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ORIGINAL RESEARCH

Cost-Effectiveness of Advanced Neuroimaging for Transient and Minor Neurological Events in the Emergency Department

Ava L. Liberman, MD; Hui Zhang, PhD; Sara K. Rostanski, MD; Natalie T. Cheng, MD; Charles C. Esenwa, MD, MS; Neil Haranhalli, MD; Puneet Singh, MD; Daniel L. Labovitz, MD, MS; Richard B. Lipton, MD; Shyam Prabhakaran, MD, MS

BACKGROUND: Accurate diagnosis of patients with transient or minor neurological events can be challenging. Recent studies suggest that advanced neuroimaging can improve diagnostic accuracy in low-risk patients with transient or minor neurological symptoms, but a cost-effective emergency department diagnostic evaluation strategy remains uncertain.

METHODS AND RESULTS: We constructed a decision-analytic model to evaluate 2 diagnostic evaluation strategies for patients with low-risk transient or minor neurological symptoms: (1) obtain advanced neuroimaging (magnetic resonance imaging brain and magnetic resonance angiography head and neck) on every patient or (2) current emergency department standard-of-care clinical evaluation with basic neuroimaging. Main probability variables were: proportion of patients with true ischemic events, strategy specificity and sensitivity, and recurrent stroke rate. Direct healthcare costs were included. We calculated incremental cost-effectiveness ratios, conducted sensitivity analyses, and evaluated various diagnostic test parameters primarily using a 1-year time horizon. Cost-effectiveness standards would be met if the incremental cost-effectiveness ratio was less than willingness to pay. We defined willingness to pay as $100 000 US dollars per quality-adjusted life year. Our primary and sensitivity analyses found that the advanced neuroimaging strategy was more cost-effective than emergency department standard of care. The incremental effectiveness of the advanced neuroimaging strategy was slightly less than the standard-of-care strategy, but the standard-of-care strategy was more costly. Potentially superior diagnostic approaches to the modeled advanced neuroimaging strategy would have to be >92% specific, >70% sensitive, and cost less than or equal to standard-of-care strategy's cost.

CONCLUSIONS: Obtaining advanced neuroimaging on emergency department patient with low-risk transient or minor neurological symptoms was the more cost-effective strategy in our model.

Key Words: cost-effectiveness ■ diagnosis ■ emergency department ■ ischemic stroke ■ transient ischemic attack

Improving diagnostic accuracy for patients with nonspecific neurological symptoms who present emergently is increasingly recognized as an important patient safety goal.[1,2] Identifying ischemic events among patients with transient or minor neurological symptoms can be challenging,[3-5] even for vascular neurologists.[6] However, accurate and timely diagnosis of minor stroke and transient ischemic attack (TIA) is essential for initiation of treatments that can significantly reduce subsequent stroke events,[7] particularly within 24 hours of symptom onset.[8,9]

Early advanced neuroimaging can aide in detecting ischemic events among patients with transient or minor neurological complaints.[10,11] Evidence of

Correspondence to: Ava L. Liberman, MD, Department of Neurology, Albert Einstein College of Medicine, Montefiore Medical Center, 3316 Rochambeau Ave, Fourth Floor, Bronx, NY 10467. E-mail: avliberm@montefiore.org

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CLINICAL PERSPECTIVE

What Is New?

- Cost-effective strategies to evaluate patients who present to emergency departments with acute low-risk transient and minor neurological symptoms are needed.
- Using a decision-analytic model based on recent clinical studies, we found that the diagnostic evaluation strategy of obtaining advanced neuroimaging (magnetic resonance imaging brain and angiography) on emergency department patients with low-risk transient and minor neurological symptoms was more cost-effective than the traditional diagnostic evaluation strategy of basic neuroimaging (computed tomography) and clinical judgment.
- Given the higher specificity and lower sensitivity of the advanced neuroimaging approach, our results imply that the costs of admitting more false-positive patients outweighs the costs of discharging some false-negative patients.

What Are the Clinical Implications?

- Our findings suggest that advanced neuroimaging protocols should be incorporated and studied in real-world diagnostic evaluation of patients with minor or transient neurological symptoms.

Nonstandard Abbreviations and Acronyms

ICER	incremental cost-effectiveness ratio

ischemia on brain diffusion-weighted magnetic resonance imaging (MRI) scans or evidence of a relevant arterial occlusion or stenosis on neurovascular imaging is a useful predictor of recurrent stroke.[12-14] In the DOUBT (Diagnosis of Uncertain-Origin Benign Transient Neurological Symptoms) prospective cohort study, brain MRI results led to a change in final diagnosis in 30% of adult patients with presumed low-risk transient or minor neurological events based on a standard clinical evaluation.[12] It is not known if the improved diagnostic accuracy derived from advanced neuroimaging in this subset of patients outweighs the cost of imaging itself and tips the scales to support changes in current diagnostic paradigms in the emergency setting.

We therefore developed a decision-analytic model to identify the most cost-effective strategy for a hospital's emergency department (ED) to adopt when determining which adult patients who present with presumed low-risk transient or minor neurological symptoms can be discharged directly to home rather than admitted to the hospital. We compare the diagnostic assessment strategy of obtaining advanced neuroimaging (brain MRI and magnetic resonance angiography [MRA]) for all patients who present with low-risk transient and minor neurological symptoms versus current ED practice (standard of care) in the United States. We also explored different test performance parameters that would be required to diagnose TIA or minor stroke among patients with low-risk symptoms to further inform the development of future diagnostic evaluation tools.

METHODS

Target Population

We designed our decision-analytical model for groups of adults presenting to a hospital's ED with any of the presumed low-risk symptoms included in the DOUBT study: a transient focal neurologic event that included either nonmotor or nonspeech symptoms of any duration, a transient focal neurological event that included motor or speech symptoms of short duration (≤5 minutes), or a National Institutes of Health Stroke Scale score ≤3 if symptoms persist.[12] All included patients had nondisabling symptoms or signs and, unlike other patients with minor stroke in whom rapid thrombolysis for disabling symptoms is indicated,[15] our study patients were not candidates for acute ischemic stroke interventions.[16]

In our primary analysis, we assumed that our study cohort of patients arriving to the ED were identical to patients included in the DOUBT study in terms of their clinical characteristics (median age, 63 years; nearly 50% with a history of hypertension; low rates of other cerebrovascular risk factors; and a normal initial neurological examination in 72% of patients) as well as cohort size (n=1028 patients).[12] In sensitivity analyses described below, we accounted for alternative cohorts of ED patients presenting with any of the aforementioned presumed low-risk symptoms who differ from the DOUBT study cohort by varying the probability that their presenting symptoms were attributable to minor stroke or TIA.[17,18]

Comparators

We modeled 2 ED-based diagnostic evaluation strategies to determine which patients with minor or transient neurological symptoms warranted hospitalization versus discharge to home. The 2 strategies were: (1) obtain advanced neuroimaging (MRI brain and MRA head and neck) in an unselected manner on all patients with presumed low-risk and transient neurological symptoms or (2) current ED

standard-of-care practice using a mix of providers' clinical judgment, which could include use of validated decision tools, and basic neuroimaging (noncontrast head computed tomography [CT]). We stipulated that, in the advanced neuroimaging strategy arm, only when either diffusion-weighted imaging sequence on MRI brain showed infarction or MRA showed a >50% stenosis or occlusion in a relevant vessel is the patient admitted. We also stipulated that, in the standard-of-care arm, whenever an ED provider suspected a patient has an ischemic event, the patient is admitted to the hospital. To determine the accuracy of identifying an ischemic event in the ED in the current practice strategy, we extrapolated from differences in predicted versus true ischemia reported in the DOUBT study (Data S1).[12]

Model Construction

We used TreeAge Pro (2019, R2. TreeAge Software, Williamstown, MA) to construct a decision-analytic model. The decision node was the 2 diagnostic evaluation strategies: advanced neuroimaging or ED standard of care. If an ischemic event was diagnosed using the chosen diagnostic evaluation strategy, patients were admitted to the hospital. If an ischemic event was not diagnosed using the chosen evaluation strategy, patients were discharged from the ED. If a patient's presenting symptoms were truly attributable to an ischemic event and he/she was hospitalized (true positive), then he/she could have 1 of 4 dispositional states after his/her hospitalization: discharge to home, discharge to acute inpatient rehabilitation, discharge to subacute rehabilitation, or death. If a patient's presenting symptoms were in fact not attributable to an ischemic event but he/she was admitted from the ED (false positive), then the patient was discharged to home following his/her index hospitalization. Patients whose presenting symptoms were not attributable to a true ischemic event and were appropriately discharged from the ED simply went home (true negative). Finally, patients whose presenting symptoms were truly ischemic and were erroneously discharged from the ED (false negative) could either have no subsequent ischemic events or experience a recurrent stroke. After a recurrent stroke, all patients were hospitalized, resulting in 1 of 4 dispositional states: discharge to home, discharge to acute inpatient rehabilitation, discharge to subacute rehabilitation, or death (Figure 1).

The main probability variables in our model were: (1) the proportion of true ischemic events (TIA or ischemic stroke) among patients with low-risk transient or minor symptoms,[12,17,18] (2) the specificity and sensitivity of each diagnostic evaluation strategy,[12,19,20] and (3) recurrent stroke rate after false-negative TIA or minor stroke.[21] We used Bayes' formula to calculate the negative and positive posttest variables included in our model (Table 1).[22] We calculated the sensitivity and specificity of the advanced imaging strategy from a study of patients admitted for probable or possible TIA as well as a study of ED patients with possible TIA (Data S1).[19,20]

Model end nodes were defined on the basis of expected clinical outcome after minor ischemic stroke or TIA[23] and expected clinical outcomes after any ischemic stroke (Table 1).[24] Previously published data were used to estimate quality-adjusted life years (QALYs) based on modified Rankin Scale score corresponding to hospital discharge disposition (Table 2).[25] We used 1 year from the index ED visit as our primary time horizon for 2 reasons. First, robust empirical data on long-term costs and long-term functional outcomes among patients who present for evaluation of transient or minor events are lacking.[14] Second, a 1-year time horizon is in keeping with hospitals' as well as managed care plans' focus on inpatient costs.[26]

Study approval was not sought from an ethical standards committee on human experimentation as no new human data were obtained or used. We followed the Consolidated Health Economic Evaluation Reporting Standards statement guidelines.[27]

Model Assumptions

To improve the generalizability of our model, we assumed that patients accurately diagnosed and admitted to the hospital from the ED at their index presentation did not have a recurrent cerebrovascular event within the study time frame. This is consistent with results from the DOUBT study, which found a <1% risk of recurrence among treated patients with minor stroke and TIA at 1 year.[12] The proportion of reported disability after minor stroke or TIA that is attributable to deficits from the index event as opposed to preexisting comorbidities, interval stroke recurrence, or subsequent poststroke medical complications in a nonclinical trial population is uncertain.[28] Therefore, to estimate clinical outcomes in our study among those correctly diagnosed at index ED visit, we assumed that patients' functional status and associated QALY remained constant after hospital or ED discharge. Among those in whom an ischemic event was missed at index ED visit (false negatives), we assumed that if a recurrent stroke occurred the clinical outcomes associated with the subsequent stroke are worse than the outcomes after a minor stroke or TIA.[23,24] If a patient's presenting transient or minor symptoms were not attributable to an ischemic event (true negative), we assumed that he/she had no subsequent complications and no functional deficits.

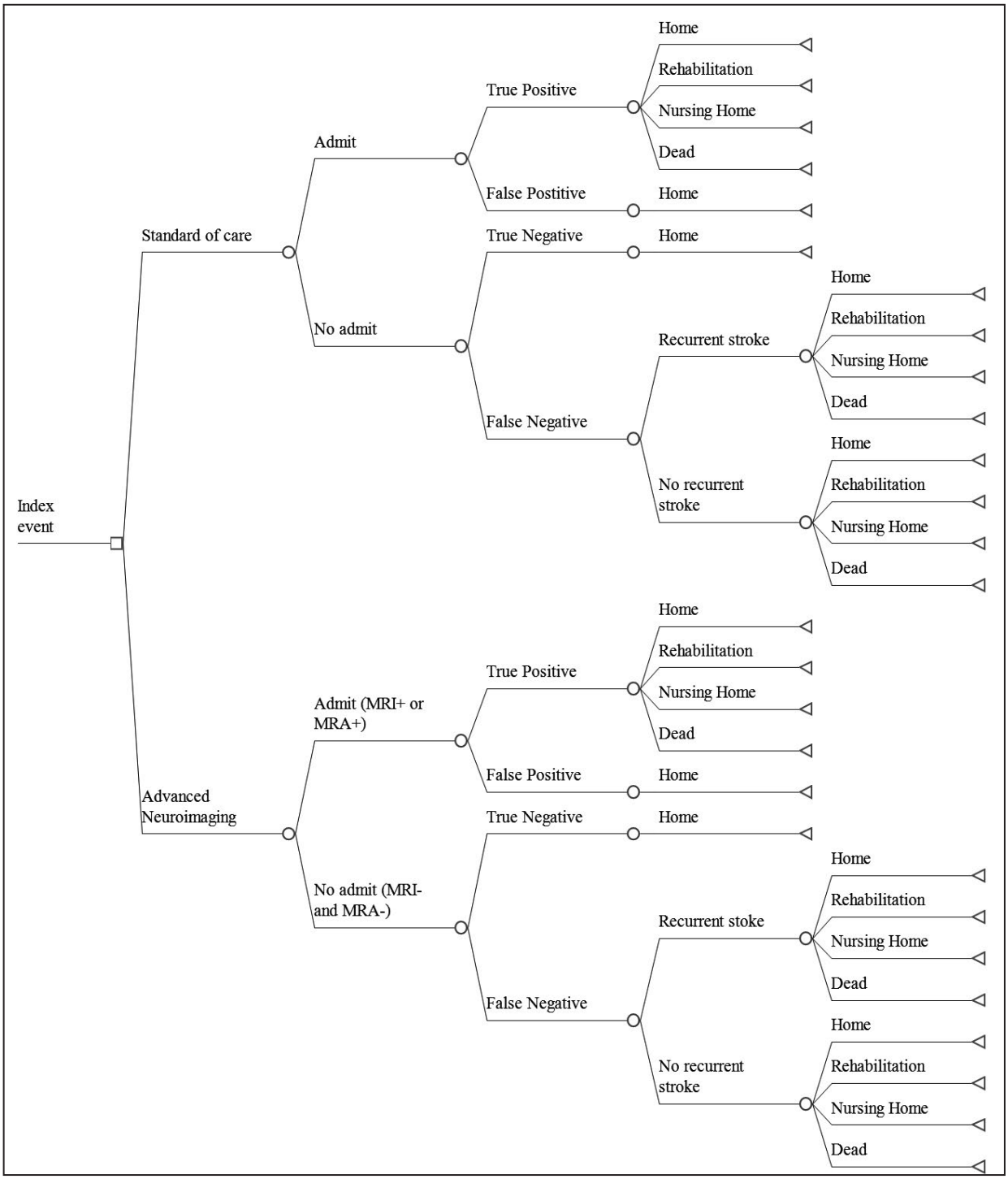

Figure 1. Decision tree.
Structure of the decision tree. The pathway after the choice node depicts both diagnostic evaluation strategies (advanced neuroimaging vs standard of care). Patient outcomes are depicted at the triangular end nodes. MRA indicates magnetic resonance angiography; and MRI, magnetic resonance imaging.

Once a patient was hospitalized, we assumed that if a patient did not have advanced neuroimaging obtained in the ED, then he/she did have advanced neuroimaging performed during his/her hospitalization. In contrast, we assumed that if a patient was readmitted for a recurrent stroke after an initial ED visit, then advanced neuroimaging was not repeated. These assumptions are based on the fact that MRI is recommended for TIA evaluations,[11] but that for most hospitalized patients with stroke, a noncontrast head CT alone suffices.[29]

Table 1. Base-Case Values, Outcome Distributions, and References of Model Input Parameters

Variable	Base-Case Value, %	1-Way Sensitivity Analysis Range, %	Distribution	Data Source
Probability				
Ischemic events in the evaluated population (pretest probability)	13.5	4–40	β	12,17,18
Recurrent stroke rate	5	0–25	β	21
Test parameter*				
Sensitivity of standard ED testing	70	50–90	β	12
Specificity of standard ED testing	70	50–90	β	
Sensitivity of advanced neuroimaging	49	29–69	β	19,20
Specificity of advanced neuroimaging	96	76–100	β	
Outcome after index presentation				
Discharge to home	71	71–91	β	14,23
Discharge to acute inpatient rehabilitation	16	5–16	(1–probability of discharge to home)×0.16/0.29	
Discharge to subacute rehabilitation	11	3–11	(1–probability of discharge to home)×0.11/0.29	
In-hospital death	2	1–2	(1–probability of discharge to home)×0.02/0.29	
Outcome distribution after recurrent stroke				
Discharge to home	47	47–67	β	24
Discharge to acute inpatient rehabilitation	21	14–21	(1–probabiliy of discharge to home)×0.21/0.53	
Discharge to subacute rehabilitation	24	15–24	(1–probabiliy of discharge to home)×0.24/0.53	
In-hospital death	8	4–8	(1–probabiliy of discharge to home)×0.08/0.53	
Calculated variable				
Negative predictive value of advanced imaging strategy	[Specificity neuroimaging×(1–pretest probability)]/{[(1–sensitivity neuroimaging)×pretest probability]+[specificity neuroimaging×(1–pretest probability)]}			
Positive predictive value of advanced imaging strategy	(Sensitivity of neuroimaging×pretest probability)/{(sensitivity neuroimaging×pretest probability)+[(1–specificity neuroimaging)×(1–pretest probability)]}			
Negative predictive value of ED standard strategy	[Specificity standard×(1–pretest probability)]/{[(1–sensitivity standard)×pretest probability]+[specificity standard×(1–pretest probability)]}			
Positive predictive value of ED standard strategy	(Sensitivity standard×pretest probability)/{(sensitivity standard×pretest probability)+[(1–specificity standard)×(1–pretest probability)]}			
Rate of hospitalization after ED standard evaluation	Sensitivity standard×pretest probability+[(1–pretest probability)×(1–specificity standard)]			
Rate of hospitalization after advanced neuroimaging (MRI brain and MRA head and neck)	Sensitivity neuroimaging×pretest probability+[(1–pretest probability)×(1–specificity neuroimaging)]			

ED indicates emergency department; MRA, magnetic resonance angiography; and MRI, magnetic resonance imaging.
*See Data S1.

Cost Calculations

We constructed our model from the payer perspective, which includes only direct healthcare costs typically incurred by healthcare payers (eg, imaging costs or inpatient care) and not indirect costs (eg, productivity losses or caregiver time). This is a meaningful way to make more explicit the implicit decisions made by providers, payers, and policy makers who consider not only the effectiveness of a particular diagnostic strategy, but also that strategy's cost.[30]

To estimate the cost of MRI and MRA in our model, we used data reported by Medicare for hospital outpatient

Table 2. Costs and Outcomes

Variable		Base-Case Value	Sources
Cost			
MRI brain without contrast, USD		230	31
MRA head and neck, USD		666	31
ED treat-and-release visit for transient neurological event, USD		572	34
Inpatient hospitalization resulting in discharge to home, USD	90 d	5026	24
	1 y	3723	33
Inpatient hospitalization resulting in discharge to acute rehabilitation, USD	90 d	6909	24
	1 y	35 345	33
Inpatient hospitalization resulting in discharge to subacute rehabilitation, USD	90 d	6868	24
	1 y	72 752	33
Inpatient hospitalization resulting in death, USD		12 861	24
Clinical outcome			
Discharge to home (mRS score, 0–2)		0.7 QALYs	25
Discharge to acute inpatient rehabilitation (mRS score, 3)		0.34 QALYs	
Discharge to subacute rehabilitation (mRS score, 4–5)		0.05 QALYs	
Dead (mRS score, 6)		0 QALYs	

ED indicates emergency department; MRA, magnetic resonance angiography; MRI, magnetic resonance imaging; mRS, modified Rankin Scale; QALY, quality-adjusted life year; and USD, US dollars.

evaluations (Table 2).[31] To account for the cost of MRA, we averaged the cost of both MRA with and MRA without contrast; only the cost of MRI brain without contrast was included. Our advanced neuroimaging protocol was conceptualized as similar to a previously published 15-minute magnetic resonance screening protocol used to rapidly evaluate ED patients with stroke,[32] but with MRA neck imaging instead of perfusion-weighted imaging obtained. Our advanced neuroimaging strategy would thus include: diffusion-weighted imaging, gradient echo, fluid-attenuated inversion recovery, intracranial MRA, and extracranial MRA.

We used previously reported cost estimates based on hospital discharge disposition to derive inpatient costs and 1-year poststroke care costs after hospital discharge (Table 2).[24,33] The cost of an ED visit for transient or minor neurological symptoms was also estimated on the basis of prior literature (Table 2).[34] All costs were adjusted for inflation to 2019 US dollars using the Consumer Price Index.[35]

Statistical Analysis

Effectiveness was measured in QALYs, and costs were measured in US dollars. We used the incremental cost-effectiveness ratio (ICER) to identify the preferred diagnostic evaluation strategy. We calculated ICER by dividing the difference in total costs (incremental cost) by the difference in effectiveness (incremental effect) between the 2 strategies, advanced neuroimaging and standard ED practice. A strategy was considered cost-effective if the ICER was <$100 000 US dollars per QALY gained, the willingness-to-pay value, in keeping with our setting of the United States.[22]

Sensitivity Analyses

We varied the likelihood that an ischemic event was the cause of minor or transient symptoms to account for different clinical cohorts of ED patients in 1-way sensitivity analyses. Specifically, we varied the pretest probability of TIA or minor stroke from 4%, based on the rate of ischemia among ED patients who complain of dizziness/vertigo,[17] to 40%, based on a study of ED patients admitted following focal transient neurological attacks.[18] For all other probability and cost variables, we conducted 1-way sensitivity analyses varied by ±20% (Table 1).

Because of uncertainty about the relationship between diagnoses and individual patient outcomes, economic evaluations of diagnostic tests are inherently more difficult than assessments of disease-specific therapeutic interventions.[30] We, therefore, evaluated different outcome scenarios after stroke hospitalization in 1-way sensitivity analyses by increasing the percentage of patients discharged to home by 20% and decreasing the remaining potential discharge outcomes proportionally (Table 1). Adjusting clinical outcomes so that 91% of patients with an ischemic cause of their presenting symptoms are nondisabled corresponds well to some previously reported outcomes after TIA or minor stroke.[8,9,14]

To further evaluate the impact of parameter uncertainty on model outputs, we performed a probabilistic sensitivity analysis using second-order

Monte Carlo simulation. We assumed the probability parameters: (1) the proportion of true ischemic events (TIA or ischemic stroke) among patients with low-risk transient or minor symptoms, (2) the specificity and sensitivity of each diagnostic evaluation strategy, (3) recurrent stroke rate after TIA and minor stroke, and (4) discharge to home after hospitalization followed a β distribution.[36-38] Specifically, the parameters of a standard β distribution were estimated on the basis of the point estimates and 95% CIs from the literature using the "prevalence" package and its "betaExpert" function in R.[39] We proportionally adjusted the probability of the other 3 dispositional states after recurrent stroke or index event based on the distribution of patients discharged to home. We assumed a normal distribution for all costs with the base-case value set as the mean and 20% of the base-case value as the SD. The simulation was run 10 000 times to capture the stability of the results. Probabilistic sensitivity analysis results are shown in an incremental cost-effectiveness scatterplot comparing the 2 diagnostic evaluation strategies.

Additional Analyses

To explore potential diagnostic evaluation strategies' testing characteristics, we used 1-way sensitivity analyses to identify optimal test performance parameters of potential future diagnostic approaches. In this threshold analysis, we varied the sensitivity and specificity of the advanced neuroimaging strategy and the current ED strategy from 0% to 100%. The cost of neuroimaging was varied from $0 to $50 000 to identify cost thresholds.

We conducted a secondary analysis using a 90-day time horizon rather than 1-year time horizon to account for the importance of short-term outcomes when evaluating ED-based decision making.[40] Costs associated with patient care after hospital discharge were not included when the shorter time horizon of 90 days was used (Table 2).

We performed an additional secondary analysis to evaluate the strategy of obtaining CT angiography of the head and neck in the ED on every patient compared with our other 2 strategies. To conduct this additional analysis, we added a third branch to the decision node (Figure S1). We stipulated that patients were admitted from the ED if >50% stenosis or occlusion in a relevant vessel was found on CT angiography and that they were discharged to home after a CT angiography study that lacked these findings. Outcomes after hospital admission or ED discharge after CT angiography were identical to those of the other diagnostic strategies. Extant literature on the sensitivity and specificity of CT angiography in our ED study population of low-risk transient and minor neurological events is sparse. We therefore estimated CT angiography testing parameters from a study of patients with TIA and from a separate study of ED patients evaluated for dizziness.[19,41] When adopting the study of dizzy patients to our model, we assumed that all patients whose CT angiography did not show a vessel stenosis did not have a vascular cause for their symptoms and that detection of fibromuscular dysplasia was a false positive.[41] We thus estimated that CT angiography has a sensitivity of 17% and a specificity of 99% for a vascular event in our study population.[19,41] We calculated the cost of CT angiography as $542 based on data reported by Medicare for Current Procedural Terminology codes 70496 and 70498.[31]

All study data will be provided at the request of other investigators for the purposes of replicating procedures and/or results.

RESULTS

In our primary study analysis, the effectiveness of the advanced neuroimaging strategy is slightly less than current ED practice, but increased costs are associated with the current ED diagnostic evaluation strategy (Figure 2). The ICER of the current ED strategy is $5 506 722 per QALY, exceeding the willingness-to-pay threshold. The total cost of the advanced neuroimaging strategy is $3210, with an effectiveness of 0.9397, whereas the total cost of the current ED strategy is $4338, with an effectiveness of 0.9399 in the primary model (Figure 2). The similar effectiveness of both strategies is largely driven by the low rate of stroke recurrence after a false-negative diagnosis. False-positive cases that were hospitalized unnecessarily, rather than recurrent stroke events following false-negative diagnosis, contributed to the higher cost of the current ED strategy.

The advanced neuroimaging strategy was cost-effective in all prespecified 1-way sensitivity analyses, including varying the probability that the index event was ischemic and the probability of stroke recurrence (Figure S2). Results of 10 000 iteration probabilistic sensitivity analyses are shown in Figure 3. Differences in the incremental effectiveness of the 2 strategies are small, and the cost of the current ED strategy is higher than that of the advanced imaging strategy in most simulation iterations. In 99.98% of the simulation runs, the advanced neuroimaging strategy is more cost-effective than current ED standard-of-care strategy.

In threshold analyses of the ED standard-of-care testing, when the specificity of ED testing for an ischemic cause of a transient or minor neurological symptom

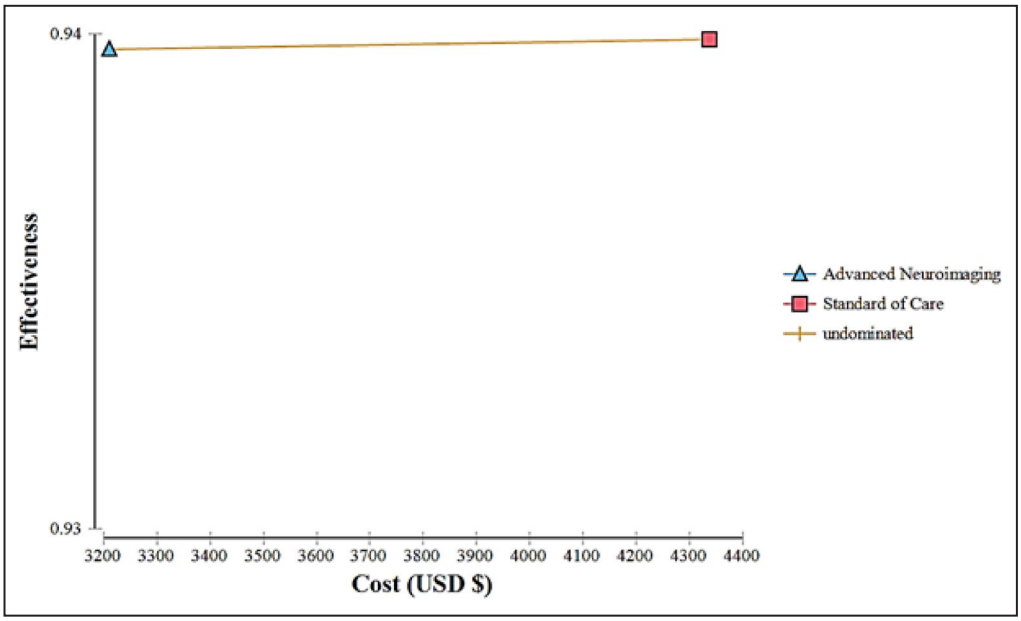

Figure 2. Primary model cost-effectiveness analysis results.
Plot of the costs and the effectiveness (quality-adjusted life years) of each diagnostic evaluation strategy in the primary analytic model. The advanced neuroimaging strategy (triangle) has an incremental cost of $1128 US dollars (USD) less than the standard-of-care strategy (square) and is 0.000205 incrementally less effective than the standard-of-care strategy.

is >91.9%, the current ED practice strategy is preferred (Figure 4). Regardless of how high the sensitivity of standard ED testing is, the advanced neuroimaging strategy is always more cost-effective. The effectiveness of both diagnostic evaluation strategies is exactly the same when sensitivity of advanced neuroimaging is equal to 70%. Varying the specificity of the advanced neuroimaging strategy in a threshold analysis reveals that the standard ED diagnostic testing strategy is only preferred when the specificity of advanced neuroimaging is <70.5%. Holding everything else constant, if the cost of advanced neuroimaging is ≥$2625, then the current ED practice strategy is more cost-effective than the advanced neuroimaging strategy (Figure 5).

In our secondary analyses with a 90-day time horizon, the advanced neuroimaging strategy remains more cost-effective in all scenarios specified in our sensitivity analyses. The cost of neuroimaging above which the advanced neuroimaging strategy is no longer preferred is $1967 using the shorter 90-day time horizon.

In an additional secondary analysis including CT angiography as a third diagnostic evaluation strategy, the total cost of the CT angiography strategy is $1848, with an effectiveness of 0.9394. Both the advanced neuroimaging strategy as well as the current standard-of-care strategy were costlier and slightly more effective than CT angiography. Compared with the CT angiography strategy, the current ED strategy had an ICER of $4 818 058 per QALY, and the advanced neuroimaging strategy had an ICER of $4 366 122 per QALY.

DISCUSSION

In our cost-effectiveness analysis of 2 ED-based diagnostic evaluation strategies (current standard of care versus advanced neuroimaging with MRI brain and MRA head and neck) for patients with low-risk transient and minor neurological symptoms, the effectiveness in diagnosing ischemic events was similar, but the advanced neuroimaging strategy was more cost-effective at 90 days and at 1 year. The robustness of this finding is supported by the results of our probabilistic sensitivity analysis. Given the low rate of recurrent stroke even among false-negative patients with minor stroke and TIA, the adverse outcomes and associated costs of a subsequent stroke hospitalization did not offset the costs of hospitalizing false-positive patients in the current ED practice strategy. Because of its lower sensitivity, the advanced neuroimaging strategy, however, does allow for more false negatives to be discharged home than current practice. These findings may have important implications for insurers and government agencies seeking to reduce healthcare costs as well as for hospitals seeking to improve admission protocols.

Our threshold analyses additionally allowed us to infer the diagnostic parameters of a potential diagnostic test or clinical decision support tool that could

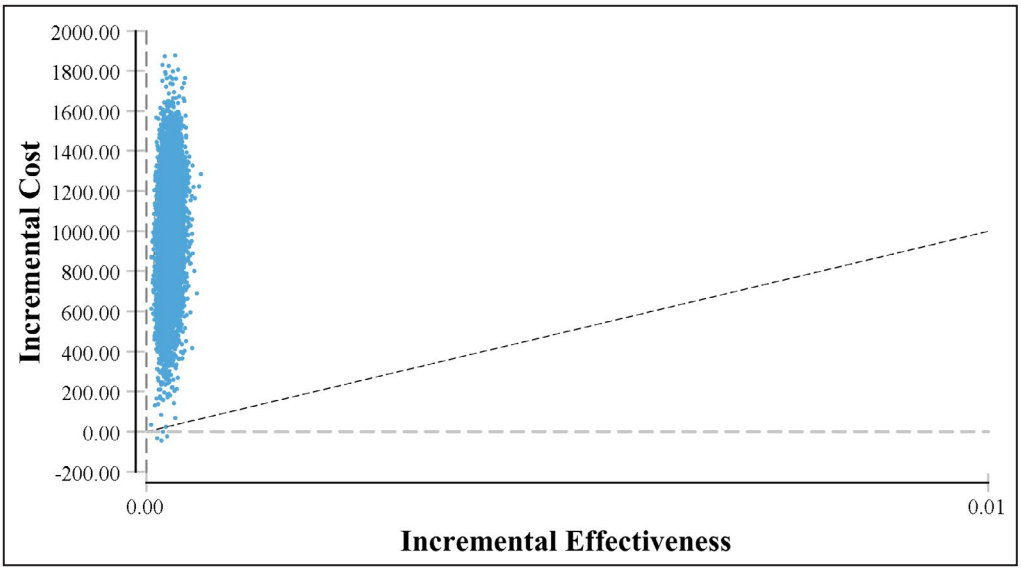

Figure 3. Incremental cost-effectiveness (ICE) scatterplot of emergency department (ED) standard of care vs advanced neuroimaging.
The ICE scatterplot includes a set of points representing pairs of incremental cost and effectiveness values from the simulation results (n=10 000) relative to a baseline (the advanced neuroimaging strategy). The comparator strategy is ED standard of care. The dashed line is the willingness-to-pay (WTP) threshold, set at US $100 000. A 95% confidence ellipse is drawn in the ICE scatterplot. In 99.98% of runs, the ED standard of care costs more and is more effective, but its ICE ratio is greater than the WTP, so advanced neuroimaging strategy is optimal.

be used to evaluate ED patients with minor or transient symptoms. Broadly speaking, clinical decision support tools are designed to improve clinical decision making at the point of care.[42] On the basis of our decision-analytic model, an example of a cost-effective testing strategy compared with obtaining advanced neuroimaging on all eligible ED patients would be one that is >92% specific, >70% sensitive, and cost less than or equal to current ED evaluation strategy using a 1-year time horizon. Designing a clinical decision support tool or new diagnostic test with these sorts of parameters may be challenging, but not impossible. For example, bedside testing maneuvers designed to improve the diagnosis of central vertigo in the ED, the head impulse, nystagmus type, test of skew (HINTS) examination, was initially reported to have a sensitivity of 96.5% and a specificity of 84.4% for stroke detection among patients presenting with dizziness.[43] Facilitating early expert consultation via telemedicine may also improve minor stroke/TIA diagnostic accuracy in the ED.[44]

Several prior studies have focused on determining the cost-effectiveness of short-term hospitalization versus expedited clinic evaluation[45-47] or the use of an ED observation unit[48] after suspected TIA or minor stroke. In contrast, we sought to determine the best evaluative strategy for a hospital's ED to adopt toward patients with low-risk neurological symptoms in the context of current clinical practice in the United States. Although expedited outpatient TIA evaluation clinics have recently been successfully implemented in the United States,[49] data from the National Emergency Department sample demonstrates that 64% of patients with TIA are admitted from the ED,[50] with a substantial proportion remaining in the hospital for ≥2 days.[51] Our analysis was also designed with the needs of emergency medicine providers in mind. In a study of emergency physicians, 1 of the top 5 clinical priorities for the development of a clinical decision rule in the ED is imaging for patients with suspected TIA.[52]

In addition to relating closely to current US practice patterns and the expressed needs of emergency medicine providers, an advantage of our study is that we explicitly accounted for recurrent stroke events following a false-negative minor stroke/TIA diagnosis in the ED. In clinical practice, delayed or missed stroke diagnosis is estimated to occur in ~9% of patients with stroke at index ED evaluation.[4] An even higher risk of diagnostic error is associated with transient, minor, or nonspecific symptoms.[4] We did not, however, account for the additional costs associated with ED-based diagnostic errors from malpractice litigation, which may be substantial[53]; we accounted only for the healthcare sector costs associated with subsequent hospitalization among false-negative patients with stroke recurrence using both 90-day and 1-year time horizons. Important

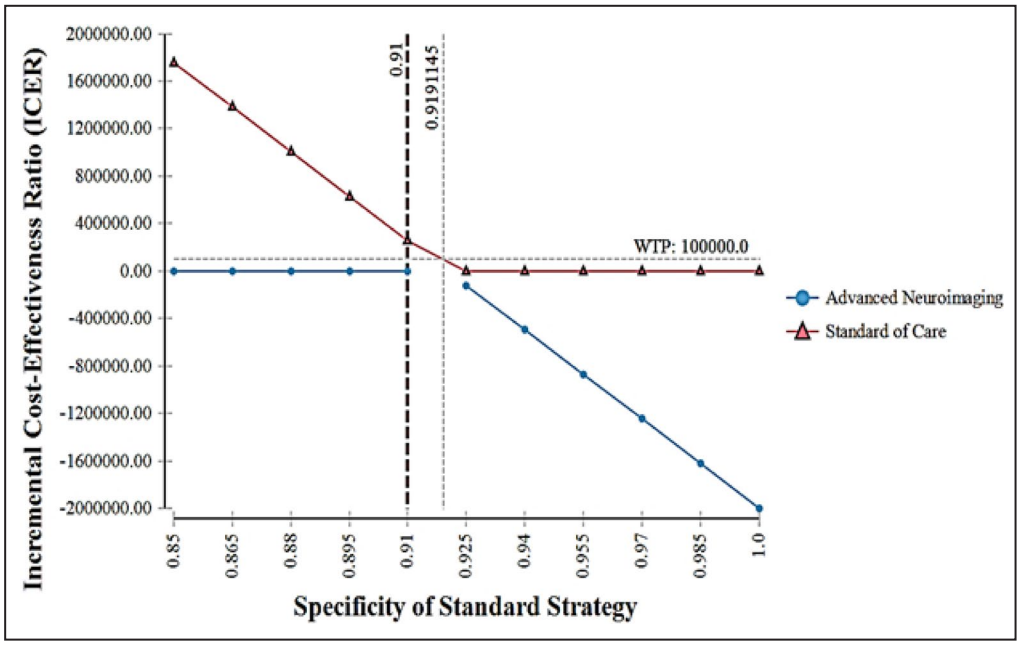

Figure 4. Varying the specificity of standard diagnostic evaluation strategy.
One-way sensitivity analyses varying the specificity of the standard-of-care strategy (triangle) from 85% to 100% in our primary analytic model. When the specificity of the standard-of-care strategy exceeds 91.9%, then the standard-of-care strategy (triangle) has an incremental cost-effectiveness ratio (ICER) below the willingness-to-pay (WTP) threshold set at US $100 000.

areas for future clinical research include accounting for additional costs of failure to diagnose stroke/TIA in the ED, the effects of a false-positive stroke diagnosis on patients and their families, and the impact of increased ED dwell time or overcrowding from increased neuroimaging use.

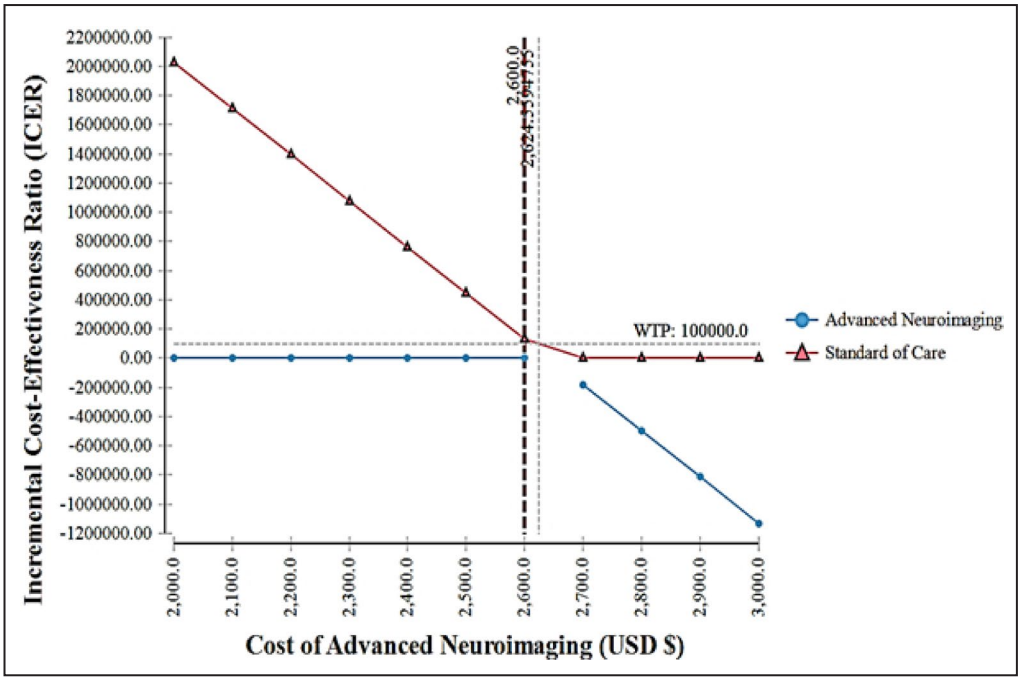

Figure 5. Varying the cost of advanced neuroimaging.
One-way sensitivity analyses varying the cost of advanced neuroimaging in our primary analytic model. If the cost of advanced neuroimaging exceeds $2624 US dollars (USD), then the standard-of-care strategy (triangle) will have an incremental cost-effectiveness ratio (ICER) below the willingness to pay (WTP), set at $100 000 USD.

The results of our secondary analysis including CT angiography as an alternative diagnostic strategy should be interpreted with extreme caution given the lack of high-quality data on the true diagnostic yield of this imaging modality among ED patients with low-risk transient and minor symptoms, our study population. Among patients with acute minor stroke with National Institutes of Health Stroke Scale score ≤6 who are eligible for acute ischemic stroke treatments, screening with CT angiography was recently shown to be cost-effective given the nontrivial rate of large-vessel occlusions in this population.[38] Using CT angiography to rapidly evaluate patients with high-risk TIA and minor stroke in the ED was recommended and has been partially adopted in Canadian EDs.[54,55] Whether or not more widespread use of screening CT angiography will improve the diagnostic evaluation of patients with low-risk neurological complaints in the emergency setting requires further study.

Our study has several additional limitations. First, we chose to evaluate diagnostic testing strategies from the payer rather than the societal perspective; this significantly limits our ability to fully inform healthcare policy.[30] We did not model a lifetime horizon and therefore do not know the long-term cost-effectiveness of either strategy. Second, our model focused on current practice paradigms in the United States; extrapolation of our results to other healthcare settings is not advisable. Some of our model assumptions may further limit generalizability, including the fact that we assumed that all ED patients with transient or minor symptoms could undergo advanced neuroimaging despite the fact that not all patients can tolerate MRI[56] and not all EDs have access to advanced imaging modalities or the funds needed to purchase, staff, and maintain this equipment. We also assumed that patients hospitalized for recurrent stroke events did not get advanced neuroimaging despite the fact that in clinical practice, MRI use among hospitalized patients with stroke is highly variable.[57] Third, the cost of obtaining advanced neuroimaging on everyone with transient or minor symptoms may be greater than the cost of the Medicare reimbursements alone because additional hospital capacity will probably be required if this diagnostic evaluation strategy is adopted. However, our threshold analysis included high neuroimaging costs, which likely encompassed some of these additional costs. Fourth, we did not distinguish between patients with versus those without focal deficits on examination or between those with multiple vascular risk factors versus those without despite the fact that in clinical practice providers often adopt different diagnostic approaches for these different patient subgroups. Finally, we also did not account for differences in provider experience, training background, or certifications in our model.

In conclusion, we found that obtaining advanced neuroimaging (MRI brain and MRA head and neck) in the ED was a cost-effective way to decide which patients presenting with low-risk transient and minor neurological symptoms can be discharged from the ED using a decision-analytic model.

ARTICLE INFORMATION

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Affiliations

Department of Neurology (A.L.L., N.T.C., C.C.E., D.L.L., R.B.L.), Department of Neurosurgery and Radiology (N.H.) and Department of Medicine (P.S.), Albert Einstein College of Medicine, Montefiore Medical Center, Bronx, NY; The Center for Health and the Social Sciences, University of Chicago, Chicago, IL (H.Z.); Department of Neurology, New York University Grossman School of Medicine, New York, NY (S.K.R.); and Department of Neurology, University of Chicago School of Medicine, Chicago, IL (S.P.).

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Supplementary Material

Data S1
Figures S1–S2

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SUPPLEMENTAL MATERIAL

Data S1.

Supplemental Methods

Main Model Test Parameters

To determine the sensitivity and specificity of the advanced neuroimaging strategy we used data from a study of hospitalized possible and probable TIA patients which reported the following results among patients with advanced neuroimaging:[19]

	MRI with infarction	MRI without infarction
MRA with stenosis in relevant vessel	31	29
MRA without stenosis in relevant vessel	105	174

We also used data from a study of possible TIA or minor stroke patients seen in the ED in whom 83 were sent directly home after MRI brain and MRA head and neck imaging as they were presumed not to have had an ischemic event.[20] The findings in the 83 patients sent home were reported as follows:

	MRI with infarction	MRI without infarction
MRA with stenosis in relevant vessel	0	1
MRA without stenosis in relevant vessel	2	80

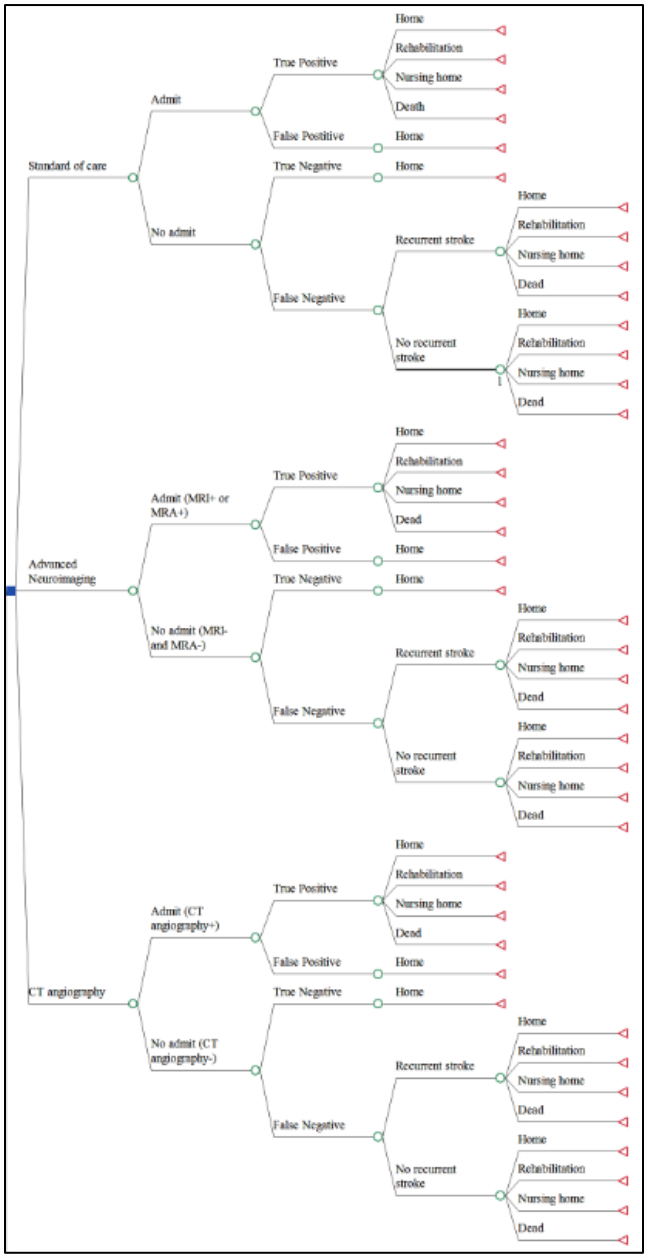
Using these two studies,[19,20] we calculated the test parameters of advanced neuroimaging in our study. We stipulated that in our model if a patient had relevant vessel stenosis or evidence of infarction on advanced imaging, they would be admitted. We also stipulated that only when both neuroimaging studies, MRI brain and MRA head and neck, showed neither infarction nor stenosis in the relevant vessel would the patient be sent home from the ED. We therefore determined that the probability of either test being abnormal in the case of a true vascular event was 48.7% ($P(\text{Test}+_{MRA} \text{ OR Test}+_{MRI}|\text{Disease})$) and the probability of both tests being normal without disease present was 96.4% ($P(\text{Test-}_{MRA} \text{ AND Test-}_{MRI}|\text{No Disease})$).

To determine the sensitivity and specificity of current ED standard of care strategy, we used data from a prospective study of patients with presumed low-risk transient or minor stroke symptoms referred from the ED or outpatient clinic.[12] We used differences between true ischemic events and predicted ischemic events to determine the sensitivity and specifity of the current care strategy based on the following results:

	True ischemic (TIA/ischemic stroke)	True non-ischemic (stroke mimic)
Predicted ischemic event	532	79
Predicted non-ischemic event	229	188

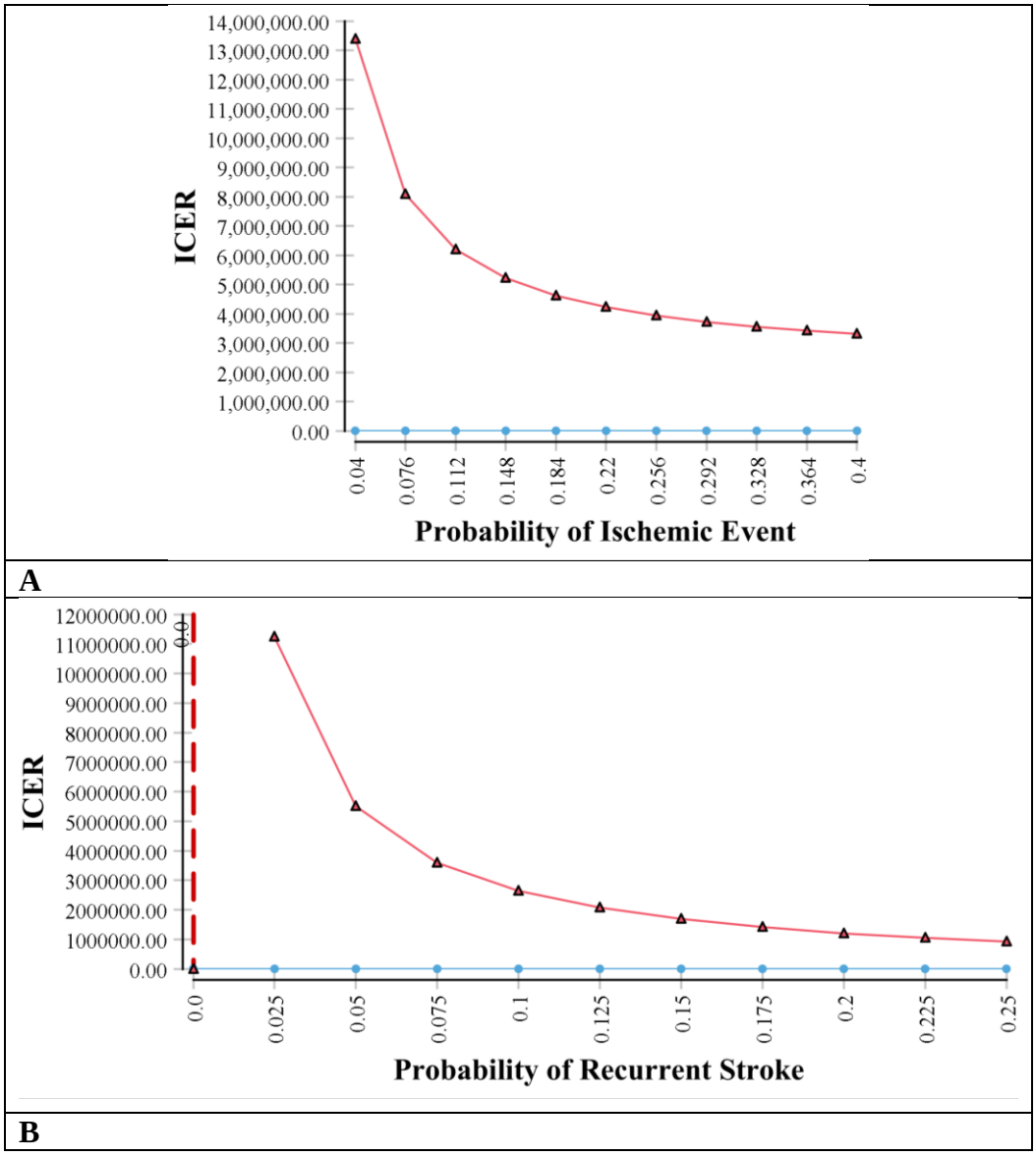
This resulted in a sensitivity of 69.9% and a specificity of 70.4% for current ED practice.

Figure S1. Secondary Analysis with CT angiography.



Structure of the decision tree revised to include compute tomography (CT) angiography. The pathway after the choice node now depicts three diagnostic evaluation strategies. Patient outcomes are depicted at the triangular end nodes

Figure S2. Additional one-way sensitivity analyses.



One-way sensitivity analyses for the probability that the (A) index event was ischemic and (B) probability of stroke recurrence after index event. Red line with triangles represents ED standard of care strategy; circles and blue line represent advance neuroimaging strategy. *ICER = Incremental Cost Effectiveness Ratio