

Data Studio

1:30–3:00pm, Wednesday, January 8, 2020

Conference Room X399, Medical School Office Building, 1265 Welch Road, Stanford, CA

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Title: Association between Paternal Medication Use Prior to Conception and Adverse Birth Outcomes

Summary:

Congenital birth defects affect 3% of births in the United States. Several parental factors, such as smoking and increasing age, been shown to modify the incidence. Given the longer and more obvious influence a mother has on gestation, most risk factors for birth defects have focused on women. However, as the age of paternity at conception increases around the developed world, paternal comorbidities increase. With that, more prospective fathers are exposed to prescription medications during spermatogenesis cycles, which lead to live births. Our ability to adequately counsel patients regarding paternal exposures to medicines is limited by sparse data. Investigators have performed studies on limited numbers of patients exposed to certain medications strongly suspected of impacting sperm DNA (e.g. anti-neoplastics). Some common medications, such as antidepressants, may affect the DNA integrity of sperm. To date, large studies of diverse medications are rare despite the crucial role the sperm contributes to fertilization and the first few days of development. This project explores the association between paternal medication use and adverse birth outcomes, including congenital birth defects. Using unique national identification numbers, we will link Danish demographic, birth, health, and medication registries for the approximately 1.3 million births from 1995 to 2015. Next, we will determine if individual medications or classes of medications with known spermatogenic effects taken by fathers just before conception are associated with a higher risk of congenital birth defects. Such findings are likely to have wide implications for couples attempting to conceive and provide guidance for the safety of medications during reproductive efforts.

Questions:

The statistical challenge of this project is to come as close to causation as possible. The aim is to establish that medication causes malformations. A challenge is that we do not have the indication for which the medication was prescribed. We do have diagnoses. How do we know if malformations are caused by medication taken by the father, caused by the father's illness for which the medication has been prescribed, or if the malformations are related to the father's constitution such that prescription of medication is more likely? We have data about malformations. These are organized in a hierarchy, some being more important than others. Possible outcome variables are: the presence of a malformation or not (binary); the number of malformations (count); some measure of malformation severity (numeric).

We can observe associations, but information on important confounders is missing. We therefore need to model as carefully as possible the potential effect of confounders. Birth defects are higher with premature births. Prematurity may also be associated with paternal comorbidity and medication use. There are also various other important confounders, some of which are measured, some of which are not. For example, we have smoking behavior of the mother, but not of the father.

For more information about Data Studio:

<https://med.stanford.edu/dbds/programs/data-studio.html>