VALIDATION OF FEBRILE SEIZURES IN THE MINI-SENTINEL POST-LICENSURE RAPID IMMUNIZATION SAFETY MONITORING (PRISM) SYSTEM

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BACKGROUND AND OBJECTIVES

- The Post-Licensure Rapid Immunization Safety Monitoring (PRISM) system is a component of the Mini-Sentinel, which was established in response to the FDA Amendments Act to monitor the safety of FDA-regulated medical products.

- We sought to evaluate the positive predictive value (PPV) of ICD9 code algorithms to identify post-vaccination febrile seizures (FS).

- Furthermore, we describe an adaptation of Brighton Collaboration (BC) definitions for seizures for use in retrospective medical record review.

METHODS

- Study population: children 6-59 months of age enrolled in a health plan associated with one of three participating Mini-Sentinel Data Partners: Aetna, HealthCore, and Humana.

- Potential FS cases were identified using ICD9 diagnosis codes for seizures in the emergency department or inpatient setting following influenza, DTaP, and PCV13 vaccines from July 1, 2010 to June 30, 2011.

- Adjudication of de-identified full text medical records was conducted to confirm case status. Each case was reviewed by two pediatrician adjudicators. Potential FS were considered confirmed if they had documentation of a seizure and a fever within 24 hours or a physician's diagnosis of FS.

- Confirmed FS were further examined to determine whether adjudication criteria based on an adaptation of BC definitions for generalized seizures were met.

RESULTS

Table 1. Characteristics of potential FS cases identified in electronic data with primary algorithm A: ICD9 diagnosis codes 780.31 [FS (simple), unspecified], 780.32 [complex FS], or 780.39 [other seizure].

Characteristic	Potential cases identified in electronic data N=252	Potential cases identified in electronic data with medical records available N=216
Age (months)		
6-11	34 (13%)	30 (14%)
12-23	145 (58%)	124 (57%)
24-35	41 (16%)	37 (17%)
36-47	14 (6%)	9 (4%)
48-59	18 (7%)	16 (7%)
Setting of diagnosis		
Emergency department	207 (82%)	177 (82%)
Inpatient	45 (18%)	39 (18%)

- The majority of potential FS cases occurred in children younger than 24 months of age and were identified in the emergency department setting.

- The subset of potential cases with medical records available was representative of all potential cases initially identified in electronic data.

Figure 1. Case disposition of potential FS identified with primary algorithm A.
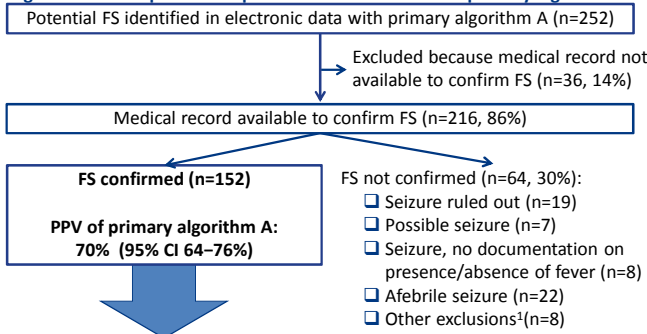
Level	Criteria based on medical record data	N (%) N=152
Meets BC criteria for generalized seizures (N=9, 6%)		
BC Level 1	Witnessed sudden loss of consciousness (LOC) and generalized tonic, tonic-clonic, or clonic motor manifestations	4 (3%)
BC Level 2	History of unconsciousness and generalized tonic, tonic-clonic, or clonic motor manifestations	2 (1%)
BC Level 3	History of unconsciousness and other generalized motor manifestations[2]	3 (2%)
Meets adaptation of BC criteria for generalized seizures (N=143, 94%)		
Level 4A	Witnessed sudden LOC and other generalized motor manifestations[2]	7 (5%)
Level 4B	Altered state of consciousness (ASC)[3] and generalized tonic, tonic-clonic, or clonic motor manifestations	39 (26%)
Level 4C	ASC[3] and other generalized motor manifestations[2]	55 (36%)
Level 4D	Clinical diagnosis of seizure	42 (28%)

[1]Cases with history of afebrile seizures, CNS infection/trauma, underlying metabolic disorders, or focal seizures not associated with complex FS were excluded.
[2]Other generalized motor manifestations include less specific descriptions such as 'shaking', 'trembling', 'shivering' and 'quivering'.
[3]Altered states of consciousness include descriptions such as 'eyes rolled back', 'unresponsive', 'post-ictal state', and 'sleepy'.

- Only 9 (6%) chart-confirmed FS met BC for generalized seizures (BC Levels 1-3).

- By including the combination of witnessed sudden LOC and other generalized motor manifestations (Level 4A), we captured an additional 7 (5%) chart-confirmed FS. By including criteria for ASC (Levels 4B and 4C), we captured an additional 94 (62%) chart-confirmed FS.

- An additional 42 (28%) chart-confirmed FS did not meet LOC/ASC and/or generalized motor manifestations criteria, but did have a clinical diagnosis of seizure.

Table 2. Chart confirmation rates for alternative FS algorithms.

Algorithm	Definition based on ICD9 diagnosis codes in electronic data	Number potential cases with medical records available N=216	Number chart-confirmed cases N=152	PPV (95% CI)
B	780.31 or 780.32 [simple or complex FS]	154	140	91% (85–95%)
C	Does not meet criteria for algorithm B and meets the following on same day: (i) 780.39 [other seizure] AND (ii) 780.6, 780.60, 780.61, 780.62 or 780.63 [fever]	5	1	20% (1–72%)
D	Does not meet criteria for algorithm B and meets the following with respect to same day: (i) 780.39 [other seizure] WITHOUT (ii) 780.6, 780.60, 780.61, 780.62 or 780.63 [fever]	57	11	19% (10–32%)

- Primary algorithm A based on any seizure code yielded a moderate PPV (70%) for FS.

- Alternative algorithm B (restriction to specific FS codes) yielded a higher PPV (91%) and accounted for 92% of confirmed FS.

- Alternative algorithms C and D (codes for other seizures in the absence of codes for FS) yielded very low PPVs, regardless of whether codes for fever were required on the same day (PPVs ranging from 19% to 20%).

CONCLUSIONS

- Future studies utilizing ICD9 coded data to identify FS without chart confirmation should consider restricting their case-finding algorithm to codes for FS.

- BC criteria for generalized seizures may not capture all clinically relevant cases of FS. In chart-review studies of FS initially identified using ICD9-coded data, investigators should consider incorporating this adaptation of BC criteria, including ASC.

FOR ADDITIONAL INFORMATION

http://www.mini-sentinel.org/work_products/PRISM/Mini-Sentinel_PRISM_Influenza-Vaccines-and-Febrile-Seizures-Report.pdf

ACKNOWLEDGEMENTS