

Mood Disorder Risk After Pregnancy: A Comparison of Gestational and Pregestational Diabetes

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Abstract

Purpose

Diabetes mellitus and depression are both major diagnoses obstetrician-gynecologists must contend with when treating pregnant patients. While previous studies have shown an association between gestational (GDM) or pregestational diabetes mellitus (PGDM) and risk of subsequent mood and substance use disorders, few studies have compared them directly, which this study addressed.

Methods

TriNetX was used to conduct this retrospective study of patients aged 18–65. Cohort 1 included patients with GDM, while cohort 2 included patients with PGDM. Each cohort was propensity-score matched to be comparable in demographics and prior diagnoses. The outcomes measured were risks of depressive episode, recurrent major depression (MDD), postpartum depression (PPD), anxiety, adjustment disorder, and substance use within 270 days of initial GDM or PGDM diagnosis.

Results

After matching, each cohort consisted of 139,725 patients. Compared to PGDM patients, GDM patients had significantly lower risks of depressive episode (RR: 0.689; 95% CI: 0.662, 0.716), recurrent MDD (RR: 0.745; 95% CI: 0.688, 0.808), anxiety (RR: 0.798; 95% CI: 0.769, 0.827), adjustment disorder (RR: 0.632; 95% CI: 0.584, 0.684), and substance use (RR: 0.667; 95% CI: 0.631, 0.705), but slightly higher risk of PPD (RR: 1.076; 95% CI: 1.024, 1.131).

Conclusion

These findings suggest that patients with PGDM are at significantly higher risk than those with GDM for subsequent mood and substance use complications. Adding to current clinical guidelines recommending mental health screening in pregnant patients, heightened awareness and support are warranted for the particular psychological burden faced by patients with PGDM.

Introduction

The CDC National Diabetes Statistics Report found that approximately 12% of the United States population has diabetes (CDC 2024) with an additional 1.5 million Americans being diagnosed annually (ADA 2023). In addition to the disease burden it places on the population at large, it presents particular challenges in pregnant patients and therefore has continued to demand attention from obstetrician-gynecologists. From 2016 to 2022, the prevalence of gestational diabetes mellitus (GDM), defined as insulin-resistant diabetes diagnosed during pregnancy, increased from 7.1 to 9.5 per 100 deliveries. The

prevalence of pregestational diabetes (PGDM), defined as diabetes mellitus diagnosed prior to and persisting throughout pregnancy, has however remained stable, at 0.3 per 100 deliveries (Fwu et al. 2026). The diagnosis of either GDM or PGDM guides clinical management due to the slew of potential complications posed to the mother and fetus. Potential maternal complications include hypertensive disorders of pregnancy, metabolic syndrome, cesarean birth, preterm birth, congenital anomalies, macrosomia, and neonatal respiratory distress syndrome (Sacks et al. 2015; Wu et al. 2020; Xu et al. 2014; Ye et al. 2022; Zhang et al. 2022). PGDM in contrast to GDM is associated with additional risks, owing in part to the autoimmune etiology, as well as due to longer years lived with disease. Diabetic ketoacidosis occurs in 5–10% of pregnant patients with PGDM. Patients with PGDM have heightened risk of myocardial infarction, retinopathy, and nephropathy. PGDM patients who had diabetic nephropathy prior to pregnancy will also have increased risks of hypertensive disorder of pregnancy, uteroplacental insufficiency, and preterm delivery (ACOG 2018).

Another issue burdening the United States at large is depression, defined as the cooccurrence of several depressive symptoms within a 2-week period: depressed mood, anhedonia, changes in weight, sleep habits, or psychomotor activity, fatigue, feelings of worthlessness, loss in concentration, and suicidal ideation. In 2021, 8.3% of adults experienced at least one major depressive episode, with women experiencing a higher prevalence at 10.3% compared to men at 6.2% (NIMH 2023). As with diabetes mellitus, depression presents unique challenges in pregnant patients, with a prevalence of about 33% during pregnancy and 40% postpartum. Maternal and infant consequences of antepartum depression include substance use, decreased attendance to prenatal visits, poor nutrition, increased suicidality, preeclampsia, impaired maternal-infant attachment, preterm delivery, fetal growth restriction, and cesarean delivery (Acheampong et al. 2021; Ciesielski et al. 2015; Dadi et al. 2020; Robinson 2015). Consequences of postpartum depression (PPD) include decreased breastfeeding, decreased attendance to postpartum well-child visits, incomplete childhood vaccination, maladaptive parenting, substance use, and suicide (Frieder et al. 2019; Stewart and Vigod 2019). Additionally, children born to mothers with postpartum depression have been found to have persisting deficits in childhood cognitive, social, and emotional development when compared to peers (Urizar and Muñoz 2021). Risk factors contributing to antepartum and postpartum depression include Asian and African American race, unemployment, incarceration, family history of depression or anxiety, intimate partner violence, medical comorbidities, and insomnia (ACOG 2023; Melville et al. 2010).

Prior studies have shown a link between diabetes and depression, including diabetes during pregnancy and depression. One meta-analysis of 11 studies demonstrated that patients with diabetes had a 24% increased association with depression (Nouwen et al. 2010). Mechanistic explanation behind the linkage of the diseases remains less studied, but a literature review by Alzoubi et al. suggested two possibilities. First, the inflammatory marker CRP is associated with both risk of depression and diabetes mellitus, so this particular cytokine may act as the third variable leading to increased comorbidity of both diseases. Second, depression is associated with a change in the hypothalamic-pituitary axis, particularly an increase in cortisol and adrenocorticotrophic hormone. Cortisol levels and insulin resistance are also

known to have significant correlation with one another. In this case, the cortisol response may be the middle factor linking depression and diabetes (Alzoubi et al. 2018).

When examining the literature regarding GDM, PGDM, and depression specifically, studies have by and large shown a strong association between diabetes in pregnancy and depression. A meta-analysis of 18 studies found patients with GDM having a 59% increased risk of PPD when compared with those without GDM (Azami et al. 2019). Another meta-analysis found a 32% increased risk (Arafa and Dong 2019). A recent meta-analysis in 2025 reviewing 29 studies found a 42% increased risk (Nourollahi and Azami 2025). The risk has also been demonstrated to be bidirectional, in that prior depression can predict risk of GDM (Fischer and Morales-Suárez-Varela 2023; Saeed et al. 2024).

While there is a robust body of literature supporting an association between diabetes in pregnancy and depression, there is little existing literature directly comparing whether GDM or PGDM is a stronger predictor for depression, despite reason to suspect a clinically meaningful difference between the risks. A patient with a new diagnosis of GDM may have to contend with the stress of a new diagnosis in addition to the challenges of the pregnancy itself, whereas a patient with PGDM has likely already familiarized themselves with their diagnosis and necessary management (Do et al. 2016; Rath and MV 2025). On the other hand, patients with PGDM may have to contend with greater disease burden due to longer proportion of life lived with disease, as well as the challenges associated with the autoimmune manifestation of diabetes when compared with the insulin resistance etiology more prevalent in GDM. Both a cross-sectional study consisting of 350 women as well as a prospective study of 80 mothers found a significantly lower risk of depression and anxiety in patients with GDM compared to those with PGDM (Aycan and Aksu 2025; Salimi et al. 2024).

Regardless, this paper aimed to address the need to directly compare GDM to PGDM at a much larger scale to determine with higher confidence whether either disease is a stronger predictor for psychiatric outcomes. A more generalizable study could help guide a differential approach in psychiatric and obstetric-gynecologic clinical decision-making and screening guidelines for patients with GDM versus PGDM based on respective psychiatric risks.

Methods

This retrospective cohort study was conducted using TriNetX, a global research platform that stores de-identified electronic medical records. The Global Collaborative Network was used in this study, with all data available as of September 2026 fielded from 160 out of 181 total healthcare organizations.

This study looked only at patients between the ages of 18 and 65. Patients with GDM were assigned to cohort 1, while patients with PGDM were assigned to cohort 2. GDM was defined as patients with the ICD-10 code O24.4. PGDM was defined as patients with any one of the ICD-10 codes O24.0, O24.1, or O24.3 for pre-existing type 1, pre-existing type 2, and unspecified pre-existing diabetes mellitus in pregnancy, childbirth, and the puerperium. Based on these parameters, 540,309 patients were eligible for cohort 1, and 140,051 for cohort 2.

To ensure similar baseline characteristics and thus comparability between cohorts, the TriNetX propensity-score matching function was run. This function assigns a propensity score to each patient based on the covariates. It then pairs a given patient from one cohort to a patient in the other cohort whose propensity score is most similar. The difference in means of a given covariate between each group is divided by the pooled standard deviation to calculate a standardized difference. The function then sets a caliper, which by default and in this study is 0.1, below which standardized differences respective to each covariate must be for cohorts to be considered adequately matched.

The covariates matched on were chosen as those most likely to influence the outcomes outside of the causal pathway that this study intended to investigate. These included demographic variables of age, race, and ethnicity. Also included were the following pre-existing diagnoses: abortive pregnancies (ICD-10 codes O00-O08), anxiety disorders (F40-F48), mood disorders (F30-F39), substance use disorders (F10-F19), personality disorders (F60-F69), childhood and adolescent behavioral disorders (F90-F98), psychotic disorders (F20-F29), and insomnia (F51.0). Other matched socioeconomic factors included: family history of mental disorders (Z81), patient noncompliance with medical treatment (Z91.1), history of psychological trauma (Z91.4), unemployment (Z56.0), and incarceration (Z65.1). After matching, each cohort consisted of 139,725 patients.

The outcomes investigated were: depression, depressive episode (F32), recurrent major depressive disorder (MDD) (F33), postpartum depression (PPD) (F53.0), anxiety (F41), adjustment disorder (F43.2), and substance use. Depression was defined by patients with at least one of three diagnoses: depressive episode, recurrent MDD, or PPD. Substance use encompassed any of the four: substance use disorder (F10-F19), or pregnancy, childbirth, and the puerperium complicated by tobacco use (O99.33), alcohol use (O99.31), or other drug use (O99.32).

These outcomes were analyzed using the native Compare Cohorts function in TriNetX, looking at first incidences within 270 days of initial diagnosis of either GDM or PGDM. For each outcome, patients fulfilling the outcome criteria prior to the studied outcome incidence were excluded from analysis. First outcome incidences, risks, risk differences (RD), risk ratios (RR), and odds ratios (OR) with 95% confidence intervals (CI) and p-values were extracted. Z-tests evaluated RD and RR estimates, while chi-square testing evaluated the OR. In addition, Kaplan-Meier survival analyses were performed, with survival curve discrepancies between cohorts evaluated with log-rank tests. Cox proportional hazards regression was used to evaluate HR with respective 95% CI. A two-sided P-value < 0.05 was used to establish statistical significance.

Results

Baseline cohort characteristics

Patients from cohort 1, GDM, and cohort 2, PGDM, were propensity-score matched based on demographics (Table 1, 3) and diagnoses (Table 2, 4) described in detail in the methods.

Table 1
Demographics of cohorts before matching

Cohort	Demographics	Mean $\pm$ SD	Patients	% of Cohort	Std. Diff.
1	Current Age	38.9 +/- 7.4	540,309	100%	0.063
2		38.4 +/- 7.6	140,051	100%	
1	Age At Index	32.0 +/- 6.1	540,309	100%	0.041
2		31.7 +/- 6.4	140,051	100%	
1	White		260,662	48.20%	0.018
2			66,326	47.40%	
1	American Indian or Alaska Native		4,792	0.90%	0.041
2			1,838	1.30%	
1	Unknown Race		111,102	20.60%	0.1
2			23,342	16.70%	
1	Native Hawaiian or Other Pacific Islander		5,079	0.90%	0.018
2			1,569	1.10%	
1	Unknown Ethnicity		155,833	28.80%	0.121
2			32,979	23.50%	
1	Not Hispanic or Latino		278,874	51.60%	0.001
2			72,207	51.60%	
1	Hispanic or Latino		105,602	19.50%	0.129
2			34,865	24.90%	
1	Black or African American		66,597	12.30%	0.231
2			29,194	20.80%	
1	Other Race		34,249	6.30%	0.009
2			9,200	6.60%	
1	Asian		57,828	10.70%	0.165
2			8,528	6.10%	

This table illustrates the initial baseline population demographic represented in each cohort, before propensity-score matching was run, based on age, race, and ethnicity. Cohort 1 is comprised of the gestational diabetes mellitus patients (n = 540,309 before matching). Cohort 2 is comprised of the pregestational diabetes mellitus patients (n = 140,051 before matching). Mean value $\pm$ standard deviation is provided for the age. The rest of the categorical values based on race and ethnicity are reported to percentages of each cohort. Std. Diff. refers to standardized difference.

Table 2
Diagnoses of cohorts before matching

Cohort	ICD-10 Code	ICD-10 Diagnosis	Patients	% of Cohort	Std. Diff.
1	O00-008	Pregnancy with abortive outcome	48,616	9.00%	0.005
2			12,419	8.90%	
1	F40-F48	Anxiety, dissociative, stress-related, somatoform and other nonpsychotic mental disorders	72,860	13.50%	0.028
2			20,225	14.40%	
1	F30-F39	Mood [affective] disorders	57,708	10.70%	0.086
2			18,866	13.50%	
1	F10-F19	Mental and behavioral disorders due to psychoactive substance use	37,205	6.90%	0.079
2			12,637	9.00%	
1	F60-F69	Disorders of adult personality and behavior	3,317	0.60%	0.035
2			1,289	0.90%	
1	F90-F98	Behavioral and emotional disorders with onset usually occurring in childhood and adolescence	11,832	2.20%	0.02
2			3,493	2.50%	
1	F20-F29	Schizophrenia, schizotypal, delusional, and other non-mood psychotic disorders	2,125	0.40%	0.052
2			1,110	0.80%	
1	Z81	Family history of mental and behavioral disorders	3,296	0.60%	0.012
2			993	0.70%	
1	Z91.1	Patient's noncompliance with medical treatment and regimen	4,888	0.90%	0.028
2			4,789	3.40%	
1	Z91.4	Personal history of psychological trauma, not elsewhere classified	1,337	0.20%	0.018
2			482	0.30%	
1	Z56.0	Unemployment, unspecified	638	0.10%	0.029
2			340	0.20%	
1	Z65.1	Imprisonment and other incarceration	215	0.00%	0.01
2			87	0.10%	
1	F51.0	Insomnia not due to a substance or known physiological condition	2,759	0.50%	0.015
2			877	0.60%	

This table illustrates the initial baseline population demographic with respect to pre-existing diagnoses. Each diagnosis accounted for has a corresponding column with respective ICD-10 codes or code ranges.

Table 3
Demographics of cohorts after matching

Cohort	Demographics	Mean $\pm$ SD	Patients	% of Cohort	Std. Diff.
1	Current Age	38.4 $\pm$ 7.5	139,725	100%	0
2		38.4 $\pm$ 7.6	139,725	100%	
1	Age At Index	31.7 $\pm$ 6.2	139,725	100%	0.002
2		31.7 $\pm$ 6.4	139,725	100%	
1	White		66,455	47.60%	0.002
2			66,295	47.40%	
1	American Indian or Alaska Native		1,910	1.40%	0.005
2			1,833	1.30%	
1	Unknown Race		23,153	16.60%	0.004
2			23,339	16.70%	
1	Native Hawaiian or Other Pacific Islander		1,501	1.10%	0.004
2			1,565	1.10%	
1	Unknown Ethnicity		32,521	23.30%	0.007
2			32,946	23.60%	
1	Not Hispanic or Latino		72,088	51.60%	0.002
2			71,968	51.50%	
1	Hispanic or Latino		35,116	25.10%	0.005
2			34,811	24.90%	
1	Black or African American		29,278	21.00%	0.006
2			28,921	20.70%	
1	Other Race		8,934	6.40%	0.007
2			9,190	6.60%	
1	Asian		8,494	6.10%	0.003
2			8,528	6.10%	

This table illustrates the baseline population demographic represented in each cohort, after propensity-score matching was run, based on age, race, and ethnicity. Both cohorts 1 and 2 consisted of n = 139,725 patients after matching.

Table 4
Diagnoses of cohorts after matching

Cohort	ICD-10 Code	ICD-10 Diagnosis	Patients	% of Cohort	Std. Diff.
1	O00-008	Pregnancy with abortive outcome	12,473	8.90%	0.003
2			12,372	8.90%	
1	F40-F48	Anxiety, dissociative, stress-related, somatoform and other nonpsychotic mental disorders	19,568	14.00%	0.011
2			20,089	14.40%	
1	F30-F39	Mood [affective] disorders	18,059	12.90%	0.014
2			18,698	13.40%	
1	F10-F19	Mental and behavioral disorders due to psychoactive substance use	12,123	8.70%	0.009
2			12,493	8.90%	
1	F60-F69	Disorders of adult personality and behavior	1,078	0.80%	0.015
2			1,269	0.90%	
1	F90-F98	Behavioral and emotional disorders with onset usually occurring in childhood and adolescence	3,030	2.20%	0.02
2			3,456	2.50%	
1	F20-F29	Schizophrenia, schizotypal, delusional, and other non-mood psychotic disorders	881	0.60%	0.018
2			1,087	0.80%	
1	Z81	Family history of mental and behavioral disorders	915	0.70%	0.006
2			986	0.70%	
1	Z91.1	Patient's noncompliance with medical treatment and regimen	4,181	3.00%	0.012
2			4,464	3.20%	
1	Z91.4	Personal history of psychological trauma, not elsewhere classified	419	0.30%	0.007
2			477	0.30%	
1	Z56.0	Unemployment, unspecified	282	0.20%	0.007
2			331	0.20%	
1	Z65.1	Imprisonment and other incarceration	73	0.10%	0.004
2			86	0.10%	
1	F51.0	Insomnia not due to a substance or known physiological condition	773	0.60%	0.009
2			867	0.60%	

This table illustrates the baseline population demographic with respect to pre-existing diagnosis after propensity-score matching. After matching, all diagnosis variables were associated with a Std. Diff. of less than 0.1, demonstrating appropriate matching.

Depression

Within 270 days of diagnosis of diabetes mellitus complicating pregnancy, 5,536 of 121,400 patients with GDM received at least one depression diagnosis (risk of 0.046) compared to 7,164 of 120,331 patients with PGDM (risk of 0.060) (Table 5).

Across all other risk metrics including survival probability, HR, RD, RR, and OR, it was demonstrated that GDM patients had a significantly lower risk of developing depression (Table 6).

Table 5
Absolute risk outcomes for depression

Cohort	Patients in cohort	Patients with outcome	Risk	Survival Probability
Gestational DM	121,400	5,536	0.046	94.38%
Pregestational DM	120,331	7,164	0.06	92.65%

This table shows the absolute number, risk percent, and survival probabilities of being diagnosed with depressive episode, recurrent major depressive disorder, or postpartum depression for patients up to 270 days after diagnosis of gestational diabetes mellitus or pregestational diabetes mellitus. Survival probabilities were estimated using the Kaplan-Meier method as implemented in the TriNetX platform. Hazard ratios were calculated using Cox proportional hazards regression. A total of 18,325 GDM patients and 19,394 PGDM patients were excluded from the analysis because they had a prior diagnosis of depressive episode, recurrent major depressive disorder, or postpartum depression.

GDM, Gestational Diabetes Mellitus. PGDM, Pregestational Diabetes Mellitus

Table 6
Measures of risk for depression outcomes

Metric	Value	95% CI	z	p-value	Chi-squared	df
Risk Difference	-0.014	(-0.016, -0.012)	-15.353	0	-	-
Risk Ratio	0.766	(0.740, 0.793)	-	-	-	-
Odds Ratio	0.755	(0.728, 0.782)	-	-	-	-
Hazard Ratio	0.767	(0.740, 0.794)	-	0	81.152	1
Log-Rank Test	-	-	-	0	222.105	1

This table shows the risk differences, risk ratios, odds ratios, hazard ratios, and log-rank tests associated with diagnosis with depressive episode, recurrent major depressive disorder, or postpartum depression

for patients up to 270 days after diagnosis of gestational diabetes mellitus or pregestational diabetes mellitus. Risk difference was calculated as the absolute difference in cumulative incidence between GDM and PGDM patients, risk ratio as the ratio of cumulative incidence, and odds ratio from the corresponding 2 × 2 contingency table. Hazard ratios were estimated using a Cox proportional hazards regression model, while Kaplan-Meier survival curves were compared using the log-rank test. Corresponding z-statistics, chi-square statistics, P-values, and 95% confidence intervals are reported for the appropriate analyses to indicate the statistical significance and precision of each estimate.

GDM, Gestational Diabetes Mellitus. PGDM, Pregestational Diabetes Mellitus

Depressive episode

Within 270 days of diagnosis of diabetes mellitus complicating pregnancy, 4,078 of 122,881 patients with GDM experienced a depressive episode (risk of 0.033) compared to 5,865 of 121,738 patients with PGDM (risk of 0.048) (Table 7).

Across all other risk metrics including survival probability, HR, RD, RR, and OR, it was demonstrated that GDM patients had a significantly lower risk of experiencing a depressive episode (Table 8).

Table 7
Absolute risk outcomes for depressive episode

Cohort	Patients in cohort	Patients with outcome	Risk	Survival Probability
Gestational DM	122,881	4,078	0.033	95.97%
Pregestational DM	121,738	5,865	0.048	94.11%

This table shows the absolute number, risk percent, and survival probabilities of being diagnosed with depressive episode for patients up to 270 days after diagnosis of gestational diabetes mellitus or pregestational diabetes mellitus. Survival probabilities were estimated using the Kaplan-Meier method as implemented in the TriNetX platform. Hazard ratios were calculated using Cox proportional hazards regression. A total of 16,844 GDM patients and 17,987 PGDM patients were excluded from the analysis because they had a prior diagnosis of depressive episode.

GDM, Gestational Diabetes Mellitus. PGDM, Pregestational Diabetes Mellitus

Table 8
Measures of risk for depressive episode

Metric	Value	95% CI	z	p-value	Chi-squared	df
Risk Difference	-0.015	(-0.017, -0.013)	-18.773	0	-	-
Risk Ratio	0.689	(0.662, 0.716)	-	-	-	-
Odds Ratio	0.678	(0.651, 0.706)	-	-	-	-
Hazard Ratio	0.688	(0.661, 0.716)	-	0	43.416	1
Log-Rank Test	-	-	-	0	340.17	1

This table shows the risk differences, risk ratios, odds ratios, hazard ratios, and log-rank tests associated with diagnosis with depressive episode for patients up to 270 days after diagnosis of gestational diabetes mellitus or pregestational diabetes mellitus. Risk difference was calculated as the absolute difference in cumulative incidence between GDM and PGDM patients, risk ratio as the ratio of cumulative incidence, and odds ratio from the corresponding 2 × 2 contingency table. Hazard ratios were estimated using a Cox proportional hazards regression model, while Kaplan-Meier survival curves were compared using the log-rank test. Corresponding z-statistics, chi-square statistics, P-values, and 95% confidence intervals are reported for the appropriate analyses to indicate the statistical significance and precision of each estimate.

GDM, Gestational Diabetes Mellitus. PGDM, Pregestational Diabetes Mellitus

Recurrent major depressive disorder

Within 270 days of diagnosis of diabetes mellitus complicating pregnancy, 1,019 of 135,851 patients with GDM were diagnosed with recurrent MDD (risk of 0.008) compared to 1,364 of 135,548 patients with PGDM (risk of 0.010) (Table 9).

Across all other risk metrics including survival probability, HR, RD, RR, and OR, it was demonstrated that GDM patients had a significantly lower risk of being diagnosed with recurrent MDD (Table 10).

Table 9
Absolute risk outcomes for recurrent major depressive disorder

Cohort	Patients in cohort	Patients with outcome	Risk	Survival Probability
Gestational DM	135,851	1,019	0.008	99.06%
Pregestational DM	135,548	1,364	0.01	98.76%

This table shows the absolute number, risk percent, and survival probabilities of being diagnosed with recurrent major depressive disorder for patients up to 270 days after diagnosis of gestational diabetes mellitus or pregestational diabetes mellitus. Survival probabilities were estimated using the Kaplan-

Meier method as implemented in the TriNetX platform. Hazard ratios were calculated using Cox proportional hazards regression. A total of 3,874 GDM patients and 4,177 PGDM patients were excluded from the analysis because they had a prior diagnosis of recurrent MDD.

GDM, Gestational Diabetes Mellitus. PGDM, Pregestational Diabetes Mellitus. MDD, Major Depressive Disorder

Table 10
Measures of risk for recurrent major depressive disorder

Metric	Value	95% CI	z	p-value	Chi-squared	df
Risk Difference	-0.003	(-0.003, -0.002)	-7.153	0	-	-
Risk Ratio	0.745	(0.688, 0.808)	-	-	-	-
Odds Ratio	0.743	(0.685, 0.807)	-	-	-	-
Hazard Ratio	0.751	(0.692, 0.814)	-	0.338	0.919	1
Log-Rank Test	-	-	-	0	48.155	1

This table shows the risk differences, risk ratios, odds ratios, hazard ratios, and log-rank tests associated with diagnosis with recurrent major depressive disorder for patients up to 270 days after diagnosis of gestational diabetes mellitus or pregestational diabetes mellitus. Risk difference was calculated as the absolute difference in cumulative incidence between GDM and PGDM patients, risk ratio as the ratio of cumulative incidence, and odds ratio from the corresponding 2 × 2 contingency table. Hazard ratios were estimated using a Cox proportional hazards regression model, while Kaplan-Meier survival curves were compared using the log-rank test. Corresponding z-statistics, chi-square statistics, P-values, and 95% confidence intervals are reported for the appropriate analyses to indicate the statistical significance and precision of each estimate.

GDM, Gestational Diabetes Mellitus. PGDM, Pregestational Diabetes Mellitus

Postpartum depression

Within 270 days of diagnosis of diabetes mellitus complicating pregnancy, 3,171 of 138,505 patients with GDM were diagnosed with PPD (risk of 0.023) compared to 2,951 of 138,747 patients with PGDM (risk of 0.021) (Table 11).

Across all other risk metrics including survival probability, HR, RD, RR, and OR, it was demonstrated that GDM patients had a significantly higher risk of being diagnosed with PPD.

This was the only outcome for which GDM patients were shown to be at higher risk compared to PGDM patients. That being said, the risk metrics were modest in magnitude, with a RD of 0.002 (95% CI: 0.001, 0.003), RR of 1.076 (95% CI: 1.024, 1.131), OR of 1.078 (95% CI: 1.025, 1.134), and HR of 1.094 (95% CI: 1.041, 1.150) (Table 12).

Table 11
Absolute risk outcomes for postpartum depression

Cohort	Patients in cohort	Patients with outcome	Risk	Survival Probability
Gestational DM	138,505	3,171	0.023	97.14%
Pregestational DM	138,747	2,951	0.021	97.31%

This table shows the absolute number, risk percent, and survival probabilities of being diagnosed with postpartum depression for patients up to 270 days after diagnosis of gestational diabetes mellitus or pregestational diabetes mellitus. Survival probabilities were estimated using the Kaplan-Meier method as implemented in the TriNetX platform. Hazard ratios were calculated using Cox proportional hazards regression. A total of 1,220 GDM patients and 978 PGDM patients were excluded from the analysis because they had a prior diagnosis of PPD.

GDM, Gestational Diabetes Mellitus. PGDM, Pregestational Diabetes Mellitus. PPD, Postpartum Depression

Table 12
Measures of risk for postpartum depression

Metric	Value	95% CI	z	p-value	Chi-squared	df
Risk Difference	0.002	(0.001, 0.003)	2.912	0.004	-	-
Risk Ratio	1.076	(1.024, 1.131)	-	-	-	-
Odds Ratio	1.078	(1.025, 1.134)	-	-	-	-
Hazard Ratio	1.094	(1.041, 1.150)	-	0	334.404	1
Log-Rank Test	-	-	-	0	12.404	1

This table shows the risk differences, risk ratios, odds ratios, hazard ratios, and log-rank tests associated with diagnosis with postpartum depression for patients up to 270 days after diagnosis of gestational diabetes mellitus or pregestational diabetes mellitus. Risk difference was calculated as the absolute difference in cumulative incidence between GDM and PGDM patients, risk ratio as the ratio of cumulative incidence, and odds ratio from the corresponding 2 × 2 contingency table. Hazard ratios were estimated using a Cox proportional hazards regression model, while Kaplan-Meier survival curves were compared using the log-rank test. Corresponding z-statistics, chi-square statistics, P-values, and 95% confidence intervals are reported for the appropriate analyses to indicate the statistical significance and precision of each estimate.

GDM, Gestational Diabetes Mellitus. PGDM, Pregestational Diabetes Mellitus

Anxiety

Within 270 days of diagnosis of diabetes mellitus complicating pregnancy, 4,905 of 120,808 patients with GDM were diagnosed with an anxiety disorder (risk of 0.041) compared to 6,125 of 120,325 patients with PGDM (risk of 0.051) (Table 13).

Across all other risk metrics including survival probability, HR, RD, RR, and OR, it was demonstrated that GDM patients had a significantly lower risk of being diagnosed with an anxiety disorder (Table 14).

Table 13
Absolute risk outcomes for anxiety disorders

Cohort	Patients in cohort	Patients with outcome	Risk	Survival Probability
Gestational DM	120,808	4,905	0.041	95.03%
Pregestational DM	120,325	6,125	0.051	93.77%

This table shows the absolute number, risk percent, and survival probabilities of being diagnosed with an anxiety disorder for patients up to 270 days after diagnosis of gestational diabetes mellitus or pregestational diabetes mellitus. Survival probabilities were estimated using the Kaplan-Meier method as implemented in the TriNetX platform. Hazard ratios were calculated using Cox proportional hazards regression. A total of 4,905 GDM patients and 6,125 PGDM patients were excluded from the analysis because they had a prior diagnosis of an anxiety disorder.

GDM, Gestational Diabetes Mellitus. PGDM, Pregestational Diabetes Mellitus

Table 14
Measures of risk for postpartum depression

Metric	Value	95% CI	z	p-value	Chi-squared	df
Risk Difference	-0.01	(-0.012, -0.009)	-12.107	0	-	-
Risk Ratio	0.798	(0.769, 0.827)	-	-	-	-
Odds Ratio	0.789	(0.759, 0.820)	-	-	-	-
Hazard Ratio	0.8	(0.770, 0.830)	-	0	30.843	1
Log-Rank Test	-	-	-	0	136.662	1

This table shows the risk differences, risk ratios, odds ratios, hazard ratios, and log-rank tests associated with diagnosis with an anxiety disorder for patients up to 270 days after diagnosis of gestational diabetes mellitus or pregestational diabetes mellitus. Risk difference was calculated as the absolute difference in cumulative incidence between GDM and PGDM patients, risk ratio as the ratio of cumulative incidence, and odds ratio from the corresponding 2 × 2 contingency table. Hazard ratios were estimated using a Cox proportional hazards regression model, while Kaplan-Meier survival curves were compared using the log-rank test. Corresponding z-statistics, chi-square statistics, P-values, and 95% confidence

intervals are reported for the appropriate analyses to indicate the statistical significance and precision of each estimate.

GDM, Gestational Diabetes Mellitus. PGDM, Pregestational Diabetes Mellitus

Adjustment disorder

Within 270 days of diagnosis of diabetes mellitus complicating pregnancy, 992 of 136,629 patients with GDM were diagnosed with adjustment disorder (risk of 0.007) compared to 1,565 of 136,153 patients with PGDM (risk of 0.011) (Table 15).

Across all other risk metrics including survival probability, HR, RD, RR, and OR, it was demonstrated that GDM patients had a significantly lower risk of being diagnosed with adjustment disorder (Table 16).

Table 15
Absolute risk outcomes for adjustment disorder

Cohort	Patients in cohort	Patients with outcome	Risk	Survival Probability
Gestational DM	136,629	992	0.007	99.10%
Pregestational DM	136,153	1,565	0.011	98.59%

This table shows the absolute number, risk percent, and survival probabilities of being diagnosed with adjustment disorder for patients up to 270 days after diagnosis of gestational diabetes mellitus or pregestational diabetes mellitus. Survival probabilities were estimated using the Kaplan-Meier method as implemented in the TriNetX platform. Hazard ratios were calculated using Cox proportional hazards regression. A total of 3,096 GDM patients and 3,572 PGDM patients were excluded from the analysis because they had a prior diagnosis of adjustment disorder.

GDM, Gestational Diabetes Mellitus. PGDM, Pregestational Diabetes Mellitus

Table 16
Measures of risk for adjustment disorder

Metric	Value	95% CI	z	p-value	Chi-squared	df
Risk Difference	-0.004	(-0.005, -0.004)	-11.474	0	-	-
Risk Ratio	0.632	(0.584, 0.684)	-	-	-	-
Odds Ratio	0.629	(0.581, 0.681)	-	-	-	-
Hazard Ratio	0.636	(0.587, 0.688)	-	0.737	0.112	1
Log-Rank Test	-	-	-	0	126.664	1

This table shows the risk differences, risk ratios, odds ratios, hazard ratios, and log-rank tests associated with diagnosis with adjustment disorder for patients up to 270 days after diagnosis of gestational

diabetes mellitus or pregestational diabetes mellitus. Risk difference was calculated as the absolute difference in cumulative incidence between GDM and PGDM patients, risk ratio as the ratio of cumulative incidence, and odds ratio from the corresponding 2 × 2 contingency table. Hazard ratios were estimated using a Cox proportional hazards regression model, while Kaplan-Meier survival curves were compared using the log-rank test. Corresponding z-statistics, chi-square statistics, P-values, and 95% confidence intervals are reported for the appropriate analyses to indicate the statistical significance and precision of each estimate.

GDM, Gestational Diabetes Mellitus. PGDM, Pregestational Diabetes Mellitus

Substance use

Within 270 days of diagnosis of diabetes mellitus complicating pregnancy, 2,022 of 125,251 patients with GDM were diagnosed with substance use (risk of 0.016) compared to 2,992 of 123,635 patients with PGDM (risk of 0.024) (Table 17).

Across all other risk metrics including survival probability, HR, RD, RR, and OR, it was demonstrated that GDM patients had a significantly lower risk of being diagnosed with substance use (Table 18).

Table 17
Absolute risk outcomes for substance use

Cohort	Patients in cohort	Patients with outcome	Risk	Survival Probability
Gestational DM	125,251	2,022	0.016	98.08%
Pregestational DM	123,635	2,992	0.024	97.10%

This table shows the absolute number, risk percent, and survival probabilities of being diagnosed with a substance use disorder, or pregnancy, childbirth, or puerperium complicated by tobacco use, alcohol use, or other drug use up to 270 days after diagnosis of gestational diabetes mellitus or pregestational diabetes mellitus. Survival probabilities were estimated using the Kaplan-Meier method as implemented in the TriNetX platform. Hazard ratios were calculated using Cox proportional hazards regression. A total of 14,474 GDM patients and 16,090 PGDM patients were excluded from the analysis because they had a prior diagnosis of substance use.

GDM, Gestational Diabetes Mellitus. PGDM, Pregestational Diabetes Mellitus

Table 18
Measures of risk for substance use

Metric	Value	95% CI	z	p-value	Chi-squared	df
Risk Difference	-0.008	(-0.009, -0.007)	-14.304	0	-	-
Risk Ratio	0.667	(0.631, 0.705)	-	-	-	-
Odds Ratio	0.662	(0.625, 0.700)	-	-	-	-
Hazard Ratio	0.667	(0.631, 0.706)	-	0	19.357	1
Log-Rank Test	-	-	-	0	200.424	1

This table shows the risk differences, risk ratios, odds ratios, hazard ratios, and log-rank tests associated with diagnosis with a substance use disorder, or pregnancy, childbirth, or puerperium complicated by tobacco use, alcohol use, or other drug use for patients up to 270 days after diagnosis of gestational diabetes mellitus or pregestational diabetes mellitus. Risk difference was calculated as the absolute difference in cumulative incidence between GDM and PGDM patients, risk ratio as the ratio of cumulative incidence, and odds ratio from the corresponding 2×2 contingency table. Hazard ratios were estimated using a Cox proportional hazards regression model, while Kaplan-Meier survival curves were compared using the log-rank test. Corresponding z-statistics, chi-square statistics, P-values, and 95% confidence intervals are reported for the appropriate analyses to indicate the statistical significance and precision of each estimate.

GDM, Gestational Diabetes Mellitus. PGDM, Pregestational Diabetes Mellitus

Discussion and Conclusions

It was found that patients with GDM generally demonstrated a significantly lower risk of developing psychiatric complications compared with patients with PGDM within 270 days of diagnosis of diabetes mellitus complicating pregnancy. These complications included risk of a depressive episode, recurrent MDD, anxiety disorder, adjustment disorder, and substance use. To note is that in contrast to all other outcomes measured, the risk of PPD was unexpectedly higher in the GDM patients when compared with patients with PGDM, albeit with a very small magnitude in difference. Except for this PPD outcome, the rest of the findings in this paper are consistent with both the cross-sectional study of 350 women (Salimi et al. 2024) and prospective study of 80 mothers (Aycan and Aksu 2025), which both found a significantly lower risk of depression and anxiety in patients with GDM compared to those with PGDM.

The explanation for why patients with GDM have lower risks for mood and substance complications compared with patients with PGDM can potentially be explained from a mechanistic, medical, and psychological standpoint. If, as Alzoubi et al. hypothesizes, the comorbidity between diabetes and depression are due to the effects of the inflammatory marker CRP, changes in the hypothalamic-pituitary axis including the actions of cortisol and adrenocorticotrophic hormone, or interaction between cortisol

and insulin resistance, then PGDM patients could have a higher risk of depression simply in relation to the comparatively longer systemic influence of these physiological factors when compared with GDM patients, who only acquired their diabetes mellitus diagnosis during the immediate pregnancy and have yet to be under chronic influence of aforementioned inflammatory and hormonal changes. However, the relationship between duration of these changes and the extent of depression has not been thoroughly studied (Fischer and Morales-Suárez-Varela 2023). From a medical and psychological standpoint, PGDM patients have a longer proportion of life lived with diabetes mellitus, so they may be under a greater cumulative disease burden related to complications and management of diabetes mellitus. It's known that PGDM when compared with GDM is associated with increased risk of medical complications such as diabetic retinopathy and nephropathy. In combination with the increased risk of complicated pregnancy such as due to a hypertension disorder, uteroplacental insufficiency, or preterm birth, it is reasonable to suggest that the comparatively higher medical burden PGDM patients experience may contribute to a higher psychological burden as well, resulting in an increased risk of a psychiatric complication or substance use associated with the pregnancy (ACOG 2018).

A notable exception to this paper's trend of lower risk of psychiatric outcomes in GDM patients is that patients with GDM were found to have a higher risk of PPD when compared with patients with PGDM. A plausible explanation for why a patient with GDM may have an increased risk of a mood complication is that GDM represents a novel diagnosis in a patient who has not been previously familiarized with the associated reality, management, and complications, in contrast to a patient with PGDM who may already be familiar with managing diabetes mellitus (Rath and MV 2025). However, although risk metrics regarding the PPD outcome were statistically significant, these findings should be interpreted in the context of their magnitudes, which were relatively small. It is therefore unclear whether extensive interpretation regarding the PPD outcome can be derived from these results, though further investigation may be warranted in future studies.

Regarding the current guidelines recommending routine perinatal mental health and substance use screening for all pregnant and postpartum patients, the findings of this paper further suggest that the higher rates of mood and substance use outcomes observed among patients with PGDM may warrant heightened clinical awareness of mental health symptoms in this population and consideration of appropriate counseling and follow-up. Patients whose pregnancies are complicated with diabetes mellitus and who have a pre-existing history of depression may require particularly close monitoring for recurrent or persistent depressive symptoms, whether their diabetes mellitus was diagnosed prior to or during the pregnancy.

One main limitation of this study is that the variables involved in propensity score matching, defining cohorts, and defining outcomes were restricted to those provided within the TriNetX database, primarily through ICD-10 codes. Thus, there was an inability to capture or design around specific modular signs and symptoms of depression, anxiety, and substance use. The differences in how clinicians arrive at diagnoses or chart outcomes also cannot be accounted for, nor can be fully captured the potential differences in healthcare utilization or healthcare access between patients with GDM and patients with

PGDM. The data itself also does not provide insight into explaining why GDM and PGDM patients may have differential outcomes, only that there is a difference.

A future study could investigate the difference in psychiatric outcomes at different timepoints after the diagnosis of GDM or PGDM to see if the difference persists long-term. Also warranted is further investigation into the reasons why differential outcomes are observed, such as whether there are differences in healthcare utilization or access between these two patient populations, or broadly which parts of diabetes mellitus contribute the most psychological burden to patients and pregnant patients. Such studies could elucidate specific and targeted ways in which clinicians can best support the mental health of patients with these challenging diagnoses outside of general screening and counseling recommendations.

Declarations

Author Contribution

H.B. devised the research question, conducted the literature search, and wrote the introduction, methods, and discussion. F.R. conducted the data collection and analysis and wrote the results and prepared the tables. E.E. assisted with editing the manuscript. All authors reviewed the manuscript.

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