Critical Review Form
Diagnostic Test

HINTS Outperforms ABCD2 to Screen for Stroke in Acute Continuous Vertigo and Dizziness. Acad Emerg Med. 2013 Oct;20(10):986-996.

Objectives: **"to compare the diagnostic accuracy of HINTS and ABCD2 in ACS [acute vestibular syndrome]." (p. 988-989)**

Methods: **This prospective study involved the analysis of data from an ongoing, prospective cross-sectional study conducted at a single academic medical center (OSF Saint Francis Medical Center, Peoria, IL). Patients were enrolled from the emergency department (ED) from 1999-2012. Patients with persistent vertigo lasting at least 1 hour in duration, but less than 1 week were screened. Inclusion required the presence of nystagmus, nausea or vomiting, head motion intolerance, gait imbalance, and at least one stroke risk factor (smoking, hypertension, diabetes, hyperlipidemia, atrial fibrillation, eclampsia, hypercoagulable state, recent cervical trauma, prior stroke, or myocardial infarction). Patients were excluded for a history of recurrent vertigo, resolution of symptoms with canalith repositioning, or an inability to participate in the exam due to lethargy.**

All patients underwent oculomotor and neurologic testing, performed by one of two neuro-ophthalmologists blinded to imaging results, and then neuroimaging (MRI in most cases). The HINTS exam consisted of head impulse testing, assessment of the direction of nystagmus, and testing for ocular skew deviation. New hearing loss was assessed as an indicator of peripheral vertigo, and included in a 4-item HINTS "Plus" tool. An ABCD2 score (Table 1) was calculated for each subject based on recorded data, or by abstraction from the medical records, with a score of 4 or more considered positive. Repeat neuroimaging was obtained in patients with initially normal neuroimaging with clinical signs concerning for a central lesion, or with the development of new neurologic signs during admission.

There were 193 patients eligible for enrollment. Three of these were excluded (two due to a lack of neuroimaging, one due to lack of blood pressure data), leaving 190 subjects in the final analysis. The median age was 61 and 60.5% were men. The percent of men diagnosed with stroke was slightly higher than percent of women (64.3% vs. 52.0%, p = 0.09).

Table 1. The ABCD2 score

Component	Score
Age ≥ 60	+1
Systolic blood pressure ≥ 140 or systolic blood pressure ≥ 90	+1
Clinical features • Unilateral weakness • Speech disturbance without weakness • Any other symptoms	 +2 +1 +0
Duration of symptoms • < 10 minutes • 10-59 minutes • ≥ 60 minutes	 +0 +1 +2
Diabetes	+1

Guide		Comments
I.	**Are the results valid?**	
A.	**Did clinicians face diagnostic uncertainty?**	Yes. Patients with acute vestibular syndrome (AVS) in whom the diagnosis of central vs. peripheral vertigo was uncertain were included in the analysis. This was, however, a moderate to high-risk group of patients with at least one risk factor for stroke.
B.	**Was there a blind comparison with an independent gold standard applied similarly to the treatment group and to the control group? (Confirmation Bias)**	Yes for HINTS exam, no for ABCD2. All patients underwent neuroimaging (97.4% MRI; 4 patients underwent CT scan only). "Examinations were conducted by one of two trained neuroophthalmology study examiners (JCK or JHP) who examined patients prior to neuroimaging or were masked to imaging results." (p. 989). The authors do not mention whether the examiners were blinded to other clinical data: we don't necessarily get accurate data on how HINTS performs in isolation; clinically you would not use HINTS in isolation, but would use results in the context of the clinical picture. Components of the ABCD2 score were abstracted from the chart by an unmasked author.
C.	**Did the results of the test being evaluated influence the decision to perform the gold standard? (Ascertainment Bias)**	Likely no. Per the protocol, all patients included in the study underwent neuroimaging, regardless of HINTS testing results. However, patients were only included in the study if they had at least one stroke risk factor; it is therefore likely that patients with higher ABCD2 score were enrolled in the study, and hence would be more likely to undergo neuroimaging.

<table>
<tr><td>II.</td><td>What are the results?</td><td></td></tr>
<tr><td>A.</td><td>What likelihood ratios were associated with the range of possible test results?</td><td>
<table>
<tr><td colspan="4">Table 1. Diagnostic accuracy of ABCD2 and HINTS for central cause of vertigo (95% CI)</td></tr>
<tr><td></td><td>ABCD2 ≥ 4</td><td>HINTS</td><td>HINTS "Plus"</td></tr>
<tr><td>Sensitivity</td><td>58.1 (49.2-66.5)</td><td>96.8 (92.4-99.0)</td><td>99.2 (96.1-100.0)</td></tr>
<tr><td>Specificity</td><td>60.6 (48.5-71.8)</td><td>98.5 (92.8-99.9)</td><td>97.0 (90.4-99.5)</td></tr>
<tr><td>PPV</td><td>73.5 (63.6-81.9)</td><td>99.2 (95.5-99.9)</td><td>98.4 (94.3-99.8)</td></tr>
<tr><td>NPV</td><td>43.5 (33.2-54.2)</td><td>94.2 (85.8-98.4)</td><td>98.5 (91.7-99.7)</td></tr>
<tr><td>LR+</td><td>1.47 (1.05-2.06)</td><td>63.9 (9.13-446.85)</td><td>32.7 (8.36-128.16)</td></tr>
<tr><td>LR-</td><td>0.69 (0.52-0.92)</td><td>0.03 (0.01-0.09)</td><td>0.01 (0.00-0.06)</td></tr>
<tr><td colspan="4">NPV/PPV and 95% CIs calculated using http://www.medcalc.org/calc/diagnostic_test.php</td></tr>
</table>

The area under the ROC curve for ABCD2 was 0.613 (95% CI 0.531 to 0.695) while the area under the curve for HINTS was 0.995 (95% CI 0.985 to 1.000).</td></tr>
<tr><td>III.</td><td>How can I apply the results to patient care?</td><td></td></tr>
<tr><td>A.</td><td>Will the reproducibility of the test result and its interpretation be satisfactory in my clinical setting?</td><td>Uncertain. The investigators did not assess the reproducibility/interrater reliability of the test with kappa or other values. The HINTS exam is a difficult test, and was performed by neuroopthalmologists in this study. The amount of training necessary for emergency physicians to become proficient with testing has not been evaluated.</td></tr>
<tr><td>B.</td><td>Are the results applicable to the patients in my practice?</td><td>Yes. Patients with vertigo frequently present to the ED. Distinguishing central from peripheral causes of vertigo is clinically difficult, and patients in whom there is clinical concern often undergo neurologic consultation, admission, and advanced neuroimaging (MRI). The ability to differentiate between these two entities by clinical exam would reduce unnecessary testing and admission and reduce the risk of missing potentially dangerous central pathology.</td></tr>
<tr><td>C.</td><td>Will the results change my management strategy?</td><td>No. In the current study, the HINTS exam was performed by neuro-ophthalmologists, who would likely be familiar and comfortable with the components of the oculomotor exam. Further studies will need to address the accuracy and reliability of the HINTS exam in the hands of the emergency physician, will need to assess the</td></tr>
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		extent of training necessary for proficiency with the exam, and should examine the impact of the exam on patient-centered outcomes, such as decreasing unnecessary testing and reducing cases of missed stroke.
D.	**Will patients be better off as a result of the test?**	Uncertain. The diagnostic test characteristics of the HINTS exam are promising, and it seems likely that its use could result in a decrease in the incidence of missed posterior circulation stroke. This is especially true in light of the risk of missed posterior circulation stroke on MRI (Oppenheim 2000, Morita 2011). Further research will need to assess the impact of the test on clinical decision-making and on patient-centered outcomes.

Limitations:

1. **Unclear why the authors chose to compare HINTS to ABCD2, which was derived to determine the risk of future stroke in patients with TIA (Tsivgoulis 2010), not to differentiate those with symptoms due to stroke from those whose symptoms are due to other etiologies.**

2. **The ABCD2 score was calculated using data abstracted from the chart by unblinded data abstractors.**

3. **The authors do not mention whether the examiners were blinded to clinical data, aside from neuroimaging results: we don't necessarily get accurate data on how HINTS performs in isolation; clinically you would not use HINTS in isolation, but would use results in the context of the clinical picture.**

4. **The authors mention using "clinical follow-up" as part of the criteria to diagnose peripheral vertigo, with a minimum of 3 months duration, they do not describe the nature of this follow-up.**

5. **This is a high-risk study population: 59.5% diagnosed with posterior fossa stroke, 65.3% diagnosed with a central etiology for their vertigo. While the prevalence of disease should not affect sensitivity or specificity, there is the possibility of spectrum bias.**

6. **The HINTS exam was performed by neuro-ophthalmologists. The external validity of the study results to application by emergency physicians is unclear.**

7. **The inter-rater reliability of the HINTS exam was not assessed.**

8. **There is the potential for false-negative tests in patients with initially normal MRI whose symptoms did not progress, potentially representing TIAs.**

Bottom Line:

The 3-part oculomotor HINTS exam had excellent diagnostic test characteristics in the study, with a LR+ of 63.9 (95% CI 9.13-446.85) and LR- of 0.03 (95% CI 0.01-0.09) for the diagnosis of central causes of vertigo. While these results are promising, the study was conducted on a high-risk patient population in which the prevalence of central disease was 65.3%. It is unclear if this test would impact the decision to perform further testing or proceed with admission in patients at such high-risk of central pathology. Further research will need to assess the impact of the test on clinical decision-making and on patient-centered outcomes, and assess its use in lower-risk patient populations.