Clinical Pathways Leading to a Diagnosis of Infantile Spasms Using a Claims Database

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Introduction

- Infantile spasms (IS) are seizures, clinically characterized by a sudden, rapid contraction of the trunk and limbs with varied intensity and often occurring in clusters
- IS is a relatively rare disorder (estimated incidence: 0.25-0.42/1000 live births per year)[1]
- The median delay in treatment of IS is 24.5 days, in part due to misdiagnosis as gastroesophageal reflux, benign sleep myoclonus, or normal infant movements[2]
- Delayed diagnosis and treatment initiation in IS can lead to long-term neurobehavioral problems[2,3]
- Predictive clinical factors that can identify infants with undiagnosed IS and/or enable a shorter time to treatment initiation represent a critical medical need
- The goal of this study was to develop predictive models to identify patients with undiagnosed IS using a population-based claims database (Symphony Health Integrated Dataverse [IDV]®) and then refer these patients to an appropriate health care professional

Methods

Cohort Identification

- The IDV database captures de-identified patient-level medical and pharmacy claims from more than 12,000 US health plans, 1.8 million prescribers, and 280 million active patients, with almost 14 years of history as of 2018
- For the present analysis, 10,837,709 patients less than 2 years old with any claims activity (prescription, diagnosis, procedure, or symptom) between May 2017 and April 2018 were identified
- Patients with a diagnosis of IS before the observation period were excluded: *International Classification of Diseases (ICD)-9*: 345.60, 345.61; *ICD-10*: G40.821-G40.824 (implemented Oct 1, 2015)
- Outcomes for patients meeting inclusion criteria were tracked from May 2017 to November 2018 to identify any subsequent diagnoses of IS

Analysis

- The project utilized input from medical experts and analyses of the IDV database to identify early presentations/diagnoses that are characteristic of IS (**Table 1**)

Table 1. Initial List of Presentations/Diagnoses Thought to Be Predictive of a Later Diagnosis of IS

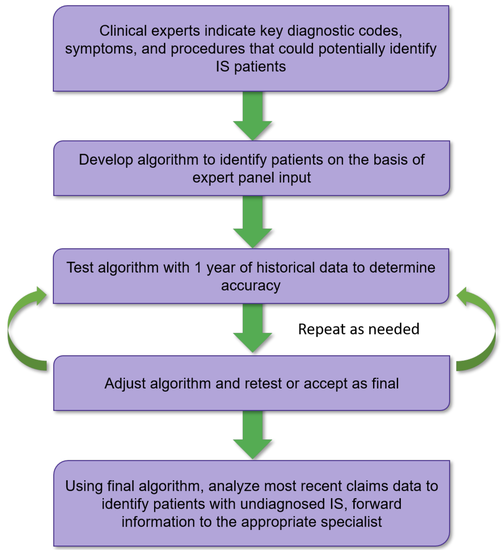
Category	Presentation/Diagnosis
Nervous system	Delays in developmental milestones Hypsarrhythmia† Encephalopathy† Brain Injury
Eye‡	Chorioretinitis Retinal tubers Chorioretinal lacuna defects/ Aicardi syndrome
Skin disorders	Tuberous sclerosis (hypopigmented skin lesions)
Metabolic disorders	Sturge-Weber syndrome Krabbe disease Neurofibromatosis
Other common misdiagnoses	Normal startle reflex Colic Reflux

† Definitive symptoms. ‡ Eye symptom–related diagnostic codes were not seen in the early data investigations.

Methods (cont'd)

- Using the list in **Table 1** as a starting point, clinical, electrographic, radiological, procedural, and medication variables associated with a diagnosis of IS were identified
- These variables were then converted to *ICD-9* and *ICD-10* diagnosis and procedure codes and drug codes
- Supervised machine learning–based algorithms were leveraged to identify combinations of these codes that were most likely to predict a subsequent diagnosis of IS
- Receiver operating characteristics were used to compare models
- The overall methodology is presented in **Figure 1**

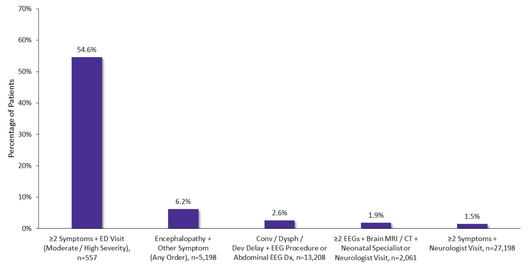
Figure 1. Algorithm Development and Patient Identification



Results

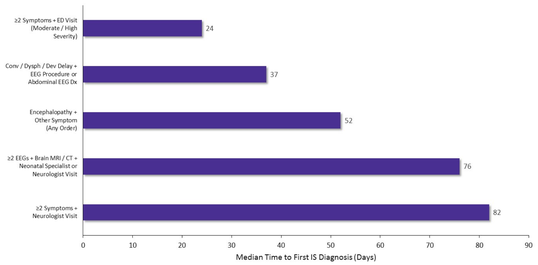
- Five combinations of clinical factors were identified that best predicted a later IS diagnosis **(Figures 2 and 3; Table 2)**
- The most successful of the predictive models identified 557 patients who had a) ≥2 symptoms pertaining to IS (diagnosis, prescription, or procedure claims from ≥2 categories of symptoms from defined lists: seizures, developmental delay, lack of eye contact, lack of muscle tone, etc) plus b) a moderate/high severity emergency department visit **(Figure 2)**
  - Of the 557 patients identified by this combination of clinical factors, 304 (54.6%) were later diagnosed with IS
  - These patients received a diagnostic code for IS within a median of 24 days of the occurrence of the predictive events **(Figure 3)**

Figure 2. Combinations of Clinical Factors Associated With an IS Diagnosis: Percentage of Identified Patients Who Were Later Diagnosed With IS



Abbreviations: CT, computed tomography; Conv, convulsions; Dev Delay, developmental delay; Dysph, dysphagia; Dx, diagnosis; ED, emergency department; EEG, electroencephalogram; IS, infantile spasm; MRI, magnetic resonance imaging.

Figure 3. Combinations of Clinical Factors Associated With an IS Diagnosis: Median Time to First IS Diagnosis



Abbreviations: CT, computed tomography; Conv, convulsions; Dev Delay, developmental delay; Dysph, dysphagia; Dx, diagnosis; ED, emergency department; EEG, electroencephalogram; IS, infantile spasm; MRI, magnetic resonance imaging.

Table 2. Combinations of Clinical Factors Predictive of IS: Positive Predictive Value

Combination of Predictive Factors	Actual IS Patients Identified (n)	Potential IS Patients Identified (n)	Positive Predictive Value (%)
≥2 Symptoms + ED Visit (Moderate / High Severity)	304	557	54.6%
Encephalopathy + Other Symptom (Any Order)	323	5,198	6.2%
Conv / Dysph / Dev Delay + EEG Procedure or Abdominal EEG Dx	345	13,208	2.6%
≥2 EEGs + Brain MRI / CT + Neonatal Specialist or Neurologist Visit	40	2,061	1.9%
≥2 Symptoms + Neurologist Visit	406	27,198	1.5%

Abbreviations: CT, computed tomography; Conv, convulsions; Dev Delay, developmental delay; Dysph, dysphagia; Dx, diagnosis; ED, emergency department; EEG, electroencephalogram; IS, infantile spasm; MRI, magnetic resonance imaging.

Conclusions

- Our analysis identified the combination of a) ≥2 symptoms plus b) a moderate/high severity ED visit as the strongest predictor (highest positive predictive value) for identification of IS in real-world patient care scenarios using our analysis set
- This combination of clinical factors identified IS patients approximately 24 days prior to diagnosis
- These results may support the application of this rule in electronic medical records to flag patients with a high probability of being diagnosed with IS. Additional validation of the algorithm in an electronic medical records database is needed
- Limitations include use of *ICD-10* for evaluation of IS, which may fail to identify all IS cases. Similarly, the rules relied on the accuracy of coding of diagnoses and procedures
- Further research is needed to examine the impact of optimization of early diagnosis and treatment on patient health outcomes

References

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