

Increased Risk of NICU Stays for Babies Born to Mothers Prescribed GLP-1 Medications in the 90 Days Before Pregnancy

Team A: Kersten Bartelt, RN; Ted Stamp

Team B: Matthew Gracianette, MD; Joe Deckert, PhD

Last updated 20 June 2024 • Check for updates at EpicResearch.org

Key Findings:

- Babies born to non-diabetic mothers prescribed glucagon-like peptide-1 receptor agonist (GLP-1) medications in the 90 days before pregnancy are 21% more likely to be admitted to the NICU than babies born to mothers not prescribed weight loss medications.
- Mothers prescribed phentermine in the 90 days before pregnancy or during the first trimester are more likely to have large babies than women not prescribed weight loss medications during pregnancy.
- Babies born to mothers prescribed phentermine or GLP-1 medications in the 90 days prior to pregnancy or during the first trimester had similar rates of failure to thrive or congenital heart defect diagnoses compared to babies born to mothers not prescribed weight loss medications.
- Few non-diabetic women are prescribed phentermine or GLP-1 medications after the first trimester of their pregnancy.

Recently, there have been reports of women who have previously struggled with infertility who were able to conceive after starting treatment with a glucagon-like peptide-1 receptor agonist (GLP-1) medication, such as semaglutide or tirzepatide.^{1,2} However, little is known about whether the use of weight loss medications, such as phentermine or GLP-1 medications, is correlated with certain pregnancy and neonatal outcomes.

We assessed 775,478 pregnancies for women with no history of diabetes and who did not develop gestational diabetes between January 2017 and April 2024. We first determined how often pregnant women were given a prescription for a weight loss medication, either phentermine or a GLP-1, in each trimester. We found that few women were prescribed weight loss medications during pregnancy, and fewer than 10 women (0.001%) were prescribed phentermine or a GLP-1 medication in the third trimester, as shown in Figure 1.

Weight Loss Medication Prescribing Rates by Trimester of Pregnancy

Medication	90 days pre-pregnancy	Trimester 1	Trimester 2	Trimester 3
Phentermine	0.41%	0.18%	0.004%	0.001%
GLP-1 Medications	0.15%	0.08%	0.003%	0.001%

N=775,478 pregnancies

"Weight Loss Medication Prescribing Rates by Trimester of Pregnancy," 2024. EpicResearch.org

Figure 1. The percentage of pregnancies with a prescription for a weight loss medication in a given trimester. Women are represented in multiple trimesters if they had multiple prescriptions ordered in separate trimesters.

To determine whether there might be a relationship between weight loss medication use immediately before or during pregnancy and various maternal and neonatal outcomes, we compared the rates of

preterm delivery, high birth weight, neonatal intensive care unit (NICU) admission, and diagnoses of failure to thrive or congenital heart defect for babies born to mothers prescribed phentermine or a GLP-1 medication in the 90 days before pregnancy or during the first trimester to those with no documented weight loss medication exposure during pregnancy. We were unable to assess the rates of these conditions for prescriptions in the second and third trimesters due to the very limited number of prescriptions for these medications during that timeframe. Women are represented in multiple trimesters if they had multiple prescriptions ordered in separate trimesters.

We found that babies born to mothers with a phentermine prescription in the 90 days prior to pregnancy were more likely to have a high birth weight than babies born to mothers not prescribed weight loss medications, as shown in Figure 2. Babies born to mothers prescribed a GLP-1 medication in the 90 days prior to pregnancy were more likely to require a NICU stay than babies born to mothers not prescribed weight loss medications. While the rates of pre-term deliveries were increased for both the phentermine and the GLP-1 group, after controlling for other risk factors, such as maternal age and BMI, the rates of pre-term delivery were similar for mothers prescribed weight loss medications and those with no weight loss medications.

Pregnancy and Neonatal Outcomes – Weight Loss Medication Prescriptions in the 90 Days Prior to Pregnancy

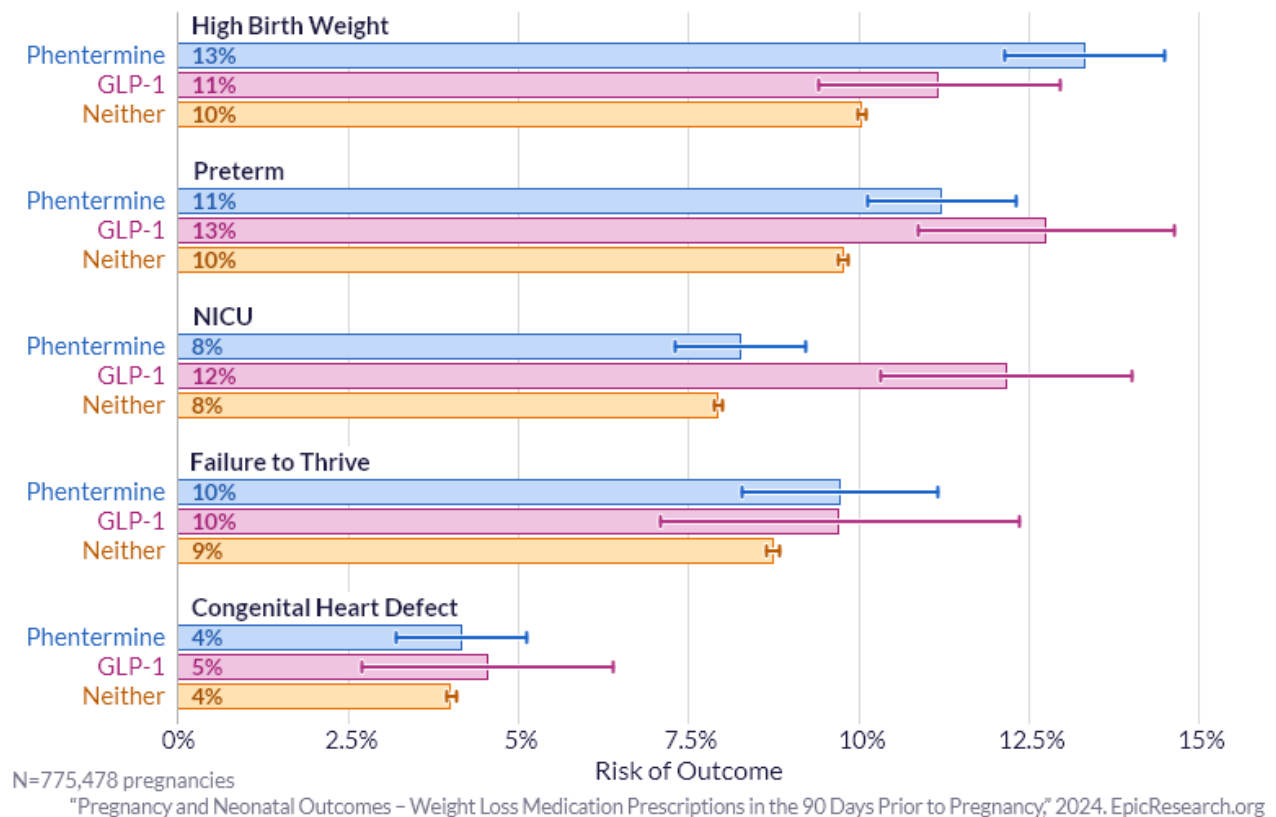
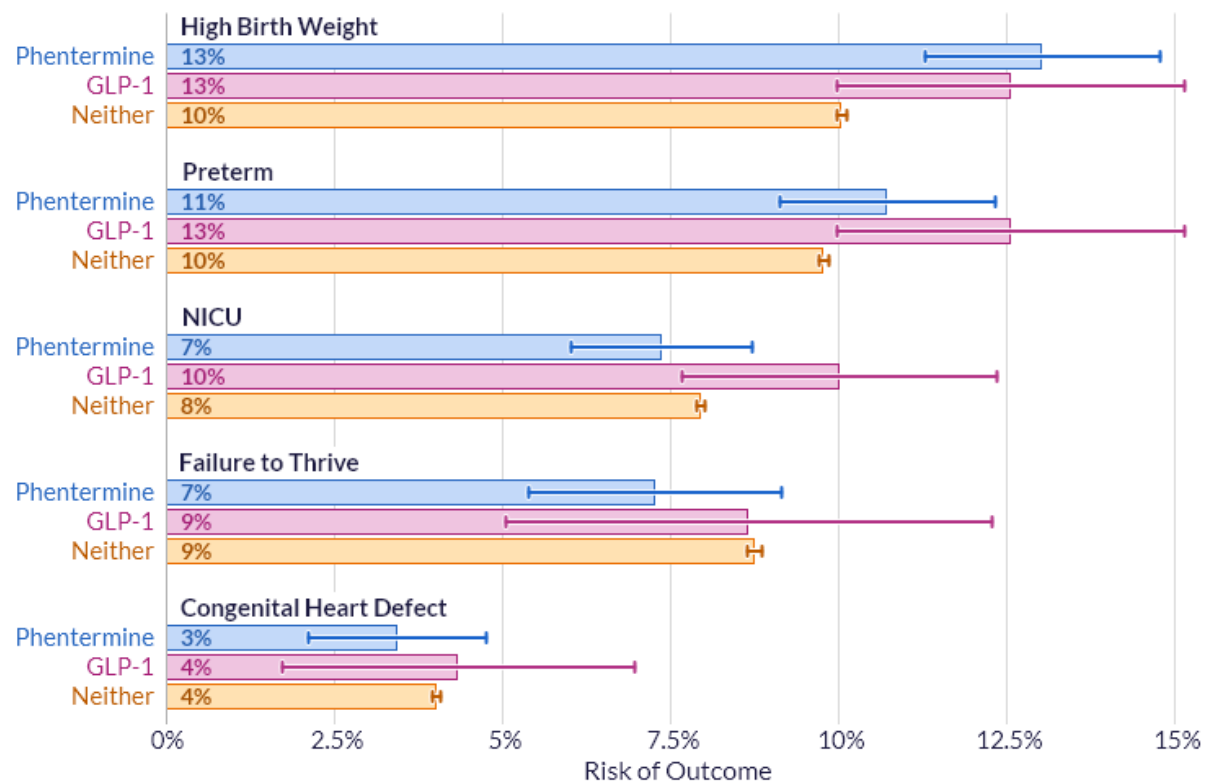


Figure 2. The unadjusted percentage of pregnancies with a given outcome by weight loss medication prescription type in the 90 days prior to pregnancy.

Exposure to phentermine or GLP-1 medications in the first trimester yielded similar results to exposure in the 90 days prior to pregnancy, as shown in Figure 3.

Pregnancy and Neonatal Outcomes – Weight Loss Medication Prescriptions in the First Trimester



N=773,143 pregnancies "Pregnancy and Neonatal Outcomes – Weight Loss Medication Prescriptions in the First Trimester," 2024. EpicResearch.org

Figure 3. The unadjusted percentage of pregnancies with a given outcome by weight loss medication prescription type in the first trimester.

These data come from Cosmos, a dataset created in collaboration with a community of Epic health systems representing more than 256 million patient records from 1,400 hospitals and more than 32,800 clinics from all 50 states and Lebanon. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions. Graphics by Brian Olson.

References

1. Schimelpfening, N. 'Ozempic Babies': How Weight Loss Drugs Can Interfere with Birth Control and Boost Fertility. *Healthline*. [Ozempic Babies: Weight Loss Drugs May be Causing Unplanned Pregnancies \(healthline.com\)](https://www.healthline.com/health/ozempic-babies). Published March 26, 2024. Accessed May 15, 2024.
2. Cheng M, Tirrell M. "'Ozempic babies': Reports of surprise pregnancies raise new questions about weight loss drugs. *CNN*. ['Ozempic babies': Reports of surprise pregnancies raise new questions about weight loss drugs | CNN](https://www.cnn.com/2024/05/08/health/ozempic-babies/index.html). Published May 8, 2024. Accessed May 15, 2024.

Data Definitions

Term	Definition
Study period	Birth date between 1/1/2017 and 4/17/2024
Study population	- Three or more prenatal visits in different gestational months - Mother's pre-birth BMI must classify them as overweight or obese

	• Prenatal visit during all trimesters, or pregnancy ended in second trimester and prenatal visits in first and second trimesters • Patient does not have type 2 diabetes or gestational diabetes
Exposures	New or reordered outpatient prescription, by trimester, 90 days before gestation, and 91-365 days before gestation: • GLP-1 medications: Generic drug name containing “semaglutide,” “liraglutide,” “dulaglutide,” “exenatide,” or “tirzepatide” • Phentermine: Generic drug name containing “phentermine HCl,” “phentermine resin,” or “phentermine/topiramate”
Outcomes	• High birth weight for gestational age: > 90% by Fenton growth chart • Pre-term birth: < 37 weeks • NICU admission: ICU stay within five days of birth • In babies that have two post-birth visits and an encounter in the first four months of life: ○ Failure to thrive: ICD-10-CM code P92.6 ○ Congenital Heart Defects: ICD-10-CM code Q24.9, Q21.0, Q21.10, Q22.4, Q22.0, Q22.1, Q22.3 Q22.8, Q21.3, Q23., Q25.0 Q25.44, 25.21, Q25.44, Q24.3, or Q26.2
Type 2 diabetes	Patients with one or more of the following: - Any diagnosis with ICD-10-CM code O24.1* or E11* - Hemoglobin A1C > 6.5% - Medication order for insulin, metformin, or glyburide
Gestational diabetes	A diagnosis with ICD-10-CM code O24.4* without a type 2 diabetes diagnosis
Insulin	Pharmaceutical class of INSULINS and route of injection, intravenous, or subcutaneous OR pharmaceutical class of ANTIHYPERGLY,INSULIN, LONG ACT GLP-1 RECEPT.AGONIST
Metformin	Generic drug name containing “metformin”
Glyburide	Generic drug name containing “glyburide,” “glyburide,micronized,” or “glyburide/metformin HCl”
Known risk factors	• Most recent pre-pregnancy BMI, classified by: ○ Underweight: < 18.5 ○ Healthy: 18.5-25 ○ Overweight: 25-30 ○ Obese: 30-40 ○ Morbidly Obese: > 40 • Mother’s race and ethnicity: Hispanic, non-Hispanic Black, non-Hispanic White, Non-Hispanic Other Race) • Sex of baby: Male, Female • Maternal age: < 18, 18-24, 25-34, 35-50 • Birth Year • Social Vulnerability Index quartile • Rural-Urban Commuting Area Code by patient home postal code: ○ Rural: 6-10 ○ Urban: 1-5 • Maternal mental health diagnoses (any time before birth): ○ Anxiety: ICD-10-CM code F40*, F41*, F06.4*, F93.0*, or F94.0* ○ Depression: ICD-10-CM code F32*, F33*, F06.31*, F06.32*, or F34.1* ○ Eating disorders: ICD-10-CM code F50*
Model specifications	• Unadjusted absolute risk values • Adjusted absolute risk values with 4:1 patient matching

- Chi Squared test for significance
- Logistic regression without patient matching

Table 1: Pregnancy and Neonatal Outcomes – Weight Loss Medication Prescriptions in the 90 Days Prior to Pregnancy and First Trimester

	Phentermine 90 days prior	Phentermine T1	GLP1 90 days prior	GLP1 T1
Is High Birth Weight Exposed Outcome	424	186	135	79
Is High Birth Weight Exposed No Outcome	2759	1241	1073	550
Is High Birth Weight Not Exposed Outcome	77441	77441	77441	77441
Is High Birth Weight Not Exposed No Outcome	693646	693646	693646	693646
Is High Birth Weight Risk Exposed	13.321%	13.034%	11.175%	12.560%
Is High Birth Weight Risk Exposed Ci Low	12.140%	11.287%	9.399%	9.970%
Is High Birth Weight Risk Exposed Ci High	14.501%	14.781%	12.952%	15.149%
Is High Birth Weight Risk Non-Exposed	10.043%	10.043%	10.043%	10.043%
Is High Birth Weight Risk Non-Exposed Ci Low	9.976%	9.976%	9.976%	9.976%
Is High Birth Weight Risk Non-Exposed Ci High	10.110%	10.110%	10.110%	10.110%
Is Preterm Exposed Outcome	357	153	154	79
Is Preterm Exposed No Outcome	2826	1274	1054	550
Is Preterm Not Exposed Outcome	75376	75376	75376	75376
Is Preterm Not Exposed No Outcome	695711	695711	695711	695711
Is Preterm Risk Exposed	11.216%	10.722%	12.748%	12.560%
Is Preterm Risk Exposed Ci Low	10.120%	9.117%	10.868%	9.970%
Is Preterm Risk Exposed Ci High	12.312%	12.327%	14.629%	15.149%
Is Preterm Risk Non-Exposed	9.775%	9.775%	9.775%	9.775%
Is Preterm Risk Non-Exposed CiLow	9.709%	9.709%	9.709%	9.709%
Is Preterm Risk Non-Exposed CiHigh	9.842%	9.842%	9.842%	9.842%
Is NICU Exposed Outcome	263	105	147	63
Is NICU Exposed No Outcome	2920	1322	1061	566
Is NICU Not Exposed Outcome	61185	61185	61185	61185
Is NICU Not Exposed No Outcome	709902	709902	709902	709902
Is NICU Risk Exposed	8.263%	7.358%	12.169%	10.016%
Is NICU Risk Exposed Ci Low	7.306%	6.003%	10.325%	7.670%

Is NICU Risk Exposed Ci High	9.219%	8.713%	14.012%	12.362%
Is NICU Risk Non-Exposed	7.935%	7.935%	7.935%	7.935%
Is NICU Risk Non-Exposed Ci Low	7.875%	7.875%	7.875%	7.875%
Is NICU Risk Non-Exposed Ci High	7.995%	7.995%	7.995%	7.995%
Is Failure To Thrive Exposed Outcome	159	53	47	20
Is Failure To Thrive Exposed No Outcome	1475	677	437	211
Is Failure To Thrive Not Exposed Outcome	28242	28242	28242	28242
Is Failure To Thrive Not Exposed No Outcome	294645	294645	294645	294645
Is Failure To Thrive Risk Exposed	9.731%	7.260%	9.711%	8.658%
Is Failure To Thrive Risk Exposed Ci Low	8.294%	5.378%	7.073%	5.031%
Is Failure To Thrive Risk Exposed Ci High	11.168%	9.143%	12.349%	12.285%
Is Failure To Thrive Risk Non-Exposed	8.747%	8.747%	8.747%	8.747%
Is Failure To Thrive Risk Non-Exposed Ci Low	8.649%	8.649%	8.649%	8.649%
Is Failure To Thrive Risk Non-Exposed Ci High	8.844%	8.844%	8.844%	8.844%
Is Congenital Heart Defects Exposed Outcome	68	25	22	
Is Congenital Heart Defects Exposed No Outcome	1566	705	462	221
Is Congenital Heart Defects Not Exposed Outcome	12952	12952	12952	12952
Is Congenital Heart Defects Not Exposed No Outcome	309935	309935	309935	309935
Is Congenital Heart Defects Risk Exposed	4.162%	3.425%	4.545%	4.329%
Is Congenital Heart Defects Risk Exposed Ci Low	3.193%	2.105%	2.690%	1.705%
Is Congenital Heart Defects Risk Exposed Ci High	5.130%	4.744%	6.401%	6.953%
Is Congenital Heart Defects Risk Non-Exposed	4.011%	4.011%	4.011%	4.011%
Is Congenital Heart Defects Risk Non-Exposed Ci Low	3.944%	3.944%	3.944%	3.944%
Is Congenital Heart Defects Risk Non-Exposed Ci High	4.079%	4.079%	4.079%	4.079%