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Original Contribution

Gestational and Postpartum Weight Trajectories Among Women With and Without Asthma

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Asthma leads to increased weight gain in nonpregnant populations, but studies have not examined this association within the context of pregnancy. The association between asthma and perinatal weight trajectories was examined in the Breathe—Wellbeing, Environment, Lifestyle, and Lung Function Study (2015–2019). Multilevel linear spline models were adjusted for age, race/ethnicity, income, marital status, education, cigarette smoking, parity, study site, and prepregnancy body mass index were used to examine differences in perinatal weight trajectories between women with ($n = 299$) and without ($n = 101$) asthma. Secondary analyses were conducted to assess whether associations differed by asthma phenotypes. At 40 weeks' gestation, women with asthma gained 16.2 kg (95% confidence interval (CI): 14.6, 17.7) and women without asthma gained 13.1 kg (95% CI: 10.9, 15.4). At 3 months postpartum, women with asthma retained 10.4 kg (95% CI: 8.9, 11.9) and women without asthma retained 8.0 kg (95% CI: 5.9, 10.2). Among women with asthma, exercise-induced asthma and step 3 asthma medications were associated with excess gestational weight gain. These study findings suggest women with asthma gain and retain more weight during pregnancy and postpartum than do women without asthma.

asthma; body mass index; exercise-induced asthma; gestational weight gain; obesity; postpartum period; postpartum weight retention; pregnancy

Abbreviations: BMI, body mass index; CI, confidence interval.

Asthma is the most common chronic respiratory disease and one of the more common conditions affecting women of childbearing age (1, 2). Findings of prior research in nonpregnant populations, and mostly among children, have suggested that asthma may contribute to excess weight gain and the development of obesity (3–10). However, to our knowledge, there has been no research on the association between asthma and weight gain and retention in pregnancy and the postpartum period.

Gestational weight gain is associated with adverse pregnancy outcomes with variation in the rate and amount of weight gain per trimester potentially contributing to different outcomes (11–17). Gestational weight gain has also been associated with long-term offspring health, including obesity and asthma development, that potentially contribute to intergenerational effects of these exposures (18, 19). Postpartum weight retention, defined as the difference between a woman's prepregnancy and postpartum weight, has been associated with changes in maternal lifetime weight trajectory, with its excess potentially contributing to detriments in cardiometabolic health (11, 16, 20). Thus, identifying factors affecting weight gain during these periods is critical.

In this study, we examined whether weight trajectories differed during pregnancy and the postpartum period between women with and without asthma. Asthma is a heterogeneous disease and any observed differences in weight trajectories during this time may be due to phenotypic characteristics of asthma. Thus, we secondarily examined whether weight-change trajectories differed by atopy status,

age at asthma onset, asthma control, asthma medications, and exercise-induced asthma.

METHODS

Study design

Participants were part of the Breathe–Wellbeing, Environment, Lifestyle, and Lung Function Study, a prospective cohort of pregnant women with active asthma ($n = 311$) or no history of asthma ($n = 107$). Women with and without active asthma were recruited from 2 study sites in the United States (Northwestern University in Chicago, Illinois; and the University of Alabama at Birmingham). Medical record review was used to identify potentially eligible participants, who were then screened for eligibility and consent. For every 2 or 3 women with asthma who were recruited, research assistants were instructed to identify and recruit 1 woman without asthma. All procedures for recruitment were similar for both women with asthma and those without. Women attended 3 study visits during pregnancy (at <15 weeks' gestation, 20–22 weeks, and 30–32 weeks) and once in the postpartum period (1–12 months).

Participant height, weight, and health status data were collected from study visit examinations and medical record abstraction. Questionnaires were administered at each in-person assessment and collected participants' sociodemographic and clinical information. Approval to use human participants was obtained from all participating sites and all the women provided informed consent. Eligibility criteria and data collection materials are available on the study website (https://b-well-mom.org).

For this analysis, we excluded individuals who were unable to be followed up to the birth (i.e., due to pregnancy loss, moving, or study withdrawal; $n = 18$). Figure 1 shows the study population enrollment and exclusions by asthma status.

Exposure assessment

Asthma status was our primary exposure. At enrollment, women were categorized as having asthma if they reported an asthma diagnosis and either used prescription medication for asthma or had asthma symptoms in the year prior to the pregnancy. Women without asthma had no history of asthma and no prior use of asthma medications.

All women with asthma were asked to complete the Asthma Control Test at visit 1 and were categorized as having well-controlled (score $>$ 19) or poorly controlled (score $\leq$ 19) asthma (21). Atopy status was determined on the basis of a positive answer to "Do you have allergies that make your asthma worse" or "Have you ever been told by a doctor/healthcare provider that you have allergies," as well as by self-report of a positive allergy skin test in the past. Women self-reported their age at asthma onset, which was defined as child onset (<18 years) or adult onset ($\geq$18 years) and whether they had exercise-induced asthma (yes/do not exercise vs. no).

Asthma medication use was determined on the basis of a positive answer to the following: "Over the past 6 months, did you use the following medications/therapies specifically for treatment of asthma: inhaled corticosteroids, short-acting beta-agonists, oral corticosteroids, etc." and "What prescription medication(s) do you use on a regular basis?" Combining answers to these questions, women were categorized as belonging to 1 of 4 asthma step-therapy categories according to the American College of Obstetricians and Gynecologists guidelines for asthma management during pregnancy (Web Table 1) (available at https://doi.org/10.1093/aje/kwaa248) (22). Corticosteroid use may be associated with weight gain; therefore, we used these same questions to classify and compare women taking inhaled corticosteroids (vs. no inhaled corticosteroids) and oral corticosteroids (vs. no oral corticosteroids) (23–25).

Outcome assessment

During pregnancy and into the postpartum period, in-person assessments were conducted at each study visit to collect participant height (m) and weight (kg). Additional measurements of weight were obtained from chart abstractions. Combining these data sources produced between 1 and 23 measures of weight (mean: 15 weight measures) throughout gestation and the postpartum period. Our primary outcome was weight change, which was calculated for each participant as the difference between each perinatal weight measurement and self-reported prepregnancy weight.

Covariates

Covariates were selected on the basis of directed acyclic graphs and informed by prior knowledge. Web Figure 1 presents a directed acyclic graph of the association between asthma and perinatal weight-change trajectories constructed using DAGitty, version 3.0 (26). Variables included age, race/ethnicity, household income below the US 2017 federal poverty level, marital status, education, cigarette smoking in the month before pregnancy or during the first trimester, parity, and prepregnancy BMI calculated on the basis of self-reported prepregnancy weight in kilograms divided by height in square meters at first study visit. All models also included adjustment for study site.

Statistical analyses

Our main analysis examined whether asthma was associated with different weight-change trajectories during gestation and postpartum. Multilevel (mixed) linear spline models were used to estimate the mean weight-change in kilograms for women with and without asthma at each week postconception up to 3 months postpartum. Each model included a subject-specific knot at week of delivery, which allowed individual trajectories to vary between pre- and postdelivery. The placement of additional knots was determined by identifying which knot placements maximized the model log-likelihood. Models were fit with up to 4 knots (models with >4 knots failed to converge), and the final number of knots was determined by comparing predicted to

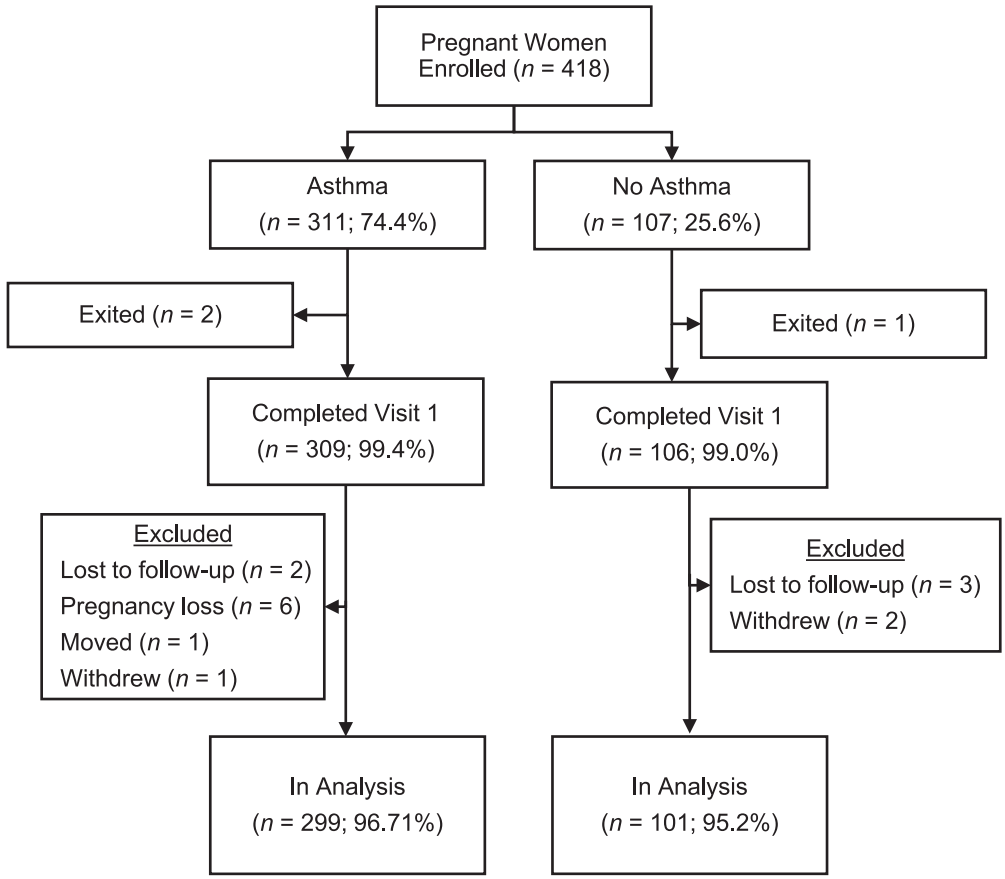

Figure 1. Flow diagram of the study population of women with and without asthma in the Breathe–Wellbeing, Environment, Lifestyle, and Lung Function Study, 2015–2019.

observed values of weight change (27, 28). The final model of perinatal weight-change trajectories contained 4 knots at 17 weeks, 32 weeks, week of delivery, and 42 weeks. All models allowed for subject-specific intercepts and slopes, and included adjustment for study site, age, race/ethnicity, household income, marital status, education, cigarette smoking, parity, and prepregnancy BMI. The LSMEANS statement in SAS was used to estimate the predicted means and differences with 95% confidence intervals in perinatal weight change for each week postconception by setting covariates to their population means (29).

To assess the association between asthma phenotypes and perinatal weight-change trajectories, we restricted our model to women with asthma and examined differences in trajectories by asthma control, asthma atopy, age at asthma onset, exercise-induced asthma, and asthma medications. The results of these analyses present perinatal weight change trajectories by asthma phenotype.

Because the National Academy of Medicine has issued recommendations for gestational weight gain for women based on prepregnancy BMI category, secondary analyses included an interaction term for asthma and prepregnancy BMI category ($\leq$24.9, 25.0–29.9, and $\geq$30) (30). The results of these analyses present perinatal weight change trajectories for women with and without asthma by pre-pregnancy BMI category.

A small percentage of women (<1%) were missing responses for asthma phenotype variables and 75 women (18.8%) were unable to recall their prepregnancy weight in the month before they became pregnant. Thus, missing data were imputed using 10 multiple chained equations and included all covariates from our primary analysis as well as employment and student status, health insurance, federal aid assistance, prepregnancy diabetes, prepregnancy hypertension, gestational age at visit 1, asthma control variables from the Asthma Control Test, asthma medication regimen, oral corticosteroid use, inhaled corticosteroid use, highest recalled weight before pregnancy, lowest recalled weight before pregnancy, prepregnancy somatotype, and visit 1 weight.

Robustness of study findings was assessed by performing several sensitivity analyses. First, to assess whether asthma medication trajectories were due to the medications as opposed to underlying severity of disease, we conducted a sensitivity analysis among women with asthma, using inverse probability treatment weights to control for baseline

Table 1. Characteristics of Women With and Without Asthma (n = 400) in the Breathe–Wellbeing, Environment, Lifestyle, and Lung Function Study, 2015–2019

Characteristic	Asthma (n = 299)		No Asthma (n = 101)		Total (n = 400)	
	No.	%	No.	%	No.	%
Gestational age at delivery, weeks	299	38.2 (3.9)[a]	101	38.6 (2.3)[a]	400	38.3 (3.5)[a]
Postpartum follow-up, weeks	270	19.1 (4.8)[a]	94	19.0 (4.8)[a]	364	19.1 (4.8)[a]
Age, years	299	29.7 (5.9)[a]	101	28.5 (5.9)[a]	400	29.4 (5.9)[a]
Race/ethnicity						
White	92	30.8	32	31.7	124	31.0
Black	157	52.5	59	58.4	216	54.0
Hispanic	29	9.7	5	5.0	34	8.5
Mixed race/other	21	7.0	5	5.0	26	6.5
Prepregnancy BMI[b]						
≤24.9	102	34.1	37	36.6	139	34.8
25.0–29.9	48	16.1	25	24.8	73	18.3
≥30.0	91	30.4	22	21.8	113	28.3
Missing data	58	19.4	17	16.8	75	18.8
Income below federal poverty line						
No	203	67.9	65	64.4	268	67.0
Yes	96	32.1	36	35.6	132	33.0
Marital status						
Divorced/separated or widowed	16	5.4	4	4.0	20	5.0
Married and/or living with partner	165	55.2	45	44.6	210	52.5
Single	118	39.5	52	51.5	170	42.5
Education						
High school or less	96	32.1	41	40.6	137	34.3
Associate's degree/some college	90	30.1	27	26.7	117	29.3
Bachelor's degree	47	15.7	15	14.9	62	15.5
Master's or advanced degree	66	22.1	18	17.8	84	21.0
Cigarette smoking						
No	237	79.3	75	74.3	312	78.0
Yes	62	20.7	26	25.7	88	22.0
Parity						
0	135	45.2	41	40.6	176	44.0
1	71	23.7	35	34.7	106	26.5
2	50	16.7	12	11.9	62	15.5
≥3	43	14.4	13	12.9	56	14.0

Abbreviation: BMI, body mass index.
[a] Values are expressed as mean (standard deviation)
[b] Weight (kg)/height (m)^2.

asthma severity (Web Appendix 1). Second, we restricted our study population to women with full-term (≥37 weeks, n = 326) deliveries only. Third, we excluded women reporting a diagnosis of prepregnancy diabetes (n = 17) or hypertension (n = 39). Fourth, we excluded women diagnosed with known pregnancy complications (specifically, gestational diabetes (n = 23) and hypertensive disorder of pregnancy (n = 65)). Fifth, we assessed the impact of excluding women with a cesarean delivery (n = 116), because recovery may have affected postpartum weight-change trajectories (16). SAS, version 9.4 (SAS Institute, Cary, NC) was used for data analysis.

Table 2. Prevalence of Asthma Phenotypes Among Women With Asthma ($n = 299$) in the Breathe–Wellbeing, Environment, Lifestyle, and Lung Function Study, 2015–2019

Characteristic	No.	%
Asthma control		
Poorly controlled	154	51.5
Well controlled	145	48.5
Asthma onset		
Adulthood	69	23.1
Childhood	228	76.3
Missing data	2	0.7
Atopy status		
Atopic	244	81.6
Nonatopic	54	18.1
Missing data	1	0.3
Exercise-induced asthma		
No	115	38.5
Yes/does not exercise	182	60.9
Missing data	2	0.7
Asthma medication regimen		
Mild intermittent	157	52.5
Mild persistent	54	18.1
Moderate persistent	56	18.7
Severe persistent	32	10.7
Corticosteroid use		
Oral	25	8.4
Inhaled	85	28.4

RESULTS

Analyses were conducted on data from 400 women (n = 299 with asthma; n = 101 without asthma). Overall sample characteristics are summarized by asthma status in Table 1. Distribution of asthma phenotypes among women with asthma are summarized in Table 2.

Perinatal weight-change trajectories diverged from one another beginning around 30 weeks' gestation and remained different until 3 months postpartum (Figure 2, Web Table 2). For an average 40-week gestation, women with asthma gained 16.2 kg (95% confidence interval (CI): 14.6, 17.7) and women without asthma gained 13.1 kg (95% CI: 10.9, 15.4). Women with asthma also retained more weight at 3 months postpartum than did women without asthma (10.4 kg (95% CI: 8.9, 11.9) and 8.0 kg (95% CI: 5.9, 10.2), respectively).

Among women with a BMI of 25, women with asthma had only slightly increased gestational weight gain compared with women without asthma; the differences in the weight-change curves at 40 weeks was 1.2 kg (95% CI: −2.1, 4.4) (Figure 3, Web Table 3). Among women with a BMI between 25 and 30, women with asthma gained an excess of 3.4 kg (95% CI: 1.1, 5.6) compared with women without asthma during a 40-week gestation, with the weight-change curves diverging around 29 weeks gestation and remaining different until the 3-month postpartum follow-up. Among women with BMI $\geq$ 30, women with asthma gained an excess of 5.6 kg (95% CI: 1.9, 9.2) compared with women without asthma during a 40-week gestation, with the weight-change curves diverging around 30 weeks gestation and remaining different until the 3-month postpartum follow-up.

There was little difference in weight gain and retention between women with asthma by control, onset, atopy, or corticosteroid use (Table 3, Web Figure 2, Web Tables 4–10). Women using step 3 (moderate persistent) asthma therapy had increased gestational weight gain compared with women using step 1 (mild intermittent) asthma therapy, with the curves diverging at approximately gestational week 18 and lasting until 31 weeks. In a 40-week gestation, women using step 3 asthma therapy gained 2.6 kg (95% CI: −0.6, 5.7) compared with women using step 1 asthma therapy. Women with exercise-induced asthma also had increased gestational weight gain and retention compared with women without exercise-induced asthma; women with exercise-induced asthma gained an excess of 2.2 kg (95% CI: −0.3, 4.6) during a 40-week gestation. Results from our primary analyses were robust to a number of sensitivity analyses (Web Tables 11–19).

DISCUSSION

To our knowledge, this is the first study in which an association of asthma with gestational and postpartum weight-change trajectories was assessed. In prior studies, researchers have examined weight gain and asthma in nonpregnant populations. Although findings of most prior research suggest weight gain is associated with the development of asthma, recent research has begun to examine whether this association between weight gain and asthma is bidirectional (3–10). Though researchers who have conducted mendelian randomization studies have concluded that the association between asthma and subsequent weight gain is unlikely to be causal, findings from recent prospective cohorts indicate an increased risk of weight gain and obesity development among children with asthma versus those without asthma (3–10). The potential mechanisms underlying the association between asthma and weight gain likely include pathways involving shared risk factors (e.g., physical activity, sleep perturbations), corticosteroid and other chronic medication use, and cardiometabolic or inflammatory pathways (10). However, research on asthma and weight trajectories among women and outside of the pediatric context is lacking.

Asthma is a heterogenous disease and prior research has identified many different asthma phenotypes and endotypes (5, 9, 31). The mechanisms underlying the link between asthma and subsequent weight gain potentially differs by phenotype (9, 32). In the present study, weight gain, when defined according to American College of Obstetricians and Gynecologist's criteria, increased among women using step 3 asthma treatment. Researchers who examined asthma phenotypes reported that persistent asthma was associated

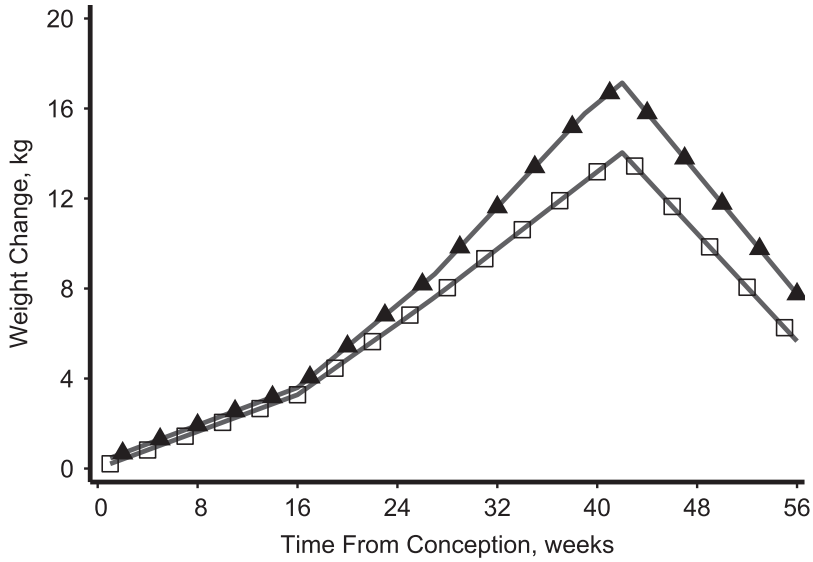

Figure 2. Plot of adjusted mean perinatal weight gain among women with and without asthma ($n = 400$) in the Breathe–Wellbeing, Environment, Lifestyle, and Lung Function Study, 2015–2019. Filled triangle indicates trajectory for women with asthma. Open square indicates trajectory for women without asthma.

with high BMI among female participants only (32). The mechanism underlying this association between an asthma phenotype requiring more intensive asthma therapy and weight gain is unknown but may involve chronic exposure to corticosteroids (24, 25, 33, 34). However, our results suggest no association between regular use of inhaled or oral corticosteroids on weight gain. This is similar to findings of prior studies, which suggest medication use does not fully explain the relationship between asthma and weight gain (4, 25). In sensitivity analyses in which we controlled for baseline asthma severity (Web Table 11) using inverse probability treatment weights, we report results similar to those of our primary analyses. Thus, the associations we observed in the group of women with moderate persistent asthma might be due to medication regimens in this group as opposed to asthma severity, though chronic oral or inhaled corticosteroid use is unlikely to be driving this association. We did not observe increased weight gain among women with severe persistent asthma compared with women with mild intermittent asthma; this likely was due to small sample sizes in the severe persistent asthma group. Interestingly, baseline asthma control was not associated with excess weight gain and retention in this study. Asthma severity, control, and therapy are highly correlated factors, because poor control is often a function of persistent asthma severity combined with poor response to the prescribed level of therapy. Thus, our lack of results regarding asthma control is puzzling but suggests that factors associated with underlying asthma severity may have a greater role in obesity than level of intercurrent control in pregnancy.

Shared lifestyle factors such as physical activity, diet, or sleep perturbations may explain the relationship between asthma and weight gain. We found that women with exercise-induced asthma/women who did not exercise had increased gestational weight gain compared with women who did not have exercise-induced asthma. In studies controlling for exercise as a covariate, authors have reported a significant association between asthma and weight gain, suggesting that exercise cannot fully explain this association (4, 32). Additional research is needed on whether exercise, diet, sleep, or other lifestyle factors may be potential mechanisms underlying the association between asthma and weight gain or if these factors are simply preexisting shared risk factors for both conditions.

Obesity, metabolic syndrome, and oxidative stress increase the risk of incident asthma, particularly childhood asthma (35, 36). It remains unclear if the same metabolic factors that promote asthma also predispose to greater weight gain in pregnancy in this cohort. Pathways including insulin resistance and cardiometabolic function are associated with both weight gain and asthma (7, 8, 37–40). Our sensitivity analyses explored whether the exclusion of women with prepregnancy hypertension or diabetes affected our results, which did not seem to be the case for most associations. Furthermore, undetected elevated cardiometabolic risk entering pregnancy may have driven the observed association. Sensitivity analyses excluding women with pregnancy and delivery complications, which included hypertensive disorders of pregnancy and gestational diabetes, still found higher mean weight gain and retention among women with asthma. Though more research is needed to fully understand the link among cardiometabolic health, weight gain, and asthma, it does not appear that diagnosed cardiometabolic disorders contributed to our observed associations.

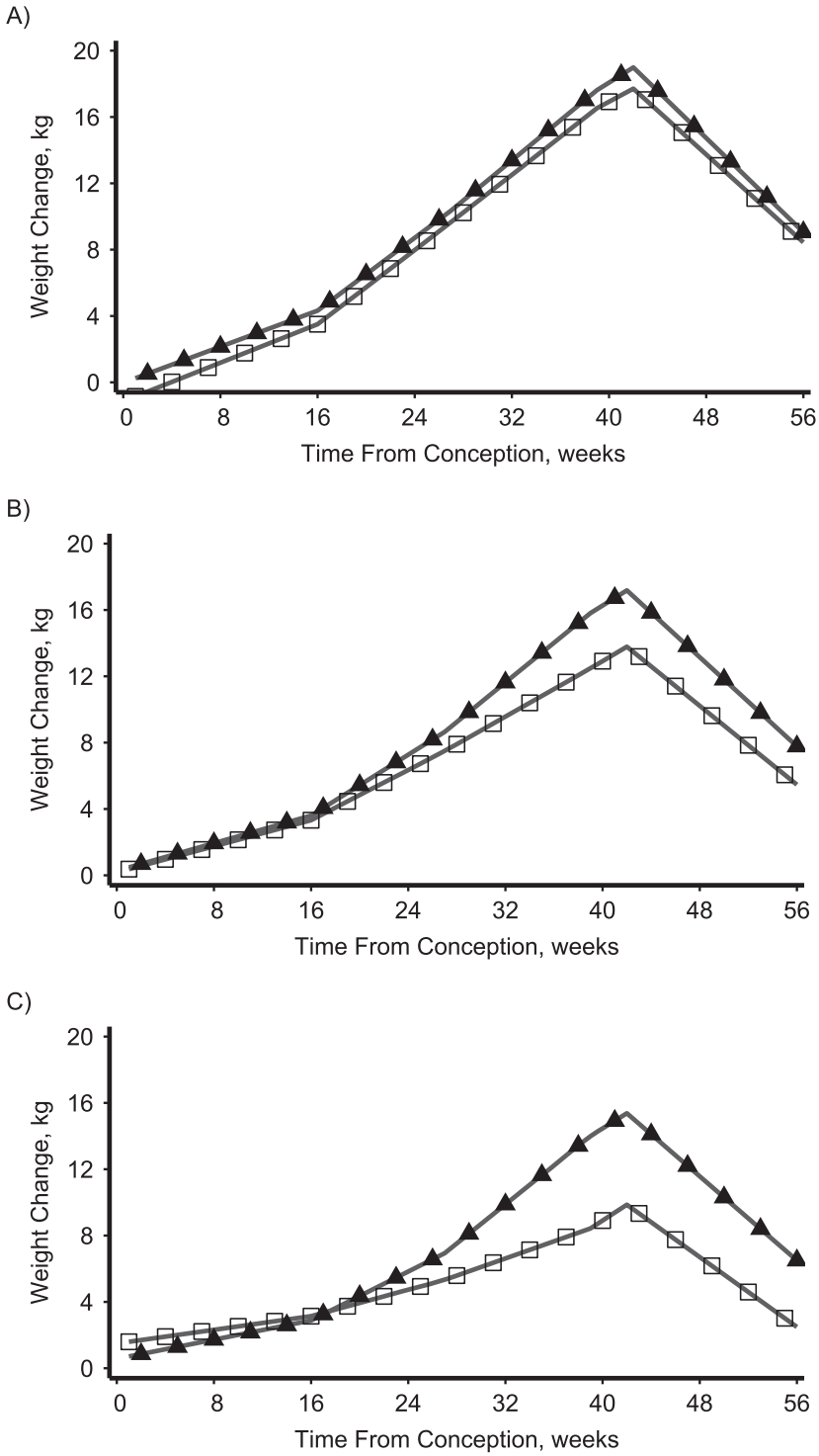

Figure 3. Plot of adjusted mean perinatal weight gain among women with and without asthma (n = 400) by prepregnancy body mass index (BMI; weight (kg)/height $(m)^2$) in the Breathe–Wellbeing, Environment, Lifestyle, and Lung Function Study, 2015–2019. A) BMI ≤24.9; B) BMI 25.0–29.9; and C) BMI ≥30.0. Filled triangle indicates trajectory for women with asthma. Open square indicates trajectory for women without asthma.

Table 3. Adjusted Mean Perinatal Weight Gain by Asthma Phenotypes Among Women With Asthma (n = 299) in the Breathe–Wellbeing, Environment, Lifestyle, and Lung Function Study, 2015–2019[a]

Asthma Phenotype	First Trimester (13 Weeks)		Second Trimester (27 Weeks)		Third Trimester (40 Weeks)		Postpartum Period (3 Months)	
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI
Asthma control								
Poorly controlled	3.2	1.8, 4.6	8.7	7.2, 10.2	16.5	14.5, 18.5	11.0	9.1, 12.8
Well controlled	2.9	1.5, 4.3	8.8	7.3, 10.3	16.3	14.4, 18.3	10.3	8.4, 12.2
Asthma onset								
Adulthood	2.7	1.1, 4.3	8.3	6.5, 10.1	15.6	12.9, 18.2	9.5	7.0, 12.0
Childhood	3.2	1.8, 4.5	8.9	7.4, 10.3	16.6	14.9, 18.4	10.9	9.2, 12.6
Atopy status								
Atopic	3.1	1.8, 4.4	8.8	7.4, 10.2	16.4	14.7, 18.1	10.6	9.0, 12.2
Nonatopic	2.9	1.1, 4.7	8.3	6.3, 10.3	15.8	12.9, 18.8	10.2	7.4, 13.0
Exercise-induced asthma								
No	3.2	1.7, 4.7	8.8	7.2, 10.4	15.0	12.9, 17.2	9.2	7.2, 11.3
Yes/does not exercise	2.9	1.5, 4.3	8.6	7.1, 10.1	17.2	15.3, 19.1	11.4	9.6, 13.2
Asthma medication regimen								
Step 1: mild intermittent	2.6	1.1, 4.0	8.1	6.6, 9.6	15.8	13.8, 17.8	10.2	8.4, 12.1
Step 2: mild persistent	3.5	1.8, 5.2	8.8	6.9, 10.8	15.9	13.0, 18.7	10.3	7.6, 13.0
Step 3: moderate persistent	3.8	1.8, 5.7	10.4	8.3, 12.5	18.4	15.4, 21.4	11.8	8.9, 14.6
Step 4: severe persistent	3.4	1.1, 5.7	8.7	6.2, 11.3	16.6	12.7, 20.4	10.5	6.8, 14.1
Corticosteroid use								
Oral corticosteroids	3.0	0.4, 5.5	7.9	5.0, 10.8	15.4	11.1, 19.7	10.0	6.0, 14.0
No oral corticosteroids	3.1	1.8, 4.4	8.8	7.4, 10.2	16.5	14.8, 18.1	10.6	9.0, 12.2
Inhaled corticosteroids	3.5	2.0, 5.1	9.3	7.6, 11.1	17.1	14.6, 19.5	10.7	8.4, 13.0
No inhaled corticosteroids	2.8	1.5, 4.2	8.5	7.1, 9.9	16.1	14.3, 17.8	10.5	8.8, 12.2

Abbreviation: CI, confidence interval.

[a] Adjusted for age, race/ethnicity, household income below federal poverty line, education, marital status, cigarette smoking, parity, and prepregnancy body mass index.

We report that gestational weight-change trajectories for women with asthma diverge from those of women without asthma with notable differences in curves from week 30 of gestation until delivery. Pregnancies complicated by asthma have higher rates of adverse outcomes, including high or low infant birthweight, preterm delivery, gestational diabetes, placenta previa, neonatal death and hospitalization, preeclampsia, and congenital malformations (41–45). Early-pregnancy weight gain has the greatest impact on fetal growth, small-for-gestational-age birth, and hypertensive disorders of pregnancy, whereas late-pregnancy weight gain has the greatest impact on large-for-gestational-age risk and postpartum weight retention (12–17). It is possible that the association between asthma and certain pregnancy complications, especially those related to infant birthweight, may be influenced by our observed differences in gestational weight gain. Though prior research has been conducted on outcomes related to gestational weight gain in pregnancies affected by asthma, most studies were focused on its contribution to severe asthma exacerbations (41, 46–48). There appears to be no consensus regarding whether gestational weight gain may be contributing to these outcomes in pregnancies affected by asthma.

Excess postpartum weight retention is a frequent occurrence, has been linked to numerous adverse cardiometabolic outcomes in women, and potentially may lead to complications in subsequent pregnancies (49–52). We observed an association between asthma and weight retention up to 3 months postpartum, even among sensitivity analyses restricted to full-term, uncomplicated, or vaginal deliveries (41, 43–45). Thus, this excess weight retention is unlikely to be due to differences in gestational age at delivery or health after pregnancy. However, it is possible that our results may be due to increased gestational weight gain among women with asthma. Because postpartum weight can take several months to resemble prepregnancy weight, weight-change trajectories beyond 3 months postpartum should be assessed to help us understand whether weight gain and retention during this critical time persists beyond the perinatal period.

Our study had several notable limitations. In addition to limitations already mentioned, we predominantly relied on self-report to determine asthma medication regimens and phenotypes, which may have resulted in exposure misclassification for some women. For example, inhaled corticosteroid use may be underreported when compared with dispensed prescriptions in electronic health records studies (53). Women often decrease their asthma medications intake during pregnancy (53). We combined the answers to 2 baseline questions related to asthma medication use, which allowed us to better estimate chronic asthma medication use in our population but may have failed to capture acute associations. We also relied on self-reported prepregnancy weight to determine gestational weight gain and postpartum weight retention. However, self-reported prepregnancy weights were highly correlated with first measured pregnancy weights ($n = 343$; $r = 0.98$) as well as chart-abstracted prepregnancy weights ($n = 118$; $r = 0.94$). Despite model adjustments, there remains the potential for residual confounding; results should therefore be interpreted with caution. Replication and examination of the question in larger cohorts with data on maternal asthma, prepregnancy BMI, and gestational weight gain would help address this concern.

Asthma was associated with greater weight gain and retention during pregnancy and postpartum in this US pregnancy cohort. The difference between gestational weight gain and postpartum retention among women with and without asthma was more pronounced with increasing prepregnancy BMI categories. The American College of Obstetricians and Gynecologists recommends that prepregnancy counseling include the importance of achieving and maintaining a healthy body weight (54). Our findings suggest this counseling may be especially important for women with asthma. Given the high global prevalence of asthma—especially among women of childbearing age—these results are of particular concern and warrant replication and additional examination of potential mechanisms and implications.

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REFERENCES

1. Centers for Disease Control and Prevention. 2018 National Health Interview Survey (NHIS) Data. 2018; https://www.cdc.gov/asthma/nhis/2018/table4-1.htm. Accessed December 21, 2019.
2. GBD 2015 Chronic Respiratory Disease Collaborators. Global, regional, and national deaths, prevalence, disability-adjusted life years, and years lived with disability for chronic obstructive pulmonary disease and asthma, 1990-2015: a systematic analysis for the global burden of disease study 2015. *Lancet Respir Med*. 2017;5(9):691–706.
3. Chen YC, Fan HY, Huang YT, et al. Causal relationships between adiposity and childhood asthma: bi-directional mendelian randomization analysis. *Int J Obes (Lond)*. 2019; 43(1):73–81.
4. Chen Z, Salam MT, Alderete TL, et al. Effects of childhood asthma on the development of obesity among school-aged children. *Am J Respir Crit Care Med*. 2017;195(9): 1181–1188.
5. Forno E, Celedon JC. The effect of obesity, weight gain, and weight loss on asthma inception and control. *Curr Opin Allergy Clin Immunol*. 2017;17(2):123–130.
6. Hossain MJ, Xie L, Lang JE, et al. Piecewise mixed effects model to compare the weight-gain patter ns before and after diagnosis of asthma in children younger than 5 years. *J Biom Biostat*. 2015;6(4):248.
7. Pradeepan S, Garrison G, Dixon AE. Obesity in asthma: approaches to treatment. *Curr Allergy Asthma Rep*. 2013; 13(5):434–442.
8. Sideleva O, Suratt BT, Black KE, et al. Obesity and asthma: an inflammatory disease of adipose tissue not the airway. *Am J Respir Crit Care Med*. 2012;186(7):598–605.
9. Tashiro H, Shore SA. Obesity and severe asthma. *Allergol Int*. 2019;68(2):135–142.
10. Zhang Y, Chen Z, Berhane K, et al. The dynamic relationship between asthma and obesity in school children. *Am J Epidemiol*. 2020;189(6):583–591.
11. Voerman E, Santos S, Patro Golab B, et al. Maternal body mass index, gestational weight gain, and the risk of

overweight and obesity across childhood: an individual participant data meta-analysis. *PLoS Med*. 2019; 16(2):e1002744.
12. Darling AM, Werler MM, Cantonwine DE, et al. Timing and amount of gestational weight gain in association with adverse birth outcomes. *Epidemiology*. 2019;30(5):695–705.
13. Feghali MN, Catov JM, Zantow E, et al. Timing of gestational weight gain and adverse perinatal outcomes in overweight and obese women. *Obstet Gynecol*. 2019;133(5):962–970.
14. Hinkle SN, Johns AM, Albert PS, et al. Longitudinal changes in gestational weight gain and the association with intrauterine fetal growth. *Eur J Obstet Gynecol Reprod Biol*. 2015;190:41–47.
15. Pugh SJ, Albert PS, Kim S, et al. Patterns of gestational weight gain and birthweight outcomes in the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development fetal growth studies-singletons: a prospective study. *Am J Obstet Gynecol*. 2017;217(3):346.e1–346.e11.
16. Sha T, Cheng G, Li C, et al. Patterns of women's postpartum weight retention and its associations with maternal obesity-related factors and parity. *Int J Environ Res Public Health*. 2019;16(22):4510.
17. Widen EM, Factor-Litvak PR, Gallagher D, et al. The pattern of gestational weight gain is associated with changes in maternal body composition and neonatal size. *Matern Child Health J*. 2015;19(10):2286–2294.
18. Morkve Knudsen T, Rezwan FI, Jiang Y, et al. Transgenerational and intergenerational epigenetic inheritance in allergic diseases. *J Allergy Clin Immunol*. 2018;142(3):765–772.
19. Polinski KJ, Liu J, Boghossian NS, et al. Maternal obesity, gestational weight gain, and asthma in offspring. *Prev Chronic Dis*. 2017;14:E109.
20. Abebe DS, Von Soest T, Von Holle A, et al. Developmental trajectories of postpartum weight 3 years after birth: Norwegian mother and child cohort study. *Matern Child Health J*. 2015;19(4):917–925.
21. Nathan RA, Sorkness CA, Kosinski M, et al. Development of the asthma control test: a survey for assessing asthma control. *J Allergy Clin Immunol*. 2004;113(1):59–65.
22. Dombrowski MP, Schatz M, ACOGC. on practice bulletins–obstetrics. ACOG practice bulletin: clinical management guidelines for obstetrician-gynecologists number 90, February 2008: asthma in pregnancy. *Obstet Gynecol*. 2008;111(2 pt 1):457–464.
23. Jani M, Ogston S, Mukhopadhyay S. Annual increase in body mass index in children with asthma on higher doses of inhaled steroids. *J Pediatr*. 2005;147(4):549–551.
24. Han J, Nguyen J, Kim Y, et al. Effect of inhaled corticosteroid use on weight (BMI) in pediatric patients with moderate-severe asthma. *J Asthma*. 2019;56(3): 263–269.
25. Contreras ZA, Chen Z, Roumeliotaki T, et al. Does early onset asthma increase childhood obesity risk? A pooled analysis of 16 European cohorts. *Eur Respir J*. 2018; 52(3):1800504.
26. Textor J, van der Zander B, Gilthorpe MS, et al. Robust causal inference using directed acyclic graphs: the R package 'dagitty'. *Int J Epidemiol*. 2016;45(6):1887–1894.
27. Macdonald-Wallis C, Lawlor DA, Palmer T, et al. Multivariate multilevel spline models for parallel growth processes: application to weight and mean arterial pressure in pregnancy. *Stat Med*. 2012;31(26):3147–3164.
28. Crozier SR, Johnson W, Cole TJ, et al. A discussion of statistical methods to characterise early growth and its impact on bone mineral content later in childhood. *Ann Hum Biol*. 2019;46(1):17–26.
29. SAS Institute Inc. SAS/STAT 15.1 User's Guide. Cary, NC: SAS Institute Inc; 2018.
30. Kominiarek MA, Peaceman AM. Gestational weight gain. *Am J Obstet Gynecol*. 2017;217(6):642–651.
31. Kuruvilla ME, Lee FE, Lee GB. Understanding asthma phenotypes, endotypes, and mechanisms of disease. *Clin Rev Allergy Immunol*. 2019;56(2):219–233.
32. Ekström S, Magnusson J, Kull I, et al. Body mass index development and asthma throughout childhood. *Am J Epidemiol*. 2017;186(2):255–263.
33. Kapadia CR, Nebesio TD, Myers SE, et al. Endocrine effects of inhaled corticosteroids in children. *JAMA Pediatr*. 2016; 170(2):163–170.
34. Loke YK, Blanco P, Thavarajah M, et al. Impact of inhaled corticosteroids on growth in children with asthma: systematic review and meta-analysis. *PLoS One*. 2015;10(7):e0133428.
35. Scott HA, Wood LG, Gibson PG. Role of obesity in asthma: mechanisms and management strategies. *Curr Allergy Asthma Rep*. 2017;17(8):53.
36. Dixon AE, Holguin F. Diet and metabolism in the evolution of asthma and obesity. *Clin Chest Med*. 2019;40(1):97–106.
37. Dixon AE, Suratt BT. Chair's summary: obesity and associated changes in metabolism, implications for lung diseases. *Ann Am Thorac Soc*. 2017;14(suppl_5):S314–S315.
38. Baffi CW, Winnica DE, Holguin F. Asthma and obesity: mechanisms and clinical implications. *Asthma Res Pract*. 2015;1:1.
39. Baffi CW, Wood L, Winnica D, et al. Metabolic syndrome and the lung. *Chest*. 2016;149(6):1525–1534.
40. Perez MK, Piedimonte G. Metabolic asthma: is there a link between obesity, diabetes, and asthma? *Immunol Allergy Clin North Am*. 2014;34(4):777–784.
41. Murphy VE, Jensen ME, Gibson PG. Asthma during pregnancy: exacerbations, management, and health outcomes for mother and infant. *Semin Respir Crit Care Med*. 2017; 38(2):160–173.
42. Murphy VE, Jensen ME, Powell H, et al. Influence of maternal body mass index and macrophage activation on asthma exacerbations in pregnancy. *J Allergy Clin Immunol Pract*. 2017;5(4):981–987.e1.
43. Flores KF, Robledo CA, Hwang BS, et al. Does maternal asthma contribute to racial/ethnic disparities in obstetrical and neonatal complications? *Ann Epidemiol*. 2015; 25(6):392–397.e1.
44. Bandoli G, Palmsten K, Forbess Smith CJ, et al. A review of systemic corticosteroid use in pregnancy and the risk of select pregnancy and birth outcomes. *Rheum Dis Clin North Am*. 2017;43(3):489–502.
45. Kemppainen M, Lahesmaa-Korpinen AM, Kauppi P, et al. Maternal asthma is associated with increased risk of perinatal mortality. *PLoS One*. 2018;13(5):e0197593.
46. Murphy VE, Jensen ME, Robijn AL, et al. How maternal BMI modifies the impact of personalized asthma management in pregnancy. *J Allergy Clin Immunol Pract*. 2020;8(1):219–228.e3.
47. Ali Z, Nilas L, Ulrik CS. Excessive gestational weight gain in first trimester is a risk factor for exacerbation of asthma during pregnancy: a prospective study of 1283 pregnancies. *J Allergy Clin Immunol*. 2018;141(2):761–767.
48. Ali Z, Nilas L, Ulrik CS. Determinants of low risk of asthma exacerbation during pregnancy. *Clin Exp Allergy*. 2018;48(1): 23–28.
49. Farpour-Lambert NJ, Ells LJ, Martinez de Tejada B, et al. Obesity and weight gain in pregnancy and postpartum: an

evidence review of lifestyle interventions to inform maternal and child health policies. *Front Endocrinol (Lausanne)*. 2018; 9:546.
50. Rooney BL, Schauberger CW, Mathiason MA. Impact of perinatal weight change on long-term obesity and obesity-related illnesses. *Obstet Gynecol*. 2005;106(6): 1349–1356.
51. Dalrymple KV, Flynn AC, Relph SA, et al. Lifestyle interventions in overweight and obese pregnant or postpartum women for postpartum weight management: a systematic review of the literature. *Nutrients*. 2018;10(11):1704.
52. Michel S, Raab R, Drabsch T, et al. Do lifestyle interventions during pregnancy have the potential to reduce long-term postpartum weight retention? A systematic review and meta-analysis. *Obes Rev*. 2019;20(4):527–542.
53. Robijn AL, Jensen ME, McLaughlin K, et al. Inhaled corticosteroid use during pregnancy among women with asthma: a systematic review and meta-analysis. *Clin Exp Allergy*. 2019;49(11):1403–1417.
54. Committee on Gynecologic Practice. ACOG Committee opinion number 762: prepregnancy counseling. *Obstet Gynecol*. 2019;133(1):e78–e89.