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Five-Year Follow Up of a Low Glycaemic Index Dietary Randomised Controlled Trial in Pregnancy—No Long-Term Maternal Effects of a Dietary Intervention

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Five-year follow up of a low glycaemic index dietary randomised controlled trial in pregnancy—no long-term maternal effects of a dietary intervention

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Objective To determine whether a dietary intervention in pregnancy had a lasting effect on maternal outcomes of diet, HbA1c and weight retention 5 years post-intervention; and to establish whether modifiable maternal behaviours were associated with these outcomes.

Design Randomised control trial of low glycaemic index (GI) diet in pregnancy with longitudinal follow up to 5 years post-intervention.

Setting Dublin, Ireland (2007–2016).

Population In all, 403 women of 759 (53.1%) were followed up at 5 years. A total of 370 (intervention $n = 188$; control $n = 182$) were included in this analysis.

Methods Fasting glucose was measured at 13 and 28 weeks' gestation and HbA1c (mmol/mol) at 5-year follow up. Weight retention (kg) from early pregnancy to 5 years post-intervention was calculated. Dietary intakes, anthropometry, and lifestyle factors were measured in pregnancy and 5 years post-intervention. Multiple linear regression models, controlling for confounders, were used for analysis.

Outcome Maternal diet, HbA1c, and weight retention at 5 years post-intervention.

Results There was no difference between the intervention and control at 5 years post-intervention for any long-term maternal outcomes measured. HbA1c at 5 years post-intervention was associated with early-pregnancy fasting glucose (*B* 1.70, 95% CI 0.36–3.04) and parity ≥3 (*B* 1.04, 95% CI 0.09–1.99). Weight retention was associated with change in well-being from pregnancy to 5 years (*B* −0.06, 95% CI −0.11 to −0.02), gestational weight gain (*B* 0.19, 95% CI 0.00–0.38), and GI (*B* 0.26, 95% CI 0.06–0.46) at 5 years.

Conclusions The ROLO low-GI dietary intervention in pregnancy had no impact on maternal dietary intakes, HbA1c or body composition 5 years post-intervention. Maternal factors and lifestyle behaviours in pregnancy have long-term effects on glucose metabolism and weight retention up to 5 years later.

Keywords Follow up, HbA1c, maternal weight retention, nutrition, pregnancy, randomised control trial.

Tweetable abstract Pregnancy factors are associated with maternal glucose metabolism and weight retention 5 years later—findings from the ROLO Study.

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Introduction

The low glycaemic index (GI) diet in pregnancy is associated with improvements in dietary intakes,[1–3] reduced gestational weight gain (GWG),[1,3] and improved glycaemic response.[4] While much research has explored offspring outcomes relating to dietary intakes and GI in pregnancy,[5–9] there is a paucity of research relating to long-term maternal outcomes following a low-GI diet in pregnancy. Long-term follow up of pregnancy intervention studies is required to develop an understanding of the impact of maternal diet during a key life stage on future health, and to assess whether lifestyle behaviours are sustained in the postpartum period after the intervention has ended.

Furthermore, the increased physiological demands of pregnancy can act as a biological stress test for life to predict a woman's future health.[10] Pregnancy is considered a 'diabetogenic state' of insulin resistance, exposure to which may result in long-term alterations of normal glucose metabolism.[11] Gestational diabetes (GDM) increases the risk of type 2 diabetes in later life,[12–15] and fasting glucose below levels used to diagnose GDM are associated with increased adverse maternal outcomes.[16] It is unclear, however, whether a continuum of increasing fasting blood glucose in pregnancy, below that diagnostic of GDM, increases maternal risk of future diabetes. In addition, weight retention in the period after pregnancy is associated with increased risk of future obesity.[17,18] Examining the modifiable behaviours that facilitate or hinder weight loss in the years after pregnancy could assist healthcare professionals to target specific maternal behaviours.[19]

Whether the immediate and lasting effects of pregnancy on a woman's metabolic health and body composition can be influenced through dietary or environmental manipulation is pertinent for all women, but requires further study. The ROLO study was a randomised control trial (RCT) of a low-GI diet in pregnancy that resulted in improved diet, less GWG, and improved glucose tolerance.[1] Due to the longitudinal nature of the ROLO study follow up, with data collected from 13 weeks' gestation to 5 years post-intervention, the findings may be used to fill some of the knowledge gaps relating to mothers' health in the years following a dietary intervention.

We aimed to determine whether a low-GI dietary intervention had a lasting effect on maternal diet, HbA1c, and weight retention 5 years post-intervention and to establish whether modifiable maternal behaviours, diet, and lifestyle factors in pregnancy and 5 years later were associated with HbA1c and weight retention 5 years post-intervention.

Methods

Study design

This is a longitudinal study of 370 women originally recruited as part of the ROLO study[1] at The National Maternity Hospital, Dublin, Ireland. In summary, the ROLO study randomised 800 secundigravida women at approximately 13 weeks' gestation, who had previously delivered a macrosomic infant (>4000 g), to receive either low-GI dietary advice or usual care (no dietary advice).[1] The primary outcome was birthweight, and secondary outcomes were GI, GWG, and glucose intolerance.[1] Two weeks post-randomisation, at approximately 15 weeks' gestation, women assigned to the intervention group attended a 2-hour group education session with the research dietitian. Women were taught the principles of healthy eating and a low-GI diet in pregnancy. The research dietitian met with intervention subjects at 28 and 34 weeks' gestation for brief reinforcement of the diet.

At 5 years post-intervention, all participants were invited to attend a follow-up visit. To be eligible for inclusion, participants must have attended the follow-up visit before the child was 5 years and 6 months of age. Institutional ethical approval and informed, written maternal consent were obtained. The study was conducted according to the guidelines laid down in the Declaration of Helsinki.

Of the 759 infants born to study mothers, 403 (53.1%) mother–child dyads were followed up at the 5-year follow-up visit. A discussion of retention rates at the 5-year follow up has been published previously.[20] Of the 403 women, 370 were included in the analysis for weight retention (reasons for exclusion: 17 did not have weight measurement at the 5-year follow up and 16 were pregnant at the time of the 5-year follow up). Of the 370 included, 188 were originally randomised to the intervention group and 182 to the control group. For analysis of HbA1c, 161 were included (reasons for exclusion: 241 did not have a blood sample available for HbA1c measurement and one had poorly controlled type 2 diabetes that was diagnosed postpartum).

Patient involvement

In February 2018, the researchers met with the ROLO Family Advisory Committee, a self-selected group of mothers who are involved in the longitudinal follow up of the ROLO Study. The central theme of this meeting was to discuss key outcomes of importance for the mothers relating to their own health and their children's health. A report of this meeting is being written for publication at present but, in brief, the mothers had greater concerns about outcomes relating to their children than themselves. In terms of maternal health, weight gain during pregnancy and postpartum was not prioritised; however, a general blood test in pregnancy, that could predict health risks in later life, was viewed positively and welcomed by the women.

Core outcome sets

A core outcome set for longitudinal follow up of mothers postpartum does not exist. However, the core outcome sets for diabetes in pregnancy[21] were consulted when deciding on the outcomes to examine. The primary reason that HbA1c, weight retention, and dietary intakes were chosen as outcomes for this piece of research is due to their placement as secondary outcomes in the original RCT (infant macrosomia was the primary outcome of the RCT).[1]

Data collection

Anthropometry and body composition

Height and weight were measured in early pregnancy (13 weeks' gestation) and at the 5-year follow-up visit. Body mass index (BMI; kg/m^2) was calculated. Weight retention was defined as the difference between weight at the early pregnancy visit and weight at the 5-year follow-up visit. GWG was calculated by subtracting the measured weight at the first antenatal visit from the final weight in pregnancy (measured at 38, 40, or 41 week's gestation). The 2009 Institute of Medicine (IOM) guidelines for total GWG[22] were used to categorise GWG. Bioimpedance analysis (BIA) was used to measure fat-free mass and fat mass at the 5-year follow-up visit using the ImpediMed Imp™ SFB7 device (ImpediMed Ltd, Brisbane, Qld, Australia).

Dietary intakes

Dietary intakes in pregnancy were collected using 3-day food diaries. All food and beverages consumed over three consecutive days were recorded by participants during each trimester. To estimate habitual dietary intakes over the previous year, participants completed the 2002 SLÁN 148-item food frequency questionnaire (FFQ), plus questions relating to milk.[23] The questionnaire was validated in an Irish population[24] and in pregnancy.[25] Dietary data were entered into dietary analysis software NETWISP version 3.0 (Tinuviel Software, Llanfechell, Anglesey, UK). The NetWISP food composition database was derived from the 6th edition of McCance and Widdowson's food composition tables.[26]

At the 5-year follow up, participants completed the 2007 SLÁN 150-item FFQ to estimate dietary intakes over the past 2 years.[27] The questionnaire was validated in an Irish population.[27] Standard food portions were assigned to each food item according to the Food Standards Agency portion sizes book.[28] The nutrient profile for each food item was set using data from the updated 2015 McCance and Widdowson's The Composition of Foods Integrated Dataset.[29]

Demographics and lifestyle

Data were collected on maternal age, parity, number of years since last pregnancy, breastfeeding for the study child, maternal educational attainment, and smoking. The World Health Organization-5 (WHO-5) well-being index was used to assess well-being in pregnancy and at the 5-year visit.[30] Physical activity was assessed in pregnancy using the 1998 SLÁN questionnaire, which was based on the Godin Leisure-Time Exercise Questionnaire.[31] At the 5-year follow-up visit, participants completed the short International Physical Activity Questionnaire (IPAQ).[32] Metabolic equivalents (METs) were calculated,[33] and participants were classified as low, medium or high. Minutes spent walking was recorded at both time points.

Blood sample

At 13 and 28 weeks' gestation, fasting blood samples were collected. A glucose challenge test (GCT), 1-hour after a 50-g glucose load, was performed at 28 weeks' gestation. Glucose intolerance in pregnancy was classified as 28 weeks' gestation fasting glucose ≥5.1 mmol/l or 28 weeks' gestation GCT >7.8 mmol/l, as previously used in the ROLO Study.[1] Fasting glucose results were also categorised according to the HAPO glucose categories.[16] At the 5-year follow-up visit, a non-fasting blood sample was collected and HbA1c concentration was determined using Tina-quant HemoglobinA1c Generation 3, analysed on a Roche Cobas 6000 (Roche Diagnostics GmbH, Mannheim, Germany).

Statistical analysis

Data were assessed for normality using the Kolmogorov–Smirnov test and visual inspection of histograms. Non-normally distributed variables were log-transformed for regression analysis. We included the maximum number of participants with complete data for each set of analysis. Correlations between maternal characteristics, and HbA1c and weight change were initially examined. Bivariate associations with a significance of $P < 0.1$ were further analysed using multiple regression models. Models were created using a forced-enter approach and were adjusted for confounders. Confounders were chosen *a priori*, based on the literature and correlations observed in the data. Models exploring HbA1c as an outcome were controlled for grouping (intervention), maternal age at the 5-year follow up, BMI at the 5-year follow up, ethnicity, energy (kcal/day) at the 5-year follow up, and physical activity (IPAQ) at the 5-year follow up. Models exploring weight retention as an outcome were controlled for grouping (intervention), maternal education, parity, smoking status at 5 years, energy (kcal/day) at the 5-year follow up, physical activity (IPAQ) at the 5-year follow up, and GWG. The model testing GWG as an independent variable was additionally controlled for early-pregnancy BMI. To improve interpretation of the results, the variables for energy were scaled (per 100 kcal/day) for the multiple linear regression analysis.

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Table 1. Maternal characteristics of those who attended the 5-year ROLO follow up

	n	
Demographics		
Age at delivery, years*	370	33.17 (3.95)
Age at 5-year follow-up visit, years*	370	38.36 (3.96)
Parity*	370	2.48 (0.64)
≥3 children**		152 (41.08)
Years since birth of youngest child***	360	5.07 (2.46)
≥2 years**		311 (86.39)
Education, completed tertiary**	324	199 (61.42)
Anthropometry		
Weight, early pregnancy, kg*	368	71.98 (12.88)
Weight, final pregnancy, kg*	297	84.80 (13.14)
Weight, 5-year follow-up visit, kg*	368	71.82 (13.45)
Gestational weight gain, kg*	296	12.83 (4.23)
Inadequate**		62 (20.95)
Adequate**		96 (32.43)
Excessive**		138 (46.62)
Weight retention from early pregnancy to 5 years, kg*	366	−0.10 (6.05)
Height, cm*	369	165.91 (6.31)
Early-pregnancy BMI, kg/m^2*	368	26.16 (4.49)
5-year follow-up visit BMI, kg/m^2*	368	26.04 (4.67)
Bioelectrical impedance		
Fat-free mass, 5-year follow-up visit, kg*	231	48.47 (7.01)
Fat-free mass %, 5-year follow-up visit*	231	68.09 (6.77)
Fat mass, 5-year follow-up visit, kg*	231	23.47 (8.50)
Fat mass %, 5-year follow-up visit*	231	31.86 (6.82)
Physical activity		
Pregnancy, walk for at least 30 min, days/week***	262	3.0 (3.0)
5-year follow-up visit, total METS*	323	1762.32 (1863.01)
High IPAQ**		98 (30.30)
Medium IPAQ**		129 (39.90)
Low IPAQ**		96 (29.70)
5-year follow-up visit, walking, min/week*	323	234.83 (305.19)
Glucose metabolism		
Early-pregnancy fasting glucose, mmol/l*	356	4.50 (0.36)
28 weeks' gestation fasting glucose, mmol/l*	347	4.49 (0.46)
1-hour GCT, 28 weeks' gestation, mmol/l*	363	6.55 (1.48)
Glucose intolerant, 28 weeks' gestation, Yes**	366	92 (25.14)
HbA1c, 5-year follow-up visit, %*	160	5.03 (0.25)
HbA1c, 5-year follow-up visit, mmol/mol*	160	31.46 (2.70)
Well-being WHO-5 percentage score		
Pregnancy*	321	58.32 (15.14)
5-year follow-up visit*	321	62.69 (14.44)
Change pregnancy to 5-year follow-up visit*	287	4.35 (15.47)
Breastfeeding practices		
No breastfeeding**	338	124 (36.70)
<26 weeks**		116 (34.30)
≥26 weeks**		98 (29.00)
Glycaemic index		
Trimester 1*	288	57.63 (3.90)
Trimester 2*	288	56.70 (3.68)
Trimester 3*	288	56.75 (3.96)
Mid-pregnancy FFQ*	325	54.50 (3.20)
5-year follow-up visit*	326	56.11 (3.82)

BMI, body mass index; IPAQ, international physical activity questionnaire; IQR, interquartile range; METS, metabolic equivalents; SD, standard deviation.
Data presented as *mean (SD), ***n* (%) or ***median (IQR).

Results

Maternal characteristics and dietary intakes

Half [*n* = 188 (50.8%)] of the women who attended the 5-year follow up ROLO study visit had been originally randomised to the intervention group of the ROLO RCT and 182 (49.2%) to the control group. Maternal characteristics are detailed in Table 1. Weight remained generally stable from early pregnancy [mean (SD) 72.0 (12.9) kg] to 5 years post-intervention [mean (SD) 71.8 (13.5) kg], with mean (SD) postpartum weight retention of −0.1 (6.1) kg (Table 1). Substantial weight retention of ≥5 kg was observed in 59 (16.1%) women. At the 5-year follow up, mean (SD) HbA1c was 31.46 (2.70) mmol/mol and 5.03% (0.25) (Table 1). Two women had an HbA1c concentration between 39 and 47 mmol/mol, classified as pre-diabetes according to the American Diabetes Association guidelines.[34] Dietary GI was similar between the food diaries in pregnancy and the FFQ instrument completed at the 5-year follow-up visit [mean (SD) in trimester 3: 56.75 (3.96) and 56.11 (3.82), respectively].

Among those who attended the 5-year follow up, no significant differences between the intervention and control groups existed in terms of GWG, excessive GWG as per the IOM guidelines, BMI at 5 years, weight retention, glucose metabolism in pregnancy, and HbA1c at 5 years (Table 2). Based on the 3-day food diaries completed in pregnancy, GI, glycaemic load (product of GI and carbohydrate intake), carbohydrate (g/day), and sugar (g) were similar between the intervention and control in trimester 1 (pre-intervention), and were significantly lower in the intervention group in trimester 2 and trimester 3 (post-intervention). In all trimesters of pregnancy, the intervention group reported consuming significantly less energy (kcal/day) and a greater percentage of energy from protein (Table 2, Supporting Information Tables S1 and S2). However, the FFQ completed at 5 years post-intervention did not detect

Table 2. Maternal characteristics at the 5-year follow-up visit (intervention versus control)

	Grouping	*N*		*P*
Demographics				
Age, 5-year follow up, years*	Control	182	38.75 3.87	0.062
	Intervention	188	37.98 4.01	
Weight				
Gestational weight gain, kg*	Control	142	13.27 4.48	0.084
	Intervention	154	12.42 3.96	
Exceed IOM weight gain guidelines**	Control	142	72 50.70	0.200
	Intervention	154	66 42.86	
Weight, 5-year follow up, kg*	Control	182	71.74 13.86	0.910
	Intervention	186	71.89 13.08	
BMI, 5-year follow up, kg/m^2*	Control	182	25.98 4.75	0.799
	Intervention	186	26.10 4.60	
Weight retention from early pregnancy to 5 years				
Weight retention, kg*	Control	181	−0.10 5.94	0.989
	Intervention	185	−0.09 6.18	
% weight retention*	Control	181	−0.06 7.82	0.801
	Intervention	185	0.15 8.00	
Bioelectrical impedance				
Fat-free mass, 5-year follow up, kg*	Control	117	48.21 7.05	0.578
	Intervention	114	48.73 7.00	
Fat-free mass %, 5-year follow up*	Control	117	68.39 7.06	0.501
	Intervention	114	67.79 6.48	
Fat mass, 5-year follow up, kg*	Control	117	23.15 9.04	0.565
	Intervention	114	23.79 7.94	
Fat mass %, 5-year follow up*	Control	117	31.52 7.15	0.445
	Intervention	114	32.21 6.48	
Glucose metabolism				
Fasting glucose, early pregnancy, mmol/l**	Control	173	4.50 0.33	0.952
	Intervention	183	4.50 0.38	
Fasting glucose, 28 weeks' gestation, mmol/l*	Control	168	4.48 0.49	0.699
	Intervention	179	4.50 0.44	
1-hour GCT, 28 weeks' gestation, mmol/l*	Control	177	6.58 1.48	0.642
	Intervention	186	6.51 1.48	
Glucose intolerant, 28 weeks' gestation*	Control	178	48 26.97	0.506
	Intervention	188	44 23.40	
HbA1c, 5-year follow up, mmol/mol*	Control	82	31.61 2.95	0.460
	Intervention	78	31.30 2.42	
Glycaemic index				
Trimester 1*	Control	150	57.66 3.94	0.894
	Intervention	138	57.60 3.88	
Trimester 2*	Control	150	57.38 3.42	0.001
	Intervention	138	55.96 3.82	
Trimester 3*	Control	150	57.39 3.95	0.004
	Intervention	138	56.05 3.87	
Mid-pregnancy FFQ*	Control	160	54.63 3.37	0.473
	Intervention	166	54.37 3.03	
5-year follow-up visit*	Control	158	55.80 3.85	0.156
	Intervention	168	56.40 3.78	

BMI, body mass index; GCT, glucose challenge test; SD, standard deviation. Glucose intolerant at 28 weeks' gestation: fasting glucose ≥5.1 mmol/l or GCT >7.8 mmol/l.
Data presented as *mean (SD) or ***n* (%).

differences in GI or any other dietary intakes between the intervention and control group (Tables 2, S1 and S2).

HbA1c at 5 years

The positive correlation between fasting glucose in pregnancy (categorised as per the HAPO study) and HbA1c at 5 years post-intervention is described in Figure S1.

On multiple linear regression, controlling for confounders, a 1 mmol/l increase in early-pregnancy fasting glucose was associated with a 1.70 (95% CI 0.36–3.04) mmol/mol increase in HbA1c; a one-category increase in HAPO glucose categories in early pregnancy was associated with a 0.53 (95% CI 0.16–0.90) mmol/l increase in HbA1c; and a trend was observed ($P = 0.050$) for an association between glucose intolerance at 28 weeks' gestation and a 1.06 (95% CI 0.00–2.12) mmol/mol increase in HbA1c (Table 3). Each additional child, after the index study child (second child), was associated with a 0.83 (95% CI 0.11–1.55) mmol/mol increase in HbA1c at the 5-year visit, and having three or more children was associated with a 1.04 (95% CI 0.09–1.99) mmol/mol higher HbA1c at the 5-year visit than those with two children (Table 3).

Weight retention

On multiple linear regression, controlling for confounders, a 1 percentage score increase in well-being from pregnancy to the 5-year visit was associated with 0.06 (95% CI 0.02–0.11) kg less weight retention; a 1-kg increase in GWG was associated with 0.19 (95% CI 0.00–0.38) kg higher weight retention (additionally controlling for early-pregnancy BMI); a 1 percentage increase in energy from protein at 5-year visit was associated with 0.30 (95% CI 0.03–0.56) kg less weight retention; 1 unit increase in GI and in glycaemic load at the 5-year visit were associated with higher weight retention (0.26 kg, 95% CI 0.06–0.46 and 0.04 kg, 95% CI 0.01–0.07, respectively; Table 4). Weight retention was positively associated with BMI ($B = 0.38$; 95% CI 0.21–0.56) and fat mass ($B = 0.22$; 95% CI 0.10–0.33) at the 5-year visit (Table 4).

Lost to follow up

Compared with women who were lost to follow up, those who attended the 5-year visit were significantly older when they were pregnant [mean (SD): 31.74 (4.42) versus 33.08 (3.92), $P < 0.001$], more likely to have completed tertiary education (48.7 versus 61.1%, $P = 0.003$), had a lower early-pregnancy BMI [kg/m^2; mean (SD): 27.38 (5.35) versus 26.10 (4.44), $P < 0.001$] and higher early-pregnancy fasting glucose [mmol/l; mean (SD): 4.42 (0.38) versus 4.49 (0.36), $P = 0.015$; Table S1]. No significant differences were observed in randomisation grouping, GWG or well-being (Table S1). Women who attended the 5-year follow-up visit reported higher energy intakes throughout pregnancy, but no other nutrients were consistently different between those who attended and those lost to follow up (Table S3).

Discussion

Main findings

This study was the 5-year longitudinal follow up of women who participated in the ROLO RCT of a low-GI diet in pregnancy. The intervention and control groups did not differ in any outcomes measured at 5 years. Higher fasting glucose in early pregnancy and parity was positively associated with HbA1c at the 5-year follow up. Lower GWG and an improved sense of well-being over time were associated with less weight retention. Habitual dietary intakes of higher energy from protein, lower GI, and lower GL in the 2 years prior to the 5-year follow-up visit were also associated with less weight retention.

Strengths and limitations

The longitudinal nature of the ROLO study and the well-characterised cohort provide novel findings relating to mothers' metabolism and body composition in the years following a dietary intervention. Strengths of this study include the objective measurement of anthropometry by trained researchers, and the prospective collection of detailed dietary and biochemical data at multiple time points. In terms of generalisability, it is probable that our findings are not applicable to populations other than educated Caucasian women living in a developed county. Furthermore, all women had previously delivered a macrosomic infant. In total, 53.1% (403/759) of the ROLO study participants completed the 5-year follow up. This is not dissimilar to the follow-up rates of similar research studies; at 6 months postpartum, the UPBEAT study followed up 45.9%;[6] at 12 months postpartum, the PIN study followed up 47.0%;[35] and at 3–6 years, Project Viva followed up 68.1%.[36] The differences in maternal characteristics between those who attended and those who were lost to follow up are discussed above and must be taken into account when interpreting these findings. Weight remained generally stable from early pregnancy to 5 years post-intervention, which is less than that quoted in the literature for 3 years (2.2 kg)[37] and 7 years (2.1 kg)[17] postpartum. It is possible that those who were not followed up had greater weight retention. In terms of statistical analysis, some of the R^2 adjusted in the multiple linear regression models are approaching zero or are negative, meaning that these models have low predictive power. Adjustment of the significance level for multiple testing was not used, increasing the risk of observing a chance finding. Finally, due to the observational nature of this study, we cannot infer causality based on these findings.

Table 3. Multiple linear regression models for associations between maternal characteristics and HbA1c (mmol/mol)

	n	B (%Δ)*	*P*	95% CI	R^2 Adj	Model *P*
Demographics and lifestyle						
Parity	136	0.83	0.025	(0.11, 1.55)	0.06	0.029
≥3 children	136	1.04	0.033	(0.09, 1.99)	0.06	0.035
Years since birth of youngest child*	134	−0.68 (−46.44%)	0.086	(−1.46, 0.10)	0.05	0.065
Walk for at least 30 minutes in pregnancy, days/week *	99	1.20 (232.01%)	0.018	(0.21, 2.18)	0.00	0.398
Glucose metabolism						
Fasting glucose, Early pregnancy, mmol/l	129	1.70	0.013	(0.36, 3.04)	0.07	0.020
Fasting glucose, Early pregnancy, HAPO glucose categories	129	0.53	0.006	(0.16, 0.90)	0.09	0.011
Fasting glucose, Early pregnancy, HAPO glucose categories, >4.4 mmol/l	129	0.79	0.106	(−0.17, 1.75)	0.05	0.071
Fasting glucose, 28 weeks' gestation, mmol/l	130	0.91	0.109	(−0.21, 2.03)	0.05	0.054
Fasting glucose, 28 weeks' gestation, HAPO glucose categories	130	0.34	0.055	(−0.01, 0.69)	0.06	0.036
1-hour GCT, 28 weeks' gestation, mmol/l	132	0.29	0.076	(−0.03, 0.61)	0.06	0.046
Glucose intolerant, 28 weeks' gestation	133	1.06	0.050	(0.00, 2.12)	0.06	0.039
Dietary intakes						
Energy						
Trimester 1, 100 kcal/day	116	0.16	0.008	(0.04, 0.27)	0.01	0.351
Trimester 2, 100 kcal/day	117	0.16	0.006	(0.04, 0.27)	0.01	0.304
Trimester 3, 100 kcal/day	116	0.13	0.028	(0.01, 0.25)	−0.01	0.582
Protein						
Trimester 2, g/day	117	0.03	0.021	(0.01, 0.06)	−0.01	0.518
Trimester 1, %energy	116	−0.21	0.014	(−0.38, −0.04)	0.00	0.452
Fat						
Trimester 2, g/day	117	0.02	0.046	(0.00, 0.04)	−0.02	0.684
Trimester 3, g/day	116	0.02	0.028	(0.00, 0.04)	−0.01	0.577
Carbohydrate						
Trimester 1, g/day	116	0.01	0.003	(0.00, 0.02)	0.02	0.207
Trimester 2, g/day	117	0.01	0.005	(0.00, 0.02)	0.02	0.261
Trimester 3, g/day	116	0.01	0.075	(0.00, 0.02)	−0.03	0.784
Glycaemic index						
Trimester 1	112	0.13	0.048	(0.00, 0.25)	−0.02	0.628
Glycaemic load						
Trimester 1	112	0.02	0.002	(0.01, 0.03)	0.04	0.127
Trimester 2	112	0.02	0.024	(0.00, 0.03)	0.00	0.489
Trimester 3	112	0.01	0.106	(0.00, 0.03)	−0.03	0.789
Sugar						
Trimester 1, g/day	116	0.01	0.021	(0.00, 0.03)	−0.01	0.529
Trimester 2, g/day	117	0.01	0.027	(0.00, 0.03)	−0.01	0.567

GCT, glucose challenge test.
Confounders: grouping (intervention), maternal age at the 5-year follow up, BMI at the 5-year follow up, ethnicity, energy (kcal) at the 5-year follow up, and physical activity (IPAQ) at the 5-year follow up. Glucose intolerant at 28 weeks' gestation: fasting glucose ≥5.1 mmol/l or GCT > 7.8 mmol/l.
*%Δ: percentage change for logged variables (non-normally distributed).

Interpretation

HbA1c at 5 years

We observed that increasing early-pregnancy fasting glucose and HAPO glucose categories were positively associated with HbA1c 5 years later. Both the HAPO study[16] and a recent systematic review by Farrar et al.[38] reported that a linear relation exists between glucose concentration in pregnancy and adverse perinatal outcomes, with no obvious threshold observed above which risk of adverse outcomes is substantially increased. It could be hypothesised that a continuum of increasing fasting blood glucose in pregnancy potentially poses longer term risks than those outlined by the aforementioned studies. In our study, a trend was observed between glucose intolerance (using a 50-g GCT) at 28 weeks' gestation and HbA1c 5 years later ($P = 0.050$). Our findings are supported by previous research that indicated an abnormal GCT was associated

Table 4. Multiple linear regression models for associations between maternal characteristics and weight retention (kg)

	n	*B* (%Δ)*	*P*	95% CI	R^2 Adj	Model *P*
Demographics and lifestyle						
Years since birth of youngest child*	268	−2.09 (−87.64%)	0.027	(−3.94, −0.24)	0.08	0.001
Change pregnancy to 5-year Well-Being (WHO-5) percentage score	263	−0.06	0.011	(−0.11, −0.02)	0.07	0.002
Anthropometry						
Final pregnancy weight, kg	218	−0.08	0.015	(−0.14, −0.01)	0.07	0.002
Gestational weight gain, kg	218	0.19	0.049	(0.00, 0.38)	0.08	0.001
Body mass index, early pregnancy, kg/m^2	270	−0.25	0.007	(−0.43, −0.07)	0.08	0.001
Body mass index, 5-year follow-up visit, kg/m^2	270	0.38	0.000	(0.21, 0.56)	0.13	<0.001
Fat-free mass, 5-year follow-up visit, kg	168	0.09	0.186	(−0.05, 0.23)	−0.04	0.910
Fat-free mass %, 5-year follow-up visit	168	−0.25	0.001	(−0.39, −0.11)	0.04	0.099
Fat mass, 5-year follow-up visit, kg	168	0.22	0.000	(0.10, 0.33)	0.06	0.048
Fat mass %, 5-year follow-up visit	168	0.25	0.001	(0.11, 0.39)	0.04	0.099
Glucose metabolism						
Fasting glucose, 28 weeks' gestation, mmol/l	253	−1.39	0.127	(−3.18, 0.40)	0.04	0.038
Fasting glucose, 28 weeks' gestation, HAPO glucose categories	253	−0.30	0.312	(−0.89, 0.28)	0.04	0.060
1-hour GCT, 28 weeks' gestation, mmol/l	264	−0.64	0.027	(−1.20, −0.07)	0.06	0.006
Dietary intakes						
Protein						
Trimester 1, g/day	241	−0.03	0.240	(−0.07, 0.02)	0.04	0.055
Trimester 1, %energy	241	−0.16	0.229	(−0.42, 0.10)	0.04	0.054
Trimester 2, %energy	244	−0.07	0.633	(−0.37, 0.23)	0.03	0.075
5-year follow up FFQ, %energy	270	−0.30	0.027	(−0.56, −0.03)	0.07	0.003
Carbohydrate						
Trimester 2, g/day	244	0.01	0.225	(−0.01, 0.02)	0.04	0.050
Trimester 1, %energy	241	0.09	0.214	(−0.05, 0.23)	0.04	0.052
Trimester 2, %energy	244	0.04	0.572	(−0.10, 0.19)	0.03	0.073
5-year follow up FFQ, %energy	270	0.11	0.071	(−0.01, 0.23)	0.06	0.006
Glycaemic index						
5-year follow up FFQ	270	0.26	0.012	(0.06, 0.46)	0.08	0.002
Glycaemic load						
Trimester 2	230	0.02	0.259	(−0.01, 0.04)	0.03	0.076
5-year follow up FFQ	270	0.04	0.017	(0.01, 0.07)	0.07	0.002
Sugar						
Trimester 1, g/day	241	0.02	0.139	(−0.01, 0.04)	0.04	0.042
Trimester 2, g/day	244	0.01	0.190	(−0.01, 0.04)	0.04	0.046

FFQ, food frequency questionnaire; GCT, glucose challenge test.
Confounders: grouping (intervention), maternal education, years since birth of youngest child, smoking status at 5 years, energy (kcal) at the 5-year follow up, physical activity (IPAQ) at the 5-year follow up, and GWG. GWG model additionally controlled for early-pregnancy BMI. Years since birth of youngest child model additionally controlled for parity. Five-year follow-up visit FFQ estimated dietary intakes over the past 2 years.
*%Δ: percentage change for logged variables (non-normally distributed).

with lower insulin sensitivity at 3 years postpartum.[37] These results suggest that subtle variations in fasting glucose and glucose tolerance in pregnancy are associated with HbA1c for up to 5 years later; however, whether this has a meaningful impact on long-term diabetes risk requires further research. Future longitudinal studies may benefit from using a 75-g oral glucose tolerance test in pregnancy, the current recommended test for diagnosis of GDM.[39]

Additionally, increasing parity was associated with HbA1c at the 5-year visit, in keeping with literature that has observed a greater risk of developing type 2 diabetes as parity increases.[11,40,41] It has been theorised that repeated exposure to the 'diabetogenic state' of insulin resistance, characteristic of pregnancy, may result in long-term alteration of normal glucose metabolism.[11]

Weight retention

Each kilogram increase in GWG was associated with 0.19 kg increase in weight retention at 5 years post-intervention. Similar rates have been reported in the literature,[42,43] whereas others have suggested that first-trimester GWG is more strongly associated with postpartum weight retention than 2nd or 3rd trimester GWG.[43] It would seem prudent to offer pregnant women lifestyle interventions that reduce GWG. Nevertheless, the ROLO intervention, which was successful in reducing GWG, was not associated with weight retention at 5 years post-intervention. Perhaps an intervention that included reinforcement in the postpartum period might have been more successful in preventing weight retention.

We observed that increased well-being from pregnancy to the 5-year visit was associated with reduced weight retention. Anxiety in pregnancy, stressful events in the early postpartum period, and postpartum depression are associated with increased weight retention,[35,44,45] suggesting that a woman's mental health is of great importance in terms of weight retention in the years following the birth of her children. Optimising well-being through the provision of appropriate support, such as parenting support, stress relief classes, self-management strategies, and behaviour change, could have the potential to alleviate stress and thus lessen weight retention.[46] It should also be noted that medications used to treat and manage anxiety and mental health conditions may be a confounding factor in the association between poor mental health and weight gain.

Weight retention 5 years post-intervention was not associated with being a member of the intervention group, dietary GI, or glycaemic load in pregnancy. Our findings are similar to those of the UPBEAT 6-month follow-up study[6] but they are contrary to findings from the Danish National Birth Cohort, which demonstrated an association between increasing glycaemic load in pregnancy and greater weight retention at 18 months post-pregnancy.[47] We did, however, observe that higher GI and glycaemic load reported at the 5-year visit (reflective of the previous 2 years) were positively associated with weight retention. This suggests that the glycaemic effect of current dietary intakes is of greater relevance to weight status than diet in pregnancy and also supports the potential benefit of reinforcements of a low-GI dietary intervention in the postpartum period.

In terms of sustainability of the ROLO study, the maternal benefits seemed to extend to 3 and 6 months post-intervention, as previously published,[48,49] but not up to 5 years post-intervention. These results are broadly similar to what was reported in the previous pregnancy RCTs, which have observed short-term (4–6 months)[6,7] but not long-term (up to 2 years)[50] maintenance of lifestyle behaviours and health benefits. To be sustainable, additional interventions that reinforce dietary changes are likely required in the postpartum period.[51]

Conclusions

Fasting glucose and GWG in pregnancy are associated with HbA1c and weight retention 5 years later, support for the hypothesis that pregnancy is a window to future maternal health. The ROLO low-GI dietary intervention in pregnancy did not have a lasting impact on dietary intakes, HbA1c or body composition 5 years later; however, the value of improving dietary intakes in pregnancy and the postpartum years should not be underestimated given the long-lasting impact that GWG potentially has on future maternal body composition. To maintain positive behaviours adopted during pregnancy, it is likely that additional interventions that reinforce dietary changes are required postpartum, an area which requires substantial research.

Disclosure of interests

The authors do not have any conflict of interests. Completed disclosure of interest forms are available to view online as supporting information.

Contribution to authorship

EOB and AG were involved in the conception, planning, carrying out, analysing, and writing up of the work. MK, EL, and JD were involved in the conception, planning, carrying out, and writing up of the work. JR and PT were involved in carrying out, analysing, and writing up of the work. EOS and JM were involved in analysing and writing up of the work. FMcA oversaw all aspects of the work and is responsible for the final content.

Details of ethics approval

The ROLO study and 5-year follow-up study were conducted according to the guidelines laid down in the Declaration of Helsinki. Ethical approval for the ROLO study was obtained from the National Maternity Hospital ethics committee in December 2006 (no reference number). Ethical approval for the 5-year follow-up study was obtained in October 2012 from the ethics committee of Our Ladies Children's Hospital, Crumlin, Dublin, Ireland (reference number: GEN/279/12).

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Supporting Information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. HbA1c at 5-year follow up and fasting blood glucose categorised according to the HAPO fasting glucose categories (a) in early pregnancy and (b) at 28 weeks' gestation.

Table S1. Maternal nutrient intakes in pregnancy from 3-day food diaries (intervention versus control).

Table S2. Maternal nutrient intakes in pregnancy and at 5-year follow-up visit using food frequency questionnaires (intervention versus control).

Table S3. Maternal characteristics (attended versus did not attend the 5-year follow-up visit). ■

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