Critical Review Form
Clinical Prediction or Decision Rule

The Role of Emergent Neuroimaging in Children with New-Onset Afebrile Seizures, *Pediatrics* 2003; 111: 1-5

Objectives: **"To better estimate the prevalence of abnormal neuroimaging, and specifically, clinically significant abnormal neuroimaging" and "to identify clinical variables that could predict which children were at high or low risk for clinically significant abnormal neuroimaging". (p.1)**

Methods:

Retrospective review of 500 consecutive children at the ED of Children's Hospital Boston with new onset afebrile seizures presenting from Oct 1996 thru July 1998. Patients with recurrent seizures, febrile seizures or with primary diagnosis other than seizure were excluded. All charts were reviewed by one investigator, except charts of abnormal imaging patients which were reviewed by three investigators.

From the medical records, the following data was abstracted: age, gender, predisposing conditions, toxic ingestions, seizure length, seizure focality, post-seizure neurological deficits, recent significant closed head injury (as defined by LOC, persistent headache, vomiting, change in mental status or visit to health care provider), temperature, mental status, intubation, admission status, chemistries, urine TOX screens, ECG, and LP. Neuroimaging findings could be CT or MRI and were divided into normal clinically insignificant abnormal, or clinically significant, abnormal. The latter were defined as "those that resulted in a change in the patient's management (tumor or stroke) or prognosis (lissencephaly) and not just a new investigation". (p. 2)

Recursive partitioning analysis was used to identify variables that could be associated with higher or lower risk for clinically significant abnormal neuroimaging. The investigators listed nine *a priori* conditions which they lumped together as a single risk-factor entitled predisposing conditions: sickle cell disease, bleeding disorders, cerebral vascular disease, malignancy, HIV, hemihypertrophy, hydrocephalus, closed head injury, or travel to an area endemic for cysticercosis (Mexico, Central or South America, Africa, Asia, Spain, or Portugal).

Guide		Comments
I.	***Is this a newly derived instrument* (Level IV)?**	
A.	Was validation restricted to the retrospective use of statistical techniques on the original database? (If so, this is a Level IV rule & is not ready for clinical application).	Retrospective derivation with statistical V-fold cross-validation. Therefore, a Level IV CDR not ready for widespread use.
II.	**Has the instrument been validated? (Level II or III). If so, consider the following:**	Not validated on unique patient population.
1a	Were all important predictors included in the derivation process?	Yes. Potential predictor variables entered into the analysis included age, sex, presence of any predisposing conditions, duration of seizure, focality of seizure, report of a focal deficit, number of seizures before evaluation, temperature, mental status, neurologic examination, and need for endotracheal intubation". (p. 2)
1b	Were all important predictors present in significant proportion of the study population?	Uncertain since the authors do not provide a breakdown of the prevalence rates for the above predictors.
1c	Does the rule make clinical sense?	Yes, the rule incorporates three variables readily obtained from the initial history and physical exam.
2	Did validation include prospective studies on several different populations from that used to derive it (II) or was it restricted to a single population (III)?	No prospective validation of this CDR is reported as noted above in IA.
3	*How well did the validation study meet the following criteria?*	
3a	Did the patients represent a wide spectrum of severity of disease?	Yes, these subjects represented 2% of all ED visits during 34-months.
3b	Was there a blinded assessment of the gold standard?	The authors do not describe who read the neuroimaging report or whether that Radiologist was blinded to all clinical data. However, "charts of all patients whose neuroimaging was abnormal were reviewed by 3 authors and any disagreements were resolved by consensus. All abnormal neuroimaging reports (clinically

		insignificant as well as clinically significant) were reviewed by a pediatric neurologist". (p. 2). Again, whether this pediatric neurologist was blinded to other clinical variables is not stated.

3c	Was there an explicit and accurate interpretation of the predictor variables & the actual rule without knowledge of the outcome?	Clinical data were recorded prior to development of the CDR, though not necessarily prior to awareness of imaging results and disposition.
3d	Did the results of the assessment of the variables or of the rule influence the decision to perform the gold standard?	Probably not since "neuroimaging was obtained in 95% (475/500) cases". (p. 2) "The remaining 5% (25/475) had neuroimaging obtained >72 hours after presentation". (p. 2). "Overall, a neuroimaging result or clinical follow-up was available in 98% of the cases. (p. 2)
4	How powerful is the rule (in terms of sensitivity & specificity; likelihood ratios; proportions with alternative outcomes; or relative risks or absolute outcome rates)?	• Among the 2,832 with ICD-9 code of seizure, 500 (18%) had new onset afebrile seizure. Their median age was 46-months with 48% female and 58% were admitted to the hospital. • Normal neuroimaging were reported in 83%, while clinically insignificant results were reported in 9%. • 38/475 (8%, 95% CI 5.7-10.8%) were clinically significant. Of this 8%, 8% (3/38) expired and 13% (5/38) required operative intervention. • Low-risk group (below) included 354 patients (75% of the cohort) and had 1.7% (95% CI 0.6-3.7%) prevalence of clinically significant abnormal neuroimaging compared with 26% rate for the high-risk subset. • Acute operative intervention was required in <1% of population. • Among the 374 normal CT's, 163 (43%) went on to have MRI and six of these cases (3.7%), the MRI showed a clinically significant abnormality.

		• The authors do not report a 2x2 table to calculate diagnostic test properties, but one can construct the following from Fig 1 (p. 3). Significant Neuroimaging / Clinically Insignificant Neuroimaging High-risk by CDR: 32 / 89 Low-risk by CDR: 6 / 348 Online LR calculator yields the following: Sensitivity = 84% Specificity = 80% LR + = 4.13 (95% CI 3.28-5.21) LR - = 0.20 (95% CI 0.09-0.40)
III.	**Has an impact analysis demonstrated change in clinical behavior or patient outcomes as a result of using the instrument? (Level I). If so, consider the following:**	
1	How well did the study guard against bias in terms of differences at the start (concealed randomization, adjustment in analysis) or as the study proceeded (blinding, co-intervention, loss to follow-up)?	No impact analysis was performed and the investigators' inclusion criteria helped avoid *selection bias* present in previous studies.
2	What was the impact on clinician behavior and patient-important outcomes?	As above.

Limitations

1) **Retrospective derivation and cross-validation so not yet ready for widespread implementation.**
2) **Investigators not blinded from clinical data when determining outcomes by neuroimaging review.**
3) **Investigators fail to list the prevalence of candidate predictor variables.**

Bottom Line

If prospectively validated, this CDR offers a simple method to identify a low-risk subset of new onset pediatric seizure patients without a fever in whom expensive neuroimaging could be deferred or avoided to alleviate parental concern and future radiation-risk. Additionally, given the neurologists preference for MRI despite CT-findings, the high-risk subset could preferentially obtain the more definitive MRI first. Future validation will need to evaluate the variables reliability and the overall rules reliability, diagnostic accuracy and validity in various populations before assessing the potential impact the rules use would have on pediatric EM practice.

The Rule