low</td>
</tr>
<tr>
<td></td>
<td>-2</td>
<td>-1</td>
<td>-1</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>

Table 5. Quality of evidence according to the Grading of recommendations, Assessment, Development and Evaluation (GRADE) system.

*Errata in Paper II. In this table the correct number of participants is reported.

**Conclusion Paper I**

As a consequence of important limitations in study design as well as inconsistencies and lack of directness, the overall quality of evidence was judged to be very low (+) (Table 5). The results of published interventional trials were of insufficient quality to enable evidence-based recommendations to be developed for clinical practice in antenatal care.

**Paper II**

A total of 445 women were randomized (221 women were allocated to intervention and 224 to standard care) to participate in the VIGA trial, 374 women remained for analysis after completing their pregnancy (Figure 10). A total of 14 maternal health care clinics in the region participated in the study. Analysis was limited to term deliveries (≥37 weeks of gestation). There was an 8% loss to follow-up in the group receiving intervention and an 11% loss to follow-up in the group receiving standard care. Data were analysed according to a modified intention to treat approach.
No significant baseline difference in maternal age, parity or mean pre-pregnancy BMI was detected between groups (Table 6). The majority of the women included were normal weight (72%). Length of gestation at inclusion and at delivery (Errata in Paper II, where the difference in gestational length at inclusion was overlooked) significantly differed (p<0.001 at inclusion and p=0.034 at delivery) between groups.
Table 6. Baseline maternal characteristics of the study population.

The proportion of women with excessive GWG was 9% smaller among women who received the intervention (41.1% vs. 50.0%) but the difference was not statistically significant (p = 0.080). There was, however, a significant difference in mean GWG (kg) between study groups in favour of intervention (14.19 kg vs. 15.31 kg, p= 0.028) (Table 7).

Table 7. Effect of intervention on proportion of women with excessive gestational weight gain (GWG) and on mean GWG in relation to study group.

No significant difference in the proportion of women gaining weight below (19% vs 16%) or within (40% vs. 34%) IOM recommendations was seen in relation to study group.

The effect of the intervention was analysed within sub-groups based on pre-pregnancy BMI and parity. A tendency towards lower weight gain among the intervention group was seen in all categories of pre-pregnancy BMI. The differences were, however, not statistically significant (Table 8).
Table 8. Effects of intervention in relation to pre-pregnancy body mass index (BMI) among women with gestational weight gain (GWG) above Institute of Medicine (IOM) recommendations.

Ancillary analysis in relation to parity showed that the intervention significantly increased the proportion of multiparous women who gained weight below IOM recommendations (22% for the intervention group vs. 12% for controls, p=0.027).

**Conclusion Paper II**

A composite, low-cost, antenatal lifestyle intervention significantly reduced mean GWG, however, the proportion of women with excessive GWG was not significantly lower in the intervention group compared with standard maternity care.

**Paper III**

Postpartum weight retention was analysed in Paper III, with the first weight measurement at the postpartum visit approximately 16 weeks after delivery and the second measurement 1 year post-delivery (Table 9). Of 445 women randomized to participate in the VIGA trial, 267 remained for analysis at first follow-up postpartum and 168 at second follow-up at 1 year postpartum (Figure 10). There were no significant differences in baseline characteristics between study groups, neither among participants remaining or lost to follow-up during the first year postpartum.
<table>
<thead>
<tr>
<th>Variable</th>
<th>Intervention group</th>
<th>Control group</th>
<th>Missing Intervention group</th>
<th>Missing Control group</th>
<th>Missing analysis p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;16 wks PP</td>
<td>137</td>
<td>130</td>
<td>55 (28.6)</td>
<td>52 (28.6)</td>
<td>NS</td>
</tr>
<tr>
<td>1 y PP</td>
<td>87</td>
<td>81</td>
<td>105 (64.7)</td>
<td>101 (55.5)</td>
<td>NS</td>
</tr>
<tr>
<td>Mean age, yrs (SD)</td>
<td>30.1 (4.4)</td>
<td>29.7 (4.7)</td>
<td>29.3 (4.5)</td>
<td>29.9 (5.2)</td>
<td>NS</td>
</tr>
<tr>
<td>Mean pre-pregnancy BMI (SD)</td>
<td>25.6 (5.2)</td>
<td>25.2 (4.7)</td>
<td>24.3 (3.9)</td>
<td>25.6 (5.1)</td>
<td>NS</td>
</tr>
<tr>
<td>Normal weight</td>
<td>93 (68)</td>
<td>95 (73)</td>
<td>45 (82)</td>
<td>35 (67)</td>
<td>NS</td>
</tr>
<tr>
<td>Overweight</td>
<td>17 (12)</td>
<td>15 (12)</td>
<td>6 (11)</td>
<td>6 (12)</td>
<td>NS</td>
</tr>
<tr>
<td>Obese</td>
<td>27 (20)</td>
<td>20 (15)</td>
<td>4 (7)</td>
<td>11 (21)</td>
<td></td>
</tr>
<tr>
<td>1 yr PP, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean pre-pregnancy BMI (SD)</td>
<td>24.5 (4.0)</td>
<td>25.1 (4.7)</td>
<td>25.8 (5.5)</td>
<td>25.6 (4.8)</td>
<td>NS</td>
</tr>
<tr>
<td>Normal weight</td>
<td>69 (79)</td>
<td>58 (72)</td>
<td>69 (66)</td>
<td>72 (71)</td>
<td>NS</td>
</tr>
<tr>
<td>Overweight</td>
<td>5 (6)</td>
<td>9 (11)</td>
<td>18 (17)</td>
<td>12 (12)</td>
<td>NS</td>
</tr>
<tr>
<td>Obese</td>
<td>13 (15)</td>
<td>14 (17)</td>
<td>18 (17)</td>
<td>17 (17)</td>
<td></td>
</tr>
<tr>
<td>Nulliparas, n (%)</td>
<td>64 (47)</td>
<td>69 (53)</td>
<td>21 (38)</td>
<td>24 (46)</td>
<td>NS</td>
</tr>
<tr>
<td>Mean GWG, kg (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;16 wks PP</td>
<td>13.9 (4.4)</td>
<td>15.5 (5.4)</td>
<td>14.8 (4.5)</td>
<td>14.9 (5.4)</td>
<td>NS</td>
</tr>
<tr>
<td>1 y PP</td>
<td>14.0 (4.2)</td>
<td>15.4 (5.1)</td>
<td>14.4 (4.7)</td>
<td>15.2 (5.6)</td>
<td>NS</td>
</tr>
<tr>
<td>Breastfeeding at &lt;16 wks PP, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>115 (88)</td>
<td>110 (85)</td>
<td>6</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>No</td>
<td>16 (12)</td>
<td>20 (15)</td>
<td></td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>Mean time PP at weight measures</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;16 w PP wks (SD)</td>
<td>10.2 (3.0)</td>
<td>10.0 (3.2)</td>
<td></td>
<td></td>
<td>NS</td>
</tr>
<tr>
<td>1 year PP mo (SD)</td>
<td>12.2 (0.8)</td>
<td>12.3 (0.7)</td>
<td></td>
<td></td>
<td>NS</td>
</tr>
</tbody>
</table>

Table 9. Baseline characteristics of the study population after delivery and at 1 year postpartum.

The intervention group had significantly lower mean PPWR at ≤16 weeks (1.81 kg vs. 3.19 kg). At 1 year postpartum, mean retention was still 0.69 kg lower in the intervention group (0.30 kg vs. 1.00 kg), but the difference was not statistically significant (Table 10).
Table 10. Effect of intervention on mean postpartum weight retention (PPWR) (kg) at two time points of maternal weight estimation.

CI = confidence interval; PP = postpartum; SD = standard deviation.

Postpartum weight retention was also analysed in sub-groups of women to explore potential differences in effects of the intervention in relation to factors such as GWG and pre-pregnancy BMI. No difference in the effect of the intervention in relation to the woman’s adherence to IOM recommendations was seen even though a significantly higher risk for high short-term PPWR was demonstrated in the category with high GWG in the whole study population.

Women with normal pre-pregnancy BMI had a significant short-term effect of the intervention on PPWR but other BMI categories did not. At the long-term follow-up there were no significant differences regarding PPWR in any of the analysed sub-
groups. Gestational weight gain above the IOM recommendations was a significant risk factor for excessive weight retention (>5 kg) 1 year after delivery (odds ratio (OR) 2.44; 95% CI: 1.08–5.52, p=0.029), independent of study group (Table 11).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Weight retention &lt; 5 kg</th>
<th>Weight retention &gt; 5 kg</th>
<th>p-value</th>
<th>OR</th>
<th>CI (95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, yrs (SD)</td>
<td>N=139</td>
<td>N=29</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>30.2 (4.8)</td>
<td>29.5 (4.2)</td>
<td>0.503</td>
<td>0.97</td>
<td>0.89-1.06</td>
</tr>
<tr>
<td>Mean pre-pregnancy BMI (SD)</td>
<td>24.6 (4.5)</td>
<td>25.8 (3.8)</td>
<td>0.161</td>
<td>1.06</td>
<td>0.98-1.16</td>
</tr>
<tr>
<td>Parity, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>61 (44)</td>
<td>13 (45)</td>
<td>0.926</td>
<td>0.98</td>
<td>0.63-1.63</td>
</tr>
<tr>
<td>&gt;1</td>
<td>78 (56)</td>
<td>16 (55)</td>
<td>1.02</td>
<td>1.02</td>
<td>0.71-1.46</td>
</tr>
<tr>
<td>Study population, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intervention</td>
<td>74 (53)</td>
<td>13 (45)</td>
<td>0.410</td>
<td>0.71</td>
<td>0.32-1.59</td>
</tr>
<tr>
<td>Control</td>
<td>65 (47)</td>
<td>16 (55)</td>
<td>1.19</td>
<td>1.19</td>
<td>0.77-1.83</td>
</tr>
<tr>
<td>Mean GWG, kg (SD)</td>
<td>14.1 (4.3)</td>
<td>17.2 (5.7)</td>
<td>0.002</td>
<td>1.16</td>
<td>1.05-1.27</td>
</tr>
<tr>
<td>Non-adherence to IOM recommendations n(%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GWG &gt;IOM</td>
<td>51 (37)</td>
<td>17 (59)</td>
<td>0.029</td>
<td>2.44</td>
<td>1.08-5.52</td>
</tr>
<tr>
<td>Mean FBW, g (SD)</td>
<td>3,544 (506)</td>
<td>3,631 (395)</td>
<td>0.426</td>
<td>1.00</td>
<td>0.99-1.00</td>
</tr>
</tbody>
</table>

| Breastfeeding, n (%)                    |                         |                         |         |     |         |
| Yes                                     | 104 (90)                | 19 (79)                 | 0.359   | 0.52| 0.13-2.16|
| No                                      | 12(10)                  | 5 (21)                  | 0.44    | 0.44| 0.14-1.39|
| Missing data                            | 23/139 (16)             | 5/29 (17)               |         |     |         |

Table 11. Risk estimates for excessive postpartum weight retention (PPWR) (>5 kg) 1 year after delivery.

BMI = body mass index; FBW = fetal birth weight; IOM = Institute of Medicine; OR = odds ratio; SD = standard deviation.

Conclusion Paper III

Women who received antenatal lifestyle intervention had significantly less short-term PPWR. One year after delivery there was no significant difference in weight retention between the study groups. Excessive GWG was a significant risk factor for excessive weight retention (>5 kg) 1 year after delivery, independent of study group.
**Paper IV**

In all, 374 children were included at birth and 300 remained for analysis at age 5. The flow of study participants is shown in Figure 10. There was no record of women not receiving the intended treatment in either study group and all offspring were analysed according to the group their mother was allocated to.

No significant difference was detected in baseline characteristics, such as sex of offspring, maternal parity, age, pre-pregnancy BMI or prevalence of breast-feeding between study groups. Mean gestational age at birth was, however, significantly higher among offspring in the intervention group (39.7 weeks vs. 39.4 weeks; 95% CI: 0.02-0.50, p=0.034) (Table 12).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Intervention group N=192</th>
<th>Control group N=182</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male offspring, n (%)</td>
<td>101 (53)</td>
<td>89 (49)</td>
<td>0.535</td>
</tr>
<tr>
<td>Gestational age at birth, wks (SD)</td>
<td>39.7 (1.2)</td>
<td>39.4 (1.2)</td>
<td>0.034</td>
</tr>
<tr>
<td>Mean maternal age, yrs (SD)</td>
<td>29.9 (4.5)</td>
<td>29.8 (4.8)</td>
<td>0.870</td>
</tr>
<tr>
<td>Mean maternal GWG, kg (SD)</td>
<td>14.19 (4.45)</td>
<td>15.31 (5.38)</td>
<td>0.029</td>
</tr>
<tr>
<td>Nulliparous mothers, n (%)</td>
<td>85 (44)</td>
<td>93 (51)</td>
<td>0.214</td>
</tr>
<tr>
<td>Mean maternal pre-pregnancy BMI, kg/m2 (SD)</td>
<td>25.2 (4.9)</td>
<td>25.3 (4.8)</td>
<td>0.822</td>
</tr>
</tbody>
</table>

**Maternal pre-pregnancy BMI group, n (%)**

<table>
<thead>
<tr>
<th></th>
<th>Intervention group</th>
<th>Control group</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>138 (72)</td>
<td>130 (71)</td>
<td>0.969</td>
</tr>
<tr>
<td>Overweight</td>
<td>23 (12)</td>
<td>21 (12)</td>
<td></td>
</tr>
<tr>
<td>Obese</td>
<td>31 (16)</td>
<td>31 (17)</td>
<td></td>
</tr>
<tr>
<td>Breast-feeding, n (%)</td>
<td>115 (60)</td>
<td>112 (62)</td>
<td>0.520</td>
</tr>
<tr>
<td>Yes</td>
<td>16 (8)</td>
<td>20 (11)</td>
<td></td>
</tr>
<tr>
<td>Missing data</td>
<td>61 (32)</td>
<td>50 (27)</td>
<td></td>
</tr>
</tbody>
</table>

Table 12. Offspring and maternal baseline characteristics.

BMI = body mass index; GWG = gestational weight gain; SD = standard deviation.

No significant difference in mean BMI z-scores was seen at birth (intervention group 0.68 vs. controls 0.56; p=0.242) or at age 5 (intervention group 0.34 vs. controls 0.26; p=0.510) and no significant difference in the proportion (%) of over- or undernutrition (BMI z-scores >+2, at birth or age 5, was seen between study groups. Adjustment for potential confounding by differences in gestational age at birth was performed without significant changes in the primary outcome results (Table 13).

Alternative measures of fetal size at birth were also analysed and no significant difference in fetal size, except for fetal length, was seen after adjusting for differences in gestational age at birth (Table 13).
### Table 13. Effect of the intervention on offspring mean body mass index (BMI) and mean BMI z-score, by study group and age. The Table also shows the effect of intervention on alternative measures of fetal size at birth.

*a Adjusted for differences in gestational age at birth.

**AGA** = average for gestational age; **FBW** = fetal birth weight; **LGA** = large for gestational age; **SD** = standard deviation; **SGA** = small for gestational age.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intervention group</th>
<th>Control group</th>
<th>Crude p-value</th>
<th>Adjusted p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean offspring BMI, kg/cm² (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth</td>
<td>14.3 (1.3)</td>
<td>14.2 (1.3)</td>
<td>0.237</td>
<td>0.473</td>
</tr>
<tr>
<td>Age 5 yrs</td>
<td>15.8 (1.4)</td>
<td>15.7 (1.4)</td>
<td>0.488</td>
<td>0.473</td>
</tr>
<tr>
<td>n=156</td>
<td>n=144</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean offspring BMI z-score, (SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth</td>
<td>0.68 (0.99)</td>
<td>0.56 (0.99)</td>
<td>0.242</td>
<td>0.479</td>
</tr>
<tr>
<td>Age 5 yrs</td>
<td>0.34 (0.96)</td>
<td>0.26 (0.96)</td>
<td>0.510</td>
<td>0.479</td>
</tr>
<tr>
<td>n=156</td>
<td>n=144</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean FBW, kg (SD)</td>
<td>3.661 (0.461)</td>
<td>3.548 (0.489)</td>
<td>0.022</td>
<td>0.109</td>
</tr>
<tr>
<td>LGA (&gt;2 SD), n (%)</td>
<td>15 (8)</td>
<td>11 (6)</td>
<td>0.501</td>
<td>0.452</td>
</tr>
<tr>
<td>AGA, n (%)</td>
<td>174 (91)</td>
<td>168 (92)</td>
<td>0.561</td>
<td>0.507</td>
</tr>
<tr>
<td>SGA (&lt;2 SD), n (%)</td>
<td>3 (2)</td>
<td>3 (2)</td>
<td>0.947</td>
<td>0.962</td>
</tr>
<tr>
<td>Mean fetal birth length, cm (SD)</td>
<td>50.5 (1.8)</td>
<td>49.9 (1.8)</td>
<td>0.005</td>
<td>0.032</td>
</tr>
<tr>
<td>FBW &gt;4,000 g, n (%)</td>
<td>47 (24)</td>
<td>28 (15)</td>
<td>0.029</td>
<td>0.091</td>
</tr>
<tr>
<td>FBW &gt;4,500 g, n (%)</td>
<td>8 (4)</td>
<td>8 (4)</td>
<td>0.913</td>
<td>0.580</td>
</tr>
<tr>
<td>Ponderal Index, weight (kg) x100/length (cm³)</td>
<td>2.84</td>
<td>2.84</td>
<td>0.861</td>
<td>0.989</td>
</tr>
</tbody>
</table>

### Table 14. Effects of the intervention on the percentage of over/undernutrition (BMI z-score > ±2 standard deviations (SDs)) in offspring, by study group and age.

*a Adjusted for differences in gestational age at birth.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intervention group</th>
<th>Control group</th>
<th>Crude p-value</th>
<th>Adjusted p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overnutrition in offspring, (BMI z-score ≥ 2 SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth, n (%)</td>
<td>18 (9)</td>
<td>15 (8)</td>
<td>0.699</td>
<td>0.932</td>
</tr>
<tr>
<td>Age 5 yrs, n (%)</td>
<td>5 (3)</td>
<td>9 (6)</td>
<td>0.221</td>
<td>0.228</td>
</tr>
<tr>
<td>n=156</td>
<td>n=144</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undernutrition in offspring, (BMI z-score ≤ -2 SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Birth, n (%)</td>
<td>2 (1)</td>
<td>0</td>
<td>0.167</td>
<td>0.995</td>
</tr>
<tr>
<td>Age 5 yrs, n (%)</td>
<td>3 (2)</td>
<td>1 (1)</td>
<td>0.347</td>
<td>0.437</td>
</tr>
<tr>
<td>n=156</td>
<td>n=144</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Mean BMI z-score was consistently slightly higher among offspring to women who had received the lifestyle intervention (Figure 12). Point-estimate comparison of mean BMI z-scores showed significantly differences at age 2.5 years only; however, in a mixed model analysis of multiple measurements, adjusted for differences in gestational age at birth, the difference in z-score was 0.16 (p=0.034; 95% CI 0.01-0.30).

![Figure 12. Trajectory of mean body mass index (BMI) z-scores in offspring from birth to age 5, in relation to study group.](image)

Independent of study group, GWG above IOM recommendations, was a significant risk factor for offspring overnutrition (BMI z-score >2 SD) at birth (OR=4.51, p<0.001; 95% CI 1.95-10.44) but not at age 5. Gestational weight gain below IOM recommendations had a significant negative association with overnutrition at birth (OR 0.89, p=0.005; 95% CI 0.86-0.93) but not at age 5 (OR 0.76, p=0.734; 95% CI 0.17-3.54) (Table 14).

Pre-pregnancy maternal BMI had no significant association with offspring overnutrition at birth (OR=1.32, p= 0.570; 95% CI 0.51-3.45), however, a strong positive association with childhood obesity at age 5 was seen, independent of maternal GWG (Figure 13). Offspring to women with normal pre-pregnancy weight had a reduced risk of obesity at age 5 and offspring to obese women had an increased risk of obesity at age 5 (Table 15).
Table 15. Risk analysis of maternal factors associated with offspring obesity (body mass index (BMI) z-score ≥2 standard deviations (SDs)) at age 5, independent of study group.

<table>
<thead>
<tr>
<th>Maternal Factor</th>
<th>Crude OR (95% CI)</th>
<th>Crude p-value</th>
<th>Adjusted OR (95% CI)</th>
<th>Adjusted p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-pregnancy maternal obesity</td>
<td>5.08 (1.70–15.18)</td>
<td>0.004</td>
<td>4.81 (1.56–14.83)</td>
<td>0.006a</td>
</tr>
<tr>
<td>Normal maternal pre-pregnancy weight</td>
<td>0.16 (0.05–0.53)</td>
<td>0.003</td>
<td>0.17 (0.05–0.56)</td>
<td>0.004a</td>
</tr>
<tr>
<td>Maternal GWG above IOM recommendations</td>
<td>1.17 (0.40–3.41)</td>
<td>0.778</td>
<td>1.01 (0.33–3.05)</td>
<td>0.991b</td>
</tr>
</tbody>
</table>

CI = confidence interval; IOM = Institute of Medicine; OR = odds ratio.

Figure 13. Mean body mass index (BMI) z-scores in offspring at age 5, in relation to maternal pre-pregnancy BMI category.
*p<0.01, significant difference between groups.
**Conclusion Paper IV**

The composite antenatal lifestyle intervention did not significantly reduce offspring mean BMI z-scores or the proportions of childhood obesity at birth or age 5. Maternal excessive GWG was not significantly associated with an increased risk of offspring obesity at age 5 but maternal pre-pregnancy obesity had a strong positive association with childhood obesity at age 5, independent of maternal GWG or study group.
DISCUSSION

Summary of main findings
The general rationale for this thesis was the need to expand knowledge of the impact of an antenatal lifestyle intervention aimed at reducing excessive GWG. Current scientific evidence was reviewed and a composite antenatal lifestyle intervention was designed and performed as a RCT.

The body of evidence from published intervention trials in 2009 was found to be insufficient to enable development of evidence-based recommendations for clinical practice in maternal health care. Our antenatal lifestyle intervention, tested within the VIGA trial, was safely performed according to study protocol and resulted in significantly reduced mean maternal GWG but no significant reduction in the proportion of women gaining excessively according to IOM recommendations. Women who received the intervention had significantly less short-term weight retention after delivery, however, no significant difference in weight retention, compared with standard care, was seen 1 year post-delivery. Offspring to women receiving the intervention did not have significantly lower mean BMI z-scores at birth or at age 5 and no effect of the intervention was seen in the proportion of children with over- or undernutrition at birth or age 5.

Strength and limitations of included studies
The choice of scientific methods in this thesis strengthens the grade of the evidence presented. The GRADE system used in Paper I, is internationally recognized and considered transparent and systematic. The randomized controlled study design, and the fact that the study was performed in a routine clinical setting strengthens our findings in Papers II-IV.

The original study population was relatively large and representative of all BMI categories except underweight women, who were not included. No self-reported body weights were used and in accordance with international guidelines, first measurement of maternal weight occurred at the time of the first antenatal visit (52). Information on participating women’s height was self-reported, as is routine in Swedish maternity care. Self-reported height is usually slightly overestimated (53), however, studies of the use of self-reported values to derive BMI have not found self-reported height to impact overall conclusions (53). The results are considered to be generalizable to other women and offspring sharing the same characteristics.

Total GWG is highly correlated with gestational duration as longer pregnancy duration provides more opportunity to gain weight. The significant difference in gestational length between study groups in Papers II-IV was a potential bias and statistical adjustment was made accordingly in the analysis. Using recently published z-score
charts of GWG for gestational age in relation to maternal BMI (25) could however have improved the depth in our analysis by providing a more exact measure of weight gain in relation to gestational age. The charts were however not available during the analysis of our data.

According to the original VIGA protocol, the women were educated and motivated to reach GWG as per IOM recommendations of 1990 (8). At the end of the study period the IOM published revised recommendations on GWG (20). Body mass index categories were adapted to WHO standards and the upper limit for women with pre-gestational obesity was set to 9 kg. A small number of the participating women would have been classified to a different BMI category based on the new guidelines. They would therefore have received a different education and a different personalized graph. The upper limit for women with pre-pregnancy obesity would have been lower. Since it was not possible to foresee how the participating women would have adhered to the intervention with these new recommendations, our data on efficiency of the intervention were analysed in accordance with our original study protocol using the IOM 1990 guidelines.

Our intervention was feasible and could be readily applied in most antenatal care settings with minimal additional funding. Our follow-up period was longer compared with the follow-up in many other, similar published trials, providing valuable information on how the efficacy of our intervention changed over time for both the women and their offspring.

There was no sign of systematic errors in the original recruitment to the different study groups, which could have confounded our data. The high rate of loss to follow-up regarding long-term PPWR limits the power to detect differences between the groups in this aspect. We considered the possibility that a differential bias had been introduced in our results during the follow-up period, and performed an analysis of missing data on mean PPWR and offspring weight and height. Participants lost to follow-up did not differ significantly in number, age, parity, pre-pregnancy BMI, offspring gender or incidence of breastfeeding between the groups. Data lost to follow-up in Papers II-IV were thereby considered missing at random.

The quality of data on breastfeeding status was low and limited any ancillary analysis of associations between breastfeeding status, PPWR and childhood obesity. Baseline incidence of breastfeeding did, however, not differ between groups and potential confounding of our results by this variable was considered unlikely. Socio-economic status and smoking habits among participants were not included in the analysis, which must be considered a limitation even though BMI can be considered a valid surrogate variable for socio-economic status in a Swedish population (54).

Measures collected to estimate maternal pre-pregnancy metabolic status and offspring obesity were limited to height and weight. The addition of circumferential measures may have increased the quality of our data and limited the major weakness
of BMI, which is its inability to distinguish between elevated adiposity and elevated lean mass. Direct measures of body composition, such as dual X-ray absorptiometry (DXA), would also have added information to our data but were not within the scope of this study. A high correlation has, however, been reported between the percentage of fat mass measured by DXA and the WHO z-scores in children (55). Weight and height are simple, inexpensive, non-invasive measurements that are routinely recorded in maternal and child health care settings. Research using a weight/height index to define obesity has advantages that outweigh its limitations. Despite the potential for misclassification of the small percentage of individuals whose high BMI is due to lean muscle mass, the great majority of individuals with high BMI do have excess body fat.

The actual “reach” of our intervention was not analysed (i.e. reasons for the decline, number of actual visits to the midwife, number of weight graphs distributed, number of prescriptions of PA, performance of PA). Neither was behavioural change objectively measured (level of PA, motivational level). This was, however, part of a conscious, pragmatic approach to our intervention. The cornerstones of our model were a motivational toolbox meant to strengthen and empower the participants’ own motivation to avoid excessive GWG and thereby increase the likelihood of more lasting behavioural changes and long-term beneficial health effects. Extensive analysis of “reach” could also influence results by enhancing effects of intervention in a manner not reproducible outside of the study setting.

Interpretation and implications of study results

The quality of evidence of antenatal intervention targeting GWG has improved since 2009, when we concluded our systematic review of current evidence (41). A review published in 2012 found moderate evidence for successful intervention to limit GWG and pointed at dietary interventions as being most effective (56). A further updated meta-analysis, published by the Cochrane Collaboration in 2015, conclude that high quality evidence indicate that diet and/or PA, during pregnancy can reduce the risk of excessive GWG by an average of 20% (RR 0.80, 95% CI: 0.73-0.87). This updated review included 65 RCTs in total, with 49 RCTs involving approximately 11,444 participants, contributing data (42). The risk of GWG below recommendations was however increased with 14% (RR 1.14, CI 95%: 1.02-1.27). Data for reduction in mean GWG were considered too heterogenous to pool and weight-related morbidity, such as risk of CS, macrosomia, preterm delivery and pre-eclampsia were not significantly reduced by interventions targeting GWG. A recent review of dietary interventions alone, revealed large methodological variability in studies performed among overweight and obese pregnant women (57). The lack of consensus still limits the ability to develop clinical guidelines and apply the evidence in clinical practice.

No evidence of harm as a result of the dietary and PA-based antenatal interventions
was seen in the VIGA trial or in other published trials, however, meta-analyses of negative maternal and fetal outcome in subgroups with increased risk are still lacking. Our ancillary analysis of offspring differences, using multiple measures recorded during childhood, demonstrated significantly higher BMI z-scores among offspring after antenatal intervention. This finding will, however, need to be confirmed in future studies before further speculation on its validity is made.

According to reports of inadequate mean GWG among underweight women in 9 out of 21 health care regions (24) in Sweden and also among 10% of Swedish women with pre-gestational obesity Grade III (25), the issue of safety is highly relevant when initiating lifestyle interventions aimed at reducing GWG in a Swedish population.

The overall modest effect of the VIGA trial intervention on GWG and PPWR and the null effect on childhood obesity concurs with several similar intervention studies in the literature (58-63). Our primary objective was to improve adherence to IOM recommendations in an overall healthy pregnant population consisting of women with predominantly normal pre-pregnancy BMI. This was, however, not achieved other than in a sub-group of parous women where significant effect was found. The reduction in mean GWG (1.12 kg) is relatively small and the clinical significance and expected relevance for future weigh-related outcome can be questioned. To significantly improve the proportion of women who achieve GWG within the IOM recommendations, a more elaborate and costly mode of intervention than tested in the VIGA trial is likely to be required. A large body of evidence based on retrospective observational studies associates excessive GWG with adverse maternal and fetal outcome in terms of high FBW and PPWR and increased risk of childhood obesity (1, 29, 64). The lack of prospectively reported positive effects on long-term maternal and offspring outcome does however pose the question as to the extent to which limiting excessive GWG is beneficial.

Avoidance of excessive GWG among severely obese women as a mean to improve maternal metabolic function and perinatal outcome has been specifically questioned by Catalano et al, who suggests that metabolic alterations affect maternal/placental function already in the first trimester of pregnancy among these women, and therefore occur before most interventions are initiated (65). According to their hypothesis, obese women would have to improve their metabolic condition already before pregnancy to decrease complications related to fetal size and GDM. The increased expression of lipogenic and inflammatory genes in maternal adipose tissue and placenta in the first trimester of pregnancy demonstrated, before any phenotypic changes in weight become apparent, implicate that severely obese women may have limited benefit from lifestyle interventions during pregnancy but this remains to be further investigated in future studies.

The highest risk of excessive GWG is however, among women with pre-pregnancy BMI between 25-35 and in a public health perspective, multiple visits to maternal
health care during pregnancy present a timely opportunity for motivation and information about the general importance of healthy lifestyle regarding diet and PA as well as tobacco and alcohol abuse. Evidence-based advice on GWG should be systematically implemented in maternal health care in order to facilitate health weight goals pre-conception, during pregnancy and postpartum.

**Future research recommendations**

Research encompassing implications of gestational weight changes on fetal and maternal outcome is still in its cradle.

Further understanding of the importance of timing and composition of excess or inadequate weight gained during pregnancy is needed as the potential metabolic impact and contribution to long-term risk is likely to vary not just in relation to maternal pre-pregnancy BMI but also depending on timing and fat mass accrual as well as the site of fat depot.

Prospective controlled studies of safety regarding GWG below IOM recommendations among obese women, stratified for grade of obesity, are needed. An ethical framework for trials involving lifestyle modification among pregnant women in a health care setting should also be developed in order to allow analysis of possible unintended consequences.

Further studies are also needed on pre-conception and intra-uterine programming of maternal adipose tissue, placenta and offspring metabolism.

Mechanisms for epigenetic modification in offspring, elicited by (either excessive or inadequate) maternal weight changes, could give us further understanding of long-term trans-generational effects.

Adequately powered and performed RCTs of pre-conception and inter-pregnancy lifestyle interventions are of particular interest to answer questions as to what intervention works for whom, why and at what cost.
CONCLUSION

Lifestyle behaviours are influenced by an accumulation of experiences during life and a life-long approach is needed on multiple levels in society to promote PA and healthy diet in order to reduce the risk of obesity-related disease. The reproductive cycle begins before conception and continues through the first year postpartum and maternal weight status throughout this entire cycle has a potential effect on mother and offspring both in the short- and in the long-term.

In a healthy, predominantly normal weight, Swedish population we found a significant but moderately sized reduction of mean GWG with our antenatal lifestyle intervention. The proportion of women exceeding recommended GWG was however not significantly reduced. The reduction in mean GWG did not affect maternal long-term PPWR or offspring adiposity at birth or age 5.

The relationship between maternal metabolic status and pre-conception, gestational and postpartum outcome is complex and the relevance of maternal weight gain as a modifier of risk needs further research. Studies included in this thesis add to the base of evidence on the topic but do not support the implementation of the tested intervention in maternal health care in Sweden.
ACKNOWLEDGEMENTS

I want to express my deepest gratitude to everyone who has helped and supported me during the process of working with this thesis. First of all I would like to thank all the participating women for finding the time and courage to contribute to research during a period in life filled with other concerns regarding pregnancy and parenthood. Your contribution has taken us further.

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REFERENCES


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SUMMARY IN SWEDISH
SAMMANFATTNING PÅ SVENSKA

Viktökning under graviditet (VIGA)
– effekter av antenatal livsstilsintervention

Överflödig viktuppgång under graviditet är vanligt förekommande i västvärlden och har kopplats till en ökad risk för komplikationer under graviditet, förlossning och postpartum för både mor och barn. Framförallt ökar risken för komplikationer som är relaterade till barnets födelsevikt men överflödig viktuppgång har även kopplats till en ökad risk för kvinnan att inte återgå till sin pregravia vikt efter förlossningen och att barnet får en framtida fetma.

En effektiv intervention som förhindrar eller begränsar överflödig viktuppgång under graviditet skulle därmed teoretiskt, kunna förbättra förlossningsutfall och även ge positiva långtidseffekter för mor och barn genom att minska risk för framtid fetma-relaterad sjuklighet. En ökande medvetenhet inom svensk mödrahälsovård om den höga förekomsten av överflödig viktuppgång och dess negativa konsekvenser var utgångspunkten för denna avhandling, som omfattar studier av livsstilsintervention med syfte att begränsa överflödig viktuppgång under graviditet.


VIGA studien jämförde standard mödrahälsovård med en kombinerad intervention bestående av utbildning om rekommenderad viktuppgång enligt internationella rekommendationer, utdelning av personlig viktgraf, fysisk aktivitet på recept (FaR) och tätare mätning av kvinnans vikt. Barnen följes med standardiserade mätningar av vikt och längd och deras tillväxt analyserades i relation till WHO’s internationella standard för tillväxt upp till fem års ålder.

Totalt 374 kvinnor kunde analyseras efter fullgången graviditet (Intervention=192, Kontroll=182). Interventionen som testades inom ramen för VIGA studien gav en signifikant lägre total viktuppgång under graviditet (medelvärde intervention=14.2 kg vs. medelvärde kontroll=15.3 kg, p=0.028). Andelen kvinnor som överskred internationella rekommendationer för viktuppgång var lägre efter intervention men skill-
ann-kristin rönnberg

Gestational Weight Gain

SUMMARY IN SWEDISH
SAMMANFATTNING PÅ SVENSKA
Viktökning under graviditet (VIGA)
– effekter av antenatal livsstilsintervention

Överflödig viktuppgång under graviditet är vanligt förekommande i västvärlden och har kopplats till en ökad risk för komplikationer under graviditet, förlossning och postpartum för både mor och barn. Framförallt ökar risken för komplikationer som är relaterade till barnets födelsevikt men överflödig viktuppgång har även kopplats till en ökad risk för kvinnan att inte återgå till sin pregravida vikt efter förlossningen och att barnet får en framtida fetma.

En effektiv intervention som förhindrar eller begränsar överflödig viktuppgång under graviditet skulle därmed teoretiskt, kunna förbättra förlossningsutfall och även ge positiva långtidseffekter för mor och barn genom att minska risk för framtida fetma-relaterad sjuklighet. En ökande medvetenhet inom svensk mödrahälsovård om den höga förekomsten av överflödig viktuppgång och dess negativa konsekvenser var utgångspunkten för denna avhandling, som omfattar studier av livsstilsintervention med syfte att begränsa överflödig viktuppgång under graviditet.


VIGA studien jämförde standard mödrahälsovård med en kombinerad intervention bestående av utbildning om rekommenderad viktuppgång enligt internationella rekommendationer, utdelning av personlig viktgraf, fysisk aktivitet på recept (FaR) och tätare mätning av kvinnans vikt. Barnen följdes med standardiserade mätningar av vikt och längd och deras tillväxt analyserades i relation till WHO’s internationella standard för tillväxt upp till fem års ålder.

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Överflödig viktuppgång under graviditet var en stark riskfaktor för överflödig viktretention (>5 kg) ett år efter förlossningen oberoende av vilken studiegrupp kvinnan tillhörde (OR 2.44; 95% CI; 1.08–5.52, p=0.029).

Alla 374 barn till kvinnor i VIGA-studien analyserades i den uppföljande studien om barnfetma. Medelvärdet för barnens BMI z-score eller andelen barn med fetma var inte lägre hos barnen i interventionsgrupp. Andelen barn med undervikt skiljde sig inte heller signifikant mellan grupperna. Överflödig viktuppgång under graviditet gav en ökad risk för barnfetma (BMI z-score ≥2) vid födelsen (OR=4.51; 95% CI 1.95-10.44, p=<0.001) men inte vid fem års ålder. Den starkaste prediktiva riskfaktorn för barnfetma vid fem års ålder var maternell pregravad obesitas (OR 4.81; 95% CI 1.56-14.83, p=0.006).

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