Critical Review Form
Clinical Prediction or Decision Rule

Higher ABCD2 Score Predicts Patients Most Likely to Have True Transient Ischemic Attack, *Stroke* 2008; 49: 3096-3098

Objective: To test the hypothesis that a "widely used risk stratification models may, in part, simply be identifying those patients most likely to have true TIA." (p. 3096)

Method: All patients diagnosed by EP's in one of 16 Kaiser-Permanente hospitals from February 1997 to February 1998 (before TIA-risk stratification CDR's like the California Rule, ABCD, or ABCD^2 were first published) were followed for 90-days after presentation. Strokes were confirmed by two neurologists. When the diagnosis of TIA was considered questionable (as labeled by qualifying adjectives like "possible TIA" or "rule-out TIA"), the charts were reviewed for the current manuscript.

An "expert neurologist" (undefined by this study) blinded to the outcome reviewed the patient charts and determined if the episode was TIA, migraine, syncope, anxiety, seizure, hypertensive encephalopathy or some other diagnosis. ABCD^2 scores were retrospectively calculated and Cochrane-Armitage trend tests were used to assess stroke risk.

Guide		Comments
I.	***Is this a newly derived instrument* (Level IV)?**	No
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).	The ABCD^2 has been previously validated prospectively (Carpenter 2009, Shah 2009).
II.	**Has the instrument been validated? (Level II or III). If so, consider the following:**	

1a	Were all important predictors included in the derivation process?	No, some predictors were not included. The $ABCD^2$ score is a combination of two previous prognostic instruments: California rule and the ABCD. To answer these questions one needs to review the original rule derivation papers. The California rule assessed a large number of cerebrovascular risk factors including, age, gender, ethnicity, DM, HTN, CAD, A. Fib, prior TIA, prior stroke, hyperlipidemia, smoking status, ASA or warfarin use, and TIA findings. TIA findings assessed included symptom duration, weakness, numbness, confusion, vision/speech changes, dizziness, vertigo, gait disturbance, heart rate, blood pressure, murmur, bruit, weakness, numbness, confusion or objective aphasia or dysasthria. (Johnston Table 1 p. 2903) Risk factors not assessed included BMI, coagulopathy history, malignancy, peripheral vascular disease, headache, palpitations, or syncope. The ABCD rule was derived from the Oxfordshire Community Stroke Project and initially evaluated the following risk factors: age, BP, HTN, unilateral weakness, speech disturbance without weakness, symptom duration, DM, gender, angina or MI history, PVD, previous atrial fib and smoking status.
1b	Were all important predictors present in significant proportion of the study population?	No, some of the variables in the derivation trials were rare in deriving the California rule. The prevalence of various risk factors ranged from 3% - 84%. Several risk factors were present in <10% of the cohort including Hispanic, Asian-American, or African-American ethnicity, atrial fibrillation, warfarin use, vertigo, numbness, confusion, gait abnormality, aphasia and dysarthria. The ABCD derivation included far

		fewer variables with predictor prevalences ranging from 4% to 54%. Only 4% had DM and only 13% had speech disturbance with weakness. (Rothwell 2005, table 1 p.31).
1c	Does the rule make clinical sense?	Yes, the elements of the $ABCD^2$ have face validity for predicting increased risk of cerebrovascular disease as opposed to other causes of TIA-like complaints.
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)?	The California and ABCD rules have been validated in distinct populations (Carpenter 2009, Shah 2009), but the $ABCD^2$ had previously only been validated in split sampling technique so it was a level IV.
3	*How well did the validation study meet the following criteria?*	
3a	Did the patients represent a wide spectrum of severity of disease?	Unknown since the authors of the derivation and validation trials, as well as the current manuscript do not detail initial stroke severity using a validated metric like the NIHSS. Instead each trial only reports dichotomous results (stroke vs. no stroke).
3b	Was there a blinded assessment of the gold standard?	Yes, "An expert neurologist, blinded to outcome, reviewed the charts of these patients and determined if the spell was likely to represent a true TIA." (p.3097) In the original California rule derivation trials (the results of which were used in the current manuscript to define stroke or no stroke), "a final stroke diagnosis required independent confirmation by 2 neurologist, who also determined whether the stroke led to hospitalization or was disabling (defined as a modified Rankin score $\geq$ 2)." (p. 2902 Johnston 2000).

3c	Was there an explicit and accurate interpretation of the predictor variables & the actual rule without knowledge of the outcome?	Possibly. "$ABCD^2$ scores were calculated for all patients" based upon chart review by one expert neurologist (p. 3097). However, "Another limitation of this study is that the expert review relied on retrospective examination of the medical record. TIA likelihood judgments may have changed if a neurologist prospectively reviewed each case; however, risk stratification models have been shown to be predictive in cohorts of patients defined in a similar retrospective manner." (p. 3098, Johnston 2007)
3d	Did the results of the assessment of the variables or of the rule influence the decision to perform the gold standard?	No. The gold standard was medical record review by 2 Neurologist which occurred for every patient regardless of California rule score in the original derivation.

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How powerful is the rule (in terms of sensitivity & specificity; likelihood ratios; proportions with alternative outcomes; or relative risks or absolute outcome rates)?

- From 1707 patients with ED-diagnosed TIA, 42% (713) had "questionable TIA" so were further reviewed by the single expert neurologist and 90% (642) were judged to have had a TIA as opposed to an alternative diagnosis.
- The following alternative diagnoses were identified: syncope (22), peripheral vestibulopathy (11), migraine (9), anxiety (9), seizure (5), medication toxicity (5), neuropathy (4), transient global amnesia (2), hypertensive encephalopathy (2), and dementia (2).
- Overall 90-day stroke risk was higher in the TIA group (24%, 95% CI 20-27%) then the not-TIA group (1.4%, 95% CI 0-7.6%) ($p < 0.0001$).

The following distribution of $ABCD^2$ scores were obtained:

$ABCD^2$ score	TIA likely		TIA Unlikely	
	Number	Stroke @ 90d (%)	Number	Stroke @ 90d (%)
0	3	0 (0%)	0	0%
1	11	1 (9%)	8	0 (0%)
2	51	3 (6%)	17	1 (6%)
3	83	7 (8%)	17	0 (0%)
4	167	34 (20%)	15	0 (0%)
5	150	39 (26%)	10	0 (0%)
6	147	55 (37%)	4	0 (0%)
7	30	13 (43%)	0	0 (0%)

- There was no relationship between $ABCD^2$ score and stroke risk in those judged unlikely to have TIA ($p = 0.73$).

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 so no randomization or adjustments were made. Probable selection bias with limited external validity since the original derivation set was primarily insured Caucasians. Furthermore, the $ABCD^2$ has thus far only underwent split set validation so it is still a Level IV clinical decision rule. Also, "the overall rate of 90-day stroke (21%) in the reviewed group was higher than the previously published rate of 10.5% in the entire cohort studied, indicating that the patients reviewed were not a representative sample." (p. 3097)
2	What was the impact on clinician behavior and patient-important outcomes?	No patient-centric outcomes or assessment of $ABCD^2$ impact on clinician behavior was assessed.

Limitations

1) **Incomplete medical record review (p.3097) by a single "expert neurologist" without defining expert or providing any assurances (i.e. subset Kappa analysis) that this expert's labeling of TIA was accurate. In fact, evidence to the contrary does exist (Kraaijeveld 1984, Koudstaal 1989, Castle 2010).**

2) **Retrospective $ABCD^2$ scoring. Skeptical readers have no assurances that busy clinicians (EP's or neurologists) would compute similar scores in the hectic, decision-dense emergency department environment.**

3) **No assessment of the $ABCD^2$ score on stroke recovery of other patient-centric outcomes.**

4) **No discussion of the implications of the current findings on subsequent use of $ABCD^2$ scores in clinical or research environments.**

5) **No assessment of ABCD^2 score relationships with 2-day or 7-day stroke risk.**

Bottom Line

Emergency Physicians in California's Kaiser Permanente system accurately label difficult clinical presentations as TIA (90% accuracy). Among those with true TIA, the ABCD^2 score is generally higher (85% in the 3-6 range) and the score correlates with 90-day stroke risk. In non-TIA patients ABCD^2 scores are generally <4 (59%) and not associated with *any* 90-day stroke risk.