2015 Report

The Iowa Registry for Congenital and Inherited Disorders (IRCID) continues to be a national leader in surveillance of congenital and inherited disorders and serves as a model program for other states. The IRCID conducts active surveillance to identify information about congenital and inherited disorders that occur in Iowa and to Iowa residents. The IRCID has collected information for over 55,000 children with various birth defects. This information has been used by health care providers and educators to provide treatment and support services. It is also used by researchers to study risk factors for birth defects and to evaluate treatments for birth defects.

The IRCID also conducts surveillance for Duchenne/Becker muscular dystrophy and has identified 140 children with this neuromuscular disease. In addition, the IRCID has collaborated with the Metropolitan Atlanta Congenital Defects Program to develop approaches to active surveillance for stillbirths and also newborn screening disorders.

The surveillance and research efforts of the IRCID and its partners provide a valuable resource for the state of Iowa. While taking care to preserve the privacy of families affected by these disorders, the IRCID provides important information to state policy makers and public health professionals. We are pleased to perform this important work on behalf of the citizens of Iowa.

Surveillance for Birth Defects

In the United States, the Centers for Disease Control and Prevention (CDC) recognize three types of surveillance systems; each is rated differently for completeness of patient ascertainment:

- Vital Records: Use of birth and fetal death certificates provided by the state's Department of Health (Rating: Poor)
- Passive Reporting: Use of medical reports submitted by staff from hospitals, clinics, or other facilities (Rating: Fair to Good)
- Active System: Use of trained personnel who systematically review records in hospitals, clinics, or other facilities (Rating: Excellent)

The term "defect" refers to abnormal development related to body structure, body function, and metabolism, or an error in body chemistry. Typically a defect is present at birth (congenital), but a recognizable defect may be diagnosed during pregnancy (prenatal) or following birth (postnatal).

The IRCID has traditionally focused on structural birth defects, which typically involve a body part that is missing or malformed. Examples include heart defects, spina bifida, and cleft lip and palate. Since 2003, the IRCID adopted the recommendations of the National Birth Defects Prevention Network (NBDPN) to focus largely on a core set of birth defects (see Table 1). Prior to this change, the IRCID included many 'minor' conditions, so this change represents a reduction in the number of conditions that it monitors.

Table 1
Prevalence for birth defects in Iowa, 2008-2012 deliveries

Condition	Total	Prevalence Estimate*
Brain/Spinal Cord		
Anencephalus	60	3.1
Encephalocele	17	0.9
Hydrocephalus without spina bifida	250	12.8
Microcephalus	228	11.7
Spina bifida without anencephalus	82	4.2
Eye		
Anophthalmia/microphthalmia	34	1.7
Congenital cataract	49	2.5
Ear		
Anotia/microtia	40	2.0
Heart		
Aortic valve stenosis	59	3.0
Atrial septal defect	594	30.4
Atrioventricular septal defect	114	5.8
Coarctation of aorta	111	5.7
Common truncus	7	0.4
Ebstein's anomaly	13	0.7
Hypoplastic left heart syndrome	47	2.4
Pulmonary valve atresia and stenosis	230	11.8
Tetralogy of Fallot	72	3.7
Total anomalous pulmonary venous return	19	1.0
Transposition of great arteries	59	3.0
Tricuspid valve atresia and stenosis	53	2.7
Ventricular septal defect	1030	52.7

Table 1 (continued from previous page)

Condition	Total	Prevalence Estimate*
Oral/Facial		
Choanal atresia	30	1.5
Cleft lip only	79	4.0
Cleft lip with cleft palate	115	5.9
Cleft palate without cleft lip	129	6.6
Digestive		
Biliary atresia	8	0.4
Esophageal atresia / tracheoesophageal fistula	51	2.6
Hirschsprung's disease (congenital megacolon)	31	1.6
Pyloric stenosis	408	20.9
Rectal and large intestinal atresia/stenosis	79	4.0
Genital/Urinary		
Bladder exstrophy	6	0.3
Hypospadias	257	25.8
Renal agenesis/hypoplasia	106	5.4
Muscle/Skeletal		
Diaphragmatic hernia	49	2.5
Gastroschisis	120	6.1
Omphalocele	53	2.7
Reduction deformity, lower limbs	44	2.3
Reduction deformity, upper limbs	91	4.7
Syndromes		
Down syndrome (Trisomy 21)	235	12.0
Edwards syndrome (Trisomy 18)	69	3.5
Patau syndrome (Trisomy 13)	30	1.5

* Prevalence rates per 10,000 live births.
† Includes second or third degree hypospadias. Excludes first degree hypospadias.
‡ Prevalence per 10,000 male live births.

Birth Defect Research

Approximately 1 in 33 newborns is affected by a major birth defect, making such conditions disturbingly common. These conditions come with personal and monetary costs, both for the families of these children and for society. Nearly 20% of all infant deaths are caused by birth defects. Hospitalizations associated with such conditions are longer than hospitalizations for other conditions. More than $8 billion is required to provide lifetime care for the children born with birth defects each year.

Because the causes of up to 70% of birth defects are unknown, research is a critical part of any strategy to prevent these conditions. For this reason, in 1996 the United States Congress directed the CDC to establish regional "centers of excellence" in birth defect research and prevention. Further, interest in fostering collaboration among state birth defect programs led to the formation of the National Birth Defects Prevention Network in 1998.

National Birth Defects Prevention Network

The National Birth Defects Prevention Network (NBDPN) is a nationwide association of birth defect programs and individuals. The IRCID is an active member of the NBDPN and participates in many of its projects. For example, the NBDPN provides a set of guidelines to help birth defect registries around the country organize their work in a consistent manner. The NBDPN also provides educational materials to birth defect abstractors, as well as informational resources to promote Birth Defects Prevention Month each January. Another goal of the NBDPN is to encourage scientific collaboration among birth defect programs. The IRCID is currently participating in NBDPN projects for gastroschisis and pyloric stenosis.

Iowa Center of Excellence for Birth Defects Research and Prevention

The Iowa Center of Excellence for Birth Defects Research and Prevention was one of eight charter centers established by the CDC to study genetic and environmental (broadly defined) risk factors for birth defects. Iowa Center investigators participated in local (state-wide) projects as well as the National Birth Defects Prevention Study (NBDPS). The NBDPS was a population-based study that investigated genetic and environmental risk factors for over 30 major birth defects. As a partner with the Iowa Center, the IRCID identified children with NBDPS-eligible birth defects and secured permission from mothers to share information with researchers. Women with a pregnancy affected by one or more of the defects and women with an unaffected pregnancy were interviewed about their health, diet, and lifestyle during their pregnancies. Biological specimens were also requested from each family to study genetic factors that may contribute to these birth defects. Over 43,000 interviews have been completed nationwide, and biological specimens have been collected from more than 25,000 families.

Over 200 research projects are currently underway nation-wide as part of the NBDPS. Some of these projects examine risk factors, such as maternal nutrition. Others examine gene and environment interaction effects. Still others examine maternal behavior during pregnancy.

The research performed by Iowa investigators has the potential to positively affect the lives of Iowans. Current studies by Iowa investigators are focused on the relationships between birth defects and agricultural chemicals, cigarette smoking, alcohol consumption, medications, and compounds in drinking water.

2015 Iowa Center Publication Using IRCID Data
(Names listed in bold designate Iowa investigators)

Wehby GL, Collett BR, **Barron S, Romitti P, Ansley T**. (2015) Children with oral clefts are at greater risk for persistent low achievement in school than classmates. Arch Dis Child 0:1-7. PMID: 26347387 doi: 10.1136/archdischild-2015-308358

2015 NBDPN Publication Using IRCID Data
(Names listed in bold designate Iowa investigators)

Anderka M, Mai CT, **Romitti PA**, Copeland G, Isenburg J, Feldkamp ML, Krikov S, Rickard R, Olney RS, Canfield MA, Stanton C, Mosley B, Kirby RS. (2015) Development and implementation of the first national data quality standards for population-based birth defects surveillance programs in the United States. BMC Public Health 15:925. PMID: 26386816 doi:10.1186/s12889-015-2223-2

2015 NBDPS Publications Using IRCID Data
(Names listed in bold designate Iowa investigators)

Botto LD, Krikov S, Carmichael SL, Munger RG, Shaw GM, Feldkamp ML, and the National Birth Defects Prevention Study. (2015) Lower rate of selected congenital heart defects with better maternal diet quality: a population-based study. Arch Dis Child Fetal Neonatal Ed 101(1):43-9. PMID: 26304461 doi: 10.1136/archdischild-2014-308013

Dawson AL, Razzaghi H, Arth A, Canfield MA, Parker SE, Reefhuis J, and the National Birth Defects Prevention Study. (2015) Maternal exposures in the National Birth Defects Prevention Study: time trends of selected exposures. Birth Defects Res A Clin Mol Teratol 103(8):703-12. PMID: 25884728 doi: 10.1002/bdra.23377

Desrosiers TA, Lawson CC, Meyer RE, Stewart PA, Waters MA, Correa A, Olshan AF, and the National Birth Defects Prevention Study. (2015) Assessed occupational exposure to chlorinated, aromatic and Stoddard solvents during pregnancy and risk of fetal growth restriction. Occup Environ Med 72(8):587-93. PMID: 26076683 doi: 10.1136/oemed-2015-102835

Howards PP, Johnson CY, Honein MA, Flanders WD, and the National Birth Defects Prevention Study. (2015) Adjusting for bias due to incomplete case ascertainment in case-control studies of birth defects. Am J Epidemiol 181(8):595-607. PMID: 25792608 doi: 10.1093/aje/kwu323

Lim H, Agopian AJ, Whitehead LW, Beasley CW, Langlois PH, Emery RJ, Waller DK, and the National Birth Defects Prevention Study. (2015) Maternal occupational exposure to ionizing radiation and major structural birth defects. Birth Defects Res A Clin Mol Teratol 103(4): 243-54. PMID: 25820072 doi: 10.1002/bdra.23340

Reeder MR, Botto LD, **Keppler-Noreuil KM**, Carey JC, Byrne JL, Feldkamp ML, and the National Birth Defects Prevention Study. (2015) Risk factors for Dandy-Walker malformation: a population-based assessment. Am J Med Genet A 167(9):2009-16. PMID: 25941000 doi: 10.1002/ajmg.a.37124

Reefhuis J, Devine O, Friedman JM, Louik C, Honein MA, and the National Birth Defects Prevention Study. (2015) Specific SSRIs and birth defects: Bayesian analysis to interpret new data in the context of previous reports. BMJ 351:h3190. PMID: 26156519 doi: 10.1136/bmj.h3190

Reefhuis J, Gilboa SM, Anderka M, Browne ML, Feldkamp ML, Hobbs CA, Jenkins MM, Langlois PH, Newsome KB, Olshan AF, **Romitti PA**, Shapira SK, Shaw GM, Tinker SC, Honein MA, and the National Birth Defects Prevention Study. (2015) The national birth defects prevention study: a review of the methods. Birth Defects Res A Clin Mol Teratol 103:656-669. PMID: 26033852 doi: 10.1002/bdra.23384

Rocheleau CM, Bertke SJ, Lawson CC, **Romitti PA**, Sanderson WT, Malik S, Lupo PJ, Desrosiers TA, Bell E, Druschel C, Correa A, Reefhuis J, and the National Birth Defects Prevention Study. (2015) Maternal occupational pesticide exposure and risk of congenital heart defects in the national birth defects prevention study. Birth Defects Res A Clin Mol Teratol 103:823-33. PMID: 26033688 doi: 10.1002/bdra.23351

Tang X, Hobbs CA, Cleves MA, Erickson SW, MacLeod SL, Malik S, and the National Birth Defects Prevention Study. (2015) Genetic variation affects congenital heart defect susceptibility in offspring exposed to maternal tobacco use. Birth Defects Res A Clin Mol Teratol 103(10):834-42. PMID: 26033827 doi: 10.1002/bdra.23370

Tinker SC, Carmichael SL, Anderka M, Browne ML, **Caspers Conway KM,** Meyer RE, Nembhard WN, Olney RS, Reefhuis J, and the National Birth Defects Prevention Study. (2015) Next steps for birth defects research and prevention: The birth defects study to evaluate pregnancy exposures (BD-STEPS). Birth Defects Res A Clin Mol Teratol 103(8):733-40. PMID: 25846741 doi: 10.1002/bdra.23373

Vuong AM, Shinde MU, Brender JD, Shipp EM, Huber JC Jr, Zheng Q, McDonald TJ, Sharkey JR, Hoyt AT, Werler MM, Kelley KE, Langlois PH, Canfield MA, and the National Birth Defects Prevention Study. (2015) Nitrosatable drug exposure during pregnancy and preterm and small-for-gestational-age births. Paediatr Perinat Epidemiol 29(1):60-71. PMID: 25492517 doi: 10.1111/ppe.12169

Wang Y, Liu G, Canfield MA, Mai CT, Gilboa SM, Meyer RE, Anderka M, Copeland GE, Kucik JE, Nembhard WN, Kirby RS, and the National Birth Defects Prevention Study. (2015)

Racial/ethnic differences in survival of United States children with birth defects: a population-based study. J Pediatr 166(4):819-826. PMID: 25641238 doi: 10.1016/j.jpeds.2014.12.025

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Zhu Y, Romitti PA, Caspers Conway KM, Shen DH, Sun L, Browne ML, Botto LD, Lin AE, Druschel CM, and the National Birth Defects Prevention Study. (2015) Maternal periconceptional alcohol consumption and congenital heart defects. Birth Defects Res A Clin Mol Teratol 103:617-629. PMID: 26118863 doi: 10.1002/bdra.23352

Muscular Dystrophy Research

Muscular dystrophy refers to a group of genetic diseases that cause progressive muscle weakness. The most common form of muscular dystrophy affecting children is Duchenne/Becker muscular dystrophy (DBMD). Duchenne muscular dystrophy is the name that historically refers to the most severe form of this disorder. DBMD usually presents with weakness in early childhood. Weakness is progressive and children lose the ability to walk in late childhood. In the severe form, death occurs in young adulthood.

DBMD is caused by mutations in the dystrophin gene on the X chromosome. Approximately 1 in 3,500 boys have DBMD. Girls rarely have the disease, but they can be carriers of the gene mutation. Approximately one-third of boys with Duchenne muscular dystrophy did not inherit the disorder.

The Muscular Dystrophy Surveillance Tracking and Research Network
MD STAR*net*, the Muscular Dystrophy Surveillance, Tracking and Research Network, is a program currently active in five states. Its goal is to identify all people with childhood-onset Duchenne/Becker muscular dystrophies (DBMD). On behalf of the MD STAR*net*, the IRCID is conducting surveillance of Iowans born since 1982 with DBMD. This surveillance consists of identification and ongoing medical chart review.

2015 MD STAR*net* Publications Using IRCID Data
(Names listed in bold designate Iowa investigators)

Caspers Conway K, Mathews KD, Paramsothy P, Oleszek J, Trout C, **Zhang Y, Romitti PA**, and the MD STAR*net*. (2015) Neurobehavioral concerns among males with dystrophinopathy using population-based surveillance data from the Muscular Dystrophy Surveillance, Tracking, and Research Network. J Dev Behav Pediatr 36:455-63. PMID: 26020585 doi: 10.1097/DBP.0000000000000177

Romitti PA, Zhu Y, Puzhankara S, James KA, **Nabukera SK,** Zamba GK, Ciafaloni E, Cunniff C, Druschel CM, **Mathews KD,** Matthews DJ, Meaney FJ, Andrews JG, **Caspers Conway KM,** Fox DJ, Street N, Adams MM, Bolen J; on behalf of the MD STAR*net*. (2015) Prevalence of Duchenne and Becker muscular dystrophies in the United States. Pediatrics 135(3):513-21. PMID: 25687144 doi: 10.1542/peds.2014-2044, Erratum in Pediatrics 135(5):945 PMID: 25934896 doi: 10.1542/peds.2015-0652

Zhu Y, Romitti PA, Caspers Conway KM, Kim S, **Zhang Y,** Yang M, **Mathews KD,** and the MD STAR*net*. (2015) Genitourinary health in a population-based cohort of males with Duchenne and Becker muscular dystrophies. Muscle Nerve 52:22-27. PMID: 25297835 doi: 10.1002/mus.24486

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The Iowa Registry for Congenital and Inherited Disorders is a collaborative program of the University of Iowa's College of Public Health and the Iowa Department of Public Health.

Acknowledgements

We gratefully acknowledge the assistance of the following collaborating Iowa agencies and organizations:

The University of Iowa
- Center for Health Effects of Environmental Contamination
- College of Liberal Arts
- Carver College of Medicine
- College of Public Health
- Craniofacial Anomalies Research Center
- Governmental Relations Office
- Hygienic Laboratory
- Iowa Cancer Registry

Iowa Department of Public Health and the members of the Center for Congenital and Inherited Disorders Advisory Committee
Iowa Regional Genetic Consultation Service
Iowa Board of Regents
March of Dimes Birth Defects Foundation
KID Coalition
ASK Resource Center

Registry surveillance activities are funded by:
State of Iowa through a special appropriation to the Board of Regents
State of Iowa through a fee on issuance of birth certificates
Centers for Disease Control and Prevention

Registry research activities are funded by:
Centers for Disease Control and Prevention
National Institutes of Health

Registry educational activities are funded by:
Centers for Disease Control and Prevention

Development and publication of this report was supported by funds appropriated by the Iowa General Assembly to the State Board of Regents.

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