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## Missed Stroke in Acute Vertigo and Dizziness: It is Time for Action, not Debate

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Vertigo and dizziness are responsible for an estimated 4.4 million emergency department (ED) visits in the US each year.<sup>1</sup> Benign peripheral vestibular disorders may account for up to 33%<sup>2</sup> (1.5 million), although it is unknown how many of these are specific, readily-diagnosed inner ear conditions, since two-thirds of these are given a symptom-only diagnosis in actual clinical practice.<sup>2</sup> Strokes account for roughly 3–5%<sup>2</sup> of all ED vertigo and dizziness presentations (130,000–220,000), and most of these are acute ischemic strokes in the brainstem, cerebellum, or both. After ruling out general medical causes, ED physicians are tasked with differentiating common, benign peripheral vestibular causes from dangerous central ones (largely stroke). This is a difficult task because vertigo is the most common posterior circulation ischemic stroke symptom, and is frequently unaccompanied by more obvious neurological symptoms.<sup>3,4</sup> The costs of US ED dizziness presentations now exceed \$10 billion per year, largely due to a combination of frequent neuroimaging, obtained in roughly half,<sup>1</sup> and admissions for nearly 20%.<sup>5</sup>

In the current edition of *Annals*, Atzema and colleagues add another major population-based study<sup>6</sup> to the now substantial body of literature on the issue of missed stroke in patients with vertigo or dizziness. Using an elegant research design (retrospective cohort study with propensity-score-matched controls) and a huge population-based regional database, the authors conclude that some patients are missed, but the absolute risk is low (0.18% at 30 days). They assert that, “Managing physicians can be reassured by these findings when discharging a patient they are confident has a diagnosis of peripheral vertigo.” This is in sharp contrast to other authors who point instead to the high relative risks of misdiagnosis and serious risks of harm seen among stroke patients presenting dizziness or vertigo.<sup>7–10</sup> So who is right?

This debate invokes three critically important public health questions: (1) how big a problem is missed stroke in vertigo or dizziness presentations?; (2) are the likely causes of misdiagnosis remediable?; and (3) would making stroke diagnoses earlier help reduce harms from stroke?

### (1) IS THIS A PROBLEM?

Atzema et al.’s conclusion that ED physicians be “reassured” is based on the notion of physician risk tolerance in the ED, where diagnostic uncertainty cannot always be completely resolved, since there are tradeoffs related to workflow inefficiencies, costs of care, and patient harms from unnecessary testing.<sup>5</sup> A commonly cited threshold for acceptable risk of missing a life-threatening disease is <1%.<sup>11</sup> Several studies suggest that

the risk of missing stroke in current clinical practice among patients with a chief symptom of vertigo or dizziness is <1%.<sup>6,12,13</sup> By this logic, the missed stroke problem is not a big one, and the authors' conclusion seems reasonable. But the foundations of this argument are not sound.

First, the public health relevance of the problem is proportional to the absolute number of patients affected, not the fraction of ED vertigo or dizziness visits they represent. Of the roughly 1.5 million ED patients given benign vestibular diagnoses and discharged, 0.18–0.70%<sup>6,12–14</sup> are hospitalized for stroke in the next 30 days (Table). This translates to roughly 2,600–10,500 patients each year in the US who are told they have a benign cause and then suffer serious harms (e.g., major stroke with disability after minor stroke) within a month. There could be many more than this, however, since the estimate does not include admitted patients (e.g., misdiagnosed as labyrinthitis or gastroenteritis and admitted to a medical service for fluid treatment, with resulting delays in stroke treatment<sup>7</sup> or admitted to the hospital and discharged with “benign” dizziness only to be readmitted later<sup>15</sup>), nor those who suffer preventable strokes later (after 30 days) or who die after discharge.<sup>10</sup> An alternate estimate is derived from the risks of adverse events among those misdiagnosed. Of the 130,000–220,000 strokes and TIAs presenting vestibular symptoms to US EDs each year, an estimated 45,000–75,000 are missed.<sup>16</sup> Based on disproportionately high adverse event rates among those missed,<sup>7</sup> it is possible there might be 15,000–25,000 stroke patients presenting acute vertigo or dizziness who suffer disability or death.<sup>16</sup>

Second, the clinical relevance of the problem depends not on whether the absolute risk of missed stroke is low, but on whether we could reasonably do better than our current performance—and there is a growing body of evidence that we could.<sup>16</sup> The relative risk of missed stroke in ED vertigo and dizziness is alarmingly high. An administrative data study of nearly 200,000 inpatient stroke admissions from nine US states found vertigo and dizziness are the symptoms most tightly linked to missed ischemic stroke.<sup>10</sup> A population-based cross sectional study (n=1666) found that 35% of ED transient ischemic attack (TIA) or stroke patients (n=16/46) presenting vestibular symptoms were initially misdiagnosed.<sup>17</sup> Another population-based registry found that 90% of isolated posterior circulation TIAs (n=23/45 presenting isolated vertigo) were initially missed at first medical contact.<sup>3</sup> The present study found that patients discharged from the ED with peripheral vestibular diagnoses are at 50-fold increased risk of stroke in the 7 days post-discharge relative to propensity score-matched controls.<sup>6</sup> These numbers suggest that our current diagnostic practices are largely ineffective<sup>18</sup> and there is substantial room for improvement.<sup>16,19</sup>

Finally, even if these missed strokes were not considered a major public health problem, the estimated \$1 billion per year we waste on unnecessary neuroimaging and inpatient admissions looking for strokes in ED patients with clear peripheral vestibular disorders should be worthy of societal attention.<sup>5,20</sup> If fixing ED diagnostic practices could save \$1 billion per year, do we really need to argue about whether the numbers of patients for whom we could prevent serious harms is closer to 5,000 or 25,000 per year?

## (2) CAN WE FIX IT?

Atzema et al. do not propose specific solutions to the problem of stroke misdiagnosis in vertigo, but they do suggest that, “a neurological examination and provocative testing, is considered sufficient to rule out central causes of vertigo.” It would be wonderful to think that a general neurological exam could effectively identify these missed stroke patients, but current best evidence suggests otherwise.

Strokes causing vertigo or dizziness are mostly located in the lateral brainstem and cerebellum.<sup>21</sup> As a result, primary motor and sensory pathways are usually intact. The lack of hemi-motor involvement is likely one of the major reasons these ‘vestibular strokes’ are not recognized in the ED. Two studies from the same ED population-based sample found that strokes are missed initially in 35% of those presenting vestibular symptoms<sup>17</sup> vs. 4% of those presenting motor symptoms.<sup>22</sup> Neurologic exams in stroke patients presenting vertigo or dizziness are non-focal in >80%, even when performed by an experienced neurology-trained neuro-otologist, and even when the highest-risk-for-stroke population is studied.<sup>23</sup> Furthermore, even when focal signs occur, they are often subtle, especially for frontline clinicians. The most common non-eye movement focal signs are Horner’s syndrome, facial hemianalgesia with preserved light touch sensation, and hoarseness.<sup>23</sup> None of these findings would normally be detected by a typical ED physician, since they require neurologic exam techniques that are rarely used (testing pupil dilation in darkness, temperature/pain sensation on the face, or vocal cord function by phonation).

Some might suggest more imaging. Certainly head CT scans are of little use in this scenario, given their low sensitivity for acute stroke, particularly in the posterior cranial fossa.<sup>16,24</sup> In fact, the authors of the present study recently published a paper demonstrating that, among those discharged with a peripheral vestibular disorder, those who underwent CT during the ED visit (with a presumptively negative result) were 2.3-times *more* likely to suffer a stroke in the next 30 days than those who received no CT at all.<sup>25</sup> This suggests ED physicians are correctly risk-stratifying patients, but being falsely reassured by a normal head CT. MRI is better than CT, but, even with diffusion-weighted imaging (DWI) misses roughly 20% of acute posterior fossa infarctions <24 hours from symptom onset.<sup>24</sup> Furthermore, MRI is not always available acutely, and its indiscriminate use in vertigo or dizziness patients as a stroke ‘rule out’ tool would increase annual costs of care by more than a billion dollars, given that it is presently used in <3%.<sup>1</sup>

Fortunately, effective bedside methods have been developed to identify patients with stroke. Classifying vertigo or dizziness by timing (episodic or continuous) and trigger (positional or not), rather than type (vertigo vs. lightheadedness vs. unsteadiness, etc.), allows for effective clinical identification of both high-risk-for-stroke and low-risk-for-stroke populations.<sup>26</sup> Those with episodic, positional vestibular symptoms lasting seconds almost always have benign paroxysmal positional vertigo (BPPV). This can be confirmed by careful examination of positional nystagmus and then treated by canalith repositioning. Those with episodic, spontaneous symptoms lasting hours mostly have vestibular migraine, Menière’s disease, or TIA. Total illness duration and vascular risk factors can usually differentiate these diseases.<sup>26</sup> Those with acute, continuous vestibular symptoms, nausea/

vomiting, intolerance of head motion, and gait unsteadiness lasting days (the ‘acute vestibular syndrome’) almost always have either vestibular neuritis or a dangerous central mimic, usually ischemic stroke. Assessing three vestibular eye movements (H.I.N.T.S. – **H**ead **I**mpulse test of the vestibulo-ocular reflex, **N**ystagmus in different fields of gaze, and **T**est for **S**kew deviation by alternate cover) distinguishes peripheral from central causes of the acute vestibular syndrome with greater accuracy than even MRI-DWI.<sup>23,27,28</sup> Video-oculography technologies may make these specialized examinations routinely available to frontline clinicians.<sup>16</sup>

### (3) WILL FIXING IT MATTER?

In the Atzema et al. study, the primary outcome is inpatient stroke admission after a treat and release discharge from the ED.<sup>6</sup> This outcome is not a good surrogate measure of stroke misdiagnosis, per se, since fewer than 15% of patients suffering TIA or minor stroke go on to major stroke within 30 days.<sup>29</sup> It is, however, a reasonable surrogate marker of important short-term harms from missed stroke, since presumably the patient would not return for care after discharge unless their symptoms or signs had progressed, rather than improving spontaneously. These adverse events disproportionately occur in the first week after discharge,<sup>6,10,12–14</sup> as with major stroke following TIA or minor stroke of all types.<sup>29</sup>

The health impact of increasing early diagnosis of vertebrobasilar strokes is unknown. Small, potentially-biased studies have suggested a very high risk of permanent morbidity (33%) or mortality (40%) among those whose posterior fossa strokes were initially missed.<sup>7</sup> These estimates are probably too high, but large studies have shown that one third of diagnostic errors, in general, lead to disability or death.<sup>30</sup> Misdiagnosis-related harms for missed stroke accrue from missed opportunities for acute thrombolysis,<sup>9</sup> early secondary prevention,<sup>31</sup> and surgical treatment of stroke complications from malignant edema.<sup>32</sup> Thus, early diagnosis with prompt, correct management could prevent disability or death for thousands.

If more accurate diagnosis of stroke vs. peripheral vestibular disorders could be accomplished quickly and inexpensively at the bedside, this would represent a positive change in care for patients with acute vertigo and dizziness. It could help correctly diagnose ~1 million previously misdiagnosed peripheral vestibular patients, decrease missed stroke for tens of thousands, and save \$1 billion per year. Even if decreasing missed strokes had minimal impact on harms, this would still be a major healthcare ‘win.’ Conclusions

## Conclusions

For some time, groups have been studying and debating the relevance of improved stroke diagnosis in acute vertigo and dizziness. Aztema and colleagues have added another rigorous study that coheres well with prior work indicating a subset of cerebrovascular patients are clearly missed and return soon thereafter with strokes severe enough to require admission. Although the absolute risk of missed stroke in vertigo or dizziness presentations is low, the relative risk is very high. These initial ED misdiagnoses constitute a major public health problem, with perhaps 45,000–75,000 missed cerebrovascular events, thousands of

whom may suffer permanent disability or death as a result. Improved diagnosis might be accomplished through effective dissemination of special eye movement exam techniques not well known to frontline clinicians.<sup>33</sup> ED physicians are aware of these issues and rate vertigo a top priority for developing new diagnostic methods.<sup>34</sup> The time for debate has passed. It is now time for action.

Future studies should focus primarily on solving this well-described problem, rather than clarifying its nature. An NIH-sponsored, phase II clinical trial of a novel diagnostic strategy based on quantitative portable video-oculography is currently underway (AVERT, Acute Video-oculography for Vertigo in Emergency Rooms for Rapid Triage; [ClinicalTrials.gov Identifier: NCT02483429](https://clinicaltrials.gov/ct2/show/study/NCT02483429)). Educational and other approaches to improving diagnosis should be studied prospectively for their real-world clinical impact. Large, pragmatic trials and dissemination/implementation studies should follow to translate efficacious interventions into routine frontline clinical practice. Clever use of administrative data similar to that performed by Atzema and colleagues may be necessary to assess outcomes of large-scale studies.

## REFERENCES

1. Saber Tehrani AS, Coughlan D, Hsieh YH, Mantokoudis G, Korley FK, Kerber KA, Frick KD, Newman-Toker DE. Rising annual costs of dizziness presentations to U.S. emergency departments. *Academic emergency medicine : official journal of the Society for Academic Emergency Medicine*. 2013;20(7):689–96. [PubMed: 23859582]
2. Newman-Toker DE, Hsieh YH, Camargo CA Jr., Pelletier AJ, Butchy GT, Edlow JA. Spectrum of dizziness visits to US emergency departments: cross-sectional analysis from a nationally representative sample. *Mayo Clin Proc*. 2008;83(7):765–75. [PubMed: 18613993]
3. Paul NL, Simoni M, Rothwell PM. Transient isolated brainstem symptoms preceding posterior circulation stroke: a population-based study. *Lancet Neurology*. 2013;12(1):65–71. [PubMed: 23206553]
4. Tarnutzer AA, Berkowitz AL, Robinson KA, Hsieh YH, Newman-Toker DE. Does my dizzy patient have a stroke? A systematic review of bedside diagnosis in acute vestibular syndrome. *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne*. 2011;183(9):E571–92. PMID: 3114934.
5. Newman-Toker DE, McDonald KM, Meltzer DO. How much diagnostic safety can we afford, and how should we decide? A health economics perspective. *BMJ Qual Saf*. 2013;22 Suppl 2:ii11–ii20.
6. Atzema CL, Grewal K, Lu H, Kapral MK, Kulkarni G, Austin PC. Outcomes among patients discharged from the emergency department with a diagnosis of peripheral vertigo. *Annals of Neurology*. 2015.
7. Savitz SI, Caplan LR, Edlow JA. Pitfalls in the diagnosis of cerebellar infarction. *Acad Emerg Med*. 2007;14(1):63–8. [PubMed: 17200515]
8. Edlow JA, Newman-Toker DE, Savitz SI. Diagnosis and initial management of cerebellar infarction. *Lancet Neurol*. 2008;7(10):951–64. [PubMed: 18848314]
9. Kuruvilla A, Bhattacharya P, Rajamani K, Chaturvedi S. Factors associated with misdiagnosis of acute stroke in young adults. *Journal of stroke and cerebrovascular diseases : the official journal of National Stroke Association*. 2011;20(6):523–7. [PubMed: 20719534]
10. Newman-Toker DE, Moy E, Valente E, Coffey R, Hines A. Missed diagnosis of stroke in the emergency department: a cross-sectional analysis of a large population-based sample. *Diagnosis*. 2014;1(2):155–66. [PubMed: 28344918]
11. Pines JM, Szyld D. Risk tolerance for the exclusion of potentially life-threatening diseases in the ED. *The American journal of emergency medicine*. 2007;25(5):540–4. [PubMed: 17543658]

12. Kim AS, Fullerton HJ, Johnston SC. Risk of vascular events in emergency department patients discharged home with diagnosis of dizziness or vertigo. *Ann Emerg Med.* 2011;57(1):34–41. [PubMed: 20855127]
13. Kerber KA, Zahuranec DB, Brown DL, Meurer WJ, Burke JF, Smith MA, Lisabeth LD, Fendrick AM, McLaughlin T, Morgenstern LB. Stroke Risk After Non-Stroke ED Dizziness Presentations: A Population-Based Cohort Study. *Annals of neurology.* 2014.
14. Lee CC, Ho HC, Su YC, Chiu BC, Lee YD, Chou P, Chien SH, Huang YS. Increased risk of vascular events in emergency room patients discharged home with diagnosis of dizziness or vertigo: a 3-year follow-up study. *PLoS One.* 2012;7(4):e35923. PMCID: 3338765. [PubMed: 22558272]
15. Lee CC, Su YC, Ho HC, Hung SK, Lee MS, Chou P, Huang YS. Risk of stroke in patients hospitalized for isolated vertigo: a four-year follow-up study. *Stroke.* 2011;42(1):48–52. [PubMed: 21127296]
16. Newman-Toker DE, Curthoys IS, Halmagyi GM. Diagnosing Stroke in Acute Vertigo: The HINTS Family of Eye Movement Tests and the Future of the “Eye ECG”. *Semin Neurol.* 2015 (in press).
17. Kerber KA, Brown DL, Lisabeth LD, Smith MA, Morgenstern LB. Stroke among patients with dizziness, vertigo, and imbalance in the emergency department: a population-based study. *Stroke.* 2006;37(10):2484–7. PMCID: 1779945. [PubMed: 16946161]
18. Kerber KA, Newman-Toker DE. Misdiagnosing Dizzy Patients: Common Pitfalls in Clinical Practice. *Neurologic clinics.* 2015;33(3):565–75. [PubMed: 26231272]
19. Kerber KA. Benign paroxysmal positional vertigo: opportunities squandered. *Annals of the New York Academy of Sciences.* 2015.
20. Cremer PD, Migliaccio AA, Pohl DV, Curthoys IS, Davies L, Yavor RA, Halmagyi GM. Posterior semicircular canal nystagmus is conjugate and its axis is parallel to that of the canal. *Neurology.* 2000;54(10):2016–20. [PubMed: 10822450]
21. Saber Tehrani AS, Kattah JC, Mantokoudis G, Pula JH, Nair D, Blitz A, Ying S, Hanley DF, Zee DS, Newman-Toker DE. Small strokes causing severe vertigo: frequency of false-negative MRIs and nonlacunar mechanisms. *Neurology.* 2014;83(2):169–73. PMCID: 4117176. [PubMed: 24920847]
22. Morgenstern LB, Lisabeth LD, Mecozi AC, Smith MA, Longwell PJ, McFarling DA, Risser JM. A population-based study of acute stroke and TIA diagnosis. *Neurology.* 2004;62(6):895–900. [PubMed: 15037689]
23. Kattah JC, Talkad AV, Wang DZ, Hsieh YH, Newman-Toker DE. HINTS to diagnose stroke in the acute vestibular syndrome: three-step bedside oculomotor examination more sensitive than early MRI diffusion-weighted imaging. *Stroke.* 2009;40(11):3504–10. [PubMed: 19762709]
24. Newman-Toker DE, Della Santina CC, Blitz A. Neurologic syndromes of the adult: when and how to image vertigo and hearing loss. *Handbook of Neuroimaging.* 2015 (in press).
25. Grewal K, Austin PC, Kapral MK, Lu H, Atzema CL. Missed Strokes Using Computed Tomography Imaging in Patients With Vertigo: Population-Based Cohort Study. *Stroke; a journal of cerebral circulation.* 2014.
26. Newman-Toker DE, Edlow JA. TiTrATE: A Novel, Evidence-Based Approach to Diagnosing Acute Dizziness and Vertigo. *Neurologic clinics.* 2015;33(3):577–99. PMCID: 4522574. [PubMed: 26231273]
27. Newman-Toker DE, Kerber KA, Hsieh YH, Pula JH, Omron R, Saber Tehrani AS, Mantokoudis G, Hanley DF, Zee DS, Kattah JC. HINTS outperforms ABCD2 to screen for stroke in acute continuous vertigo and dizziness. *Academic emergency medicine : official journal of the Society for Academic Emergency Medicine.* 2013;20(10):986–96. [PubMed: 24127701]
28. Cohn B Can Bedside Oculomotor (HINTS) Testing Differentiate Central From Peripheral Causes of Vertigo? *Annals of emergency medicine.* 2014.
29. Rothwell PM, Buchan A, Johnston SC. Recent advances in management of transient ischaemic attacks and minor ischaemic strokes. *Lancet Neurol.* 2006;5(4):323–31. [PubMed: 16545749]
30. Singh H, Giardina TD, Meyer AN, Forjuoh SN, Reis MD, Thomas EJ. Types and origins of diagnostic errors in primary care settings. *JAMA Internal Medicine.* 2013;173(6):418–25. [PubMed: 23440149]

31. Gulli G, Khan S, Markus HS. Vertebrobasilar stenosis predicts high early recurrent stroke risk in posterior circulation stroke and TIA. *Stroke*. 2009;40(8):2732–7. [PubMed: 19478210]
32. Wijdicks EF, Sheth KN, Carter BS, Greer DM, Kasner SE, Kimberly WT, Schwab S, Smith EE, Tamargo RJ, Wintermark M. Recommendations for the management of cerebral and cerebellar infarction with swelling: a statement for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke; a journal of cerebral circulation*. 2014;45(4):1222–38.
33. Kerber KA, Morgenstern LB, Meurer WJ, McLaughlin T, Hall PA, Forman J, Fendrick AM, Newman-Toker DE. Nystagmus assessments documented by emergency physicians in acute dizziness presentations: a target for decision support? *Acad Emerg Med*. 2011;18(6):619–26. PMID: 3117268. [PubMed: 21676060]
34. Eagles D, Stiell IG, Clement CM, Brehaut J, Kelly AM, Mason S, Kellermann A, Perry JJ. International survey of emergency physicians' priorities for clinical decision rules. *Academic emergency medicine : official journal of the Society for Academic Emergency Medicine*. 2008;15(2):177–82. [PubMed: 18275448]

**Table.**

Incidence of stroke following a “benign” vertigo or dizziness discharge from the ED in large, population-based studies

Study	ED Discharge Population (n)	Study Design (Case Capture)	Cumulative Incidence of Stroke (%)				
			7 d	30 d	90 d	180 d	365 d
Atzema, 2015 <sup>6</sup>	Age 18; final ICD-10 peripheral vestibular diagnosis (excludes ‘symptom-only’ codes for vertigo or dizziness) (n=41,794)	Retrospective, population-based cohort study in Ontario, CA (administrative database search for inpatient stroke admission)	0.14 (50) <sup>*</sup>	0.18 (9.3) <sup>*</sup>	0.25 (6.1) <sup>*</sup>	-	0.41 (2.5) <sup>*</sup>
Kerber, 2014 <sup>13</sup>	Age 45; vestibular presenting symptom or disease (vertigo, dizziness, BPPV, vestibular neuritis, or similar listed in ‘top 3’ ED complaints) (n=1,245)	Ambispective, population-based cohort study (active and passive surveillance with clinical record-level data abstraction; stroke revisit to ED or inpatient)	0.48	0.56	0.56	0.73	1.42
Kim, 2011 <sup>12</sup>	Age 18; final ICD-9-CM peripheral <sup>‡</sup> vestibular diagnosis or symptom-only vestibular diagnosis (vertigo or dizziness) (n=31,159)	Retrospective, population-based cohort study in California, USA (administrative database search for inpatient stroke admission)	0.20 <sup>‡</sup>	0.30 <sup>‡</sup>	0.45 <sup>‡</sup>	0.63	-
Lee, 2012 <sup>14</sup>	Age 18; final ICD-9-CM peripheral <sup>‡</sup> vestibular diagnosis or symptom-only vestibular diagnosis (vertigo or dizziness) (n=1,118)	Retrospective, population-based cohort study in Taiwan (administrative database search for inpatient stroke admission)	0.50 <sup>§</sup>	0.70 <sup>§</sup>	0.80 <sup>§</sup>	1.0	1.8 (2.1) <sup>°</sup>

\* Relative risk of stroke admission after discharge when compared to propensity score-matched renal colic discharges.

<sup>‡</sup> Also included one infrequently-used diagnosis code for “vertigo of central origin” (ICD-9 386.2).

<sup>‡</sup> Values not directly reported in Kim et al. Estimate here is a graphical approximation based on manuscript Figure 1.

<sup>§</sup> Values not directly reported in Lee et al. Estimate here is a graphical approximation based on manuscript Figure 2a.

<sup>°</sup> The study by Lee et al. also reported cumulative incidence at 2 years (2.7%) and 3 years (3.3%). The hazard ratio for dizziness and vertigo patients compared to those without was 2.1 in the first year and 1.1 between the second and third years.