Year : 2121

Maternal mental and metabolic health during the perinatal period

Gilbert Gilbert

UNIL | Université de Lausanne
Faculté de biologie et de médecine

Département de Médecine

Maternal mental and metabolic health during the perinatal period

Thèse de doctorat ès sciences de la vie (PhD)

présentée à la

Faculté de biologie et de médecine
de l'Université de Lausanne

par

Leah GILBERT

Master en psychologie de l'enfant et de l'adolescent (MSc), Université de Lausanne, Suisse.

Jury

Prof. Nicole Sekarski-Hunkeler, Présidente
Prof. Jardena Puder, Directrice de thèse
Prof. Antje Horsch, Co-directrice de thèse
Prof. Nadine Messerli, Experte
PD Dr med. François Jornayvaz, Expert

Lausanne
2021

UNIL | Université de Lausanne
Faculté de biologie et de médecine

Département de Médecine

Maternal mental and metabolic health during the perinatal period

Thèse de doctorat ès sciences de la vie (PhD)

présentée à la

Faculté de biologie et de médecine
de l'Université de Lausanne

par

Leah GILBERT

Master en psychologie de l'enfant et de l'adolescent (MSc), Université de Lausanne, Suisse.

Jury

Prof. Nicole Sekarski-Hunkeler, Présidente
Prof. Jardena Puder, Directrice de thèse
Prof. Antje Horsch, Co-directrice de thèse
Prof. Nadine Messerli, Experte
PD Dr med. François Jornayvaz, Expert

Lausanne
2021

UNIL | Université de Lausanne
Faculté de biologie et de médecine

Ecole Doctorale
Doctorat ès sciences de la vie

Imprimatur

Vu le rapport présenté par le jury d'examen, composé de

Président·e	Madame	Prof.	Nicole	**Sekarski-Hunkeler**
Directeur·trice de thèse	Madame	Prof.	Jardena	**Puder**
Co-directeur·trice	Madame	Prof.	Antje	**Horsch**
Expert·e·s	Madame	Prof.	Nadine	**Messerli**
	Monsieur	Dr	François	**Jornayvaz**

le Conseil de Faculté autorise l'impression de la thèse de

Madame Leah Gilbert

Maîtrise universitaire ès Sciences en psychologie en psychologie, Université de Lausanne

intitulée

Maternal mental and metabolic health during the perinatal period

Date de l'examen : 13 janvier 2021

Date d'émission de l'imprimatur : Lausanne, le 11 février 2021

pour le Doyen
de la Faculté de biologie et de médecine

Prof. Niko GELDNER
Directeur de l'Ecole Doctorale

I. ACKNOWLEDGEMENTS

Surround yourself with the dreamers and the doers, the believers and thinkers, but most of all, surround yourself with those who see greatness within you, even when you don't see it yourself - Edmund Lee

This quote fits the people I would like to thank perfectly. First of all, I would like to thank my supervisor Jardena Puder and my co-supervisor Antje Horsch for giving me the opportunity of conducting this thesis. Throughout the years you have taught me to be brave, independent and strong; you have helped me evolve tremendously as a person and a scientist during my PhD and I will be forever grateful. Antje, I have known you the longest, and without you, I would never have known about this PhD position, you have been my greatest supporter since we met in September 2014, I am thankful beyond words. I still remember, with a smile on my face, my first interview with Jardena pretending to be a pregnant and stubborn lady and asking me to conduct a "motivational interview" on the spot; since then you have taught me to be quick on my feet and ready for any situation.

Besides my supervisors, I would like to thank Professor Nicole Sekarski-Hunkeler, Professor Nicole Messerli and Privatdozent François Jornayvaz for accepting to be my thesis' committee and for critically evaluating my work and giving me valuable guidance during my half-thesis exam.

A wholehearted thanks goes to the *MySweetHeart* team, the collaborators, the clinicians, the parents and children taking part in our study. I would like to thank Doctors Stefano Lanzi & Amar Arhab for being the great big brothers I have always dreamed of having; I thank them for their emotional support, advice and laughs we shared throughout my thesis. A special thanks goes to Justine Gross who has helped me find everything I needed to help coach the patients, helped me improve my documents by making them look beautiful and for the way you have always found solutions to every imaginable problem, Justine; you have made my PhD smoother and my motherhood less stressful. I would also like to thank Olivier LeDizès and Magali Andrey for the discussions we had about the patients and the jokes we shared. Olivier, I even sometimes regret quitting smoking as I miss our daily cigarettes together. Thanks also to Dan Quansah for the friendship we have built throughout the years even if we had a rocky start; you have clearly become one of my go-to guys for any worry or scientific question I might have and I treasure our laughs and the emotional support you bring me. The *MySweetHeart trial* would not have been as fun without the help of the student interns I co-supervised and for that I thank Giada Ostinelli, Agnès Bacso, Chloé Beutler, Michelle Grossglauser, Marie-Josée Meuwly, Svenia Quieros, Seyda Demircan, Lucia Volpato, Cécile Bétrix, Victoria Gendre, Axelle Bourgeois, Arnaud Gruélat, Aude Guex-Crosier, Nivitha Sivaneshan, Laurie Schwab and Giada Maspoli.

Indeed, I think supervising young scientists has taught me a lot about how to manage a team and how human interactions play a tremendous role in the science worlds. My early morning testings would also not have been as easy to go through without the ever smiling and positive minded Dominique Stulz, Debora Degen and Linda Elvins. I would specifically like to thank Dominique for accepting me in the team, as you have the strongest veto power, but also for sharing personal feelings about life and about the team work. Debora and Linda, thank you so much for being so reactive, for telling me when you felt things were not going in the right direction and for your extreme adaptability. Another great team which I was lucky enough to accompany to London in 2019 was the Lausanne Perinatal Research Group with Vania Sandoz, Camille Deforges and Suzannah Ravenscroft, these three women are exceptional scientists and always integrated me as a part of their team. Thanks to Vania and Camille who have also helped me in the correction of this thesis.

Nothing would have been the same without my pillar and mentor Professor Valerie D'Acremont. If someone were to ask me what kind of professor I would like to be in the future, I would have to say I want to be as close to you as I can. You have given me precious advice you have taught me to say no, to be strong and to get what I needed to go through the thesis. You have empowered me in my professional and personal life and I hope we can keep this precious relationship.

Thanks to the Gilbert and Sägesser families for your advice and your enormous support and encouragements throughout this thesis. Mum and Dad thanks for always believing in my capacities and teaching me from a young age to be curious about everything, this has helped build the scientist I am today, also thanks for your help regarding my spelling mistakes. Thanks also for the education you gave me, which has served me to a great extent through the thesis process. Andrea, my sister, thanks for teaching me to take some time for myself, and for creating the *MySweetHeart* recruitment video. Thanks to my best friend and man of honor Fanneau Lecygne for our time together, you have kept me re-freshed and positive minded all along. Improvizanyon, you are like a family to me and without our get-togethers which have absolutely nothing to do with science I would have not had the "breather" I needed.

Finally, the biggest thanks go to my husband Yannick Sägesser for supporting me throughout all my endeavors, this thesis would have been much harder if you weren't there to reassure me and empower me on a daily basis. Your advice has been precious and your presence was essential! You are my rock, you are my best friend and I cannot believe how lucky I am to have a man like you by my side.

I also cannot believe how lucky we are to have become the parents of our beautiful and cheeky little girl, Ariane. Ariane, you have taught me more than anyone ever could, you bring a smile to my face

every time I think of you and you probably are the most knowledgeable baby on GDM; I guess it may even be one of your first words. You have been to a lot of “acqua conferences” and you seemed to like them and now you are on your own path of adventures and I am sure you are going to be awesome at everything you do!

II.I ABSTRACT (ENGLISH)

Aims

This thesis aimed to understand the role of psychosocial well-being (self-efficacy, social support and mental health; comprised of both depression and well-being scores) in women with gestational diabetes mellitus (GDM) by **1**: conducting an integrative review synthetizing previous research on how diet, physical activity and psychosocial well-being interact and which type of intervention (psychosocial well-being, diet or physical activity) lowers adverse outcomes associated with GDM, **2**: testing the effects of a novel interdisciplinary and psychosocial well-being intervention created on the basis of the results of 1, in the form of a randomized controlled trial (RCT) protocol and, **3**: investigating the evolution of mental health and, **4**: its association with weight, weight gain and the need for glucose-lowering medication in two prospective clinical cohort studies.

Methods

The search strategy for aim 1 included carefully selected terms that corresponded to domains of interest in women with GDM. For aim 2, the efficacy of a the new intervention is tested by comparing its health outcomes to a control group. Aims 3 and 4 are based on a prospective clinical cohort of women diagnosed with GDM attending a Swiss University Hospital. The outcomes include self-report questionnaires and data which was extracted from the patient's medical records.

Results

The review showed that even if psychosocial well-being was positively associated with lifestyle behaviors, it was not a part of previous lifestyle interventions. These lifestyle interventions mostly improved diet and physical activity, psychological factors and some metabolic outcomes. The data collection for the RCT is still ongoing. Mental health evolved positively between GDM diagnosis and 6-8 weeks postpartum. Only clinically relevant symptoms of depression after GDM diagnosis were associated to subsequent weight gain in pregnancy. There were no other association between mental health and weight or weight gain in pregnancy. Mental health symptoms and glucose-lowering medication did not influence each other in an unfavorable way.

Clinical implications

This thesis focused on the field of psychosocial well-being in women with GDM, which is still insufficiently studied today. The results demonstrate that psychosocial well-being has an impact on lifestyle behaviors and on some of the investigated metabolic outcomes (i.e. weight gain). Hence, women with GDM should be screened for mental health symptoms and treated accordingly.

II.II RESUME (FRANCAIS)

Objectifs

Cette thèse a étudié le rôle du bien-être psychosocial (l'efficacité de soi, le soutien social et la santé mentale ; contenant des scores de dépression et de bien-être) chez les femmes atteintes de diabète gestationnel (DG) **1** : en menant une revue intégrative de la littérature explorant l'interaction entre la diététique, l'activité physique et le bien–être psychosocial et quel type d'intervention (psychosocial, diététique et activité physique) réduit le plus les risques liés au DG, **2** : en testant les effets d'une nouvelle intervention interdisciplinaire et psychosociale, élaborée à partir des résultats de 1, par un protocole d'essai randomisé contrôlé (ERC) et **3** : en investiguant l'évolution de la santé mentale et **4** : son impact sur le poids, la prise de poids et le besoin de médicaments réduisant la glycémie, par des études observationnelles de cohorte clinique et prospectives.

Méthodes

Les recherches pour l'objectif 1 se sont basées sur un choix de mots clefs relatifs à des domaines d'intérêt dans le DG. Pour l'objectif 2, l'efficacité de la nouvelle intervention a été testée en comparant ses impacts sur la santé avec ceux du groupe contrôle. Les objectifs 3 et 4 ont étudié une cohorte de femmes ayant un DG du Centre Hospitalier Universitaire Vaudois. Les variables ont été mesurées par des questionnaires auto-reportés et par des données extraites des dossiers médicaux des patientes.

Résultats

La revue a démontré que le bien-être psychosocial était associé positivement à l'activité physique et aux choix diététiques, mais il n'était pas un composant des interventions à ce jour. Pour la plupart, les interventions amélioraient la diététique, l'activité physique, des données psychologiques et certains résultats métaboliques. La récolte de données de l'ERC n'est pas encore terminée. La santé mentale a évolué positivement entre le diagnostic de DG et 6-8 semaines postpartum. Seuls les symptômes de dépression après le diagnostic de DG étaient associés à une prise de poids ultérieure. Il n'y avait pas d'autres associations entre la santé mentale et le poids pendant la grossesse. La santé mentale et les médicaments réduisant la glycémie n'avaient pas d'impact négatif l'une sur l'autre.

Implications cliniques

Cette thèse portait sur le bien-être psychosocial dans le DG, qui est une thématique sous-étudiée. Les résultats indiquent que le bien-être psychosocial impacte les comportements de santé et des variables métaboliques testées (par ex. la prise de poids). Un dépistage de dépression dans cette population devrait être systématique, ainsi qu'un plan de traitement, mis en place, le cas échéant.

III. Table of contents

IV. GLOSSARY AND DEFINITIONS

LIFESTYLE BEHAVIORS/LIFESTYLE INTERVENTIONS – In this thesis, as in most scientific articles in women with GDM, this term regroups diet and physical activity behaviors or interventions that contain specific health goals for diet and physical activity [1-14]. This term is mostly used in studies A and B.

PSYCHOSOCIAL WELL-BEING – Similarly to previous reviews, in this thesis, "psychosocial well-being" will be used as an umbrella term, which will regroup mental health and mental health symptoms as well as social support and self-efficacy [15]. In previous research, this term also regrouped mental health and social well-being [16], social support [17] and self-efficacy [18]. When psychosocial well-being is low, for example, in cases of social marginalization, mental health symptoms, such as depression, can arise [19, 20] and it can also affect an individual's self-efficacy [21]. Thus, mental health symptoms (such as symptoms of depression) are also contained in that term for the purpose of this thesis. Psychosocial well-being is discussed in detail in study A and in study B and may be used as a predictor or an outcome in this thesis.

MENTAL HEALTH – This term is used as a construct and regroups positive (i.e. well-being) and negative (i.e. depression) concepts related to mental health. Generally, mental health is described as "*a state of well-being in which the individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community*" [22]. It derives from positive psychology as it is not only a lack of illness but also a presence of well-being [23]. Mental health can also be seen as the positive end of a continuum between mental illness and mental health [23], where an absence of mental health could, to that end, mean a presence of depression. Similarly to this thesis, previous descriptions of mental health contained mental health symptoms such as depression [24, 25]. The validated and self-report questionnaires used to measure well-being and depression in this thesis are described in detail in studies C and D.

MENTAL HEALTH SYMPTOMS – This term regroups only negative mental health, such as symptoms of depression or low well-being. In the literature, mental health symptoms usually also comprise symptoms such as depression, which may lead to an impairment in daily life functioning [26].

SELF-EFFICACY – As in this thesis, this concept generally describes a person's beliefs in his/her ability to influence events that affect his/her life, which allow performance accomplishments, motivation, and emotional well-being [27]. Also, self-efficacy is associated with health related choices and self-care in the domains of diet, physical activity and blood glucose testing in populations with diabetes [28, 29].

SOCIAL SUPPORT – In this thesis, the term social support will regroup all forms of help a woman with GDM can get either from her family, friends or from professionals [30]. Social support from family and friends has been shown to be an enabler, as well as a barrier, to conduct healthy lifestyle behaviors in women with GDM. Studies show that if family and friends have unhealthy lifestyle behaviors this may be a barrier for women to have healthy behaviors [31]. Therefore, an integration of the family in lifestyle interventions may offer more efficient social support which may then lead to an overall healthier lifestyle and peer support may also allow emotional support for women with GDM [32].

V. LIST OF FIGURES

VI. LIST OF TABLES

VII. LIST OF ABBREVIATIONS

ADA: American Diabetes Association

AH: Antje Horsch

BMI: Body Mass Index

CBT: Cognitive Behavioral Therapy

CHUV: Centre Hospitalier Universitaire Vaudois

DYQ: Dan Yedu Quansah

EPDS: Edinburgh Postnatal Depression Scale

FPG: Fasting Plasma Glucose

GDM : Gestational Diabetes Mellitus

HAPA: Health Action Process Approach

HbA1c : Glycated Hemoglobin

HDL: High-Density Lipoprotein (cholesterol)

IADPSG: International Association of Diabetes and Pregnancy Study Groups

JBI: Joanna Briggs Institute

LDL: Low-Density Lipoprotein (cholesterol)

LG: Leah Gilbert

LGA: Large for Gestational Age (at birth)

NICE: National Institute for Health and Care Excellence

oGTT: oral Glucose Tolerance Test

RCT: Randomized Controlled Trial

WHO-5: World Health Organization well-being index - Five

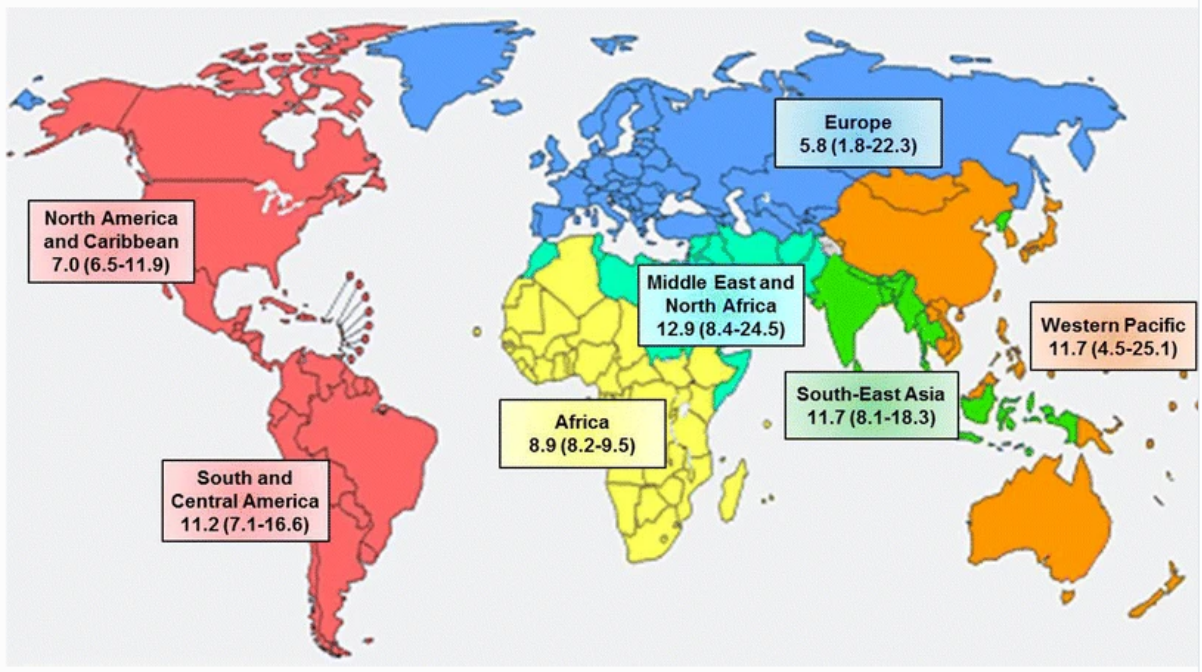
1. INTRODUCTION

1.1 Gestational Diabetes Mellitus definition

Gestational Diabetes Mellitus (GDM) is described as a glucose intolerance diagnosed in the second or third trimester of pregnancy that does not fulfil the criteria of type 1 or type 2 diabetes [34, 35]. This illness affects around 12% of pregnancies worldwide and these rates have augmented over time [36].

In Switzerland, 10.8% of women are diagnosed with GDM during pregnancy [37]. These rates are comparable to what can be found in other countries; 9.2% in the USA [38], 6.8% in China [39], 16.3% in Qatar [40] and 7.8% in an ethnically diverse population [41] (see Figure 1).

Figure 1. Median prevalence (%) of GDM by WHO region 2005–2015 [33].



Although these rates vary around 10%, the prevalence of GDM has increased in the past years. In the United States, GDM rates have doubled between 1994 and 2002 [42] and the prevalence of GDM has increased by 16 to 127% worldwide [43]. These numbers underline the importance of screening for GDM, as this illness can have multiple impacts on the mother and the infant.

1.2 GDM screening in pregnancy

GDM screening is subject to different recommendations worldwide. This thesis will focus on two very important and widely used recommendations that have also been the base for the Swiss Recommendations [44, 45]. Therefore, the thesis will only discuss the IADPSG (International

Association of Diabetes and Pregnancy Study Groups) and ADA (American Diabetes Association) recommendations.

Both the recommendations of the IADPSG and the American Diabetes Association (ADA), derive from the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) study: a large-scale multinational cohort study (*n*=23'000) [46]. Both advocate an universal screening at 24-28 weeks of gestation. The IADPSG recommends a one-step approach to test for GDM at 24-28 weeks of gestation using an oGTT (oral Glucose Tolerance Test) test with 75g of glucose [46]. The diagnosis of GDM is established when any of the following plasma glucose values are met or exceeded; FPG: 92 mg/dL (5.1 mmol/L), one hour: 180 mg/dL (10.0 mmol/L), two hour: 153 mg/dL (8.5 mmol/L). The ADA recommends either the same one-step approach or a two-step approach, as recommended by their panel of the National Institutes of Health in 2013 [47]. Thereby, there is an initial screening test using a 1h 50g glucose load test and for women that find themselves above a certain threshold (mostly around 7.8 mmol/l) this initial screening is followed by a 3h 100g oGTT [35].

In this thesis, the studied population comes from the Centre Hospitalier Universitaire Vaudois (CHUV) situated in Lausanne, Switzerland. Women either directly undergo a 75 g oGTT or are initially screened with their FPG levels. If their fasting glucose is ≥5.1 mmol/l, they do not need to undergo the oGTT. The cut-offs used to diagnose GDM are in accordance with the IAPDSG and Swiss Recommendations [45, 46].

1.3 Risk factors for GDM and the role of psychosocial well-being

Even though insulin sensitivity decreases in the second and third trimester of pregnancy in all women [48, 49] and thereby the universal screening for GDM should be performed for all pregnant women, some subjects are at higher risk than others. The ADA describes women that are considered at risk for GDM with the following criteria: overweight or obese women who have one or more of the following conditions; BMI ≥ 25 kg/m^2, or ≥ 23 kg/m^2 in Asian-Americans, diabetes in first degree relatives, high risk ethnicities (such as African American, Latino, Native American, Asian American, Pacific Islander), history of cardiovascular disease, hypertension, HDL (High-Density Lipoprotein) cholesterol level < 35 mg/dL (0.90 mmol/L) and/or a triglyceride level > 0.250 mg/dL (2.82 mmol/L), polycystic ovary syndrome, physical inactivity or other clinical conditions associated with insulin resistance [50]

Currently research corroborates these criteria established by the ADA. However, research also shows that there are other potential risk factors for GDM that originate in lifestyle behavior and psychosocial well-being.

Lifestyle behaviors, such as physical activity and diet quality, are described as both protective or risk factors. Women who are physically active before pregnancy lower their risk of developing GDM by 55% and women who are physically active during pregnancy lower their risk of developing GDM by 24% [51]. Thus, as described by the ADA, sedentary behaviors constitute a risk factor for GDM [50]. Another risk factor in lifestyle behaviors is diet quality; indeed lipids, saturated fat and cholesterol if consumed often, can lead to an augmented risk of developing GDM [52]. Animal protein and heme iron are also correlated to the risk of developing GDM [53].

Research on psychosocial well-being risk factors for the development of GDM is still lacking today. Nevertheless, mental health symptoms, such as depression, have shown to be associated to higher levels of FPG during the oGTT test [54]. There is also mounting evidence that depressive symptoms are associated to the risk of developing GDM [55, 56], although more research is needed. Indeed, women with high first-trimester depression scores experience a twofold significantly increased risk of future GDM compared with women with low first trimester depression [55]. A recent meta-analysis has also demonstrated that a history of depression is associated to a 20% increased risk of developing GDM [56].

In summary, risk factors leading to GDM development may also contain lifestyle behavior and psychosocial well-being factors. As research on these specific risk factors is still lacking and as GDM has adverse consequences on the health of the women and their child, it is of interest to investigate any potential risk factors for the development of GDM. As will be illustrated by this thesis, these risk factors may also play a role in the development of adverse outcomes associated to GDM.

1.4 Adverse outcomes associated with GDM

GDM carries multiple adverse health short term and long term consequences for the mother and her child. There are obstetric, pediatric, cardiovascular, metabolic and mental health adverse outcomes related to GDM. Obstetric adverse outcomes in women with GDM include: a higher risk of preeclampsia, premature rupture of membranes, preterm delivery, and cesarean delivery [57, 58].

GDM is also related to adverse outcomes in the infant including an increased risk of macrosomia, being large for gestational age (LGA) at birth, and a higher risk of perinatal mortality [57, 58]. The following long-term adverse outcomes related to GDM for the child and adolescent have been described. Hereafter, the highest odds ratio was extracted from original research articles that compared outcomes in children whose mothers had GDM in pregnancy, with children whose mothers did not have GDM in pregnancy. In children aged six, there is a 2.32 higher risk of having hypertension, and a 1.89 higher risk for high blood pressure [59] and a 2.20 higher risk of having attention deficit hyperactivity disorder [60]. In children aged between 11 and 14, there is a 1.42 higher risk of having

impaired glucose tolerance and a 1.22 higher risk of having impaired fasting glucose [61]. In children aged between 10 and 16, there is 4.05 higher risk of overweight [62, 63] and a 1.30 higher risk of obesity [63, 64] and a two-fold higher risk of developing impaired glucose tolerance [63, 65]. In adolescents aged 16 there is a 3.82 higher risk of having abdominal obesity [62] and a 3.53 higher risk of having a metabolic syndrome [66]. Finally, in adults aged between 19 and 27, there is an eight-fold higher risk of developing diabetes or prediabetes in adulthood (19-27 years old) [65].

Maternal long-term adverse outcomes related to GDM concern cardiovascular and metabolic health. Mothers with GDM have a 3.4 higher risk of developing a glucose disorder (described as type 2 diabetes and prediabetes together) [67]. Furthermore, they present a two to three-fold higher risk of developing a cardiovascular disease in the decade following childbirth, even in the absence of diabetes [68].

Finally, GDM has lately been associated with mental health symptoms. Up to 30% of women suffer from depression following their GDM diagnosis [69], which is three times higher than in pregnancies without GDM [70]. In addition, prevalence of postpartum symptoms of depression is up to 4.9 times higher in women with GDM compared to women without GDM [71, 72].

1.5 Care of GDM patients

The ADA [35] and the Endocrine Society [73] suggest treating women that are diagnosed with GDM (24-28 weeks of gestation) through lifestyle interventions that mainly consists of diet and physical activity goals and recommend measurement of glucose values. Glucose-lowering medication is introduced when glucose values remain above targets, despite lifestyle behavior (diet and physical activity) changes. This procedure is used at the GDM clinic at the CHUV, which serves as the base for the clinical studies of this thesis. Details regarding different glucose-lowering medications are discussed under section 1.5.2.

1.5.1 Lifestyle interventions

Following their diagnosis, women followed at the GDM clinic at the CHUV are seen by physicians, diabetes educators, dieticians and physiotherapists. These clinical appointments may allow women with GDM to improve their lifestyle behaviors, to reduce their glucose values, and to keep their weight gain within the recommendations for pregnancy [74]

The dieticians follow recommendations regarding eating habits, glucose values, and weight gain in women diagnosed with GDM [73, 75, 76]. Thereby, dieticians focus on how to balance carbohydrate intake over several meals and snacks [73], how to limit the intake of free sugars to less than 10% [77], and how to increase fiber intake to up to 30 g per day [78].

All health care providers and particularly specialized physiotherapists encourage patients to increase their physical activity [73]. The physiotherapy session(s) consists of teaching women to perform a combination of aerobic and resistance physical activity, in a moderate intensity, under professional supervision. Women are advised to repeat exercises, ideally, more than once a day and, ideally, in the postprandial period to reduce their glucose values [79, 80].

In an ideal situation, the patients are able to limit their weight gain [74], and to reduce their glucose values by following these lifestyle interventions. However, changing behaviors and adherence to lifestyle interventions are highly dependent on other underlying factors.

1.5.1.1 Psychosocial well-being correlates and determinants of adherence to lifestyle interventions.

Psychosocial well-being is associated with and determines one's adherence to lifestyle interventions during pregnancy (both terms described in Chapter IV). Nonetheless, pregnancy is a difficult time for psychological and physiological reasons [81]. This is especially true for women with GDM, as 30% of these women suffer from symptoms of depression [69]. Moreover, 10% of women with GDM show severe symptoms of depression [69]. Mental health symptoms, such as depression can reduce adherence to lifestyle behavior change [82]. Diet quality is impacted by mental health symptoms, as they lead individuals to lose control over eating, to eat comfort food and so, to have a higher intake of caloric, energy dense and nutrient poor foods [83-87]. Finally, the motivation to conduct physical activity is reduced in the presence of mental health symptoms. Depression is associated with a lower motivation to be active [85] and to less time spent in moderate to vigorous physical activity a day [88]. Thus, mental health symptoms are important factors to consider with regards to adherence to lifestyle behavior changes or to general lifestyle behavior.

Self-efficacy and social support (described in Chapter IV) are two factors that can improve adherence to lifestyle interventions, as they help women to positively change their lifestyle behavior [87, 89-91]. Self-efficacy and social support are both known to improve mental health [27, 92]. Conversely, an absence of social support and self-efficacy may bring women to experience increased mental health symptoms, which may then reduce adherence to lifestyle behavior changes. Previous research has also shown that in individuals who suffer from severe mental health symptoms, have a reduced self-efficacy [93-95]. Social support and self-efficacy also have a direct impact on lifestyle behavior changes. This association will be described in more detail in studies A and B.

1.5.1.2 Consequences of non-adherence to lifestyle interventions

As mentioned above, mental health symptoms may lead women to a lower adherence to lifestyle interventions, and consequently bring to adverse outcomes in women with GDM, such as a higher weight gain and/or a lower control over glucose values [73, 96-99].

In women with GDM, excessive weight gain is known to have multiple adverse obstetric, neonatal and long-term consequences for the mother. Obstetric and neonatal consequences consist of preterm or cesarean delivery, macrosomia or higher birth weight [64, 96-98, 100]. Consequences for the mother consist of a higher risk of type 2 diabetes and cardiovascular disease and a higher weight retention in the postpartum period [96, 97, 100-103]. Thus, it is important to know if women with poorer mental health are at risk for excessive weight gain in pregnancy, as they might require more clinical attention following their GDM diagnosis. Nonetheless, the direct relationship between poor mental health and weight (gain) in women with GDM has yet to be investigated.

If women with mental health symptoms cannot implement the necessary lifestyle behavior changes to reduce their glucose values [73, 99], this may results in medication intake to achieve glycemic targets [44, 104]. However, the direct relationship between mental health symptoms and glucose-lowering medication intake in women with GDM has not been studied so far.

1.5.2 Glucose-lowering medication

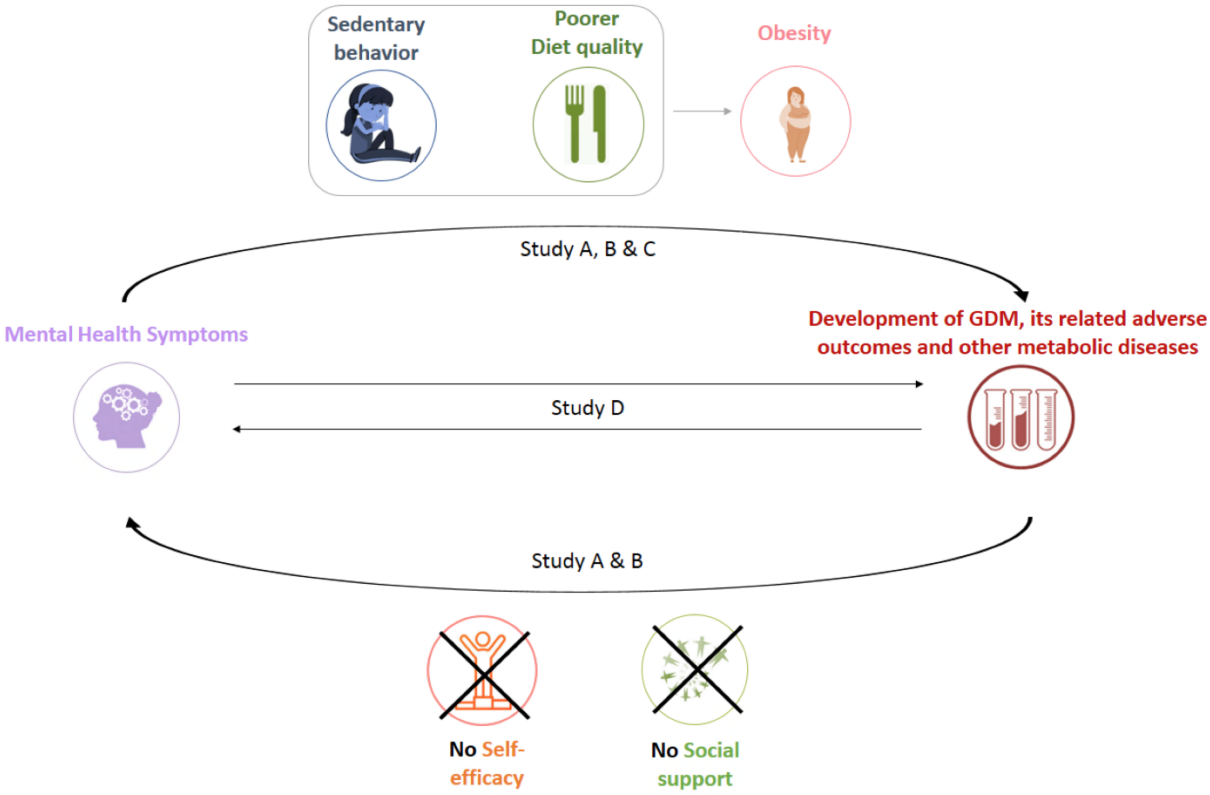
Glucose-lowering medication is introduced when glucose values remain above targets two or more times during a one to two-week period (FPG > 5.3 mmol/l, 1h postprandial glucose > 8 mmol/l and 2h postprandial glucose > 7 mmol/l) [35, 44, 104]. The ADA and the National Institute for Health and Care Excellence (NICE) recommend insulin for the treatment of hyperglycemia. Indeed, the oral glucose-lowering medications; metformin and glyburide cross the placenta, which might affect the fetus [50, 105] and/or lead to additional adverse cardio-metabolic consequences in the infant [106]. In this situation, especially the use of glyburide has been discouraged [50]. Notwithstanding, in the context of specific cultural and personal situations, metformin can be used if the patient remains above targets after attempting lifestyle interventions and does not wish insulin injections [105, 107].Depending on the type of glucose-lowering medication, women may have more or less difficulty in accepting medication [108] and this can be a source of additional stress for these women. Overall, lifestyle behavior change is always proposed as the first solution to control weight gain and reduce glucose values in women with GDM [50].

1.6 Overarching Aim of thesis

In summary, biological, psychological, social and mental health factors interact in women with GDM. Consequently, the aims of this thesis and the presented studies were based on and emanate

from the biopsychosocial theoretical model of mental health. This model is developed below, but it a few words, it shows how different biological, psychological and social factors interact with an individual's mental health and hence, seems highly pertinent for the thesis at hand. The relationships between the factors were operationalized as follows.

Figure 2. Adapted theoretical biopsychosocial model of mental health.



This model was inspired by the theoretical biopsychosocial model of mental health and by two other models demonstrating the association between mental health and metabolic health [109, 110]. Indeed, Robinson and colleagues demonstrate that mental health symptoms are more frequent in individuals with diabetes, and conversely individuals with mental health symptoms have a higher risk of developing diabetes [109]. This concept is displayed in the center of Figure 2 and demonstrates the bi-directional relationship between mental health symptoms and metabolic issues (development of GDM, its related adverse outcomes and other metabolic diseases). According to Reece and colleagues, GDM is a growing problem in our society and argue that psychological and behavioral factors may contribute to its development [110]. In the adapted model above, the biological factors are depicted in salmon and red and were adapted to GDM, they contain obesity and metabolic issues (i.e. the

development of GDM, its adverse outcomes and other metabolic diseases). The psychological factors in the model contain self-efficacy, and behavioral factors, such as sedentary behavior and poor diet quality. Lastly, the social factor in this model is social support and the mental health factor is mental health symptoms. The relationship between these factors was conceptualized in the following way; in women with GDM, the absence of social support [92, 111] and self-efficacy [27, 29] may contribute to the development of mental health symptoms. These mental health symptoms may, in turn, lead to sedentary behaviors and a poorer diet quality [82, 85, 87], which may increase the risk of obesity [112-114]. Sedentary behavior, poor diet quality and obesity may contribute to a higher risk for metabolic issues (i.e. developing GDM, adverse outcomes related to GDM and other metabolic diseases) [64, 85, 96-99, 102, 109, 110].

Thus, the overall objective of this thesis was to investigate how psychosocial well-being influences lifestyle behaviors and metabolic health in women with GDM. To reach this objective, the following aims were created:

- Aim 1: The thesis synthetized evidence (a) on how diet, physical activity and psychosocial well-being interacted in women with GDM and their offspring, and (b) on how effective interventions were in reducing adverse outcomes related to GDM (study A).
- Aim 2: The thesis aims to test the effect of an interdisciplinary lifestyle and psychosocial well-being continuous perinatal intervention in women with GDM on maternal, infant and paternal metabolic and mental health outcomes (study B).
- Aim 3: The thesis investigates the evolution of mental health (specifically depression and well-being) through time (studies C and D).
- Aim 4: The thesis investigates the associations between mental health and adverse outcomes related to GDM such as (a) weight (gain) (study C) and (b) the intake glucose-lowering medication during and/or after GDM pregnancy (study D).

The titles of the studies are in the following order:

- Study A - *How diet, physical activity and psychosocial well-being interact in women with gestational diabetes mellitus: an integrative review*
- Study B - *Improving cardiometabolic and mental health in women with gestational diabetes mellitus and their infant: study protocol for MySweetHeart Trial, a randomized controlled trial*
- Study C - *Mental health and its associations with weight in women with gestational diabetes mellitus. A prospective clinical cohort study*

- Study D - *Mental health and its associations with glucose-lowering medication in women with gestational diabetes mellitus. A prospective clinical cohort study*

1.6.1 Link between the studies

Firstly, to gain a broad knowledge of psychosocial well-being and mental health in women with GDM, an integrative literature review (Study A) was conducted to synthetize evidence on (1a) how diet, physical activity and psychosocial well-being interacted in women with GDM and their offspring, and on (1b) how effective interventions were in reducing adverse outcomes related to GDM. Secondly, based on the literature review results, an innovative RCT was developed. This RCT aimed (2) at testing the effect of an interdisciplinary lifestyle and psychosocial well-being continuous perinatal intervention on maternal, infant and paternal metabolic and mental health outcomes (Study B). Thirdly, the bi-directional relationship between mental health and adverse outcomes related to GDM was investigated in women who were not receiving any psychosocial well-being intervention, observational studies were conducted in a cohort of women with GDM. These studies investigated (3) the evolution of mental health through time and the association between mental health and adverse outcomes related to GDM such as (4a) weight (gain) (Study C) and (4b) glucose-lowering medication (Study D) during and/or after GDM pregnancy, as both of these elements are important factors to consider in women with GDM.

2. THESIS STUDIES

The studies of this thesis were all conducted at the GDM clinic of the Woman-Mother-Child Department (DFME) of the CHUV. In the following section, the four studies integrated in this thesis will be presented one after the other as they all differ in methodology. Studies C and D will have a common part for their methodology, as they share certain elements relative to the cohort they were based upon.

2. 1: Study A: How diet, physical activity and psychosocial well-being interact in women with gestational diabetes mellitus: an integrative review

Authors: **Leah Gilbert**, Justine Gross, Stefano Lanzi, Dan Yedu Quansah, Jardena Puder and Antje Horsch

Published in: ***BMC Pregnancy and Childbirth, 2019***.

2.1.1 Aims

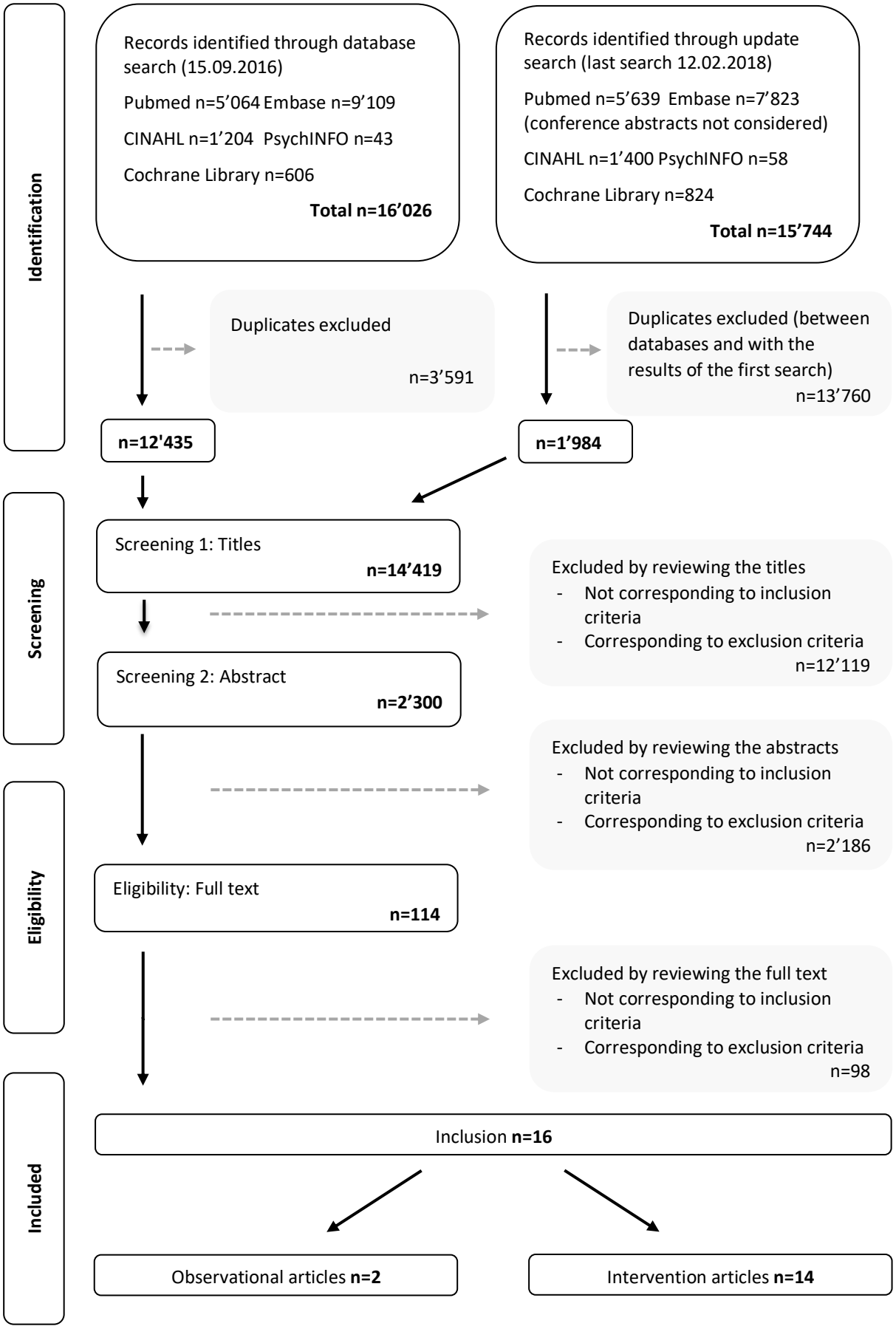
This study was conducted as a base for the study protocol (study B). Therefore, it aimed to synthetize evidence on (1a) how three domains of interest, i.e., diet, physical activity and psychosocial well-being interacted in women with GDM and their offspring and on (1b) how effective interventions were in reducing adverse outcomes related to GDM. Hereafter is a summary of the integrative literature review (for more details, see the published paper in Appendix 8.1).

2.1.2 Methods

2.1.2.1 Search strategy

Search terms corresponding to the domains of interest (see detailed list in Appendix 8.1) were entered in the following databases: CINAHL, PsycINFO, Embase, Pubmed, and Cochrane. This research was conducted twice. The first one was conducted on articles published between 1980 and September, 15th 2016 which provided 16'026 articles. The update took into account articles published between the 15th of September 2016 and the 12th of February 2018 and yielded 15'744 articles. The articles were imported into EndNote Library X7 and divided among members of the research team. In line with PRISMA guidelines [115], the team screened through the titles, abstracts and, finally, the full-texts. Articles were included if they corresponded to the inclusion criteria, as described in the flow chart below.

Figure 3. Prisma flow-chart for study A.



2.1.2.2. Inclusion and exclusion criteria

Inclusion: Articles were included if they were published in English in peer-reviewed journals. They had to contain data on women with GDM (or women and their partner), or a history of GDM, with clinical outcomes reported for women (or women and their baby). The type of studies included could be either observational or intervention studies that focused on at least two of the domains of interest (i.e. diet, physical activity and psychosocial well-being). No articles published prior to 1980 were included, in order to stay in line with more up-to-date clinical practice and objectives for glycaemic thresholds.

Exclusion: Articles were excluded if they exclusively investigated women with type 1 and type 2 diabetes. Studies concerning dietary supplements only were excluded, as were intervention studies that only tested pharmacological interventions. Genetic, epigenetic, genomic and animal research, as well as papers addressing exclusively the microbiome were excluded. Finally, study protocols, conference abstracts, recommendation papers, guidelines, qualitative studies, and review articles were excluded.

2.1.2.3 Data extraction and synthesis

As shown in the flow-chart (Figure 3), 114 articles were selected for detailed evaluation. The data from the 114 articles was extracted systematically in a modified Joanna Briggs Institute (JBI) form [116-119]. As suggested by Whittemore and Knafl, findings from the included studies were synthesized according to the objectives of the study in a thematic manner [120]. This synthesis provided answers for both of the research questions. The associations (1a) between the different domains of interest were outlined. The effects (1b) of interventions on clinical outcomes related to GDM were summarised. Consequently, a conceptual model was drawn.

2.1.2.4 Quality appraisal

Four different checklists corresponding to the original paper's design were used to evaluate the quality of the included studies: the JBI critical appraisal Checklist for Randomized Controlled Trials [117], Checklist for quasi-experimental studies (non-randomized experimental studies) [119], Checklist for Analytical Cross Sectional Studies [116] and Checklist for Cohort studies [118]. The quality appraisal was conducted by two independent ratters (LG & DYQ), and discrepancies in score ratings were resolved by consensus.

2.1.3 Results

2.1.3.1 Characteristics of included studies

This review included 16 studies (Figure 3): two observational studies and 14 intervention studies combining a total of 20'285 participants, with n=19'884 in the intervention and n=401 in the

observational studies. All combined intervention studies focused solely on diet and physical activity and none included psychosocial well-being in their intervention. For clarity, these interventions combining diet and physical activity were named: “lifestyle interventions” [1-14]. Both observational studies investigated the associations between diet, physical activity and psychosocial well-being variables (n=2/2) [30, 121]. According to the Joanna Briggs Institute Appraisal Tools (2017), the majority of included articles were rated to be of good quality (see Tables 1 and 2 in Appendix 8.1). Only one study was rated as having poor quality [12].

2.1.3.2 Interactions between domains of interest (diet, physical activity and psychosocial well-being)

In both observational studies, social support and self-efficacy were associated with the adherence to healthy lifestyle behaviours (i.e. diet and physical activity). The lifestyle interventions studies led to clear improvements in diet in all the studies observing this outcome (n=7) and, in physical activity, which improved in six out of nine studies. Two studies also demonstrated that lifestyle interventions also led to lower stress perception and higher quality of life and less fatalistic and cultural diabetes beliefs.

2.1.3.3 Effectiveness of the lifestyle interventions on the reduction of adverse outcomes related to GDM

Regarding anthropometric outcomes, one observational study indicated that social support and self-efficacy had no significant association with BMI. The lifestyle interventions led to decreased waist and hip circumference in five out of seven studies and to decreased body fat in the two studies measuring it. However, the results of lifestyle interventions concerning weight and BMI were inconsistent, as out of the eight studies measuring these outcomes, only four yielded improvements.

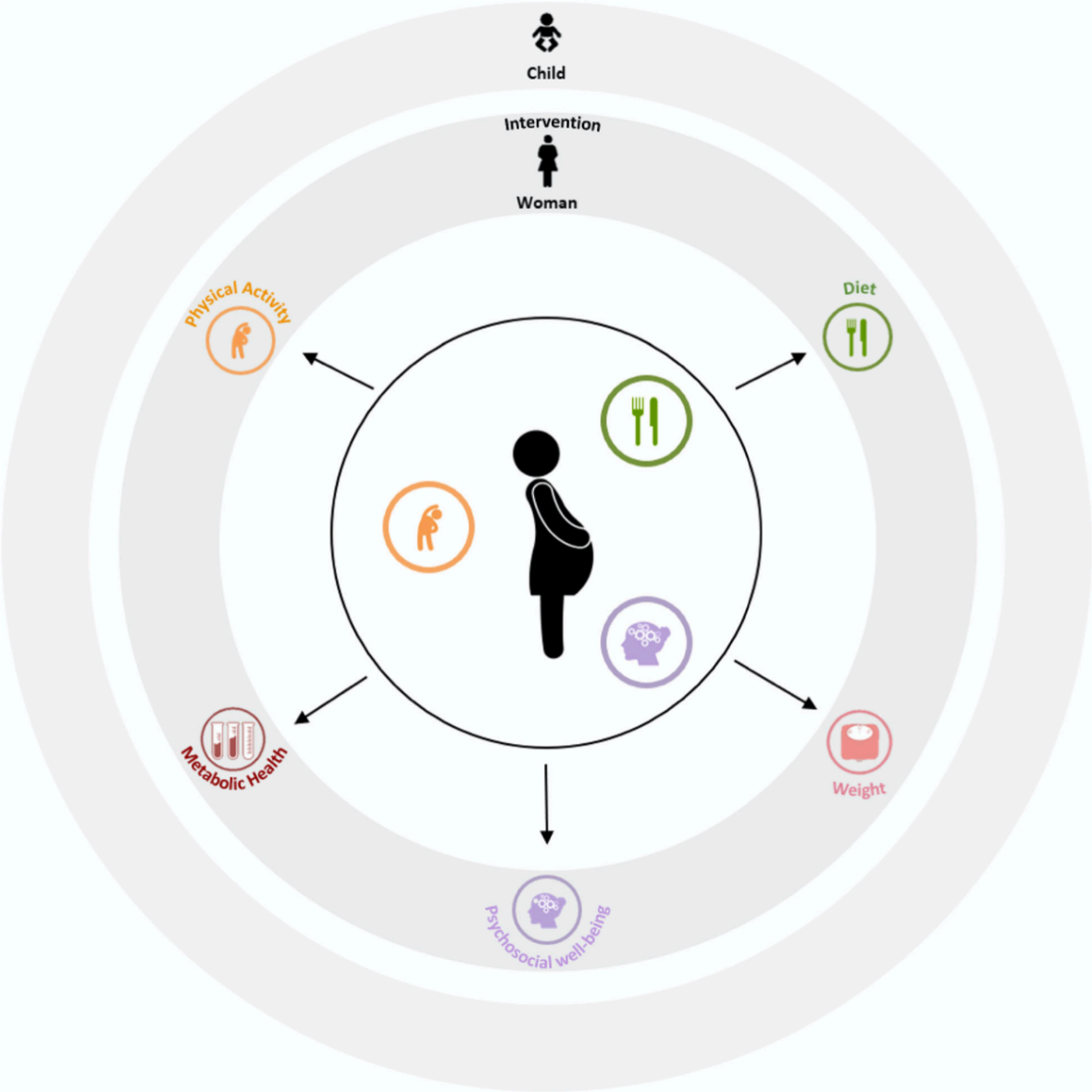
Lifestyle intervention studies led to a decrease in total and LDL (Low-Density Lipoprotein) cholesterol in the three studies that measured it, triglycerides in the two studies where it was measured, and in glucose values. For the glucose values measured in three studies, the decrease in values depended on the measure. Indeed, oGTT and postprandial measures were reduced by lifestyle interventions in the three studies that measured this. FPG was reduced in two out of three studies and insulin resistance was only reduced in one out of three studies. There was also a reduced risk of postpartum diabetes in the two studies that evaluated this outcome. Concerning results for systolic blood pressure, these were similar throughout groups and time in the two studies measuring this outcome. Inconsistencies were found regarding glycated haemoglobin (HbA1c), HDL cholesterol, diastolic blood pressure and total cholesterol. HbA1c decreased in two studies but increased in one study. HDL cholesterol rose in one study and remained the same in the other. Diastolic blood pressure was reduced in one study and remained unchanged in the other. Finally total cholesterol was either

reduced or stayed consistent in the two studies measuring it. Regarding delivery outcomes, only macrosomia was measured in more than one study, and was similar in the control and lifestyle intervention group. For all the outcomes, no conclusions were drawn on outcomes which were only measured in one study. Results concerning the health of the child after delivery were not found. Also, no results were found regarding the health of the partner of women with GDM.

2.1.4 Conclusion

This integrative review showed that (1a) diet, physical activity and psychosocial well-being interact in women with GDM. It also demonstrated that social support and self-efficacy were associated with healthy lifestyle behaviours in two studies. Lifestyle interventions (1b) led to improved adherence to a healthy diet and mostly improved physical activity. Lifestyle interventions often improved waist and hip circumference, LDL cholesterol, triglycerides, oGTT, postprandial glucose values, and postpartum diabetes status and two lifestyle interventions led to improvements in stress, quality of life and fatalistic beliefs. Results related to weight, BMI and macrosomia were inconsistent and other birth outcomes were only measured in one study and thus do not allow a solid interpretation. Furthermore, no results regarding health outcomes of the partner, or the child after delivery were found. As this review would serve as a basis to develop the *MySweetHeart trial*, a conceptual model of the results was developed, as shown in Figure 4 below.

Figure 4. Conceptual model representing the integration of a psychosocial well-being component in lifestyle interventions, extracted from study A.



This model suggests that lifestyle interventions should not only include diet and physical activity domains, but should also include psychosocial well-being components, such as strategies for improving social support, self-efficacy and mental health. Indeed, the results from this integrative review demonstrated that psychosocial well-being improved adherence to lifestyle behaviors (diet, physical activity), and also improved psychological variables. Given that adding a psychosocial well-being component could lead to a higher adherence to lifestyle interventions, it would have the potential to improve adverse outcomes related to GDM. Furthermore, it could probably improve the obstetric and neonatal outcomes. Psychosocial well-being interventions may necessitate three important components to improve adherence to diet and physical activity. First of all, a strong social

support from professionals and from the family of the patient, are important [122]. Secondly, the patients should be mentally healthy to be able to carry out behavioral changes in diet and physical activity and thereby would benefit from treatments regarding potential symptoms of depression and stress relief techniques [123-125]. Finally, women should benefit from a positive belief that they are able to make behavioral changes, thus developing their self-efficacy would help [126], although self-efficacy is also dependent on the first two pillars; the support the women have and their current mental health. This model suggests that only with such a fine-tuned intervention can women improve their adherence to lifestyle interventions and, as a result, make changes in their behaviors and thereby, improve their potential adverse outcomes related to GDM.

2.1.5 Personal Contribution

The candidate significantly participated in the conception and design of the study, coordinated the study and the data collection, collected data, participated in the data analysis, participated in the interpretation of data, drafted and adapted the manuscript.

2.2: Study B. Improving cardiometabolic and mental health in women with gestational diabetes mellitus and their infant: study protocol for *MySweetHeart Trial*, a randomised controlled trial

Authors: Antje Horsch, **Leah Gilbert**, Stefano Lanzi, Justine Gross, Bengt Kayser, Yvan Vial, Umberto Simeoni, Didier Hans, Alexandre Berney, Urte Scholz, Ruben Barakat, Jardena J Puder, on behalf of *MySweetHeart* Research Group

Published in: **BMJ Open, 2018.**

2.2.1 Aims

This RCT aims (2) to test the effect of an interdisciplinary lifestyle and psychosocial well-being continuous perinatal intervention in women with GDM on maternal, infant and paternal metabolic and mental health outcomes. The main effect of this intervention will be assessed especially through the primary outcomes which are weight and symptoms of depression in the mother. To assess this, the differences in the changes in maternal weight and in the symptoms of depression will be measured. These differences will be measured between the first *MySweetHeart* assessment taking place at the second GDM visit and the last assessment taking place at one year postpartum and between the intervention and the control groups. Hereafter is a summary of the study protocol (for more details, see the published paper in Appendix 8.2).

2.2.2. Methods

2.2.2.1 Inclusion and exclusion criteria

Inclusion: Women were integrated in the *MySweetHeart trial* if they were diagnosed with GDM according to IADPSG criteria, between 24-32 weeks of gestation [46, 127]. These women also had to be aged 18 or older, and able to understand French or English.

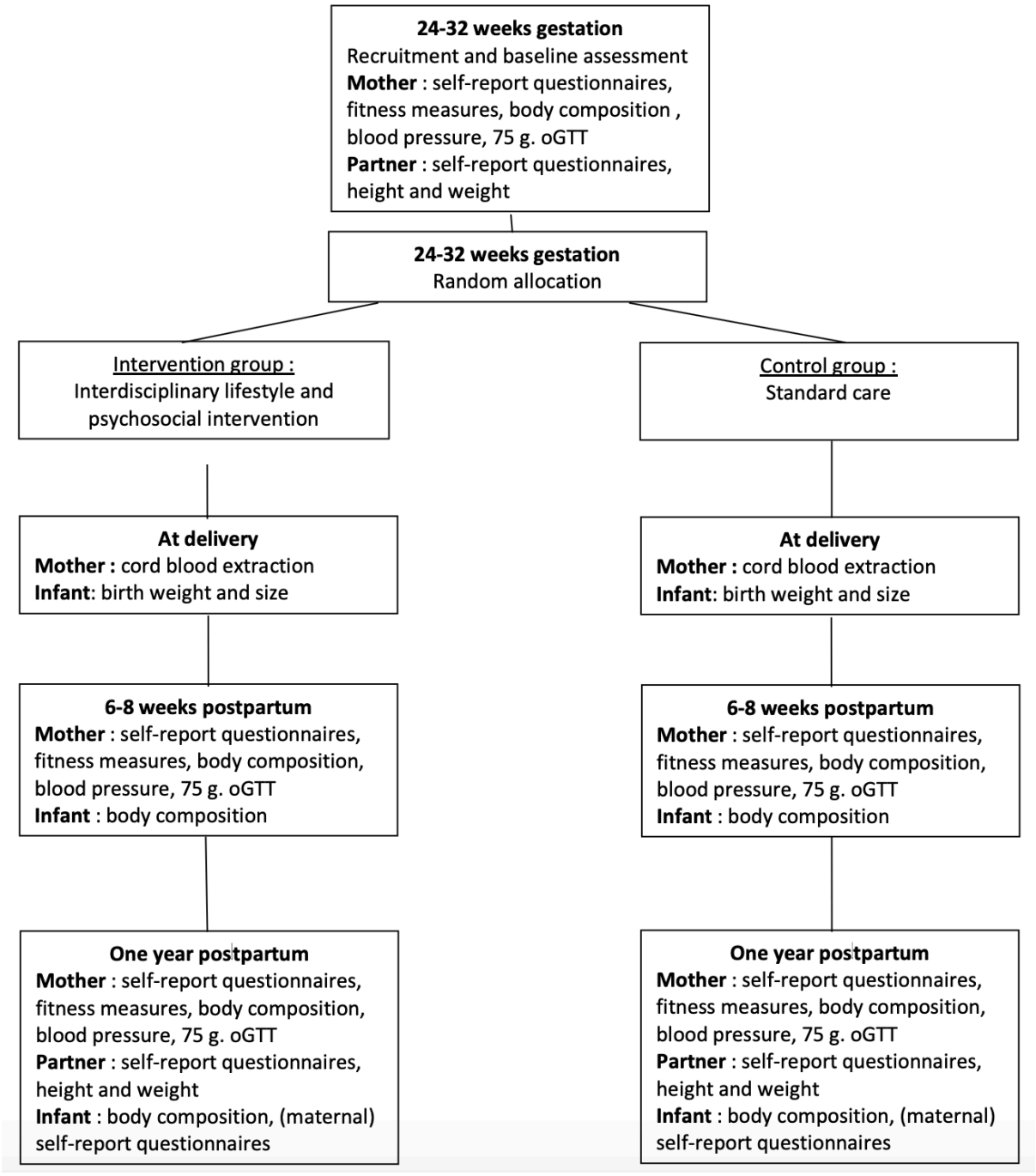
Exclusion: Women were excluded from the trial if they were on strict bed-rest and/or had pre-existing diabetes mellitus. They were also excluded if they had a current episode of severe mental disorder, such as a current psychotic episode or suicidality.

2.2.2.2 Consent, recruitment and group allocation

The recruitment for the study took place either at the GDM clinic at the CHUV or through private practices or other regional hospitals. During recruitment, after GDM diagnosis, women received information about the study and were called a few days later to assess interest in taking part in the study. As shown in Figure 5, women who consented to participate underwent the first assessment. At the end of this first assessment, women were randomly allocated either to standard care (control group) or to the intervention group of the study through a concealed envelope. The

allocation ratio of randomization was 1:1, using the block randomization method (blocks of 4) established by the CONSORT guidelines [128].

Figure 5. Prisma flow-chart for study B.

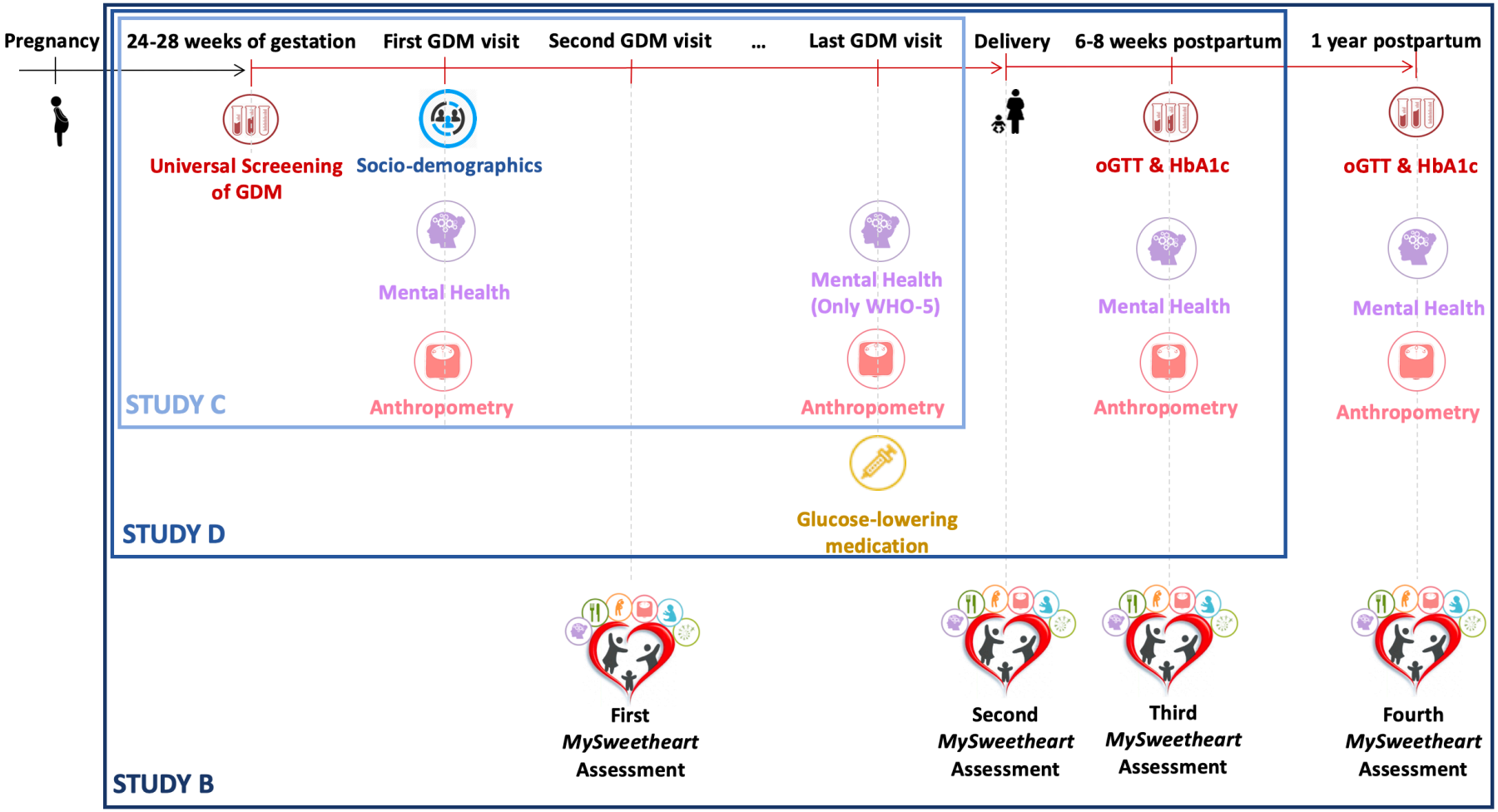


2.2.2.2 Data collection visits

As women were recruited at the GDM clinic at the CHUV (or in other centers) for the *MySweetHeart trial*, data collection and visits were in line with the visits for women in standard care and thus, with the assessments of studies C and D (all represented in Figure 6). For the *MySweetHeart*

trial, the first baseline assessments, took place between 24-32 weeks of gestation. Other *MySweetHeart trial* assessments occurred at delivery (second assessment), at 6-8 weeks postpartum (third assessment) and finally at one year postpartum (fourth assessment).

Figure 6. Overview of data collection visits for studies B, C and D.



The assessments specific to the *MySweetHeart trial* are listed below in overview Table 1 and are described in detail in the published protocol that can be found in Appendix 8.2.

Table 1. Overview of data collection visits for the *MySweeHeart* trial.

	First *MySweetHeart* Assessment	Second *MySweetHeart* Assessment	Third *MySweetHeart* Assessment	Fourth *MySweetHeart* Assessment
	Second GDM Visit	At delivery	6-8 weeks postpartum	One year postpartum
Self-report questionnaires	x		x	x
Fitness measures	x			x
Body composition	x		x	x
Blood pressure and 75 g. oGTT	x		x	x
Cord-blood extraction		x		
Bone Densitometry (DEXA) if additional consent is signed				x
Infant's birth weight and size extracted from the hospital birth record.		x		
Infant's body composition			x	x
Infant's BIA (bio-impedance)				x
Partner's self-report questionnaires, height and weight	x			x

2.2.2.3 Primary and secondary outcomes

The two primary outcomes of this study are changes in symptoms of depression [assessed through the Edinburgh Postnatal Depression Scale (EPDS)] and in weight in mothers. To measure symptoms of depression, the women filled-out the self-report and validated questionnaire; the EPDS [129]. For weight, patients were measured in light clothes and without shoes to the nearest 0.1 kgs with a regularly calibrated Seca Scale. Both of these primary outcome measures were assessed at the first, third and last *MySweetHeart* assessment. As these outcomes are also measured in the cohort of the GDM clinic at the CHUV, they are described in more detail in the sections that describe this cohort.

Therefore, measures of depression are described in section 2.3.2.7 and measures of weight in section 2.3.2.8. The secondary outcomes were diet, physical activity, cardiometabolic outcomes, social support and infant as well as paternal outcomes; as these secondary outcomes are not of main importance in this thesis, they will not be described (see Appendix 8.2 for details).

2.2.2.4 Sample size calculation

To determine the required sample size, a power analysis for the primary outcomes was conducted. Regarding weight, the calculations were based on the pilot data and goals for weight retention. A weight reduction of 8.4 kg (SD: 5.5) between the baseline *MySweetHeart* assessment and the last *MySweetHeart* assessment at one year postpartum was assumed for the control group, compared with a weight reduction of 10.9 kg (SD: 5.5) in the intervention group between these same visits. The required sample size was 76 women in each study group to have a statistical significant difference with a power of 80% and an alpha-level set at 0.05 (two-sided). Concerning the depression score, this 76 women sample size was also sufficient to observe significant differences in this primary outcome, as a reduction in symptoms of depression between the above-mentioned two time points was expected to be 0.2 (SD: 4.3) in the control group and 2.2 (SD: 4.4) in the intervention group. Considering a maximum attrition rate of 30%, a sample consisting of 100 women in the control and 100 in the intervention group would provide adequate power. The recruitment of women for this trial took place between September 2016 and September first 2020 with a total of 213 women included in the study. On the 25th of November 2020, the total number of drop-outs was 31.

2.2.2.5 Intervention design

The control group

The standard care given to the control group was the same as the care given to women in the cohort and is thereby described in section 2.3.2 of this thesis. Contrarily to the usual practice regarding physical activity counselling described in section 1.5.1, women in the *MySweetHeart trial* control group received advice from the physicians/specialized nurse practitioners or dietitians instead of physiotherapists. This implies these women received less specific advice on how to conduct physical activity.

The intervention group

Women in the intervention group followed an evidence-based interdisciplinary and personalized lifestyle intervention where psychosocial well-being, diet and physical activity were the main domains of intervention. The care and the goals of the intervention group were adapted to the patient's needs to reduce the adverse outcomes related to GDM, especially with regards to weight. A

personal lifestyle coach followed the women from inclusion up to one year postpartum, to enable them to reach the goals described below.

The psychosocial well-being part of the intervention contained three components; social support, self-efficacy and mental health. As social support is an important factor for psychosocial well-being, this trial provided support by the healthcare providers in the research team, and especially by the lifestyle coach (LG) to women with GDM. Additionally, the lifestyle coach (LG) arranged for the perinatal clinic to give breastfeeding support to the women once they give birth (if at the CHUV). Social support was also improved by offering one prenatal and one postnatal group workshops to the patients, so that they met other women in their condition. In the prenatal workshop, the structure and organization of the women's daily life was discussed. Whereas in the postnatal workshop, diet and physical activity were discussed and integrated goals for the infant and the partner. Furthermore, the partners were invited to the pre and postnatal consultations and workshops so that they understood their partner's health goals and so that they could then support them towards these healthy habits. To improve self-efficacy, the lifestyle coach (LG) used Health Action Process Approach (HAPA) and motivational techniques [130, 131]. Through the HAPA, the objective for the coach was to lead the patient from the motivational phase, during which goals were created and discussed via motivational techniques, to the volitional phase. In the volitional phase, the lifestyle coach and the patient planned actions (i.e. when and how the new behavior should take place) and coping (i.e. identifications of barriers which could bring the new behavior to fail). The HAPA, being highly depended on the patient's self-efficacy and perception of advantages emanating from the new behavior, implied the coach had to set behavioral goals which would be best adapted to the patient's capacities and needs. As shown by the adapted theoretical biopsychosocial model of mental health, both social support and self-efficacy should improve mental health [27, 92]. Although, in some women additional help for mental health symptoms was given. To identify if mental health symptoms were present, all women visiting the GDM clinic were screened for symptoms of depression through the EPDS (described in section 2.3.2.6) at the first GDM visit, at 6-8 weeks, 7 months (only in the intervention group) and one year postpartum. When the EPDS scores were ≥ 10, women were offered individual sessions with a clinical psychologist (AH). These sessions aimed at preventing and reducing symptoms of depression through Cognitive Behavioral Therapy (CBT) techniques. This technique aimed at challenging the most unhelpful negative cognitions, scheduling at least one pleasurable activity a day, increasing social contacts, improving sleep routine and identifying the most stressful situations to apply cognitive behavioral strategies for their management [132-134]. The goals set by the clinical psychologist were then followed up by the lifestyle coach (LG). At seven months

postpartum, there was also a session which focused specifically on mental health and on the structure of the day, to make sure women had time for pleasurable activities.

In the dietary part of the intervention, women met the dietician in three sessions. In the first session, they were advised to distribute carbohydrates over several meals and snacks [73], to limit the intake of free sugar to less than 10% of total energy intake and to avoid added sugars and sugar naturally present in honey, syrups and fruit juices [77]. Women were also encouraged to increase fiber intake to up to 30 g. per day [78, 135]. The second visit with the dietician focused on lipids, where women were instructed to limit total fat to less than 30% [136] and saturated fat to less than 10% of total energy intake [137], to prioritize higher quality fats such as monounsaturated fat [138, 139] and to reduce the intake of red or processed meat [138]. During the third visit, women were taught mindful eating; to develop awareness regarding their hunger and satiety cues, to slow down the pace of eating and to reduce emotional eating [140-142]. At four months postpartum, women were encouraged to structure their meals and to avoid snacking [73], and the goals from pregnancy were re-visited and adapted to the postpartum period.

Regarding the physical activity part of the intervention, all women receive the suggestion to reduce sedentary behavior by being active at least once an hour [143]. Women in the prepartum period were guided towards conducting aerobic and resistance physical activity, twice a day, every day for at least 20 minutes, at a moderate intensity and, ideally, one to one and a half hour(s) after their meal [144-146]. At the ten months postpartum visit, women were prescribed to conduct aerobic physical activity for 150 minutes a week and resistance physical activity twice a week, all at a moderate intensity [147]. Moderate intensity was taught to the patient through walking exercises with the lifestyle coach (LG) and a doctor in sport sciences.

Finally, the interventions described in the three domains of interest (psychosocial well-being, diet and physical activity) above were supposed to help women with their weight gain in pregnancy and their weight loss in the postpartum period. However, in women for which difficulties in the domain of weight were noticed, additional guidance was given. These women were advised to gain weight in pregnancy in accordance with the Institute of Medicine and National Research Council guidelines [74], and for them to return to pregravid weight or to 5% less if their BMI was ≥25 kg at one year postpartum [148]. Specific interventions for the three domains of interest were also offered to the parents for their infant, but will not be discussed in this thesis, as the primary focus is on the mother (see Appendix 8.2 for details).

2.2.2.6 Statistical analysis

As the primary outcome concerns differences in the changes in maternal weight and symptoms of depression between the first GDM visit and one year postpartum in the control versus intervention group, linear regressions will be conducted for these outcomes. Concerning the secondary outcomes, differences in changes between both groups and the four assessments of the *MySweetHeart trial*, illustrated above in Figure 6, will be examined by using linear regressions in women, the infant and the partner. All analysis will be adjusted by controlling for important baseline variables and confounding variables, such as maternal age, sex of the children, the presence of prenatal, perinatal and early postnatal conditions/complications, BMI, the EPDS score, and socioeconomic status where applicable. Subgroup analyses will also be conducted according to weight, mental health (EPDS score <10 vs ≥10) and prediabetes status at 6-8 weeks postpartum, as well as the sex of the infant. A Bonferroni correction for multiple analyses will be applied [149]. In order to assess fidelity and quality of implementation, to clarify causal mechanisms and to identify contextual factors associated with variation in outcomes, a process evaluation nested inside the trial will be conducted [149].

2.2.3 Conclusion

The results of this RCT will help addressing the current gap in the literature regarding psychosocial well-being interventions in women with GDM and their potential to reduce adverse outcomes related to GDM (2). It will permit to evaluate if this type of intervention adds an increased value in the reduction of adverse outcomes related to GDM in the mother, in comparison to a simple lifestyle intervention – as practiced in the control group. It will also allow to evaluate the infant and paternal behaviors and their related health outcomes. Indeed, integrating novel psychosocial well-being components such as techniques to augment social support, self-efficacy, well-being, and to reduce symptoms of depression, might improve several outcomes in these women and maybe even in their infant and partner.

2.2.4 Personal Contribution

The candidate significantly contributed to the establishment and refinement of study procedures and critically revised the manuscript. The candidate is also the coordinator of the trial and has been coaching the majority of the patients in the intervention group and is the co-supervisor of psychology student interns assisting in the study. Finally, the candidate developed or co-developed all the educational materials given to the intervention patients of the trial and developed or co-developed the SOPs (Standard Operating Procedures) of the trial. The study was added to thesis, as

the candidate played an important role in the setting up (educational materials and SOPs), intellectual input and functioning of the study and the team around it.

2.3: Study C: Mental health and its associations with weight in women with gestational diabetes mellitus. A prospective clinical cohort study.

Authors: **Leah Gilbert**, Jean-Benoît Rossel, Dan Yedu Quansah, Jardena J. Puder* and Antje Horsch*

*joint last authors

Study C Submitted in: **Journal of Psychosomatic Research** on the 05.08.20, currently under revision.

2.3.1 Aims

The aims of study C were to investigate (3) the evolution of well-being through time and (3^{bis}) its association with depression and the association between mental health and adverse outcomes related to GDM such as ($4a^1$) weight and ($4a^2$) weight gain during pregnancy in women with GDM. Concerning aim 3^{bis}, the association between well-being and depression was measured solely to assess the utility of using both the depression and well-being scores in women with GDM in relation to adverse outcomes related to GDM, such as weight. This aim (3^{bis}) is considered as a secondary outcome in this study and in this thesis, therefore it will not be discussed in detail. Hereafter is a summary of study C (for more details, see the submitted paper in Appendix 8.3). As study C is currently under review, it is described in more detail than studies A & B.

2.3.2 Methods

This method section for study C is also applicable to study D up to and not including section 2.3.2.9. This common method section concerns the prospective observational cohort of women at the GDM clinic at the CHUV, shared by both studies, and the STROBE statement, applied to both studies [150].

2.3.2.1 Patients

The analysis of this cohort (shared by studies C & D) focused on women treated at the GDM clinic at the CHUV with a GDM. These women were diagnosed between 24 and 28 weeks of gestation according to the ADA and the IADPSG recommendations [46, 50] (see introduction section 1.2 for further details on diagnosis). All of these women are seen by a multidisciplinary team of specialists and undergo the care described in section 1.5.

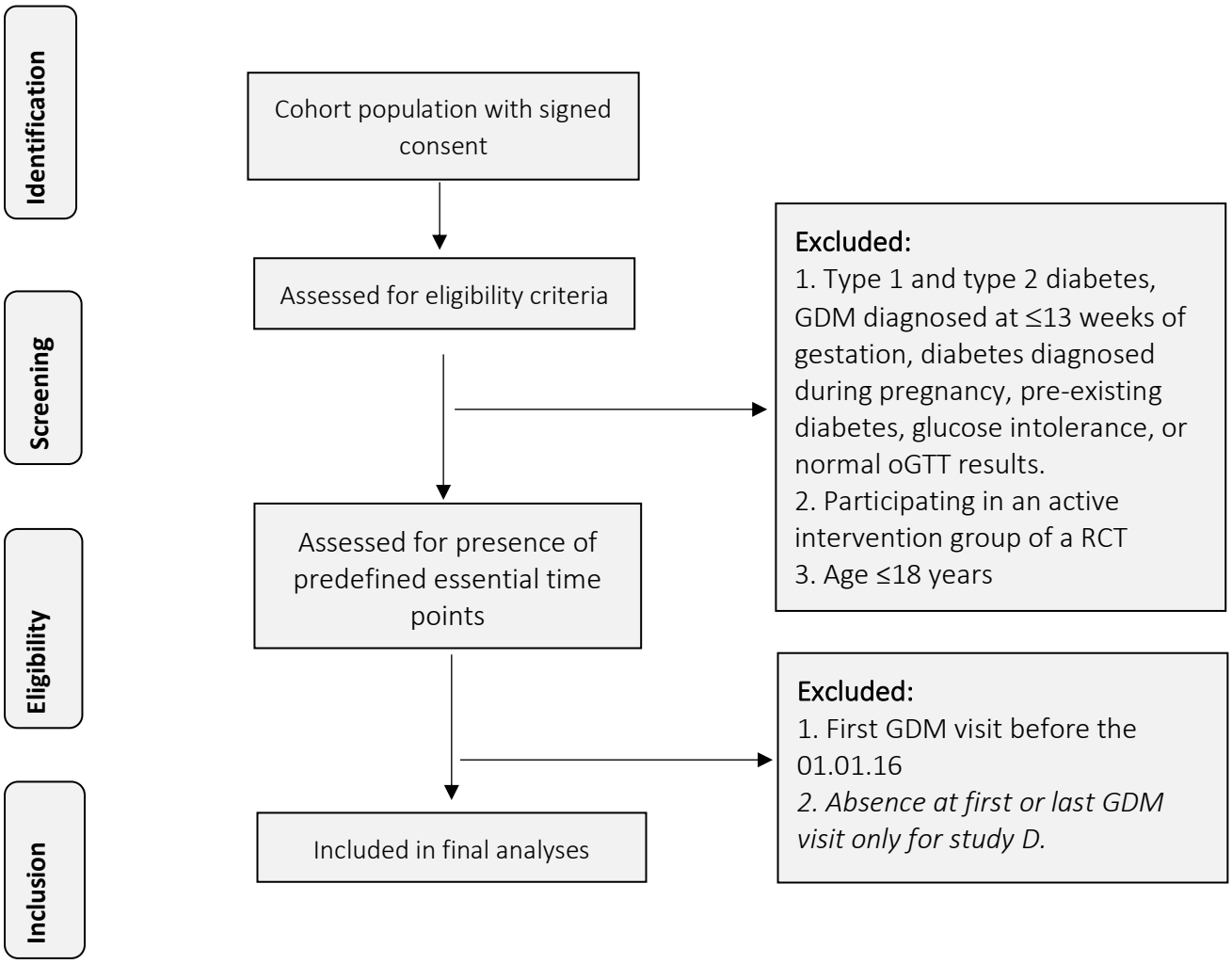
2.3.2.2 Inclusion and exclusion criteria

Both prospective clinical cohort studies integrated in this thesis had shared inclusion and exclusion criteria. Nevertheless Figure 7 below illustrates minor differences *in italics.*

Inclusion: Women were integrated in both studies if they had a GDM diagnosis. They were only included if they had given written consent for usage of their data.

Exclusion: Women were excluded from both studies if they were diagnosed with any other type of diabetes than GDM (i.e. type 1 and type 2 diabetes, GDM diagnosed at ≤13 weeks of gestation, diabetes diagnosed during pregnancy, pre-existing diabetes, or glucose intolerance) or if they had normal oGTT results. Women that were participating in study B's intervention group were also excluded, as they received a specific intervention including support to reduce mental health symptoms. Women that were ≤18 years of age were excluded as well. Finally, women were excluded if their first GDM visit took place before the first of January 2016, as mental health data only started to be routinely collected at this date. Further exclusion criteria were applied for study D. For this study, women had to be present at both the first and at the last GDM visits, as baseline mental health (assessed at the first GDM visit) and a record of glucose-lowering medication (assessed at the last GDM visit) had to be accounted for. Thus, women who did not attend one of these two visits or both were excluded, as shown in italics in the flow-chart below.

Figure 7. Prisma flow-chart for studies C and D.



2.3.2.3 Consent and recruitment

All patients followed up at the GDM clinic are asked to take part in the ongoing GDM cohort by the research team and are given a consent form to sign containing further information on data usage. The « Commission Cantonale (VD) d'éthique de la recherche sur l'être humain (CER-VD) » approved the study protocol "Impact du diabète gestationnel sur la mère et son enfant pendant et après la grossesse" (study n° 326/15).

2.3.2.4 Cohort data base

The women are seen regularly from their diagnosis and up to three years postpartum. Data including information on mental health, anthropometry, metabolism, and socio-demographic variables are collected and saved in "SecuTrial", a secure database, which was started in October 2011. Mental health questionnaires only started to be systematically collected from January 2016 and the three years postpartum visit has only been added recently.

2.3.2.5 Data collection visits

There were three data collection visits for studies C and D. The first data collection took place at the first GDM visit at which anthropometric, mental health and socio-demographic outcomes were collected. The second data collection took place at the last GDM visit, at which anthropometric, mental health outcomes and information about the intake of glucose-lowering medication (for study D only) were collected. In study D only, a third data collection took place at the 6-8 weeks postpartum visit during which mental health outcomes were collected.

2.3.2.6 Mental health outcomes and measures

Mental health outcomes included depression and well-being. For study C and D, these mental health outcomes were assessed with the help of two validated questionnaires: the EPDS and the World Health Organization Well-being Index-Five (WHO-5) both described below.

The EPDS measured symptoms of depression in the preceding seven days [151]. Self-report questionnaires were distributed in French and in English. For women who did not understand these languages, a certified professional translator was provided by the GDM clinic at the CHUV to help women complete the questionnaire. This was done to ensure that the multi-ethnicity and diversity of the women coming at the GDM clinic at the CHUV was accounted for. Each item of the EPDS measured symptoms of depression with items, such as: "I have been able to laugh and see the funny side of things" on a 4-point scale, the minimum and maximum total scores being 0 and 30, respectively. In both studies, a dichotomous variable using a cut-off of ≥ 11 to separate women with or without clinically relevant depression scores was created [152]. For this cut-off, the terminology "clinically relevant symptoms of depression" was chosen, given that clinical interviewing represents the gold

standard to diagnose depression [153]. The EPDS has been validated in pregnant women [152], as well as in a French sample. Good psychometric properties have been reported, with good criterion validity and internal consistency (Cronbach's alpha: 0.76), as well as good short term test-retest reliability (0.98) [154].

The WHO-5 assessed the subjective well-being of the participants with five questions [155]. As the WHO-5 is validated in 31 different languages, it was administered in a variety of different languages in accordance with the ethnical diversity of the patients. The items are unidimensional and measured well-being with items such as: "I have felt cheerful and in good spirits" on a 5-point Likert scale ranging from 0 'at no time' to 5 'all of the time'. The final score was then calculated by multiplying the total score by 4. Thereby, the final score ranged from 0 to 100. The WHO-5 was originally designed to measure well-being (coping with illness), negative well-being (depression and anxiety) and energy, it used to be comprised of 28 items and was then reduced to fewer items [156]. When the five-item version was created, studies demonstrated that it could be used to measure depression, indicated by a total score of <13 [157] or < 50 for the final score [158]. In other studies, the WHO-5 also has been demonstrated to be highly negatively associated with observer-rated and self-report measures of symptoms of depression [159]. As the relationship between well-being and metabolic health in GDM pregnancy had not been studied when this study was initiated, this questionnaire was used to measure well-being [160]. The scale has shown to have adequate validity and good psychometric properties, as the Cronbach's alpha was of 0.88 and good internal consistency in French in a previous study [155]. This scale has been applied successfully across a wide range of study fields, though it has been used most extensively in endocrinology [161].

For study C, the EPDS was collected at the first GDM visit, whilst the WHO-5 was completed at the first and last GDM visits. For study D, data from the EPDS and the WHO-5 was additionally collected at 6-8 weeks postpartum. Please see an overview of these data collection visits in Figure 6.

2.3.2.7 Anthropometric outcomes and measures

In this thesis, anthropometric outcomes included weight, weight gain, height and BMI. Weight was measured in light clothes and without shoes to the nearest 0.1 kg and height was measured to the nearest 0.1 cm both these measures were assessed with a regularly calibrated electronic scale (Seca®). Body Mass Index (BMI) was calculated based on the measured height and weight using the formula weight(kg)/[height(m)]^2. For study C only, a "weight gain during pregnancy" variable was calculated by subtracting the weight at first GDM visit from the weight at the last GDM visit. In study C, anthropometrics from the first and last GDM visit were used. In study D, only BMI was used as a confounder in some of the analysis.

2.3.2.8 Socio-demographic variables

For both studies C and D, additional socio-demographic variables were collected during the clinical visits or extracted from medical records. These variables were social support, maternal age, educational level, prior GDM diagnosis, family history of diabetes and HbA1c; which was measured via a chemical photometric method (conjugation with boronate; Afinion®) [162, 163] These variables were all collected at the first GDM visit except for gestational age which was collected at both the first and the last GDM visits.

2.3.2.9 Statistical analysis

Hereafter, only the analyses that took place for study C are described. All analyses were carried out with Stata/SE 15.0 (StataCorp LLC, TX, USA). Continuous and normally distributed variables were described as means and standard deviations and ordinal outcomes were described as frequencies and percentages. Statistical significance was set at $p<0.05$. Additionally to means and standard deviations for continuous variables, normality of distribution was graphically assessed with normal QQ-plots.

Analysis: For aim 3, investigating the evolution of well-being through time and (3^{bis}) its association with depression, a paired t-test was conducted to study if well-being changed between the first and the last GDM visits. The association between well-being and depression was then measured at the first GDM visit through univariate linear regressions with the depression score and cut-off of ≥ 11 as independent variables and the well-being score as the dependant variable.

For aim 4, investigating the prospective association between mental health variables, weight ($4a^1$), and weight gain ($4a^2$), univariate linear regressions were conducted with the depression score and the cut-off of ≥ 11 and the well-being score all measured at the first GDM visit as the independent variables. The dependant variables were weight at the first GDM visit and weight gain between the first and the last GDM visits.

Models: For all regressions, two models were used. In Model 1, no adjustments were made for confounders in order to assess the raw associations between two variables of interest. In Model 2, adjustments for the following confounding variables were made: maternal age, gestational age, educational level, and social support all at the first GDM visit. For aim 3 and $4a^2$, BMI at the first GDM was added as a confounder. The reason these confounders were added is because they are usually used as such in the current research in GDM (maternal age and BMI). More specifically, gestational age was added as it has an impact on the mother's weight [164] and the educational level [165] and social support status [166] have an impact on the mother's mental health.

Missing variables: At the first GDM visit, there were missing cases for the following variables: height (7), weight (18), BMI (19), weight gain (53), gestational age (2), ethnicity (5), social support (25), educational level (57), the depression score and cut-off (42), the well-being score (39). At the last GDM visit, there were missing cases for gestational age (120) and the well-being score (105). Therefore, imputations based on the Missing at Random assumption were conducted by using the Multiple Imputation by Chained Equations method [167]. Given that this led to similar results, the original data was used for this study.

2.3.3 Results

The 334 women integrated in this study had a mean age of 33.4±5.5 years, a mean gestational age of 28.9±3.3 weeks, a mean weight of 78.3±14.8 kg, a mean well-being score of 60.1±20.2 and a mean depression score of 7.5±5.5, with 26.0% of women having clinically relevant symptoms of depression at the first GDM visit. At the last GDM visit, the mean gestational age was 36.2±1.9 weeks, the mean weight was 80.6±14.8 kg and the mean well-being score was 67.2±18.3.

2.3.3.1 Evolution of mental health variables through time in pregnancy

The well-being score increased from 60.3 ± 20.5 at the first GDM visit to 67.4 ± 17.9 at the last GDM visit, indicating a 7.1 point (± 16.5) or an 11.8% increase on average among study participants (CI=4.9-9.3; p<0.0001), see Table 1 in the appendix section 8.3 for more details.

Table 2 below shows that the well-being and depression scores were negatively associated in both the models, whether the depression scores or cut-off of ≥ 11 were used. Strong and inverse correlations between the well-being and depression scores (r= -0.55; p<0.0001) were also found. The same association was weaker when the cut-off of ≥11 was used for depression (r= -0.47; p<0.0001).

Table 2. Associations between mental health variables at the first GDM visit.

	Model 1	Model 2
	β-Coefficient (95% confidence interval)	*β-Coefficient (95% confidence interval)*
	Well-being score	
Depression score	-2.077 (-2.445 – -1.708)**	-1.953 (-2.373 – -1.532)**
Depression cut-off of ≥ 11	-21.773 (-26.502 – -17.044)**	-20.933 (-26.203 – -15.622)**

** p<0.05, ** p<0.01*

Model 1 was an unadjusted linear regression model. Model 2 was a linear regression model with adjustments for: Maternal age, gestational age, educational level, social support and BMI at the first GDM visit.

2.3.3.2 Associations between mental health and weight variables

Table 3 below shows that mental health at the first GDM visit was not associated with weight at the same visit. In spite of that, after adjustments in model 2, there was a trend towards an inverse association between the well-being score and weight at the first GDM visit (β=-0.09; *p*=0.07).

Table 3. Associations between mental health variables and weight at the first GDM visit.

	Model 1	Model 2
	β-Coefficient (95% confidence interval)	*β-Coefficient (95% confidence interval)*
	Weight (kg)	
Depression score	0.048 (-0.259 – 0.356)	0.043 (-0.309 – 0.394)
Depression cut-off of ≥ 11	0.780 (-3.009 – 4.567)	1.534 (-2.794 – 5.861)
Well-being score	-0.055 (-0.138 – 0.027)	-0.088 (-0.184 – 0.008)

** p<0.05, ** p<0.01*

Model 1 was an unadjusted linear regression model. Model 2 was a linear regression model with adjustments for: Maternal age, gestational age, educational level and social support at the first GDM visit.

Table 4 below shows that mental health at the first GDM visit was not associated with weight gain between the first and last GDM visit, except for women with clinically relevant symptoms of depression. Indeed, in these women, the depression cut-off of ≥11 at the first GDM visit was significantly associated with subsequent weight gain in the unadjusted model.

Table 4. Associations between mental health variables at the first GDM visit and subsequent weight gain.

	Model 1	Model 2
	β-Coefficient (95% confidence interval)	*β-Coefficient (95% confidence interval)*
	Weight gain (kg) between the first GDM visit and the last GDM visit	
Depression score	0.056 (-0.029 – 0.142)	-0.011 (-0.104 – 0.082)
Depression cut-off of ≥ 11	1.249 (0.203 – 2.294)*	0.237 (-0.910 – 1.383)
Well-being score	0.007 (-0.016 – 0.030)	0.011 (-0.014 – 0.036)

** p<0.05, ** p<0.01*

Model 1 was an unadjusted linear regression model. Model 2 was a linear regression model with adjustments for: Maternal age, gestational age, educational level, social support and BMI at the first GDM visit.

2.3.4 Conclusion

This study showed that (3) mental health, and more specifically, well-being evolved positively between the first and last GDM visit. Secondly, it showed that (3^{bis}) the well-being and depression scores were inversely and overall moderately associated with one another as the well-being scores explained around 25% of the variance in the depression scores. This implies that other factors might impact both mental health variables and that it is more informative to measure them both. As this secondary aim was conducted solely to assess the usefulness of using both the well-being and depression scales, this association will not be discussed further in the thesis and both the scales will be used in study D. Clinically relevant symptoms of depression (cut-off of ≥ 11) were associated with subsequent weight gain (4), although none of the other measures of mental health were associated with weight or weight gain in this prospective clinical cohort of women with GDM.

2.3.5 Personal Contribution

The candidate significantly participated in the conception and design of the study, coordinated the study and the data collection, collected data, participated in the data analysis, participated in the interpretation of data, drafted and adapted the manuscript.

2.4 Study D: Mental health and its associations with glucose-lowering medication in women with gestational diabetes mellitus. A prospective clinical cohort study

Authors for D: **Leah Gilbert**, Argyro Nikolaou, Dan Yedu Quansah, Jean-Benoît Rossel, Antje Horsch* and Jardena J. Puder*

* joint last authors

Published in: **Psychoneuroendocrinology, 2020.**

2.4.1 Aims

The aims of study D were to investigate (3) the evolution of mental health in women with GDM up to the 6-8 weeks postpartum visit and ($4b^1$) if the intake of glucose-lowering medication independently modified this evolution and ($4b^2$) if mental health symptoms in women with GDM predicted an intake of glucose-lowering medication during GDM pregnancy. Clinically relevant symptoms of depression (4^{bis}) were also added as an interaction factor to investigate if the associations (4b) would change in their presence, i.e., if they were different in the presence of symptoms of depression. Hereafter is a summary of study D (for more details, see the last version of the proof of the accepted paper in Appendix 8.4).

2.4.2 Methods

As a reminder, the methods described in study C are applicable to study D from section 2.3.2 up to, but not including section 2.3.2.9, as both studies were conducted on the same prospective clinical cohort of women seen at the GDM clinic at the CHUV. Below, only the methods applicable to study D are described.

2.4.2.1 Glucose-lowering medication outcome and measures

Glucose-lowering medication was both an outcome and a predictor. It included two types of variables. First, a dichotomous (yes, no) variable named “glucose-lowering medication” was created to separate women who did or did not take glucose-lowering medication during their pregnancy. For additional and more detailed analysis, a second variable was computed with four categories: (1) no glucose-lowering medication intake, (2) metformin only (oral medication), (3) long-acting (basal) bedtime insulin (±metformin), and (4) short-acting (meal) insulin (± long-acting bedtime insulin and/or metformin). These categories of glucose-lowering medication were formed based on degrees of burden to the participants: from (1) putting no strain on women to (4) being most burdensome (as women have to carry syringes with them wherever they go and inject before the meals, often outside of their home). This variable is named “detailed glucose-lowering medication” in study D and the

reference category is 1=no glucose-lowering medication intake. The information regarding glucose-lowering medication intake was retrieved from the medical records at the last GDM visit.

2.4.2.2 Statistical Analysis

All analyses were carried out with SPSS (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). Descriptive statistics were conducted for socio-demographic variables. Continuous and normally distributed variables were described as means and standard deviations and ordinal outcomes were described as frequencies and percentages. Statistical significance was set at $p<0.05$.

Analysis : For aim 3, the trajectory of the depression and well-being scores between the first and last GDM visit and the 6-8 weeks postpartum were investigated. For this evolution, a linear mixed effects model was computed.

For aim $4b^1$ that investigated if this evolution of mental health was modified by the intake of glucose-lowering medication, prospective associations between the use of glucose-lowering medication and subsequent mental health at the last GDM visit and the 6-8 weeks postpartum visit, were assessed. For this aim a linear regression was performed when glucose-lowering medication was a binary predictor and a general linear model was performed when the detailed glucose-lowering medication was a categorical predictor. For aim $4b^2$, investigating the prospective association between mental health and the subsequent intake of glucose-lowering medication, logistic regression analyses were conducted with the intake of glucose-lowering medication (yes, no) as the dependent variable and with depression and well-being as the predictors. Finally, for aim 4^{bis}, to see if these associations were different in women with clinically relevant symptoms of depression, an interaction analysis was conducted and if the interaction terms were significant, a stratification analysis followed.

Models: For all regressions, two models were used. In Model 1, adjustments were made for maternal age and gestational weeks at the first GDM visit [168, 169]. In Model 2, variables that were significantly correlated with the respective dependent variable were added on top of Model 1. The following potential confounding variables were tested: family history of diabetes, prior GDM diagnosis, BMI, HbA1c, social support, and educational level all evaluated at the first GDM visit. Based on the results of the correlational analysis and for aim $4b^1$, only family history of diabetes was added as a confounder in Model 2 when the dependent variable was well-being, while there was no Model 2 when the dependent variable was depression, as none of the tested confounders correlated with this score. For aim $4b^2$ family history of diabetes, social support, educational level, and HbA1c were added as confounders in Model 2. Furthermore, the regressions were adjusted for baseline mental

health variables assessed at the first GDM visit and completely unadjusted models were also tested. As both these analysis did not change the results, models 1 and 2 were selected.

Missing variables: At the first GDM visit, there were missing cases for maternal education (55), social support (22), family history of diabetes (22), gestational age (5) and HbA1c values (10) and there were missing cases for gestational age at the last GDM visit (109) too. For the well-being scores, there were missing variables at the first (33) and last GDM visits (99) and at the 6-8 weeks postpartum visit (50). For the depression scores, there were missing cases at the first GDM visit (36) and at the 6-8 weeks postpartum visit (51). Missing data were not imputed.

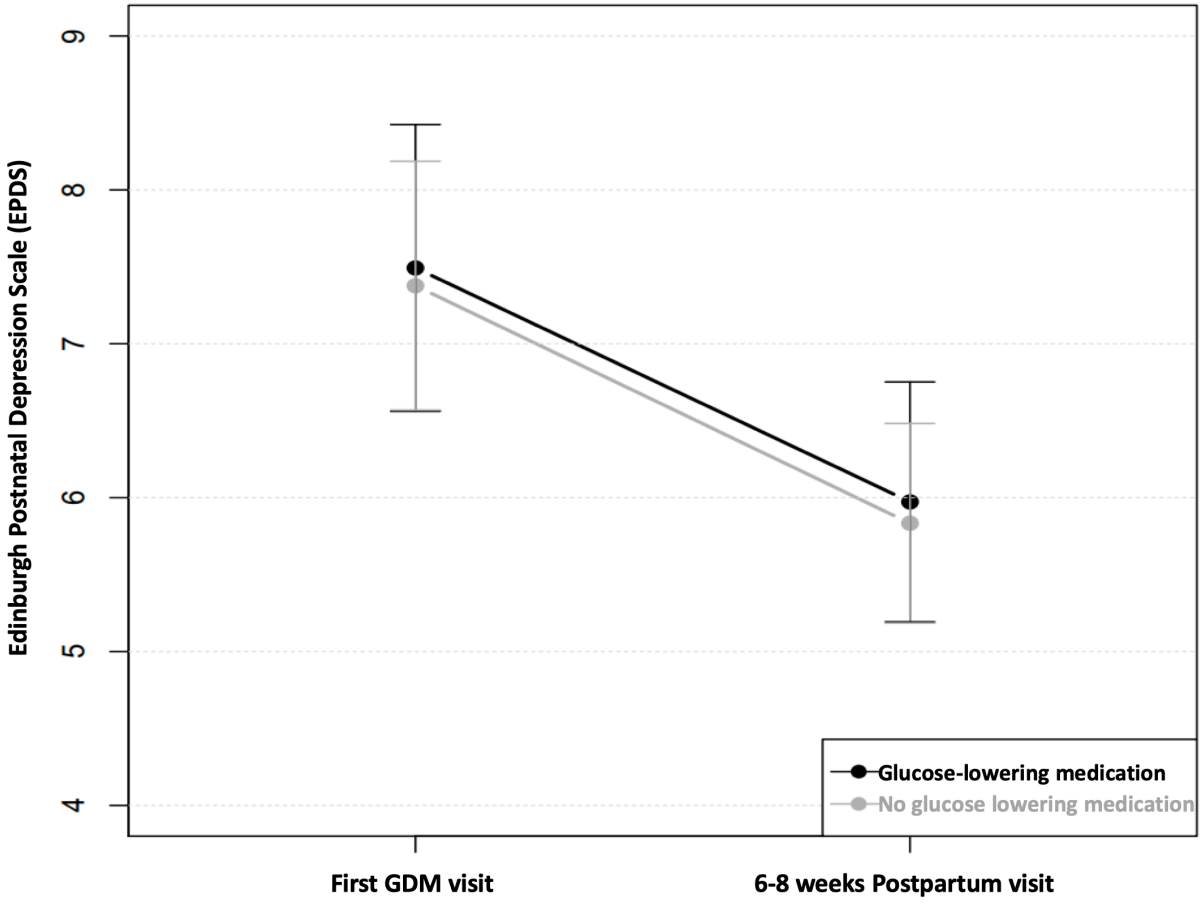
2.4.3 Results

The 341 women integrated in this study had a mean age of 33.62±5.34 years and a mean gestational age of 28.85±3.38 weeks at the first GDM visit. 25.2% of them suffered from clinically relevant symptoms of depression, and 47.8% of women took glucose-lowering medication during their GDM pregnancy, see Table 1 in appendix 8.4 for more details.

2.4.2.1 Evolution of mental health variables between the first GDM and the 6-8 weeks postpartum visits

Figure 8 below shows that the depression scores decreased by 26% between the first GDM visit and the 6-8 weeks postpartum visit (B=-1.74, CI= -2.22 – -1.26, p<0.01). Specifically, mean scores changed from a 7.43 ± 5.46 at the first GDM visit to 5.90 ± 4.40 at 6-8 weeks postpartum.

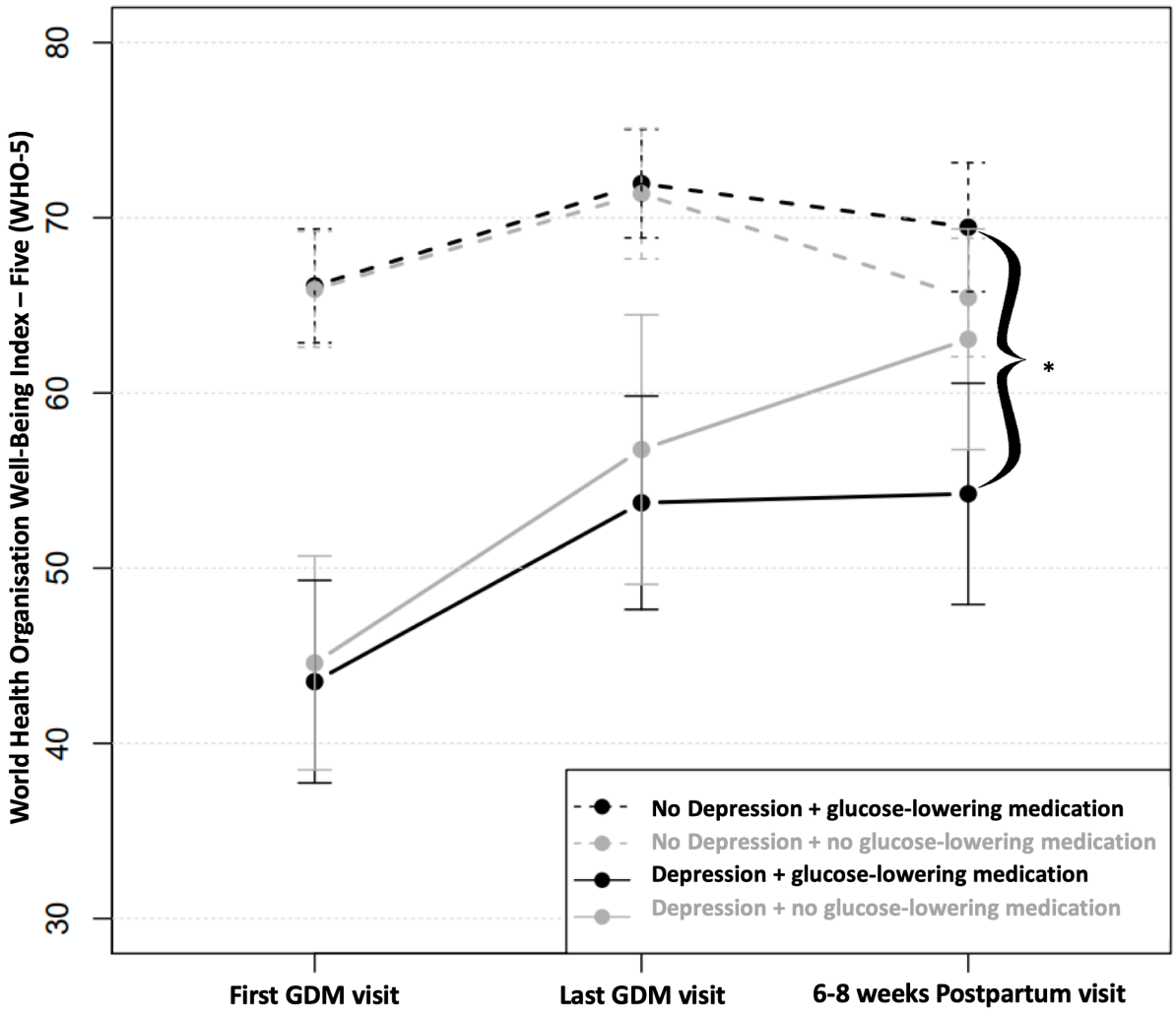
Figure 8. Evolution of the depression scores in study D.



Values are shown as means and standard errors. For illustrative purposes, women with and without glucose-lowering medication were separated and the figure demonstrates an overall effect of time with significant decreases in mean depression (EPDS) (B=-1.74, CI= -2.22 – -1.26, p<0.01) in both groups.

Figure 9 below also shows time had a positive effect on the well-being scores. Indeed, they increased overall by 7% between the first GDM and the 6-8 weeks postpartum visits (*B*=2.49, CI= 1.34 – 3.64, *p*<0.01). More specifically, the mean well-being scores changed from 60.55 ± 20.368 at the first GDM visit to 67.59 ± 17.96 at the last GDM visit, and to 65.43 ± 18.79 at 6-8 weeks postpartum visit.

Figure 9. Evolution of the well-being scores in study D.



*Values are shown as means and standard errors. For illustrative purposes, women with and without glucose-lowering medication were separated and the figure demonstrates the overall effect of time with significant increases in the well-being (WHO-5) scores in the overall sample (B=2.49, CI= 1.34 – 3.64, p<0.01). Of all interaction effects tested, the only significant finding relates to the presence or not of clinically relevant depression at the first GDM visit on the association between glucose-lowering medication in pregnancy and the well-being score at 6-8 weeks postpartum (*p for interaction=0.01).*

2.4.3.2 Associations between the intake of glucose-lowering medication and subsequent mental health during and after pregnancy

The intake of glucose-lowering medication (as a dichotomous variable and as a four categories variable) during pregnancy had no impact on this positive evolution of mental health either during or after pregnancy. There was one exception, in the 13 women using metformin during pregnancy, there was an improvement in the well-being scores at the postpartum visit compared to women with no glucose-lowering medication (using the 4-categories variable, *p*=0.03, see Table 5 below).

Table 5. Associations between detailed glucose-lowering medication treatment during pregnancy and subsequent mental health.

	Model 1	Model 2
	Well-being scores at the last GDM visit	
Metformin vs none	B= -0.62 (CI= -11.66 – 10.43)	B= -0.99 (CI= -11.63 – 9.65)
Long-acting Insulin vs none	B= -2.95 (CI= -8.86 – 2.96)	B= -1.99 (CI= -7.79 – 3.82)
Short-acting Insulin vs none	B= -0.54 (CI= -6.22 – 5.13)	B= -0.24 (CI= -5.84 – 5.36)
	Well-being scores at 6-8 weeks postpartum	
Metformin vs none	B= 11.65 (CI= 1.06 – 22.24)*	B= 11.42 (CI= 0.92 – 21.92)*
Long-acting Insulin vs none	B= -1.97 (CI= -7.60 – 3.67)	B= -1.41 (CI= -7.16 – 4.34)
Short-acting Insulin vs none	B= 1.26 (CI= -4.04 – 6.55)	B= 1.57 (CI= -3.81 – 6.95)
	Depression scores at 6-8 weeks postpartum	
Metformin vs none	B= -0.15 (CI= -2.64 – 2.34)	-
Long-acting Insulin vs none	B= 1.00 (CI= -0.34 – 2.31)	-
Short-acting Insulin vs none	B= 0.46 (CI= -1.72 – 0.80)	-

** p <0.05*

Results were reported as β-Coefficient (95% confidence interval) from a general linear model.

The following three categories are compared to (1) "no glucose-lowering medication" (termed "none") being used as a reference category: (2) metformin only, (3) long-acting (basal) bedtime insulin (±metformin), and (4) short-acting (meal) insulin (± long-acting bedtime insulin and/or metformin).

Model 1 was adjusted for maternal age and gestational age at first GDM visit.

Model 2 was adjusted for maternal age, gestational age, family history of diabetes and well-being at the first GDM visit, except for the analyses with the depression scores at 6-8 weeks postpartum, for which no additional confounders were added as no additional variables were correlated to the dependent variable.

Moreover, when analyzing the interaction effect of clinically relevant symptoms of depression on the association between glucose-lowering medication and subsequent mental health, one interaction effect was significant. In women with clinically relevant symptoms of depression, glucose-lowering medication in pregnancy was associated with a lower improvement in the well-being score

between the first GDM and the 6-8 weeks postpartum visit compared to women without clinically relevant symptoms of depression (*p* for interaction=0.01, Figure 9). Thus, further stratification analysis were conducted and showed that, in women with clinically relevant symptoms of depression, glucose-lowering medication was associated with a non-significant -8.82 (*p*=0.063) point decrease in the well-being scores at the 6-8 weeks postpartum visit. In women without symptoms of depression, glucose-lowering medication lead to a non-significant increase of 4.02 points (*p*=0.12) in the well-being scores at 6-8 weeks postpartum. There was no other interaction effect of clinically relevant symptoms of depression on the associations between glucose-lowering medication during pregnancy and subsequent mental health.

2.4.3.3 Associations between mental health and the subsequent intake of glucose-lowering medication during pregnancy

Neither the depression (OR=1.0 (CI=0.96 – 1.04; *p*=0.94) nor the well-being scores (OR=0.99 (CI=0.98 – 1.01; *p*=0.29) at the first GDM visit predicted a subsequent intake of glucose-lowering medication during pregnancy in this prospective clinical cohort of women with GDM. These results remained similar in Model 2 [(OR=0.99 (CI=0.93 – 1.04; *p*=0.62) and (OR=0.99 (CI=0.98 – 1.01; *p*=0.30)]. Clinically relevant symptoms of depression at the first GDM visit did not change the association between the well-being score and the subsequent intake of glucose-lowering medication (*p* for interaction=0.80).

2.4.4 Conclusion

This prospective clinical cohort study showed that (3) mental health evolved positively through time in this cohort of women with GDM. The study also ($4b^1$) did not find that the intake of glucose-lowering medication impacted overall on this positive evolution of mental health, neither during nor after pregnancy. However, the interaction analysis (4^{bis}) demonstrated that in women that had clinically relevant symptoms of depression at the first GDM visit, glucose-lowering medication led to less improvements in the well-being scores at the 6-8 weeks postpartum visit compared to women with no symptoms of depression. No other interaction effect was found in the investigated associations ($4b^1$ and $4b^2$). Furthermore, mental health ($4b^2$) was not associated with a subsequent intake of glucose-lowering medication. Thus, this study demonstrated that glucose-lowering medication could be prescribed without the risk of worsening mental health symptoms and that women with symptoms of depression may benefit from psychosocial well-being interventions.

2.4.5 Personal Contribution

The candidate significantly participated in the conception and design of the study, coordinated the study and the data collection, collected data, conducted the data analysis, participated in the interpretation of data, and drafted and adapted the manuscript.

3. GENERAL DISCUSSION AND PERSPECTIVES

This thesis set out to investigate how psychosocial well-being factors influence lifestyle behaviors and metabolic health in women with GDM through four different studies. The first aim of this thesis (study A) was to synthetize evidence on (1a) how diet, physical activity and psychosocial well-being interact in women with GDM and their offspring and on (1b) how effective interventions were in reducing adverse outcomes related to GDM. The key finding for study A was that psychosocial well-being had never been integrated as a part of lifestyle interventions in women with GDM, although social support and self-efficacy were associated with improvements in lifestyle behaviors, such as diet and physical activity, in both observational studies measuring these associations. Study A also demonstrated that lifestyle interventions were associated with diet and frequently to physical activity, and with some improved adverse outcomes related to GDM (i.e. waist and hip circumference, LDL cholesterol, triglycerides, oGTT, postprandial glucose values, and postpartum diabetes status) and with psychological factors (i.e. stress, quality of life and fatalistic beliefs). The second aim of this thesis (study B) was to test the effect of an interdisciplinary lifestyle and psychosocial well-being continuous perinatal intervention in women with GDM on maternal, infant and paternal metabolic and mental health outcomes. As this trial is still ongoing, the thesis solely presented the study protocol. The third aim of this thesis was to investigate the evolution of mental health (specifically depression and well-being) through time (studies C and D). The key findings of these last two studies was that mental health evolved positively between the first and the last GDM and the 6-8 weeks postpartum visits and that it was unaffected by the intake of glucose-lowering medication, except in women with clinically relevant symptoms of depression. In this last subgroup, the intake of glucose-lowering medication was associated with less improvements in the well-being scores at the 6-8 weeks postpartum visit. The fourth aim of this thesis investigated the associations between mental health and adverse outcomes related to GDM such as weight (4a[1]), weight gain (4a[2]) (study C), and glucose-lowering medication (4b) during and/or after GDM pregnancy (study D). The key findings of studies C and D were that mental health was not associated with weight, weight gain or glucose-lowering medication after GDM diagnosis. Nevertheless, an exception was again observed in women with clinically relevant symptoms of depression, whereby these symptoms were associated with subsequent weight gain during pregnancy in this cohort of women with GDM.

3.1 Interpretation of findings

3.1.1 Key finding 1: Psychosocial well-being, lifestyle interventions and outcomes

The first key finding showed that psychosocial well-being was not a part of lifestyle interventions, although psychosocial well-being variables such as social support and self-efficacy were

associated with a healthy diet and physical activity. Furthermore, lifestyle interventions improved diet and mostly physical activity as well as some of the adverse outcomes related to GDM and stress, quality of life and fatalistic beliefs (in study A). The fact that no previous studies were found on psychosocial well-being interventions was not surprising, given that psychosocial well-being in women with GDM has only started to be investigated recently, as can be seen on PubMed [170]. The fact that psychosocial well-being improved adherence to diet and physical activity can be corroborated by the adapted theoretical biopsychosocial model of mental health, and by previous research showing an effect of psychosocial well-being on lifestyle behaviors in women with GDM [30-32].

Study A also demonstrated that only social support and self-efficacy were associated with lifestyle behaviors, and no information was found on the direct impact of mental health symptoms on these lifestyle behaviors. This is surprising because mental health symptoms are known to be important barriers to adopt healthy lifestyle behaviors in women with a history of GDM [31]. Consequently, mental health symptoms should be taken into account when investigating women's lifestyle behaviors. One could hypothesize that the improvements found in diet and physical activity in study A, could be caused by a positive evolution of mental health following improvements in self-efficacy and social support [27, 29, 92, 111]. The *MySweetHeart trial's* protocol which was based on the results of study A will contains factors which should enable the adherence to lifestyle interventions in women with GDM by inserting a psychosocial well-being intervention. Hence, as described in section 2.2.2.5, the trial contains interventions which aim to improve social support, self-efficacy and mental health. This could and hopefully will, in turn, reduce sedentary behavior and poor diet quality [82, 85], which should reduce the risk of obesity [112-114]. Both the healthy lifestyle behaviors and the reduced obesity risk will then help to reduce adverse outcomes related to GDM and the development of metabolic diseases [64, 85, 96-98, 102, 109, 110]. This reduction of adverse outcomes related to GDM was only partly shown in study A, as lifestyle interventions only led to improvements in waist and hip circumference, LDL cholesterol, triglycerides, oGTT, postprandial glucose values, and postpartum diabetes status. Although, in the conceptual model that derived from study A, it is hypothesized that as psychosocial well-being improved adherence to lifestyle behaviors (diet, physical activity), it would have the potential to improve adverse outcomes related to GDM to a higher extent than a stand-alone lifestyle intervention. Furthermore, it could probably improve the obstetric and neonatal outcomes, which had shown inconsistent results in study A. Therefore, the *MySweetHeart trial* may have the potential to improve the adverse outcomes related to GDM in the mother, the infant and perhaps also, in the partner.

Finally, the fact that lifestyle interventions led to the reduction in stress and fatalistic beliefs and to improvements in the quality of life could be explained by the fact that the women following a

lifestyle intervention feel empowered [1]. A lifestyle intervention may allow them to gain control over their GDM and this may therefore reduce their stress levels and augment their quality of life as they have new resources to deal with GDM management. The education they receive may also lead to a new comprehension of their illness and therefore to less fatalistic beliefs with regards to their diabetes [1, 121]. Furthermore, reductions in stress, fatalistic beliefs and augmentation in quality of life may, in turn, reduce mental health symptoms such as depression [171-173]. This last hypothesis can also be corroborated by the second key finding discussed below, as it showed a positive evolution of mental health in women with GDM treated through a lifestyle intervention at the GDM clinic at the CHUV.

3.1.2: Key finding 2: The positive evolution of mental health

The second key finding was the positive evolution of mental health through time in studies C and D in the short time separating GDM diagnosis and the 6-8 weeks postpartum visit. This positive evolution was unaffected by glucose-lowering medication and was influenced by clinically relevant symptoms of depression. The overall positive evolution of mental health shows that even if women with GDM suffer from mental health symptoms in the perinatal period more often [174], they are still able to attain similar mental health scores at the 6-8 week postpartum visit compared to women without GDM [175]. This positive evolution could be due to the social support they receive from the clinicians that care for them [176, 177]. The results also demonstrated that this positive evolution of mental health could also simply be due to a time-effect, and it could be explained by a recovery after the initial disappointment or shock of the diagnosis [92].

This positive evolution of mental health was unaffected by the presence of glucose-lowering medication, as demonstrated in study D and as shown by previous research in women with GDM [82]. This could imply that, in this prospective clinical cohort, glucose-lowering medication is well accepted. Previous studies have shown that insulin and metformin are generally well accepted during pregnancy in women with GDM [108], although insulin can also be a source of fear and anxiety in women with GDM [178]. Based on the data, the intake of glucose-lowering medication is not an additional burden that could impact mental health, as initially hypothesized and as illustrated in the adapted theoretical biopsychosocial model of mental health, demonstrating a bidirectional relationship between mental health symptoms and glucose-lowering medication (that is given only in the case of high glucose values represented as red factors in the model).

Notwithstanding, the positive evolution of mental health was reduced in women who had both clinically relevant symptoms of depression and glucose-lowering medication. Indeed, these women experienced a lower increase of the well-being scores at the 6-8 weeks postpartum visit,

compared to women with no symptoms of depression. This finding was not surprising, because, in the general population is has been shown that depression is negatively associated with well-being [179] and, to that end, depression in pregnancy could have directly affected well-being in the postpartum period. Secondly, as these women stop glucose-lowering medication at delivery, there could be an increase in stress related to the oGTT test that takes place at 6-8 weeks postpartum (see illustration of visits in Figure 6). These women may be more stressed by the results of this test, as they are used to experiencing high glucose values and to taking glucose-lowering medication to control them. As stress is known to lead to symptoms of depression in pregnancy and in the postpartum [171-173] and given that these women already had clinically relevant symptoms of depression in pregnancy, all of this together may lead them to attain lower levels of well-being.

3.1.3 Key Finding 3: Mental health and its impact on metabolic health

The third key finding was the fact that mental health was not associated with subsequent weight, weight gain or the intake of glucose-lowering medication. An exception was found for clinically relevant symptoms of depression which were associated with subsequent weight gain in pregnancy. As operationalized by the bidirectional relationship illustrated at the center of the adapted model, mental health symptoms should affect adverse outcomes related to GDM, such as weight or weight gain, and lead to higher glucose values [99], which could then lead to the intake of glucose-lowering medication [35, 44, 104]. Conversely, well-being should improve adverse outcomes related to GDM and therefore may be negatively associated with weight, weight gain or the intake of glucose-lowering medication. Surprisingly, there were no associations between mental health or mental health symptoms and either of these outcomes, except in women with clinically relevant symptoms of depression. This last finding is in line with previous studies which demonstrate that depression is associated with weight gain in pregnancy [112, 180] and in the general population [114]. However, the rest of the findings showing no association between mental health and weight are in contradiction with previous studies. These studies show that symptoms of depression are associated with weight [113, 181], and that well-being is negatively associated with weight in the general population [182]. Moreover, in previous research, mental health symptoms were associated with metabolic issues (i.e. GDM development, its related adverse outcomes and other metabolic diseases) and should therefore be associated with higher glucose values in GDM pregnancy and thereby lead to a higher intake of glucose-lowering medication [71, 109].

Regarding the fact that no significant association between mental health and weight or weight gain were found, this may be due, firstly, to the short time period separating the first and last GDM visit. There was a mean of seven weeks separating the first and the last GDM visits. The mean weight gain between these two visits was low, as it was around 2.4 (±3.5) kgs. In a similar cohort of women

with GDM, our team has shown that women usually gain 12.75 (±5.96) kgs over the whole pregnancy [183]. The time frame chosen for study C might have then, been too short to capture the potential effects of mental health on weight and weight gain in pregnancy. Associations between mental health symptoms before GDM diagnosis and weight or weight gain over the whole pregnancy may have been found, as shown in previous research [184]. Also, if these associations would have been studied in the postpartum period, they could have yielded different results. Indeed, previous research has shown associations between mental health symptoms and weight retention in the postpartum period [185]. There may also have been an impact of the care women with GDM received between the first GDM visit and last GDM visit at the GDM clinic at the CHUV on their weight gain. As this population of women received diet and physical activity counselling and their weight gain was discussed shortly after their GDM diagnosis (as described in section 1.5), there may be have been an effect of these interventions on weight gain, as supported by some of the results in study A [3, 5, 9, 13] and by the adapted theoretical biopsychosocial model of mental health. Finally, previous research has shown that the relationship between depression and gestational weight gain may differ depending on the timing of onset depression and that weight gain may even be reduced in women with pre-pregnancy depression [186]. Thus, in women with previous depression in the cohort, this could explain why no association between mental health symptoms and weight or weight gain were found.

Concerning the fact that no association between mental health symptoms and the subsequent intake of glucose-lowering medication were found, this can be interpreted in light of the care women receive in the cohort. Indeed, the healthcare providers at the CHUV offer social support to women with GDM which may lead to improvements in mental health [92, 176] as well as to subsequent changes in lifestyle behaviors [82, 85, 87]. The social support and/or the positive evolution of mental health and/or the positive changes in lifestyle behavior might all have been confounders in the associations between mental health and glucose values. Indeed, one can hypothesize that at least one of these factors might have confounded the bidirectional association which was investigated between mental health and the subsequent intake of glucose-lowering medication. The same can be concluded with regards to the fact that no association between well-being and glucose-lowering medication were found. Indeed, as well-being is considered to be the opposite of depression [179], this would have either yielded significant findings for the association between both mental health variables and glucose-lowering medication or none.

3.2 Clinical implications of findings

3.2.1 Key Finding 1: The unanswered questions that remain

As this thesis's first key finding demonstrates, there is a gap in the scientific literature with regards to the impact of mental health on lifestyle behaviors, but also in the clinical integration of psychosocial well-being interventions in women with GDM. It also demonstrated that lifestyle interventions improved some adverse outcomes related to GDM as well as led to reductions in stress, fatalistic beliefs and augmented the quality of life in these women. This has important clinical implications on mothers with GDM and potentially also on their infants and partners. The gap in the literature may be filled by the *MySweetHeart trial* as it will allow an investigation of the combination of different approaches aimed at improving social support, self-efficacy (HAPA model and motivational interviewing), mental health (CBT approaches if indicated by a score of ≥10 on the EPDS), diet and physical activity. Hence, this trial will allow to measure the efficiency of this novel and interdisciplinary lifestyle and psychosocial well-being approach on the improvements in social support, self-efficacy, mental health and on the adherence to lifestyle behaviors [82, 85, 87], and, on the reduction of the adverse outcomes related to GDM [96, 98, 102]. This will be done by comparing the control group, receiving usual care described in section 1.5, to women receiving the novel lifestyle and psychosocial well-being intervention described in section 2.2.2.5. This may have broad implications for the guidelines that are currently used in women with GDM, as this would be a first step in showing that psychosocial well-being interventions need to be integrated into the care given to women with GDM. On the contrary if the women following the intervention have a similar perception of social support, self-efficacy, mental health symptoms, comparable lifestyle behaviors and cardio-metabolic outcomes than women in the control group, there would be no need for an integration of a psychosocial well-being intervention of this type for the overall GDM population. Specific sub-groups (for example, women treated through CBT for their symptoms of depression) would then need to be analyzed to see if there were different benefits, and investigate what other type and duration of intervention would best be suited to these women's needs. Moreover, this trial was also designed to integrate the infant and the partner of women with GDM and may yield interesting results. Partners and infants related to women in the intervention group may also have improved mental health and metabolic outcomes. The results from the *MySweetHeart trial* will thus allow to inform future clinical practice in women with GDM and also, guidelines in a variety of other fields such as diabetes, obstetrics, pediatrics, child development, sport, nutrition and public health. Moreover, if the stand-alone lifestyle interventions in study A allowed a reduction in stress and fatalistic beliefs and augmented quality of life in women, the *MySweetHeart trial* will also have the potential to improve these psychological elements. The motivational part of the intervention will empower women to make healthy lifestyle

behavior changes and this may also reduce stress, fatalistic beliefs related to GDM and augment the women's quality of life [1, 121].

3.2.2 Key Finding 2: The clinical and medical care in women with GDM

The second key finding showing there is a positive evolution of mental health regardless of the intake of glucose-lowering medication, except in women with both glucose-lowering medication and clinically relevant symptoms of depression, has implications for clinical work. The first clinical implication is that this shows that even without the integration of a psychosocial well-being intervention most women evolve positively between the first GDM and the 6-8 weeks postpartum visit, showing that women at the GDM clinic at the CHUV seem to receive sufficient care and support to soften the initial shock of their GDM diagnosis. In spite of that, it is important to note these studies were only conducted over a short period of time. Another important clinical finding is the fact that the intake of glucose-lowering medication did not change this positive evolution of mental health. This is reassuring for the clinicians prescribing this medication to women with GDM, as it demonstrates that glucose-lowering medication can be prescribed without the risk of worsening mental health symptoms. The third clinical implication that can be extracted from this second key finding is that in women with both clinically relevant symptoms of depression and glucose-lowering medication in pregnancy, there is a lower improvement in the well-being scores at the 6-8 weeks postpartum visit. This may imply that it would be interesting to offer psychological support to these women from pregnancy and up to the postpartum period.

3.2.3 Key Finding 3: The importance of screening and treating mental health symptoms

Finally, the third key finding showed that mental health symptoms did not influence adverse outcomes related to GDM (weight, weight gain and glucose-lowering medication) in women with GDM with the exception of women with clinically relevant symptoms of depression. The association between clinically relevant symptoms of depression and weight gain in pregnancy (and the lower levels of well-being in the postpartum discussed above) has important clinical implications. This finding demonstrates the importance of assessing and treating symptoms of depression, as recommended by the National Institute for Health and Clinical Excellence [187]. Furthermore, clinically relevant symptoms of depression should be treated as they may lead to multiple adverse outcomes in the mother and infant and in their relationship. To cite a few examples, mental health symptoms are associated with a lower duration of breastfeeding [188]. They may also lead to relationship difficulties between the mother and her infant, which have shown to be prospectively associated with suboptimal development of cognitive and emotional functioning of the infant [189, 190] in the postpartum period. These symptoms should also be treated as they have an effect on

weight gain in pregnancy, which is known to be an important risk factor for adverse outcomes in the mother and the infant. Research has shown that, in GDM women both weight and excessive weight gain can increase hypertensive disorders during pregnancy and weight retention in the postpartum period, and augment the risk of developing type 2 diabetes and cardiovascular disease later in life [101-103, 191, 192]. Excessive gestational weight gain in women with GDM may also lead to perinatal complications, such as a higher risk of preterm and caesarean delivery, macrosomia, and to birth weights over the 90th percentile for age and sex [64, 96-98]. Given all the implications that may be related to clinically relevant symptoms of depression it seems important to screen for these symptoms and propose adapted care.

3.3 Theoretical implications of findings and perspectives for future research

The overall objective of this thesis was to investigate how psychosocial well-being factors influence lifestyle behavior and metabolic health in women with GDM. To answer this objective, the thesis was based on the adapted theoretical biopsychosocial model of mental health, which allowed a careful selection of the associations to investigate between the factors. This section lists and illustrates which associations from the model this thesis was able to corroborate, which findings contradicted the model, the inconsistencies that were found or the gaps in the literature and the remaining associations, which warrant further investigations.

3.3.1 Findings that supported the biopsychosocial model of mental health

The associations shown in this thesis are depicted in black in Figure 10 below. Firstly, were able to demonstrate the association between social support, self-efficacy and lifestyle behavior. Indeed, study A demonstrated that both social support and self-efficacy and lifestyle interventions improved the adherence to lifestyle behaviors, especially to diet. Study A also demonstrated that lifestyle interventions led to improvements in some of the adverse outcomes related to GDM. Finally, study A demonstrated that lifestyle interventions had the potential to influence psychological factors from the original theoretical biopsychosocial model of mental health such as stress, fatalistic beliefs and quality of life. Therefore, the findings in black reinforce these associations from the adapted theoretical biopsychosocial model of mental health.

3.3.2 Findings that contradicted the biopsychosocial model of mental health

The findings from studies C and D, illustrated in pink, contradicted the theoretical biopsychosocial model of mental health. The original model shows a bi-directional relationship between mental health and biological factors [(in this thesis these biological factors were: obesity and metabolic issues (i.e. the development of GDM, its related adverse outcomes and other metabolic

diseases)]. Contrarily, studies C and D demonstrated there was no relationship between mental health and the variables weight and weight gain and no bi-directional relationship between mental health and glucose-lowering medication, all of which are related to biological factors. This finding has theoretical and research implications as it shows that mental health might not directly impact adverse outcomes related to GDM, as demonstrated in the adapted theoretical biopsychosocial model of mental health. Indeed, the model was inspired from other models showing that mental health symptoms lead to adverse outcomes related to GDM and other metabolic diseases but the time-frame in which these diseases develop are not discussed [109, 110]. Nonetheless, mental health symptoms may have an impact on the health of these women and their infant in the long run [85, 193-196]. Therefore, research should focus on exploring the adverse outcomes related to GDM in the postpartum period, which may derive from mental health symptoms in the perinatal period. Moreover, mental health symptoms in the postpartum period were not assessed in this thesis, while they may lead to postpartum weight retention, which is also known to have detrimental metabolic impacts in the mother [183, 185, 197, 198]; so, this should be investigated in future studies. Furthermore, even if mental health and the intake of glucose-lowering medication in pregnancy did not influence each other in this thesis, mental health symptoms may affect glucose values [54] and, thus, postpartum diabetes status in these women. Also, glucose values and other adverse outcomes related to GDM in the postpartum, may affect subsequent mental health, as demonstrated by the model [109, 110]. As this bi-directional relationship was not studied in the postpartum period in this thesis and as it was contradicted by the results of studies C and D in pregnancy, research is still needed to elucidate this theoretical relationship. In summary, judging by the current literature implying a potential impact of mental health symptoms on adverse outcomes related to GDM, the theoretical model should be adapted to contain time-effects. Future research should focus on the effect of mental health symptoms in the perinatal period on adverse metabolic outcomes in the postpartum period and therefore investigate this through longitudinal studies. Studies should also investigate how the development of adverse outcomes related to GDM may affect subsequent mental health in this population. The *MySweetHeart trial* may allow to shed light on these associations in the first postpartum year.

3.3.3 Inconsistencies, gaps and research that still needs to be conducted to reinforce the biopsychosocial model of mental health

There were inconsistencies in some relationships between the factors, as illustrated by the grey arrows below. Study A demonstrated inconsistencies in the associations between lifestyle interventions and anthropometric and birth outcomes. Also, in study C, mental health was only associated with weight gain when women had clinically relevant symptoms of depression. However,

this result became non-significant when confounding variables were added (i.e. maternal age, gestational age, educational level, social support and BMI all at the first GDM visit) and no other mental health variables were associated to weight or weight gain. Given these inconsistencies, there is a need to further investigate these associations in future research. The *MySweetHeart trial* may shed some light on the effect of lifestyle interventions and of the more complex and novel psychosocial well-being intervention on anthropometry and birth outcomes as well as on weight and weight gain as hypothesized in the conceptual model from study A. Nevertheless, before investigating the effect of this novel psychosocial well-being intervention on these outcomes, it may be interesting to investigate this in the control group (receiving only a standard care, lifestyle intervention) from study B to either confirm or infirm these findings.

The grey, broken arrows demonstrate associations that were investigated but for which no results were found. Firstly, this concerned the association between social support, self-efficacy and mental health and the impact of all of these factors together (psychosocial well-being) on lifestyle behaviors. As shown in the adapted theoretical biopsychosocial model of mental health, psychosocial well-being impacts lifestyle behaviors and, consequently, may impact future disease risk. However, even if this model shows that the absence of adherence to lifestyle intervention theoretically augments future disease risk, the current literature on women with GDM does not enable us to conclude that by augmenting psychosocial well-being, overall adherence to lifestyle interventions could be improved and consequently increase overall future health [1, 121]. Nevertheless, findings from study A already showed improvements in lifestyle behavior when social support and self-efficacy were present. The *MySweetHeart trial* described in study B will only be a starting point to evaluate this theoretical improvement in future cardio-metabolic health in women with GDM through a novel psychosocial well-being and lifestyle intervention. This trial will also allow an evaluation of the - currently theoretical - impact of mental health on lifestyle behaviors.

Secondly, the grey, broken arrows demonstrate an absence of consideration of these associations if taken from the inverse perspective. This inverse perspective would be that lifestyle interventions may lead to improvements in mental health which would then lead to improvements in self-efficacy which would finally lead to improvements in lifestyle behaviors. Indeed, the adapted model did not conceptualize these associations in that direction. Although, some findings from study A indicate that this relationship between lifestyle interventions and subsequent psychosocial well-being may also work in that direction. Study A showed that lifestyle interventions improved psychological factors such as stress, fatalistic beliefs and quality of life. From these results, one could hypothesize that lifestyle interventions may also lead to direct improvements in mental health. As stress was reduced by lifestyle interventions, depression may also be reduced as a result of lifestyle

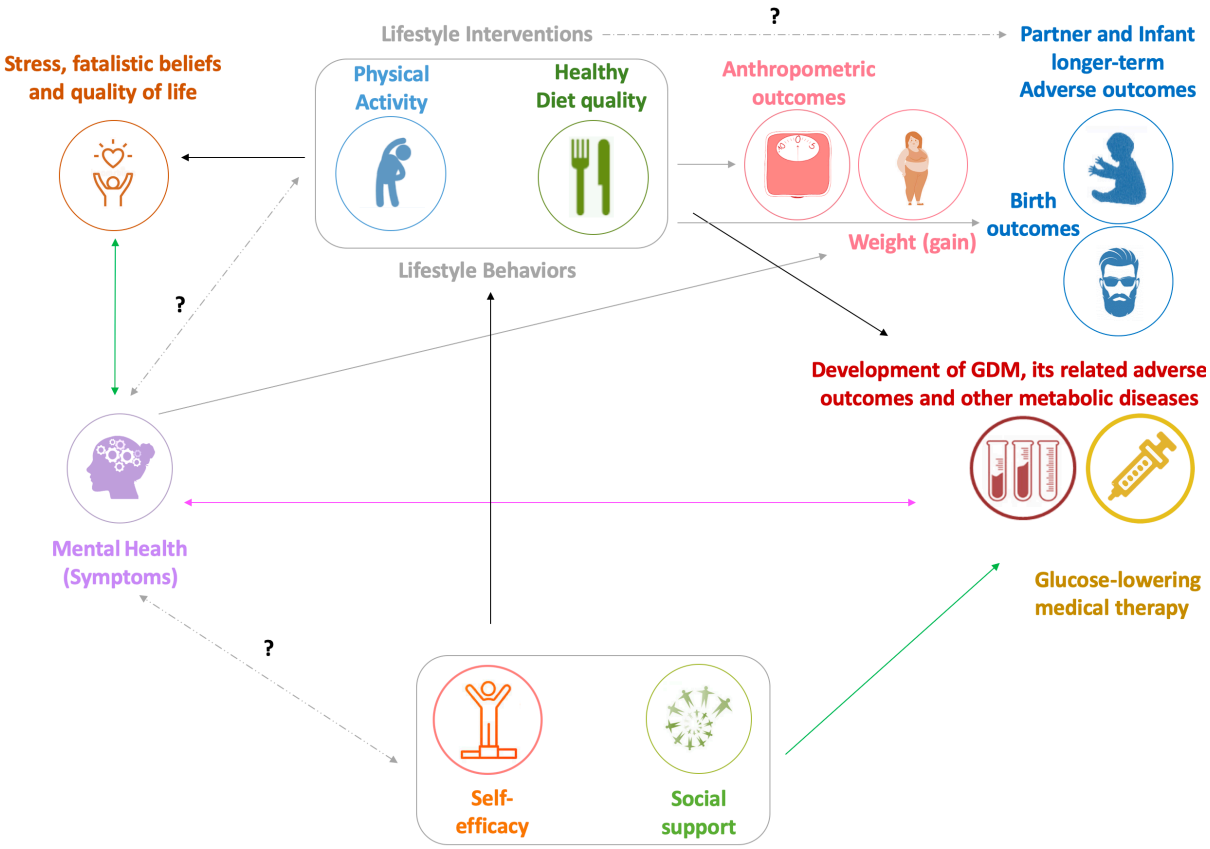
interventions, especially when considering the fact that stress and depression are associated to one another in pregnancy and in the postpartum [171-173]. Moreover, no conclusions can be drawn either on the direct impact of mental health on self-efficacy. Indeed, the literature review demonstrated an absence of consideration of the theoretical impact of mental health symptoms on the reduction of self-efficacy [27, 93, 95]. The control group from *MySweetHeart trial* following a lifestyle intervention only may allow an evaluation of the impact of lifestyle interventions on mental health and self-efficacy. This may therefore improve the theoretical biopsychosocial model of mental health and show that these associations function in both directions.

Finally, the grey, broken lines also demonstrate the absence of findings regarding the impact of lifestyle interventions on infant adverse outcomes after birth and on the health of the partner. The infants of women with GDM may suffer from this illness through different pathways. First, through the in utero environment, which contains higher levels of glucose, shunted towards the fetus through the placenta and which may lead to adverse birth outcomes [199, 200]. Secondly, as women with GDM suffer from mental health symptoms more frequently than women without GDM [174], there is an increased risk that they cannot respond appropriately to their child's needs. Indeed, this may lead to a misinterpretation of the child's hunger and satiety signals [193, 194], which may in turn augment the infant's obesity risk [195, 196]. Furthermore, the mother, infant and partner inevitably share common lifestyle behaviors with the mother [201, 202]. With the lack of appropriate psychosocial well-being interventions integrating the whole family and augmenting their adherence to healthy lifestyle behaviors, comes a risk for them to suffer from metabolic issues [203]. To that end, the transgenerational impact of GDM on the infant's health risk and the impact of GDM on the partner's health need to be investigated. Again, as the *MySweetHeart trial* integrated both the partner and infant in the intervention, this will allow an evaluation of their mental and metabolic health in general and also, the impact of a combined lifestyle and psychosocial well-being intervention on improvements in their health outcomes. Nevertheless, this will only be investigated up to one year postpartum and therefore, there may be a necessity to re-contact the fathers and infants later to assess their longer-term health outcomes.

There are also associations in the biopsychosocial model of mental health, which have not been investigated in this thesis as shown by the green arrows. There may be interesting associations between social support, self-efficacy and the intake of glucose-lowering medication, the development of adverse outcomes related to GDM or other metabolic diseases. One may hypothesize that the intake of glucose-lowering medication and the development of adverse outcomes related to GDM or other metabolic diseases may be reduced in the presence of high social support and self-efficacy. Indeed, previous research in diabetes has shown that self-efficacy and social support play an

important role in diabetes self-care, which may then influence glycemic control [28, 29, 204]. Finally, as study A showed, there were improvements in stress, fatalistic beliefs and quality of life following lifestyle interventions. The psychological factors such as the ones cited above may have the potential to influence mental health symptoms, indeed, stress is known to be related to symptoms of depression [171-173] and therefore, reductions in stress may lead to improvements in mental health symptoms. Conversely, reductions in mental health symptoms may lead to improvements in stress, fatalistic beliefs and quality of life. Therefore, this should be tested in future research. To summarize, comparing women in the intervention group of the *MySweetHeart trial,* receiving extra social support, to the women from the control group, may allow to evaluate the prospective impact of higher social support and perceived self-efficacy and the subsequent intake of glucose-lowering medication and of the development of adverse outcomes related to GDM or other metabolic diseases. Finally, it will allow to investigate the potential bidirectional relationship between psychological factors (stress, fatalistic beliefs and quality of life) and mental health.

Figure 10. Final adapted theoretical biopsychosocial model of mental health.



3.4 Strengths and limitations of the thesis

3.4.1 Strengths of thesis

The thesis at hand has many strengths. First of all, the topic of the thesis is innovative, as it is the first to investigate how psychosocial well-being influences lifestyle behaviors in women with GDM through a literature review (study A). Study B's protocol also proposes a novel interdisciplinary lifestyle and psychosocial well-being intervention and integrates the health of partners and infants of women with GDM. In addition, and as exposed in section 3.3, study B will enable a broad comprehension of psychosocial well-being in women with GDM up to one year postpartum and it will fill in the current gaps in the literature with regards to the associations illustrated in the final adapted model. Studies C and D have also addressed a gap in the literature regarding the impact of mental health on important adverse outcomes related to GDM, such as weight and weight gain and on the bi-directional relationship between mental health and glucose-lowering medication in pregnancy and in the early postpartum. Finally, it is also innovative as the studies of the thesis measured or are measuring outcomes in the pre- and postpartum period in women with GDM, their infants and partners. The results which will emanate from these measures will allow a global understanding of the mechanisms involved in GDM and the development of adverse outcomes related to GDM and other metabolic diseases through time, using a family-centered approach.

Secondly, this thesis followed a clear theoretical framework inspired by the theoretical biopsychosocial model of mental health. Such a framework has many strengths. Firstly, this allowed to define the subject at hand philosophically, epistemologically, methodologically and analytically [205], making findings which derive from the model more meaningful and generalizable [206]. The adapted biopsychosocial model of mental health also served as a foundation on which the research at hand was built, by adapting it to the GDM population [207]. The arrows between the factors presented in the adapted theoretical biopsychosocial model of mental health provided guidance on which associations to investigate and thereby prevented this thesis from deviating from the confines of the accepted theories. This allowed a final, and scholarly contribution to knowledge in women with GDM [207]. Finally, the selection of a theoretical framework testifies to the quality of this thesis as it required an understanding of the problem at hand, the purpose of each study, the significance of research questions and it allowed a final representation of the findings and what still needs to be investigated in research [207].

Thirdly, this thesis ensured methodological rigor by following research guidelines, by using validated self-report questionnaires and by controlling for important confounding factors. For each study design specific guidelines were followed; the PRISMA [115] and Whittemore and Knafl's [120]

guidelines for study A, the CONSORT guidelines for study B [128] and the STROBE statement [150] for studies C and D, hence insuring a quality-control of the reported research and methodological rigor. Studies B, C and D used well-developed and validated self-report questionnaires to measure mental health. Prior to conducting the analyses in Studies C and D, important confounding variables were identified through the literature and through testing correlations between potential confounders and the dependent variable (study D). This control for confounding variables allowed to confirm the validity of the results.

Fourthly, the studies in this thesis provided representativeness of both the current literature in women with GDM and of the ethnical diversity of the population at the GDM clinic at the CHUV. Firstly, Study A regrouped the largest possible scope of the literature, by using an integrative design [120]. This led study A to contain articles which had different designs and topics, allowing a comprehensive, thorough and up to date portrayal of the existing literature in women with GDM. Secondly, women from many ethnic backgrounds were integrated in the analyses of studies C and D. Indeed, the questionnaires measuring well-being were developed in a large number of languages and for questionnaires measuring symptoms of depression, women had the help of a professional translator.

Finally, there were important clinical and research implications which arose from the results of the studies. As these implications are discussed in section 3.2 and section 3.3 above, they will not be repeated here. There will also be more and important implications that will derive from the analysis of *the MySweetHeart trial* data in the near future.

3.4.2 Limitations of thesis

As described above, this thesis was based on a theoretical model so that the research questions were guided by a framework. Notwithstanding, the design of studies A (integrative literature review), C and D (prospective clinical cohort) do not allow to draw causal relationships between the investigated factors. The findings thus just allow to reinforce or question the associations depicted in the adapted biopsychosocial model. Furthermore, the model did not allow an illustration of longitudinal associations between the factors and as explained in section 3.3.3 this will need to be investigated in future studies. Lastly, the model portrays “clockwise” associations, although study A demonstrated that there were also “counterclockwise” associations (i.e. lifestyle interventions improved psychological factors and thus may influence mental health) which still need to be explored. The last two elements, if studied in future research, may allow a reinforcement of the final adapted model.

Even though the thesis provided methodological rigor through using guidelines, validated questionnaires and controlling for confounding variables, some pitfalls need to be addressed. In studies A and B, there are a few outcomes for which participants and clinicians were not blinded, which means that some of the results emanating from these studies could be biased. Indeed, in intervention studies in which the researchers measuring the outcomes are aware of the group (control versus intervention) the women belong to, may lead to biased reporting. Studies C and D share common limitations, such as the short time frame in which outcomes were measured. Longer periods of time might have yielded different results, especially regarding weight gain. Other potential confounders, such as the impact of the clinical care (number of appointments, and profession of the person giving advice) or diet and physical activity behaviors, may have had an effect on the studied predictors and outcomes. Regarding mental health measures in studies C and D, previous mental health symptoms or other potential mental health issues (such as anxiety and stress) were not measured and may have led to different findings or given a broader portrayal of mental health in women with GDM. Also, mental health was measured by self-report questionnaires, which have known weaknesses, such as cognitive biases (for example interpretation bias or catastrophizing which are especially present in depressed populations). Furthermore, these self-report questionnaire often have high sensitivity for the detection of depression and low sensitivity to changes in the patients [208-210]. The EPDS also has known specific weaknesses, such as its ambiguous questions or exclusion of participants with high levels of distress [211].

Regarding the objective of making the integrative review and the prospective cohort studies as representative as possible, this may have led to some issues. For example, studies with large heterogeneities were integrated in study A as an integrative design was used and that this design does not place restrictions on the design of original articles [120]. These heterogeneities mostly concerned the duration of the interventions, the general design and the reported outcomes. This implies that the results need to be interpreted with caution, as they may have concerned only a restricted period of time and may be measured during different phases of pregnancy and of the postpartum. Moreover, study A is prone to publication bias, as studies with no significant results are published less frequently [212]. Issues related to representativeness are also present in studies C and D as women were included regardless of their weeks of gestation at first and last GDM visits. However, in study D the results from the selected sample were compared with a smaller sample including only women that were between 24-32 weeks of gestation at the first GDM visit and that came after 36 weeks of gestation at the last GDM visit and the results from both samples were similar. To that end, this limitation can be considered to be minor. In studies C and D and given the clinical cohort context, there may be a high attrition rate. In study D for example, patients who did not attend both GDM visits were excluded and

this may have biased the results, as the study population was restricted. Finally, as the women from the GDM clinic at the CHUV receive a specific and efficient care regarding their GDM, they may not be representative with regards to the status of worldwide mental and metabolic health in women with GDM.

4. GENERAL CONCLUSION

This thesis set out to investigate how psychosocial well-being factors influence lifestyle behaviors and metabolic health in women with GDM through four different studies. The main findings of this thesis are that psychosocial well-being was never a part of lifestyle interventions in women with GDM, although it was always associated with improvements in lifestyle behaviors, such as diet and physical activity. The thesis also demonstrated that lifestyle interventions were mostly associated with improvements in some adverse outcomes related to GDM and in psychological factors (i.e. stress, fatalistic beliefs and quality of life). Furthermore, women from the prospective clinical cohort at the GDM clinic at the CHUV had a positive evolution in their mental health between the first GDM and the 6-8 weeks postpartum visits. This evolution was not influenced by glucose-lowering medication, except in women with clinically relevant symptoms of depression for which the well-being scores at the 6-8 weeks postpartum visit were less improved. Finally, it demonstrated that there was no association between mental health and weight, weight gain or glucose lowering medication. Again, there was an exception as clinically relevant symptoms of depression at first GDM visit were associated with a subsequent weight gain in pregnancy.

These results clearly illustrate that the psychological factors from the adapted theoretical biopsychosocial model of mental health (self-efficacy and lifestyle behaviors) are important in determining adverse outcomes related to GDM and may be associated to improvements in mental health. Firstly, because lifestyle interventions mostly improved adverse outcomes related to GDM in study A. Secondly, because it is through lifestyle interventions that the women in the prospective clinical cohort at the CHUV are treated and, during this treatment, their mental health evolved positively. The results and previous research also suggest that social support may have played a role in the positive evolution of mental health in the studied cohort. Social support may also be the reason why the investigations conducted on the bi-directional association between mental health and adverse outcomes related to GDM were either inconsistent or disproven. Therefore, this thesis shows that psychological factors are central elements in women with GDM and social support needs to be taken into account as a potential moderator in the bi-directional relationship between mental health and GDM and its adverse outcomes in pregnancy and surely also in the postpartum period.

The thesis also yielded strong clinical implications. Firstly, it demonstrated that the current care given to women with GDM in the prospective clinical cohort is sufficient for them to recover from the initial shock of their GDM diagnosis. Secondly, the fact that glucose-lowering medication was not associated with mental health symptoms means that this type of medication can be safely prescribed without the risk of harming the mental health status in women with GDM. Finally, this thesis

demonstrated that clinically relevant symptoms of depression seem to be an important factor to consider. These symptoms were associated with a smaller improvement in the well-being scores in the postpartum period in women who also took glucose-lowering medication. These symptoms were also associated with a subsequent weight gain in pregnancy and this could potentially lead to harmful outcomes in the mother and infant. This thesis therefore suggests that these clinically relevant symptoms should be screened for and treated.

While the adapted theoretical biopsychosocial model of mental health challenged some theoretical associations (pink arrow), provided insight into which associations would benefit from further investigation (grey arrows) and highlighted the current gaps in the literature and from the model (grey, broken and green arrows), it limited the longer-term vision. For example, the potential long-term impact of the GDM diagnosis, its adverse outcomes or the development of other metabolic diseases on the postpartum development of mental health symptoms were not investigated here. This can also be applied to the long-term impact of mental health symptoms in the perinatal period on the development of adverse outcomes related to GDM and metabolic diseases. This model was also very useful in showing inconsistencies in the results, which therefore warrant further research. Finally, the model showed gaps in knowledge. These gaps were related to the specific mechanisms between social support, self-efficacy, mental health and psychological factors. There were also gaps in the literature with regards to the health outcomes of infants and partners of women with GDM. Finally, the direct impact of social support and self-efficacy on adverse outcomes related to GDM and the bi-directional associations between mental health and psychological factors would benefit from being studied further. The *MySweeheart trial* results will inevitably enrich these findings and also provide further insight on these mechanisms in pregnancy and in the postpartum period.

5. OUTPUT AND CONTRIBUTION TO SCIENCE

This thesis was developed in collaboration with a multidisciplinary team of researchers composed of psychologists, physicians, dieticians, sport scientists, physiotherapists and student interns. Thus, the coordination work I had with regards to study B involved a tight collaboration with all of these researchers. Furthermore, regarding the *MySweetHeart trial*, I was co-supervising student interns on patient testing and coaching, addressed and answered questions from student interns and clinicians on testing procedures and the trial protocol, and I co-developed the intervention material for the patients, as well as the standard operating procedures we used for the data collection. The analyses of this ongoing trial, which includes mental health variables, will be a part of my Postdoctoral project, which will focus on the associations between mental health and metabolic outcomes in mothers and infants. I presented abstracts linked to the prospective clinical cohort (study C and D) in 6 conferences and abstracts linked to studies A and B in 4 conferences. I also presented my thesis in other settings, such as teaching and *"Ma thèse en 180 secondes"* (see Table 6). During my PhD, I also reviewed manuscripts for peer-reviewed journals (see Table 7 in Appendix 8.6.1), had teaching activities (see Table 8 in Appendix 8.6.2), and co-supervised a number of different student interns (see Table 9 in Appendix 8.6.3). Furthermore, I trained in a diversity of different domains, such as research (Good Clinical Practice), motivational interviewing, mindful eating, cognitive-behavioral therapy, physical activity, obesity in children and in interactive parent-child guidance practices (see detailed list in Appendix 8.5). Finally, I had several scientific outreach activities (see the list in Appendix 8.6), and participated as first author in one published article, one accepted article and on submitted article and as co-author in nine published articles (see Chapter 7).

Table 6. Participation in conferences, workshops and symposia.

Study	Title	Type of presentation	Place, date	Conference
D	Mental health and its associations with glucose-lowering medical therapy in gestational diabetes pregnancy: a prospective clinical cohort study.	Poster and walking presentation by Jardena Puder for which I recorded the presentation	Virtual 22-23.09.20	European Association for the study of Diabetes
D	Mental health and its association with glucose-lowering medical therapy in gestational diabetes pregnancy: a prospective clinical cohort study	Oral	Utrecht (virtual) 04.09.20	Diabetes in Pregnancy Study Groups

D	Mental health and its association with glucose-lowering therapy in GDM pregnancy. A prospective clinical cohort study.	Oral (presented by Jardena Puder as I was on maternity leave)	Bern, Switzerland, 14-15.11.19	Swiss Society of Endocrinology and Diabetes.
C	Mental health and its associations with weight in women with gestational diabetes mellitus. A prospective clinical cohort study.	Oral	Bern, Switzerland 11.09.19	Swiss Psychology Society
Other	Workshop for early career researchers on different themes.	Workshop	London, 03-06.09.19	Society for Reproductive and Infant Psychology
A + B	Role of psychosocial factors and mental health issues in GDM	Symposia	London, 03-06.09.19	Society for Reproductive and Infant Psychology
C	Mental health and its associations with weight in women with gestational diabetes mellitus. A prospective clinical cohort study.	Oral	London, 03-06.09.19	Society for Reproductive and Infant Psychology
C	Mental health and its associations with weight in women with gestational diabetes mellitus. A prospective clinical cohort study.	Oral and poster	CHUV, Lausanne, Switzerland 17.05.19	Swiss Perinatal Research Day
A	How diet, physical activity and psychosocial well-being interact in women with Gestational Diabetes Mellitus: An integrative review.	Poster and walking presentation	CHUV, Lausanne, Switzerland 21.02.19	Journée de recherche du département de médecine
A	How diet, physical activity and psychosocial well-being interact in women with Gestational Diabetes Mellitus: An integrative review.	Poster	Bern, Switzerland 16.11.18	Swiss Society of Endocrinology and Diabetology
Other	La santé mentale et métabolique pendant la période périnatale	Oral (competition)	UniFr, Fribourg, Switzerland 08.06.18	Ma thèse en 180 secondes, finale suisse
Other	La santé mentale et métabolique pendant la période périnatale	Oral (competition ; won third jury prize)	UniL, Lausanne, Switzerland, 22.03.18	Ma thèse en 180 secondes.

Other	Maternal stress during pregnancy is associated with obstetric and neonatal outcomes and can be influenced by glucose values.	Oral	CHUV, Lausanne, Switzerland 02.03.18	Journée de recherche en pédiatrie
Other	Maternal stress during pregnancy is associated with obstetric and neonatal outcomes and can be influenced by glucose values.	Oral	Bern, Switzerland 17.11. 17	Swiss Society of Endocrinology and Diabetology
Other	Maternal stress during pregnancy is associated with obstetric and neonatal outcomes and can be influenced by glucose values.	Poster	Zurich, Switzerland 07-09.09.17	International Society of Psychoneuroendocrinology
Other	Potentially modifiable predictors of adverse neonatal outcomes in pregnancies complicated by gestational diabetes.	Poster	Montreux, Switzerland, 17-18.11.2016.	Groupement Romand de la Société Suisse de Gynécologie et Obstétrique

6. BIBLIOGRAPHY

1. O'Dea, A., et al., *Can the onset of type 2 diabetes be delayed by a group-based lifestyle intervention in women with prediabetes following gestational diabetes mellitus (GDM)? Findings from a randomized control mixed methods trial.* Journal of diabetes research, 2015. **2015**.
2. Ferrara, A., et al., *A pregnancy and postpartum lifestyle intervention in women with gestational diabetes mellitus reduces diabetes risk factors: a feasibility randomized control trial.* Diabetes care, 2011: p. DC_102221.
3. Peacock, A., et al., *A randomised controlled trial to delay or prevent type 2 diabetes after gestational diabetes: walking for exercise and nutrition to prevent diabetes for you.* International journal of endocrinology, 2015. **2015**.
4. Philis-Tsimikas, A., et al., *Dulce Mothers: an intervention to reduce diabetes and cardiovascular risk in Latinas after gestational diabetes.* Translational behavioral medicine, 2014. **4**(1): p. 18-25.
5. Ratner, R.E., et al., *Prevention of diabetes in women with a history of gestational diabetes: effects of metformin and lifestyle interventions.* The Journal of Clinical Endocrinology & Metabolism, 2008. **93**(12): p. 4774-4779.
6. Pérez-Ferre, N., et al., *Diabetes mellitus and abnormal glucose tolerance development after gestational diabetes: A three-year, prospective, randomized, clinical-based, Mediterranean lifestyle interventional study with parallel groups.* Clinical Nutrition, 2015. **34**(4): p. 579-585.
7. Rautio, N., et al., *Lifestyle intervention in prevention of type 2 diabetes in women with a history of gestational diabetes mellitus: one-year results of the FIN-D2D project.* Journal of Women's Health, 2014. **23**(6): p. 506-512.
8. Jovanovic-Peterson, L., E.P. Durak, and C.M. Peterson, *Randomized trial of diet versus diet plus cardiovascular conditioning on glucose levels in gestational diabetes.* Am J Obstet Gynecol, 1989. **161**(2): p. 415-9.
9. Hu, G., et al., *Tianjin Gestational Diabetes Mellitus Prevention Program: study design, methods, and 1-year interim report on the feasibility of lifestyle intervention program.* Diabetes Res Clin Pract, 2012. **98**(3): p. 508-17.
10. Artal, R., et al., *A lifestyle intervention of weight-gain restriction: diet and exercise in obese women with gestational diabetes mellitus.* Appl Physiol Nutr Metab, 2007. **32**(3): p. 596-601.
11. Youngwanichsetha, S., S. Phumdoung, and T. Ingkathawornwong, *The effects of mindfulness eating and yoga exercise on blood sugar levels of pregnant women with gestational diabetes mellitus.* Applied Nursing Research, 2014. **27**(4): p. 227-230.
12. Mukerji, G., et al., *An Innovative Home-Based Cardiovascular Lifestyle Prevention Program for Women With Recent Gestational Diabetes: A Pilot Feasibility Study.* Canadian journal of diabetes, 2015. **39**(6): p. 445-450.
13. Liu, H., et al., *One-year weight losses in the Tianjin Gestational Diabetes Mellitus Prevention Programme: A randomized clinical trial.* Diabetes, Obesity and Metabolism, 2018. **20**(5): p. 1246-1255.
14. Wang, C., et al., *Exercise intervention during pregnancy can be used to manage weight gain and improve pregnancy outcomes in women with gestational diabetes mellitus.* BMC pregnancy and childbirth, 2015. **15**(1): p. 255.
15. Schouten, B., et al., *Systematic screening and assessment of psychosocial well-being and care needs of people with cancer.* Cochrane Database of Systematic Reviews, 2019(3).
16. Admiraal, K.R., *Psychosocial well-being among older adults with cancer*. 2015: Michigan State University.

17. Teoh, V., J. Sims, and J. Milgrom, *Psychosocial predictors of quality of life in a sample of community-dwelling stroke survivors: a longitudinal study.* Topics in stroke rehabilitation, 2009. **16**(2): p. 157-166.
18. Herget, S., et al., *Psychosocial well-being of adolescents before and after a 1-year telephone-based adiposity prevention study for families.* Journal of Adolescent Health, 2015. **57**(3): p. 351-354.
19. Lovibond, S.H. and P.F. Lovibond, *Manual for the depression anxiety stress scales*. 1996: Psychology Foundation of Australia.
20. Melato, S.R., et al., *Coping self-efficacy and psychosocial well-being of marginalised South African youth.* Journal of Psychology in Africa, 2017. **27**(4): p. 338-344.
21. Chesney, M.A., et al., *A validity and reliability study of the coping self-efficacy scale.* British journal of health psychology, 2006. **11**(3): p. 421-437.
22. World Health Organization, *Strengthening mental health promotion.* Fact sheet, 2001. **20**.
23. Westerhof, G.J. and C.L. Keyes, *Mental illness and mental health: The two continua model across the lifespan.* Journal of adult development, 2010. **17**(2): p. 110-119.
24. Ryff, C.D., *Psychological well-being in adult life.* Current directions in psychological science, 1995. **4**(4): p. 99-104.
25. Headey, B., J. Kelley, and A. Wearing, *Dimensions of mental health: Life satisfaction, positive affect, anxiety and depression.* Social indicators research, 1993. **29**(1): p. 63-82.
26. Krutsch, W., et al., *Injury and Health Risk Management in Sports: A Guide to Decision Making*. 2020: Springer.
27. Bandura, A., *Self-efficacy.* The Corsini encyclopedia of psychology, 2010: p. 1-3.
28. Williams, K. and M. Bond, *The roles of self-efficacy, outcome expectancies and social support in the self-care behaviours of diabetics.* Psychology, health & medicine, 2002. **7**(2): p. 127-141.
29. Wallston, K.A., R.L. Rothman, and A. Cherrington, *Psychometric properties of the perceived diabetes self-management scale (PDSMS).* Journal of behavioral medicine, 2007. **30**(5): p. 395-401.
30. Kim, C., et al., *Self-efficacy, social support, and associations with physical activity and body mass index among women with histories of gestational diabetes mellitus.* The Diabetes Educator, 2008. **34**(4): p. 719-728.
31. Razee, H., et al., *Beliefs, barriers, social support, and environmental influences related to diabetes risk behaviours among women with a history of gestational diabetes.* Health Promotion Journal of Australia, 2010. **21**(2): p. 130-137.
32. Ingstrup, M.S., et al., *Women's experience with peer counselling and social support during a lifestyle intervention among women with a previous gestational diabetes pregnancy.* Health Psychology and Behavioral Medicine, 2019. **7**(1): p. 147-159.
33. Zhu, Y. and C. Zhang, *Prevalence of gestational diabetes and risk of progression to type 2 diabetes: a global perspective.* Current diabetes reports, 2016. **16**(1): p. 7.
34. Association, A.D., *Introduction: standards of medical care in diabetes—2018*. 2018, Am Diabetes Assoc.
35. American Diabetes Association, *14. Management of Diabetes in Pregnancy: Standards of Medical Care in Diabetes—2020.* Diabetes Care, 2020. **43**(Supplement 1): p. S183-S192.
36. Khajehei, M. and H. Assareh, *Temporal trend of diabetes in pregnant women and its association with birth outcomes, 2011 to 2017.* Journal of Diabetes and its Complications, 2020: p. 107550.
37. Ryser Rüetschi, J., et al., *Fasting glycaemia to simplify screening for gestational diabetes.* BJOG: An International Journal of Obstetrics & Gynaecology, 2016. **123**(13): p. 2219-2222.
38. DeSisto, C.L., S.Y. Kim, and A.J. Sharma, *Peer reviewed: Prevalence estimates of gestational diabetes mellitus in the United States, pregnancy risk assessment monitoring system (prams), 2007–2010.* Preventing chronic disease, 2014. **11**.

39. Zhang, F., et al., *Increasing prevalence of gestational diabetes mellitus in Chinese women from 1999 to 2008.* Diabetic Medicine, 2011. **28**(6): p. 652-657.
40. Bener, A., N.M. Saleh, and A. Al-Hamaq, *Prevalence of gestational diabetes and associated maternal and neonatal complications in a fast-developing community: global comparisons.* International journal of women's health, 2011. **3**: p. 367.
41. Contreras, R., W. Chen, and D.A. Sacks, *Trends in the Prevalence of Preexisting Diabetes and Gestational Diabetes Mellitus Among a Racially/Ethnically Diverse Population of Pregnant Women, 1999-2005.* Diabetes care, 2008. **31**(5): p. 899.
42. Dabelea, D., et al., *Increasing prevalence of gestational diabetes mellitus (GDM) over time and by birth cohort: Kaiser Permanente of Colorado GDM Screening Program.* Diabetes care, 2005. **28**(3): p. 579-584.
43. Ferrara, A., *Increasing prevalence of gestational diabetes mellitus: a public health perspective.* Diabetes care, 2007. **30**(Supplement 2): p. S141-S146.
44. Lehmann, R., Troendle, and Brändle, *Neue Erkenntnisse zur Diagnostik und Management des Gestationsdiabetes.* Therapeutische Umschau, 2009. **66**(10): p. 695-706.
45. Surbek, D. *Gynäkologie und Geburtshilfe: Gestationsdiabetes: endlich eine einheitliche Screening-Strategie!* in *Swiss Medical Forum*. 2011. EMH Media.
46. Metzger, B.E., et al., *International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy.* Diabetes Care, 2010. **33**(3): p. 676-682.
47. Vandorsten, J.P., et al., *NIH consensus development conference: diagnosing gestational diabetes mellitus.* NIH consensus and state-of-the-science statements, 2013. **29**(1): p. 1-31.
48. Catalano, P.M., et al., *Longitudinal changes in glucose metabolism during pregnancy in obese women with normal glucose tolerance and gestational diabetes mellitus.* American journal of obstetrics and gynecology, 1999. **180**(4): p. 903-916.
49. Catalano, P.M., et al., *Longitudinal changes in insulin release and insulin resistance in nonobese pregnant women.* American journal of obstetrics and gynecology, 1991. **165**(6): p. 1667-1672.
50. American Diabetes Association, *2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes—2020.* Diabetes Care, 2020. **43**(Supplement 1): p. S14-S31.
51. Tobias, D.K., et al., *Physical activity before and during pregnancy and risk of gestational diabetes mellitus: a meta-analysis.* Diabetes care, 2011. **34**(1): p. 223-229.
52. Bowers, K., et al., *A prospective study of prepregnancy dietary fat intake and risk of gestational diabetes.* The American journal of clinical nutrition, 2012. **95**(2): p. 446-453.
53. Bowers, K., et al., *A prospective study of prepregnancy dietary iron intake and risk for gestational diabetes mellitus.* Diabetes care, 2011. **34**(7): p. 1557-1563.
54. Horsch, A., et al., *Stress exposure and psychological stress responses are related to glucose concentrations during pregnancy.* British Journal of Health Psychology, 2016: p. n/a-n/a.
55. Hinkle, S.N., et al., *A longitudinal study of depression and gestational diabetes in pregnancy and the postpartum period.* Diabetologia, 2016. **59**(12): p. 2594-2602.
56. Arafa, A. and J.-Y. Dong, *Depression and risk of gestational diabetes: A meta-analysis of cohort studies.* Diabetes research and clinical practice, 2019. **156**: p. 107826.
57. Wendland, E.M., et al., *Gestational diabetes and pregnancy outcomes-a systematic review of the World Health Organization (WHO) and the International Association of Diabetes in Pregnancy Study Groups (IADPSG) diagnostic criteria.* BMC pregnancy and childbirth, 2012. **12**(1): p. 23.
58. Xiong, X., et al., *Gestational diabetes mellitus: prevalence, risk factors, maternal and infant outcomes.* International Journal of Gynecology & Obstetrics, 2001. **75**(3): p. 221-228.
59. Lu, J., et al., *Maternal gestational diabetes is associated with offspring's hypertension.* American journal of hypertension, 2019. **32**(4): p. 335-342.

60. Nomura, Y., et al., *Exposure to gestational diabetes mellitus and low socioeconomic status: effects on neurocognitive development and risk of attention-deficit/hyperactivity disorder in offspring.* Archives of pediatrics & adolescent medicine, 2012. **166**(4): p. 337-343.
61. Scholtens, D.M., et al., *Hyperglycemia and Adverse Pregnancy Outcome Follow-up Study (HAPO FUS): maternal glycemia and childhood glucose metabolism.* Diabetes Care, 2019. **42**(3): p. 381-392.
62. Pirkola, J., et al., *Risks of overweight and abdominal obesity at age 16 years associated with prenatal exposures to maternal prepregnancy overweight and gestational diabetes mellitus.* Diabetes care, 2010. **33**(5): p. 1115-1121.
63. Lowe, W.L., et al., *Hyperglycemia and adverse pregnancy outcome follow-up study (HAPO FUS): maternal gestational diabetes mellitus and childhood glucose metabolism.* Diabetes Care, 2019. **42**(3): p. 372-380.
64. Hillier, T.A., et al., *Childhood obesity and metabolic imprinting: the ongoing effects of maternal hyperglycemia.* Diabetes care, 2007. **30**(9): p. 2287-2292.
65. Damm, P., *Future risk of diabetes in mother and child after gestational diabetes mellitus.* International Journal of Gynecology & Obstetrics, 2009. **104**: p. S25-S26.
66. Vääräsmäki, M., et al., *Adolescent manifestations of metabolic syndrome among children born to women with gestational diabetes in a general-population birth cohort.* American journal of epidemiology, 2009. **169**(10): p. 1209-1215.
67. Lowe, W.L., et al., *Association of gestational diabetes with maternal disorders of glucose metabolism and childhood adiposity.* Jama, 2018. **320**(10): p. 1005-1016.
68. Kramer, C.K., S. Campbell, and R. Retnakaran, *Gestational diabetes and the risk of cardiovascular disease in women: a systematic review and meta-analysis.* Diabetologia, 2019. **62**(6): p. 905-914.
69. Damé, P., et al., *Depressive Symptoms in Women with Gestational Diabetes Mellitus: The LINDA-Brazil Study.* Journal of Diabetes Research, 2017. **2017**.
70. Bennett, H.A., et al., *Prevalence of depression during pregnancy: systematic review.* Obstetrics & Gynecology, 2004. **103**(4): p. 698-709.
71. Hinkle, S.N., et al., *A longitudinal study of depression and gestational diabetes in pregnancy and the postpartum period.* Diabetologia, 2016. **59**(12): p. 2594-2602.
72. Azami, M., et al., *The association between gestational diabetes and postpartum depression: A systematic review and meta-analysis.* diabetes research and clinical practice, 2019. **149**: p. 147-155.
73. Blumer, I., et al., *Diabetes and pregnancy: an endocrine society clinical practice guideline.* The Journal of Clinical Endocrinology & Metabolism, 2013. **98**(11): p. 4227-4249.
74. Institute of Medicine, *Weight gain during pregnancy; Reexamining the guidelines.* Washington DC: National Academy of Sciences, 2009.
75. Sox, H.C. and S. Greenfield, *Comparative effectiveness research: a report from the Institute of Medicine.* Annals of internal medicine, 2009. **151**(3): p. 203-205.
76. Yaktine, A.L. and K.M. Rasmussen, *Weight Gain During Pregnancy:: Reexamining the Guidelines*. 2009: National Academies Press.
77. Nishida, C., *Guideline: sugars intake for adults and children*. 2016.
78. Montonen, J., et al., *Whole-grain and fiber intake and the incidence of type 2 diabetes.* The American journal of clinical nutrition, 2003. **77**(3): p. 622-629.
79. Colberg, S.R., K. Castorino, and L. Jovanovic, *Prescribing physical activity to prevent and manage gestational diabetes.* World J Diabetes, 2013. **4**(6): p. 256-62.
80. Barakat, R., A. Lucia, and J.R. Ruiz, *Resistance exercise training during pregnancy and newborn's birth size: a randomised controlled trial.* Int J Obes (Lond), 2009. **33**(9): p. 1048-57.
81. Mulder, E.J., et al., *Prenatal maternal stress: effects on pregnancy and the (unborn) child.* Early human development, 2002. **70**(1-2): p. 3-14.

82. Nicklas, J.M., et al., *Factors associated with depressive symptoms in the early postpartum period among women with recent gestational diabetes mellitus.* Maternal and child health journal, 2013. **17**(9): p. 1665-1672.
83. Christenson, A., et al., *Women's perceived reasons for their excessive postpartum weight retention: a qualitative interview study.* PloS one, 2016. **11**(12): p. e0167731.
84. Fowles, E.R., C. Murphey, and R.J. Ruiz, *Exploring relationships among psychosocial status, dietary quality, and measures of placental development during the first trimester in low-income women.* Biological research for nursing, 2011. **13**(1): p. 70-79.
85. Carter, J. and W. Swardfager, *Mood and metabolism: anhedonia as a clinical target in type 2 diabetes.* Psychoneuroendocrinology, 2016. **69**: p. 123-132.
86. Wolfe, B.E., et al., *Validity and utility of the current definition of binge eating.* international Journal of Eating disorders, 2009. **42**(8): p. 674-686.
87. Kasten, S., et al., *The influence of pre-motivational factors on behavior via motivational factors: a test of the I-Change model.* BMC psychology, 2019. **7**(1): p. 7.
88. De Wit, L., et al., *Physical activity, depressed mood and pregnancy worries in European obese pregnant women: results from the DALI study.* BMC pregnancy and childbirth, 2015. **15**(1): p. 158.
89. Znoj, H.-J., et al., *Psychotherapeutic process of cognitive–behavioral intervention in HIV-infected persons: Results from a controlled, randomized prospective clinical trial.* Psychotherapy Research, 2010. **20**(2): p. 203-213.
90. Mason, A.E., et al., *Effects of a mindfulness-based intervention on mindful eating, sweets consumption, and fasting glucose levels in obese adults: data from the SHINE randomized controlled trial.* Journal of behavioral medicine, 2016. **39**(2): p. 201-213.
91. Jelsma, J.G., et al., *Beliefs, barriers, and preferences of European overweight women to adopt a healthier lifestyle in pregnancy to minimize risk of developing gestational diabetes mellitus: an explorative study*. Journal of pregnancy, 2016. **2016**.
92. Carolan, M., *Women's experiences of gestational diabetes self-management: A qualitative study.* Midwifery, 2013. **29**(6): p. 637-645.
93. Kavanagh, D.J., *Self-efficacy and depression.* Self-efficacy: Thought control of action, 1992: p. 177-193.
94. Bandura, A., *Self-efficacy conception of anxiety.* Anxiety research, 1988. **1**(2): p. 77-98.
95. Linde, J.A., et al., *Binge eating disorder, weight control self-efficacy, and depression in overweight men and women.* International Journal of obesity, 2004. **28**(3): p. 418.
96. Durnwald, C. *Gestational diabetes: linking epidemiology, excessive gestational weight gain, adverse pregnancy outcomes, and future metabolic syndrome*. in *Seminars in Perinatology*. 2015. Elsevier.
97. Kim, S.Y., et al., *Association of maternal body mass index, excessive weight gain, and gestational diabetes mellitus with large-for-gestational-age births.* Obstetrics and gynecology, 2014. **123**(4): p. 737.
98. Cheng, Y.W., et al., *Gestational weight gain and gestational diabetes mellitus: perinatal outcomes.* Obstetrics & Gynecology, 2008. **112**(5): p. 1015-1022.
99. Ruchat, S.M. and M.F. Mottola, *The important role of physical activity in the prevention and management of gestational diabetes mellitus.* Diabetes/metabolism research and reviews, 2013. **29**(5): p. 334-346.
100. American Diabetes Association, *2. Classification and diagnosis of diabetes: standards of medical care in diabetes—2018.* Diabetes care, 2018. **41**(Supplement 1): p. S13-S27.
101. Bellamy, L., et al., *Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis.* The Lancet, 2009. **373**(9677): p. 1773-1779.
102. Dalfra, M., et al., *Antepartum and early postpartum predictors of type 2 diabetes development in women with gestational diabetes mellitus.* Diabetes & metabolism, 2001. **27**(6): p. 675-680.

103. Gilmore, L.A., M. Klempel-Donchenko, and L.M. Redman. *Pregnancy as a window to future health: excessive gestational weight gain and obesity*. in *Seminars in Perinatology*. 2015. Elsevier.
104. Metzger, B.E., et al., *Summary and recommendations of the fifth international workshop-conference on gestational diabetes mellitus.* Diabetes care, 2007. **30**(Supplement 2): p. S251-S260.
105. Webber, J., M. Charlton, and N. Johns, *Diabetes in pregnancy: management of diabetes and its complications from preconception to the postnatal period (NG3).* British Journal of Diabetes, 2015. **15**(3): p. 107-111.
106. Tarry-Adkins, J.L., C.E. Aiken, and S.E. Ozanne, *Neonatal, infant, and childhood growth following metformin versus insulin treatment for gestational diabetes: A systematic review and meta-analysis.* PLoS medicine, 2019. **16**(8): p. e1002848.
107. Butalia, S., et al., *Short-and long-term outcomes of metformin compared with insulin alone in pregnancy: a systematic review and meta-analysis.* Diabetic Medicine, 2017. **34**(1): p. 27-36.
108. Rowan, J.A., et al., *Metformin versus insulin for the treatment of gestational diabetes.* New England Journal of Medicine, 2008. **358**(19): p. 2003-2015.
109. Robinson, D.J., M. Luthra, and M. Vallis, *Diabète et santé mentale.* Canadian Journal of Diabetes, 2013. **37**: p. S459-S465.
110. Reece, E.A., G. Leguizamón, and A. Wiznitzer, *Gestational diabetes: the need for a common ground.* The Lancet, 2009. **373**(9677): p. 1789-1797.
111. Ragland, D., et al., *Depressive Symptoms in Pregnant Women: Does Diabetes Have an Impact.* J Women's Health Care, 2012. **1**(118): p. 2167-0420.1000118.
112. Matthews, J., et al., *Psychosocial predictors of gestational weight gain and the role of mindfulness.* Midwifery, 2018. **56**: p. 86-93.
113. McPhie, S., et al., *Relationships between mental health symptoms and body mass index in women with and without excessive weight gain during pregnancy.* Midwifery, 2015. **31**(1): p. 138-146.
114. Murphy, J.M., et al., *Obesity and weight gain in relation to depression: findings from the Stirling County Study.* International Journal of Obesity, 2009. **33**(3): p. 335.
115. Moher, D., et al., *Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement.* PLOS Medicine, 2009. **6**(7): p. e1000097.
116. The Joanna Briggs Institute, C.A.t.f.u.i.J.S.R., *Checklist for Analytical Cross Sectional Studies*. 2017.
117. The Joanna Briggs Institute, C.A.t.f.u.i.J.S.R., *Checklist for Randomized Controlled Trials*. 2017.
118. The Joanna Briggs Institute, C.A.t.f.u.i.J.S.R., *Checklist for Cohort Studies*. 2017.
119. The Joanna Briggs Institute, C.A.t.f.u.i.J.S.R., *Checklist for Quasi-Experimental Studies (non-randomized experimental studies)*. 2017.
120. Whittemore, R. and K. Knafl, *The integrative review: updated methodology.* Journal of advanced nursing, 2005. **52**(5): p. 546-553.
121. Kaiser, B., E. Jeannot, and C. Razurel, *Determinants of health behaviors after gestational diabetes mellitus: a prospective cohort study in Geneva.* Journal of Midwifery & women's health, 2016. **61**(5): p. 571-577.
122. Brantley, P.J., et al., *Psychosocial predictors of weight regain in the weight loss maintenance trial.* Journal of behavioral medicine, 2014. **37**(6): p. 1155-1168.
123. Martini, J., et al., *Anxiety disorders before birth and self-perceived distress during pregnancy: associations with maternal depression and obstetric, neonatal and early childhood outcomes.* Early human development, 2010. **86**(5): p. 305-310.
124. Zhu, P., et al., *New insight into onset of lactation: mediating the negative effect of multiple perinatal biopsychosocial stress on breastfeeding duration.* Breastfeeding Medicine, 2013. **8**(2): p. 151-158.

125. Horsch, A., et al., *Diabète gestationnel--quelles sont les approches non médicales [Gestational diabetes--what are the non-medical approaches?].* Revue medicale suisse, 2016. **12**(521): p. 1089-1091.
126. Ashford, S., J. Edmunds, and D.P. French, *What is the best way to change self-efficacy to promote lifestyle and recreational physical activity? A systematic review with meta-analysis.* British journal of health psychology, 2010. **15**(2): p. 265-288.
127. Nolan, C.J., *Controversies in gestational diabetes.* Best Practice & Research Clinical Obstetrics & Gynaecology, 2011. **25**(1): p. 37-49.
128. CONSORT Group, *CONSORT 2010 checklist of information to include when reporting a randomized trial.* Retrieved August, 2010. **21**: p. 2019.
129. Cox, J., J. Holden, and R. Sagovsky, *Edinburgh postnatal depression scale (EPDS).* Br J psychiatry, 1987. **150**: p. 782-786.
130. Selçuk-Tosun, A. and H. Zincir, *The effect of a transtheoretical model–based motivational interview on self-efficacy, metabolic control, and health behaviour in adults with type 2 diabetes mellitus: A randomized controlled trial.* International journal of nursing practice, 2019. **25**(4): p. e12742.
131. Schwarzer, R., *Modeling health behavior change: How to predict and modify the adoption and maintenance of health behaviors.* Applied Psychology, 2008. **57**(1): p. 1-29.
132. NIfHaC, E., *Antenatal and postnatal mental health: clinical management and service guidance.* London: National Institute for Health and Care Excellence, 2014.
133. Sockol, L.E., *A systematic review of the efficacy of cognitive behavioral therapy for treating and preventing perinatal depression.* Journal of Affective Disorders, 2015. **177**: p. 7-21.
134. van Ravesteyn, L.M., et al., *Interventions to treat mental disorders during pregnancy: A systematic review and multiple treatment meta-analysis.* PLoS One, 2017. **12**(3): p. e0173397.
135. *Les hydrates de carbone dans l'alimentation: résumés des chapitres*, in *Les hydrates de carbone dans l'alimentation*, F.s.d. Federal Office of Public Health, Switzerland, Editor. 2009: Berne
136. SSN. *Swiss Society for Nutrition. Nutritional recommendations for Germany, Autria and Switzerland (DACH): Les valeurs de référence DACH pour les apports nutritionnels, 2ème édition*. 2015; Available from: http://www.sge-ssn.ch/fr/science-et-recherche/denrees-alimentaires-et-nutriments/recommandations-nutritionnelles/valeurs-de-reference-dach/].
137. Ansermet, O. and A. Aebi, *Influence des protéines et des lipides chez le diabétique de type 1*. 2016, Haute école de santé Genève.
138. Ley, S.H., et al., *Prevention and management of type 2 diabetes: dietary components and nutritional strategies.* The Lancet, 2014. **383**(9933): p. 1999-2007.
139. Marathe, P.H., H.X. Gao, and K.L. Close, *American D iabetes A ssociation S tandards of M edical C are in D iabetes 2017.* Journal of diabetes, 2017. **9**(4): p. 320-324.
140. Mantzios, M. and J.C. Wilson, *Mindfulness, eating behaviours, and obesity: a review and reflection on current findings.* Current obesity reports, 2015. **4**(1): p. 141-146.
141. L Medina, W., et al., *Effects of mindfulness on diabetes mellitus: rationale and overview.* Current diabetes reviews, 2017. **13**(2): p. 141-147.
142. Mathieu, J., *What should you know about mindful and intuitive eating?* Journal of the Academy of Nutrition and Dietetics, 2009. **109**(12): p. 1985.
143. Healy, G.N., et al., *Breaks in sedentary time: beneficial associations with metabolic risk.* Diabetes care, 2008. **31**(4): p. 661-666.
144. Committee, A., *Opinion No. 650: physical activity and exercise during pregnancy and the postpartum period.* Obstet Gynecol, 2015. **126**(6): p. e135-42.
145. Colberg, S.R., et al., *Physical Activity/Exercise and Diabetes: A Position Statement of the American Diabetes Association.* Diabetes Care, 2016. **39**(11): p. 2065-2079.

146. Barakat, R., A. Lucia, and J.R. Ruiz, *Resistance exercise training during pregnancy and newborn's birth size: a randomised controlled trial.* International journal of obesity, 2009. **33**(9): p. 1048-1057.
147. Organization, W.H., *Global strategy on diet, physical activity and health.* 2004.
148. Retnakaran, R. and B.R. Shah, *Mild glucose intolerance in pregnancy and risk of cardiovascular disease: a population-based cohort study.* CMAJ, 2009. **181**.
149. Rothman, K.J., *No adjustments are needed for multiple comparisons.* Epidemiology, 1990: p. 43-46.
150. Von Elm, E., et al., *The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies.* Annals of internal medicine, 2007. **147**(8): p. 573-577.
151. Cox, J.L., J.M. Holden, and R. Sagovsky, *Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale.* The British journal of psychiatry, 1987. **150**(6): p. 782-786.
152. Bunevicius, A., et al., *Screening for antenatal depression with the Edinburgh Depression Scale.* Journal of Psychosomatic Obstetrics & Gynecology, 2009. **30**(4): p. 238-243.
153. Watson, L.C., et al., *Practical depression screening in residential care/assisted living: five methods compared with gold standard diagnoses.* The American Journal of Geriatric Psychiatry, 2009. **17**(7): p. 556-564.
154. Guedeney, N. and J. Fermanian, *Validation study of the French version of the Edinburgh Postnatal Depression Scale (EPDS): new results about use and psychometric properties.* European psychiatry, 1998. **13**(2): p. 83-89.
155. Topp, C.W., et al., *The WHO-5 Well-Being Index: a systematic review of the literature.* Psychotherapy and psychosomatics, 2015. **84**(3): p. 167-176.
156. Bech, P., C. Gudex, and K.S. Johansen, *The WHO (Ten) well-being index: validation in diabetes.* Psychotherapy and psychosomatics, 1996. **65**(4): p. 183-190.
157. Awata, S., et al., *Reliability and validity of the Japanese version of the World Health Organization-Five Well-Being Index in the context of detecting depression in diabetic patients.* Psychiatry and clinical neurosciences, 2007. **61**(1): p. 112-119.
158. Hajós, T.R., et al., *Psychometric and screening properties of the WHO-5 well-being index in adult outpatients with Type 1 or Type 2 diabetes mellitus.* Diabetic Medicine, 2013. **30**(2): p. e63-e69.
159. Krieger, T., et al., *Measuring depression with a well-being index: further evidence for the validity of the WHO Well-Being Index (WHO-5) as a measure of the severity of depression.* Journal of affective disorders, 2014. **156**: p. 240-244.
160. Newnham, E.A., G.R. Hooke, and A.C. Page, *Monitoring treatment response and outcomes using the World Health Organization's Wellbeing Index in psychiatric care.* Journal of affective disorders, 2010. **122**(1-2): p. 133-138.
161. Hochberg, G., et al., *WHO-5, a tool focusing on psychological needs in patients with diabetes: the French contribution to the DAWN study.* Diabetes & metabolism, 2012. **38**(6): p. 515-522.
162. Panel, C.C.a.C.T.D. *FDA Public Advisory Meeting Alere Afinion™ HbA1c Dx*. 2016; Available from: https://www.fda.gov/media/99241/download.
163. Wood, J.R., et al., *Accuracy and precision of the Axis-Shield Afinion hemoglobin A1c measurement device.* Journal of diabetes science and technology, 2012. **6**(2): p. 380-386.
164. Nicklas, J.M. and L.A. Barbour, *Optimizing weight for maternal and infant health: tenable, or too late?* Expert review of endocrinology & metabolism, 2015. **10**(2): p. 227-242.
165. Bjelland, I., et al., *Does a higher educational level protect against anxiety and depression? The HUNT study.* Social science & medicine, 2008. **66**(6): p. 1334-1345.
166. Penninx, B.W., et al., *Effects of social support and personal coping resources on depressive symptoms: different for various chronic diseases?* Health Psychology, 1998. **17**(6): p. 551.

167. White, I.R., P. Royston, and A.M. Wood, *Multiple imputation using chained equations: issues and guidance for practice.* Statistics in medicine, 2011. **30**(4): p. 377-399.
168. Crowther, C.A., et al., *Effect of treatment of gestational diabetes mellitus on pregnancy outcomes.* New England Journal of Medicine, 2005. **352**(24): p. 2477-2486.
169. Ruohomäki, A., et al., *The association between gestational diabetes mellitus and postpartum depressive symptomatology: A prospective cohort study.* Journal of affective disorders, 2018. **241**: p. 263-268.
170. Campaigne, B. and K. Wishner, *Gender-specific health care in diabetes mellitus.* The journal of gender-specific medicine: JGSM: the official journal of the Partnership for Women's Health at Columbia, 2000. **3**(1): p. 51.
171. Beck, C.T., *Predictors of postpartum depression: an update.* Nursing research, 2001. **50**(5): p. 275-285.
172. Dennis, C.L., P.A. Janssen, and J. Singer, *Identifying women at-risk for postpartum depression in the immediate postpartum period.* Acta Psychiatrica Scandinavica, 2004. **110**(5): p. 338-346.
173. Woods, S.M., et al., *Psychosocial stress during pregnancy.* American journal of obstetrics and gynecology, 2010. **202**(1): p. 61. e1-61. e7.
174. Wilson, C., et al., *Is there an increased risk of perinatal mental disorder in women with gestational diabetes? A systematic review and meta-analysis.* Diabetic Medicine, 2019.
175. Mortazavi, F., et al., *Validation of the World Health Organization-5 Well-Being Index; assessment of maternal well-being and its associated factors.* Turk Psikiyatri Dergisi, 2015. **26**(1): p. 1-7.
176. Barger, S.D., N. Messerli-Bürgy, and J. Barth, *Social relationship correlates of major depressive disorder and depressive symptoms in Switzerland: nationally representative cross sectional study.* BMC public health, 2014. **14**(1): p. 273.
177. Martis, R., et al., *Enablers and barriers for women with gestational diabetes mellitus to achieve optimal glycaemic control–a qualitative study using the theoretical domains framework.* BMC pregnancy and childbirth, 2018. **18**(1): p. 91.
178. Morrison, M.K., J.M. Lowe, and C.E. Collins, *Australian women's experiences of living with gestational diabetes.* Women and Birth, 2014. **27**(1): p. 52-57.
179. Wersebe, H., et al., *Well-being in major depression and social phobia with and without comorbidity.* International Journal of Clinical and Health Psychology, 2018.
180. Altazan, A.D., et al., *Mood and quality of life changes in pregnancy and postpartum and the effect of a behavioral intervention targeting excess gestational weight gain in women with overweight and obesity: a parallel-arm randomized controlled pilot trial.* BMC pregnancy and childbirth, 2019. **19**(1): p. 50.
181. Blaine, B., *Does depression cause obesity? A meta-analysis of longitudinal studies of depression and weight control.* Journal of health psychology, 2008. **13**(8): p. 1190-1197.
182. Ryff, C.D., et al., *Psychological well-being and ill-being: do they have distinct or mirrored biological correlates?* Psychotherapy and psychosomatics, 2006. **75**(2): p. 85-95.
183. Quansah, D.Y., et al., *Predictors and consequences of weight retention in the early and late postpartum period in women with gestational diabetes.* Diabetes Research and Clinical Practice, 2020: p. 108238.
184. Braig, S., et al., *Psychosocial stress and longitudinally measured gestational weight gain throughout pregnancy: The Ulm SPATZ Health Study.* Scientific reports, 2020. **10**(1): p. 1-8.
185. Herring, S.J., et al., *Association of postpartum depression with weight retention 1 year after childbirth.* Obesity (Silver Spring, Md.), 2008. **16**(6): p. 1296-1301.
186. Badon, S.E., et al., *Pre-and Early Pregnancy Onset Depression and Subsequent Rate of Gestational Weight Gain.* Journal of Women's Health, 2019. **28**(9): p. 1237-1245.
187. National Collaborating Centre for Mental Health. *Antenatal and postnatal mental health: Clinical management and service guidance: Updated edition*. 2014. British Psychological Society.

188. Cato, K., et al., *Antenatal depressive symptoms and early initiation of breastfeeding in association with exclusive breastfeeding six weeks postpartum: a longitudinal population-based study.* BMC pregnancy and childbirth, 2019. **19**(1): p. 49.
189. Grace, S.L., A. Evindar, and D. Stewart, *The effect of postpartum depression on child cognitive development and behavior: a review and critical analysis of the literature.* Archives of Women's Mental Health, 2003. **6**(4): p. 263-274.
190. Cooper, P.J. and L. Murray, *Postnatal depression.* Bmj, 1998. **316**(7148): p. 1884-1886.
191. American Diabetes Association, *13. Management of diabetes in pregnancy: Standards of Medical Care in Diabetes—2018.* Diabetes Care, 2018. **41**(Supplement 1): p. S137-S143.
192. Gibson, K.S., T.P. Waters, and P.M. Catalano, *Maternal weight gain in women who develop gestational diabetes mellitus.* Obstetrics & Gynecology, 2012. **119**(3): p. 560-565.
193. Farrow, C.V. and J.M. Blissett, *Is maternal psychopathology related to obesigenic feeding practices at 1 year?* Obesity research, 2005. **13**(11): p. 1999-2005.
194. Grigoriadis, S., et al., *The impact of maternal depression during pregnancy on perinatal outcomes: a systematic review and meta-analysis.* The Journal of clinical psychiatry, 2013. **74**(4): p. 321-341.
195. Khalsa, A.S., et al., *Parental intuitive eating behaviors and their association with infant feeding styles among low-income families.* Eating behaviors, 2019. **32**: p. 78-84.
196. Scaglioni, S., et al., *Determinants of children's eating behavior.* The American journal of clinical nutrition, 2011. **94**(suppl_6): p. 2006S-2011S.
197. Nicklas, J., *A Web-Based Lifestyle Intervention for Women With Recent Gestational Diabetes Mellitus: A Randomized Controlled Trial.* Obstetric Gynecology, 2014.
198. Nicklas, J.M., C.A. Zera, and E.W. Seely, *Predictors of very early postpartum weight loss in women with recent gestational diabetes mellitus.* The Journal of Maternal-Fetal & Neonatal Medicine, 2020. **33**(1): p. 120-126.
199. Haig, D., *Genetic conflicts in human pregnancy.* The Quarterly review of biology, 1993. **68**(4): p. 495-532.
200. Hartling, L., et al., *Benefits and harms of treating gestational diabetes mellitus: a systematic review and meta-analysis for the US Preventive Services Task Force and the National Institutes of Health Office of Medical Applications of Research.* Annals of internal medicine, 2013. **159**(2): p. 123-129.
201. Koletzko, B., et al., *Early nutrition programming of long-term health.* Proceedings of the Nutrition Society, 2012. **71**(3): p. 371-378.
202. Leong, A., E. Rahme, and K. Dasgupta, *Spousal diabetes as a diabetes risk factor: a systematic review and meta-analysis.* BMC medicine, 2014. **12**(1): p. 1-12.
203. Pace, R., et al., *Conjoint associations of gestational diabetes and hypertension with diabetes, hypertension, and cardiovascular disease in parents: a retrospective cohort study.* American journal of epidemiology, 2017. **186**(10): p. 1115-1124.
204. Gao, J., et al., *Effects of self-care, self-efficacy, social support on glycemic control in adults with type 2 diabetes.* BMC family practice, 2013. **14**(1): p. 66.
205. Osanloo, A. and C. Grant, *Understanding, selecting, and integrating a theoretical framework in dissertation research: Creating the blueprint for your "house".* Administrative issues journal: connecting education, practice, and research, 2016. **4**(2): p. 7.
206. Akintoye, A., *Developing theoretical and conceptual frameworks.* Jedm. oauife. edu. ng.(Accessed on the 22nd February2017), 2015.
207. Adom, D., et al., *Theoretical and conceptual framework: Mandatory ingredients of a quality research.* Journal of Education and Human Development, 2016. **5**(3): p. 158-172.
208. Nieto, I., E. Robles, and C. Vazquez, *Self-reported cognitive biases in depression: A meta-analysis.* Clinical Psychology Review, 2020: p. 101934.

209. Cuijpers, P., et al., *Self-reported versus clinician-rated symptoms of depression as outcome measures in psychotherapy research on depression: a meta-analysis.* Clinical psychology review, 2010. **30**(6): p. 768-778.
210. Heun, R., et al., *Validity of the five-item WHO Well-Being Index (WHO-5) in an elderly population.* European archives of psychiatry and clinical neuroscience, 2001. **251**(2): p. 27-31.
211. Matthey, S. and F. Agostini, *Using the Edinburgh Postnatal Depression Scale for women and men—some cautionary thoughts.* Archives of women's mental health, 2017. **20**(2): p. 345-354.
212. Joober, R., et al., *Publication bias: what are the challenges and can they be overcome?* Journal of psychiatry & neuroscience: JPN, 2012. **37**(3): p. 149.

7. PUBLICATION LIST

1. **Gilbert L**, Nikolaou A, Quansah DY, Rossel JB, Horsch A, Puder JJ. *Mental health and its association with glucose-lowering medication in women with gestational diabetes mellitus. A prospective clinical cohort study*. DOI: https://doi.org/10.1016/j.psyneuen.2020.105095 https://www.sciencedirect.com/science/article/pii/S0306453020305187

2. Antoniou M.-C., **Gilbert L.**, Gross J., Rossel J.-B., Fisher Fumeaux C. J., Vial Y., Puder J. Main Fetal Predictors of Adverse Neonatal Outcomes in Pregnancies with Gestational Diabetes Mellitus. 2020. Journal of Clinical Medicine. DOI: doi:10.3390/jcm9082409 https://www.mdpi.com/2077-0383/9/8/2409/htm

3. Quansah D. Y., Gross J., **Gilbert L.**, Arhab A., Horsch A., Puder J. Predictors and consequences of weight retention in the early and late postpartum period in women with gestational diabetes. 2020. Diabetes Research and Clinical Practice. DOI : https://doi.org/10.1016/j.diabres.2020.108238 https://www.sciencedirect.com/science/article/pii/S0168822720304885?dgcid=coauthor

4. Antoniou M.-C., **Gilbert L.**, Gross J., Rossel J.-B., Fisher Fumeaux C. J., Vial Y., Puder J. Potentially modifiable predictors of adverse neonatal and maternal outcomes in pregnancies with gestational diabetes mellitus: can they help for future risk stratification and risk-adapted patient care? 2019. BMC Pregnancy and Childbirth. DOI: 10.1186/s12884-019-2610-2. https://link.springer.com/article/10.1186/s12884-019-2610-2

5. Quansah D. Y., **Gilbert L.**, Gross J., Horsch A. and Puder J.J. Intuitive eating is associated with improved health indicators at 1- year postpartum in women with gestational diabetes mellitus, 2019. Journal of Health Psychology. DOI: 10.1177/1359105319869814 https://journals.sagepub.com/doi/abs/10.1177/1359105319869814

6. Quansah D. Y., Gross J., **Gilbert L.**, Helbling C., Horsch A., Puder J. J. 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, 2019. Eating Behaviors. DOI: https://doi.org/10.1016/j.eatbeh.2019.101304 https://www.sciencedirect.com/science/article/pii/S1471015319300558

7. **Gilbert L.**, Gross J., Lanzi S., Quansah D. Y., Puder J. J., & Horsch A. How diet, physical activity and psychosocial well-being interact in women with gestational diabetes mellitus: an integrative review, 2019. BMC Pregnancy and Childbirth, 19(1), 60. DOI: 10.1186/s12884-019-2185-y https://link.springer.com/article/10.1186/s12884-019-2185-y

8. Horsch A., **Gilbert L.**, Lanzi S., Kang J.S., Vial Y., Puder J.J. Associations between maternal stress during pregnancy and fasting glucose with obstetric and neonatal outcomes, 2019. BMC Pregancy and Childbirth. DOI: https://doi.org/10.1016/j.jpsychores.2019.109795 https://www.sciencedirect.com/science/article/pii/S0022399919305860

9. Horsch A., **Gilbert L.**, Lanzi S., Gross J., Kayser B., Vial Y., Simeoni U., Hans D., Berney A., Brand-Miller J., Scholz U., Barakat R., Puder J.J. Improving cardio-metabolic and mental health in women with gestational diabetes mellitus and their offspring: Study protocol for MySweetHeart Trial, a randomized controlled trial, 2018. 8(2): p. e020462. DOI: 10.1136/bmjopen-2017-020462 https://bmjopen.bmj.com/content/8/2/e020462.abstract

10. Horsch A., Jacobs I., **Gilbert L.**, Favrod C., Schneider J., Morisod Harari M., Bickle Graz M. Impact of perinatal asphyxia on parental mental health and bonding with the offspring: a questionnaire survey of Swiss parents, 2017. 1(1). DOI:10.1136/bmjpo-2017- 000059 https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5862159/

11. Horsch A., Tolsa J.F., **Gilbert L.**, Jan du Chêne L., Müller-Nix C., Bickle Graz M. Improving Maternal Mental Health Following Preterm Birth Using an Expressive Writing Intervention: A Randomized Controlled Trial, 2015. p. 1-12. DOI: 10.1007/s10578-015- 0611-6 https://pubmed.ncbi.nlm.nih.gov/26659113/

The following article has been submitted and is currently under revision:

1. **Gilbert L.**, Rossel J.-B., Quansah D. Y., Puder J. J, Horsch A. *Mental health and its associations with weight in women with gestational diabetes mellitus. A prospective clinical cohort study.* Submitted to Journal of Psychosomatic research on the fifth of August 2020.

8. APPENDIX

8.1 Publication A

Published in BMC Pregnancy and Childbirth in 2019.

How diet, physical activity and psychosocial well-being interact in women with Gestational Diabetes Mellitus: An integrative review

Leah Gilbert[1*], Justine Gross[1], Stefano Lanzi[1,2], Dan Yedu Quansah[1], Jardena Puder[1, 3†], Antje Horsch[1,4,5]†

[1]Service of Endocrinology, Diabetes & Metabolism, Lausanne University Hospital, 1011 Lausanne, Switzerland

[2]Division of Angiology, Heart and Vessel Department, Lausanne University Hospital, 1011 Lausanne, Switzerland

[3]Division of Pediatric Endocrinology, Diabetology and Obesity, Lausanne University Hospital, 1000 Lausanne, Switzerland

[4]Institute of Higher Education and Research in Healthcare (IUFRS), University of Lausanne, 1010 Lausanne, Switzerland

[5]Woman-Mother-Child Department, Lausanne University Hospital, 1011 Lausanne, Switzerland

†shared last authors

Email addresses:

Leah Gilbert: leah.gilbert@chuv.ch

Justine Gross : justine.gross@hospvd.ch

Stefano Lanzi: stefano.lanzi@chuv.ch

Dan Yedu Quansah: dan.quansah@chuv.ch

Jardena Puder : jardena.puder@chuv.ch

Antje Horsch: antje.horsch@chuv.ch

***Corresponding author:** Leah Gilbert – Office 6041 of the CHUV Maternity clinic – Avenue Pierre-Decker 2 – 1011 Lausanne, Switzerland. Mail: leah.gilbert@chuv.ch

Phone: 0041213144778

Abstract

Background. Gestational Diabetes Mellitus (GDM) is associated with future cardio-metabolic risks for the mother and her child. In addition, one-third of women with recent GDM develop postpartum

depression. Given these adverse impacts of GDM on the health of the mother and her offspring, it is important to intervene on modifiable factors, such as diet, physical activity, and psychosocial well-being. This integrative review therefore explored evidence on how these modifiable factors interact in women with GDM and their offspring, and how effective combined interventions are on reducing adverse impacts of GDM.

Methods. A comprehensive search strategy included carefully selected terms that corresponded to the domains of interest (diet, physical activity and psychosocial well-being). The databases searched for articles published between 1980 and February 2018 were: CINAHL, PsycINFO, Embase, Pubmed and Cochrane. Studies that were included in this review were either observational or intervention studies that included at least two domains of interest. Articles had to at least report data on maternal outcomes of women with GDM.

Results. The search strategies identified 14'419 citations after excluding duplicates. After screening titles and then abstracts, 114 articles were selected for detailed evaluation of their full text, and 16 were included in this review: two observational and 14 intervention studies. Results from observational studies showed that psychosocial well-being (social support and self-efficacy) were positively associated with physical activity and dietary choice. Intervention studies always included diet and physical activity interventions, although none integrated psychosocial well-being in the intervention. These lifestyle interventions mostly led to increased physical activity, improved diet and lower stress perception. Many of these lifestyle interventions also reduced BMI and postpartum diabetes status, improved metabolic outcomes and reduced the risk of preterm deliveries and low birth weight.

Conclusion. This integrative review showed that psychosocial well-being interacted with diet as well as with physical activity in women with GDM. We recommend that future studies consider integrating psychosocial well-being in their intervention, as observational studies demonstrated that social support and self-efficacy helped with adopting a healthy lifestyle following GDM diagnosis.

Keywords: Intervention, Exercise, Nutrition, Mental Health, Pregnancy

Introduction

Gestational Diabetes Mellitus (GDM) is defined when a women has a glucose intolerance with onset and first recognition between 24 to 28 weeks of gestation [1, 2]. It usually resolves after childbirth [2, 3], although it carries pre-, peri-, and postnatal risks of adverse outcomes in the mother and the child [1]. For example, up to 40% of women with GDM are known to have pre-diabetes in the

early postpartum period [4]. The prevalence of GDM is 10.8% in Switzerland [5], 9.2% in the USA [6], 6.8% in China [7], 16.3% in Qatar [8] and 7.8% among a racially/ethnically diverse population [9].

Mothers have a risk of up to 70% of GDM recurrence, a seven-fold higher five to ten-year risk of type 2 diabetes, and an increased risk of cardiovascular diseases [10-13]. GDM is also associated with reduced psychosocial well-being: women with GDM are two to four times [14] more likely to develop antenatal or postpartum depression. Evidence shows that approximately one-third of women with recent GDM develop postpartum depression [15]. Postpartum depression in turn is associated with an increase in comfort eating and a decrease in physical activity [16], thus putting the women at higher risk of weight gain and future diabetes [15].

With regards to negative consequences for the child, GDM is associated with macrosomia at birth (> 4kg birth weight), excess body fat and paediatric obesity [17-24]. Intrauterine exposure to GDM also doubles the risk for type 2 diabetes in the children of GDM mothers [25]. Apart from GDM, maternal pre-pregnancy overweight and excessive gestational weight gain also predict higher birth weight and adiposity during infancy [26, 27]. Furthermore, maternal lifestyle behaviour, such as a high fat diet or lack of physical activity during pregnancy, can influence offspring adiposity independent of maternal obesity [27, 28].

Given the deleterious impact of GDM during pregnancy on the health of the mother and her offspring, it appears crucial to work on modifiable risk factors during the pre-, peri-and postnatal period, namely diet, physical activity, and psychosocial well-being [29]. Excessive gestational weight gain [30] is very frequent in women with GDM and strongly associated with lifestyle factors during pregnancy [31]. High fat consumption particularly saturated fat, trans fat and cholesterol, increases GDM risk [32-34]. A higher intake of added sugar and lower intake of vegetable and fruit fiber are independently linked to increased fasting glucose [34]. Animal protein intake is positively and vegetable protein inversely associated with GDM risk [35]. Another important domain that can address risk factors of GDM is physical activity, which decreases insulin resistance, reduces future risk of type 2 diabetes [36], and limits gestational weight gain by increasing energy expenditure and altering food intake [37]. Thus, physical activity has a protective effect on the development of GDM [38, 39]. Finally, psychological factors also play an important role in GDM. Higher stress exposure and perceived stress are associated with increased fasting glucose levels in pregnant women, even before they know their diagnosis [40]. Psychological stress and negative life events can be associated with higher salivary cortisol levels during pregnancy, which might influence glucose levels [41]. Depressive symptoms in early pregnancy also increase the risk for GDM [14, 39].

Many modifiable risk factors that relate to GDM also interact with each other. In this review, the term “interaction” covers correlations or associations, found in the original papers, between our

domains of interest [diet (including breastfeeding), physical activity and psychosocial well-being (including depression, anxiety, stress, sleep, self-efficacy and social support)]. For example, physical activity may reduce symptoms of depression [42], probably by reducing plasma kynurenine [43, 44]. Physical activity increases energy expenditure [45], can influence total food intake [45, 46], reduces stress-induced food intake [47] and can also regulate eating behavior via endocrine mediators such as insulin, leptin, and ghrelin [48-50]. Eating behavior, such as emotional eating or unhealthy habitual eating plays an important role in explaining the depression-BMI relationship [51-55]. Finally, the higher risk for maternal postpartum depression is also associated with reduced parenting skills, which may have negative consequences for the development of the child [56-58]. Given the interaction of these domains, designing interventions that integrate more than one domain of interest (diet, physical activity and psychosocial well-being) may be promising. Many interventions in women with GDM focus on either diet [59-61], physical activity [62-66], or combined diet and physical activity interventions [67, 68]. However, to our knowledge, there are no interventions combining diet and/or physical activity with psychosocial well-being. Therefore, this integrative review explored how physical activity, diet, and psychosocial well-being interact in women with GDM and in their offspring by analyzing and synthetizing observational and intervention studies. In addition, we investigated how effective interventions that address more than one domain of interest are in reducing risk factors associated with GDM. Addressing these questions may help to identify effective ingredients of interventions to counter the negative impact of GDM in women and their offspring.

Methods

Design

This integrative review follows the guidelines elaborated by Whitemore and Knafl (2005) [69]. As we were investigating a new topic, we needed a design that would allow us to explore this topic in a broad manner and to produce evidence-based results. We followed Whitemore and Knafl's design firstly by identifying variables of interest and elaborating specific research questions. We then used computerized databases to augment efficiency as well as the scope of our review. Secondly, we defined inclusion and exclusion criteria that guided the decision to exclude irrelevant articles, and we evaluated the quality of each original article. When analysing data, we categorized, summarized and ordered our data extracted from primary articles and organized the results according to subgroups. Whitemore and Knafl (2005) [69] also recommend creating data displays; thus, we summarized our findings in tables (see additional file 1) and created a conceptual model integrating all of our results (see Figure 2). Finally, we specified the implications for clinical practice, as recommended by the authors.

Search strategy

A comprehensive search strategy included carefully selecting terms that corresponded to the domains of interest [diet (including breastfeeding), physical activity and psychosocial well-being (including depression, anxiety, stress, sleep, self-efficacy and social support)] (please refer to additional file 2 for details on the search strategy) by consulting a team of interdisciplinary experts and a specialised librarian. The databases searched for articles were: CINAHL, PsycINFO, Embase, for which usual subject headings were used and Pubmed, for which the strategy was completed with free-text terms to also collect the non-indexed articles, and finally, Cochrane, for which the strategy used only free search terms. All studies identified during the search were assessed for relevance to the review based on the information provided in the title and abstract. For all papers that appeared to meet the inclusion criteria, full papers were retrieved. Full papers were again assessed for eligibility in order to determine relevance to the review objective. The period considered was from 1980 to the date of the first search (September, 15 2016) and this first search identified 16'026 articles. An update of the search was performed between the 15 of September 2016 and the 12 of February 2018 and identified 15'744 articles. This contained articles found in the first search as well as new ones; for this reason, a large number of duplicates were removed after the second search (13'760) (Figure 1). The second literature search yielded fewer articles than the first one because we were able to exclude the time period related to our first search in Pubmed, thus avoiding the exclusion of duplicates in this database.

Inclusion criteria

Inclusion criteria were either observational or intervention studies in women with GDM that focused on at least two domains of interest. Articles were published in English in peer-reviewed journals and had to contain data on women with GDM (or women and their partner), or previous GDM, with clinical outcomes reported for women (or women and their baby). The decision to include articles from 1980 was made in order to stay in line with more up-to-date clinical practice and objectives for glycemic thresholds.

Exclusion criteria

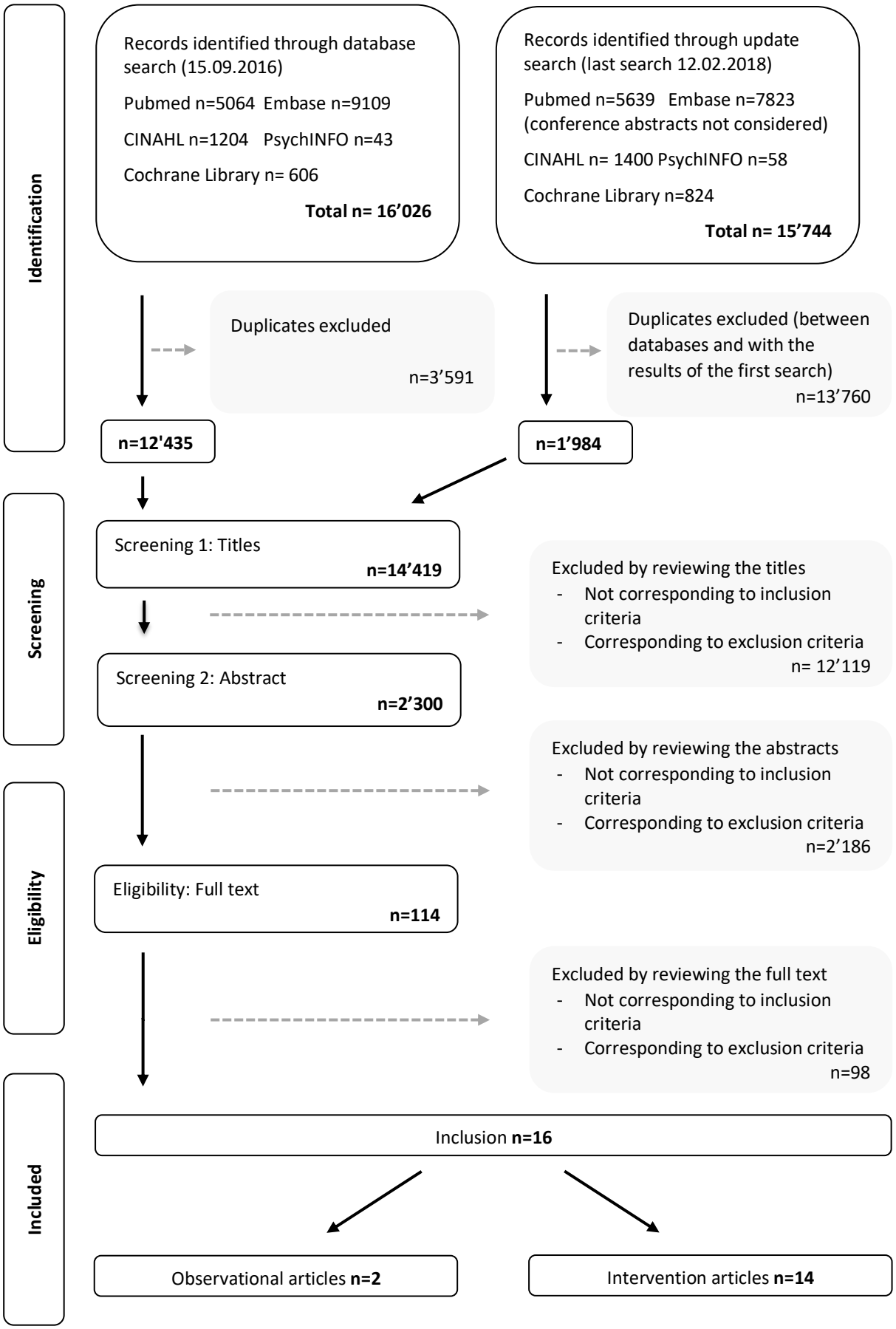
We excluded study protocols, conference abstracts, recommendation papers, guidelines, qualitative studies, and review articles. Articles that exclusively investigated women with type 1 and type 2 diabetes were excluded. Intervention studies that only tested pharmacological interventions were also excluded, as were genetic, epigenetic and genomic studies. Studies on diet, which focused

only on dietary supplements were also excluded. Animal research and papers addressing exclusively the microbiome were also excluded.

Data extraction and quality appraisal

All identified citations were collated in a citation management system (Endnote X7) and duplicates were removed. The search strategies identified 14'419 citations after excluding duplicates (see above and Figure 1). After screening titles and then abstracts, 114 articles were selected for detailed evaluation of their full text, and 16 were included in this review.

Figure 1. ***Prisma Flowchart***



This Prisma flowchart illustrates the process through which articles for this integrative review were included or excluded.

Data from the 114 articles were extracted systematically from all eligible papers with a modified Joanna Briggs Institute (JBI) data extraction form for review and research synthesis designed by LG. This allowed for sequential extraction of articles by LG and DYQ to make final decisions on which papers to include and those to exclude. Any disparities or disagreements were resolved by consensus-based discussions with AH.

Following this, JG and SL independently extracted the data and produced tables 1 and 2 (see tables 1 and 2 in additional file 1). The quality of included studies was assessed with the JBI critical appraisal *Checklist for Randomized Controlled Trials* [70], *Checklist for quasi-experimental studies (non-randomized experimental studies)* [71], *Checklist for Analytical Cross Sectional Studies* [72] and *Checklist for Cohort studies* [73]. Two reviewers (LG & DYQ) undertook the quality assessment independently and later resolved discrepancies in score ratings by consensus. The appraisal checklists assessed the aims of the study, sampling procedure, data collection methods, main findings, and limitations.

Synthesis of findings

Findings from the included studies were synthesized according to the objectives of the study in a thematic manner, as suggested by Whittemore and Knafl (2005) [69]. Firstly, links between the different domains of interest in the observational and intervention studies were synthesized, forming the base for a conceptual framework. Secondly, the effects of interventions on clinical outcomes were summarized.

Results

Characteristics of included studies

This review included 16 studies (Figure 1): two observational studies and 14 intervention studies. The observational studies were conducted in the USA (n=1/2) [74] and Switzerland (n=1/2) [75], employing a cross-sectional (n=1/2) [74] or a prospective cohort design (n=1/2) [75]. The 14 intervention studies took place in eight different countries, with the highest number of them conducted in the USA (n=5/14) [76-80] and China (n=3/14) [81-83]. The remaining studies were carried out in Australia (n=1/14) [84], Canada (n=1/14) [85], Finland (n=1/14) [86], Ireland (n=1/14) [87], Spain (n=1/14) [88] and Thailand (n=1/14) [89]. Of these intervention studies, the large majority were randomized controlled trials (RCTs) (n=9/14) [76, 78, 79, 81, 82, 84, 87-89] and the remaining studies

were intervention trials (n=5/14), with two of them (n=2/5) containing a control group [80, 83] and the other three (n=3/5) using a pre/post-test design [77, 85, 86]. The majority of the included studies were published between 2011 and 2015 (n=10/16) [76, 77, 81, 83-89], whereas the remaining studies were published between 2006-2010 (n=3/16) [74, 78, 80] and 2016-2018 (n=2/16) [75, 82]. One study (n=1/16) [79] was published in 1989.

All combined intervention studies focused solely on diet and physical activity and none included psychosocial well-being in their intervention. For reasons of simplicity and clarity, these combined studies will be named “lifestyle interventions”.

In these intervention studies, the extracted data for this review focused on outcomes of the intervention groups which were always compared to the respective other GDM control groups; thus we will not mention this in our result section, to increase readability. Only one intervention study (n=1/14) [83] contained more than two groups. Indeed, this study had five different groups (lifestyle, diet only, physical activity only, no intervention and a “no GDM” group). We chose to report results for the lifestyle intervention compared to the “no intervention group” only, to be in line with the other studies integrated in this review. An exception remains for three studies (n=3/14) that were designed differently. Indeed, one study compared the lifestyle intervention group at the end of the study (one year) to the baseline of that same lifestyle intervention group and thus did not contain a control group (n=1/14) [86]. For the second study, the authors used a single-group pre-post design and measured the effect of the intervention across time [77]. Finally, the last study was a single arm pilot before and after intervention study [85]. For these studies, these design details will always be mentioned in our results section.

Lifestyle interventions lasted from six weeks [79] to four years [82] and either contained results at the end of the intervention [76, 78-86, 88, 89] or, for only two studies, after a follow-up period [77, 87]. As time effects (baseline to end of the study or to follow-up) are always present in initial papers for intervention groups and given that they vary largely, they will be mentioned in detail in our results section.

Study participants

A total of 20285 participants were included in the studies, with n=19884 in the intervention and n=401 in the observational studies. The lowest number of participants in a study was 17 [85] and the largest study consisted of 14168 participants [83].

Associations measured in the observational studies

Both observational studies investigated the associations between diet, physical activity and psychosocial variables (n=2/2) [74, 75]. Specifically, the authors assessed the link between social support and diet and physical activity, and the relationship between psychosocial well-being (self-efficacy, social support and self-efficacy and social support) and diet and physical activity.

Lifestyle interventions investigated

The lifestyle intervention adopted in all intervention studies consisted of combined diet and physical activity interventions (n=14/14). The dietary components of the study interventions required participants to follow either the American Diabetes Association (ADA) diet [76], the Diabetes Prevention Program (DPP) guidelines [77, 78], the Canada's Food Guide [85], a Mediterranean diet [88] or other types of dietary guidelines [79-84, 86, 87, 89, 90]. In most studies, participants were advised to either conduct moderate to vigorous physical activity for around 150 minutes a week [76-78, 85] or 30 minutes a day [81, 82], to be more active and incorporate light and moderate physical activity as much as possible in daily life [83], to increase the number of steps (walking) a day to 10'000 [84], or to have a specific yoga routine (nine postures) [89]. In four studies, participants were asked to exercise at moderate intensity [79, 80, 87, 88]. In one study, intervention participants were provided with a study pedometer to track their daily steps [84]. In another study [86], training with a coach provided empowerment during physical activity.

All outcome variables were tested either during pregnancy [80, 83, 89] or in the postpartum period [74-88] In intervention studies, the interventions started either during pregnancy [76, 79, 80, 82, 83, 89] or in the postpartum period [77, 78, 81, 84-88] (for details, please refer to Tables 1 and 2 in additional file 1).

Interactions between domains of interest (diet, physical activity and psychosocial well-being)

Focusing on the *observational studies*, one prospective observational study (n=1/2) [75] revealed that the main normative influences for healthy behaviors (diet and physical activity) were the husband/partner (68%) and other family members (56%). After controlling for significant individual factors, the study showed that a lower level of social support was related to a lower adherence to a healthy lifestyle in the postpartum period.

Regarding diet and its relationship with self-efficacy, the authors of the cross-sectional study [74] showed that women reported low self-efficacy for not overeating. They further demonstrated that self-efficacy for not overeating was associated with better dietary quality, although this association missed significance after adjusting for covariates.

In terms of the relationship between diet and social support, women reported moderate social support for consuming a healthy diet [74]. Higher social support from both friends and family for a healthy diet correlated with better dietary quality, with a trend towards statistical significance. The authors further demonstrated that after adjustment for covariates, stronger social support from family and friends for dietary habits was associated with better dietary quality.

Regarding physical activity and its relationship with self-efficacy, Kim et al. (2008) demonstrated in the cross-sectional observational study that women reported low self-efficacy for physical activity [74]. However, greater self-efficacy for physical activity was associated with a greater number of hours spent walking and greater leisure time spent in vigorous intensity activity, but not with walking intensity. When the authors adjusted their analysis for covariates, greater self-efficacy for physical activity was associated with more than four hours per week spent walking and with spending at least 20 minutes three times a week in a vigorous activity.

Regarding associations between physical activity and social support, the cross-sectional study (n=1/2) [74] observed that women reported moderate social support for physical activity. Furthermore, they observed that social support from friends for physical activity was associated with a greater number of hours spent walking and greater leisure time spent in vigorous activity. Moreover, social support for physical activity was associated with greater leisure time physical activity, but not with the total number of hours spent walking. Furthermore, after adjustment for covariates, social support from friends was also associated with more than four hours spent walking per week, but not with walking intensity and leisure time activity. In the prospective observational study (n=1/2) [75] observing the link between social support and physical activity, women indicated a need for personalized advice (65%) and sport facilities where their children can be looked after (69%) to facilitate their physical activity practice.

All *intervention studies* were combined physical activity and diet lifestyle interventions (n=14/14). The lifestyle interventions led to a decreased fat intake in two studies, one during the intervention period (seven months) (n=1/2) [76] and one at six months follow-up after a three-month intervention, compared to baseline [77] (n=1/2) . In one study, the lifestyle intervention lead to a higher diet adherence at the one-year follow-up after a 12-week intervention (n=1/1) [87]. Higher diet self-efficacy was seen in two studies, once at one-year follow-up after a three-month intervention [87] and also at the end of the intervention [84]. In addition, there was a higher proportion of women who partially or exclusively breastfed during the intervention (seven months) in one study (n=1/1) [76]. Other outcomes for diet in the lifestyle intervention studies demonstrated that participants reported a higher fibre intake at the end of the intervention (four years) (n=1/1) [82] and a healthier diet pattern in the consumption of unsaturated fat, saturated fat and healthy fat at the end of the intervention

(three years) (n=1/1) [88]. In summary, all studies that investigated a dietary outcome showed an improved dietary outcome.

Concerning physical activity, women in the lifestyle intervention group had higher physical activity, leisure or commuting time activity and exercise at the end of each intervention (n=4/4) [78, 81, 82, 88], a higher exercise capacity at the end of the intervention (six months), compared to baseline (n=1/1) [85] and higher aerobic activity, flexibility and strength at six months follow-up after a three-month intervention, compared to baseline (n=1/1) [77]. In contrast, three studies (n=3/3) revealed no significant differences between physical activity levels between inclusion and after the interventions at three months [84], seven months [76] or during the one-year follow-up after a three-month intervention [87]. Thus, six studies showed a positive impact on physical activity, while three demonstrated no change.

With regards to psychosocial outcomes, the lifestyle interventions led to lower stress perception and higher quality of life at the end of the study (one year) after a three-month intervention (n=1/1) [87] and less fatalistic and cultural diabetes beliefs at six months follow-up after a three-month intervention compared to baseline (n=1/1) [77]. Thus, two studies looked at psychosocial well-being as outcomes and found an improved outcome.

In summary, observational studies demonstrated that there were interactions between lifestyle domains. The studies hint at social support being an important factor for adhering to a healthy lifestyle. Moreover, there were positive relationships between diet and self-efficacy and social support. These two factors were also positively associated with physical activity, more specifically time and intensity were higher when women had higher self-efficacy and social support. The intervention studies demonstrated that most lifestyle interventions improved diet and physical activity, although the effect of physical activity was not sustained in the long term. Lifestyle interventions also augmented psychosocial well-being, but this was only investigated in two studies.

Clinical outcomes

Anthropometric outcomes

Anthropometric outcomes measured in the integrated studies contained BMI, weight, gestational weight gain, waist and hip circumference, body composition and percentage body fat. These outcomes were measured during the postpartum period, except for gestational weight gain, which was measured during pregnancy. In the *observational studies*, only one (n=1/2) study looked at anthropometric outcomes, and more specifically BMI [74]. This study revealed no significant associations between self-efficacy against overeating, and social support from family for diet and BMI, with the exception of a weak correlation between friends' social support for diet and BMI. After

adjustment for the healthy diet index score, dietary self-efficacy and social support were not associated with BMI. The same authors also looked for associations between physical activity-oriented self-efficacy and social support for BMI and found no significant associations between these types of self-efficacy and social support for physical activity and BMI.

Regarding *intervention studies*, 12 interventions (n=12/14) assessed anthropometric outcomes. BMI was reported in eight different studies (n=8/12). This outcome decreased significantly in four studies (n=4/8) at the end of interventions: lasting three months [84], one year [81], three years [88], or four years [82]. However, no significant difference was observed in three other studies (n=3/8) at the follow-up measures at one year after a three-month intervention [87] and at six months after a three-month intervention, compared to baseline [77] and at the end of a six-month intervention, compared to baseline [85]. One study (n=1/8) observed that women following a diet and exercise intervention during pregnancy had a higher pre-pregnancy BMI compared to other groups [83]. The same study (n=1/8) also showed that in women following a lifestyle intervention, BMI increased significantly less between pre- and late pregnancy and between mid and late pregnancy. Waist and/or hip circumference was measured in seven studies (n=7/12) and significantly decreased in five studies (n=5/7), always at the end of the intervention at three months [84] or six months compared to baseline [85], one year [81], three years [88] and four years [82]. In contrast, two other studies reported no significant change in waist and hip circumference (n=2/7), at the end of a one-year intervention compared to baseline in one study [86] and at one year follow-up after a three-month intervention in another study [87]. Participants' weight was assessed in eight studies (n=8/12). Four studies (n=4/8) revealed a significant decrease in weight after the interventions that lasted three months [84], one year [81], three years [78] or four years [82]. However, three other studies (n=3/8) showed no apparent change in weight compared to the control groups after interventions that lasted six months compared to baseline [85] and after a follow-up period of six months after a three-month intervention, compared to baseline [77] and a follow-up period of one year after a three-month intervention [87]. A fourth study (n=1/8) also showed no apparent change after a one-year intervention compared to baseline [86]. One study revealed a trend towards reaching the recommended 12-months postpartum weight goal at the end of a 12-month intervention (n=1/1) [76]. One study demonstrated that gestational weight gain was lower at the end of a 7.7 weeks intervention (n=1/1) [80]. In two intervention studies measuring body fat (n=2/2), there was a significant decrease in body fat at the end of the one-year intervention (n=1/1) [81]. Another study showed no difference in percent body fat at the end of the six-month intervention, compared to baseline (n=1/1) [85]. In addition, one study showed no change in body composition at the end of the three-month intervention (n=1/1) [84].

In summary, observational studies indicated that social support and self-efficacy had no significant association with BMI. Intervention studies demonstrated a decreased waist and hip circumference and body fat, although the results of lifestyle interventions concerning weight and BMI were inconsistent.

Metabolic outcomes

Metabolic outcomes included insulin, glucose, lipid profile, cholesterol, triglycerides, HbA1c, and Apo lipoprotein. None of the *observational studies* assessed metabolic outcomes. Seven of the *intervention studies* (n=7/14) measured metabolic outcomes. Fasting plasma glucose (n=3/7) remained unchanged at the one-year follow-up of a three-month intervention (n=1/3) [87], although it was reduced significantly at the end of two other interventions (n=2/3) that lasted six [79] and eight weeks [89], respectively. Concerning other glucose-related values (n=3/7), all of these values were reduced in the intervention groups (n=3/3), demonstrating lower one-hour glucose after OGTT at study end (six weeks) (n=1/1) [79], lower two-hour glucose after OGTT at the one year follow-up of a three-month intervention [87] and lower two-hour postprandial blood glucose at the end of an eight-week intervention (n=1/1) [89]. Interestingly, insulin resistance, which was measured in three studies (n=3/7), decreased at the end of a three-year intervention (n=1/3) [88], but no significant change was observed in two other studies (n=2/3) at the end of a three-month intervention [84] or at a one-year follow-up after a three-month intervention [87] (n=2/3). In three studies, HbA1c (glycated haemoglobin) (n=3/7) was measured. It significantly increased between baseline and the six-month follow-up after a three-month intervention compared to baseline in one study (n=1/3) [77] but significantly decreased in the two remaining studies (n=2/3) after a six-week intervention [79] and an eight-week intervention [89]. Three studies measured LDL (low density lipoprotein) –cholesterol (n=3/7); this decreased after a one-year intervention compared to baseline in one study (n=1/3) [86], after a three-year intervention in another [88], and at a six-month follow-up after a three-month intervention compared to baseline in the last study (n=1/3) [77]. Two studies measured HDL (high density lipoprotein)-cholesterol. One study demonstrated a rise in HDL at the end of a one-year intervention compared to the intervention baseline (n=1/2) [86], whilst in the other study it remained the same as during baseline assessments at the six-month follow-up after a three-month intervention (n=1/2) [77]. Two studies measured triglycerides (n=2/7) that decreased in both studies (n=2/2): at a six-month follow-up after a three-month intervention compared to baseline (n=1/2) [77] and at the end of a three-year intervention (n=1/2) [88]. In two separate studies, reductions in total cholesterol at a six-month follow-up after a three-month intervention, compared to baseline (n=1/1) [77], and consistency was seen in the lipid profile at the one-year follow-up after a three-month intervention in

one study (n=1/1) [87]. Intervention groups had lower fasting plasma insulin levels and Apo lipoprotein at the end of a three-year intervention (n=1/1) [88] or lower plasma insulin levels at the end of a one-year intervention (n=1/1) [81].

In summary, the majority of the studies that included metabolic outcomes revealed a decrease in total and LDL cholesterol, triglycerides, and in glucose values. Results in HbA1c and HDL cholesterol were inconsistent and the other outcomes were not measured in enough studies to draw conclusions.

Postpartum diabetes status

This outcome was not reported in the *observational studies*. Only two lifestyle *intervention studies* (n=2/14) measured postpartum diabetes status at the end of the intervention (after a three-year intervention in both studies). One intervention study revealed a significant reduction in the risk of diabetes progression (n=1/2) [78]. Another study (n=1/2) [88] showed a 25% decrease in the development of glucose disorders (impaired fasting glucose and impaired glucose tolerance) as well as a 35% decrease in the rate of type 2 diabetes.

In summary, lifestyle interventions led to a reduced risk of postpartum diabetes in the two studies that evaluated this outcome.

Delivery and other clinical outcomes

None of the *observational studies* measured delivery or other clinical outcomes. Two of the lifestyle *intervention studies* (n=2/14) measured outcomes related to the delivery, such as macrosomia, adverse pregnancy outcomes, preterm delivery, low birth weight, and caesarean deliveries; two other studies measured other clinical outcomes, such as blood pressure (n=2/14).

In the studies measuring macrosomia (n=2/2), both (n=1/2) demonstrated similar rates of macrosomia in both groups at the end of a 13.2-week intervention [83] and after a 7.7-week intervention [80]. This last study also showed no differences in the rate of adverse pregnancy outcomes [80].

Preterm delivery, low birth weight, and cesarean deliveries were only measured in one study (n=1/1); a significantly decreased risk of preterm delivery and low birth weight at the end of a 13.2-week intervention was found, but there were similar rates of caesarean deliveries compared to a GDM control group [83].

In the studies measuring other clinical outcomes (n=2/14), one study showed a reduction in diastolic blood pressure and no change in systolic blood pressure at the six-month follow-up after a three-month intervention, compared to baseline (n=1/2) [77]. The second study showed that systolic

and diastolic blood pressure were unchanged at the end of a one-year intervention compared to baseline [86].

In summary, compared to GDM women in control groups, women in lifestyle interventions showed no differences between the rates of macrosomia, adverse pregnancy outcomes and caesarean section, although there was a decreased risk of preterm deliveries and low birth weight. Concerning results for systolic blood pressure were similar throughout groups and time and the results for diastolic blood pressure were inconsistent.

Quality of studies reviewed

Authors (LG & DYQ) rated the majority of included articles to be of good quality [74-84, 86-89] based on the Joanna Briggs Institute Appraisal Tools (2017) (see tables 1 and 2 in additional file 1). The checklist for analytical cross-sectional studies [72] was used for the cross sectional observational study [74], the checklist for cohort studies [73] was used for the prospective cohort study [75] whereas for intervention studies, the checklist for randomized controlled trials [70] was employed for the randomized controlled trials [76, 78, 79, 81, 82, 84, 87-89]. For the remaining intervention studies [77, 80, 83, 85, 86], we used the checklist for quasi-experimental studies [71]. Studies rated as having a good quality described in detail the design and methodology used, the process of recruiting participants and the study setting, gave clear and detailed presentation of findings and had study limitations that were unlikely to affect the reliability and validity of study findings. The only study rated as having poor quality [85] did not explain the reasons for drop out in participants and did not conduct analysis to compare the drop outs to the participants remaining in the study. It thus had limited information on data analysis and a small sample size, both of which could lead to a high risk of bias and a poor generalizability of the study.

Discussion

This integrative review synthesized evidence on the interaction between three different domains: diet (including breastfeeding), physical activity, and psychosocial well-being (including depression, anxiety, sleep, and social support) in women with GDM and their offspring. Moreover, it summarized the effectiveness of interventions addressing more than one lifestyle domain, including diet and physical activity on anthropometric, metabolic, delivery and other clinical outcomes. To the best of our knowledge, this integrative review is the first to synthesize evidence on the relationships and interaction between different lifestyle behaviors, psychosocial well-being, and the efficacy of combined lifestyle interventions in women with GDM and their offspring.

Results from this review indicated that the *interaction between lifestyle domains* produced desirable outcomes. The two observational studies integrated in this review demonstrated that psychosocial well-being such as social support and self-efficacy were important factors associated with adherence to a healthy lifestyle. Indeed, the observational studies demonstrated that social support and self-efficacy were associated to positive changes in diet and physical activity. This is in line with another intervention study showing that psychosocial well-being, such as self-efficacy and social support was positively associated with lifestyle modifications or changes [91]. Similarly, results from the intervention studies showed that lifestyle interventions improved diet and physical activity and augmented psychosocial well-being in study participants, although this last outcome (psychosocial well-being) was only evaluated in two studies. These results underline the importance of apprehending health behavior changes in individuals via more than one domain, thus focusing on a more holistic approach of the individual.

Regarding *anthropometric outcomes,* observational studies demonstrated that psychosocial well-being had no significant association with BMI. This result is not in line with previous research showing that social support and self-efficacy for diet are associated with greater success in weight control [92] and that self-efficacy over dietary behaviours such as emotional eating and dietary restrictions generally lead to healthier weight [93]. This might be due to the fact that only one study investigated this relationship. Results from the intervention studies suggested that most lifestyle interventions achieved successes with regards to waist/hip circumference and body fat. This is in line with previous research demonstrating that diet has an important role to play in weight loss, healthier BMI and other measures of adiposity [94, 95]. Indeed, it is well known that diets setting limits on the intake of energy, trans and saturated fat, and/or energy from carbohydrate and increased fiber intake help GDM women with weight management [2]. Physical activity might also play a role in the relationship between lifestyle interventions and an improvement in anthropometric outcomes, as studies also suggest that physical activity is associated with positive changes in eating self-regulation and may lead to healthy eating. In particular, it improves psychosocial well-being and could prevent emotional eating, consumption of foods high in calories, and binge eating [96]. Higher adherence to physical activity could therefore increase eating self-regulation and may lead to lower anthropometric outcomes such as weight, BMI and waist circumference measures. Even though the results of lifestyle intervention studies led to decreases in some anthropometric outcomes, weight and BMI demonstrated inconsistent results. This might partly be due to the diversity of diet and physical activity interventions, as well as the length of the studies and adherence to the intervention.

Regarding *metabolic outcomes*, the intervention studies led to a decrease in total cholesterol, LDL cholesterol, triglycerides and glucose values compared to the control groups, although results for

HbA1c and HDL cholesterol were inconsistent. For the decreasing outcomes, the diet component of the intervention studies might have had an impact on these findings. Indeed, previous research has shown that the high dietary fiber intake may reduce appetite and food consumption, delay gastric emptying, slow food digestion and absorption [97]. This should have led to a decrease glucose absorption and also plasma insulin levels [98]. Our results are in line with these findings, as three interventions measured glucose values and two studies lead to improvements in two measured glucose values. The third study led to improvements in two-hour glucose after OGTT and to similar results in fasting plasma glucose. Research shows that the consumption of a DASH diet leads to a decrease in lipids and fasting glucose, as it has a positive impact on the lipid profile in women with GDM [99], as well as in other populations [100, 101]. In our review, the Mediterranean diet was associated with overall improved metabolic health outcomes. In pregnancy, these diets may have protective benefits for overweight and obese women who are at risk for both short and long-term metabolic outcomes [102]. The physical activity component of the intervention studies might have also played a role in the improvements of some of these metabolic outcomes. Indeed, previous research has shown that regular exercise increases insulin action by stimulating glucose uptake in the muscle through glucose transport proteins (GLUT4) that mediate insulin-dependent glucose uptake [103], and our results showed improvements in 2.5/3 of the studies analyzing glucose as an outcome. A meta-analysis of randomized controlled trials in women with GDM showed that exercise significantly improved postprandial glucose and lowered fasting blood glucose [104]. It was therefore not surprising that participants who had lifestyle interventions had lower fasting plasma insulin levels and two-hour postprandial blood glucose than those in the control group. Results for HDL cholesterol were inconsistent in the intervention studies. This might be explained by the fact that the interventions were probably not intense enough. Indeed, the two studies measuring this outcome did not have any specific physical activity training but recommended women to exercise. Another explanation could be the low adherence to the intervention regime. A third argument could be that, as HDL is also influenced by oestrogen status, it might be a strong confounder for this outcome in this population and might have impacted these results [105].

Two intervention studies showed reductions in the rate of *postpartum diabetes status,* [78, 88]. In a systematic review that examined the cumulative incidence of type 2 diabetes in women with GDM, the progression to type 2 diabetes after GDM increased steadily within the first five years after delivery [106]. According to Tobias et al., diet plays a role in the reduction of postpartum diabetes status, as higher adherence to a Mediterranean diet was associated with a 40% lower risk of diabetes compared to those in the lower adherence group in their cohort study [107]. In the same study, similar risk reductions were observed for the DASH diet, even after multiple adjustments of covariates [107].

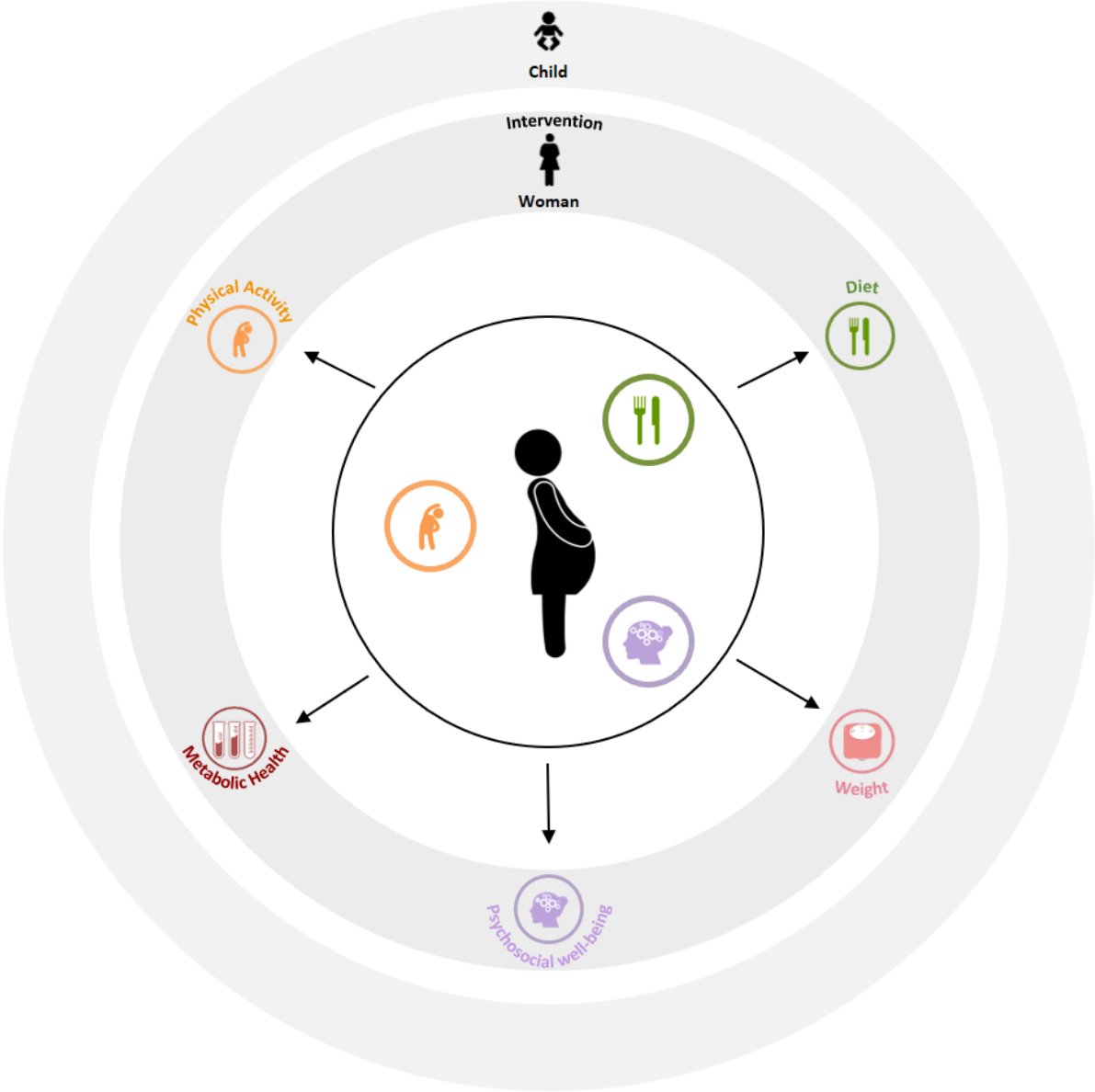
Elevated fasting glucose and HbA1c levels during pregnancy may be associated with a more pronounced progression to diabetes after GDM [108-110]. Adherence to a lifestyle intervention designed to lower weight gain and improve metabolic health during pregnancy may prevent the development of postpartum diabetes, as observed in this review. Physical activity has also been implicated in the prevention or delay in postpartum diabetes in women with GDM [111]. A prospective cohort study recently showed that women with GDM within the Nurses Health Study II cohort had a 9% reduced risk for postpartum diabetes for every 100 minutes of moderate intensity physical activity. Interestingly, an increase of 150 minutes per week of moderate intensity physical activity led to a 47% lower risk of diabetes after GDM [36].

Regarding *delivery and other clinical features,* the results of one study demonstrated a decrease in preterm delivery rates and low birth weight. Regarding preterm delivery, this outcome can be caused by various pre-existing conditions in the mother [112] and thus might not depend on lifestyle interventions. Concerning low birth weight, one of the studies found fewer low birth weight after a 13.2-week intervention [83]. Thus, our results are not in line with a previous systematic review and meta-analysis of randomized controlled trials of dietary interventions in women with GDM showing that dietary interventions were associated with lower birth weight compared with controls [113]. One explanation could relate to the fact that women in the integrated study might not have all received the same type of lifestyle intervention. Indeed this study mentioned that the lifestyle interventions were retrospectively auto-reported by questionnaire [83]. Finally, we found similarities in the rates of macrosomia, in the intervention studies in the control as well as intervention groups [80, 83]. Thus, our results are not in line with the findings of a recent review indicating that diet and physical activity interventions can lead to a reduced risk of macrosomia in overweight and obese women [114]. Previous research has shown that macrosomia, adverse pregnancy outcomes and caesarean sections are dependent on a number of different factors and/or on the maternal diabetes status [1, 115, 116] and thus, lifestyle interventions might have little to no effect on these outcomes. The results for systolic blood pressure were similar between baseline and at six months follow-up after a three-month intervention [77] and similar compared to baseline in the other [86]. Finally, for diastolic blood pressure, our results were inconsistent. These results are comparable with previous research showing no difference in systolic and diastolic blood pressure between different control groups and GDM women [117], except for one of the integrated studies demonstrating a decrease in diastolic blood pressure at six months follow-up after a three-month intervention, compared to baseline [77].

Overall, evidence from this integrative review suggests that *lifestyle interventions* including a psychosocial intervention during pregnancy could augment the women's adherence to diet and

physical activity, which in turn might have complementary and interactive effects on the physiological and psychological health of women with GDM. We therefore propose that combined diet, physical activity, and psychosocial interventions could positively influence physiological and psychological processes toward healthy outcomes (Figure 2) and should be tested. Arguments that cognitive-behaviorally supported exercises, self-efficacy and social support can facilitate changes in eating behavior through associated psychological changes have emerged, also outside of pregnancy. This is partly because diet and physical activity domains of a lifestyle intervention may also benefit from improved psychosocial outcomes. Thus, exercise during pregnancy can influence physiological processes, such as energy metabolism and appetite, as well as psychological factors, including self-efficacy, body image, or mood [118, 119]. The interactive mechanisms of these factors could lead to stronger motivation and confidence, which could improve adherence to physical activity. Long-term exercise adherence, as well as eating self-regulation and dietary compliance may also result in gestational weight gain control, metabolic outcomes, and again higher levels of psychosocial well-being during pregnancy and in the post-partum period. On the other hand, psychosocial vulnerability (including depression, stress, and lack of social support), lack of diet self-regulation and physical inactivity may negatively influence birth outcomes, including caesarean deliveries, macrosomia and other infant physiological disorders, such as hypoglycemia, as well as adverse outcomes in the mother during the post-partum period [90, 120-122]. According to our results and proposed model (see Figure 2), interventions targeted at mitigating the risks associated with a GDM pregnancy should not only include diet and physical activity domains but may also integrate and/or include strategies for improving self-efficacy and self-regulation of eating, exercise, psychosocial well-being, and social/ family support. After all, the success of a combined diet and exercise intervention may also depend on the mothers' psychosocial well-being (depression, stress, self-efficacy and social support) during pregnancy.

Figure 2. ***Integrative model***



Conceptual model resulting from the integrative review proposes that interventions targeted at mitigating the risks associated with a GDM pregnancy should not only include diet and physical activity domains but may also integrate and/or include strategies for improving self-efficacy and self-regulation of eating, exercise, psychosocial well-being, and social/ family support. In the first black circle, diet, physical activity, and psychosocial well-being interventions for women with GDM are represented. In the second gray circle, the outcomes which are improved for the mother following a diet, physical activity and psychosocial intervention are illustrated. Finally, the largest gray circle represents the neonatal outcomes which may also be improved if the mother follows a diet, physical activity and psychosocial intervention.

Strengths and limitations

This integrative review has many strengths. This study followed the PRISMA guidelines as well as Whitemore and Knafl's recommendations We used a comprehensive search strategy and independent reviewers carried out identification of relevant studies. The majority of our included studies were of RCT design with large sample sizes and follow-up periods. We also included psychosocial well-being and focused on combined interventions, which, to our knowledge, has not been done before. Nevertheless, some limitations need to be addressed. Firstly, conducting an integrative literature review lead to integrating studies with large heterogeneities regarding the intervention and follow-up periods across studies, as well as in the types of lifestyle interventions used in each individual studies. Thus, our results need to be interpreted with caution. In addition, psychosocial well-being was only investigated in observational studies, even though it was assessed in intervention studies as an outcome. Moreover, although we had also searched for terms, such as depression, anxiety and sleep in the psychosocial well-being domain, no results were found for these outcomes. This might be due to the fact that, as mentioned, psychosocial well-being was only present in two observational studies and as an outcome in two intervention studies. Furthermore, although we had also screened for articles for parenting, we found no results concerning the partner except in observational studies. Indeed, in the observational studies, the partners appeared as "social support from family" but no other results were found. The different components of the lifestyle interventions and types of diet and physical activity as well as the approach and the patient population may account for the differences in study results and conclusions. In addition, the inability of the lifestyle interventions to account for or adjust for individual attitudes and behaviors, particularly psychosocial factors, might have influenced the results of these studies. This is because positive results on changing diet and physical activity habits are often related to self-efficacy or social support, as seen in the observational studies. Finally, the issue of publication bias can be a limitation to this study, as studies reporting no significant results are rarely published [123].

Clinical implications and future directions

The findings of this integrative literature review reveal that diet, physical activity, and psychosocial well-being relate and interact in women with GDM. On the one hand, diet and physical activity were associated with psychosocial well-being. On the other hand, this review showed that psychosocial well-being, such as self-efficacy and social support may be important when adopting a healthy diet and physical activity habits. Thus, we propose that any intervention focusing on behavioral change, should evaluate and consider integrating psychosocial well-being as part of the intervention components, as this might add to the lack of research in this domain. Even though diet

and physical activity interventions may reduce some of the risks associated with GDM, the findings of this integrative review suggest that there may be merit in further exploring the option of psychosocial well-being in future interventions. This may increase patients' willingness to change attitudes and inform positive behavioral changes that would expand the current scope of strategies in reducing the risk associated with GDM. Future studies that plan to adopt psychosocial interventions should focus on self-efficacy and/or social support, as both elements are associated with diet and physical activity habits. However, this might not be easy, as it implies that women already have a support system on which they can rely to help them change their behavior and that self-efficacy can be improved in this life period within a lifestyle intervention. It is also known that prenatal maternal stress exposure and stress perception are associated with less favorable obstetric outcomes, such as caesarean section [90, 120, 121]. Thus, future interventions may focus on the psychosocial well-being of women with GDM to help alleviate and/or ameliorate stress symptoms [124]. Furthermore, partners of women could also be integrated as social support for women with GDM that need to make lifestyle changes. Finally, it would also be interesting to conduct a review on qualitative studies to identify participant perception and lived experiences with lifestyle interventions in women with GDM in order to fine-tune future interventions.

Conclusion

This integrative review showed that diet, physical activity and psychosocial well-being interact in women with GDM. We found that lifestyle interventions led to a better dietary quality in all studies, improvements in physical activity in more than half of the studies measuring this outcome, lower stress perception, higher quality of life, less fatalistic and cultural diabetes beliefs, some better anthropometric and metabolic health outcomes, lower rates of diabetes progression following GDM and to less preterm deliveries and a higher birth weight. The observational studies also demonstrated the importance of social support and self-efficacy in relation to a healthy lifestyle in women with GDM. Given that psychosocial well-being, such as social support and self-efficacy, are associated with physical activity and healthy dietary choices, we recommend that future intervention studies consider integrating psychosocial well-being in a combined diet and physical activity intervention to investigate the role of self-efficacy and social support on GDM.

List of abbreviations

GDM : gestational diabetes mellitus

OGTT: Oral Glucose Tolerance Test

Declarations

Ethics approval and consent to participate

Not applicable.

Consent to publish

Not applicable.

Availability of data and materials

All relevant data are within the paper and its Supporting Information files.

Competing interests

The authors declare that they have no competing interests.

Funding

This review is a pilot study of a project grant by the Swiss National Science Foundation (SNF 32003B_176119). This study also received funding from an unrestricted educational grant from NovoNordisk. The funding organizations had no role in the preparation of this manuscript for submission.

Author's contributions

LG participated in the conception and design of the study, coordinated the study and the data collection, participated in the data analysis, interpretation of data and in the writing of the manuscript. SL & JG conducted the data analysis, assisted with the interpretation of the data, and commented on the manuscript. DYQ participated in the interpretation of data and co-wrote the manuscript. JP participated in the conception and design of the study, assisted in the interpretation of the data and commented on the manuscript. AH participated in the conception and design of the study and co-wrote the manuscript. All authors read and approved the final manuscript.

Acknowledgements

We would like to give a special thanks to Cécile Jaques, librarian at the Medical Library of the Lausanne University Hospital for her help in the literature databases search. We also would like to thank Shota Dzemali, Giada Ostinelli, Céline Helbling and Agnès Bacso for their help in the selection process of the titles and abstracts. We would like to thank Andrew Dwyer for helpful discussions at the conception stage.

References

1. American Diabetes Association: **Standards of medical care in diabetes—2014**. *Diabetes Care* 2014, **37**(Supplement 1):S14-S80.
2. Blumer I, Hadar E, Hadden DR, Jovanovič L, Mestman JH, Murad MH, Yogev Y: **Diabetes and pregnancy: an endocrine society clinical practice guideline**. *The Journal of Clinical Endocrinology & Metabolism* 2013, **98**(11):4227-4249.
3. Association AD: **Standards of Medical Care in Diabetes-2017: Summary of Revisions**. *Diabetes Care* 2017, **40**(Suppl 1):S4-s5.
4. Benhalima K, Jegers K, Devlieger R, Verhaeghe J, Mathieu C: **Glucose Intolerance after a Recent History of Gestational Diabetes Based on the 2013 WHO Criteria**. *PloS one* 2016, **11**(6):e0157272.
5. Ryser Rüetschi J, Jornayvaz F, Rivest R, Huhn E, Irion O, Boulvain M: **Fasting glycaemia to simplify screening for gestational diabetes**. *BJOG: An International Journal of Obstetrics & Gynaecology* 2016.
6. DeSisto CL, Kim SY, Sharma AJ: **Peer reviewed: Prevalence estimates of gestational diabetes mellitus in the United States, pregnancy risk assessment monitoring system (prams), 2007–2010**. *Preventing chronic disease* 2014, **11**.
7. Zhang F, Dong L, Zhang C, Li B, Wen J, Gao W, Sun S, Lv F, Tian H, Tuomilehto J: **Increasing prevalence of gestational diabetes mellitus in Chinese women from 1999 to 2008**. *Diabetic Medicine* 2011, **28**(6):652-657.
8. Bener A, Saleh NM, Al-Hamaq A: **Prevalence of gestational diabetes and associated maternal and neonatal complications in a fast-developing community: global comparisons**. *International journal of women's health* 2011, **3**:367.
9. Contreras R, Chen W, Sacks DA: **Trends in the Prevalence of Preexisting Diabetes and Gestational Diabetes Mellitus Among a Racially/Ethnically Diverse Population of Pregnant Women, 1999-2005**. *Diabetes Care* 2008, **31**(5):899.
10. Bellamy L, Casas JP, Hingorani AD, Williams D: **Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis**. *Lancet* 2009, **373**(9677):1773-1779.
11. Lauenborg J, Hansen T, Jensen DM, Vestergaard H, Mølsted-Pedersen L, Hornnes P, Locht H, Pedersen O, Damm P: **Increasing Incidence of Diabetes After Gestational Diabetes A long-term follow-up in a Danish population**. *Diabetes Care* 2004, **27**(5):1194-1199.
12. Retnakaran R, Shah BR: **Mild glucose intolerance in pregnancy and risk of cardiovascular disease: a population-based cohort study**. *Canadian Medical Association Journal* 2009, **181**(6-7):371-376.
13. Harreiter J, Dovjak G, Kautzky-Willer A: **Gestational diabetes mellitus and cardiovascular risk after pregnancy**. *Women's Health* 2014, **10**(1):91-108.
14. Hinkle SN, Buck Louis GM, Rawal S, Zhu Y, Albert PS, Zhang C: **A longitudinal study of depression and gestational diabetes in pregnancy and the postpartum period**. *Diabetologia* 2016, **59**(12):2594-2602.
15. Nicklas J, Miller L, Zera C, Davis R, Levkoff S, Seely E: **Factors Associated with Depressive Symptoms in the Early Postpartum Period Among Women with Recent Gestational Diabetes Mellitus**. *Matern Child Health J* 2013, **17**(9):1665-1672.
16. Staiano AE, Marker AM, Martin CK, Katzmarzyk PT: **Physical activity, mental health, and weight gain in a longitudinal observational cohort of nonobese young adults**. *Obesity* 2016, **24**(9):1969-1975.
17. Nehring I, Chmitorz A, Reulen H, Kries R, Ensenauer R: **Gestational diabetes predicts the risk of childhood overweight and abdominal circumference independent of maternal obesity**. *Diabetic Medicine* 2013, **30**(12):1449-1456.
18. Crume T, Ogden L, West N, Vehik K, Scherzinger A, Daniels S, McDuffie R, Bischoff K, Hamman R, Norris J: **Association of exposure to diabetes in utero with adiposity and fat distribution**

in a multiethnic population of youth: the Exploring Perinatal Outcomes among Children (EPOCH) Study. *Diabetologia* 2011, **54**(1):87-92.

19. Chandler-Laney PC, Bush NC, Granger WM, Rouse DJ, Mancuso MS, Gower BA: **Overweight status and intrauterine exposure to gestational diabetes are associated with children's metabolic health**. *Pediatric obesity* 2012, **7**(1):44-52.
20. Mehta SH, Kruger M, Sokol RJ: **Is maternal diabetes a risk factor for childhood obesity?** *Journal of Maternal-Fetal and Neonatal Medicine* 2012, **25**(1):41-44.
21. Pettitt DJ, McKenna S, McLaughlin C, Patterson CC, Hadden DR, McCance DR: **Maternal glucose at 28 weeks of gestation is not associated with obesity in 2-year-old offspring: the Belfast Hyperglycemia and Adverse Pregnancy Outcome (HAPO) family study**. *Diabetes Care* 2010, **33**(6):1219-1223.
22. Zhao P, Liu E, Qiao Y, Katzmarzyk PT, Chaput J-P, Fogelholm M, Johnson WD, Kuriyan R, Kurpad A, Lambert EV *et al*: **Maternal gestational diabetes and childhood obesity at age 9–11: results of a multinational study**. *Diabetologia* 2016, **59**(11):2339-2348.
23. Logan KM, Emsley RJ, Jeffries S, Andrzejewska I, Hyde MJ, Gale C, Chappell K, Mandalia S, Santhakumaran S, Parkinson JRC *et al*: **Development of Early Adiposity in Infants of Mothers With Gestational Diabetes Mellitus**. *Diabetes Care* 2016, **39**(6):1045-1051.
24. Kamana K, Shakya S, Zhang H: **Gestational diabetes mellitus and macrosomia: a literature review**. *Annals of Nutrition and Metabolism* 2015, **66**(Suppl. 2):14-20.
25. Clausen TD, Mathiesen ER, Hansen T, Pedersen O, Jensen DM, Lauenborg J, Damm P: **High prevalence of type 2 diabetes and pre-diabetes in adult offspring of women with gestational diabetes mellitus or type 1 diabetes the role of intrauterine hyperglycemia**. *Diabetes Care* 2008, **31**(2):340-346.
26. Russo MD, Ahrens W, De Vriendt T, Marild S, Molnar D, Moreno L, Reeske A, Veidebaum T, Kourides Y, Barba G: **Gestational weight gain and adiposity, fat distribution, metabolic profile, and blood pressure in offspring: the IDEFICS project**. *International journal of obesity* 2013, **37**(7):914-919.
27. Poston L: **Maternal obesity, gestational weight gain and diet as determinants of offspring long term health**. *Best Practice & Research Clinical Endocrinology & Metabolism* 2012, **26**(5):627-639.
28. Harrod CS, Chasan-Taber L, Reynolds RM, Fingerlin TE, Glueck DH, Brinton JT, Dabelea D: **Physical Activity in Pregnancy and Neonatal Body Composition: The Healthy Start Study**. *Obstetrics & Gynecology* 2014, **124**(2, PART 1):257-264.
29. Horsch A, Gilbert L, Lanzi S, Gross J, Kayser B, Vial Y, Simeoni U, Hans D, Berney A, Scholz U: **Improving cardiometabolic and mental health in women with gestational diabetes mellitus and their offspring: study protocol for MySweetHeart Trial, a randomised controlled trial**. *BMJ open* 2018, **8**(2):e020462.
30. Yaktine AL, Rasmussen KM: **Weight Gain During Pregnancy:: Reexamining the Guidelines**: National Academies Press; 2009.
31. Hui A, Back L, Ludwig S, Gardiner P, Sevenhuysen G, Dean H, Sellers E, McGavock J, Morris M, Bruce S: **Lifestyle intervention on diet and exercise reduced excessive gestational weight gain in pregnant women under a randomised controlled trial**. *BJOG: An International Journal of Obstetrics & Gynaecology* 2012, **119**(1):70-77.
32. Bowers K, Tobias DK, Yeung E, Hu FB, Zhang C: **A prospective study of prepregnancy dietary fat intake and risk of gestational diabetes**. *The American journal of clinical nutrition* 2012, **95**(2):446-453.
33. Koivusalo SB, Rono K, Klemetti MM, Roine RP, Lindstrom J, Erkkola M, Kaaja RJ, Poyhonen-Alho M, Tiitinen A, Huvinen E *et al*: **Gestational Diabetes Mellitus Can Be Prevented by Lifestyle Intervention: The Finnish Gestational Diabetes Prevention Study (RADIEL): A Randomized Controlled Trial**. *Diabetes Care* 2016, **39**(1):24-30.

34. Ley SH, Hanley AJ, Retnakaran R, Sermer M, Zinman B, O'Connor DL: **Effect of macronutrient intake during the second trimester on glucose metabolism later in pregnancy**. *The American journal of clinical nutrition* 2011, **94**(5):1232-1240.
35. Bao W, Bowers K, Tobias DK, Hu FB, Zhang C: **Prepregnancy Dietary Protein Intake, Major Dietary Protein Sources, and the Risk of Gestational Diabetes Mellitus A prospective cohort study**. *Diabetes Care* 2013:DC_122018.
36. Bao W, Tobias DK, Bowers K, Chavarro J, Vaag A, Grunnet LG, Strøm M, Mills J, Liu A, Kiely M: **Physical activity and sedentary behaviors associated with risk of progression from gestational diabetes mellitus to type 2 diabetes mellitus: a prospective cohort study**. *JAMA internal medicine* 2014, **174**(7):1047-1055.
37. Wang C, Guelf K, Yang H: **Exercise and its role in gestational diabetes mellitus**. *Chronic Diseases and Translational Medicine 2* 2016:208-214.
38. Dode MASdO, dos Santos IS: **Non classical risk factors for gestational diabetes mellitus: a systematic review of the literature**. *Cadernos De Saúde Pública* 2009, **25 Suppl 3**:S341-S359.
39. Sauder KA, Starling AP, Shapiro AL, Kaar JL, Ringham BM, Glueck DH, Leiferman JA, Siega-Riz AM, Dabelea D: **Diet, physical activity and mental health status are associated with dysglycaemia in pregnancy: the Healthy Start Study**. *Diabetic medicine : a journal of the British Diabetic Association* 2016, **33**(5):663-667.
40. Horsch A, Kang JS, Vial Y, Ehlert U, Borghini A, Marques-Vidal P, Jacobs I, Puder JJ: **Stress exposure and physiological stress responses are related to glucose concentrations during pregnancy.** *British Journal of Health Psychology* Accepted for publication.
41. Giesbrecht GF, Campbell T, Letourneau N, Kooistra L, Kaplan B: **Psychological distress and salivary cortisol covary within persons during pregnancy**. *Psychoneuroendocrinology* 2012, **37**(2):270-279.
42. Perales M, Refoyo I, Coteron J, Bacchi M, Barakat R: **Exercise during pregnancy attenuates prenatal depression: a randomized controlled trial**. *Evaluation & the health professions* 2015, **38**(1):59-72.
43. Schlittler M, Goiny M, Agudelo LZ, Venckunas T, Brazaitis M, Skurvydas A, Kamandulis S, Ruas JL, Erhardt S, Westerblad H *et al*: **Endurance exercise increases skeletal muscle kynurenine aminotransferases and plasma kynurenic acid in humans**. *American journal of physiology Cell physiology* 2016, **310**(10):C836-840.
44. Mudry JM, Alm PS, Erhardt S, Goiny M, Fritz T, Caidahl K, Zierath JR, Krook A, Wallberg-Henriksson H: **Direct effects of exercise on kynurenine metabolism in people with normal glucose tolerance or type 2 diabetes**. *Diabetes/metabolism research and reviews* 2016, **32**(7):754-761.
45. Thivel D, Isacco L, Montaurier C, Boirie Y, Duché P, Morio B: **The 24-h Energy Intake of Obese Adolescents Is Spontaneously Reduced after Intensive Exercise: A Randomized Controlled Trial in Calorimetric Chambers**. *PloS one* 2012, **7**(1):e29840.
46. Martins C, Morgan L, Truby H: **A review of the effects of exercise on appetite regulation: an obesity perspective**. *International journal of obesity (2005)* 2008, **32**(9):1337-1347.
47. Horsch A, Wobmann M, Kriemler S, Munsch S, Borloz S, Balz A, Marques-Vidal P, Borghini A, Puder JJ: **Impact of physical activity on energy balance, food intake and choice in normal weight and obese children in the setting of acute social stress: a randomized controlled trial**. *BMC Pediatrics* 2015, **15**(1):1-10.
48. Broom DR, Stensel DJ, Bishop NC, Burns SF, Miyashita M: **Exercise-induced suppression of acylated ghrelin in humans**. *Journal of applied physiology* 2007, **102**(6):2165-2171.
49. Wardle J, Steptoe A, Oliver G, Lipsey Z: **Stress, dietary restraint and food intake**. *Journal of psychosomatic research* 2000, **48**(2):195-202.
50. King JA, Wasse LK, Broom DR, Stensel DJ: **Influence of brisk walking on appetite, energy intake, and plasma acylated ghrelin**. *Med Sci Sports Exerc* 2010, **42**(3):485-492.

51. Antoniou EE, Bongers P, Jansen A: **The mediating role of dichotomous thinking and emotional eating in the relationship between depression and BMI**. *Eating behaviors* 2017, **26**:55-60.
52. Huang C, Momma H, Cui Y, Chujo M, Otomo A, Sugiyama S, Ren Z, Niu K, Nagatomi R: **Independent and combined relationship of habitual unhealthy eating behaviors with depressive symptoms: A prospective study**. *Journal of epidemiology* 2017, **27**(1):42-47.
53. Mantzios M, Wilson JC: **Making concrete construals mindful: a novel approach for developing mindfulness and self-compassion to assist weight loss**. *Psychol Health* 2014, **29**(4):422-441.
54. Mantzios M, Wilson JC: **Exploring Mindfulness and Mindfulness with Self-Compassion-Centered Interventions to Assist Weight Loss: Theoretical Considerations and Preliminary Results of a Randomized Pilot Study**. *Mindfulness* 2015, **6**(4):824-835.
55. Alberts HJ, Mulkens S, Smeets M, Thewissen R: **Coping with food cravings. Investigating the potential of a mindfulness-based intervention**. *Appetite* 2010, **55**(1):160-163.
56. Lovejoy MC, Graczyk PA, O'Hare E, Neuman G: **Maternal depression and parenting behavior: A meta-analytic review**. *Clinical psychology review* 2000, **20**(5):561-592.
57. Carter AS, Garrity-Rokous FE, Chazan-Cohen R, Little C, Briggs-Gowan MJ: **Maternal depression and comorbidity: predicting early parenting, attachment security, and toddler social-emotional problems and competencies**. *Journal of the American Academy of Child & Adolescent Psychiatry* 2001, **40**(1):18-26.
58. Hoffman C, Crnic KA, Baker JK: **Maternal depression and parenting: Implications for children's emergent emotion regulation and behavioral functioning**. *Parenting: Science and Practice* 2006, **6**(4):271-295.
59. Asemi Z, Samimi M, Tabassi Z, Sabihi S-s, Esmaillzadeh A: **A randomized controlled clinical trial investigating the effect of DASH diet on insulin resistance, inflammation, and oxidative stress in gestational diabetes**. *Nutrition* 2013, **29**(4):619-624.
60. Hu Z-G, Tan R-S, Jin D, Li W, Zhou X-Y: **A low glycemic index staple diet reduces postprandial glucose values in Asian women with gestational diabetes mellitus**. *Journal of Investigative Medicine* 2014, **62**(8):975-979.
61. Moses RG, Casey SA, Quinn EG, Cleary JM, Tapsell LC, Milosavljevic M, Petocz P, Brand-Miller JC: **Pregnancy and Glycemic Index Outcomes study: effects of low glycemic index compared with conventional dietary advice on selected pregnancy outcomes–**. *The American journal of clinical nutrition* 2013, **99**(3):517-523.
62. Barakat R, Lucia A, Ruiz JR: **Resistance exercise training during pregnancy and newborn's birth size: a randomised controlled trial**. *International journal of obesity* 2009, **33**(9):1048-1057.
63. Halse RE, Wallman KE, Dimmock JA, Newnham JP, Guelfi KJ: **Home-Based Exercise Improves Fitness and Exercise Attitude and Intention in Women with GDM**. *Med Sci Sports Exerc* 2015, **47**(8):1698-1704.
64. Halse RE, Wallman KE, Newnham JP, Guelfi KJ: **Home-based exercise training improves capillary glucose profile in women with gestational diabetes**. *Med Sci Sports Exerc* 2014, **46**(9):1702-1709.
65. Oostdam N, van Poppel MN, Wouters MG, Eekhoff EM, Bekedam DJ, Kuchenbecker WK, Quartero HW, Heres MH, van Mechelen W: **No effect of the FitFor2 exercise programme on blood glucose, insulin sensitivity, and birthweight in pregnant women who were overweight and at risk for gestational diabetes: results of a randomised controlled trial**. *BJOG : an international journal of obstetrics and gynaecology* 2012, **119**(9):1098-1107.
66. Stafne SN, Salvesen KA, Romundstad PR, Eggebo TM, Carlsen SM, Morkved S: **Regular exercise during pregnancy to prevent gestational diabetes: a randomized controlled trial**. *Obstetrics and gynecology* 2012, **119**(1):29-36.

67. de Barros MC, Lopes MA, Francisco RP, Sapienza AD, Zugaib M: **Resistance exercise and glycemic control in women with gestational diabetes mellitus**. *Am J Obstet Gynecol* 2010, **203**(6):556 e551-556.
68. Luoto R, Kinnunen TI, Aittasalo M, Kolu P, Raitanen J, Ojala K, Mansikkamaki K, Lamberg S, Vasankari T, Komulainen T *et al*: **Primary prevention of gestational diabetes mellitus and large-for-gestational-age newborns by lifestyle counseling: a cluster-randomized controlled trial**. *PLoS Med* 2011, **8**(5):e1001036.
69. Whittemore R, Knafl K: **The integrative review: updated methodology**. *Journal of advanced nursing* 2005, **52**(5):546-553.
70. Reviews TJBICAtfuiJS: **Checklist for Randomized Controlled Trials**. In.; 2017.
71. Reviews TJBICAtfuiJS: **Checklist for Quasi-Experimental Studies (non-randomized experimental studies)**. In.; 2017.
72. Reviews TJBICAtfuiJS: **Checklist for Analytical Cross Sectional Studies**. In.; 2017.
73. Reviews TJBICAtfuiJS: **Checklist for Cohort Studies**. In.; 2017.
74. Kim C, McEwen LN, Kieffer EC, Herman WH, Piette JD: **Self-efficacy, social support, and associations with physical activity and body mass index among women with histories of gestational diabetes mellitus**. *The Diabetes Educator* 2008, **34**(4):719-728.
75. Kaiser B, Jeannot E, Razurel C: **Determinants of health behaviors after gestational diabetes mellitus: A prospective cohort study in geneva**. *Journal of midwifery & women's health* 2016, **61**(5):571-577.
76. Ferrara A, Hedderson MM, Albright CL, Ehrlich SF, Quesenberry CP, Peng T, Feng J, Ching J, Crites Y: **A pregnancy and postpartum lifestyle intervention in women with gestational diabetes mellitus reduces diabetes risk factors: a feasibility randomized control trial**. *Diabetes Care* 2011:DC_102221.
77. Philis-Tsimikas A, Fortmann AL, Dharkar-Surber S, Euyoque JA, Ruiz M, Schultz J, Gallo LC: **Dulce Mothers: an intervention to reduce diabetes and cardiovascular risk in Latinas after gestational diabetes**. *Translational behavioral medicine* 2014, **4**(1):18-25.
78. Ratner RE, Christophi CA, Metzger BE, Dabelea D, Bennett PH, Pi-Sunyer X, Fowler S, Kahn SE, Group DPPR: **Prevention of diabetes in women with a history of gestational diabetes: effects of metformin and lifestyle interventions**. *The Journal of Clinical Endocrinology & Metabolism* 2008, **93**(12):4774-4779.
79. Jovanovic-Peterson L, Durak EP, Peterson CM: **Randomized trial of diet versus diet plus cardiovascular conditioning on glucose levels in gestational diabetes**. *American Journal of Obstetrics & Gynecology* 1989, **161**(2):415-419.
80. Artal R, Catanzaro RB, Gavard JA, Mostello DJ, Friganza JC: **A lifestyle intervention of weight-gain restriction: diet and exercise in obese women with gestational diabetes mellitus**. *Appl Physiol Nutr Metab* 2007, **32**(3):596-601.
81. Hu G, Tian H, Zhang F, Liu H, Zhang C, Zhang S, Wang L, Liu G, Yu Z, Yang X: **Tianjin Gestational Diabetes Mellitus Prevention Program: study design, methods, and 1-year interim report on the feasibility of lifestyle intervention program**. *Diabetes research and clinical practice* 2012, **98**(3):508-517.
82. Liu H, Wang L, Zhang S, Leng J, Li N, Li W, Wang J, Tian H, Qi L, Yang X: **One-year weight losses in the Tianjin Gestational Diabetes Mellitus Prevention Programme: A randomized clinical trial**. *Diabetes, Obesity and Metabolism* 2018, **20**(5):1246-1255.
83. Wang C, Zhu W, Wei Y, Feng H, Su R, Yang H: **Exercise intervention during pregnancy can be used to manage weight gain and improve pregnancy outcomes in women with gestational diabetes mellitus**. *BMC pregnancy and childbirth* 2015, **15**(1):255.
84. Peacock A, Bogossian FE, Wilkinson S, Gibbons K, Kim C, McIntyre H: **A randomised controlled trial to delay or prevent type 2 diabetes after gestational diabetes: walking for exercise and nutrition to prevent diabetes for you**. *International journal of endocrinology* 2015, **2015**.

85. Mukerji G, McTavish S, Glenn A, Delos-Reyes F, Price J, Wu W, Harvey P, Lipscombe LL: **An Innovative Home-Based Cardiovascular Lifestyle Prevention Program for Women With Recent Gestational Diabetes: A Pilot Feasibility Study**. *Canadian journal of diabetes* 2015, **39**(6):445-450.
86. Rautio N, Jokelainen J, Korpi-Hyövälti E, Oksa H, Saaristo T, Peltonen M, Moilanen L, Vanhala M, Uusitupa M, Tuomilehto J: **Lifestyle intervention in prevention of type 2 diabetes in women with a history of gestational diabetes mellitus: one-year results of the FIN-D2D project**. *Journal of women's health* 2014, **23**(6):506-512.
87. O'Dea A, Tierney M, McGuire BE, Newell J, Glynn LG, Gibson I, Noctor E, Danyliv A, Connolly SB, Dunne FP: **Can the onset of type 2 diabetes be delayed by a group-based lifestyle intervention in women with prediabetes following gestational diabetes mellitus (GDM)? Findings from a randomized control mixed methods trial**. *Journal of diabetes research* 2015, **2015**.
88. Pérez-Ferre N, Del Valle L, Torrejón MJ, Barca I, Calvo MI, Matía P, Rubio MA, Calle-Pascual AL: **Diabetes mellitus and abnormal glucose tolerance development after gestational diabetes: A three-year, prospective, randomized, clinical-based, Mediterranean lifestyle interventional study with parallel groups**. *Clinical Nutrition* 2015, **34**(4):579-585.
89. Youngwanichsetha S, Phumdoung S, Ingkathawornwong T: **The effects of mindfulness eating and yoga exercise on blood sugar levels of pregnant women with gestational diabetes mellitus**. *Applied Nursing Research* 2014, **27**(4):227-230.
90. Martini J, Knappe S, Beesdo-Baum K, Lieb R, Wittchen H-U: **Anxiety disorders before birth and self-perceived distress during pregnancy: associations with maternal depression and obstetric, neonatal and early childhood outcomes**. *Early human development* 2010, **86**(5):305-310.
91. Brantley PJ, Stewart DW, Myers VH, Matthews-Ewald MR, Ard JD, Coughlin JW, Jerome GJ, Samuel-Hodge C, Lien LF, Gullion CM: **Psychosocial predictors of weight regain in the weight loss maintenance trial**. *Journal of behavioral medicine* 2014, **37**(6):1155-1168.
92. Fuglestad PT, Jeffery RW, Sherwood NE: **Lifestyle patterns associated with diet, physical activity, body mass index and amount of recent weight loss in a sample of successful weight losers**. *International Journal of Behavioral Nutrition and Physical Activity* 2012, **9**(1):79.
93. Nezami BT, Lang W, Jakicic JM, Davis KK, Polzien K, Rickman AD, Hatley KE, Tate DF: **The effect of self-efficacy on behavior and weight in a behavioral weight-loss intervention**. *Health Psychology* 2016, **35**(7):714.
94. Muros JJ, Pérez FS, Ortega FZ, Sánchez VMG, Knox E: **The association between healthy lifestyle behaviors and health-related quality of life among adolescents**. *Jornal de Pediatria (Versão em Português)* 2017, **93**(4):406-412.
95. Al-Hazzaa HM, Abahussain NA, Al-Sobayel HI, Qahwaji DM, Musaiger AO: **Physical activity, sedentary behaviors and dietary habits among Saudi adolescents relative to age, gender and region**. *International Journal of Behavioral Nutrition and Physical Activity* 2011, **8**(1):140.
96. Mata J, Silva MN, Vieira PN, Carraça EV, Andrade AM, Coutinho SR, Sardinha LB, Teixeira PJ: **Motivational "spill-over" during weight control: Increased self-determination and exercise intrinsic motivation predict eating self-regulation**. *Health Psychology* 2009, **28**(6):709.
97. Yao M, Roberts SB: **Dietary energy density and weight regulation**. *Nutr Rev* 2001, **59**(8):247-258.
98. Shepherd E, Gomersall JC, Tieu J, Han S, Crowther CA, Middleton P: **Combined diet and exercise interventions for preventing gestational diabetes mellitus**. *The Cochrane Library* 2017.
99. Asemi Z, Tabassi Z, Samimi M, Fahiminejad T, Esmaillzadeh A: **Favourable effects of the Dietary Approaches to Stop Hypertension diet on glucose tolerance and lipid profiles in gestational diabetes: a randomised clinical trial**. *British Journal of Nutrition* 2013, **109**(11):2024-2030.

100. Azadbakht L, Mirmiran P, Esmaillzadeh A, Azizi T, Azizi F: **Beneficial effects of a Dietary Approaches to Stop Hypertension eating plan on features of the metabolic syndrome**. *Diabetes Care* 2005, **28**(12):2823-2831.
101. Asemi Z, Samimi M, Tabassi Z, Shakeri H, Sabihi S-S, Esmaillzadeh A: **Effects of DASH diet on lipid profiles and biomarkers of oxidative stress in overweight and obese women with polycystic ovary syndrome: a randomized clinical trial**. *Nutrition* 2014, **30**(11-12):1287-1293.
102. Oteng-Ntim E, Varma R, Croker H, Poston L, Doyle P: **Lifestyle interventions for overweight and obese pregnant women to improve pregnancy outcome: systematic review and meta-analysis**. *BMC medicine* 2012, **10**(1):47.
103. Ryder J, Chibalin A, Zierath J: **Intracellular mechanisms underlying increases in glucose uptake in response to insulin or exercise in skeletal muscle**. *Acta physiologica Scandinavica* 2001, **171**(3):249-257.
104. Harrison AL, Shields N, Taylor NF, Frawley HC: **Exercise improves glycaemic control in women diagnosed with gestational diabetes mellitus: a systematic review**. *Journal of physiotherapy* 2016, **62**(4):188-196.
105. Montelongo A, Lasunción MA, Pallardo LF, Herrera E: **Longitudinal study of plasma lipoproteins and hormones during pregnancy in normal and diabetic women**. *Diabetes* 1992, **41**(12):1651-1659.
106. Kim C, Newton KM, Knopp RH: **Gestational diabetes and the incidence of type 2 diabetes: a systematic review**. *Diabetes Care* 2002, **25**(10):1862-1868.
107. Tobias DK, Hu FB, Chavarro J, Rosner B, Mozaffarian D, Zhang C: **Healthful dietary patterns and type 2 diabetes mellitus risk among women with a history of gestational diabetes mellitus**. *Archives of internal medicine* 2012, **172**(20):1566-1572.
108. Noctor E, Dunne FP: **Type 2 diabetes after gestational diabetes: the influence of changing diagnostic criteria**. *World journal of diabetes* 2015, **6**(2):234.
109. Malinowska-Polubiec A, Sienko J, Lewandowski Z, Czajkowski K, Smolarczyk R: **Risk factors of abnormal carbohydrate metabolism after pregnancy complicated by gestational diabetes mellitus**. *Gynecological endocrinology* 2012, **28**(5):360-364.
110. Ekelund M, Shaat N, Almgren P, Groop L, Berntorp K: **Prediction of postpartum diabetes in women with gestational diabetes mellitus**. *Diabetologia* 2010, **53**(3):452-457.
111. Qiao Q, Pang Z, Gao W, Wang S, Dong Y, Zhang L, Nan H, Ren J: **A large-scale diabetes prevention program in real-life settings in Qingdao of China (2006–2012)**. *Primary care diabetes* 2010, **4**(2):99-103.
112. Goldenberg RL, Culhane JF, Iams JD, Romero R: **Epidemiology and causes of preterm birth**. *The lancet* 2008, **371**(9606):75-84.
113. Viana LV, Gross JL, Azevedo MJ: **Dietary intervention in patients with gestational diabetes mellitus: a systematic review and meta-analysis of randomized clinical trials on maternal and newborn outcomes**. *Diabetes Care* 2014, **37**(12):3345-3355.
114. Muktabhant B, Lawrie TA, Lumbiganon P, Laopaiboon M: **Diet or exercise, or both, for preventing excessive weight gain in pregnancy**. *The Cochrane Library* 2015.
115. Ornoy A: **Prenatal origin of obesity and their complications: Gestational diabetes, maternal overweight and the paradoxical effects of fetal growth restriction and macrosomia**. *Reproductive toxicology* 2011, **32**(2):205-212.
116. Porreco RP, Thorp JA: **The cesarean birth epidemic: trends, causes, and solutions**. *American journal of obstetrics and gynecology* 1996, **175**(2):369-374.
117. Linné Y, Barkeling B, Rössner S: **Natural course of gestational diabetes mellitus: long term follow up of women in the SPAWN study**. *BJOG: An International Journal of Obstetrics & Gynaecology* 2002, **109**(11):1227-1231.
118. Carraça EV, Silva MN, Markland D, Vieira PN, Minderico CS, Sardinha LB, Teixeira PJ: **Body image change and improved eating self-regulation in a weight management intervention in women**. *International Journal of Behavioral Nutrition and Physical Activity* 2011, **8**(1):75.

119. Annesi JJ: **Psychosocial predictors of decay in healthy eating and physical activity improvements in obese women regaining lost weight: translation of behavioral theory into treatment suggestions**. *Translational behavioral medicine* 2016, **6**(2):169-178.
120. Saunders TA, Lobel M, Veloso C, Meyer BA: **Prenatal maternal stress is associated with delivery analgesia and unplanned cesareans**. *Journal of Psychosomatic Obstetrics & Gynecology* 2006, **27**(3):141-146.
121. Zhu P, Hao J, Jiang X, Huang K, Tao F: **New insight into onset of lactation: mediating the negative effect of multiple perinatal biopsychosocial stress on breastfeeding duration**. *Breastfeeding Medicine* 2013, **8**(2):151-158.
122. Moyer C, Reoyo OR, May L: **The influence of prenatal exercise on offspring health: a review**. *Clinical Medicine Insights: Women's Health* 2016, **9**:CMWH. S34670.
123. Joober R, Schmitz N, Annable L, Boksa P: **Publication bias: What are the challenges and can they be overcome?** *Journal of psychiatry & neuroscience: JPN* 2012, **37**(3):149.
124. Horsch A, Gross J, Jornayvaz F, Lanzi S, Puder J: **Diabète gestationnel--quelles sont les approches non médicales [Gestational diabetes--what are the non-medical approaches?]**. *Revue medicale suisse* 2016, **12**(521):1089-1091.

Additional file 1

Table 1. ***Summary of observational articles integrated in the review.***

Authors (year) **Country**	**Study design** **Sample** **Objective**	**Selection criteria**	**Diet, physical activity & psychosocial assessment**	**Major findings**	**Quality** JBI quality appraisal tools
Kim et al. (2008) U.S.A	Cross-sectional n=228 To examine the associations between two potential facilitators of healthy behaviors (self-efficacy and social support) on diet, physical activity and BMI among women with histories of GDM	**Inclusion** Women with GDM within the past 5 years and with ≥ 1 health-care utilization event during the past year **Exclusion** Women with T1DM or T2DM before their pregnancy, denied having had GDM, were currently pregnant without GDM or unable to give informed consent	**Diet** Weight Efficacy Lifestyle Questionnaire **Physical Activity** 5-item scale **Psychosocial** Scale	Self-efficacy and social support from family and friends was associated with better dietary scores and physical activity. No significant associations existed between psychosocial constructs and BMI.	Good
Kaiser et al. (2016) Switzerland	Prospective Cohort Study n=173 To specify the determinants of postpartum physical activity and dietary habits after a pregnancy complicated by GDM in a population of Swiss women	**Inclusion** Women with diagnosis of GDM in the current or in a previous pregnancy without diagnosis of T1DM or T2DM; ≥ 18 years; if they could read, write, and speak French.	**Diet & Physical activity** Rapid Eating and Activity Assessment for Participants, short version questionnaire **Psychosocial** Social support and self-efficacy scale	Multivariate regression analysis found that Lower level of social support ($p<0.001$) and more perceived barriers to a healthy lifestyle ($p = 0.002$) were determinants in a low adherence to healthy lifestyle in the postpartum period after GDM	Good

Legend: BMI: Body mass index; GDM: gestational diabetes mellitus; T1DM: type 1 diabetes mellitus; T2DM: type 2 diabetes mellitus.

Table 2. ***Summary of Intervention studies integrated in the review.***

Authors (year) **Country**	**Study design** **Sample** **Objective**	**Selection criteria**	**Diet & physical activity assessment**	**Intervention**	**Major findings in intervention group**	**Quality** JBI quality appraisal tools
O'Dea et al. (2015) Ireland	RCT n=50 To evaluate a 12-week group-based lifestyle intervention program for women with pre-diabetes following GDM	**Inclusion** IFG, or IGT, or IR and at least two CV risk factors **Exclusion** T2DM, current pregnancy, insufficient English language fluency	**Diet** Mediterranean diet score **Physical Activity** Self-reported	**Starting in the postpartum period** **Diet and Physical Activity** 12-week intensive lifestyle program, delivered by a multidisciplinary team, consisting of 2.5 h/wk spread over a group exercise program, a group education seminar, and a one-to-one session involving a motivational interview and individual goal setting	**At the end of the study, at 1-year follow-up, after a three months intervention, compared to control group** ↗ (trend) diet adherence, diet self-efficacy = PA levels ↙ stress perception, ↗ quality of life = BMI, weight, waist circumference ↙ 2hr glucose after OGTT = Insulin resistance, FPG and lipid profile	Good
Ferrara et al. (2011) U.S.A.	RCT n=197 To pilot the feasibility of a prenatal/postpartum intervention that aimed to reduce diabetes risk factors among women with GDM	**Inclusion** Women with GDM **Exclusion** Aged< 18; multiple gestation; diabetic retinopathy; high-risk pregnancy, thyroid diseases diagnosed in the last 30 days, non-English speaker.	**Diet** FFQ **Physical Activity** Interview questionnaire	**Starting during pregnancy** The intervention program aims to modify **diet and Physical Activity** in 3 phases: **Prenatal phase** Encourage women to follow the ADA diet and engage in moderate intensity PA for 150 min/wk **Postpartum phase** Encourage women to perform 150 min of moderate or harder PA/wk and to consume ≤ 25% of total calories from fat/day **Maintenance phase** Reinforce the positive behavioral changes achieved and address relapse	**7 months postpartum, compared to control group** ↙ fat intake, ↗ (trend) proportion of women who partially or exclusively breastfed = PA levels **At the end of the study, at 12 months postpartum, compared to control group** ↗ (trend) proportion of women who reached the PP weight goal. The intervention was more effective among women who did not exceed the recommended GWG	Good

Authors (year) Country	Study design Sample Objective	Selection criteria	Diet & physical activity assessment	Intervention	Major findings in intervention group	Quality JBI quality appraisal tools
Peacock et al. (2015) Australia	RCT n=31 To develop a program to support behavior changes in diet and physical activity for women with a history of GDM and BMI to delay or prevent T2D	**Inclusion** Women with GDM who had been diagnosed and treated for GDM, with a self-reported BMI >25 $kg \cdot m^{-2}$ **Exclusion** Women currently pregnant, T2DM, not fluent in English, using hypoglycaemic medications	**Diet** Fibre Index, Health and Wellbeing Self Efficacy Survey **Physical Activity** Interview questionnaire (Australian Women's Activity Survey)	**Starting in the postpartum period** **Diet (nutrition coaching)** Four one-hour group sessions to facilitate behavior change **Physical Activity** Weekly goals (web-based) were generated based on the previous weeks steps recorded with a pedometer. The goals were gradually increased, until the maximum of 10'000 steps/d was reached	**At the end of the study, at 3 months, compared to control group** ↗ self-efficacy related to food choices = PA ↙ weight, BMI, hip and waist circumference = body composition = HOMA-IR	Good
Philis-Tsimikas et al. (2014) U.S.A.	Interventional n=84 To evaluate the effectiveness of a lifestyle intervention to reduce T2DM and CVD risk among low income Latinas with a history of GDM	**Inclusion** Latinas with GDM in the past 3 years **Exclusion** Women with T2DM, who were pregnant, and/or who had a serious health condition	**Diet** Questionnaire (Food Screener) **Physical Activity** Questionnaire (rapid assessment of physical activity)	**Starting in the postpartum period** The intervention was adapted from the DPP **Diet and Physical Activity** Achieve and maintain a weight reduction of at least 7% of initial body weight, and to achieve and maintain a level of PA of at least 150 min/wk through moderate intensity activity	**At the end of the study, at 6 months follow-up after a 3 months intervention, compared to baseline** ↙ dietary fat intake ↗ aerobic activity, ↗ flexibility/strength ↙ fatalistic, ↙ diabetes-specific cultural beliefs = weight and BMI ↙ Total cholesterol; ↙ LDL, =HDL, ↙ TG; ↗ HbA1c = systolic blood pressure, ↙ diastolic blood pressure	Good
Ratner et al. (2008) U.S.A.	RCT n=2190 To identify individuals with IGT and intervene in an effort to prevent or delay their progression to diabetes To examine the differences between women with and without a reported GDM	**Inclusion** Women with a history of GDM aged ≥ 25, BMI ≥ 24 $kg \cdot m^{-2}$ (≥ 22 for Asian-Americans), FPG of 95–125 mg/dL, 2-h glucose 140-199 mg/dL in the OGTT **Exclusion** Recent myocardial infarction, symptoms of coronary heart disease, serious illness, or use of medications known to impair glucose tolerance.	**Diet** Semiquantitative FFQ **Physical Activity** Standardized questionnaires	**Starting in the postpartum period** The intervention group followed the DPP **Diet and Physical Activity** Achieve and maintain a weight reduction of at least 7% of initial body weight, and to achieve and maintain a level of PA of at least 150 min/wk through moderate intensity activity	**At the end of the study, at 3 years, compared to control group** ↙ weight ↗ of PA (~1.5h/wk) at 1 yr follow-up; not sustained in women with a history of GDM at 3 yr follow-up ↙ risk of progression to T2DM	Good

Authors (year) Country	**Study design Sample Objective**	**Selection criteria**	**Diet & physical activity assessment**	**Intervention**	**Major findings in intervention group**	**Quality** JBI quality appraisal tools
Pérez-Ferre et al. (2015) Spain	RCT n=237 To evaluate the efficacy of a lifestyle intervention for the prevention of glucose disorders in women with prior GDM	**Inclusion** Women diagnosed with GDM. **Exclusion** Impaired fasting plasma glucose (≥ 100 mg/dL) in the first postpartum evaluation and plan for new pregnancy during the three years of follow-up.	**Diet and Physical Activity** Semiquantitative questionnaire (Lifestyle questionnaire)	**Starting in the postpartum period** **Diet** Adherence as much as possible to the Mediterranean diet **Physical activity** 4x/week, two days at the hospital and two days at home with duration of 50-60 min during 10 weeks between 3-6 months post-delivery. The sessions consisted in progressive aerobic activities and muscular conditioning performed at moderate intensity	**At the end of the study, at 3 years, compared to control group** ↗ nutrition pattern, healthier pattern in the consumption of unsaturated fat, saturated fat and healthy fat ↗ PA pattern as in the control group ↙ BMI; ↙ waist circumference ↙ fasting plasma insulin; ↙ HOMA-IR; ↙ LDL-cholesterol; ↙ TG; ↙ Apo lipoprotein B ↙ of ~25% in the conversion rate to glucose disorder and ↙ of 35% in the conversion rate to T2DM	Good
Rautio et al. (2014) Finland	Interventional n=265 To compare cardio-metabolic risk profile and responses to a 1-year lifestyle intervention program in women with and without history of GDM	**Inclusion** Women with GDM, IFG, IGT or coronary heart disease **Exclusion** NA	**Diet and Physical Activity** Questionnaire	**Starting in the postpartum period** **Physical Activity & Diet** Mainly based on the principles of empowerment developed during exercise or weight maintenance groups, lectures or individual counseling	**At the end of the study, at 1 year, compared to baseline** = weight, waist circumference ↗ HDL-cholesterol, ↙ LDL-cholesterol = systolic & diastolic blood pressure	Good

Authors (year) Country	Study design Sample Objective	Selection criteria	Diet & physical activity assessment	Intervention	Major findings in intervention group	Quality JBI quality appraisal tools
Jovanovic-Peterson et al. (1989) U.S.A.	RCT n=19 Evaluate the impact of a training program on glucose tolerance in GDM	**Inclusion** Women with GDM **Exclusion** NA	NA	**Starting during pregnancy** **Diet** Control & intervention groups followed a 6 weeks of standards diet containing 40% of CHO, 20% protein & 40% fat. Energy requirement was calculated at 24-30 kcal/kg/24h divided in 3 meals and 3 snacks **Physical Activity Intervention** Exercise program of 6 weeks' duration that consisted of 20 min of supervised aerobic training. The patients were monitored for 20 min of cardiovascular work during which they maintained their target heart rate, which was calculated to be equal to (220 - age) x 70%. As each patient adapted to her workload in terms of perceived exertion and heart rate, the workload (or resistance) (kg x meters x min-l) was increased or decreased by 10% to 20%; thus maternal heart rate was maintained in the training range. The exercise session never exceeded 50% maximal oxygen consumption $V0_2max$ in any case. 50% oxygen consumption was estimated based on their previous work that related maternal heart rate in beats/min to the V02 at steady state utilizing a metabolic cart (Beckman model S/N 614, D/N 11265, Fullerton, Calif.)	**At the end of the study, at 6 weeks, compared to control group** ↙ HbA1c, FPG, 1hr glucose after OGTT	Good

Authors (year) Country	Study design Sample Objective	Selection criteria	Diet & physical activity assessment	Intervention	Major findings in intervention group	Quality JBI quality appraisal tools
Hu et al. (2012) China	RCT n=1180 To assess whether lifestyle intervention can reduce type 2 diabetes risk in women with prior GDM in the Tianjin GDM Prevention Program	**Inclusion** Aged 20–49, women with GDM between 2005 and 2009. **Exclusion** Aged <20 or ≥50, at the screening visit: FPG ≥7.0 mmol/l or 2-h glucose ≥ 11.1 mmol/l in the OGTT, taking medicines known to alter OGTT, presence of any chronic diseases, currently pregnant, planning to become pregnant in the next 2 yrs	**Diet** 5 x 3-day 24-h food records; questionnaire **Physical Activity** Questionnaire	**Starting in the postpartum period** **Diet** Reduction of at least 10% of total calories of their normal meals to lose 5–10% of initial body weight in women with BMI ≥ 24 kg/m^2 Consume <30% of energy from total fat, <10% of energy from saturated fat, 55-65% of energy from carbohydrate, 20–30 g/d of fiber **Physical Activity** Gradually increase the physical activity to reach 30 min/day in moderate or vigorous physical activity 7 d/wk	**At the end of the study, at 1 year, compared to control group** ↗ leisure time activity ↙ weight, ↙ BMI, body fat, waist circumference ↙ plasma insulin level	Good
Artal et al. (2007) U.S.A.	Interventional n=96 To assess whether weight-gain restriction regimen, with or without exercise, would impact glycemic control, pregnancy outcome, and total pregnancy weight gain in obese subjects with GDM	**Inclusion** < 33 GA, BMI > 25 kg/m^2, not yet managed with insulin, aged > 18 **Exclusion** ACOG contraindication to exercise	NA	**Starting during pregnancy** **Diet** Meal plan was prescribed for both group by a registered dietitian according the energy needs calculated on the prepregnancy BMI and which content 40-45% of carbohydrates. **Physical Activity** Moderate exercise program not to exceed the 60% $VO_{2\,max}$. Encouraged to exercise once a week by walking on a treadmill or by riding a semi recumbent cycle ergometer based on an exercise prescription under the supervision of an exercise routine on the remaining 6 days/week at home	**At the end of the study, at a calculated mean of 7.7 weeks, compared to control group** ↙ GWG = macrosomia, adverse pregnancy outcome	Good

Authors (year) Country	Study design Sample Objective	Selection criteria	Diet & physical activity assessment	Intervention	Major findings in intervention group	Quality JBI quality appraisal tools
Youngwanichsetha et al. (2014) Thaïland	RCT n=170 To investigate the effect of mindfulness eating and yoga exercise on blood sugar levels among pregnant women with GDM	**Inclusion** Pregnant Thai women diagnosed with GDM with 24–30 wk GA, FPG < 105 mg/dl, postprandial blood glucose < 120 mg/dl, not receiving insulin therapy, having no serious complications **Exclusion** NA	NA	**Starting during pregnancy** 8 weeks to perform mindfulness eating and yoga exercise **Diet** Mindfulness eating composed of five steps: 1) setting a goal for blood glucose control, 2) integrating medical nutrition therapy including carbohydrate choices and low glycemic index food, 3) considering portion size, 4) being aware while consuming diabetic food, and 5) eating slowly for 30-45 min. **Physical activity** Yoga exercise at home five times a week using deep-breathing techniques and posture and movements. It was designed for 15–20 minutes daily practice, corresponding to 9 postures repeated for ten times	**At the end of the study, at 8 weeks, compared to control group** ↙ FPG, 2hr postprandial blood glucose and HbA1c	Good
Mukerji et al. (2015) Canada	Interventional n= 17 To assess the feasibility and effectiveness of a 6-month customized, home-based lifestyle program for women with recent GDM	**Inclusion** Women aged > 18 with GDM and prepregnancy BMI ≥ 25 $kg \cdot m^{-2}$ **Exclusion** Not english speaking, prepregnancy T1DM or T2DM, pregnant again, significant medical or fetal complications	**Physical Activity** Weekly 15-minute telephone calls	**Starting in the postpartum period** **Diet** General diet counselling using Canada's Food Guide **Physical Activity** A personalized home-based exercise program, incorporating the participants' baseline fitness, and current exercise habits. All women were counselled to meet 150 min of moderate aerobic exercise/wk and to keep an exercise log/wk. Weekly telephone calls were scheduled with an exercise specialist to provide coaching, review adherence to exercise logs, advance goals and address barriers	**At the end of the study, at 6 months, compared to baseline** ↗ exercise capacity ↙ waist circumference = weight, BMI, % body fat	Poor

Authors (year) Country	Study design Sample Objective	Selection criteria	Diet & physical activity assessment	Intervention	Major findings in intervention group	Quality JBI quality appraisal tools
Liu et al. (2018) China	RCT n=1180 To report the weight loss findings after the first year of a lifestyle intervention trial among women with GDM	**Inclusion** Women aged 20–49, with GDM between 2005 and 2009. **Exclusion** Aged <20 or ≥50, at the screening visit: FPG ≥7.0 mmol/l or 2-h glucose ≥ 11.1 mmol/l in the OGTT, taking medicines known to alter OGTT, presence of any chronic diseases, currently pregnant, planning to become pregnant in the next 2 years	**Diet** 5 x 3-day 24-h food records; questionnaire **Physical Activity** Questionnaire	**Starting during pregnancy** **Diet** Each participant met one-on-one with a dietician who instructed the participant on how to achieve several goals: reduction of 5% to 10% of initial body weight in women with BMI ≥24 kg/m2 by reducing at least 10% of total calories in their normal meals; total fat intake <30% of energy consumed; carbohydrate intake 55% to 65% of energy consumed; fiber intake 20-30 g/d **Physical Activity** During the first 4wk of intervention, the level of PA increased to at least 30 min of moderate-to-vigorous PA per day, 7 days/wk; and was then maintained during the entire period Each participant completed a questionnaire on changes in major dietary and PA habits from the last visit, and 3-day 24-hour food records 5 times during the first year for assessment by the dietician. 2 phone calls were performed during the first year to encourage compliance to intervention	**At the end of the study, at 4 years, compared to control group** ↗ fibre intake ↗ commute and leisure time activity, exercise ↙ weight, BMI, waist circumference, body fat	Good
Wang et al. (2015) China	Interventional n=14'168 To evaluate whether exercise intervention can be applied to pregnant women with GDM for controlling gestational weight gain and combating GDM-related outcomes.	**Inclusion** NA **Exclusion** pre-existing diabetes, multiple births, and missing data on major items	**Diet and Physical Activity** Individual interview	**Starting during pregnancy** **Diet** Reduce intake of sugar, eat more vegetables, reduce fat intake, and the total energy intake 1800 kcal/j **Physical Activity** Sit less, take more steps, be more active, incorporate light and moderate PA as much as possible into their daily life.	**At the end of the study, at a calculated mean of 13.2 weeks, compared to control group** ↙ BMI increase between pre and late-pregnancy and between mid and late-pregnancy ↙ risk of preterm birth, low birth weight = macrosomia, caesarean	Good

Legend:
↙: significant reduction, ↗: significant augmentation; =: no significant difference; BMI: body mass index; CVD: cardiovascular disease; DBP: diastolic blood pressure; DPP: diabetes prevention program; FFQ: Food Frequency Questionnaire; FPG: fasting plasma glucose; GDM: gestational diabetes mellitus; GWG: gestational weight gain ; HbA1c : glycosylated hemoglobin; HOMA-IR: homeostasis model assessment-insulin resistance; IFG: impaired fasting glucose; IGT: impaired glucose tolerance; ILS: intensive lifestyle intervention; OGTT: oral glucose tolerance test; PA: physical activity; RCT: randomized control trial; SES: socioeconomic status; T2DM: type 2 diabetes mellitus; TG: Triglycerides

Additional file 2

Full search strategy

PubMed

(("Diabetes, Gestational"[Mesh]) AND (("Exercise"[Mesh] OR "Physical Fitness"[Mesh] OR "Motor Activity"[Mesh]OR "Bicycling"[Mesh]) OR ("Feeding Behavior"[Mesh] OR "Hunger"[Mesh] OR "Satiation"[Mesh] OR "Dietary Fats"[Mesh] OR "Diet"[Mesh] OR "Dietary Carbohydrates"[Mesh] OR "Body Weight"[Mesh] OR "Body Composition"[Mesh] OR "Waist Circumference"[Mesh]) OR ("Life Style"[Mesh] OR "Attitude to Health"[Mesh] OR "Health Behavior"[Mesh] OR "Depressive Disorder"[Mesh] OR "Depression"[Mesh] OR "Stress, Psychological"[Mesh] OR "Parenting"[Mesh] OR "Parent-Child Relations"[Mesh] OR "Anxiety"[Mesh:NoExp] OR "Anxiety Disorders"[Mesh] OR "Postpartum Period"[Mesh])) NOT ("animals"[mh] NOT "humans"[mh])) OR ((Pregnancy-Induced Diabete*[tiab] OR Gestational diabete*[tiab]) AND (Exercise[tiab] OR Swimming[tiab] OR Stretching[tiab] OR Walking[tiab] OR Physical activit*[tiab] OR Aerobic[tiab] OR "Strength training"[tiab] OR Sedentary[tiab] OR inactivity[tiab] OR Cycling[tiab] OR running[tiab] OR resistance training[tiab] OR feeding behav*[tiab] OR eating behav*[tiab] OR Feeding Pattern*[tiab] OR Eating Pattern*[tiab] OR Food habit*[tiab] OR Eating habit*[tiab] OR Diet habit*[tiab] OR Dietary habit*[tiab] OR Breast feeding[tiab] OR Breastfeeding[tiab] OR (Mindful*[tiab] AND eating[tiab]) OR Intuitive eating[tiab] OR Food intake[tiab] OR Hunger[tiab] OR satiation[tiab] OR dietary fat*[tiab] OR diet[tiab] OR diets[tiab] OR sugar*[tiab] OR carbohydrate*[tiab] OR sucrose[tiab] OR weight[tiab] OR overweight[tiab] OR obesity[tiab] OR body composition[tiab] OR appetite[tiab] OR energy intake[tiab] OR Stressful event*[tiab] OR Life change*[tiab] OR Lifestyle*[tiab] OR Depression*[tiab] OR Depressive disorder*[tiab] OR Stress*[tiab] OR Anxiety[tiab] OR Postpartum[tiab] OR parenting[tiab]) *AND (publisher[sb] OR inprocess[sb])) AND ("1980/01/01"[PDat] : "3000/12/31"[PDat])*

5064 references from 1980 to 15.09.2016

5639 *references from 1980 to 24.01.2018 (Update) the terms in italics were added*

Embase.com

('pregnancy diabetes mellitus'/de AND ('physical activity, capacity and performance'/exp OR 'fitness'/de OR 'motor activity'/exp OR 'feeding behavior'/exp OR 'hunger'/de OR 'satiety'/de OR 'dietary intake'/exp OR 'diet'/exp OR 'body weight'/exp OR 'body composition'/exp OR 'lifestyle and related phenomena'/de OR 'life event'/de OR 'lifestyle'/de OR 'lifestyle modification'/de OR 'sedentary

lifestyle'/de OR 'health behavior'/de OR 'attitude to health'/de OR 'health belief'/de OR 'depression'/exp OR 'stress'/exp OR 'child parent relation'/exp OR 'parenting education'/de OR 'anxiety'/de OR 'anxiety disorder'/exp OR 'puerperium'/exp OR 'meal'/de OR 'waist circumference'/de OR 'attitude to illness'/de)) NOT ([animals]/lim NOT [humans]/lim) *NOT 'conference abstract'/it) AND [1980-2018]/py*

9109 references from 1980 to 15.09.2016

7823 *references from 1980 to 12.02.2018 (Update, conference abstracts not considered): the terms in italics were added*

CINAHL

MH "Diabetes Mellitus, Gestational" AND ((MH "Exercise+") OR (MH "Physical Activity") OR (MH "Physical Fitness+") OR (MH "Swimming") OR (MH "Cycling") OR (MH "Walking") OR (MH "Relaxation") OR (MH "Running+") OR (MH "Motor Activity") OR (MH "Eating Behavior+") OR (MH "Hunger") OR (MH "Appetite") OR (MH "Eating") OR (MH "Postprandial Period") OR (MH "Diet+") OR (MH "Food Intake+") OR (MH "Satiation") OR (MH "Dietary Fats+") OR (MH "Dietary Carbohydrates+") OR (MH "Meals+") OR (MH "Body Weight+") OR (MH "Waist Circumference") OR (MH "Waist-Hip Ratio") OR (MH "Body Composition+") OR (MH "Life Style+") OR (MH "Attitude to Health+") OR (MH "Attitude to Illness") OR (MH "Attitude to Obesity") OR (MH "Attitude to Pregnancy") OR (MH "Attitude to Change") OR (MH "Depression+") OR (MH "Anxiety") OR (MH "Stress+") OR (MH "Anxiety Disorders") OR (MH "Parenting") OR (MH "Parental Behavior") OR (MH "Paternal Behavior") OR (MH "Parent-Child Relations") OR (MH "Postnatal Period+"))

1204 references from 1980 to 15.09.2016

1400 references from 1980 to 25.01.2018 (Update)

PsycINFO

gestational diabetes/ AND (exp physical activity/ or active living/ or exp physical fitness/ OR sedentary behavior/ OR exp eating behavior/ or exp appetite/ or diets/ or eating attitudes/ or food intake/ OR satiation/ OR exp health attitudes/ or exp lifestyle/ or health behavior/ or exp major depression/ OR exp stress/ OR anxiety/ or exp anxiety disorders/)

43 references from 1980 to 15.09.2016

58 references from 1980 to 24.01.2018 (Update)

Cochrane Library Wiley

("Pregnancy-Induced" NEXT/1 Diabete* OR Gestational NEXT/1 diabete*) AND (Exercise OR Swimming OR Stretching OR Walking OR Physical NEXT/1 activit* OR Aerobic OR "Strength training" OR Sedentary OR inactivity OR Cycling OR running OR "resistance training" OR feeding NEXT/1 behav* OR eating NEXT/1 behav* OR Feeding NEXT/1 Pattern* OR Eating NEXT/1 Pattern* OR Food NEXT/1 habit* OR Eating NEXT/1 habit* OR Diet NEXT/1 habit* OR Dietary NEXT/1 habit* OR Breast NEXT/1 feeding OR Breastfeeding OR (Mindful* NEAR/3 eating) OR Intuitive NEXT/1 eating OR Food NEXT/1 intake OR Hunger OR satiation OR dietary NEXT/1 fat* OR diet OR diets OR sugar* OR carbohydrate* OR sucrose OR weight OR overweight OR obesity OR body NEXT/1 composition OR appetite OR energy NEXT/1 intake OR Stressful NEXT/1 event* OR Life NEXT/1 change* OR Lifestyle* OR Depression* OR Depressive NEXT/1 disorder* OR Stress* OR Anxiety OR Postpartum OR parenting):ab,ti

606 references from 1980 to 15.09.2016

Cochrane Database of Systematic Reviews : Issue 9 of 12, September 2016

Cochrane Central Register of Controlled Trials : Issue 8 of 12, August 2016

Database of Abstracts of Reviews of Effect : Issue 2 of 4, April 2015

824 references from 1980 to 24.01.2018 (Update)

Cochrane Database of Systematic Reviews : Issue 1 of 12, January 2018

Cochrane Central Register of Controlled Trials : Issue 12 of 12, December 2017

8.2 Publication B

Published in BMJ Open in 2018.

Improving cardiometabolic and mental health in women with gestational diabetes mellitus and their offspring: study protocol for *MySweetHeart Trial*, a randomized controlled trial

Antje Horsch,[1,2] Leah Gilbert,[3] Stefano Lanzi,[3,4] Justine Gross,[3] Bengt Kayser,[5] Yvan Vial,[1] Umberto Simeoni,[6] Didier Hans,[7] Alexandre Berney,[8] Urte Scholz,[9] Ruben Barakat,[10] Jardena J Puder,[2,11] on behalf of MySweetHeart Research Group

[1]Woman-Mother-Child Department, Lausanne University Hospital, Lausanne,Switzerland

[2]Institute of Higher Education and Research in Healthcare (IUFRS), University of Lausanne, Lausanne, Switzerland

[3]Service of Endocrinology, Diabetes and Metabolism, Lausanne University Hospital, Lausanne, Switzerland

[4]Service of Angiology, Heart and Vessel Department, Lausanne University Hospital, Lausanne, Switzerland

[5]Institute of Sport Sciences, University of Lausanne, Lausanne, Switzerland

[6]DOHad Laboratory, Pediatrics Division, Woman-Mother-Child Department, Lausanne University Hospital, Lausanne, Switzerland

[7]Center of Bone Diseases, Rheumatology Service, Bone and Joint Department, Lausanne University Hospital, Lausanne, Switzerland

[8]Consultation Liaison Psychiatry, Lausanne University Hospital, Lausanne, Switzerland

[9]Applied Social and Health Psychology, Department of Psychology, University Research Priority Program Dynamics of Healthy Aging, University of Zurich, Lausanne, Switzerland

[10]Facultad de Ciencias de la Actividad Física y del Deporte-INEF, Universidad Politécnica de Madrid, Madrid, Spain

[11]Service of Pediatric Endocrinology, Diabetology and Obesity, Lausanne University Hospital, Lausanne, Switzerland

Abstract

Introduction Gestational diabetes mellitus (GDM) carries prenatal and perinatal risk for the mother and her offspring as well as longer-term risks for both the mother (obesity, diabetes, cardiovascular disease) and her child (obesity, type 2 diabetes). Compared with women without GDM, women with GDM are twice as likely to develop perinatal or postpartum depression. Lifestyle interventions for

GDM are generally limited to physical activity and/or nutrition, often focus separately on the mother or the child and take place either during or after pregnancy, while their results are inconsistent. To increase efficacy of intervention, the multifactorial origins of GDM and the tight link between mental and metabolic as well as maternal and child health need to be heeded. This calls for an interdisciplinary transgenerational approach starting in, but continuing beyond pregnancy.

Methods and analysis This randomised controlled trial will assess the effect of a multidimensional interdisciplinary lifestyle and psychosocial intervention aimed at improving the metabolic and mental health of 200 women with GDM and their offspring. Women with GDM at 24–32 weeks gestational age who understand French or English, and their offspring and partners can participate. The intervention components will be delivered on top of usual care during pregnancy and the first year postpartum. Metabolic and mental health outcomes will be measured at 24–32 weeks of pregnancy, shortly after birth and at 6–8 weeks and 1 year after childbirth. Data will be analysed using intention-to-treat analyses. The MySweetHeart Trial is linked to the MySweetHeart Cohort (clinicaltrials. gov/ ct2/ show/ NCT02872974).

Ethics and dissemination We will disseminate the findings through regional, national and international conferences and through peer-reviewed journals.

Trial registration number NCT02890693; Pre-results.

Strengths and limitations of this study

► The study will test the effects of a novel multidimensional interdisciplinary lifestyle and psychosocial intervention for women with gestational diabetes mellitus.

► The intervention focuses on both metabolic and mental health, of the mother and her offspring, which starts during pregnancy and continues beyond birth.

► The intervention draws on theories of health behaviour change through motivational and systemic approaches.

► Methodological rigour, including concealment of random allocation, blinded outcome assessors, regular monitoring and prospective trial registration and publication, should limit risk of bias.

► Unblinded participants and clinicians for some of the secondary outcomes may increase the risk of bias.

Introduction

Definition and prevalence of gestational diabetes mellitus (GDM)

GDM is characterised by glucose intolerance diagnosed during pregnancy not fulfilling the criteria for diabetes.[1,2] It often resolves after childbirth, although up to 40% of women have prediabetes in the early postpartum period.[3] In Switzerland, the prevalence of GDM is 10.8%.[4]

Morbidity of GDM and related conditions

GDM carries prenatal and perinatal risk for the mother and her child and is also linked to postnatal risks. Long-term maternal risks include a 30%–70% GDM recurrence, a 7-fold higher 5–10 year risk of type 2 diabetes and an increased risk of metabolic syndrome and cardiovascular disease.[5–8] Compared with women without GDM, women with GDM are twice to four times[9] as likely to develop antenatal or postpartum depression and approximately one-third of women with recent GDM develop postpartum depression.[10] Postpartum depression leads to an increase in comfort eating and a decrease in physical activity,[11] thus putting the women at higher risk of weight gain and future diabetes.[10] Regarding the child, the importance of the intrauterine and early postnatal environments for metabolic programming and modifications of the epigenome is increasingly recognised,[12–14] particularly for metabolic diseases such as obesity and diabetes.[15] Thus, GDM is related to macrosomia at birth (>4 kg), to excess body fat and (central) obesity and to insulin secretion in infants and children, the obesity being in part mediated by maternal body mass index (BMI) or birth weight.[16–23] Intrauterine exposure to GDM also doubles the risk for subsequent type 2 diabetes in offspring compared with offspring of mothers with a high genetic predisposition for type 2 diabetes, but with normal glucose tolerance during the index pregnancy.[24] Maternal prepregnancy overweight and excessive gestational weight gain also predict high birth weight and adiposity during infancy.[12 25] This is highly relevant, as up to 60%–70% of women with GDM are overweight or obese before pregnancy.[26] Finally, maternal lifestyle behavior such as a high fat diet or lack of physical activity during pregnancy can influence offspring adiposity independent of maternal obesity.[12 27] The higher risk for maternal postpartum depression is also associated with reduced parenting skills, which may have negative consequences for the development of the child.[28–30] Parents of obese children may lack effective parenting skills providing both a consistent structured frame and emotional support.[31] In women with GDM, psychosocial vulnerability including low levels of social and family networks is associated with more adverse neonatal outcomes, especially increased birth weight.[32] Thus, there is a tight interaction between maternal lifestyle, weight status, mental health, social support as well as between maternal and child's overall health. In view of the high worldwide prevalence of (childhood) obesity and associated metabolic problems, this close link between maternal and child metabolic health and the

resulting vicious cycle are very relevant.[33 34] Because of the deleterious impact of GDM and lifestyle during pregnancy on the health of the mother and her offspring, it is crucial to intervene during the prenatal, perinatal and postnatal period.

Modifiable risk factors of GDM

Risk factors for GDM that are modifiable during pregnancy include excessive weight gain which is a very frequent phenomenon that is observed in a majority of pregnant women (in up to 75% of pregnancies).[35 36] Further modifiable risk factors include lifestyle behaviours such as low levels of physical activity, high fat and animal protein consumption, high intake of added sugar and low intake of vegetable and fruit fiber.[37] Regular food intake and avoidance of snacking can have beneficial effects on weight and glucose tolerance, but this has mostly been tested outside of pregnancy.[38–42] Another key factor is mental health. Higher stress exposure and perceived stress during pregnancy have been linked to GDM and/or higher glucose levels in women.[43–45] Psychological stress and negative life events can be associated with higher salivary cortisol levels during pregnancy, which might relate to higher glucose levels.[46] Higher depression scores early in pregnancy also increase the risk for GDM.[9 47] On the other hand, social support has been shown to be protective regarding mental health and depression in particular.[9 48 49] Physical activity, nutrition and depression are interlinked. Physical activity can reduce symptoms of depression,[50] and there is a two-directional relationship between unhealthy eating and the incidence of symptoms of depression.[51] Mindfulness and mindful eating can have a beneficial impact on weight loss and food cravings.[52–54]

Prior studies having evaluated lifestyle interventions in GDM

Most interventions in GDM focus either on dietary or on physical activity changes and only last during pregnancy. Dietary advice is recommended for all women with GDM to improve glycaemic control and to provide adequate nutrition.[1] Of the few existing trials, the majority focused on either low carbohydrate or low glycaemic index foods. Results were not consistent and effect sizes were small, but low glycaemic diets, sometimes in combination of higher fibre intake, were found to have a favourable impact on insulin requirements, birth weight and/or maternal weight gain.[55–57] A recent Cochrane review found that more evidence is needed to assess the effects of different types of dietary advice to give to women with GDM.[58] As fat, especially saturated fat, is a risk factor for both GDM and type 2 diabetes, decreasing animal fat intake represents an interesting novel approach.[59–62] Indeed, a high-complex carbohydrate/low-fat diet improved glycaemic values and insulin resistance in women with GDM as well as infant adiposity in a pilot study of women with GDM.[63] Regarding eating

behaviour, a recent intervention focusing on mindfulness-based eating awareness that aimed at increasing awareness of inner cues, such as hunger and satiety, at identification of emotional eating and eating triggers, had a beneficial impact on glycaemic control.[64 65] Although recommended for GDM treatment, guidelines do not specify the type of physical activity or its timing in regards to meal intake.[66 67] Aerobic and resistance exercise can be accomplished during pregnancy in the absence of contraindications,[68] but motivation, compliance, perceived health and lack of time appear to be major limiting factors.[48 69] A recent review concluded that physical activity, both aerobic and resistance exercise, may improve glycaemic control and/or limit insulin use in women with GDM.[70] Regular physical activity can

also limit pregnancy weight gain, stabilise maternal mood and reduce fetal fat mass (FM) and physiological stress responses in the offspring.[27 69 71] To our knowledge, there are no evidence-based psychological interventions for women with GDM and no international guidelines for psychosocial management exist,[72] although evidence shows that inclusion of partners can be helpful.[73 74]

Postpartum follow-up and interventions

Due to the increased risk of development or persistence of prediabetes and diabetes, management of women with GDM in the postpartum period is essential. The American Diabetes Association, the American College of Obstetricians and Gynaecologists and the National Diabetes Education Program recommend testing within 4–12 weeks postpartum with a 2 hour 75 g oral glucose tolerance test (oGTT).[2 75 76] Weightloss is an important predictor to prevent diabetes in this high-risk population. Thus, in the Diabetes Prevention Program, weight loss after GDM reduced future diabetes incidence by 16% for every kilogram lost.[77] The Nurses Health Study found that healthy diet patterns such as a Mediterranean diet, a Dietary approaches to stop hypertension (DASH) pattern diet or an Alternative Healthy Eating diet reduced diabetes incidence by 40%–57% in women who had GDM 14 years before.[78] Evidence of the Gestational Diabetes' Effects on Moms study shows that a lifestyle intervention that starts during pregnancy and continues postpartum is feasible and may prevent pregnancy weight retention and help overweight women lose weight.[79 80] In the postpartum period after GDM, low social support was related to low adherence to a healthy lifestyle, thus contributing to an increased risk of type 2 diabetes.[81] In another study, social support was a key factor for the adoption of physical activity among women after GDM.[82] Finally, integrating partners into the intervention helped to maximise participation in an intervention that aimed to prevent type 2 diabetes after GDM.[74]

Prevention strategies for the child

Offspring of women with GDM are at higher risk for childhood obesity[83] and intervening in the early postpartum period is therefore essential. Several modifiable risk or protective factors have been identified, such as infant feeding mode (bottle vs breastfeeding), parental responsiveness to infant feeding cues and infant distress, the age of bottle weaning, timing of the introduction of solid food, sweetened beverage consumption and lack of physical activity.[84–88] Inactivity can delay motor development and further increases the risk for early childhood obesity.[85 89–91] Parenting skills interventions that focus on these factors provide anticipatory guidance and teach parents how to identify and respond appropriately to infant cues and distress to positively influence self-regulatory capacities, well-being and the developing control of the infant's food intake in order to avoid eating in the absence of hunger have shown beneficial results.[84 85 92 93]

Theoretical framework for behaviour change interventions

The chosen theoretical framework for the behavior change interventions is the Health Action Process Approach (HAPA).[94] The HAPA distinguishes between a motivational and a volitional phase of behavioural change. In the motivational phase, the process of forming an intention to engage in a health behaviour takes place. Being aware of a personal risk due to the unhealthy behaviour, perceiving more benefits than disadvantages of changing the behavior (outcome expectancies) and believing in one's own abilities to change the behaviour (self-efficacy) are the factors that the HAPA specifies to increase the likelihood of a behavioural intention to change the behaviour. After an intention has been set, the individual enters the volitional phase. Here, action control, action planning, coping planning and again self-efficacy are assumed to be crucial for translating the intention into behaviour. Action control and its components (ie, the awareness of one's own standards for the new behaviour, self-monitoring and regulatory effort in case of a discrepancy between the intended and the actual behaviour) have been demonstrated in several populations and across several behaviours, among them physical activity and diet, to be effective in promoting behavioural change.[95] Moreover, action planning and coping planning are crucial postintentional variables in the HAPA. Action planning, which is also known as implementation intentions,[96 97] refers to if-then plans regarding the exact planning of when, where and how a behavior will be implemented. Implementation intentions have been demonstrated to be an effective tool of behavioural change in numerous settings and behaviours, displaying medium to strong effect sizes.[98–100] Coping plans refer to plans that specify a critical barrier to the intended/ planned behaviour and a specific strategy on how to cope with this barrier.[101] A recent systematic review attests that the combination of action planning and coping

planning seems to be most effective for behavioural change.[102] Self-efficacy has also been shown to be a crucial factor in health behaviour change across different behaviours and different populations.

Development of a complex multidimensional interdisciplinary lifestyle intervention

Given that single risk factor interventions have shown limited efficacy, and considering the multifactorial origins of GDM, complex interdisciplinary approaches that start in pregnancy and continue postpartum, targeting both the mother and the child could be more efficient. This is especially important with regard to the intergenerational transmission of risk.[103] Some authors specifically called for the need to integrate psychological support in a lifestyle intervention.[104] Typical characteristics of complex interventions are that they contain several interacting components, their high number of outcomes and that a high degree of flexibility or tailoring of the intervention is permitted.[105] Furthermore, complex interventions work best if tailored to local circumstances rather than completely standardised.[105]

Aims

This study aims to test the effect of an evidence-based, complex interdisciplinary lifestyle and psychosocial continuous prepartum and postpartum intervention in women with GDM on maternal and offspring metabolic and mental health outcomes up to 1 year postpartum. It also aims to investigate longitudinal associations, thus increasing the understanding of the development of maternal and child obesity, glucose intolerance and mental health problems.

Methods

Study design

We will conduct a monocentric superiority open Randomised Controlled Trial (RCT) with minimal risk aiming to test the effect of a multidimensional interdisciplinary lifestyle and psychosocial intervention for pregnant women with GDM and their offspring, compared with treatment-as-usual (figure 1).

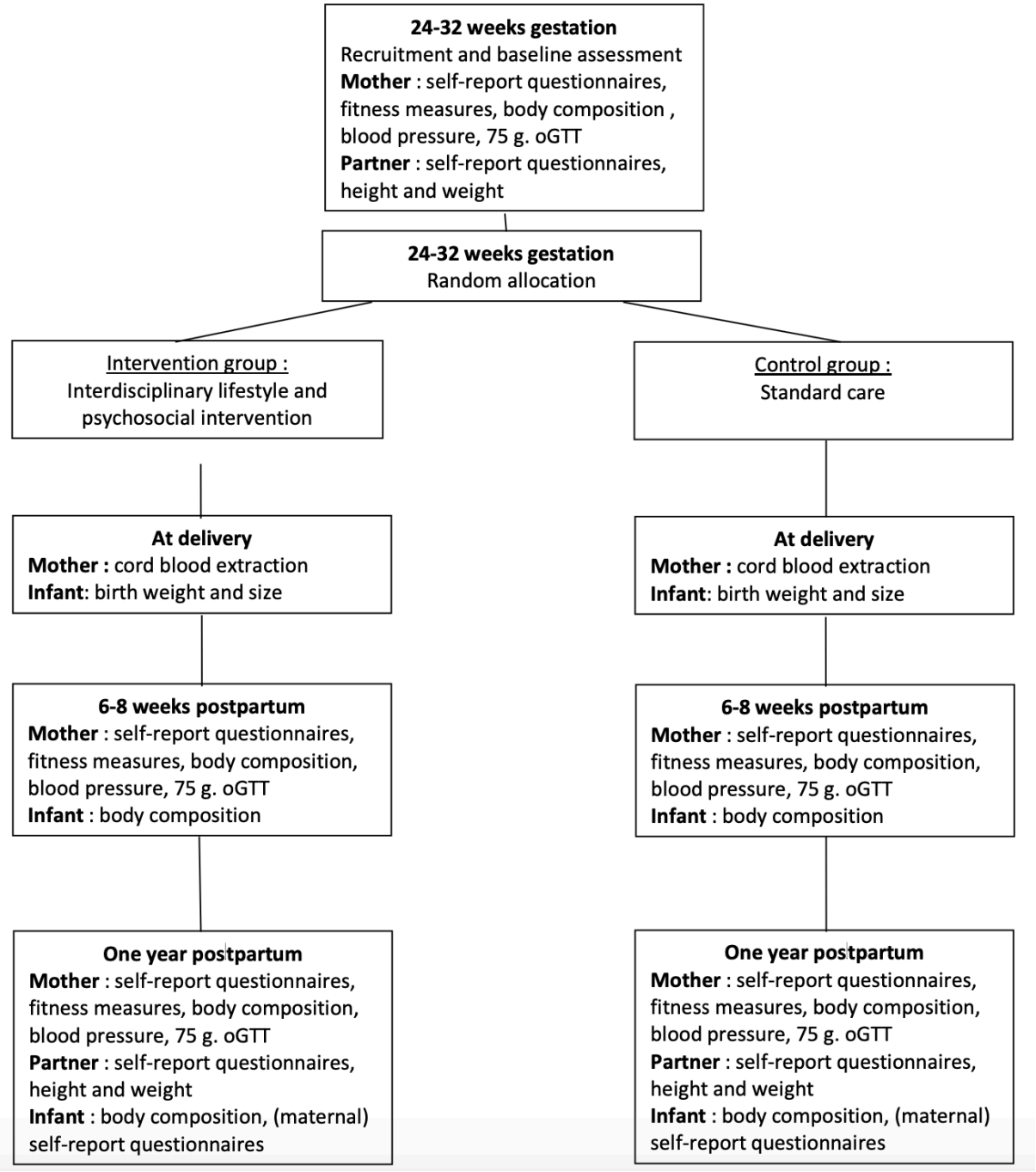


Figure 1 Trial flowchart.

Study population, recruitment, group allocation and blinding

Women diagnosed with GDM according to IADPSG criteria[106 107] will be recruited (1) in our diabetes and pregnancy clinic, where patients both from the University Hospital Vaud (CHUV) antenatal care clinic and from obstetricians in private practice are referred to or (2) referred to our clinic for the study from diabetologists in private practice and from regional hospitals

in the canton Vaud. Following their first clinical appointment, the study coordinator will explain the study and give the information sheet to the patient. Participating women will receive for their time, effort as well as the fees for their frequent travels CHF 250 at the 6–8 week postpartum visit and then CHF 200 at the 1 year visit. The inclusion criteria are as follows: pregnant women aged ≥18 years, with GDM at 24–32 weeks of gestation and understanding French or English. Women on strict bed-rest, with pre-existing DM or current episode of severe mental disorder will be excluded. The allocation ratio of randomisation is 1:1, using the block randomisation method (blocks of 4) after stratification for the place of the usual care (at the CHUV or the respective private diabetologist/regional hospital). Thus, each referral centre represents its own control. However, all intervention components and all the evaluations take place at the CHUV hospital. For allocation of the participants, a computer-generated list of random blocks is used (https://www. sealedenvelope. com/ simple- randomiser). The allocation sequence will be concealed from the research staff assessing the primary outcomes in sequentially numbered, opaque, sealed envelopes. Envelopes will be opened only after the enrolled participants gave signed consent and completed all baseline assessments. Assessors of primary outcomes and the statistician will be blind to group allocation.

Control group

The control group will receive treatment-as-usual, which is based on the current guidelines of the American Diabetes Association[2] and of the Endocrine Society.[1] Patients are first seen at 24–32 weeks of gestation by a physician and/ or a specialised nurse practitioner who will then provide follow-up until childbirth. During the first visit, patients learn about GDM and how to perform self-control of blood glucose 4 times a day (fasting and 2 hours postprandially).[1 108] Regarding the weight, lifestyle and mental health goals, details are provided in tables 1A and B. Standard advice about gestational weight gain according to the Institute of Medicine recommendations[109 110] will be given. Patients have one appointment with a registered dietician in order to receive individualised dietary advice, with a focus on how to distribute carbohydrate intake over several meals and snacks, limit the intake of free sugars to less than 10%, and increase fibre intake to up to 30 g per day. Patients are encouraged to increase physical activity according to the Endocrine Society Guidelines.[1] If despite lifestyle measures, glucose values remain above targets,[1 2] twice or more during a 2-week period,[108] metformin or insulin treatment is installed depending on glucose values (eg, insulin in case of relatively high glycaemic values) and patient preference.[111] In the postpartum period, patients then undergo a 75 g oGTT at 6–8 weeks postpartum and are seen afterwards by the physician and a dietician jointly to discuss results and further management and provide general advice on lifestyle measures.[1 2] Patients then resume

usual care by their healthcare provider outside of the clinic. The frequency of blood glucose self-control, the thresholds for initiating treatment, the choice of the medical treatment and the first visit with the dietician will be the same in the control and in the intervention group.

Intervention group

The complex, multidimensional, interdisciplinary lifestyle and psychosocial intervention will be offered on top of usual care. Details for the goals of the intervention group are provided in tables 1A and B. All goals will be individually tailored and set by the respective experts (dietician and physiotherapist) during the face-to-face prepartum consultations, based on the patients' context and capacities[112] and transmitted to the coach (see below). The goals will also be discussed during bimonthly interdisciplinary meetings in the postpartum period and exchanges regarding further adaptations.[83–86 89–93 113–124] Counselling about gestational weight gain according to the Institute of Medicine recommendations and about weight retention will be given.[109 110] In addition to the dietary goals set in the control group, the intervention aims to reduce intake of total lipid intake,[125] saturated fat,[126] to prioritise higher quality fats such as monounsaturated fat present in the Mediterranean,[127 128] DASH and plant-based diets and to reduce red or processed meat intake.[127] It also aims to encourage mindful eating[129–131] and regular, structured eating.[1] The intervention also includes the promotion of continuous breastfeeding for at least 6 months. The intervention encourages aerobic and resistance physical activity[66 68 132 133] and aims to reduce sedentary behaviour.[134] Regarding the psychosocial part,[135] patients will be screened for depression at study beginning, at 6–8 weeks, at 7 months postpartum and at 1 year postpartum. According to a stepped care approach (based on the patient's Edinburgh Postnatal Depression Scale (EPDS) score), facilitated self-help with the coach or individual cognitive behavioural therapy sessions with the clinical psychologist will be offered.[135] Common elements are: (1) challenge most unhelpful negative cognitions, (2) schedule at least one pleasurable activity per day, (3) increase social contacts, (4) improve sleep routine, (5) identify most stressful situations and apply cognitive behavioural strategies to improve their management.[135 136] Patients who require a psychiatric evaluation will be referred to a psychiatry liaison service. Treatment goals for the offspring focus on diet, breastfeeding, nutrition, physical activity[137] and emotional regulation, all of which will be addressed via psychoeducation and parenting training (see tables 1A and B). The intervention will take place during pregnancy and during the first year postpartum and will be delivered in individual sessions during the prepartum period with members of the multidisciplinary team, in 3–4 monthly individual interdisciplinary sessions in the postpartum period covering both the mother and the child or during group workshops. Throughout the pregnancy and up to 1 year

postpartum, patients will be accompanied and supported by a lifestyle coach (with regular supervision by a clinical psychologist) who will monitor adherence to the intervention, provide booster messages, identify barriers and facilitators, discuss action plans, provide support and teach strategies to work towards the individual goals. The coach will offer different behaviour change techniques[138] targeting the HAPA[90] constructs relevant for the respective phase participants are in. Depending on the needs and the progress of participants, the content of theory- based interventions will be tailored to the individuals. Self-monitoring by the patient will help to clarify the situation and adjust the goals. During pregnancy, the coach will have approximately 15 min of biweekly contact (by phone, videophone and/or face to face after clinical visits). During the first year postpartum, the coach will have phone/videophone contact with the mother every 3 weeks until 6 months and then monthly. Patients will receive a folder with written materials and resources and worksheets or text messages (according to preferences) to monitor their personalised tailored goals and action plans in the different domains throughout the study period. Close collaboration with paediatricians, obstetricians and existing healthcare networks that form part of the patients' usual clinical care will be ensured. Social support will be encouraged on three levels.[139–141] First, partners will be invited

Table 1A Goals (for the mother)

Domains	Intervention group	Control group
Weight goals	**Prepartum** Attain gestational weight gain according to the Institute of Medicine and National Research Council[110] **Postpartum** Weight retention: return to pregravid weight (or 5% less if BMI≥25 kg) at 1 year postpartum[79 180]	**Prepartum** Standard advice to attain gestational weight gain according to the Institute of Medicine and National Research Council[110]
Diet	**Prepartum and postpartum** *Carbohydrates* Distribute carbohydrates over several meals and snacks.[1] Limit the intake of free sugar to less than 10% of total energy intake avoiding added sugars and sugar naturally present in honey, syrups, fruit juices.[181] Increase fibre intake to up to 30 g per day[182 183] *Lipids* Limit total fat to less than 30%[125] and saturated fat to less than 10% of total energy intake,[126] Prioritise higher quality fats such as monounsaturated fat[127 128] Reduce red or processed meat[127] *Mindful eating* Improve eating regulation in developing an awareness of physical hunger and satiety cues, slowing down pace of eating and reduce emotional eating[129–131] *Regular eating* Structure eating into 2–3 small- to moderate-sized meals and structured snacks if necessary; avoid snacking[1]	**Prepartum** *Carbohydrates* Distribute carbohydrates over several meals and snacks.[1] Limit the intake of free sugar to less than 10% of total energy intake avoiding added sugars and sugars naturally present in honey, syrups, fruit juices.[181] Increase fibre intake to up to 30 g per day[182 183] **Postpartum** Provide general clinical advice on lifestyle measures[1]
Physical activity	**Prepartum**[66 68 132]: ► Type: combined aerobic and resistance physical activity. ► Frequency: 2 times per day; 7 days per week. ► Duration: at least 20 min per session. ► Intensity: moderate intensity (RPE=12–14 on Borg's scale). ► Timing: 1 hour to 1 hour 30 min postprandial (to target postprandial glycaemia). **Postpartum**[133]: ► Type: combined aerobic and resistance physical activity without specific timing. ► Frequency and duration: 150 min per week of aerobic physical activity and at least 2x/week of resistance physical activity. ► Intensity: moderate intensity. Sedentary behaviour: break sedentary time with physical activity every hour[134]	**Prepartum** Provide usual recommendations of 30 min per day of moderate physical activity as recommended by the Endocrine Society Guidelines[1] **Postpartum** Provide general clinical advice on lifestyle measures[1]

Continued

Table 1A Continued

Domains	Intervention group	Control group
Mental health	**Prepartum and postpartum** *Depression symptoms: Screening and treatment of moderate depressive symptoms* EPDS at first antenatal visit, 6–8 weeks postpartum and 1 year postpartum. Based on the EPDS score a stepped care approach[135] will be offered. The focus is on prevention and early intervention of depression symptoms, with facilitated self-help offered in case of mild symptoms, and individual sessions with a clinical psychologist integrated in the team in case of moderate to severe symptoms (EPDS=10+) *General prevention and treatment elements for all*[136] Common elements are: (1) challenge most unhelpful negative cognitions, (2) schedule at least one pleasurable activity per day, (3) increase social contacts, (4) improve sleep routine, (5) identify most stressful situations and apply cognitive behavioural strategies to their management	**Prepartum** *Depression symptoms: Screening and referral for moderate to severe depressive symptoms* EPDS at first antenatal visit and 1 year postpartum. If EPDS=13+, referral to Psychiatry Liaison Service as for usual clinical practice[135]
Social support	**Prepartum and postpartum**[139–141]: *Attain satisfactory social support on three levels* Healthcare providers: ensure that all adequate perinatal support services have been proposed Peers: offer support by group sessions to initiate exchange and contact Partner: integrate the partner in the consultations, groups sessions and the personal established goals	No specific intervention

Table 1B Goals for the infant up to 1 year (targeted through parent education)

Domains	Intervention group	Control group
Diet	Breastfeeding: encourage continuation for at least 6 months[184] Soothing: propose alternative methods than feeding[85 92 121] Hunger and satiety: recognise the respective cues[92 120] Food: introduce solid food after at least 4–6 months of age[185]	Provide general recommendation for breastfeeding[184]
Physical activity	Physical activity: encourage physical activity during waking hours, reaching 180 min/day at 1 year of age[137] Sedentary behaviour: no screen time[137]	No specific intervention
Mental health	Parental regulation of infant distress and self regulation capacity: increased through parent education during prenatal and postnatal workshops and postpartum interdisciplinary sessions and reinforced by coach[85 92]	No specific intervention

BMI, body mass index; EPDS, Edinburgh Postnatal Depression Scale; RPE, rate of perceived exertion.

to attend individual and group sessions during both the prepartum and postpartum period. If partners are unable to attend those sessions, a phone/videophone contact at the end of the sessions will be offered. Second, small peer support groups will be formed during the prepartum and postpartum workshops. Third, the coach will also transmit information about other local support offers and will refer the patient to a lactation consultant, if desired by the patient. There are no specific other intervention parts for the partners except their integration in the maternal and offspring goals, which include a family approach.

Primary outcomes

The primary outcomes are differences between the intervention and the control groups in (1) the decrease in maternal weight (calibrated Seca scale) between 24–32 weeks gestational age (GA) and 1 year postpartum and (2) attenuation in maternal symptoms of depression (EPDS) during the same time period.

Secondary outcomes

Maternal outcomes

The following lifestyle behaviours will be measured: carbohydrate and fat intake (Food Frequency Questionnaire (FFQ), see below), eating behaviour (French Intuitive Eating Scale (IES), see below), breastfeeding (self-report), physical activity (accelerometer GENEActiv), sleep (Pittsburgh Sleep Quality Index (PSQI), see below). Aerobic fitness will be estimated using the Chester step test (see below) and muscular fitness will be assessed with the hand grip strength using a Jamar dynamometer (see below). Body composition measures include bioelectrical impedance analysis (BIA), the sum of four skinfolds (Harpenden callipers) as well as Dual-Energy-X-ray absorptiometry (iDXA device, GEHC-Lunar, Madison, Wisconsin, USA). Cardiometabolic laboratory variables and miRNA will be measured (for more details, see Di Bernardo et al[142]). Additional mental health indicators include anxiety (Anxiety subscale of the Hospital Anxiety and Depression Scale (HADS), see below), depression (EPDS and Whooley questions, see below), well-being (WHO Well-Being Index, see below), social support (Medical Outcomes Study Social Support Survey-short form (mMOS-SS), see below) and parenting stress (Parenting Stress Scale-short form (PSI-SF), see below).

Offspring outcomes

Cardiometabolic laboratory variables and miRNA will be measured in the cord blood (for more details, see Di Bernardo et al[142]). Body composition measures include height, weight (standardized tools for infants), BIA and the sum of four skinfolds (Harpenden callipers). Mental health indicators include self-regulation (Difficult Child subscale of the Parenting Stress Index-Short form, see below) and sleep (Brief Infant Sleep Questionnaire (BISQ), see below).

Data collection and visits

The study started in September 2016. The participation in the study is voluntary and involves a sequence of events and measurements as summarised in table 2. At 24–32 weeks GA, baseline assessments are carried out (visit 1), including the validated questionnaires, physical activity and fitness measures, body composition assessments and laboratory variables. If the women agree, their partners are also informed about the study and invited to participate using a separate information sheet and consent form. Once they have signed a separate consent form, research staff will measure the partner's weight and height and ask him to complete validated self-report questionnaires (table 2). During childbirth (visit 2), maternal blood will be drawn at the entry into the delivery room. After childbirth, blood will be drawn from the cord following clamping and birth weight will be recorded. Offspring birth weight and height will be collected from the hospital birth record. At 6–8 weeks postpartum (visit 3), while attending a clinical appointment, women will be asked to complete a series

of validated self-report questionnaires online, and physical activity and fitness measures, body composition assessments and laboratory variables will be measured. They will undergo a 75 g oGTT with blood sampling. Body composition assessments of their offspring will be assessed. At 1 year postpartum (final visit, visit 4), participants will be asked to complete a series of validated self-report questionnaires online, and physical activity, aerobic and muscular fitness, body composition and laboratory variables will be measured. Women, who sign an additional consent, will also undergo Bone Densitometry (DEXA) measures for more detailed body composition. They will undergo a 75 g oGTT with blood sampling and blood pressure (three measures) will be measured. Body composition measures of their offspring will again be assessed.

Partners

Partners of participating women who also agree to participate will be asked to complete validated questionnaires and body composition assessments at study entry and study end (when the women are at 24–32 weeks GA and at 1 year postpartum, respectively).

Measures

All measures and their timings are listed in detail in table 2.

Self-report questionnaires: mother and partner

Symptoms of depression in the preceding 7 days are assessed with EPDS,[143] which has been validated for pregnant women.[144] Each item is scored on a 4-point scale, the minimum and maximum total scores being 0 and 30, respectively. The EPDS has been validated in a French sample and good psychometric properties have been reported.[145] The original authors suggested a cut-off score of 12.5 as an indication of clinically significant depression but others reported that a score of 10 was the most useful cut-off in a French sample of postnatal women.[145] Exposure to life events is measured with the Life Events Questionnaire (see below), in which participants are given a list of three negative pregnancy-related major events (suspected growth retardation, vaginal bleeding, premature contractions) as well as 10 negative pregnancy-unrelated major life events (death of someone they were close to, serious illness, exposure to abuse, exposure to violence, serious accident, unemployment, disability, alcohol/drug abuse, divorce, moving house) and have to indicate whether they have been exposed to any of these events in the last 12 months.[146 147] Carbohydrate and fat intake is assessed with the FFQ.[148 149] The FFQ comprises 97 items listing different types of food and drinks (tea, butter, tomatoes, chicken and so on) and six available spaces which allow the

Table 2 Overview of assessment variables, measures and time points

Domain	Variables	Measures	Timing			
			Visit 1 24–32 GA	Visit 2 Birth	Visit 3 6–8 weeks pp	Visit 4 1 year pp
Mother						
Physical examination	Weight, height, BMI (pregravid weight will be obtained from medical charts and gestational weight gain and weight retention will be calculated)	Calibrated scale (Seca), standard stadiometer	X		X	X
	Total fat mass	Bioimpedance, skinfolds (callipers)	X		X	X
	Total and regional fat mass	Dual-Energy X-ray absorptiometry (Lunar)—optional				X
	Blood pressure	Oscillometric Sphygmomanometer	X		X	X
Sociodemographic background	Sociodemographic variables, exposure to life events	Sociodemographic questionnaire, Life Events Questionnaire[146 147]	X			X
Lifestyle behaviours	Carbohydrate and fat intake	Food Frequency Questionnaire[148]	X			X
	Eating behaviour	French Intuitive Eating Scale[150 151]	X			X
	Breastfeeding	Self-report (duration and exclusiveness)			X	X
	Food to soothe	Food to Soothe Questionnaire[87]				X
	Hunger/satiety clues	Infant Feeding Style Questionnaire: Satiety subscale[165]				X
	Physical activity	Accelerometer (GeneActiv): Total counts/min and time spent in different intensities	X			X
Fitness	Aerobic fitness	Chester step test with VO_{2max} estimation[170]	X			X
	Grip strength	Jamar dynamometer[172]	X			X
	miRNA (in plasma)	Plasma; various miRNA	X	X		X
	Overall metabolic control	HbA1c	X		X	X
Laboratory biomarkers	Glucose tolerance	75 g oGTT			X	X
	Other cardiometabolic laboratory biomarkers	Glucose, insulin, HbA1c, lipid profile, indices of insulin resistance (during oGTT)[186] and other metabolic laboratory biomarkers	X		X	X
Mental Health	Depression	Edinburgh Postnatal Depression Scale[143]	X		X	X
	Anxiety	Anxiety subscale of Hospital Anxiety and Depression Scale[153]	X			X
	Well-being	WHO Well-Being Index[156]	X		X	X
	Parenting stress	Parenting Stress Scale-short form[187]	X			X
	Sleep duration and quality	Pittsburgh sleep quality index[160]				
Social support	Social support	Medical Outcomes Study Social Support Survey-short form[162]	X			X
Partner						

Continued

Table 2 Continued

Domain	Variables	Measures	Timing			
			Visit 1 24–32 GA	Visit 2 Birth	Visit 3 6–8 weeks pp	Visit 4 1 year pp
Physical examination	Weight, height, BMI	Calibrated scale (Seca), standard stadiometer	X			X
Sociodemographic background	Sociodemographic variables, exposure to life events	Sociodemographic questionnaire, Life Events Questionnaire[146 147]	X			X
Lifestyle behaviours	Eating behaviour	French Intuitive Eating Scale[150 151]	X			X
Mental Health	Depression	Edinburgh Postnatal Depression Scale[143]	X			X
	Anxiety	Anxiety subscale of Hospital Anxiety and Depression Scale[153]	X			X
	Well-being	WHO Well-Being Index[156]	X			X
	Parenting stress	Parenting Stress Scale-short form[187]	X			X
Social support	Social support	Medical Outcomes Study Social Support Survey-short form[162]	X			X
Offspring						
Physical examination	Weight, height, BMI	Calibrated baby scale (Seca), portable length board		X	X	X
	Total fat mass	Bioimpedance				X
		Skinfolds (callipers)			X	X
Laboratory biomarkers	miRNA	Cord blood; various miRNA		X		
	Other cardiometabolic laboratory biomarkers	Cord blood		X		
Mental health	Self-regulation	Difficult Child' subscale of Parenting Stress Index-short form[188]				X
	Sleep duration and quality	Brief infant sleep questionnaire[167]				X

BMI, body mass index; GA, gestational age; HbA1c, glycated haemoglobin; oGTT, oral glucose tolerance test; Pp, postpartum.

person to write any additional food or drinks she/he might have taken over a 4-week period. Each item is rated for frequency of use on a 6-point Likert scale ranging from 1 'never in the past 4 weeks' to 6 'twice a day'. The items are also rated on a quantity scale which allows the person to compare the portion they took in comparison with a reference portion (ie, 150 g, one piece and so on) with three response choices: 'less', 'same' or 'more'. Eating behaviour is measured with the French IES,[150] [151] assessing an individuals' tendency to follow their physical hunger and satiety cues when determining when, what and how much to eat.[152] In the current study, the IES was modified by taking out the unconditional permission to eat scale, as women with GDM are given strict diet counselling. Women respond using a 5-point Likert scale ranging from 1 'strongly disagree' to 5 'strongly agree'. To calculate the scale scores, negative items are reversed, so that high scores on the total measure and subscales indicate greater intuitive eating. The individual scores of items under each subscale are then summed to obtain subscale scores ranging from 1 to 5. The French version of the IES-2 demonstrated good psychometric properties.[151] Anxiety symptoms are assessed with the HADS,[153–155] which has seven items measuring state-anxiety in the last 7 days. Each item is scored from 0 to 3, with higher scores indicating greater anxiety. Scores from 8 to 10 indicate possible clinical disorder and scores between 11 and 21 indicate probable clinical disorder. Furthermore, it may be used as a measure of symptom severity from normal (0–7), mild (8–10), moderate (11–14), to severe (15–21). The HADS has good psychometric properties.[154] Well-being is measured with the WHO Well-Being Index (WHO-5),[156] which consists of 5 questions assessing the subjective well-being of the respondents. The items are measured on a 5-point Likert scale ranging from 0 'at no time' to 5 'all of the time'. The scale has adequate validity both as a screening tool for depression and as an outcome measure in clinical trials and has been applied successfully across a wide range of study fields. The scale has been used most extensively in endocrinology[156] and has good psychometric properties in French.[157] Parenting stress is assessed with the PSI-SF.[158] It has 36 items and consists of three subscales that assess parental distress, dysfunctional parent–child interactions and child difficulties. Items are rated using a 5-point Likert scale from 1 'totally agree' to 5 'totally disagree'. The PSI has good psychometric properties.[159] Sleep duration and quality are measured with the PSQI,[160] which has 19 items and measures retrospective sleep quality and disturbances over a 1-month period. It discriminates between good and poor sleepers and provides a brief, clinically useful assessment of multiple sleep disturbances. The 19 items are grouped into seven equally weighted component scores: Subjective Sleep Quality, Sleep Latency, Sleep Duration, Habitual Sleep Efficiency, Sleep Disturbances, Use of Sleeping Medication and Daytime Dysfunction. Items 1–4 are free entry of: usual bed and wake times, minutes of total sleep time and sleep latency (minutes). Items 5–18 are rated on a 4-point Likert

scale responses pertaining to problem frequency: ranging from 0 'not during the past month' to 3 'three or more times a week'. Item 19 is rated on a 4-point Likert scale rating of overall sleep quality ranging from 0 'very good' to 3 'very bad.' All component scores range from 0 to 3. The Global Score ranges from 0 to 21, with a higher score indicating poorer sleep quality and a cut-off score of >5 distinguishing poor sleepers from good sleepers. The questionnaire is validated in French.[160] The English questionnaire was retrieved directly from the author.[161] Social support is measured with the mMOS-SS,[162] which has two subscales assessing emotional and instrumental social support composed of four items to identify potentially modifiable social support deficits. It has good psychometric properties[162] and was translated into French.[163] Food to soothe is assessed with the Food to Soothe Questionnaire,[87] the first subscale of the Baby's Basic Needs Questionnaire.[87] It measures parents' likeliness to use food to sootheir child by 33 items with a Likert scale ranging from 1 to 5. Twenty-six items present scenarios in which parents might use food to soothe. Seven items measure the use of food to encourage/discourage child behaviour. Five items are specified as 'other' so that the parents can fill in specific scenarios that might not be addressed in the questionnaire. There are also two more questions inviting parents to share more information about the use of food to soothe and the use of food to encourage or discourage behaviours.[87] The scales were retrieved by personal communication with the author[164] and translated into French using standard techniques.[163] Parental response to hunger/satiety clues is assessed with the Infant Feeding Style Questionnaire: Satiety subscale,[165] designed to assess parental feeding practices. This parent-report measure consists of five subscales that tap parental control practices and attitudes in child feeding.[87] In this study, we use the satiety subscale. Two of the items probe beliefs and are coded on a 5-point Likert scale ranging from 1 'disagree' to 5 'agree'. The five other items probe behaviours and are coded on a 5-point Likert scale ranging from 1 'never' to 5 'always'. The scales were obtained directly from the author[166] and translated into French using standard techniques.[163]

Self-report questionnaires: offspring

Offspring sleep duration and quality are measured with the BISQ.[167] The role of the responder is asked as well as the age, gender and birth order of the child. The parent rates their child's nocturnal sleep duration, daytime sleep duration, number of night waking, duration of wakefulness during the night hours, nocturnal sleep-onset time, settling time, method of falling asleep, location of sleep and preferred body position during the past week. It has 14 items, which all have specific scoring measures related to the type of question. BISQ scores correlate significantly with sleep measures derived from actigraphy and sleep diaries.[167] The scales were obtained directly from the author[168] and translated

into French using standard techniques.[163] Offspring self-regulation is assessed with the PSI-SF[158] (see above).

Physical activity and fitness measures

Physical activity (total physical activity and its intensity) is assessed using an accelerometer (GeneActiv) that is worn on the right wrist during 10 consecutive days.[169] The Chester Step Test, a multistage submaximal exercise test, is performed to estimate aerobic fitness (maximal oxygen uptake (V'O2max)).[170] Before starting the test, patients are instructed and experience a 30 s familiarisation. During the test, the step rate (assessed by an audiotape) starts at 15 step/min and increases of 5 step/min every 2 min. Patients are asked to step up and down for a maximum of 10 min. Step height (15, 20 or 25 cm) can be adapted depending on the physical characteristics and/or activity level of the patients. Heart rate (HR) and rate of perceived exertion (RPE) on Borg's scale are monitored at the end of each 2 min stage. The test is stopped when patients reach 80% of the estimated HRmax (220-age), when RPE≥15 or when the patient shows signs of distress during the test. The VO2max is then estimated using a standardised equation. The Chester step-test was validated against indirect calorimetry and demonstrated reasonable validity.[171] Muscular fitness is assessed with a hand grip strength dynamometer (Jamar dynamometer) following standard procedure.[172] Before starting the test, patients are instructed on the correct use of the dynamometer (hand and wrist position during squeezing). Then, patients are seated in a chair and are asked to squeeze the dynamometer as tightly as possible. A verbal encouragement is given during the test. Three measures are taken for each hand and the highest value is considered for analysis.

Physical examination: body composition assessments

Weight is measured in mothers, fathers as well as their babies to the closest 100 g. For the mothers and fathers, a calibrated scale (Seca Model 220) is used. Participants are asked to remove their shoes as well as any heavy clothing (jeans, jacket, scarf and so on). For babies, a calibrated scale (model Seca 336) is used and they are weighed without any clothes or nappy. Height is measured in mothers, fathers as well as length in babies to the closest mm. For the mothers and fathers, a calibrated scale (Seca Model 220) is used and they are asked to remove their shoes. For babies, a calibrated scale (Seca model 336) is used. The infant's head is placed against the head positioner (Seca model 419), then the experimenter lightly presses on the infant's knees and measures the infant's length with the measuring rod (Seca Model 232). Total fat mass of the mother and her offspring are measured with BIA and skinfolds. BIA measures the reactance and the resistance of the patient.[173] Any metallic objects

such as watches, bracelets or others are removed before starting the BIA. The participant needs to lie down, arms and legs spread away from each other, so that there is no contact between the limbs. Four electrodes are positioned; two on the right hand and two on the right foot, at a distance of 3–4 cm from each other (BIA 101, Akern, Italy). Obese women with an altered body composition can be identified and monitored using vector BIA.[174] A relaxation phase of 10 min is respected before measurements are taken. Skinfolds are measured with a Harpenden skinfold calliper (HSK-BI, British Indicators, UK) on the biceps, the triceps, the subscapular and the iliac crest. Muscle tissues are not included in the skinfolds. Measures for the mothers are taken on the right side of the body while standing up. Measurements are taken twice, and a third time if the difference between the two first measures is over 1 mm. A mean between the two or three values is calculated.[175 176] For the babies, the measures are taken once on the left hand side while their mothers are holding them.[177] Total and regional fat mass measured by Dual-Energy X-ray absorptiometry (mother). Participants are asked to remove all metal items before densitometry and are examined while wearing only their underwear and a cloth gown. The subjects are placed in a supine position with their arms at their sides but held slightly separated from their trunk and correctly centred on the scanning field. Regions of interest are defined by the analytical programme, and include different corporeal districts: total body, trunk, head, pelvic, upper limbs, lower limbs, android and gynoid region. For each region, DXA scans bone mineral content, bone areal size and weight (in grams) of total mass, FM and non-bone lean mass. For the android and gynoid regions, the ratio between android and gynoid fat distribution is also assessed. Also calculated are a FM index (kg/m2), computed as the ratio of total body FM over height squared and a skeletal muscle mass index (kg/m2), computed as the ratio of appendicular skeletal muscle mass over height squared. Finally, the intravisceral fat index is assessed using a special algorithm provided by the manufacturer. Blood pressure in mothers and their partners is measured by obtaining three readings at 2 min intervals with a clinically validated oscillometric sphygmomanometer (OMRON HEM-907, Japan).

Laboratory variables

Mother

Cardiometabolic laboratory variables such as HbA1c, lipid levels, gamma-GT, B12 vitamin, ferritin will be measured at study beginning, at 6–8 weeks and at 1 year postpartum and miRNA will be additionally also measured at birth. At 6–8 weeks and at 1 year postpartum, a 75 g oGTT with blood sampling at 30 min intervals for 2 hour will be performed to assess glucose tolerance and indices of insulin secretion and sensitivity.

Offspring

Cord blood sample will be obtained at the time of birth to measure lipid levels, glucose, HbA1c and other cardiometabolic laboratory parameters as well as miRNA (for more details, see Di Bernardo et al[142]). A sample of the respective blood draw will be kept for future potential analyses.

Sample size calculation

Sample size was computed based on the expected difference in primary outcomes between the control and the intervention group. The weight assumptions are based on our pilot data and goals for weight retention. Regarding maternal weight, we assumed a weight reduction of 8.4 kg (SD: 5.5) between study enrolment at 24–32 GA, after GDM diagnosis and 1 year postpartum in women allocated to the control group compared with a weight reduction of 10.9 kg (SD: 5.5) in women allocated to the intervention group. The required sample size is 76 women in each study group to have a statistical significant difference with a power of 80% and an alpha-level set at 0.05 (two-sided). This sample size is also sufficient to observe statistical significant differences in the reduction in the Edinburgh Postnatal Depression Scale, if we assume that the reduction in the depression score between the above-mentioned two time points is 0.2 (SD: 4.3) in women allocated to the control group and 2.2 (SD: 4.4) in women allocated to the intervention group. Assuming a maximum attrition rate of 30%, we will include 100 women in the control and 100 in the intervention groups to provide adequate power.

Statistical analysis

For the primary aim, differences in the changes in maternal weight and the EPDS symptoms score between enrolment after GDM diagnosis and 1 year postpartum at the end of the study between the intervention and the control group will be analysed using linear regression analysis. For the secondary aims, the analyses will be performed both for differences in changes between the intervention and the control group and for differences between groups at different time points (baseline at inclusion, childbirth, 6–8 weeks and 1 year postpartum) in maternal metabolic health outcomes, maternal mental health outcomes and offspring metabolic and mental health outcomes. This will be tested using linear regression analysis. We will compare the proportion of patients meeting guidelines for gestational weight gain and for weight retention at 1 year postpartum between the two groups using logistic regression analyses. Associations between outcomes will be tested using linear regression analyses. Differences between groups will be adjusted for the respective baseline values in case they differ. Variables will be transformed if residuals are not normally distributed. We will include potential

confounding variables, if necessary. These include maternal age, sex of the children, the presence of prenatal, perinatal and early postnatal conditions/complications, BMI, EPDS symptoms score and socioeconomic status where applicable. Subgroup analyses will be performed according to weight status, mental health status (EPDS score <10 vs ≥10), prediabetes status at the initial postpartum evaluation (6–8 weeks postpartum) as well as sex (for the children). Analyses will be conducted with STATA V.14.0. For confirmatory analyses, a Bonferroni correction for multiple analyses will be applied. For initial exploratory analyses, no such correction will be used.[178] For the partners, we will evaluate changes between groups and differences between groups at different time points (baseline at inclusion, 1 year postpartum) in weight and paternal eating behaviour and mental health outcomes. Finally, a process evaluation nested inside the trial will be conducted in order to assess fidelity and quality of implementation, to clarify causal mechanisms and to identify contextual factors associated with variation in outcomes.[179]

Adverse events

All expected and unexpected adverse events will be recorded during the entire study period. A recognized potential risk is the occurrence of early contractions due to intense physical activity. In order to monitor and mitigate this potential risk, patients will be closely supervised by a physician and a physiotherapist. In case of early contractions, participants will be requested to reduce or stop their physical activity.

Data management

All study data will be entered by research staff (PhD students and study co-ordinator). All data will be precoded and stored in a secured database (Secutrial), which will be regularly updated by the IT Service of the Lausanne University Hospital. Double data entry will be done for the primary outcomes. For the rest of the data, a random 5% will be double-checked.

Monitoring

Monitoring will be performed by a qualified person independent of the study group and will be organized in two parts: the initial visit took place before the start of recruitment and the second visit after approximately 10% of the study population have been recruited.

Ethics and dissemination

The trial poses little to no risk to participants and their offspring. Signed informed consent is obtained from all participating women. Participation in the study does not interfere with the typical care patients receive during pregnancy and after childbirth. Results from this study will be disseminated at regional and international conferences and in peer-reviewed journals. The MySweetHeart Trial is a registered trial (clinicaltrials. gov/ ct2/ show/ NCT02890693) and linked to the MySweetHeart Cohort (clinicaltrials. gov/ ct2/ show/ NCT02872974).

Significance and outlook

This project will provide relevant findings regarding understanding of GDM, potential pathways and its link to lifestyle, mental health and the development and trajectories of obesity and diabetes in the mothers and obesity in their offspring. It will also provide relevant findings regarding treatment of GDM and its impact on complications such as diabetes and obesity and may thus help to elucidate potential solutions, thus leading to significant changes in clinical practice and guidelines. Due to its interdisciplinary nature, this research is of interest for clinicians, educators and researchers in the field of diabetes, obstetrics, paediatrics and development, psychology, sport and nutrition sciences and public health.

Acknowledgements We would like to thank Dominique Stulz, Céline Helbling, Véronique Pidoux, Giada Ostinelli, Chloé Beutler and Agnes Bacso for their help with administration and data collection. We are grateful to Olivier Le Dizes, Magali Andrey, Andrea Orechio, Laura Marino, Antonella Corcillo, Carine Mekoguem, Christophe Kosinski, Sylvie Girardin, Stephanie Roudet, for delivering the usual care condition and to Nelly Pitteloud and Jean-François Tolsa for departmental support.

Collaborators The following are members of MySweetHeart Research Group (including the authors of the present article), listed in alphabetical order: Ruben Barakat, PhD, Professor (Facultad de Ciencias de la Actividad Física y del Deporte- INEF, Universidad Politécnica de Madrid, Madrid, Spain; barakatruben@gmail.com), Alexandre Berney, MD, Professor (Consultation Liaison Psychiatry, Lausanne University Hospital, Lausanne, Switzerland; alexander.berney@chuv.ch), Pascal Bovet, MD MPH, Professor (Institute of Social and Preventive Medicine (IUMSP), Lausanne University Hospital, Lausanne, Switzerland; pascal.bovet@chuv.ch), Jenni Brand-Miller, AM, FAIFST, FNSA, Professor (School of Life and Environmental Sciences and Charles Perkins Centre, University of Sydney, Australia; jennie.brandmiller@sydney.edu.au); Arnaud Chiolero, MD PhD, Senior lecturer (Institute of Social and Preventive Medicine (IUMSP), Lausanne University Hospital, Lausanne, Switzerland; Department of Epidemiology, Biostatistics, and Occupational Health, McGill University, Montreal Canada; Institute of

Primary Health Care (BIHAM), University of Bern, Switzerland; arnaud.chiolero@chuv.ch), Stefano Di Bernardo, MD, Lecturer (Pediatric Cardiology Unit, Woman-Mother-Child Department, Lausanne University Hospital, Lausanne, Switzerland; stefano.di-bernardo@chuv.ch), Adina Epure, MD (Pediatric Cardiology Unit, Woman-Mother-Child Department; Institute of Social and Preventive Medicine (IUMSP), Lausanne University Hospital, Lausanne, Switzerland; adina-mihaela.epure@chuv.ch), Sandrine Estoppey, M.Sc. (Institute of Social and Preventive Medicine (IUMSP), Lausanne University Hospital, Lausanne, Switzerland; sandrine.estoppey@chuv.ch), Leah Gilbert, M.Sc. (Service of Endocrinology, Diabetes and Metabolism, Department of Medicine, Lausanne University Hospital, Lausanne, Switzerland; leah.gilbert@chuv.ch), Elena Gonzalez-Rodriguez, MD (Service of Endocrinology, Diabetes and Metabolism, Department of Medicine, Lausanne University Hospital, Lausanne, Switzerland; elena-gonzalez@chuv.ch), Justine Gross, HES (Service of Endocrinology, Diabetes and Metabolism, Department of Medicine, Lausanne University Hospital, Lausanne, Switzerland; justine.gross@chuv.ch), Didier Hans, MD (Center of Bone Diseases, Rheumatology Service, Bone & Joint Department, Lausanne University Hospital, Lausanne, Switzerland; didier.hans@chuv.ch), Antje Horsch, DClinPsych, Professor (Institute of Higher Education and Research in Healthcare (IUFRS), University of Lausanne and Woman-Mother-Child Department, Lausanne University Hospital, Lausanne, Switzerland; antje.horsch@chuv.ch), Bengt Kayser, MD, PhD, Professor (Institute of Sport Sciences, University of Lausanne; bengt.kayser@unil.ch), Stefano Lanzi, PhD (Service of Endocrinology, Diabetes and Metabolism, Department of Medicine and Service of Angiology, Heart and Vessel Department, Lausanne University Hospital, Lausanne, Switzerland; stefano.lanzi@chuv.ch), Yvan Mivelaz, MD, Lecturer (Pediatric Cardiology Unit, Woman-Mother-Child Department, Lausanne University Hospital, Lausanne, Switzerland; yvan.mivelaz@chuv.ch), Jardena J Puder, MD, Professor (Service of Endocrinology, Diabetes and Metabolism, Department of Medicine and Service of Pediatric Endocrinology, Diabetology and Obesity, Lausanne University Hospital, Lausanne, Switzerland; jardena.puder@chuv.ch), Dan Quansah, MPH (Service of Endocrinology, Diabetes and Metabolism, Department of Medicine, Lausanne University Hospital, Lausanne, Switzerland), Urte Scholz, PhD, Professor (Applied Social and Health Psychology, Department of Psychology & University Research Priority Program Dynamics of Healthy Aging, University of Zurich, Zurich, Switzerland; urte.scholz@psychologie.uzh.ch), Nicole Sekarski, MD, Professor (Pediatric Cardiology Unit, Woman-Mother-Child Department, Lausanne University Hospital, Lausanne, Switzerland; nicole.sekarski@chuv.ch), Umberto Simeoni, MD, Professor (DOHad Laboratory, Pediatrics Division, Woman-Mother- Child Department, Lausanne University Hospital, Lausanne, Switzerland; umberto.simeoni@chuv.ch), Benazir Siddeek, Ph.D. (DOHad Laboratory, Pediatrics

Division, Woman-Mother-Child Department, Lausanne University Hospital, Lausanne, Switzerland; benazir.siddeek@chuv.ch), Yvan Vial, MD, Professor (Obstetrics and Gynecology Division, Woman-Mother-Child Department, Lausanne University Hospital, Lausanne, Switzerland; yvan.vial@chuv.ch).

Contributors JJP and AH designed the study with input from all other authors. AH and JJP drafted the manuscript and contributed equally to the present work. LG, SL, JG, BK, YV, USi, DH, AB, USc and RB significantly contributed to the establishment and refinement of study procedures and critically revised the manuscript. All authors approved the final version of the manuscript.

Funding This study is funded by a project grant by the Swiss National Science Foundation (SNF 32003B_176119).

Competing interests None declared.

Patient consent Obtained.

Ethics approval Ethical approval was granted by the Human Research Ethics Committee of the Canton de Vaud (study number 2016-00745).

Provenance and peer review Not commissioned; peer reviewed for ethical and funding approval prior to submission.

Data sharing statement Individual participant data collected during the trial (after deidentification) that underlie the publications from MySweetHeart research group will be available on reasonable request.

References

1. Blumer I, Hadar E, Hadden DR, et al. Diabetes and pregnancy: an endocrine society clinical practice guideline. J Clin Endocrinol Metab 2013;98:4227–49.

2. Association AD. Standards of medical care in diabetes-2017: Summary of revisions. Diabetes Care 2017;40:S4–s5.

3. Benhalima K, Jegers K, Devlieger R, et al. Glucose intolerance after a recent history of gestational diabetes based on the 2013 who criteria. PLoS One 2016;11:e0157272.

4. Ryser Rüetschi J, Jornayvaz FR, Rivest R, et al. Fasting glycaemia to simplify screening for gestational diabetes. BJOG 2016;123:2219–22.

5. Bellamy L, Casas JP, Hingorani AD, et al. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. Lancet 2009;373:1773–9.

6. Lauenborg J, Hansen T, Jensen DM, et al. Increasing incidence of diabetes after gestational diabetes: a long-term follow-up in a Danish population. Diabetes Care 2004;27:1194–9.

7. Retnakaran R, Shah BR. Mild glucose intolerance in pregnancy and risk of cardiovascular disease: a population-based cohort study. CMAJ 2009;181:371–6.

8. Harreiter J, Dovjak G, Kautzky-Willer A. Gestational diabetes mellitus and cardiovascular risk after pregnancy. Womens Health 2014;10:91–108.

9. Hinkle SN, Buck Louis GM, Rawal S, et al. A longitudinal study of depression and gestational diabetes in pregnancy and the postpartum period. Diabetologia 2016;59:2594–602.

10. Nicklas JM, Miller LJ, Zera CA, et al. Factors associated with depressive symptoms in the early postpartum period among women with recent gestational diabetes mellitus. Matern Child Health J 2013;17:1665–72.

11. Staiano AE, Marker AM, Martin CK, et al. Physical activity, mental health, and weight gain in a longitudinal observational cohort of nonobese young adults. Obesity 2016;24:1969–75.

12. Poston L. Maternal obesity, gestational weight gain and diet as determinants of offspring long term health. Best Pract Res Clin Endocrinol Metab 2012;26:627–39.

13. Hanson MA, Gluckman PD. Early developmental conditioning of later health and disease: physiology or pathophysiology? Physiol Rev 2014;94:1027–76.

14. Simeoni U, Yzydorczyk C, Siddeek B, et al. Epigenetics and neonatal nutrition. Early Hum Dev 2014;90 Suppl 2:S23–S24.

15. Gluckman PD, Hanson MA, Cooper C, et al. Effect of in utero and early-life conditions on adult health and disease. N Engl J Med 2008;359:61–73.

16. Nehring I, Chmitorz A, Reulen H, et al. Gestational diabetes predicts the risk of childhood overweight and abdominal circumference independent of maternal obesity. Diabet Med 2013;30:1449–56.

17. Crume TL, Ogden L, West NA, et al. Association of exposure to diabetes in utero with adiposity and fat distribution in a multiethnic population of youth: the Exploring Perinatal Outcomes among Children (EPOCH) Study. Diabetologia 2011;54:87–92.

18. Chandler-Laney PC, Bush NC, Granger WM, et al. Overweight status and intrauterine exposure to gestational diabetes are associated with children's metabolic health. Pediatr Obes 2012;7:44–52.

19. Mehta SH, Kruger M, Sokol RJ. Is maternal diabetes a risk factor for childhood obesity? J Matern Fetal Neonatal Med 2012;25:41–4.

20. Pettitt DJ, McKenna S, McLaughlin C, et al. Maternal glucose at 28 weeks of gestation is not associated with obesity in 2-yearold offspring: the Belfast Hyperglycemia and Adverse Pregnancy Outcome (HAPO) family study. Diabetes Care 2010;33:1219–23.

21. Zhao P, Liu E, Qiao Y, et al. Maternal gestational diabetes and childhood obesity at age 9-11: results of a multinational study. Diabetologia 2016;59:2339–48.

22. Logan KM, Emsley RJ, Jeffries S, et al. Development of early adiposity in infants of mothers with gestational diabetes mellitus. Diabetes Care 2016;39:1045–51.

23. Kc K, Shakya S, Zhang H. Gestational diabetes mellitus and macrosomia: a literature review. Ann Nutr Metab 2015;66 Suppl 2:14–20.

24. Clausen TD, Mathiesen ER, Hansen T, et al. High prevalence of type 2 diabetes and pre-diabetes in adult offspring of women with gestational diabetes mellitus or type 1 diabetes: the role of intrauterine hyperglycemia. Diabetes Care 2008;31:340–6.

25. Dello Russo M, Ahrens W, De Vriendt T, et al. Gestational weight gain and adiposity, fat distribution, metabolic profile, and blood pressure in offspring: the IDEFICS project. Int J Obes 2013;37:914–9.

26. Black MH, Sacks DA, Xiang AH, et al. The relative contribution of prepregnancy overweight and obesity, gestational weight gain, and IADPSG-defined gestational diabetes mellitus to fetal overgrowth. Diabetes Care 2013;36:56–62.

27. Harrod CS, Chasan-Taber L, Reynolds RM, et al. Physical activity in pregnancy and neonatal body composition: the Healthy Start study. Obstet Gynecol 2014;124:257–64.

28. Lovejoy MC, Graczyk PA, O'Hare E, et al. Maternal depression and parenting behavior: a meta-analytic review. Clin Psychol Rev 2000;20:561–92.

29. Carter AS, Garrity-Rokous FE, Chazan-Cohen R, et al. Maternal depression and comorbidity: predicting early parenting, attachment security, and toddler social-emotional problems and competencies. J Am Acad Child Adolesc Psychiatry 2001;40:18–26.

30. Hoffman C, Crnic KA, Baker JK. Maternal Depression and Parenting: Implications for Children's Emergent Emotion Regulation and Behavioral Functioning. Parenting 2006;6:271–95.

31. Wake M, Nicholson JM, Hardy P, et al. Preschooler obesity and parenting styles of mothers and fathers: Australian national population study. Pediatrics 2007;120:e1520–e1527.

32. Cosson E, Bihan H, Reach G, et al. Psychosocial deprivation in women with gestational diabetes mellitus is associated with poor fetomaternal prognoses: an observational study. BMJ Open 2015;5:e007120.

33. Ng M, Fleming T, Robinson M, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: A systematic analysis for the global burden of disease study 2013. Lancet 2014;384:766–81.

34. Hirst JE, Villar J, Papageorghiou AT, et al. Preventing childhood obesity starts during pregnancy. Lancet 2015;386:1039–40.

35. Koivusalo SB, Rönö K, Klemetti MM, et al. Gestational diabetes mellitus can be prevented by lifestyle intervention: The finnish gestational diabetes prevention study (radiel): A randomized controlled trial. Diabetes Care 2016;39:24–30.

36. Brownfoot FC, Davey MA, Kornman L. Routine weighing to reduce excessive antenatal weight gain: a randomised controlled trial. BJOG 2016;123:254–61.

37. Bao W, Bowers K, Tobias DK, et al. Prepregnancy dietary protein intake, major dietary protein sources, and the risk of gestational diabetes mellitus: a prospective cohort study. Diabetes Care 2013;36:2001–8.

38. Garaulet M, Madrid JA. Chronobiological aspects of nutrition, metabolic syndrome and obesity. Adv Drug Deliv Rev 2010;62:967–78.

39. Pot GK, Almoosawi S, Stephen AM. Meal irregularity and cardiometabolic consequences: results from observational and intervention studies. Proc Nutr Soc 2016;75:475–86.

40. Alhussain MH, Macdonald IA, Taylor MA. Irregular meal-pattern effects on energy expenditure, metabolism, and appetite regulation: a randomized controlled trial in healthy normal-weight women. Am J Clin Nutr 2016;104:21–32.

41. Renault KM, Carlsen EM, Nørgaard K, et al. Intake of sweets, snacks and soft drinks predicts weight gain in obese pregnant women: Detailed analysis of the results of a randomised controlled trial. PLoS One 2015;10:e0133041.

42. Fuglestad PT, Jeffery RW, Sherwood NE. Lifestyle patterns associated with diet, physical activity, body mass index and amount of recent weight loss in a sample of successful weight losers. Int J Behav Nutr Phys Act 2012;9:79.

43. Hosler AS, Nayak SG, Radigan AM. Stressful events, smoking exposure and other maternal risk factors associated with gestational diabetes mellitus. Paediatr Perinat Epidemiol 2011;25:566–74.

44. Spirito A, Ruggiero L, Bowen A, et al. Stress, coping, and social support as mediators of the emotional status of women with gestational diabetes. Psychol Health 1991;5:111–20.

45. Horsch A, Kang JS, Vial Y, et al. Stress exposure and psychological stress responses are related to glucose concentrations during pregnancy. Br J Health Psychol 2016;21:712–29.

46. Giesbrecht GF, Campbell T, Letourneau N, et al. Psychological distress and salivary cortisol covary within persons during pregnancy. Psychoneuroendocrinology 2012;37:270–9.

47. Sauder KA, Starling AP, Shapiro AL, et al. Diet, physical activity and mental health status are associated with dysglycaemia in pregnancy: the Healthy Start Study. Diabet Med 2016;33:663–7.

48. Leppänen M, Aittasalo M, Raitanen J, et al. Physical activity during pregnancy: predictors of change, perceived support and barriers among women at increased risk of gestational diabetes. Matern Child Health J 2014;18:2158–66.

49. Lydon K, Dunne FP, Owens L, et al. Psychological stress associated with diabetes during pregnancy: a pilot study. Ir Med J 2012;105:26–8.

50. Perales M, Refoyo I, Coteron J, et al. Exercise during pregnancy attenuates prenatal depression: a randomized controlled trial. Eval Health Prof 2015;38:59–72.

51. Huang C, Momma H, Cui Y, et al. Independent and combined relationship of habitual unhealthy eating behaviors with depressive symptoms: A prospective study. J Epidemiol 2017;27:42–7.

52. Mantzios M, Wilson JC. Making concrete construals mindful: a novel approach for developing mindfulness and self-compassion to assist weight loss. Psychol Health 2014;29:422–41.

53. Mantzios M, Wilson JC. Exploring mindfulness and mindfulness with self-compassion-centered interventions to assist weight loss: Theoretical considerations and preliminary results of a randomized pilot study. Mindfulness 2015;6:824–35.

54. Alberts HJ, Mulkens S, Smeets M, et al. Coping with food cravings. Investigating the potential of a mindfulness-based intervention. Appetite 2010;55:160–3.

55. Louie JC, Brand-Miller JC, Markovic TP, et al. Glycemic index and pregnancy: a systematic literature review. J Nutr Metab 2010;2010:1–8.

56. Viana LV, Gross JL, Azevedo MJ. Dietary intervention in patients with gestational diabetes mellitus: a systematic review and metaanalysis of randomized clinical trials on maternal and newborn outcomes. Diabetes Care 2014;37:3345–55.

57. Wei J, Heng W, Gao J. Effects of low glycemic index diets on gestational diabetes mellitus: A meta-analysis of randomized controlled clinical trials. Medicine 2016;95:e3792.

58. Han S, Middleton P, Shepherd E, et al. Different types of dietary advice for women with gestational diabetes mellitus. Cochrane Database Syst Rev 2017;2:Cd009275.

59. Bowers K, Tobias DK, Yeung E, et al. A prospective study of prepregnancy dietary fat intake and risk of gestational diabetes. Am J Clin Nutr 2012;95:446–53.

60. Risérus U, Willett WC, Hu FB. Dietary fats and prevention of type 2 diabetes. Prog Lipid Res 2009;48:44–51.

61. Schoenaker DA, Mishra GD, Callaway LK, et al. The role of energy, nutrients, foods, and dietary patterns in the development of gestational diabetes mellitus: A systematic review of observational studies. Diabetes Care 2016;39:16–23.

62. Bao W, Li S, Chavarro JE, et al. Low carbohydrate-diet scores and long-term risk of type 2 diabetes among women with a history of gestational diabetes mellitus: A prospective cohort study. Diabetes Care 2016;39:43–9.

63. Hernandez TL, Van Pelt RE, Anderson MA, et al. Women with gestational diabetes mellitus randomized to a higher-complex carbohydrate/low-fat diet manifest lower adipose tissue insulin resistance, inflammation, glucose, and free fatty acids: A pilot study. Diabetes Care 2016;39:39–42.

64. Youngwanichsetha S, Phumdoung S, Ingkathawornwong T. The effects of mindfulness eating and yoga exercise on blood sugar levels of pregnant women with gestational diabetes mellitus. Appl Nurs Res 2014;27:227–30.

65. Mason AE, Epel ES, Kristeller J, et al. Effects of a mindfulnessbased intervention on mindful eating, sweets consumption, and fasting glucose levels in obese adults: data from the SHINE randomized controlled trial. J Behav Med 2016;39:201–13.

66. Anon. ACog committee opinion no. 650: Physical activity and exercise during pregnancy and the postpartum period. Obstet Gynecol 2015;126:e135–42.

67. Colberg SR, Sigal RJ, Yardley JE, et al. Physical activity/exercise and diabetes: A position statement of the american diabetes association. Diabetes Care 2016;39:2065–79.

68. Colberg SR, Castorino K, Jovanovič L. Prescribing physical activity to prevent and manage gestational diabetes. World J Diabetes 2013;4:256–62.

69. Melzer K, Schutz Y, Boulvain M, et al. Physical activity and pregnancy. Sports Medicine 2010;40:493–507.

70. Ruchat SM, Mottola MF. The important role of physical activity in the prevention and management of gestational diabetes mellitus. Diabetes Metab Res Rev 2013;29:334–46.

71. May LE, Scholtz SA, Suminski R, et al. Aerobic exercise during pregnancy influences infant heart rate variability at one month of age. Early Hum Dev 2014;90:33–8.

72. Horsch A, Gross J, Jornayvaz FR, et al. [Gestational diabetes– what are the non-medical approaches?]. Rev Med Suisse 2016;12:1089–91.

73. Brazeau AS, Leong A, Meltzer SJ, et al. Group-based activities with on-site childcare and online support improve glucose tolerance in women within 5 years of gestational diabetes pregnancy. Cardiovasc Diabetol 2014;13:104.

74. Dasgupta K, Da Costa D, Pillay S, et al. Strategies to optimize participation in diabetes prevention programs following gestational diabetes: a focus group study. PLoS One 2013;8:e67878.

75. Brown HL. Acog guidelines at a glance: Gestational diabetes mellitus. Obstetrics and gynecology 2013;122:406–16.

76. Gabbe SG, Landon MB, Warren-Boulton E, et al. Promoting health after gestational diabetes: A national diabetes education program call to action. Obstet Gynecol 2012;119:171.

77. Sattar N, Wannamethee SG, Forouhi NG. Novel biochemical risk factors for type 2 diabetes: pathogenic insights or prediction possibilities? Diabetologia 2008;51:926–40.

78. Tobias DK, Hu FB, Chavarro J, et al. Healthful dietary patterns and type 2 diabetes mellitus risk among women with a history of gestational diabetes mellitus. Arch Intern Med 2012;172:1566–72.

79. Ferrara A, Hedderson MM, Albright CL, et al. A pregnancy and postpartum lifestyle intervention in women with gestational diabetes mellitus reduces diabetes risk factors: a feasibility randomized control trial. Diabetes Care 2011;34:1519–25.

80. Ferrara A, Hedderson MM, Albright CL, et al. A pragmatic cluster randomized clinical trial of diabetes prevention strategies for women with gestational diabetes: design and rationale of the Gestational Diabetes' Effects on Moms (GEM) study. BMC Pregnancy Childbirth 2014;14:21.

81. Kaiser B, Jeannot E, Razurel C. Determinants of health behaviors after gestational diabetes mellitus: A prospective cohort study in geneva. J Midwifery Womens Health 2016:571–7.

82. Koh D, Miller YD, Marshall AL, et al. Health-enhancing physical activity behaviour and related factors in postpartum women with recent gestational diabetes mellitus. J Sci Med Sport 2010;13:42–5.

83. Woo Baidal JA, Locks LM, Cheng ER, et al. Risk factors for childhood obesity in the first 1,000 days: A systematic review. Am J Prev Med 2016;50:761–79.

84. Birch LL, Anzman-Frasca S, Paul IM. Starting early: obesity prevention during infancy. Nestle Nutr Inst Workshop Ser 2012;73:81–94.

85. Paul IM, Bartok CJ, Downs DS, et al. Opportunities for the primary prevention of obesity during infancy. Adv Pediatr 2009;56:107–33.

86. Redsell SA, Edmonds B, Swift JA, et al. Systematic review of randomised controlled trials of interventions that aim to reduce the risk, either directly or indirectly, of overweight and obesity in infancy and early childhood. Matern Child Nutr 2016;12:24–38.

87. Stifter CA, Anzman-Frasca S, Birch LL, et al. Parent use of food to soothe infant/toddler distress and child weight status. An exploratory study. Appetite 2011;57:693–9.

88. Wardle J, Sanderson S, Guthrie CA, et al. Parental feeding style and the inter-generational transmission of obesity risk. Obes Res 2002;10:453–62.

89. Reilly JJ, Armstrong J, Dorosty AR, et al. Early life risk factors for obesity in childhood: cohort study. BMJ 2005;330:1357.

90. Wen LM, Baur LA, Rissel C, et al. Correlates of body mass index and overweight and obesity of children aged 2 years: findings from the healthy beginnings trial. Obesity 2014;22:1723–30.

91. de Vries AG, Huiting HG, van den Heuvel ER, et al. An activity stimulation programme during a child's first year reduces some indicators of adiposity at the age of two-and-a-half. Acta Paediatr 2015;104:414–21.

92. Paul IM, Williams JS, Anzman-Frasca S, et al. The Intervention Nurses Start Infants Growing on Healthy Trajectories (INSIGHT) study. BMC Pediatr 2014;14:184.

93. French GM, Nicholson L, Skybo T, et al. An evaluation of mothercentered anticipatory guidance to reduce obesogenic infant feeding behaviors. Pediatrics 2012;130:e507–517.

94. Schwarzer R. Modeling Health Behavior Change: How to Predict and Modify the Adoption and Maintenance of Health Behaviors. Appl Psychol 2008;57:1–29.

95. Berli C, Stadler G, Inauen J, et al. Action control in dyads: A randomized controlled trial to promote physical activity in everyday life. Soc Sci Med 2016;163:89–97.

96. Leventhal H, Singer R, Jones S. EFFECTS OF FEAR AND SPECIFICITY OF RECOMMENDATION UPON ATTITUDES AND BEHAVIOR. J Pers Soc Psychol 1965;2:20–9.

97. Gollwitzer PM. Implementation intentions: Strong effects of simple plans. Am Psychol 1999;54:493–503.

98. Gollwitzer PM, Sheeran P. Implementation intentions and goal achievement: A meta-analysis of effects and processes. Adv Exp Soc Psychol 2006;38:69–119.

99. Hagger MS, Luszczynska A. Implementation intention and action planning interventions in health contexts: state of the research and proposals for the way forward. Appl Psychol Health Well Being 2014;6:1–47.

100. Hagger MS, Luszczynska A, de Wit J, et al. Implementation intention and planning interventions in Health Psychology: Recommendations from the Synergy Expert Group for research and practice. Psychol Health 2016;31:814–39.

101. Sniehotta FF, Scholz U, Schwarzer R. Action plans and coping plans for physical exercise: A longitudinal intervention study in cardiac rehabilitation. Br J Health Psychol 2006;11:23–37.

102. Kwasnicka D, Presseau J, White M, et al. Does planning how to cope with anticipated barriers facilitate health-related behavior change? A systematic review. Health Psychol Rev 2013;7:129–45.

103. Seshiah V, Balaji V. Primordial prevention: maternal health and diabetes. Diabetes Manag 2013;3:333–41.

104. Halperin IJ, Feig DS. The role of lifestyle interventions in the prevention of gestational diabetes. Curr Diab Rep 2014;14:452.

105. Craig P, Dieppe P, Macintyre S, et al. Developing and evaluating complex interventions: the new Medical Research Council guidance. Int J Nurs Stud 2013;50:587–92.

106. Metzger BE, Gabbe SG, Persson B, et al. International Association of Diabetes and Pregnancy Study Groups Recommendations on the Diagnosis and Classification of Hyperglycemia in Pregnancy: Response to Weinert. Diabetes Care 2010;33:e98–82.

107. Nolan CJ. Controversies in gestational diabetes. Best Pract Res Clin Obstet Gynaecol 2011;25:37–49.

108. Crowther CA, Hiller JE, Moss JR, et al. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. N Engl J Med 2005;352:2477–86.

109. Sox HC, Greenfield S. Comparative effectiveness research: a report from the Institute of Medicine. Ann Intern Med 2009;151:203–5.

110. Yaktine AL, Rasmussen KM. Weight gain during pregnancy: reexamining the guidelines. Washington (DC): National Academies Press, 2009.

111. Carroll DG, Kelley KW. Review of metformin and glyburide in the management of gestational diabetes. Pharm Pract 2014;12:528.

112. Ferrer RL, Carrasco AV. Capability and clinical success. Ann Fam Med 2010;8:454–60.

113. Daniels LA, Mallan KM, Nicholson JM, et al. Outcomes of an early feeding practices intervention to prevent childhood obesity. Pediatrics 2013;132:e109–118.

114. Farrow C, Blissett J. Does maternal control during feeding moderate early infant weight gain? Pediatrics 2006;118:e293–e298.

115. Gunderson EP, Hurston SR, Ning X, et al. Lactation and Progression to Type 2 Diabetes Mellitus After Gestational Diabetes Mellitus: A Prospective Cohort Study. Ann Intern Med 2015;163:889–98.

116. Herring SJ, Rich-Edwards JW, Oken E, et al. Association of postpartum depression with weight retention 1 year after childbirth. Obesity 2008;16:1296–301.

117. Hori H, Teraishi T, Sasayama D, et al. Relationship of temperament and character with cortisol reactivity to the combined dexamethasone/CRH test in depressed outpatients. J Affect Disord 2013;147:128–36.

118. Iglowstein I, Jenni OG, Molinari L, et al. Sleep duration from infancy to adolescence: reference values and generational trends. Pediatrics 2003;111:302–7.

119. Mallan KM, Daniels LA, Wilson JL, et al. Association between maternal depressive symptoms in the early post-natal period and responsiveness in feeding at child age 2 years. Matern Child Nutr 2015;11:926–35.

120. Mallan KM, Sullivan SE, de Jersey SJ, et al. The relationship between maternal feeding beliefs and practices and perceptions of infant eating behaviours at 4 months. Appetite 2016;105:1–7.

121. Paul IM, Savage JS, Anzman SL, et al. Preventing obesity during infancy: a pilot study. Obesity 2011;19:353–61.

122. Redsell SA, Weng S, Swift JA, et al. Validation, Optimal Threshold Determination, and Clinical Utility of the Infant Risk of Overweight Checklist for Early Prevention of Child Overweight. Child Obes 2016;12:202–9.

123. Taveras EM, Blackburn K, Gillman MW, et al. First steps for mommy and me: a pilot intervention to improve nutrition and physical activity behaviors of postpartum mothers and their infants. Matern Child Health J 2011;15:1217–27.

124. Zarrinpar A, Chaix A, Panda S. Daily Eating Patterns and Their Impact on Health and Disease. Trends Endocrinol Metab 2016;27:69–83.

125. SSN. Swiss Society for Nutrition. Nutritional recommendations for Germany, Autria and Switzerland (DACH): Les valeurs de référence DACH pour les apports nutritionnels. 2ème édn, 2015.

126. Ansermet O, Aebi A. Influence des protéines et des lipides chez le diabétique de type 1. Genève, Switzerland: Haute école de santé, 2016.

127. Ley SH, Hamdy O, Mohan V, et al. Prevention and management of type 2 diabetes: dietary components and nutritional strategies. Lancet 2014;383:1999–2007.

128. Marathe PH, Gao HX, Close KL. American Diabetes Association Standards of Medical Care in Diabetes 2017. J Diabetes 2017;9:320–4.

129. Mantzios M, Wilson JC. Mindfulness, Eating Behaviours, and Obesity: A Review and Reflection on Current Findings. Curr Obes Rep 2015;4:141–6.

130. Mathieu J. What should you know about mindful and intuitive eating? J Am Diet Assoc 2009;109:1982–7.

131. Medina WL, Wilson D, de Salvo V, et al. Effects of Mindfulness on Diabetes Mellitus: Rationale and Overview. Curr Diabetes Rev 2017;13:141–7.

132. Barakat R, Lucia A, Ruiz JR. Resistance exercise training during pregnancy and newborn's birth size: a randomised controlled trial. Int J Obes 2009;33:1048–57.

133. Organization WH. Global strategy on diet, physical activity and health: WHO, 2017.

134. Healy GN, Dunstan DW, Salmon J, et al. Breaks in sedentary time: beneficial associations with metabolic risk. Diabetes Care 2008;31:661–6.

135. Excellence NIfHaC. Antenatal and postnatal mental health: clinical management and service guidance. London: National Institute for Health and Care Excellence, 2014.

136. Sockol LE. A systematic review of the efficacy of cognitive behavioral therapy for treating and preventing perinatal depression. J Affect Disord 2015;177:7–21.

137. Tremblay MS, Leblanc AG, Carson V, et al. Canadian Physical Activity Guidelines for the Early Years (aged 0-4 years). Appl Physiol Nutr Metab 2012;37:345–56.

138. Michie S, Richardson M, Johnston M, et al. The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: building an international consensus for the reporting of behavior change interventions. Ann Behav Med 2013;46:81–95.

139. Da Costa D, Dritsa M, Larouche J, et al. Psychosocial predictors of labor/delivery complications and infant birth weight: a prospective multivariate study. J Psychosom Obstet Gynaecol 2000;21:137–48.

140. Devsam BU, Bogossian FE, Peacock AS. An interpretive review of women's experiences of gestational diabetes mellitus: proposing a framework to enhance midwifery assessment. Women Birth 2013;26:e69–e76.

141. Wadhwa PD, Entringer S, Buss C, et al. The contribution of maternal stress to preterm birth: issues and considerations. Clin Perinatol 2011;38:351–84.

142. S db, M Y, E A, et al. Assessing the consequences of gestational diabetes mellitus on offspring's cardiovascular health: MySweetHeart Cohort study protocol, Switzerland. BMJ Open in press 2017;7:e016972.

143. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. Br J Psychiatry 1987;150:782–6.

144. Bunevicius A, Kusminskas L, Pop VJ, et al. Screening for antenatal depression with the Edinburgh Depression Scale. J Psychosom Obstet Gynaecol 2009;30:238–43.

145. Guedeney N, Fermanian J. Validation study of the French version of the Edinburgh Postnatal Depression Scale (EPDS): new results about use and psychometric properties. Eur Psychiatry 1998;13:83–9.

146. Koch FS, Sepa A, Ludvigsson J. Psychological stress and obesity. J Pediatr 2008;153:839–44.

147. Obel C, Hedegaard M, Henriksen TB, et al. Stress and salivary cortisol during pregnancy. Psychoneuroendocrinology 2005;30:647–56.

148. Jean-Marc T. Plan de codage des variables: questionnaires activité physique (PAFQ) et alimentaires (FFQ), 2009.

149. Theler. Food frequency questionnaire. Switzerland, 2016.

150. Daundasekara SS, Beasley AD, O'Connor DP, et al. Validation^of the intuitive Eating Scale for pregnant women. Appetite 2017;112:201–9.

151. Camilleri GM, Méjean C, Bellisle F, et al. Cross-cultural validity of the Intuitive Eating Scale-2. Psychometric evaluation in a sample of the general French population. Appetite 2015;84:34–42.

152. Tylka TL, Kroon Van Diest AM. The Intuitive Eating Scale-2: item refinement and psychometric evaluation with college women and men. J Couns Psychol 2013;60:137–53.

153. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. Acta Psychiatr Scand 1983;67:361–70.

154. Bocéréan C, Dupret E. A validation study of the Hospital Anxiety and Depression Scale (HADS) in a large sample of French employees. BMC Psychiatry 2014;14:1.

155. Herrmann C, Buss U, Snaith R. Hospital Anxiety and Depression Scale–Deutsche Version [Ein Fragebogen von Angst und Depressivität in der somatischen Medizin]. Bern, Schweiz: Hans Huber, 1995.

156. Topp CW, Østergaard SD, Søndergaard S, et al. The WHO-5 Well-Being Index: a systematic review of the literature. Psychother Psychosom 2015;84:167–76.

157. Hochberg G, Pucheu S, Kleinebreil L, et al. WHO-5, a tool focusing on psychological needs in patients with diabetes: the French contribution to the DAWN study. Diabetes Metab 2012;38:515–22.

158. Abidin R, Index PS. Parenting Stress Index (PSI). Odessa, FL: Psychological Assessment Resources:Inc, 1995.

159. Singer LT, Salvator A, Guo S, et al. Maternal psychological distress and parenting stress after the birth of a very low-birth-weight infant. JAMA 1999;281:799–805.

160. Smith MT, Wegener ST. Measures of sleep: The Insomnia Severity Index, Medical Outcomes Study (MOS) Sleep Scale, Pittsburgh Sleep Diary (PSD), and Pittsburgh Sleep Quality Index (PSQI). Arthritis & Rheumatism 2003;49:S184–196.

161. Raphael H. Pittsburgh sleep quality index, 2016.

162. Moser A, Stuck AE, Silliman RA, et al. The eight-item modified Medical Outcomes Study Social Support Survey: psychometric evaluation showed excellent performance. J Clin Epidemiol 2012;65:1107–16.

163. Wild D, Grove A, Martin M, et al. Principles of Good Practice for the Translation and Cultural Adaptation Process for Patient-Reported Outcomes (PRO) Measures: report of the ISPOR Task Force for Translation and Cultural Adaptation. Value Health 2005;8:94–104.

164. Stifter C. Food to soothe questionnaire, 2016.

165. Thompson AL, Mendez MA, Borja JB, et al. Development and validation of the Infant Feeding Style Questionnaire. Appetite 2009;53:210–21.

166. Thompson A. Infant feeding style questionnaire: satiety subscale, 2016.

167. Sadeh A. A brief screening questionnaire for infant sleep problems: validation and findings for an Internet sample. Pediatrics 2004;113:e570–e577.

168. Sadeh A. Brief infant sleep questionnaire. 2016.

169. Esliger DW, Rowlands AV, Hurst TL, et al. Validation of the GENEA Accelerometer. Med Sci Sports Exerc 2011;43:1085–93.

170. Sykes K, Roberts A. The Chester step test—a simple yet effective tool for the prediction of aerobic capacity. Physiotherapy 2004;90:183–8.

171. Melzer K, Lazzeri M, Armand S, et al. Validation of the Actiheart for estimating physical activity related energy expenditure in pregnancy. Espen J 2012;7:e5–e10.

172. Roberts HC, Denison HJ, Martin HJ, et al. A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach. Age Ageing 2011;40:423–9.

173. Bertrand PC. Marche à suivre pour la mesure de la composition corpoirelle par BIA (Body impedance analyser RJL systems- AKERN). Lausanne, Suisse: CCHU, 2008.

174. Guida B, Trio R, Pecoraro P, et al. Impedance vector distribution by body mass index and conventional bioelectrical impedance analysis in obese women. Nutr Metab Cardiovasc Dis 2003;13:72–9.

175. Knonthropometry ISftao. International standards for anthropometric assessment: International Society for the advancement of Knonthropometry.

176. Durnin JV, Womersley J. Body fat assessed from total body density and its estimation from skinfold thickness: measurements on 481 men and women aged from 16 to 72 years. Br J Nutr 1974;32:77–97.

177. Dauncey MJ, Gandy G, Gairdner D. Assessment of total body fat in infancy from skinfold thickness measurements. Arch Dis Child 1977;52:223–7.

178. Rothman KJ. No adjustments are needed for multiple comparisons. Epidemiology 1990;1:43–6.

179. Oakley A, Strange V, Bonell C, et al. Process evaluation in randomised controlled trials of complex interventions. BMJ 2006;332:413–6.

180. Ferrara A, Hedderson MM, Brown SD, et al. The comparative effectiveness of diabetes prevention strategies to reduce postpartum weight retention in women with gestational diabetes mellitus: The Gestational Diabetes' Effects on Moms (GEM) cluster randomized controlled trial. Diabetes Care 2016;39:65–74.

181. Nishida C. Guideline: sugars intake for adults and children, 2016.

182. Les hydrates de carbone dans l'alimentation: résumés des chapitres. Les hydrates de carbone dans l'alimentation. Berne, Switzerland: Federal Office of Public Health Fsd, 2009.

183. Montonen J, Knekt P, Järvinen R, et al. Whole-grain and fiber intake and the incidence of type 2 diabetes. Am J Clin Nutr 2003;77:622–9.

184. Lake AC M. Breastfeeding: a key to sustainable development. World breastfeeding week Message 2016: Organization UWH, 2016.

185. Swiss Society for Nutrition Nutritional recommendations. L'alimentation du nourrisson durant la première année de vie. Berne: Swiss Society for Nutrition Nutritional recommendations, 2012.

186. Phillips DI, Clark PM, Hales CN, et al. Understanding oral glucose tolerance: comparison of glucose or insulin measurements during the oral glucose tolerance test with specific measurements of insulin resistance and insulin secretion. Diabet Med 1994;11:286–92.

187. Berry JO, Jones WH. The parental stress scale: initial psychometric evidence. J Soc Pers Relat 1995;12:463–72.

188. Abidin RR, Brunner JF. Development of a parenting alliance inventory. J Clin Child Psychol 1995;24:31–40.

8.3 Submitted Study C

In revision in Journal of Psychosomatic Research.

Mental health and its associations with weight in women with gestational diabetes mellitus. A prospective clinical cohort study.

Short title: **Mental health and weight in pregnancy.**

The work was conducted at the Obstetric service, Department Woman-Mother-Child, Lausanne University Hospital, Lausanne, Switzerland

Leah Gilbert MSc*[1], Jean-Benoît Rossel PhD[1], Dan Yedu Quansah PhD[1], Jardena J. Puder Prof.#[1] and Antje Horsch Prof.#[2,3]

[1] Obstetric service, Department Woman-Mother-Child, Lausanne University Hospital, Lausanne, Switzerland

[2] Institute of Higher Education and Research in Healthcare (IUFRS), University of Lausanne, Lausanne, Switzerland

[3] Neonatology Service, Department Woman-Mother-Child, Lausanne University Hospital, Lausanne, Switzerland

*Corresponding author information: Leah Gilbert, Avenue Pierre-Decker 2, 1011 Lausanne (e-mail: leah.gilbert@chuv.ch).

Joint last authors

Highlights

- Women with GDM (gestational diabetes mellitus) generally have poorer mental health.
- In our population, well-being increased between GDM diagnosis and late pregnancy.
- Well-being and depression were inversely associated after GDM diagnosis.
- Depression was positively associated with weight gain during pregnancy.

Abstract

Objective Despite the prevalence of depression in women with gestational diabetes mellitus (GDM) and the relationship of mental health (depression and well-being) with metabolic health, little is known about mental health and its metabolic impact in GDM pregnancy. This prospective clinical

cohort study aimed to investigate the association between 1) well-being and depression, and 2) between mental health and weight/weight gain in women with GDM.

Methods We included 334 pregnant women with GDM treated at a University Hospital between January 2016 and December 2018. They completed two self-report questionnaires: The World Health Organization well-being index (WHO-5) at the first (29 weeks of gestation) and last visit (36 weeks of gestation) at the GDM clinic and the Edinburgh Postnatal Depression Scale (EPDS) at the first visit; a cut-off of ≥ 11 was selected for the latter to indicate the presence of clinically relevant symptoms of depression.

Results Well-being increased by 11.8% (7.1± 16.5 points; CI=4.9-9.3; ; p<0.0001) during GDM pregnancy. There was an inverse association between the well-being and depression scores at the first GDM visit (r= -0.55; p<0.0001). Concerning associations between mental health and weight, clinically relevant depression symptoms at the first GDM visit were associated with subsequent weight gain until the end of pregnancy (β=1.249; *p*=0.019).

Conclusions In women with GDM, patients with clinically relevant depression symptoms are at risk of gaining more weight during pregnancy.

Keywords:

cohort, depression, EPDS, pregnancy, well-being, weight, WHO-5

Introduction

In women with GDM (gestational diabetes mellitus), mental health is still understudied, particularly with regards to its association with metabolic health parameters, such as weight (1). However, mental health and weight are both important factors to consider in women with GDM, for several reasons. Regarding mental health, depression in pregnancy is associated with multiple adverse metabolic and mental health outcomes for both, the mother and the child (2, 3). Firstly, depression in pregnancy often leads to low birth weight and preterm delivery (4) and is associated with a higher risk of instrumental delivery (5, 6). Secondly, it is associated with difficulties in breastfeeding (7) and poor attachment with the new-born (8). Finally, depression during pregnancy is also associated with a higher risk of developing GDM (9-11), and women with GDM have a three times higher risk of developing depressive symptoms during late pregnancy (12-14). Nevertheless, the effect of depression during a GDM pregnancy is still understudied.

It is important to capture mental health in a comprehensive way. Although depression plays an important role in women with GDM, it is also essential to investigate well-being, as positive emotional health is an important factor to consider when studying diabetes (15). Furthermore, depression and well-being might be related, and there is a lack of research on well-being in women with GDM. Well-being, more precisely, emotional well-being as measured by the World Health Organisation – Five Well-Being Index (WHO-5) (16), can be described as "the emotional quality of an individual's everyday experience—the frequency and intensity of experiences of joy, stress, sadness, anger, and affection that make one's life pleasant or unpleasant" (17). Thus, the first aim of this study was to analyse the association between well-being and depression.

In GDM, both weight and excessive weight gain are essential health parameters, and weight gain is higher in this population (18). It can increase adverse outcomes, such as hypertensive disorders during pregnancy (19) and weight retention in the postpartum period, and augment the risk of developing type 2 diabetes and cardiovascular disease later in life (20-23). Excessive gestational weight gain in women with GDM may also lead to perinatal complications, such as a higher risk of preterm and caesarean delivery, macrosomia, and to birth weights over the 90th percentile for age and sex (24-26). Given the numerous adverse consequences related to excessive weight or weight gain in women with GDM, it is important to understand all factors which might influence weight during GDM pregnancy.

In the general pregnant population, antepartum depression can have consequences on metabolic health, especially on weight gain (27-29). Indeed, individuals with psychological and emotional discomfort tend to eat as a strategy to relieve themselves of negative symptoms (30). Also, depression and stress may diminish coping abilities in individuals and can result in disordered eating behaviours and lower dietary quality (31). Pregnant women experiencing depression and stress are more likely to consume energy-dense, nutrient-poor foods, thus decreasing their dietary quality and increasing their risk for excessive gestational weight gain and subsequent obesity (31). Well-being is also important to consider, as well-being between pregnancy and five years later is associated with less weight retention in the general population (32). Moreover, outside of pregnancy, a higher score of well-being in diabetic patients is associated with a better diet and higher physical activity (15) and thus might also be related to health behaviour impacting weight in women with GDM. Although the link between depression, well-being and weight or weight gain is particularly relevant in women with GDM, this is an understudied area. Thus, our second aim was to investigate the association between

mental health (depression and well-being) and weight and weight gain in these women during pregnancy.

Materials and Methods

Setting

This prospective clinical cohort study included pregnant women diagnosed with GDM after their first visit at the GDM clinic at a University Hospital in Switzerland between January 2016 and December 2018. During the first clinical visit that takes place at around 29 weeks of gestation (Mean=28.9 ±SD=3.3), patients are generally seen by a clinical nurse specialist in GDM or a physician; they receive information on GDM, and are taught how to perform a capillary blood glucose test. Women are usually seen by a dietician one week later and then followed up by a nurse or a physician about once every two weeks. Women commonly attend their last GDM visit before giving birth at around 36 weeks of gestation (Mean=36.2 ±SD=1.9)

Participant consent and recruitment

Women who were diagnosed with GDM according to the American Diabetes Association (ADA) guidelines and the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) (21, 33), were asked to take part in the GDM cohort by the research team and were given a consent form to sign containing further information on data usage. The « Commission Cantonale (VD) d'éthique de la recherche sur l'être humain (CER-VD) » approved the study protocol "Impact du diabète gestationnel sur la mère et son enfant pendant et après la grossesse" (study n° 326/15).

Inclusion and exclusion criteria

Subjects were eligible if they had a GDM diagnosis, were followed up in our clinic between 2016 (when we started to routinely collect mental health data) and December 2018, and gave written consent to participate. Therefore, 334 consecutive women were included in this study.

Measures

Maternal depression symptoms

Edinburgh Postnatal Depression Scale (EPDS) : This scale is used to measure symptoms of depression in the preceding seven days (34). Each item is scored on a 4-point scale, the minimum and maximum scores being 0 and 30, respectively. The EPDS has been validated in pregnant women (35) as well as in a French sample of women in the postpartum period and the scale had good criterion

validity and internal consistency (Cronbach's alpha: 0.76) and good short term test-retest reliability (0.98) (36). In this study, we used the EPDS score as a continuous variable (depression score) and we also created a dichotomous variable with a cut-off of ≥ 11 (depression cut-off) as a score of ≥ 11 can indicate the presence of a major depressive disorder in pregnancy (35). Nonetheless, as the gold standard for depression screening is clinical interviewing (37), we interpreted a score of ≥ 11 as clinically relevant symptoms of depression. This questionnaire was given to the patients by the research team at the first GDM visit, in French or English. In order to ensure that we were accounting for the multi-ethnicity and diversity of women coming to our clinic, a professional certified translator assisted women who did not speak French or English to complete this questionnaire.

Maternal Well-being Index

World Health Organization - Five Well-Being Index (WHO-5): Well-being was measured with the WHO-5, which consists of 5 questions assessing the subjective well-being of the participants (38). The items are unidimensional and measure well-being by statements such as: "I have felt cheerful and in good spirits" on a 5-point Likert scale ranging from 0 'at no time' to 5 'all of the time'. The final score is then calculated by multiplying the score by 4, thus the score ranges from 0 to 100. The WHO-5 was originally designed to measure positive well-being (coping with illness), negative well-being (depression and anxiety) and energy, it used to be comprised of 28 items and was then reduced to fewer items (39). When the five-item version was developed studies demonstrated that it could be used to measure depression, indicated by a score of <13 (40) or < 50 if the score is multiplied by 4 (16). In other studies it also has been demonstrated to be highly negatively associated with self-reported and observer-rated measures of depressive symptoms (41). As the relationship between well-being and metabolic health in GDM pregnancy has not been studied so far, we chose to use this questionnaire to measure positive well-being (42). The scale has adequate validity, has good psychometric properties in French as the Cronbach's alpha is 0.88, confirming good internal consistency, it has been applied successfully across a wide range of study fields, though it has been used most extensively in endocrinology and (38, 43). This questionnaire was given at the first and last GDM visit to the patients by the research team. As the WHO-5 is validated in 31 different languages, we were able to distribute them in a variety of different languages.

Maternal anthropometric, obstetric and sociodemographic variables

At the first GDM visit, women were weighed in light clothes and without shoes, and their height was measured. Age, gestational age and educational level were assessed by interview or

extracted from obstetric charts. Additionally, patients answered questions about their social support (lives with partner vs lives alone) during the first GDM visit. At the last GDM visit, their weight was measured again. The weight gain variable was thus calculated by subtracting the weight at first GDM visit from the weight at last GDM visit.

Data analysis

All analyses were carried out with Stata/SE 15.0 (StataCorp LLC, TX, USA). Descriptive statistics were carried out for socio-demographic variables (please refer to Table 1). Ordinal outcomes were described as frequencies and percentages. For continuous variables, normality of distribution was graphically assessed with normal QQ-plots. Those variables were then described with their mean and standard deviation. Univariate linear regressions analyses were conducted for all aims (Model 1) in order to evaluate the raw associations between two variables of interest. These associations were then adjusted for confounding variables (Model 2, see below).

We first conducted a paired t-test to study if well-being changed between first GDM visit and the end of pregnancy (i.e., last GDM visit). For the first aim, we performed a linear regression where the independent variables were the depression score and cut-off of ≥ 11 at the first GDM visit and the dependent variable was the well-being score at the first GDM visit. For the second aim, the independent variables were the depression score and the cut-off of ≥ 11 and the well-being score, all at the first GDM visit; the dependent variables were weight at the first GDM visit and weight gain between the first and the last GDM visit. Adjustments for the following confounding variables were made for all linear regressions (Model 2): maternal age, gestational age, educational level, and social support. For the first aim, we also added BMI (Body Mass Index) at the first GDM visit as a confounder. For the second aim, we only added BMI as a confounder when the dependent variable was weight gain. Gestational age was added as a confounder, as it can have an impact on the mother's weight (44). Maternal educational level (45) and social support status (46) were added as confounders, as they have an impact on the mother's mental health. At the first GDM visit, there were seven missing cases for height, 18 missing cases for weight, 19 missing cases for BMI, 53 missing cases for weight gain, two missing cases for gestational age, five missing cases for ethnicity of the patients, 25 missing cases for social support, 57 missing cases for educational level, 42 missing cases for the depression score and cut-off, 39 missing cases for the well-being score at the first GDM visit. At the last GDM visit, there were 120 missing cases for gestational age and 105 missing cases for the well-being score. Based on the Missing at Random assumption, we conducted imputations by using the Multiple Imputation

by Chained Equations method. This led to similar results (data not shown; available upon request); thus, we chose to use the original data for the present analysis.

Data sharing statement

Data is available from the first author upon request.

Results

Sample characteristics

Sample characteristics are described in Table 1. At the first GDM visit, participants had a mean age of 33.4±5.5 years, a mean gestational age of 28.9±3.3 weeks, a mean weight of 78.3±14.8 kg, a mean well-being score of 60.1±20.2 and a mean depression score of 7.5±5.5, with 26.0% of women having clinically relevant symptoms of depression. At the last GDM visit, the mean gestational age was 36.2±1.9 weeks, the mean weight was 80.6±14.8 kg and the mean well-being score 67.2±18.3.

Table 1. Sample characteristics: Maternal sociodemographic, anthropometric, obstetric, and mental health variables.

	Mean (SD)	*n* (%)
Maternal sociodemographic and anthropometric variables		
Age (years)	33.4 (5.5)	
Educational level		
Compulsory education not completed		20 (7.2%)
Compulsory education completed		58 (20.9%)
Secondary school		40 (14.4%)
Apprenticeship		52 (18.8%)
University degree		107 (38.6%)
Social support		
Lives with partner		280 (90.6%)
Lives alone		29 (9.4%)
Weight (kg) at the first GDM visit	78.3 (14.8)	
Weight (kg) at the last GDM visit	80.6 (14.8)	
Weight gain (kg) between the first and last GDM visit	2.4 (3.5)	
BMI at the first GDM visit	29.2 (5.3)	
Obstetric variables		
Gestational age (weeks) at first GDM visit	28.9 (3.3)	
Gestational age (weeks) at last GDM visit	36.2 (1.9)	
Mental health variables		
Depression score at first GDM visit	7.5 (5.5)	

Depression cut-off ≥ 11 at first GDM visit		76 (26.0%)
Well-being score at first GDM visit	60.3 (20.5)	
Well-being score at last GDM visit	67.4 (17.9)	

BMI: body mass index.

Changes and associations between mental health variables during pregnancy

The well-being score increased from 60.3 ± 20.5 at the first GDM visit to 67.4 ± 17.9 at the end of pregnancy, indicating a 7.1 point (± 16.5) or an 11.8% increase on average in the in well-being score among study participants (CI=4.9-9.3; p<0.0001). An inverse strong association between the well-being score and the depression score (β=-2.08; r= -0.55; p<0.0001) and an inverse moderate association between the well-being score and the depression cut-off ≥11 at the first GDM visit (β=-21.77; r= -0.47; p<0.0001, see Table 2) were found. These associations remained significant after adjustments for confounders (β=-1.95; p<0.0001 and β=-20.93; p<0.0001; see Table 2).

Table 2. Association between mental health variables in women with GDM.

	Model l	Model 2
	β-Coefficient (95% confidence interval)	*β-Coefficient (95% confidence interval)*
	Well-being at the first GDM visit	
Depression score at the first GDM visit	-2.077 (-2.445 – -1.708)**	-1.953 (-2.373 – -1.532)**
Depression cut-off ≥ 11 at the first GDM visit	-21.773 (-26.502 – -17.044)**	-20.933 (-26.203 – -15.622)**

** p < 0.05, ** p < 0.01*

Model 1 was an unadjusted linear regression model. Model 2 was a linear regression model with adjustments for: Maternal age, gestational age, educational level, social support and BMI at the first GDM visit.

Associations between mental health and weight variables

We found no significant associations between the depression score and the cut-off ≥11 at the first GDM visit and weight at the same moment (β=0.05; p=.76 and β=0.78; p=0.69), even after adjustments for confounders (β=0.04 and β=1.53; both p≥0.49; see Table 3a). There were no significant associations between the depression score at the first GDM visit and subsequent weight gain, regardless of adjustments (β=0.06; p=0.19 in Model 1 and β=-0.01; p=0.82 in Model 2). On the

other hand, positive and significant associations between the depression cut-off ≥11 at the first GDM visit and subsequent weight gain during pregnancy were found (β=1.25; p=0.02). After controlling for confounders, this association did not remain significant (β=0.24; p=0.69; see Table 3b).

The associations between the well-being score at first GDM visit with concurrent weight and subsequent weight gain (β=-0.06; p=0.19 and β=0.007; p=0.53) were not significant. After adjustments, there was a trend towards an inverse association between the well-being score and weight at the first GDM visit, but not with weight gain (β=-0.09; p=0.07 and β=0.01; p=0.38; see Tables 3a and 3b).

Table 3a. Association between mental health variables and weight in women with GDM.

	Model l	Model 2
	β-Coefficient (95% confidence interval)	*β-Coefficient (95% confidence interval)*
	Weight (kg) at the first GDM visit	
Depression score at the first GDM visit	0.048 (-0.259 – 0.356)	0.043 (-0.309 – 0.394)
Depression cut-off of ≥ 11 at the first GDM visit	0.780 (-3.009 – 4.567)	1.534 (-2.794 – 5.861)
Well-being score at the first GDM visit	-0.055 (-0.138 – 0.027)	-0.088 (-0.184 – 0.008)

** p < 0.05, ** p < 0.01*

Model 1 was an unadjusted linear regression model. Model 2 was a linear regression model with adjustments for: Maternal age, gestational age, educational level and social support at the first GDM visit.

Table 3b. Associations between mental health variables and weight gain in women with GDM.

	Model l	Model 2
	β-Coefficient (95% confidence interval)	*β-Coefficient (95% confidence interval)*
	Weight gain (kg) between the first and last GDM visit	
Depression score at the first GDM visit	0.056 (-0.029 – 0.142)	-0.011 (-0.104 – 0.082)
Depression cut-off of ≥ 11 at the first GDM visit	1.249 (0.203 – 2.294)*	0.237 (-0.910 – 1.383)

Well-being score at the first GDM visit	0.007 (-0.016 – 0.030)	0.011 (-0.014 – 0.036)

** p < 0.05, ** p < 0.01*

Model 1 was an unadjusted linear regression model. Model 2 was a linear regression model with adjustments for: Maternal age, gestational age, educational level, social support and BMI at the first GDM visit.

Discussion

This prospective clinical cohort study aimed at investigating associations of maternal mental health variables (well-being and depression symptoms) over the course of pregnancy in women with GDM. It also examined associations between these mental health variables and weight/weight gain.

The well-being score increased between first and last GDM visit and the well-being score at first GDM visit was inversely associated with the depression score and the depression cut-off ≥11. Regarding the association between mental health and weight, our results indicated that a depression cut-off ≥11 was positively associated with subsequent weight gain during pregnancy in the unadjusted analyses, whereas, no other mental health parameters were significantly associated with weight or weight gain.

This study addressed an important gap in the literature regarding the trajectory and associations in mental health in women with GDM. Well-being increased by 11.8% between the short period of time separating the first GDM visit after diagnosis and the last GDM visit before delivery; a context of significant changes for pregnant women with GDM. Granting this, one study investigated the change in well-being in a primary care setting of psychiatric patients (42) and showed that a change of 11 points on the WHO-5 scale would demonstrate clinically significant change in well-being. The increase of 7.1 points in our patients could be due to the fact that they are seen by various professionals, which counsel, accompany and help them with regards to their understanding of the GDM diagnosis, their lifestyle and glucose management. This might bring some reassurance to these women, as they might feel cared for. This is corroborated by a study showing that women with GDM receiving dietary advice, blood glucose monitoring, and insulin therapy, as needed, from 24-34 weeks of gestation improved their mood, quality of life and decreased their rates of depression at three months postpartum compared to a routine care group (47). In our patients, this improvement in mental health could have already started earlier, i.e., in the prepartum period, as shown by the increase in well-being. It would therefore be interesting to investigate further possible changes in well-being in the postpartum period.

It seems compelling that the well-being score would be inversely associated with the depression score and cut-off ≥11 and, indeed, this was demonstrated by our results for the first time in pregnancy. Wersebe and colleagues had previously established that well-being was lower in non-pregnant participants suffering from major depression compared to individuals not suffering from depression (48). We also showed that well-being only explained around 25% of our two depression variables (both r around 0.5). This means that depression and well-being items also give distinct information and, thus, are both important to investigate. This finding is corroborated by another study concluding that while mild and moderate levels of depression were negatively associated with well-being, the WHO-5 demonstrates inefficacy in detecting severe and extreme forms of depression (41). Nevertheless, in primary care for psychiatric patients, in the general population, or in type 1 and type 2 diabetes, studies have used the WHO-5 to measure depressive symptoms (16, 41, 49). However, further investigations are needed in the pregnant population, particularly in women diagnosed with GDM who are at higher risk of developing depression.

Despite the fact that depression has been shown to be associated with metabolic health, especially with weight, in the general pregnant population (27-29, 50), we did not find any associations between the depression variables and weight in our sample of pregnant women with GDM. The inverse prospective association we found between clinically relevant symptoms of depression (cut-off ≥11) and subsequent weight gain is novel and interesting. However, it did not remain significant when we controlled for confounding factors. The fact that we did not find an association between the general depression score with weight gain could be due to the fact that there may be a non-linear association between mental and metabolic health that is only present above a certain cut-off when depression symptoms are more clinically relevant. The time interval might also be too short to show sufficient significant changes regarding this relationship. In previous studies, weight and depression were associated. Indeed, during an episode of depression, obese individuals from the general population were five times more likely than the non-obese individuals to overeat, leading to weight gain (51). Furthermore, depression measured by the EPDS (as a score as well as a cut-off ≥12) or by the DASS (Depression Anxiety Stress Scales) using five different cut-off scores, was associated with excessive weight gain in pregnancy and in the general population (28, 29). Nonetheless, data is lacking in women with GDM, which is surprising, considering that women with GDM are more susceptible to higher weight gain during pregnancy, as well as to a higher risk of depressive symptoms (12, 13, 18). In these women, there might even be a synergistic effect of depression and weight gain that amplifies adverse outcomes in the mother and the infant. Thus, it would be helpful to investigate this topic in larger studies.

Finally, we found no association between the well-being score and weight. Our results are in conflict with other studies, where well-being has been inversely associated with weight outside of pregnancy (52) and with weight retention in the postpartum period (32). It seems that other clinical factors might have played a role and thus, we suggest that future research investigates the relationship between well-being and weight gain, as our results were close to significant and might have been significant if the timing between the measures was longer or the population larger.

Clinical implications

Our results showing that well-being augmented by 11.8% between the first and last GDM visit is of clinical relevance. Indeed, this may suggest that a good and comprehensive clinical follow-up may counteract the negative emotional impact of a GDM diagnosis (12), although this would need to be confirmed by a RCT. Our findings demonstrating that well-being was inversely correlated to depression and explained around 25% of its variance imply that other factors might impact both mental health variables and that it is more informative to measure them both.

Of further clinical relevance is the association of the depression cut-off ≥11 with higher weight gain during GDM pregnancy. This highlights the importance of screening women's mental health during pregnancy, as recommended by the National Institute for Health and Clinical Excellence (53) and the ADA (54) . As weight gain in pregnancy and in women with GDM may have a deleterious impact on the mother and the child (6, 31, 45, 55-57), actions may be taken to lower their depressive symptoms as a means to restricting weight gain during pregnancy. Given our results and the results of a recent review together (1), women with GDM may benefit from being screened but also treated for mental health symptoms early after their GDM diagnosis.

Strengths and limitations

This study has many strengths, including the prospective design investigating a "real-life" clinical cohort of consecutive women, the use of validated self-report questionnaires, and the inclusion of influential confounding variables. This study also included women speaking other languages then French and English, thus increasing generalizability and reflecting the GDM population in Switzerland. Nevertheless, some limitations need to be addressed. First, a longer time period might have yielded more pronounced results regarding the relationship between mental health and weight gain, as weight gain was only 2.4 kg. It would be interesting to investigate these relationships up to the postpartum period. Second, additional confounders that could not be accounted for might have affected our results. Third, these women also met different professionals during their pregnancy,

advising them about their diet and lifestyle behavior, which might have influenced their weight gain. As this paper has an explorative nature, we did not account for previous mental health diagnosis, as is the case for similar papers in this domain (12). Finally, there is a high attrition rate, as this study took place in a clinical setting.

Conclusion

This prospective clinical cohort study indicated that in women with GDM, well-being increased by 11.8% between their first GDM visit after GDM diagnosis and the end of pregnancy. The well-being score was inversely related to the depression score and cut-off ≥ 11 and explained around 25% of their variability. This shows positive emotional health should be considered in relation to metabolic health in women with GDM. Furthermore, clinically relevant symptoms of depression (cut-off of ≥ 11) were associated with subsequent weight gain, showing the importance of screening mental health in women with GDM, as it may impact not only weight as shown in this paper, but also other metabolic health factors. Thus, future research might aim at investigating how mental health impacts postpartum weight retention or pregnancy and postpartum metabolic factors.

List of abbreviations

ADA: American Diabetes Association

BMI: Body mass index

EPDS: Edinburg Postnatal Depression Scale

WHO-5: World Health Organization Five - Well-Being Index

Funding

This work was supported by the Swiss National Science Foundation [SNF 32003B_176119] and by an unrestricted educational grant from NovoNordisk.

Declarations of interest

None.

Acknowledgements:

We would like to give a special thanks to our colleagues that collected and entered data for this study: Isabelle Cohen, Justine Gross, Céline Helbling, Stefano Lanzi, Giada Ostinelli and Dominique Stulz.

References

1. Gilbert L, Gross J, Lanzi S, Quansah DY, Puder J, 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.

2. Grote NK, Bridge JA, Gavin AR, Melville JL, Iyengar S, Katon WJ. A meta-analysis of depression during pregnancy and the risk of preterm birth, low birth weight, and intrauterine growth restriction. Archives of general psychiatry. 2010;67(10):1012-24.

3. Grigoriadis S, VonderPorten EH, Mamisashvili L, Tomlinson G, Dennis C-L, Koren G, et al. The impact of maternal depression during pregnancy on perinatal outcomes: a systematic review and meta-analysis. 2013.

4. Schetter CD, Tanner L. Anxiety, depression and stress in pregnancy: implications for mothers, children, research, and practice. Current opinion in psychiatry. 2012;25(2):141.

5. Chung TK, Lau TK, Yip AS, Chiu HF, Lee DT. Antepartum depressive symptomatology is associated with adverse obstetric and neonatal outcomes. Psychosomatic Medicine. 2001;63(5):830-4.

6. Horsch A, Gilbert L, Lanzi S, Kang JS, Vial Y, Puder JJ. Prospective associations between maternal stress during pregnancy and fasting glucose with obstetric and neonatal outcomes. Journal of Psychosomatic Research. 2019;125:109795.

7. Cato K, Sylvén SM, Georgakis MK, Kollia N, Rubertsson C, Skalkidou A. Antenatal depressive symptoms and early initiation of breastfeeding in association with exclusive breastfeeding six weeks postpartum: a longitudinal population-based study. BMC pregnancy and childbirth. 2019;19(1):49.

8. Carter AS, Garrity-Rokous FE, Chazan-Cohen R, Little C, Briggs-Gowan MJ. Maternal depression and comorbidity: predicting early parenting, attachment security, and toddler social-emotional problems and competencies. Journal of the American Academy of Child & Adolescent Psychiatry. 2001;40(1):18-26.

9. Morrison C, McCook JG, Bailey BA. First trimester depression scores predict development of gestational diabetes mellitus in pregnant rural Appalachian women. Journal of Psychosomatic Obstetrics & Gynecology. 2016;37(1):21-5.

10. Hinkle SN, Louis GMB, Rawal S, Zhu Y, Albert PS, Zhang C. A longitudinal study of depression and gestational diabetes in pregnancy and the postpartum period. Diabetologia. 2016;59(12):2594-602.

11. Horsch A, Kang JS, Vial Y, Ehlert U, Borghini A, Marques-Vidal P, et al. Stress exposure and psychological stress responses are related to glucose concentrations during pregnancy. British Journal of Health Psychology. 2016:n/a-n/a.

12. Damé P, Cherubini K, Goveia P, Pena G, Galliano L, Façanha C, et al. Depressive Symptoms in Women with Gestational Diabetes Mellitus: The LINDA-Brazil Study. Journal of Diabetes Research. 2017;2017.

13. Bennett HA, Einarson A, Taddio A, Koren G, Einarson TR. Prevalence of depression during pregnancy: systematic review. Obstetrics & Gynecology. 2004;103(4):698-709.

14. Daniells S, Grenyer BF, Davis WS, Coleman KJ, Burgess J-AP, Moses RG. Gestational diabetes mellitus: is a diagnosis associated with an increase in maternal anxiety and stress in the short and intermediate term? Diabetes care. 2003;26(2):385-9.

15. Robertson SM, Stanley MA, Cully JA, Naik AD. Positive emotional health and diabetes care: concepts, measurement, and clinical implications. Psychosomatics. 2012;53(1):1-12.

16. Hajos TR, Pouwer F, Skovlund S, Den Oudsten BL, Geelhoed-Duijvestijn P, Tack C, et al. Psychometric and screening properties of the WHO-5 well-being index in adult outpatients with Type 1 or Type 2 diabetes mellitus. Diabetic Medicine. 2013;30(2):e63-e9.

17. Kahneman D, Deaton A. High income improves evaluation of life but not emotional well-being. Proceedings of the national academy of sciences. 2010;107(38):16489-93.

18. Gibson KS, Waters TP, Catalano PM. Maternal weight gain in women who develop gestational diabetes mellitus. Obstetrics & Gynecology. 2012;119(3):560-5.

19. Durnwald C, editor Gestational diabetes: linking epidemiology, excessive gestational weight gain, adverse pregnancy outcomes, and future metabolic syndrome. Seminars in Perinatology; 2015: Elsevier.

20. Gilmore LA, Klempel-Donchenko M, Redman LM, editors. Pregnancy as a window to future health: excessive gestational weight gain and obesity. Seminars in Perinatology; 2015: Elsevier.

21. American Diabetes Association. 13. Management of Diabetes in Pregnancy: Standards of Medical Care in Diabetes-2018. Diabetes Care. 2018;41(Suppl 1):S137.

22. Bellamy L, Casas J-P, Hingorani AD, Williams D. Type 2 diabetes mellitus after gestational diabetes: a systematic review and meta-analysis. The Lancet. 2009;373(9677):1773-9.

23. Dalfra M, Lapolla A, Masin M, Giglia G, Dalla BB, Toniato R, et al. Antepartum and early postpartum predictors of type 2 diabetes development in women with gestational diabetes mellitus. Diabetes & metabolism. 2001;27(6):675-80.

24. Kim SY, Sharma AJ, Sappenfield W, Wilson HG, Salihu HM. Association of maternal body mass index, excessive weight gain, and gestational diabetes mellitus with large-for-gestational-age births. Obstetrics and gynecology. 2014;123(4):737.

25. Cheng YW, Chung JH, Kurbisch-Block I, Inturrisi M, Shafer S, Caughey AB. Gestational weight gain and gestational diabetes mellitus: perinatal outcomes. Obstetrics & Gynecology. 2008;112(5):1015-22.

26. Hillier TA, Pedula KL, Vesco KK, Schmidt MM, Mullen JA, LeBlanc ES, et al. Excess gestational weight gain: modifying fetal macrosomia risk associated with maternal glucose. Obstetrics & Gynecology. 2008;112(5):1007-14.

27. Altazan AD, Redman LM, Burton JH, Beyl RA, Cain LE, Sutton EF, et al. Mood and quality of life changes in pregnancy and postpartum and the effect of a behavioral intervention targeting excess gestational weight gain in women with overweight and obesity: a parallel-arm randomized controlled pilot trial. BMC pregnancy and childbirth. 2019;19(1):50.

28. Matthews J, Huberty J, Leiferman J, Buman M. Psychosocial predictors of gestational weight gain and the role of mindfulness. Midwifery. 2018;56:86-93.

29. McPhie S, Skouteris H, Fuller-Tyszkiewicz M, Hill B, Jacka F, O'Neil A. Relationships between mental health symptoms and body mass index in women with and without excessive weight gain during pregnancy. Midwifery. 2015;31(1):138-46.

30. Christenson A, Johansson E, Reynisdottir S, Torgerson J, Hemmingsson E. Women's Perceived Reasons for Their Excessive Postpartum Weight Retention: A Qualitative Interview Study. PloS one. 2016;11(12):e0167731.

31. Fowles ER, Murphey C, Ruiz RJ. Exploring relationships among psychosocial status, dietary quality, and measures of placental development during the first trimester in low-income women. Biological research for nursing. 2011;13(1):70-9.

32. O'Brien E, Geraghty AA, O'Sullivan E, Riordan J, Horan MK, Larkin E, et al. Five-year follow up of a low glycaemic index dietary randomised controlled trial in pregnancy—no long-term maternal effects of a dietary intervention. BJOG: An International Journal of Obstetrics & Gynaecology. 2019;126(4):514-24.

33. Metzger BE, Gabbe SG, Persson B, Buchanan TA, Catalano PA, Damm P, et al. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy. Diabetes Care. 2010;33(3):676-82.

34. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. The British journal of psychiatry. 1987;150(6):782-6.

35. Bunevicius A, Kusminskas L, Pop VJ, Pedersen CA, Bunevicius R. Screening for antenatal depression with the Edinburgh Depression Scale. Journal of Psychosomatic Obstetrics & Gynecology. 2009;30(4):238-43.

36. Guedeney N, Fermanian J. Validation study of the French version of the Edinburgh Postnatal Depression Scale (EPDS): new results about use and psychometric properties. European psychiatry. 1998;13(2):83-9.

37. Watson LC, Zimmerman S, Cohen LW, Dominik R. Practical depression screening in residential care/assisted living: five methods compared with gold standard diagnoses. The American Journal of Geriatric Psychiatry. 2009;17(7):556-64.

38. Topp CW, Østergaard SD, Søndergaard S, Bech P. The WHO-5 Well-Being Index: a systematic review of the literature. Psychotherapy and psychosomatics. 2015;84(3):167-76.

39. Bech P, Gudex C, Johansen KS. The WHO (Ten) well-being index: validation in diabetes. Psychotherapy and psychosomatics. 1996;65(4):183-90.

40. Awata S, Bech P, Yoshida S, Hirai M, Suzuki S, Yamashita M, et al. Reliability and validity of the Japanese version of the World Health Organization-Five Well-Being Index in the context of detecting depression in diabetic patients. Psychiatry and clinical neurosciences. 2007;61(1):112-9.

41. Krieger T, Zimmermann J, Huffziger S, Ubl B, Diener C, Kuehner C, et al. Measuring depression with a well-being index: further evidence for the validity of the WHO Well-Being Index (WHO-5) as a measure of the severity of depression. Journal of affective disorders. 2014;156:240-4.

42. Newnham EA, Hooke GR, Page AC. Monitoring treatment response and outcomes using the World Health Organization's Wellbeing Index in psychiatric care. Journal of Affective Disorders. 2010;122(1-2):133-8.

43. Hochberg G, Pucheu S, Kleinebreil L, Halimi S, Fructuoso-Voisin C. WHO-5, a tool focusing on psychological needs in patients with diabetes: the French contribution to the DAWN study. Diabetes & metabolism. 2012;38(6):515-22.

44. Nicklas JM, Barbour LA. Optimizing weight for maternal and infant health: tenable, or too late? Expert review of endocrinology & metabolism. 2015;10(2):227-42.

45. Bjelland I, Krokstad S, Mykletun A, Dahl AA, Tell GS, Tambs K. Does a higher educational level protect against anxiety and depression? The HUNT study. Social science & medicine. 2008;66(6):1334-45.

46. Penninx BW, van Tilburg T, Boeke AJP, Deeg DJ, Kriegsman DM, van Eijk JTM. Effects of social support and personal coping resources on depressive symptoms: different for various chronic diseases? Health Psychology. 1998;17(6):551.

47. Crowther CA, Hiller JE, Moss JR, McPhee AJ, Jeffries WS, Robinson JS. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes. New England Journal of Medicine. 2005;352(24):2477-86.

48. Wersebe H, Lieb R, Meyer AH, Miche M, Mikoteit T, Imboden C, et al. Well-being in major depression and social phobia with and without comorbidity. International Journal of Clinical and Health Psychology. 2018;18(3):201-8.

49. Henkel V, Mergl R, Kohnen R, Maier W, Möller H, Hegerl U. The WHO-5 wellbeing index performed the best in screening for depression in primary care. Evidence Based Medicine. 2003;8(5):155.

50. Blaine B. Does depression cause obesity? A meta-analysis of longitudinal studies of depression and weight control. Journal of health psychology. 2008;13(8):1190-7.

51. Murphy JM, Horton NJ, Burke Jr JD, Monson RR, Laird NM, Lesage A, et al. Obesity and weight gain in relation to depression: findings from the Stirling County Study. International Journal of Obesity. 2009;33(3):335.

52. Ryff CD, Love GD, Urry HL, Muller D, Rosenkranz MA, Friedman EM, et al. Psychological well-being and ill-being: do they have distinct or mirrored biological correlates? Psychotherapy and psychosomatics. 2006;75(2):85-95.

53. National Collaborating Centre for Mental Health. Antenatal and postnatal mental health: the NICE guideline on clinical management and service guidance. 2014.

54. American Diabetes Association. Standards of medical care in diabetes—2014. Diabetes Care. 2014;37(Supplement 1):S14-S80.

55. Parker JD, Abrams B. Prenatal weight gain advice: an examination of the recent prenatal weight gain recommendations of the Institute of Medicine. Obstetrics and gynecology. 1992;79(5 (Pt 1)):664-9.

56. Hedderson MM, Gunderson EP, Ferrara A. Gestational weight gain and risk of gestational diabetes mellitus. Obstetrics and gynecology. 2010;115(3):597.

57. Kac G, Benício MH, Velásquez-Meléndez G, Valente JG, Struchiner CuJ. Gestational weight gain and prepregnancy weight influence postpartum weight retention in a cohort of Brazilian women. The Journal of nutrition. 2004;134(3):661-6.

8.4 Publication D

Published in Psychoneuroendocrinology in 2021.

Mental health and its associations with glucose-lowering medication in women with gestational diabetes mellitus. A prospective clinical cohort study

Leah Gilbert[a*], Argyro Nikolaou[b], Dan Yedu Quansaha, Jean-Benoît Rossel[c], Antje Horsch[d,e,1], Jardena J.Puder[a,1]

[a] Obstetric Service, Woman-Mother-Child Department, Lausanne University Hospital, Avenue Pierre-Decker 2, 1011 Lausanne, Switzerland

[b] Clinical Pharmacology and Toxicology Division, Geneva University Hospital, Rue Gabrielle-Perret-Gentil 4, Geneva, Switzerland

[c] Clinical Trials Unit, University of Bern, Mittelstrasse 43, 3012 Bern, Switzerland

[d] Institute of Higher Education and Research in Healthcare (IUFRS), University of Lausanne, Route de la Corniche 10, 1010 Lausanne, Switzerland

[e] Neonatology Service, Woman-Mother-Child Department, Lausanne University Hospital, Avenue Pierre-Decker 2, 1011 Lausanne, Switzerland

[*]Corresponding author.

Highlights

- Gestational diabetes (GDM) is usually associated with mental health symptoms.
- In our sample, mental health improves after GDM diagnosis; during and after pregnancy.
- Mental health symptoms does not increase the need for medical therapy in GDM.
- Medical therapy does not impact on mental health during and after pregnancy.

Structured Abstract

Aims

Mental health symptoms are frequent in women with gestational diabetes mellitus (GDM) and may influence glycemic control. We therefore investigated if mental health symptoms (high depression and low well-being scores) predicted a need for glucose-lowering medication and if this use of medication influenced the trajectory of mental health during pregnancy and in the postpartum period.

Methods

We included 341 pregnant women from a cohort of GDM women in a Swiss University Hospital. The World Health Organization Well-being Index-Five was collected at the first and last GDM and at the postpartum clinical visits and the Edinburgh Postnatal Depression Scale at the first GDM and the

postpartum clinical visits. Medication intake was extracted from participants' medical records. We conducted linear and logistic regressions with depression as an interaction factor.

Results

Mental health symptoms did not predict a need for medication (all $p \geq 0.29$). Mental health improved over time (both $p \leq 0.001$) and use of medication did not predict this change (all $p \geq 0.40$). In women with symptoms of depression, medication was associated with less improvement in well-being at the postpartum clinical visit (p for interaction=0.013).

Conclusions

Mental health and glucose-lowering medication did not influence each other in an unfavourable way in this cohort of women with GDM.

Key Words: Depression ; Insulin ; Metformin ; Postpartum; Pregnancy; Well-being

1. Introduction

Gestational diabetes mellitus (GDM) is defined as a glucose intolerance diagnosed in the second or third trimester of pregnancy that does not fulfil the criteria of overt diabetes (Cefalu et al., 2019). Lifestyle interventions focusing on diet and physical activity are usually recommended as the primary therapeutic strategy (Blumer et al., 2013, Gilbert et al., 2019, Cefalu et al., 2019, American Diabetes Association, 2020) for glucose control during pregnancy. When lifestyle interventions fail to achieve glycemic targets (Lehmann et al., 2009, Blumer et al., 2013, Metzger et al., 2007, American Diabetes Association, 2020), glucose-lowering medication is initiated. In accordance with the American Diabetes Association (ADA) guidelines, insulin is prescribed more frequently in Switzerland, as it does not cross the placenta (Cefalu et al., 2019, American Diabetes Association, 2020), although metformin can also be prescribed (Webber et al., 2015). According to a recent study and similarly to our practice, insulin is the most frequently used glucose-lowering medication during GDM pregnancy across countries (Cesta et al., 2019).

Women with GDM are more likely to suffer from mental health symptoms. Indeed, women with GDM have higher rates of depression during pregnancy and in the postpartum period, compared to women without GDM (Alexandre et al., 2017, Bennett et al., 2004, Damé et al., 2017, Daniells et al., 2003, Wilson et al., 2019). Mental health symptoms therefore represent an important factor to consider in women with GDM, as they may interfere with their capacity to adhere to lifestyle interventions (Molyneaux et al., 2018). Indeed, symptoms of depression may reduce an individual's

coping abilities and may lead to disordered eating behaviors and lower dietary quality (Fowles et al., 2011). Depression may also lead individuals to eat as a strategy to relieve themselves of negative symptoms (Christenson et al., 2016) and may decrease women's motivation to conduct physical activity (Carter and Swardfager, 2016). Thus, mental health symptoms may impact both diet and physical activity and lead to higher glycaemia during pregnancy (Blumer et al., 2013, Ruchat and Mottola, 2013). Secondly, mental health symptoms may be directly related to worsened metabolic control in women with GDM. Overall, depression is associated with a higher risk of future GDM (Hinkle et al., 2016). Similarly, higher anxiety and depression scores, as well as stress perception, are associated with higher glycaemia during pregnancy (Horsch et al., 2016, Hinkle et al., 2016). However, even if mental health symptoms can have a direct impact on glycaemia and adherence to lifestyle interventions, it is not clear if it increases the need for glucose-lowering medication in women with GDM. In addition, we are not aware of any study investigating whether the presence of clinically relevant symptoms of depression might augment the need for glucose-lowering medication. This could have an important impact on the identification and care of these women.

Conversely, there might also be an association between the need for glucose-lowering medication and subsequent mental health symptoms. Indeed, our clinical experience shows that many women are willing to adjust their lifestyle in order to avoid medication and particularly the burden of insulin injections. In addition, the need for glucose-lowering medication could lead to a feeling of failure. To our knowledge, only one study showed that insulin use was not a predictor for postpartum depression in women with GDM (Nicklas et al., 2013). Thus, the potential impact of glucose-lowering medication on the mental health of women with GDM and in the postpartum period remains understudied. It is important to study this question, as mental health symptoms have been shown to be higher in the postpartum period in women with GDM (Wilson et al., 2019) and may have important adverse effects on the health of the mother (Christenson et al., 2016, Herring et al., 2008) and the infant (Grace et al., 2003, Cooper and Murray, 1998, Cato et al., 2019). To study these questions, we chose both symptoms of depression (Hinkle et al., 2016, Blumer et al., 2013, Ruchat and Mottola, 2013) and well-being (Robertson et al., 2012, Hochberg et al., 2012) as markers of mental health, as they had either shown their impact on glycemic control or were studied in patients with diabetes.

This study was therefore conducted to 1) investigate if mental health symptoms, described here as high symptoms of depression and low well-being scores, in women with GDM, predict a need for glucose-lowering medication during pregnancy and 2) describe the overall trajectory of mental health in these women and investigate if the need for glucose-lowering medication independently predicts

mental health symptoms during and after pregnancy. We also studied if clinically relevant symptoms of depression would influence these associations, i.e., if they are different in the presence of symptoms of depression.

2. Materials and Methods

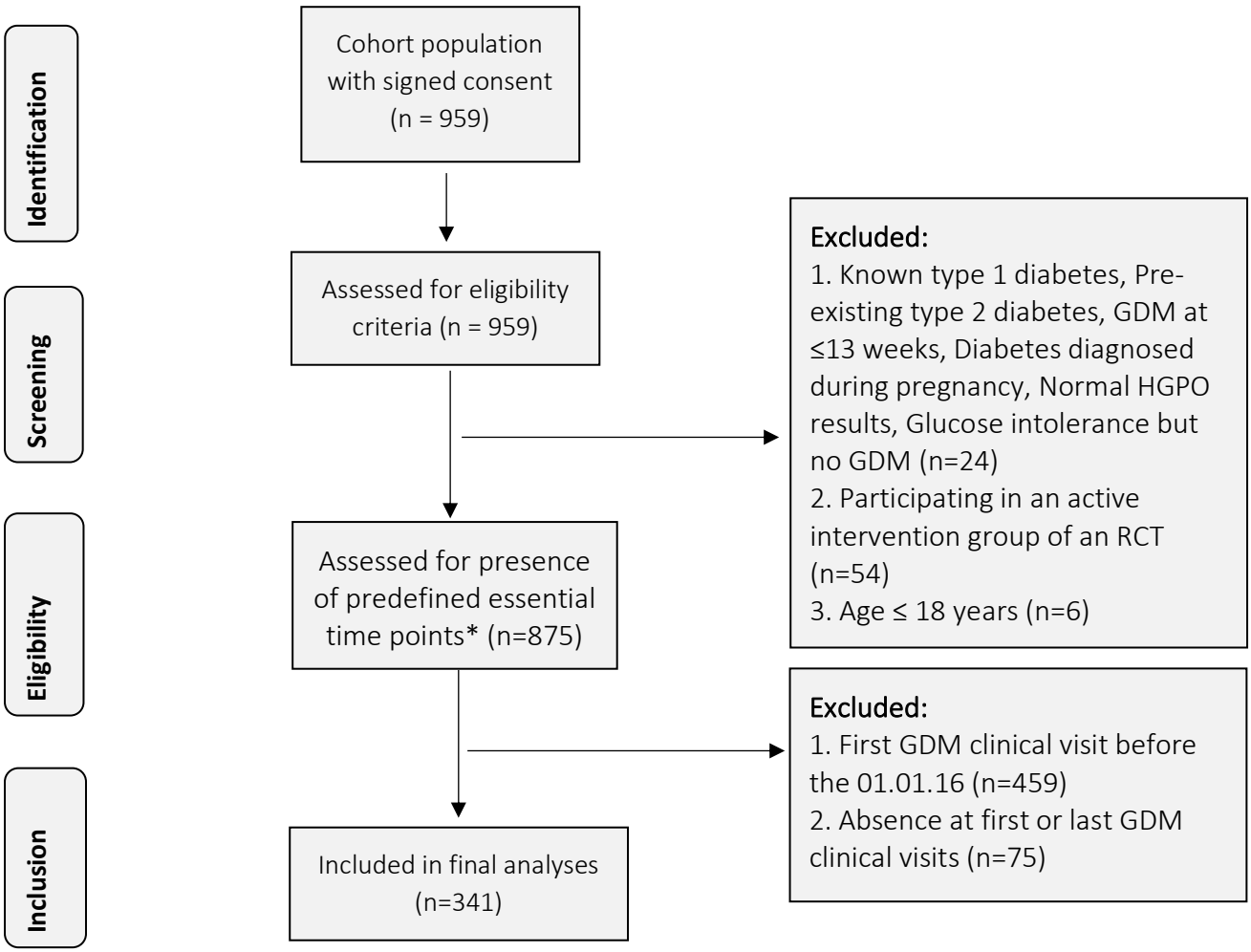
2.1 Setting and patient population

This prospective clinical cohort study included pregnant women diagnosed with GDM according to the International Association of the Diabetes and Pregnancy Study Groups (IADPSG) and ADA guidelines (American Diabetes, Association, 2019, Blumer et al., 2013, Metzger et al., 2010). These women were taken care of in the Diabetes and Pregnancy Unit at the Lausanne University Hospital (Switzerland) between 2016 and 2019. The Human Research Ethics Committee of the Canton de Vaud, Switzerland approved the study protocol (326/15).

2.2 Inclusion and exclusion criteria

This study is part of an ongoing prospective clinical cohort of women with GDM, for which participating women provided signed consent for data usage. Out of the 959 participating women, we selected those who corresponded to our eligibility criteria (n = 875) (please see Fig. 1), who presented after January 2016 (when we started systematically distributing mental health questionnaires) (n = 800), and were present during predefined time points that are essential (first and last GDM visit) in order to have baseline mental health assessed and valid information regarding glucose-lowering medication (the two main aims of the study). Thus, 341 women with GDM were included in the current analysis.

Figure 1:



Flow chart describing how the study participants were selected.

*Systematic distribution of mental health questionnaires started on 01.01.2016 and women that were followed before this time point were excluded. First and last GDM clinical visit were the predefined essential time points providing indispensable information regarding the two main aims: baseline mental health and valid information regarding glucose-lowering medication. Women that were absent at either one of these time points were therefore also excluded.

2.3 GDM management/clinical care

At the first clinical visit after the confirmation of GDM diagnosis, women receive information on GDM from a nurse or medical doctor specialized in GDM and are taught to perform capillary blood glucose (CBG) measures. Women are then asked to monitor their CBG 4 times per day (fasting blood glucose

(FBG) in the morning and 2-hour (or 1-hour) postprandial blood glucose after each meal) (Arditi et al., 2017, American Diabetes Association, 2020). A week later, women are seen by a dietician and receive recommendations regarding their CBG, eating habits and weight gain (Blumer et al., 2013) and are encouraged to increase their physical activity (Colberg et al., 2013). If despite lifestyle changes (diet and physical activity) glucose values remain above targets two or more times during a 1–2-week period, glucose-lowering medication is introduced (Lehmann et al., 2009, Metzger et al., 2007). Glucose-lowering medication type depends on glucose values (i.e., insulin in case of relatively high values), patient characteristics (i.e., Body Mass Index (BMI)) and patient preference, but in the vast majority of cases insulin is the preferred treatment over metformin. Short-acting insulin analogues are introduced and adapted to achieve a 2-hour postprandial glucose value ≤7 mmol/l (alternatively 1-hour postprandial glucose ≤8 mmol/l), and long-acting insulin analogues to achieve FBG ≤5.3 mmol/l (American Diabetes Association, 2020, American Diabetes, Association, 2019, Carroll and Kelley, 2014). Women are then followed until delivery and an oral glucose tolerance test (oGTT) is performed between 6 and 8 weeks postpartum (American Diabetes Association, 2020).

2.4 Measures

2.4.1 Maternal symptoms of depression

The Edinburgh Postnatal Depression Scale (EPDS): The EPDS was used in the current study to measure symptoms of depression. The questionnaire has been validated in pregnant women (Bunevicius et al., 2009), as well as in a French population, and good psychometric properties have been reported (Guedeney and Fermanian, 1998). Symptoms of depression in the preceding 7 days were assessed (Cox, Holden, and Sagovsky, 1987) at the women's first GDM clinical visit and at the 6–8 weeks postpartum clinical visit. We distributed this self-report questionnaire in French and in English. For women who did not understand these languages, we ensured that a certified professional translator helped them complete it. Each item of this questionnaire is scored on a 4-point scale, the minimum and maximum total scores being 0 and 30, respectively. For our interaction analysis, we additionally created a dichotomous variable using a cut-off of ≥ 11 to separate women with and without clinically relevant depression scores (Bunevicius et al., 2009). For this cut-off, the terminology "clinically relevant symptoms of depression" was chosen, given that clinical interviewing represents the gold standard to diagnose depression (Watson et al., 2009).

2.4.2 Maternal well-being index

The World Health Organisation Well-Being Index-Five (WHO-5): The WHO-5 was used to measure well-being in our sample, as this questionnaire has shown adequate validity as an outcome measure in clinical studies (Henkel et al., 2003, Topp et al., 2015). It has been used extensively in endocrinology, and the French version has shown good psychometric properties (Topp et al., 2015, Hochberg et al., 2012). This 5-item self-report questionnaire assessed the subjective well-being of the participants (Topp et al., 2015) at the first and last GDM clinical visit and at the 6–8 weeks postpartum clinical visit. In accordance with the ethnical diversity of our patients, we used validated versions of the questionnaire in several languages. The items are measured on a 5-point Likert scale ranging from 0 'at no time' to 5 'all of the time'. The final score is then calculated by multiplying the total score by 4; thus, the final score ranges from 0 to 100.

2.4.3 Glucose-lowering medication

Information regarding glucose-lowering medication intake was retrieved from the medical records at the last GDM clinical visit. With this information, two types of variables were generated. First, a dichotomous (yes, no) variable named "glucose-lowering medication" was created to know if women did or did not take glucose-lowering medication during their pregnancy. For additional and more detailed analysis, a second variable was comprised of four categories: no glucose-lowering medication intake (1), metformin only (2), long-acting (basal) bedtime insulin (± metformin) (3), and short-acting (meal) insulin (± long-acting bedtime insulin and/or metformin) (4). These categories of glucose-lowering medication were formed based on degrees of burden to the participants: the injections with short-acting insulins were considered being most burdensome (as women have to carry syringes with them wherever they go and inject before the meals, often outside of their home), and no glucose-lowering medication, was considered as putting a lower strain on women and metformin was in between. Indeed, previous research has shown that metformin is better accepted in women with GDM and that insulin is more burdensome (Rowan et al., 2008). This variable is named "detailed glucose-lowering medication" and the reference category was 1 =no glucose-lowering medication intake.

2.4.4 Sociodemographic, medical and anthropometric variables

At the first GDM clinical visit, maternal age, weeks of gestation, educational level, social support, prior GDM diagnosis, and family history of diabetes information were collected during the clinical consultation or extracted from medical records. Furthermore, glycated haemoglobin (HbA1c) was measured using a chemical photometric method (conjugation with boronate; Afinion®) (Clinical Chemistry and Clinical Toxicology Devices Panel, FDA Public Advisory Meeting Alere Afinion™ HbA1c

Dx. https://www.fda.gov/media/99241/download.Clinical Chemistry and Clinical Toxicology Devices Panel, 2016Panel, Clinical Chemistry and Clinical Toxicology Devices , 2016. FDA Public Advisory Meeting Alere Afinion™ HbA1c Dx, 2016. https://www.fda.gov/media/99241/download., Wood et al., 2012) and Body Mass Index (BMI) at first GDM clinical visit was calculated based on measured height and weight using the formula weight (kg)/[height(m)]^2.

2.5 Data analysis

All analyses were carried out with SPSS (IBM Corp. Released 2017. IBM SPSS Statistics for Windows, Version 25.0. Armonk, NY: IBM Corp.). Descriptive statistics were conducted for socio-demographic variables (Table 1). Continuous and normally distributed variables were described as means and standard deviations and ordinal outcomes were described as frequencies and percentages. Statistical significance was set at $p < 0.05$.

Table 1. Descriptive maternal sociodemographic and medical parameters.

	All	With glucose-lowering medication	Without glucose-lowering medication
	Mean (SD) or n (%)	*Mean (SD) or n (%)*	*Mean (SD) or n (%)*
Maternal sociodemographic variables			
Age (years)	33.62 (5.34)	33.39 (5.27)	33.84 (5.41)
Educational level			
No education	3 (0.9%)	1 (0.6%)	2 (1.1%)
Compulsory education not completed	17 (5%)	8 (4.9%)	9 (5.1%)
Compulsory education completed	60 (17.6%)	33 (20.3%)	27 (15.2%)
Secondary school	38 (11.1%)	18 (11%)	20 (11.2%)
Apprenticeship	55 (16.1%)	29 (17.8%)	26 (14.6%)
University degree	113 (33.1%)	46 (28.2%)	67 (37.6%)
Social support			
Lives: alone without support, alone with support, with partner	13 (3.8%), 14 (4.1%), 292 (85.6%)	9 (5.5%), 2 (1.2%), 138 (84.7%)	4 (2.2%), 12 (6.7%), 154 (86.5)*

Obstetric variables			
Gestational age at first GDM clinical visit	28.85 (3.38)	28.13 (3.85)	29.51 (2.74) *
Gestational age at last GDM clinical visit	36.44 (1.28)	36.34 (1.31)	36.53 (1.25)
GDM variables			
HbA1c at first GDM clinical visit % - (mmol/mol)	5.4 (0.43) – (35 (4.32))	5.5 (0.51) – (37 (5.09))	5.3 (0.31) (34 (3.11))*
Family history of diabetes: None, First and Second degree relative	126 (37%), 122 (35.8%), 71 (20.8%)	56 (34.4%), 63 (38.7%), 33 (20.2%)	70 (39.2%), 59 (33.1%), 38 (21.3%)
Mental health variables			
Depression score at first GDM clinical visit	7.43 (5.46)	7.49 (5.75)	7.38 (5.20)
Women with clinically relevant symptoms of depression (cut-off of ≥ 11) at first GDM clinical visit	77 (25.2%)	42 (28.8%)	35 (22%)

Detailed glucose-lowering medication for the overall sample	
	n (%)
No glucose-lowering medication intake (1)	178 (52.2%)
Metformin only (2)	15 (4.4%)
Long-acting (basal) bedtime insulin (±metformin) (3)	64 (18.8%)
Short-acting (meal) insulin (± long-acting bedtime insulin and/or metformin) (4)	84 (24.6%)

Continuous and normally distributed variables were described as means and standard deviations and ordinal outcomes were described as frequencies and percentages. *Indicates a significant difference (p<0.05) between the subgroups with and without glucose-lowering medication, respectively.

BMI: body mass index.

Regarding the first objective, investigating the prospective association between mental health symptoms and the subsequent need for glucose-lowering medication, we conducted logistic regression analyses with the dichotomous glucose-lowering medication variable as the dependent variable. To see if this relationship was different in women with higher depression scores, we added the "clinically relevant symptoms of depression" interaction term (dichotomous variable created from the EPDS scale) for the association between well-being and the glucose-lowering medication

dichotomous variable. This was possible, as the correlation between the predictor (well-being scores) and the interaction term (clinically relevant symptoms of depression) was only small to moderate (correlation coefficient $r = -0.47$). This interaction term could not be added when the depression scores were the predictor, as the correlation was too high between this predictor and the interaction term (clinically relevant symptoms of depression; correlation coefficient $r = 0.81$) and both of these measures; depression scores and clinically relevant symptoms of depression are derived from the same questionnaire. Given that none of the interactions were significant in our first objective, we did not conduct further stratification analyses.

Regarding the second objective, we first evaluated the trajectory of the depression and well-being scores over time during and after pregnancy in women with GDM using a linear mixed effects model. Indeed, it seemed important to first gain knowledge about the general trajectory of mental health in women with GDM in pregnancy and in the postpartum period. Then, we assessed the prospective association between the use of glucose-lowering medication and subsequent mental health at the end of pregnancy (well-being scores) and in the postpartum period (well-being and depression scores). We performed linear regressions with occurrence of glucose-lowering medication as a binary predictor (yes, no), and also with the detailed glucose-lowering medication as a categorical predictor. Finally, to see if the impact of glucose-lowering medication (yes, no) on mental health was different if clinically relevant symptoms of depression were present, we added the "clinically relevant symptoms of depression" interaction term. If any of the interactions were significant, we conducted further stratification analyses, separating women with clinically relevant symptoms of depression from those without. This was only the case for the association between the dichotomous glucose-lowering medication variable during pregnancy and well-being at the postpartum clinical visit.

For all regressions, we used two models (model 1 & 2). In model 1, we adjusted for maternal age and gestational weeks at the first GDM clinical visit (Crowther et al., 2005, Ruohomäki et al., 2018). In model 2, we added variables that were significantly correlated with the respective dependent variable. We tested the following potential confounder variables: family history of diabetes, prior GDM diagnosis, BMI and HbA1c at the first GDM clinical visit, social support, and educational level. For the first objective, family history of diabetes, social support, educational level, and HbA1c were added as confounders in model 2. For the second objective, only family history of diabetes was added as a confounder in model 2 when the dependent variable was well-being. There was no model 2 when the dependent variable was depression, as none of the additional confounders were correlated with this score. In an additional step, we also adjusted for baseline mental health variables at the first GDM

clinical visit in order to investigate if the associations changed. Given that this did not change the results (data not shown), we used the simpler model (model 2). In analogy, we also tested completely unadjusted models. However, as is common practice, we adjusted for age and gestational age in our basic model 1.

3. Results

Table 1 shows detailed descriptive information regarding sociodemographic and medical parameters. Women had a mean age of 33.62 ± 5.34 years and a mean gestational age of 28.85 ± 3.38 weeks at the first GDM clinical visit and a mean gestational age of 36.44 ± 1.28 at the last GDM clinical visit. 25.2% of women suffered from clinically relevant symptoms of depression and 47.8% of women took glucose-lowering medication during their GDM pregnancy. In our sample, 120 (35.2%) women were pregnant for the first time and 167 (49%) had no previous babies. Out of 174 (51%) women who were multiparas, 9.2% (*n* = 16) had previous GDM.

3.1 Prospective associations between mental health and the subsequent need for glucose-lowering medication during pregnancy

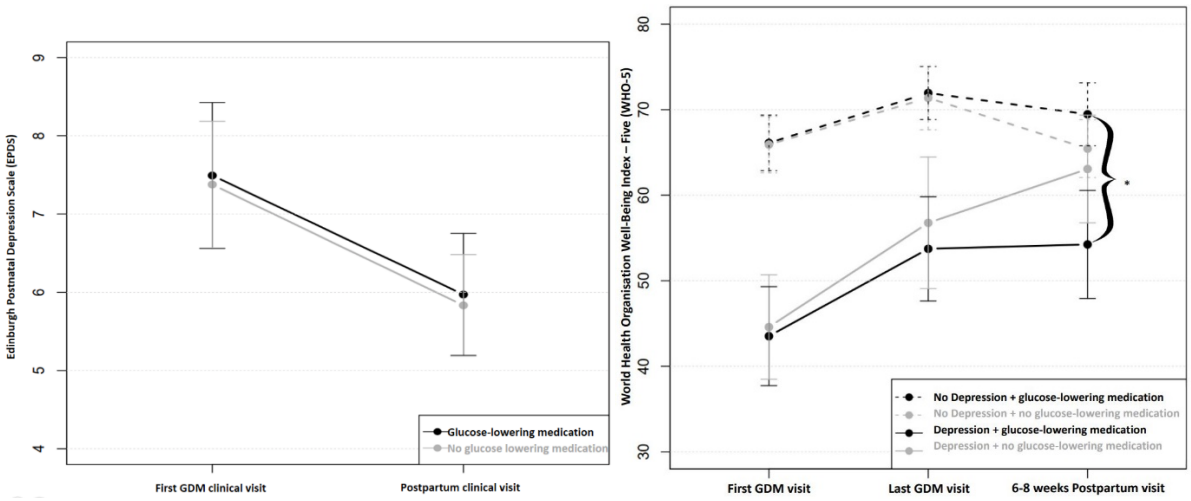
Women's mental health at the first GDM clinical visit did not predict a subsequent need for glucose lowering medication during pregnancy, neither for the depression (OR=1.0 (CI=0.96 – 1.04; $p = 0.94$) nor for the well-being scores (OR=0.99 (CI=0.98–1.01; $p = 0.29$). These results remained similar in model 2 (OR=0.99 (CI=0.93 – 1.04; $p = 0.62$) and (OR=0.99 (CI=0.98 – 1.01; $p = 0.30$)).

The association between the well-being score and the subsequent need for glucose-lowering medication was not significantly different between women with or without clinically relevant symptoms of depression at the first GDM clinical visit (*p* for interaction = 0.80).

3.2 Prospective associations between the need for glucose-lowering medication and subsequent mental health during and after pregnancy

Mental health improved significantly over time in the whole sample (see Fig. 2a & 2b). Thus, the depression scores decreased by 26% between the first GDM clinical visit and the postpartum clinical visit (B=−1.74, CI= −2.22 to −1.26, $p < 0.01$). Specifically, mean scores changed from a 7.43 ± 5.46 at the first GDM clinical visit to 5.90 ± 4.40 at the postpartum clinical visit. The well-being scores increased overall by 7% between the first GDM clinical visit and the postpartum clinical visit (*B*=2.49, CI= 1.34 – 3.64, $p < 0.01$). More specifically, the mean well-being scores changed from 60.55 ± 20.368 at the first GDM clinical visit to 67.59 ± 17.96 at the last GDM clinical visit, and to 65.43 ± 18.79 at the postpartum clinical visit.

Figure 2:



2a **2b**

Overall effect of time showing significant decreases in mean depression (Fig. 2a; Edinburgh Postnatal Depression Scale (EPDS)) and well-being (Fig. 2b; World Health Organization Well-being Index-Five; (WHO-5)) scores in the overall sample (B=−1.74, CI= −2.22 to –1.26, p < 0.01 and B=2.49, CI= 1.34 – 3.64, p < 0.01). For illustrative purposes, women with and without glucose-lowering medication are separated. Of all interaction effects tested, the only significant finding relates to the presence or not of clinically relevant symptoms of depression (named "depression" in the figures) at the first GDM visit on the association between glucose-lowering medication in pregnancy and well-being at the postpartum visit (p for interaction = 0.01 and shown as a star on Fig. 2b). Values are shown as means and standard errors.

The need for glucose-lowering medication during pregnancy had no impact on subsequent mental health during and after pregnancy. This was the case for the depression scores at the postpartum clinical visit (*B*=0.29 (CI=−0.76 to 1.34; *p* = 0.59)), the well-being scores at the end of pregnancy (*B*=2.01 (CI=−6.72 to 2.69; *p* = 0.40) in model 1, *B*= 2.26 (CI=−6.84 to 2.32; *p* = 0.33) in model 2) and the well-being scores at the postpartum clinical visit (*B*=−0.15 (CI=−4.59 to 4.30; *p* = 0.95) in model 1, *B*= 0.25 (CI=−4.18 to 4.69; *p* = 0.91) in model 2). These results remained unchanged when controlled for baseline mental health at the first GDM clinical visit (data not shown).

When looking at the detailed glucose-lowering medication, we found very similar results (see Table 2), with the exception of metformin, used in 13 women, that was associated with improved well-being in the postpartum period compared to no glucose-lowering medication (*p* = 0.03, see Table 2).

Table 2. Prospective associations between detailed glucose-lowering medication during pregnancy and subsequent mental health.

	Model 1	Model 2
	Well-being scores at the last GDM clinical visit	
Metformin vs none	B= -0.62 (CI= -11.66 – 10.43)	B= -0.99 (CI= -11.63 – 9.65)
Long-acting Insulin vs none	B= -2.95 (CI= -8.86 – 2.96)	B= -1.99 (CI= -7.79 – 3.82)
Short-acting Insulin vs none	B= -0.54 (CI= -6.22 – 5.13)	B= -0.24 (CI= -5.84 – 5.36)
	Well-being scores at the postpartum clinical visit	
Metformin vs none	B= 11.65 (CI= 1.06 – 22.24)*	B= 11.42 (CI= 0.92 – 21.92)*
Long-acting Insulin vs none	B= -1.97 (CI= -7.60 – 3.67)	B= -1.41 (CI= -7.16 – 4.34)
Short-acting Insulin vs none	B= 1.26 (CI= -4.04 – 6.55)	B= 1.57 (CI= -3.81 – 6.95)
	Depression scores at the postpartum clinical visit	
Metformin vs none	B= -0.15 (CI= -2.64 – 2.34)	-
Long-acting Insulin vs none	B= 1.00 (CI= -0.34 – 2.31)	-
Short-acting Insulin vs none	B= 0.46 (CI= -1.72 – 0.80)	-

Results reported as β-Coefficient (95% confidence interval) from a general linear model.

The following three categories are compared to "no glucose-lowering medication" (termed "none") being used as a reference category (1), metformin only (2), long-acting (basal) bedtime insulin (± metformin) (3), and short-acting (meal) insulin (± long-acting bedtime insulin and/or metformin) (4).

Model 1 adjusted for maternal age and gestational age at the first GDM clinical visit.

Model 2 adjusted for maternal age, gestational age, family history of diabetes and well-being at the first GDM clinical visit, except for the analyses with the depression score at the postpartum clinical visit for which no additional confounders were added, as no additional confounders were significantly correlated to this dependent variable.

* p <0.05

Regarding the interaction effect of clinically relevant symptoms of depression on the association between glucose-lowering medication and mental health, we found no interaction effect on the depression score at the postpartum clinical visit (p = 0.93), nor on the well-being score at the end of pregnancy (p = 0.49). However, in women with clinically relevant symptoms of depression, glucose-

lowering medication in pregnancy was associated with a lower improvement in the well-being score at the postpartum clinical visit compared to women without clinically relevant symptoms of depression (p for interaction = 0.01, Fig. 2b). Further stratification analysis revealed that, in women with clinically relevant symptoms of depression, glucose-lowering medication led to a non-significant decrease in well-being of −8.82 points ($p = 0.063$), whereas in women without symptoms of depression, glucose-lowering medication lead to a non-significant increase in the well-being scores of 4.02 points ($p = 0.12$).

4. Discussion

This study investigated a clinical cohort of women with GDM and demonstrated that mental health symptoms at the first GDM clinical visit did not predict a later need for glucose-lowering medication. Furthermore, mental health improved throughout pregnancy and in the early postpartum period. Importantly, the need for glucose-lowering medication was not associated with future mental health symptoms during and after pregnancy. Clinically relevant symptoms of depression at the first GDM clinical visit did not interact with these investigated associations, except for the well-being scores at the postpartum clinical visit, which improved less in women with clinically relevant symptoms of depression.

To the best of our knowledge, this is the first study to report that there is no association between mental health symptoms and the subsequent need for glucose-lowering medication in women with GDM. Previous research shows that mental health symptoms are associated with both a lower adherence to lifestyle interventions and thus can lead to higher glycaemia (Molyneaux et al., 2018, Carter and Swardfager, 2016, Ruchat and Mottola, 2013), and, that mental health symptoms are also directly associated with a higher glycaemia in pregnancy (Hinkle et al., 2016, Horsch et al., 2016). Both, low adherence to lifestyle interventions and higher glycaemia would be expected to lead to a more frequent need for glucose-lowering medication. Surprisingly, this was not the case in our population, nor was this influenced by the presence of clinically relevant symptoms of depression. These symptoms were present in 25.2% of our cohort and the mean score was 7.43 at the first GDM clinical visit, which is comparable to other studies in women with GDM and, for some, in normal pregnancies (Damé et al., 2017, Varela et al., 2017, Mak et al., 2019, Wilson et al., 2019). In our sample, the symptoms of depression declined by 26% to a mean score of 5.9 at the postpartum clinical visit. This score is similar to a previous sample of GDM women in the postpartum period (Nicklas et al., 2013). In the current sample, the well-being scores also augmented by 7% between the first GDM clinical visit and the postpartum clinical visit, and attained similar scores as previously reported in

healthy pregnancies and in the postpartum period (Mortazavi et al., 2015). The scores at the last GDM clinical visit cannot be compared to previous research as we are not aware of such studies. The fact that well-being at the first GDM clinical visit and the postpartum clinical visit in our sample is not lower than that of normal pregnancies is reassuring, given that women with GDM usually have higher depression scores than the general population (Bennett et al., 2004, Damé et al., 2017), and that depression is known to be negatively associated with well-being in pregnancy (Wersebe et al., 2018). We believe that the improvements found in mental health over time could be due to the social support the patients receive from clinicians (Barger et al., 2014). Indeed, women are seen a for a few clinical appointments during their pregnancy and receive tailored advice and attention from our team of specialized clinicians. This could also have improved well-being and lowered depression in our population, despite the need for frequent glucose monitoring and lifestyle adjustments.

The improvements found in mental health were not influenced by glucose-lowering medication intake, as glucose-lowering medication did not predict the future well-being or depression scores during or after pregnancy. This result is comparable to one previous study in women with GDM showing that use of insulin during pregnancy was not associated with symptoms of depression in the postpartum period (Nicklas et al., 2013), while overall well-being or mental health during pregnancy has not been previously investigated. These findings may reassure clinicians when they need to initiate glucose-lowering medication with patients, as mental health does not seem to be affected by medication intake, at least in our population. This could possibly mean that women do not view glucose-lowering medication as a failure of their lifestyle behavior change, but rather as another acceptable solution to lower their glucose. Also, glucose-lowering medication may bring them some relief if lifestyle adaptations alone did not yield the desired effect (Rowan et al., 2008). Another novel, yet, secondary finding was that the use of metformin was associated with improved well-being in the postpartum period. Although, this result is in line with previous research showing that metformin is the preferred type of medication in women with GDM (Rowan et al., 2008), this result should be interpreted with caution and needs to be replicated in future research, as this concerned only a very small number of women (n = 13, 3.8%).

The presence of clinically relevant symptoms of depression did not interact with our findings except with the association between glucose-lowering medication during pregnancy and the well-being scores in the postpartum period. Indeed, the results demonstrated that in women with both clinically relevant symptoms of depression and glucose-lowering medication, there was a lower improvement in the postpartum well-being scores compared to women with no clinically relevant symptoms of

depression. In these women, the combination of glucose-lowering medication, higher depression scores and having to care for a newborn might cumulate and contribute to the lower increase and lower absolute well-being scores. Hajos et al. showed that a score of 50 on the WHO-5, which is close to the mean score of 54 in our subgroup of women, can be interpreted as suboptimal well-being and warrants further testing for depression (Hajos et al., 2013). This is especially important, as depression in the postpartum period can have adverse impacts on the mother's cardio-metabolic health (Christenson et al., 2016, Herring et al., 2008, Carter and Swardfager, 2016). Depression in the postpartum may also lead to negative consequences for the infant, such as lower duration of breastfeeding (Cato et al., 2019) and to relationship difficulties between the mother and her infant, which have shown to be prospectively associated with a suboptimal development of cognitive (for example language development) and emotional functioning of the infant (Grace et al., 2003, Cooper and Murray, 1998). Thus, these women should be identified and may need psychological interventions.

4.1 Strengths and limitations

This study has several strengths. First, we included a "real-life", multiethnic and diverse population in which patients completed the questionnaires either in their native language or with the help of a certified professional translator. Second, we included influential confounding variables; in our basic model we controlled for variables of interest in the GDM population (Crowther et al., 2005, Ruohomäki et al., 2018), and in our second model, we added confounding variables that correlated significantly to our dependent variables. Finally, we also made sure that the well-being and depression scores at the first GDM clinical visit did not alter the results by controlling for these results with a third model (data not shown).

Limitations of the study include the lack of information about the women's physical activity and diet behaviors, which could have been important confounders for the intake of glucose-lowering medication. Furthermore, we do not have information about mental health variables before the first GDM clinical visit or mental health measurements other than depression or well-being scores after their GDM diagnosis (such as anxiety symptoms), which could be seen as a limitation. The data about metformin needs to be interpreted with caution, as this only concerns 13 (3.8%) of women and the choice to treat with metformin might be biased. As no exclusion criteria were applied for the timings of the clinical visits, this could have had an influence on the women's mental health variables. Women came for their first GDM clinical visit at a mean of 28.85 (3.38) weeks of gestation. Allover, 8 (2.4%) women came before 20 or 24 weeks of gestation, as no women came between 20 and 24 weeks of

gestation and 29 (8.7%) came later than 32 weeks of gestation for their first GDM clinical visit. The last GDM clinical visit took place at a mean of 36.44 (1.28) weeks; all of the women came between 32 and 40 weeks of gestation and of those, 55 (23.7%) came before 36 weeks of gestation. We therefore performed the main analyses in a limited sample of 157 women who came between 24 and 32 weeks of gestation at the first GDM clinical visit and who were at 36 weeks of gestation or more at the last GDM clinical visit and the results did not significantly change.

5. Conclusion

This prospective clinical cohort study found that mental health symptoms did not lead to a higher subsequent need for glucose-lowering medication in women with GDM. This finding is reassuring, as it means that even if mental health symptoms can impact both on lifestyle behavior and on glycaemia, it does not necessarily implicate a higher need for glucose-lowering medication. Secondly, glucose-lowering medication did not worsen the trajectory of mental health symptoms in this GDM population. This is reassuring for clinicians, as it demonstrates that glucose-lowering medication can be prescribed without the risk of worsening mental health symptoms (symptoms of depression and lower well-being in particular). Even if mental health symptoms did not affect the need for glucose-lowering medication in our pregnant population, it may influence lifestyle behavior and/or glucose values in the postpartum period and thus increase the risk of later prediabetes or diabetes. Similarly, further research should investigate, if the diagnosis of prediabetes and/or diabetes would worsen mental health symptoms in the following months and years and define the trajectory for such a change in order to intervene early. Further studies should also aim at investigating the relationship between use of medication and other mental health symptoms, such as anxiety in the GDM population.

CRediT authorship contribution statement

LG lead the conception and design of the current aims of the study, lead the choices on methodology and supported the data curation, performed the formal analysis, lead the interpretation of data, and wrote the original draft the manuscript. AN delivered the information and literature regarding medication use. DQ lead the data curation, completed the database and equally edited and reviewed the manuscript. JBR supported the interpretation of the data, and edited and reviewed the manuscript. JP is responsible for the overall cohort and participated in the conception and design of the study, choices on methodology, and lead the editing and reviewing of the manuscript and lead the acquiring of funds for the study, lead the supervision of the study. AH equally participated in the conception and design of the study, supported the choices on methodology, also lead the editing and

reviewing of the manuscript, and equally supervised the study. All authors read and approved the final manuscript.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgements

We would like to give a special thanks to our colleagues that collected and entered data for this study: Isabelle Cohen, Justine Gross, Céline Helbling, Stefano Lanzi, Giada Ostinelli and Dominique Stulz.

This study is a pilot project of a study supported by the Swiss National Science Foundation (SNF 32003B_176119), Switzerland and received an unrestricted educational grant from NovoNordisk, Switzerland. The funding organizations had no role in the study design, the collection, analysis or interpretation of data, nor in the writing of the report or the decision to submit for publication.

Bibliography

Alexandre, Ketia, Olivier Desrichard, Bernard Burnand, and Isabelle Peytremann-Bridevaux. 2017. Factors influencing self-management in adults with diabetes: an umbrella review protocol, JBI database of systematic reviews and implementation reports, 15: 2630-37.

American Diabetes, Association. 2019. 14. Management of Diabetes in Pregnancy: Standards of Medical Care in Diabetes-201', DIABETES CARE, 42: S165-S72.

American Diabetes Association. 2020. 14. Management of Diabetes in Pregnancy: Standards of Medical Care in Diabetes—2020, DIABETES CARE, 43: S183-S92.

Arditi C, Burnand B, Puder J. 2017. "Recommendations pour la pratique clinique 2017." In.

Barger, Steven D, Nadine Messerli-Bürgy, and Jürgen Barth. 2014. Social relationship correlates of major depressive disorder and depressive symptoms in Switzerland: nationally representative cross sectional study, BMC public health, 14: 273.

Bennett, Heather A, Adrienne Einarson, Anna Taddio, Gideon Koren, and Thomas R Einarson. 2004. Prevalence of depression during pregnancy: systematic review, Obstetrics & Gynecology, 103: 698-709.

Blumer, Ian, Eran Hadar, David R Hadden, Lois Jovanovič, Jorge H Mestman, M Hassan Murad, and Yariv Yogev. 2013. Diabetes and pregnancy: an endocrine society clinical practice guideline, The Journal of Clinical Endocrinology & Metabolism, 98: 4227-49.

Bunevicius, Adomas, Laima Kusminskas, Victor J Pop, Cort A Pedersen, and Robertas Bunevicius. 2009. Screening for antenatal depression with the Edinburgh Depression Scale, Journal of Psychosomatic Obstetrics & Gynecology, 30: 238-43.

Carroll, Dana G, and Kristi W Kelley. 2014. Review of metformin and glyburide in the management of gestational diabetes, Pharmacy practice, 12.

Carter, Jasmine, and Walter Swardfager. 2016. Mood and metabolism: anhedonia as a clinical target in type 2 diabetes, Psychoneuroendocrinology, 69: 123-32.

Cato, Karin, Sara M Sylvén, Marios K Georgakis, Natasa Kollia, Christine Rubertsson, and Alkistis Skalkidou. 2019. Antenatal depressive symptoms and early initiation of breastfeeding in association with exclusive breastfeeding six weeks postpartum: a longitudinal population-based study, BMC pregnancy and childbirth, 19: 49.

Cefalu, William T, Erika Gebel Berg, Mindy Saraco, Matthew P Petersen, Sacha Uelmen, and Shamera Robinson. 2019. Management of Diabetes in Pregnancy: Standards of Medical Care in Diabetes-2019, DIABETES CARE, 42: S165-S72.

Cesta, Carolyn E, Jacqueline M Cohen, Laura Pazzagli, Brian T Bateman, Gabriella Bröms, Kristjana Einarsdóttir, Kari Furu, Alys Havard, Anna Heino, and Sonia Hernandez-Diaz. 2019. Antidiabetic medication use during pregnancy: an international utilization study, BMJ Open Diabetes Research and Care, 7.

Christenson, Anne, Eva Johansson, Signy Reynisdottir, Jarl Torgerson, and Erik Hemmingsson. 2016. Women's Perceived Reasons for Their Excessive Postpartum Weight Retention: A Qualitative Interview Study, PloS one, 11: e0167731.

Colberg, Sheri R, Kristin Castorino, and Lois Jovanovič. 2013. Prescribing physical activity to prevent and manage gestational diabetes, World journal of diabetes, 4: 256.

Cooper, Peter J, and Lynne Murray. 1998. Postnatal depression, Bmj, 316: 1884-86.

Cox, J. L., J. M. Holden, and R. Sagovsky. 1987. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale, The British journal of psychiatry, 150: 782-86.

Crowther, Caroline A, Janet E Hiller, John R Moss, Andrew J McPhee, William S Jeffries, and Jeffrey S Robinson. 2005. Effect of treatment of gestational diabetes mellitus on pregnancy outcomes, New England Journal of Medicine, 352: 2477-86.

Damé, Patrícia, Kadhija Cherubini, Pâmella Goveia, Geórgia Pena, Leony Galliano, Cristina Façanha, and Maria Angélica Nunes. 2017. Depressive Symptoms in Women with Gestational Diabetes Mellitus: The LINDA-Brazil Study, Journal of diabetes research, 2017.

Daniells, Suzie, Brin FS Grenyer, Warren S Davis, Keith J Coleman, Julie-Anne P Burgess, and Robert G Moses. 2003. Gestational diabetes mellitus: is a diagnosis associated with an increase in maternal anxiety and stress in the short and intermediate term?, DIABETES CARE, 26: 385-89.

Fowles, Eileen R, Christina Murphey, and Roberta Jeanne Ruiz. 2011. Exploring relationships among psychosocial status, dietary quality, and measures of placental development during the first trimester in low-income women, Biological research for nursing, 13: 70-79.

Gilbert, L., J. Gross, S. Lanzi, D. Y. Quansah, J. Puder, and A. Horsch. 2019. How diet, physical activity and psychosocial well-being interact in women with gestational diabetes mellitus: an integrative review, BMC Pregnancy Childbirth, 19: 60.

Grace, Sherry L, Alexandra Evindar, and DE Stewart. 2003. The effect of postpartum depression on child cognitive development and behavior: a review and critical analysis of the literature, Archives of women's mental health, 6: 263-74.

Guedeney, N, and J Fermanian. 1998. Validation study of the French version of the Edinburgh Postnatal Depression Scale (EPDS): new results about use and psychometric properties, European psychiatry, 13: 83-89.

Hajos, Tibor RS, F Pouwer, SE Skovlund, Brenda L Den Oudsten, PHLM Geelhoed-Duijvestijn, CJ Tack, and Frank J Snoek. 2013. Psychometric and screening properties of the WHO-5 well-being index in adult outpatients with Type 1 or Type 2 diabetes mellitus, Diabetic Medicine, 30: e63-e69.

Henkel, Verena, Roland Mergl, Ralf Kohnen, Wolfgang Maier, Hans-Jürgen Möller, and Ulrich Hegerl. 2003. Identifying depression in primary care: a comparison of different methods in a prospective cohort study, Bmj, 326: 200-01.

Herring, Sharon J, Janet W Rich-Edwards, Emily Oken, Sheryl L Rifas-Shiman, Ken P Kleinman, and Matthew W Gillman. 2008. Association of postpartum depression with weight retention 1 year after childbirth, Obesity, 16: 1296-301.

Hinkle, Stefanie N., Germaine M. Buck Louis, Shristi Rawal, Yeyi Zhu, Paul S. Albert, and Cuilin Zhang. 2016. A longitudinal study of depression and gestational diabetes in pregnancy and the postpartum period, Diabetologia, 59: 2594-602.

Hochberg, G, S Pucheu, L Kleinebreil, S Halimi, and C Fructuoso-Voisin. 2012. WHO-5, a tool focusing on psychological needs in patients with diabetes: The French contribution to the DAWN study, Diabetes & metabolism, 38: 515-22.

Horsch, Antje, Ji Seon Kang, Yvan Vial, Ulrike Ehlert, Ayala Borghini, Pedro Marques-Vidal, Ingo Jacobs, and Jardena J. Puder. 2016. Stress exposure and psychological stress responses are related to glucose concentrations during pregnancy, British journal of health psychology: n/a-n/a.

Lehmann, Roger, Troendle, and Brändle. 2009. Neue Erkenntnisse zur Diagnostik und Management des Gestationsdiabetes, Therapeutische Umschau, 66: 695-706.

Mak, Jonathan KL, Andy H Lee, Ngoc Minh Pham, Li Tang, Xiong-Fei Pan, Colin W Binns, and Xin Sun. 2019. Gestational diabetes and postnatal depressive symptoms: A prospective cohort study in Western China, Women and Birth, 32: e427-e31.

Metzger, Boyd E, Thomas A Buchanan, Donald R Coustan, Alberto De Leiva, David B Dunger, David R Hadden, Moshe Hod, John L Kitzmiller, Siri L Kjos, and Jeremy N Oats. 2007. Summary and recommendations of the fifth international workshop-conference on gestational diabetes mellitus, DIABETES CARE, 30: S251-S60.

Metzger, Boyd E., Steven G. Gabbe, Bengt Persson, Thomas A. Buchanan, Patrick A. Catalano, Peter Damm, Alan R. Dyer, Alberto de Leiva, Moshe Hod, John L. Kitzmiler, Lynn P. Lowe, H. David McIntyre, Jeremy J. N. Oats, Yasue Omori, and Maria Ines Schmidt. 2010. International association of diabetes and pregnancy study groups recommendations on the diagnosis and classification of hyperglycemia in pregnancy, DIABETES CARE, 33: 676-82.

Molyneaux, Emma, Shahina Begum, Annette L Briley, Paul T Seed, Louise M Howard, and Lucilla Poston. 2018. Do elevated symptoms of depression predict adherence and outcomes in the UPBEAT randomised controlled trial of a lifestyle intervention for obese pregnant women?, BMC pregnancy and childbirth, 18: 378.

Mortazavi, Forough, S-A Mousavi, Reza Chaman, and Ahmad Khosravi. 2015. Validation of the World Health Organization-5 Well-Being Index; assessment of maternal well-being and its associated factors, Turk Psikiyatri Dergisi, 26: 1-7.

Nicklas, Jacinda M, Laura J Miller, Chloe A Zera, Roger B Davis, Sue E Levkoff, and Ellen W Seely. 2013. Factors associated with depressive symptoms in the early postpartum period among women with recent gestational diabetes mellitus, Maternal and child health journal, 17: 1665-72.

Clinical Chemistry and Clinical Toxicology Devices Panel, FDA Public Advisory Meeting Alere AfinionTM HbA1c Dx. https://www.fda.gov/media/99241/download.Clinical Chemistry and Clinical Toxicology Devices Panel, 2016Panel, Clinical Chemistry and Clinical Toxicology Devices , 2016. FDA Public Advisory Meeting Alere AfinionTM HbA1c Dx, 2016. https://www.fda.gov/media/99241/download.

Robertson, S. M., M. A. Stanley, J. A. Cully, and A. D. Naik. 2012. Positive emotional health and diabetes care: concepts, measurement, and clinical implications, Psychosomatics, 53: 1-12.

Rowan, J. A., W. M. Hague, W. Gao, M. R. Battin, M. P. Moore, and G. Trial Investigators Mi. 2008. Metformin versus insulin for the treatment of gestational diabetes, N Engl J Med, 358: 2003-15.

Ruchat, Stephanie-May, and Michelle F Mottola. 2013. The important role of physical activity in the prevention and management of gestational diabetes mellitus, Diabetes/metabolism research and reviews, 29: 334-46.

Ruohomäki, Aleksi, Elena Toffol, Subina Upadhyaya, Leea Keski-Nisula, Juha Pekkanen, Jussi Lampi, Sari Voutilainen, Tomi-Pekka Tuomainen, Seppo Heinonen, and Kirsti Kumpulainen. 2018. The association between gestational diabetes mellitus and postpartum depressive symptomatology: A prospective cohort study, Journal of affective disorders, 241: 263-68.

Topp, C. W., S. D. Østergaard, S. Søndergaard, and P. Bech. 2015. The WHO-5 Well-Being Index: A Systematic Review of the Literature, Psychotherapy and psychosomatics, 84: 167-76.

Varela, Pinelopi, Areti C Spyropoulou, Zacharias Kalogerakis, Eleni Vousoura, Martha Moraitou, and Iannis M Zervas. 2017. Association between gestational diabetes and perinatal depressive symptoms: evidence from a Greek cohort study, Primary health care research & development, 18: 441-47.

Watson, Lea C, Sheryl Zimmerman, Lauren W Cohen, and Rosalie Dominik., 2009. Practical depression screening in residential care/assisted living: five methods compared with gold standard diagnoses. The American Journal of Geriatric Psychiatry 17: 556-64.

Webber, Jonathan, Mary Charlton, and Nina Johns. 2015. Diabetes in pregnancy: management of diabetes and its complications from preconception to the postnatal period (NG3), British Journal of Diabetes, 15: 107-11.

Wersebe, Hanna, Roselind Lieb, Andrea H Meyer, Marcel Miche, Thorsten Mikoteit, Christian Imboden, Jürgen Hoyer, Klaus Bader, Martin Hatzinger, and Andrew T Gloster. 2018. Well-being in

major depression and social phobia with and without comorbidity, International Journal of Clinical and Health Psychology.

Wilson, C, J Newham, J Rankin, K Ismail, Emily Simonoff, RM Reynolds, N Stoll, and LM Howard. 2019. Is there an increased risk of perinatal mental disorder in women with gestational diabetes? A systematic review and meta-analysis, Diabetic Medicine.

Wood, Jamie R, Brett M Kaminski, Craig Kollman, Roy W Beck, Callyn A Hall, Jason P Yun, Eda Cengiz, Michael J Haller, Krishna Hassan, and Georgeanna J Klingensmith. 2012. Accuracy and precision of the Axis-Shield Afinion hemoglobin A1c measurement device, Journal of diabetes science and technology, 6: 380-86.

8.5 Trainings

8.5.1 Research

1. Good Clinical Practice (GCP) : March 2019 – In-service training by Clinical epidemiology center IUMSP (CHUV), Clinical Research Center FBM (CHUV) and “Centre des formations” (CHUV)

8.5.2 Clinical

2. Motivational Interviewing: December 2015 – In-service training by the swiss society of general medicine - Société Suisse de Médecine Générale (SSMG)
3. Mindful Eating : February 2016 – In-service training by https://www.londonmindful.com
4. Cognitive-Behavioural Therapy : November 2017 – In-service training by the federal office of public health - l’office fédéral de la santé publique (OFSP)
5. Promotion of physical activity in children: Mai 2016 – In-service training by “ça marche ! Bouger plus, manger mieux” and the medical and chirurgical department of pediatrics - département médical de chirurgie et de pédiatrie DMCP (CHUV)
6. Individual and multidisciplinary therapy of childhood obesity: Mai 2016 – In-service training by Swiss society of pediatrics - société Suisse de pédiatrie (SSP) and Swiss Association of Graduate Dieticians – association Suisse des diététicien(ne)s diplômé(e)s (ASDD)
7. Interactive guidance: a brief parent-child therapy to support family resources: October 2016 – In service training by the child and adolescent psychiatric service - service de psychiatrie de l’enfant et de l’adolescent (SPEA)

8.6 Scientific Outreach Activities

8.6.1 Reviewing activities

Table 7. Reviewing activities.

Journal	Reference	Date
Journal of the American College of Nutrition	UACN-2020-0387	September 2020
Diabetes Research and Clinical Practice	DIAB_2019_370	June 2019
BMC Pregnancy and Childbirth (under supervision by Prof. Jardena Puder)	PRCH-D-18-00936	September 2018

8.6.2 Teaching activities

Table 8. Teaching activities

Course title	Students	Infrastructure	Place	Date
Motivational Interviewing in the context of a pregnancy complicated by gestational diabetes	Trained specialized practitioner nurses (IPS)	The Institute of Higher Education and Research in Healthcare (IUFRS),	Virtual	05.05.20
Motivational Interviewing in the context of a pregnancy complicated by gestational diabetes	Trained specialized practitioner nurses (IPS)	The Institute of Higher Education and Research in Healthcare (IUFRS)	Lausanne, Switzerland	03.05.19
Mental and metabolic health in the prepartum and postoartum period, what is psychology's role?	Master of Advances Studies (MAS) in Health Psychology	IDEAHP (Institut de hautes études en administration publique),	University of Lausanne (UniL)	12.04.19
Nutrition, Pregestational and gestational diabetes. A non-medical and multidisciplinary approach.	Professional dieticians	University of applied sciences and arts of Western Switzerland (HES-SO)	CHUV, Lausanne	28.11.17

8.6.3 Co-supervision of student interns

Table 9. Co-supervision of the student interns for the testing, organization and coaching of patients in the *MySweetHeart trial* together with Professor Horsch and Professor Puder.

Names	Studies
Giada Ostinelli & Agnès Bacso	Postmaster students
Chloé Beutler, Julia Primavesi & Giada Maspoli	MSc Sports Sciences at the University of Lausanne
Michelle Grossglauser, Svenia Queiros & Arnaud Guélat	MSc Psychology at the University of Fribourg,

Marie-Josée Meuwly, Seyda Demircan, Lucia Volpato, Cécile Bétrix, Victoria Gendre, Axelle Bourgeois, Marie Couvreu, Nina Canova, Aude Guex-Crosier, Nivitha Sivaneshan & Laurie Schwab	MSc Psychology at the University of Lausanne.

8.6.4 Media presence

Swiss National Television & Youtube https://www.youtube.com/watch?v=1l8n21HxDhU

https://www.youtube.com/watch?v=9ATaN3y9U2A

Swiss National Radio "Couleur3" https://www.rts.ch/play/radio/pony-express/audio/pony-express?id=9419810 (2h41).

Swiss Regional Press https://www.lacote.ch/articles/regions/district-de-nyon/ma-these-en-180-secondes-leah-gilbert-concurrente-de-nyon-762731