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Developing algorithms for identifying major structural birth defects using automated electronic health data

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Abstract

Purpose: Given the 2015 transition to *International Classification of Diseases, Tenth Revision, Clinical Modification* (*ICD-10-CM*) diagnostic coding, updates to our previously published algorithms for major structural birth defects (BDs) were necessary. Aims of this study were to update, validate, and refine algorithms for identifying selected BDs, and then to use these algorithms to describe BD prevalence in the vaccine safety datalink (VSD) population.

Methods: We converted our ICD-9-CM list of selected BDs to ICD-10-CM using available crosswalks with manual review of codes. We identified, chart reviewed, and adjudicated a sample of infants in the VSD with ≥2 ICD-10-CM diagnoses for one of seven common BDs. Positive predictive values (PPVs) were calculated; for BDs with suboptimal PPV, algorithms were refined. Final automated algorithms were applied to a cohort of live births delivered 10/1/2015–9/30/2017

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SUPPORTING INFORMATION

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at eight VSD sites to estimate BD prevalence. This research was approved by the HealthPartners Institutional Review Board, by all participating VSD sites, and by the CDC, with a waiver of informed consent.

Results: Of 573 infants with ≥2 diagnoses for a targeted BD, on adjudication, we classified 399 (69.6%) as probable cases, 31 (5.4%) as possible cases and 143 (25.0%) as not having the targeted BD. PPVs for the final BD algorithms ranged from 0.76 (hypospadias) to 1.0 (gastroschisis). Among 212 857 births over 2 years following transition to ICD-10-CM coding, prevalence for the full list of selected defects in the VSD was 1.8%.

Conclusions: Algorithms can identify infants with selected BDs using automated healthcare data with reasonable accuracy. Our updated algorithms can be used in observational studies of maternal vaccine safety and may be adapted for use in other surveillance systems.

Keywords

birth defects; ICD-10; pharmacoepidemiology; pregnancy

1 | INTRODUCTION

Prelicensure clinical trials of medications and vaccines with intended use in pregnancy are seldom powered to evaluate risks for rare outcomes such as major structural birth defects (BDs).[1] In addition, pregnant women may be excluded from trials due to concerns regarding the potential for fetal harm. Following licensure, observational studies utilizing automated healthcare data may provide further evidence on the risk or safety of medication or vaccine exposures in pregnant women. Continued surveillance is also important for therapeutics with frequent formulation changes, such as the influenza vaccine.[2]

The first trimester of pregnancy is a critical period for fetal organogenesis and susceptibility to potentially teratogenic exposures. In the United States, and in many countries worldwide, the influenza vaccine is recommended for routine administration in any trimester of pregnancy.[3,4] Additional vaccine exposures may occur in the first trimester, before a pregnancy is recognized.[5] To date, studies on both recommended and inadvertent first trimester maternal vaccination and risks for birth defects in offspring have been reassuring,[6–13] yet continued monitoring is needed.

Accurate identification of BD outcomes from automated healthcare data is necessary to reduce risks for misclassification bias in observational cohort studies of maternal vaccine safety.[14] As part of the vaccine safety datalink (VSD), a collaboration between the Centers for Disease Control and Prevention (CDC) and several large healthcare organizations[15] that includes over 2% of U.S. births each year, our team previously derived algorithms for identifying selected BDs in automated healthcare data based on *International Classification of Diseases*, *Ninth Revision*, *Clinical Modification* (ICD-9-CM) coding.[1] In this prior work, definitions and algorithms were guided by expert opinion, observed patterns of care, estimated BD prevalence, and limited chart review, with modifications applied in an iterative process. The ICD-9-CM-based algorithms have been successfully applied in studies of maternal vaccine safety.[7,10,11]

As of October 1, 2015, U.S. health care organizations transitioned from ICD-9-CM to ICD-10-CM diagnostic coding.[16] To continue surveillance of vaccines currently administered to reproductive-age women, and to prepare to monitor vaccines that may be licensed in the coming months to years,[17,18] our previously-validated ICD-9-CM-based algorithms require updating to ICD-10-CM. Our overall goals were to update and validate algorithms for selected BDs to be used in large cohort studies of maternal vaccine safety where detailed review of all BDs would not be feasible. Specific aims of our study were to:(1) update, validate and refine previous ICD-9-CM-based algorithms for identifying selected major structural BDs and (2) use the ICD-10-CM-based algorithms to estimate BD prevalence among live births occurring over a two-year period across the VSD.

2 | METHODS

We aimed to identify selected major structural BDs, consistent with the Global Alignment on Immunization Assessment (GAIA) definitions, which are: (1) of prenatal origin; (2) present at the time of live birth or fetal demise, or in utero; and (3) affecting the health, survival, or physical or cognitive functioning of the individual.[14]

Our approach included multiple steps. First, we linked the ICD-9-CM codes from our previously published list of BDs[1] to ICD-10-CM codes, applying definitions from the National Birth Defects Prevention Network (NBDPN).[19] We manually reviewed each ICD-10-CM code and removed nonspecific diagnoses or minor anomalies introduced through the crosswalk (e.g., the ICD-9-CM 749.02 unilateral cleft palate mapped to the minor anomaly, ICD-10-CM Q35.7 cleft uvula).

Second, based on our prior work, we targeted the seven most prevalent BDs or groups of BDs[1] for chart validation: (1) neural tube defects; (2) congenital microcephaly; (3) cleft lip or palate; (4) severe cardiac defects; (5) intestinal atresia or stenosis; (6) hypospadias; and (7) abdominal wall defects (gastroschisis or omphalocele). We adapted probable and possible case definitions from those used by the NBDPN and GAIA in consultation with clinical experts in pediatrics (E. O. K. and M. B. D.), and BD research (P. A. R.). BDs included and probable and possible case definitions for these defects are listed in Table S1.

Third, we identified a sample of live births following transition to ICD-10-CM and delivered from 10/1/2015 through 9/30/2017 at seven of eight VSD infrastructure sites (Kaiser Permanente Northern California, Kaiser Permanente Southern California, Kaiser Permanente Northwest, Kaiser Permanente Washington, Kaiser Permanente Colorado, HealthPartners and Marshfield Clinic) for chart review. With limitations in sample size for some defects and our preference to focus available resources on probable cases, we selected live born infants with at least 1 day of insurance enrollment in the first year of life, at least two diagnoses within the same grouping for a targeted BD on different care dates, and at least one outpatient visit at a VSD site. Infants were identified using standardized VSD files, including enrollment, inpatient, emergency, and outpatient diagnostic codes, birth and mortality files.[15] We also captured head circumference measurements from the birth hospitalization to evaluate microcephaly diagnoses. Head circumference percentiles at birth were primarily calculated using Intergrowth-21st Fetal Growth Standards.[20] For infants born

at 33 weeks' gestation or earlier, head circumference was calculated using Fenton Preterm Growth Charts.[21] We performed chart reviews for all eligible infants with suspected neural tube defects ($N = 57$). For the remaining BDs, based on total number of eligible infants and available resources, we selected a random sample of 80 infants each of suspected congenital microcephaly, cleft lip or palate, intestinal atresia or stenosis, and abdominal wall defects (gastroschisis or omphalocele), 90 with suspected hypospadias and 110 with suspected severe cardiac defects. Compared to the other targeted BDs, the number of infants with suspected hypospadias was increased due to its higher prevalence, whereas the number with severe cardiac defects was increased due to it being the most common and heterogeneous group of BDs. We conducted structured chart reviews using REDCap[22] with data collection forms specific to each BD or group of BDs. Trained chart abstractors, (2–10 per site), or clinical investigators performed chart reviews with site-based review of data entered and follow-up of potential outliers, in order to ensure data quality. Two abstractors performed duplicate chart review of 10% of infants. Differences were identified as areas for additional training and were reconciled by sites. Investigators with clinical expertise in pediatrics (E. O. K or M. B. D) adjudicated all completed charts, based on the information abstracted and entered into REDCap. We assessed agreement in final case classification using the kappa statistic.

Chart validation was a multistep process. We first described probable and possible cases for having two or more ICD-10-CM diagnoses. Then, for each BD undergoing chart review, we applied our previously validated (ICD-9-CM-based) algorithms,[1] but with ICD-10-CM codes, and calculated positive predictive values (PPV) and 95% confidence intervals (CIs). Finally, for algorithms with an initial PPV at or near 0.75, we reviewed and modified algorithm components, such as inclusion or exclusion of specific ICD-10-CM codes, aiming for final automated algorithms to have a PPV of 0.75 or higher. This approach allowed us to compare the use of simple definitions (two or more diagnoses) versus more complex algorithms, and to identify specific defects where refinement was indicated.

We then created a cohort of live births in the VSD delivered from 10/1/2015–9/30/2017 for estimating BD prevalence. The updated cohort included all eight VSD infrastructure sites (Denver Health added). To reduce missing diagnosis data for this cohort, we required infants surviving the first year of life to have at least at least 1 month of insurance enrollment in the first 3 months of life, 4 months of enrollment total in the first year, and one outpatient encounter.

We applied the final automated algorithms in our live birth cohort to describe BD prevalence estimates (per 100 for overall prevalence and per 10 000 live births for specific defects or groups of defects). We explored variation in BD prevalence by site and maternal race/ethnicity. For descriptive purposes, we compared results for individual defects or groups of defects among live birth in three sources: (1) our previously published estimates from the VSD using ICD-9-CM algorithms (2004–2013),[1] (2) the European Registration of Congenital Anomalies and Twins (EUROCAT) (2015–2017)[23] and (3) California State Birth Defects Surveillance (2012–2016).[24]

This research was approved by the HealthPartners Institutional Review Board, by all participating VSD sites, and by the CDC, with a waiver of informed consent.

3 | RESULTS

The final list of BDs and corresponding ICD-10-CM codes by organ system, is shown in Table 1.

3.1 | Chart validation

We identified 2104 suspected BDs with two or more ICD-10-CM diagnoses on different care dates for one of the seven targeted BDs, corresponding to 2045 infants born over a two-year period. We initially selected 577 BDs for full chart review among 568 unique infants. We excluded one infant with suspected microcephaly but no link to a medical record, and 3 infants (2 with intestinal atresia, 1 with gastroschisis) determined to be ineligible on subsequent review as their two diagnoses were on the same care date; thus, we analyzed 573 unique suspected BDs among 564 unique infants. On adjudication, 399 (69.6%) of BDs were identified as probable, 31 (5.4%) as possible and 143 (25.0%) as not the BD of interest (definitions for probable and possible cases are provided in Table S1 and classification by BD is shown in Table 2). For subsequent analyses, we grouped “probable” and “possible” BDs as confirmed. Fifty-five charts underwent duplicate chart review and adjudication; there was substantial agreement on final case classification for these (kappa = 0.76 [95% CI: 0.54–0.98]).

Using our previously published algorithm for microcephaly, one inpatient diagnosis *or* two outpatient diagnoses or one outpatient diagnosis and death in first year,[1] updated for ICD-10-CM, the PPV for the algorithm was 0.62 and required refinement (Table 2). After updating the algorithm to include either a head circumference measurement <5th percentile during the birth hospitalization, identified through automated EHR data, or three microcephaly diagnoses in the first 3 months of life, the PPV of the congenital microcephaly algorithm increased to 0.80 (95% CI: 0.65–0.95), based on 30 potential cases (Table 2). We explored applying a lower threshold for head circumference percentile (e.g. <3rd percentile) or including additional head circumference measurements from outpatient visits; however, these approaches neither increased the PPV, nor increased the proportion of true diagnoses identified.

Severe cardiac defects had an initial PPV of 0.76, lower than anticipated and attributed in part to lack of specificity in a subset of diagnostic codes. The ICD-10-CM Q24.5 was included to capture infants with congenital anomalous left coronary artery, a severe defect. However, during chart review, we discovered that most infants with this code had a less severe defect, anomalous right coronary artery. The ICD-10-CM Q22.1 was evaluated to identify pulmonary stenosis, a severe cardiac defect, but most infants with this diagnosis instead had transient peripheral pulmonary stenosis. Similarly, we observed that many infants diagnosed with pulmonary or tricuspid valve defects (Q22.0, Q22.3, Q22.4) had mild pulmonary or tricuspid stenosis and did not require surgery, cardiac catheterization, or other intervention. We also reclassified two nonspecific cardiac defect codes (Q20.8, Q20.9) as “other cardiac.” We revised the list of ICD-10 diagnoses for severe cardiac defects,

reclassifying or excluding 18 with two or more diagnoses (3 of whom had met the initial algorithm criteria) and modestly improved the algorithm PPV to 0.79 (95% CI: 0.70–0.89). (Table 2).

In addition, we updated the initial BD algorithms to account for the availability of unique ICD-10-CM codes for omphalocele and gastroschisis. Prior to 2010, there was a single ICD-9-CM code for omphalocele and gastroschisis; the ICD-9-CM-based algorithm accommodated both diagnoses. Omphalocele is the most severe form of exomphalos (ICD-10-CM code Q79.2). This diagnostic code also includes umbilical hernia, a milder form of exomphalos. As such, in order to avoid inclusion of umbilical hernias, we restricted the algorithm for omphalocele to diagnoses in the first 3 months of life, observing a PPV of 0.95 (95% CI: 0.85–1.0). There is not a similar, milder form of gastroschisis; for the gastroschisis final algorithm, we required one inpatient or two outpatient diagnoses in the first year of life, increasing the sensitivity, without adversely impacting the PPV. The final ICD-10-CM algorithms for all selected defects are shown in Table 3. Comparisons between the initial and final algorithms, for defects undergoing medical record review, are shown in Table S2.

PPVs for the original and final ICD-10-CM algorithms for the BDs that underwent medical record review are shown in Table 2. The final PPVs ranged from 0.76 (hypospadias) to 1.0 (gastroschisis). Additional detail regarding timing and number of BD diagnoses among those who did and did not meet final algorithm definitions, among infants with at least one diagnosis, is in Table S3.

3.2 | Description of birth defect prevalence in the VSD, 10/1/2015–9/30/2017

We identified 212 857 live births across eight VSD sites over a 24-month period immediately after transition to ICD-10-CM coding. The cohort was 48.8% female, 33.9% white, non-Hispanic and 16.6% were publicly insured. The overall prevalence of selected BDs using the updated ICD-10-CM algorithms was 1.8 per 100 live births (95% CI: 1.4–2.2 per 100 live births). BD prevalence by race/ethnicity varied from 1.5 to 1.9 per 100 live births. Site-based prevalence of BDs ranged from 1.5 to 2.9. (Table 4) The overall prevalence of selected BDs for 2015–2017 was consistent with that we reported for 2004–2013, using ICD-9-CM-based algorithms (1.8 per 100 live births versus 1.7 per 100 live births, respectively). Absolute change in prevalence estimates by time period were evident by defect. For most BDs, prevalence estimates increased in recent years, using ICD-10-CM algorithms. However, for several BDs, including congenital diaphragmatic hernia and gastroschisis, prevalence estimates were slightly lower using the ICD-10-CM-based algorithms. (Table 5) Most prevalence rates for specific BDs were similar to those described in European and California surveillance systems.[23,24].

4 | DISCUSSION

In this large observational study, we demonstrate the validity of algorithms applied to automated healthcare data, including inpatient, emergency, and outpatient diagnoses in the first year of life, and mortality files, for identifying infants with selected major BDs. Despite variability by BD, the overall prevalence for selected BDs for our 2015–2017 ICD-10-CM

cohort was 1.8%, nearly identical to that we previously reported for births from our 2004–2013 ICD-9-CM cohort.[1] Prevalence estimates for specific defects were also consistent with published population-based estimates.[23–26] For the BDs or groups of BDs undergoing chart validation and case adjudication, algorithm PPVs approached 80% or higher for most defects.

Despite the overall validity of the algorithms we describe, some areas merit further discussion. First, only 62% of infants selected for chart review met the initial algorithm for congenital microcephaly, and even with inclusion of head circumference measurements, the algorithm PPV was only 80%. These data highlight challenges unique to congenital microcephaly. First, the diagnostic code Q02 does not distinguish between congenital and acquired microcephaly. More importantly, variability in measurement and interpretation of head circumference data are common. Head circumference measurements can be affected by molding at delivery, presence of a cephalohematoma, or technique. Calculation of head circumference percentiles may vary by the growth chart used and whether the percentiles account for gestational week at birth.[21,27] Furthermore, definitions for congenital microcephaly vary, the highest level of diagnostic certainty in the GAIA definitions requires a head circumference two standard deviations below the M or <3rd percentile measured 24–36 hrs after birth.[28] In a recent report of congenital microcephaly surveillance from New York for 2013–2015, 499 (94%) of 529 infants initially identified were confirmed as having physician diagnosed congenital microcephaly, whereas only 284 (57% of those confirmed by physician diagnosis) also had a head circumference at birth <3rd percentile.[29] Thus, similar to our evaluation, many infants are diagnosed with microcephaly even when the recorded head circumference does not meet case definitions.

Second, the PPV for severe cardiac defects was 0.79, lower than we had anticipated but still slightly higher than that reported in other ICD-9-CM era studies using Medicaid or health system data.[30–32] Of note, in most instances where a severe cardiac defect was not confirmed, the error was due to miscoding, and on adjudication, we identified a nonsevere congenital cardiac defect. For example, infants with isolated atrial septal defects (Q21.1) and ventricular septal defects (Q21.0) were coded as having a more severe atrioventricular septal defect (Q21.2). In addition, as severe cardiac defects require confirmation through postnatal diagnostic imaging and most also require an immediate intervention, PPVs would increase with the addition of common procedural terminology (CPT) codes. This approach was not utilized for our final algorithms in order to reduce algorithm complexity and to minimize the need for updates, as interventions and billing procedures may vary by VSD site and over time.[33]

A final BD worth reviewing is hypospadias. It is the most common isolated BD occurring in males; thus, misclassification could adversely impact overall BD prevalence estimates. Based on our prior research and clinical experience, we anticipated that the PPV for hypospadias may be low and difficult to improve through updates to the algorithm. Mild cases of hypospadias are often diagnosed in outpatient settings but may not undergo surgical repair, or they may undergo repair after 12 months of age. As our goal was to identify moderate to severe cases, requiring surgical repair, there was potential for both misclassification and loss to follow-up in our data. Both the ICD-9-CM and the ICD-10-

CM codes for hypospadias include defects of variable severity. Our final algorithm for hypospadias had a PPV of 0.76. Of note, 70% of infants meeting the hypospadias algorithm definition were adjudicated as probable: (1) diagnosed following surgical repair or (2) diagnosed by a urologist, geneticist or neonatologist. In comparison, Cooper et al reported a PPV for hypospadias based on ICD-9-CM codes as 91% but only 17% of infants with a hypospadias diagnosis in that study underwent surgical repair.[31]

A few limitations should be noted. The BD prevalence we report is an estimate for selected defects. We were unable to include data from stillbirths or elective terminations and have incomplete ascertainment of defects among infants who died during their birth hospitalization. We also did not adjust prevalence estimates to account for the PPVs from chart review and adjudication. Finally, we developed and validated algorithms for seven targeted BDs in the same population. External validation of these algorithms in a new population was not feasible within the scope of this project. In addition, although the algorithms allowed for a single diagnosis, they were validated in a population with at least two diagnoses. As such, the PPVs we report may be an overestimate; PPVs may be lower when applied in a new population, in particular where this initial restriction is not imposed. Despite these limitations, our study demonstrates the validity of ICD-10-CM-based algorithms for identifying selected BDs in automated healthcare data. These algorithms will be used in ongoing studies of maternal vaccine safety and can be considered for use in pharmacovigilance studies in similar populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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KEY POINTS

- Identification of birth defects (BDs) in automated health care data is prone to misclassification.
- Algorithms can enhance the validity of automated health care data for identifying selected major structural BDs.
- Prevalence of selected major structural BDs in the vaccine safety datalink for births during 2015–2017, primarily using ICD-10-CM diagnoses, is consistent with prevalence reported for births during 2004–2013, using ICD-9-CM diagnoses.
- The algorithms presented can be used for ongoing observational studies of maternal medication and vaccine safety for the major structural defects evaluated.

TABLE 1

Selected major structural birth defects (BDs) by organ system and final list of ICD-10-CM codes for identifying these defects in automated healthcare data (shading denotes those BDs undergoing validation through chart review)

Organ system	Specific diagnoses and their associated ICD-10-CM Codes
Central nervous system	Neural tube defects: Encephalocele, Cranial Meningocele, Encephalomyelocele (Q01.x); Spina Bifida (Q05.x, Q07.01, Q07.03)
	Microcephaly (Q02)
	Holoprosencephaly (Q04.2)
Eye	Anophthalmia, Microphthalmia (Q11.1, Q11.2); Cataracts and Other Lens Defects. (Q12.0, Q12.3, Q12.4, Q12.8)
Ear	Anotia, Microtia (Q16.0, Q16.1, Q17.2)
Cardiac	Severe cardiac defects: Single ventricle, tricuspid atresia, ebstein anomaly, hypoplastic left heart, hypoplastic right heart, common truncus, transposition, atrioventricular septal defects, tetralogy of fallot, aortic valve atresia or stenosis, coarctation, total anomalous pulmonary venous return, double outlet right ventricle, double outlet left ventricle, (Q20.0, Q20.1, Q20.2, Q20.3–Q20.5, Q21.2–Q21.4, Q22.5–Q22.6, Q23.0, Q23.4, Q25.1, Q25.2x, Q25.3, Q25.41, Q25.42, Q25.5, Q26.2)
	Other cardiac defects: Septal defects, heterotaxy, pulmonary valve atresia, tricuspid stenosis, partial anomalous pulmonary venous return (Q20.8, Q20.9, Q21.0, Q21.8, Q21.9, Q22.0, Q22.3, Q22.4, Q26.3, Q26.4, Q89.3)
Orofacial/respiratory	Choanal atresia (Q30.0)
	Cleft lip and/or cleft palate (Q35.1–Q35.5, Q35.9, Q36.x, Q37.x)
Gastrointestinal	Biliary atresia (Q44.2)
	Intestinal atresia or stenosis (Q41.x, Q42.x)
	Esophageal atresia with or without tracheoesophageal fistula (Q39.0–Q39.3)
	Pyloric stenosis (Q40.0)
	Bladder exstrophy (Q64.1x)
Genitourinary/renal	Hypospadias (Q54.0–Q54.3, Q54.8, Q54.9);
	Renal dysplasia (Q61.4)
	Renal agenesis or hypoplasia (Q60.0–Q60.6)
	Posterior urethral valves (Q64.2)
Musculoskeletal	Gastroschisis (Q79.3)
	Omphalocele (Q79.2)
	Congenital diaphragmatic hernia (Q79.0)
	Limb deficiency (Q71.0x – Q71.6x, Q71.89x, Q71.9x, Q72.0x – Q72.7x, Q72.89x, Q72.9x, Q73.x)

TABLE 2

Counts and case classification for charts reviewed, and positive predictive values (PPV) and 95% confidence intervals (CIs) for initial and final birth defect algorithms (n = 573)

			Met initial automated algorithm	Met final automated algorithm
Birth defect	**Reviewed**[a]	**Case classification Probable/possible/not a case**[b]	**Defect confirmed**[b] **PPV (95% CI)**	**Defect confirmed**[b] **PPV (95% CI)**
Neural tube defects	57	49/1/7	57	57
			50	50
			0.88 (0.79–0.97)	0.88 (0.79–97)
Microcephaly	79	30/19/30	79	30
			49	24
			0.62 (0.51–0.73)	0.80 (0.65–0.95)
Severe cardiac defects	110	70/0/40	80	77
			61	61
			0.76 (0.67–0.86)	0.79 (0.70–0.89)
Cleft lip/palate	80	72/2/6	80	80
			74	74
			0.93 (0.87–0.98)	0.93 (0.87–0.98)
Intestinal atresia / stenosis	78	60/4/14	78	78
			64	64
			0.82 (0.73–0.91)	0.82 (0.73–0.91)
Hypospadias	90	56/5/29	76	76
			58	58
			0.76 (0.67–0.86)	0.76 (0.67–0.86)
Gastroschisis	42	42/0/0	41	42
			41	42
			1.0 (−)	1.0 (−)
Omphalocele	37	20/0/17	20	20
			19	19
			0.95 (0.85–1.0)	0.95 (0.85–1.0)

[a]Infants were randomly selected for chart review based on having two diagnoses (inpatient, emergency or outpatient) in the first year of life; For neural tube defects, all 57 eligible charts were reviewed; For microcephaly, 79 of 80 selected charts were reviewed, 1 infant with suspected microcephaly could not be linked to medical records; For severe cardiac defects 92 of 110 randomly selected charts were reviewed and retained in the data; 18 charts (including 3 probable cases) initially reviewed were reclassified as other cardiac defects (Q20.8, Q20.9, Q22.0, Q22.3, Q22.4) or excluded (Q22.1, Q24.5) in the

updated severe cardiac defect case definition. Of the 110 initially identified charts, 80 met the criteria for the initial severe cardiac defect algorithm (15 of the 30 cases that did not meet the algorithm criteria would also have been excluded based on our reclassification of the severe cardiac defects). The remaining 3 of the 18 reclassified cases were removed in the final algorithm; For cleft lip/palate, 80 of 80 selected charts were reviewed; For intestinal atresia/stenosis, 78 of 80 selected charts were reviewed and retained in the data, 2 charts initially reviewed were not eligible as their 2 diagnoses were on same care date; For hypospadias, 90 of 90 randomly selected charts were reviewed; For gastroschisis and omphalocele, 79 of 80 randomly selected charts were reviewed and retained in the data; 1 chart initially reviewed was not eligible as 2 diagnoses were on the same care date; One additional case of gastroschisis was identified using the final algorithm because it allowed for one inpatient or two outpatient diagnoses in the first year of life (compared to the initial algorithm which required an inpatient diagnosis in the first 3 months of life).

[b]Based on chart review and adjudication cases classified as probable and possible were considered confirmed. For neural tube defects, microcephaly, cleft lip / palate, and intestinal atresia/stenosis the number of potential cases did not change based on having two diagnostic codes versus meeting the initial algorithm.

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TABLE 3

Selected major structural birth defects (BDs) and updated algorithms for identifying these defects in automated healthcare data (shading denotes those BDs undergoing validation through chart review)

Organ system	Specific diagnoses (ICD-10-CM Codes)	Updated algorithms
Central nervous system	Neural tube defects: Encephalocele, cranial Meningocele, encephalomyelocele, spina bifida	1 inpatient diagnosis or 2 outpatient diagnoses or 1 diagnosis and death in first year
	Microcephaly	1 diagnosis at birth or head circumference <5%ile at birth or 3 diagnoses in first 3 months or 1 diagnosis and death in the first year
	Holoprosencephaly	2 outpatient diagnoses or 1 diagnosis and death in first year
Eye	Anophthalmia, microphthalmia, cataracts and other Lens defects	2 outpatient diagnosis or 1 diagnosis and death in first year
Ear	Anotia, Microtia	2 outpatient diagnoses or 1 diagnosis and death in first year
Cardiac	Severe cardiac defects: Single ventricle, tricuspid atresia, ebstein anomaly, hypoplastic left heart, hypoplastic right heart, common truncus, transposition, atrioventricular septal defects, tetralogy of fallot, aortic valve atresia or stenosis, coarctation, total anomalous pulmonary venous return	2 inpatient diagnoses or 1 inpatient and 1 outpatient diagnosis or 1 diagnosis and death in first year
	Other cardiac defects: Septal defects, heterotaxy, pulmonary valve atresia, tricuspid stenosis, partial anomalous pulmonary venous return	2 diagnoses or 1 diagnosis and death in first year
Orofacial/Respiratory	Choanal atresia	2 outpatient diagnoses or 1 diagnosis and death in first year
	Cleft lip and/or Cleft palate	1 inpatient diagnosis or 2 outpatient diagnoses or 1 diagnosis and death in first year
Gastrointestinal	Biliary atresia	1 inpatient diagnosis or 2 outpatient diagnoses or 1 diagnosis and death in first year
	Intestinal atresia or stenosis	1 inpatient diagnosis or 2 outpatient diagnoses or 1 diagnosis and death in first year
	Esophageal atresia with or without tracheoesophageal fistula	2 outpatient diagnoses or 1 inpatient and 1 outpatient diagnosis or 1 diagnosis and death in first year
	Pyloric stenosis	1 inpatient diagnosis or 1 diagnosis and death in first year
	Bladder exstrophy	1 inpatient diagnosis by 3 months of age and 1 outpatient diagnosis by 1 year or 1 diagnosis and death in the first year
Genitourinary/Renal	Hypospadias	2 outpatient diagnoses or 1 diagnosis and death in first year; males only
	Renal dysplasia	2 outpatient diagnoses or 1 diagnosis and death in first year;
	Renal agenesis or hypoplasia	1 inpatient diagnosis and 1 outpatient diagnosis or 1 diagnosis and death in first year
	Posterior urethral valves	2 outpatient diagnoses or 1 diagnosis and death in first year; males only
Musculoskeletal	Gastroschisis	1 inpatient diagnosis or 2 outpatient diagnoses or 1 diagnosis and death in first year
	Omphalocele	1 inpatient diagnosis by 3 months of age or 1 diagnosis and death in first year
	Congenital diaphragmatic hernia	1 inpatient diagnosis by 3 months of age or 1 diagnosis and death in first year

Organ system	Specific diagnoses (ICD-10-CM Codes)	Updated algorithms
	Limb deficiency	1 inpatient or 2 outpatient diagnoses and 1 diagnosis within 3 months or 1 diagnosis and death in first year

TABLE 4

Birth cohort at eight vaccine safety datalink sites, 10/1/2015–9/30/2017, and prevalence of selected major structural birth defects (BDs)

			BD	BD
	N	**%**	**n**	**Per 100 live births**
Full cohort	212 857	100	3742	1.76
Birth year				
2015	26 186	12.3	495	1.89
2016	107 202	50.4	1810	1.69
2017	79 469	37.3	1437	1.81
Race				
Asian	30 659	14.4	464	1.51
Black	14 394	6.8	250	1.74
Hispanic	64 229	30.2	1144	1.78
White	72 164	33.9	1399	1.94
Other/missing	31 411	14.7	485	1.54
Sex				
Female	103 925	48.8	1493	1.44
Male	108 925	51.2	2249	2.07
Insurance				
Medicaid	35 306	16.6	722	2.05
Private	177 551	83.4	3020	1.70
Site				
A	81 475	38.3	1299	1.59
B	9418	4.4	214	2.27
C	8557	4.0	149	1.74
D	3917	1.8	114	2.91
E	10 161	4.8	236	2.32
F	4953	2.3	75	1.51
G	84 885	39.9	1477	1.74
H	9491	4.5	178	1.88

TABLE 5

Major structural birth defects by condition for births 2015–2017 at 8 VSD sites versus births 2004–2013 at 7 VSD sites, prevalence per 10 000 live births

Organ system	Defect	VSD 2015–2017, ICD-10-CM	EUROCAT 2015–2017, ICD-10-CM	California Surveillance 2012–2016	VSD 2004–2013, ICD-9-CM
Central nervous system	Neural tube defects	3.2	1.9	4.7	1.9
	Microcephaly	8.5	2.0	NA	12.9
	Holoprosencephaly	4.8	0.3	1.7	3.3
Eye	Anophthalmia, microphthalmia	0.7	0.9	1.8	0.8
	Cataracts	3.8	1.2	1.7	3.8
Cardiac	Severe cardiac	19.9	18.1	32.9	16.9
	Other cardiac	64.9	50.1	23.3	54.1
Orofacial	Choanal atresia or stenosis	0.8	0.8	0.5	0.5
	Cleft lip or palate	14.1	12.3	15.1	14.5
Gastrointestinal	Intestinal atresia or stenosis	8.4	4.7	7.8	7.8
	Esophageal atresia or stenosis	1.3	2.3	2.0	1.4
	Biliary atresia	1.2	0.3	0.4	1.2
	Pyloric stenosis	9.8	NA	NA	14.7
Genitourinary/renal	Hypospadias[a]	65.1	16.9	40.3	59.2
	Renal dysplasia, agenesis, hyposplasia, posterior urethral valves[a]	9.2	5.1	6.2	2.9
Musculoskeletal	Gastroschisis	2.7	2.0	5.7	2.9[b]
	Omphalocele	1.5	1.2	2.1	0.9[b]
	Congenital diaphragmatic hernia	1.5	2.2	2.7	1.7
	Limb defects	3.4	3.0	3.3	1.5

Note: Shading denotes defects that were chart reviewed. Abbreviations: VSD, vaccine safety datalink.

[a]Among males.

[b]For births 2010–2013.