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Original Contribution

External validation of the Ottawa subarachnoid hemorrhage clinical decision rule in patients with acute headache☆,☆☆,★,★★

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ABSTRACT

We aim to externally validate the Ottawa subarachnoid hemorrhage (OSAH) clinical decision rule. This rule identifies patients with acute nontraumatic headache who require further investigation. We conducted a medical record review of all patients presenting to the emergency department (ED) with headache from January 2011 to November 2013. Per the OSAH rule, patients with any of the following predictors require further investigation: age 40 years or older, neck pain, stiffness or limited flexion, loss of consciousness, onset during exertion, or thunderclap. The rule was applied following the OSAH rule criteria. Patients were followed up for repeat visits within 7 days of initial presentation. Data were electronically harvested from the electronic medical record and manually abstracted from individual patient charts using a standardized data abstraction form. Calibration between trained reviewers was performed periodically. A total of 5034 ED visits with acute headache were reviewed for eligibility. There were 1521 visits that met exclusion criteria, and 3059 had headache of gradual onset or time to maximal intensity greater than or equal to 1 hour. The rule was applied to 454 patients (9.0%). There were 9 cases of subarachnoid hemorrhage (SAH), yielding an incidence of 2.0% (95% confidence interval [CI], 1.0%-3.9%) in the eligible cohort. The sensitivity for SAH was 100% (95% CI, 62.9%-100%); specificity, 7.6% (95% CI, 5.4%-10.6%); positive predictive value, 2.1% (95% CI 1.0%-4.2%); and negative predictive value, 100% (95% CI, 87.4%-100%). The OSAH rule was 100% sensitive for SAH in the eligible cohort. However, its low specificity and applicability to only a minority of ED patients with headache (9%) reduce its potential impact on practice.

1. Introduction

Headache is a common complaint in emergency departments (EDs) across the United States, accounting for up to 4% of ED visits [1,2]. Identifying the small number of patients with a life-threatening headache among the majority with benign primary headache (eg, migraine or tension) is an important and common problem. Failure to recognize a serious underlying cause of the headache can have potentially fatal consequences. A careful history and physical examination remain the most important elements of the assessment of the headache patient, enabling the clinician to determine the risk of a dangerous etiology and the need for additional workup [3,4].

Use of computed tomography (CT) to identify a potential serious underlying cause of nontraumatic headache has increased dramatically in the past 15 years [5]. The number of patients presenting to the ED with nontraumatic headache who underwent CT imaging increased from 13% to 31% over a 10-year period [3]. However, the incidence of subarachnoid hemorrhage (SAH) among those presenting with headache is relatively low and is estimated to be 0.5% to 6% [1,4,6,7].

A recently published clinical decision rule, the Ottawa SAH (OSAH) rule, seeks to identify the few cases of SAH among patients presenting with acute nontraumatic headache. The OSAH rule was 100% sensitive and 15% specific for detection of SAH among patients presenting to the ED with acute nontraumatic headache reaching maximum intensity within 1 hour and a normal neurologic examination [7].

Clinical decision rules require validation in diverse clinical settings before they should be broadly used [8,9]. In this investigation, we externally validate the OSAH rule to assess its classification performance in an independent patient population and to estimate the potential impact of implementing the rule in a US setting.

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★★ Ethics approval: This study was approved by the institutional review board at Mayo Clinic, and patients not consenting for medical records review for research were excluded in accordance with the Minnesota State Law.

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2. Methods

2.1. Study design

We conducted a health records review of consecutive patients presenting with headache at [Institution name here] ED, an academic center with approximately 73 000 annual visits located in [Institution city here]. All visits from January 2011 to November 2013 were screened for inclusion. Patients were identified through our electronic medical record system based on a chief complaint of headache. This study was approved by the institutional review board.

2.2. Study setting and population

All patients older than 15 years with nontraumatic headache were potentially eligible. Inclusion and exclusion criteria were determined before data collection and were based on the original study by Perry et al [7]. Potentially eligible patients had a headache determined to be sudden in onset, reaching maximal intensity within 1 hour. Patients with head trauma within 7 days; new neurologic deficits; and any prior history of cerebral aneurysm, SAH, hydrocephalus, cerebral neoplasm, or established recurrent headache syndromes were excluded. Criteria for inclusion and exclusion as well as a coding guide to maintain the uniformity of data abstraction and decrease the risk of introducing bias in the process of patient selection were defined a priori and applied by trained, closely supervised data abstractors (Appendix A).

2.3. Methods, measurements, data collection, and outcomes

We electronically abstracted the following data from the electronic medical record and administrative databases within [Institution name] health records system: demographic variables, chief complaint, workup in the ED including head CT, CT angiogram and/or lumbar puncture (LP), initial vital signs, pain score, final diagnosis, disposition, and return to the ED within 7 days.

We manually reviewed electronic medical records to obtain the following data: onset and duration of the headache, whether it was described as thunderclap or reached maximum intensity within 1 hour, neck pain or stiffness, limited neck flexion, presence of neurologic deficits, loss of consciousness, concomitant symptoms, CT scan and other imaging modalities, LP, diagnosis at discharge, and outcomes at 7 days. Patients were followed up through health record review for 7 days from the index ED visit to determine whether there was a return visit to the ED and any potential missed diagnoses. For patients who did not have a subsequent visit documented in the electronic medical record, we searched the Social Security Death Index database to ascertain any potentially missed adverse events that occurred within 7 days of the ED visit.

We used the same definition as Perry et al [7] for the diagnosis of SAH: subarachnoid blood on CT, xanthochromia in the cerebrospinal fluid, or red blood cells in the final tube of cerebrospinal fluid, with an aneurysm or arteriovenous malformation on cerebral angiography. We selected a consecutive sample, thus diminishing the risk of selection bias. Any conflicting entries (staff, resident, and nurses) were resolved using the staff physician information first, resident second, and nurse information third. We piloted the data abstraction form and revised it after approximately 50 charts were reviewed. The abstractors met periodically with the primary investigator to review any questions that arose in the data abstraction process and to resolve disagreement between abstractors. Abstractors were not blinded to the study objectives and hypothesis. Study data were collected using a standardized data abstraction form and entered into a Research Electronic Data Capture Web-based interface made secure by an intrainstitutional firewall. Research Electronic Data Capture is a secure, Web-based application designed to support data capture for research studies, providing an intuitive interface for validated data entry, audit trails for tracking data manipulation, and export procedures [10].

2.4. Data analysis

According to the OSAH rule, patients with any of the following characteristics require further investigation for their headache: age 40 years or older, neck pain or stiffness, witnessed loss of consciousness, onset during exertion, thunderclap character, or limited neck flexion. We assessed the classification performance of the OSAH rule using 2×2 contingency tables to generate estimates for sensitivity, specificity, positive predictive value, and negative predictive value (NPV). We calculated 95% confidence intervals (CIs) for each proportion using the method described by Newcombe and Robert [11]. Data were analyzed with JMP Statistical Discovery software version 11 (SAS, Cary, NC). We report categorical data as frequency counts and percentages and continuous data as mean (SD) or median (interquartile range [IQR]) as appropriate for the distribution of the data.

This study was partially funded by The Andison Family Foundation. The Foundation had no role in the design or reporting of the study.

3. Results

We screened 5409 records of patients presenting to the ED with headache during the study period. There were 1521 records that met exclusion criteria. Three hundred seventy-five patients did not give consent for the use of their medical records for research purposes and were excluded from analysis in accordance with Minnesota state law (Fig. 1). Records were also excluded because the headache did not reach maximum intensity within 1 hour (n = 1440), was described as gradual in onset (n = 1309), or lacked a description of onset in the records (n = 310) (Fig. 1). There were 454 patients (8.4%) who met eligibility criteria and were included in the final analysis.

Table 1 displays the baseline characteristics of the 454 included patients. Mean age was 44.5 years (IQR, 30-55), 45% were younger than 40 years, 63% were female, and 16% arrived by ambulance. Eighty-nine percent described a thunderclap or sudden onset headache; 25% had neck pain or stiffness; 6%, onset during exertion; 24%, vomiting; 2%, limited neck flexion; and 1%, witnessed loss of consciousness. In the ED, 79% had a CT scan performed during their ED visit, 17% had an LP, and 10% underwent cerebral angiography. Most patients (80%) were discharged home after the ED evaluation, and 4% were admitted to the intensive care unit. Four percent of patients returned to the ED within 7 days; none of these patients had an SAH.

There were 9 cases of SAH, yielding an incidence of 2.0% (95% CI, 1.0%-3.9%). Table 2 displays a 2-by-2 contingency table from which we generated the following classification performance estimates: sensitivity 100% (95% CI, 62.9%-100%), specificity 7.6% (95% CI, 5.4%-10.6%), positive predictive value 2.1% (95% CI, 1.0%-4.2%), and NPV 100% (95% CI, 87.4%-100%). There were 34 patients without SAH for whom the rule suggested no further investigation (true negatives). One of these cases required further management of a cerebrospinal fluid leak. Overall, if the rule were applied in practice, 94.4% of the patients would require further investigation with head CT and/or LP.

There were 360 patients (79%) who had a cranial CT, and 76 (17%) underwent LP. Among the 34 patients for whom the rule suggested no further investigation, 13 underwent CT, and none, LP. Indications for cranial CT listed by the clinician for these 13 patients were new onset headache, immunosuppression, suspected postoperative cerebrospinal fluid leak, and hypertensive emergency.

Among the 420 patients for whom the rule suggested further investigation, 347 underwent CT, 76 underwent LP, and 71 had no further investigations performed (Fig. 2). All 9 cases of SAH were diagnosed by CT. Application of the rule in real time in this cohort could have prevented 13 CTs and would have suggested that additional workup is indicated in 71 patients.

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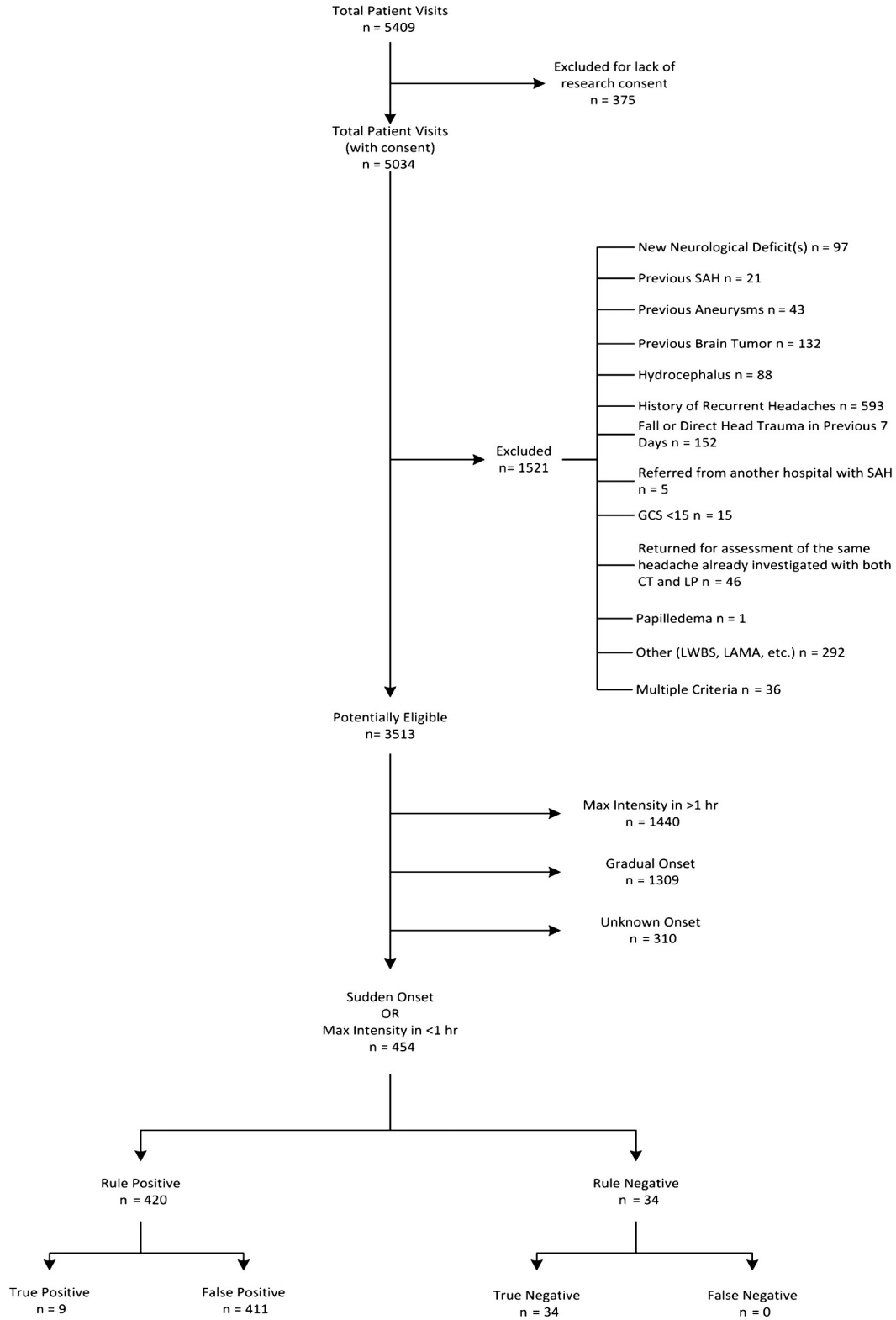

Fig. 1. Flow diagram of patient selection.

Table 3 shows the discharge diagnoses for patients who did and did not meet eligibility criteria for the rule. There were 13 cases of SAH in the excluded cohort (0.3%); these patients were excluded because of a history of aneurysms, previous SAH, referral from another hospital with a diagnosis of SAH, a Glasgow Coma Scale score less than 15, or trauma in the previous 7 days.

4. Discussion

In this external validation of the Ottawa clinical decision rule to rule out SAH for acute headache, we found a sensitivity of 100%, a specificity of 7.6%, and NPV of 100%. We found similar sensitivity compared to the original derivation study [7]. However, the specificity was lower than

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Table 1
Summary of features for visits included in the rule, n = 454

Feature	Mean (median; IQR; range)
Age at visit (y)	44.5 (42; 30-55; 16-91)
Systolic blood pressure	140.7 (137; 125-156; 66-213)
Diastolic blood pressure	82.2 (81; 73-91; 18-171)
Temperature (n = 451)	36.7 (36.7; 36.5-36.8; 36.0-38.8)
Pulse rate	80.2 (77; 68-89; 26-148)
Respiratory rate	17.2 (16; 16-18; 9-36)
Oxygen saturation	97.9 (98; 97-100; 88-100)
Pain score (n = 442)	6.8 (7; 5-9; 0-10)
Sex	n (%)
Male	166 (37)
Female	288 (63)
Age at visit (y)	
<40	205 (45)
≥40	249 (55)
Transport arrival	
ALS/BLS surface ambulance	72 (16)
Private vehicle/walk in	379 (84)
Other	3 (1)
Neck pain/stiffness (n = 452)	112 (25)
Witnessed LOC (n = 452)	6 (1)
Onset during exertion (n = 418)	24 (6)
Thunderclap headache (n = 441)	393 (89)
Limited neck flexion (n = 451)	7 (2)
Vomiting (n = 447)	109 (24)
CT scan done	360 (79)
Angiography done	45 (10)
Lumbar puncture done	76 (17)
Patient returned within 7 d	18 (4)

that which was previously reported, and only a small proportion of patients who presented with headache (8.4%) were eligible for the rule. These data suggest that the OSAH rule would likely apply to only a small proportion of patients who present to the ED with headache and, if applied, would suggest further testing is indicated in nearly 93% of patients.

Our incidence of SAH was 2.0% in comparison to the original study by Perry et al [7] that had an incidence of 6%. When compared to the original OSAH derivation study, our study had a similar sex and age distributions. We had a lower proportion of patients arriving by ambulance (16% vs 26%) and lower mean pain scores (6.8 vs 8.7); however, the OSAH study measured pain at "peak," and we measured pain at the time of ED presentation. We had a slightly lower proportion of patients with headache onset during exertion (6% vs 11%) but similar rates of patients with witnessed loss on consciousness (1% vs 3.7%), neck pain or stiffness (25% vs 34%), limited neck flexion (2% vs 4%), and vomiting (24% vs 29%). Conversely, we had a higher proportion of patients with thunderclap headache (89% vs 53%). Our cohort had a similar rate of CT (79% vs 83%) and cerebral angiography (10% vs 15%) but a lower rate of LP (17% vs 39%). We also had a greater proportion of patients admitted to the hospital (20% vs 9%). We had similar final diagnoses in the included cohort, with most of the patients having benign headache. Whether these differences between cohorts represent an expected degree of variation between cohorts or are due to the retrospective design of our study is not entirely clear.

Table 2
Performance of the OSAH rule

	SAH present	SAH absent
Rule positive	9	411
Rule negative	0	34

Sensitivity 100% (95% CI, 62.9%-100%); specificity 7.6% (95% CI, 5.4%-10.6%); positive predictive value 2.1% (95% CI, 1.0%-4.2%); negative predictive value 100% (95% CI, 87.4%-100%). Estimated proportion of patients requiring testing if applied in practice: 92.5% (95% CI, 89.7%-94.6%).

Diagnosing SAH is challenging and the OSAH rule aims to recognize SAH in the cases most difficult to diagnose, that is, in patients who are alert and neurologically intact. Our study highlights that the rule only applies to a minority of patients presenting with headache. In that group, the rule was 100% sensitive and had low specificity for the diagnosis of SAH. A very sensitive rule is indeed needed to avoid missing dangerous diagnoses. However, the lack of applicability of the rule to the large majority of patients presenting with headache to the ED deserves attention.

In our cohort, 80% of patients underwent cranial CT or LP, and no cases of SAH were missed in the usual course of patient care. Application of the rule in our cohort would have suggested further investigation indicated in nearly 93% of patients, a 16% increase (absolute increase of 13%). These data suggest that applying the rule to our practice setting would increase health care utilization without improving patient safety [12].

4.1. Limitations

Our study has several potential limitations. First, in medical record review studies, missing data can occur [13]. We excluded 310 patients in whom whether the headache reached maximal intensity in less than 1 hour was not recorded, which may have introduced bias into our results. The [Hospital name here] ED is an academic tertiary care center and potentially prone to referral bias. To decrease the risk of referral bias, patients referred with the diagnostic of SAH were excluded. It is possible that a few patients with SAH were dismissed from the ED and subsequently diagnosed at another medical facility or died in the out-of-hospital setting. However, the exhaustive detail and reliable follow-up data available from review of the original inpatient and outpatient medical records in our setting suggest that this is unlikely [14]. We also reviewed the Social Security Death Index database for patients who did not have a subsequent visit documented in the electronic medical record (7.9% of the patients) and did not identify any deaths within 30 days of the ED visit.

In summary, the OSAH rule is relatively simple, uses data easily available in the history and physical examination, and is very sensitive. However, its applicability to only a small minority of patients presenting to the ED with headache and no increase in the rate of diagnosis of SAH limits its potential impact in our setting.

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Appendix A. Definitions for SAH study

1. Headache reaching maximum intensity in 1 hour
   - "Yes" = Clear documentation of headache that peaked and reached maximum intensity within 1 hour
   - "Unknown" = No clear documentation. Further classified by the following options:
     - Sudden: Fast, sudden onset, or acute (included for data analysis as a "yes" but delineated separately for data integrity)
     - Gradual: Suspected to be slow, such as onset over multiple hours or days (will be analyzed as a "no" but delineated here for data integrity), insidious onset.
     - Unknown: No onset description given, or unclear documentation
2. No = Clear documentation that headache was gradual in onset and reached maximum intensity over greater than 1 hour or an initially sudden onset headache that is clearly described as progressive over greater than 1 hour's time. Thunderclap headache: Headache that was sudden in onset, also described as fast onset or acute onset. No requirement for severity for this descriptor.

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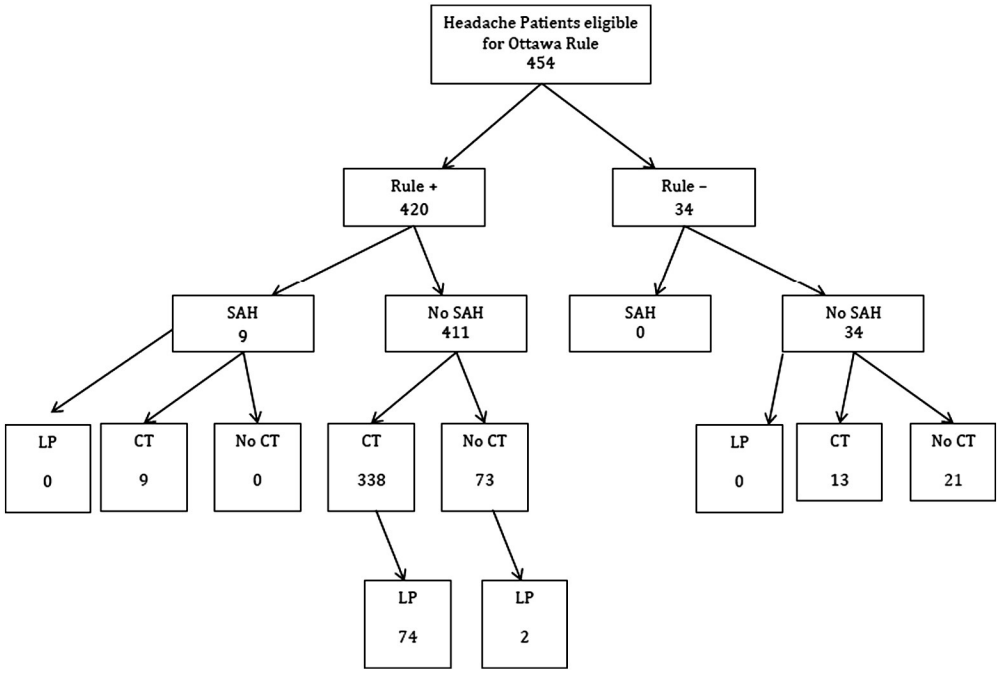

Fig. 2. Resource utilization and testing among the eligible patients.

3. Neck pain: Pain that originates in neck or radiates down from the head to the neck, stiff neck, pain in the paravertebral muscles or midline of the neck.
4. New neurologic deficit: Objective demonstration of neurologic deficit on the examination in the emergency department, including visual deficit, gait change, balance change, motor deficit, or sensory deficit if measurable. Also includes confusion, altered mental status, and seizures.
5. History of recurrent headaches: Patient who is described to have "chronic headaches" (assumed to be ≥6 months and ≥3 episodes if not explicitly mentioned) and who is presenting for evaluation of headache similar in character and intensity to their usual headache, regardless of duration.
6. Hydrocephalus: Any documented history of hydrocephalus including pseudotumor cerebri/idiopathic intracranial hypertension.
7. History of brain tumor: Any documented history of intracranial mass including benign lesions such as meningioma or schwannoma and pituitary tumors.

Diagnosis Categories:

Benign headache: Cephalgia, acute cephalgia, chronic headache, tension headache, headache due to decreased analgesia, acute headache, headache, head pain, headache, headache NOS, indeterminate headache, intermittent headache, mixed type HA, generalized HA, persistent HA, recurrent HA, stress HA

Migraine: 1-sided headache, migraine headache

Other benign headache: neuropathic pain, cluster headache, post-GI procedure headache, shingles, postoperative headache, post-LP, trigeminal neuralgia, V3 distribution cephalgia, postchemotherapy, occipital neuralgia.

Ischemic stroke: CVA.

Transportation:

Other: fixed wing aircraft, helicopter, law enforcement, carried, helicopter external

ALS/BLS Surface ambulance: Medical van, ALS/BLS ambulance

Table 3
Comparison of discharge diagnosis by inclusion in the rule, n = 4866

Discharge diagnosis	Excluded, n = 4412	Included, n = 454
	n (%)	n (%)
Benign headache	1888 (43)	295 (65)
Migraine headache	1051 (24)	62 (14)
Other benign cause	117 (3)	9 (2)
SAH	13 (<1)	9 (2)
Viral illness	82 (2)	1 (<1)
Postcoital headache	0	2 (<1)
Ischemic stroke or transient ischemic attack	25 (1)	7 (2)
Sinusitis	71 (2)	2 (<1)
Vasovagal syncope	7 (<1)	0
Neck strain	35 (1)	3 (1)
Intracerebral hemorrhage	11 (<1)	1 (<1)
Subdural hematoma	28 (1)	1 (<1)
Brain tumor	12 (<1)	1 (<1)
Bacterial meningitis	0	1 (<1)
Other	1072 (24)	60 (13)

One hundred sixty-eight visits were missing a discharge diagnosis.

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