



An evaluation of national birth certificate data for neonatal seizure epidemiology

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SUMMARY

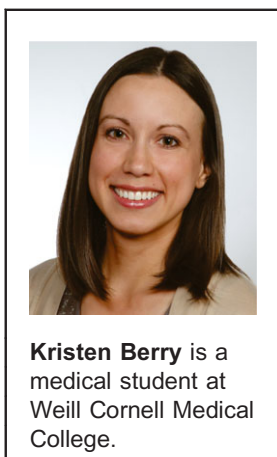
Objective: Seizures are a common manifestation of neurologic dysfunction in neonates and carry a high risk for mortality and adverse long-term outcomes. U.S. birth certificates are a potentially valuable source for studying the epidemiology of neonatal seizures. However, the quality of the data is understudied.

Methods: We reviewed all U.S. birth records from 2003 to 2013 to describe the following: (1) rates of missing data, (2) evidence of underreporting, and (3) effect of the 2003 revision of the birth certificate form. We evaluated missingness by state, year, demographic, infant health, and medical care factors using bivariate analyses. To measure potential underreporting, we compared estimates to a published reference (0.95 per 1,000 term births). We developed criteria for data plausibility, and reported which states met these criteria.

Results: Of 22,834,395 live term births (≥ 36 weeks of gestation) recorded using the revised form from 2005 to 2015, there were 5,875 with neonatal seizures, suggesting an incidence of 0.26 per 1,000 term births, one fourth of the expected incidence. Although the overall degree of missing seizure data was low (0.5%), missingness varied significantly by state, year, demographic, infant health, and medical care factors. After the 2003 birth certificate form revision, missing data and evidence of potential underreporting increased. Nine states met criteria for plausibility.

Significance: The value of U.S. birth certificate data for neonatal seizure epidemiology is limited by biased missingness, evidence suggestive of underreporting, and changes in reporting subsequent to the 2003 revision. There are plausible data from nine states, which merit investigation for further research.

KEY WORDS: Neonatal seizure, Birth certificate, Epidemiology.



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Seizures are a common manifestation of neurologic dysfunction in the neonatal period and are associated with high risk for early death and adverse long-term outcomes.^{1,2} Neonatal seizures may result from neonatal onset epilepsy,² or they may be acutely symptomatic of an infection, metabolic derangement, or a congenital or acquired structural brain lesion.

It is important to track neonatal seizures in the general population to identify risk factors, inform clinical practice, monitor epidemiologic trends over time, and prioritize research funding. This importance was emphasized in the Institute of Medicine's report *Epilepsy Across the Spectrum*, which recommended that the epilepsy research community find better data sources to measure the incidence

KEY POINTS

- U.S. birth certificates are a potentially valuable source for studying the epidemiology of neonatal seizures
- The data have limitations: evidence of underreporting, biased missingness, and changes in reporting after a form revision in 2003
- Data from nine states are sufficiently plausible to merit further validation work: IA, MT, NE, OR, SD, UT, VT, WA, and WY
- There are ongoing efforts to improve the quality of U.S. birth certificate data. Our findings can inform their work

of epilepsy over time and across specific populations.³ The report also encourages the epilepsy community to develop and evaluate screening tools to identify epilepsy in high risk groups to lay the foundation for epilepsy prevention.

High quality birth certificate data could help address several unanswered questions about the causes of neonatal seizures, and their relationship to future development of epilepsy. For example, an analysis of births in California from 1998 to 2002 found several prenatal risk factors for neonatal seizures, raising the possibility that some neonatal seizures may be preventable. However, the contribution of modifiable risk factors is underdescribed, and it is unclear if the risk factors have persisted over time.⁴ As a second example, in the population of neonates with seizures from hypoxic ischemic encephalopathy, it is unclear if (and for how long) seizures should be treated with antiepileptic medication, and if neonatal seizures are causally related to the subsequent development of epilepsy.⁵⁻⁷

U.S. birth certificates are a potentially valuable source for the epidemiologic study of neonatal seizures; they track 4 million yearly births and include detailed prenatal and perinatal information. However, there are several potential limitations of the data. Some items have uncertain validity,⁸⁻¹¹ data quality varies by state and hospital,⁸ and neonatal seizures are often underreported.¹²⁻¹⁵ Furthermore, the birth certificate form was revised in 2003, with uncertain effect on the quality of data.

In order to use U.S. birth certificate data to study neonatal seizures, several important questions must be addressed. First, how complete are the data (i.e., what is the degree of missingness)? Second, has the 2003 revision of the birth certificate form affected the quality of neonatal seizures reporting? Third, is there a particular subset of high-quality data that may be suitable for epidemiology studies? This study addresses all three questions.

METHODS

We used a retrospective serial cross-sectional design to examine the quality of national birth certificate data for neonatal seizures from 2003 to 2013. We used a restricted dataset received from the Centers for Disease Control and Prevention National Center for Health Statistics (NCHS) that included geographic information. This study was approved by Weill Cornell Medical College Institutional Review Board.

Birth certificate registration is estimated near 100% in the United States.¹⁶ The NCHS has contracts with 57 jurisdictions (50 states, New York City, District of Columbia, and 5 territories) to receive electronic files of birth certificates, and the NCHS publishes a national dataset online each year.¹⁷ The NCHS provides jurisdictions with feedback about data quality, such as a summary of the jurisdiction's quality problems (completeness of data, out-of-range values, and inconsistencies across items) and email attachments illustrating problems.¹⁸ Each of the 57 jurisdictions is tasked with improving the data quality of individual hospitals and facilities.¹⁹ Most jurisdictions focus their evaluations on data quality (e.g., completeness and logic checks), whereas a few jurisdictions evaluate validity by comparing a sample of birth certificates to medical records.

Birth certificate revision

The birth certificate was revised in 2003 to improve the completeness and quality of data,²⁰ and states implemented the revision on a rolling basis from 2003 to 2015. The data published by the NCHS on neonatal seizures vary from 2003 to 2006. From 2003 to 2004, data include seizure information collected by states using only the unrevised form. From 2005 to 2006, data include seizure information collected from states using either form. Some states have both unrevised and revised records, because there was not consistent use of one form across the state during this time period. After 2006, data include seizure information collected using only the revised form. Thus our analysis includes births using only the unrevised form in 2003–2004, both forms in 2005 and 2006, and only the revised form in 2007–2013.

Published estimates of neonatal seizure incidence

We found estimates of neonatal seizure incidence through a literature search (search terms: newborn seizures, neonatal seizures, incidence, population-based, and epidemiology) and by reviewing references from neonatal seizure review articles. Among six studies (Table 1), one⁴ used methods that closely approximate what would be expected in birth certificates. That study, a review of statewide administrative data and discharge data from California, counted seizures occurring only during the birth admission (rather than 28 days after birth). Therefore, we used their estimate as the

Table 1. Population-based studies estimating the incidence of neonatal seizures per 1,000 among all live births and term live births^{4,34-38}

Study	Time period	Observation window	All live births			Term		
			Number of seizures	Sample size	Incidence per 1,000	Number of seizures	Sample size	Incidence per 1,000
Holden et al. ³⁷	1959–1966	Within 28 days of birth	245	54,000	4.5	–	–	–
Lanska and Lanska ³⁸	1980–1991	Within 30 days of birth	131,161	46,159,220	2.8	–	–	–
Lanska et al. ¹²	1985–1989	Within 28 days of birth	58	16,428	3.5	–	–	–
Ronen et al. ³⁶	1990–1994	28 days for term; 44 weeks postconception for preterm ^a	9,000	34,615	2.6	5,843	30,753	1.9
Saliba et al. ¹³	1992–1994	28 days for term; 44 weeks postconception for preterm ^a	189	103,399	1.8	122	80,398	1.5
Glass et al. ⁴	1999–2002	During birth hospitalization	–	–	–	2,213	2,332,803	0.95
Current study ^b	2005–2013	During birth hospitalization	7,353	24,740,630	0.30 ^b	5,875	22,834,395	0.26 ^b

^aSeizures occurring within 28 days of birth for term infants and up to 44 weeks postconception for preterm infants.

^bCrude estimate of national neonatal seizure incidence using the 2003 revised birth certificate. Interpret cautiously; see Discussion.

best available reference (0.95 per 1,000) and refer to it as the “California incidence” or “California study.”

Outcome—definition

On both the unrevised and revised forms, neonatal seizures are reported in an item called “Abnormal Conditions of the Newborn (check all that apply).” On the unrevised birth certificate form, there was a check box item labeled “Seizure.” On the revised form, the check box is labeled “Seizure or other serious neurological condition” (Fig. 1).

Analysis

Crude national neonatal seizure incidence

We report the crude estimates of the overall national neonatal seizure incidence for two groups: (1) all live births

and (2) term live births only (≥ 36 weeks of gestation), using data from births recorded using the revised form during 2005–2013. We used a sensitivity analysis to evaluate the impact of missing data—we recoded births with missing seizure data as normal findings and recalculated incidence.

Reporting of seizures

We performed four analyses to evaluate the effect of the 2003 revision of the birth certificate form on reporting of neonatal seizures. We included regions that had both unrevised and revised data available, including 40 states and the District of Columbia (D.C.).

First, we identified states and years with decreased reporting of seizures compared to the California incidence, potentially reflecting underreporting of seizures in birth certificate data. We used a chi-square test to compare the

Unrevised birth certificate	2003 Revised birth certificate
<div style="border: 1px solid black; padding: 5px;"> <p>42. Abnormal Conditions of the Newborn (Check all that apply)</p> <ul style="list-style-type: none"> <input type="checkbox"/> Anemia (Hct. <38/Hgb.<13) <input type="checkbox"/> Birth injury <input type="checkbox"/> Fetal alcohol syndrome <input type="checkbox"/> Hyaline membrane dresses/RDS <input type="checkbox"/> Meconium aspiration syndrome <input type="checkbox"/> Assisted ventilation \leq 30 min <input type="checkbox"/> Assisted ventilation > 30 min <input checked="" type="checkbox"/> Seizures <input type="checkbox"/> None <input type="checkbox"/> Other (Specify) _____ </div>	<div style="border: 1px solid black; padding: 5px;"> <p>54. ABNORMAL CONDITIONS OF THE NEWBORN (Check all that apply)</p> <ul style="list-style-type: none"> <input type="checkbox"/> Assisted ventilation required immediately following delivery <input type="checkbox"/> Assisted ventilation required for more than six hours <input type="checkbox"/> NICU admission <input type="checkbox"/> Newborn given surfactant replacement therapy <input type="checkbox"/> Antibiotics received by the newborn for suspected neonatal sepsis <input checked="" type="checkbox"/> Seizure or serious neurologic dysfunction <input type="checkbox"/> Significant birth injury (skeletal fracture(s), peripheral nerve injury, and/or soft tissue/solid organ hemorrhage which requires intervention) <input type="checkbox"/> None of the above </div>

Figure 1.

Comparison of the “Abnormal Conditions of the Newborn” section in the unrevised and revised birth certificate. In the revised form, the check box is labeled “Seizure or serious neurologic dysfunction,” compared to the unrevised form labeled “Seizures.”

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number of state-years with seizure incidence below the California incidence using unrevised versus revised forms. Second, we compared the distribution of seizure incidence in the unrevised versus revised form using a Wilcoxon signed-rank test. Third, we examined the percent change in seizure incidence from 2003 (unrevised form) to 2013 (revised form) for each state. Fourth, we compared 2003 to the first year that the revised form was implemented, which varied from state to state.

We provide two visualizations to demonstrate changes in incidence over time. First, to highlight notable examples, we selected states with a large percent change and plotted seizure incidence by year. Second, to show the distribution of changes across all states, we split states into tertiles based on their 2003 seizure incidence, and plotted seizure incidence for 2003 and 2013.

Missing seizure data

The instructions for the birth certificate form specify that the item “Abnormal Conditions of the Newborn” should not be left blank. Users of the form can indicate “None” in the unrevised form, or “None of the above” in the revised form. If the entire item was left blank, the data element for seizure was considered missing, that is, because it was uncertain if the newborn did not have seizures, or if the individual filling out the form did not complete the item. We performed an analysis of missingness for all live births from 2003 to 2013 as follows.

First, we tested if missingness varied by state and year using a two-way analysis of variance (ANOVA).

Second, we performed bivariate analyses to determine whether missing data varied by maternal demographic factors, infant health factors, and medical care factors. The maternal predictors were as follows: age (<20, 20–24, 25–34, 35–44, and ≥45 years), education (less than high school, high school, some college, Bachelor’s degree or more), race/ethnicity (Hispanic, white non-Hispanic, black non-Hispanic, and other non-Hispanic), and insurance status. Insurance status was divided in two groups: families that paid for birth admission using private insurance or self-pay versus public insurance (i.e., Medicaid, Indian Health Service, Champus/Tricare, and other government insurance).⁴ The infant health predictors included gestational age (<36, ≥36 weeks), birth weight (<2,500, 2,500–4,000, >4,000 g), and Apgar score ≤3 or >3 at 5 min. The medical care factors included the title/degree of the attending (Doctor of medicine – M.D., Doctor of osteopathic medicine – D.O., certified nurse-midwife other midwife), and place of delivery (hospital, freestanding birthing center, clinic/doctor’s office, home/residence).

Third, in order to examine if variations in missingness persisted in the most recent data, we repeated the bivariate analyses using only data from the revised birth certificate in 2013.

Fourth, we evaluated if missingness changed following the revision by comparing the proportion of missing seizure data for unrevised forms in 2003 versus revised forms in 2013 using a chi-square test. We restricted this analysis to the 40 states and D.C. that had data available for both years.

Recommended cohort

Through consensus, we developed a working definition for a state to have plausible data. A state had to meet three criteria: (1) use of the revised form for at least 4 years (2010–2013), (2) <1% missing data in 2013, and (3) seizure incidence within 50% of the California incidence (0.5–1.4 per 1,000 live births) in 2013. We selected a relatively large window (within 50% of the California incidence) to account for changes over time, possible differences between California and other states, and inherent limitations of the California study.

Statistical tools

We performed statistical analyses with R version 3.2.1 and RStudio version 0.99.465, supplemented by “data.table” package.^{21,22}

RESULTS

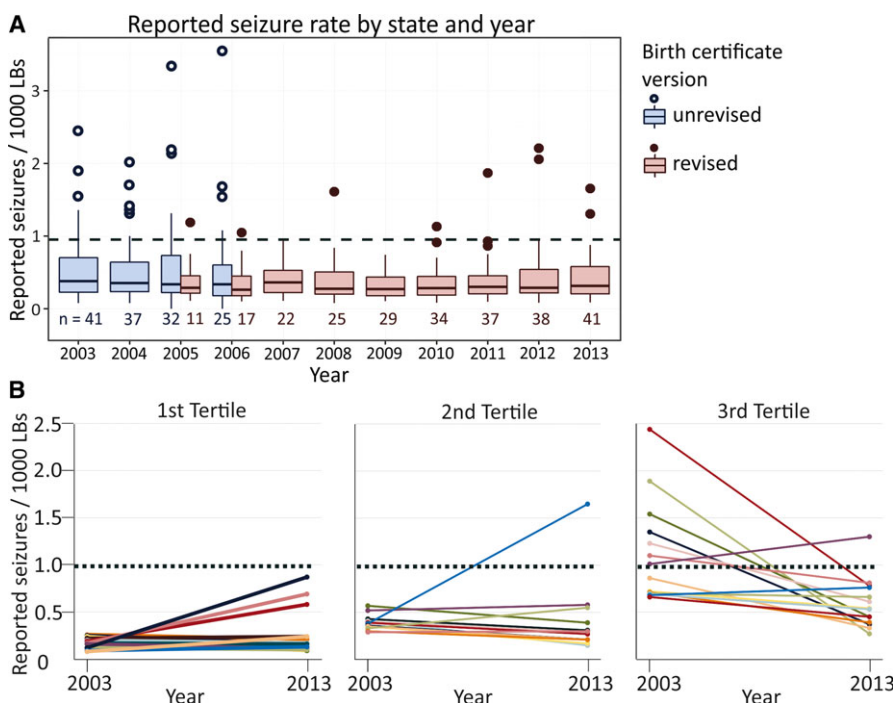
From 2003 to 2013, 45.22 million live born infants were registered using the U.S. Standard National Certificate of Birth. We excluded cases collected using the revised form before 2005 (0.98 million) and unrevised after 2006 (7.06 million), as the seizure field for these cases is not included in the NCHS dataset. Of the remaining sample, 36.97 of 37.18 million (99.5%) had seizure data, including 34.01 of 34.18 million (99.5%) infants born at term (Fig. S1).

Crude national neonatal seizure incidence

Using the revised form, we identified 7,353 infants with seizures during their birth hospitalization among 24,740,630 live births from 2005 to 2013, yielding a crude national neonatal seizure incidence of 0.30 per 1,000 live births. There were 5,875 infants with seizures among 22,834,395 term births (≥36 weeks)—a crude national neonatal seizure incidence of 0.26 per 1,000 term live births, which is 27% of the California incidence. In our sensitivity analysis (in which we assumed births with missing seizure data were normal), the crude incidence changed from 0.257 to 0.256 (i.e., a decline of 0.001 per 1,000 term live births), indicating that missing data overall had only a small effect on the reported crude seizure incidence.

Reporting of seizures

The yearly median seizure incidence for term newborns across all states, including both unrevised and revised data, ranged from 0.21 to 0.39/1,000, which was consistently

**Figure 2.**

(A) Seizure rates among term infants were plotted for each state (dots) by year, boxplots indicate median and 25th and 75th percentiles. Median seizure rates were lower than the previously reported 0.95/1,000 California rate (dashed line) for all years. However, there were fewer state-years with seizure rates above the California rate using the revised form: 9 of 245 versus 25 of 110 state-years. (B) States were split into tertiles based on their 2003 seizure rate, and plotted by seizure rate and year. The majority of states (70.7%) had a decrease in reported seizure rates from 2003 (unrevised) to 2013 (revised).

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below the California incidence (Fig. 2A). Only 34 (9.5%) of 355 state-years reported a seizure incidence above the California incidence. More state-years had a seizure incidence below the California incidence using the unrevised (25 of 110) versus the revised (9 of 245) form, $p < 0.001$. In addition, the reported seizure incidence using the revised form in 2013 had a lower median and tighter interquartile interval (median 0.31 [interquartile interval 0.21–0.58]), compared to the unrevised form in 2003 (0.38 [0.22–0.70]), $p < 0.05$.

We split states into tertiles based on their 2003 seizure incidence (Fig. 2B). In the first tertile, no states reported seizure incidence above the California incidence in 2003 or 2013. In the second tertile, there was no state with a seizure incidence above the California incidence in 2003, and one state above in 2013. In the third tertile, seven states reported seizure incidence above the California incidence in 2003, and one state above in 2013. The majority of states (29 of 41, 70.7%; Fig. 3) had a reduction in reported seizure incidence from 2003 to 2013 (using unrevised vs. revised). For example, Michigan had an 86% decrease in reported seizure incidence. The median percent change was a 26% decrease across all states. Of note, eight of nine states above the California incidence in 2003 declined below the California incidence in 2013 (Table S1). Finally, when we measured the percent change using the revised form in 2003 versus the first year that the revision was implemented, the median percent change was an 18% decrease across all states, and the majority of states (27 of 41, 66%) had a decrease in reporting.

Missing seizure data

In general, we found low levels of missing seizure data in birth certificates. Only a small number of state-years had $>5\%$ missing seizure data using the unrevised (8 of 167 from four states) or the revised form (10 of 272 from two states). The level of missing seizure data varied by state and year, $p < 0.001$. For example, rates of missing data in New Hampshire ranged from 3.00% to 6.19% by year, and rates of missing data in Georgia decreased from 14.65% to 3.06% between 2003 and 2013 (Table S2).

In bivariate analysis, the proportion of missing data varied by factors related to the birth (Table 2). We found more data missing for infants born to black non-Hispanic mothers (odds ratio [OR] 1.81, 95% confidence interval [CI] 1.79–1.83) and fewer missing data for Hispanic mothers (OR 0.72, 95% CI 0.71–0.73), compared to white non-Hispanic mothers. There were fewer missing data among families with public insurance (OR 0.71, 95% CI 0.67–0.74), compared to private insurance/self-pay. More data was missing for preterm infants versus term infants (OR 1.48, 95% CI 1.46–1.51), low birthweight versus normal birth weight (1.49, 1.47–1.51), and Apgar score <4 at 5 min versus 4 or higher (3.68, 3.56–3.80). In addition, more data were missing when infants were delivered by a certified nursing midwife (OR 1.22, 1.20–1.23) or other midwife (2.76, 2.67–2.86), and fewer missing data when infants were delivered by provider with a D.O. degree (0.73, 0.72–0.75), compared to a physician with an M.D. degree. We found more data missing for infants born in a freestanding birthing center (3.37, 3.24–3.51), clinic/doctor's office (5.70, 4.69–6.93),

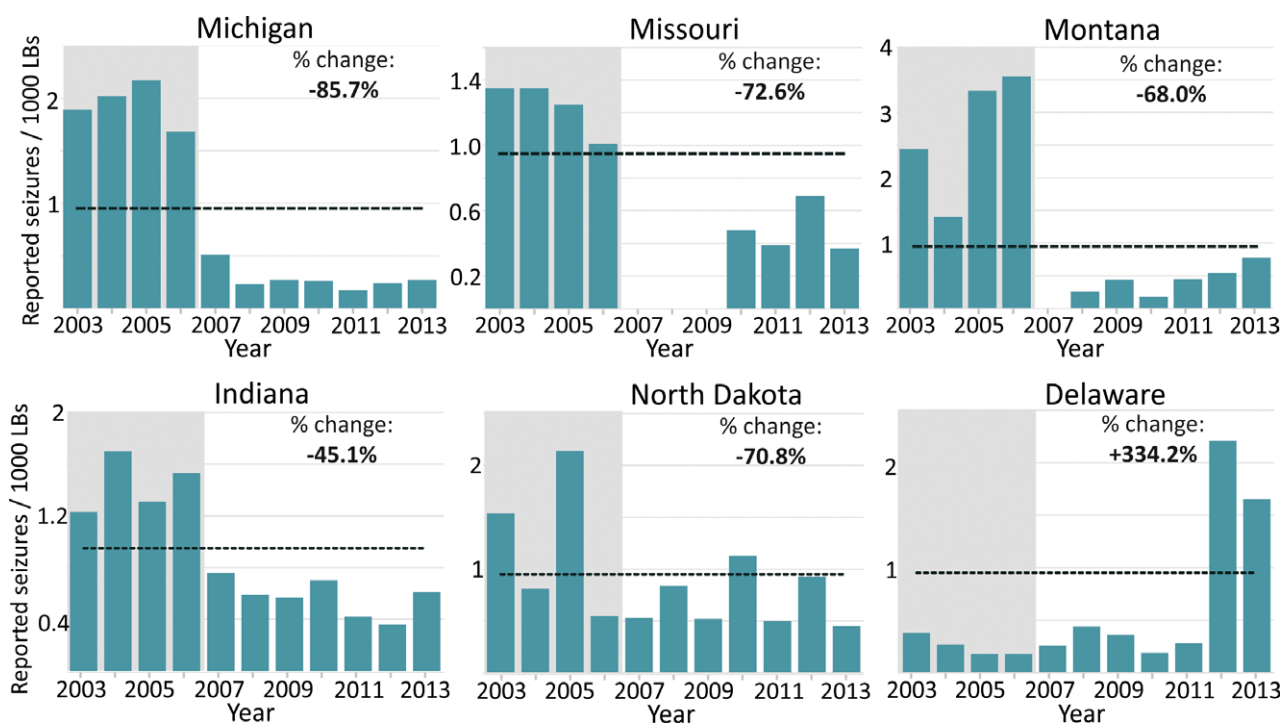


Figure 3.

Selected states with a large change in reporting from unrevised (gray box) to revised forms. The % change from 2003 to 2013 is displayed in text. Plots illustrate a clear change in reporting after implementation of the revision. Delaware was the only state below the 0.95/1,000 California rate (dashed line) in 2003 and above in 2013.

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and home/residence (2.30, 2.23–2.39), compared to a hospital. Similar results were observed when analysis was restricted to only 2013 data (Table S4). Finally, more seizure data were missing when the revised (0.53%) versus unrevised form (0.44%) was used, $p < 0.001$ (Tables S2 and S3).

Recommended cohort

Nine states met our basic criteria for data plausibility: Iowa, Montana, Nebraska, Oregon, South Dakota, Utah, Vermont, Washington, and Wyoming. As an example, Georgia did not meet our plausibility criteria because it had 3.06% missing data and reported 0.17 newborns with seizures per 1,000 term births (an incidence that is less than one fifth of the California incidence). As a second example, Virginia did not meet our criteria, because it had data available using only the revised form for 2 years and reported a seizure incidence of only 0.09/1,000 (an incidence that is one tenth of the California incidence).

DISCUSSION

In this evaluation of the quality of newborn seizure data on U.S. national birth certificates for years 2003–2013, we found the following three major limitations: (1) lower reporting of seizures compared to previous estimates (by

>70%), (2) increased missing data and decreased reporting of neonatal seizures following the 2003 revision, and (3) biased missingness of data by demographic, infant health, and medical care factors. More missing seizure data were observed among families with black non-Hispanic race or families with private/self-pay insurance status; infants with preterm gestational age, low birthweight, or low Apgar score; and delivery by a midwife and outside a hospital. We recommend nine states that met basic plausibility criteria as a starting point for future studies.

The low number of reported neonatal seizures in birth certificates can be interpreted two ways. It is possible that birth certificates accurately estimate seizure incidence, and that other reports have consistently overestimated neonatal seizures throughout the United States. Alternatively, birth certificates underreport neonatal seizures, leading to a falsely low estimate of neonatal seizure incidence. Our findings, in the context of the published literature, strongly support the second interpretation (i.e., that birth certificate underreport neonatal seizures) for the following three reasons.

First, validation studies have consistently found underreporting of neonatal seizures when comparing birth certificate data to multiple other data sources (hospital records,^{12–15} death certificates,^{12–15} and maternal interviews¹⁵). As an example, a recent sampling of 372 birth certificates in

Table 2. Frequency of missing seizure data and odds ratios by demographic, infant health, and medical care factors

	Missing, % (x of y)	Bivariate OR (95% CI)
Demographic factors		
Maternal age, years		
<20	0.56 (19.8K of 3.5M)	1.02 (1.00–1.04)
20–24	0.55 (49.8K of 9085.9K)	Reference
25–34	0.52 (100.6K of 19.2M)	0.96 (0.95–0.97)*
35–44	0.57 (30.0K of 5.3M)	1.03 (1.02–1.05)*
≥45	0.67 (441 of 65.8K)	1.23 (1.12–1.35)*
Maternal race/ethnicity		
Hispanic	0.36 (34.1K of 9.4M)	0.72 (0.71–0.73)*
White, non-Hispanic	0.51 (100.7K of 19.9M)	Reference
Black, non-Hispanic	0.91 (47.4K of 5.2M)	1.81 (1.79–1.83)*
Other, non-Hispanic	0.43 (10.5K of 2.4M)	0.84 (0.83–0.86)*
Maternal education		
Less than high school	0.52 (39.0K of 7.5M)	0.97 (0.95–0.98)*
High school	0.54 (53.7K of 10.0M)	Reference
Some college	0.50 (46.8K of 9.4M)	0.92 (0.91–0.94)*
Bachelor's degree or more	0.51 (50.8K of 9.9M)	0.95 (0.94–0.97)*
Public insurance	0.26 (1.9K of 714.2K)	0.71 (0.67–0.74)*
Private insurance or self-pay	0.37 (57.2K of 15.4M)	Reference
Infant health factors		
Male	0.54 (103.3K of 19.0M)	1.01 (1.00–1.02)
Female	0.54 (97.4K of 18.1M)	Reference
Gestational age < 36 weeks	0.75 (21.3K of 2.8M)	1.48 (1.46–1.51)*
Gestational age ≥ 36 weeks	0.51 (173.7K of 34.2M)	Reference
Birth weight, g		
<2,500	0.76 (22.7K of 3.0M)	1.49 (1.47–1.51)*
2,500–4,000	0.51 (159.7K of 31.2M)	Reference
>4,000	0.51 (15.1K of 3.0M)	1.00 (0.98–1.01)
Apgar ≤ 3 at 5 min	1.98 (3.8K of 192.4K)	3.68 (3.56–3.80)*
Apgar > 3 at 5 min	0.55 (184.8K of 33.8M)	Reference
Medical care factors		
Attending		
Medical doctor (M.D.)	0.52 (166.2K of 31.9M)	Reference
Doctor of osteopathic medicine (D.O.)	0.38 (7.4K of 1.9M)	0.73 (0.72–0.75)*
Certified nurse-midwife	0.63 (18.1K of 2.9M)	1.22 (1.20–1.23)*
Other midwife	1.43 (3.2K of 221.8K)	2.76 (2.67–2.86)*
Facility		
Hospital	0.53 (194.0K of 36.7M)	Reference
Freestanding birthing center	1.76 (2.4K of 137.9K)	3.37 (3.24–3.51)*
Clinic/doctor's office	2.94 (104 of 3.5K)	5.70 (4.69–6.93)*
Home/residence	1.21 (3.2K of 263.6K)	2.30 (2.23–2.39)*

*p < 0.05.

Second, our comparison study, the California study,⁴ estimated a much higher incidence (0.95 per 1,000) than suggested by birth certificate data. The California study has many strengths: it is the most recently available estimate of incidence, has the largest sample size among recent studies, and provides a separate estimate for term versus all live births. Although we acknowledge that the California study has limitations, its weaknesses are not sufficient to explain the large discrepancy between their findings and ours. For example, the California study used administrative data containing International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnoses of seizures rather than chart review, raising the possibility of coding errors. However, these codes are reasonably accurate when compared to chart review (for example, one studied showed 97% sensitivity and 75% positive predictive value).¹² As another example, the California study was conducted in earlier years than our study (1999–2002 vs. 2003–2013). However, the published incidence using birth certificate data had little change in years 1999–2002 (0.3–0.4 per 1,000 live births^{23–26}) compared to our study in 2003–2013 (0.3 per 1,000). During the same 4-year period, the published incidences using birth certificate data remain much lower than the California incidence (0.3–0.4 vs. 0.95 per 1,000 live births).^{4,23–26} Note that the published incidences using birth certificates included all live births (regardless of gestational age) and that the California study included only term live births. Therefore, we would expect published birth certificate estimates to be larger than in the California study.

Third, we found an abrupt decrease in reporting of neonatal seizures after states implemented the 2003 revision. It is possible that this reflects a real reduction in seizure incidence over time, since unrevised forms were collected in earlier years than revised forms (2003–2006 vs. 2005–2013) and there were important changes in care over the intervening period (for example, therapeutic hypothermia for hypoxic-ischemic encephalopathy became available in 2005). However, the majority of states reported a reduction in seizure incidence following implementation of the revision regardless of the year, which strongly implicates a change in how the revised form tracks seizures, rather than an actual change in seizure incidence.

Our work and others^{12–15} indicate an ongoing gap in the quality of U.S. birth certificate data, particularly for neonatal seizure epidemiology. Of important note, there are prior and current efforts to improve the quality of birth certificate data. The birth certificate was revised in 2003 to improve data quality following recommendations from an expert panel and subgroups who reviewed literature, surveys, and testimony.²⁰ Since the 2003 revision, NCHS has conducted two large validation studies^{8,27} and further evaluated three individual data items.^{28–30} They have an ongoing study that involves interviewing hospital staff in four states to understand how birth certificates are completed in different

Michigan found 38 records of neonatal seizures across three data sources (discharge abstracts, maternal interviews, and birth certificates), although only one of 38 was recorded in birth certificates.¹⁵

settings.³¹ In addition, a Birth Data Quality workgroup was developed to identify data quality problems and effective solutions.⁸ The workgroup is evaluating how jurisdictions currently ensure data quality, and the workgroup plans to develop a national model for quality control.¹⁹

We were surprised to learn, however, that the NCHS did not include the seizure item in a recent validation study, despite including all other items in the “Abnormal conditions of the newborn” section.⁸ This presents an opportunity for the neonatology, neurology, and epilepsy communities to advocate for improvement of items relevant to our fields, including the neonatal seizure item. Recognizing this opportunity early is important, because revising the birth certificate form is a lengthy process. For example, it took 13 years for all states to implement the revised birth certificate.²⁷

We were also surprised to find a decrease in reported seizures following implementation of the revision. We expected that language from the revised birth certificate (“Seizure or serious neurologic dysfunction”) would include more infants than the language from the unrevised (“Seizures”). It is unclear how the average user interprets the seizure item, although we can speculate possibilities. For example, the revised seizure item may be misinterpreted to mean including isolated seizures that are not associated with other checklist items (e.g., assisted ventilation, sepsis, and neonatal intensive care unit [NICU] admission), and therefore the seizure item may be left blank when other items seem more appropriate. Or, the item may be interpreted to mean “seizures AND serious neurological dysfunction,” which would bias toward excluding less seriously ill newborns.

We found that some groups have more seizure data missing, including more missing data among high-risk infants and infants born out of the hospital. We can speculate about potential explanations. For example, high-risk infants have more transitions in care (e.g., transfer from labor and delivery unit to intensive care unit) and this may explain missing data. As another example, higher rates of missing data for out-of-hospital births may suggest gaps in training, procedures, or incentives for providers who supervise home births. More work is needed to understand the underlying explanation for differences, as well as to test the efficacy of potential solutions (e.g., telephone support service for midwives and pediatricians recording out-of-hospital births).

Despite the limitations of birth certificate data for neonatal seizure epidemiology, nine states passed our plausibility criteria: IA, MT, NE, OR, SD, UT, VT, WA, and WY. Future work might start with additional validation studies in these states.

Limitations

Three limitations merit discussion. First, we have relied on other published work rather than chart review (or administrative data)^{12–15} to evaluate the validity of neonatal

seizure reporting in birth certificates. National validation of birth certificates is beyond the scope of our work here.

Second, interpreting birth certificate data is complicated by the known variability in reporting across hospitals and states.⁸ Our data show important variations between states, although variability is more pronounced in earlier years using the unrevised form. These variations may be explained by how hospitals diagnose seizures, their interpretation of “other serious neurological dysfunction,” how much the hospital emphasizes the value of birth certificates, and the resources available. In addition, there may be variability in when birth certificate forms are completed (e.g., immediately following birth vs. at discharge).

Finally, unregistered births are an important contemporary public health problem throughout the world,¹⁶ raising the possibility that unregistered births in the United States could bias epidemiologic estimates drawn from birth certificates. Unregistered births were common in the United States as recently as the 1940s.^{32,33} However, at present, there are few data to suggest that there are a large number of unregistered births in the United States, and international agencies regularly estimate that U.S. birth registration is at or near 100%.¹⁶

CONCLUSION

National birth certificates are a valuable data source for epidemiologic studies, because they track nearly all live births in the United States and collect a range of information about the births. However, our study demonstrates a gap in the utility of using birth certificates to track neonatal seizures. We found that birth certificates estimate a much lower seizure incidence compared to other published estimates. Furthermore, we found more missing seizure data and fewer reports of neonatal seizures following implementation of a 2003 revision of the birth certificate form. A unifying explanation of our findings and those of others is that neonatal seizures are often underreported in birth certificates. We recommend nine states that met basic plausibility criteria as a starting point for future studies using birth certificate data for neonatal seizure epidemiology.

DISCLOSURE OF CONFLICT OF INTEREST

Ms. Berry and Ms. Seirup have no potential conflicts of interest to disclose. Dr. Pesko receives grant funding from the National Institutes of Health, the American Cancer Society, the Agency for Healthcare Research & Quality, and the Centers for Disease Control and Prevention. Dr. Pesko has no conflicts of interest to disclose. Dr. Hesdorffer receives grant funding from the Patient-Centered Outcomes Research Institute, the Centers for Disease Control and Prevention, Finding a Cure for Epilepsy and Seizures, the Citizens United for Research in Epilepsy, Clinical and Genetic Predictors of Outcomes and Therapeutic Insights, the Epilepsy Study Consortium, and the National Institute of Neurological Disorders and Stroke. She is a consultant for Cyberonics, on the advisory board at Upsher-Smith, an associate editor at *Epilepsia*, and a consultant at Mount Sinai Injury Prevention

Center. Dr. Hesdorffer has no conflicts of interest to disclose. Dr. Shellhaas receives grant funding from the National Institutes of Health, the Patient-Centered Outcomes Research Institute, the Pediatric Epilepsy Research Foundation, the American Sleep Medicine Foundation, and the University of Michigan Department of Pediatrics & Communicable Diseases. She receives royalties from UpToDate and serves as a consultant to the Epilepsy Study Consortium. Dr. Shellhaas has no conflicts of interest to disclose. Dr. Grinspan receives grant funding from the Centers for Disease Control and Prevention, the New York State Department of Health, the Nanette Laitman Clinical Scholars Program, and the Pediatric Epilepsy Research Foundation. He has consulted for the U.S. Department of Justice and for Supernus Pharmaceuticals. Dr. Grinspan has no conflicts of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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SUPPORTING INFORMATION

Additional Supporting Information may be found in the online version of this article:

Figure S1. Flow chart of birth certificate data. Gray boxes indicate excluded and missing data.

Table S1. Seizure rates by state using the unrevised form in 2003 and revised form in 2013, including 40 states and

D.C. with data available for both years/versions.

Table S2. Percent of missing seizure data across states and years, using the 2003 revised birth certificate.

Table S3. Percent of missing seizure data across states and years, using the unrevised birth certificate.

Table S4. Frequency of missing seizure data and odds ratios by demographic and infant health characteristics, using data from revised birth certificates in 2013.