FDA's Private, Virtual Listening Session With Antidepressant Petitioners

Overview of Petition to Require Balanced, Evidence-Based Pregnancy Warnings for Serotonin Reuptake Inhibitors (SRIs)
FDA-2025-P-6094

March 23, 2026

Azza AbuDagga, Ph.D.
Public Citizen's Health Research

Conflicts of Interest Disclosure

We have no financial or other conflicts of interest to disclose.

SRIs With Mental-Health Indications

Generic Names	Brand Names
Serotonin-norepinephrine reuptake inhibitors (SNRIs)	
desvenlafaxine	PRISTIQ
duloxetine	DRIZALMA SPRINKLE
levomilnacipran	FETZIMA
venlafaxine	EFFEXOR XR
Selective serotonin reuptake inhibitors (SSRIs)	
citalopram	CELEXA
escitalopram	LEXAPRO
fluoxetine	PROZAC, SYMBYAX
fluvoxamine	LUVOX
paroxetine	PAXIL
sertraline	ZOLOFT
vilazodone	VIIBRYD
vortioxetine	TRINTELLIX

Requested Enhanced Warnings Re. Poor Neonatal Adaptation Syndrome

- Poor neonatal adaptation syndrome (PNAS)

Use of SNRIs and SSRIs (including x drug) in the third trimester of pregnancy can cause PNAS in about 30% of exposed neonates. Signs of PNAS include apnea, respiratory distress, cyanosis, seizures, temperature instability, feeding difficulty, vomiting, hypoglycemia, change in muscle tone, hyperreflexia, tremors, jitteriness, irritability, and constant crying. These signs can occur immediately after birth.

There is evidence that SRI-induced PNAS may be dose-related. Unlike serotonin reuptake inhibitor withdrawal syndrome in adults, PNAS may be serious if not recognized and treated promptly. Advise pregnant patients taking SNRIs and SSRIs to deliver in a hospital to ensure that management by neonatology experts will be readily available upon delivery, when needed. At least 24 hours of close monitoring of these neonates is recommended. Neonates with severe PNAS should be monitored in a neonatal intensive care unit.

Prolonged hospitalization, respiratory support, and tube feeding may be required. In some cases, PNAS is not limited to the first two weeks after birth.

- Avoid concomitant use of serotonin reuptake inhibitors with benzodiazepines or other central nervous system depressants during the last trimester of pregnancy.

Green highlights are new requested warnings.

Animal Studies

- Rodent studies show that blockade of serotonin transport (including through SSRI exposure) during developmentally sensitive periods affects brain development in key brain regions (amygdala, hippocampus, and prefrontal cortex).
- These brain changes seem to predispose exposed rodents to anxiety-like behaviors and depression that do not typically emerge until the peri-adolescent period.
- However, animal studies may not always be representative of human response, and the clinical importance of the findings from the limited human studies that are available is unclear.

Uncertain Effects in MRI Studies

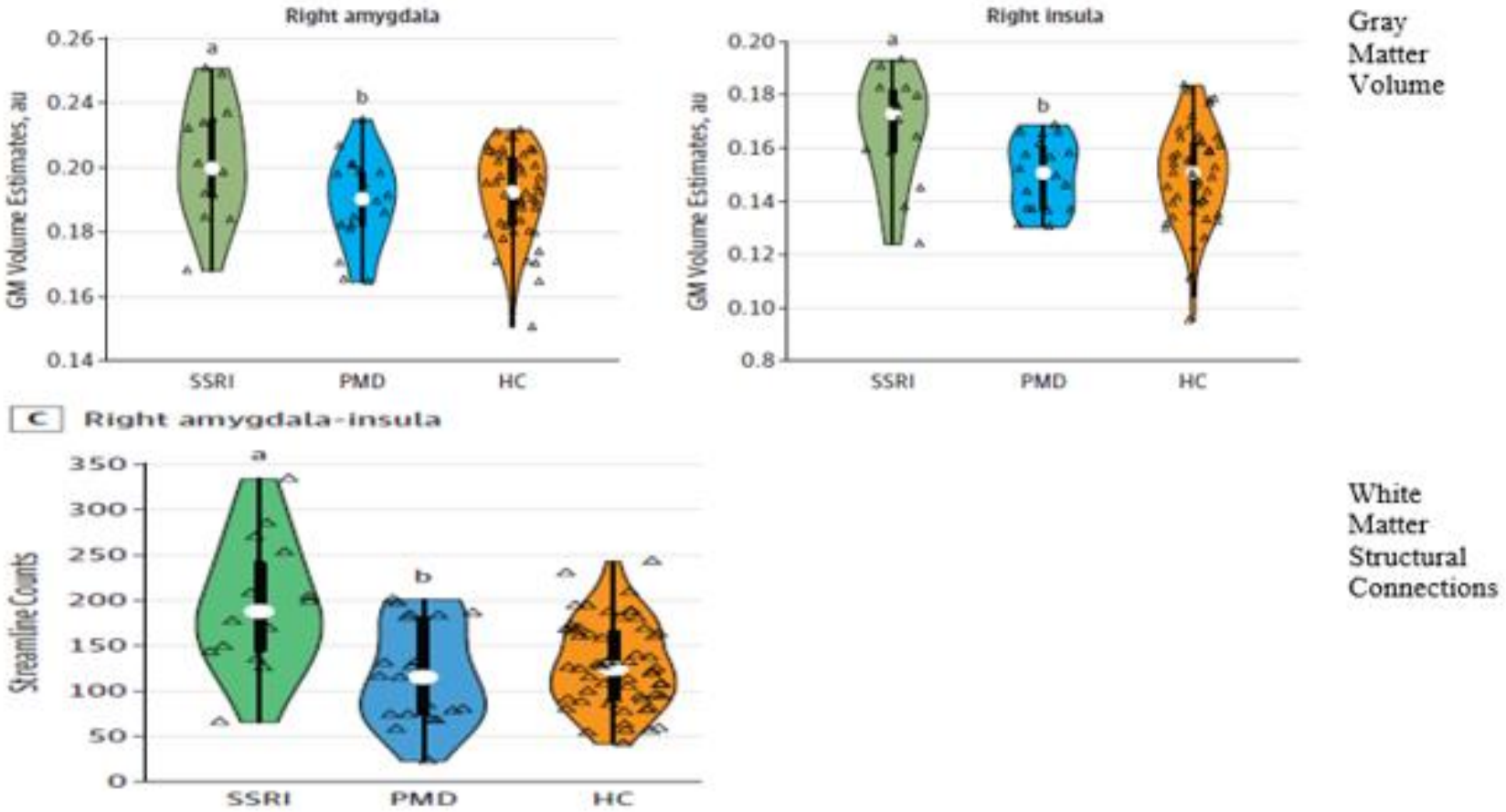

Figure 1. Effect of SSRI Exposure on Brain Structure in Lugo-Candelas et al. 2018. (HC, healthy control; PMD, prenatal maternal depression)

- Small sample: 16 infants born to mothers with prenatal SSRI use, 21 born to nondrug-treated depressed mothers, and 61 born to healthy (control) mothers.
- SSRI-treated mothers might have been more severely depressed than those who were not treated for depression during pregnancy. In addition, the study groups differed in some sociodemographic factors (maternal education, income, race/ethnicity, and birth weight).
- Therefore, the researchers called for further research to better disentangle the role of prenatal SSRI exposure in fetal brain development and other outcomes later in life.

Generation R Study

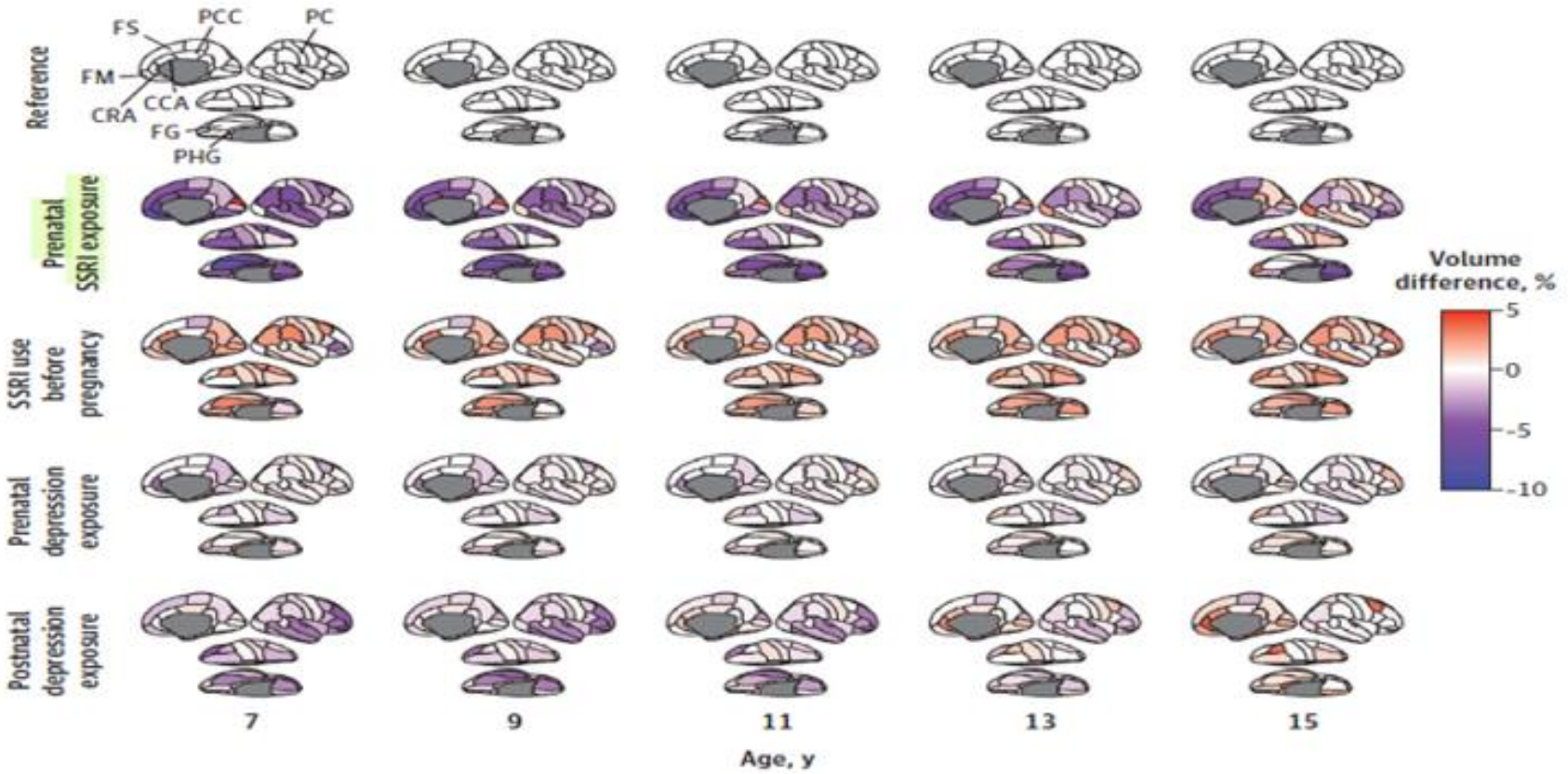

Figure 2. Cortical Maps of Estimated Volume Differences in Cortical Regions Between Each Exposure Group and the Reference Group During Follow-Up (Koc et al. 2023)

- Sample: 41 children with gestational SSRI exposure, 77 children whose mothers had used SSRIs only before pregnancy, 257 children whose mothers had prenatal depressive symptoms but did not use SSRIs during pregnancy, 74 children whose mothers only had postnatal depressive symptoms, and 2,749 children whose mothers did not use SSRIs and had low scores for depressive symptoms during pregnancy (control group).
- Talati 2023 noted that i**t is still early to draw clinical conclusions**: The clinical significance of the findings are unclear, especially as key limbic regions, including the amygdala, normalized over time. If future evidence links brain anomalies to adverse youth outcomes, this will need to be calibrated into the risk-benefit profile. Until then, it seems unwise to overinterpret such findings to either promote or discourage antidepressant medication use during pregnancy.

Observational Studies

- Danish Registry Data, emotional regulation

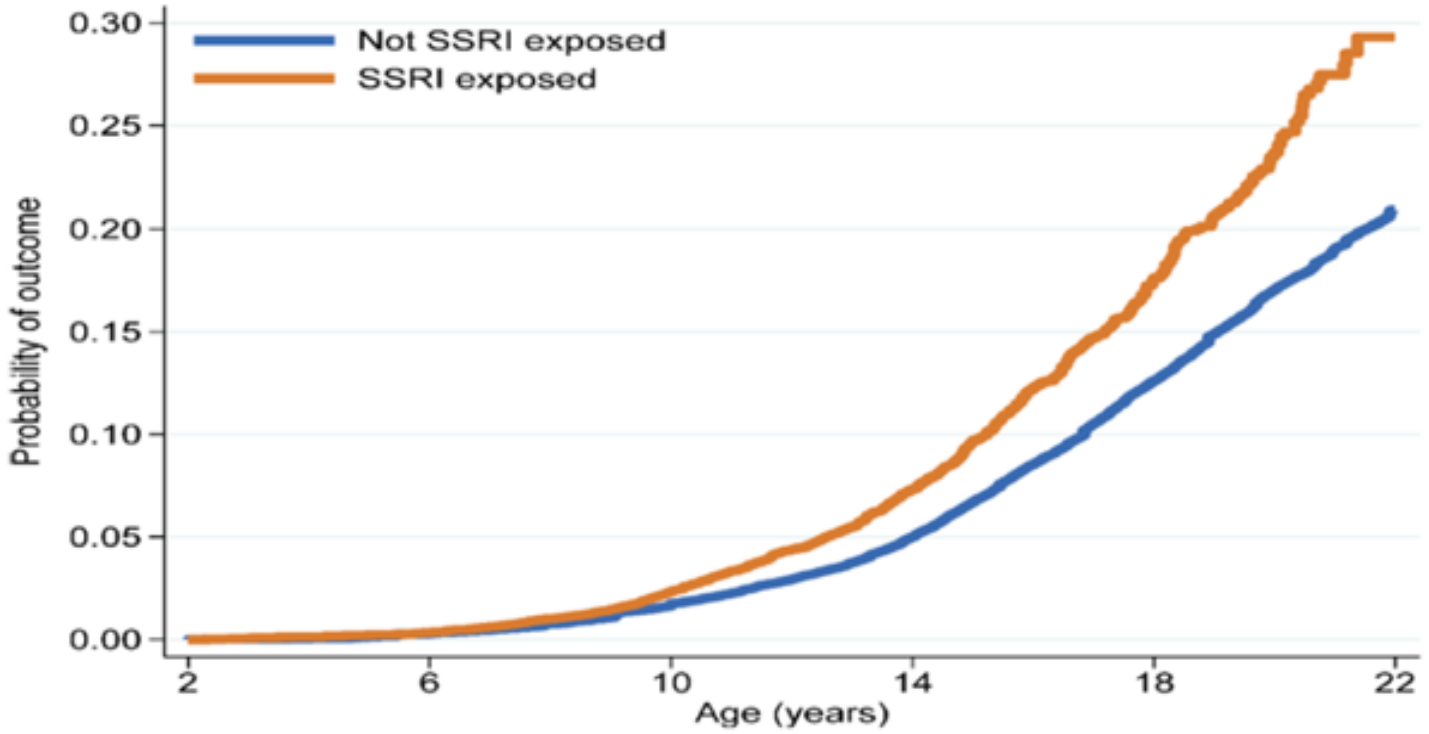

Figure 3. Failure Plot on Hazard Rates for Emotional Disorder Diagnosis or Prescription in Offspring by Maternal Exposure to SSRI During Pregnancy in Denmark, 1997-2015 (Bliddal et al. 2023)

Caveats: The associations with clinical disorders may be more strongly driven by parental depression and its correlates. Regardless of the underlying mechanism, SSRI-exposed children reflect a higher-risk group for depression and anxiety than the general population and may warrant increased clinical screening as they pass through the age of risk.

U.S. Observational Study

- Mayo Clinic Rochester Epidemiology Project data, Talati et al. 2025

- A geographically defined cohort involving three groups of live, singleton children born between 1997 and 2010: those whose mothers used SRIs during pregnancy (n = 837), those whose mothers used antidepressants in the year prior to pregnancy (n = 399), and those whose mothers did not use antidepressants (n = 863).

- After tracking the **psychiatric diagnoses of these children** through 2021 and accounting for maternal mental health and other relevant variables, the researchers found that children of SRI users during pregnancy **did not differ** from children of nonusers in the onset of the first diagnosis of a unipolar depressive or anxiety disorder.

Requested Studies to Address Uncertainty

- The FDA should require SRI manufacturers to conduct a comprehensive post-marketing safety surveillance study to compare short- and long-term outcomes of prenatal SRI exposure in the offspring.
- The agency may conduct its own assessment of SRI risks using data from the Sentinel Initiative.

Requested Warnings Re. Cautious Use of SRIs During Pregnancy

- Untreated maternal depression during pregnancy is associated with profound adverse effects on the mother and the baby. Therefore, it is important to treat maternal mental illness whenever it occurs.
- The use of these medications during pregnancy should ***only*** **be considered if their potential benefits outweigh their potential risks**, taking into account the risks associated with untreated mental illness.
- If the use of SRIs during pregnancy is deemed necessary, especially in patients who were using these medications before pregnancy, the smallest effective dose should be used for the shortest period necessary to reduce fetal exposure.
- It is important to monitor pregnant SRI users and their children more frequently than usual.
- Due to the potential serious health consequences of mental illness, especially around the time of delivery, and the potential risk of antidepressant discontinuation symptoms, SRIs should not be discontinued suddenly, but tapered gradually, as needed.

Health Research Group

Public Citizen

Washington, D.C.

www.citizen.org