The Comparative Effectiveness of Diabetes Prevention Strategies to Reduce Postpartum Weight Retention in Women With Gestational Diabetes Mellitus: The Gestational Diabetes' Effects on Moms (GEM) Cluster Randomized Controlled Trial

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OBJECTIVE

To compare the effectiveness of diabetes prevention strategies addressing postpartum weight retention for women with gestational diabetes mellitus (GDM) delivered at the health system level: mailed recommendations (usual care) versus usual care plus a Diabetes Prevention Program (DPP)–derived lifestyle intervention.

RESEARCH DESIGN AND METHODS

This study was a cluster randomized controlled trial of 44 medical facilities (including 2,280 women with GDM) randomized to intervention or usual care. The intervention included mailed gestational weight gain recommendations plus 13 telephone sessions between 6 weeks and 6 months postpartum. Primary outcomes included the following: proportion meeting the postpartum goals of *1*) reaching pregravid weight if pregravid BMI <25.0 kg/m^2 or *2*) losing 5% of pregravid weight if BMI ≥25.0 kg/m^2; and pregravid to postpartum weight change.

RESULTS

On average, over the 12-month postpartum period, women in the intervention had significantly higher odds of meeting weight goals than women in usual care (odds ratio [OR] 1.28 [95% CI 1.10, 1.47]). The proportion meeting weight goals was significantly higher in the intervention than usual care at 6 weeks (25.5 vs. 22.4%; OR 1.17 [1.01, 1.36]) and 6 months (30.6 vs. 23.9%; OR 1.45 [1.14, 1.83]). Condition differences were reduced at 12 months (33.0 vs. 28.0%; OR 1.25 [0.96, 1.62]). At 6 months, women in the intervention retained significantly less weight than women in usual care (mean 0.39 kg [SD 5.5] vs. 0.95 kg [5.5]; mean condition difference −0.64 kg [95% CI −1.13, −0.14]) and had greater increases in vigorous-intensity physical activity (mean condition difference 15.4 min/week [4.9, 25.8]).

CONCLUSIONS

A DPP-derived lifestyle intervention modestly reduced postpartum weight retention and increased vigorous-intensity physical activity.

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MANAGEMENT OF GESTATIONAL DIABETES MELLITUS

Type 2 diabetes is a costly disease affecting $\sim$12.6 million women in the U.S. Randomized efficacy trials (1–4) demonstrated that weight loss programs can prevent diabetes. Diabetes prevention is critical for women with gestational diabetes mellitus (GDM), which affects 7–14% of pregnancies (5), as women with GDM are seven times more likely to develop type 2 diabetes than parous women without GDM (6). Postpartum weight retention increases diabetes risk (7), and postpartum weight management for women with GDM is recommended (8). Yet evidence to support health system adoption of postpartum diabetes prevention programs for women with GDM is lacking. In addition to traditional clinical trials enrolling carefully selected volunteers with a history of GDM under ideal conditions (4), pragmatic trials evaluating the effectiveness of diabetes prevention programs in real-world clinical settings among diverse populations are needed to increase generalizability and inform health system adoption (9).

The Gestational Diabetes' Effects on Moms (GEM) cluster randomized controlled trial compared an existing postpartum diabetes prevention program of mailed recommendations delivered by the Kaiser Permanente Northern California (KPNC) Perinatal Center (10) (usual care) to usual care plus a Diabetes Prevention Program (DPP)–derived lifestyle intervention (1). The DPP-derived intervention was delivered on behalf of the KPNC Perinatal Center and offered as an optional routine care program (11). The goal of the intervention was to help women with GDM *1*) reach pregravid weight if their pregravid BMI was <25.0 kg/m^2 or *2*) lose 5% of pregravid weight if their pregravid BMI was $\geq$25.0 kg/m^2 (11). Primary outcomes were the proportion of women who reached postpartum weight goals and weight change from pregravid to postpartum across the 12-month postpartum follow-up period. Secondary outcomes included changes from pregnancy to postpartum in daily total energy intake, percent of calories from fat, physical activity, hypertension, and depression. An exploratory outcome was postpartum prediabetes or diabetes incidence.

RESEARCH DESIGN AND METHODS
The rationale and methods of the GEM trial are described elsewhere (11). The

Kaiser Foundation Research Institute Human Subjects Committee approved the trial and waived the requirement for informed consent for the intervention. Women provided verbal consent for the survey component of the trial after all medical facilities were randomized (11).

Setting, Randomization, and Masking
The setting was KPNC, an integrated health care delivery system with 44 medical facilities managing $\sim$33,000 births annually. KPNC membership closely approximates the surrounding population (12) and is dynamic with respect to enrollment. All 44 KPNC facilities were randomized to either usual care or intervention conditions. Randomization was blocked on facility size (i.e., the expected annual number of women with GDM, in three strata: <25, 25–74, and $\geq$75). A restricted randomization scheme was used to ensure acceptable between-condition balance (i.e., maximum between-condition relative difference) in expected racial/ethnic distributions and the number of women contacted by an ongoing unrelated observational study, both overall and within facility size stratum (11,13). All investigators, data collectors, and health care providers were blinded to condition assignment.

Participants
Potentially eligible women included pregnant women $\geq$18 years old diagnosed with GDM ($n = 2,480$) according to the Carpenter and Coustan criteria between March 2011 and March 2012, as recommended by the American College of Obstetricians and Gynecologists (14) during this period and implemented across all 44 KPNC medical facilities. Women were excluded if they did not have any telephone contact with the KPNC Perinatal Center during pregnancy ($n = 142$), were missing data on pregravid BMI ($n = 40$), or had a neonatal loss ($n = 18$), leaving 2,280 women: 1,087 in the intervention condition and 1,193 in usual care (Fig. 1). Follow-up ended on December 2013.

Usual Care
All women with GDM at KPNC are offered supplemental care from the KPNC Perinatal Center consisting of telephone-based case management for glucose control during pregnancy (10). At

6 weeks postpartum, the KPNC Perinatal Center sends a letter encouraging women to be screened for diabetes and provides printed materials that emphasize a healthy BMI, participation in 30 min of physical activity daily, and healthy eating. If screening results indicate prediabetes, women are mailed materials about lifestyle prevention strategies and educational classes.

DPP-Derived Lifestyle Intervention
In addition to usual care, women attending medical facilities assigned to the intervention were mailed, within 2 weeks of the GDM diagnosis, a tailored letter detailing a personalized goal for gestational weight gain with healthy eating and physical activity tips (11). After delivery, women were offered a print/telephone-based lifestyle program modeled after the DPP intervention (11). The program was presented as optional routine care and delivered by GEM coaches on behalf of the KPNC Perinatal Center. During the core of the postpartum intervention (6 weeks to 6 months), the primary target was to help women achieve the postpartum weight goals: *1*) reaching pregravid weight if their pregravid BMI was <25.0 kg/m^2 or *2*) losing 5% of pregravid weight if their pregravid BMI was $\geq$25.0 kg/m^2 (11). Women were mailed a 13-session guidebook to review via telephone with a lifestyle coach, a registered dietitian employed for the trial and based at the KPNC Perinatal Center. Women were encouraged to set weekly goals for daily fat and caloric intake and to work up to or continue participating in 150 min of moderate- to vigorous-intensity physical activity per week (11). Behavior change techniques were individualized to women's preferences, resources, and cultural context using motivational interviewing and theoretical constructs derived from social cognitive theory (15) and the Transtheoretical Model (16). All telephone sessions were audiotaped; a random 10% were coded using a brief checklist of intervention components to assess fidelity to the protocol. Fidelity was high (mean proportion of intervention components present = 95%, range 60–100%). During the maintenance phase (7–12 months postpartum), women were mailed three newsletters encouraging maintenance of healthy behaviors. Lifestyle coaches tracked the time spent scheduling and
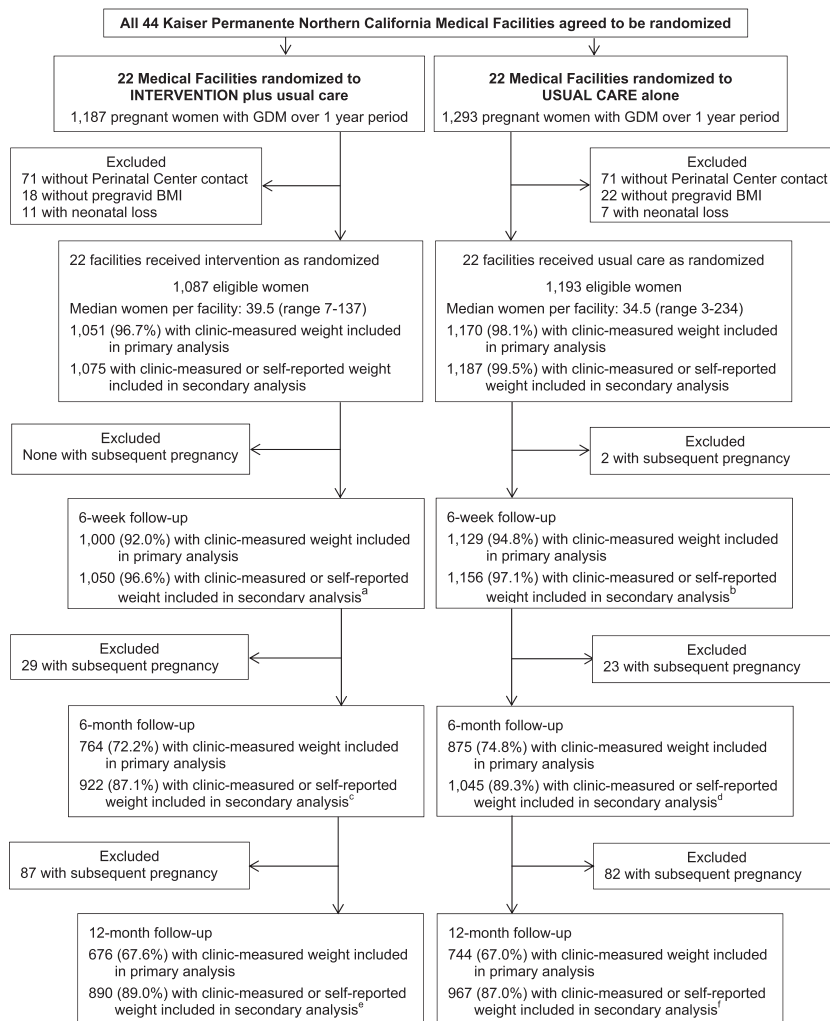
Figure 1—Trial flow. a, 12 women were not health plan members and did not have clinic-measured weight, 5 of them provided self-reported weight; b, 9 women were not health plan members and did not have clinic-measured weight, 4 of them provided self-reported weight; c, 37 women were not health plan members and did not have clinic-measured weight, 26 of them provided self-reported weight; d, 36 women were not health plan members and did not have clinic-measured weight, 25 of them provided self-reported weight; e, 84 women were not health plan members and did not have clinic-measured weight, 61 of them provided self-reported weight; f, 101 women were not health plan members and did not have clinic-measured weight, 66 of them provided self-reported weight only.

conducting telephone sessions. The direct cost of the intervention included coaches' work hours, calculated using the May 2012 median annual wage for registered dietitians (17) plus fringe benefits (29% of annual wages), and the cost of printing and mailing materials.

Data Collection

All 2,280 eligible women in the 44 medical facilities were invited to complete study surveys (11); 1,783 (78.2%) completed the baseline survey during pregnancy after the GDM diagnosis (mean gestational age at completion 29.4 weeks [SD 6.1]). Survey responders did not differ from nonresponders except for being less likely to be of non-Hispanic white origin (11). Responders to the baseline survey were asked to complete surveys at 6 weeks, 6 months, and 12 months postpartum (11), with 91.6, 87.9, and 84.0% retention rates, respectively. Pregravid BMI was calculated from clinic-measured pregravid weight obtained through the electronic health record (EHR; 86.0%), weight ascertained at the first prenatal clinic visit before 10 weeks' gestation (10.5%, from the EHR), or self-reported pregravid weight on the GEM pregnancy survey (3.5%).

Clinic-measured postpartum weight was obtained through the EHR for each time point, regardless of participation in the intervention or the GEM surveys. Postpartum weight was also self-reported at each GEM survey.

The Block Food Frequency questionnaire (18) and the Pregnancy Physical Activity Questionnaire (19) were used at baseline and 6 months postpartum to assess usual daily total energy intake and weekly physical activity over the past 3 months. Hypertension was defined as present during pregnancy and at each postpartum time point by searching the EHR for any abnormal blood pressure measurements (systolic blood pressure $\geq$140 mmHg or diastolic blood pressure $\geq$90 mmHg) or for use of antihypertensive medications. Depression was defined as present during pregnancy and at each postpartum time point by searching the EHR for diagnoses of depression, use of antidepressant medications, or depression score $\geq$10 on Patient Health Questionnaire 9 (PHQ-9) (20) or score $\geq$10 on PHQ-8 (21) from surveys at each time point. Age, race/ethnicity, parity, and laboratory test results were also obtained from the EHR. Prediabetes and diabetes were defined according to American Diabetes Association glycemic thresholds (22) (see Supplementary Methods).

Power and Statistical Analysis

The sample size of 2,280, of which 97.4% had at least one clinic-measured weight during the 12-month postpartum follow-up period, allowed for robust estimation of the average effect of the intervention on postpartum weight goals assessed through clinic-measured weight across the 12-month postpartum follow-up period. We focused post hoc minimum detectable effect estimation at each point in time accounting for the cluster randomization. Of the sample, 93.4, 71.9, and 62.3% had clinic-measured weight at 6 weeks, 6 months, and 12 months postpartum, respectively, which led to a minimum detectable absolute difference in the proportion meeting postpartum weight goals ranging from 5.6 to 10.2%, 6.2 to 10.6%, and 6.6 to 11.0%, respectively, across the range in expected proportion meeting goals in the usual care condition (15–25%, based on our pilot trial [24%] and across the range in expected intraclass correlation [0.01–0.05]) (see Supplementary Methods). We note the additional

power and precision gained in the analysis of treatment effects by incorporating the repeated measures of meeting postpartum weight goals.

Analyses were intent to treat. Analyses used marginal regression models to estimate population average intervention effects, using logistic regression with estimation via generalized estimating equations in analyses of meeting the weight goals and other dichotomous outcomes, and linear mixed regression in analyses of weight change and changes in other continuous outcomes after adjusting for baseline values. Regression models accounted for the within-medical facility correlation between patients and within-person correlation among repeated measurements for valid estimation of treatment effects and associated standard errors. Variations in treatment condition differences over time were examined via the introduction of appropriate cross-product terms. For all analyses, if women had a subsequent pregnancy, they were censored at the estimated time of conception.

Primary outcome analysis for the effect of the intervention included only clinic-measured postpartum weights. Sensitivity analyses to address potential bias from missing clinic-measured weight included clinic-measured or self-reported postpartum weight collected during postpartum surveys. Additional sensitivity analyses included clinic-measured or imputed postpartum weight (23). The fully conditional specification imputation method was used, with 10 imputations performed. Subgroup analyses were performed after stratifying by pregravid BMI. Two exploratory analyses assessed intervention effectiveness across number of sessions completed and using an instrumental variable to estimate the complier average causal effect, a measure of the effectiveness of the intervention among those who comply with assigned treatment, with the randomization indicator used as the instrumental variable (24). For this analysis, "all or none" compliance was defined as completing one or more telephone sessions (25). A key applicable assumption is that the outcomes among noncompliers are not affected by randomization condition assignment. Exploratory outcome analysis of prediabetes or diabetes incidence used Cox

proportional hazards regression to estimate hazard ratios associated with the intervention, controlling for pregnancy fasting and 3-h glucose values and pregravid BMI. All analyses were conducted using SAS 9.3 (Cary, NC).

RESULTS

The intervention and usual care conditions were comparable on prerandomization characteristics such as medical facility size (Fig. 1) and racial/ethnic and BMI distributions; however, they differed by fasting and 3-h glucose (Table 1). Among the 1,087 women in the intervention, 50.3% completed one or more telephone sessions; specifically, 18.8% completed 1–3 sessions, 16.2% completed 4–12 sessions, and 15.3% completed all 13 sessions.

Primary Outcomes

Clinic-measured postpartum weight was obtained at least once during the 12-month postpartum follow-up for 97.4% of women ($n = 2,221$). In the primary analysis that included only clinic-measured postpartum weight, on average, over the 12-month postpartum period, women in the medical facilities assigned to the intervention had a statistically significant 28% higher odds (odds ratio [OR] 1.28 [95% CI 1.10, 1.47]) of meeting postpartum weight goals than women in the medical facilities assigned to usual care (Table 2). The proportion meeting weight goals was significantly higher in the intervention facilities than usual care facilities at 6 weeks (25.5 vs. 22.4%; 1.17 [1.01, 1.36]) and 6 months postpartum (30.6 vs. 23.9%; 1.45 [1.14, 1.83]). At 12 months (6 months after the intervention ended), the condition difference was reduced (33.0 vs. 28.0%; 1.25 [0.96, 1.62]) and no longer statistically significant. The absolute difference between conditions was 3.1% at 6 weeks, 6.7% at 6 months, and 5.0% at 12 months postpartum. In analyses examining weight change from pregravid to postpartum (Table 2), women in the intervention facilities retained less weight than women in usual care facilities at 6 months postpartum (mean 0.39 kg [SD 5.5] vs. 0.95 kg [5.5]; adjusted mean condition difference −0.64 kg [95% CI −1.13, −0.14]); the condition difference was attenuated at 12 months postpartum and no longer statistically significant (−0.43 kg [−0.98, 0.11])

(Table 2). Sensitivity analyses that included self-reported or imputed weight if the clinic-measured weight was missing yielded similar results (Tables 2 and 3). The intervention was equally effective across racial/ethnic groups (P value for condition × race/ethnicity interactions >0.25). The intervention was also equally effective across BMI strata (Supplementary Tables 1 and 2).

In exploratory analyses, the instrumental variable estimates of the absolute differences between conditions among compliers (defined as completing one or more telephone sessions) were almost double the absolute differences observed in the primary analysis: estimates for proportions meeting weight goals were 6.2% at 6 weeks, 13.3% at 6 months, and 9.9% at 12 months; estimates for differences in mean weight change were −0.62 kg at 6 weeks, −1.27 kg at 6 months, and −0.86 kg at 12 months postpartum.

In additional exploratory analyses, women who completed all 13 sessions had significantly higher odds of meeting the postpartum weight goals than women in usual care at 6 months (3.97 [2.75, 5.72]) and 12 months postpartum (2.16 [1.52, 3.07]) (Fig. 2A). In analyses examining weight change from pregravid to postpartum (Fig. 2B), women who completed 4–12 sessions retained less weight than women in usual care at 6 months postpartum (mean 0.13 kg [SD 5.7] vs. 0.94 kg [5.5], adjusted mean condition difference −1.1 kg [95% CI −1.8, −0.41]) and at 12 months postpartum (0.06 kg [5.6] vs. 0.50 kg [5.4]; −1.0 kg [−1.9, −0.13]). Women who completed all 13 sessions lost more weight than women in usual care at 6 months (mean −1.89 kg [SD 5.5] vs. 0.94 kg [5.5], adjusted mean condition difference −2.3 kg [95% CI −3.1, −1.5]) and 12 months postpartum (−1.19 kg [6.1] vs. 0.50 kg [5.4]; −1.6 kg [−2.4, −0.68]).

Secondary Outcomes

At 6 months postpartum, women in both conditions increased minutes per week spent in vigorous-intensity activity; however, women in the intervention facilities showed a significantly greater increase (adjusted mean condition difference 15.4 min/week [95% CI 4.9, 25.8]) (Table 3). No condition differences were observed for time spent in moderate-intensity activity

Table 1—Baseline characteristics by treatment condition: the GEM trial

	Intervention, N = 1,087	Usual care, N = 1,193	Entire sample, N = 2,280
	n (%)	n (%)	n (%)
Age (years)			
18–24	59 (5.4)	58 (4.9)	117 (5.1)
25–29	238 (21.9)	289 (24.2)	527 (23.1)
30–34	425 (39.1)	425 (35.6)	850 (37.3)
35–39	280 (25.8)	330 (27.7)	610 (26.8)
40–50	85 (7.8)	91 (7.6)	176 (7.7)
Race-ethnicity			
Asian	458 (42.1)	481 (40.3)	939 (41.2)
Non-Hispanic white	268 (24.7)	305 (25.6)	573 (25.1)
Hispanic	236 (21.7)	270 (22.6)	506 (22.2)
African American	47 (4.3)	57 (4.8)	104 (4.6)
Multiracial	37 (3.4)	37 (3.1)	74 (3.3)
Other	26 (2.4)	16 (1.3)	42 (1.8)
Pacific Islander	13 (1.2)	25 (2.1)	38 (1.7)
Missing	2 (0.2)	2 (0.2)	4 (0.2)
Pregravid BMI (kg/m^2)			
15.9–19.9	61 (5.6)	59 (5.0)	120 (5.3)
20.0–24.9	324 (29.8)	343 (28.8)	667 (29.3)
25.0–29.9	319 (29.4)	352 (29.5)	671 (29.4)
30.0–34.9	201 (18.5)	216 (18.1)	417 (18.3)
35.0–59.7	182 (16.7)	223 (18.7)	405 (17.8)
Parity			
0	451 (41.5)	501 (42.0)	952 (41.8)
1	363 (33.4)	398 (33.4)	761 (33.4)
2	174 (16.0)	157 (13.2)	331 (14.5)
3+	84 (7.7)	117 (9.8)	201 (8.8)
Missing	15 (1.4)	20 (1.7)	35 (1.5)
Hypertension			
Yes	80 (7.4)	82 (6.9)	162 (7.1)
No	1,005 (92.5)	1,111 (93.1)	2,116 (92.8)
Missing	2 (0.2)	0 (0)	2 (0.1)
Depression			
Yes	206 (19.0)	237 (19.9)	443 (19.4)
No	833 (76.6)	887 (74.4)	1,720 (75.4)
Missing	48 (4.4)	69 (5.8)	117 (5.1)
	Mean (SD)	Mean (SD)	
Pregravid body weight (kg)	73.5 (19.9)	74.7 (20.2)	74.2 (20.0)
Pregravid BMI (kg/m^2)	28.5 (6.8)	28.9 (6.9)	28.7 (6.8)
BMI at GDM diagnosis (kg/m^2)	31.0 (6.5)	31.4 (6.4)	31.2 (6.5)
Gestational age at GDM diagnosis (weeks)	25.2 (6.4)	25.3 (6.6)	25.3 (6.5)
100-g, 3-h OGTT			
Fasting glucose (mmol/L)*	5.0 (0.7)	5.1 (0.7)	5.1 (0.7)
1-h glucose (mmol/L)	11.0 (1.4)	11.1 (1.5)	11.0 (1.4)
2-h glucose (mmol/L)	9.8 (1.5)	9.8 (1.5)	9.8 (1.5)
3-h glucose (mmol/L)*	7.3 (1.8)	7.1 (1.8)	7.2 (1.8)
Systolic blood pressure (mmHg)	116.7 (13.0)	116.7 (13.6)	116.7 (13.3)
Diastolic blood pressure (mmHg)	72.9 (10.0)	72.6 (10.2)	72.7 (10.1)
Daily total energy intake (kcal/day)†	1,743.5 (662.5)	1,736.7 (660.7)	1,740.0 (661.4)
Daily percent of kcal from fat†	42.2 (7.0)	42.2 (7.0)	42.2 (7.0)
Walking (min/week)‡	446.3 (355.2)	427.9 (364.1)	436.8 (359.8)
Moderate physical activity (min/week)‡	38.2 (62.9)	32.1 (55.8)	35.1 (59.4)
Vigorous physical activity (min/week)‡	23.5 (53.3)	19.0 (46.2)	21.2 (49.8)
Total volume of physical activity (MET min/week)‡	1,667.9 (1,312.9)	1,554.4 (1,212.6)	1,609.2 (1,262.7)

Hypertension was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or use of antihypertensive medications. Depression was defined as score ≥10 on PHQ-8 or PHQ-9, physician diagnosis, or use of antidepressant medications. OGTT, oral glucose tolerance test. *$P < 0.05$ for the comparison with the intervention condition by two-tailed Student t test. All other comparisons had a $P \geq 0.05$. †639 women in the intervention and 668 women in usual care with valid diet data at baseline and 6 months postpartum (e.g., those with daily total energy intake ≥600 and ≤4,000 kcal at both time points). ‡522 women in the intervention and 560 women in usual care with valid physical activity data at baseline and 6 months postpartum (e.g., those with ≤20 h/week of total physical activity and ≤9 h/week of moderate physical activity at both time points).

Table 2—Proportion of women meeting the postpartum weight goals with ORs estimating differences between conditions and mean changes in weight from pregravid to postpartum with mean differences between conditions: the GEM trial

Proportion of women meeting postpartum weight goals:

	Primary analysis						Sensitivity analysis							
	Measured postpartum weights						Measured or self-reported postpartum weights						Measured or imputed postpartum weights	
	Intervention		Usual care				Intervention		Usual care					
	n	% meeting weight goals	n	% meeting weight goals	OR (95% CI)	P value*	n	% meeting weight goals	n	% meeting weight goals	OR (95% CI)	P value*	OR (95% CI)	P value*
Average effect of intervention	1,051		1,170		1.28 (1.10, 1.47)	<0.01	1,075		1,187		1.23 (1.08, 1.39)	<0.01	1.25 (1.11, 1.42)	<0.01
6 weeks postpartum	1,000	25.5	1,129	22.4	1.17 (1.01, 1.36)	0.04	1,050	25.0	1,156	22.7	1.16 (1.00, 1.34)	0.05	1.18 (0.98, 1.44)	0.09
6 months postpartum	764	30.6	875	23.9	1.45 (1.14, 1.83)	<0.01	922	31.6	1,045	25.4	1.37 (1.13, 1.67)	<0.01	1.33 (1.09, 1.62)	0.01
12 months postpartum	676	33.0	744	28.0	1.25 (0.96, 1.62)	0.09	890	33.5	967	30.2	1.16 (0.95, 1.41)	0.14	1.24 (0.97, 1.59)	0.08

Mean changes in weight from pregravid to postpartum:

| | Intervention | | Usual care | | Adjusted† mean weight condition difference (95% CI) | P value* | Intervention | | Usual care | | Adjusted† mean weight condition difference (95% CI) | P value* | Adjusted† mean weight condition difference (95% CI) | P value* |
	n	Mean weight (SD)	n	Mean weight (SD)			n	Mean weight (SD)	n	Mean weight (SD)				
Average effect of intervention	1,051		1,170		−0.29 (−0.69, 0.11)	0.16	1,075		1,187		−0.26 (−0.65, 0.13)	0.19	−0.24 (−0.67, 0.19)	0.28
6 weeks postpartum	1,000	0.64 (5.57)	1,129	0.75 (5.46)	−0.21 (−0.64, 0.23)	0.35	1,050	0.64 (5.53)	1,156	0.71 (5.44)	−0.20 (−0.63, 0.22)	0.35	−0.19 (−0.63, 0.26)	0.41
6 months postpartum	764	0.39 (5.55)	875	0.95 (5.47)	−0.64 (−1.13, −0.14)	0.01	922	0.17 (5.46)	1,045	0.64 (5.54)	−0.55 (−1.02, −0.09)	0.02	−0.51 (−0.99, −0.02)	0.04
12 months postpartum	676	0.20 (5.84)	744	0.50 (5.43)	−0.43 (−0.98, 0.11)	0.12	890	0.01 (5.81)	967	0.15 (5.73)	−0.32 (−0.82, 0.19)	0.22	−0.35 (−0.98, 0.29)	0.28

*P value for condition differences; P values for treatment × follow-up time point interaction >0.05. †Adjusted for pregravid weight.

Table 3—Mean changes in physical activity and diet from pregnancy to 6 months postpartum with mean differences between conditions: the GEM trial

	Primary analysis (Self-reported data)					Sensitivity analysis (Self-reported or imputed data)				
	Intervention n	Intervention Mean (SD)	Usual care n	Usual care Mean (SD)	Adjusted* mean condition difference (95% CI)	Intervention n	Intervention Mean (SD)	Usual care n	Usual care Mean (SD)	Adjusted* mean condition difference (95% CI)
Moderate activity (min/week)										
During pregnancy	522	38.2 (62.9)	560	32.1 (55.8)		1,083	39.1 (2.6)	1,187	34.1 (2.5)	
6 months postpartum	522	42.8 (67.2)	560	33.7 (61.8)		1,083	47.0 (2.5)	1,187	35.4 (3.1)	
Mean change (95% CI)		4.5 (−1.8, 10.8)		1.6 (−4.5, 7.7)	7.0 (−0.8, 14.7)		8.0 (1.8, 14.1)		1.9 (−6.5, 10.3)	9.5 (0.7, 18.3)
Vigorous activity (min/week)										
During pregnancy	522	23.5 (53.3)	560	19.0 (46.2)		1,083	22.9 (1.8)	1,187	19.6 (1.6)	
6 months postpartum	522	47.2 (78.9)	560	30.6 (68.4)		1,083	47.6 (2.9)	1,187	32.5 (2.9)	
Mean change (95% CI)		23.7 (16.9, 30.5)		11.7 (5.1, 18.2)	15.4 (4.9, 25.8)		24.9 (18.0, 31.7)		13.3 (6.3, 20.3)	14.0 (5.0, 22.9)
Total volume of physical activity (MET min/week)										
During pregnancy	522	1,667.9 (1,312.9)	560	1,554.4 (1,212.6)		1,083	1,816.6 (58.6)	1,187	1,781.7 (53.3)	
6 months postpartum	522	1,753.9 (1,300.5)	560	1,610.0 (1,354.7)		1,083	1,843.0 (64.4)	1,187	1,727.6 (54.0)	
Mean change (95% CI)		88.0 (−48.5, 224.6)		58.4 (−79.1, 195.9)	113.8 (−78.0, 305.6)		33.5 (−135.8, 202.8)		−47.4 (−203.0, 108.3)	100.5 (−83.7, 284.7)
Daily total energy intake (kcal)										
During pregnancy	639	1,763.1 (655.7)	668	1,740.2 (644.1)		1,187	1,754.6 (28.4)	1,187	1,785.7 (26.4)	
6 months postpartum	639	1,591.4 (614.7)	668	1,583.4 (608.0)		1,187	1,580.4 (27.5)	1,187	1,622.7 (25.9)	
Mean change (95% CI)		−171.8 (−221.2, −122.4)		−153.9 (−203.7, −104.1)	−5.3 (−64.6, 53.9)		−175.5 (−232.9, −118.1)		−162.7 (−214.8, −110.6)	−26.6 (−88.3, 35.1)
Daily percent of calories from fat										
During pregnancy	639	42.1 (6.9)	668	42.2 (7.0)		1,187	42.0 (0.3)	1,187	42.2 (0.3)	
6 months postpartum	639	40.2 (6.3)	668	39.8 (6.7)		1,187	40.1 (0.3)	1,187	39.8 (0.3)	
Mean change (95% CI)		−1.8 (−2.5, −1.1)		−2.3 (−3.0, −1.6)	0.4 (−0.3, 1.1)		−2.0 (−2.6, −1.3)		−2.4 (−3.1, −1.8)	0.3 (−0.4, 1.1)

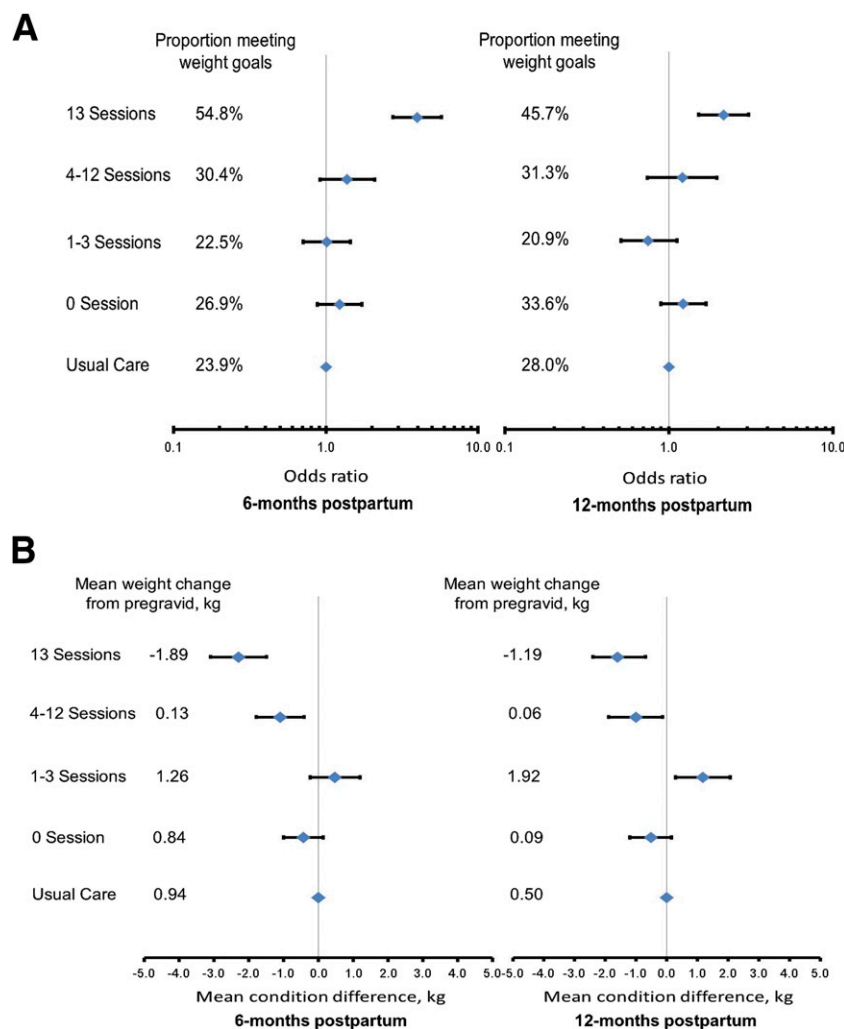*Adjusted for baseline values.

A

B

Figure 2—OR (95% CI) estimating the condition difference in meeting the postpartum weight goals (*A*) and adjusted mean condition difference (95% CI) (*B*) for weight change from pregravid by number of intervention sessions completed and time since delivery: the GEM trial. At 6 months postpartum, the number of women by number of completed telephone sessions were as follows: 338 for 0 sessions, 151 for 1–3 sessions, 171 for 4–12 sessions, and 104 for 13 sessions. At 12 months, the number of women by number of completed telephone sessions were as follows: 301 for 0 sessions, 134 for 1–3 sessions, 112 for 4–12 sessions, and 129 for 13 sessions.

or total volume of activity (i.e., MET minutes per week). Women in intervention facilities and usual care facilities reported similar reductions in daily total energy intake and percent of calories from fat, with no condition differences (Table 3). Similar results for diet and physical activity were observed in sensitivity analyses that included imputed values if survey data were missing (Table 3). No condition differences were observed for hypertension or depression (Supplementary Table 3).

Exploratory Outcomes
After excluding women with possible pregestational diabetes (21 in the intervention and 29 in usual care), 873 (83.5%) women in the intervention and 974

(85.4%) in usual care completed postpartum diabetes screening. Fewer women in the intervention facilities developed prediabetes or diabetes than in usual care facilities (310 [29.7%] and 37 [3.5%] in intervention facilities and 370 [32.4%] and 50 [4.4%] in usual care facilities, respectively). However, the risk estimate for prediabetes/diabetes combined did not reach statistical significance (33.2 vs. 36.8%; hazard ratio 0.90 [95% CI 0.78, 1.04]) (Supplementary Fig. 1).

Intervention Process Measures and Economic Cost
The mean number of call attempts to reach women and complete telephone sessions was 2.2 (SD 1.8). The first

session lasted a mean of 28.2 min (8.6); subsequent sessions lasted a mean of 18.8 min (7.4). Direct intervention costs per person among all 1,087 women in the intervention were $78.00 ($19.00 for printing and mailing and $59.00 for telephone sessions); costs increased to $121.00 ($19.00 for printing and mailing and $102.00 for telephone sessions) if the cost of telephone sessions was calculated among women who completed one or more telephone sessions.

Adverse Events
During the 12 months postpartum, there were no significant differences between intervention and usual care in the proportion of women who had an emergency room visit for sprains/strains (*n* = 9 [0.8%] vs. *n* = 16 [1.3%]; *P* = 0.24) or fractures (*n* = 2 [0.2%] vs. 6 [0.5%]; *P* = 0.29). The proportion of women in the intervention and usual care who were hospitalized or had an emergency room visit was 2.1 vs. 1.8% (*P* = 0.64) and 7.8 vs. 10.1% (*P* = 0.05), respectively. No condition differences were observed in underlying medical diagnosis except that fewer women had emergency room visits due to gallbladder disorders in the intervention than usual care (*n* = 3 [0.3%] vs. *n* = 15 [1.2%]; *P* = 0.008).

CONCLUSIONS
This cluster randomized trial demonstrated that a health system–based print/telephone lifestyle intervention derived from the DPP modestly reduced postpartum weight retention and increased vigorous-intensity physical activity among women with GDM. Postpartum weight retention and weight gain are associated with increased risk for diabetes (7), recurrent GDM (26), and abnormal cardiometabolic profile (27). The reductions in postpartum weight retention and the suggestion of reductions in prediabetes/diabetes incidence, for which GEM was not powered, might be explained by the significant increase in vigorous-intensity activity among women in the intervention facilities, since no condition differences were observed for changes in daily total energy intake and percent of calories from fat. It has been reported that vigorous-intensity activity is associated with decreased risk of diabetes

among women with a history of GDM (28) and greater sports participation is associated with reduced postpartum weight retention (27).

Condition differences in weight observed in GEM were similar to that observed in other cluster randomized trials. In the Tianjin Gestational Diabetes Prevention Program cluster randomized trial (29), women in a lifestyle intervention weighed ~1 kg less than women in the control condition at 12 months postpartum. The GEM condition difference was also similar to that observed at 12 months in the Da Qing cluster randomized trial (3) of adults with prediabetes, in which lifestyle intervention led to 40 and 60% reductions in diabetes risk at 6 years (3) and 20 years (30), respectively, suggesting potential long-term beneficial effects of modest weight loss. In GEM, condition differences in the proportion meeting postpartum weight goals were statistically significant, on average, over the entire 12-month postpartum period, and at 6 weeks and 6 months postpartum. Although condition differences at the 12-month postpartum time point were not statistically significant, they were similar in magnitude to those at 6 months postpartum, when the intervention ended.

It is noteworthy that intervention effects on postpartum weight retention among women with GDM are greater in trials randomized at the individual level (31,32) than cluster randomized trials (29), since only a select group of motivated volunteers participate in the former. Although in cluster randomized trials such as GEM only a portion of eligible women participate, it should be noted that the effect sizes reported are for all women in the facilities assigned to the intervention. Instrumental variable analysis suggested that the intervention effect would be at least twofold greater if all women had completed one or more sessions, suggesting a potential for great impact if we can improve patient engagement in such lifestyle interventions. To illustrate, in the pilot study that preceded GEM, with randomization at the individual level, more women in the intervention met the postpartum weight goals, with a 16% absolute difference between conditions by 12 months postpartum (31). A trial among 75 women with GDM found women in a web-based lifestyle intervention were closer to their pregravid weight than control subjects at 12 months postpartum (−0.7 vs. +4.0 kg) (32).

Limitations of the GEM trial include missing clinic-measured weight for 26.4% of women at 6 months and 32.7% at 12 months postpartum. These missing data are due to the pragmatic nature of the GEM trial; participants did not volunteer for a study with 12 months of longitudinal follow-up on body weight measurements. We obtained women's weights from the EHR, although this required women to visit their medical facility. Still, 97.4% of women contributed to the analysis of measured weight across the entire 12-month postpartum period. Furthermore, results based on clinic-measured postpartum weight were comparable to those of sensitivity analyses. Observed differences in postpartum weight retention remained significant in a sensitivity analysis that included clinic-measured weight or self-reported weight (with only 13.7 and 18.6% still missing at 6 and 12 months, respectively) and a sensitivity analysis that imputed missing clinic-measured weight. Given the robustness of our results, it is unlikely that missing clinic-measured weight data created bias.

Strengths of this cluster randomized trial include the ability to randomize all medical facilities in the KPNC region; the large number of facilities and women, and their racial/ethnic diversity; intent-to-treat analyses including all facilities and women; blinding of investigators, data collectors, and health care providers; and follow-up extending 6 months beyond the end of the intervention. A unique strength was that the primary analysis was based on clinic-measured weight obtained via EHR, regardless of women's participation in the surveys or intervention. These features provide generalizable, real-world findings.

GEM features several aspects of pragmatic trials, which prioritize generalizability at the potential expense of effect size given implicit sample heterogeneity and lower intervention adherence (33). In contrast to traditional clinical trials, GEM had minimal exclusion criteria and the intervention was delivered at the health system level as optional routine care to an unselected population (i.e., regardless of motivation, perinatal complications, or comorbidities), which likely contributed to the 50.3% intervention uptake. Although this uptake is high for a pragmatic trial (34,35)—and considerably higher than,

for example, the recently reported uptake of 13% in the health system–based Veterans Health Administration MOVE! lifestyle change program, the largest such program in the U.S. (36)—uptake likely impacted the condition differences observed and shows how challenging it is to engage patients in prevention programs. In GEM, intervention effectiveness increased with the number of sessions completed. Although prespecified categories for the number of completed sessions were used, women were not randomized to these categories, and those who completed more sessions may have lost more weight due to increased motivation for a healthy lifestyle. Nevertheless, these dose-response analyses (37) suggest that to increase the effectiveness of lifestyle interventions, strategies are needed to increase and sustain patient engagement. If health systems were to adopt postpartum interventions for women with GDM, clinician referrals and other strategies to increase patient engagement might increase uptake and effectiveness (38). Finally, the cost per woman of the GEM intervention was relatively modest, and the printed/telephone modality is easily translatable to other settings.

In conclusion, this cluster randomized trial of diabetes prevention strategies delivered at the health system level to women with GDM demonstrated that a DPP-derived, print/telephone-based lifestyle intervention was superior to usual care in reducing postpartum weight retention, a risk factor for diabetes, and increasing physical activity. Although condition differences were modest, differences of similar magnitude have been shown to reduce long-term diabetes incidence in at-risk adults (30). These findings, from a trial embedded in real-world practice, may encourage health systems to adopt DPP-derived postpartum interventions to help women with GDM manage their weight and increase physical activity, thereby potentially preventing or delaying the onset of diabetes.

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