



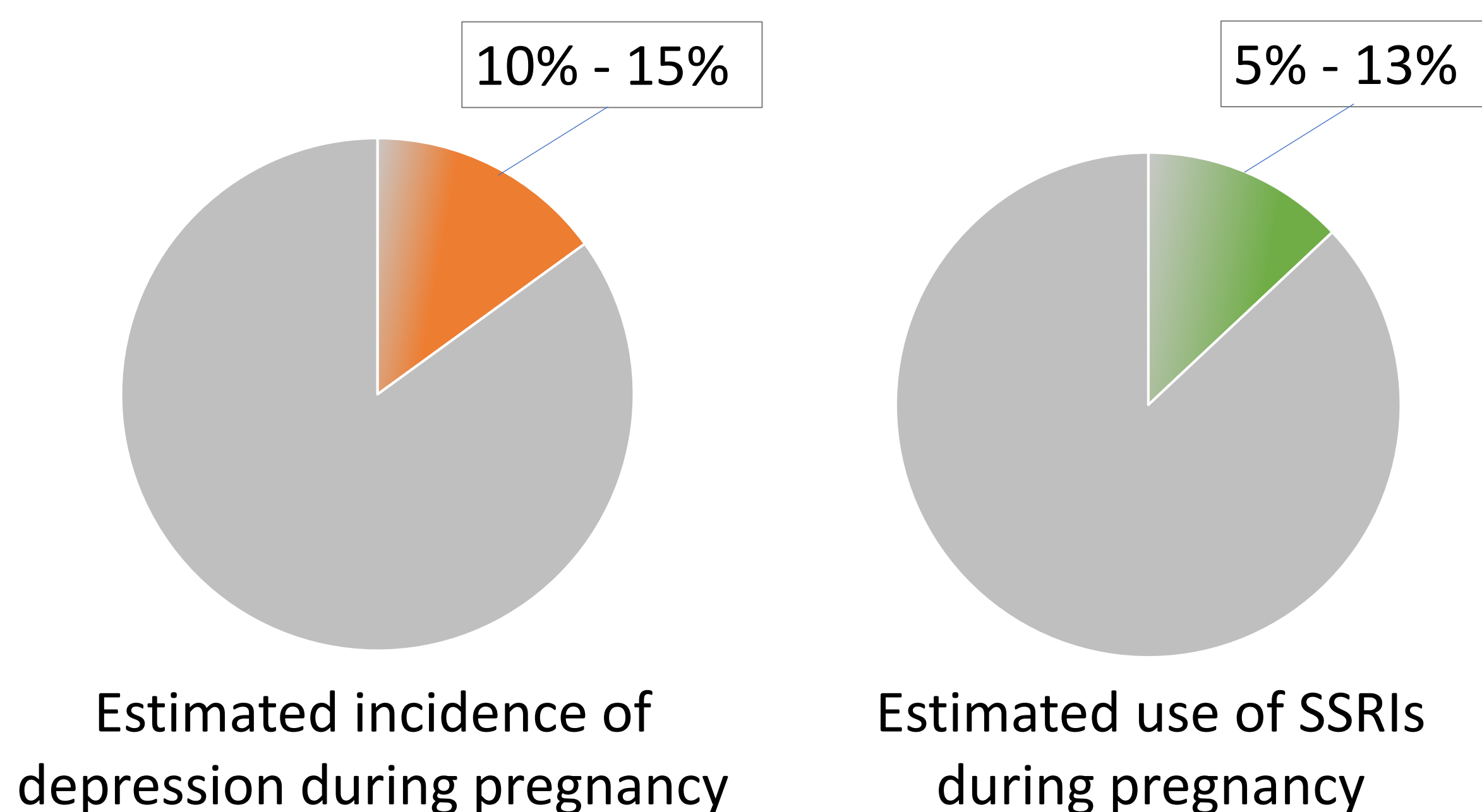
Neurobehavioral effects of prenatal SSRI exposure

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Background

- About 10-15% of people experience depression during pregnancy.¹
- The use of antidepressant medication during pregnancy is estimated at between 5%-13%, namely Selective Serotonin Reuptake Inhibitors (SSRIs).²
- Research in this area has focused on adverse neonatal outcomes, which are generally short-lived and resemble either withdrawal or toxicity symptoms observed in adults.
- There is limited understanding of the long-term effects of prenatal SSRI use on children's development and behavior.



SSRIs and the Fetal Environment

- SSRIs can readily cross the placenta, which may increase serotonin in the fetal environment.^{3,4}
- Abnormally high serotonin levels during the fetal stage may produce negative feedback loops that could reduce long-term serotonin sensitivity.
- This may be especially important for areas of the brain known to contain high concentrations of serotonin receptors, such as the amygdala and insula.^{5,6}

Neural/Behavioral Outcomes

- An early study found no differences on key developmental indicators between SSRI-exposed children and controls.⁷
- More recent studies document a number of changes in neurodevelopment associated with prenatal exposure to SSRIs, including:
 - An increase in connectivity between the right amygdala and the right insula, which may result in changes to fear circuitry.¹⁰
 - Alterations in language development.⁹
 - Hyperconnectivity in regions within the auditory network in the temporal cortex and parietal lobe.⁸

Parental Depression

- Disentangling the effects of SSRIs from the underlying pathology, parental depression, is a major challenge in this work.
- Parental depression can extend far beyond the pre/perinatal period and have substantial effects on the child's development, which complicates efforts to isolate the effects of individual variables.¹³

Evidence for the role of depression

- MRI data in infants with prenatal depression exposure has found atypical connectivity between the amygdala and prefrontal cortex, suggesting that neural physiology may be altered by exposure to depression alone.¹²
- A study comparing mood disorder-exposed neonates with SSRI-exposed neonates suggests that DNA methylation in the fetus is affected more by the parent's depression/anxiety than by use of SSRIs.¹¹
- A 3-year longitudinal study found effects of both parental mood disturbances and prenatal SSRI exposure on behavioral changes in children.¹⁴

Future Direction

- More research in this domain can provide critical information to clinicians and patients to help inform decisions that support the health of both the pregnant parent and the fetus.
- Future research should focus on long-term follow-ups with children to assess behaviors influenced by serotonergic processes, such as fear circuitry, to understand how long-lasting these effects may be.
- One such study is currently underway here at Columbia's DAN Lab, following up with children who were exposed to depression and/or SSRIs in the womb to assess cognitive/behavioral development and neural connectivity.



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