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Q: What are the key findings of this study?

D’Onofrio: Our study suggests that some of the risks associated with maternal antidepressant use during the first trimester of pregnancy for children may not be as severe as previously suggested.

We used several research designs to help understand the effects of antidepressant exposure early in pregnancy independent of the influence of factors that contribute to the use of antidepressants in the first place, such as maternal depression or anxiety.

We found that after accounting for other factors, exposure to antidepressants during the first trimester of pregnancy was associated with a slightly higher risk for preterm birth (i.e., before 37 weeks of gestation) but was not associated with risk for poor fetal growth, autism spectrum disorder, or attention deficit hyperactivity disorder (ADHD).

Q: How do these results differ from previous studies on the effect of taking antidepressants during pregnancy?

Previous studies have found that prenatal exposure to antidepressants is associated with adverse birth outcomes, such as preterm birth and low fetal growth. Furthermore, previous studies have found that children exposed to antidepressants during pregnancy were more likely to be diagnosed with autism spectrum disorder or ADHD.

Our findings suggest that these previous studies may not have adequately accounted for other explanations for the observed associations. Thus, these studies may have overestimated the risk of mothers’ antidepressant use during the first trimester of pregnancy.

Q: What are some important ways this study’s methods differ from previous studies on this subject?

- First, our study is one of the largest studies on this topic, which enabled us to study rare-but-serious outcomes that are associated with significant burdens and costs.
- Second, we were able to assess antidepressant use based both upon when women reported using these medications and when they were actually provided the medication through a pharmacy, whereas previous studies typically rely on only one of these measures.

- Third, and most importantly, our study used several methods to account for alternative explanations for the associations between antidepressant use and problems in children. Specifically, while most previous studies relied on the use of measured variables only, we also used three additional approaches that were able to more rigorously test alternative explanations for the associations. This is important because families with mothers who use antidepressants during pregnancy differ in numerous ways from families with mothers who do not use antidepressants during pregnancy.

Q: How does this provide a more accurate picture of the effect of taking antidepressants during pregnancy?

Notably, mothers who use antidepressants during pregnancy are more likely to have depression than mothers who do not use these medications. Thus, it is possible that depression, stress, or other family factors could explain why children exposed to antidepressants during pregnancy have higher risk of some adverse outcomes.

Previous studies generally match children exposed or unexposed to antidepressants in the womb with respect to measured maternal characteristics, such as age and socioeconomic status. Our study was able to match exposed and unexposed children on specific measured characteristics of both the mothers and the fathers.

Importantly, we used three additional methods to test alternative explanations. First, we compared siblings where mothers had used antidepressants in some pregnancies but not others. Second, we compared children of women who used antidepressants before pregnancy but not during or after pregnancy to children of women who used antidepressants during the first trimester of pregnancy. And, third, we assessed the risk of the outcomes among children of fathers who took antidepressants during the first trimester of pregnancy.

Each of these designs provides additional information that can't be obtained from merely matching individuals on measured characteristics.

Q: This study measures the effect of depression medications known as Selective Serotonin Reuptake Inhibitors, or SSRIs. Why focus on these drugs, and what are some common SSRIs?

SSRIs are the most commonly prescribed class of antidepressants in the study population. In our sample, over 80 percent of the children exposed to antidepressants during pregnancy were specifically exposed to SSRIs. Commonly used SSRIs include sertraline (e.g., Zoloft), citalopram (e.g., Celexa), and fluoxetine (e.g., Prozac).

Q: Why is it significant that you saw higher rates of ADHD, Autism and poor fetal growth in the children of both fathers who took antidepressants and mothers who took these medications before (but not during) pregnancy?

We found that fetal growth problems, autism spectrum disorder or attention-deficient

hyperactivity disorder were equally likely in the children of mothers who used antidepressants before – but not during or after pregnancy – as those who only used the drugs during the first trimester of pregnancy. These findings suggest that factors related to mothers' antidepressant use around the time of pregnancy may be responsible for the increased risk of these outcomes rather than a specific effect of exposure during pregnancy.

We also found that fathers' antidepressant use during the first trimester of pregnancy was associated with autism spectrum disorder and ADHD. These findings provide further support that family factors, rather than the specific exposure during pregnancy, explain associations between maternal antidepressant use during pregnancy and autism spectrum disorder and ADHD.

Q: This study examines parents' use of antidepressants and their effects on children in Sweden. How do the results apply to people in the United States?

While we don't know if the results would apply to people in other countries, the general associations we observe in this population are comparable to findings from studies conducted on samples from different countries. Additionally, it is unlikely that biological mechanisms of antidepressants would differ across countries.

Q: What are some of the risks associated with ceasing depression medication during pregnancy?

Untreated maternal depression is associated with psychological problems for mothers, poorer maternal health practices during pregnancy, and adverse birth and neurodevelopmental problems in the children. Organizations including the American Congress of Obstetricians and Gynecologists, American Academy of Pediatrics, and the U.S. Prevention Services Task Force have called for routine screening of pregnant women and coordinated integrative treatment of depression.

While our study focused on understanding the risks associated with antidepressant use during the first trimester of pregnancy, it is important to stress that there are also risks associated with not treating depression. Thus, women should not discontinue their medication treatment before consulting with their health care provider.

Q: How do doctors balance the risks of depression versus the risk of complications from antidepressants during pregnancy?

It can be difficult for patients and doctors to weigh the risks and benefits of antidepressant use during pregnancy. Our study suggests that the risks associated with use in early pregnancy may be smaller than suggested by previous studies.

Additionally, we want to emphasize that maternal depression is associated with problems in

both mothers and their children. There are a variety of effective treatment options for depression, including antidepressant medication, as well as evidence-based psychotherapy.

Q: What advice would you give mothers taking antidepressants who are considering getting pregnant?

Although our study suggests that antidepressant exposure during the first trimester of pregnancy may result in fewer adverse outcomes than previously thought, it did not assess associations with second- and third-trimester antidepressant exposure, and no one study can definitively determine the safety of a medication. Therefore, women on antidepressants considering getting pregnant should discuss the topic with their doctors.

Additionally, our findings suggest that the increased occurrence of adverse outcomes among the children of women who use antidepressants during pregnancy may be due to the underlying conditions for which the medications are prescribed. Therefore, doctors should screen for and, if necessary, treat maternal depression during pregnancy.