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Population-Based Microcephaly Surveillance in the United States, 2009 to 2013: An Analysis of Potential Sources of Variation

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Additional Supporting information may be found in the online version of this article.

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Abstract

Background—Congenital microcephaly has been linked to maternal Zika virus infection. However, ascertaining infants diagnosed with microcephaly can be challenging.

Methods—Thirty birth defects surveillance programs provided data on infants diagnosed with microcephaly born 2009 to 2013. The pooled prevalence of microcephaly per 10,000 live births was estimated overall and by maternal/infant characteristics. Variation in prevalence was examined across case finding methods. Nine programs provided data on head circumference and conditions potentially contributing to microcephaly.

Results—The pooled prevalence of microcephaly was 8.7 per 10,000 live births. Median prevalence (per 10,000 live births) was similar among programs using active (6.7) and passive (6.6) methods; the interdecile range of prevalence estimates was wider among programs using passive methods for all race/ethnicity categories except Hispanic. Prevalence (per 10,000 live births) was lowest among non-Hispanic Whites (6.5) and highest among non-Hispanic Blacks and Hispanics (11.2 and 11.9, respectively); estimates followed a U-shaped distribution by maternal age with the highest prevalence among mothers <20 years (11.5) and ≥40 years (13.2). For gestational age and birth weight, the highest prevalence was among infants <32 weeks gestation and infants <1500 gm. Case definitions varied; 41.8% of cases had an HC ≥ the 10th percentile for sex and gestational age.

Conclusion—Differences in methods, population distribution of maternal/infant characteristics, and case definitions for microcephaly can contribute to the wide range of observed prevalence estimates across individual birth defects surveillance programs. Addressing these factors in the setting of Zika virus infection can improve the quality of prevalence estimates.

Keywords

microcephaly; surveillance; prevalence; head circumference

Introduction

Since the first reports of an increased number of infants born with microcephaly in Brazil in September 2015, great strides have been made in characterizing the causal relationship between Zika virus infection during pregnancy and congenital microcephaly, as well as other serious brain abnormalities (Rasmussen et al., 2016; Schuler-Faccini et al., 2016). This work emphasized the value of comprehensive population-based surveillance data on these defects. The National Birth Defects Prevention Network (NBDPN) was established in 1997 with the mission of improving population-based surveillance of birth defects in the United States (http://www.nbdpn.org). Since 2000, the NBDPN has released annual reports containing state-specific, population-based data on the prevalence of major birth defects; however,

ascertaining infants with microcephaly can present challenges for birth defects surveillance programs.

To illustrate, the prevalence of microcephaly for the years 2006 to 2010 estimated by surveillance programs included in the NBDPN Annual Report 2013 ranged from 0.5 to 19.0 per 10,000 live births (Mai et al., 2013). Differences in the clinical definition of microcephaly, the timing and setting of diagnosis, case ascertainment methods, and other factors may have contributed to this wide variation in observed prevalence. For these reasons, microcephaly was dropped from the list of defects requested in the NBDPN Annual Report in 2014 (Mai et al., 2014), but many programs have continued to monitor its prevalence.

The purpose of this report is to describe the estimated prevalence of microcephaly in the United States from 2009 to 2013 using data from thirty population-based birth defects surveillance programs and to explore potential reasons for some of the observed variation in prevalence.

BACKGROUND ON MICROCEPHALY

Microcephaly is the clinical finding of a small head when compared with infants of the same sex and age, or gestational age if measured at birth. The head circumference (HC), also known as the occipitofrontal circumference, is used to assess the volume of the underlying brain (Bray et al., 1969; Cooke et al., 1977). Measurements of HC are compared with standard references and described in terms of percentiles or SDs above or below the mean for the reference population. Clinicians can differ in the reference value they use as the threshold for defining microcephaly or as a trigger for evaluation of an infant for an underlying abnormality. Commonly used thresholds are less than 3rd percentile or more than 2 SD below the mean. Other thresholds used are less than the 5th or 10th percentiles, or more than 3 SDs below the mean (Opitz and Holt, 1990; Raymond and Holmes, 1994; Ashwal et al., 2009). Complicating classification further is that measurement of HC in the newborn or young infant can be inaccurate due to molding of the head following vaginal birth, infant movement, use of tapes that measure only to the nearest half centimeter, and other factors. It is critical to assess head growth, and thus growth of the brain, routinely throughout childhood (Holden, 2014). Microcephaly is confirmed when repeated HC measurements over time remain smaller than expected, or become progressively smaller, compared with infants of the same sex and age.

While the finding of a small HC may suggest an abnormality in the underlying brain, it does not confirm an abnormality or define its nature. Some infants who are constitutionally small overall will have an HC below a given threshold without any underlying brain abnormality. Others may have a small HC due to limitations on growth in utero that are unrelated to brain structure or function. Microcephaly is disproportionate when the HC is small in proportion to infant length and weight, which may be normal for sex and age; or proportionate when the HC, length, and weight are all small for the infant's sex and age, but proportional to each other (Leviton et al., 2002). In congenital microcephaly, the decreased HC is present prenatally or at the time of delivery. However, microcephaly can be acquired postnatally due to a delivery complication or a subsequent insult, such as infection or trauma (Baxter et al.,

2009; von der Hagen et al., 2014). In addition, microcephaly that is due to a genetic syndrome may not be present at birth but develop postnatally.

Although most cases of congenital microcephaly have unknown etiology, some causes of congenital microcephaly have been identified (Ashwal et al., 2009). Microcephaly is a known component of some chromosomal abnormalities and single gene disorders (Opitz and Holt, 1990). It is a component of fetal alcohol syndrome and a manifestation of several congenital infections (e.g., cytomegalovirus, toxoplasmosis, and rubella). Congenital microcephaly has been associated with other exposures or conditions including placental insufficiency in utero, poorly controlled maternal diabetes, high levels of radiation exposure, and in utero exposure to the medication hydantoin. The clinical implications, natural history, and developmental potential for infants with microcephaly vary depending on the cause and severity.

Taken together, variations in how microcephaly is defined, the existence of different types, the timing of diagnosis, and the accuracy of gestational age estimates at birth can contribute to variation in the reported prevalence of microcephaly. Microcephaly surveillance is particularly challenging when programs use different methods in terms of the settings where cases are identified (e.g., birth hospitals only, birth and pediatric hospitals, out-patient specialty clinics) and the maximum age at which affected children are ascertained (e.g., newborn only, up to 1 year, up to 3 years). For many programs, limitations on types of data sources and time period for case ascertainment and follow-up are critical. However, the recent increased focus on microcephaly as a consequence of congenital Zika virus infection has led to heightened interest in re-examining the epidemiologic characteristics of microcephaly and improving case ascertainment of this condition.

Materials and Methods

The NBDPN issued a call to state and territorial birth defects surveillance programs for data on infants born from 2009 to 2013 who have a diagnosis of microcephaly (see Supplementary Materials, which are avaiable online). A total of thirty programs provided data. Typically, cases were identified by the presence of an ICD-9-CM hospital discharge code for microcephaly or mention of microcephaly in the medical record regardless of the HC size. One program was known to have required that the HC measurement be less than the 3rd percentile by sex and gestational age for inclusion in the surveillance. Data provided for each case included the year of birth, maternal race/ethnicity and age at delivery, infant sex, gestational age, birth weight, and plurality. Eight programs also provided information on the specific HC measurement or value of the HC percentile for each case; a ninth provided the number of cases within categories of HC percentiles. These nine programs also included data on the infant's age at the time of the first HC measurement ascertained by the surveillance program, whether the certainty of the microcephaly diagnosis was considered confirmed (definite) or questionable (possible/probable), and the presence of additional conditions that might contribute to microcephaly.

Participating programs were divided into those with active case finding methods and those with passive case finding methods. Generally, in active case finding, children with birth

defects are identified through review and abstraction of medical records at data sources, which may include birth and pediatric hospitals, prenatal diagnostic offices, subspecialty offices and other sources; in passive case finding, children with birth defects are identified and reported to the program from administrative datasets at the sources. Some passive programs verify reported diagnoses through subsequent medical record review. Maternal race/ethnicity was categorized as: non-Hispanic White, non-Hispanic Black, Hispanic, non-Hispanic Asian or Pacific Islander, and non-Hispanic American Indian or Alaskan Native, other, and unknown. Infants identified as being of more than one race were bridged to a single race category using data from the National Center for Health Statistics, when available.

When these bridged data were not available, infants of more than one race were assigned to the category of other and unknown race. Maternal age at delivery was categorized as less than 20 years, 20 to 24 years, 25 to 29 years, 30 to 34 years, 35 to 39 years, 40 or more years, and unknown. Gestational age was categorized as term (37 weeks or greater), preterm (32–36 weeks), very preterm (less than 32 weeks), and unknown. Birth weight was categorized as normal (2500 gm or more), low (1500–2499 gm), very low (less than 1500 gm), and unknown. Plurality was categorized as singleton, twin, triplet or higher multiple, and unknown.

The percentile for each newborn HC value from the eight programs that provided these data was calculated using the INTERGROWTH-21st international standards for newborn weight, length, and head circumference by gestational age and sex (available at: https://intergrowth21.tghn.org/articles/international-standards-newborn-weight-length-and-head-circumference-gestational-age-and-sex-newborn-cross-sectional-study-inte/). The INTERGROWTH-21st standards include reference values for term, preterm, and very preterm newborns. The percentile for each HC value taken beyond the birth hospitalization from the programs that provided these data was calculated using the World Health Organization Child Growth Standards (available at: http://www.who.int/childgrowth/standards/hc_for_age/en/). For those cases where HC measurements were not available (less than 1% of cases), the percentile values provided by the state programs were used. Percentiles for HC were categorized as less than 3rd percentile, 3rd to less than 5th percentile, 5th to less than 10th percentile, and greater or equal to 10th percentile. Percentiles for HC were not calculated for infants less than 24 weeks gestation or greater than 42 weeks gestation because reference standards for these infants were not available through INTERGROWTH-21.

Additional conditions that might contribute to microcephaly included other birth defects (neural tube defects, holoprosencephaly, craniosynostosis, and conjoined twins), chromosomal abnormalities and/or clinical syndromes (including fetal alcohol syndrome), and non-Zika in utero infections. All chromosomal abnormalities, clinical syndromes, and in utero infections were included as possibly contributing regardless of whether they were known to be associated with microcephaly. Cases with more than one additional contributing condition were included in each category for which they had a condition.

STATISTICAL ANALYSIS

Data were pooled across thirty programs and the unadjusted prevalence of microcephaly was estimated as the number of reported cases divided by the total live birth population from the corresponding time period overall and by maternal and infant characteristics (Mason et al., 2005). The 95% confidence intervals (CIs) around all prevalence estimates were calculated using the Clopper-Pearson method (Clopper and Pearson, 1934). Prevalence estimates for microcephaly by plurality and gestational age categories (estimates by gestational age category were restricted to singleton infants only) were also stratified by maternal race/ethnicity. To assess variability in the prevalence of microcephaly across programs, the mean, median, interquartile (25^{th} to 75^{th} percentile) and interdecile (10^{th} to 90^{th} percentile) ranges were calculated overall, by case finding methodology (active, passive), and by race/ethnicity. A similar analysis was performed for HC percentiles with the mean, median, interquartile and interdecile ranges calculated by gestational age category.

Results

In Table 1, the counts, unadjusted prevalence estimates, and 95% CIs for microcephaly are presented using pooled data for 2009 to 2013 from all 30 participating birth defects surveillance programs. The total surveillance population covered over 11 million live births during this time period. The pooled unadjusted prevalence for microcephaly was 8.7 per 10,000 live births (95% CI, 8.5–8.9), or approximately 1 in 1150 births.

MATERNAL AND INFANT CHARACTERISTICS

Prevalence estimates for microcephaly (per 10,000 live births) were lowest among non-Hispanic Whites (6.5) and non-Hispanic Asian or Pacific Islanders (7.6), and highest among non-Hispanic Blacks (11.2) and Hispanics (11.9). Prevalence estimates (per 10,000 live births) by maternal age followed a U-shaped pattern with the highest estimates observed in the youngest (less than 20 years) and oldest (40 years or greater) age categories (11.5 and 13.2, respectively). This U-shaped pattern was generally consistent across all race/ethnicity groups (data not shown).

The estimated prevalence of microcephaly increased with decreasing gestational age and with decreasing birth weight. For gestational age, the estimated prevalence (per 10,000 live births) was highest among very preterm births at less than 32 weeks gestation (58.0) and lowest among term births at 37 weeks or more gestation (6.2). For birth weight, the estimated prevalence (per 10,000 live births) was highest among infants with very low birth weight of less than 1500 gm (74.1) and lowest among infants with normal birth weight of 2500 gm or greater (5.0). The estimated prevalence of microcephaly (per 10,000 live births) also was higher among twins (12.0) and triplets or higher multiples (17.3) compared with that for singletons (8.5).

Because race/ethnicity can be associated with the distribution of preterm and multiple births in a population, microcephaly prevalence estimates for these characteristics were stratified by maternal race/ethnicity (Table 2). Prevalence estimates of microcephaly increased with decreasing gestational age among singleton births within every maternal race/ethnicity

category, although the CIs were particularly wide for non-Hispanic American Indians and Alaska Natives due to the small number of affected infants. Similarly, prevalence estimates for twins and triplets or higher multiples were generally greater compared with singletons across maternal racial/ethnic categories.

CASE FINDING METHODOLOGY

In Table 3, the mean with standard deviation, median (P50), interquartile interval range (P25–P75) and interdecile range (P10–P90) for the prevalence estimates of microcephaly are presented for birth defects surveillance programs by type of case finding methodology (active, passive) stratified by maternal race/ethnicity. In this analysis, each program carried an equal weight regardless of population size. The accompanying figure displays the mean (circle), median (middle vertical bar), interquartile range (outer vertical bars), and interdecile interval (horizontal lines). The vertical width of each box represents the percent of total cases contributed by each race/ethnicity group. Non-Hispanic Whites are shown in green, non-Hispanic Blacks in pink, Hispanics in blue, and total for all race/ethnicities in white. Race/ethnicity categories that provided less than 10% of the total cases are not shown. A visual explanation of a similar figure was presented in the 2015 NBDPN Annual Report (Mai et al., 2015).

Among programs with active case finding, the mean estimated prevalence of microcephaly (per 10,000 live births) was 7.3 and the median was 6.7, with 80% of programs reporting a prevalence between 3.4 and 12.1 (Table 3). Among programs with passive case finding, the mean estimated prevalence of microcephaly (per 10,000 live births) was 7.7 and the median was 6.6, with 80% of programs reporting a prevalence between 1.9 and 18.7. The variability in prevalence estimates, as indicated by the width of the interdecile range, was greater for birth defects surveillance programs with passive compared with active case finding for all race/ethnicity categories except Hispanic ethnicity. Programs that used active case finding methods reported the highest mean prevalence (per 10,000 live births) among Hispanics (9.9). Hispanics also accounted for the largest proportion of total cases among programs with active case finding. The next highest mean prevalence (per 10,000 live births) among programs with active case finding was for non-Hispanic Blacks (8.6) followed by non-Hispanic Whites (5.6).

Programs that used passive case finding methods reported the highest mean prevalence (per 10,000 live births) among non-Hispanic Blacks (11.5), followed by Hispanics (7.1) and non-Hispanic Whites (6.2). Non-Hispanic Whites accounted for the largest proportion of total cases among these programs. The median estimated prevalence of microcephaly among programs with active and those with passive case finding were similar for all race/ethnicity categories except non-Hispanic Black. Non-Hispanic Black was also the race/ethnicity category that contributed the lowest proportion of cases regardless of case finding methodology. For both types of programs, the median prevalence estimates were lower than the mean estimates, presumably because the median value is less influenced by outliers and less subject to skewing by data from programs with very high prevalence estimates.

ADDITIONAL DATA ON MICROCEPHALY DIAGNOSES

Additional data on microcephaly diagnoses provided by nine birth defects surveillance programs are presented in Table 4. Six of the nine programs provided information on the certainty of the microcephaly diagnosis. Almost 95% of the cases reported by these six programs were considered to have a definite microcephaly diagnosis; 5.3% (205/3851) were considered to have a possible/probable diagnosis. Seven programs were able to provide data on additional conditions that might contribute to microcephaly. Almost 30% of cases from these programs had at least one additional contributing condition; 22.9% had a chromosomal abnormality or syndrome, 2.2% had documentation of a non-Zika in utero infection, and 6.7% had other birth defects (neural tube defects, holoprosencephaly, craniosynostosis, or conjoined twins).

One of the nine programs was dropped from the analysis of HC percentiles because their case definition required that cases have an HC less than the 3rd percentile for gestational age and sex to be included in the surveillance. Among the remaining eight programs, 27.8% of cases had a HC measurement less than 3rd percentile; 41.8% had a HC measurement greater than or equal to the 10th percentile. Head circumference percentiles could not be calculated for 14.7% of cases from these eight programs due to missing HC measurements, sex, or gestational age values, or because the infants were less than 24 weeks or greater than 42 weeks gestation at birth. Slightly more than 98% of the HC measurements provided were taken during the birth hospitalization.

Analysis of the variability of HC percentiles by gestational age category is presented for seven programs in Table 5. The figure accompanying Table 5 displays the mean (circle), median (middle vertical bar), interquartile range (outer vertical bars), and interdecile range (horizontal lines) for HC percentiles. The one program that provided only the number of cases within each HC percentile category was dropped from this analysis. In general, the mean HC percentile increased with decreasing gestational age (22.2 among term births, 23.4 among preterm births and 37.6 among very pretem births). The median HC percentile was the same for term and preterm births (8.7) but much higher for very preterm births (29.0). While the interdecile ranges were similar for all three groups, the interquartile range for very preterm births was much wider (7.4–65.2) than for term or preterm births (1.4–34.5 and 1.6–36.1, respectively).

Discussion

The pooled estimated prevalence of microcephaly from 2009 to 2013 among 30 population-based birth defects surveillance programs in the United States was 8.7 per 10,000 live births (95% CI, 8.5–8.9). Worldwide, the reported prevalence of microcephaly varies widely. The European Surveillance of Congenital Anomalies (EUROCAT) reported an overall prevalence of microcephaly of 2.85 per 10,000 live births (95% CI, 2.69–3.02) among full member registries for birth years 2008 to 2012 (http://www.eurocat-network.eu/ACCESSPREVALENCEDATA/PrevalenceTables). Among population-based programs included in the 2014 annual report of the International Clearinghouse for Birth Defects, the prevalence estimates for microcephaly for the most recent available birth year (2011, 2012,

or 2013) varied widely from 0.42 to 21.24 per 10,000 live births (http://www.icbdsr.org/filebank/documents/ar2005/Report2014.pdf).

The data in this report demonstrate several factors that could contribute to the observed variation in the prevalence of microcephaly across U.S. birth defects surveillance programs. While there was little difference in the median prevalence estimates of microcephaly among programs with active versus passive surveillance methods, the estimates among programs with active case finding generally showed less variability. This may be due to a combination of more rigorous case finding and confirmation of suspected cases. A higher estimated prevalence of defects other than microcephaly by programs with active compared with passive case finding has been demonstrated, presumably reflecting more complete case ascertainment (Parker et al., 2010; Mai et al., 2015).

In this issue of the journal, investigators with the Utah Birth Defect Network (UBDN) evaluated their ascertainment of microcephaly (Steele et al., 2016). Their results demonstrated the variability of ascertainment depending on the source and method of case finding. The UBDN uses a combination of active and passive case finding methods. They found that 53% of all potential cases of microcephaly reported to the UBDN were subsequently confirmed as true cases. The sources of case ascertainment with the highest positive predictive value for confirmed microcephaly included tertiary neonatal intensive care units and pediatric specialty clinics including genetics and ophthalmology. Approximately 50% of reports from vital records and hospital discharge data were subsequently confirmed to have microcephaly. Cases reported by multiple sources were more likely to be true cases of microcephaly.

The distribution of HC percentiles among birth defects surveillance programs that were able to submit these data demonstrates wide variation in the clinical definition of microcephaly. Almost 42% of the cases had an HC greater than or equal to the 10^{th} percentile for age and sex. Such differences in the definition of microcephaly may account for much of the variation in prevalence estimates across surveillance programs, and is one reason that surveillance for microcephaly is considered particularly problematic. Identification of children with mention of microcephaly in the medical record, the approach taken by many birth defects surveillance programs, will include children with a wide range of HC percentiles. In contrast, identification of all children with an HC below a certain percentile value would inevitably include some children who are constitutionally small but otherwise clinically normal, and currently is not logistically practical on a population basis.

The data in this report show a striking increase in the prevalence of microcephaly with decreasing gestational age and birth weight. Reference data for growth parameters at birth for very preterm infants tend to be based on smaller samples than for term infants, which may affect the precision of the reference values. The small size of these infants overall also might lead to increased mention of small head size in the medical record relative to that for larger preterm or term infants. Regardless of the accuracy of the measurement or diagnosis, variations in the proportion of preterm infants and low birth weight infants in populations could contribute to differences in the resulting estimates of the prevalence of microcephaly.

The estimated prevalence of microcephaly in these data also varied by maternal race/ethnicity, maternal age, and plurality. Children of Hispanic and non-Hispanic Black mothers had a substantially higher estimated prevalence of microcephaly compared with children of non-Hispanic White mothers and a moderately higher prevalence compared with children of non-Hispanic Asian or Pacific Island mothers. The increased variability among prevalence estimates for Hispanics from programs using active case finding methods may partly be driven by the high proportion of this ethnic group in the active program that contributed the largest number of microcephaly cases. The fact that the median prevalence estimate among non-Hispanic Blacks was the highest regardless of ascertainment method supports the finding of a true higher prevalence of microcephaly in non-Hispanic Blacks.

As a result, the racial/ethnic distribution of mothers giving birth in different populations could contribute to differences in observed prevalence estimates for microcephaly. A U-shaped distribution of microcephaly prevalence by maternal age was apparent for all racial/ethnic groups examined, indicating that the age distribution of mothers in different populations also could contribute to differences in observed prevalence estimates. Similarly, the proportion of mothers giving birth to twin or higher multiple infants in different populations also could affect the estimated prevalence of microcephaly. While these deliveries generally constitute a small proportion of most populations, the increasing use of artificial reproductive technology and resultant increase in multiple births may vary across populations.

CONCLUSIONS

The recent spread of Zika virus highlights the critical role that birth defects surveillance programs can play in response to an emerging epidemic or other public health threat affecting mothers and infants. This includes characterizing the public health impact of an exposure and monitoring the effects of prevention efforts. High quality population-based birth defects surveillance data can support a timely response to these threats. However, few birth defects surveillance programs in the United States currently have the infrastructure, resources, and personnel in place to conduct “rapid” surveillance for birth defects while simultaneously ensuring accuracy and completeness. Timeliness of reporting, case ascertainment, and data collection are all areas of potential improvement. The NBDPN continues to develop standards and tools to support programs to achieve this goal. In the absence of a nationwide population-based registry for birth defects, the data collected from state and territorial birth defects surveillance programs through the NBDPN provides the largest source of data regarding the prevalence of birth defects, including microcephaly, in the United States

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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TABLE 1

Microcephaly Counts,[a] Prevalence per 10,000 Live Births, and 95% CIs for 30 Birth Defects Surveillance Programs,[b] 2009 to 2013

	Cases		Live births			
	n	(%)	*n*	(%)	Prev	95% CI
Total cases	9,678	(100.0)	11,110,665	(100.0)	8.7	8.5–8.9
Maternal race/ethnicity						
Non-Hispanic White	3,856	(39.8)	5,973,376	(53.8)	6.5	6.3–6.7
Non-Hispanic Black	1,972	(20.4)	1,758,491	(15.8)	11.2	10.7–11.7
Hispanic	3,071	(31.7)	2,585,605	(23.3)	11.9	11.5–12.3
Non-Hispanic Asian or Pacific Islander	429	(4.4)	566,353	(5.1)	7.6	6.9–8.3
Non-Hispanic American Indian or Alaska Native	54	(<1.0)	51,646	(<1.0)	10.5	7.9–13.6
Maternal age (years)						
<20	1,094	(11.3)	955,420	(8.6)	11.5	10.8–12.1
20–24	2,506	(25.9)	2,608,005	(23.5)	9.6	9.2–10.0
25–29	2,487	(25.7)	3,142,705	(28.3)	7.9	7.6–8.2
30–34	2,010	(20.8)	2,765,901	(24.9)	7.3	7.0–7.6
35–39	1,089	(11.3)	1,312,477	(11.8)	8.3	7.8–8.8
40+	426	(4.4)	322,730	(2.9)	13.2	12.0–14.5
Infant sex						
Male	4,288	(44.3)	5,685,094	(51.2)	7.5	7.3–7.8
Female	5,371	(55.5)	5,425,361	(48.8)	9.9	9.6–10.2
Gestational age						

	Cases		Live births			
	n	(%)	*n*	(%)	Prev	95% CI
Term birth (37+ weeks)	6,200	(64.1)	9,960,699	(89.6)	6.2	6.1–6.4
Preterm birth (32 – 36 weeks)	2,271	(23.5)	933,452	(8.4)	24.3	23.3–25.4
Very preterm birth (<32 weeks)	1,088	(11.2)	187,601	(1.7)	58.0	54.6–61.5
Birth weight						
Normal birth weight (2,500+ grams)	5,115	(52.9)	10,169,612	(91.5)	5.0	4.9–5.2
Low birth weight (1,500–2,499 grams)	3,140	(32.4)	760,346	(6.8)	41.3	39.9–42.8
Very low birth weight (<1,500 grams)	1,243	(12.8)	167,771	(1.5)	74.1	70.0–78.3
Plurality						
Singleton	9,130	(94.3)	10,715,456	(96.4)	8.5	8.3–8.7
Twin	455	(4.7)	378,151	(3.4)	12.0	11.0–13.2
Triplet or higher	27	(<1.0)	15,645	(<1.0)	17.3	11.4–25.1

[a] Categories of missing/other/unknown are not shown.

[b] States and territories with surveillance programs contributing to the table: Arkansas, Colorado, Delaware (2009–2012), Florida, Georgia (Metropolitan Atlanta), Hawaii (2012), Illinois, Iowa, Kansas, Kentucky, Louisiana, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Nebraska, Nevada, New Jersey, New York, North Carolina, North Dakota, Oregon, Puerto Rico (2013), Rhode Island, South Carolina, Texas, Utah, West Virginia, Wisconsin

Prev, prevalence; CI, Confidence Interval.

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TABLE 2

Microcephaly Counts, Prevalence per 10,000 Live Births, and 95% CIs by Maternal Race/Ethnicity, Plurality, and Gestational Age for 30 Birth Defects Surveillance Programs,[a] 2009 to 2013

Plurality and gestational age	Maternal race/ethnicity																	
	Non-Hispanic White			Non-Hispanic Black			Hispanic			Non-Hispanic Asian or Pacific Islander			Non-Hispanic American Indian or Alaska Native			Total[b]		
	Cases	Prev	95% CI	Cases	Prev	95% CI	Cases	Prev	95% CI	Cases	Prev	95% CI	Cases	Prev	95% CI	Cases	Prev	95% CI
Singleton	3,637	6.3	6.1–6.5	1,863	11.0	10.5–11.5	2,927	11.6	11.2–12.0	399	7.3	6.6–8.0	52	10.4	7.7–13.6	9,130	8.5	8.3–8.7
Term birth (37+ weeks)	2,480	4.7	4.5–4.9	1,117	7.5	7.1–8.0	1,962	8.5	8.1–8.9	290	5.7	5.1–6.4	37	8.1	5.7–11.2	6,062	6.2	6.0–6.3
Preterm birth (32 – 36 weeks)	782	21.7	20.2–23.3	482	31.2	28.5–34.1	683	38.7	35.8–41.7	81	23.8	18.9–29.5	12	30.8	15.9–53.8	2,082	28.1	26.9–29.4
Very preterm birth (< 32 weeks)	352	64.9	58.3–72.1	249	54.7	48.1–61.9	273	87.1	77.1–98.1	25	48.8	31.6–72.1	<5	26.2	3.2–94.8	919	65.8	61.6–70.2
Twin	193	8.6	7.4–9.8	102	15.5	12.6–18.8	124	20.5	17.0–24.4	22	12.3	7.7–18.6	<5	14.1	1.7–50.9	455	12.0	11.0–13.2
Triplet or higher	10	9.5	4.6–17.5	<5	22.5	6.1–57.6	8	38.1	16.4–75.1	5	67.8	22.0–158.1	0	--	--	27	17.3	11.4–25.1

[a] States and territories with surveillance programs contributing to the table: Arkansas, Colorado, Delaware (2009–2012), Florida, Georgia (Metropolitan Atlanta), Hawaii (2012), Illinois, Iowa, Kansas, Kentucky, Louisiana, Massachusetts, Michigan, Minnesota, Mississippi, Missouri, Nebraska, Nevada, New Jersey, New York, North Carolina, North Dakota, Oregon, Puerto Rico (2013), Rhode Island, South Carolina, Texas, Utah, West Virginia, Wisconsin

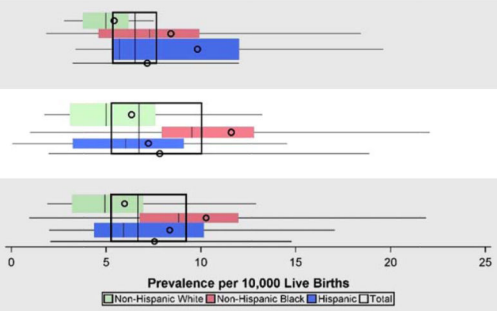
[b] Missing/other/unknown are included in the total.

Prev, prevalence; CI, Confidence Interval.

TABLE 3

Microcephaly Prevalence Estimates per 10,000 Live Births: Measures of Central Tendency and Dispersion by Maternal Race/Ethnicity and Case Finding Methodology for 30 Birth Defects Surveillance Programs,[a] 2009 to 2013

Case finding methodology		Non-Hispanic White	Non-Hispanic Black	Hispanic	Total[b]
Active case finding	Mean (SD)	5.6 (2.8)	8.6 (6.4)	9.9 (8.5)	7.3 (3.9)
	P50 (P10-P90)	5.1 (3.0-7.7)	7.4 (2.0-18.5)	5.9 (3.6-19.7)	6.7 (3.4-12.1)
	(P25-P75)	(3.9-6.3)	(4.8-10.1)	(5.5-12.1)	(5.5-7.8)
Passive case finding	Mean (SD)	6.2 (4.4)	11.5 (10.3)	7.1 (6.3)	7.7 (5.3)
	P50 (P10-P90)	4.9 (1.7-13.1)	9.4 (0.9-21.9)	5.9 (0.0-14.4)	6.6 (1.9-18.7)
	(P25-P75)	(3.0-7.5)	(7.8-12.7)	(3.2-9.0)	(5.2-9.9)
All programs	Mean (SD)	6.0 (3.8)	10.3 (8.9)	8.4 (7.3)	7.5 (4.7)
	P50 (P10-P90)	4.9 (1.9-12.9)	8.8 (0.9-21.9)	5.9 (2.0-17.0)	6.7 (2.0-14.8)
	(P25-P75)	(3.2-6.9)	(6.8-12.0)	(4.3-10.1)	(5.2-9.2)



In the figure, the circle indicates the mean prevalence estimate, the middle vertical bar indicates the median prevalence estimate, the outer vertical bars indicate the interquartile range of prevalence estimates, and the horizontal lines indicate the interdecile range of prevalence estimates.

[a]States and territories with active case finding surveillance programs contributing to the table: Arkansas, Delaware (2009–2012 only), Georgia (Metropolitan Atlanta), Hawaii (2012 only), Iowa, Louisiana, Massachusetts, Minnesota, North Carolina, Puerto Rico (2013 only), South Carolina, Texas, Utah; States with passive case finding surveillance programs contributing to the table: Colorado, Florida, Illinois, Kansas, Kentucky, Michigan, Mississippi, Missouri, Nebraska, Nevada, New Jersey, New York, North Dakota, Oregon, Rhode Island, West Virginia, Wisconsin.

[b]Asian and Pacific Islander, American Indian/Alaska Native, and missing/other/unknown are included in the total.

P10, 10th percentile; P25, 25th percentile; P50, 50th percentile (Median); P75, 75th percentile; P90, 90th percentile; SD, Standard Deviation.

TABLE 4

Microcephaly Counts[a] for Select Variables, Nine Birth Defects Surveillance Programs,[b] 2009 to 2013

	Cases	
	n	**(%)**
Total cases	4,766	(100.0)
Time at which earliest HC measurements were taken[c]		
Measured at birth	4,067	(98.4)
Measured beyond the birth hospitalization	51	(1.2)
Unknown	17	(0.4)
HC percentiles[d]		
HC <3rd percentile for age and sex	1,320	(27.8)
HC 3rd to <5th percentile for age and sex	253	(5.3)
HC 5th to <10th percentile for age and sex	494	(10.4)
HC ≥10th percentile for age and sex	1,983	(41.8)
Unknown HC percentile	696	(14.7)
Certainty of diagnosis[e]		
Possible/probable	205	(5.3)
Definite	3,646	(94.7)
Causes[f]		
Documented cause	1,344	(29.5)
Chromosomal abnormality and/or syndrome[g]	1,042	(22.9)
Non-Zika in utero infection	100	(2.2)
Other birth defect potentially associated with microcephaly[h]	304	(6.7)
No documented cause	3,206	(70.5)

[a]The total counts for each variable differ because some programs were unable to provide all of the variables.

[b]States and territories with surveillance programs contributing to the table: Georgia (Metropolitan Atlanta), Massachusetts, Michigan, Minnesota, North Carolina, Puerto Rico (2013 only), Rhode Island, Texas, Utah.

[c]Includes only cases with an HC measurement available from 9 birth defects surveillance programs (n = 4,135).

[d]Includes data for eight birth defects surveillance programs (n = 4,746); one program was excluded because their case definition required an HC less than 3rd percentile.

[e]Includes data for six birth defects surveillance programs (n = 3,851).

[f]Includes data for seven birth defects surveillance programs (n = 4,550). Cases with more than one potential cause are included in each category for which they had a condition.

[g]Includes fetal alcohol syndrome.

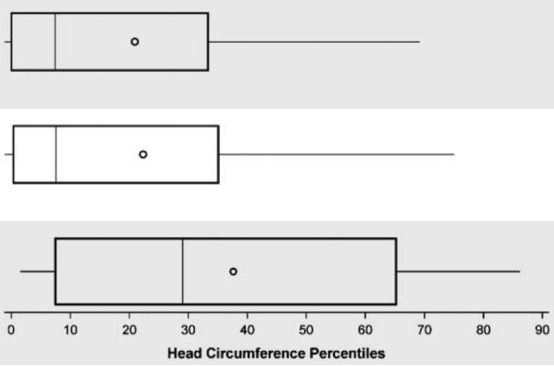
[h]Includes neural tube defects, holoprosencephaly, craniosynostosis, and conjoined twins.

HC, Head Circumference.

TABLE 5

Microcephaly HC Percentiles:[a] Measures of Central Tendency and Dispersion by Gestational Age for Seven Birth Defects Surveillance Programs,[b] 2009 to 2013

Gestational age		HC percentiles
Term birth (37+ weeks)	Mean (SD)	22.2 (28.0)
	P50 (P10-P90)	8.7 (0.2-70.2)
	(P25-P75)	(1.4-34.5)
Preterm birth	Mean (SD)	23.4 (29.3)
(32 - 36 weeks)	P50 (P10-P90)	8.7 (0.1-75.9)
	(P25-P75)	(1.6-36.1)
Very preterm birth	Mean (SD)	37.6 (31.9)
(< 32 weeks)	P50 (P10-P90)	29.0 (1.5-86.2)
	(P25-P75)	(7.4-65.2)



In the figure, the circle indicates the mean HC percentile, the middle vertical bar indicates the median HC percentile, the outer vertical bars indicate the interquartile range of HC percentiles, and the horizontal lines indicate the interdecile range of HC percentiles.

[a] Limited to microcephaly cases with head circumference measurements taken at birth; includes twins and higher multiples.

[b] States with surveillance programs contributing to the table: Georgia (Metropolitan Atlanta), Michigan, Minnesota, North Carolina, Rhode Island, Texas, Utah.

P10, 10th percentile; P25, 25th percentile; P50, 50th percentile (Median); P75, 75th percentile; P90, 90th percentile; SD, Standard Deviation; HC, Head Circumference.