

Prenatal Depression Correlated with Increased Autism Risk in Children

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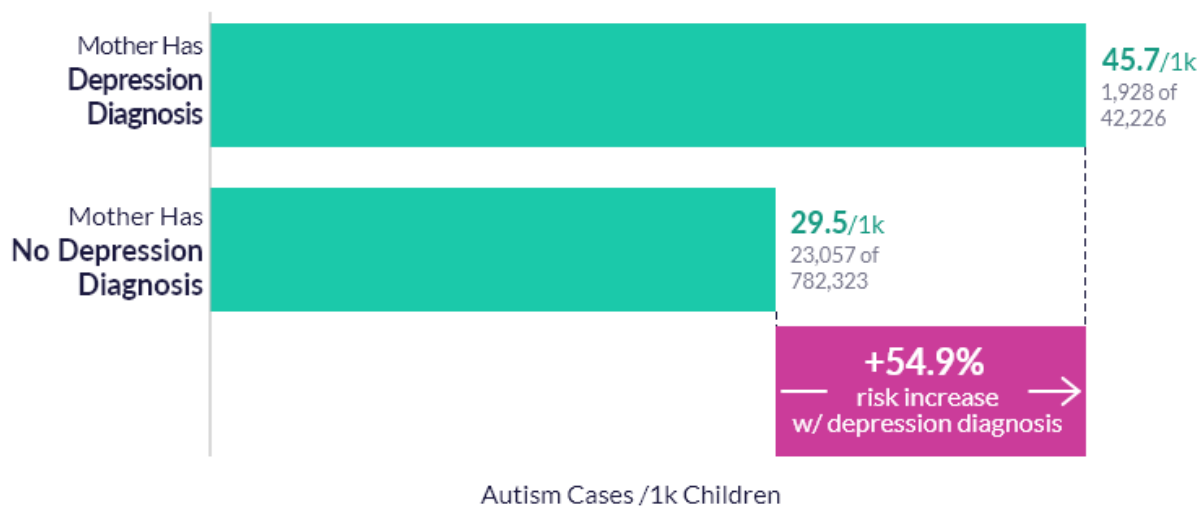
Key Findings:

- Babies born to mothers with depression but not prescribed antidepressants are 54.9% more likely to be diagnosed with an autism spectrum disorder (ASD) than those born to mothers without depression.
- Antidepressant prescriptions during pregnancy may slightly increase the risk of the child being diagnosed with ASD compared to children born to mothers who did not have an antidepressant prescription. However, this increase may be the result of confounding factors, such as severity of maternal depression.

Both antidepressant use and autism spectrum disorder (ASD) diagnoses have increased over the last several decades.^{1,2} The coincidental timing of these increases have led to the hypothesis that antidepressant use during pregnancy may be related to the increase in ASD diagnoses. Some previous studies have shown a possible causal link while others have not.³⁻⁵

To better understand whether antidepressant use during pregnancy increases the risk of children developing ASD, we first examined the effect of prenatal maternal depression on the development of ASD in 824,549 children whose mother did not have an antidepressant prescription during pregnancy. We compared the rate of ASD between those born to mothers with and without depression, as shown in Figure 1. Children whose mother had depression were 54.9% more likely to be diagnosed with ASD than those whose mother did not have depression during pregnancy. We did not assess how behavioral, environmental, or genetic factors surrounding maternal depression may affect the risk of a child developing ASD as part of this study.

Autism Rate for Children Born to Mothers with No Antidepressant Prescription



"Autism Rate for Children Born to Mothers with No Antidepressant Prescription," 2023. EpicResearch.org

Figure 1. Rate of ASD in children born to mothers who did not have an antidepressant prescription during pregnancy stratified by whether the mother had prenatal depression. The difference between the two groups represents the relative risk.

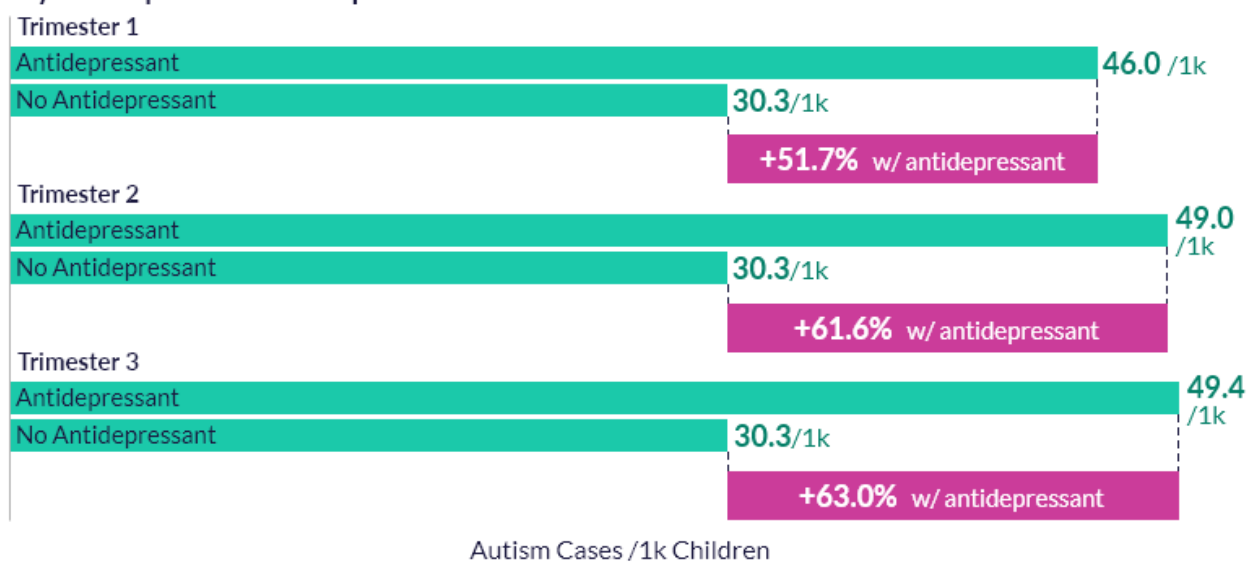
We then examined how the use of antidepressants during pregnancy affects the risk of ASD diagnosis compared to the risk from depression alone, as shown in Figure 2. We studied 50,976 children who were born to mothers who had an active prescription for antidepressants at some point during pregnancy and compared them with the 824,549 children who were born to mothers who did not have an antidepressant prescription during pregnancy. While there is a slightly higher risk for children whose mother was prescribed antidepressants during the second or third trimesters, this increase is not statistically significant. These increases may be caused by confounding factors, such as severity of depression, rather than an effect of the medication.

Autism Risk by Maternal Depression Diagnosis and Antidepressant Prescriptions

By Depression Diagnosis (No Antidepressants)



By Antidepressant Prescription



"Autism Risk by Maternal Depression Diagnosis and Antidepressant Prescription," 2023. EpicResearch.org

Figure 2. The diagnosis rates and relative risk of developing ASD based on trimester of prenatal antidepressant exposure. Children whose mother had an antidepressant prescription during multiple trimesters are included in all trimesters during which the prescription was active.

Comparisons between different classes of antidepressants, such as selective serotonin reuptake inhibitors (SSRIs) and selective norepinephrine reuptake inhibitors (SNRIs) did not show significant differences in ASD rates. Comparisons between siblings where the mother had an antidepressant prescription during one pregnancy but not the other also showed no significant difference. These findings are consistent with some previous research that showed any effect of antidepressant use during pregnancy on the development of ASD is small.⁵

These data come from Cosmos, a HIPAA-defined Limited Data Set of more than 190 million patients from 203 Epic organizations including 1,176 hospitals and more than 25,300 clinics, serving patients in 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.

References

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Data Definitions

Term	Definition
Study period	3/20/2005 – 12/31/2022
Study population	Patients born 3/20/2005 - 12/28/2017 and at least five years old who have a linked mother in Cosmos and at least one encounter after their fifth birthday
Mothers with depression	Mothers whose child is part of the study population who had at least one prenatal depression diagnosis
Autism diagnosis	A diagnosis with ICD-10-CM code F84.0
Prenatal depression diagnosis	A diagnosis with ICD-10-CM codes F32*, F33*, or F39* in the mother prior to childbirth
SSRIs	Medication with a pharmaceutical class or subclass of “Selective Serotonin Reuptake Inhibitors”
SNRIs	Medication with a pharmaceutical class or subclass of “Selective Norepinephrine Reuptake Inhibitors”
Antidepressant medications	SSRIs, SNRIs, and medications with a pharmaceutical class or subclass of Antidepressant Tricyclics, Benzodiazepine, Phenothiazine, or Serotonin-2 Agonist-Reuptake Inhibitors

Table 1: Relative Risk of ASD for Children Born to Mothers with No Antidepressant Prescription

	Autism	No autism	Autism %
Diagnosed with depression	1,928	40,298	4.57%
Not diagnosed	23,057	759,266	2.95%
Increased Risk:			54.9%
	<i>P-value: <0.0001</i>		<i>Confidence Interval: [48.0%, 62.1%]</i>

Table 2a: Relative Risk of ASD for Children Born to Mothers with an Antidepressant Prescription During the First Trimester

	Autism	No autism	Autism %
Medication prescribed	1,775	36,839	4.60%
Not prescribed	24,985	799,564	3.03%
Increased Risk:			51.7%
	<i>P-value: <0.0001</i>		<i>Confidence Interval: [44.7%, 59.0%]</i>

Table 2b: Relative Risk of ASD for Children Born to Mothers with an Antidepressant Prescription During the Second Trimester

	Autism	No autism	Autism %
Medication prescribed	1,550	30,110	4.90%
Not prescribed	24,985	799,564	3.03%
Increased Risk:			61.6%
	<i>P-value: <0.0001</i>		<i>Confidence Interval: [53.7%, 69.9%]</i>

Table 2c: Relative Risk of ASD for Children Born to Mothers with an Antidepressant Prescription During the Third Trimester

	Autism	No autism	Autism %
Medication prescribed	1,664	32,023	4.94%
Not prescribed	24,985	799,564	3.03%
Increased Risk:			63.0%
	<i>P-value: <0.0001</i>		<i>Confidence Interval: [55.3%, 71.1%]</i>