



This information has been gathered by The Cleft Lip & Palate Foundation of Smiles. We are responding to the fact that a number of our members have questions concerning the safety of medications that they had taken during pregnancy, or may take during a future pregnancy. These medications may be the cause of craniofacial differences. Our goal is to ensure that our families have resources and facts about the medications that may be taken during pregnancy, so you can have informed discussions with the treating doctors.

Online at www.cleftsmile.org

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The Cleft Lip & Palate Foundation of Smiles provides research on craniofacial causes (genetics, environmental, prescription drugs), treatments (cleft palate teams, medical devices, therapies), and available support for families.

This PDF is about SSRI birth defect risks for women who get pregnant. This article is by no means conclusive but generally outlines some of the more common birth defects from the more well known brands of SSRIs. As with any prescription drug, do not stop taking or reduce the dosage without discussing the repercussions with your doctor first.



RESEARCH AND RECENT STUDIES

Causes of Cleft Lip and Palate: SSRIs

What are SSRIs?

Selective serotonin reuptake inhibitors are a class of compounds typically used as antidepressants for the treatment of depression, anxiety disorders, and some personality disorders.

Some brands of SSRIs include Paxil, Prozac, Wellbutrin, Zoloft, Lexapro, Celexa, Cymbalta, Effexor, Remeron, and Symbyax, to name a few.

SSRIs block the reabsorption of the neurotransmitter serotonin in the brain. Changing the balance of serotonin seems to help brain cells send and receive chemical messages, which in turn boosts mood. SSRIs are called selective because they seem to primarily affect serotonin, not other neurotransmitters.

What prescription drugs are SSRI medications?

SSRI drugs include the following: Celexa, Cymbalta, Effexor, Lexapro, Paxil, Prozac, Remeron, Symbyax, Wellbutrin, Zoloft. Formulations of SSRI medications are offered by a number of different pharmaceutical manufacturers.

Who makes SSRIs?

Celexa—Forest Laboratories
Cymbalta—Lilly
Effexor—formerly Wyeth Laboratories/now Pfizer
Lexapro—Lundbeck/Forest Laboratories
Paxil—GlaxoSmithKline
Prozac—Lilly
Remeron—Organon
Symbyax—Lilly
Wellbutrin—GlaxoSmithKline
Zoloft—Pfizer

What birth defects are associated with SSRIs?

The most common birth defects are heart defects, cleft lip and cleft palate, Down syndrome and spina bifida.

SSRIs are not considered major teratogens. However, they cross the placenta and may affect your newborn. Zoloft and Paxil and the SSRI as a group have been associated with congenital malformations, particularly septal defects.



PPHN / persistent pulmonary hypertension of the newborn

A recently published case-control study has shown that [infants born to mothers](#) who took SSRIs after the 20th week of pregnancy were six times more likely to have persistent pulmonary hypertension (PPHN) than infants born to mothers who did not take antidepressants during pregnancy. PPHN is a life-threatening disorder in which the newborn's arteries to the lungs remain constricted after delivery, limiting the amount of blood flow to the lungs and therefore the amount of oxygen into the bloodstream.

The background risk of a woman giving birth to an infant affected by PPHN in the general population is estimated to be about 1 to 2 infants per 1,000 live births. Neonatal PPHN is associated with significant morbidity and mortality.

SSRI brands that affect PPHN include Celexa, Fluvoxamine, Lexapro, Paxil, Prozac, Symbyax, and Zoloft.

Congenital heart defects, ASD, VSD

The Food and Drug Administration (FDA) has determined that [exposure to paroxetine, Paxil, Paxil CR, and Pexeva in the first trimester of pregnancy](#) may increase the risk for congenital malformations, particularly cardiac malformations. At the FDA's request, the manufacturer GlaxoSmithKline changed Paxil's pregnancy category from C to D and added new data and recommendations to the "Warnings" section of the prescribing information.

Most of the cardiac defects observed in these studies were atrial septal defects (ASD) or ventricular septal defects (VSD), conditions in which the wall between the right and left sides of the heart is not completely developed.

Wellbutrin, a popular antidepressant, has been linked to heart-related birth defects for women

who took the drug one month prior to getting pregnant and during the first trimester of pregnancy.

Cleft palate and cleft lip

There was also a notable rise in facial malformations such as cleft lip and palate. A cleft is a gap resulting from an incomplete closing of a structure during development. Clefts that occur in the lip and palate or roof of the mouth are called oral-facial clefts. Some babies only have a cleft lip. Many babies who have cleft lip also have a cleft palate. Cleft palate also can occur without cleft lip.

Omphalocele

[Omphalocele is a congenital defect in the abdominal wall](#) in which variable amounts of abdominal contents protrude into the base of the umbilical cord. Until about week 10 of pregnancy, it is normal for the bowel to be outside of the baby's belly. After 10 weeks the bowel or intestines should be inside the belly.

According to the Centers for Disease Control and Prevention (CDC) about 775 babies in the United States are born with an omphalocele per year.

One of the causes of [omphalocele](#) is taking SSRIs during pregnancy. Some brands of SSRIs include Paxil, Prozac, Zoloft, Lexapro, Celexa, Asentra.

How many people take SSRIs?

According to an August 2009 article in USA Today, about 10% of Americans—or 27 million people—were taking antidepressants in 2005, the last year for which data was available at the time the

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study was written. That's about twice the number in 1996, according to the study of nearly 50,000 children and adults in today's *Archives of General Psychiatry*. Yet the majority weren't being treated for depression. Half of those taking antidepressants used them for back pain, nerve pain, fatigue, sleep difficulties, or other problems.

What are alternative drugs and treatments? Are there safer drugs?

Because of the concern for SSRIs and birth defects, guidelines were released last year by the [American Psychiatric Association](#) and the [American College of Obstetricians and Gynecologists](#) stating that psychotherapy may be an effective alternative to antidepressants for pregnant women with mild to moderate depression.

However, the guidelines say, women with a history of more severe depression, or other major psychiatric disorders, may need to continue with their medication.

Also while antidepressants may be covered by health insurance, psychotherapy or psychiatry is usually not.

Short summary of studies about SSRI risks for pregnant women:

► In the fall of 2005, GlaxoSmithKline released [some information](#) from their recently collected safety data indicating an increased risk of major congenital malformations among infants exposed during organ development to Paxil. Among 527 fetuses exposed to Paxil in the first trimester, 23 were born with major congenital malformations. Most of the malformations were cardiovascular, and the majority of those were ventricular septal defects (VSD). As compared with infants born to women taking any other antidepressant agent during the first trimester, the adjusted odds ratio for any malformation was 2.2, 1.3 to 3.6. Previously published studies were generally smaller and had not produced clear evidence.

► Boston: The Slone Epidemiology Center at Boston University, the Genetics Unit, Massachusetts General Hospital for Children, and the Department of Epidemiology, Harvard School of Public Health assessed associations between first-trimester maternal use of SSRIs and the risk of birth defects among 9,849 infants with and 5,860 infants without birth defects participating in the Slone Epidemiology Center Birth Defects Study. Among outcomes previously reported to be associated with SSRI use, there were 127 cases of omphalocele, 115 cases of craniosynostosis, and 3,724 cases of congenital heart defects.

► A SSRI used in combination with benzodiazepines (examples are valium, Librium, Xanax, Atavan, etc.) increased the risk of Congenital Heart Disease (CHD) by 1.19 percentage points compared with no exposure. The risk difference remained statistically significant. SSRI alone (or monotherapy) did not increase the risk overall when compared with no exposure. The risk for ventral septal defect (VSD) did not increase with poly-drug exposure while the risk for atrial septal defect (ASD) increased with using SSRIs alone.

► Clinical trials are not practiced on pregnant women. Data is culled from pregnancy registries. In 6 of 7 studies comparing developmental outcomes of children exposed to antidepressants in utero with non-exposed children reported no significant differences. Most of these antidepressant medications remain relatively safe in pregnancy, but some significant areas of concern exist—particularly some evidence of higher risk of preterm birth, neonatal adaptation difficulties and congenital cardiac malformations (with Paxil).





Do you have more questions? Do you need resources?

For questions and resources about cleft lip and cleft palate, please contact: [The Cleft Lip and Palate Foundation of Smiles](#). Cleft lip or palate is one of the most common birth defects, currently affecting one in 600 children in the United States. The Foundation was formed by a young mother of twins both born with cleft lip and palate. The

Foundation offers positive support to parents of children with cleft birth defects by updating news, [resources](#), [birth registry listings](#), and state by state [support groups](#) and cleft teams.

Do you want more information about SSRIs? Do you question as to whether the SSRIs you were prescribed could be related to your child's cleft lip and cleft palate? Please contact [Rachel Mancuso](#) for assistance.

References

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Other Research from The Cleft Lip & Palate Foundation of Smiles

Research and Recent Studies:

- [Causes of Cleft Lip and Palate: Birth Defects](#)
- [Causes of Cleft Lip and Palate: Clomid](#)
- [Causes of Cleft Lip and Palate: Health Insurance](#)
- [Causes of Cleft Lip and Palate: Hydrocodone](#)
- [Causes of Cleft Lip and Palate: Special Education](#)
- [Causes of Cleft Lip and Palate: Topamax](#)