Critical Review Form
Diagnostic Test

HINTS to diagnose stroke in the acute vestibular syndrome: three-step bedside oculomotor examination more sensitive than early MRI diffusion-weighted imaging. Stroke. 2009 Nov;40(11):3504-10.

Objectives: **"to assess the overall sensitivity and specificity of a 3-step bedside oculomotor examination (Head-Impulse, Nystagmus, Test-of-Skew [HINTS]) for differentiating stroke from APV in AVS." (p. 3505)**

Methods: **This prospective, cross-sectional study involved data derived from an ongoing study. Patients were enrolled at a single, urban academic center. Patients with rapid onset of vertigo with associated nausea, vomiting, and gait ataxia (with or without nystagmus) were enrolled primarily from the emergency department (ED). Patients admitted to the hospital for cerebellar infarction were also enrolled. Eligibility required the presence of at least one risk factor for stroke (smoking, hypertension, diabetes, hyperlipidemia, atrial fibrillation, eccampsia, hypercoagulable state, recent cervical trauma, or prior stroke or myocardial infarction). Patients with a prior history of recurrent vertigo were excluded.**

A neuro-ophthalmologist conducted neurological and vestibular testing on all subjects, including evaluation of h-HIT, nystagmus, and skew deviation (HINTS exam). All patients underwent neuroimaging, generally after examination, consisting primarily of MRI with DWI. If performed prior to examination, the neurooptthalmologist was blinded to imaging results. The criterion standard for stroke was considered a positive MRI with diffusion-weighted imaging (DWI). All patients enrolled were admitted to the hospital for observation and serial examination.

Of 121 patients screened, 19 were excluded for a history of recurrent vertigo, and one subject refused enrollment. A total of 101 subjects were enrolled. The mean age was 62 years and 65% were men. In 30% of subjects only one stroke risk factor was present; all other patients had 2 or more stroke risk factors. HINTS exam was performed within 24 hours of symptom onset in the majority (75%) of patients. CT alone was performed in 3 patients, all with unequivocal signs of cerebellar stroke; all other patients had MRI performed. Twenty-five subjects were diagnosed with peripheral vertigo and 76 with a central lesion (69 with ischemic stroke, 4 with hemorrhage, and 2 with demyelinating disease).

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. "All patients underwent neuroimaging, generally after bedside evaluation. If neuroimaging was performed before the study evaluation, the examiner was masked to these results at the time of clinical assessment." (p. 3505). 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. All but 3 patients underwent MRI with DWI; these 3 patients had CT scans showing unequivocal signs of cerebellar stroke.
C.	**Did the results of the test being evaluated influence the decision to perform the gold standard? (Ascertainment Bias)**	No. Per the protocol, all patients included in the study underwent neuroimaging, regardless of HINTS testing results.
II.	**What are the results?**	
A.	**What likelihood ratios were associated with the range of possible test results?**	• All 76 subjects with central pathology had abnormal HINTS testing, while 24 of 25 patients without a central lesion had negative testing. The sensitivity was 100% (95% CI 95.2-100.0*), specificity was 96% (95% CI 79.6-99.3*), PPV was 98.7% (95% CI 93.0-99.8)*, NPV was 100.0 (95% CI 85.6-100.0)*, LR+ was 25 (95% CI 3.66 to 170.59), and LR- was 0.00 (95% CI 0.00 to 0.11). • Eight patients with initially normal MRI underwent repeat imaging 2 to 10 days later due to signs concerning for brainstem pathology, all positive for infarction. Therefore, the sensitivity of initial MRI for stroke was 88%, specificity was 100%, positive LR was infinity, and negative LR was 0.12 (95% CI 0.06-0.22). *Calculated using http://www.medcalc.org/calc/diagnostic_test.php
III.	**How can I apply the**	

	results to patient care?	
A.	**Will the reproducibility of the test result and its interpretation be satisfactory in my clinical setting?**	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.
B.	**Are the results applicable to the patients in my practice?**	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.
C.	**Will the results change my management strategy?**	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 extent of training necessary for proficiency with the exam, and 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. Further research will need to assess the impact of the test on clinical decision-making and on patient-centered outcomes.

Limitations:

1. **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.**

2. **The authors do not mention any patient follow-up.**

3. **This is a high-risk study population: almost 3/4 diagnosed with a central etiology for their vertigo, and 69% diagnosed with posterior fossa stroke. While the prevalence of disease should not affect sensitivity or specificity, there is the possibility of spectrum bias.**

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

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

6. **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 25 (95% CI 3.66 to 170.59), and LR- of 0.00 (95% CI 0.00 to 0.11) for the diagnosis of central causes of vertigo. The sensitivity of initial MRI was only 88%, compared to 100% for the HINTS exam. While these results are promising, the study was conducted on a high-risk patient population in which the prevalence of central disease was ~75%. 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.