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The Metropolitan Atlanta Congenital Defects Program: 35 Years of Birth Defects Surveillance at the Centers for Disease Control and Prevention

Adolfo Correa-Villaseñor,* Janet Cragan, James Kucik, Leslie O'Leary, Csaba Siffel, and Laura Williams

Division of Birth Defects and Developmental Disabilities, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, Atlanta, Georgia 30333

BACKGROUND: The Metropolitan Atlanta Congenital Defects Program (MACDP) is a population-based birth defects surveillance program administered by the Centers for Disease Control and Prevention (CDC) that has been collecting, analyzing, and interpreting birth defects surveillance data since 1967. This paper presents an overview of MACDP current methods and accomplishments over the past 35 years. **METHODS:** MACDP actively monitors major birth defects among infants born to residents of five counties of metropolitan Atlanta, an area with approximately 50,000 annual births. Cases are ascertained from multiple sources, coded using a modified British Pediatric Association six-digit code, and reviewed and classified by clinical geneticists. **RESULTS:** MACDP has monitored trends in birth defects rates and has served as a case registry for descriptive, risk factor, and prognostic studies of birth defects, including studies of Agent Orange exposure among Vietnam War veterans, maternal use of multivitamins, diabetes, febrile illnesses, and survival of children with neural tube defects. MACDP has served as a data source for one of the centers participating in the National Birth Defects Prevention Study, and for developing and evaluating neural tube defects prevention strategies related to the periconceptional use of folic acid supplements. **CONCLUSIONS:** Since its inception, MACDP has served as a resource for the development of uniform methods and approaches to birth defect surveillance across the United States and in many other countries, monitoring birth defects rates, and as a case registry for various descriptive, etiologic, and survival studies of birth defects. MACDP has also served as a training ground for a large number of professionals active in birth defects epidemiology. *Birth Defects Research (Part A) 67:617–624, 2003.* Published 2003 Wiley-Liss, Inc.†

INTRODUCTION

Birth defects are a leading cause of infant mortality in many parts of the world (Rosano et al., '00). In the United States, birth defects account for 21% of all deaths among infants (CDC, '98; Petrini et al., '02). Most children who are born with major birth defects and survive infancy are affected physically, mentally, or socially and can be at increased risk for morbidity from various health disorders. Because birth defects have a substantial public health impact on mortality, morbidity, disability, and health care costs (Hall et al., '78; MacLeod, '93; Yoon et al., '97; Rosano et al., '00), there has been a growing interest in defining their causes and in developing, implementing, and evaluating prevention programs. Public health surveillance systems for birth defects play an important role in collecting and analyzing data on birth defects in human populations and enable us to learn about occurrence patterns. This knowledge is essential in identifying the causes of birth defects, informing health policy decisions, and developing and evaluating prevention programs.

The Metropolitan Atlanta Congenital Defects Program (MACDP) is a population-based birth defects surveillance program created in 1967 following the thalidomide tragedy. MACDP is designed to provide early warning of increases in the prevalence of defects by monitoring trends over time. Founded as a collaboration of the Centers for Disease Control and Prevention (CDC), Emory University, and the Georgia Mental Health Institute, and administered by CDC, MACDP has been collecting, analyzing, and interpreting birth defects surveillance data on an ongoing basis. "Birth defects (i.e., congenital defects) are reportable conditions in Georgia, and the Georgia Department of Human Resources (DRH) has given MACDP the authority, renewed annually, to conduct active surveillance of birth defects in metropolitan Atlanta with and on behalf of the Georgia Division of Public Health, DRH." The specific objectives of MACDP today are essentially the same as when the program started (CDC, '89): (1) to monitor, regularly and systematically, births of malformed infants in the population for changes in incidence or unusual patterns suggestive of environmental influences, including drugs, infections, and chemical and physical agents; (2) to develop and maintain a case registry for use in epidemiologic and genetic studies; (3) to quantify the morbidity and mortality associated with birth defects; and (4) to provide

*Correspondence to: Adolfo Correa-Villaseñor, National Center on Birth Defects and Developmental Disabilities, Centers for Disease Control and Prevention, 1600 Clifton Road, Mailstop E-86, Atlanta, GA 30333.
E-mail: acorrea@cdc.gov

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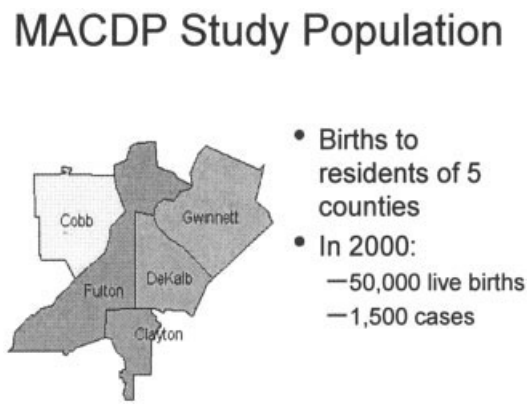


Figure 1. Metropolitan Atlanta Congenital Defects Program: Study Population.

data for education and health policy decisions leading to prevention.

Over the years, MACDP has served as a model for birth defects surveillance programs in the United States and in other countries, a source of cases for epidemiologic studies, and a training ground for birth defects investigators (Khoury and Edmonds, '92). In this paper, we present an overview of methods, accomplishments, and future plans for MACDP in celebration of its 35th anniversary.

METHODS

Population Covered

The population covered by MACDP includes all births occurring to residents of five counties in Metropolitan Atlanta (Figure 1): Clayton, Cobb, DeKalb, Fulton, and Gwinnett. The metropolitan Atlanta area has grown over the past two decades and now includes over 15 counties surrounding the 5 MACDP counties. The number of yearly births and the racial and ethnic composition of the base population have also changed over the years, and one of the challenges for MACDP has been to keep up with such growth. MACDP started with about 26,000 births per year and 587 cases of birth defects in 1968. In 2000, there were approximately 50,000 live births and 1,500 cases of birth defects. The percentage of non-white births has increased over time, from about 27% in 1968 to 48% in 2000.

Case Definition

Congenital anomalies, congenital malformations, and birth defects are synonymous terms used to describe an abnormality of structure, or function present at birth that is fatal or can result in physical or mental disability. For practical reasons, the inclusion criteria used for case ascertainment by MACDP are as follows:

1. Residence of birth mother in the five-county metropolitan Atlanta area at the time of delivery;
2. Presence of serious or major structural defects that can have adverse effects on health or development;
3. Ascertainment made by 6 years of age; and
4. Gestation of 20 weeks or more.

Whenever possible, MACDP also ascertains affected pregnancies that are prenatally diagnosed and terminated prior to 20 weeks of gestation. Because of incomplete ascertainment, records of prenatally diagnosed cases are analyzed separately.

Case subjects not included in MACDP are children with functional or metabolic disorders (e.g., cerebral palsy or phenylketonuria), hematological disorders (e.g., sickle cell disease, thalassemia, or hemophilia), minor defects (e.g., preauricular tags), and normal variants. Nevertheless, if a child has one or more major defects, then all defects, major and minor, and the presence of metabolic conditions are recorded because information on all defects can be helpful in the recognition of syndromes or patterns of multiple congenital anomalies.

Case Ascertainment

Cases in MACDP are identified on an ongoing basis by trained abstractors who actively search newborn hospitals, pediatric hospitals, and other sources. At newborn hospitals, CDC abstractors review all available logs, including: obstetric logs, newborn nursery logs, neonatal intensive care unit logs, postmortem logs, surgery records, and disease indices. Several conditions prompt abstractors to review thoroughly the medical records of infants, including any birth defect mentioned, preterm infants (<37 weeks) and low birth weight infants (<2500 grams), stillbirths and neonatal deaths, newborn surgical procedures, and all newborns in high-risk or special care nurseries.

At pediatric hospitals, abstractors also review computerized discharge indices and surgery and pathology records, if available. Any mention of a birth defect prompts abstractors to review thoroughly the medical records of infants and children.

Searches are also made through birth certificates, fetal death and death certificates obtained from the Georgia Department of Human Resources. Records of pathology reports for terminations, abortion records, autopsy records, and records of cytogenetic laboratories are also reviewed periodically.

Use of multiple sources for case ascertainment is more resource intensive and requires more time to prepare a database for analysis compared to programs that use more limited sources. However, use of multiple-source case ascertainment in MACDP has ensured a more complete case recording, more precise and accurate diagnoses, availability of maternal and infant data, and relative ease for researchers to conduct follow-up studies of children with birth defects.

Data Collection

A special abstraction form is used by abstractors to collect information on infants and children who meet the MACDP case definition. Data collected and coded include:

1. Identifying information on each infant, mother, and father that allows for comparison and linkage of multiple sources of case ascertainment;
2. Demographic information, including sex, maternal age, race and, ethnicity;
3. Diagnostic information on each type of birth defect;
4. Pregnancy information from prenatal and obstetric records, including plurality, gestational age, date of last

Table 1
A sample of Defects in the Metropolitan Atlanta Birth Defects Program Reported to the National Birth Defects Prevention Network, and Their International Classification of Diseases 9th Revision, Clinical Modification Codes, and Centers for Disease Control-British Pediatric Association Codes

Birth defects	ICD-9 CM codes	CDC-BPA codes
Central Nervous System		
Anencephaly	740.0–740.1	740.00–740.10
Spina bifida without anencephaly	741.0, 741.9 w/o 740.0, 740.1	741.00–741.99 w/o 740.00–740.10
Hydrocephalus without spina bifida	742.3 w/o 741.0, 741.9	742.30–742.39 w/o 741.00–740.99
Encephalocele	742.0	742.00–742.09
Microcephaly	742.1	742.10
Eye		
Anophthalmia/microphthalmia	743.0, 743.1	743.00–743.10
Congenital cataract	743.30–743.34	743.32–743.326
Aniridia	743.45	743.42
Ear		
Anotia/microtia	744.01, 744.23	744.01, 744.21
Cardiovascular		
Common truncus	745.0	745.00–745.01
Transposition of great arteries	745.10, .11, .12, .19	745.10–745.19
Tetralogy of Fallot	745.2	745.20–745.21, 746.84
Ventricular septal defect	745.4	745.40–745.490
Atrial septal defect	745.5	745.51–745.59
Endocardial cushion defect	745.60, .61, .69	745.60–745.69
Pulmonary valve atresia and stenosis	746.01, 746.02	746.00–746.01
Tricuspid valve atresia and stenosis	746.1	746.10
Ebstein anomaly	746.2	746.20
Aortic valve stenosis	746.3	746.30
Hypoplastic left heart syndrome	746.7	746.70
Patent ductus arteriosus	747.0	747.00
Coarctation of the aorta	747.10	747.10–747.19
Orofacial		
Cleft palate without cleft lip	749.00–749.04	749.00–749.09
Cleft lip with and without cleft palate	749.0–749.2	749.10–749.29
Choanal atresia	748.0	748.00

Source: CDC (2000).

menstrual period, estimated date of delivery, and birth weight;

5. Outcome information (e.g., stillbirth, neonatal death, and age at death); and

6. Hospital and physician information to facilitate follow-up procedures.

Coding and Classification of Birth Defects

For each affected infant, information is collected on up to 24 individual defects. These defects are coded by trained abstractors using a modified British Pediatric Association (BPA) six-digit code (BPA, '79) that is more detailed than the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM codes) (WHO, '79). Table 1 provides a sample of the major defects monitored by MACDP and reported to the National Birth Defects Prevention Network along with two coding schemes, ICD-9-CM (codes 740.0 to 759.9) and the BPA system. This list represents a sample of the more than 100 major defects monitored by MACDP. In an effort to improve on the anatomic specificity and pathogenetic classification of defects, we are currently developing a new birth defect six-digit code that will be based on the ICD-10 code.

All incoming case abstract forms are evaluated routinely by a clinical geneticist or dysmorphologist for accuracy and completeness of diagnosis, as well as for defect coding. This clinical review also assists in the classification of cases into patterns of associated defects (isolated, sequences, syndromes with recognized cause, and multiples defects) (Spranger et al., '82).

Quality Control Procedures

To evaluate the completeness and accuracy of MACDP, we have conducted several projects, including reabstraction of records, reviews of new computerized discharge summary indices, linkages with prenatal records, and special projects. One of these special projects made use of capture-recapture methods to evaluate the sensitivity of case ascertainment by MACDP, which was estimated to be 87% at 1 year after birth and 95% 2 years after birth (Honein and Paulozzi, '99).

Data Analysis and Dissemination

The frequency of birth defects is measured as prevalence at birth, expressed as the number of affected infants per 1,000 live births. Data on major birth defects are analyzed quarterly for changes in birth defects rates. Such changes are monitored by statistical evaluation of the difference between observed and expected numbers of specific de-

fects or defect combinations for a specified time. Expected numbers are obtained from baseline prevalence data for the previous 2 years. The CUSUM technique (Lucas, '85) is used to signal statistically significant changes in birth defects rates. Follow-up studies are conducted on occasion when appropriate.

MACDP provides reports on rates of birth defects to local and state officials and international programs on a regular basis. These include reports to the National Birth Defects Prevention Networks and to the International Clearinghouse for Birth Defects Monitoring Systems, an international consortium of 35 birth defects programs (ICBD, '02). MACDP is currently developing a more detailed technical report on birth defects rates for regular dissemination to local and state officials. Routine compilation of rates and reports of temporal trends and regional variations can be useful to health-care providers and to local and state officials.

RESULTS

During its 35 years of operation, MACDP has made several contributions to birth defects surveillance, epidemiology, and prevention.

Surveillance

MACDP has been collecting, analyzing, and interpreting birth defects surveillance data on an ongoing basis, and has identified almost 40,000 babies with serious birth defects. MACDP has served as a prototype for active case ascertainment surveillance systems across the United States and in many other countries, and as a model for surveillance programs for other adverse reproductive outcomes, such as developmental disabilities (Metropolitan Atlanta Developmental Disabilities Surveillance Program [MADDSP]) and fetal alcohol syndrome (Fetal Alcohol Syndrome Surveillance Network [FASSNet]).

MACDP has developed tools and methodology to support birth defect surveillance in the United States and worldwide (Edmonds et al, '81). MACDP has defined surveillance procedures for birth defect case ascertainment and validation and worked towards developing a standard coding format for use in birth defect programs (Oakley, '84; Lynberg et al., '93).

MACDP has been documenting long-term trends in a number of defects (CDC, '79, '81), such as declines in the rates of neural tube defects before the widespread use of prenatal diagnosis and food fortification with folic acid (Yen et al., '92) (Figure 2), increasing rates of hypospadias (Paulozzi et al., '97), and increasing rates of heart defects (Figure 3) (Botto et al., '01). Surveillance data from MACDP have been used to address important public health issues, such as a decline in congenital rubella syndrome with the decline in prevalence of maternal rubella (Cochi et al., '89), and the impact of prenatal diagnosis and new diagnostic techniques on birth defect rates (Roberts et al., '95). MACDP data have been essential in assisting state health departments in their response to public concerns about apparent clusters of birth defects and in serving as baseline rates in comparison studies of birth defects frequencies in special populations, such as pregnant women taking specific medications (Safra and Oakley '75, '76) and Gulf War veterans (Araneta et al, '97).

Through the use of cooperative agreements, CDC has supported the development of state birth defect surveillance programs. Using MACDP as a basis, the National Birth Defects Prevention Network (NBDPN) was formed and now has 40 state birth defect surveillance programs as members. This network publishes annual reports on the prevalence of birth defects in approximately one-half of the U.S. birth population (NBDPN, '00, '01, '02).

Epidemiology

MACDP data have allowed the conduct of studies on the descriptive epidemiology of birth defects, evaluation of potential teratogenic exposures, and examination of possible etiologic factors contributing to birth defects (Table 2).

MACDP served as the source of data on babies born with major structural birth defects for the Atlanta Birth Defects Case-Control (ABDCC) Study (Erickson et al., '84). Results from that study of births occurring during 1968-1980 led to the conclusion that there was no strong evidence to support the position that Vietnam veterans had a greater risk than other men of fathering babies with serious birth defects. Other analyses from this large database have greatly increased understanding of risk factors associated with birth defects, such as prescription medications (Safra & Oakley, '75, '76), cocaine abuse (Chavez et al., '89), maternal rubella (Cochi et al., '89), maternal diabetes mellitus (Becerra et al., '90), obesity (Watkins et al., '96, '01), febrile illnesses (Lynberg et al., '94; Botto et al., '01), vitamin A use (Khoury et al., '96), alcohol use (Moore et al., '97), maternal smoking (Honein et al., '00), and the effect modification of maternal diabetes by multivitamins (Correa et al., 03).

MACDP served as a source of case data for the Atlanta Birth Defects Risk Factors Surveillance project, a case-control study of birth defects that served as a precursor to the National Birth Defects Prevention Study (NBDPS). The NBDPS is a multicenter case-control study of genetic and environmental risk factors for birth defects that currently has collected data on 10,000 case and control infants (Yoon et al., '01). MACDP also serves as a source of case data for a collaborative study of risk factors for Down syndrome with Emory University School of Medicine (Yang et al., '99).

More recently, MACDP data have been linked with the National Death Index and Georgia vital statistics. This linkage has allowed two recent population-based studies of the survival experience of and prognostic factors for children with spina bifida (Wong and Paulozzi, '01) and encephalocele (Siffel et al., '03) in recent years.

Prevention

Data from the MACDP-based ABDCC Study corroborated initial studies (Smithells et al., '80, '83) that found a reduced risk for NTDs in the offspring of mothers who used periconceptional multivitamins (CDC, '88; Mulinare et al., '88). This and other studies (Milunsky et al., '89; Bower et al., '89) supported the implementation of randomized controlled trials of folic acid (MRC, '91) that ultimately led to the 1992 U.S. Public Health Service recommendation for folic acid consumption in women of childbearing age (CDC, '92), and to mandatory food fortification in 1998 (FDA, '96). Data from the Beijing Medical University-CDC community intervention project in China that used surveillance methodology adapted from

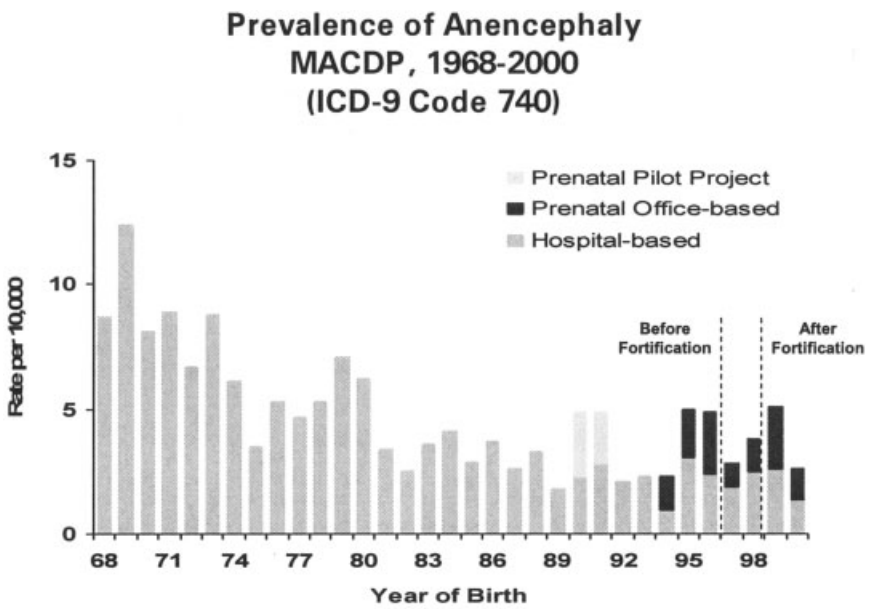
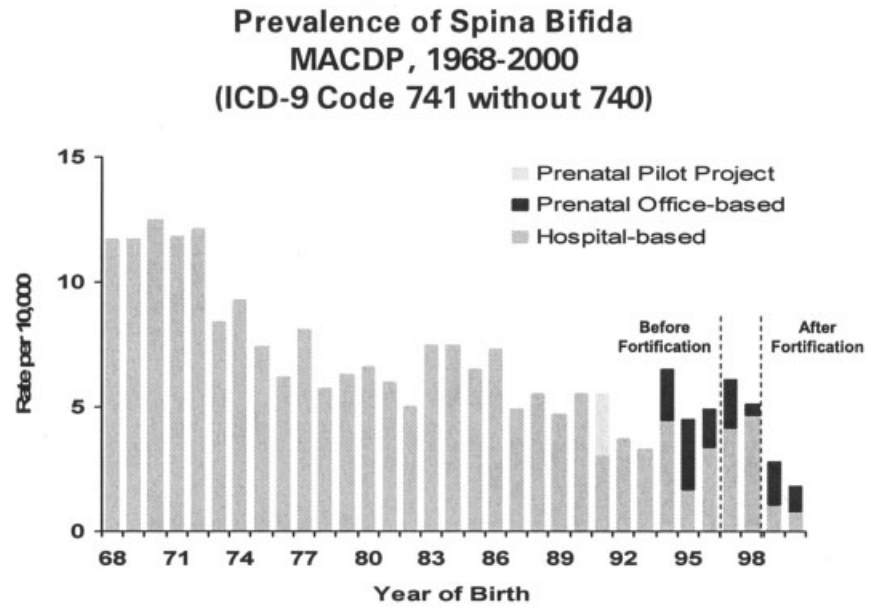


Figure 2. Trends in anencephaly and spina bifida, including prenatally ascertained cases, before and after fortification, Metropolitan Atlanta Congenital Defects Program, 1968-2000.



MACDP confirmed that 400 micrograms of folic acid daily significantly reduces the risk for NTDs (Berry et al., '99). Additional analyses using these data sets indicate that the risks for other birth defects might be reduced as well with use of multivitamins or folic acid (Botto et al., '96; Yang et al., '97; Itikala et al., '01; Myers et al., '01).

Efforts to evaluate the effectiveness of the folic acid prevention activities in the United States rely on the ability to document a decrease in the birth prevalence of NTDs. MACDP data, pooled with data from the NBDPN, have shown a significant decrease in NTD rates in the years after fortification (Williams et al., '02).

MACDP-based studies of other risk factors have led also to additional recommendations to reduce the risk of birth defects. For example, a study using MACDP data along with data from six other state programs found a six-fold increased risk for transverse limb reductions after chorionic villus sampling (Olney et al., '95). This led to recommendations for counseling women considering prenatal diagnosis (CDC, '95).

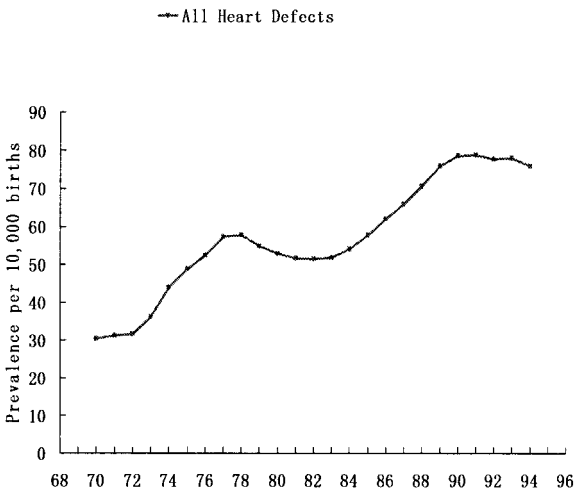


Figure 3. Reported prevalence of congenital heart defects, Metropolitan Atlanta Congenital Defects Program, 1968-1998.

DISCUSSION

Since its inception, MACDP has served as a model for many state-based programs, a resource for the development of uniform methods and approaches to birth defect surveillance and a prototype for active case ascertainment surveillance across the United States and around the world. The program has served as a training ground for a large number of professionals active in birth defects epidemiology, including CDC Epidemic Intelligence Service Officers, visiting scientists, fellows, preventive medicine residents, and medical and public health students. Such training has been important for building professional capacity in birth defects epidemiology in state health departments, federal agencies, universities, and private industry.

In its 35 years of continuous operation, MACDP has provided data from which numerous valuable scientific findings have been made in the field of birth defects epidemiology. Ongoing analyses of data from current studies and contributions to collaborative studies are certain to further extend our knowledge of the etiology of birth defects.

As birth defects continue to be an important cause of morbidity and mortality in children and as the causes of many birth defects remain unknown, there is a need to evaluate our current birth defects monitoring and research activities and to consider ways of enhancing such efforts. Current projects that represent an expansion of our surveillance capabilities and tools are: (1) development of an electronic database that will allow for more efficient inte-

Table 2
Examples of Uses of Data from the Metropolitan Atlanta Congenital Defects Program, 1971–2001

Year	Author	Concern	Type of study	Findings
1972	Rachelefalsy	Increased rate of phocomelia with use of tricyclic antidepressants	Case review	None of the mothers of cases with reduction deformity used the drugs
1973	CDC	Increased rates of birth defects with increased sales of spray adhesives	Secular trends	No change in rates of birth defects
1975	Saffra	Diazepam and cleft lip	Case-control	Possible association
1976	Erickson	Water fluoridation and birth defects	Ecologic	No association
1979	Edmonds	Airport noise and birth defects	Case-control	No association
1980	Layde	Maternal fever and neural tube defects	Case-control	Findings support an association
1984	Erickson	Vietnam veterans and birth defects	Case-control	No association
1988	Mulinare	Periconceptional use of multivitamins and neural tube defects	Case-control	Reduction in risk among offspring of users of multivitamins
1989	Cochi	Maternal rubella and birth defects	Secular trends	Decline in congenital rubella
1990	Becerra	Maternal diabetes and birth defects	Case-control	Association with several defects
1994	Sylvester	Anesthesia and birth defects	Case-control	No association
1995	Olney	Chorionic villus sampling and transverse digital deficiency	Case-control	An association
1995	Roberts	Impact of prenatal diagnosis on at birth prevalence of birth defects	Case review and secular trends	Decrease in at birth prevalence of anencephaly
1996	Botto	Periconceptional multivitamin use and heart defects	Case-control	Reduction in risk of conotruncal defects
1996	Watkins	Maternal obesity and neural tube defects	Case-control	Possible association
2000	Honein	Maternal smoking, family history and clubfoot	Case-control	Possible gene-environment interaction
2001	Botto	Temporal trends and racial variations in heart defects	Secular trends	Increasing and decreasing trends with racial variations
2001	Itikala	Periconceptional multivitamin use and orofacial clefts	Case-control	Possible reduction in risk
2003	Siffel	Survival of and prognostic factors for infants with encephalocele	Cohort	Improved survival over time; prognostic factors include presence of other defects, low birth weight, race

gration of the data collection, review, and report preparation; (2) development of software for statistical analysis and plotting of temporal trends; (3) linkage of MACDP data with MADDSP data to allow further evaluations of the prevalence of developmental disabilities among children with birth defects; (4) geocoding MACDP data to allow evaluation of regional variations in prevalence and mortality of birth defects; and (5) linkage of MACDP data with environmental data to facilitate environmental tracking. Because MACDP covers a limited geographic area, we plan to continue to work with states to design, implement, and coordinate population-based birth defect programs to provide a nationwide coverage for birth defect surveillance and etiologic studies with the goal of preventing birth defects.

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