

1 ***SUPPLEMENTARY MATERIALS***

2 **SUPPLEMENTAL METHODS**

3 **NOVEL APPROACHES TO EXAMINING WEIGHT CHANGE IN PREGNANCIES AFFECTED BY OBESITY**

4 AMY R. NICHOLS, FEI XU, NATALIE BURNS, SARALYN F. FOSTER, RACHEL RICKMAN,

5 MONIQUE M. HEDDERSON, ELIZABETH M. WIDEN

6

7 *Fitting the Latent Class Models*

8 Latent class trajectories of gestational weight change (GWC) were fit using function *hlme*
9 that utilized a Gaussian distribution from package *lcmm* in R (16) to characterize distinct patterns
10 by class-specific linear mixed models using maximum likelihood estimation (16, 17). Trajectory
11 models were stratified by obesity grade *a priori*. Grouping structure (argument *subject*) was
12 specified to be by pregnancy. Random effects (argument *random*) of gestational age by subject
13 were included to allow for individual random slopes that account for intrasubject correlation
14 between measurements. Random intercepts were not included by subject as part of the model
15 specification since each participant trajectory curve begins at 0 kg weight change at 0 weeks
16 gestation. The initial intercept was constrained through use of a categorical independent dummy
17 variable to reflect the weight change constant of 0 kg weight change at 0 weeks gestation shown
18 in the data (18).

19 To improve numerical stability of the model, gestational age in weeks was normalized for
20 each observation by dividing gestational weeks by 38 weeks (or 34 weeks in preterm models) so
21 that all values for gestational age were between 0 and 1. All prenatal weights >38 weeks
22 gestation (or >34 weeks in preterm models) were excluded so later weight change would not
23 skew trajectory patterns or drive class predictions and membership. As in our previous work (19,
24 20), we designated equidistant knots at 0, 10, 20, 30, and 38 weeks (34 weeks in preterm models)
25 because the majority of pregnancies had weight measurements at these times; likewise, these
26 times coincide with routine prenatal visits (i.e., establishing prenatal care by 10 weeks,

27 diagnostic testing at 20 weeks, and increasing visit frequency in the third trimester around 30
28 weeks). We defined the spline design matrix of random coefficients multiplied by a flexible low-
29 rank thin-plate spline penalty matrix (19, 20) to avoid overfitting while capturing non-linearity as
30 described by Crainiceanu *et al.* (21). Initial values (argument *B*) were randomly generated using
31 an expectation-maximization algorithm per parameter to identify local maxima and support
32 model convergence (16, 17). Prepregnancy BMI affects probability of belonging to a particular
33 latent class and, thus, was included as a class predictor (*classmb*). Models for obesity grade 1,
34 grade 2, and grade 3 that identified three to six latent classes (argument *ng*) were examined for
35 fit; hence, there were 3 primary models to 38 weeks and 3 preterm models to 34 weeks (obesity
36 grades 1, 2, and 3). To visualize GWC per obesity grade, we predicted (function *predictY*) class-
37 specific longitudinal markers for each latent class by gestational age in weeks (**Figure 2**).

38 The implications of GWC for infant health outcomes differ per prepregnancy BMI, and
39 GWC patterns across pregnancy differ by BMI category (1). Thus, latent class models were
40 examined stratified by prepregnancy obesity grade. We examined models that identified between
41 4 and 6 latent classes for fit using lower Akaike and Bayesian Information Criteria (AIC, BIC),
42 higher mean probability of belonging to the assigned class (i.e., examining for classes with a
43 posterior probability of group membership $\geq 80\%$), and ensuring a sample size per GWC latent
44 class of ≥ 150 pregnancies ($\sim 5\%$ of analytic sample) (**Supplemental Table 2**). When the fit
45 statistics for models with 4 to 6 classes were compared, the six-class model for each obesity
46 grade generated marginally lower AIC and BIC, although the six-class model for obesity grade 2
47 was only able to identify 5 distinct classes. Additionally, the six-class models identified parallel,
48 but non-overlapping, adjacent trajectories in each obesity grade that we believe would limit
49 clinical usefulness. Ultimately, the five-class model for each BMI grade was selected. The

50 smallest latent class was observed in grade 3 obesity (n=156, 4.6%; 94.4% posterior probability
51 of belonging to this class). To examine associations between GWC trajectories and preterm birth
52 while limiting the influence of later weight change on class membership, additional five-class
53 models were fit censoring prenatal weights >34 weeks since the mean gestational age at delivery
54 for preterm pregnancies was 34.1 weeks.

55 **SUPPLEMENTAL TABLES**

56 **NOVEL APPROACHES TO EXAMINING WEIGHT CHANGE IN PREGNANCIES AFFECTED BY OBESITY**

57 AMY R. NICHOLS, FEI XU, NATALIE BURNS, SARALYN F. FOSTER, RACHEL RICKMAN,

58 MONIQUE M. HEDDERSON, ELIZABETH M. WIDEN

SUPPLEMENTAL TABLE 1

Sample characteristics (n=22,355) compared to those excluded from analyses (n=12,671)

	Included	Excluded
n (%)	22,355	12,671
Age, y	29.8 ± 5.5	31.0 ± 5.8
Height, cm	163.0 ± 7.3	162.7 ± 7.4
Parity <3	19,911 (89.1)	10,497 (82.8)
GA, ¹ wk	38.9 ± 1.9	38.4 ± 2.2
BMI, kg/m ²	35.3 ± 4.9	36.6 ± 5.3
Grade 1, n(%)	13,180 (59.0)	6003 (47.4)
Grade 2, n(%)	5787 (25.9)	3831 (30.2)
Grade 3, n(%)	3388 (15.2)	2837 (22.4)
Ethnicity		
White	8308 (37.2)	4096 (32.3)
Hispanic	8133 (36.4)	4756 (37.5)
Black	2791 (12.5)	1510 (11.9)
Asian	1860 (8.3)	1538 (12.1)
Other ²	1263 (5.7)	771 (6.1)
Total GWC, ³ kg	11.1 ± 6.9	8.5 ± 7.0
GWC z-score	-0.06 ± 0.80	-0.29 ± 0.88
Comparison to IOM ⁴		
Above IOM	13,515 (60.5)	5590 (44.1)
Within IOM	4874 (21.8)	3065 (24.2)
Below IOM	3966 (17.7)	4016 (31.7)
Sex, m	11,353 (50.8)	6428 (50.7)
Preterm ⁵	1586 (7.1)	1374 (10.8)
Birthweight, g	3478.2 ± 580.1	3455.2 ± 657.4
Birthweight z-score	0.34 ± 1.10	0.48 ± 1.18
Macrosomia ⁶	3679 (16.5)	2150 (17.0)
Low birthweight ⁷	1006 (4.5)	777 (6.1)
LGA ⁸	3200 (14.3)	2398 (18.9)
SGA ⁹	1668 (7.5)	855 (6.7)

Values are n(%) or mean ± SD. ¹Gestational age; ²Includes unknown/not reported; ³Gestational weight change; ⁴IOM guidelines, 5-9kg; ⁵Delivery <37wk; ⁶Birthweight ≥4000g; ⁷Birthweight ≤2500g; ⁸Large for gestational age, birthweight >90th percentile; ⁹Small for gestational age, birthweight <10th percentile.

SUPPLEMENTAL TABLE 2

Five-class gestational weight change latent class model statistics by prepregnancy obesity grade

	AIC ¹	BIC ²	n(%) by Latent Class					
			Class 1	Class 2	Class 3	Class 4	Class 5	
Obesity Grade 1								
Base Model ³	536679.7	536979.1	2264 (17.2)	5090 (38.6)	2303 (17.5)	2450 (18.6)	1073 (8.1)	
Preterm Model ⁴	433299.4	433598.8	2359 (17.9)	4423 (33.6)	2317 (17.6)	3177 (24.1)	904 (6.9)	
Obesity Grade 2								
Base Model	248823.6	249090.2	1067 (18.4)	2368 (40.9)	1104 (19.1)	836 (14.5)	412 (7.1)	
Preterm Model	201364.5	201631.0	1068 (18.5)	2526 (43.7)	971 (16.8)	835 (14.4)	387 (6.7)	
Obesity Grade 3								
Base Model	154953.6	155198.7	729 (21.5)	1172 (34.6)	725 (21.4)	606 (17.9)	156 (4.6)	
Preterm Model	124173.4	124418.5	497 (14.7)	1530 (45.2)	498 (14.7)	653 (19.3)	210 (6.2)	

¹AIC, Akaike Information Criterion; ²BIC, Bayesian Criterion Information; ³Weight trajectories modeled to ≤ 38 weeks; ⁴Weight trajectories modeled to ≤ 34 weeks.

SUPPLEMENTAL TABLE 3

Adjusted associations between gestational weight change latent class and infant outcomes by prepregnancy obesity grade (n=22,355)

	Birthweight, g β (95% CI)	Macrosomia¹ β (95% CI)
Grade 1 (n=13,180)		
Class 1	<i>Referent</i>	
Class 2	18.12 (-3.23, 39.47)	1.02 (0.91, 1.15)
Class 3	-8.63 (-33.99, 16.73)	1.03 (0.90, 1.19)
Class 4	68.04 (43.31, 92.77)	1.25 (1.10, 1.43)
Class 5	72.86 (41.14, 104.58)	1.39 (1.19, 1.62)
Grade 2 (n=5787)		
Class 1	<i>Referent</i>	
Class 2	25.96 (-6.30, 58.23)	1.27 (1.07, 1.51)
Class 3	24.62 (-13.41, 62.66)	1.25 (1.03, 1.53)
Class 4	107.28 (67.01, 147.55)	1.43 (1.17, 1.73)
Class 5	116.63 (65.27, 167.98)	1.75 (1.39, 2.19)
Grade 3 (n=3388)		
Class 1	<i>Referent</i>	
Class 2	-46.64 (-90.76, -2.51)	0.86 (0.70, 1.05)
Class 3	36.15 (-13.12, 85.42)	1.27 (1.04, 1.55)
Class 4	71.74 (21.10, 122.39)	1.22 (0.99, 1.50)
Class 5	59.26 (-22.69, 141.21)	1.15 (0.80, 1.65)

Values are estimated β -coefficients for multivariable linear regression models. Class 1 serves as the reference group for each prepregnancy obesity grade. ¹Birthweight \geq 4000 grams. **Bold values** indicate confidence interval does not contain 0 (β -coefficient) or 1 (IRR).

SUPPLEMENTAL TABLE 4

Adjusted associations between gestational weight change z-score and infant outcomes by prepregnancy obesity grade (n=22,355)

	Birthweight, g β (95% CI)	Macrosomia¹ β (95% CI)
Grade 1 (n=13,180)		
>1	117.19 (89.14, 145.24)	1.54 (1.37, 1.72)
-1 to 1	<i>Referent</i>	
<-1	-141.90 (-162.99, -120.81)	0.47 (0.39, 0.55)
Grade 2 (n=5787)		
>1	132.03 (90.41, 173.65)	1.57 (1.35, 1.83)
-1 to 1	<i>Referent</i>	
<-1	-159.60 (-199.19, -120.00)	0.54 (0.41, 0.70)
Grade 3 (n=3388)		
>1	174.91 (110.97, 238.84)	1.63 (1.31, 2.03)
-1 to 1	<i>Referent</i>	
<-1	-171.02 (-247.71, -94.34)	0.53 (0.32, 0.86)

Values are estimated β -coefficients for multivariable linear regression models. GWC z-score of -1 to 1 serves as the reference group for each prepregnancy obesity grade. ¹Birthweight ≥ 4000 grams. **Bold values** indicate confidence interval does not contain 0 (β -coefficient) or 1 (IRR).

SUPPLEMENTAL TABLE 5

Adjusted associations between gestational weight change latent class and infant outcomes by prepregnancy obesity grade in the analytic (n=22,355) and term (n=20,769) samples

	LGA ¹ , IRR (95% CI)		SGA ² , IRR (95% CI)		Birthweight GA z-score, β (95% CI)		Low Birthweight ³ , IRR (95% CI)	
	Analytic Sample	Term Sample	Analytic Sample	Term Sample	Analytic Sample	Term Sample	Analytic Sample	Term Sample
Grade 1	n=13,180		n=12,288					
Class 1	<i>Referent</i>							
Class 2	1.00 (0.88, 1.14)	1.01 (0.88, 1.16)	1.01 (0.86, 1.20)	0.99 (0.84, 1.18)	0.05 (-0.00, 0.10)	0.05 (0.00, 0.11)	0.76 (0.60, 0.97)	0.80 (0.52, 1.24)
Class 3	1.02 (0.87, 1.19)	1.01 (0.86, 1.19)	1.18 (0.97, 1.43)	1.11 (0.90, 1.35)	-0.02 (-0.08, 0.04)	-0.01 (-0.07, 0.06)	0.99 (0.73, 1.35)	1.36 (0.86, 2.16)
Class 4	1.27 (1.10, 1.46)	1.29 (1.11, 1.49)	0.81 (0.66, 1.00)	0.78 (0.63, 0.97)	0.18 (0.12, 0.24)	0.18 (0.12, 0.24)	0.77 (0.58, 1.01)	0.56 (0.31, 1.01)
Class 5	1.47 (1.24, 1.74)	1.49 (1.25, 1.78)	0.82 (0.62, 1.08)	0.81 (0.61, 1.07)	0.18 (0.10, 0.26)	0.18 (0.10, 0.26)	0.93 (0.67, 1.29)	0.65 (0.30, 1.41)
Grade 2	n=5787		n=5358					
Class 1	<i>Referent</i>							
Class 2	1.40 (1.14, 1.71)	1.39 (1.13, 1.71)	1.14 (0.88, 1.47)	1.14 (0.87, 1.50)	-0.00 (-0.09, 0.09)	0.08 (0.00, 0.16)	1.05 (0.72, 1.53)	0.72 (0.38, 1.38)
Class 3	1.51 (1.20, 1.90)	1.54 (1.22, 1.94)	1.06 (0.78, 1.45)	0.97 (0.70, 1.36)	0.08 (-0.01, 0.17)	0.11 (0.02, 0.21)	1.55 (1.05, 2.28)	0.75 (0.35, 1.63)
Class 4	2.02 (1.61, 2.52)	1.97 (1.57, 2.47)	0.87 (0.61, 1.23)	0.88 (0.62, 1.27)	0.27 (0.17, 0.36)	0.26 (0.16, 0.36)	0.68 (0.40, 1.16)	0.96 (0.42, 2.20)
Class 5	1.98 (1.52, 2.58)	2.03 (1.55, 2.65)	1.18 (0.79, 1.78)	1.18 (0.76, 1.82)	0.24 (0.13, 0.36)	0.32 (0.19, 0.45)	1.12 (0.68, 1.85)	0.20 (0.03, 1.46)
Grade 3	n=3388		n=3123					
Class 1	<i>Referent</i>							
Class 2	0.83 (0.67, 1.04)	0.86 (0.69, 1.08)	1.12 (0.79, 1.58)	1.14 (0.79, 1.64)	-0.11 (-0.22, -0.01)	-0.10 (-0.21, 0.01)	1.14 (0.76, 1.72)	1.17 (0.50, 2.75)
Class 3	1.30 (1.04, 1.62)	1.38 (1.10, 1.74)	1.23 (0.84, 1.78)	1.16 (0.77, 1.73)	0.07 (-0.05, 0.19)	0.12 (0.00, 0.24)	1.27 (0.78, 2.06)	1.10 (0.40, 3.07)
Class 4	1.18 (0.94, 1.48)	1.19 (0.94, 1.50)	0.72 (0.45, 1.14)	0.77 (0.48, 1.23)	0.18 (0.06, 0.30)	0.18 (0.06, 0.30)	0.81 (0.47, 1.39)	0.92 (0.32, 2.67)
Class 5	1.20 (0.82, 1.73)	1.28 (0.88, 1.86)	1.11 (0.60, 2.05)	1.17 (0.62, 2.23)	0.13 (-0.07, 0.32)	0.18 (-0.03, 0.38)	1.56 (0.87, 2.80)	1.31 (0.39, 4.37)

Values are estimated Incidence-Rate Ratios for multivariable Poisson regression or β -coefficients for multivariable linear regression models adjusted for maternal age, ethnicity, height (cm), gestational age at delivery, and infant sex. Weight trajectories modeled to ≤ 38 weeks in base models and ≤ 34 weeks in preterm models. Class 1 serves as the reference group for each prepregnancy obesity grade. ¹Large for gestational age, birthweight >90th percentile; ²Small for gestational age, birthweight <10th percentile; ³Birthweight ≤ 2500 grams. **Bold values** indicate confidence interval does not contain 0 (β -coefficient) or 1 (IRR).