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Gestational Diabetes and Metabolic Outcomes

Quansah Dan Yedu

UNIL | Université de Lausanne

Faculté de biologie
et de médecine

Département de Médicine

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Thèse de doctorat ès sciences de la vie (Ph.D.)

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Par

Dan Yedu QUANSAH

Maîtrise en santé publique (MPH), Seoul National University, Republic of Korea

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Prof. Jean-François TOLSA, Président
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Prof. Niko GELDNER
Directeur de l'Ecole Doctorale

DEDICATION

To Mum and Dad for all the sacrifices

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ABSTRACT

Women with gestational diabetes mellitus (GDM) have increased weight and higher glucose levels during pregnancy and in the postpartum period compared to women without GDM. It is therefore recommended to prevent excess gestational weight gain (GWG) and also return to pre-pregnancy weight at 1-year postpartum. This is essential as higher postpartum weight retention (PPWR) at 1-year postpartum is a significant risk factor for long-term weight gain and the most important predictor of future diabetes in women with GDM. To tackle weight and subsequent metabolic health problems such as weight and glucose control in these women, there is a need to comprehend their risk and to investigate different lifestyle approaches. This thesis provides a better understanding of the novel concept of intuitive eating during and after pregnancy and its associations with metabolic health. It also investigates the predictors and consequences of PPWR in a cohort of women with GDM.

This thesis utilized data from the Lausanne University Hospital (CHUV) GDM longitudinal cohort. We assessed the cross-sectional and longitudinal associations between intuitive eating and metabolic health outcomes during pregnancy and in the postpartum period in women with GDM. We also investigated the predictors and consequences of weight retention in this cohort.

The cross-sectional analysis showed that intuitive eating during and after pregnancy was significantly associated with metabolic health outcomes, both with weight and with glucose control. The longitudinal analyses revealed that intuitive eating during pregnancy was also related to later metabolic health outcomes, at the end of pregnancy, but also in the early (6-8 weeks) and late (1-year) postpartum period. Regarding the predictors and consequences of PPWR, GWG predicted higher PPWR, both in the early and late postpartum period. Women with PPWR had worsened glucose control at 1 year postpartum that was not observed in the early postpartum period.

These results suggest that intuitive eating could represent a novel approach to weight and glucose management in women with GDM. Our data regarding the consequences of PPWR also suggest that clinical care with a strong focus on lifestyle interventions in order to improve weight and glucose control should be essential up to the late postpartum.

RÈSUME

Les femmes avec un diabète gestationnel (DG) ont un poids plus élevé ainsi qu'un contrôle glycémique moins favorable que les femmes sans DG durant leur grossesse ainsi qu'en post-partum. Les recommandations visent donc à prévenir une prise de poids excessive durant la grossesse ainsi que de revenir au poids d'avant la grossesse dans l'année qui suit l'accouchement. En effet, ne pas avoir perdu le poids pris durant la grossesse à un an post-partum est un facteur de risque significatif pour une évolution pondérale défavorable sur le long terme que pour le risque de DMII indépendamment du poids et de l'IMC avant grossesse. Aborder l'évolution du poids ainsi que les paramètres métaboliques chez ces femmes par de nouvelles approches impliquant le style de vie serait dès lors pertinent. Cette thèse a pour but d'apporter un nouvel éclairage sur l'association entre l'alimentation intuitive durant et après la grossesse et les paramètres métaboliques chez des femmes avec un diabète gestationnel. Elle recherche également les prédicteurs ainsi que les conséquences de la rétention de poids en post-partum chez les femmes avec un DG.

Les données utilisées pour évaluer les associations transversales et longitudinales entre l'alimentation intuitive et les paramètres métaboliques durant la grossesse mais également en post-partum sont issues d'une cohorte longitudinale de femmes suivies au Centre Hospitalier Universitaire Vaudois pour leur DG. Des analyses sur les conséquences d'une rétention pondérale ainsi que ses prédicteurs ont aussi été réalisées. Les analyses transversales ont démontré une association significative entre l'alimentation intuitive et la santé métabolique durant la grossesse ainsi qu'en post-partum. Les analyses longitudinales ont révélé une association entre l'alimentation intuitive et l'amélioration des paramètres métaboliques aussi bien à la fin de la grossesse, à 6-8 semaines post-partum ainsi qu'à 1 an post-partum. La prise de poids durant la grossesse était un prédicteur pour la rétention de poids après grossesse aussi bien à 6-8 semaines qu'à un an post-

partum et ses conséquences étaient des issues métaboliques défavorables à 1 an, mais pas à 6-8 semaines post-partum.

Ces résultats suggèrent que pratiquer une alimentation intuitive pourrait être une nouvelle approche dans la gestion le poids ainsi que l'équilibre métabolique chez des femmes avec un diabète gestationnel. Ces données sur la rétention de poids et la santé métabolique laissent penser qu'un accompagnement, au-delà des recommandations, pourrait être nécessaire chez ces femmes avec un antécédent de DG afin d'améliorer plus spécifiquement leur contrôle glycémique ainsi que pondéral.

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LIST OF ABBREVIATIONS

GDM: Gestational diabetes mellitus

IE: Intuitive eating

PPWR: Postpartum weight retention

WHO: World health organization

ADA: American diabetes association

IADPSG: International Association of Diabetes and Pregnancy Study Groups

GWG: Gestational weight gain

MNT: Medical nutrition therapy

GI: Glycemic index

BMI: Body mass index

IOM: Institute of medicine

HbA1c: Glycated hemoglobin

IES-2: Intuitive eating scale-2

CHUV: Lausanne university hospital

oGTT: Oral glucose tolerance test

RCT: Randomized controlled trials

EPR: Eating for Physical rather than Emotional Reasons

RHSC: Reliance on Hunger and Satiety cues

HAPO: Hyperglycemia and Adverse Pregnancy Outcome

1.0 GENERAL INTRODUCTION

1.1 Background

The main interest of this thesis lies in the field of gestational diabetes mellitus (GDM) and metabolic health outcomes during and after pregnancy. Most importantly, the relationship between nutrition and eating behavior (intuitive eating) with weight and higher glucose levels during and after pregnancy in women diagnosed with GDM. This introductory chapter summarizes the different thesis themes. These themes are GDM and metabolic outcomes during and after pregnancy, the potential novel role of intuitive eating (IE) in the management of GDM and the predictors and consequences of postpartum weight retention (PPWR) in the early and late postpartum period in women with GDM.

1.2 Gestational diabetes mellitus (GDM)

GDM is defined as any degree of glucose intolerance or hyper-glycaemia with onset or first recognition during pregnancy that does not fulfil the criteria of overt diabetes prior to gestation (1). It is usually diagnosed in the second or third trimester of pregnancy. GDM develops when beta cells fail to keep pace with the increase in insulin resistance that is observed around 20-24 weeks of gestation. This then causes an imbalance between demand and supply of insulin production and action and raises glucose levels, especially during the second and third trimester (2). GDM is one of the most common pregnancy complications. Between 3-20% of pregnant women develop GDM globally (3) and about 11% of all pregnancies in Switzerland are complicated by GDM (4).

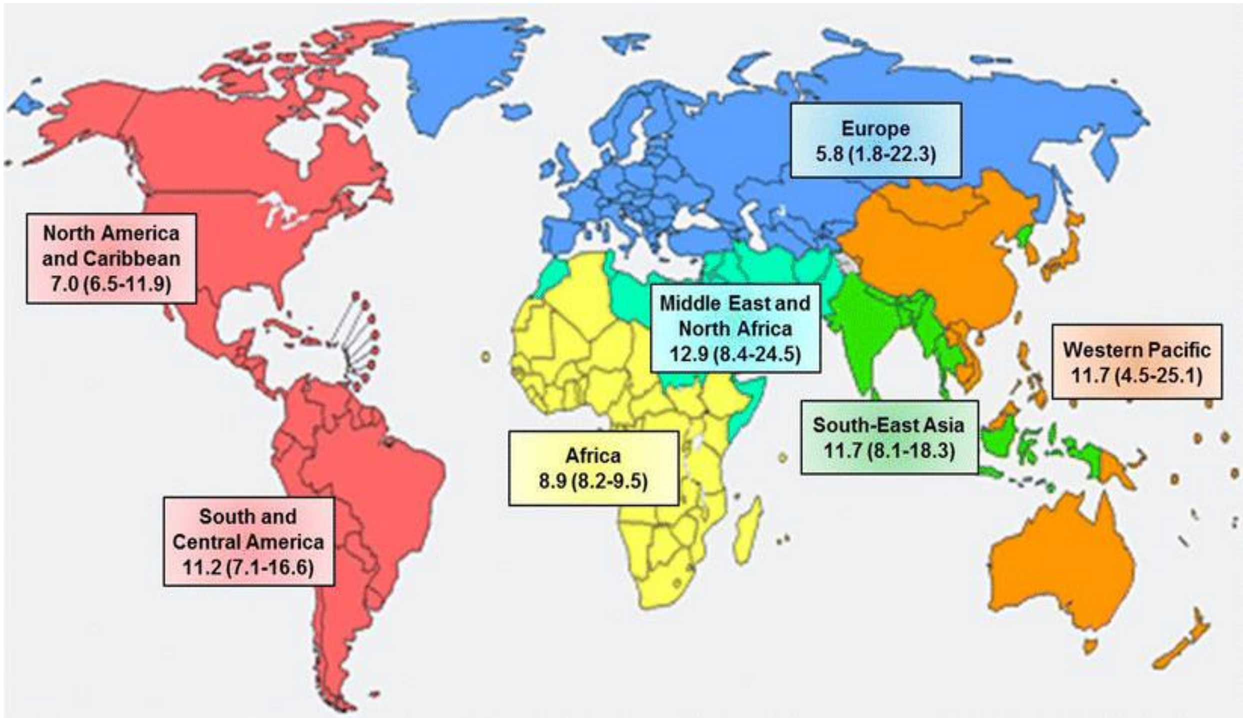

Fig 1: Median (interquartile range) prevalence (%) of GDM by WHO region 2005–2015 (5)

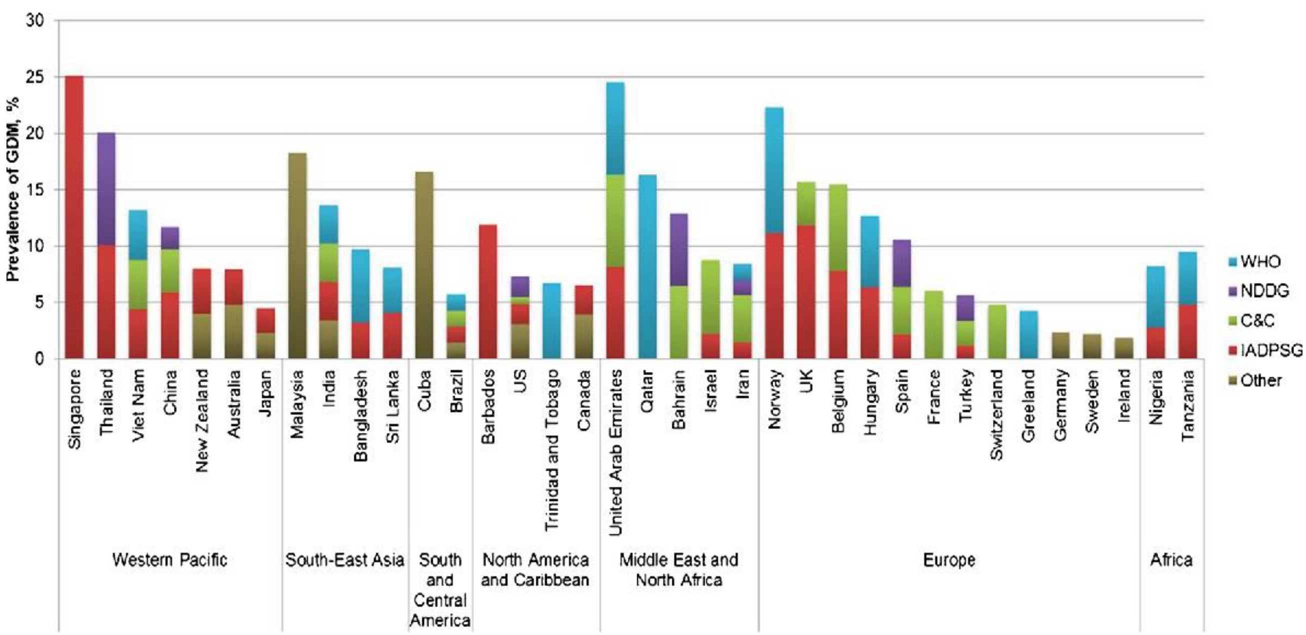

Fig 2: Country-specific prevalence of GDM according to different diagnostic criteria.
C&C: Carpenter and Coustan criteria, IADPSG: International Association of Diabetes and Pregnancy Study Groups, NDDG: National Diabetes Data Group, WHO: World Health Organization, other included International Classification of Diseases codes and local guidelines or criteria (5).

1.3 Detection and diagnosis

Pregnant women with increased risk of GDM are recommended to undergo testing during the first prenatal visit (1). If results are negative during the initial screening, there is the need for another screening test between 24 and 28 weeks of pregnancy. Women with an average risk are however recommended to be screened at 24–28 weeks.

During pregnancy, screening for abnormal glucose level is generally recommended as a routine component of prenatal care (1,6,7). This is because an abnormal glucose levels in pregnancy are associated with both short and long-term maternal and fetal risks. Several health organizations/countries have different and diverse recommendations for screening, diagnosis, management, and follow-up of GDM (8). Most of these proposals or recommendations for GDM are contentious because some of them were developed from unscientific studies, based on expert-opinion, catered to preserve resources and subjectively modified for convenience. Because of the diverse recommendations, the approach to GDM can be extremely different from one country to another (8). This lack of consensus creates problems in addressing prevalence, complications, efficacy of treatment and follow-up of GDM.

The American diabetes association (ADA) and the International Association of Diabetes and Pregnancy Study Groups (IADPSG) recommendations are widely used and accepted (1,9). These recommendations are based on the results from the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study. The HAPO study is a large-scale multinational cohort study of more than 23,000 pregnant women, which showed that the risk of adverse maternal and neonatal outcomes continuously increased as a function of maternal glycaemia during the oral glucose tolerance test (oGTT) at 24–28 weeks of gestation (9). The ADA recommendation for GDM diagnosis consists of two strategies; the “one step” and the “two step” approaches.

The "one-step" approach is derived from the IADPSG criteria, which is based on a 75g oGTT with plasma glucose measurement at 1and 2h after an 8-hour overnight fasting. The "two-step" approach consist of, 1) performing a 50g glucose load test (non-fasting) with plasma glucose measurement at 1hour. If the plasma glucose level is ≥ 7.2, 7.5 or 7.8 mmol/L respectively then a 100g oGTT is followed. 2) A 100g oGTT is performed when the patient is fasting.

Although differences exist in the management of GDM according to the ADA and the IADPSG guidelines, the screening guidelines somewhat remains the same except the two-step approach recommended by the ADA (10). Both guidelines recommend screening between 24 and 28 weeks. When a patient exceeds one or more threshold values, the diagnosis of GDM can be made. The threshold values for the ADA ("one step" approach) and IADPSG are; fasting glucose ≥5.1 mmol/l, 1h ≥10.0 mmol/l and 2h ≥8.5 mmol/l. The threshold for the ADA "two-step" approach are fasting glucose ≥5.3 mmol/l, 1h ≥10.0 mmol/l, 2h ≥8.6 mmol/l and 3h ≥7.8 mmol/l. Recommendation with relatively low cut-off points leads to a relatively high incidence rate of GDM, including many women with mild hyperglycemia and vice versa (8).

Table 1 Diagnosis of GDM with an HGPO of 75 g of glucose between 24-28 weeks of amenorrhea (plasma venous blood sugar)

Glucose	**mmol/l**
Fasting	**≥ 5.1**
1-h	**≥ 10.0**
2-h	**≥8.5**

Table 2 Comparison of some diagnostic criteria of GDM

Organization	**Glucose Load, Grams**	**Glucose Thresholds (mmol/L)**				**Number of OGTT Values for Diagnosis ≥**
		Fasting	**1-h**	**2-h**	**3-h**	
NDDG (ACOG)	100	5.8	10.5	9.2	8.0	2
C&C(ACOG)	100	5.3	10.0	8.6	7.8	2
IADPSG/ADA/WHO/ADIPS/FIGO/BSD	75	5.1	10.0	8.5	-	1
CDA	75	5.3	10.6	9.0	-	1
NICE	75	5.6	-	7.8	-	1
DIPSI	75	-	-	7.8		-

ACOG: American College of Obstetrics and Gynecology. ADA: American Diabetes Organization. ADIPS: Australian Diabetes in Pregnancy Society. BSD: Brazilian Society of Diabetes. CDA: Canadian Diabetes Association. C&C: Carpenter and Coustan. DIPSI: Diabetes in Pregnancy Study group in India. FIGO: The International Federation of Gynecology and Obstetrics. FPG: Fasting plasma glucose. IADPSG: The International Association of Diabetes and Pregnancy Study Groups. NDDG: National Diabetes Data Group. NICE: National Institute for Health and Care Excellence. WHO: World Health Organization.

1.4 GDM risk factors and adverse outcomes

The adverse maternal consequences of GDM are well documented (10). A meta-analysis of observational studies (11,12) showed that higher pre-pregnancy body mass index (BMI), excess gestational weight gain (GWG), pregnancy-induced hypertension, family history of diabetes, polycystic ovary syndrome and multi-parity are significant risk factors of GDM (13). According to the ADA, individual who have a first-degree relative with diabetes, high-risk race/ethnicity (e.g., African American, Latino, Native American, Asian American, Pacific Islander), history of cardiovascular disease, hypertension, high-density lipoprotein, cholesterol level <35 mg/dl and/or a triglyceride level >250 mg/dl and physical inactivity are at a higher risk for GDM and diabetes in general (7).

Other non-classical risk factors in pregnancy include excessive GWG, hypothyroidism, life events such as psychological stress, depression and other clinical conditions associated with insulin resistance (14). It has also been shown that women with preexisting β-cell dysfunction have reduced ability to increase insulin secretion to compensate for the decreasing insulin sensitivity as pregnancy progresses leading to an impaired glucose tolerance and the development of GDM.

GDM of any severity increases the risk of fetal and maternal complications both during and after pregnancy (15). Generally, adverse outcomes that are increased in the offspring of women with GDM include spontaneous abortion, fetal anomalies, preeclampsia, fetal demise, macrosomia, shoulder dystocia, neonatal hypoglycemia, hyperbilirubinemia, neonatal respiratory distress syndrome and preeclampsia among several others. In addition, GDM may increase the risk of obesity, hypertension and future diabetes in the offspring later in life (6,9,16,17). GDM is associated with an increased frequency of maternal hypertensive disorders and the need for cesarean delivery. Higher glycemic values lead to increased fetal glucose uptake which in turn stimulates fetal insulin secretion (18). This increases fetal adiposity and neonatal hypoglycemia once the neonate leaves the hyperglycemic maternal environment but its hyperinsulinemia still continues.

In the postpartum period, women with GDM have a higher risk of prediabetes and of future diabetes. Around 48% of women with GDM develop prediabetes and between 20%–60% of them develop diabetes in the postpartum period (2). The conversion of GDM to prediabetes and subsequent development of diabetes continues to be on the rise making GDM one of the important risk factor for diabetes (19). GDM also leads to longer-term risk of metabolic syndrome and cardiovascular morbidity and mortality (15,18,20–23).

A recent systematic review and meta-analysis including 9 studies in more than 5 million women found that GDM was associated with a 56% higher risk of future cardiovascular events and conferred a 2.3-fold increased risk of cardiovascular events within the first decade after pregnancy (24). This risk remained increased even in the absence of the development of diabetes (24).

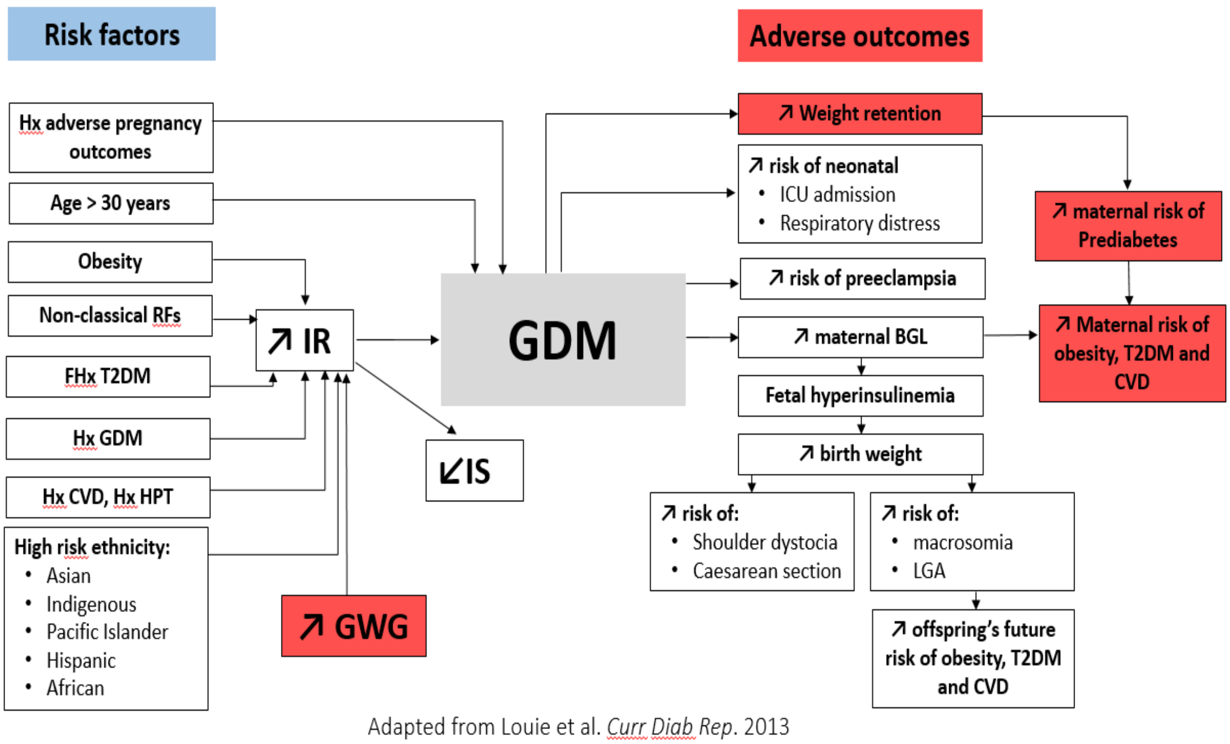

Fig 3: Risk factors and adverse outcomes of gestational diabetes (25).

The figure above however focuses more on insulin resistance and has little information on the reduction in insulin secretion in women with GDM. It does not also capture all the risk factors associated with GDM (indicated above) which include for example polycystic ovarian syndrome, history of cardiovascular disease including hypertension and physical inactivity as well as non-classical risk factors including excessive gestational weight gain, life events and depression.

GDM: gestational diabetes mellitus; IR: insulin resistance; IS: Insulin secretion; T2DM: type 2 diabetes mellitus; CVD: cardiovascular diseases; FHx: family history; BGL: blood glucose level

1.5 GDM and postpartum weight retention

Postpartum weight retention (PPWR) is defined as the difference between pre-pregnancy weight and weight at the 1-year postpartum period (26). PPWR is frequent (27) and represents a huge public health concern because of its contribution to the increase in non-communicable diseases and associated morbidities (28,29). Specifically, although women are advised to return to their pre-pregnancy weight after delivery, a significant proportion of pregnant women are unable to meet this recommendation (30,31). At 6-8 weeks postpartum for example, women with or without GDM retain an average of 3–7kg of GWG and at least two-thirds of women will still be above their pre-pregnancy weight even at 1-year postpartum (29,31). In the long term, PPWR leads to an upwards weight trajectory for women following childbirth and may lead to the development of several metabolic outcomes (32–34). It has been shown that modest PPWR increases the risk of obesity and higher PPWR leads to an increased risk of permanent obesity 5-10years after birth, risk of diabetes and other cardiovascular diseases (35). In women with GDM (36), PPWR is associated with a higher risk of overweight/obesity (37), of prediabetes (38), of recurrent GDM (39) and of future diabetes (40,41). According to a study, PPWR of 4.5kg during a 7.5year follow-up was independently associated with a two-fold increase in the risk of future diabetes in women with GDM (42). In a 23 years follow-up, 42% of women with PPWR developed diabetes while the incidence of diabetes was almost half in the women without PPWR (43).

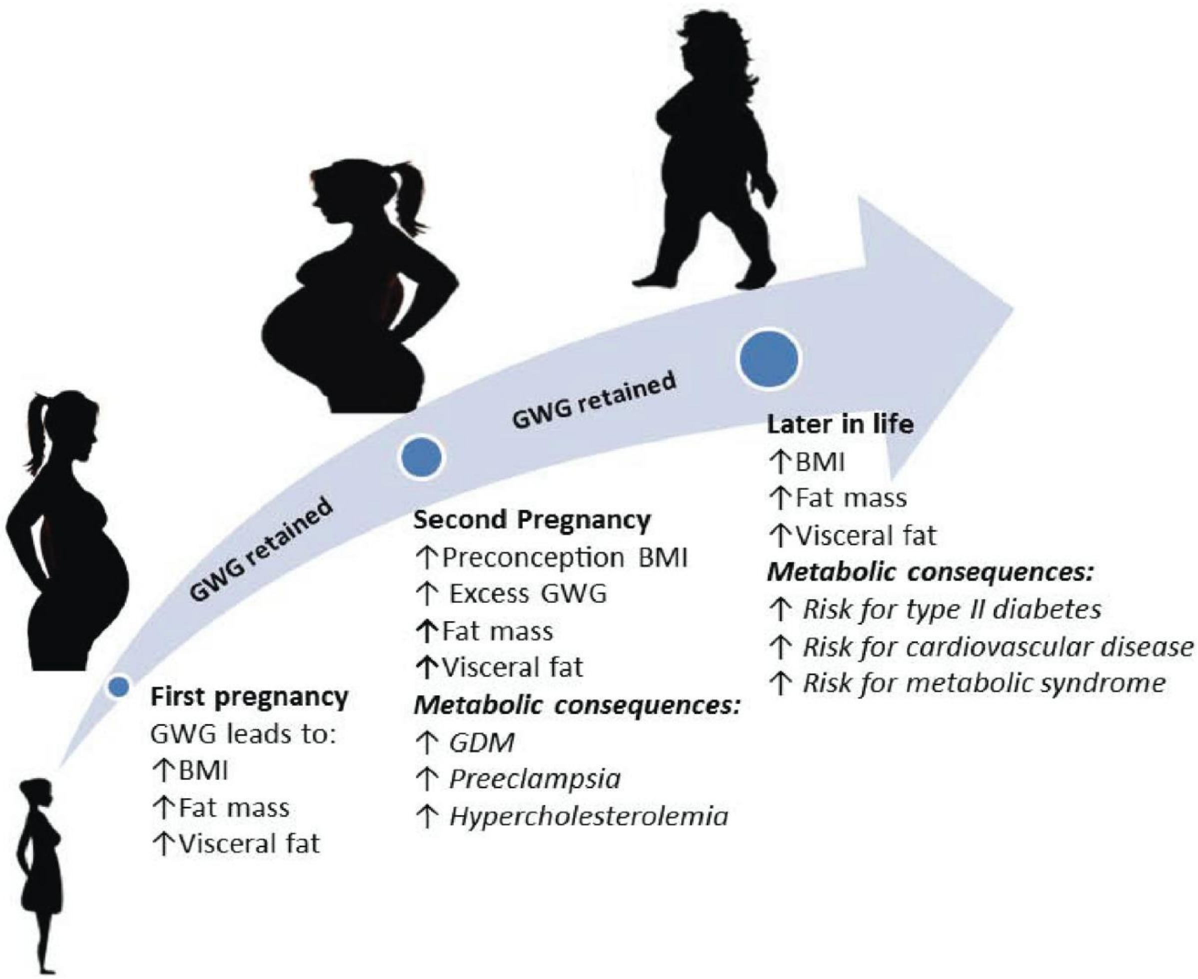

Fig 4: Long and short-term metabolic consequences of (excess) gestational weight gain (GWG) and postpartum weight retention in reproductive age women. (44).
BMI: body mass index; GDM: gestational diabetes mellitus

1.6 Predictors of PPWR

Knowledge of the factors associated with PPWR can help to focus efforts and target optimal timing for interventions to reduce the long-term complications of PPWR in women with GDM. In the general population, the most important predictors of PPWR are higher pre-pregnancy BMI and excessive GWG (45,46). Other studies have also associated high fat and high energy-dense diets, physical inactivity, age, single women (47–49) and minority ethnic groups with PPWR (50).

A study reported that excess GWG, physical inactivity and increased amount of food intake in the postpartum period have increases the risk of PPWR (49). A systematic review also indicated that women aged below 20 or over 40 years at delivery, single women and women with lower income have a higher risk for PPWR (49). Other studies have shown that eating behavior (increase in intuitive eating habits), exclusive breastfeeding and lack of depression during and after pregnancy are protective factors for PPWR (51–53). It has been show that exclusive breastfeeding over 6 months and up to 24 months is protective of diabetes in women with GDM (54). In non-GDM populations many studies support excess GWG as a strong and pronounced predictor of PPWR at 6 weeks (55) and up to 12 months postpartum (56–59). Other studies suggest that exceeding the institute of medicine (IOM) guidelines according to pre-pregnancy BMI increases the risk of PPWR at 6 to 18 months (60–62). In 2009, the IOM published a revision of GWG guidelines that are based on pre-pregnancy BMI. These GWG recommendations were 12.5–18kg for underweight (<18.5kg/m^2), 11.5–16kg for normal weight (18.5–24.9kg/m^2), 7–11kg for overweight (25.0–29.9kg/m^2) and 7kg for obese women (≥30kg/m^2). These recommendations were supported by the WHO and were independent of age, parity, smoking history, race and ethnic background (63). However, studies in non-GDM populations only investigated excessive GWG without including total or absolute GWG. No study has investigated the effect of both exceeding IOM guidelines (=excessive GWG) and total GWG on PPWR and in the current population these guidelines may not be appropriate (anymore). In women with GDM, only one small study (n=75) has investigated the predictors of weight loss or lack of PPWR in women with GDM but it exclusively focused on the early postpartum period (6 weeks postpartum) (31). In that study, less GWG and no insulin use during pregnancy predicted a loss of at least 75% of GWG.

It is however not clear if those are also predictors of the recommended "complete" lack of PPWR (i.e. no weight increase at all when compared to the pre-pregnancy weight) and it is also not clear from a pathophysiological point of view why the authors chose a loss of at least 75% and not the recommended lack of PPWR.

1.7 Interventions to manage GDM

The goal of GDM management is to promote glucose control and improve pregnancy outcomes (2). As part of the recommendation for the management of GDM, all women with GDM are to receive nutritional and physical activity counseling. This is to help improve and stabilize glycemic targets. If nutritional and physical activity counselling are not sufficient to improve glycemic targets, other approaches such as medical nutrition therapy (MNT), insulin therapy or oral anti-diabetic pharmacological therapies including metformin are adopted (6,64).

Regarding the use of MNT, provision for adequate calories and nutrients to meet the needs of pregnancy are made to be consistent with established maternal blood glucose goals. Non-caloric sweeteners are to be used in moderation and for obese women, a 30–33% calorie restriction (to 25 kcal/kg actual weight per day) has been shown to reduce hyperglycemia (65,66). The ADA medical nutrition therapy recommendations for women with GDM include developing an individualized nutrition plan based on a minimum of 175g of carbohydrate, a minimum of 71g of protein, 28g of fiber and to have a diet low in saturated fat (6). The Endocrine society recommends 35-45% of carbohydrates, 3 small-to-moderate-sized meals, 2 to 4 snacks for non-obese women and restricting one-third of 1600-1800kcal/d calorie intake for obese women (67). The objectives of these guidelines are to provide optimal calorie intake needed to promote fetal/neonatal and maternal health while achieving glycemic goals and promoting optimal GWG.

A recent Cochrane review suggested that although dietary advice is the main strategy for managing GDM, it however remains unclear what type of advice is best and hence more evidence on the type of nutritional advice is needed (68). Studies show that a restriction of carbohydrates to 35–40% of calories decreases maternal glucose levels and improves maternal and fetal outcomes (69).

Regular physical activity during pregnancy in general improves or maintains physical fitness, promotes weight and glucose control and enhances psychological well-being. Although there are no specific or detailed physical activity guidelines for women with GDM, it is recommended to engage in both aerobic (including walking, jogging, aerobic dance, swimming, hydrotherapy aerobics, rope skipping, hiking and rowing) and resistance exercise (e.g. weightlifting) at a moderate intensity of a minimum of three times a week (30-60min each time for at least 150minutes per week) (70).

Regarding GDM treatment recommendations, the ADA recommends insulin as the preferred medication for treating hyperglycemia. The use of metformin and glyburide is not recommended as first-line agents as both drugs cross the placenta to the fetus. It also recommends that metformin should be discontinued at the end of the first trimester if it is used to treat polycystic ovary syndrome and induce ovulation (6). The use of insulin together with MNT also reduces fetal morbidities.

It is worthy to note that several other recommendations include the use of metformin for women with GDM (71). For example, the National Institute for Health and Care Excellence (NICE), recommends insulin over metformin for women with GDM. However, metformin can be administered if blood glucose targets are not met even after changes in diet and exercise (71).

Regarding long-term GDM management and the prevention of future metabolic risks, a routine screening at 4-12weeks postpartum is recommended (1). Metabolic changes after pregnancy turn back to “normal” around 4-6weeks after delivery. Due to insurance purposes, this screening is performed before 8weeks postpartum in Switzerland. The ADA recommends performing a 75g oGTT. Diagnostic criteria are the same as outside of pregnancy or the perinatal period and are as follows: normal glucose: if fasting glucose is <5.6mmol/l, 2h is < 7,8 mmol/l and HbA1c is < 5.7%; prediabetes/glucose intolerance: if either fasting glucose is 5.6-6.9 mmol/l, or 2h is 7.8-11.0 mmol/l or HbA1c is 5.7- 6.4% and diabetes is diagnosed if fasting glucose is ≥7.0, mmol/l, or 2h is ≥11.1 mmol/l or HbA1c is ≥6.5% (7).

If glucose levels are normal at around 6weeks postpartum, reassessment of glycaemia at 1-3 yearly interval is recommended using fasting glucose and/or HbA1c (1). Women with impaired fasting glucose or impaired glucose tolerance at 6weeks postpartum need annual testing; these patients are to receive intervention because of their higher diabetes risk (9). Educating and counselling patients with previous GDM on lifestyle modifications helps to lower the risk of insulin resistance including maintenance of normal body weight through healthy nutritional habits and physical activity. Education should also include the need for family planning to ensure optimal glycemic regulation before and from the start of any subsequent pregnancy.

1.8 Role of lifestyle interventions in GDM management

The cornerstone of GDM treatment requires nutrition/diet and exercise intervention to achieve weight and glucose control and also to reduce the need for medical therapy (64). These interventions are collectively termed as lifestyle interventions. These interventions provide dietary and lifestyle advice as the primary prevention strategy for women with GDM (10,72).

Regarding nutrition several diets such as low glycemic index (GI) diet, total energy restriction diet, low carbohydrate diet and ethnic or traditional diets, such as the Mediterranean diets are have been studied for the management of weight and glycemic control in women with GDM. Regarding physical activity/exercise intervention several exercise regimes also exist.

The results of these lifestyle interventions have however been unsatisfactory and their sustained effects have been controversial (10,73). In a Cochrane review of lifestyle intervention trials among women with GDM, only one trial found a difference between the intervention and the control group regarding the incidence of type-2 diabetes and prediabetes in the postpartum period (10). In a study involving lifestyle intervention during and after pregnancy in women with GDM, there were no significant differences in postpartum weight and in physical activity between the intervention and control group but the intervention group had a decreased dietary fat intake (74). In another recent systematic review and meta-analysis of 15 trials in women with previous GDM, half of the lifestyle interventions led to a marginal reduction in weight and the incidence of diabetes but effect sizes were small and their sustained effects remain controversial (75). It is therefore of utmost importance to explore new approaches to weight and glucose control in these women. In addition inconsistency, imprecision and the variation in the content of the lifestyle intervention is of major concern.

1.9 Eating behavior and GDM

Eating behavior relates to food choices and motives, eating practices, dieting, and eating-related problems such eating and feeding disorders (76). Eating behavior focuses on the etiology, prevention, treatment of eating disorders as well as the promotion of healthy eating patterns (76). Poor dietary behaviors are prevalent among women with GDM and hence confidence associated with healthy eating behaviors can help improve GDM outcomes (77).

Skills in cooking healthy foods along with family food preferences and time pressures are important influences on eating habits (78). Behavioral and cognitive factors mediate healthy behaviors by improving eating behaviors and habits (79).

Negative emotions such as depression are psychological factors related to eating disorders. Some individuals who struggle with their weight engage in a maladaptive eating behavior termed emotional eating (80). Emotional eating refers to the tendency to eat in response to aversive negative states (81) and has been related to both obesity and depressive symptoms (80,82). Individuals who engage in disordered eating tend to think of food as either "good or bad", themselves as being "on" or "off" a diet and their weight as "acceptable" or "totally unacceptable" (83). Rigid dietary rules and all-or-nothing cognitions are generally present in individuals with weight and glucose problems such as those with GDM. Eating behavior plays an important role in explaining weight-BMI relationships and cardio-metabolic outcomes (79,84–87). Therefore, in the context of identifying interventions to promote healthy weight and glucose levels during and after pregnancy in women with GDM due to the inconsistent and controversial results from typical lifestyle interventions, other interventions that promote eating behavior and not exclusively focused on food choices could play a novel role.

1.10 The intuitive eating concept

Research suggests that adaptive eating behaviors that encourage people to recognize and respond to their internal signs of hunger and satiety prevents emotional eating and dietary restriction (88–90) and may lead to lower weight and BMI (91). One such adaptive eating behavior is intuitive eating (IE). IE is characterized by eating in response to physiological hunger and satiety cues rather than external and/or emotional cues (92,93).

IE has interoceptive abilities that determine when and how much to eat and to accurately perceive and respect one's hunger and satiety cues. IE tendencies are related to emotional, psychological and physical well-being (94). The concept of IE as interoceptive comprises of sensing the physiological condition of the body as well as the representation of the internal state (95).

IE is a more sustainable long-term eating behavior than dieting and is known to be associated with lower levels of cholesterol and cardiovascular risk. It is also inversely associated with disordered eating behavior, leads to body shape satisfaction and is associated with lower weight and glucose control in cross-sectional studies (96,97).

IE is assessed with the Intuitive Eating Scale-2 (IES-2); a validated self-report questionnaire (91). The original version of the IES-2 (English version) consists of four subscales. These subscales are 1) Eating for physical rather than emotional reasons subscale that assesses how much eating is affected by emotional responses. 2) The Reliance on hunger and satiety cues subscale that evaluates the extent to which individuals are aware and able to trust internal signals rather than relying on external rules/cues. 3) The Unconditional permission to eat when hungry subscale that assesses whether an individual purposefully tries to ignore hunger and satiety signals and 4) the Body-Food Choice Congruence subscale (91). The validated French version however contains three subscales. These are the eating for physical rather than emotional reasons subscale, the reliance on hunger and satiety subscale and the unconditional permission to eat subscale (98).

1.11 Intuitive eating and dietary intake

Despite that fact that IE has shown benefits for psychological wellbeing and improvements in physical health and wellbeing, there is scarce information on the relationship between IE and food/dietary intake (99).

One could attribute this to the concern that nutritionists do not promote IE due to a concern that individuals may consume high levels of high fat or high sugar foods (100). On the contrary however, IE involves the idea of 'body wisdom' (101) and eating intuitively is expected to lead and promote healthy dietary patterns and food intakes (102). One principle of IE specifically refers to making "food choices that honor your health and taste buds while making you feel well". Since restrained eaters tend to overeat (103) and emotional eaters tend to consume more fatty or sweet foods over time (104), reductions in restraint and emotional eating through IE may rather lower intakes of such foods. Few studies have explored the relationships between food intake and IE among men and non-pregnant women (105). A study that explored the first three dimensions of the intuitive eating scale-2 (IES-2; eating for physical rather than emotional reasons subscale, reliance on hunger and satiety cues subscale and the unconditional permission to eat subscale) reported that different aspects of IE relate to food intake in different ways (105). Few studies have explored the impact of IE interventions on food intake outside of pregnancy and findings were mixed. Three studies reported a positive impact on diet quality scores (102,106,107), while others found a relationship between higher IE scores and healthy dietary intake (108,109). Results from the Swiss food panel study also revealed that the four subscales of IES-2 showed different relationships with food intake (99). In contrast to the other subscales, unconditional permission to eat moderately correlated with poorer diet quality scores and consistently showed associations with a more negative self-evaluation of eating behavior. The other three IES-2 subscales showed a few small positive and negative correlations with food intake including positive associations of diet quality scores in women with the eating for physical rather than emotional reasons and the reliance on hunger and satiety cues subscales.

There is therefore the need for further studies to investigate the relationship between IE and dietary intake in a quest to find strategies to promote healthy weight and improve glucose control in women with GDM.

1.12 Intuitive eating and metabolic outcomes

Dietary intake mediates the relationship between IE and metabolic health outcomes and hence there is the need to identify strategies that promote both healthy dietary eating and intuitive eating. IE practices promote metabolic health by preventing disordered and emotional eating that are associated with adverse metabolic health outcomes (88). Compared to studies (110,111) that focused on lifestyle interventions and nutritional advice such as total energy intake, macronutrient contents of foods, type of carbohydrates, portion sizes and eating frequency, IE represents an interesting and different approach to weight loss and glycemic control. Outside of pregnancy, evidence from cross-sectional studies suggest that IE is associated with lower BMI (112–114) with weight loss in an intervention trial (115,116) and with glycemic control in two observational studies involving the general adult population (117,118) and with lower weight and fasting glucose in the postpartum period (119). Studies have confirmed the association between IE with improved metabolic outcomes such a weight, BMI and fasting glucose (91,93,120). Furthermore, eating in response to hunger and satiety signals predicted lower BMI in a study involving 1600 New-Zealand women aged 40–50 years. In a study involving adolescent with type-1 diabetes, increased adherence to IE was associated with 11% lower HbA1c per unit increase in IE score (117). In another cross-sectional study, the relationship between IE and BMI was partially mediated by frequency of binge eating. This suggests that higher adherence to IE may prevent disordered eating and in turn influence weight and BMI outcomes (114).

A large population based study (9581 men and 31,955 women) in France indicated a stronger cross-sectional association between higher IE scores with lower odds of overweight or obesity in both men and women and thus support earlier findings using smaller sample sizes that IE adherence leads to favorable metabolic health outcomes (116).

According to a review of 26 studies (17 cross-sectional survey studies and 9 clinical studies, 8 of which were randomized controlled trials) cross-sectional surveys found an inverse association between IE and BMI (118). IE was positively associated with various health indicators such as blood pressure and cholesterol levels (118). Results from 9 clinical trials involving a total of 941 obese/overweight women found that IE leads to weight maintenance and improves physical health indicators including glucose control (118). Research on IE has increased in recent years. Past research demonstrates substantial and consistent associations between IE and metabolic health. These notwithstanding, no study have investigated the potential association between IE during pregnancy with any metabolic health outcomes including weight and glucose levels. Specifically, there is no study focusing on women with GDM either during pregnancy or in the postpartum period. It is therefore important that future studies explore the relationship between IE and weight and glucose levels outcomes in women with GDM in the perinatal period as they are at a higher risk of weight gain and metabolic disturbances such as prediabetes and diabetes during this critical time period. This is particularly important in view of the low success of lifestyle interventions and the need for new approaches to weight loss and glucose control.

2.0 AIMS OF THE THESIS

2.1 Overall thesis goal

The overall goal of this thesis was to study the relationship between nutrition behavior (focusing on intuitive eating (IE)) with weight and glucose levels in women with GDM. It sought to primarily determine cross-sectional and longitudinal relationships between IE and weight and glucose levels during and after pregnancy in these women. It also investigated the predictors and consequences of PPWR in the early and late postpartum period.

2.2 Thesis outline and study objectives

This thesis is divided into three different studies/articles. Below are the individual studies and their specific objectives.

1. Intuitive eating is associated with metabolic health during pregnancy and in the early postpartum period in women with GDM (Study 1)

Objective: To investigate the cross-sectional and longitudinal associations between IE and metabolic health during pregnancy and in the early post-partum period.

Hypothesis: IE is associated with weight and glycemic control during pregnancy and in the early postpartum period in women with GDM.

2. Intuitive eating is associated with improved health indicators at 1-year postpartum in women with GDM (Study 2)

*Objective***:** To evaluate the associations between IE during and after pregnancy with metabolic health outcomes at 1-year postpartum in all women with GDM who were followed beyond the early postpartum period and in high-risk GDM subgroups with pre-pregnancy overweight/obesity or with postpartum prediabetes.

Hypothesis: There are longitudinal and cross-sectional associations between IE during and after pregnancy with metabolic health at 1-year postpartum in women with GDM and in high-risk GDM subgroups with overweight/obesity or with prediabetes.

3. Predictors and consequences of weight retention in the early and late postpartum period in women with GDM (Study 3)

Objective: To determine the predictors and consequences of PPWR in the early and late postpartum period in women with GDM.

Hypothesis: Anthropometric (e.g. pre-pregnancy weight, changes in weight, BMI) and glucose control variables (fasting glucose, HbA1c) are predictors of PPWR and women with PPWR have increased adverse metabolic consequences in the early and late postpartum period compared to those with no PPWR.

It is worthy to note that, all three studies (1-3) are published. Details of these studies can be found in the appendix section.

3.0 GENERAL METHODS

The first part of this section of the thesis provides a summary of the main methods involved in this thesis and the second part summarizes the specific individual methods involved in the different studies. Complete and detailed methods used in each study/article can be found in the appendix section.

3.1 Summary of the general methods

3.2 General participant consent and recruitment

This thesis utilized data from an ongoing cohort of women with GDM. We invited pregnant women diagnosed with GDM to participate in this cohort at the GDM clinic in the Lausanne University Hospital (CHUV). Our participants were pregnant women referred by the CHUV antenatal clinic and by obstetricians in private practice in the Canton de Vaud. The Human Research Ethics Committee of the Canton de Vaud approved the study protocol (326/15).

3.3 Cohort database

This ongoing longitudinal cohort started in October 2011. The database consists of data from women with GDM followed during pregnancy and in the postpartum period at the GDM clinic in the CHUV. In August 2015 we extended the follow-up period from 6-8 weeks postpartum to 1-year and subsequently also included IE assessment. The individual studies involved in this thesis utilized data during pregnancy, in the 6-8 weeks and 1-year postpartum period depending on the objective of the individual study/article.

3.4 General data collection and assessments

Data from women in this cohort and involved in this thesis were retrieved from seven time points that correspond to six clinical visits.

Initially, women are screened for GDM using an oGTT (pre-GDM/ first time point). This first visit is not in the GDM clinic. Then women are seen for the first time in the GDM clinic (first GDM visit/ second time point) where anthropometric measures, HbA1c, assessment of intuitive eating (since 2015) and demographic characteristics are assessed. A dietary counseling by a dietitian then follows after 1week where participants are advised on the carbohydrate content of their foods and drinks and the need to avoid or limit certain foods in order to improve their eating habits and glycemic profile (third time point). The fourth time point is the last visit during pregnancy prior to delivery. During this visit metabolic and anthropometric variables were again assessed. At delivery (fifth time point) obstetric and neonatal outcomes of the study participants and their offspring are assessed. This visit is not in the GDM clinic. Women then attend a 6-8weeks postpartum (sixth time point) visit after delivery, which is characterized by glucose control assessment i.e. the performance of an oGTT and HbA1c, and collection of anthropometric data, intuitive eating assessments and a clinical visit with a physician and dietician together. The last visit (seventh time point) is the 1-year postpartum visit. During this visit, women are assessed again for glucose control assessment i.e. fasting glucose and HbA1c, anthropometric data, and intuitive eating measurements. Below is a detailed presentation of the GDM clinic set-up, visits and the measures at each time point.

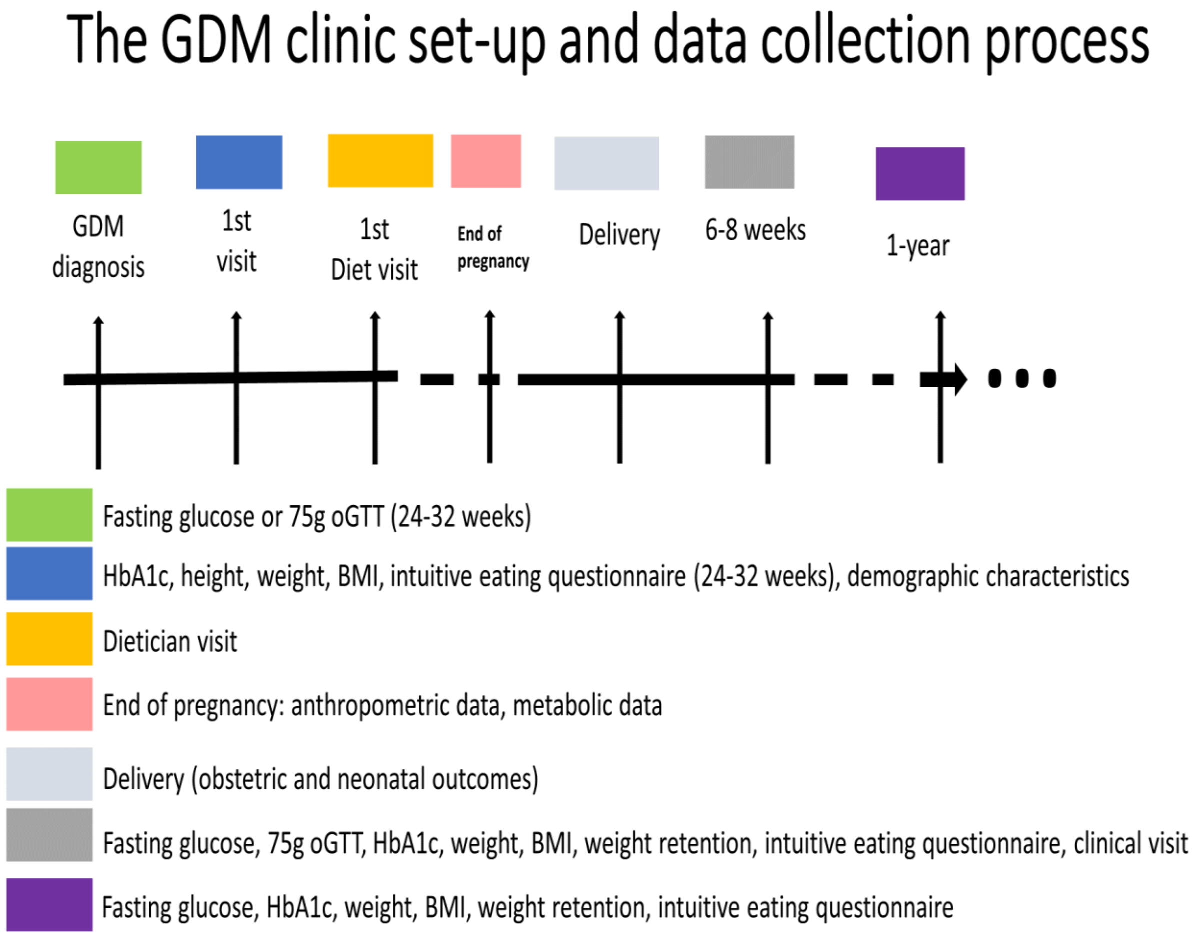

Fig 5: GDM cohort set-up and data collection process.

The cohort database is hosted by an online data management resource called *SecuTrial***,** which is jointly managed by the CHUV information technology unit and the GDM research unit. Below is an image of the various time points and individual data stored. The ongoing longitudinal cohort has 1441 participants who are at various stages of the data collection as of 31.01.2020.

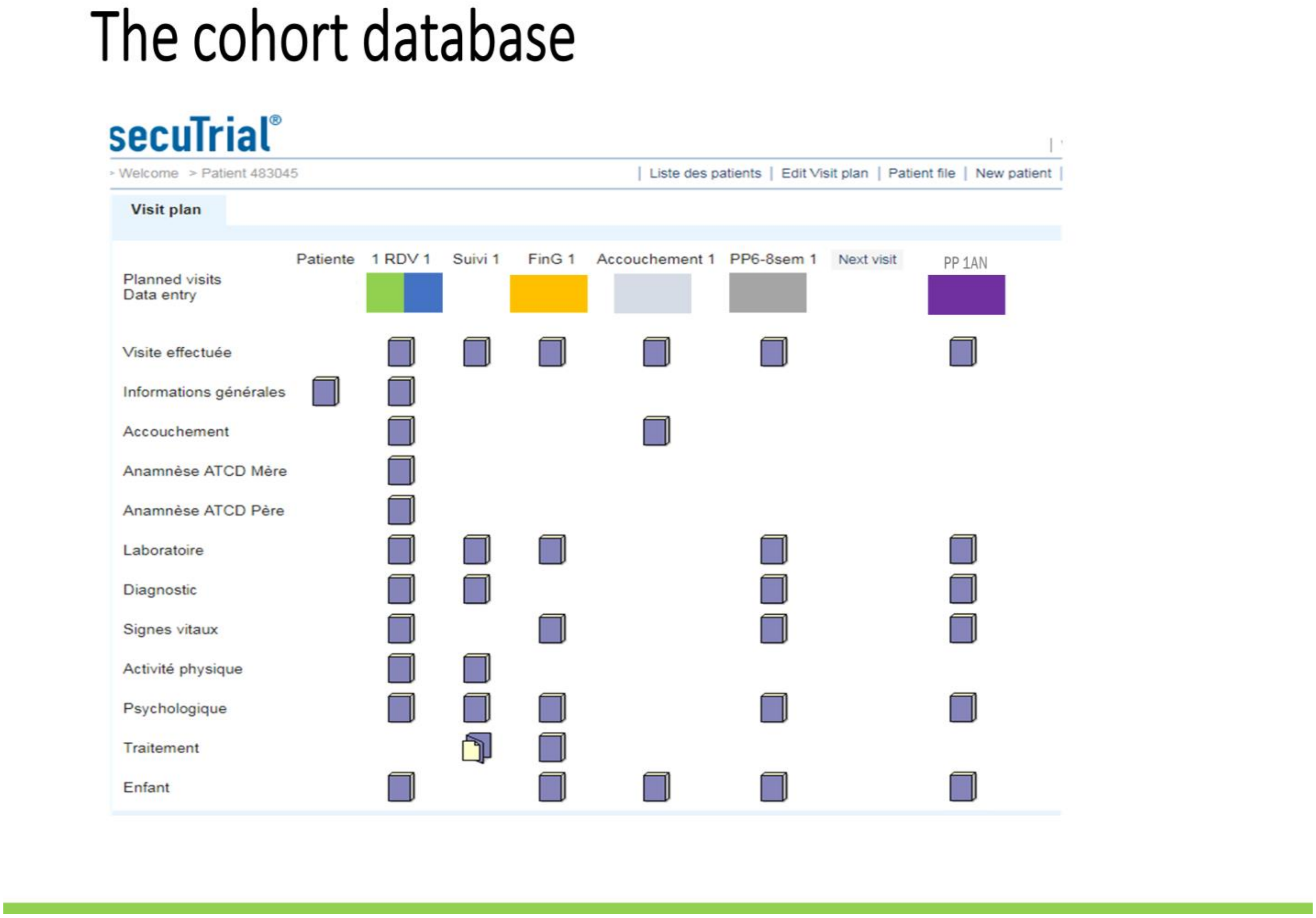

Fig 6: The online data management platform of the cohort data

3.5 General inclusion and exclusion criteria

The general inclusion criteria in this thesis were women who were ≥18 years with GDM diagnosis that were followed in the GDM clinic, who understood French or English and consented to participate. Data used in all the analyses of this thesis first excluded those with known type-1 diabetes, type-2 diabetes, newly diagnosed diabetes in pregnancy, glucose intolerance but no GDM, those with normal oGTT results, with GDM diagnosed at ≤13 weeks and those participating in an active lifestyle intervention study.

Depending on the specific study objective, other exclusion criteria were applied. This included the removal of those who did not attend the 6-8 weeks postpartum visit, those without IE scores or those without data for the 1-year postpartum visit.

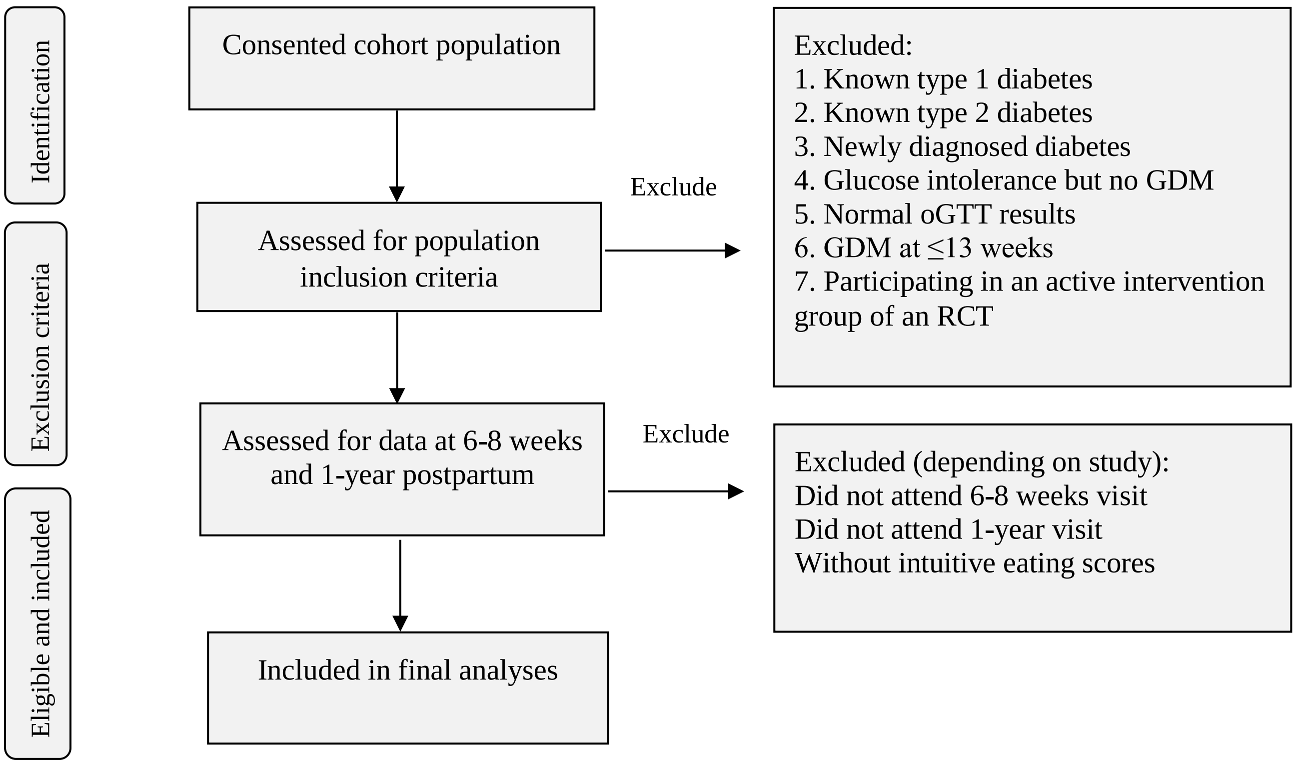

Fig 7. Flow chart describing the selection of study participants
oGTT: oral glucose tolerance test; GDM: gestational diabetes mellitus; RCT: randomized controlled trials

3.6 Specific inclusion/exclusion criteria (studies 1-3)

In addition to the general inclusion/exclusion criteria, had additional exclusion criteria for studies 1-3 depending on the specific study objective:

Study 1: *Intuitive eating is associated with metabolic health during pregnancy and in the early postpartum period in women with GDM*

For this study, the additional exclusion criteria in addition to those mentioned in section 3.5 (page 25) were women who did not complete an IE questionnaire at the first GDM visit and those who did not attend the 6-8 weeks postpartum appointment visit.

The flow of selecting study participants for this specific study is as follows: out of the cohort population of 1000 participants (at the time of analysis of this analysis) that were followed in our clinic (2011-2017), we excluded those who did not complete an IE questionnaire at the first GDM visit (N=533) and those who did not attend the 6-8 weeks postpartum visit (N=32). Out of the eligible cohort population of 435 participants, we then excluded those who did not sign an informed consent (N= 145). Participants with known type 1 diabetes (N= 7), known type 2 diabetes (N= 9), GDM diagnosed at ≤13 weeks (N= 11), diabetes diagnosed during pregnancy at ≤20 weeks (N= 19), normal (i.e. negative) oGTT results (N= 7), with glucose intolerance but no GDM (N= 2) and those participating in a form of an active lifestyle randomized controlled trial (RCT) intervention (N= 21) were also excluded. Overall, 214 women were included in the final analysis.

Study 2: *Intuitive eating is associated with improved health indicators at 1-year postpartum in women with GDM*

For this study, the additional exclusion criteria in addition to those mentioned in section 3.5 (page 25) were women who did not complete the IES-2 at the first GDM visit and at 1-year visit and those who did not attend the 1-year postpartum appointment visit.

The flow of selecting study participants for this specific study is as follows: out of a cohort population of 1068 participants (at the time of this analysis) that were followed at our clinic from 2011-2018 we first excluded those who did not sign an informed consent (N= 177) and did not complete the IES-2 at the first GDM visit and at 1-year visit (N=558). Out of a cohort population of 333 participants that consented, we removed participants who did not come for 1-year postpartum appointment visit (N=144) as they did not have valid data for our main questions and hypothesis. Participants with known type 1 diabetes (N= 2), known type 2 diabetes (N= 6), had GDM at ≤13 weeks (N= 10), had diabetes diagnosed during pregnancy at ≤20 weeks (N= 8), with oGTT results that were normal (N= 3), with glucose intolerance but no GDM (N= 1) and were participating in a lifestyle intervention study (N=42) who are part of our cohort database were also excluded as they did not meet the inclusion criteria. Overall, 117 women were eligible and thus included in the final analysis. Figure 1 shows the details of how participants in this study were selected.

Study 3: *Predictors and consequences of weight retention in the early and late postpartum period in women with GDM*

For this study, the additional exclusion criteria in addition to those mentioned in section 3.5 (page 25) were women who did not attend the postpartum appointment visits (i.e. both the 6-8 weeks and 1-year visits).

The flow of selecting study participants for this specific study is as follows: out of a total consented cohort population of 1039 women (at the time of this analysis) we first excluded those with known type 1 diabetes (N=13), type 2 diabetes (N=18), newly diagnosed diabetes in pregnancy (N=9), glucose intolerance but no GDM (N=2), with normal oGTT results (N=8), with GDM diagnosed at ≤13 weeks (N=13), and those participating in an active lifestyle intervention study (N=53).

We then excluded those who did not attend the 6-8 weeks postpartum visit (N=61). Following this, 862 women were eligible and were included in our final analysis. Of these 862 women, all of them had completed the 6-8 weeks postpartum visit, whereas 259 (30%) had completed the 1-year postpartum visit at the time of this analysis. The main reason for the low numbers of patients at 1-year postpartum visit is that the implementation of the 1-year postpartum follow-up visit started in August 2015.

The following paragraphs summarize the variables and measures used in my thesis project in either of the three studies.

3.7 Assessment of Intuitive eating (IE)

We assessed IE (Studies 1 &2) with the French Intuitive Eating Scale-2 (IES-2) corresponding to the language of our population.

The French IES-2 is an18-item validated self-report questionnaire that assesses individuals' tendency to follow their physiological, hunger and satiety in relation to eating. The French IES-2 consists of three (3) subscales. These are (1) the Eating for physical rather than emotional reasons (EPR, 8 items) subscale; that assesses how much eating is affected by emotional responses, (2) the Reliance on hunger and satiety cues (RHSC, 6 items) subscale; that evaluates the extent to which individuals are aware and able to trust internal signals rather than relying on external rules/cues.

The Unconditional permission to eat (UPE, 4 items) when hungry subscale (3) that assesses whether an individual purposefully tries to ignore hunger and satiety signals (116,121). The English IES-2 (23-item questionnaire), however, consists of four subscales. These are the EPR (8 items) subscale, the RHSC (6 items) subscale, the UPE (4 items) and the Body-Food Choice Congruence (BFC-C, 5 items) subscale (88,91). Both French and English IES-2 questionnaires have demonstrated good psychometric properties in pregnant women (121). In an earlier study, the Cronbach's alphas (α) for the two subscales were 0.92 and 0.87 for EPR and RHSC respectively which suggests a good internal reliability among the subscales (121). IE has interoceptive abilities that are suggested to determine when/how much to eat, and to accurately perceive and respect one's hunger and satiety cues. Thus IE tendencies are related to emotional, psychological, and physical well-being (94). Details of the IES-2 questionnaire have been previously described (91). For the purpose of this thesis, we removed the UPE subscale (4 items) from the French IES-2. This is because women involved in this study had in general one pre-partum visit with a registered dietician during pregnancy and another visit in the early post-partum period (6-8 weeks postpartum).

This second visit in the early postpartum period was of short duration and done together with the diabetologist or diabetes educator and focused predominantly on reporting the results of the postpartum oral glucose tolerance testing (oGTT).

Women had no further dietician appointment after this visit. In the general population of our women with gestational diabetes, about 85% are usually seeing a dietician and the main reasons for not seeing one are: appointment-scheduling problems or arrival at the GDM clinic at a very advanced stage of pregnancy. We believe that, discussions during diet counselling could significantly influence participant responses to the UPE subscale questions such as: "I try to avoid certain foods high in fat, carbohydrates, or calories", as participants were advised on carbohydrate content of their foods and to avoid or limit certain food like soft drinks, sweet products, added sugar and fruits juice in order to improve their eating habits and glycemic profile. We therefore only used the EPR and RHSC subscales of the French IES-2 and an English translation using the forward-backward translation and cultural adaption method (122) made by our research team (with the same 14 items; EPR has 8 items and RHSC has 6 items); they were then given to participants who speak French and English, respectively. Women completed the EPR and RHSC subscales of the IES-2 questionnaire during the first GDM visit (study1 & 2) and at one-year postpartum visit (study 2) by responding to a 5-point Likert scale response ranging from one (1) 'strongly disagree' to five (5) 'strongly agree' to each item in both subscales. We then calculated the EPR and RHSC subscale scores as recommended by dividing the total scores obtained from the sum of 1-5 from each item by the total number of items in each subscale (EPR by 8 and RHSC by 6) leading to a possible subscale score between one and five (0 and 5). Higher scores indicated greater levels of IE. A higher score of the EPR subscale reflects eating as an answer to hunger and a lower score meant eating to cope with emotional distress, whereas a higher score of the RHSC subscale signifies trust in internal cues, and a lower score reflects less ability to regulate food intake.

3.8 Assessment of glycemic control variables

Participants underwent a 75g oral glucose tolerance test (oGTT) during pregnancy at 24-32 weeks of gestation unless an initial fasting glucose was ≥ 5.1 mmol/L. Women were diagnosed of GDM if one of the following criteria were met: fasting glucose ≥ 5.1 mmol/L, 1-hr glucose ≥ 10.0 mmol/L, or 2-hr glucose ≥ 8.5 mmol/L using the IAPDSG (17) and ADA guidelines (7). At the first GDM visit, HbA1c was measured using a chemical photometric method (conjugation with boronate; Afinion®). At 6-8 weeks and 1-year postpartum, an oGTT was performed to measure fasting glucose, 2-hr glucose and HbA1c with a high performance liquid chromatography method (HPLC). Both methods are traceable to the international federation of clinical chemistry and laboratory medicine (IFCC) reference method for measurement of HbA1c (123). Prediabetes was diagnosed when a participant's fasting glucose at the postpartum period was between 5.6-6.9 mmol/l, the 2h glucose was between 7.8-11.0 mmol/l or HbA1c at 1-year postpartum was between 5.7- 6.4%.

3.9 Anthropometric variables

Pre-pregnancy weight was taken from participants' medical charts or, if missing was self-reported (for the 1-2 months before pregnancy). We measured weight at the first GDM visit, at the end of pregnancy, at 6-8 weeks and at 1-year postpartum to the nearest 0.1 kg in women wearing light clothes and no shoes with a regularly calibrated electronic scale (Seca®). We measured height at the first GDM visit to the nearest 0.1 cm with a regularly calibrated Seca® height scale. GWG was defined as the difference between pre-pregnancy weight and weight at the end of pregnancy. We calculated the BMI as the ratio of weight in kilograms to the square of height in meters (kg/m^2). We defined overweight and obesity as BMI between 25.0-29.9 Kg/m^2 and ≥30 kg/m^2 respectively.

Based on the pre-pregnancy BMI and GWG, women were classified as being below (inadequate), within (adequate) or above (excessive) the Institute of Medicine (IOM) GWG recommendations (124). We calculated PPWR by either subtracting the pre-pregnancy weight from the weight at 6-8 weeks postpartum (early PPWR) and from the weight at 1-year postpartum (late PPWR). Information on GDM treatment during pregnancy (use of insulin and/or metformin; yes/no) and caesarean section (yes/no) were obtained from medical charts.

3.9 Socio-demographic characteristics and additional health variables

During the first GDM visit, information on participants' characteristics including age, educational level, and ethnic origin, family history of type-2 diabetes, history of previous GDM, parity, gravida, and smoking during pregnancy were obtained during a structured face-to-face interview. We categorized educational level into "no formal education; compulsory school achieved; general and vocational training levels; high school and university education" (125,126). Information on partner support was obtained during the face-to-face interview and was categorized as either "living with a partner or not". We categorized family history of type-2 diabetes, as either "first-degree, second degree or none" whereas previous history of GDM and smoking during pregnancy were categorized as either 'yes' or 'no'. We grouped parity into "none, one, two and ≥ three" whereas gravida consisted of "one, two or three". In the routine clinical visit at 6-8 weeks postpartum, information about breastfeeding (yes/no) and contraception use (yes/no) were obtained. To assess their mental health, women completed the Edinburgh Postnatal Depression Scale (EPDS) questionnaire during their first GDM visit (at 24-32 weeks) and in the postpartum period. This questionnaire is a ten-item self-report questionnaire designed and validated to screen women for symptoms of depression during pregnancy and in the postnatal period (127).

The possible scores of the EPDS questionnaire range from 0 to 30 points, with a higher total score indicating more severe depressive symptoms.

3.10 Statistical analyses (studies 1-3)

Study 1: *Intuitive eating is associated with metabolic health during pregnancy and in the early postpartum period in women with GDM.*

All analyses were conducted using the SPSS software version 25 (32). All descriptive variables were presented as either means (±standard deviation) or in percentages (%) where appropriate.

Both predictor (EPR and RHSC subscales of the IES-2 questionnaire) and outcome (BMI, weight and glycemic control including fasting glucose, 1hr glucose, 2hr glucose and HbA1c at the different time points) variables were normally distributed. The correlation between the two subscales of IES-2 questionnaire was low-to moderate ($r=0.35$, $P<0.01$). We conducted a linear regression analysis to determine the cross-sectional and longitudinal associations between the two subscales of IES-2 at the first GDM visit with BMI, weight, fasting glucose, 1hr glucose, 2hr glucose and HbA1c during pregnancy (cross-sectional analysis), at the end of pregnancy and at 6-8 weeks postpartum, respectively (longitudinal analysis). We made use of three models in the regression analyses. Model 1 consisted of unadjusted regression estimates. In model 2, we adjusted for socio-demographic characteristics that showed significance with at least one of metabolic health outcome variables (BMI, weight, fasting glucose, 1h or 2h glucose, HbA1c) at either the first GDM visit or at 6-8 weeks postpartum. This was tested for age, gestational age, education level, nationality, employment status, family history of type-2 diabetes, history of GDM, smoking and alcohol intake during pregnancy, gravida, parity, and medical treatment during pregnancy.

Of these potential confounder variables, age, gestational age, smoking during pregnancy, parity, and medical treatment during pregnancy showed significance with one of the metabolic health outcome variables and were thus included in Model 2 as confounder variables. We did not adjust for medical treatment in our cross-sectional analysis because women had not started medical treatment during the first GDM visit, as this had no effect on the potential associations between IE and metabolic health at the first GDM visit. We however adjusted for this in our longitudinal analyses. When the outcome was glycemic control (fasting glucose and HbA1c), we added a third model: model 3, where we adjusted for weight at the respective time points (at the first GDM visit and at 6-8 weeks postpartum). All analyses were conducted separately for both subscales of the IES-2 questionnaire. All statistical significances were two sided and accepted at $p < 0.05$.

Study 2: *Intuitive eating is associated with improved health indicators at 1-year postpartum in women with GDM*

All descriptive variables were presented as either means (±standard deviation) or in percentages (%), where appropriate. Both predictor (EPR and RHSC subscales of the IES-2 questionnaire at first GDM visit and at 1-year postpartum visit) and outcome (BMI, weight retention, HbA1c and fasting glucose at the different time points) variables were normally distributed. The EPR and RHSC subscales showed a moderate correlation of 0.42 ($p<0.001$) at the first GDM visit and 0.51 ($p<0.001$) at 1-year postpartum. We conducted a linear regression analysis to determine the associations between IE at the first GDM visit (longitudinal) and at the 1-year postpartum visit (cross-sectional) with BMI, weight retention, fasting glucose, and HbA1c at 1-year postpartum. We adjusted for socio-demographic characteristics that showed statistical significance with at least one of the metabolic health outcome variables (BMI, weight, weight retention, fasting glucose and HbA1c) at 1-year postpartum.

We tested for age, gestational age at the first GDM visit, education level, nationality, employment status, family history of type-2 diabetes, history of GDM, smoking and alcohol intake during pregnancy, parity, and breastfeeding in the early postpartum period. Of these potential confounder variables, age and gestational age showed significance with at least one of the metabolic health outcomes. We therefore adjusted for age and gestational age at the first GDM visit as confounders for all analyses. When the outcome was glycemic control (HbA1c or fasting glucose), we further adjusted for BMI at first GDM visit. We did this to see if the relationship was mediated by BMI. We conducted all analyses separately for EPR and RHSC subscales at the first GDM visit and at 1-year postpartum. We also evaluated the associations between the two IE subscales at the first GDM visit and at 1-year postpartum with metabolic health outcomes in the high-risk GDM subgroups with prediabetes or overweight/obesity and in the respective low-risk subgroups. Both IE scores at both time points were analyzed using correlation analyses and paired t-tests (between first visit and 1-year postpartum). All statistical significances were two sided and accepted at $p < 0.05$.

Study 3*: Predictors and consequences of weight retention in the early and late postpartum period in women with GDM*

Demographic and other descriptive variables are presented as either means (±standard deviation) or in percentages (%). PPWR variable and all outcome parameters were normally distributed. We categorized this continuous variable (PPWR) into two groups: either no PPWR when the difference between a participant’s weight before pregnancy and weight at the postpartum period (either 6-8 weeks or 1-year visit) was ≤0kg and into PPWR if the difference is ≥0.1kg. We performed an ANOVA analysis to compare the anthropometric and metabolic characteristics (independent continuous variables) of participants according to weight retention categories.

In order to determine the predictors of PPWR at 6-8 weeks and at 1-year postpartum, we conducted an initial univariate logistic regression analysis. We selected potential predictors for the univariate regression analyses based on the existing literature. These variables were; age, educational level, nationality, history of GDM, family history of diabetes, parity, gravida, delivery by caesarean section, partner support, GDM treatment, contraception use, breastfeeding and depression score at the first GDM visit, pre-pregnancy weight, fasting, 1hr and 2hr glucose after oGTT at GDM diagnosis, total GWG, excess GWG according to IOM guidelines, fasting glucose, 2hr glucose after oGTT and HbA1c, all at 6-8 weeks postpartum. We then modeled the odds of PPWR (at the 6-8 weeks and 1-year postpartum visits) using multivariable logistic regression models with backward elimination by including variables with $p<0.25$ in the initial univariate regression analysis. Based on this, the following predictor variables were included in the 6-8 weeks postpartum model: family history of diabetes, partner support, breastfeeding and depression score at the first GDM visit, pre-pregnancy weight, 2hr glucose after oGTT at GDM diagnosis, total and excess GWG according to IOM guidelines. The following predictor variables were included in the 1-year postpartum model: age, family history of diabetes, partner support, depression score at the first GDM visit, total GWG, excess GWG, and HbA1c at 6-8 weeks postpartum visit. For the 1-year postpartum analysis, we made use of two models; one in parallel to the model performed at 6-8 weeks postpartum and thus without any variable obtained after delivery i.e., without HbA1c at 6-8 weeks postpartum (model 1) and one including significant variables after delivery, i.e. HbA1c at 6-8 weeks postpartum (model 2). We then selected the regression model with the lowest Akaike information criterion (AIC) as our final model for both time points. We tested for collinearity of the included predictor variables, and none displayed excessive collinearity. The variance inflation factor (VIF) in the regression models were less than 2 (between 1.0-1.4), and thus acceptable. All statistical significances were two sided and accepted at $p< 0.05$.

4.0 GENERAL RESULTS

The section of the thesis provides a summary of the main results of the studies involved in this thesis. The complete and detailed results of each study can be found in the appendix section.

Study 1: Intuitive eating is associated with metabolic health during pregnancy and in the early postpartum period in women with GDM

Cross-sectional associations between intuitive eating during pregnancy and metabolic outcomes during pregnancy

This study included 214 women. Their mean score of the eating for physical rather than emotional reasons subscale at first GDM visit was 3.8 ± 0.9, whereas the mean score of the reliance on hunger and satiety subscale was 3.5 ± 0.9. **Table 3** below shows the cross-sectional associations between the two scales of intuitive eating scale-2 (IES-2) with BMI, weight and glycemic control at the first GDM visit. Cross-sectional analyses showed that both subscales of IES-2 at the first GDM visit were associated with lower weight and BMI before pregnancy, weight, fasting glucose and HbA1c at the first GDM visit (β= -0.171 to -0.222, all $p \leq 0.01$). However the reliance on hunger and satiety subscale was not significantly associated with HbA1c at the first GDM visit. After adjusting for confounders including age, gestational age, smoking, and parity (model 2) the associations between the two subscales of IES-2 with weight and BMI before pregnancy and weight at first GDM visit remained unchanged. The association between eating for physical rather than emotional reasons subscale with fasting glucose and HbA1c also remained largely unchanged, except that the association between the reliance on hunger and satiety subscale with fasting glucose was attenuated (p=0.095), albeit with a similar beta-coefficient. When fasting glucose or HbA1c was the outcome, we adjusted for weight at first GDM visit as a potential confounder (model 3).

The relationship between the eating for physical rather than the emotional subscale with fasting glucose and HbA1c were attenuated (both $p \leq 0.07$), while the relationship between the reliance on hunger and satiety subscale and fasting glucose remained insignificant ($p=0.261$). This shows that weight partly mediates the relationship between IE and fasting glucose in our sample.

Longitudinal associations between intuitive eating during pregnancy and metabolic outcomes at 6-8 weeks postpartum

Table 4 shows the longitudinal associations between IES-2 at the first GDM visit with BMI, weight and glycemic control at the end of pregnancy and at 6-8 weeks postpartum visit. Both subscales of IES-2 at first GDM visit were associated with lower weight at the end of pregnancy, weight, BMI and fasting glucose at 6-8 weeks postpartum ($\beta=-0.139$ to -0.242, all $P \leq 0.046$) (model 1). None of the IES-2 subscales was related to weight at first GDM visit, change in weight at the end of pregnancy and change in weight at 6-8 weeks postpartum. After adjusting for confounders including age, gestational age, smoking, parity, and medical treatment during pregnancy (model 2), the significant associations between the two subscales of IES-2 with weight at the end of pregnancy, weight, BMI and fasting glucose at 6-8 weeks postpartum remained unchanged (all $p \leq 0.004$). However, the association between reliance on hunger and satiety subscale and weight at 6-8 weeks postpartum was attenuated ($p=0.057$), albeit with a similar beta-coefficient. When fasting glucose and HbA1c were the outcome variables, we adjusted for weight at 6-8 weeks postpartum visit (model 3). Thus, the inverse association between the eating for physical rather than the emotional reasons subscale and fasting glucose at 6-8 weeks postpartum remained unchanged ($p= 0.038$) whereas the association between the reliance on hunger and satiety subscale and fasting glucose at 6-8 weeks postpartum was attenuated ($p \leq 0.059$).

[Table 3] **Cross-sectional associations between the two subscales of intuitive eating scale-2 and weight, BMI and glycemic control at first GDM visit**

	Model 1				Model 2				Model 3			
Variable	**regression coefficient**	**95% CI**		**P-value**	**regression coefficient**	**95% CI**		**P-value**	**regression coefficient**	**95% CI**		**P-value**
EPR												
Weight before pregnancy *(n=213)*	-0.203	-5.329	-1.107	**0.003**	-0.181	-5.002	-0.745	**0.008**	NA			
BMI before pregnancy (*n=213)*	-0.216	-1.936	-0.463	**0.002**	-0.194	-1.824	-0.332	**0.005**	NA			
Weight at first GDM visit (*n=211)*	-0.205	-5.355	-1.126	**0.003**	-0.191	-5.168	-0.871	**0.006**	NA			
HbA1c at first GDM visit (*n=211)*	-0.171	-0.126	-0.015	**0.013**	-0.170	-0.127	-0.013	**0.016**	-0.123	-0.106	0.004	0.070
Fasting glucose at first GDM visit *(n=206)*	-0.195	-0.278	-0.050	**0.005**	-0.196	-0.280	-0.049	**0.005**	-0.124	-0.213	0.007	0.066
1-hr glucose at first GDM visit *(n=163)*	0.122	-0.058	0.490	0.122	0.154	-0.009	0.556	0.058	0.112	-0.081	0.465	0.166
2-hr glucose at first GDM visit *(n=164)*	-0.030	-0.336	0.226	0.698	-0.033	-0.351	0.232	0.689	-0.065	-0.404	0.169	0.420
RHSC												
Weight before pregnancy *(n=213)*	-0.194	-5.394	-0.999	**0.005**	-0.181	-5.171	-0.800	**0.008**	NA			
BMI before pregnancy (*n=213)*	-0.222	-2.046	-0.518	**0.001**	-0.215	-2.007	-0.482	**0.002**	NA			
Weight at first GDM visit (*n=211)*	-0.190	-5.365	-0.934	**0.006**	-0.188	-5.331	-0.886	**0.006**	NA			
HbA1c at first GDM visit (*n=211)*	-0.061	-0.085	0.032	0.376	-0.061	-0.085	0.033	0.389	-0.004	-0.060	0.056	0.954
Fasting glucose at first GDM visit *(n=206)*	-0.148	-0.248	-0.010	**0.033**	-0.117	-0.222	0.018	0.095	-0.076	-0.182	0.050	0.261
1-hr glucose at first GDM visit *(n=163)*	0.072	-0.149	0.409	0.359	0.097	-0.108	0.459	0.224	0.043	-0.209	0.359	0.605
2-hr glucose at first GDM visit *(n=164)*	-0.072	-0.417	0.153	0.361	-0.068	-0.416	0.165	0.394	-0.124	-0.526	0.070	0.132

Gestational age at first GDM visit is 24-32 weeks
EPR means Eating for Physical Rather than Emotional Reasons subscale of the Intuitive Eating scale2 (IES-2). Higher scores means higher adherence to the EPR subscale
RHSC means Reliance on Hunger and Satiety Cues subscale of the Intuitive Eating scale2 (IES-2). Higher scores means higher adherence to the RHSC subscale
Model 1: Unadjusted regression estimates
Model 2: Adjusted for age, gestational age, smoking, and parity
Model 3: Adjusted for weight at first GDM visit

[Table 4] **Longitudinal associations between two subscales of intuitive eating scale-2 and weight, BMI and glycemic control at the end of pregnancy and in early postpartum (6-8 weeks)**

	Model 1				**Model 2**				**Model 3**			
Variable	**regression coefficient**	**95% CI**		**P-value**	**regression coefficient**	**95% CI**		**P-value**	**regression coefficient**	**95% CI**		**P-value**
EPR												
Weight at end of pregnancy (*n=198)*	-0.223	-5.450	-1.297	**0.002**	-0.212	-5.373	-1.063	**0.004**	NA			
Weight at 6-8 weeks postpartum (*n=207)*	-0.237	-5.700	-1.592	**0.001**	-0.219	-5.536	-1.267	**0.002**	NA			
BMI at 6-8 weeks postpartum *(n=205)*	-0.242	-2.003	-0.574	**0.000**	-0.226	-1.956	-0.474	**0.001**	NA			
Δweight first GDM visit and end of pregnancy (*n=192)*[1]	-0.007	-0.562	0.509	0.922	0.025	-0.452	0.642	0.732	NA			
Δweight first GDM visit and 6-8 weeks PP (*n=205)*[2]	-0.061	-1.137	0.438	0.382	-0.062	-1.154	0.448	0.386	NA			
HbA1c at 6-8 weeks postpartum(n=206)	-0.002	-0.053	0.051	0.978	-0.003	-0.056	0.054	0.968	0.017	-0.047	0.060	0.815
Fasting glucose 6-8 weeks postpartum (n=207)	-0.200	-0.159	-0.031	**0.004**	-0.191	-0.158	-0.026	**0.007**	-0.144	-0.132	-0.004	**0.038**
2-hr glucose 6-8 weeks postpartum (n=206)	-0.020	-0.261	0.194	0.775	-0.005	-0.253	0.235	0.943	-0.018	-0.264	0.205	0.806
RHSC												
Weight at end of pregnancy (*n=198)*	-0.193	-5.276	-0.868	**0.007**	-0.175	-5.059	-0.545	**0.015**	NA			
Weight at 6-8 weeks postpartum (*n=207)*	-0.139	-4.486	-0.040	**0.046**	-0.134	-4.435	0.065	0.057	NA			
BMI at 6-8 weeks postpartum *(n=205)*	-0.164	-1.691	-0.155	**0.019**	-0.165	-1.708	-0.156	**0.019**	NA			
Δ weight first GDM visit and end of pregnancy (*n=192)*	0.092	-0.200	0.926	0.205	0.102	-0.159	0.974	0.157	NA			
Δ weight first GDM visit and 6-8 weeks PP(*n=205)*	0.105	-0.198	1.467	0.135	0.064	-0.444	1.216	0.360	NA			
HbA1c at 6-8 weeks postpartum(n=206)	-0.074	-0.084	0.025	0.291	-0.072	-0.085	0.028	0.315	-0.065	-0.081	0.030	0.358
Fasting glucose 6-8 weeks postpartum (n=207)	-0.163	-0.151	-0.014	**0.019**	-0.140	-0.140	-0.002	**0.045**	-0.128	-0.131	0.003	0.059
2-hr glucose 6-8 weeks postpartum (n=206)	-0.025	-0.284	0.196	0.717	-0.006	-0.262	0.239	0.930	-0.024	-0.284	0.201	0.736

[1]Means the difference in weight at the end of pregnancy and at first GDM visit

[2]Means the difference between weight at the 6-8 weeks postpartum visit and first GDM visit

EPR means Eating for Physical Rather than Emotional Reasons subscale of the Intuitive Eating scale 2 (IES-2). Higher scores means higher adherence to the EPR subscale

RHSC means Reliance on Hunger and Satiety Cues subscale of the Intuitive Eating scale 2 (IES-2). Higher scores means higher adherence to the RHSC subscale

Model 1: Unadjusted regression estimates

Model 2: Adjusted for age, gestational age smoking, parity and medical treatment during pregnancy

Model 3: Adjusted for weight 6-8 weeks post-partum

PP means postpartum

Study 2: Intuitive eating is associated with improved health indicators at 1-year postpartum in women with GDM

This study included 117 women. Their mean eating for physical rather than emotional reasons subscale at the first GDM visit was 3.86 and 3.76 at 1-year postpartum ($p<0.001$), and the mean scores for reliance on hunger and satiety cues subscale were 3.53 and 3.42 respectively ($p<0.001$). Correlation between the first GDM visit and 1-year postpartum were 0.42 for the eating for physical rather than emotional reasons and 0.32 for the reliance on hunger and satiety subscales (both $p<0.001$).

Associations between intuitive eating during and after pregnancy with metabolic outcomes at 1-year postpartum

Table 5 represents the longitudinal and cross-sectional associations between the two subscales of IES-2 at the first GDM visit and at 1-year postpartum with metabolic health indicators at 1-year postpartum. After adjusting for confounders (age and gestational age at the first GDM visit), the eating for physical rather than emotional reasons subscale at the first GDM visit was associated with lower BMI ($p=0.017$), fasting glucose ($p=0.014$) and tended to predict lower HbA1c ($p=0.062$) at 1-year postpartum. On the other hand, reliance on hunger and satiety subscale at the first GDM visit had no association with any of the metabolic health variables at 1-year postpartum (all $p>0.2$). However, both eating for physical rather than emotional reasons and reliance on hunger and satiety subscales at 1-year postpartum were associated (cross-sectional) with lower weight retention (both $p\leq0.037$) and lower BMI (both $p\leq0.012$). The eating for physical rather than emotional reasons subscale was also associated with lower HbA1c and lower fasting glucose (both $p=0.018$).

When fasting glucose and HbA1c were the outcome variables, we further adjusted for BMI at the first GDM visit as a potential confounder, which led to the attenuation of the observed associations between the two subscales of IES-2 and metabolic parameters (all $p \geq 0.066$).

Associations between intuitive eating during and after pregnancy with metabolic health stratified by overweight/obese or with prediabetes

We also focused on two high-risk GDM subgroups with pre-pregnancy overweight/obese or with prediabetes and their lower-risk counterparts. After adjusting for age and gestational age at the first GDM visit, in the subgroup of women with prediabetes **(Table 6)**, eating for physical rather than emotional reasons and reliance on hunger and satiety subscales at the first GDM visit predicted lower fasting glucose at 1-year postpartum (both $p \leq 0.024$). At 1-year postpartum, both physical rather than emotional reasons and reliance on hunger and satiety subscales were associated with less postpartum weight retention (both $p \leq 0.034$) and lower BMI (both $p \leq 0.005$) in women with prediabetes, while no associations were observed in the women with normal glucose tolerance (all $p \geq 0.10$) after adjustments for confounders (age and gestational age). In the subgroup of women with overweight/obese **(Table 7)**, the physical rather than emotional reasons subscale at the first GDM visit predicted lower fasting glucose at 1-year postpartum ($p=0.041$), whereas the reliance on hunger and satiety subscale showed no significance with any of the metabolic variables. At 1-year postpartum, both physical rather than emotional reasons and reliance on hunger and satiety subscales were associated with lower weight retention (both $p \leq 0.009$) and fasting glucose (both $p=0.030$). The physical rather than emotional reasons subscale was also associated with lower BMI ($p<0.001$). Thus, in both high-risk subgroups, measures of IE were associated with measures of metabolic health such as anthropometric parameters or glucose control variables.

Specifically, in both high-risk subgroups, the associations of IES-2 subscales with fasting glucose were independent of BMI. However, we found no associations between the two subscales of IES-2 and metabolic health in the subgroup of women with normal weight.

[Table 5] Associations between the two subscales of IES-2 at the first GDM visit and at 1-year postpartum and metabolic health at 1-year postpartum in the total population

Variable	Regression coefficient	95% CI		P-value[a]	P-value[b]
IES-2 at the first GDM visit (longitudinal)					
EPR at the first GDM visit					
Metabolic health at 1-yr pp					
ΔWeight retention (kg)[1]	-0.087	-2.026	0.730	0.350	
BMI (kg/m^2)	-0.219	-2.281	-0.151	**0.017**	
HbA1c (%)	-0.171	-0.119	0.008	0.062	0.137
Fasting glucose (mmol/l)	-0.229	-0.251	-0.026	**0.014**	**0.068**
RHSC at the first GDM visit					
Metabolic health at 1-yr pp					
ΔWeight retention (kg)[1]	0.078	-0.815	2.084	0.400	
BMI (kg/m^2)	-0.090	-1.637	0.645	0.332	
HbA1c (%)	0.044	-0.048	0.086	0.634	0.327
Fasting glucose (mmol/l)	-0.104	-0.184	0.058	0.272	0.458
IES-2 at 1-yr pp (cross-sectional)					
EPR at 1-yr pp					
Metabolic health at 1-yr pp					
ΔWeight retention (kg)[1]	-0.230	-2.976	-0.370	**0.012**	
BMI (kg/m^2)	-0.337	-2.825	-0.829	**<0.001**	
HbA1c (%)	-0.216	-0.129	-0.008	**0.018**	**0.066**
Fasting glucose (mmol/l)	-0.222	-0.236	-0.018	**0.018**	0.237
RHSC at 1-yr pp					
Metabolic health at 1-yr pp					
ΔWeight retention (kg)[1]	-0.193	-2.847	-0.083	**0.037**	
BMI (kg/m^2)	-0.243	-2.469	-0.313	**0.012**	
HbA1c (%)	-0.095	-0.098	0.032	0.311	0.547
Fasting glucose (mmol/l)	-0.194	-0.230	0.002	0.042	0.208

[1]means the difference in weight at 1-yr postpartum and pre-pregnancy weight
EPR means Eating for Physical Rather than Emotional Reasons subscale of the Intuitive Eating scale2 (IES-2)
RHSC means Reliance on Hunger and Satiety Cues subscale of the Intuitive Eating scale2 (IES-2)
PP means postpartum
P-value[a]: adjusted for age and gestational age at the first GDM visit
P-value[b]: adjusted for age and gestational age and BMI at the first GDM visit

Table 6] Associations between the two subscales of IES-2 at first GDM visit and at one-year postpartum visit with metabolic health at one year postpartum stratified by glucose tolerance

	Prediabetes (n=54)					**Normal (n=63)**			
Variable	**Regression coefficient**	**95% CI**		**P-value[a]**	**P-value[b]**	**Regression coefficient**	**95% CI**		**P-value**
IES-2 at first GDM visit (longitudinal)*									
EPR at the first GDM visit									
ΔWeight retention (kg) [1]	-0.098	-2.598	1.239	0.480		-0.052	-2.461	1.628	0.685
BMI (kg/m^2)	-0.169	-2.415	0.576	0.223		-0.214	-2.748	0.213	0.092
HbA1c (%)	-0.173	-0.158	0.036	0.211	0.189	-0.076	-0.095	0.051	0.553
Fasting glucose (mmol/l)	-0.437	-0.303	-0.063	**0.001**	**0.004**	-0.029	-0.106	0.084	0.820
RHSC at the first GDM visit									
ΔWeight retention (kg) [1]	-0.090	-2.459	1.254	0.518		0.294	0.453	4.959	0.076
BMI (kg/m^2)	-0.075	-1.857	1.068	0.591		-0.082	-2.300	1.178	0.521
HbA1c (%)	0.043	-0.080	0.109	0.760	0.751	0.060	-0.064	0.104	0.641
Fasting glucose (mmol/l)	-0.308	-0.247	-0.004	**0.024**	**0.025**	0.101	-0.066	0.152	0.432
IES-2 at 1-year pp (cross-sectional)									
EPR at 1-yr pp									
ΔWeight retention (kg)[1]	-0.288	-3.572	-0.142	**0.034**		-0.114	-3.111	1.184	0.373
BMI (kg/m^2)	-0.384	-3.248	-0.645	**0.004**		-0.180	-2.698	0.450	0.158
HbA1c (%)	-1.582	-0.159	0.019	0.120	0.125	-0.001	-0.077	0.077	0.995
Fasting glucose (mmol/l)	-0.204	-0.207	0.031	0.142	0.765	0.083	-0.067	0.132	0.515
RHSC at 1-yr pp									
ΔWeight retention (kg) [1]	-0.394	-4.388	-0.935	**0.003**		-0.030	-2.361	1.861	0.814
BMI (kg/m^2)	-0.378	-3.376	-0.639	**0.005**		-0.047	-1.851	1.272	0.712
HbA1c (%)	-0.130	-0.139	0.050	0.349	0.253	0.157	-0.028	0.121	0.219
Fasting glucose (mmol/l)	-0.137	-0.190	0.065	0.329	0.842	-0.043	-0.114	0.082	0.740

*for the fasting glucose, this corresponds to the time point of the GDM diagnosis before the first GDM visit.
[1]means the difference in weight at 1-yr postpartum and pre-pregnancy weight
EPR means Eating for Physical Rather than Emotional Reasons subscale of the Intuitive Eating scale2 (IES-2)
RHSC means Reliance on Hunger and Satiety Cues subscale of the Intuitive Eating scale2 (IES-2)
P-value[a]: Adjusted for age and gestational age at the first GDM visit
P-value[b]: Adjusted for age, gestational age and BMI at the first GDM visit
PP means postpartum

[Table 7] Associations between the two subscales of IES-2 and metabolic health at one year postpartum stratified by BMI category

Variable	**Obese/overweight (n=54)**					**Normal weight (n=63)**			
	Regression coefficient	**95% CI**		**P-value[a]**	**P-value[b]**	**Regression coefficient**	**95% CI**		**P-value**
IES-2 at first GDM visit (longitudinal)*									
EPR at the first GDM visit									
ΔWeight retention (kg) [1]	-0.111	-3.466	1.475	0.422		0.026	-1.281	1.567	0.842
BMI (kg/m^2)	-0.132	-1.779	0.643	0.351		-0.144	-1.183	0.304	0.241
HbA1c (%)	-0.195	-0.157	0.037	0.165	0.169	-0.076	-0.112	0.061	0.553
Fasting glucose (mmol/l)	-0.288	-0.337	0.003	**0.041**	**0.043**	-0.083	-0.191	0.098	0.522
RHSC at the first GDM visit									
ΔWeight retention (kg) [1]	0.176	-0.924	4.241	0.203		0.054	-1.188	1.819	0.676
BMI (kg/m^2)	0.213	-0.319	2.219	0.137		-0.073	-1.028	0.556	0.554
HbA1c (%)	-0.010	-0.108	0.101	0.967	0.963	0.194	-0.020	0.160	0.127
Fasting glucose (mmol/l)	-0.111	-0.260	0.111	0.419	0.424	0.039	-0.130	0.176	0.765
IES-2 at 1-year pp (Cross-sectional)									
EPR at 1-yr									
ΔWeight retention (kg) [1]	-0.347	-5.152	-0.562	**0.009**		0.006	-1.349	1.409	0.965
BMI (kg/m^2)	-0.430	-2.873	-0.735	**<0.001**		-0.098	-1.019	0.442	0.432
HbA1c (%)	-0.177	-0.156	0.034	0.201	0.233	-0.155	-0.134	0.032	0.225
Fasting glucose (mmol/l)	-0.301	-0.345	-0.015	**0.030**	**0.025**	0.001	-0.140	0.140	0.997
RHSC at 1-yr									
ΔWeight retention (kg) [1]	-0.405	-6.529	-1.494	**0.002**		0.077	-0.891	1.656	0.550
BMI (kg/m^2)	-0.245	-2.467	-1.370	0.780		-0.120	-1.036	0.371	0.348
HbA1c (%)	-0.135	-0.162	0.055	0.329	0.299	0.074	-0.055	0.100	0.564
Fasting glucose (mmol/l)	-0.302	-0.395	-0.021	**0.030**	**0.032**	0.040	-0.110	0.151	0.755

*for the fasting glucose, this corresponds to the time point of the GDM diagnosis before the first GDM visit
[1]means the difference in weight at 1-yr postpartum and pre-pregnancy weight
EPR means Eating for Physical Rather than Emotional Reasons subscale of the Intuitive Eating scale2 (IES-2)
RHSC means Reliance on Hunger and Satiety Cues subscale of the Intuitive Eating scale2 (IES-2)
P-value[a]: Adjusted for age and gestational age at the first GDM visit
P-value[b]: Adjusted for age, gestational age, and BMI at the first GDM visit
PP means postpartum

Study 3: Predictors and consequences of weight retention in the early and late postpartum period in women with GDM

Anthropometric and metabolic characteristics of study participants

This study included 862 and 259 participants that had data at 6-8 weeks and/or 1-year postpartum respectively based on the inclusion criteria. **Table 8** shows the anthropometric and metabolic characteristics of the study participants. The mean pre-pregnancy BMI was 25.6±5.4kg/m^2 and 52.6%, 27.5% and 19.9% of patients had initial normal weight, overweight or were obese before pregnancy, respectively. Total GWG was 12.7±5.9kg. The mean PPWR at 6-8 weeks and at 1-year postpartum were 4.6±5.7kg and 4.0±7.4kg respectively. In the subgroup of women with 1-year data, the mean fasting glucose increased by 0.48±0.2mmol/l between 6-8 weeks and 1-year postpartum, while the mean HbA1c decreased by 0.03±0.01%.

Anthropometric differences and metabolic consequences of participants according to postpartum weight retention categories

Table 9a shows the participants' anthropometric differences and metabolic consequences according to PPWR categories at 6-8 weeks postpartum. At this time point, 81% of women had PPWR. Women with PPWR had significantly higher anthropometric parameters before, during and after pregnancy (early postpartum period) compared to those with no PPWR. Specifically, they had a 4±3.7kg higher pre-pregnancy weight, a higher pre-pregnancy BMI, a 7.5±0.2kg higher total GWG and a 0.23 ±0.1kg higher excess GWG, a higher weight at GDM diagnosis and at the end of pregnancy, as well as a 12±2.0kg higher weight at 6-8 weeks postpartum (all p≤0.02). In addition, the 2hr glucose after oGTT at GDM diagnosis was slightly higher (p=0.034). However, there were no differences in the metabolic parameters (fasting and 2h glucose, HbA1c) between both groups at the early postpartum period.

At 1-year postpartum, 66.4% of women had PPWR. Compared to those with no PPWR, women with PPWR had no differences in anthropometric parameters before and during pregnancy, but had a 4±0.4kg higher total GWG, a higher BMI at 6-8 weeks and at 1-year postpartum, and were 7±4.2kg heavier at 1-year postpartum (all $p \leq 0.04$) (**Table 9b)**. Women with no PPWR, on the other hand, had a minimal increase in excess GWG of 0.2 ±0.03kg ($p<0.001$). In the group of women with PPWR, weight did not decrease between the early and late postpartum period. The metabolic consequences at 1-year postpartum period showed a 0.2±0.2 mmol/l higher fasting glucose in women with PPWR compared to those without PPWR, and a more pronounced increase in fasting glucose and in HbA1c between the early and late postpartum period (both $p \leq 0.03$). We also evaluated the differences in metabolic and medical characteristics at 6-8 weeks postpartum in the 259 women with complete 1-year data. The results were similar to those in Table 9a.

Predictors of postpartum weight retention

In the multivariate logistic regression analysis (Tables 10a and 10b), higher pre-pregnancy weight and total GWG predicted higher risk of PPWR at 6-8 weeks postpartum (OR: 1.1, 95% CI: 1.03-1.15) and (OR: 1.6, 95% CI: 1.32-1.91), respectively). Higher total GWG also predicted higher risk of PPWR at 1-year postpartum (OR: 1.15, 95% CI: 1.07-1.23; model 1). This prospective association remained significant in model 2 (OR: 1.2, 95% CI: 1.07-1.24) when HbA1c at 6-8 weeks postpartum was included as potential predictor. In model 2, higher HbA1c at 6-8 weeks postpartum (OR: 0.16, 95% CI: 0.05-0.49) was associated with less PPWR at 1-year postpartum.

Table 8: Anthropometric and metabolic characteristics of study participants

Variable	Mean	SD
Pre-pregnancy weight (Kg) (n=862)	69.09	15.38
Pre-pregnancy BMI (Kg/m^2)[1] (n=862)	25.62	5.45
Weight at the first GDM visit (Kg) (n=862)	79.53	15.36
BMI at the first GDM visit (Kg/m^2) (n=862)	29.72	5.41
Fasting glucose at the first GDM visit (mmol/l) (n=862)	5.15	0.75
1hr glucose after oGTT at GDM diagnosis (mmol/l) (n=862)	9.63	1.85
2hr glucose after oGTT at GDM diagnosis (mmol/l) (n=862)	7.85	1.83
HbA1c at the first GDM visit (%) (n=862)	5.44	0.41
Weight at the end of pregnancy (Kg) (n=862)	81.86	15.42
Total gestational weight gain (Kg) (n=862)	12.75	5.96
Weight at the 6-8 weeks pp (Kg) (n=862)	73.58	15.05
BMI at the 6-8 weeks pp (Kg/m^2) (n=862)	27.54	5.35
Fasting glucose at the 6-8 weeks pp (mmol/l) (n=862)	5.00	0.52
2hr glucose after oGTT at 6-8 weeks pp (mmol/l) (n=862)	5.50	1.68
HbA1c at the 6-8 weeks pp (%)(n=862)	5.35	0.38
Weight at 1-year pp (Kg) (n=259)	73.49	17.15
BMI at 1-year pp (Kg/m^2) (n=259)	27.41	6.30
Fasting glucose at 1-year pp (mmol/l) (n=259)	5.48	0.67
HbA1c at 1-year pp (%)(n=259)	5.32	0.39
Weight retention at 6-8 weeks pp[2] (n=862)	4.61	5.79
Weight retention at 1-year pp[3] (n=259)	3.99	7.36

[1]Data taken from the medical charts or reported at the first GDM visit
[2]Weight retention means the difference in weight at 6-8 weeks postpartum and pre-pregnancy weight
[3]Weight retention means the difference in weight at 1-year postpartum and pre-pregnancy weight
BMI means body mass index
GDM means gestational diabetes mellitus
oGTT means oral glucose tolerance test
HbA1c means glycated hemoglobin
pp means postpartum period

Table 9: Anthropometric differences and metabolic consequences of participants according to postpartum weight retention categories

9a: At 6-8 weeks postpartum

6-8 weeks postpartum	Weight retention category at 6-8 weeks PP (n=862)[1]				
	Weight retention (n=700)		No weight retention (n=162)		
General and metabolic health variables*	**Mean**	**SD**	**Mean**	**SD**	**p value**
Age (years)	33.39	5.43	32.91	5.77	0.340
Gestational age at delivery (weeks)	38.68	1.49	38.38	3.52	0.283
Pre-pregnancy weight (Kg)	70.49	17.51	66.76	13.81	**<0.001**
Pre-pregnancy BMI (Kg/m^2)[2]	26.35	6.26	24.75	4.86	**<0.001**
Weight at the first GDM visit (Kg)	80.93	16.96	71.45	14.76	**<0.001**
Fasting glucose at first GDM visit (mmol/l)	5.16	0.65	5.15	0.77	0.843
1hr glucose after oGTT at GDM diagnosis (mmol/l)	9.70	1.70	9.62	1.88	0.658
2hr glucose after oGTT at GDM diagnosis (mmol/l)	8.18	1.70	7.78	1.85	**0.034**
Weight at the end of pregnancy (Kg)	84.63	16.66	73.58	14.23	**0.015**
Total gestational weight gain (Kg)	14.16	5.14	6.63	5.36	**<0.001**
Excess gestational weight gain (Kg)	1.73	0.44	1.50	0.50	**<0.001**
Weight at 6-8 weeks pp (Kg)	75.40	16.66	63.14	14.62	**0.002**
BMI at 6-8 weeks pp (Kg/m^2)	27.10	5.91	23.40	5.19	**0.020**
Fasting glucose at 6-8 weeks pp (mmol/l)	4.99	0.50	5.01	0.52	0.643
2hr glucose after oGTT at 6-8 weeks pp (mmol/l)	5.37	1.57	5.53	1.70	0.269
HbA1c at 6-8 weeks pp (%)	5.32	0.40	5.35	0.37	0.357
Predictor variables*	**n**	**%**	**n**	**%**	**P value**
EPDS score at first GDM visit (n=346)					
<13	237	84.0	45	16.0	**0.031**
≥13	46	71.9	18	28.1	
Breastfeeding in the postpartum period					
Yes	548	80.1	136	19.9	0.065
No	152	85.4	26	14.6	
Medication use in pregnancy (n=777)					
None	292	80.0	73	20.0	**0.041**
Insulin	284	82.8	59	17.2	
Metformin	48	69.6	21	30.4	
Caesarean delivery					
Yes	281	82.4	60	17.6	0.477
No	419	80.4	102	19.6	
Contraception use after delivery (n=305)					
Yes	140	82.4	30	17.6	0.897
No	110	81.5	25	18.5	
Lives with partner					
Yes	566	80.2	140	19.8	0.097
No	134	85.9	22	14.1	
Exceed IOM guidelines					
Yes	347	89.0	43	11.0	**≤0.001**
No	353	74.8	119	25.2	
EPR at first GDM visit (Mean ±SD)	3.89	0.911	3.93	0.86	0.774
RHSC at first GDM visit (Mean ±SD)	3.50	0.88	3.56	0.82	0.669

[1]Weight retention means the difference in weight at 6-8 weeks and pre-pregnancy weight
[2]Data reported at the first GDM visit or taken from the medical charts
GDM means gestational diabetes mellitus; BMI means body mass index; oGTT means oral glucose tolerance test
HbA1c means glycated hemoglobin; EPR means eating for physical rather than emotions; RHSC means reliance on hunger and satiety cues; EPDS means Edinburg postnatal depression scale; IOM means institute of medicine; pp means postpartum period; P value derived from ANOVA for continuous variables and Chi-square for categorical variables
Bold p values are significant. *All n's are 826 unless otherwise stated.

9b: At 1-year postpartum

1-year postpartum	Weight retention category at 1-year PP (n=259)[1]				
	Weight retention (n=172)		No weight retention (n=87)		
General and metabolic health variables*	**Mean**	**SD**	**Mean**	**SD**	**p value**
Age (years)	32.93	5.86	34.00	4.74	0.147
Gestational age at delivery (weeks)	38.78	1.71	38.82	1.86	0.888
Pre-pregnancy weight (Kg)	68.78	15.42	69.97	14.10	0.564
Pre-pregnancy BMI (Kg/m^2)[2]	25.81	5.67	25.62	5.18	0.792
Weight at the first GDM visit (Kg)	80.28	15.97	78.58	13.48	0.427
Fasting glucose at first GDM visit (mmol/l)	5.24	1.00	5.11	0.77	0.328
1hr glucose after oGTT at GDM diagnosis (mmol/l)	9.68	2.00	9.61	1.96	0.817
2hr glucose after oGTT at GDM diagnosis (mmol/l)	7.85	2.02	7.99	1.85	0.651
Weight at the end of pregnancy (Kg)	82.82	15.47	80.02	13.60	0.188
Total gestational weight gain (Kg)	14.16	6.15	10.08	5.76	**<0.001**
Excess gestational weight gain (Kg)	1.44	0.49	1.68	0.46	**<0.001**
Weight at 6-8 weeks pp (Kg)	74.88	14.92	71.96	13.01	0.121
BMI at 6-8 weeks pp (Kg/m^2)	28.08	5.36	26.66	4.66	**0.044**
Fasting glucose at 6-8 weeks pp (mmol/l)	5.00	0.518	4.97	0.45	0.618
2hr glucose after oGTT at 6-8 weeks pp (mmol/l)	5.26	1.42	5.22	1.63	0.841
HbA1c at 6-8 weeks pp (%)	5.27	0.36	5.40	0.34	**0.009**
Weight at 1-year pp (Kg)	75.79	18.08	68.67	13.92	**0.002**
BMI at 1-year pp (Kg/m^2)	28.42	6.55	25.05	4.93	**<0.001**
EPR at 1-year pp	3.64	0.92	3.75	10.4	0.478
RHSC at 1-year pp	3.31	0.94	3.59	0.95	0.057
Fasting glucose at 1-year pp (mmol/l)	5.55	0.72	5.35	0.55	**0.026**
HbA1c at 1-year pp (%)	5.33	0.42	5.31	0.33	0.739
ΔFasting glucose[3]	0.54	0.61	0.37	0.54	**0.032**
ΔHbA1c[3]	0.05	0.39	-0.08	0.37	**0.006**

[1]Weight retention means the difference in weight at 6-8 weeks and pre-pregnancy weight. [2]Data reported at the first GDM visit or taken from the medical charts. [3]Change in metabolic variables (fasting glucose and HbA1c) between 6-8 weeks and 1year postpartum. GDM means gestational diabetes mellitus; BMI means body mass index; oGTT means oral glucose tolerance test; HbA1c means glycated hemoglobin; EPR means eating for physical rather than emotions; RHSC means reliance on hunger and satiety cues; EPDS means Edinburg postnatal depression scale; IOM means institute of medicine; pp means postpartum period; P value derived from ANOVA for continuous variables and Chi-square for categorical variables. *All the N's are 259 unless otherwise stated. Bold p values are significant.

9b: At 1-year postpartum (continued)

1-year postpartum	Weight retention category at 1-year PP (n=259)[1]				
	Weight retention (n=172)		No weight retention (n=87)		
Predictor variables*	**n**	**%**	**n**	**%**	**P value**
EPDS score at first GDM visit (n=172)					
<13	99	71.7	39	28.3	0.144
≥13	20	58.8	14	41.2	
EPDS score at first 1-year pp (n=213)					
<13	119	64.7	65	35.3	0.930
≥13	19	65.5	10	34.5	
Breastfeeding in the postpartum period					
Yes	152	67.3	74	32.7	0.450
No	20	60.6	13	39.4	
Medication use in pregnancy (n=248)					
None	75	68.2	35	31.8	0.791
Insulin	83	69.2	37	30.8	
Metformin	11	61.1	7	38.9	
Caesarean delivery					
Yes	70	64.8	38	35.2	0.690
No	102	6705	49	32.5	
Contraception use after delivery (n=134)					
Yes	39	61.9	24	38.1	0.217
No	53	74.6	18	25.4	
Lives with partner					
Yes	146	68.2	68	31.8	0.177
No	26	57.8	19	42.2	
Exceed IOM guidelines					
Yes	96	78.0	27	22.0	**≤0.001**
No	76	55.9	60	44.1	
EPR at first GDM visit (Mean ±SD)	3.84	0.94	3.85	0.90	0.962
RHSC at first GDM visit (Mean ±SD)	3.50	0.87	3.39	0.86	0.465

[1]Weight retention means the difference in weight at 6-8 weeks and pre-pregnancy weight. [2]Data reported at the first GDM visit or taken from the medical charts. [3]Change in metabolic variables (fasting glucose and HbA1c) between 6-8 weeks and 1year postpartum. GDM means gestational diabetes mellitus; BMI means body mass index; oGTT means oral glucose tolerance test; HbA1c means glycated hemoglobin; EPR means eating for physical rather than emotions; RHSC means reliance on hunger and satiety cues; EPDS means Edinburg postnatal depression scale; IOM means institute of medicine; pp means postpartum period; P value derived from ANOVA for continuous variables and Chi-square for categorical variables. *All the N's are 259 unless otherwise stated. Bold p values are significant.

Table 10: Predictors of weight retention

10a: Predictors at 6-8 weeks postpartum (n=862)

Variable	OR	95% CI		P value*
Pre-pregnancy weight (Kg)	1.09	1.035	1.150	**<0.001**
Total gestational weight gain (Kg)	1.59	1.324	1.919	**<0.001**
Excess gestational weight gain (Kg)	4.08	0.857	19.466	0.077

Weight retention means the difference in weight at 6-8 weeks postpartum and pre-pregnancy weight
*P value from the final model of the multivariable logistic regression with backward elimination
Variables entered in the multivariable regression models were: family history of diabetes, partner support, breastfeeding and depression score at the first GDM visit, pre-pregnancy weight, 2hr glucose after oGTT at GDM diagnosis, total GWG, and excess GWG according to IOM guidelines.

10b: Predictors at 1-year postpartum (n=259)

	Model 1				Model 2			
Variable	**OR**	**95% CI**		**P value***	**OR**	**95% CI**		**P value***
Total Gestational weight gain (kg)	1.15	1.072	1.231	**<0.001**	1.15	1.076	1.245	**<0.001**
HbA1c at 6-8 weeks pp (%)					0.16	0.052	0.490	**<0.001**

pp means postpartum period
Weight retention means the difference in weight at 1-yr postpartum and pre-pregnancy weight
Model 1: without HbA1c at 6-8 weeks pp
Model 2: included HbA1c at 6-8 weeks pp
* P value from the final model of the logistic regression with backward elimination
Variables entered in the multivariable regression model were: age, family history of diabetes, partner support, depression score at the first GDM visit, total GWG, excess GWG, and HbA1c at 6-8 weeks postpartum visit

5.1 ABSTRACT OF STUDY 1

Intuitive Eating Is Associated with Weight and Glucose Control during Pregnancy and in the Early Postpartum Period in Women with Gestational Diabetes Mellitus: A Clinical Cohort Study

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QUANSAH DY, Gross J, Gilbert L, Helbling C, Horsch A, Puder JJ. Intuitive eating is associated with weight and glucose control during pregnancy and in the early postpartum period in women with gestational diabetes mellitus (GDM): A clinical cohort study. **Poster communication** at the 2018 Swiss Society of Endocrinology and Diabetology (SSED) annual meeting. Inselpital, Bern; 15-16.11.2018.

QUANSAH DY, Gross J, Gilbert L, Helbling C, Horsch A, Puder JJ. Intuitive eating is associated with weight and glucose control during pregnancy and in the early postpartum period in women with gestational diabetes mellitus (GDM): A clinical cohort study. **Poster communication** at the Journée de la recherche du Département de médecine; CHUV; 21.02.2019.

QUANSAH DY, Gross J, Gilbert L, Helbling C, Horsch A, Puder JJ. Intuitive eating is associated with weight and glucose control during pregnancy and in the early postpartum period in women with gestational diabetes mellitus (GDM): A clinical cohort study. **Poster communication at the** Die Arbeitsgruppe Lipide und Atherosklerose **(**AGLA) State of the Art and Progress on Lipids and Atherosclerosis conference; Inselpital, Bern; 07.02.2019**.**

Author contribution

QUANSAH DY, designed the study, contributed to data collection, performed all the data extraction, all analyses, contributed to interpretation of data and wrote the manuscript.

Abstract

Introduction: High pre-pregnancy weight and body mass index (BMI) increase the risk of gestational diabetes mellitus (GDM) and diabetes after pregnancy. To tackle weight and metabolic health problems, there is a need to investigate novel lifestyle approaches. Outside of pregnancy, higher adherence to intuitive eating (IE) is associated with lower BMI and improved glycemic control. This study investigated the association between IE and metabolic health during pregnancy and in the early postpartum period among women with GDM.

Methods: Two-hundred and fourteen consecutive women aged ≥18, diagnosed with GDM between 2015 and 2017 and completed the "Eating for Physical rather than Emotional Reasons (EPR)" and "Reliance on Hunger and Satiety cues (RHSC) subscales" of the French Intuitive Eating Scale-2 (IES-2) questionnaire at the first GDM clinic visit was included in this study.

Results: Participants' mean age was 33.32±5.20 years. Their weight and BMI before pregnancy were 68.18±14.83kg and 25.30±5.19kg/m^2 respectively. After adjusting for confounding variables, the cross-sectional analyses showed that the two subscales of IES-2 at the first GDM visit were associated with lower weight and BMI before pregnancy, and lower weight at the first GDM visit (β=-0.181 to -0.215, all p≤ 0.008). In addition, the EPR subscale was associated with HbA1c and fasting plasma glucose at the first GDM visit (β=-0.170 and to -0.196; all p≤ 0.016). In the longitudinal analyses, both subscales of IES-2 at first GDM visit were associated with lower weight at the end of pregnancy, BMI and fasting plasma glucose at 6-8 weeks postpartum (β=-0.143 to -0.218, all P≤ 0.040) after adjusting for confounders.

Conclusions*:* Increase adherence to IE could represent a novel approach to weight and glucose control during and after pregnancy in women with GDM.

5.2 ABSTRACT OF STUDY 2

Intuitive Eating is associated with Improved Health Indicators at 1-Year Postpartum in Women with Gestational Diabetes Mellitus

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The full length article is in appendix 2

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QUANSAH DY, Gilbert L, Gross J, Horsch A, Puder JJ. Intuitive eating is associated with improved health indicators at 1-year postpartum in women with gestational diabetes mellitus. **Oral communication** at the Swiss Perinatal Research Conference; CHUV; 17.05.2019

QUANSAH DY, Gilbert L, Gross J, Horsch A, Puder JJ. Intuitive eating is associated with improved health indicators at 1-year postpartum in women with gestational diabetes mellitus. **Poster communication** Diabetes in pregnancy (DIP) 2019: The 10th International Symposium on Diabetes, Hypertension, Metabolic Syndrome and Pregnancy; Florence, Italy; 29.05-01.06.2019.

QUANSAH DY, Gilbert L, Gross J, Horsch A, Puder JJ. Intuitive eating is associated with improved health indicators at 1-year postpartum in women with gestational diabetes mellitus. **Poster flash communication** at the American Diabetes Association (ADA) 79th Scientific Sessions; San Francisco, California; 7-11.06.2019

Author contribution

QUANSAH DY, designed the study, contributed to data collection, performed all the data extraction, all analyses, contributed to interpretation of data and wrote the manuscript.

Abstract

Introduction: In women with GDM, there is a need to investigate novel lifestyle approaches to reduce the risk of future diabetes. We evaluated the associations between IE during and after pregnancy with BMI, fasting glucose and HbA1c at 1-year postpartum (PP) in women with GDM and in high-risk GDM subgroups with prediabetes or overweight/obesity prior to pregnancy.

Methods: 117 women with GDM who consented and completed the "*Eating for Physical rather than Emotional Reasons* (EPR)" and *"Reliance on Hunger and Satiety cues* (RHSC)" subscales of the validated Intuitive Eating Scale-2 questionnaire during the first GDM clinic visit at 24-32 weeks of gestation and at 1-year PP were included.

Results: Participants mean age was 33.21±5.37 years, weight and BMI before pregnancy and at 1-year PP were 69.46±13.99kg, 25.82±4.69kg/m^2 and 72.79±16.22kg, 27.06±5.54kg/m^2, respectively. EPR at the first GDM visit predicted lower BMI (β=-0.219, p=0.017) and fasting glucose (β=-0.229, p=0.014) at 1-year PP, while associations were not significant for RHSC. At 1-year PP, EPR and RHSC were associated with lower BMI (β= -0.337 and -0.243 both p≤ 0.012) and weight retention (β=-0.230 and -0.193, both p=0.037) and EPR was also associated with lower fasting glucose and HbA1c (both β= -0.22, both p=0.018). In the subgroup of women with prediabetes, EPR and RHSC at the first GDM visit predicted lower fasting glucose at 1-year PP, while in the overweight/obese subgroup this was only significant for EPR (all p≤0.02). At 1-year PP however, both EPR and RHSC were inversely associated with BMI in women with prediabetes and with fasting glucose in overweight/obese women (all p≤0.03).

Conclusion: Interventions to increase IE could represent a novel approach for PP weight and glycemic control in women with previous GDM, particularly in high-risk subgroups with prediabetes or obesity.

5.3 ABSTRACT OF STUDY 3

Predictors and Consequences of Weight Retention in the Early and Late Postpartum Period in Women with Gestational Diabetes

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QUANSAH DY, Gross J, Gilbert L, Arhab A, Horsch A, Puder JJ. Predictors and differences in early and late postpartum weight retention in women previously diagnosed with Gestational diabetes; a clinical cohort study. **Poster flash communication** at the Journee de la Recherche du Dèpartment femme-mère-enfant 2020 conference, on Thursday, March 12th 2020 at CHUV, Lausanne.

Author contribution

QUANSAH DY, designed the study, contributed to data collection, performed all the data extraction, all analyses, contributed to interpretation of data and wrote the manuscript.

Abstract

Aims: We investigated the predictors and consequences of postpartum weight retention (PPWR) in the early and late postpartum period in women with gestational diabetes (GDM), to assist preventive strategies.

Methods: 862 women with GDM were prospectively included between 2011 and 2019. We investigated PPWR at 6-8 weeks and 1-year postpartum. Potential predictors included gestational weight gain (GWG), weight, BMI, and glucose control parameters during and after pregnancy.

Results: PPWR at 6-8 weeks and 1-year postpartum were 4.6±5.7kg and 4.0 ±7.4kg. At 6-8 weeks postpartum, women with PPWR had higher pre-pregnancy weight, 7.5±0.2kg higher GWG and higher postpartum weight (all $p \leq 0.02$), without presenting metabolic differences. At 1-year postpartum, there were no differences in anthropometric parameters before and during pregnancy between women with or without PPWR, except for a 4±0.4kg higher GWG ($p<0.001$). However, women with PPWR had increased postpartum weight and BMI, higher fasting glucose and more pronounced increases in Δfasting glucose and ΔHbA1c at 1-year (all $p \leq 0.03$). GWG predicted higher PPWR at both 6-8 weeks and at 1-year PP (all $p<0.001$).

Conclusion: Women with PPWR had increased anthropometric parameters and adverse metabolic consequences at 1-year postpartum. GWG was the most relevant predictor of PPWR.

6.0 GENERAL DISCUSSION

This thesis provides more insights into the novel cross-sectional and longitudinal relationships between IE and weight and fasting glucose levels in women with GDM. It also identifies the predictors and the consequences of PPWR in the early and late postpartum period in women with GDM.

Cross-sectional association between intuitive eating and metabolic outcome (Study 1 & 2)

Our analyses revealed a novel association between IE during pregnancy (at the first GDM visit) with lower BMI and weight before and during pregnancy as well as with fasting glucose and/or HbA1c during pregnancy (study 1). The relationship between IE and fasting glucose was partly mediated by weight (study 1). In study 2, we found that, IE at 1-year postpartum was associated with lower BMI, lower weight retention, fasting glucose and HbA1c at 1-year postpartum. Our results corroborate the findings of a cross-sectional review which indicated that IE was positively related with improved dietary intake and/or healthy eating behaviors. Those factors are drivers for weight loss and glucose maintenance (118). Eating intuitively is known to improve hunger and satiety cues, exert more cognitive control over eating and increase response to physiological signals which leads to lower weight and BMI (36). The results of study 1 and 2 are also consistent with a cross-sectional study among postpartum women where higher practice or adherence to IE was associated with accelerated rates of postpartum weight loss (119). Following a more IE approach to food consumption may encourage postpartum weight loss without the required diet restrictions, calorie counting and exercise regimes all of which are features of traditional weight loss programs. Regarding glycemic control, the findings of this study are in line with those of Wheeler and colleagues who showed that higher adherence to the eating for physical rather than emotional reasons subscale of the IES-2 was associated with lower HbA1c in a cross-sectional study (128).

They are also in line with a cross-sectional review in which IE was associated with improvements in metabolic health indicators, including fasting glucose (118). The eating for physical rather than emotional reasons subscale is known to be negatively associated with disordered eating behaviors and may lead to lower fasting glucose and HbA1c levels (38). These results indicate that aiming to improve IE during pregnancy and the ability to keep this practice stable and even higher in the postpartum period may help to improve weight and fasting glucose levels in these women.

Longitudinal association between intuitive eating and metabolic outcomes (Study 1 & 2)

We also explored the longitudinal relationship between IE with weight and fasting glucose levels during the early and late postpartum period. We found that IE during pregnancy (at the first GDM visit) was associated with lower weight at the end of pregnancy, lower BMI and lower fasting glucose at 6-8 weeks postpartum (study 1). Also, eating for physical rather than emotional reasons during pregnancy (at the first GDM visit) was associated with lower BMI at 1-year postpartum (study 2). These findings are in concordance with a previous study conducted in a general non-pregnant population where IE was associated with lower weight gain and BMI decreases at 1-year postpartum (119). IE assesses the extent to which eating is affected by emotion (92) and women with GDM who engage in eating habits or behaviors driven by emotion rather than physical symptoms of hunger during and after pregnancy may have more problems with weight loss and fasting glucose control in the postpartum period (119). Adhering to IE prevents or reduces eating in response to negative emotional states such as anxiety, depression, boredom or loneliness that often leads to overeating, weight retention, higher BMI and poor glucose control in women with GDM (129). IE could therefore offer an alternative approach that may be rewarding and less exhausting to aid early and late postpartum weight loss in women with GDM (119).

In study 2, we also found that both subscales of IES-2 during pregnancy (at the first GDM visit) were associated with lower fasting glucose at 1-year postpartum in all women with GDM and in women with prediabetes at 1-year postpartum. Also the eating for physical rather than emotional reasons during pregnancy (at the first GDM visit) predicted lower fasting glucose in women with obese/overweight BMI. The relationship between IE and lower fasting glucose in women with prediabetes and obese/overweight showed that special focus should be placed on these women for follow-up. This is particularly important because in women with GDM and in high-risk GDM subgroups (with prediabetes and obese/overweight) each kilogram of weight lost in the postpartum period is associated with a 16% decrease in the risk of diabetes (130–132). It should also be noted that although women with GDM might have normal glucose values after delivery (133), up to 50% develop prediabetes between 6 weeks and 12 months as observed in our sample and confirmed by another study (22).

On the contrary, we found no longitudinal association between the reliance on hunger and satiety cues subscale during pregnancy (at the first GDM visit) with either weight or glucose control variables studied at 1-year postpartum. This lack of association between the reliance on hunger and satiety cues subscale and the weight and fasting glucose variables in our longitudinal analyses suggests that in the long-term eating for physical rather than emotional reasons overshadows the potential importance of relying on one's hunger and satiety signals to regulate food intake in this sample. Outside of pregnancy, intervention studies have revealed that IE is associated with weight loss (115,116) leads to weight maintenance and improves physical health indicators including glucose control (102,108). Our results have important clinical implications which suggest that IE could represent a novel approach for weight and glycemic control during and after pregnancy in women diagnosed with GDM. However, intervention studies should be performed to verify these hypotheses.

Predictors of PPWR (Study 3)

In women with GDM, one previous study exists regarding the predictors of PPWR (31). It demonstrated that less GWG, increasing age and lack of insulin use during pregnancy were associated with losing ≥75% of pregnancy weight at 6-8 weeks postpartum. In our study GWG was also associated with PPWR but we did not find an association with age or insulin use during the initial univariate regression analyses and hence these variables were not included in the main predictor models. In non-GDM populations, many studies support GWG as a strong and pronounced predictor of PPWR at 6 weeks (55) and up to 12 months postpartum (56–59) as found in our study. Our results are also consistent with those of other studies conducted in non-GDM populations which showed that women with PPWR had higher GWG leading to higher weight status in the late postpartum period (53,134,135). This is explained by the role of excess adipose tissue due to sub-optimal diet and physical activity behaviors before/during pregnancy that leads to excess weight gain and extends into the postpartum period leading to a higher weight retention in the late postpartum period (136–138). Other studies indicate that exceeding IOM guidelines (=excessive GWG) increases the risk of PPWR at 6 to 18 months (60–62). To our knowledge, these latter studies only investigated excessive GWG without including total or absolute GWG. In this study however, although exceeding IOM guidelines (=excessive GWG) was associated with PPWR, this relationship did not remain significant after adjusting for total GWG. This means that excessive GWG does not impact on PPWR beyond the impact of total GWG. Total GWG was the most important predictor of PPWR in our cohort. This is even more relevant as excess GWG was not very pronounced and represented less than 2kg even in women with PPWR. Based on the results, at least regarding postpartum metabolic health, the currently existing IOM guidelines are probably too flexible for a multicultural population with GDM and hence should be revised.

Consequences of weight retention (Study 3)

Study 3 revealed that women with and without PPWR at 6-8 weeks postpartum differed significantly in anthropometric characteristics (weight, BMI, GWG) before, during and after pregnancy. At 1-year postpartum however, they only differed in anthropometric characteristics in the postpartum period, i.e. both in the early (BMI) and late (weight, BMI) postpartum periods. Regarding metabolic consequences, no differences were seen in the early postpartum period between women with and without PPWR. In the late postpartum period, women with PPWR had higher fasting glucose and more pronounced increases in both fasting glucose and HbA1c between the early and late postpartum period. Thus, regarding metabolic consequences, differences between women with and without PPWR were only seen at 1-year postpartum. This finding suggests that late PPWR had an impact on glucose control at 1-year postpartum which might not reveal itself yet in the early postpartum period. Reasons such as sub-optimal diet and physical activity behaviors before/during/after pregnancy (136–138), depressive symptoms and/or short sleep duration (139,140) or breastfeeding (54) and its discontinuation as most of these patients do not breastfeed beyond 6 months could account for the differences in the anthropometric characteristics observed in women with PPWR. Regarding breastfeeding, 85% of women in our cohort who were still breastfeeding at 6-8 weeks postpartum had no PPWR in the late postpartum period. Findings of one previous study parallels our results (21): it demonstrated that weight gain in the first year postpartum was associated with a significant increase in fasting and 2-h glucose in women with GDM.

It is thus essential to focus on prevention of later PPWR e.g. at 1-year postpartum, which actually concerns two thirds of women in our cohort and in published populations. A lack of PPWR or of metabolic complications at 6-8 weeks postpartum although reassuring should therefore not lead to complacency.

This is especially important as only a minority (10%) continues to lose weight after the early postpartum period in our study and those with PPWR at 1-year even demonstrated a small weight gain between the early and late postpartum period. These findings contradict the usual clinical recommendation that the PPWR at 6-8 weeks postpartum is not important as women will anyway loose more weight in the first year postpartum.

Our data regarding the consequences of PPWR also suggest that clinical care with a strong focus on lifestyle interventions in order to improve weight and glucose control beyond a pure screening should be essential up to the late postpartum. This postpartum follow-up should not be limited to screening for metabolic health indicators only but must focus on lifestyle changes. This is because even women without PPWR had a significant increase in fasting glucose between the early and late postpartum period despite almost a 3kg weight loss between these time points suggesting the need for an extended postpartum follow-up period.

7.0 STRENGTHS, LIMITATIONS AND PERSPECTIVES

Strengths of this thesis

This study has several strengths. It is the first to investigate the relationship between IE with metabolic health during and after pregnancy. It is also the first to investigate IE and metabolic health in women with GDM and in a real-life clinical setting. We used a well-developed and validated tool to measure IE. Clinically, our results if confirmed by an intervention trial could help address the issue of postpartum weight retention in women with GDM. It could also help augment the management and prevention of diabetes in women with GDM in general and in the high-risk subgroups with prediabetes or overweight/obese specifically (141). This is even more important, as lifestyle interventions continue to show inconsistent results and effect sizes are small (10,73,75). This study is also the first to investigate both total and excessive GWG as predictors of PPWR as most studies focus exclusively on excessive GWG. In our cohort, total GWG showed a more important role in PPWR prediction than excess GWG. In terms of metabolic consequences of PPWR, adverse metabolic differences and outcomes were only seen in the late postpartum period.

Limitations of this thesis

Even though the results of this thesis are novel, they must be interpreted with caution and some limitations prevail. One limitation of this thesis is the lack of food and dietary intake data in the cohort database. Although we focused on the role of nutritional behavior and metabolic outcomes in women with GDM, it should be important now to investigate the relationship between IE with dietary intake and food quality in these women. In addition, factors such as dietary counseling and use of medication during pregnancy could influence weight and glycemic control and may account for some observed relationships in our longitudinal analysis, even though we measured study variables before dietary counselling and also adjusted for medication use during pregnancy in our analyses.

Furthermore, women had no medication intake in the postpartum period. The lack of a total IES-2 score in our analyses may be a source of limitation as it would have been interesting to see the overall effect of IES-2 on our outcomes. Even though the IES-2 has been validated both in the general and pregnant population, it is not validated in women with GDM and could be a limitation of our study. Other limitations such as a relatively small sample size in our longitudinal analyses may limit our ability to generalize those findings. In addition, several psychosocial and behavioral factors including family support, smoking status in the postpartum period, willingness and change in attitudes following GDM diagnosis which were not the focus of this thesis could influence weight changes especially in the postpartum period. Another limitation is the inability to test the causality of these associations in an intervention trial as data is still ongoing in our randomized controlled intervention trial.

Perspectives for future research

This prospective clinical cohort of women with GDM showed that IE could potentially be a novel approach for weight and glucose management during pregnancy and in the postpartum period. **Studies 1 and 2,** found that, the eating for physical rather than emotional reasons subscale of the IES-2 was a better predictor of improved cardio-metabolic outcomes than the reliance on hunger and satiety cues subscale independent of covariate adjustment. It is therefore important that future studies investigates the individual subscales of the IES-2 as well as the influence of the total IES-2 score and its contribution to both weight and glucose control in women with GDM. Dietary counseling during pregnancy, can both influence weight and glycemic control in the long-term and hence future research should investigate its potential longitudinal influence. Most importantly, research that utilizes IE as an intervention for weight retention and glucose control in a larger and multicultural population during pregnancy is needed to determine the causality of these novel associations we have found.

In studies outside of the perinatal period, IE could be modulated and thus can be influenced. This hints to the assumption that IE is not just a trait, but also a state that could be influenced.

In our ongoing lifestyle interventional trial in women with GDM, we hope test the association between an IE intervention with metabolic health outcome during and after pregnancy. We will also investigate the relationship between dietary intake and IE and if indeed higher IE scores relates to dietary quality as well as their relationship with metabolic outcomes. We will also investigate the relationship between maternal diet quality and intuitive eating during pregnancy with offspring metabolic outcomes.

Regarding the predictors of weight retention, our results indicate that currently existing IOM guidelines for (excess) GWG maybe too relaxed concerning postpartum weight and metabolic health in women with GDM. It is thus essential to control GWG. It will also be pertinent for these guidelines to be reviewed for women with GDM. It is essential for future research to focus on postpartum weight retention even after the recommended postpartum routine screenings because the lack of postpartum weight retention or of metabolic complications at 6-8weeks postpartum, although reassuring, should not lead to complacency as only a minority continues to lose weight after the early postpartum period. There is therefore the need to extend the postpartum follow-up period with special focus on lifestyle interventions.

8.0 GENERAL CONCLUSION

This thesis provides insights into the relationships between nutrition behavior (focusing on intuitive eating (IE)) and weight and fasting glucose outcomes in women with GDM. It also provides an understanding of the predictors and consequences of weight retention in the postpartum period in women with GDM. In a prospective clinical cohort of women with GDM, we found a novel cross-sectional association between IE, specifically the two subscales of IES-2 (eating for physical rather than emotional reasons and reliance on hunger and satiety cues) with lower weight and BMI before, during pregnancy and at the 6-8 weeks and 1-year postpartum in both study 1 and 2. The eating for physical rather than emotional reasons subscale was also associated with lower HbA1c and fasting glucose in the cross-sectional analyses. Our longitudinal analyses (study 1 & 2) confirmed the novel relationship between the eating for physical rather than emotional reasons subscale and lower fasting glucose and HbA1c in our cross-sectional associations in **study 1.** In the high-risk GDM subgroups with overweight/obesity or prediabetes, IE was associated with lower BMI, weight retention and fasting glucose. These cross-sectional and longitudinal relationships between IE with weight and fasting glucose outcomes during and after pregnancy reveals that IE could be a future target for screening and a potential intervention in women with GDM especially when success from traditional lifestyle interventions remains low.

In **Study 3,** total GWG was the most important predictor of PPWR beyond the impact of excess GWG. Regarding metabolic consequences between women with and without PPWR, differences were only seen in the late postpartum period. However, all women showed an increase in fasting glucose between the 6-8 weeks and 1-year postpartum. Our data regarding PPWR and metabolic health suggest that beyond the recommended postpartum screenings, there is a need for a continuous lifestyle intervention for women with GDM.

Weight loss or lifestyle interventions should also focus on GWG and could help reduce the risk of PPWR and importantly to improve cardio-metabolic consequences. In conclusion, the findings of this thesis imply that IE might have practical implications on weight and glucose control during and after pregnancy in women with GDM and in high-risk GDM subgroups with prediabetes or overweight/obesity. It also demonstrates that studying the pattern of PPWR can help to focus efforts and target optimal timing for interventions in women with GDM in the postpartum period in order to prevent diabetes and other cardio-metabolic outcomes. Most importantly intervention studies should be performed in order to test our hypotheses.

8.1 Personal contribution to data acquisition and management

The GDM research group is a multidisciplinary research group composed of dieticians, physiotherapist, physicians and researchers including psychologists, sport scientists and graduate students. I participate in two projects managed by the research group. These are the GDM longitudinal cohort and a lifestyle intervention trial. In the lifestyle intervention trial (Improving Cardio-metabolic and Mental Health in Women With Gestational Diabetes Mellitus and their Offspring (MySweetHeart); NCT02890693), I coordinate the participant recruitment in English, supervises interns on patient testing, addresses and answer questions from interns and clinicians on testing procedures and the trial protocol. The analyses of this ongoing trial which include an IE intervention will be part of my Postdoctoral training which will focus on testing the hypotheses involved in this thesis. In both the cohort and intervention trial, I manage the Secutrial research database and supervises data input by master's students and performs data extraction for different research purposes. In this role, I produced a detailed systematic and regular update of data input guideline to aid data input. I also supervise and coordinate the preparation of research kits for blood drawing and responsible for weekly contact with laboratory for blood samples, analysis and assistance in blood drawing.

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10.0 PUBLICATION LIST

First authored publications related to this Ph.D. thesis

1. **QUANSAH DY**, Gross J, Gilbert L, Helbling C, Horsch A, Puder JJ. Intuitive eating is associated with weight and glucose control during pregnancy and in the early postpartum period in women with gestational diabetes mellitus (GDM): A clinical cohort study. ***Eating Behaviors*** 34 (2019):1013042.
2. **QUANSAH DY**, Gilbert L, Gross J, Horsch A, Puder JJ. Intuitive eating is associated with improved health indicators at 1-year postpartum in women with gestational diabetes mellitus. ***J Health Psychol***. 22 (2019):1359105319869814.
3. **QUANSAH DY**, Gross J, Gilbert L, Arhab A, Horsch A, Puder JJ. Predictors and consequences of weight retention in the early and late postpartum period in women with gestational diabetes. ***Diabetes Res and Clin Prac.*** *(2020).* doi: https://doi.org/10.1016/j.diabres.2020.108238

Other co-uthored publications related to the Ph.D. studies (pubblished or submitted)

4. Gilbert L, Gross J, Lanzi S, **QUANSAH DY**, Puder JJ, Horsch A. How diet, physical activity and psychosocial well-being interact in women with gestational diabetes mellitus: an integrative review. ***BMC Pregnancy Childbirth***. 2019; 19 (1):60
5. Gilbert L, Rossel JB, **QUANSAH DY**, Puder JJ, Horsch A. Mental health and its associations with weight in women with gestational diabetes mellitus (GDM). A prospective clinical cohort study. ***Submitted***
6. Kosinski, C, Gross J, Helbling C, **QUANSAH DY**, Rossel JB, Collet TH, Puder JJ. Gestational Diabetes Mellitus and Metabolic Health in the Early and Late Postpartum Period: A prospective clinical cohort study. ***Submitted***
7. Gilbert L, Nikolaou A, **QUANSAH DY**, Rossel JB, Horsch A, JJ. Mental health and its associations with medication intake in women with gestational diabetes mellitus. A prospective clinical cohort study. ***Psychoneuroendocrinology***, under review.

11.0 APPENDIX

The appendix contains 3 manuscripts/articles which are all published.

APPENDIX 1

STUDY 1: Intuitive eating is associated with weight and glucose control during pregnancy and in the early postpartum period in women with gestational diabetes mellitus: A clinical cohort study

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Abstract

Introduction: High pre-pregnancy weight and body mass index (BMI) increase the risk of gestational diabetes mellitus (GDM) and diabetes after pregnancy. To tackle weight and metabolic health problems, there is a need to investigate novel lifestyle approaches. Outside of pregnancy, higher adherence to intuitive eating (IE) is associated with lower BMI and improved glycemic control. This study investigated the association between IE and metabolic health during pregnancy and in the early postpartum period among women with GDM. **Methods:** Two-hundred and fourteen consecutive women aged ≥18, diagnosed with GDM between 2015 and 2017 and completed the "Eating for Physical rather than Emotional Reasons (EPR)" and "Reliance on Hunger and Satiety cues (RHSC) subscales" of the French Intuitive Eating Scale-2 (IES-2) questionnaire at the first GDM clinic visit was included in this study. **Results:** Participants' mean age was 33.32±5.20 years. Their weight and BMI before pregnancy were 68.18±14.83kg and 25.30±5.19kg/m^2 respectively. After adjusting for confounding variables, the cross-sectional analyses showed that the two subscales of IES-2 at the first GDM visit were associated with lower weight and BMI before pregnancy, and lower weight at the first GDM visit (β=-0.181 to -0.215, all p≤ 0.008). In addition, the EPR subscale was associated with HbA1c and fasting plasma glucose at the first GDM visit (β=-0.170 and to -0.196; all p≤ 0.016). In the longitudinal analyses, both subscales of IES-2 at first GDM visit were associated with lower weight at the end of pregnancy, BMI and fasting plasma glucose at 6-8 weeks postpartum (β=-0.143 to -0.218, all P≤ 0.040) after adjusting for confounders. **Conclusions***:* Increase adherence to IE could represent a novel approach to weight and glucose control during and after pregnancy in women with GDM.

Keywords: Intuitive eating; Gestational diabetes mellitus; Body mass index; Glycemic control; Pregnancy; Postpartum

1. Introduction

Gestational diabetes mellitus (GDM) refers to any degree of glucose intolerance that is diagnosed in the second or third trimester of pregnancy but does not fulfil the criteria of overt diabetes prior to gestation (1). The negative maternal consequences of GDM are well documented (2,3). Pre-pregnancy BMI and weight gain during pregnancy also increase the risk for complications, such as cesarean delivery and maternal postpartum weight retention (4). Although pre-pregnancy overweight or obesity increase the risk of GDM (5), excess weight gain in women with GDM may increase the risk of developing diabetes in the postpartum period (5,6).

The cornerstone of GDM treatment requires nutrition/diet and exercise intervention to achieve weight and glucose control and also to reduce the need for medical therapy (7). Regarding nutrition, several diets, such as low glycemic index (GI) diet, total energy restriction diet, low carbohydrate diet, and ethnic or traditional diets, such as the Mediterranean diets, have been used to manage weight and glycemic control in women with GDM (8). Although lifestyle interventions (diet and physical activity) led to a lower postpartum weight gain according to a recent Cochrane review (9), the review found no differences regarding postpartum glucose tolerance, postnatal weight retention or return to pre-pregnancy weight in women with GDM between those who had a lifestyle intervention and the control group (9). This evidence suggests that, research should focus on interventions targeting specific lifestyle aspects to address the long-term outcomes of GDM. BMI and weight are independent risk factors of GDM and of the development of diabetes after pregnancy. Therefore, additional methods that improve or maintain weight and promote healthier eating options during pregnancy and in the postpartum period need to be explored especially in women with GDM.

Research suggests that, adaptive eating behaviors that encourage people to recognize and respond to their internal signs of hunger and satiety prevent emotional eating and dietary restriction (10–12), and may lead to lower weight and BMI (13). One such adaptive eating behavior is intuitive eating (IE). IE is characterized by eating in response to physiological hunger and satiety cues rather than external and/or emotional cues (14,15). IE is a more sustainable long-term eating behavior than dieting and is known to be associated with lower levels of cholesterol and cardiovascular risk. It is also inversely associated with disordered eating behavior and leads to body shape satisfaction, lower weight and glucose maintenance (16,17).

Outside of pregnancy, evidence suggests that IE is associated with lower BMI (18–20), weight loss (21,22) and glycemic control in the general population (23,24). In the postpartum period, higher IE practices were associated with lower weight compared to those who engaged in fewer IE practices (25). Even though IE is associated with long-term weight maintenance or weight loss (26), no study has investigated the potential benefit of IE in pregnancy, although the IE questionnaire has been validated in samples of pregnant women (27). Considering that, IE is correlated with BMI, weight and glycemic control as indicated above, we hypothesize that, higher adherence to IE may be beneficial for weight and glycemic control in women with GDM during and after pregnancy. The objective of this study therefore was to investigate the cross-sectional and longitudinal associations between IE and BMI, weight and glycemic control, both during pregnancy and in the early postpartum period among women with GDM.

2. Methods

2.1 Participant consent and recruitment

Pregnant women diagnosed with GDM according to the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) and American Diabetes Association (ADA) guidelines (28,29) were invited to participate in the study at the diabetes in pregnancy clinic, where patients from both the University Hospital, Lausanne (CHUV) antenatal care clinic and obstetricians in private practice are referred. This study is part of an ongoing cohort of women with GDM at the Lausanne University Hospital. Women who agreed to participate in the study signed a consent form. The Human Research Ethics Committee of the Canton de Vaud approved the study protocol (326/15).

2.2 Inclusion criteria and exclusion criteria

Women ≥18 years, with GDM diagnosis and were followed in our clinic between 2015 and 2017, who understood French or English, consented to the cohort, and completed the French IE questionnaire at their first GDM visit, were included in this study.

Out of the cohort population of 1000 participants that were followed in our clinic, we excluded those who did not complete an IE questionnaire at the first GDM visit (N=533) and those who did not attend postpartum visit (N=32). Out of the eligible cohort population of 435 participants, we then excluded those who did not sign an informed consent (N= 145). Participants with known type 1 diabetes (N= 7), known type 2 diabetes (N= 9), GDM diagnosed at ≤13 weeks (N= 11), diabetes diagnosed during pregnancy at ≤20 weeks (N= 19), normal (i.e. negative) HGPO results (N= 7), with glucose intolerance but no GDM (N= 2), and those participating in a form of an active lifestyle randomized controlled trial (RCT) intervention (N= 21) were also excluded. Overall, 214 women were included in the final analysis.

2.3 Data collection

2.3.1 Assessment of Intuitive eating (IE)

We assessed IE with the French Intuitive Eating Scale-2 (IES-2); an 18-item validated self-report questionnaire that assesses individuals' tendency to follow their physiological, hunger and satiety cues in determining when, what and how much to eat.

The French IES-2 contains 3 subscales. These are (1) the Eating for physical rather than emotional reasons (EPR, 8 items) subscale; that assesses how much eating is affected by emotional responses, (2) the Reliance on hunger and satiety cues (RHSC, 6 items) subscale; that evaluates the extent to which individuals are aware and able to trust internal signals rather than relying on external rules/cues, and (3) the Unconditional permission to eat (UPE, 4 items) when hungry subscale that assesses whether an individual purposefully tries to ignore hunger and satiety signals (27). The English IES-2 (23-item questionnaire), however, consists of 4 subscales. These are (1) the Eating for physical rather than emotional reasons (EPR, 8 items) subscale; (2) the Reliance on hunger and satiety cues (RHSC, 6 items) subscale, (3) the Unconditional permission to eat (UPE, 4 items) when hungry subscale and 4) the Body-Food Choice Congruence (BFC-C, 5 items) subscale (13,15). The French IES-2, just like the English version, has demonstrated good psychometric properties in samples of pregnant women (27). In an earlier study, the IES-2 indicated a good internal reliability among the subscales. The Cronbach's alphas (α) for the two subscales were 0.92 and 0.87 for EPR and RHSC respectively (25). The IES-2 measures interoceptive abilities. These abilities determine when and how much to eat, and help to accurately perceive and respect one's hunger and satiety cues. Thus, higher IE scores are related to emotional, psychological, and physical well-being (30).

It is also important to note that the conceptualization of IE as interoceptive comprises of sensing the physiological condition of the body as well as the representation of the internal state (31). For the purpose of our study, we removed the UPE subscale (4 items) from the French IES-2. This is because women involved in this study had in general one pre-partum diet visit with a registered dietician during pregnancy and one post-partum visit after pregnancy. We believe that discussions during diet counselling could significantly influence participants' responses to the UPE subscale such as "I try to avoid certain foods high in fat, carbohydrates, or calories". "If I am craving for a certain food, I allow myself to have it".

“I have forbidden foods that I don’t allow myself to eat”. “I allow myself to eat what food I desire at any moment”. “I do NOT follow eating rules or dieting plans that dictate what, when, and/or how much to eat”. This is because during the one-hour dietary counseling, participants’ were advised on the carbohydrate content of their foods and to avoid or limit certain foods in order to improve their eating habits and glycemic profile.

In our hospital, 85% of women with gestational diabetes see a dietician. In the general clinic population, reasons for not being able to see a dietician included appointment-scheduling problems or participants’ visited the GDM clinic at an advanced stage of their pregnancy, leaving no time to schedule a dietary counseling session. Before the pre-partum and postpartum dietary counseling, glycemic control variables, weight, and BMI were measured.

We therefore gave the two subscales, i.e., the EPR and RHSC subscales of the French IES-2 and its English translated version produced by our team (with the same 14 items; EPR has 8 items and RHSC has 6 items); to participants who speak French and English respectively. Women completed the EPR and RHSC subscales of the IES-2 questionnaire during the first GDM visit by responding to a 5-point Likert scale response ranging from one (1) ‘strongly disagree’ to five (5) ‘strongly agree’ to each item in both subscales.

We then calculated the EPR and RHSC subscale scores as recommended; by dividing the total scores obtained from the sum of 1-5 from each item by the total number of items in each subscale (EPR by 8 and RHSC by 6), leading to a possible subscale score between one and five. Higher scores indicated greater levels of IE. Higher score of the EPR subscale reflects eating as an answer to hunger and lower score meant eating to cope with emotional distress whereas higher score of the RHSC subscale signifies trust in internal cues and lower score reflects less ability to regulate food intake.

2.3.2 Anthropometric measures

We measured height and weight of participants' during the first GDM visit. When available, weight before pregnancy was obtained from patients' medical charts and records. Otherwise this was self-reported. During the first GDM visit, body weight was measured to the nearest 0.1kg in women wearing light clothes and no shoes with an electronic scale (Seca®), height was measured to the nearest 0.1 cm with a Seca® height scale. The electronic scales were regularly calibrated. We also measured participants' weight at the end of pregnancy, and at the 6-8 weeks postpartum visit. We calculated gestational weight gain as the difference between weight at the end of pregnancy and weight before pregnancy. We also calculated the difference between weight at 6-8 weeks postpartum and weight at the first GDM visit. We expressed BMI as the ratio of weight in kilograms to the square of height in meters (kg/m2).

2.3.3 Assessment of glycemic control variables

Participants underwent a 75g oral glucose tolerance test (oGTT) during pregnancy at 24-32 weeks of gestation, unless an initial fasting glucose was ≥ 5.1 mmol/L. Women were diagnosed of GDM if one of the following criteria were met: fasting glucose ≥ 5.1 mmol/L, 1-hr glucose ≥ 10.0 mmol/L, or 2-hr glucose ≥ 8.5 mmol/L using the IAPDSG guidelines (28).

At the first GDM visit, HbA1c was measured using a chemical photometric method (conjugation with boronate; Afinion®). At 6-8 weeks postpartum, an oGTT was performed to measure fasting glucose, 2-hr glucose and HbA1c using a High Performance Liquid Chromatography method (HPLC). Both methods are traceable to the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Reference Method for Measurement of HbA1c (32).

2.3.4 Measurement of covariates and other variables

Potential covariates were age and gestational age at the first GDM visit (model 2) and weight when the outcome was fasting glucose or HbA1c (model 3).

For descriptive analyses, the following parameters that were recorded at the first GDM visit were used: Socio-demographic characteristics, including age, education level, nationality, employment status, family history of type-2 diabetes, history of GDM, gravida and parity, habits (smoking and alcohol status during pregnancy), and medical treatment during pregnancy (either metformin or insulin). Age was analyzed as a continuous variable. We grouped education level into four categories. These were compulsory school achieved; general and vocational training levels; high school; and university education. Nationality consisted of Switzerland; Europe and North America; Africa; Asia and Western pacific; and Latin America. Employment status was categorized as student; employed; housewife/at home; and unemployed. We categorized family history of type-2 diabetes, history of GDM, smoking and alcohol intake during pregnancy as either ‘yes’ or ‘no’.

2.4 Statistical analysis

All analyses were conducted using the SPSS software version 25 (32). All descriptive variables were presented as either means (±standard deviation) or in percentages (%) where appropriate. Both predictor (EPR and RHSC subscales of the IES-2 questionnaire) and outcome (BMI, weight and glycemic control including fasting glucose, 1hr glucose, 2hr glucose and HbA1c at the different time points) variables were normally distributed. The correlation between the two subscales of IES-2 questionnaire was low-to moderate ($r=0.35$, $P<0.01$). We conducted a linear regression analysis to determine the cross-sectional and longitudinal associations between the two subscales of IES-2 at the first GDM visit with BMI, weight, fasting glucose, 1hr glucose, 2hr glucose and HbA1c during pregnancy (cross-sectional analysis), at the end of pregnancy and at 6-8 weeks postpartum, respectively (longitudinal analysis). We made use of three models in the regression analyses. Model 1 consisted of unadjusted regression estimates. In model 2, we adjusted for socio-demographic characteristics that showed significance with at least one of metabolic health outcome variables (BMI, weight, fasting glucose, 1h or 2h glucose, HbA1c) at either the first GDM visit or at 6-8 weeks postpartum. Thus, this was tested for age, gestational age, education level, nationality, employment status, family history of type-2 diabetes, history of GDM, smoking and alcohol intake during pregnancy, gravida, parity, and medical treatment during pregnancy. Of these potential confounder variables, age, gestational age, smoking during pregnancy, parity, and medical treatment during pregnancy showed significance with one of the metabolic health outcome variables and were thus included in Model 2 as confounder variables. We did not adjust for medical treatment in our cross-sectional analysis. This is because women had not started medical treatment during the first GDM visit (Table 3), as this had no effect on the association between IE and metabolic health at the first GDM visit. However, we adjusted for this in our longitudinal analyses. When the outcome was glycemic control, we added a third model: model 3, where we adjusted for weight at the respective time points (at the first GDM visit and at 6-8 weeks postpartum). All analyses were conducted separately for both subscales of the IES-2 questionnaire. All statistical significances were two sided and accepted at $p < 0.05$.

3. Results

Table 1 shows the socio-demographic characteristics of the participants (N=214). The mean age of participants was 33.3 ± 5.2 years and the mean gestational age at first GDM visit was 27.4 ± 3.4 weeks. A third (32.2 %) of the participants was university graduates, and 41% were of Swiss nationality. Few women had a history of previous GDM (5.2%) and majority had a family history of type-2 diabetes (60.7%). 44% of the women had no medical treatment for GDM during pregnancy.

The mean weight before and during pregnancy, variables regarding glycemic control and the scores of the two subscales of the IES-2 at the first GDM visit is shown in Table 2. Mean weight and BMI before pregnancy were 68.2 ± 14.8kg and 25.3 ± 5.2kg/m2 respectively. Mean weight and HbA1c at first GDM visit were 79.2 ± 14.9kg and 5.4 ± 0.4% respectively. The mean score of the EPR subscale at first GDM visit was 3.8 ± 0.9, whereas the mean score of the RHSC subscale was 3.5 ± 0.9. Table 3 shows the cross-sectional associations between the two scales of IES-2 with BMI, weight and glycemic control at the first GDM visit. Cross-sectional analyses showed that both subscales of IES-2 at the first GDM visit were associated with lower weight and BMI before pregnancy, weight, fasting glucose and HbA1c at the first GDM visit (β= -0.171 to -0.222, all p≤ 0.01), however the RHSC subscale was not significantly associated with HbA1c at the first GDM visit. After adjusting for confounders including age, gestational age, smoking, and parity (model 2) the associations between the two subscales of IES-2 with weight and BMI before pregnancy and weight at first GDM visit remained unchanged. The association between the EPR subscale with fasting glucose and HbA1c also remained largely unchanged, except that the association between the RHSC subscale with fasting glucose was attenuated (p=0.095), albeit with a similar beta-coefficient. When fasting glucose or HbA1c was the outcome, we adjusted for weight at first GDM visit as a potential confounder (model 3).

The relationship between the EPR subscale with fasting glucose and HbA1c were attenuated (both p≤0.07), while the relationship between the RHSC subscale and fasting glucose remained insignificant (p=0.261). This shows that weight partly mediates the relationship between IE and fasting glucose in our sample. Table 4 shows the longitudinal associations between IES-2 at the first GDM visit with BMI, weight and glycemic control at the end of pregnancy and at 6-8 weeks postpartum visit. Both subscales of IES-2 at first GDM visit were associated with lower weight at the end of pregnancy, weight, BMI and fasting glucose at 6-8 weeks postpartum (β=-0.139 to -0.242, all P≤ 0.046) (model 1).

None of the IES-2 subscales was related to change in weight at the end of pregnancy and change in weight at 6-8 weeks postpartum and weight at first GDM visit. After adjusting for confounders including age, gestational age, smoking, parity, and medical treatment during pregnancy (model 2), the significant associations between the two subscales of IES-2 with weight at the end of pregnancy, weight, BMI and fasting glucose at 6-8 weeks postpartum remained unchanged (all $p \leq 0.004$). However, there was an attenuation of the association between RHSC subscale and weight at 6-8 weeks postpartum ($p=0.057$), albeit with a similar beta-coefficient. When fasting glucose and HbA1c were the outcome variables, we adjusted for weight at 6-8 weeks postpartum visit (model 3) as a potential confounder. Thus, the inverse association between the EPR subscale and fasting glucose at 6-8 weeks postpartum remained unchanged ($p= 0.038$), whereas the association between the RHSC subscale and fasting glucose at 6-8 weeks postpartum was attenuated ($p \leq 0.059$).

4. Discussion

We investigated the relationship between the two subscales of IES-2 with weight and glucose control during pregnancy and in the early postpartum period in women diagnosed with GDM.

To the best of our knowledge, this has not been previously studied in a general pregnant population or in women with GDM. In this prospective cohort of women followed in a clinical setting, we found that, the two subscales of IES-2 ("Eating for physical rather than emotional reasons" and "Reliance on hunger and satiety cues" subscales) during pregnancy were associated with lower BMI and weight before pregnancy, weight, fasting glucose and/or HbA1c during pregnancy and in the early postpartum period. The relationship between intuitive eating and fasting glucose was partly mediated by weight.

Although certain lifestyle interventions such as low GI diets can lead to a decrease in weight gain and postprandial glucose among women with GDM (9,33), the effect size of their impact on weight and their influence on fasting glucose and HbA1c remains controversial (9,33,34). As opposed to those previous studies that focused on macronutrient contents of foods, type of carbohydrates, portion sizes and eating frequency, IE represents an interesting and different approach that has never been studied in pregnancy in general and in women with GDM in particular (33,34). To fill this gap during pregnancy, where feelings and cues of hunger and satiety are distinct from out of pregnancy-states, and in women with GDM where increased weight gain during pregnancy and weight retention in the postpartum period can lead to recurrent GDM, obesity and future development of diabetes, this study evaluated the associations between IE with weight and glucose control during and after pregnancy in an observational design.

Results of our cross-sectional analyses showed that the two subscales of IES-2 at the first GDM visit were associated with lower weight and BMI before pregnancy and weight at the first GDM visit. These associations may exist due to the following reasons. First, the EPR subscale of the IES-2 measures the extent to which individuals use food to satisfy hunger rather than to cope with negative emotional states, such as anxiety, depression, boredom, or loneliness, that can lead to overeating, weight gain, and an eventual increase in BMI (35).

The RHSC subscale, on the other hand, uses one's innate ability to respond to satiety cues by determining when, what, and how much to eat. Eating intuitively therefore may lead to improved hunger and satiety cues, more cognitive control, and increased response to physiological signals. Improvement in cognitive control and response to physiological cues may in turn lead to lower weight and BMI (36).

The association between the EPR subscale with fasting glucose and HbA1c independent of adjustment for confounders in our cross-sectional analyses indicates that eating habits driven by emotions and cravings during pregnancy may lead to higher glycemic values (10). This may be explained by the following mechanisms: frequent snacking and reduced time without food intake might impact on increased hepatic insulin resistance and subsequent increased overnight glucose production, which may lead to increased fasting glucose levels (37). On the other hand, higher adherence to the EPR subscale prevents disordered eating behaviors and thus may lead to lower fasting glucose and HbA1c levels (38). In contrast, the lack of association between the RHSC subscale with HbA1c and with fasting glucose after adjustments indicates that when it comes to pregnancy, elements of RHSC that assesses the degree of awareness of internal hunger and satiety signals may be overshadowed by the potential importance of eating for physical rather than emotional reasons. This could be the reason why the adherence to the RHSC subscale was comparatively lower than the EPR subscale in our sample. One of the possible reasons why IE was not related to the one and two-hour glucose levels was that during the oGTT, a fixed amount of 75 g of glucose was given regardless of any signs of IE. In addition, the oGTT test overrides all internal stimuli. As explained above, the associations between the two subscales of IES-2 with lower weight at the end of pregnancy and lower weight and BMI at 6-8 weeks postpartum in the longitudinal analyses could indicate that the sustained adherence to IE over a period of time may improve emotional states and disordered eating behaviors, as well as help to increase one's ability to innately recognize hunger and satiety cues. This could be beneficial in lowering cognitive restraint that usually lead to weight gain and higher BMI. In this context of a clinical setting, women with GDM were followed by either a nurse or a physician and likely had a pre-partum and postpartum dietary counseling sessions with a dietician.

During the postpartum dietary counselling, the general goal was for women to return to their weight before pregnancy within one year after delivery. This is because gestational weight retention is a known risk factor for recurrent GDM and type-2 diabetes. Therefore, the sustained practice of IE and the desire to lose postpartum weight itself may account for the observed association regarding weight and BMI outcomes in our longitudinal analyses. The lack of associations between IE with weight gain (at the end of pregnancy) and weight retention at 6-8 weeks postpartum visit remains unclear, however, factors such as little variation and short time periods between these time points may be reasons for the lack of association.

The lack of associations between the two subscales of IES-2 with HbA1c in our longitudinal analyses can be explained by the following reasons: in the postpartum period, eating habits, such as frequent overeating (especially excess animal fat intake), may influence glucose level and can impact on HbA1c (39). Similarly, medical treatment may also have an impact in the longitudinal analyses, as it lower fasting and postprandial glucose levels and may confound our findings. We therefore adjusted for medical treatment in our longitudinal analysis. In our study, the majority (52.5%) of our participants' received medical treatment during pregnancy either in the form insulin or insulin and metformin. The possible impact of iron deficiency anemia (40) and the changes in insulin sensitivity in the early weeks after delivery may be implicated in the lack of longitudinal associations between the two subscales of IES-2 and HbA1c. Other factors, such as breastfeeding in the postpartum period also act to reduce glucose levels and may affect HbA1c levels (41).

Our results corroborate the findings of a cross-sectional review outside of pregnancy which indicated that IE was positively related with improved dietary intake and/or healthy eating behaviors that are drivers for weight loss and maintenance (24). The results of our study are also consistent with a study among postpartum women where the higher practice or adherence to IE was associated with accelerated rates of postpartum weight loss (25).

Several attempts by weight loss programs that mainly consists of lifestyle intervention to address postpartum weight retention have been inconsistent (42). Difficulties in adhering to specific structured diet and physical activity recommendations have been named as the possible reason. Following a more IE approach to food consumption may encourage postpartum weight loss without the required diet restrictions, calorie counting and exercise regimes, all of which are features of traditional weight loss programs. IE could offer an alternative approach that may be rewarding and less exhausting for new mothers who have busy lives, limited available time and new to parenting (25). Regarding glycemic control, the findings of this study are in line with those of Wheeler and colleagues who showed that, higher adherence to the EPR subscale was associated with lower HbA1c in a cross-sectional study (43) and with a review in which IE led to improvements in metabolic health indicators, including fasting glucose (24).

Our results have important clinical implications and suggests that IE could represent a novel approach for weight and glycemic control in women diagnosed with GDM. Future epidemiologic/intervention studies should investigate the long-term and sustained effect of IE during pregnancy and in the postpartum period among women with GDM.

This study has several strengths. It is the first to investigate the relationship between IE with BMI, weight and glycemic control in women with GDM in a real-life clinical setting. We used a well-developed and validated tool to measure IE during pregnancy. However, the results of this study must be interpreted with the following limitations. Factors such as dietary counseling and use of medication during pregnancy can influence both weight and glycemic control may account for the observed relationships in our longitudinal analysis even though we adjusted for medication use during pregnancy in our analyses. We believe that visiting a dietician did not impact on our cross-sectional results because we measured weight, BMI and glucose control variables at the first GDM visit before the appointment with a dietician was scheduled.

Even for the longitudinal results, the impact was probably not major, as we measured the outcome variables only at 6-8 weeks postpartum. In this context, we do not believe that one hour of consultation with the dietician during pregnancy that focused on the carbohydrate content of foods would influence our outcomes in a major way, considering that, many habits changes in the postpartum period. Missing data of some socio-demographic characteristics is a possible limitation because these variables were potential confounders in our analyses. The lack of a total IES-2 score in our analyses may be a source of limitation as it would have been interesting to see the overall effect of IES-2 on our outcomes would have been interesting. Other limitations such as a relatively small sample size limit our ability to generalize our findings. We obtained weight before pregnancy from patients' medical chart when available, otherwise we relied on self-reported pre-pregnancy weight which may be a limitation. In addition, several psychosocial and behavioral factors including family support, willingness and change in attitudes following GDM diagnosis were not investigated could influence weight changes especially in the postpartum period. Further research that utilizes IE as an intervention for weight retention and glucose control in a larger population during pregnancy and in the postpartum period is needed to determine the causality of these associations found in women with GDM.

5. Conclusions

In this prospective cohort of women with GDM, cross-sectional analyses showed that the two subscales of IES-2 at the first GDM visit were associated with lower weight and BMI before pregnancy and weight at first GDM visit after adjusting for confounders. The EPR subscale was also associated with lower HbA1c and fasting glucose at the first GDM visit. In the longitudinal analyses, both subscales of IES-2 at first GDM visit were associated with lower weight at the end of pregnancy, BMI and fasting plasma glucose at 6-8 weeks postpartum after adjusting for confounders. The EPR subscale was also associated with weight at 6-8 weeks postpartum.

None of the IES-2 subscales was associated with weight changes at the end of pregnancy and at 6-8 weeks postpartum. These results suggest that practicing IE may be beneficial and could represent an interesting approach to weight and glucose management during and after pregnancy in women with GDM. In addition, higher adherence to IE may reduce the risk of developing diabetes in the postpartum period in women with GDM.

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Author contribution

DYQ, JG, LG, AH and JP designed the study. DYQ, JG, CH, LG were involved in data collection. DYQ extracted the data, performed all the analyses and wrote the draft manuscript. DYQ, JG and JP interpreted the data. JG, LG, AH and JP reviewed the manuscript.

All authors revised and accepted the manuscript for submission. JP had the idea of the cohort and co-supervised all the work with AH.

Conflict of interest

None

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STUDY 1 Tables and captions

[Table 1] Socio-demographic characteristics of study participants

Variable	Mean	SD	Frequency	Percent (%)
Age (year) N= 214)	33.32	5.20		
Gestational age at the first GDM visit (weeks) (N= 214)	27.43	3.36		
Educational level (N=164)				
Compulsory school achieved[1]			28	13.1
CFC[2]			40	18.7
High school			27	12.6
University			69	32.2
Ethnic origin (N=212)				
Switzerland			88	41.1
Europe + North America			80	37.4
Africa			25	11.7
Asia + western pacific			15	7.0
Latin America			4	1.9
Employment status (N=186)				
Student			5	2.3
Employed			137	64.0
Unemployed			22	10.3
At home/housewife			22	10.3
Family history of Type-2 Diabetes (N= 214)				
1st degree[3]			71	33.2
2nd degree[4]			59	27.5
No			84	39.2
History of GDM (N= 214)				
Yes			11	5.2
No			203	94.8
Smoking status during pregnancy (N= 214)				
Yes			45	21.0
No			169	79.0
Alcohol intake during pregnancy (N= 214)				
Yes			14	6.5
No			200	93.5
Gravida (N= 214)				
1			89	41.6
2			68	31.8
≥3			57	26.6
Parity (N= 214)				
0			116	54.2
1			70	32.7
2			22	10.3
≥3			6	2.8
Medical treatment during pregnancy (N=207)				
None			95	44.4
Metformin			7	3.4
Insulin and Metformin			105	49.1

[1]Includes 1 patient who did not complete compulsory school

[2]CFC means general and vocational education

[3]1st degree means 1 degree of relationship of the participant (at least 50% of genetic link, which included mother, father, brother, sister, daughter, son)

[4]Second degree means 2nd degree of kinship of the participant (at least 25% of genetic link that included grandparents, grandchildren, nephews, niece, half-brother, half-sister)

All results are frequency and percentage unless otherwise stated

[Table 2] Mean distribution of study variables at first GDM visit or before pregnancy

Variable	N	Mean	SD
Weight before pregnancy (kg) (self-reported)	213	68.18	14.83
BMI before pregnancy (kg/m^2)	213	25.30	5.19
Weight at first GDM visit (kg) (measured)	211	79.16	14.87
∆Weight before pregnancy and at First GDM visit (kg)	210	10.92	4.58
HbA1c at First GDM visit (%)	211	5.36	0.39
Fasting glucose at first GDM visit (mmol/l)	206	5.08	0.79
1hr glucose at first GDM visit (mmol/l)	163	9.73	1.70
2hr glucose at first GDM visit (mmol/l)	164	7.87	1.74
EPR at first GDM visit	214	3.88	0.93
RHSC at first GDM visit	214	3.54	0.90

GDM means gestational diabetes mellitus
HbA1c means glycated hemoglobin
BMI means body mass index
EPR means Eating for Physical Rather than Emotional Reasons subscale of the Intuitive Eating scale2 (IES-2). Higher scores means higher adherence to the EPR subscale
RHSC means Reliance on Hunger and Satiety Cues subscale of the Intuitive Eating scale2 (IES-2). Higher scores means higher adherence to the RHSC subscale
The differences in Frequency of Fasting glucose, 1hr and 2hr glucose is because GDM was diagnosed with a 75-G oral glucose-tolerance test unless an initial fasting glucose was ≥5.1 mmol/L.

[Table 3] Cross-sectional associations between the two subscales of intuitive eating scale-2 and weight, BMI and glycemic control at first GDM visit

	Model 1				Model 2				Model 3			
Variable	**regression coefficient**	**95% CI**		**P-value**	**regression coefficient**	**95% CI**		**P-value**	**regression coefficient**	**95% CI**		**P-value**
EPR												
Weight before pregnancy *(n=213)*	-0.203	-5.329	-1.107	**0.003**	-0.181	-5.002	-0.745	**0.008**	NA			
BMI before pregnancy (*n=213)*	-0.216	-1.936	-0.463	**0.002**	-0.194	-1.824	-0.332	**0.005**	NA			
Weight at first GDM visit (*n=211)*	-0.205	-5.355	-1.126	**0.003**	-0.191	-5.168	-0.871	**0.006**	NA			
HbA1c at first GDM visit *(n=211)*	-0.171	-0.126	-0.015	**0.013**	-0.170	-0.127	-0.013	**0.016**	-0.123	-0.106	0.004	0.070
Fasting glucose at first GDM visit *(n=206)*	-0.195	-0.278	-0.050	**0.005**	-0.196	-0.280	-0.049	**0.005**	-0.124	-0.213	0.007	0.066
1-hr glucose at first GDM visit *(n=163)*	0.122	-0.058	0.490	0.122	0.154	-0.009	0.556	0.058	0.112	-0.081	0.465	0.166
2-hr glucose at first GDM visit *(n=164)*	-0.030	-0.336	0.226	0.698	-0.033	-0.351	0.232	0.689	-0.065	-0.404	0.169	0.420
RHSC												
Weight before pregnancy *(n=213)*	-0.194	-5.394	-0.999	**0.005**	-0.181	-5.171	-0.800	**0.008**	NA			
BMI before pregnancy (*n=213)*	-0.222	-2.046	-0.518	**0.001**	-0.215	-2.007	-0.482	**0.002**	NA			
Weight at first GDM visit (*n=211)*	-0.190	-5.365	-0.934	**0.006**	-0.188	-5.331	-0.886	**0.006**	NA			
HbA1c at first GDM visit *(n=211)*	-0.061	-0.085	0.032	0.376	-0.061	-0.085	0.033	0.389	-0.004	-0.060	0.056	0.954
Fasting glucose at first GDM visit *(n=206)*	-0.148	-0.248	-0.010	**0.033**	-0.117	-0.222	0.018	0.095	-0.076	-0.182	0.050	0.261
1-hr glucose at first GDM visit *(n=163)*	0.072	-0.149	0.409	0.359	0.097	-0.108	0.459	0.224	0.043	-0.209	0.359	0.605
2-hr glucose at first GDM visit *(n=164)*	-0.072	-0.417	0.153	0.361	-0.068	-0.416	0.165	0.394	-0.124	-0.526	0.070	0.132

Gestational age at first GDM visit is 24-32 weeks
EPR means Eating for Physical Rather than Emotional Reasons subscale of the Intuitive Eating scale2 (IES-2). Higher scores means higher adherence to the EPR subscale
RHSC means Reliance on Hunger and Satiety Cues subscale of the Intuitive Eating scale2 (IES-2). Higher scores means higher adherence to the RHSC subscale
Model 1: Unadjusted regression estimates
Model 2: Adjusted for age, gestational age, smoking, and parity
Model 3: Adjusted for weight at first GDM visit

[Table 4] Longitudinal associations between two subscales of intuitive eating scale-2 and weight, BMI and glycemic control at the end of pregnancy and in early postpartum (6-8 weeks)

	Model 1				**Model 2**				**Model 3**			
Variable	**regression coefficient**	**95% CI**		**P-value**	**regression coefficient**	**95% CI**		**P-value**	**regression coefficient**	**95% CI**		**P-value**
EPR												
Weight at end of pregnancy (*n=198)*	-0.223	-5.450	-1.297	**0.002**	-0.212	-5.373	-1.063	**0.004**	NA			
Weight at 6-8 weeks postpartum (*n=207)*	-0.237	-5.700	-1.592	**0.001**	-0.219	-5.536	-1.267	**0.002**	NA			
BMI at 6-8 weeks postpartum *(n=205)*	-0.242	-2.003	-0.574	**0.000**	-0.226	-1.956	-0.474	**0.001**	NA			
Δweight first GDM visit and end of pregnancy (*n=192)*[1]	-0.007	-0.562	0.509	0.922	0.025	-0.452	0.642	0.732	NA			
Δweight first GDM visit and 6-8 weeks PP (*n=205)*[2]	-0.061	-1.137	0.438	0.382	-0.062	-1.154	0.448	0.386	NA			
HbA1c at 6-8 weeks postpartum(n=206)	-0.002	-0.053	0.051	0.978	-0.003	-0.056	0.054	0.968	0.017	-0.047	0.060	0.815
Fasting glucose 6-8 weeks postpartum (n=207)	-0.200	-0.159	-0.031	**0.004**	-0.191	-0.158	-0.026	**0.007**	-0.144	-0.132	-0.004	**0.038**
2-hr glucose 6-8 weeks postpartum (n=206)	-0.020	-0.261	0.194	0.775	-0.005	-0.253	0.235	0.943	-0.018	-0.264	0.205	0.806
RHSC												
Weight at end of pregnancy (*n=198)*	-0.193	-5.276	-0.868	**0.007**	-0.175	-5.059	-0.545	**0.015**	NA			
Weight at 6-8 weeks postpartum (*n=207)*	-0.139	-4.486	-0.040	**0.046**	-0.134	-4.435	0.065	0.057	NA			
BMI at 6-8 weeks postpartum *(n=205)*	-0.164	-1.691	-0.155	**0.019**	-0.165	-1.708	-0.156	**0.019**	NA			
Δ weight first GDM visit and end of pregnancy (*n=192)*	0.092	-0.200	0.926	0.205	0.102	-0.159	0.974	0.157	NA			
Δ weight first GDM visit and 6-8 weeks PP(*n=205)*	0.105	-0.198	1.467	0.135	0.064	-0.444	1.216	0.360	NA			
HbA1c at 6-8 weeks postpartum(n=206)	-0.074	-0.084	0.025	0.291	-0.072	-0.085	0.028	0.315	-0.065	-0.081	0.030	0.358
Fasting glucose 6-8 weeks postpartum (n=207)	-0.163	-0.151	-0.014	**0.019**	-0.140	-0.140	-0.002	**0.045**	-0.128	-0.131	0.003	0.059
2-hr glucose 6-8 weeks postpartum (n=206)	-0.025	-0.284	0.196	0.717	-0.006	-0.262	0.239	0.930	-0.024	-0.284	0.201	0.736

[1]Means the difference in weight at the end of pregnancy and at first GDM visit

[2]Means the difference between weight at the 6-8 weeks postpartum visit and first GDM visit

EPR means Eating for Physical Rather than Emotional Reasons subscale of the Intuitive Eating scale 2 (IES-2). Higher scores means higher adherence to the EPR subscale

RHSC means Reliance on Hunger and Satiety Cues subscale of the Intuitive Eating scale 2 (IES-2). Higher scores means higher adherence to the RHSC subscale

Model 1: Unadjusted regression estimates

Model 2: Adjusted for age, gestational age smoking, parity and medical treatment during pregnancy

Model 3: Adjusted for weight 6-8 weeks post-partum

PP means postpartum

APPENDIX 2

STUDY 2: Intuitive eating is associated with improved health indicators at 1-year postpartum in women with Gestational Diabetes Mellitus

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Abstract

We evaluated the associations between intuitive eating during and after pregnancy with metabolic health at 1-year postpartum in women with gestational diabetes mellitus (GDM) and in high-risk GDM subgroups. One-hundred-and-seventeen women who consented and completed the French intuitive eating questionnaire during and after pregnancy were included. We found an association between intuitive eating during and after pregnancy with lower BMI, weight retention, fasting glucose and HbA1c at 1-year postpartum in women with GDM and in high-risk GDM subgroups with overweight/obese or with prediabetes in the postpartum period. Our results suggest that, intuitive eating could be an effective intervention for weight and glucose control in women with GDM.

Keywords: Intuitive eating; Gestational diabetes mellitus; Body mass index; Glycemic control; Weight retention

Introduction

Gestational diabetes mellitus (GDM) refers to any degree of glucose intolerance that is diagnosed in the second or third trimester of pregnancy but does not fulfil the criteria of overt diabetes (American Diabetes Association (ADA), 2019). Between 3-20% of pregnant women develop GDM globally (Feig et al., 2018) and 10.9% of all pregnancies in Switzerland are complicated with GDM (Rüetschi et al., 2016). The adverse maternal and fetal outcomes of GDM are well known (Damm et al., 2016; Nehring et al., 2011). Indeed, about 48% of women with GDM are at risk of prediabetes (Huopio et al., 2014) and between 20%–60% of women with GDM develop diabetes 5 to 10 years after delivery (Buchanan et al., 2012). Overall, the conversion of GDM to prediabetes and subsequent development of diabetes is well known and continues to be on the rise, making GDM a significant risk factor of type 2 diabetes (Feig, 2018).

Pre-pregnancy body mass index (BMI), excess weight gain during pregnancy and postpartum (PP) weight retention contribute to the risk of prediabetes and diabetes among women with GDM (Kim, 2015; Miao et al., 2017). Weight retention is indeed a prevalent problem: Studies show that, at the early postpartum period, women retain an average of 2–7kg of weight gained during pregnancy, and at least two-thirds of women will still be above their pre-pregnancy weight (Fadzil et al., 2018; Ha et al., 2019; Walker et al., 2005). Given that postpartum weight retention is predictive for GDM recurrence (Ehrlich et al., 2011), prediabetes and future diabetes (Bao et al., 2015; Liu et al., 2014), weight loss in the postpartum period is critical for women with previous GDM. In the Diabetes Prevention Program (DPP) for example, weight loss reduced the risk of future diabetes by 16% for every kilogram of weight lost (Hamman et al., 2006) and an intensive lifestyle intervention also led to 50% reduction in the risk of diabetes (Ratner et al., 2008).

Apart from overweight/obesity, prediabetes in the postpartum period has also been shown to augment the risk of diabetes in women with GDM (Bao et al., 2015; Meron and Grajower, 2017). Focusing on these two high-risk groups (i.e., overweight/obese women and women with prediabetes) is therefore crucial.

Lifestyle interventions are usually recommended as the primary therapeutic strategy in the postpartum period for women with previous GDM to reduce diabetes risk factors (Gilbert et al., 2019). These interventions consist of nutrition and physical activity advice for weight and glucose control to reduce and or prevent the risk of diabetes in these women. Even though lifestyle interventions have achieved some results in women with GDM, recent systematic and meta-analyses have shown that results from lifestyle intervention studies have been unsatisfactory and inconsistent. In a recent Cochrane review of lifestyle intervention trials among women with GDM, three trials included the incidence of type-2 diabetes and prediabetes in the postpartum period, but only one found a difference between the intervention and the control group (Brown et al., 2017). In another recent systematic review and meta-analysis of 15 trials in women with previous GDM, half of the lifestyle interventions led to a reduction of weight and the incidence of diabetes, but effect sizes were small and their sustained effects were inconsistent (Goveia et al., 2018).

There is therefore a need to identify other novel approaches that can help reduce weight gain during pregnancy and weight retention in order to lower the risk of prediabetes and future diabetes in women previously diagnosed with GDM. Compared to studies (Moses et al., 2009; Xu and Ye, 2018) that focused on lifestyle interventions and nutritional advice, such as total energy intake, macronutrient contents of foods, type of carbohydrates, portion sizes and eating frequency, intuitive eating (IE) represents an interesting and different approach to weight loss and glycemic control.

IE is an adaptive eating behavior that deals with the ability to accurately interpret and adhere to instinctive feedback regarding the required amount of food and when to eat (Tylka, 2006). IE correlates with lower weight, BMI and improved glycemic control in the general population (Van Dyke and Drinkwater, 2014; Wheeler et al., 2016). A study that evaluated the relationship between IE and weight in women in the late postpartum period found that IE was associated with weight loss and lower BMI (Leahy et al., 2017). Even though we have earlier demonstrated that, IE is associated with weight and glucose control during pregnancy and in the early postpartum period in women with GDM (Quansah et al., 2019), no study has investigated the potential long-term association between IE during and after pregnancy with weight, weight retention and glycemic control in the general perinatal population nor in women with GDM and their metabolically high-risk subgroups with high BMI or prediabetes. In these high-risk subgroups, the risk of diabetes is higher. To fill this gap, we evaluated the associations between IE during and after pregnancy with BMI, weight retention and glycemic control at 1-year postpartum in all women with GDM and in high-risk GDM subgroups with pre-pregnancy overweight/obesity or with prediabetes in the postpartum period.

Methods

Participant consent and recruitment

This study is part of an ongoing cohort of women with GDM. We invited pregnant women diagnosed with GDM according to the American Diabetes Association (ADA) and the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) guidelines (Dorsey et al., 2018; Metzger, 2010) to participate in the GDM cohort at the gestational diabetes clinic at a Swiss University Hospital. We sought for written informed consent before participation in the cohort. The Human Research Ethics Committee of the Canton de Vaud approved the study protocol (326/15).

Inclusion and exclusion criteria

Women who were ≥18 years, with GDM diagnosis in the second trimester (Metzger et al., 2010) that were followed in our clinic between 2015 and 2018, who understood French or English, consented to participate, and completed the French Intuitive Eating Scale-2 (IES-2) questionnaire at their first visit and at the 1-year visit were included in this study.

Out of a cohort population of 333 participants that consented, we removed participants who did not come for 1-year postpartum appointment visit (N=144) as they did not have valid data for our main questions and hypothesis. Participants with known type 1 diabetes (N= 2), known type 2 diabetes (N= 6), had GDM at ≤13 weeks (N= 10), had diabetes diagnosed during pregnancy at ≤20 weeks (N= 8), with HGPO results that were normal (N= 3), with glucose intolerance but no GDM (N= 1) and were participating in a lifestyle intervention study (N=42) who are part of our cohort database were also excluded as they did not meet the inclusion criteria. Overall, 117 women were eligible and thus included in the final analysis. Figure 1 shows the details of how participants in this study were selected.

Assessment of Intuitive eating (IE)

We assessed IE with the French Intuitive Eating Scale-2 (IES-2) due to the language capacities of our population (Camilleri et al., 2015). The French IES-2 is an18-item validated self-report questionnaire that assesses individuals' tendency to follow their physiological, hunger and satiety in relation to eating. The French IES-2 contains three (3) subscales. These are (1) the Eating for physical rather than emotional reasons (EPR, 8 items) subscale; that assesses how much eating is affected by emotional responses, (2) the Reliance on hunger and satiety cues (RHSC, 6 items) subscale; that evaluates the extent to which individuals are aware and able to trust internal signals rather than relying on external rules/cues, and (3) the Unconditional permission to eat (UPE, 4 items) when hungry subscale that assesses whether an individual purposefully tries to ignore hunger and satiety signals (Camilleri et al., 2015; Daundasekara et al., 2017). The English IES-2 (23-item questionnaire), however, consists of four subscales. These are the EPR (8 items) subscale, the RHSC (6 items) subscale, the UPE (4 items) and the Body-Food Choice Congruence (BFC-C, 5 items) subscale (Tylka, 2006; Tylka and Van Diest, 2013). Both the French and English IES-2 questionnaires have demonstrated good psychometric properties in pregnant women (Daundasekara et al., 2017). In an earlier study, the Cronbach's alphas (α) for the two subscales were 0.92 and 0.87 for EPR and RHSC respectively, which suggests a good internal reliability among the subscales (Daundasekara et al., 2017). IE has interoceptive abilities that are suggested to determine when and how much to eat, and to accurately perceive and respect one's hunger and satiety cues. Thus, IE tendencies are related to emotional, psychological, and physical well-being (Saunders and Nichols-Lopez, 2018). Details of the IES-2 questionnaire have been previously described (Tylka and Van Diest, 2013).

For the purpose of our study, we removed the UPE subscale (4 items) from the French IES-2. This is because women involved in this study had in general one pre-partum visit with a registered dietician during pregnancy and another one in the early post-partum period (6-8 weeks postpartum). The latter was of short duration and done together with the diabetologist or diabetes educator and focused predominantly on reporting the results of the postpartum oral glucose tolerance testing (oGTT). Women had no further dietician appointment after this visit. Allover, in the general population of our women with gestational diabetes, about 85% see a dietician, but we do not have the exact numbers for the study population. In the general clinic population, reasons for not being able to see a dietician included appointment-scheduling problems or participants visited the GDM clinic at an advanced stage of their pregnancy.

We believe that, discussions during diet counselling could significantly influence participant responses to the UPE subscale questions such as “I try to avoid certain foods high in fat, carbohydrates, or calories”. This is because during the one-hour diet counselling during the pregnancy, participants were advised on carbohydrate content of their foods and to avoid or limit certain food like soft drinks, sweet products, added sugar and fruits juice in order to improve their eating habits and glycemic profile. We measured weight, BMI and glycemic control variables before the pre-partum counseling with the dietician. This was to ensure that, diet counselling with a dietician does not influence study outcomes. We then measured the metabolic health outcomes again at 1 year postpartum.

We therefore used the EPR and RHSC subscales of the French IES-2 and, an English translation using the forward-backward translation and cultural adaption method (Wild et al., 2005) made by our research team (with the same 14 items; EPR has 8 items and RHSC has 6 items); they were given to participants who speak French and English, respectively. Women completed the EPR and RHSC subscales of the IES-2 questionnaire during the first GDM visit and at the one-year postpartum visit by responding to a 5-point Likert scale ranging from one ‘strongly disagree’ to five ‘strongly agree’ to each item in both subscales. We then calculated the EPR and RHSC subscale scores as recommended, by dividing the total scores obtained from the sum of 1-5 from each item by the total number of items in each subscale (EPR by 8 and RHSC by 6), leading to a possible subscale score between one and five. Higher scores indicated greater levels of IE. A higher score of the EPR subscale reflects eating as an answer to hunger and a lower score meant eating to cope with emotional distress, whereas a higher score of the RHSC subscale signifies trust in internal cues, and a lower score reflects less ability to regulate food intake.

Assessment of glycemic control variables

All women involved in this study were diagnosed with GDM during pregnancy (at 24-32 weeks) if one of the following criteria were met during a 75g oGTT: fasting venous glucose ≥ 5.1 mmol/L, 1-hr glucose ≥ 10.0 mmol/L, or 2-hr glucose ≥ 8.5 mmol/L, using the IAPDSG guidelines (Metzger, 2010). For the purpose of this analysis, we used the fasting glucose at GDM diagnosis, as women with fasting glucose of ≥ 5.1 mmol/L did not have an oGTT. During the first GDM visit after diagnosis, we measured HbA1c using a chemical photometric method (conjugation with boronate; Afinion®). At 1-year PP, patients had a fasting venous glucose and HbA1c measured. The HbA1c was measured using a High Performance Liquid Chromatography method (HPLC) (Jeppsson et al., 2002). Both methods are traceable to the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Reference Method for Measurement of HbA1c (Jeppsson et al., 2002). Prediabetes was diagnosed when a participant's fasting glucose at 1-year postpartum was between 5.6-6.9 mmol/l, or HbA1c at 1-year postpartum was between 5.7- 6.4%.

Anthropometric measures

We measured the height and weight of participants during the first GDM visit. Weight and BMI before pregnancy were taken from participants' medical charts or, if missing, was self-reported; we asked for the weight in the 1-2 months before pregnancy if this information is not available in the participants' medical chat. We measured weight at 1-year postpartum to the nearest 0.1 kg in women wearing light clothes and no shoes with an electronic scale (Seca®) and height at the first GDM visit to the nearest 0.1 cm with a regularly calibrated Seca® height scale. We calculated weight retention as the difference between weight at 1-year postpartum and weight before pregnancy.

We calculated BMI as the ratio of weight in kilograms to the square of height in meters (kg/m2). We defined overweight and obesity as BMI between 25.0-29.9 Kg/m^2 and ≥30 kg/m^2 respectively.

Measurement of other variables

Sociodemographic characteristics of our participants included age, educational level, nationality, employment status, family history of type-2 diabetes, history of GDM, parity, and smoking and alcohol status during pregnancy. These were obtained from the patients' medical charts, which were completed during the first face-to-face visit. We grouped educational level into four categories. These were compulsory school achieved; general and vocational training levels; high school and university education. Nationality consisted of the following five regions: Switzerland; Europe and North America; Africa; Asia and Western pacific; and Latin America. Employment status was categorized as student; employed; housewife/at home; and unemployed. We categorized family history of type-2 diabetes, history of GDM, smoking, and alcohol intake during pregnancy as either 'yes' or 'no'.

Statistical analyses

We performed all analyses with the SPSS software version 25 (IBM Corp., 2017). All descriptive variables were presented as either means (±standard deviation) or in percentages (%), where appropriate (Table 1 & 2). Both predictor (EPR and RHSC subscales of the IES-2 questionnaire at first GDM visit and at 1-year postpartum visit) and outcome (BMI, weight retention, HbA1c and fasting glucose at the different time points) variables were normally distributed. The EPR and RHSC subscales showed a moderate correlation of 0.42 ($p<0.001$) at the first GDM visit and 0.51 ($p<0.001$) at 1-year postpartum.

We conducted a linear regression analysis to determine the associations between IE at the first GDM visit (longitudinal) and at the 1-year postpartum visit (cross-sectional) with BMI, weight retention, fasting glucose, and HbA1c at 1-year postpartum (Table 3). We adjusted for socio-demographic characteristics that showed statistical significance with at least one of the metabolic health outcome variables (BMI, weight, weight retention, fasting glucose and HbA1c) at 1-year postpartum. Thus, we tested for age, gestational age at the first GDM visit, education level, nationality, employment status, family history of type-2 diabetes, history of GDM, smoking and alcohol intake during pregnancy, parity, and breastfeeding in the early postpartum period (at 6-8 weeks postpartum,). Of these potential confounder variables, age and gestational age showed significance with at least one of the metabolic health outcomes. We therefore adjusted for age and gestational age at the first GDM visit as confounders for all analyses. When the outcome was HbA1c or fasting glucose, we further adjusted for BMI at first GDM visit (Table 3). We did this to see if the relationship was mediated by BMI. We conducted all analyses separately for EPR and RHSC subscales at the first GDM visit and at 1-year postpartum. We also evaluated the associations between the two subscales of IES-2 at the first GDM visit and at 1-year postpartum with metabolic health outcomes in the high-risk GDM subgroups with prediabetes or overweight/obesity and in the respective low-risk subgroups (Tables 4 & 5). In the Supplementary Analyses, we also compared the metabolic health outcomes with the IE scores between the high-risk and low-risk subgroups by performing an ANOVA test (Supplementary Table 1 & 2). Both IE scores at both time points were analyzed using correlation analyses and paired t-tests (between first visit and 1-year postpartum, Supplementary Table 3). All statistical significances were two sided and accepted at $p < 0.05$.

Results

Table 1 shows the summary of the general characteristics of our study participants (N=117). The mean age, gestational age at the first GDM visit, and gestational age at delivery were 33.21±5.4 years, 28.83±2.87 weeks and 38.8±1.6 weeks, respectively. More than one-third of the study participants were university graduates (38.2%) and 44.8% were of Swiss nationality. About 59% of the participants had a family history of diabetes and only 4.3% had a history of GDM.

Table 2 describes the study variables at the first GDM visit and at 1-year postpartum. The mean pre-pregnancy weight and BMI were 69.46±13.99 kg and 25.82±4.69 kg/m^2 respectively. At 1-year postpartum, these numbers were 72.79±16.22 kg and 27.06±5.54 kg/m^2, which translates to weight retention of 3.32±7.18 kg. Mean HbA1c was 5.37±0.42% at the first GDM visit and 5.27±0.33% at 1-year postpartum, while fasting glucose at diagnosis was 5.24±0.93 mmol/l and 5.49±0.58 mmol/l at 1-year postpartum. Before pregnancy, 46.2% of women were overweight/obese and this was the same at 1-year postpartum. At 1-year postpartum, 46.1% women had prediabetes. The mean EPR subscale at the first GDM visit was 3.86 and 3.76 at 1-year postpartum ($p<0.001$), and these numbers were 3.53 and 3.42 for the mean RHSC subscales ($p<0.001$). Correlation between the first GDM visit and 1-year postpartum were 0.42 for the EPR and 0.32 for the RHSC subscales (both $p<0.001$, see also Supplementary Table 3). Table 3 represents the associations between the two subscales of IES-2 at the first GDM visit and at 1-year postpartum with metabolic health indicators at 1-year postpartum. After adjusting for confounders the EPR subscale at the first GDM visit was associated with lower BMI ($p=0.017$), fasting glucose ($p=0.014$) and tended to predict lower HbA1c ($p=0.062$) at 1-year postpartum. On the other hand, RHSC at the first GDM visit had no association with any of the metabolic health variables at 1-year postpartum (all $p>0.2$).

However, both EPR and RHSC at 1-year postpartum were associated with lower weight retention (both $p \leq 0.037$) and lower BMI (both $p \leq 0.012$). The EPR subscale was also associated with lower HbA1c and lower fasting glucose (both $p=0.018$). When fasting glucose and HbA1c were the outcome variables, we further adjusted for BMI at the first GDM visit as a potential confounder, which led to the attenuation of the observed associations between the two subscales of IES-2 and metabolic parameters (all $p \geq 0.066$).

We also focused on two high-risk GDM subgroups with pre-pregnancy overweight/obese or with prediabetes and their lower-risk counterparts. The Supplementary Table 1 shows that at 1-year postpartum all metabolic health indicators, including weight retention, were significantly higher in women with prediabetes (all $p \leq 0.026$), whereas women with normal glucose values had significantly higher scores of the EPR ($p=0.025$). The Supplementary Table 2 shows that all metabolic health indicators at 1 year postpartum except weight retention were significantly higher in women who were overweight/obese (all $p \leq 0.042$) and they had significant higher scores of the EPR subscale ($p=0.040$). In the subgroup of women with prediabetes (Table 4), EPR and RHSC at the first GDM visit predicted lower fasting glucose at 1-year postpartum (both $p \leq 0.024$). At 1-year postpartum, both EPR and RHSC were associated with lower weight retention (both $p \leq 0.034$) and BMI (both $p \leq 0.005$), while no associations were observed in the women with normal glucose tolerance (all $p \geq 0.10$).

In the subgroup of women with overweight/obese (Table 5), EPR at the first GDM visit predicted lower fasting glucose at 1-year postpartum ($p=0.041$), whereas the RHSC subscale showed no significance with any of the metabolic variables. At 1-year postpartum, both EPR and RHSC subscales were associated with lower weight retention (both $p \leq 0.009$) and fasting glucose (both $p=0.030$). The EPR was also associated with lower BMI ($p<0.001$).

We found no associations between the two subscales of IES-2 and metabolic health in the subgroup of women with normal weight. In both high-risk subgroups, the associations of IES-2 subscales with fasting glucose were independent of BMI.

Discussion

To our knowledge, no previous study has looked at the relationship between intuitive eating and metabolic health during pregnancy up to the 1-year postpartum period. In the context of identifying novel approaches to prevent weight retention and diabetes in women after GDM, we evaluated the longitudinal and cross-sectional associations between the two subscales of the French intuitive eating questionnaire (the EPR and RHSC subscales) during and after pregnancy with weight retention, BMI, fasting glucose, and HbA1c at 1-year postpartum in women with GDM. This was also studied in two high-risk GDM subgroups, those with prediabetes (46.1%) and those with overweight/obese status (46.2%). IE at the first GDM visit and at 1-year postpartum visit was associated with better metabolic health at 1-year postpartum in all women with GDM and in the two high-risk subgroups. Specifically, the longitudinal analyses revealed that the EPR subscale at the first GDM visit predicted lower postpartum BMI and fasting glucose. In the cross-sectional analyses, the EPR and RHSC subscales at 1-year postpartum visit were associated with lower BMI and lower weight retention, while the EPR subscale was additionally associated with lower fasting glucose and HbA1c. The (cross-sectional and longitudinal) associations between IE and improved metabolic health were also observed in both GDM high-risk subgroups (those with overweight/obese and those with prediabetes), but not in the respective low-risk subgroups.

In women with GDM, there is a tight relationship between weight gain during pregnancy, weight retention, and diabetes in the postpartum period (Mamun et al., 2013; Bao et al., 2015; Institute of Medicine (IOM), 2009; Nehring et al., 2011).

Increased weight retention is related to increased insulin resistance, subsequent dysfunction of the beta cells, and development of glucose intolerance (Moyce and Dolinsky, 2018). This is partly attributed to the subtle changes in appetite regulatory mechanisms associated with weight gain and weight retention (Ciampolini et al., 2010; Perry and Wang, 2012). Alterations in leptin (a hormone released from fat cells in adipose tissue altering food intake and control energy expenditure over the long term) signaling also act to increase the risk of diabetes in these women (Moyce and Dolinsky, 2018; Oh et al., 2018). It is therefore of utmost importance to decrease weight retention and to improve glucose control in order to reduce diabetes risk in this population. Traditional lifestyle interventions that are used to manage weight and glucose control and to prevent the progression to diabetes in the postpartum period have, however, been unsatisfactory and their sustained effects are controversial (Brown et al., 2017; Michel et al., 2018). In order to reduce weight retention and improve glycemic control in women with GDM, eating intuitively could help to exert less cognitive control over eating and rely more on satiety cues, irrespective of current innate satiety cues, and help to eat in response to hunger and satiety signals. We thus explored the relationship between IE and metabolic health in women with GDM.

In our longitudinal analyses, we found that the EPR subscale at the first GDM visit was associated with lower BMI and fasting glucose at 1-year postpartum. These findings are in concordance with a previous study conducted in a general non-pregnant population where the EPR subscale was associated with lower weight gain and lower fasting glucose (39). The EPR subscale assesses the extent to which eating is affected by emotion (Tylka, 2006), and women with GDM who engage in eating habits or behaviors driven by emotion rather than physical symptoms of hunger during and after pregnancy may have more problems with weight loss and glucose control in the postpartum period (Leahy et al., 2017).

Adhering to IE prevents or reduces eating in response to negative emotional states, such as anxiety, depression, boredom, or loneliness that often leads to overeating, weight retention, higher BMI, and poor glucose control in women with GDM (Lauzon-Guillain et al., 2006). Compared to a study that found a cross-sectional association between the EPR subscale with lower levels of HbA1c in a population with type-1 diabetes, our results found a weak longitudinal relationship between this subscale and HbA1c ($p=0.06$). In addition to frequent (emotional) overeating, loss of sleep (Dashti et al., 2015) in the postpartum period might influence weight and glucose metabolism and confound some of these findings (Kim et al., 2015; St-Onge, 2017). Other factors, such as breastfeeding in the postpartum period reduce glucose levels and may influence HbA1c levels, and also confound some of the analyses (Gunderson et al., 2012). Indeed, about 87% of women in our sample reported they were breastfeeding during the early postpartum period, but breastfeeding was not a significant confounder in our analyses.

We found no longitudinal relationship between the RHSC subscales at the first GDM visit with any of the metabolic health variables studied at 1 year postpartum. This lack of association between RHSC and the metabolic health variables such as BMI, weight retention, fasting glucose, and HbA1c in our longitudinal analyses suggests that in the long-term, eating for physical rather than emotional reasons overshadows the potential importance of relying on one's hunger and satiety signals to regulate food intake in this sample. Therefore, it was not surprising that the mean difference between the scores of the EPR subscale during and after pregnancy was around 10% higher than that of the RHSC subscale.

In our cross-sectional analyses however, IE at the 1-year postpartum visit was associated with several metabolic health parameters. Thus, the EPR subscale was associated with lower weight retention, BMI, fasting glucose and HbA1c, while the RHSC subscale was associated with lower weight retention and BMI.

Either other parameters interfere less in the cross-sectional analyses, or the nature of IE in the postpartum in general relates better to metabolic health compared to the pregnancy period and may account for these associations. Thus, aiming to improve IE in pregnancy and the ability to keep this practice stable and higher in the postpartum period might help to improve overeating and metabolic health in these women.

Despite their future diabetes risk, most women with GDM have normal glucose values after delivery (Retnakaran et al., 2010), but up to 50% have prediabetes within 12 months as observed in our sample and that of another study (Huopio et al., 2014). It is important to prevent further glucose intolerance in these GDM subgroups with prediabetes and overweight/obese who are at higher risk of progressing to diabetes (Feig, 2018). In the subgroup of women with prediabetes or with overweight/obese, we found that IE was associated with fasting glucose in the longitudinal analyses and with weight retention, BMI and/or fasting glucose in the cross-sectional analysis. This results show that special focus should be placed on these women for follow-up, but also to test early interventions to improve IE. This is particularly important because, in women with GDM and in high-risk GDM subgroups, each kilogram of weight lost in the postpartum period is associated with a 16% decrease in the risk of diabetes (Bao et al., 2015; Hamman et al., 2006; Meron and Grajower, 2017). The EPR and RHSC subscales moderately correlated with each other during the first GDM visit (r=0.41) and at 1-year postpartum (r=0.51). The mean score of the EPR subscale was about 10% higher than the mean score of the RHSC subscale. Our results are consistent with another study involving a healthy non-pregnant population (correlation between EPR and RHSC subscale: r=0.35 and 0.37 in women and men respectively) (Tylka and Van Diest, 2013). Although these subscales correlate with each other, only 20% of the variability of one subscale seemed to be explained by the other and thus they cover different aspects of IE.

Our study has several strengths. Clinically, our results if confirmed by an intervention trial could help address the issue of postpartum weight retention in women with GDM. It could also help augment the management and prevention of diabetes in women with GDM and in the high-risk subgroups with prediabetes or overweight/obese, especially when results from several existing lifestyle interventions still remain controversial (Gilbert et al., 2019) and inconsistent (Brown et al., 2017; Goveia P et al., 2018; Michel et al., 2018). We studied the novel relationship between IE with BMI, weight retention and glycemic control during pregnancy and in the postpartum period up to 1 year postpartum in a longitudinal cohort of women with GDM. We also measured IE with a validated tool that has shown to have construct validity and reliability among pregnant women (Camilleri et al., 2015, Daundasekara et al., 2017).

A limitation of this study is the relatively small sample size, which may limit our ability to generalize our findings. Furthermore, the nature of the observational study design does not allow the modification of IE scores, reduces the control over external, confounding variables, although we did test and adjust for potential significant confounders in our regression models, as described in the statistics section above. The inability to include the UPE subscale due to the fact that, discussions during diet counselling could significantly influence participant responses to the UPE subscale may be a source of limitation since the effect of an overall IES-2 subscale would have been interesting. Other factors, such as the intention to lose weight in the postpartum period and a variety of other behavioral or socioeconomic variables that could influence weight loss or impact on metabolic health were not studied. Even though the IES-2 has been validated both in the general and pregnant population, it is not validated in women with GDM and could be a limitation of our study. It is also important to indicate that the IES-2 questionnaire is self-reported, and therefore the likelihood of over- or under-reporting may influence our analyses.

We obtained weight before pregnancy from patients' medical chart when available; otherwise, we relied on self-reported pre-pregnancy weight, which may be a limitation. Further research that utilizes IE as an intervention to reduce weight retention and improve glucose control in a larger population during pregnancy and in the postpartum period is needed to determine the causality of these associations in women in general and specifically those with GDM.

Conclusions

We found an association between IE during and after pregnancy with lower BMI and weight retention at 1-year postpartum, both in cross-sectional and longitudinal analyses. In addition, eating for physical rather than emotional reasons was associated with lower fasting glucose and HbA1c in this cohort of women with GDM. High-risk GDM subgroups with prediabetes or overweight/obese each represented almost 50% of the population. In these high-risk groups, IE was associated with lower BMI, weight retention, and fasting glucose. Our results suggest that higher sustenance of IE behavior could represent an interesting and novel approach for reduced BMI, weight retention, and improved glucose control in women with GDM, and especially in high-risk subgroups. IE could therefore be a future target for screening and a potential intervention in women with GDM.

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Conflict of interest

Authors declare that there is no conflict of interest.

Author contribution

DYQ, JG and JP designed the study. DYQ, extracted the data, performed all the analysis and wrote the draft manuscript under the supervision of JP. JG, LG, AH and JP reviewed the manuscript. All authors revised and accepted the manuscript for submission. JP had the idea of the cohort and co-supervised all the work with AH.

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STUDY 2 Tables and Captions

[Table 1] General characteristics of study participants

Variable	Mean	SD	Frequency	Percent (%)
Age (yr.) (N=117)	33.21	5.37		
Gestational age at the first GDM visit (N=117)	28.83	2.82		
Education level (N=89)				
Compulsory school achieved			15	16.9
High school			13	14.6
General and vocational education			27	30.3
University			34	38.2
Nationality (N=116)				
Swiss			52	44.8
Europe + North America			37	31.9
Asia + Western pacific			6	5.2
Africa			20	17.2
Latin America			1	0.9
Employment status (N=109)				
Student			1	0.9
Professional worker			82	75.2
Housewife			13	11.9
Unemployed			13	11.9
Family history of diabetes (N=117)				
1st degree[1]			41	35.0
2nd degree[2]			28	23.9
No			48	41.0
History of previous GDM (N=117)				
No			112	95.7
Yes			5	4.3
Smoking status during pregnancy (N=117)				
Yes			22	18.8
No			95	81.2
Alcohol intake during pregnancy (N=117)				
Yes			6	5.1
No			111	94.9
Parity (N=117)*				
0			68	58.1
1			36	30.8
2			11	9.4
≥3			2	1.7
Breastfeeding (N=117)[3]				
Yes			102	87.2
No			15	12.8

[1]1st degree means 1 degree of relationship of the participant (at least 50% of genetic link, which included mother, father, brother, sister, daughter, son)

[2]2nd degree means 2nd degree of kinship of the participant (at least 25% of genetic link that included grandparents, grandchildren, nephews, niece, half-brother, half-sister)

[3]At 6-8 weeks postpartum

*10.2% of women who were multiparous had history of previous GDM

All results are frequency and percentage unless otherwise stated

GDM means gestational diabetes mellitus

[Table 2] Mean and standard deviations of study variables (N=117)

Variable	Mean	SD
First GDM visit		
Pre-pregnancy weight (kg)[1]	69.46	13.99
Pre-pregnancy BMI (Kg/m^2)[2]	25.82	4.69
Weight at the first GDM visit (kg)	80.26	14.55
BMI at the first GDM visit (Kg/m^2)	29.87	4.89
HbA1c at the first GDM visit (%)	5.37	0.42
Fasting glucose at GDM diagnosis (mmol/l)	5.24	0.93
EPR at the first GDM visit	3.86	0.94
RHSC at the first GDM visit	3.53	0.89
1-year postpartum		
Weight at 1-yr postpartum (kg)	72.79	16.22
ΔWeight retention (kg)[3]	3.32	7.18
BMI at 1-yr postpartum (kg/m^2)	27.06	5.54
Waist circumference at 1-yr postpartum (cm)	88.82	11.99
HbA1c at 1-yr postpartum (%)	5.27	0.33
Fasting glucose at 1-yr postpartum (mmol/l)[4]	5.49	0.58
EPR at 1-yr postpartum	3.76	0.97
RHSC at 1-yr postpartum	3.42	0.94

[1]Data reported at the first GDM visit or taken from the medical charts

[2]Body mass index before pregnancy; data reported at the first GDM visit or taken from the medical charts

[3]Weight retention means the difference in weight at 1-yr postpartum and pre-pregnancy weight

[4]N=116; one missing

GDM means gestational diabetes mellitus

HbA1c means glycated hemoglobin

BMI means body mass index

EPR means Eating for Physical Rather than Emotional Reasons subscale of the Intuitive Eating scale2 (IES-2)

RHSC means Reliance on Hunger and Satiety Cues subscale of the Intuitive Eating scale2 (IES-2)

[Table 3] Associations between the two subscales of IES-2 at the first GDM visit and at 1-year postpartum and metabolic health at 1-year postpartum

Variable	Regression coefficient	95% CI		P-value[a]	P-value[b]
IES-2 at the first GDM visit (longitudinal)					
EPR at the first GDM visit					
Metabolic health at 1-yr pp					
ΔWeight retention (kg)[1]	-0.087	-2.026	0.730	0.350	
BMI (kg/m^2)	-0.219	-2.281	-0.151	**0.017**	
HbA1c (%)	-0.171	-0.119	0.008	0.062	0.137
Fasting glucose (mmol/l)	-0.229	-0.251	-0.026	**0.014**	**0.068**
RHSC at the first GDM visit					
Metabolic health at 1-yr pp					
ΔWeight retention (kg)[1]	0.078	-0.815	2.084	0.400	
BMI (kg/m^2)	-0.090	-1.637	0.645	0.332	
HbA1c (%)	0.044	-0.048	0.086	0.634	0.327
Fasting glucose (mmol/l)	-0.104	-0.184	0.058	0.272	0.458
IES-2 at 1-yr pp (cross-sectional)					
EPR at 1-yr pp					
Metabolic health at 1-yr pp					
ΔWeight retention (kg)[1]	-0.230	-2.976	-0.370	**0.012**	
BMI (kg/m^2)	-0.337	-2.825	-0.829	**<0.001**	
HbA1c (%)	-0.216	-0.129	-0.008	**0.018**	**0.066**
Fasting glucose (mmol/l)	-0.222	-0.236	-0.018	**0.018**	0.237
RHSC at 1-yr pp					
Metabolic health at 1-yr pp					
ΔWeight retention (kg)[1]	-0.193	-2.847	-0.083	**0.037**	
BMI (kg/m^2)	-0.243	-2.469	-0.313	**0.012**	
HbA1c (%)	-0.095	-0.098	0.032	0.311	0.547
Fasting glucose (mmol/l)	-0.194	-0.230	0.002	0.042	0.208

[1]means the difference in weight at 1-yr postpartum and pre-pregnancy weight
EPR means Eating for Physical Rather than Emotional Reasons subscale of the Intuitive Eating scale2 (IES-2)
RHSC means Reliance on Hunger and Satiety Cues subscale of the Intuitive Eating scale2 (IES-2)
PP means postpartum
P-value[a]: adjusted for age and gestational age at the first GDM visit
P-value[b]: adjusted for age and gestational age and BMI at the first GDM visit

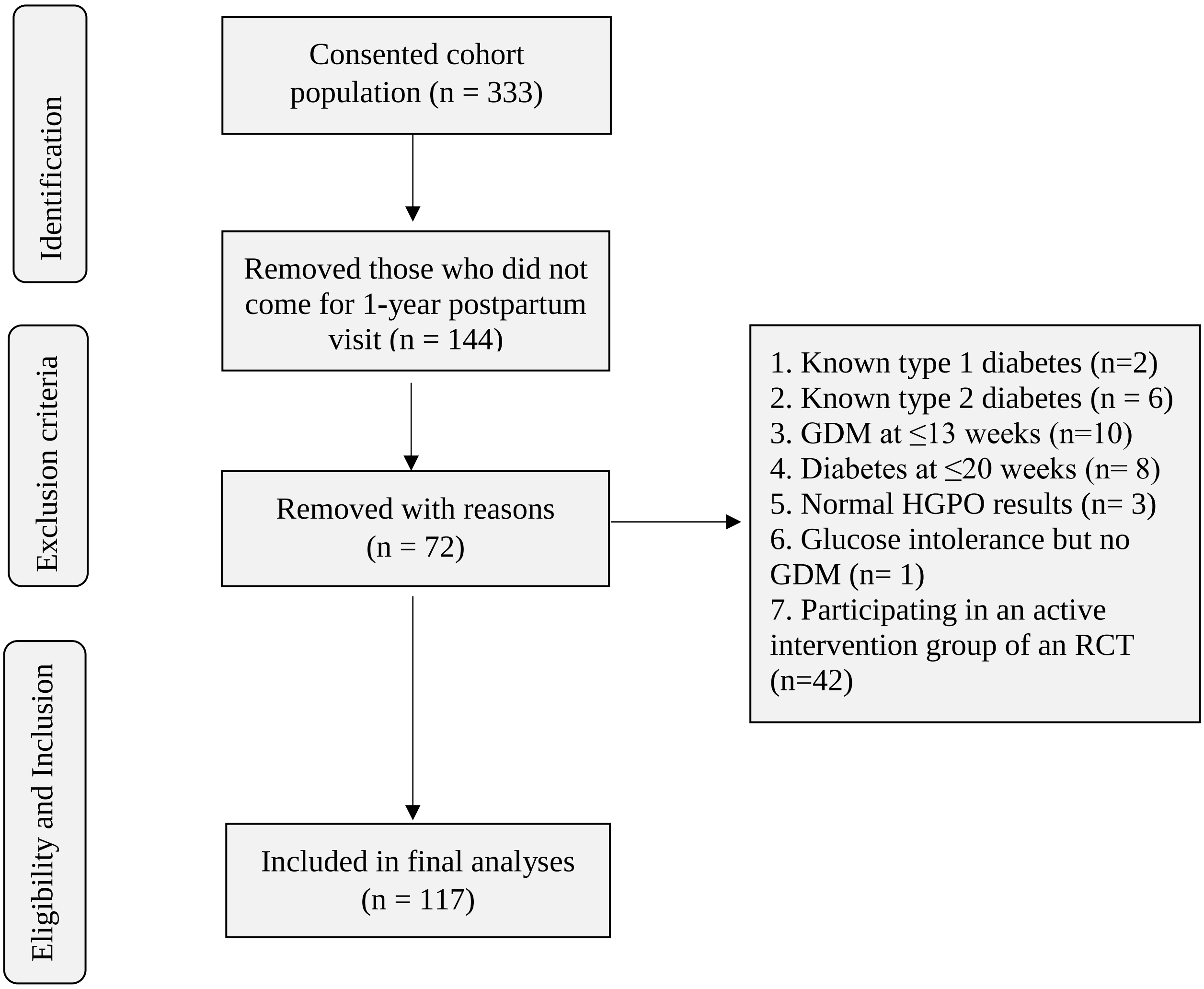

Fig 1. Flow chart describing how the study participants were selected. Removed participants did not meet the inclusion criteria (see methods section).

[Table 4] Associations between the two subscales of IES-2 at first GDM visit and at one-year postpartum visit with metabolic health at one year postpartum stratified by glucose tolerance

	Prediabetes (n=54)					Normal (n=63)			
Variable	Regression coefficient	95% CI		P-value[a]	P-value[b]	Regression coefficient	95% CI		P-value
IES-2 at first GDM visit (longitudinal)*									
EPR at the first GDM visit									
ΔWeight retention (kg) [1]	-0.098	-2.598	1.239	0.480		-0.052	-2.461	1.628	0.685
BMI (kg/m^2)	-0.169	-2.415	0.576	0.223		-0.214	-2.748	0.213	0.092
HbA1c (%)	-0.173	-0.158	0.036	0.211	0.189	-0.076	-0.095	0.051	0.553
Fasting glucose (mmol/l)	-0.437	-0.303	-0.063	**0.001**	**0.004**	-0.029	-0.106	0.084	0.820
RHSC at the first GDM visit									
ΔWeight retention (kg) [1]	-0.090	-2.459	1.254	0.518		0.294	0.453	4.959	0.076
BMI (kg/m^2)	-0.075	-1.857	1.068	0.591		-0.082	-2.300	1.178	0.521
HbA1c (%)	0.043	-0.080	0.109	0.760	0.751	0.060	-0.064	0.104	0.641
Fasting glucose (mmol/l)	-0.308	-0.247	-0.004	**0.024**	**0.025**	0.101	-0.066	0.152	0.432
IES-2 at 1-year pp (cross-sectional)									
EPR at 1-yr pp									
ΔWeight retention (kg)[1]	-0.288	-3.572	-0.142	**0.034**		-0.114	-3.111	1.184	0.373
BMI (kg/m^2)	-0.384	-3.248	-0.645	**0.004**		-0.180	-2.698	0.450	0.158
HbA1c (%)	-1.582	-0.159	0.019	0.120	0.125	-0.001	-0.077	0.077	0.995
Fasting glucose (mmol/l)	-0.204	-0.207	0.031	0.142	0.765	0.083	-0.067	0.132	0.515
RHSC at 1-yr pp									
ΔWeight retention (kg) [1]	-0.394	-4.388	-0.935	**0.003**		-0.030	-2.361	1.861	0.814
BMI (kg/m^2)	-0.378	-3.376	-0.639	**0.005**		-0.047	-1.851	1.272	0.712
HbA1c (%)	-0.130	-0.139	0.050	0.349	0.253	0.157	-0.028	0.121	0.219
Fasting glucose (mmol/l)	-0.137	-0.190	0.065	0.329	0.842	-0.043	-0.114	0.082	0.740

*for the fasting glucose, this corresponds to the time point of the GDM diagnosis before the first GDM visit.
[1]means the difference in weight at 1-yr postpartum and pre-pregnancy weight
EPR means Eating for Physical Rather than Emotional Reasons subscale of the Intuitive Eating scale2 (IES-2)
RHSC means Reliance on Hunger and Satiety Cues subscale of the Intuitive Eating scale2 (IES-2)
P-value[a]: Adjusted for age and gestational age at the first GDM visit
P-value[b]: Adjusted for age, gestational age and BMI at the first GDM visit
PP means postpartum

[Table 5] Associations between the two subscales of IES-2 and metabolic health at one year postpartum stratified by BMI category

Variable	Obese/overweight (n=54)					Normal weight (n=63)			
	Regression coefficient	**95% CI**		**P-value[a]**	**P-value[b]**	**Regression coefficient**	**95% CI**		**P-value**
IES-2 at first GDM visit (longitudinal)*									
EPR at the first GDM visit									
ΔWeight retention (kg) [1]	-0.111	-3.466	1.475	0.422		0.026	-1.281	1.567	0.842
BMI (kg/m^2)	-0.132	-1.779	0.643	0.351		-0.144	-1.183	0.304	0.241
HbA1c (%)	-0.195	-0.157	0.037	0.165	0.169	-0.076	-0.112	0.061	0.553
Fasting glucose (mmol/l)	-0.288	-0.337	0.003	**0.041**	**0.043**	-0.083	-0.191	0.098	0.522
RHSC at the first GDM visit									
ΔWeight retention (kg) [1]	0.176	-0.924	4.241	0.203		0.054	-1.188	1.819	0.676
BMI (kg/m^2)	0.213	-0.319	2.219	0.137		-0.073	-1.028	0.556	0.554
HbA1c (%)	-0.010	-0.108	0.101	0.967	0.963	0.194	-0.020	0.160	0.127
Fasting glucose (mmol/l)	-0.111	-0.260	0.111	0.419	0.424	0.039	-0.130	0.176	0.765
IES-2 at 1-year pp (Cross-sectional)									
EPR at 1-yr									
ΔWeight retention (kg) [1]	-0.347	-5.152	-0.562	**0.009**		0.006	-1.349	1.409	0.965
BMI (kg/m^2)	-0.430	-2.873	-0.735	**<0.001**		-0.098	-1.019	0.442	0.432
HbA1c (%)	-0.177	-0.156	0.034	0.201	0.233	-0.155	-0.134	0.032	0.225
Fasting glucose (mmol/l)	-0.301	-0.345	-0.015	**0.030**	**0.025**	0.001	-0.140	0.140	0.997
RHSC at 1-yr									
ΔWeight retention (kg) [1]	-0.405	-6.529	-1.494	**0.002**		0.077	-0.891	1.656	0.550
BMI (kg/m^2)	-0.245	-2.467	-1.370	0.780		-0.120	-1.036	0.371	0.348
HbA1c (%)	-0.135	-0.162	0.055	0.329	0.299	0.074	-0.055	0.100	0.564
Fasting glucose (mmol/l)	-0.302	-0.395	-0.021	**0.030**	**0.032**	0.040	-0.110	0.151	0.755

*for the fasting glucose, this corresponds to the time point of the GDM diagnosis before the first GDM visit
[1]means the difference in weight at 1-yr postpartum and pre-pregnancy weight
EPR means Eating for Physical Rather than Emotional Reasons subscale of the Intuitive Eating scale2 (IES-2)
RHSC means Reliance on Hunger and Satiety Cues subscale of the Intuitive Eating scale2 (IES-2)
P-value[a]: Adjusted for age and gestational age at the first GDM visit
P-value[b]: Adjusted for age, gestational age, and BMI at the first GDM visit
PP means postpartum

Supplementary tables

[Table 1] 1-year postpartum metabolic health indicators and IE scores according to glucose tolerance

Variable	N	Mean	SD	P-value*
Weight at 1-year pp (kg)				
Normal	63	69.15	15.07	**0.008**
Prediabetes	54	77.03	16.62	
ΔWeight retention (kg)[1]				
Normal	63	1.96	7.22	**0.026**
Prediabetes	54	4.92	6.86	
BMI (kg/m^2)				
Normal	63	25.72	5.35	**0.004**
Prediabetes	54	28.63	5.40	
HbA1c (%)				
Normal	63	5.14	0.25	**<0.001**
Prediabetes	54	5.41	0.34	
Fasting glucose (mmol/l)				
Normal	63	5.10	0.33	**<0.001**
Prediabetes	54	5.96	0.46	
EPR				
Normal	63	3.95	0.85	**0.025**
Prediabetes	54	3.55	1.06	
RHSC				
Normal	63	3.53	0.87	0.171
Prediabetes	54	3.29	1.01	

[1]means the difference in weight at 1-yr postpartum and pre-pregnancy weight
*P-value from ANOVA test
GDM means gestational diabetes mellitus
HbA1c means glycated hemoglobin
BMI means body mass index
EPR means Eating for Physical Rather than Emotional Reasons subscale of the Intuitive Eating scale2 (IES-2)
RHSC means Reliance on Hunger and Satiety Cues subscale of the Intuitive Eating scale2 (IES-2)
PP means postpartum

[Table 2] 1-year postpartum metabolic health indicators and IE scores according to weight status/category

Variable	N	Mean	SD	P-value*
Weight at 1-year pp (kg)				
Normal	63	61.79	7.70	**<0.001**
OW/OB	54	85.61	13.98	
∆Weight retention (kg)[1]				
Normal	63	2.13	4.78	**0.053**
OW/OB	54	4.71	9.08	
BMI (kg/m^2)				
Normal	63	23.11	2.61	**<0.001**
OW/OB	54	31.67	4.37	
HbA1c (%)				
Normal	63	5.21	0.29	**0.042**
OW/OB	54	5.33	0.36	
Fasting glucose (mmol/l)				
Normal	63	5.34	0.48	**0.002**
OW/OB	53	5.67	0.64	
EPR				
Normal	63	3.94	0.88	**0.040**
OW/OB	54	3.57	1.04	
RHSC				
Normal	63	3.55	0.95	0.110
OW/OB	54	3.27	0.91	

[1]means the difference in weight at 1-yr postpartum and pre-pregnancy weight
*P-value from ANOVA test
GDM means gestational diabetes mellitus
HbA1c means glycated hemoglobin
BMI means body mass index
EPR means Eating for Physical Rather than Emotional Reasons subscale of the Intuitive Eating scale2 (IES-2)
RHSC means Reliance on Hunger and Satiety Cues subscale of the Intuitive Eating scale2 (IES-2)
PP means postpartum
OW/OB means Overweight/Obese

[Table 3] Paired t-test and correlation between the two scales of IES-2 at the first GDM visit and at 1-year postpartum (N=117)

Variable	Mean	SD	P-value (t-test)	r.	P-value (r)
EPR at the first GDM visit	3.86	0.94	0.862	0.422	<0.001
EPR at 1-yr pp	3.76	0.97			
RHSC at the first GDM visit	3.53	0.89	0.995	0.320	<0.001
RHSC at 1-yr pp	3.42	0.94			
EPR at the first GDM visit	3.86	0.94	<0.001	0.415	<0.001
RHSC at the first GDM visit	3.42	0.89			
EPR at 1-yr pp	3.76	0.97	<0.001	0.510	<0.001
RHSC at 1-yr pp	3.42	0.94			

EPR means Eating for Physical Rather than Emotional Reasons subscale of the Intuitive Eating scale2 (IES-2)
RHSC means Reliance on Hunger and Satiety Cues subscale of the Intuitive Eating scale2 (IES-2)
PP means postpartum
r means correlation

APPENDIX 3

STUDY 3: Predictors and consequences of weight retention in the early and late postpartum period in women with gestational diabetes

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Abstract

Aims: We investigated the predictors and consequences of postpartum weight retention (PPWR) in the early and late postpartum period in women with gestational diabetes (GDM), to assist preventive strategies. **Methods:** 862 women with GDM were prospectively included between 2011 and 2019. We investigated PPWR at 6-8 weeks and 1-year postpartum. Potential predictors included gestational weight gain (GWG), weight, BMI, and glucose control parameters during and after pregnancy. **Results:** PPWR at 6-8 weeks and 1-year postpartum were 4.6±5.7kg and 4.0 ±7.4kg. At 6-8 weeks postpartum, women with PPWR had higher pre-pregnancy weight, 7.5±0.2kg higher GWG and higher postpartum weight (all p≤0.02), without presenting metabolic differences. At 1-year postpartum, there were no differences in anthropometric parameters before and during pregnancy between women with or without PPWR, except for a 4±0.4kg higher GWG (p<0.001). However, women with PPWR had increased postpartum weight and BMI, higher fasting glucose and more pronounced increases in Δfasting glucose and ΔHbA1c at 1-year (all p≤0.03). GWG predicted higher PPWR at both 6-8 weeks and at 1-year PP (all p<0.001). **Conclusion:** Women with PPWR had increased anthropometric parameters and adverse metabolic consequences at 1-year postpartum. GWG was the most relevant predictor of PPWR.

Keywords: Postpartum weight retention; Gestational diabetes mellitus; Gestational weight gain; Anthropometric; Metabolic consequences; Predictors

1.0 Introduction

Postpartum weight retention (PPWR) is the difference between pre-pregnancy weight and weight in the postpartum period (1). This includes the immediate PPWR at the early postpartum (6-8 weeks after birth), or a long-term PPWR at different stages in the postpartum period (such as at 6 months or at 12 months) (2). It is recommended for women to return to their pre-pregnancy weight 12 months after childbirth in order to avoid any PPWR (3–5). Unfortunately, PPWR is frequent (3) and represents a significant public health concern (6,7) because, in the long term, PPWR leads to an upwards weight trajectory following childbirth (8–10). Modest PPWR increases the risk of obesity and higher PPWR leads to an increased risk of permanent obesity 5-10 years after birth (11). For any preventive efforts, it is important to understand the pattern of PPWR (3).

In women with a history of gestational diabetes mellitus (GDM) (12), PPWR is associated with a higher risk of overweight/obesity (13), of prediabetes (14) and of recurrent GDM (4). Higher PPWR also augments the risk for future diabetes (15,16). In these women, weight changes in the postpartum period have been associated with higher risk of future diabetes (15–17). One study revealed that, in this population, PPWR of 4.5kg during a 7.5-year follow-up after pregnancy was independently associated with a twofold increase in the risk of future diabetes (18). In another study, 42% of women with PPWR developed diabetes after 23years of follow-up, while the incidence of diabetes was almost half in the women without PPWR (19). These results show that PPWR is an independent risk factor of diabetes and its related morbidities in women with GDM. Reducing PPWR or weight loss is therefore recommended (13,14). For example, in a sample of 72 women, weight loss of ≥2 kg during the postpartum period led to a significant improvement in glucose control at 1-year postpartum period (17).

In the general population, the most important predictors of PPWR are higher pre-pregnancy body mass index (BMI) and excessive gestational weight gain (GWG) (20,21). Other studies have also associated diet, physical activity, age, marital status, and ethnicity with PPWR (22–24). We are only aware of one small study (n=75) that investigated predictors of weight loss or no PPWR in women with GDM exclusively in the early postpartum period (25). In that study, less GWG and no insulin use during pregnancy predicted a loss of at least 75% of GWG. However, it is not clear if those factors are also predictors of the recommended lack of PPWR (i.e., no weight increase at all compared to the pre-pregnancy weight). To our knowledge, no previous study has investigated the differences between women with and without PPWR, the metabolic consequences and the predictors of PPWR in the early and late postpartum period in women with GDM. This can help to focus efforts and target optimal timing to reduce long-term complications of GDM. We therefore conducted this study to determine the anthropometric characteristics and differences between women with and without PPWR and the adverse metabolic consequences of PPWR in the early and late postpartum period in a cohort of women with GDM. This prospective cohort study also aimed to identify the predictors associated with PPWR in the early and late postpartum period.

2.0 Methods

2.1 Study design and patient population

This is a prospective observational clinical cohort of women with GDM followed in the Diabetes and Pregnancy Unit at the Lausanne University Hospital (CHUV) between 2011-2019 (26–28). Pregnant women diagnosed with GDM between 24-32 weeks of gestation according to the American Diabetes Association (ADA) and the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) guidelines (29,30) were invited to participate.

The Human Research Ethics Committee of the Canton de Vaud (326/15) approved the study protocol. All participating women signed an informed consent. The total cohort population consisted of 1039 women who understood French and English and consented to participate. We first excluded those with known type 1 diabetes (N=13), type 2 diabetes (N=18), newly diagnosed diabetes in pregnancy (N=9), glucose intolerance but no GDM (N=2), those with normal oral glucose tolerance test (oGTT) results (N=8), with GDM diagnosed at ≤13 weeks (N=13), and those participating in an active lifestyle intervention study (N=53). We then excluded those who did not attend the 6-8 weeks postpartum visit (N=61). Following this, 862 women were eligible and were included in our final analysis. Figure 1 shows the details of the participants' selection. Of these 862 women, all of them had completed the 6-8 weeks pp visit, whereas 259 (30%) had completed the 1-year postpartum visit at the time of this analysis. The main reason for the low numbers of patients at 1-year postpartum visit is that the implementation of the 1-year postpartum follow-up visit started in August 2015.

2.2 Measures

2.2.1 Socio-demographic characteristics

During the first GDM visit, information on participants' characteristics including age, educational level, and ethnic origin, family history of type-2 diabetes, history of previous GDM, parity, gravida, and smoking during pregnancy were obtained during a structured face-to-face interview. We categorized educational level into "no formal education; compulsory school achieved; general and vocational training levels; high school and university education" (27,28). Information on partner support was obtained during the face-to-face interview and was categorized as either "living with a partner or not". We categorized family history of type-2 diabetes, as either "first-degree, second degree or none" whereas previous history of GDM and smoking during pregnancy were categorized as either 'yes' or 'no'.

We grouped parity into "none, one, two and ≥ three" whereas gravida consisted of "one, two or three" (see Table 1 for more details).

2.2.2 Anthropometric and other health variables

Pre-pregnancy weight was taken from participants' medical charts or, if missing, was self-reported (for the 1-2 months before pregnancy). We measured weight at the first GDM visit, at the end of pregnancy, at 6-8 weeks and at 1-year postpartum to the nearest 0.1 kg in women wearing light clothes and no shoes with a regularly calibrated electronic scale (Seca®). We measured height at the first GDM visit to the nearest 0.1 cm with a regularly calibrated Seca® height scale. GWG was defined as the difference between pre-pregnancy weight and weight at the end of pregnancy. We calculated the body mass index (BMI) as the ratio of weight in kilograms to the square of height in meters (kg/m2). Based on the pre-pregnancy BMI and GWG, women were classified as being below (inadequate), within (adequate) or above (excessive) the Institute of Medicine (IOM) GWG recommendations (31). PPWR was the outcome variable for our main analyses. We calculated PPWR by either subtracting the pre-pregnancy weight from the weight at 6-8 weeks postpartum (early PPWR) and from the weight at 1-year postpartum (late PPWR). Information on GDM treatment during pregnancy (use of insulin and/or metformin; yes/no) and caesarean section (yes/no) were obtained from medical charts. In the routine clinical visit at 6-8 weeks postpartum, information about breastfeeding (yes/no) and contraception use (yes/no) at this time point were obtained. During the first GDM visit (at 24-32 weeks), women completed the Edinburgh Postnatal Depression Scale (EPDS) questionnaire. This is a ten-item self-report questionnaire designed and validated to screen women for symptoms of depression during pregnancy and in the postnatal period (32). The possible scores of the EPDS questionnaire range from 0 to 30 points, with a higher total score indicating more severe depressive symptoms.

2.2.3 Metabolic health variables

All women involved in this study were diagnosed with GDM during pregnancy (at 24-32 weeks of gestational age) if one of the following criteria were met during a 75g oGTT: fasting venous glucose ≥5.1 mmol/L, 1-hr glucose ≥10.0 mmol/L, or 2-hr glucose ≥8.5 mmol/L, using the IAPDSG guidelines (29,30). At 6-8 weeks postpartum visit, another oGTT was performed to measure fasting glucose, 2-hr glucose and HbA1c using a High Performance Liquid Chromatography method (HPLC). At the 1-year postpartum visit, women had a fasting venous glucose and HbA1c measured using a High Performance Liquid Chromatography method (HPLC) (33). Both methods are traceable to the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Reference Method for the Measurement of HbA1c (33).

2.3 Statistical analysis

We performed all statistical analyses with the SPSS software version 26 (34). Demographic and other descriptive variables are presented as either means (±standard deviation) or in percentages (%), where appropriate (Table 1 and 2). PPWR variable and all outcome parameters described in Table 2 were normally distributed. We categorized this continuous variable (PPWR) into two groups: either no PPWR when the difference between a participant's weight before pregnancy and weight at the postpartum period (either 6-8 weeks or 1-year visit) was ≤0kg and into PPWR if the difference is ≥0.1kg.

We performed an ANOVA analysis to compare the anthropometric and metabolic characteristics (independent continuous variables) of participants according to no PPWR and PPWR (at 6-8 weeks and at 1-year postpartum) (Table 3a and 3b). In order to determine the predictors of PPWR at 6-8 weeks and at 1-year postpartum (outcome variable), we first conducted a univariate logistic regression analysis. We selected potential predictors tested in the univariate regression analyses based on the existing literature.

These variables were; age, educational level, nationality, history of GDM, family history of diabetes, parity, gravida, delivery by caesarean section, partner support, GDM treatment, contraception use, breastfeeding and depression score at the first GDM visit, pre-pregnancy weight, fasting, 1hr and 2hr glucose after oGTT at GDM diagnosis, total GWG, excess GWG according to IOM guidelines (31), fasting glucose, 2hr glucose after oGTT and HbA1c, all at 6-8 weeks postpartum. We then modeled the odds of PPWR (at the 6-8 weeks and 1-year postpartum visits) using multivariable logistic regression models with backward elimination by including variables with $p<0.25$ in the univariate regression analysis. Based on this, the following predictor variables were included in the 6-8 weeks postpartum model (Table 4a): family history of diabetes, partner support, breastfeeding and depression score at the first GDM visit, pre-pregnancy weight, 2hr glucose after oGTT at GDM diagnosis, total GWG, and excess GWG according to IOM guidelines. The following predictor variables were included in the 1-year postpartum model (Table 4b): age, family history of diabetes, partner support, depression score at the first GDM visit, total GWG, excess GWG, and HbA1c at 6-8 weeks postpartum visit. For the 1-year postpartum analysis, we made use of two models; one in parallel to the model performed at 6-8 weeks postpartum and thus without any variable obtained after delivery i.e., without HbA1c at 6-8 weeks pp (model 1) and one including significant variables after delivery, i.e. HbA1c at 6-8 weeks postpartum (model 2).

We then performed a multivariate logistic regression analysis with backward elimination and selected the regression model with the lowest Akaike information criterion (AIC) as our final model for both time points (25). We tested for collinearity of the included predictor variables, and none displayed excessive collinearity. The variance inflation factor (VIF) in the regression models were less than 2 (between 1.0-1.4), and thus acceptable. All statistical significances were two sided and accepted at $p< 0.05$.

3.0 Results

Table 1 shows the socio-demographic characteristics of the 862 study participants. Their mean maternal age and gestational age at delivery were 33.0±5.7years and 38.4±3.2weeks respectively. The majority of the study participants had a vocational or university education (68%), 28% were Swiss and 33% were Europeans or from North America (33%). In addition, 44% of the women were nulliparous. Overall, only 6% of the women had a previous history of GDM (11.6% of those were multiparous), whereas 50% had a family history of diabetes. Table 2 shows the anthropometric and metabolic characteristics of the study participants. The mean pre-pregnancy BMI was 25.6±5.4kg/m^2 and the total GWG was 12.7±5.9kg. The mean PPWR at 6-8 weeks and at 1-year postpartum were 4.6±5.7kg and 4.0±7.4kg respectively. In the subgroup of women with 1-year data, the mean fasting glucose increased by 0.48±0.2mmol/l between 6-8 weeks and 1-year postpartum, while the mean HbA1c decreased by 0.03±0.01%. Table 3a summarizes the participants' anthropometric differences and metabolic consequences according to PPWR categories at 6-8 weeks postpartum. At this time point, 81% of women had PPWR. Women with PPWR had significant higher anthropometric parameters before, during and after pregnancy (early postpartum period) compared to those with no PPWR.

Specifically, they had a 4±3.7kg higher pre-pregnancy weight, a higher pre-pregnancy BMI, a 7.5±0.2kg higher total GWG and a 0.23 ±0.1kg higher excess GWG, a higher weight at GDM diagnosis and at the end of pregnancy, as well as a 12±2.0kg higher weight at 6-8 weeks postpartum (all p≤0.02). In addition, the 2hr glucose after oGTT at GDM diagnosis was slightly higher (p=0.034). However, there were no differences in the metabolic parameters (fasting and 2h glucose, HbA1c) between both groups at the early postpartum period (all p=ns). Table 3b summarizes the participants' anthropometric differences and metabolic consequences according to PPWR categories at 1-year postpartum in the subgroup of patients (n=259/862; 30%) who had attended the 1-year postpartum visit.

At 1-year postpartum, 66.4% of women had PPWR. Compared to those with no PPWR, women with PPWR had no differences in anthropometric parameters before and during pregnancy, but had a 4±0.4kg higher total GWG, a higher BMI at 6-8 weeks and at 1-year postpartum, and were 7±4.2kg heavier at 1-year postpartum (all $p \leq 0.04$). Women with no PPWR, on the other hand, had a minimal increase in excess GWG of 0.2 ±0.03kg ($p<0.001$). In the group of women with PPWR, weight did not decrease between the early and late postpartum period. The metabolic consequences at 1-year postpartum period showed a 0.2±0.2 mmol/l higher fasting glucose in women with PPWR compared to those without PPWR, and a more pronounced increase in fasting glucose and in HbA1c between the early and late postpartum period (both $p \leq 0.03$). We also evaluated the differences in metabolic and medical characteristics at 6-8 weeks postpartum in the 259 women with complete 1-year data (supplementary Table 1). The results were similar to those in Table 3a.

3.1 Predictors of postpartum weight retention

In the multivariate logistic regression analysis (Tables 4a and 4b), higher pre-pregnancy weight and total GWG predicted higher risk of PPWR at 6-8 weeks postpartum (OR: 1.1, 95% CI: 1.03-1.15) and (OR: 1.6, 95% CI: 1.32-1.91), respectively).

Higher total GWG also predicted higher risk of PPWR at 1-year postpartum (OR: 1.15, 95% CI: 1.07-1.23; model 1). This prospective association remained significant in model 2 (OR: 1.2, 95% CI: 1.07-1.24) when HbA1c at 6-8 weeks postpartum was included as potential predictor. In model 2, higher HbA1c at 6-8 weeks postpartum (OR: 0.16, 95% CI: 0.05-0.49) was associated with less PPWR at 1-year postpartum.

4.0 Discussion

In this clinical cohort of women with GDM, we found that women with and without PPWR at 6-8 weeks postpartum differed significantly in anthropometric characteristics (weight, BMI, GWG) before, during and after pregnancy. At this time point, there were no differences regarding metabolic consequences between both groups. On the other hand, women with and without PPWR at 1-year postpartum did not differ significantly in weight or BMI before or during pregnancy, except for less pronounced differences in GWG. However, they differed in anthropometric characteristics in both the early (BMI) and late (weight, BMI) postpartum period. Regarding adverse metabolic consequences, women with late PPWR had higher fasting glucose and more pronounced increases in both fasting glucose and HbA1c between the early and late postpartum period than those without PPWR. Although excessive GWG beyond the IOM guidelines was less than 2kg, total GWG was the most important predictor of PPWR, both in the early and late postpartum period. Although women are advised to return to their pre-pregnancy weight after delivery, a significant proportion of pregnant women are unable to meet this recommendation (25,35). At 6-8 weeks postpartum for example, women with or without GDM retain an average of 3–7kg of GWG, and at least two-thirds of women will still be above their pre-pregnancy weight at 1-year postpartum (7,25). Our results are in accordance with the literature: mean PPWR at 6-8 weeks postpartum was 4.6±5.7kg and 4.0±7.4kg at 1-year postpartum and two-third (66%) of the women had PPWR at 1-year.

Given that PPWR is predictive of adverse long-term cardio-metabolic outcomes (17) in women with GDM (36,37), it is important to study the pattern of PPWR in order to develop prevention/intervention strategies and to define their optimal timing. To fill this gap, we conducted this study to determine the anthropometric differences and metabolic consequences of PPWR and the predictors of PPWR in the early and late postpartum period in a clinical cohort of women with GDM.

According to our results, women with PPWR in the early postpartum period differed in BMI and weight before, during, and after pregnancy and in GWG, whereas those with PPWR at 1-year postpartum differed in GWG and especially in BMI and/or weight during the postpartum period. In women with PPWR, we found that differences in GWG in the late postpartum period were about half of those observed in the early postpartum period. Importantly, women with PPWR in the late postpartum period had small and non-significant weight differences compared to their counterparts in the early postpartum period, but they did not continue to lose weight up to 1-year postpartum.

Several reasons could account for the differences in the anthropometric characteristics observed in women with PPWR. Excess adipose tissue due to sub-optimal diet and physical activity behaviors before/during pregnancy leads to excess weight gain that extends into the postpartum period, leading to an increased risk of obesity in the late postpartum period (38–40). Studies have also shown that women who breastfeed several months after delivery have lower PPWR due to the energy cost of producing breast milk (41). Hence, breastfeeding may potentially have an impact or at least represent a marker for beneficial lifestyle behavior in our cohort. In our cohort, 85% of women who were still breastfeeding at 6-8 weeks postpartum had no PPWR at the late postpartum period. Depressive symptoms and lower/short sleep duration could also reduce weight loss in the postpartum period by influencing energy expenditure and appetite regulation (42).

Our results are consistent with those of other studies conducted in non-GDM populations which showed that, women with PPWR had a higher GWG, leading to higher weight status in the late postpartum period (43–45). Regarding adverse metabolic consequences, differences between women with and without PPWR were seen at 1-year postpartum only. At 1-year postpartum, women with PPWR had higher fasting glucose values and more pronounced increases in metabolic parameters (increases in Δfasting glucose and ΔHbA1c) than their counterparts did.

This finding suggests that late PPWR had an impact on glucose control at 1-year postpartum, which might not reveal itself yet in the early postpartum period. It is thus essential to focus on prevention of PPWR at 1-year postpartum, which actually concerns two thirds of women in this cohort and previous ones. A lack of PPWR or of metabolic complications at 6-8weeks postpartum, although reassuring, should not lead to complacency. This is especially important, as only a minority continues to lose weight after the early postpartum period and those with PPWR at 1-year demonstrated a small weight gain, between the early and late postpartum period. The findings of one previous study parallels our results (17): it demonstrated that weight gain in the 1-year postpartum was associated with a significant increase in fasting and 2-h glucose in women with GDM.

The link between PPWR and deteriorations in glucose control is mediated by the lack of further, more pronounced, weight loss during the later postpartum period (38). Lack of sleep in the postpartum period also increases insulin resistance in women with PPWR by impacting on metabolic pathways (42). Our data showed that clinical care beyond a pure screening with a focus on metabolic health should be essential in the late postpartum. Importantly, even women without PPWR had a significant ($p<0.001$) increase in fasting glucose between the early and late postpartum period, despite almost a 3kg weight loss.

These findings suggest the need to extend the postpartum follow-up period from 6-8 weeks to at least 1-year with special focus on metabolic health.

In women with GDM, a previous study (25) demonstrated that less GWG, increasing age, and lack of insulin use during pregnancy were associated with losing ≥75% of pregnancy weight at 6-8 weeks postpartum. In our study, GWG was associated with PPWR, but found no association with age or insulin use. In non-GDM populations, many studies support GWG as a strong and pronounced predictor of PPWR at 6 weeks (46) and up to 12 months postpartum, as found in our study (47–50).

Other studies indicate that exceeding IOM guidelines according to pre-pregnancy BMI increases the risk of PPWR at 6 to 18 months (51–53). To our knowledge, these latter studies only investigated excessive GWG without including total or absolute GWG. In our study however, exceeding IOM guidelines (=excessive GWG) was not associated with PPWR beyond the impact of total GWG. Total GWG was the most important predictor of PPWR in our cohort, although excess GWG beyond the IOM guidelines was less than 2kg, even in women with PPWR. These data suggest that, at least regarding postpartum weight and metabolic health, the currently existing IOM guidelines for GWG are too indulgent for a multicultural population with GDM and should be refined for these women. Other potential predictors of PPWR, such as sociodemographic characteristics, physical activity, eating behavior (intuitive eating) exclusive breastfeeding, and depression scores during and after pregnancy were not significantly associated with PPWR in our study in contrast to some studies in non-GDM populations (44,54,55).

This study has several strengths. This is the first study to investigate the anthropometric differences and metabolic consequences in women with and without PPWR in both the early and late postpartum period in a large clinical cohort of women with GDM. We also identified the most essential role of GWG on PPWR in these women. This study seems to be the first to investigate both total GWG and excess GWG based on IOM guidelines on PPWR, as most studies focus exclusively on excess GWG. Excess GWG is based on guidelines that may be subject to change. Indeed, in our cohort, total GWG has shown to have a more important role than excess GWG. One of the limitations of this study is that, the associations found in this study may be correlational and not necessarily causal, despite its prospective design. We obtained weight before pregnancy from patients' medical chart when available; otherwise, we relied on self-reported pre-pregnancy weight.

However, there was a strong correlation between clinically measured weight during and after pregnancy with self-reported pre-pregnancy weight. Other factors, such as the intention to lose weight in the postpartum period and a variety of other variables, including sleep in the postpartum period, which were not investigated in this study, may have influenced these associations.

5.0 Conclusion

In this prospective clinical cohort of women with GDM, 81% had PPWR at 6-8 weeks postpartum, whereas two-third had PPWR at 1-year postpartum. Women with PPWR in the early postpartum period showed significant differences in anthropometric characteristics (weight, BMI, GWG) before, during and after pregnancy, while those in the late postpartum period showed mainly differences in the postpartum. Importantly, adverse metabolic consequences between women with and without PPWR were only seen in the late postpartum period. Regarding predictors of PPWR, total GWG was the most important predictor of PPWR, beyond the impact of excess GWG, which was rather small. These results suggest that currently existing IOM guidelines for (excess) GWG maybe too relaxed concerning postpartum weight and metabolic health in these women. Our data regarding PPWR and metabolic health suggest that beyond the recommended postpartum screenings, there is a need for a continuous follow-up of women with GDM, focusing specifically on weight and glucose control.

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Conflict of interest

Authors declare that there is no conflict of interest.

Author contribution

DYQ, JG and JP designed the study. DYQ, extracted the data, performed all the analysis and wrote the draft manuscript under the supervision of JP. JG, LG, AA, AH and JP reviewed the manuscript. All authors revised and accepted the manuscript for submission. JP had the idea of the cohort and co-supervised all the work with AH.

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STUDY 3 Tables and captions

Table 1: Socio-demographic characteristics of study participants (N=862)

Variable	Frequency (n)	Percent (%)
Age (years) *mean ±SD*	33.00	5.71
Gestational age at delivery (weeks) *mean ±SD*	38.43	3.23
Education level* (N=488)		
No formal education	3	0.8
Compulsory school achieved	69	18.4
High school	47	12.6
General and vocational education	85	22.7
University	170	45.5
Nationality		
Switzerland	247	28.7
Europe + North America	285	33.1
Africa	143	16.6
Asia + western pacific	116	13.5
Latin America	39	4.5
Others	32	3.7
Employment status		
Student	23	2.7
Professional worker	388	45.0
Housewives/unemployed	451	52.3
Smoking during pregnancy		
Yes	132	15.3
No	730	84.7
Previous history of GDM[1]		
No	807	93.6
Yes	55	6.4
Family history of diabetes[2]		
First degree	272	31.5
Second degree	160	18.6
No	430	49.9
Parity (N=842)		
0	375	44.5
1	283	33.6
2	119	14.1
≥3	65	7.7
Gravida (N=842)		
1	257	30.5
2	247	29.3
3	338	40.1

[*]488 participants had missing data on education

[1]GDM means gestational diabetes mellitus (11.6 % of women who were multiparous had previous history of GDM)

[2]First degree means 1 degree of relationship of the participant (at least 50% of genetic link, which included mother, father, brother, sister, daughter, son). Second degree means 2nd degree of kinship of the participant (at least 25% of genetic link that included grandparents, grandchildren, nephews, niece, half-brother, half-sister)

All results are frequency and percentage unless otherwise stated

Table 2: Anthropometric and metabolic characteristics of study participants

Variable	Mean	SD
Pre-pregnancy weight (Kg)	69.09	15.38
Pre-pregnancy BMI (Kg/m^2)[1]	25.62	5.45
Weight at the first GDM visit (Kg)	79.53	15.36
BMI at the first GDM visit (Kg/m^2)	29.72	5.41
Fasting glucose at the first GDM visit (mmol/l)	5.15	0.75
1hr glucose after oGTT at GDM diagnosis (mmol/l)	9.63	1.85
2hr glucose after oGTT at GDM diagnosis (mmol/l)	7.85	1.83
HbA1c at the first GDM visit (%)	5.44	0.41
Weight at the end of pregnancy (Kg)	81.86	15.42
Total gestational weight gain (Kg)	12.75	5.96
Weight at the 6-8 weeks pp (Kg)	73.58	15.05
BMI at the 6-8 weeks pp (Kg/m^2)	27.54	5.35
Fasting glucose at the 6-8 weeks pp (mmol/l)	5.00	0.52
2hr glucose after oGTT at 6-8 weeks pp (mmol/l)	5.50	1.68
HbA1c at the 6-8 weeks pp (%)	5.35	0.38
Weight at 1-year pp (Kg)	73.49	17.15
BMI at 1-year pp (Kg/m^2)	27.41	6.30
Fasting glucose at 1-year pp (mmol/l)	5.48	0.67
HbA1c at 1-year pp (%)	5.32	0.39
Weight retention at 6-8 weeks pp[2]	4.61	5.79
Weight retention at 1-year pp[3]	3.99	7.36

[1]Data taken from the medical charts or reported at the first GDM visit
[2]Weight retention means the difference in weight at 6-8 weeks postpartum and pre-pregnancy weight
[3]Weight retention means the difference in weight at 1-year postpartum and pre-pregnancy weight
BMI means body mass index
GDM means gestational diabetes mellitus
oGTT means oral glucose tolerance test
HbA1c means glycated hemoglobin
pp means postpartum period

Table 3: Anthropometric differences and metabolic consequences of participants according to postpartum weight retention categories

3a: At 6-8 weeks postpartum

6-8 weeks postpartum	**Weight retention category at 6-8 weeks PP (n=862)[1]**				
	Weight retention (n=700)		**No weight retention (n=162)**		
Variable	**Mean**	**SD**	**Mean**	**SD**	**p value**
Age (years)	33.39	5.43	32.91	5.77	0.340
Gestational age at delivery (weeks)	38.68	1.49	38.38	3.52	0.283
Pre-pregnancy weight (Kg)	70.49	17.51	66.76	13.81	**<0.001**
Pre-pregnancy BMI (Kg/m^2)[2]	26.35	6.26	24.75	4.86	**<0.001**
Weight at the first GDM visit (Kg)	80.93	16.96	71.45	14.76	**<0.001**
Fasting glucose at first GDM visit (mmol/l)	5.16	0.65	5.15	0.77	0.843
1hr glucose after oGTT at GDM diagnosis (mmol/l)	9.70	1.70	9.62	1.88	0.658
2hr glucose after oGTT at GDM diagnosis (mmol/l)	8.18	1.70	7.78	1.85	**0.034**
Weight at the end of pregnancy (Kg)	84.63	16.66	73.58	14.23	**0.015**
Total gestational weight gain (Kg)	14.16	5.14	6.63	5.36	**<0.001**
Excess gestational weight gain (Kg)	1.73	0.44	1.50	0.50	**<0.001**
Weight at 6-8 weeks pp (Kg)	75.40	16.66	63.14	14.62	**0.002**
BMI at 6-8 weeks pp (Kg/m^2)	27.10	5.91	23.40	5.19	**0.020**
Fasting glucose at 6-8 weeks pp (mmol/l)	4.99	0.50	5.01	0.52	0.643
2hr glucose after oGTT at 6-8 weeks pp (mmol/l)	5.37	1.57	5.53	1.70	0.269
HbA1c at 6-8 weeks pp (%)	5.32	0.40	5.35	0.37	0.357

[1]Weight retention means the difference in weight at 6-8 weeks and pre-pregnancy weight
[2]Data reported at the first GDM visit or taken from the medical charts
GDM means gestational diabetes mellitus
BMI means body mass index
oGTT means oral glucose tolerance test
HbA1c means glycated hemoglobin
pp means postpartum period
P value derived from ANOVA for continuous variables

3b: At 1-year postpartum

1-year postpartum	Weight retention category at 1-year PP (n=259)[1]				
	Weight retention (n=172)		No weight retention (n=87)		
Variable	**Mean**	**SD**	**Mean**	**SD**	**p value**
Age (years)	32.93	5.86	34.00	4.74	0.147
Gestational age at delivery (weeks)	38.78	1.71	38.82	1.86	0.888
Pre-pregnancy weight (Kg)	68.78	15.42	69.97	14.10	0.564
Pre-pregnancy BMI (Kg/m^2)[2]	25.81	5.67	25.62	5.18	0.792
Weight at the first GDM visit (Kg)	80.28	15.97	78.58	13.48	0.427
Fasting glucose at first GDM visit (mmol/l)	5.24	1.00	5.11	0.77	0.328
1hr glucose after oGTT at GDM diagnosis (mmol/l)	9.68	2.00	9.61	1.96	0.817
2hr glucose after oGTT at GDM diagnosis (mmol/l)	7.85	2.02	7.99	1.85	0.651
Weight at the end of pregnancy (Kg)	82.82	15.47	80.02	13.60	0.188
Total gestational weight gain (Kg)	14.16	6.15	10.08	5.76	**<0.001**
Excess gestational weight gain (Kg)	1.44	0.49	1.68	0.46	**<0.001**
Weight at 6-8 weeks pp (Kg)	74.88	14.92	71.96	13.01	0.121
BMI at 6-8 weeks pp (Kg/m^2)	28.08	5.36	26.66	4.66	**0.044**
Fasting glucose at 6-8 weeks pp (mmol/l)	5.00	0.518	4.97	0.45	0.618
2hr glucose after oGTT at 6-8 weeks pp (mmol/l)	5.26	1.42	5.22	1.63	0.841
HbA1c at 6-8 weeks pp (%)	5.27	0.36	5.40	0.34	**0.009**
Weight at 1-year pp (Kg)	75.79	18.08	68.67	13.92	**0.002**
BMI at 1-year pp (Kg/m^2)	28.42	6.55	25.05	4.93	**<0.001**
Fasting glucose at 1-year pp (mmol/l)	5.55	0.72	5.35	0.55	**0.026**
HbA1c at 1-year pp (%)	5.33	0.42	5.31	0.33	0.739
ΔFasting glucose[3]	0.54	0.61	0.37	0.54	**0.032**
ΔHbA1c[3]	0.05	0.39	-0.08	0.37	**0.006**

[1]Weight retention means the difference in weight at 6-8 weeks and pre-pregnancy weight
[2]Data reported at the first GDM visit or taken from the medical charts
[3]Change in metabolic variables (fasting glucose and HbA1c) between 6-8 weeks and 1-year pp
GDM means gestational diabetes mellitus
BMI means body mass index
oGTT means oral glucose tolerance test
HbA1c means glycated hemoglobin
pp means postpartum period
P value derived from ANOVA for continuous variables

Table 4: Predictors of weight retention

4a: Predictors at 6-8 weeks postpartum

Variable	OR	95% CI		P value*
Pre-pregnancy weight (Kg)	1.09	1.035	1.150	**<0.001**
Total gestational weight gain (Kg)	1.59	1.324	1.919	**<0.001**
Excess gestational weight gain (Kg)	4.08	0.857	19.466	0.077

Weight retention means the difference in weight at 6-8 weeks postpartum and pre-pregnancy weight
* P value from the final model of the multivariable logistic regression with backward elimination

4b: Predictors at 1-year postpartum

	Model 1				Model 2			
Variable	**OR**	**95% CI**		**P value***	**OR**	**95% CI**		**P value***
Total Gestational weight gain (kg)	1.15	1.072	1.231	**<0.001**	1.15	1.076	1.245	**<0.001**
HbA1c at 6-8 weeks pp (%)					0.16	0.052	0.490	**<0.001**

pp means postpartum period
Weight retention means the difference in weight at 1-yr postpartum and pre-pregnancy weight
Model 1: included HbA1c at 6-8 weeks pp
Model 2: without HbA1c at 6-8 weeks pp
* P value from the final model of the logistic regression with backward elimination

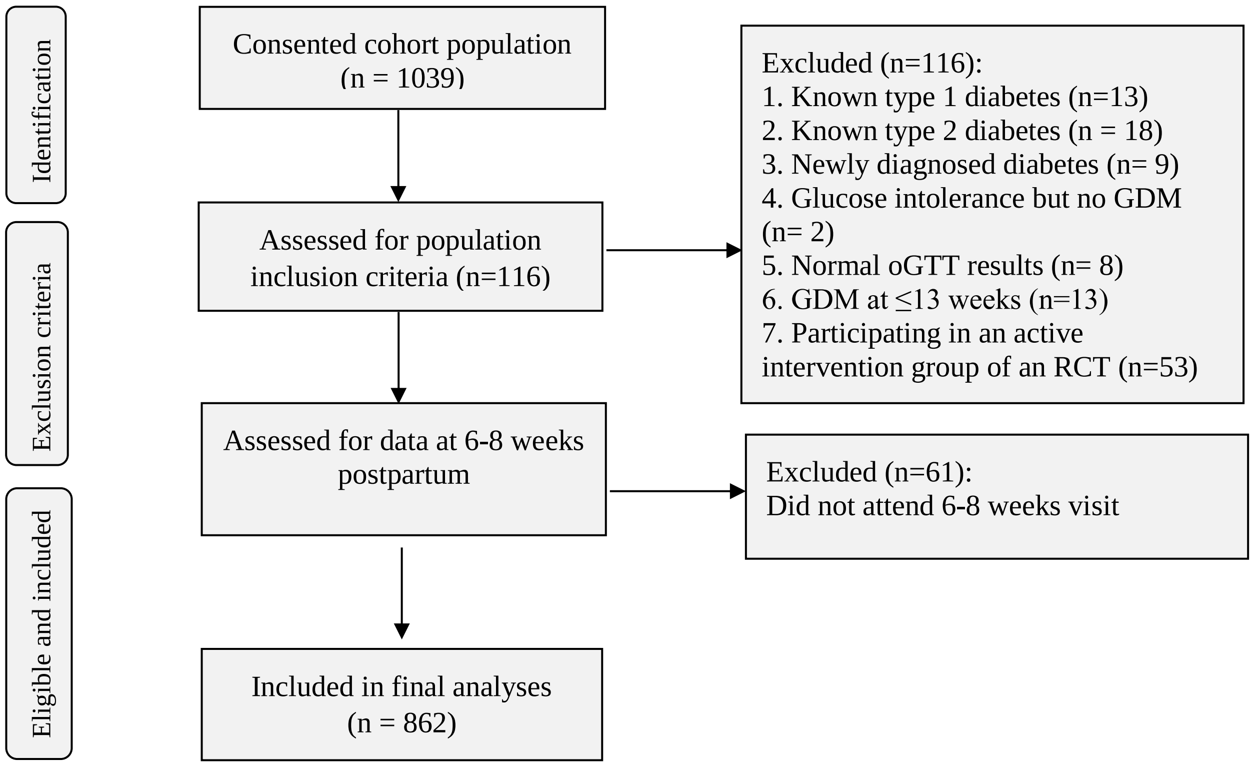

Fig 1. Flow chart describing the selection of study participants

[Supplementary tables]

Table 1: Anthropometric differences and metabolic consequences of participants with 1-year data at the 6-8 weeks postpartum

6-8 weeks postpartum*	**Weight retention at 1-year (n=259)[1]**				
	Weight retention (n=201)		**No Weight retention (n=58)**		**p value**
Variable	**Mean**	**SD**	**Mean**	**SD**	
Age (years)	33.33	5.42	33.27	5.42	0.937
Gestational age at delivery (weeks)	39.03	1.85	38.72	1.85	0.238
Pre-pregnancy weight (Kg)[2]	72.83	12.19	65.69	12.19	**<0.001**
Pre-pregnancy BMI (Kg/m^2)[3]	27.15	4.38	24.47	4.38	**<0.001**
Weight at first GDM visit (Kg)	78.06	13.95	69.87	13.95	**<0.001**
Fasting glucose at first GDM visit (mmol/l)	5.25	0.96	5.18	0.96	0.631
1hr glucose at GDM diagnosis (mmol/l)	9.84	2.02	9.61	2.02	0.527
2hr glucose at GDM diagnosis (mmol/l)	8.13	1.99	7.83	1.99	0.394
HbA1c at first GDM visit (%)	5.50	0.41	5.39	0.41	0.079
End of pregnancy weight (Kg)	86.33	13.83	71.61	13.83	**0.014**
Gestational weight gain (Kg)	14.54	5.26	6.72	5.26	**<0.001**
Excess gestational weight (Kg)	1.68	0.50	1.47	0.50	**0.004**
Weight at 6-8 weeks pp (Kg)[4]	77.58	13.39	63.84	13.39	**0.026**
BMI at 6-8 weeks pp (Kg/m^2)	28.04	4.72	24.21	4.72	**0.019**
Fasting glucose at 6-8 weeks pp (mmol/l)	4.92	0.50	5.01	0.50	0.253
2hr glucose at 6-8 weeks pp (mmol/l)	5.04	1.47	5.30	1.47	0.242
HbA1c at 6-8 weeks pp (%)	5.34	0.35	5.30	0.35	0.450

*Data at 6-8 weeks are shown for the subgroup of participants who have valid data at 1 year postpartum
[1]Weight retention means the difference in weight at 6-8 weeks and pre-pregnancy weight
[2]Data reported at the first GDM visit or taken from the medical charts
GDM means gestational diabetes mellitus
BMI means body mass index
oGTT means oral glucose tolerance test
HbA1c means glycated hemoglobin
pp means postpartum period
P-value derived from ANOVA