How to Read a Research Paper: An Exercise Using a Study on Continuation vs. Discontinuation of Antidepressants during Pregnancy

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ABSTRACT

The ability to critically read a research paper is a skill that all postgraduate students and academicians require because the findings of a study must be interpreted in the context of its strengths and limitations. This article summarizes a recent study on continuation vs. discontinuation of antidepressants during pregnancy; preterm birth and low-birth weight were the outcomes of interest. The strengths and limitations of the study are considered, as are the best and worst case scenarios related to antidepressant use during pregnancy. It is hoped that this exercise will increase the reader's awareness of statistical and methodological issues that emerge when a study is critically examined.

Key words: *Antidepressants, confounding variables, depression, how to read a research paper, pregnancy*

It takes much knowledge of the field and the knowledge of statistics and research methods to know how to read a journal article critically; yet, beginnings can be made with a little assistance. This article illustrates how to critically read a research paper, using a study[1] on continuation vs. discontinuation of antidepressants during pregnancy as an example. Readers are recommended to read this open access study[1] first so that the rest of this article will be understood in context.

Observational studies show that antidepressant use during pregnancy is associated with diverse adverse gestational outcomes. It is not known whether the adverse outcomes are because of the antidepressants, the illness for which the antidepressant was prescribed, or confounding variables[2] that cannot be controlled for because patients were not randomized to antidepressant vs. control groups. Because randomized controlled trials (RCTs) are considered unethical during pregnancy, some researchers have compared depressed women who did vs. did not receive antidepressant drugs during pregnancy. However, because women who do vs. do not require antidepressants differ in many ways, other researchers have used propensity score matching[3] to pair treated and untreated women who had an equal baseline probability of being treated with an antidepressant; this approximates an RCT situation.

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The study, and what it found

Cantarutti *et al*.[1] presented a different approach. They described a population-based study of 384,673 mother-infant pairs identified from a healthcare database in Italy. There were 3295 women who had received an antidepressant during pregnancy (users), 6548 women who had received an antidepressant during the 9 months preceding pregnancy but not during pregnancy (previous users), and 374,830 women who had not received antidepressant treatment either during pregnancy or during the preceding 9 months (nonusers).

Women who had previous or current antidepressant exposure were older, less educated, less likely to have married, and more likely to have medical comorbidities. These differences were adjusted for in regression analyses.

Preterm birth (<37 weeks gestation) and low-birth weight (<2.5 kg) were identified in 5.2% and 5.1% of pregnancies, respectively. Relative to *nonusers*, antidepressant users were 20% (95% CI, 10–40%) more likely to have a preterm delivery. However, relative to *previous users*, this risk was not significantly increased. Further, relative to antidepressant *nonusers*, antidepressant users were 20% (95% CI, 10–40%) more likely to deliver a low-birth weight infant. However, relative to *previous users*, this risk was again not significantly increased. Importantly, the risk of both outcomes was raised (by 10%) at a borderline line of significance (95% CI, 0% – 20 to 30%) in *previous users* relative to *nonusers*. The findings were closely similar when selective serotonin reuptake inhibitors and other antidepressants were analyzed separately.

The authors reasonably interpreted these findings to indicate that it is depression, for which the antidepressants were prescribed, that must have driven the risk of preterm birth and low-birth weight, and not antidepressant drug use during pregnancy, by itself.

DISCUSSION

The reader is now asked to think about the study. What are its strengths and limitations? One strength is the large sample with a reasonably large number of women in each group. Another strength is the research design with *previous users* as controls; identification of adverse outcomes in *previous users* allowed the inference that the indication for antidepressants, rather than antidepressant use, drove the risk of adverse gestational outcomes.

However, statistical and methodological limitations were many. The authors did not adjust birth weight for gestational age; low-birth weight may merely have been a function of preterm birth, explaining why the values for the two outcomes were almost identical. They did not examine either effects of antidepressant dose or trimester during which the antidepressant exposure took place. They did not control for known confounds such as smoking, alcohol use, illicit substance use, and other medication use. For greater precision, they could have analyzed time of delivery and birth weight as continuous rather than as categorical variables. Finally, their propensity matching could not have adjusted for inadequately measured, unmeasured, and unknown confounds, though it was better than no matching, at all.

As a general note, the authors could not know whether women who were dispensed with antidepressant medications actually took the medications; however, this is a known limitation of studies with this research design. Regrettably, the authors did not examine other pregnancy outcomes such as maternal complications and major congenital malformations; these outcomes would surely have been available in the database.

At best, this study suggests that antidepressant exposure is a marker for adverse gestational outcomes and not the cause of the adverse outcomes. At worst, the study shows that the antidepressant-associated absolute risk is very small. If the absolute risk of preterm birth and low-birth weight is approximately 5% each (as reported in the study), and if antidepressant exposure increases the risk of each by 20% (as reported in the study), then the absolute risk after antidepressant exposure will be approximately 6%. In other words, the absolute risk is increased by 1%, yielding a number needed to harm[4] value of 100. This worst case scenario risk should be weighed against the potential benefits associated with effective, antidepressant-based treatment of depression during pregnancy.

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Conflicts of interest

There are no conflicts of interest.

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