Updated National Birth Prevalence Estimates for Selected Birth Defects in the United States, 2004–2006

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BACKGROUND: The National Birth Defects Prevention Network collects state-specific birth defects surveillance data for annual publication of prevalence estimates and collaborative research projects. In 2006, data for 21 birth defects from 1999 through 2001 were presented as national birth prevalence estimates. The purpose of this report was to update these estimates using data from 2004 through 2006. **METHODS:** Population-based data from 11 active case-finding programs, 6 passive case-finding programs with case confirmation, and 7 passive programs without case confirmation were used in this analysis. Pooled birth prevalence estimates for 21 birth defects, stratified by case ascertainment approach, were calculated. National prevalence estimates, adjusted for maternal race/ethnicity and maternal age (trisomy 13, trisomy 18, and Down syndrome only) were determined using data from 14 programs. The impact of pregnancy outcomes on prevalence estimates was also assessed for five specific defects. **RESULTS:** National birth defects prevalence estimates ranged from 0.72 per 10,000 live births for common truncus to 14.47 per 10,000 live births for Down syndrome. Stratification by type of surveillance system showed that active programs had a higher prevalence of anencephaly, anophthalmia/microphthalmia, cleft lip with or without cleft palate, reduction defect of upper limbs, and trisomy 18. The birth prevalence of anencephaly, trisomy 13, and trisomy 18 also varied substantially with inclusion of elective terminations. **CONCLUSION:** Accurate and timely national estimates of the prevalence of birth defects are needed for monitoring trends, assessing prevention efforts, determining service planning, and understanding the burden of disease due to birth defects in the United States. *Birth Defects Research (Part A) 88:1008–1016, 2010.* © 2010 Wiley-Liss, Inc.

Key words: birth defects; surveillance; prevalence; national estimates; United States

INTRODUCTION

Major birth defects (i.e., structural malformations with a significant impact on the health and development of a child) remain an important public health issue because they are a leading cause of infant mortality and lifelong disabilities; in addition, they substantially impact health care costs. Birth defects contributed to more than 5500

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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infant deaths in 2005, accounting for 20% of infant mortality in the United States (Mathews and MacDorman, 2008). An estimated 2.3% of cases of premature death and disability, as measured by disability-adjusted life years, among the United States population were due to congenital abnormalities (McKenna et al., 2005). In 2004, hospital costs alone for those admitted principally for treatments of birth defects in the United States totaled $2.6 billion (Russo and Elixhauser, 2007).

Since 1997, the National Birth Defects Prevention Network (NBDPN) has collected birth defects surveillance data for publication in its annual report, and for use in multistate collaborative projects. These multistate collaborations have included investigations of the declining rates of spina bifida, anencephaly, and other birth defects after folic acid fortification of the U.S. grain supply; the epidemiology of club foot; and the association between birth defects and preterm delivery (Canfield et al., 2005; Honein et al., 2009; Parker et al., 2009; Williams et al., 2002; Williams et al., 2005). In 2006, national birth prevalence estimates were published for the first time for 21 birth defects, based on surveillance data from 1999 through 2001 (Canfield et al., 2006).

National birth prevalence estimates have provided points of reference for several epidemiologic studies of birth defect risk factors and have guided public health research agendas for specific birth defects, such as Down syndrome (Rasmussen et al., 2008). Timely estimates of the national birth prevalence of specific birth defects are needed to enable researchers to examine the contribution of prevention activities to improved outcomes, and to provide information to families and health practitioners concerning the actual prevalence of these conditions. The purpose of this project was to provide updated national birth prevalence estimates using the most recently available data from 2004 through 2006.

MATERIALS AND METHODS

The NBDPN annually publishes state/regional level data on 45 major birth defects from over 30 population-based surveillance programs as part of a special issue of *Birth Defects Research Part A*. These programs vary in their ascertainment approaches. For this study, the eligible programs were grouped into three general categories based on their primary method of case-finding and verification. Programs that used abstractors to review medical records for case-finding were grouped into the active case-finding category. Programs that relied on administrative datasets for case-finding and then verified the cases through medical record review or other follow-up methods were grouped into passive case-finding with follow-up, and the remaining programs without case confirmation were grouped into passive case-finding without follow-up.

Twenty-one birth defects were selected and grouped into the following categories for this study: central nervous system defects (anencephaly, spina bifida without anencephaly, and encephalocele), eye defects (anophthalmia/microphthalmia), cardiovascular defects (common truncus, transposition of great arteries [TGA], tetralogy of Fallot, atrioventricular septal defect [AVSD], and hypoplastic left heart syndrome), orofacial defects (cleft palate, cleft lip with or without cleft palate), gastrointestinal defects (esophageal atresia/tracheoesophageal fistula, rectal and large intestinal atresia/stenosis), musculoskeletal defects (reduction defects of the upper limbs, reduction defects of the lower limbs, gastroschisis, omphalocele, and diaphragmatic hernia), and chromosomal anomalies (trisomy 13, trisomy 18, and trisomy 21 [Down syndrome]). These defects were selected because they are usually diagnosed at birth or soon after birth, and diagnostic accuracy of these defects is not expected to vary widely between surveillance systems (Canfield et al., 2006). The *International Classification of Diseases, Clinical Modification* (*ICD-9-CM*) codes and the Centers for Disease Control and Prevention (CDC) coding based on the British Pediatric Association codes for each defect are listed in the NBDPN annual report appendix (National Birth Defects Prevention Network, 2009a).

For this study, we included data only from participating programs that were able to provide individual year data continuously from 2004 through 2006 as part of the 2009 NBDPN annual report data request. The data collection methods and specifications for the NBDPN annual report have been described previously (National Birth Defects Prevention Network, 2009a).

Population-Based Surveillance Data by Case Ascertainment Method

Population-based birth defects surveillance data were first stratified by case ascertainment methodology and then pooled to determine unadjusted birth prevalence estimates and 95% confidence intervals (CIs) for the selected defects. There were 11 active case-finding programs (Arkansas, Arizona, California [8-county Central Valley], Georgia [5-county metropolitan Atlanta], Iowa, Massachusetts, North Carolina, Oklahoma, Puerto Rico, Texas, and Utah); 6 passive with follow-up programs (Colorado, Illinois, Kentucky, New Jersey, New Mexico, and New York); and 7 passive surveillance programs (Florida, Indiana, Michigan, Tennessee, Virginia, Wisconsin, and West Virginia).

Birth defect prevalence (hereinafter referred to simply as ''prevalence'') reflected the frequency of a given birth defect within a birth cohort at the time of delivery. Cases might have included live born infants, fetal deaths (typically 20 weeks gestation or greater), and elective terminations. Prevalence was expressed as the number of cases per 10,000 live births, even though the numerator included cases of any pregnancy outcomes (live births, fetal deaths, and elective terminations). The 95% CI was estimated with the assumption that the observed number of cases followed a Poisson distribution. Data were analyzed using SAS 9.1 (SAS Institute, Cary, NC).

National Prevalence Estimates

The national prevalence estimates for each of the selected defects were derived using data from a subset of the programs. Programs that met the following two criteria were included in this subset: (1) active case-finding or passive case-finding with verification of all cases reported for the defects and (2) inclusion of at least live birth and stillbirth cases. Therefore, programs that confirmed only a percentage of the reported cases for a specific defect or those that limited their case definition to only live births were excluded. After excluding programs that did not meet the inclusion criteria, 14 programs were used to cal-

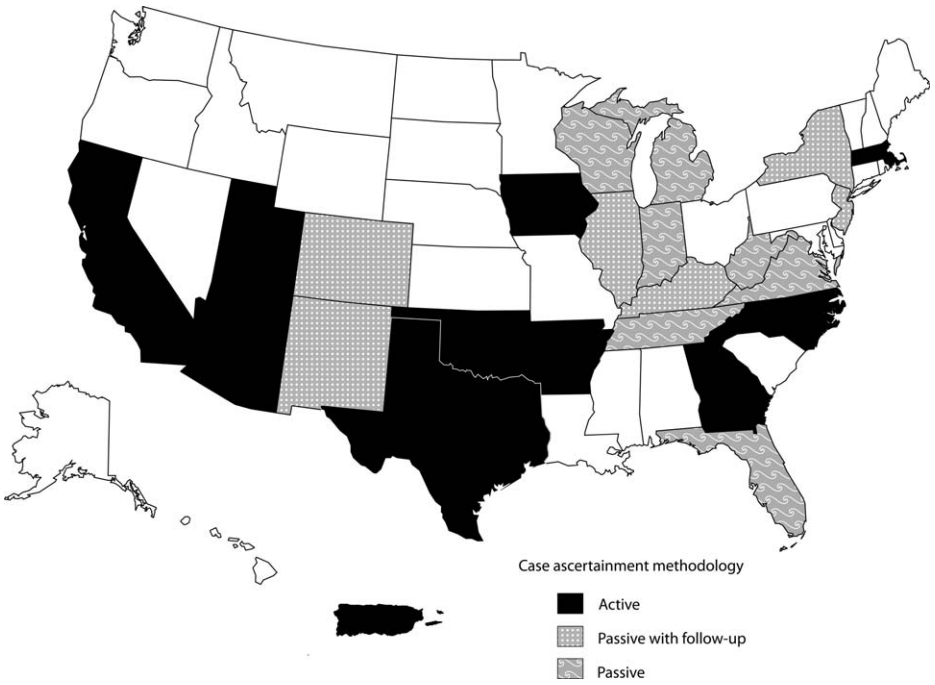

Figure 1. Surveillance programs and ascertainment method for 24 programs, 2004–2006.

culate the national prevalence estimates. These were all 11 of the active programs, nine of which included elective terminations in their case definition, and three of the passive with follow-up programs (Colorado, Illinois, and Kentucky). Colorado data were excluded from the analyses on eye defects, three cardiovascular defects (common truncus, tetralogy of Fallot, and AVSD), and the gastrointestinal defects because of a lack of case confirmation for these defects. Similarly, Kentucky data were excluded from the analyses on all cardiovascular defects. Two of the active surveillance systems did not collect data on all defects; Arizona was excluded from estimates on AVSD and rectal and large intestinal atresia/stenosis, and Puerto Rico was excluded from estimates for eye defects, gastrointestinal defects, and diaphragmatic hernia. The denominators of total live births reflected the programs in each defect-specific prevalence estimate.

The crude national prevalence estimates were standardized to the racial and ethnic distribution of the United States live birth population from 2004 through 2006, which totaled 12,515,956 births. Additionally, the estimated national prevalence for the chromosomal anomalies was standardized to the maternal age distribution. Maternal age was categorized as younger than 35 years of age or 35 years of age or older. Data on the United States live birth population for 2004 through 2006 were obtained from the National Center on Health Statistics (Martin et al., 2006; Martin et al., 2007; Martin et al., 2009). The new national estimates were compared to the previous estimates published in Canfield et al. (2006) using a Z-test for independent proportions.

Prevalence by Pregnancy Outcome

The NBDPN began collecting information on pregnancy outcomes for five specific defects as part of the 2009 annual report data request. Cases of anencephaly, spina bifida, trisomy 13, trisomy 18, and Down syndrome stratified by live births, stillbirths, and elective terminations were requested. Three active case-finding surveillance programs (Georgia, Iowa, and Utah) performing enhanced prenatal case ascertainment with added data sources, such as prenatal diagnostic facilities and cytogenetic laboratories, were able to provide stratified data for 2004 through 2006, which then were pooled to determine the contribution of each pregnancy outcome on the prevalence of the five specific defects.

RESULTS

Population-Based Surveillance Data by Case Ascertainment Method

Twenty-four population-based birth defects programs provided yearly data for the 21 selected defects for the period January 1, 2004, through December 31, 2006 (Fig. 1). The participating programs covered the Northeast, Southeast, and Southwest regions of the United States, areas with a total of approximately 2.4 million births per year during the study period.

After stratification of the programs based on their surveillance methodologies, the pooled unadjusted prevalence estimates and 95% CIs for the selected defects were calculated for each of the three types of surveillance systems (Table 1). Down syndrome was the most common condition we examined, with a prevalence ranging from 13.08 per 10,000 live births among programs using strictly passive case-finding methods to 13.48 per 10,000 live births among programs using active case ascertainment. The least common defects among all surveillance systems were encephalocele and common truncus. Among the passive surveillance programs, trisomy 13 had the lowest unadjusted prevalence.

Table 1
Pooled Prevalence of Selected Birth Defects by Type of Surveillance System, United States, 2004–2006

Birth Defects	Active (N = 11)[a]			Passive with Follow-up (N = 6)[b]			Passive (N = 7)[c]		
	Cases	Prevalence [d]	95% CI	Cases	Prevalence [d]	95% CI	Cases	Prevalence [d]	95% CI
Central nervous system defects									
Anencephaly	697	2.23	2.07–2.41	211	1.02	0.89–1.16	192	0.89	0.78–1.03
Spina bifida without anencephaly	1162	3.72	3.52–3.94	561	2.70	2.49–2.94	820	3.82	3.57–4.09
Encephalocele[1]	261	0.84	0.74–0.94	125	0.63	0.53–0.75	184	0.86	0.74–0.99
Eye defects									
Anophthalmia/microphthalmia[1,2]	623	2.10	1.94–2.27	217	1.09	0.95–1.24	209	0.97	0.85–1.12
Cardiovascular defects									
Common truncus[1]	231	0.74	0.65–0.84	134	0.67	0.57–0.80	184	0.86	0.74–0.99
Transposition of great arteries	948	3.04	2.85–3.24	610	2.94	2.71–3.18	1083	5.05	4.76–5.38
Tetralogy of Fallot	1264	4.05	3.83–4.28	798	3.84	3.59–4.12	1003	4.68	4.39–4.97
Atrioventricular septal defect[1,3]	1330	4.70	4.45–4.96	661	3.32	3.08–3.58	891	4.15	3.89–4.44
Hypoplastic left heart syndrome	720	2.31	2.14–2.48	457	2.20	2.01–2.41	624	2.91	2.69–3.15
Orofacial defects									
Cleft palate without cleft lip	2012	6.45	6.17–6.74	1197	5.77	5.45–6.10	1359	6.33	6.01–6.68
Cleft lip with or without cleft palate	3397	10.89	10.53–11.26	1814	8.74	8.35–9.15	2024	9.43	9.03–9.85
Gastrointestinal defects									
Esophageal atresia/tracheoesophageal fistula[1,2]	629	2.12	1.96–2.29	506	2.54	2.33–2.77	506	2.36	2.16–2.57
Rectal and large intestinal atresia/stenosis[1,2,3]	1304	4.86	4.61–5.14	840	4.22	3.94–4.51	915	4.27	4.00–4.55
Musculoskeletal defects									
Reduction deformity, upper limbs	1136	3.64	3.43–3.86	514	2.48	2.27–2.70	433	2.02	1.84–2.22
Reduction deformity, lower limbs	514	1.65	1.51–1.80	294	1.42	1.26–1.59	289	1.35	1.20–1.51
Gastroschisis	1473	4.72	4.49–4.97	671	3.23	3.00–3.49	N/A[4]	N/A[4]	N/A[4]
Omphalocele[1]	600	1.92	1.77–2.08	285	1.43	1.27–1.61	N/A[4]	N/A[4]	N/A[4]
Diaphragmatic hernia[1,2]	772	2.60	2.42–2.79	499	2.51	2.29–2.74	617	2.88	2.66–3.11
Chromosomal anomalies									
Trisomy 13	375	1.20	1.09–1.33	217	1.05	0.92–1.19	181	0.84	0.73–0.98
Trisomy 21 (Down syndrome)	4208	13.48	13.08–13.90	2735	13.17	12.69–13.68	2806	13.08	12.60–13.57
Trisomy 18	795	2.55	2.38–2.73	371	1.79	1.61–1.98	288	1.34	1.20–1.51

[a]Eleven active birth defects surveillance systems, number of live births 2004–2006 = 3,120,605.
[b]Six passive surveillance systems with case confirmation component, number of live births 2004–2006 = 2,075,973.
[c]Seven passive surveillance systems, number of live births 2004–2006 = 2,145,287.
[d]Prevalence per 10,000 live births.
[1]Passive with follow-up data exclude New Mexico.
[2]Active surveillance data exclude Puerto Rico.
[3]Active surveillance data exclude Arizona.
[4]Not applicable, gastroschisis and omphalocele cannot be distinguished by passive surveillance programs.
CI, confidence interval.

Table 2
Adjusted National Prevalence Estimates and Estimated Number of Births Affected in the United States, 2004–2006

	Estimated National Prevalence per 10,000 Live births	95% Confidence Interval	Cases per Births	Estimated Annual Number of Cases Nationally	95% Confidence Interval
Adjusted for maternal race and ethnicity[a]					
Central nervous system defects					
Anencephaly	2.06	1.92–2.20	1 in 4859	859	800–918
Spina bifida without anencephaly	3.50	3.31–3.68	1 in 2858	1460	1383–1537
Encephalocele	0.82	0.73–0.91	1 in 12,235	341	304–378
Eye defects					
Anophthalmia/microphthalmia	1.87	1.73–2.01	1 in 5349	780	721–839
Cardiovascular defects					
Common truncus	0.72	0.63–0.81	1 in 13,876	301	265–337
Transposition of great arteries	3.00	2.83–3.17	1 in 3333	1252	1180–1324
Tetralogy of Fallot	3.97	3.77–4.17	1 in 2518	1657	1572–1742
Atrioventricular septal defects	4.71	4.48–4.94	1 in 2122	1966	1870–2061
Hypoplastic left heart syndrome	2.30	2.15–2.45	1 in 4344	960	898–1023
Orofacial defects					
Cleft palate without cleft lip	6.35	6.11–6.60	1 in 1574	2651	2549–2754
Cleft lip with and without cleft palate	10.63	10.32–10.95	1 in 940	4437	4304–4570
Gastrointestinal defects					
Esophageal atresia/tracheoesophageal fistula	2.17	2.02–2.32	1 in 4608	905	843–968
Rectal and large intestinal atresia/stenosis	4.68	4.45–4.91	1 in 2138	1952	1855–2048
Musculoskeletal defects					
Reduction deformity, upper limbs	3.49	3.30–3.67	1 in 2869	1454	1378–1530
Reduction deformity, lower limbs	1.68	1.56–1.81	1 in 5949	701	649–754
Gastroschisis	4.49	4.28–4.69	1 in 2229	1871	1784–1958
Omphalocele	1.86	1.73–1.99	1 in 5386	775	720–830
Diaphragmatic hernia	2.61	2.45–2.77	1 in 3836	1088	1020–1155
Chromosomal anomalies					
Trisomy 13	1.28	1.18–1.39	1 in 7784	536	491–581
Trisomy 21 (Down syndrome)	13.56	13.20–13.92	1 in 737	5657	5506–5808
Trisomy 18	2.64	2.48–2.80	1 in 3788	1101	1036–1166
Adjusted for maternal age[a]					
Chromosomal anomalies					
Trisomy 13	1.26	1.16–1.37	1 in 7906	528	482–573
Trisomy 21 (Down syndrome)	14.47	14.11–14.83	1 in 691	6037	5886–6188
Trisomy 18	2.66	2.50–2.81	1 in 3762	1109	1044–1174

[a]Adjustments based on United States live birth population, 2004–2006.

The prevalence of specific defects varied among the different types of surveillance systems. Defects with considerable variation among the surveillance methodology groups included anencephaly; anophthalmia/microphthalmia; cleft lip with or without cleft palate; rectal and large intestinal atresia/stenosis; reduction defect of the upper limbs; gastroschisis; omphalocele; and trisomy 18, for which the crude prevalence estimates were notably higher among the active surveillance systems relative to corresponding prevalence estimates among the passive systems. Specific defects for which the prevalence appeared to be higher among passive than among active systems were TGA; tetralogy of Fallot; and hypoplastic left heart syndrome. The prevalence of gastroschisis and omphalocele were not available for strictly passive programs due to their reliance on *ICD-9-CM* coding and the inability of the coding system to distinguish between these two defects.

National Prevalence Estimates

The adjusted national estimates of the selected defects, based on data from 14 population-based birth defects registries are presented in Table 2. The number of live births represented by the catchment areas for these 14 programs from 2004 through 2006 was 4,038,506. After adjustment for maternal race and ethnicity, Down syndrome remained the most common birth defect of those examined, with an estimated adjusted national prevalence of 13.56 per 10,000 live births or 1 in 737 live births. Cleft lip with or without cleft palate was the second most common condition, with an adjusted prevalence of 10.63 per 10,000 live births or 1 in 940 live births. After adjusting the chromosomal anomalies for maternal age, the estimated national prevalence of Down syndrome increased significantly to 14.47 per 10,000 live births, while estimates for trisomy 13 and trisomy 18 remained similar.

In addition to variation based on the type of surveillance system, there also was variation in the reported prevalence of specific defects across the states. State-specific prevalence data for the 14 programs used to estimate the national prevalence are presented in Figure 2. Program-specific prevalence estimates for individual defects tended to cluster together with occasional outliers. Cleft lip with or without cleft palate exhibited considerable variation in prevalence across states, whereas the cardiovascular defects consistently appeared to have some of the least varying estimates. Down syndrome had very consistent estimates, with the exception of two states reporting considerably higher prevalence.

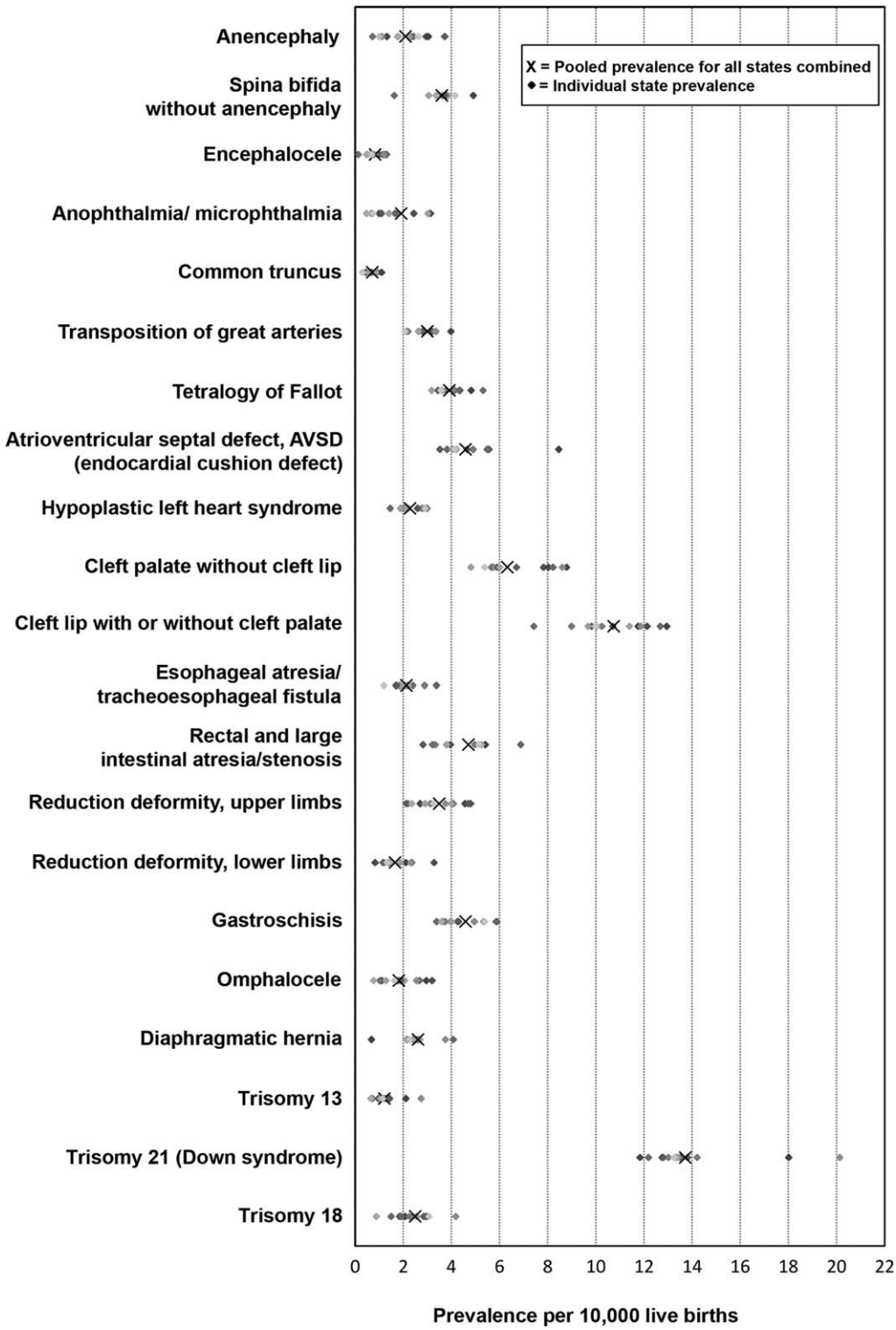

Figure 2. State-specific and pooled prevalence for 21 selected defects from 14 surveillance programs, 2004–2006.

Prevalence by Pregnancy Outcome

Three active case-finding surveillance systems with additional prenatal data sources provided data for five selected defects stratified by pregnancy outcome. The prevalence of all defects increased from the initial live birth prevalence as stillbirths and elective terminations were subsequently added to the case definition (Table 3).

Table 3
Prevalence of Selected Defects by Pregnancy Outcome Inclusions, 2004–2006[a]

Defect	Prevalence[b] by Pregnancy Outcomes		
	Live births	Live births and Stillbirths	Live births, Stillbirths, and Terminations
Anencephaly	0.55	1.02	2.54
Spina Bifida	3.40	3.51	4.41
Trisomy 13	0.81	1.11	1.89
Trisomy 21 (Down syndrome)	13.51	14.14	16.08
Trisomy 18	1.50	2.38	3.60

[a]Data from three active case-finding surveillance systems, Georgia, Iowa, and Utah.
[b]Prevalence per 10,000 live births.

The prevalence of anencephaly increased from 0.55 to 1.02 with the addition of stillbirth cases and then further increased to 2.54 as elective termination cases were added. The addition of pregnancy outcomes, other than live births, contributed to a 4½-fold increase in the estimated prevalence of anencephaly. The prevalence of trisomy 13 and trisomy 18 also were influenced strongly by the inclusion of additional pregnancy outcomes, increasing from 0.81 to 1.89 and 1.50 to 3.60, respectively. Spina bifida and Down syndrome showed the least amount of change with added pregnancy outcomes.

DISCUSSION

National Prevalence Estimates

The national prevalence estimates for 21 major birth defects were determined using data from 14 population-based surveillance systems, representing 32.3% of all live births in the United States from 2004 through 2006. The birth defects selected for this study included major structural malformations of several systems, such as the central nervous, cardiovascular, and gastrointestinal systems, and chromosomal anomalies. This study provides an update to previous national estimates of selected birth defects, which were based on data from 1999 through 2001 (Canfield et al., 2006).

The national estimates for the selected defects we presented have several strengths. The estimates were based on confirmed cases of birth defects from population-based surveillance systems that represented both demographic and geographic variations in the United States. Additionally, availability of data on maternal race and ethnicity allowed for adjustment, given reported variation in prevalence of defects based on race and ethnicity (Canfield et al., 2006; Canfield et al., 2009; Carmichael et al., 2004; Nembhard et al., 2010; Williams et al., 2005). Furthermore, adjustments for maternal age were made for chromosomal anomaly rates. The number of annual estimated cases increased slightly for Down syndrome when maternal age was taken into account. This increase was explained by the higher prevalence of Down syndrome among offspring of older mothers and the increasing contribution to the total birth population (Allen et al., 2009).

An additional strength of the national estimates was the inclusion of cases other than live births, which allowed for a more accurate estimation of the prevalence of the selected defects. Of the 14 programs used in determining the national estimates, nine ascertained cases among live births, stillbirths, and elective terminations, while the remaining five included both live births and stillbirths. Limiting the data to live birth cases only can greatly underestimate the prevalence of certain birth defects. The inclusion of stillbirths and elective terminations influences the prevalence of specific conditions more so than others, with fatal and severe conditions affected the most (Schechtman et al., 2002). For the majority of the selected defects, the updated national estimates remained similar to those reported previously (Canfield et al., 2006). Changes in the surveillance methodology of individual birth defects programs, coding modifications of congenital heart malformations between the two data collection periods, and slightly differing designs in the study methods could have accounted for some of the variability between the two reports.

Significant changes in the estimated national prevalence were observed for anencephaly, TGA, and gastroschisis. The decrease in prevalence of anencephaly from 2.51 to 2.06 ($p < 0.01$) was consistent with previous reports of the decrease of neural tube defect (NTD)-affected pregnancies since folic acid fortification. A study of the prevalence of spina bifida and anencephaly during the post-fortification period observed a significant decrease in the prevalence of anencephaly, but not spina bifida, from the period 1999 through 2000 to the period 2003 through 2004 (Boulet et al., 2008). A possible explanation for the post-fortification decrease in the birth prevalence of anencephaly (vs. spina bifida) over time might have been due to changes in prenatal diagnostic practices that could have made it more difficult for population-based surveillance systems to ascertain this fatal condition. Peller et al. (2004) found increases in prenatal screening and elective terminations for anencephaly from 1974 through 1999. If diagnostic tests were done earlier during pregnancy, or if elective terminations were performed in an outpatient clinic that surveillance systems did not routinely cover, then such cases would not have been captured by the surveillance system and the birth prevalence of selected defects could have been underestimated. Another reason for the decrease could have been the secular trend of decreasing NTD rates since the late 1960s (Lary and Edmonds, 1996; Yen et al., 1992).

The decline in the estimated prevalence of TGA from 4.73 to 3.00 ($p < 0.01$) could have been explained by changes made to the heart defect code inclusions in the 2009 NBDPN annual report data request. A study conducted using data from the Metropolitan Atlanta Congenital Defects Program (MACDP) demonstrated that relying strictly on administrative defect codes produced many false positives for TGA when compared to the use of a more clinically relevant nomenclature (Strickland et al., 2008). Subsequently, in an effort to improve the accuracy of reporting, the NBDPN revised its cardiovascular defect code list to exclude certain subtypes of TGA codes that might not actually have represented true cases of the TGA defect. Other cardiovascular defects that underwent changes in code inclusion criteria included tetralogy of Fallot and AVSD. This also explained the findings in our analysis of prevalence based on the method of surveillance, that passive systems showed a higher pooled prevalence for these heart defects. The elevated prevalence of specific heart defects among passive sur-

veillance programs might be explained by the contribution of false positives. Such systems rely on reports from administrative data sources and do not use a follow-up system to confirm the cases. Reliance only on physician diagnoses might result in greater misclassification of cases than if a confirmatory diagnostic test is required for inclusion (Hobbs et al., 2001).

In addition to anencephaly and TGA, gastroschisis showed a significant change between the two time periods. The increase observed in the prevalence of gastroschisis, 3.73 to 4.49 ($p < 0.01$), compared to previous national estimates, was in concordance with studies from California, North Carolina, Texas, and Utah, all of which reported significant increases in gastroschisis the past decade (Benjamin et al., 2010; Hougland et al., 2005; Laughon et al., 2003; Vu et al., 2008).

Several defects showed slight, nonsignificant decreases in the national estimated prevalence between the two time periods. These changes in prevalence might have been explained by the inclusion of programs with passive case ascertainment in the updated estimates. With the exception of the chromosomal anomalies, all estimates remained similar or increased when the analysis was limited to just the active programs. None of the observed changes were significant (unpublished data).

State-Specific Variation

Although we limited the programs included in the national estimates to those with either an active ascertainment methodology or an active case confirmation component, some variation in state-specific prevalence still remained across programs. Birth defect studies using data from multiple surveillance systems have observed variations in the reported prevalence of defects such as spina bifida and Down syndrome (Lary and Edmonds, 1996; Shin et al., 2009). A study of the effect of grain fortification on the prevalence of 16 birth defects based on data from 23 surveillance programs showed considerable state-to-state variation in the calculated prevalence ratios comparing prefortification and postfortification estimates. Heterogeneity in state-specific prevalence rates is to be expected and does not invalidate aggregating state-level data (Canfield et al., 2005). Sources of variation might include varying case inclusion criteria, such as age of case ascertainment or disease coding system. Variation also could be explained by differing surveillance methodologies, such as whether a state includes all pregnancy outcomes. The higher prevalence of anencephaly, anophthalmia/microphthalmia, and trisomy 18 among active programs might be explained by the inclusion of elective terminations (Ethen and Canfield, 2002). Of the 11 active surveillance programs, nine included elective terminations in their case definition; only one of the passive surveillance programs did. Furthermore, several of these active programs conducted specialized prenatal ascertainment involving abstraction at prenatal diagnostic facilities and clinical genetics facilities, ultimately increasing their ability to ascertain additional prenatal cases (National Birth Defects Prevention Network, 2009b).

Pregnancy Outcome

The availability of pregnancy outcome information for a subset of the selected defects provided the opportunity to describe the contribution of each individual pregnancy outcome toward the overall prevalence. Pregnancy outcome data for NTDs, anencephaly and spina bifida, and chromosomal anomalies were collected based on previous studies indicating the contribution of elective terminations on the prevalence of these defects (Forrester et al., 1998; Schechtman et al., 2002). The prevalence of anencephaly was impacted the most with the inclusion of elective terminations, increasing 149% from the prevalence among live births and stillbirths. Studies consistently have shown the strong impact of including elective terminations on the prevalence of anencephaly (Forrester et al., 1998; Peller et al., 2004; Velie and Shaw, 1996). A study from MACDP showed a 128% increase in the prevalence of anencephaly when elective terminations were included (Cragan and Gilboa, 2009).

Other defects influenced by the inclusion of elective terminations were trisomy 13 and trisomy 18. When elective terminations were included, they made up 41.5% and 34.0% of all cases ascertained, respectively. These findings were consistent with an analysis of MACDP data that indicated elective terminations accounted for 45.8% of trisomy 13 cases and 48.4% of trisomy 18 cases (Crider et al., 2008). The three birth defects surveillance programs selected for the pregnancy outcome analysis had enhanced prenatal data ascertainment from multiple sources, including prenatal diagnostic facilities and cytogenetic laboratories; however, underascertainment of prenatal cases was still likely. These findings highlight the importance of including additional pregnancy outcomes to enhance the surveillance of birth defects.

Although our study provided prevalence estimates based on surveillance methodology, updated national estimates, and detailed information on the impact of ascertaining additional pregnancy outcomes on the prevalence of selected defects, several limitations should be noted. First, the birth defect categories were not composed of a homogenous group of cases. Isolated and nonisolated patterns were combined within categories and might have had very different etiologies. Second, with the exception of race and ethnicity and maternal age, information on other possible covariates was unavailable, and was not accounted for in the national estimates. Maternal age adjustments were made for the chromosomal anomalies, but such adjustments could not be made for other defect categories. Third, cases with multiple birth defects were included in each relevant category, thereby overestimating the total number of affected births.

CONCLUSION

This study provides an update of the national estimates of 21 selected birth defects. Data contributing to this update represented nearly one-third of all live births in the United States during the study period. Timely national estimates on the prevalence of birth defects are imperative to aid in better understanding the burden of birth defects in the United States and to provide a benchmark that communities and health professionals can use to assess which areas might be at elevated risk for specific birth defects. In addition, national estimates are important for examining patterns or trends over time, evaluating prevention programs and interventions, and planning services. The NBDPN continually works to promote uniform case definitions and standardized data collection methods for state birth defect registries. Standardizing

case definitions and methodologies for estimating national prevalences will allow for frequent updates of the national estimates and future monitoring of trends over time in the prevalence of major birth defects.

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