

The Centers for Birth Defects Research and Prevention (CBDRP) and the Centers for Disease Control and Prevention (CDC) distribute BD-STEPs News.

This newsletter informs study participants and the public of the Centers' activities and current news about birth defects.

About the Birth Defects Study to Evaluate Pregnancy exposureS (BD-STEPs)

BD-STEPs builds on the promising findings of the National Birth Defects Prevention Study (NBDPS), whose researchers have been looking at possible causes of birth defects for 20 years.

Through BD-STEPs, researchers continue to study factors that may place a woman at higher risk for having a baby with a birth defect. The study focuses primarily on factors that a woman might change to reduce the chance of her baby being born with a birth defect. Factors under study that could affect the risk of birth defects include:

- Diabetes and obesity;
- Treatments for long term health conditions, such as asthma and high blood pressure;
- Infertility treatments; and
- Other medicines.

In July 2014, BD-STEPs began telephone interviews with women from seven states:

- Arkansas
- California
- Georgia
- Iowa
- Massachusetts
- New York
- North Carolina

The women in these states had pregnancies affected by birth defects or pregnancies unaffected by birth defects. Comparing factors between these two groups can help us to understand which factors might place a woman at higher risk for having a baby with a birth defect.

Recent Findings from the National Birth Defects Prevention Study (NBDPS)

We completed interviews for the NBDPS in March 2013, but researchers will analyze this rich source of information for years to come. During the 14 years of interviews, 43,000 women from 10 states (Arkansas, California, Georgia, Iowa, Massachusetts, New Jersey, New York, North Carolina, Texas, and Utah) took part in the study. We also have cheek cell genetic samples from over 23,000 families we will use to understand how genetics play a role in birth defects. Over 300 scientific papers using NBDPS data have already been published. Here are some of the recent research findings.

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Centers for Disease Control and Prevention
National Center on Birth Defects and Developmental Disabilities

Genetics and Congenital Heart Defects (CHDs)

CHDs are the most common type of birth defect as they affect about 1 in every 100 babies born in the United States. Genetic factors play an important role in the development of CHDs. However, the genes and other factors that may affect the development of CHDs are largely unknown.



Using the genetic samples provided by NBDPS families, investigators have found that changes (often referred to as variants) within several genes are more likely to be passed down from parents to infants with CHDs than from parents to infants without CHDs. This finding shows that these genetic variants may be linked to the development of CHDs and infants who inherit these genetic changes from their parents may have an increased risk of being born with a CHD. Further research needs to be done to understand the functions of these genes and to confirm the study findings. This study is one of the first using NBDPS data to look at multiple genetic variants and CHDs.

Li M, Li J, He Z, Lu Q, Witte JS, Macleod SL, Hobbs CA, Cleves MA; NBDPS. Testing allele transmission for a SNP-set with a family-based generalized genetic random field method. *Genetic Epidemiology*. 2016 May; 40(4): 341-51. PMID: 27061818. PMCID: PMC5061344.

Gastroschisis and Mother’s Residence in Early Pregnancy

Gastroschisis is a birth defect of the abdominal (belly) wall. The baby’s intestines lie outside the baby’s body through a hole beside the belly button. The hole can be small or large and sometimes other organs, such as the stomach and liver, can also lie outside the baby’s body. The causes of gastroschisis are unknown, but there have been reports of clusters of babies born with gastroschisis in the same geographic area.

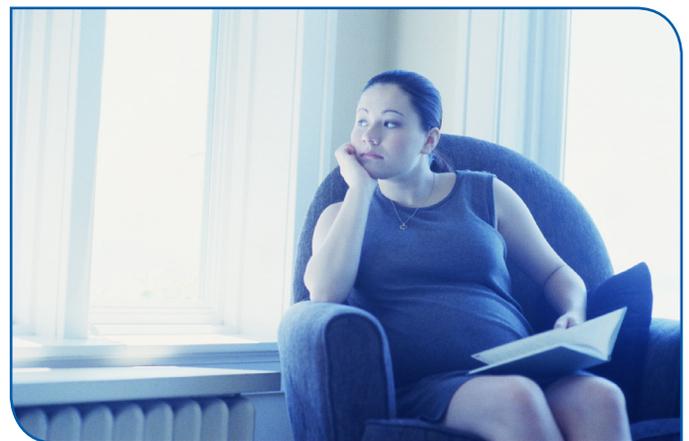
NBDPS researchers used information on where mothers lived in early pregnancy to investigate if there were any clusters within certain areas of Arkansas, California, and Utah. Studying patterns in birth defects can help

to determine if there are environmental factors that may increase the risk of birth defects. The researchers found patterns in specific locations where the moms lived but could not rule out that these patterns resulted from random chance. Researchers still need to find out if gastroschisis occurs in geographic clusters.

Yazdy MM, Werler MM, Feldkamp ML, et al. Spatial analysis of gastroschisis in the National Birth Defects Prevention Study. *Birth defects research Part A, Clinical and molecular teratology*. 2015; 103(6):544-553. doi:10.1002/bdra.23375.

Maternal Stress and Social Support and the Risks of Gastroschisis or Hypospadias

Stressful life events may affect fetal development during pregnancy. Using data from the National Birth Defects Prevention Study, researchers examined the association of maternal stressful life events and social support with risks for gastroschisis and hypospadias, which are birth defects that affect the abdominal wall and urogenital system. Mothers who had a stressful life event, such as relationship difficulties, legal/financial problems, violence/crime, illness/injury, or a change in residence or employment, during pregnancy had a higher risk for gastroschisis but only among non-teenage mothers. They saw no differences for risk of hypospadias. The greater the social support a mother had was associated with lower risks for birth defects. The potentially harmful impact of stress on the development of specific birth defects requires further study.



Carmichael SL, Ma C, Tinker S, Shaw GM, National Birth Defects Prevention Study. Maternal Stressors and Social Support and Risks of Delivering Babies With Gastroschisis or Hypospadias. *American Journal of Epidemiology*. 2017 May 13; 185(12):1240-6.

Twinning and Major Birth Defects

Twins are on the rise! The rate of twin births has increased by over 75 percent since 1980. One reason for the increasing number of twins is the growing use of fertility treatments among couples seeking to become pregnant. Previous studies have shown that twins are at a higher risk of certain birth outcomes such as premature birth, low birth weight, and birth defects compared to single babies. Some studies have reported a higher risk of negative birth



outcomes among identical (monozygotic) twins compared to fraternal (dizygotic) twins. However, previous studies of birth defects in twins could not include important information about other risk factors, including the mothers' use of fertility treatments.

NBDPS researchers used information on over 28,000 babies to see if a twin's risk of birth defects was affected by the mother's use of fertility treatments and whether the twin was identical or fraternal.

The NBDPS study found that twins were more likely to have certain birth defects than single babies, and that identical twins were more likely than fraternal twins to have certain birth defects. Researchers found that twins whose mother did not use fertility treatments to become pregnant had a higher risk of birth defects than twins whose mother did.

While more research is needed, this study can help clinicians better advise their patients seeking to become pregnant about the risk of birth defects in twins.

Dawson AL, Tinker SC, Jamieson DJ, Hobbs CA, Berry RJ, Rasmussen SA, Anderka M, Kepler-Noreuil KM, Lin AE, Reefhuis J; National Birth Defects Prevention Study. Twinning and major birth defects, National Birth Defects Prevention Study, 1997-2007. *J Epidemiol Community Health*. 2016 Nov;70(11):1114-1121.

Risk Factors for Cloacal Defects

Multiple risk factors during pregnancy were tested for cloacal exstrophy and persistent cloaca, which are rare

birth defects that involve the abdominal wall and the gastrointestinal and genitourinary systems. Researchers found that infants with these defects were more likely to be born premature, and those with cloacal exstrophy were more likely to be from twin pregnancies. Both cloacal exstrophy and persistent cloaca were linked with the use of fertility medications and assisted reproductive technology procedures (such as In Vitro Fertilization). Cloacal exstrophy was linked with x-ray exposure, and persistent cloaca was associated with the use of certain medications. All findings will need to be confirmed in future studies, but this study provides important knowledge about potential risk factors.

Kepler-Noreuil KM, Conway KM, Shen D, Rhoads AJ, Carey JC, Romitti PA and the National Birth Defects Prevention Study. Clinical and Risk Factor Analysis of Cloacal Defects in the National Birth Defects Prevention Study. *Am J of Med Genet*. 2017 Aug; DOI: 10.1002/ajmg.a.38469

Antioxidant Consumption and Limb Defects

About 1 in 2,000 babies in the United States is born with a limb defect, which happens when a baby's arms or legs do not fully form while developing in the uterus. Previous research shows that a mother's usual diet (the foods she typically eats) around the time of early pregnancy is important for healthy development of the baby. Using information from participants in NBDPS, researchers studied whether a mother's dietary intake of antioxidants is related to having a baby with a limb defect. Antioxidants found in many fruits and vegetables are important for many functions in our bodies. They found that mothers who ate a lot of fruits and vegetables were about 20 percent less likely to have a baby with a limb defect than mothers who did not eat as many fruits and vegetables. The researchers also found that mothers with diets high in three particular antioxidants (beta-carotene, lycopene, and lutein) were about 30 percent less likely to have a baby with a limb defect. These results reaffirm the importance of healthy eating during early pregnancy. Additional research will help with understanding how antioxidants might reduce the risk of limb defects.



Pace, N. D., Desrosiers, T. A., Carmichael, S. L., Shaw, G. M., Olshan, A. F., Siega-Riz, A. M. and the National Birth Defects Prevention Study (2017), Antioxidant Consumption is Associated with Decreased Odds of Congenital Limb Deficiencies. *Paediatr. Perinat. Epidemiol.* [PPE] doi:10.1111/ppe.12403 [Epub ahead of print]

Antihypertensive Medication and Congenital Heart Defects (CHDs)

Chronic hypertension or high blood pressure complicates around 2 percent of pregnancies; the effects of antihypertensive medication, or medication used to treat high blood pressure, on the developing baby are not well understood. Researchers used data from NBDPS to study the relationship between antihypertensive medication and the risks for CHDs. They found that mothers who reported antihypertensive medication use during early pregnancy were about twice as likely to have a pregnancy affected by certain CHDs (coarctation of the aorta, pulmonary valve stenosis, perimembranous ventricular septal defect, or secundum atrial septal defect). Use of specific types of antihypertensive medications, beta-blockers and renin-angiotensin system blockers, were most strongly associated with the risk for these CHDs, but other types of antihypertensive medications were associated with increased risk. Because uncontrolled hypertension can be harmful during pregnancy, women with high blood pressure who are considering becoming pregnant should discuss treatment options with their doctors before pregnancy.



Fisher SC, Van Zutphen AR, Werler MM, Lin AE, Romitti PA, Druschel CM, Browne ML and the National Birth Defects Prevention Study. Maternal antihypertensive medication use and congenital heart defects: Updated results from the National Birth Defects Prevention Study. *Hypertension.* 2017 May; 69(5):798-805. doi: 10.1161/HYPERTENSIONAHA.116.08773. Epub 2017 Apr 3.

Spotlight on BD-STEPS Research Centers and the Project Coordinators

BD-STEPS Research Centers and their Project Coordinators work together to collect and to analyze data. Read about each of the Research Centers and Project Coordinators below.

ARKANSAS

Each year in Arkansas, about 1,300 babies are born with a birth defect. The Arkansas Center for Birth Defects Research and Prevention collects data from the Arkansas Reproductive Health Monitoring System, one of the oldest active birth defects monitoring systems in the United States.

Research at the Arkansas Center focuses on genetic (inherited) factors that might increase the risk for birth defects, specifically congenital heart defects and hypospadias. The Arkansas Center also looks at how genes might be influenced by a woman's lifestyle habits and exposures such as tobacco smoke.

Dr. Jenny Naylor is the Project Coordinator for Arkansas. Jenny received a PhD in Neuroscience from the University of Mississippi Medical Center in 2015 and completed a post-doctoral fellowship at the US FDA National Center for Toxicological Research (NCTR) in the Department of Neurotoxicology in October of 2017. Over the past seven years, she has developed a strong passion for the management and design of research projects, and she is excited to apply this skill set while coordinating BD-STEPS.



What Jenny most enjoys about BD-STEPS are the collaborative efforts of everyone involved and the knowledge that everyone is working together towards a common goal to improve the lives of children and their families. Jenny recognizes that participants are the most crucial part of this study and that this work would not be possible without their involvement and willingness to be part of this research.

Jenny's favorite travel destination is France. While she loves Paris, she would like to return to the Loire Valley in the central part of France where there are many historic towns, castles, and beautiful landscapes to explore.

GEORGIA/CDC

About 4,000 births are affected by birth defects in Georgia each year. CDC coordinates BD-STEPS study activities and serves as the Georgia Center for Birth Defects Research and Prevention. CDC studies how medicine is used among pregnant women and also how certain medicines might affect the risk for birth defects. CDC tracks the number of birth defects in Atlanta through the Metropolitan Atlanta Congenital Defects Program. The program has collected data in Atlanta since 1968 and continues to serve as a model for other state birth defects tracking systems.

Brandi Martell is the Project Coordinator for the Georgia Center. Brandi grew up in San Diego, California and completed her Master's in Public Health from San Diego State University while working as a Program Specialist in alcohol research. She began her CDC career in 2012 as a research and evaluation fellow in violence prevention and later worked to identify tobacco-related disparities among vulnerable populations. Brandi enjoys working with the team of staff and researchers who are dedicated to helping mothers and families identify risk factors associated with birth defects to allow families to grow and to thrive in healthy communities. Participants' contributions in this study are invaluable for future mothers-to-be. In her spare time, Brandi enjoys practicing yoga, trying new recipes, and traveling with family and friends.



factors related to congenital defects has contributed to earlier identification, improved treatments and longer lives for children, including her nephew. As a scientist, she appreciates the great amount of information provided to the study by participating mothers and families. This information allows scientists to study many different pathways that may contribute to these complex health conditions. Outside of work, her favorite role is as a grandmother to her sparkly granddaughter, who was born with Down syndrome. She looks forward to continuing to collect and to analyze the important information provided by the study.



MASSACHUSETTS

About 1,700 pregnancies are affected by birth defects in Massachusetts each year. The Massachusetts Center for Birth Defects Research and Prevention started in 1997. It is a partnership between the Massachusetts Department of Public Health, Boston University's Slone Epidemiology Center, and the Genetics Unit at Massachusetts General Hospital for Children. The Massachusetts Center has experts in many research areas including congenital heart defects and other birth defects.

The Massachusetts Center is a leader in research on the safety and risks of medication use during pregnancy, including a study showing that medicine use during pregnancy has increased over the past 30 years.

Rebecca Lovering is the Study Coordinator for the Massachusetts Center at the Massachusetts Department of Public Health. She has been with the Massachusetts Center in her role as Study Coordinator since 2004 and recently completed her 20th year at the Massachusetts Department of Public Health. Her interest in public health began when she served



as a Peace Corps Volunteer in Sierra Leone, West Africa and then in Panama. In her role coordinating BD-STEPS for Massachusetts, Rebecca most enjoys the variety of the work. She keeps track of all the details of the data collection component of the study, and she keeps all parts running smoothly. This role allows her to have contact not only with the data but with the study participants as well.

Through the many years that Rebecca has been working in birth defects research, she remains in awe of and has

IOWA

Each year, over 1,500 pregnancies are affected by birth defects in Iowa. The Iowa Center studies pregnancies across Iowa, an area that includes over 3 million people comprised of urban and rural residents who have differences in personal behaviors, such as smoking, alcohol use, and exposure to farming chemicals and other toxins. The Iowa Registry for Congenital and Inherited Disorders was established partly to study how a person's genes and their behaviors might affect birth defect risks. For BD-STEPS, the Iowa Center will look at the impact of personal behaviors and environmental exposures, along with genes, on birth defects.

Dr. Kristin M Conway is a Research Scientist for the Iowa Center, who analyzes data for the project. She has a PhD in Human Development and Family Studies, with an emphasis in child development, from Iowa State University. She has worked with the Center since 2009 and has personal and professional interests in the research. Personally, her nephew was born with a rare congenital heart defect, hypoplastic right heart syndrome, in 1995. Research into

immense respect for the study participants' willingness to help others. She hopes that participants know the importance of their contribution to the study: "We could not do this without them!"

In her spare time, Rebecca wants to learn more Tai Chi and fit it regularly into her busy schedule.

NEW YORK

Over 12,000 babies are born with a major birth defect every year in New York State. Experts at the New York Center study medicine use during pregnancy and environmental exposures that might lead to birth defects. The Center often collaborates with the Wadsworth Center, the research-focused public health laboratory at the New York State Department of Health. Their colleagues at Wadsworth have developed ways to do genetic and environmental analyses of newborn screening blood spots for birth defects research.

Briana Borgolini is the BD-STEPS Coordinator for New York. Briana grew up in the Albany area and later attended Brown University, where she graduated in 2014 with her Bachelor's degree in Human Biology. While at Brown, Briana was a varsity athlete, a Public Health teaching assistant, and completed her senior honors thesis with a professor at Brown's School of Public Health. Before joining the New York BD-STEPS Team, she was a Research Coordinator at The Miriam Hospital in Providence, Rhode Island.



Briana's favorite thing about coordinating BD-STEPS is that she gets to work with great people every day who are dedicated to helping women have healthier pregnancies. Briana would like participants to know every contribution is valuable in identifying modifiable risk factors. Knowing more about these risk factors can help women make the best possible decisions for a healthy pregnancy. Briana enjoys running, reading, and cooking, and she hopes to pick up ceramics someday.

NORTH CAROLINA

Over 3,500 babies are born with major birth defects in North Carolina each year. The North Carolina Center carries out birth defects research in 33 counties in central North Carolina. Children with birth defects are identified through the North Carolina Birth Defects Monitoring Program a state-run program since 1995. The North Carolina Center has two partners: the Department of Epidemiology at the University of North Carolina (UNC) Gillings School of Global Public Health in Chapel Hill and the North Carolina Birth Defects Monitoring Program at the State Center for Health Statistics, Division of Public Health in Raleigh.

Researchers in the North Carolina Center focus on factors that increase the risk for birth defects that might be changed, including diet, obesity, exercise, and work exposures; the role of genes and how genes interact with environmental exposures; and new methods of studying birth defects.

Alison Woomert, PhD, is the Project Director for North Carolina. She enjoys working with the dedicated and caring teams both in North Carolina and around the country; she realizes that everyone cares deeply about discovering ways to prevent birth defects and to improve the lives of children and their families. Alison believes that BD-STEPS participants are our partners in this research and are the key to learning about birth defects. She appreciates the families who so generously share their time and experiences with the study, without which we could not learn about the risks and causes of birth defects. In her spare time, Alison enjoys reading, especially historical novels and science fiction, and traveling to national parks and being outdoors for short hikes and camping.



Resource Corner

Listed below are several resources that might be of interest. The Centers are not responsible for the content found on these websites.

MEDICINE AND PREGNANCY:

The **Mother to Baby** website contains a library of factsheets about different medications. These sheets answer questions about the use of each medicine during pregnancy and breastfeeding. <https://mothertobaby.org/fact-sheets-parent/>

CDC and partners are working together to provide better information to women and their healthcare providers about medication use during pregnancy. **Treating For Two**, an index site of CDC.gov, provides this information and other resources. <http://www.cdc.gov/treatingfortwo/>

The **American College of Allergy, Asthma, and Immunology** has a webpage on asthma and allergies during pregnancy. It provides guidance for pregnant women dealing with these conditions. <http://acaai.org/resources/connect/letters-editor/letters-to-web-editor-5>

STRESS AND PREGNANCY:

The **March of Dimes** website on life changes during pregnancy talks about causes of stresses and ways to reduce stress during pregnancy. http://www.marchofdimes.com/pregnancy/lifechanges_indepth.html

The **Mother to Baby** website has a fact sheet on stress during pregnancy, available in English and Spanish. It covers what stress is, if moms-to-be should be concerned, ways to reduce stress, and where to go for help. <http://www.mothertobaby.org/files/stress.pdf>

CONGENITAL HEART DEFECTS:

CDC's website has an entire index of webpages on **congenital heart defects**, including information on specific heart defects, research, and statistics, among other useful resources. <http://www.cdc.gov/ncbddd/heartdefects/>

CDC's website also has a webpage on **critical congenital heart defects**. The webpage has information on screening, current research activities, and information for healthcare providers. <http://www.cdc.gov/ncbddd/heartdefects/cchd-facts.html>

CLEFT LIP AND PALATE:

CDC's website has a webpage on **cleft lip and cleft palate**, providing information on the conditions, some of the known causes of cleft lip and palate, and diagnosis and treatment options. <http://www.cdc.gov/ncbddd/birthdefects/cleftlip.html>

The Cleft Palate Foundation has information for parents of children with cleft lip with or without cleft palate. <http://www.cleftline.org/parents-individuals/>

Children's Craniofacial Association website has information about birth defects of the head and face. They have resources on connecting with other parents and families as well as information on each condition. <https://ccakids.org/>

CHOANAL ATRESIA:

The **Children's Choanal Atresia Foundation** has a website that provides information, research, and support for choanal atresia or birth defects of the nasal passage. <http://choanalatresia.org/index.html>

GASTROSCHISIS:

CDC's website has a webpage on **gastroschisis**. It talks about what gastroschisis is, how common it is, how it is diagnosed, and how it is treated. <http://www.cdc.gov/ncbddd/birthdefects/gastroschisis.html>

Avery's Angels is a foundation that is helping children and families affected by gastroschisis. The website has resources for connecting with other families and ways to raise awareness about gastroschisis. <http://www.averysangels.org/>

GENETICS:

CDC has a unique **Family Health History and Genetics** index of web pages that provide a great deal of information on the role genetics plays on the health of families, newborn screening, and many other useful resources. <https://www.cdc.gov/genomics/famhistory/>

Directory of the Research Centers

To reach a BD-STEPS project coordinator, please email us at BD-STEPS@cdc.gov. Below is the contact information for each BD-STEPS Center.

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The logo features the word "share" in a stylized font where each letter is inside a colored square (s: green, h: orange, a: blue, r: yellow, e: red). To the right of "share" is the phrase "your stories" in a dark grey, sans-serif font.

share your stories

Newsletter Ideas and Mailing:

Please contact your Center listed in the directory if you:

- Want to share your experience about the NBDPS
- No longer wish to receive this newsletter
- Need to update your mailing address
- Would like to receive the newsletter via e-mail

Also, please let us know if you have topic ideas for future issues.