Effects of a Lifestyle Intervention During Pregnancy and First Postpartum Year: Findings From the RADIEL Study

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Context: Women with a history of gestational diabetes (GDM) have a sevenfold risk of developing type 2 diabetes.

Objective: To assess the effects of a lifestyle intervention during pregnancy and first postpartum year on glucose regulation, weight retention, and metabolic characteristics among women at high GDM risk.

Design: In the Finnish Gestational Diabetes Prevention study, trained study nurses provided lifestyle counseling in each trimester and 6 weeks, 6 months, and 12 months postpartum.

Setting: Three maternity hospitals in the Helsinki area and one in Lappeenranta.

Patients: In total, 269 women with previous GDM and/or a prepregnancy body mass index $\geq$30 kg/m^2 were enrolled before 20 gestational weeks and allocated to either a control or an intervention group. This study includes the 200 participants who attended study visits 6 weeks and/or 12 months postpartum.

Intervention: The lifestyle intervention followed Nordic diet recommendations and at least 150 minutes of moderate exercise was recommended weekly.

Main Outcome Measure: The incidence of impaired glucose regulation (impaired fasting glucose, impaired glucose tolerance, or type 2 diabetes) during the first postpartum year.

Results: Impaired glucose regulation was present in 13.3% of the women in the control and in 2.7% in the intervention group [age-adjusted odds ratio, 0.18 (95% confidence interval, 0.05 to 0.65), *P* = 0.009] during the first postpartum year. There were no differences between the groups in weight retention, physical activity, or diet at 12 months postpartum.

Conclusions: A lifestyle intervention during pregnancy and the first postpartum year successfully reduced the incidence of postpartum impairment in glucose regulation. ***(J Clin Endocrinol Metab* 103: 1669–1677, 2018)**

The incidence of type 2 diabetes is increasing worldwide, causing an extensive burden on the health care system as well as on those suffering from the disease. Along with the obesity epidemic, the incidence of gestational diabetes (GDM) is also rising, reaching 18% in Finland (1). Women with a history of GDM form an important risk group because they have a sevenfold risk of developing type 2 diabetes (2) compared with women

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Abbreviations: AUC, area under the curve; BMI, body mass index; CI, confidence interval; GDM, gestational diabetes; IFG, impaired fasting glucose; IGT, impaired glucose tolerance; OGTT, oral glucose tolerance test; OR, odds ratio; RADIEL, Finnish Gestational Diabetes Prevention Study; SD, standard deviation.

without a history of GDM and also have a higher risk for other metabolic disturbances later in life (3, 4).

There is strong evidence showing that type 2 diabetes can be prevented by lifestyle intervention (5, 6). Furthermore, our recently published study findings have also shown that GDM can be prevented (7). There have been a few type 2 diabetes prevention studies, applying both lifestyle and pharmaceutical interventions, targeting women with previous GDM. Some of them have succeeded in moderately reducing the incidence of type 2 diabetes (8–11). Only limited data exist, however, on how a lifestyle intervention during pregnancy will affect the future risk of type 2 diabetes and cardiovascular risk (12–14). There are suggestions that an intervention initiated during pregnancy and continued after delivery might be feasible and even more successful (15).

In the Finnish Gestational Diabetes Prevention Study (RADIEL), we aimed to assess the effects of a lifestyle intervention initiated in prepregnancy or early pregnancy and continuing up to 1 year after delivery. The lifestyle intervention initiated in early pregnancy reduced the incidence of GDM by 36% (7). In the current study, our aim was to evaluate the effects of the intervention on glucose regulation during the first postpartum year, as well as on weight retention and other metabolic characteristics in women recruited in early pregnancy with normal oral glucose tolerance test (OGTT) at recruitment.

Materials and Methods

Study design

RADIEL is a multicenter randomized, controlled, intervention trial targeting women at high risk for GDM, recruited either in prepregnancy or early pregnancy before 20 gestational weeks (16). The study was conducted in Finland between February 2008 and January 2014 in all three maternity hospitals in the Helsinki metropolitan area (Helsinki University Hospital, Department of Obstetrics and Gynecology; Kätilöopisto Maternity Hospital; Jorvi Hospital) and in the South-Karelia Central Hospital in Lappeenranta. The design of the RADIEL intervention trial has been presented in detail previously (16). This study focuses on a subgroup of women recruited in early pregnancy with normal OGTT at recruitment (7) with follow-up data available in the postpartum period.

The intervention consisted of 3 study visits during pregnancy, 1 in each trimester, and 3 visits during the postpartum year (6 weeks, 6 months, and 12 months after delivery). Participants in the intervention group were given individualized lifestyle counseling by dietitians and study nurses who were midwives trained to work as diabetes nurses (7). The lifestyle counseling concerning diet quality and exercise goals was similar during the pregnancy and postpartum periods. The dietary recommendations were based on the Nordic guidelines emphasizing an increased intake of vegetables, fruits, high-fiber grains, and fish; replacing animal fat with vegetable oil; replacing high-fat with low-fat dairy and meats; and limiting intake of high-energy products. The physical activity goal was 150 minutes of moderate intensity physical activity per week. For the overweight and obese women [prepregnancy body mass index (BMI) ≥30 kg/m^2], no gestational weight gain was recommended in the first and second trimesters. After delivery, the participants were supported and encouraged to reach their prepregnancy weight; for overweight women, a weight loss of 5% to 10% was recommended. Women in the intervention group were guided to dietary changes that they could maintain. Breastfeeding was encouraged, and counseling emphasis was on beneficial long-term lifestyle changes for the whole family.

The control group visited the study nurse at the same time points as the women in the intervention group for anthropometric measurements and laboratory testing. They received general advice and leaflets regarding diet and physical activity, usually provided by the local antenatal clinics.

Participants

The study participants were pregnant women, 18 years of age or older, with a history of GDM or a prepregnancy BMI ≥30 kg/m^2, or both, at <20 weeks of gestation at inclusion. Exclusion criteria in the current study were overt diabetes at enrollment, multiple pregnancies, physical disability, current substance abuse, severe psychiatric disorders, difficulties in cooperation, and regular medication influencing glucose metabolism. The only exclusion criterion in the RADIEL intervention study in relation to diabetes was overt type 1 or type 2 diabetes at enrollment. The women with GDM diagnosed before 20 gestational weeks (so-called "early GDM") were randomized as previously described (16), but were excluded from this substudy. For the definition of abnormal glucose regulation in the first trimester, we used the same diagnostic thresholds as in the second trimester.

Initially, the RADIEL study aimed for a sample size of 1000, but eventually 787 women were enrolled in the study. In total, 540 women were recruited in early pregnancy; of those, 492 were randomized. Among the women recruited in early pregnancy, 269 had a normal OGTT before 20 gestational weeks. Our previous report includes the findings from the pregnancy period of this subgroup (7). This present study focuses on the first postpartum year of those women and includes the participants who had at least one OGTT done after delivery (n = 200) (Fig. 1).

The Ethics Committees of Helsinki University Hospital and South-Karelia Central Hospital approved the study protocol, and the study has been registered at clinicaltrials.gov. All participants provided written informed consent.

Outcomes

The primary outcome was impaired glucose regulation defined as the presence of impaired fasting glucose (IFG), impaired glucose tolerance (IGT), or type 2 diabetes during the first postpartum year. The definition according to the World Health Organization (17) for IFG is fasting glucose 6.1 to 6.9 mmol/L; for IGT 2-hour glucose with 75 g OGTT 7.8 to 11.0 mmol/L; and for type 2 diabetes fasting glucose ≥7.0 mmol/L or 2-hour glucose with OGTT >11.0 mmol/L. OGTT was performed both 6 weeks and 12 months postpartum, independent of previous results.

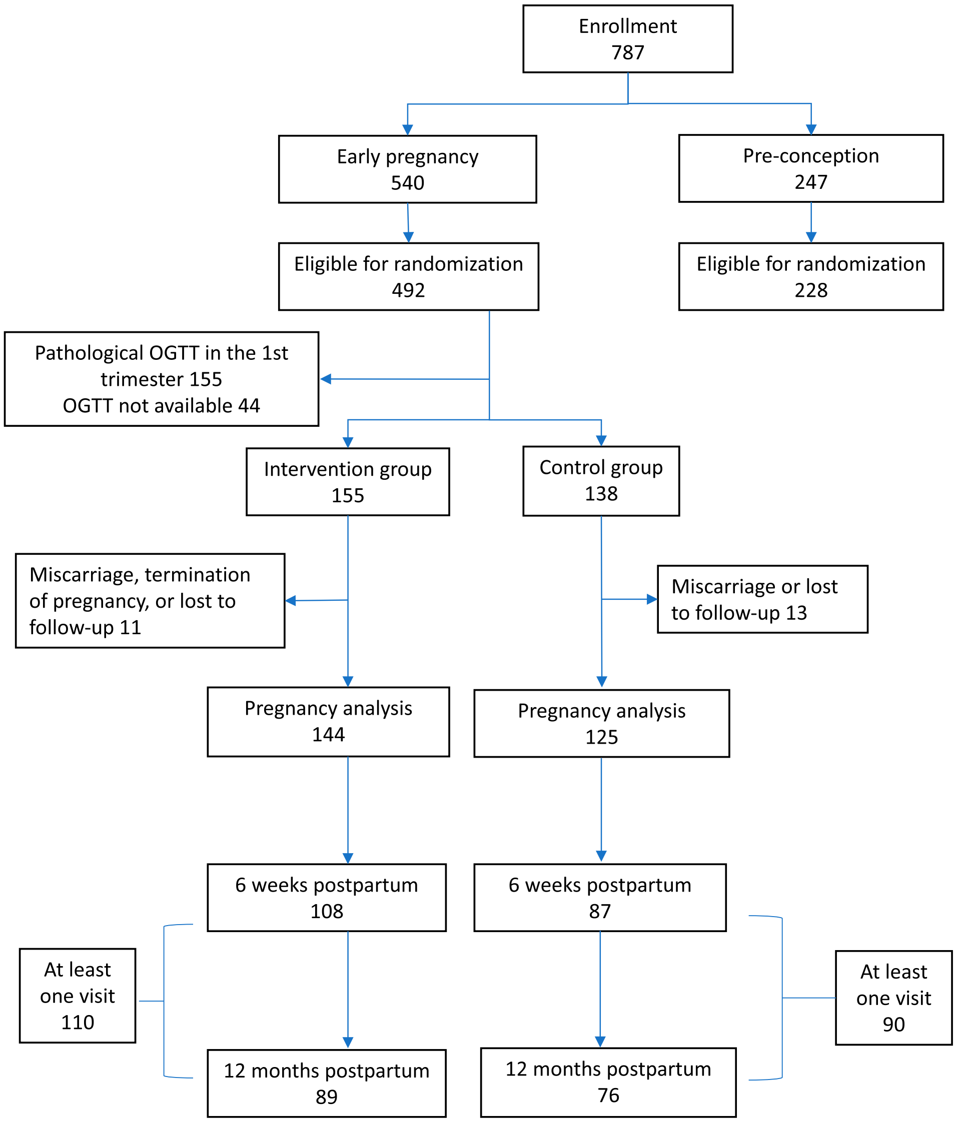

Figure 1. Flowchart of the study participants in the RADIEL study.

Other outcome measures included weight change, lipid metabolism, and changes in diet and physical activity. Laboratory tests performed in conjunction with study visits included fasting measurements of glucose metabolism (75-g 2-hour OGTT, glycated hemoglobin, fasting insulin) and lipids (cholesterol, triglycerides, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol). The methods have been previously described (18). Area under the curve (AUC) of the OGTT was calculated with the trapezoidal method (19). Anthropometric measurements (height, weight, waist, and hip circumference) were also taken, and blood pressure was measured at each study visit. Weight change was calculated between the self-reported prepregnancy weight and the weight at the study visit 12 months after delivery.

Each study visit included questionnaires about health, socioeconomic status, psychological wellbeing, diet, and physical activity. A food frequency questionnaire provided information on dietary intake and was the basis for calculating a diet quality index. Previous reports include the description (7) and validation (20) of the diet quality index designed for the RADIEL study. It is based on 11 food components in accordance with the National Dietary Guidelines and scored according to the reported frequency of intake with higher scores indicating better diet quality (score range, 0 to 17). Evaluation of leisure time physical activity was based on self-reported time spent on at least moderately strenuous physical activity per week.

Statistics

Results are expressed as means with standard deviation (SD) and as odds ratios (ORs) with 95% confidence intervals (CIs). Statistical comparison between groups was performed by *t* test, permutation test, χ^2 test, or Fisher exact test, when appropriate. Logistic regression models were used to produce age-adjusted OR of impaired glucose regulation at 6 weeks and 12 months after delivery. Repeated measures (glucose tolerance and weight change) were analyzed using generalized estimating equation models with an unstructured covariance structure; models included age as a covariate. In the case of violation of the assumptions (*e.g.*, nonnormality), a bootstrap-type test and CI estimation was used. The bootstrap method was used when the theoretical distribution of the test statistics was unknown or in the case of violation of the assumptions. The normality of the variables was tested by using the Shapiro-Wilk W test. STATA 14.1 (StataCorp LP, College Station, TX) statistical package was used for analyses.

Results

Table 1 presents the baseline characteristics of the study participants at the first antenatal visit, on average at 13 weeks of gestation. At baseline, there were no important differences between the groups in metabolic parameters or other characteristics. Among those 200 women who participated in the postpartum follow-up, GDM was diagnosed during pregnancy in 17 participants (15%) in the intervention group and in 19 (21%) in the control group (P = 0.30). During the postpartum year, 76% of the women in the intervention group and 72% in the control group continued in the study. In the control group, the dropouts were not significantly different when comparing age, BMI, family history of diabetes, and previous GDM, but in the intervention group the dropouts were significantly younger (mean difference, −2.5 years; P = 0.004). In total, 75% of the participants attended all six visits, and the mean number of visits was 5.7 (4.0 to 6.0).

At 6 weeks after delivery, impaired glucose regulation (IFG/IGT/type 2 diabetes) was diagnosed in 7.2% (6/83) of participants in the control group and in 1.0% (1/105) in the intervention group (P = 0.045). After adjustment for age, the OR was 0.11 (95% CI, 0.01 to 0.97), P = 0.047. The prevalence of impaired glucose regulation at 12 months after delivery was 9.5% (7/74) in the control group and 2.4% (2/85) in the intervention group (P = 0.053). After adjustment for age, the OR was 0.23 (95% CI, 0.05 to 1.14), P = 0.07. During postpartum follow-up, impaired glucose regulation was present, either at 6 weeks and/or at 12 months in 13.3% (12/90) of the participants in the control group and in 2.7% (3/110) (P = 0.005) of the participants in the intervention group; age-adjusted OR was 0.18 (95% CI, 0.05 to 0.65), P = 0.009. In the total study sample of women who participated in the follow up (n = 200) among those not diagnosed with GDM, 4.27% developed impaired glucose regulation (7/164), whereas the corresponding number among those with GDM was 22.2% (8/36) ($P < 0.001$). All diagnosed cases of impairment in glucose regulation were based on the 2-hour glucose value.

Type 2 diabetes was diagnosed in one participant in the control group. When glucose metabolism was assessed by glucose AUC, it was not significantly lower in the intervention group at 6 weeks (P = 0.12), but at 12 months postpartum, the difference was significant between the intervention and control groups (P = 0.04) (Fig. 2). Additionally, there were substantial differences in the glucose concentrations of the OGTT both 6 weeks and 12 months postpartum (Fig. 2).

Clinical and lifestyle characteristics 6 weeks and 12 months after delivery are presented in Table 2. There were no substantial differences between the groups. Weight changes among the participants from prepregnancy to 1 year after delivery are presented in Fig. 3. There were no differences in postpartum weight changes between the control and the intervention groups.

During the intervention period, from the first trimester to 12 months after delivery, the diet quality index

Table 1 Baseline Characteristics of the Participants at First Antenatal Visit (Average, 13 Gestational Weeks)

	Control Group (N = 90)	Intervention Group (N = 110)	*P* Value
Age (y)	32 (5)	32 (5)	0.65
Weight (kg)	89 (17)	89 (18)	0.99
Prepregnancy BMI (kg/m^2)	32.2 (5.7)	31.9 (6.0)	0.73
Educational attainment (y)	14.6 (1.8)	14.5 (2.1)	0.77
Previous deliveries, n (%)	49 (54)	64 (58)	0.60
History of GDM, n (%)	27 (30)	40 (36)	0.34
Blood pressure (mm Hg)			
Systolic	122 (14)	123 (12)	0.59
Diastolic	77 (9)	78 (9)	0.63
Total cholesterol (mmol/L)	4.83 (0.82)	4.95 (0.91)	0.34
LDL cholesterol (mmol/L)	2.74 (0.67)	2.83 (0.81)	0.45
HDL cholesterol (mmol/L)	1.74 (0.28)	1.73 (0.32)	0.85
Total triacylglycerol (mmol/L)	1.36 (0.79)	1.33 (0.57)	0.78
Fasting plasma glucose (mmol/L)	4.87 (0.25)	4.87 (0.24)	0.94
2-h glucose in 75-g OGTT (mmol/L)	5.94 (1.10)	5.87 (1.00)	0.66
HbA_{1c} (%)	5.20 (0.27)	5.23 (0.26)	0.48
HbA_{1c} (mmol/mol)	33 (3)	34 (3)	0.53
Fasting plasma insulin (pmol/L)	58.3 (32.3)	55.0 (29.2)	0.46
Physical activity at baseline (min/wk), median (IQR)	90 (30, 150)	60 (30, 130)	0.12
Dietary index at baseline	9.8 (2.7)	10.2 (2.7)	0.32

Values are presented as means (SD) unless otherwise indicated.

Abbreviations: HbA_{1c}, glycolated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

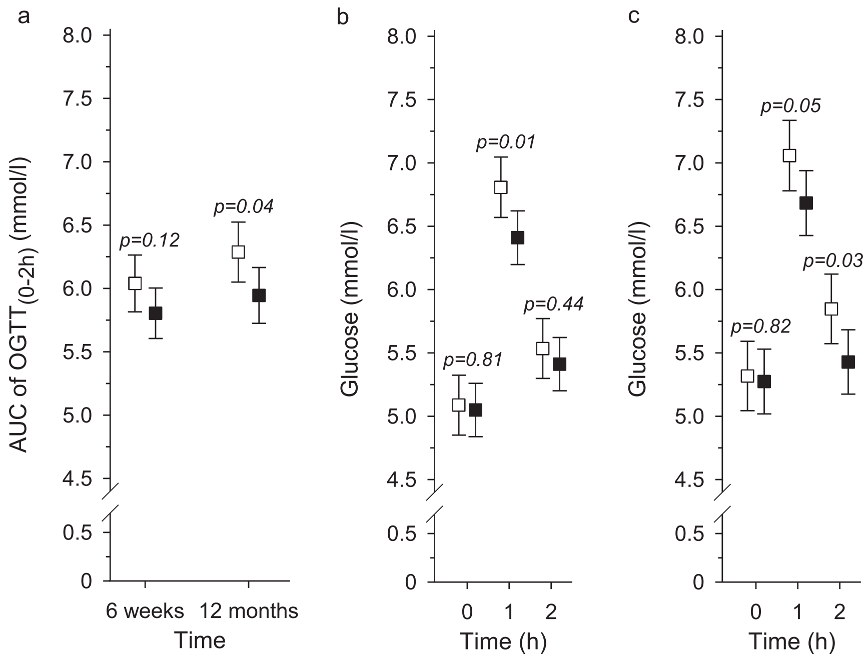

Figure 2. Glucose tolerance after delivery. (a) Glucose AUC values at 6 weeks and 12 months postpartum. (b) Plasma glucose concentrations during a 75-g, 2-hour OGTT at 6 weeks postpartum. (c) Plasma glucose concentrations in 75-g, 2-hour OGTT at 12 months postpartum. Values are adjusted for age. □, control group; ■, intervention group.

decreased in the control group, depicting a change toward an unhealthier diet; there was no such change in the intervention group [−0.9 (95% CI, −1.6 to −0.3), *P* = 0.01; and −0.3 (95% CI, −1.0 to 0.35), *P* = 0.36, respectively]. The increase in physical activity was similar in both groups (control group, median 17 minutes/week [interquartile range (IQR), −60 to 60]; intervention group, median 30 minutes/week [IQR, −30 to 90]. *P* = 0.28).

Six weeks after delivery 57% of the participants in the control group and 63% in the intervention group were exclusively breastfeeding (*P* = 0.44). The number of breastfeeding women decreased during the first year; these changes were similar in both groups. One year after delivery, 26% in the control group and 32% in the intervention group (*P* = 0.40) were still partially breastfeeding. Breastfeeding was not associated with weight change from prepregnancy to 12 months postpartum or with glucose regulation when adjusted for prepregnancy BMI.

Discussion

Our promising results from the RADIEL study, analyzing participants recruited in early pregnancy with normal glucose tolerance, demonstrate that a lifestyle intervention during pregnancy and the first postpartum year effectively reduced glucose intolerance, defined as IFG, IGT, or type 2 diabetes, in high-risk women. There were no differences in diet, physical activity, or weight retention between the groups 12 months postpartum.

During the first postpartum year, the effect of the intervention on the incidence of glycemic impairments seemed to decline, a phenomenon seen also in the Gestational Diabetes' Effects on Moms study (21). According to current understanding (22), however, the early postpartum OGTT is most sensitive in diagnosing women in high risk for type 2 diabetes. Hypothetically, normal glucose tolerance soon after delivery indicates a faster

Table 2. Metabolic Characteristics, Diet Quality Index, and Physical Activity 6 Weeks and 12 Months Postpartum

	6 Weeks Postpartum			12 Months Postpartum		
	Control Group (N = 87)	Intervention Group (N = 108)	*P* Value	Control Group (N = 76)	Intervention Group (N = 89)	*P* Value
Weight (kg)	89 (16)	89 (17)	0.83	88 (18)	88 (19)	0.80
Blood pressure (mm Hg)						
Systolic	122 (13)	122 (14)	0.69	121 (13)	121 (11)	0.83
Diastolic	80 (10)	81 (9)	0.37	80 (10)	80 (8)	0.92
Total cholesterol (mmol/L)	5.32 (0.95)	5.41 (0.99)	0.59	4.60 (0.84)	4.63 (0.91)	0.86
LDL cholesterol (mmol/L)	3.40 (0.94)	3.49 (0.91)	0.58	2.94 (0.81)	2.93 (0.80)	0.90
HDL cholesterol (mmol/L)	1.58 (0.30)	1.58 (0.34)	0.96	1.43 (0.29)	1.45 (0.33)	0.68
Total triacylglycerol (mmol/L)	1.13 (0.56)	1.11 (0.63)	0.87	0.96 (0.43)	0.97 (0.57)	0.91
HbA_{1c} (%)				5.39 (0.31)	5.36 (0.29)	0.49
HbA_{1c} (mmol/mol)				35 (3)	35 (3)	0.73
Fasting plasma insulin (pmol/L)	46.85 (29.1)	44.84 (25.0)	0.63	59.0 (27.4)	56.0 (35.6)	0.56
Physical activity (min/wk), median (IQR)	60 (0, 120)	60 (30, 150)	0.72	120 (45, 180)	100 (60, 180)	0.94
Dietary index				9.0 (2.7)	9.7 (3.1)	0.13

Values are presented as means (SD) unless otherwise indicated.

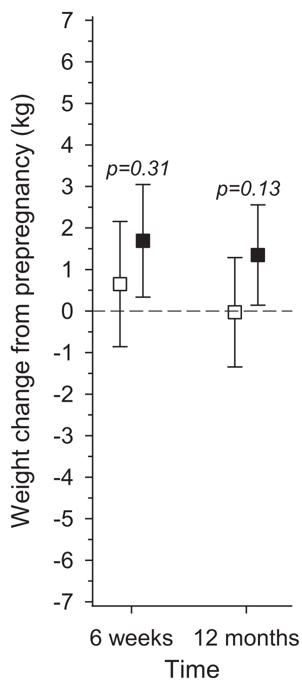

Figure 3. Weight change. Age-adjusted weight change from prepregnancy to 6 weeks and to 12 months postpartum. □, control group; ■, intervention group.

recovery from the pregnancy-related insulin resistance state and stress to beta cells. This might have positive implications for the future.

In addition to the traditional definitions of the prediabetic state (IFG and IGT), new models of glucose metabolism assessment also exist. Glucose AUC and 1-hour plasma glucose could be even better predictors of future type 2 diabetes risk and declining beta cell function (23, 24). The shape of the OGTT curve could also be used to evaluate glucose metabolism (25). In this study, 1-hour plasma glucose was significantly lower in the intervention group 6 weeks postpartum; this was also the case for the glucose AUC and 2-hour glucose at 12 months postpartum.

The strength of this trial lies in its unique study design: this GDM prevention study, in which the intervention was initiated in the beginning of pregnancy and continued during the first postpartum year, aimed also at postpartum weight control and type 2 diabetes prevention. We have data on metabolic and other characteristics from the first trimester onwards, unlike in previous intervention studies on women with a history of GDM, which have been performed only after delivery (8–11). Our study findings are in accordance with results from previous postpartum intervention studies. A recent systematic review (8) demonstrated that postpartum lifestyle interventions directed at women with prior GDM seem to have some beneficial effects in reducing progression to type 2 diabetes, although the results are inconsistent. According to Ferrara *et al.,* however, an intervention initiated during pregnancy and continued during the first postpartum year might be even more effective (15).

The changes during the intervention period in our study reflect potentially important changes in lifestyle. Neither of the groups showed substantial changes in their reported physical activity, but the intervention group was able to maintain a better dietary quality. Similar small but important changes were seen during the pregnancy period, leading to a lower GDM incidence (7), which may explain our positive results on the incidence of glycemic disturbances also noted in the postpartum period.

Postpartum weight retention has been associated with several adverse health outcomes, including type 2 diabetes, cardiovascular disease, and GDM in the next pregnancy (26). Weight retention is characteristic of the postpartum period (27); this is a major factor promoting obesity in young women of reproductive age. A recent study has shown positive effects of a postpartum lifestyle intervention on weight change and glycemic disturbances 6 months postpartum, but the differences were no longer substantial 1 year after delivery (21). In our study, however, the groups showed no differences in postpartum weight change. This might be explained partly by the beneficial effect of routine study visits and the motivation also in the control group. In addition, all the participants belonged to a high-risk group and were therefore also given enhanced counseling in local antenatal clinics.

Breastfeeding has been reported to be beneficial for both mother and child, and it was encouraged in our intervention. It has beneficial effects on maternal glucose metabolism and weight control after GDM (28, 29), and possibly reduces future overweight and incidence of diabetes in children (30). In previous intervention studies, breastfeeding has been associated with better postpartum weight control (14). There were no such associations in the current study, probably because of the overall high rates of breastfeeding among all participants, similar to the Finnish average (31).

Women with GDM have a sevenfold risk of developing type 2 diabetes and up to 15% to 60% will be diagnosed within 5 to 15 years after pregnancy (32). Annual type 2 diabetes incidence rates among women with prior GDM range from 5.4% to 12.1% (33–35). In this study, we used impaired glucose regulation as our primary outcome measure because of its strong association with future risk of type 2 diabetes (36). The overall prevalence of disturbances in glucose regulation was, however, lower compared with other studies. Women with a pathological OGTT in early pregnancy were excluded from this study and, because "early GDM" might not only be a more severe form of GDM but also indicate preexisting impaired glucose regulation, this will certainly influence the incidence of impaired glucose regulation after delivery. It should also be acknowledged that women coming to an intervention trial are motivated, and even participants in the control group are more determined to achieve general lifestyle goals. This selection bias might be even more prominent during a long follow-up selecting the most successful participants. Additionally, because age is a known risk factor for GDM, the drift of older participants to continue in the intervention group may have potentially influenced our results. Hypothetically, without such a difference, the effect of the intervention might have been even more pronounced.

All the study participants were of Caucasian origin, which therefore limits the generalizability of the study results to other ethnic populations. Additionally, prepregnancy weight and physical activity were self-reported and can be considered a weakness of the study; however, this is the case in most other studies as well. There was a 26% loss to follow-up, similar to other studies (21), which affected the sample size. This rather small number of participants limits the statistical power of our analysis. Potentially, this might also pose a selection bias because the participants staying in the study could be more motivated or possibly more receptive to treatment. In the dropout analysis, however, we did not find any observable differences between the groups, and the intervention and control groups were similar with the exception that participants continuing in the intervention group were older. Another limitation is that this study was not a randomized clinical trial but a follow-up of women recruited in early pregnancy. However, a similar number of women from both the original intervention and control groups were excluded and baseline characteristics were similar between the groups (Table 1).

Because interventions have proven effective in both reducing the incidence of GDM (7) and type 2 diabetes (5, 6) it will be of great interest to see the long-term effects of a lifestyle intervention during pregnancy and the first postpartum year. The results of our RADIEL trial are promising: they support the GDM initiative of the International Federation of Obstetrics and Gynecology (37) in highlighting the importance of the postpartum period to initiate early preventive strategies for future type 2 diabetes. We believe that creating possibilities for a better lifestyle during pregnancy and the first postpartum year promote better metabolic health also later in life.

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Author Contributions: E.H. participated in the implementation of the study, literature search, data interpretation, and the drafting and editing of the article. S.B.K. initiated, participated in the design of, and coordinated the study; and helped in the drafting and editing of the article. A.V. and J.M. participated in the implementation and statistical analyses of the nutrition aspects of the study and the drafting of the article. A.T. and K.R. participated in the design of the study and helped with the drafting and editing of the article. B.S.-L. participated in the design of the study, coordinated the study in Lappeenranta, and helped with the statistical analyses and drafting of the article. J.G.E. is the principal investigator of the study, participated in the implementation of the study, and advised on editing the article. All authors have read and approved the final version of the manuscript. E.H. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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