Original Article
CLINICAL TRIALS AND INVESTIGATIONS

Obesity

Increased Visceral Adipose Tissue Without Weight Retention at 59 Weeks Postpartum

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Objective: This study aimed to determine whether controlling maternal gestational weight gain (GWG) influences adipose tissue distribution at 1 year postpartum.

Methods: Women with overweight or obesity ($n = 210$, BMI ≥25 or ≥30) were randomized to a lifestyle intervention (LI) designed to control GWG or to usual obstetrical care (UC). Measures included anthropometry, whole-body magnetic resonance imaging for visceral (VAT), intermuscular, and subcutaneous adipose tissue, and cardiometabolic risk factors in pregnancy (15 and 35 weeks) and after delivery (15 and 59 weeks).

Results: Baseline (15 weeks) characteristics were similar (mean [SD]: age, 33.8 [4.3] years; weight, 81.9 [13.7] kg; BMI, 30.4 [4.5]; gestational age at randomization, 14.9 [0.8] weeks). LI had less GWG (1.79 kg; $P = 0.003$) and subcutaneous adipose tissue gain at 35 weeks gestation ($P < 0.01$). UC postpartum weight (2.92 kg) was higher at 15 weeks but not different from baseline or LI at 59 weeks postpartum. Postpartum VAT increased from baseline in LI by 0.23 kg at 15 weeks and 0.55 kg at 59 weeks; in UC, it increased by 0.34 kg at 15 and 59 weeks. Intermuscular adipose tissue remained elevated in LI (0.22 kg) at 59 weeks. VAT was associated with several cardiometabolic risk factors at 59 weeks.

Conclusions: Despite no weight retention at 59 weeks postpartum, women had increased VAT by ~30%. Postpartum modifiable behaviors are warranted to lower the risk of VAT retention.

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Study Importance

What is already known?

- Pregnancy is associated with a central deposition of fat.
- Pregnancy weight gain and weight retention after delivery are associated with later maternal obesity and comorbidities

What does this study add?

- There is strong evidence of a pregnancy-induced increase in visceral adipose tissue, on the order of 30% at 59 weeks postpartum, despite a return to baseline weight.
- Visceral adipose tissue mass is associated with elevated cardiometabolic risk factors at 59 weeks postpartum, implying a negative health effect.
- Pregnant women with overweight and obesity enrolled in a lifestyle intervention to control excess gestational weight gain during the second and third trimesters had returned to early pregnancy body weight by 15 weeks postpartum compared with a nonintervention group that had not.

Introduction

Postpartum weight retention contributes to the risk for obesity and its comorbidities (1,2). This excess weight includes central fat (3,4) which, if maintained, is associated with an increased later risk of cardiovascular disease (CVD) (5,6). Few studies have obtained serial measurements from early pregnancy to 1 year postpartum to assess fat gain or loss. The Coronary Artery Risk Development in Young Adults (CARDIA) study (4) reported a threefold greater increase in visceral adipose tissue (VAT) from preconception to 5 years postpartum compared with nulliparous women. In a multiethnic cohort, excessive gestational weight gain (GWG) was associated with a 3.5-cm greater waist circumference and 300% increased risk of abdominal adiposity compared with values for adequate GWG (7). Whether fat mass gained during pregnancy is retained after delivery and whether the fat distribution is different have not been adequately studied.

A major barrier confronting investigations of pregnancy-related adiposity changes has been the lack of validated measures to assess body composition during the pregnant state (8). Available *in vivo* methods cannot differentiate between mother and fetus (9), so values for fat and fat-free mass reflect the combined units. Also, total body water increases during pregnancy by about 5 to 8 L (10-12), and the composition of lean tissue changes as pregnancy progresses, thereby invalidating a basic assumption that 73% of the adult's fat-free mass compartment is water (11,13,14).

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An understanding of pregnancy-induced changes in body composition requires a prepregnancy measure followed by one in the early postpartum period, yet there have been few such studies (15) and none with magnetic resonance imaging (MRI)-specific adipose tissue distribution.

The purpose of this study involved secondary Lifestyle Intervention For Two (LIFT) (16) aims, investigating the effects of controlling GWG on maternal adipose tissue distribution through 1 year postpartum and relating changes in adipose tissue depots with changes in cardiometabolic parameters. The intervention was developed to control GWG, not to target fat mass. Yet measuring fat depot changes is clinically insightful because excess fat tends to be centrally distributed, which, if maintained, correlates with an increased metabolic risk (7,17). We present adipose tissue distribution from early pregnancy through 1 year postpartum.

Methods

Study design

LIFT is in the Lifestyle Interventions For Expectant Moms (LIFE-Moms) consortium (18,19) consisting of seven independent randomized controlled trials (RCTs), a Coordinating Unit, and NIH as the sponsor, collaborating but with different strategies for reducing GWG in women with overweight or obesity. Described previously (16), LIFT was a parallel-group RCT with women assigned in a 1:1 ratio at the beginning of the second trimester to a lifestyle intervention (LI) or to usual care (UC). A secondary hypothesis of LIFT was that maternal body fat and VAT would be lower for LI compared with UC. The study was approved by the Institutional Review Boards of St. Luke's-Roosevelt Hospital and Columbia University.

Participants

Women were recruited from hospital-affiliated private and clinic practices from February 2013 to October 2015. Eligibility criteria included age ≥ 18 years, BMI ≥ 25 at baseline measurement, singleton pregnancy, gestational age between 9 weeks 0 days and 15 weeks 6 days confirmed by dating ultrasound, and intention to deliver at St. Luke's-Roosevelt Hospital. Exclusion criteria included body size that exceeded the MRI field of view, metal implants, and claustrophobia.

Assessment visits

During pregnancy. The baseline visit immediately preceded randomization and occurred between 12 weeks 0 days and 15 weeks 6 days, corresponding approximately to the beginning of the second trimester of pregnancy. The final prenatal core visit occurred between 35 weeks 0 days and 36 weeks 6 days at approximately the end of the third trimester.

Postpartum. There were two scheduled visits, one between 13 weeks 0 days and 15 weeks 0 days and another between 48 weeks 0 days and 56 weeks 6 days after delivery.

Measurements

Details on anthropometric measurements are provided in online Supporting Information Appendix 1. Height, weight, and waist and hip circumferences were measured, and BMI was calculated.

Total adipose tissue (TAT), including total VAT, intermuscular (IMAT), and subcutaneous (SAT), and SAT subdivisions were measured during pregnancy and after delivery by using whole-body multisection MRI with the participant in a fasted state (6X Horizon; GE, Milwaukee, Wisconsin) (20,21). See details in online Supporting Information Appendix 1. The assessment of VAT in this study reflects all visible VAT extending from the tip of the sacrum/coccyx throughout the abdomen to where the lungs appear. The coefficient of variation for VAT (1.97%) in our laboratory is from the blind reanalysis or rereading of the same three scans by the same MRI analyst. In an individual with 1.5 kg of VAT, a coefficient of variation of 2.0% translates to an SD of 0.030 kg.

Total body fat and fat-free mass were measured by air displacement plethysmography using the BOD POD (COSMED USA, Inc., Concord, California) (22). Total body fat, lean mass, and total body water were measured by quantitative magnetic resonance (QMR) (EchoMRI; EchoMRI LLC, Houston, Texas) (23). The BOD POD and QMR measures were done only postpartum. See details in online Supporting Information Appendix 1.

Secondary variables

Additional measures obtained at pregnancy and postpartum included the 2010 Healthy Eating Index (HEI) based on a single day 24-hour recall, validated in pregnant women (24). A wrist-worn ActiGraph GT3X+ (ActiGraph, Pensacola, Florida) accelerometer provided estimates of total physical activity (25). Blood pressure was measured after the participant had been sitting quietly for 5 minutes. Clinical biochemistry involving fasting serum assays for cholesterol, high-density lipoprotein (HDL) cholesterol, Friedewald low-density lipoprotein (LDL) cholesterol, glucose, insulin, C-peptide, leptin, adiponectin, albumin, glycated albumin, tumor necrosis factor-α (TNF-α), and interleukin 6 (IL-6) were obtained. See online Supporting Information Appendix 1.

Statistical analysis

Within each group, descriptive statistics, means, and SDs for continuous variables and percentages for discrete variables were calculated. At each visit, an analysis of covariance tested the null hypothesis that the adjusted mean values for the two groups were equal. The covariates include ethnicity, age, baseline BMI, baseline weight, gestational diabetes mellitus, and the baseline value of the dependent variable. For each variable, the change from baseline was calculated. At each follow-up visit, the paired *t* test tested the null hypothesis that the mean change was equal to zero within each group. A *t* test tested the null hypothesis that the mean changes from baseline for the two groups were equal. Correlation, partial correlation, and regression analyses explored relationships among body composition variables and weight, physical activity, and HEI variables. Statistical analyses were performed using SAS version 9.2 (SAS Institute Inc., Cary, North Carolina) and Stata version 12 (StataCorp LP, College Station, Texas). The level of significance was 0.05, two-tailed.

Results

Study participants

Figure 1 shows enrollment, randomization ($n = 210$), and retention. To maximize retention, the last study window was extended and occurred between 48 and 184 weeks (59 [17] weeks) after delivery. Baseline group characteristics were similar (Table 1). Gestational diabetes mellitus prevalence was 10.3% for LI and 6.1% for UC ($P = 0.28$).

Intervention adherence

Adherence was measured by attendance at bimonthly visits and weekly food and exercise logs. Median attendance of LI women was good at

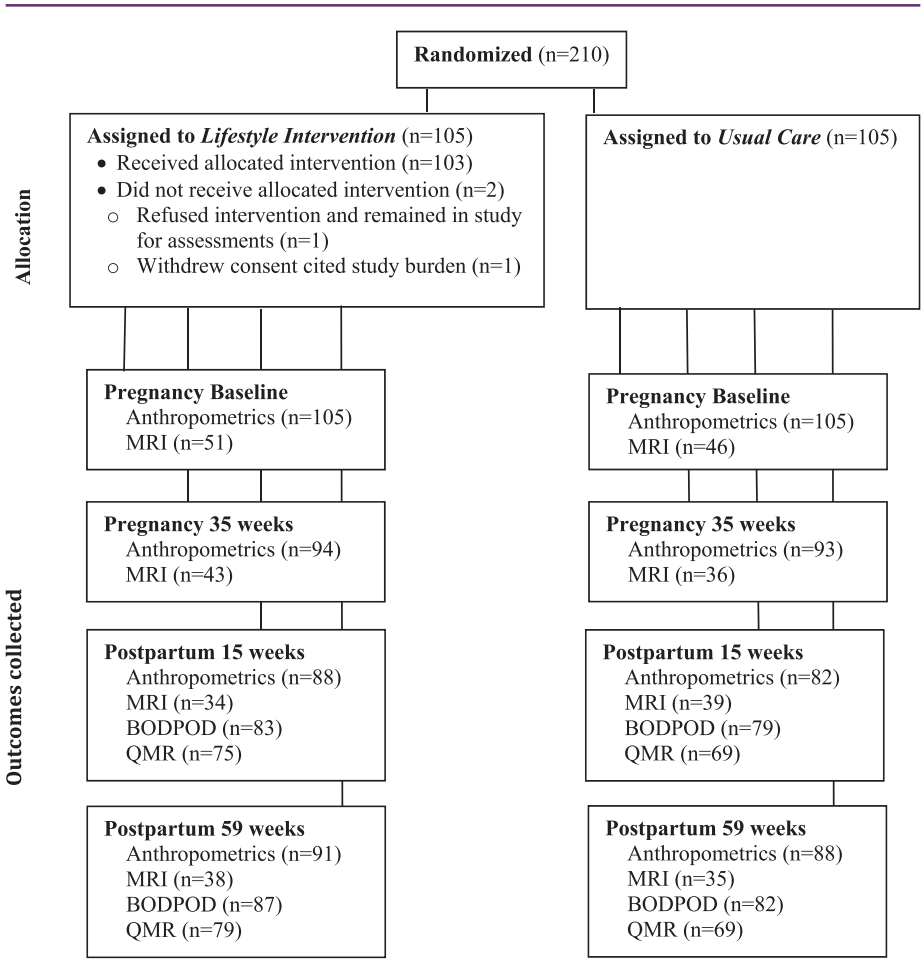

Figure 1 Randomization and follow-up of study participants showing sample size (*n*) at each time point.

87.5% of visits through the end of the second trimester and 72% of visits through the end of pregnancy. Adherence to submitting weekly food logs was moderate, with a median rate of 67.5% in the second trimester and 51.1% overall. Adherence to submitting weekly exercise logs had a median rate of 52.5% in the second trimester and 34.2% overall. Exercise class attendance rate was extremely poor at 9.7%.

Intervention effects on GWG

In the entire sample, LI GWG was 1.79 kg (standard error difference [SED] = 0.59 kg) less than in UC ($P < 0.003$) (16). Among the women with overweight ($25.0 \geq BMI \leq 29.9$), LI GWG was not statistically lower than UC (−1.32 kg, SED = 0.70 kg, $P = 0.06$). Among the women with obesity ($BMI > 30.0$), LI weight gain was 2.68 kg (SED = 0.96 kg, $P = 0.007$) less than UC. LI GWG in the second trimester compared with UC was 0.97 kg less among women with overweight (SED = 0.42 kg, $P = 0.02$) and 2.27 kg less among women with obesity (SED = 0.57 kg, $P < 0.001$). GWG in the third trimester did not differ (0.64 kg, SED = 0.38 kg, $P = 0.09$) between groups. Notably, in women with obesity, LI GWG was 69% of UC GWG (6.07 kg, SD = 4.24 kg vs. 8.75 kg, SD = 4.27 kg, SED = 0.96 kg, $P < 0.007$) (16). GWG per week above the Institute of Medicine guidelines was 19% in LI compared with 38% in UC ($P = 0.002$) (16).

Diet components during pregnancy and after delivery

There were no between-group differences in HEI at baseline (Supporting Information Table S1) except for higher total dairy for LI. At 35 weeks gestation, LI compared with UC had a higher total HEI score, higher total fruit, and higher whole fruit, reflecting a healthier maternal diet, as well as higher solid fats, alcohol, and added sugar score, indicating a lower consumption of calories from this category. The change in total HEI by 35 weeks for LI (5.33, $P = 0.01$) was greater ($P = 0.03$) than the change for UC (−1.03, $P = 0.62$). At 59 weeks postpartum, LI continued to have higher total HEI scores, total vegetables, dark greens/organs/legumes, and refined grains compared with UC. The change in HEI from baseline to 59 weeks for UC (−5.57, $P = 0.02$) was less ($P = 0.03$) than the change for LI (1.48, $P = 0.49$), reflecting a less healthy diet in UC at 59 weeks.

Cardiometabolic parameters during pregnancy and after delivery

Cardiometabolic values during pregnancy and after delivery are presented in Supporting Information Table S2. There were no differences between the groups for any cardiometabolic variable at baseline, at

TABLE 1 Maternal baseline characteristics

	Lifestyle intervention ($n=105$)	Usual care ($n=105$)
Age (y)	33.8 ± 4.0	33.8 ± 4.7
Race		
White	48 (46%)	50 (48%)
Black	25 (24%)	25 (24%)
Other	26 (25%)	22 (21%)
More than one race	5 (5%)	8 (8%)
Unknown	1 (1%)	0 (0%)
Ethnicity		
Not Hispanic/Latina	72 (69%)	80 (76%)
Hispanic	32 (30%)	25 (24%)
Unknown	1(1%)	0 (0%)
Height (cm)	164.3 ± 5.4	163.5 ± 7.0
Baseline weight (kg)	81.5 ± 12.4	82.2 ± 15.0
Baseline BMI (kg/m^2)	30.1 ± 4.1	30.7 ± 5.0
Baseline BMI categories		
Overweight (25.0-29.9 kg/m^2)	65 (62%)	60 (57%)
Obesity (> 30.0 kg/m^2)	40 (38%)	45 (43%)
Parity		
0	39 (37%)	38 (36%)
1	30 (29%)	31 (30%)
≥ 2	36 (34%)	36 (34%)
Gestational age at randomization (wk)	14.96 ± 0.72	14.82 ± 0.78

Values are *n* (%) for categorical variables and means ± SDs for continuous variables. Differences in baseline characteristics between treatment groups were not significant.

35 weeks gestation, or at 59 weeks postpartum. The change scores from baseline to 35 weeks differed between the groups for total cholesterol, HDL cholesterol, and leptin, reflecting increases in UC compared with LI. The increased leptin in UC was consistent with an increase in TAT (2.50 [3.31] kg, $P=0.009$) with no changes in either leptin or adipose tissue observed in LI.

Body composition at baseline

There were no between-group differences for any anthropometric or MRI-derived variable at baseline. Among LI and UC, 49% and 44%, respectively, had an MRI scan (Table 2). Participants who had an MRI scan had a lower body weight (−7.2 [13.3] kg, $P<0.0001$) compared with those with no scan among both LI and UC.

Body composition in late pregnancy

Measurements were acquired at 35 weeks gestation in LI ($n=94$) and UC ($n=93$) (Table 2). Among the MRI measurement subgroup, body weight was 2.49 kg (SED = 0.96 kg) lower in LI ($n=43$) compared with UC ($n=36$), which was reflected in less SAT (−1.78 kg, SED = 0.66 kg) in LI in late pregnancy. There were no between-group differences in IMAT or skeletal muscle at this time.

Pregnancy changes. Within-group changes for weight, BMI, and hip circumference from baseline to late pregnancy are in Table 3.

MRI changes. Results are presented for LI ($n=42$) and UC ($n=34$) participants who had an MRI at baseline and 35 weeks gestation (Table 3). Within LI, increases occurred in IMAT (0.13 [0.31] kg) and skeletal muscle (0.73 [1.14] kg), but not for TAT. Within UC, increases occurred in TAT (2.50 [3.31] kg), including SAT (2.54 [2.93] kg) and IMAT (0.18 [0.26] kg), and in skeletal muscle (1.32 [1.13] kg). We deemed our efforts to quantify VAT measures at 35 weeks to be unreliable, and results are not included. Late in pregnancy, the heavily distended uterus compresses the surrounding maternal tissues, including the intra-abdominal VAT tissue, abdominal SAT, and presumably abdominal skeletal muscle, preventing an accurate quantification of the tissues in the abdomen at this visit.

Body composition after delivery: 15 weeks

The first postpartum measurements were acquired at 15 weeks postpartum in LI ($n=88$) and UC ($n=82$) (Table 2). LI had lower body weight (−2.92 [0.68] kg), BMI, and circumferences of hip and waist than UC. LI had lower fat mass and percent fat by BOD POD (−3.00 [0.86] kg; −2.02% [0.81%]) and lower fat mass by QMR (−3.18 [0.88] kg) than UC, and there were no between-group differences in fat-free mass or lean mass. Among the MRI subgroups, LI weight was less (−3.80 [1.14] kg) than UC, reflected in less total SAT (−2.24 kg). Among the SAT depots, LI had less abdominal superficial SAT (−0.41 [0.11] kg) than UC. There were no between-group differences in VAT, IMAT, or skeletal muscle.

Changes from baseline. Within-group changes in body composition variables from baseline to 15 weeks postpartum are presented in Table 3. In LI, body weight was not different from baseline body weight at 15 weeks postpartum. However, waist and hip circumferences were significantly lower than baseline. In UC, body weight (2.43 [4.62] kg), BMI, and hip circumference remained above baseline values.

MRI adipose tissue changes. Results are presented for LI ($n=33$) and UC ($n=36$) participants who had an MRI at baseline and at 15 weeks postpartum (Table 3). Within LI, body weight was not different from baseline. VAT (0.23 [0.54] kg; Figure 2) and IMAT (0.18 [0.41] kg) were increased, and skeletal muscle mass was lower (−0.59 [1.21] kg) compared with baseline. In UC, body weight and adipose tissue subdivisions, with the exception of abdominal deep SAT and femoral peri-muscular SAT, continued to be above baseline.

Body composition after delivery: 59 weeks

Measurements were acquired at 59 weeks postpartum in LI ($n=91$) and UC ($n=88$) (Table 2). There were no statistically significant between-group differences for any variable.

Changes from baseline. Within-group changes in body composition variables from baseline to 59 weeks postpartum are presented in Table 3. In LI, waist circumference remained below baseline. In UC, body weight was not different from baseline. The overall mean group changes (baseline to 59 weeks) did not differ between groups for any anthropometric measure.

MRI changes from baseline. Results are presented for LI ($n=38$) and UC ($n=30$) participants who had an MRI at baseline and 59 weeks postpartum (Table 3). VAT remained above baseline in LI (0.54 [0.71] kg) and UC (0.34 [0.54] kg), whereas body weight was not different from baseline for either group. Only in LI were abdominal

TABLE 2 Maternal body composition during early and late pregnancy and after delivery, mean (SD)

	Pregnancy						Postpartum					
	LI, baseline, *n* = 105	UC, baseline, *n* = 105	Adj diff (SED)[a]	LI, 35 weeks, *n* = 94	UC, 35 weeks, *n* = 93	Adj diff (SED)	LI, 15.3 weeks, *n* = 88	UC, 15.4 weeks, *n* = 82	Adj diff (SED)	LI, 58 weeks, *n* = 91	UC, 59.34 weeks, *n* = 88	Adj diff (SED)
Gestational age (wk)	15.0 (0.72)	14.8 (0.78)		35.7 (0.72)	35.9 (0.92)		—	—		—	—	
Weeks after delivery	—	—	—	—	—	—	15.1 (2.9)	15.2 (3.5)	−0.02 (0.51)	57.7 (13.4)	59.3 (20.2)	−2.37 (2.47)
Weight (kg)	81.5 (12.4)	82.2 (15.0)	−0.58 (1.89)	89.6 (12.0)	92.1 (14.6)	**−1.87 (0.58****	81.8 (13.3)	84.6 (15.0)	**−2.81 (0.69)***	81.8 (14.8)	83.7 (17.0)	−1.44 (0.92)
BMI (kg/m^3)	30.1 (4.1)	30.7 (5.0)	−0.48 (0.62)	33.0 (3.8)	34.4 (4.9)	**−0.73 (0.22)***	30.3 (4.3)	31.5 (5.1)	**−1.06 (0.26)***	30.2 (5.0)	31.2 (5.9)	−0.57 (0.34)
Circumferences												
Hip (cm)	112.0 (8.2)	112.7 (8.6)	−0.14 (0.50)	113.4 (8.3)	115.3 (11.4)	−1.37 (0.93)	111.3 (9.1)	114.0 (10.1)	**−2.61 (0.66)***	111.4 (10.2)	112.9 (11.0)	−0.97 (0.77)
Waist (cm)	95.1 (8.7)	95.4 (10.4)	0.48 (0.67)	—	—	—	94.0 (9.5)	95.7 (10.7)	**−1.77 (0.84)*****	93.5 (10.8)	94.8 (12.8)	−1.15 (1.02)
BOD POD							***n*=83**	***n*=79**		***n*=87**	***n*=82**	
Weeks after delivery	—	—	—	—	—	—	15.3 (3.9)	15.4 (4.6)	−0.13 (0.70)	57.8 (13.4)	57.6 (14.4)	−1.07 (2.01)
Percentage fat (%)	—	—	—	—	—	—	37.95 (6.03)	40.05 (6.84)	**−1.99 (0.82)*****	37.60 (8.55)	38.41 (7.77)	−0.53 (0.94)
Fat mass (kg)	—	—	—	—	—	—	31.57 (9.00)	34.61 (11.53)	**−2.96 (0.87)*****	31.94 (12.16)	33.25 (12.95)	−0.95 (1.02)
Fat-free mass (kg)	—	—	—	—	—	—	50.34 (6.15)	50.04 (5.93)	0.26 (0.56)	50.37 (5.39)	50.75 (5.80)	−0.32 (0.51)
QMR							***n*=75**	***n*=69**		***n*=79**	***n*=69**	
Weeks after delivery	—	—	—	—	—	—	15.3 (3.9)	16.3 (5.5)	−1.03 (0.84)	58.6 (13.9)	58.5 (15.5)	−1.31 (2.27)
Fat mass (kg)	—	—	—	—	—	—	31.22 (8.54)	34.61 (10.99)	**−3.14 (0.90)***	31.92 (11.35)	33.85 (13.19)	−1.56 (1.09)
Lean mass (kg)	—	—	—	—	—	—	40.91 (6.14)	42.02 (5.6)	−0.56 (0.86)	42.10 (6.67)	43.06 (5.59)	−0.69 (0.82)
Total body water (kg)	—	—	—	—	—	—	33.93 (6.38)	34.25 (7.03)	−0.02 (1.08)	33.95 (7.44)	34.27 (7.45)	−0.38 (1.19)
MRI (kg)	***n*=51**	***n*=46**		***n*=43**	***n*=36**		***n*=34**	***n*=39**		***n*=38**	***n*=35**	
Gestational age (wk)	14.98 (0.74)	15.03 (0.57)	−0.02 (0.13)	35.66 (0.67)	35.8 (0.70)	−0.00 (0.16)	—	—		—	—	
Weeks after delivery	—	—	—	—	—	—	14.34 (1.1)	15.4 (3.8)	−1.30 (0.79)	57.03 (11.0)	61.8 (29.0)	−7.67 (6.22)
Weight (kg)	78.6 (9.6)	78.8 (9.5)	−0.70 (1.98)	85.8 (9.1)	88.9 (9.8)	**−2.32 (0.99)*****	77.2 (10.4)	82.0 (9.7)	**−2.97 (1.25)*****	78.4 (13.1)	79.8 (10.3)	−0.42 (1.67)
Total adipose (kg)	32.8 (7.6)	33.3 (6.0)	−0.13 (0.73)	32.8 (7.2)	36.0 (5.9)	**−2.01 (0.80)*****	32.6 (8.0)	36.1 (7.0)	−1.86 (0.99)	34.0 (11.7)	34.2 (8.3)	1.58 (1.50)
Subcutaneous (kg)	30.0 (7.1)	30.6 (5.4)	−0.09 (0.63)	30.3 (6.7)	33.4 (5.7)	**−1.85 (0.69)****	29.7 (7.4)	32.8 (6.4)	−1.83 (0.94)	30.5 (10.5)	30.9 (7.4)	0.98 (1.32)
Abdominal deep	2.92 (0.81)	3.11 (0.68)	−0.08 (0.15)	—	—	—	2.95 (0.91)	3.28 (0.79)	−0.10 (0.13)	2.96 (1.12)	2.99 (0.77)	0.17 (0.17)
Abdominal superficial	2.91 (0.96)	2.99 (0.75)	0.04 (0.14)	—	—	—	2.95 (0.88)	3.29 (0.82)	**−0.37 (0.11)***	3.11 (1.20)	3.03 (0.93)	0.08 (0.14)
Femoral SAT	10.50 (2.39)	11.49 (1.93)	−0.68 (0.43)	10.69 (2.73)	12.37 (2.78)	−0.76 (0.42)	10.69 (2.73)	12.37 (2.78)	−0.67 (0.43)	11.06 (3.36)	11.44 (2.88)	0.68 (0.50)
Peri-muscular SAT	0.50 (0.13)	0.48 (0.10)	0.03 (0.03)	0.49 (0.12)	0.48 (0.10)	−0.01 (0.03)	0.49 (0.12)	0.48 (0.10)	−0.00 (0.03)	0.49 (0.12)	0.47 (0.11)	0.05 (0.03)
Visceral (kg)	1.45 (0.84)	1.45 (0.99)	-0.05 (0.17)	—	—	—	1.57 (0.74)	1.78 (1.08)	−0.05 (0.12)	1.99 (1.11)	1.94 (1.26)	**0.31 (0.15)*****
Intermuscular (kg)	1.27 (0.54)	1.28 (0.47)	0.001 (0.10)	1.42 (0.54)	1.43 (0.43)	−0.03 (0.07)	1.38 (0.56)	1.48 (0.51)	0.04 (0.09)	1.46 (0.67)	1.38 (0.52)	0.17 (0.09)
Skeletal muscle (kg)	20.4 (3.1)	20.2 (3.1)	0.21 (0.44)	21.1 (2.6)	21.3 (3.1)	−0.39 (0.26)	19.8 (2.9)	20.8 (3.0)	−0.38 (0.29)	20.5 (2.9)	20.8 (2.8)	−0.37 (0.33)

[a]Adjusted difference at each time point calculated using the following covariates: variable's baseline value, mother's baseline age, weight, BMI, and ethnicity. For 35-week analysis, additional covariates included gestational diabetes mellitus and gestational age. For the postpartum visit, additional covariates included weeks since delivery and gestational diabetes mellitus.
Statistically significant *P* values are in bold.
**P* < 0.001.
***P* < 0.01.
****P* < 0.05.
LI, lifestyle intervention; UC, usual care; SED, standard error difference.

TABLE 3 Maternal body composition changes within group, mean (SD)

	Pregnancy			Postpartum			Postpartum		
	Baseline to 35 weeks			Baseline to 15 weeks postpartum			Baseline to 59 weeks postpartum		
	LI change, *n* = 94	UC change, *n* = 93	*P* value	LI change, *n* = 88	UC change, *n* = 82	*P* value	LI change, *n* = 91	UC change, *n* = 87	*P* value
Weight (kg)	**8.01 (4.01)***	**9.81 (4.20)***	**0.0031**	−0.22 (4.09)	**2.43 (4.62)***	**0.0001**	−0.39 (5.78)	1.16 (6.02)	0.0821
BMI (kg/m^3)	**2.95 (1.47)***	**3.68 (1.60)***	**0.0014**	−0.10 (1.51)	**0.89 (1.75)***	**0.0001**	−0.15 (2.10)	0.45 (2.23)	0.0650
Hip circumference (cm)	**1.48 (3.51)***	**2.35 (7.90)****	0.3354	**−0.92 (3.62)*****	**1.32 (4.74)*****	**0.0007**	−0.95 (4.64)	−0.10 (5.36)	0.2553
Waist circumference (cm)	—	—		**−1.59 (5.52)****	0.51 (5.43)	**0.0133**	**−2.21 (6.70)****	−0.81 (6.69)	0.1613
MRI (kg)	*n* = 42	*n* = 34		*n* = 33	*n* = 36		*n* = 38	*n* = 30	
Weight (g)	**7.61 (3.73)***	**10.26 (4.70)***	**0.0097**	−0.29 (3.92)	**2.97 (4.85)***	**0.0030**	0.06 (5.97)	0.60 (6.22)	0.7157
Total adipose (kg)	0.46 (3.22)	**2.50 (3.31)***	**0.0086**	0.78 (3.25)	**2.91 (3.87)***	**0.0155**	1.80 (5.81)	0.61 (5.30)	0.3834
Subcutaneous (kg)	0.68 (2.70)	**2.54 (2.93)***	**0.0059**	0.37 (2.95)	**2.41 (3.55)***	**0.0114**	1.04 (5.04)	0.22 (4.74)	0.4917
Abdominal deep	—	—	—	0.03 (0.32)	0.17 (0.52)	0.1985	0.03 (0.52)	−0.11 (0.59)	0.3088
Abdominal superficial	—	—	—	0.04 (0.42)	**0.31 (0.38)***	**0.0137**	**0.20 (0.52)*****	0.05 (0.50)	0.2541
Femoral SAT	0.18 (1.05)	**0.88 (1.58)**	**0.0217**	0.18 (1.05)	**0.88 (1.58)****	0.0518	0.55 (1.61)	−0.04 (1.80)	0.1826
Peri-muscular SAT	−0.01 (0.12)	**0.00 (0.10)**	0.8508	−0.01 (0.12)	0.00 (0.10)	0.7686	−0.00 (0.11)	−0.02 (0.11)	0.6238
Visceral (kg)	—	—	—	**0.23 (0.54)*****	**0.34 (0.52)***	0.4075	**0.54 (0.71)***	**0.34 (0.54)****	0.2210
Intermuscular (kg)	**0.13 (0.31)*****	**0.18 (0.26)***	0.4015	**0.18 (0.41)*****	**0.17 (0.34)****	0.8759	**0.22 (0.41)****	0.05 (0.35)	0.0703
Skeletal muscle (kg)	**0.73 (1.14)***	**1.32 (1.13)***	**0.0262**	**−0.59 (1.21)****	−0.06 (1.21)	0.0771	−0.05 (1.25)	0.57 (1.20)	**0.0444**

Significant within-group changes indicated in bold typeface using paired *t* test. Between-group *P* values calculated using *t* test adjusted for unequal variances.
*$P < 0.001$.
**$P < 0.01$.
***$P < 0.05$.
LI, lifestyle intervention; UC, usual care.

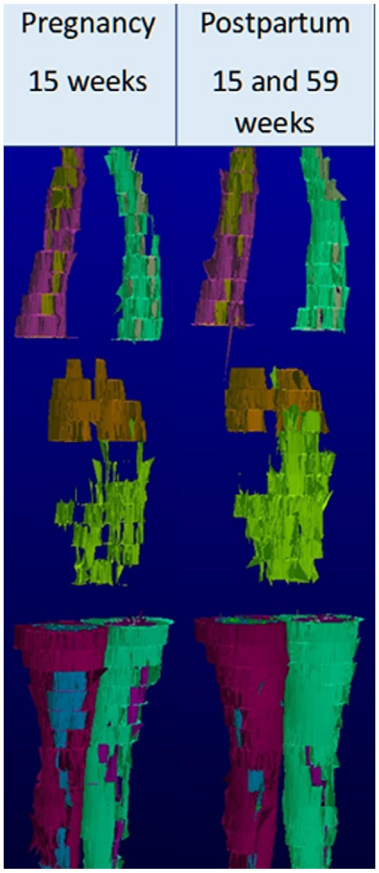

Figure 2 Processed three-dimensional volume rendering of VAT mass (green) in a single study participant at 15 weeks gestation (weight, 84.7 kg; VAT, 1.64 kg) and at 15 weeks postpartum (weight, 83.5 kg; VAT, 2.93 kg). Participant is positioned in the MRI scanner with arms extended above head.

superficial SAT (0.20 kg, $P<0.05$) and IMAT (0.22 kg, $P=0.05$) marginally elevated compared with baseline. Presented in Figure 3 are the individual participant data, showing percentage change in VAT and corresponding percentage change in weight, for the period from 15 weeks gestation (our baseline pregnancy time point) to 59 weeks postpartum.

Relationship with GWG. The partial correlations of total GWG with maternal body composition variables during pregnancy (35 weeks) and after delivery (Supporting Information Table S3) for combined groups were calculated and adjusted for time (35 weeks gestation, 15 and 59 weeks postpartum) and baseline values for age, weight, and BMI. Total GWG was positively correlated with all 35-week body composition variables and with changes in body composition variables from baseline to 35 weeks of pregnancy (Supporting Information Table S4). At 15 weeks postpartum, GWG was positively correlated with waist and hip circumferences, total and percentage body fat, abdominal deep SAT, and femoral SAT but not VAT. There were significant positive correlations between GWG and changes in waist and hip circumferences, total SAT, including femoral SAT (all $P<0.001$), and skeletal muscle mass ($P<0.02$). At 59 weeks postpartum, GWG was positively correlated with QMR fat mass ($P<0.05$) and changes in waist circumference ($P<0.04$) and skeletal muscle ($P<0.03$) from baseline to 59 weeks.

Relationship with HEI. The HEI total score at the concurrent visit was included as an additional independent variable in regression models containing group, ethnicity, baseline values for age, weight, and BMI, time to measurement, and the baseline value of the variable to predict body composition variables (Supporting Information Table S5). HEI total score was a significant predictor of hip circumference ($P<0.04$) and VAT ($P<0.03$) only at 15 weeks postpartum; that is, an increase in HEI score was associated with an increase in VAT, although we do not consider this relationship to be biologically significant.

Relationship with physical activity. Total physical activity (mean amplitude deviation [MAD]) was included as an additional independent variable in regression models to predict the maternal body composition variables (Supporting Information Table S6). At 35 weeks gestation, the MAD coefficient was significant for the following three models: TAT ($P=0.02$), total SAT ($P=0.03$), and total IMAT ($P=0.01$); that is, less physical activity was associated with greater TAT, SAT, and IMAT. At 59 weeks, the MAD coefficient was significant for BOD POD fat mass ($P=0.02$); that is, less physical activity was associated with great BOD POD fat mass.

Relationship of change in VAT to metabolic parameters. At 59 weeks postpartum (Table 4), VAT was positively associated with 59-week triglycerides ($P=0.04$) and cholesterol/HDL ratio ($P=0.02$) and negatively associated with HDL ($P=0.03$).

Safety events

Through the end of pregnancy, 13.3% of women in LI ($n=14$) and 14.3% in UC ($n=15$) ($P=0.84$) reported serious adverse events. Maternal hospitalizations accounted for 79.3% of these. None was considered related to the study intervention.

Discussion

These prospective data were among the first to report on the effects of pregnancy and the early postpartum period on adipose tissue distribution, including VAT mass by MRI. VAT mass was elevated by 30% at 1 year postpartum despite body weight having returned to baseline/first trimester levels in both LI and UC. The LI promoting healthy diet and physical activity during the second and third trimesters in women with overweight or obesity, designed to restrict excessive GWG, had no effect on preventing or lessening the increase in VAT.

The first postpartum measure showed no weight retention, but there was increased VAT (0.23 kg; 16%) and IMAT in LI compared with baseline values, whereas UC retained weight (3.0 kg), VAT (23%), and total SAT that was reflected in abdominal superficial SAT and femoral SAT subdivisions. The earlier return to baseline weight in LI may reflect less total GWG (~2.0 kg) and therefore less excess weight to shed compared with UC. By 59 weeks postpartum, however, neither group showed weight retention compared with baseline, yet VAT remained elevated by 37% and 23% in LI and UC, and only in LI did IMAT remain elevated (~6%). A study with follow-up at 7 years of changes in VAT

TABLE 4 Regression coefficient (standard error [SE]) of VAT (kg) at 15 weeks in pregnancy and at 59 weeks postpartum and Spearman correlation between VAT (kg) and cardiometabolic risk factors at 59 weeks postpartum

	Pregnancy		Postpartum		Postpartum	
	15 weeks		59 weeks		59 weeks	
	β (SE)[a]	*P*	β (SE)[a]	*P*	*r*[b]	*P*
DBP (mm Hg)	0.775 (0.796)	0.3330	0.089 (0.568)	0.8761	−0.10	0.4151
SBP (mm Hg)	1.022 (1.073)	0.3433	1.011 (0.969)	0.3011	−0.06	0.5938
Triglycerides (mg/dL)	14.396 (4.415)	**0.0016**	11.769 (6.124)	0.0596	0.41	**0.0003**
Cholesterol (mg/dL)	3.971 (3.986)	0.3219	−0.872 (3.411)	0.7992	0.20	0.0912
HDL (mg/dL)	−2.775 (1.966)	0.1618	−3.209 (1.328)	**0.0189**	−0.26	**0.0280**
Cholesterol/HDL (ratio)	0.183 (0.082)	**0.0279**	0.159 (0.084)	0.0625	0.37	**0.0012**
Friedewald LDL cholesterol (mg/dL)	3.889 (3.433)	0.2604	0.205 (2.898)	0.9439	0.28	**0.0151**
Insulin (uU/mL)	1.962 (0.570)	**0.0009**	0.495 (0.726)	0.4978	0.32	**0.0051**
Glucose (mg/dL)	1.933 (0.860)	**0.0272**	0.494 (1.075)	0.6475	0.29	**0.0116**
HOMA-IR	9.404 (2.719)	**0.0008**	2.910 (3.387)	0.3939	0.36	**0.0017**
C-peptide (ng/mL)	0.223 (0.046)	**0.0001**	0.074 (0.078)	0.3507	0.52	**0.0001**
Glycated serum protein (umol/L)			−3.487 (4.184)	0.4079	−0.34	**0.0033**
Glycated albumin (%)			−0.159 (0.150)	0.2947	−0.38	**0.0010**
Albumin (g/dL)			0.003 (0.027)	0.9187	−0.03	0.8004
Leptin (ug/L)	3.640 (1.928)	0.0624	8.777 (4.273)	**0.0446**	0.40	**0.0005**
Adiponectin (mg/dL)	−543.58 (278.91)	0.0546	−195.96 (222.21)	0.3815	−0.17	0.1539
TNF-α (pg/mL)	0.099	0.0526				
IL-6 (pg/mL)	0.34	**0.0014**				

[a]Regression model included VAT (kg), baseline metabolic variable, group, ethnicity, baseline age, baseline weight, baseline BMI, and weeks after delivery. Gestational diabetes mellitus was an additional covariate for the 59-week regression models. Statistically significant *P* values are in bold.
[b]Spearman correlations between VAT (kg) and cardiometabolic risk factors at 59 weeks postpartum.
HMW, high molecular weight.

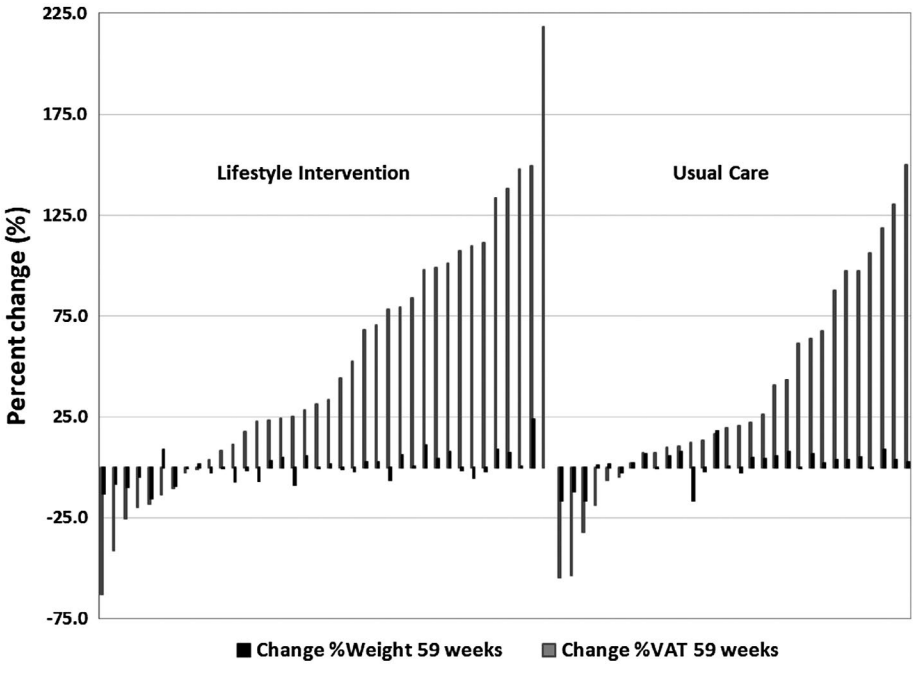

Figure 3 Change in percentage VAT and corresponding change in percentage weight in individual participants from 15 weeks gestation to 59 weeks postpartum.

found that having 1 versus 0 births was associated with a greater increase in VAT and concluded that childbearing was associated with a threefold greater increase in VAT deposition from preconception to postpartum compared with nulliparous women (4). An increase in VAT by 0.30 kg to 0.50 kg (Table 3) from a single pregnancy in women who are relatively early in their life course sets them on a negative health trajectory. In women (BMI ≥ 30) in the Netherlands Epidemiology of Obesity Study, a 1-SD higher VAT was associated with an OR of 5.77 (3.02-11.01) on having at least one cardiometabolic risk factor compared with individuals without any risk factors (26). In the presence of no change in body weight, increased VAT with no change in SAT is comparable to the adipose tissue distribution profile of aging older adults.

We found no evidence of changes in abdominal deep SAT or peri-muscular femoral SAT during pregnancy and after delivery. In previous studies, deep abdominal SAT correlated strongly with insulin resistance, but superficial SAT did not, in nonpregnant adults with overweight and obesity (27); peri-muscular adipose tissue adjacent to skeletal muscle was associated with insulin resistance in women with polycystic ovary syndrome (28).

Implications and clinical relevance

An expanded VAT is associated with hypertrophic adipocytes and a migration of inflammatory macrophages into the VAT depot (29,30). Intra-abdominal adipose tissue and resident macrophages within this tissue are considered the primary source of cytokines relevant to metabolic disease. Adipose tissue is a source of proinflammatory cytokines and chronic inflammation in VAT and is importantly associated with the development of type 2 diabetes mellitus, dyslipidemia, metabolic syndrome, and CVD in individuals with overweight and obesity (31-33). The observed between-group difference in leptin was consistent with increased TAT (2.56 kg, $P=0.009$; Table 3) in UC, with no changes in either leptin or adipose tissue observed in LI. The between-group differences for change (baseline to 35 weeks gestation; Supporting Information Table S2) in total cholesterol (−10.7 mg/dL, $P=0.019$), HDL cholesterol (−3.76 mg/dL, $P=0.017$), and leptin (−6.34 ug/L, $P=0.05$) were reflective of stable values in LI during the intervention period compared with positive and nonsignificant increases in UC.

In the combined cohort of women with prepregnancy overweight and obesity, while acknowledging that hormonal changes that occur in pregnancy influence the levels of many cardiometabolic risk factors, after adjusting for baseline metabolic variables, age, weight, BMI, group, and ethnicity, VAT was a significant predictor of five cardiometabolic risk factors, triglycerides, cholesterol/HDL ratio, insulin, glucose, homeostatic model assessment of insulin resistance (HOMA-IR), c-peptide, and the IL-6 marker of inflammation (Table 4) at baseline. At 59 weeks postpartum, VAT was a significant predictor of triglycerides and cholesterol/HDL ratio and a negative predictor of HDL cholesterol (inflammatory markers not measured). Moreover, at 59 weeks postpartum, VAT was unfavorably correlated with four established CVDs (triglycerides, HDL, cholesterol/HDL ratio, low-density lipoprotein) and six metabolic risk factors (insulin, glucose, HOMA-IR, c-peptide, glycated serum protein, and glycated albumin).

At 15 weeks postpartum in LI, waist and hip circumferences were lower than baseline (15 weeks gestation), suggesting that baseline values may have been elevated compared with prepregnancy values and the 15-week postpartum circumferences are reflecting prepregnancy values. LI gained less skeletal muscle compared with UC during pregnancy, and LI showed an unexplained 3% loss of skeletal muscle mass at 15 weeks postpartum compared with baseline that had normalized at 59 weeks.

GWG was associated with increases in weight and adipose tissue; however, by 15 weeks postpartum, these effects were dissipating, and by 1 year, the only persistent effects of GWG were on fat mass by QMR (Supporting Information Table S3). GWG was correlated with changes in waist circumference and skeletal muscle mass at 59 weeks postpartum (Supporting Information Table S4). Total physical activity by accelerometry (MAD) was negatively associated with TAT, including subdivisions SAT and IMAT at 35 weeks of pregnancy; that is, greater physical activity was associated with less adipose tissue. At 59 weeks, the MAD negative coefficient was associated with BOD POD fat mass ($P=0.02$) only; that is, greater physical activity was associated with less fat mass.

Study entry measures collected at 15 weeks gestation cannot be assumed to reflect prepregnancy values because of changes in weight and shape. Because of the RCT design, first trimester weight gain and body composition changes could not be determined. Waist and hip circumference measures at 15 weeks postpartum were significantly lower than values recorded at baseline (15 weeks gestation), which could possibly suggest a return to prepregnancy values.

Limitations

A significant percentage of our cohort was larger than could be accommodated by MRI, which impacts the extrapolation of our findings to persons larger than the current MRI cohort. Quantifying VAT late in pregnancy was unsuccessful because of compression effects of the highly distended uterus on the VAT. We cannot address the confounding influences of lifestyle factors (e.g., physical activity, diet, medications, and lactation) on changes in body composition as well as cardiometabolic risk measures between childbirth and 15 weeks and again between 15 and 59 weeks. Cytokines (TNF-α and IL-6) were unavailable for analysis relative to VAT at 59 weeks.

Next steps

Observational studies have shown that breastfeeding for >3 months is associated with reduced VAT at 7 years postpartum (7,34), breastfeeding women have less abdominal adiposity through to age of menopause (35-37), and breastfeeding is associated with lower postpartum weight retention in all categories of prepregnancy BMI (38).The mechanism may be through the additional energy cost of lactation. We did not collect information on lactation in LIFT.

There is an established and growing body of literature supporting the superior and independent effects of aerobic exercise over caloric restriction on reducing VAT in persons with overweight and obesity (39). Even in the absence of weight loss following exercise training, VAT loss can occur (40). No studies, however, have been conducted in postpartum populations, and appropriately, designed studies involving exercise interventions, factored on lactation, are needed to document efficacy to reduce VAT. Findings could guide health promotion practices in women both during their reproductive years and longer term.

Conclusion

In women with preconception overweight and obesity, pregnancy resulted in a ~30% increase in VAT that persisted at 59 weeks postpartum

despite a return to baseline weight. Moreover, VAT was significantly associated with several cardiometabolic risk factors at 59 weeks postpartum. Finally, women enrolled in a LI to control excess GWG during the second and third trimesters had returned to early pregnancy body weight by 15 weeks postpartum compared with the nonintervention group that had not. O

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Author contributions: IJ and DG designed the maternal MRI phenotyping protocol; IJ supervised all MRI acquisition and analyzed MRI scans; DG and FXP are coprincipal investigators of the LIFT trial and were responsible for supervision of data collection; BR was responsible for obstetrical care; TTR, EW, and MH were responsible for maternal outcome measures; CP and SG were responsible for medical supervision; MH was the primary project coordinator; JC was the primary lifestyle interventionist; SL was responsible for data management; JCT was responsible for data analysis; DG and FXP had primary responsibility for final content. All authors read and approved the final manuscript.

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Supporting information: Additional Supporting Information may be found in the online version of this article.

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