2021 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. IRCID conducts active surveillance to identify information about congenital and inherited disorders that occur in Iowa and to Iowa residents.

Since 1983, IRCID has collected information for nearly 60,000 children with various birth defects. This information is used by health care providers and educators to provide treatment and support services, and by researchers to study risk factors for birth defects and evaluate treatments for birth defects.

IRCID also conducts surveillance for nine muscular dystrophies – Duchenne, Becker, congenital, distal, Emery-Dreifuss, facioscapulohumeral, limb-girdle, myotonic, and oculopharyngeal. In addition, IRCID has collaborated with the Centers for Disease Control and Prevention (CDC) to develop approaches to conduct active surveillance for stillbirths, newborn screening disorders, and birth defects that may be related to Zika virus infection. Most recently, IRCID has collaborated with CDC to conduct active statewide surveillance for pregnant people who tested positive for SARS-CoV-2.

The surveillance and research efforts of 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, 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, CDC recognizes three surveillance approaches, each rated differently for completeness of ascertainment of pregnancies with a birth defect.

- Vital Record Reporting: 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 Reporting: 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).

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

Table 1. Prevalence (per 10,000 live births) for birth defects in Iowa, 2014-2018 deliveries

Birth Defect	Total	Prevalence
Brain/Spinal Cord		
Anencephalus	47	2.4
Encephalocele	26	1.3
Holoprosencephaly	36	1.8
Spina bifida without anencephalus	90	4.6
Eye		
Anophthalmia/microphthalmia	33	1.7
Congenital cataract	72	3.7
Ear		
Anotia/microtia	72	3.7
Heart		
Aortic valve stenosis	50	2.6
Atrial septal defect	518	26.6
Atrioventricular septal defect	104	5.3
Coarctation of aorta	136	7.0
Common truncus	15	0.8
Double outlet right ventricle	38	2.0
Ebstein anomaly	19	1.0
Hypoplastic left heart syndrome	54	2.8
Interrupted aortic arch	14	0.7
Pulmonary valve atresia and stenosis	190	9.8
Single ventricle	8	0.4
Tetralogy of Fallot	70	3.6
Total anomalous pulmonary venous return	19	1.0
Transposition of great arteries	54	2.8
Tricuspid valve atresia and stenosis	53	2.7
Ventricular septal defect	1091	56.1
Oral/Facial		
Choanal atresia	12	0.6
Cleft lip only	86	4.4
Cleft lip with cleft palate	134	6.9
Cleft palate without cleft lip	142	7.3

Table 1. (continued from previous page)

Birth Defect	Total	Prevalence
Gastrointestinal		
Biliary atresia	9	0.5
Esophageal atresia/tracheoesophageal fistula	44	2.3
Hirschsprung's disease (congenital megacolon)	29	1.5
Pyloric stenosis	356	18.3
Rectal and large intestinal atresia/stenosis	68	3.5
Small intestinal atresia and stenosis	74	3.8
Genital/Urinary		
Bladder exstrophy	7	0.4
Cloacal exstrophy	1	0.1
Congenital posterior urethral valves	18	0.9
Hypospadias[*,†]	635	63.8
Renal agenesis/hypoplasia	129	6.6
Muscle/Skeletal		
Clubfoot	371	19.1
Craniosynostosis	108	5.5
Diaphragmatic hernia	61	3.1
Gastroschisis	77	4.0
Limb deficiencies (reduction defects)	106	5.4
Omphalocele	60	3.1
Syndromes/Chromosomes		
Deletion 22q11.2	34	1.7
Down syndrome (Trisomy 21)	304	15.6
Edwards syndrome (Trisomy 18)	71	3.6
Patau syndrome (Trisomy 13)	39	2.0
Turner syndrome[‡]	40	4.2

[*] Includes first, second, and third degree hypospadias.

[†] Prevalence per 10,000 male live births.

[‡] Prevalence per 10,000 female live births.

Birth Defect Research

Approximately 1 in 33 newborns is affected by a major birth defect in the United States. These defects come with personal and monetary costs, both for families of these children and for society. Nearly 20% of all infant deaths are caused by major birth defects. Hospitalizations associated with major birth defects are longer than hospitalizations for other conditions and account for nearly $9 billion annually for infants under one year of age.

Because the causes of up to 70% of major birth defects that occur are unknown, research is a critical part of any strategy to prevent these defects. As such, in 1996 the United States Congress directed 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 (NBDPN)

The NBDPN is a nationwide association of birth defect programs and individuals. IRCID is an active member of NBDPN and participates in many NBDPN projects. For example, NBDPN provides a set of guidelines to help birth defect surveillance programs around the country organize their work in a consistent manner. 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 NBDPN is to encourage scientific collaboration among birth defect surveillance programs. IRCID has participated in several of these collaborations.

2021 NBDPN Publication Using IRCID Data (Names in bold designate Iowa investigators)

Heinke D, Isenburg J, Stallings E, Short T, Le M, Fisher S, Shan X, Kirby R, Nguyen H, Nestoridi E, Nembhard WN, **Romitti P**, Salemi J, Lupo P. (2021) Prevalence of structural birth defects among infants with Down syndrome, 2013-2017: a U.S. population-based study. Birth Defects Res 113:189-202.

Iowa Center for Birth Defects Research and Prevention (CBDRP)

The Iowa CBDRP was one of eight centers established by CDC to study genetic and environmental (broadly defined as non-inherited) risk factors for birth defects and continues as one of seven currently funded centers. Iowa CBDRP investigators have participated in local (statewide) projects and the National Birth Defects Prevention Study (NBDPS), as well as currently participating in the Birth Defects Study To Evaluate Pregnancy exposureS (BD-STEPS).

NBDPS was a population-based study that investigated risk factors for over 30 major birth defects. Partnering with the Iowa CBDRP, IRCID identified children with NBDPS-eligible birth defects and secured permission from mothers to share information with researchers. Mothers with a pregnancy affected by one of these birth defects and those with an unaffected pregnancy were interviewed about their health, diet, and lifestyle during their pregnancies. Biological specimens were requested from each family to study genetic factors. Over 43,000 interviews were completed nationwide, and specimens were collected from more than 25,000 families.

Nearly 300 projects have been conducted with NBDPS data. Some projects examine risk factors, such as maternal nutrition. Others examine gene and environment interaction effects. Projects conducted by Iowa investigators have the potential to positively impact the lives of Iowans. These projects examine relationships between birth defects and agricultural chemicals, cigarette smoking, alcohol consumption, diet, medications, and compounds in drinking water, along with genetic risk factors and their interactions with these exposures.

2021 NBDPS Publications Using IRCID Data (Names in bold designate Iowa investigators)

Cao Y, **Rhoads A**, **Burns TL**, **Carnahan R**, **Conway KM**, Werler MM, Mitchell A, **Romitti PA** and the National Birth Defects Prevention Study. (2021) Maternal use of cough medications during early pregnancy and selected birth defects: a USA, multisite case-control study. BMJ Open 11:e053604.

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Patel J, Bircan E, Tang X, Orloff M, Hobbs CA, Browne ML, Botto LD, Finnell RH, Jenkins MM, Olshan A, **Romitti PA**, Shaw GM, Werler M, Li J, Nembhard WN and the National Birth Defects Prevention Study. (2021) Paternal genetic variants and risk of obstructive heart defects: A parent-of-origin approach. PLoS Genet. 17:e1009413.

Petersen JM, Yazdy MM, Getz KD, Anderka MT, Werler MM, National Birth Defects Prevention Study. (2021) Short interpregnancy intervals and risks for birth defects: support for the nutritional depletion hypothesis. Am J Clin Nutr 113:1688-1699.

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Schrager NL, Adrien N, Werler MM, Parker SE, Van Bennekom C, Mitchell AA, National Birth Defects Prevention Study. (2021) Trends in first-trimester nausea and vomiting of pregnancy and use of select treatments: Findings from the National Birth Defects Prevention Study. Paediatr Perinat Epidemiol 35:57-64.

Siegel MR, Rocheleau CM, Broadwater K, Santiago-Colón A, Johnson CY, Herdt ML, Chen IC, Lawson CC, National Birth Defects Prevention Study. (2021) Maternal occupation as a nail technician or hairdresser during pregnancy and birth defects, National Birth Defects Prevention Study, 1997-2011. Occup Environ Med 79:17-23.

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Surveillance for Muscular Dystrophy

Muscular dystrophies (MDs) are a group of genetic progressive muscle diseases affecting an estimated 33 per 100,000 individuals and are characterized by worsening muscle weakness. Historically, types of MDs were diagnosed by known changes in muscle and clinical presentation; presently, diagnosis is determined largely by genetic analysis. Ages at symptom onset of MDs can range from birth through late adulthood. In children, Duchenne is the most common childhood MD, followed by congenital MDs. In adults, myotonic dystrophy is the most common MD, followed by facioscapulohumeral MD.

Muscular Dystrophy Surveillance Tracking and Research Network (MD STARnet)

The MD STAR*net* is a surveillance program currently active in seven states (Florida, Iowa, New York, North Carolina, South Carolina, Utah, Virginia) and funded by CDC. The goals of MD STAR*net* are to define and describe the MD population in the United States, define and describe healthcare needs and outcomes for individuals living with MD, and collect information to guide MD care, treatment, and policy. On behalf of MD STAR*net*, IRCID is conducting surveillance of Iowans who are diagnosed with one of eight MDs and meet residence, diagnostic, and treatment period criteria (Table 2). This surveillance consists of identification and ongoing medical chart review. In the current phase, we will identify individuals who have at least one eligible MD diagnostic code (International Classification of Disease [ICD], ICD-9, ICD-10).

Table 2. Number of individuals identified with a muscular dystrophy among Iowa residents

Phase of Surveillance/Muscular Dystrophy	Total
Phase I*	
Duchenne or Becker	140
Phase II†	
Becker	52
Congenital	24
Distal	5
Duchenne	105
Emery-Dreifuss	12
Facioscapulohumeral	81
Limb-Girdle	66
Myotonic	253
Oculopharyngeal	17
Phases III and IV	
Becker‡	20
Congenital^	35
Distal^	8
Duchenne‡	77
Emery-Dreifuss^	20
Facioscapulohumeral^	131
Limb-Girdle^	135
Myotonic^	418
Oculopharyngeal§	37

*Resident individual with MD diagnosis born on or after January 1, 1982 through December 31, 2011 who lived in Arizona, Colorado, Georgia, Hawaii, Iowa, or western New York.

†Resident individual with MD diagnosis and health encounter from January 1, 2007 through December 31, 2011 who lived in Arizona, Colorado, Iowa, or western New York.

‡Phase III: Resident individual with MD diagnosis born on or after January 1, 2000 and health encounter from January 1, 2000 through December 31, 2015 who lived in Colorado, Iowa, western New York, North Carolina, South Carolina, or Utah.

Phase IV: Resident individual with MD diagnosis born on or after January 1, 2000 and health encounter from January 1, 2000 through December 31, 2021 who lived in Florida, Iowa, western New York, North Carolina, South Carolina, Utah, or Virginia.

^Phase III: Resident individual with MD diagnosis since January 1, 2008 and health encounter from January 1, 2008 through December 31, 2016 who lived in Colorado, Iowa, western New York, North Carolina, South Carolina, or Utah.

Phase IV: Resident individual with MD diagnosis and health encounter from January 1, 2008 through December 31, 2019 who lived in Florida, Iowa, western New York, North Carolina, South Carolina, Utah, or Virginia.

§Phase III: Resident individual with MD diagnosis and health encounter from January 1, 2006 through December 31, 2016 who lived in Colorado, Iowa, western New York, North Carolina, South Carolina, or Utah.

2021 MD STAR*net* Publications Using IRCID Data (Names in bold designate Iowa investigators)

Haber G, **Conway KM**, Paramsothy P, Roy A, Rogers H, Ling X, Kozauer N, Street N, **Romitti PA**, Fox DJ, Phan HC, Matthews D, Ciafaloni E, Oleszek J, James KA, Galindo M, Whitehead N, Johnson N, Butterfield RJ, Pandya S, Venkatesh S, Bhattaram VA. (2021) Association of genetic mutations and loss of ambulation in childhood-onset dystrophinopathy. Muscle Nerve 63:181-191.

Mathews KD, **Conway KM**, **Gedlinske AM**, Johnson N, Street N, Butterfield RJ, Hung M, Ciafaloni E, **Romitti PA**. (2021) Characteristics of Clinical Trial Participants with Duchenne Muscular Dystrophy: Data from the Muscular Dystrophy Surveillance, Tracking, and Research Network (MD STARnet). Children 8:835.

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Zhang Y, Mann JR, James KA, McDermott S, **Conway KM**, Paramsothy P, Smith T, Cai B; MD STARnet. (2021) Duchenne and Becker muscular dystrophies' prevalence in MD STARnet surveillance sites: An examination of racial and ethnic differences. Neuroepidemiology 55:47-55.

Surveillance for Emerging Threats to Mothers and Babies Network (SET-NET)

CDC SET-NET aims to understand the effects of emerging and reemerging threats on pregnant people and their infants. To accomplish this, surveillance programs that participate in SET-NET work to detect the effects of these health threats by collecting data from pregnancy through childhood and use these data to inform clinical decision-making and public health action. IRCID is participating in SET-NET projects for Zika and SARS-CoV-2 infection during pregnancy.

Microcephaly and Other Birth Defects Related to Zika Virus Exposure

Congenital microcephaly (MC) is a serious birth defect characterized by an abnormally small head size in affected infants compared to infants of the same sex and gestational age. A dramatic increase in MC in infants in Brazil was linked to pregnant people infected with Zika virus. Zika virus exposure poses a serious risk to an unborn fetus; thus, more timely surveillance is needed

for monitoring MC and other birth defects that may be related to Zika virus exposure among pregnant people. To conduct this surveillance, IRCID created a rapid response team comprised of experienced surveillance professionals. Along with rapid surveillance, our team participated in national projects led by CDC to translate our surveillance data into public health action.

Outcomes Related to SARS-CoV-2 Infection among Pregnant People

In 2021, IRCID joined the CDC SET-NET to study outcomes for pregnant people infected by the SARS-CoV-2 virus and their offspring. The initial focus of this work is to conduct statewide surveillance of birth outcomes among pregnant people with a laboratory-confirmed SARS-CoV-2 infection in 2020. To date, IRCID has identified more than 3,000 deliveries among pregnant people in Iowa with SARS-CoV-2 infection during pregnancy.

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