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RESEARCH SUBMISSIONS

Epidemiology, investigation, management, and outcome of headache in emergency departments (HEAD study)—A multinational observational study

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Abstract

Objective: To describe the epidemiology of nontraumatic headache in adults presenting to emergency departments (EDs).

Abbreviations: CT, computed tomography; CTA, computed tomography angiogram; ED, emergency department; MRI, magnetic resonance imaging; NSAID, nonsteroidal anti-inflammatory drugs; SAH, subarachnoid hemorrhage.

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Background: Headache is a common reason for presentation to EDs. Little is known about the epidemiology, investigation, and treatment of nontraumatic headache in patients attending EDs internationally.

Methods: An international, multicenter, observational, cross-sectional study was conducted over one calendar month in 2019. Participants were adults (≥18 years) with nontraumatic headache as the main presenting complaint. Exclusion criteria were recent head trauma, missing records, interhospital transfers, re-presentation with same headache as a recent visit, and headache as an associated symptom. Data collected included demographics, clinical assessment, investigation, treatment, and outcome.

Results: We enrolled 4536 patients (67 hospitals, 10 countries). "Thunderclap" onset was noted in 14.2% of cases (644/4536). Headache was rated as severe in 27.2% (1235/4536). New neurological examination findings were uncommon (3.2%; 147/4536). Head computed tomography (CT) was performed in 36.6% of patients (1661/4536), of which 9.9% showed clinically important pathology (165/1661). There was substantial variation in CT scan utilization between countries (15.9%–75.0%). More than 30 different diagnoses were made. Presumed nonmigraine benign headache accounted for 45.4% of cases (2058/4536) with another 24.3% classified as migraine (1101/4536). A small subgroup of patients have a serious secondary cause for their headache (7.1%; 323/4536) with subarachnoid hemorrhage (SAH), stroke, neoplasm, non-SAH intracranial hemorrhage/hematoma, and meningitis accounting for about 1% each. Most patients were treated with simple analgesics (paracetamol, aspirin, or nonsteroidal anti-inflammatory agents). Most patients were discharged home (83.8%; 3792/4526). In-hospital mortality was 0.3% (11/4526).

Conclusion: Diagnosis and management of headache in the ED is challenging. A small group of patients have a serious secondary cause for their symptoms. There is wide variation in the use of neuroimaging and treatments. Further work is needed to understand the variation in practice and to better inform international guidelines regarding emergent neuroimaging and treatment.

KEYWORDS
emergency department, headache, imaging

INTRODUCTION

Headache disorders are the commonest neurological problems globally and a major public health problem.[1] It is a common reason for presentation to emergency departments (EDs) around the world. The proportion of ED attendances attributed to headache varies according to geographical regions, ranging from 1.35% in Australia[2] to 2.5% in the United States,[3] 2.9% in Italy, and 3.5% in Austria.[4]

There are a wide range of possible causes of headache including primary headaches (migraine, tension-type headache, trigeminal autonomic cephalalgias, etc.) and secondary headaches including those attributable to trauma, a cranial or cervical vascular disorder, nonvascular intracranial disorders, infection, substance/substance withdrawal, and disorders of the head/neck structures.[5] In previous studies, most cases had a benign cause, and the vast majority of patients were discharged home.[2,6,7]

Little is known about the epidemiology of nontraumatic headache in patients attending EDs internationally. Diagnoses, patterns of investigation, treatment, and outcome may vary across countries or regions. For example, the proportion of patients with headache in the ED who undergo head computed tomography (CT) varies considerably, with studies reporting rates between 14.0% and 53.2%.[4,6] National and international guidelines for neuroimaging in headache disorders rely on clinical judgment, International Headache Society diagnostic criteria, focal neurological signs, and the so-called "red flag" features to guide decision-making about the need for neuroimaging and the mode of neuroimaging.[8–10]

Data on treatment provided to people presenting to the ED with headache are limited, although there is known variation in practice.[1–13] Whether this variation is at the clinician, hospital, or regional level, or a combination of these factors is unknown. It is also unknown whether the variation in practice is due to lack of evidence

with respect to effective treatment options. There is also international concern about the use of opioids (especially codeine and pethidine/meperidine) and their negative health and societal impacts.[14] Headache is one condition implicated in this debate.[13,15]

The assessment of headache in the ED is complicated by a multiplicity of guidelines and rules. These may be general such as the Australasian College for Emergency Medicine guidelines on diagnostic imaging (including head CT),[9] the American College of Emergency Physicians clinical policy in the evaluation and management of acute headache,[10] and UK guidelines such as those produced by the Royal College of Emergency Medicine and the National Institute for Health and Care Excellence.[16,17] There are also condition-specific clinical decision rules (such as the Ottawa Subarachnoid Hemorrhage (SAH) Rule[18]) and treatment guidelines for individual conditions.[19]

This study aims to describe the real-world epidemiology of nontraumatic headache in adults presenting to the ED internationally, including clinical features, investigations, treatment, diagnosis, and outcome and to describe associations between clinical features and a defined serious secondary headache diagnosis.

METHODS

Design and settings

This multicenter, observational, cross-sectional study was conducted over one calendar month in 2019 (for most sites in March 2019; the last site was in October 2019). There were minor variations in the data collection period because of ethical approval process delays. Participating sites were recruited from ED research networks established for previous studies in Europe, Asia, Australasia, and by contact with emerging research groups. Sites vary in size from small rural centers to large tertiary hospitals.

Participants and recruitment

Participants were adult patients (age ≥18 years) who reported (either individually or via a carer) nontraumatic headache as their main presenting complaint, irrespective of the presence of acute neurological features. Exclusion criteria were history of trauma to the head within 48 h of presentation, missing records, interhospital transfers, representation with the same headache as a recent previous visit, and headache as an associated symptom rather than the main complaint. Determination of whether headache was the primary complaint was at the discretion of the local researcher based on all available data. Except in jurisdictions where consent was required (see below), participating institutions were instructed to include all patients presenting with headache within the enrolment period.

Qualifying adult patients presenting during the study period were identified from ED data management systems. Patients were identified prospectively but, depending on site resources, some data were collected retrospectively. There was a need for data collection flexibility because some sites did not have the research support infrastructure to collect truly prospective data, especially if the local ethics committee required informed consent. We considered that the advantages, particularly generalizability, of including as many EDs as possible, outweighed the limitations associated with retrospective data collection.

Data collected and data collection process

Data collected included patient characteristics, clinical assessment, investigation, treatment, diagnosis, disposition, and outcome. Data were collected from clinical records by local researchers onto piloted data forms or directly into the study database (depending on local processes and resources). Study data were collected and managed using Research Electronic Data Capture (REDcapTM) tools.[20] A copy of the data collection tool is included as Appendix 1. Hospitals were also asked to complete an online survey that included data on total ED presentations and disposition for the study period and availability of CT and magnetic resonance imaging (MRI) scans at their site.

Outcomes of interest

Our main aims were to describe the epidemiology and clinical outcomes of patients presenting to the ED with nontraumatic headache and associations between clinical features and a defined serious secondary headache diagnosis. We also aimed to describe neuroimaging rates, the proportion of patients with a defined serious secondary cause for headache, the distribution of patient characteristics and clinical features, the distribution of physician-based ED diagnoses, treatment patterns, disposition from the ED, in-hospital mortality, the proportion of headache patients in the ED, hospital and intensive care unit patient loads, and between-hospital and between-country variation of investigation rates. Note, we have chosen to report migraine and nonmigraine primary headache separately because of potentially different therapeutic approaches.

Definitions

Severe headache was defined as pain score 7–10. Thunderclap onset headache was defined as headache peaking instantly or almost instantly and lasting at least 5 min. This was distinguished from headache that reached peak intensity within 1 h but not instantly. New neurological signs on examination were neurological signs not known to be pre-existing based on all available data including patient/carer report. We defined important findings on head CT as SAH, intracranial hemorrhage/hematoma (acute or chronic), signs suggestive of intracranial hypertension, venous thrombosis, stroke, neoplasm (benign or malignant), vascular abnormality without bleeding (aneurysm, arteriovenous malformation, etc.), hydrocephalus, and signs

suggestive of intracranial infection, irrespective of their relationship to final diagnosis. We defined nonmigraine benign headache as the composite of those classified as primary, tension-type, cluster, or musculoskeletal headache. Migraine is reported separately. We defined serious secondary headache as the composite of headache due to SAH, intracranial hemorrhage, meningitis, encephalitis, cerebral abscess, neoplasm, hydrocephalus, vascular dissection, stroke, hypertensive crisis or pregnancy-related hypertension, temporal arteritis, idiopathic intracranial hypertension, or ventriculoperitoneal shunt complications. We chose to use physician-based diagnosis rather than International Classification of Headache Disorders (ICHD) classification because most ED data management systems have coding that does not map to ICHD classifications and they are rarely used in the ED.

Analysis and sample size

This is the primary analysis of these data. Analyses were predominantly descriptive in nature (median, interquartile range [IQR], frequency, percent). Comparison of proportions was made by the chi-squared test (one-sided) or Fisher's exact test (two-sided), as appropriate. Assumptions were verified using histograms. Confidence intervals were calculated using the Wilson method without continuity correction. Statistical significance was defined as $p < 0.05$. The level of missing data for variables is reported. Cases with missing data for a variable were excluded from analyses related to that variable but included in other analyses. Intraclass correlations were calculated to identify similarities (if any) between patient outcomes, specifically whether an investigation was performed. A multilevel binary logistic regression analysis was performed to explore variations in investigations between hospitals and between countries. Analyses were performed using Stata v16 (College Station, TX) and included intraclass correlation. Formal sample size calculation was not performed due to the descriptive nature of the study.

RESULTS

We enrolled 4536 patients from 67 hospitals in 10 countries (Australia 28, New Zealand 9, Turkey 9, United Kingdom 7, Singapore 4, Belgium 4, France 3, Romania 1, Hong Kong 1, and Israel 1). The largest contributing country was Australia (39.2% of cases), followed by Turkey (21.7%), New Zealand (13.1%), and Singapore (12.8%). All other countries contributed <10% of cases (Online Appendix 2).

Patient demographics, comorbidity, and chronic medications

The median age was 41 (IQR: 29–55) years with a predominance of female patients (64.1%, 95% CI: 62.7%–65.5%) (Table 1). Most patients (65.2%, 95% CI: 63.8%–66.6%) self-presented to the ED without any physician referral or ambulance conveyance. Headache had been present for <24 h in 45.4% of patients (95% CI: 44.0%–46.9%). Past medical history and chronic medications are shown in Online Appendix 3. A large proportion (43.1%, 95% CI: 41.6%–44.5%) of patients had no relevant past medical history, and 72.7% (95% CI: 71.3%–73.9%) did not take regular medications. Of note, 21% of patients (95% CI: 19.9%–22.2%) had previous physician-diagnosed migraine, and a further 14.1% (95% CI: 13.1%–15.1%) had a history of nonmigraine recurrent headache. A variety of preventive medications were taken (Online Appendix 3). Long-term codeine preparations were taken by 1.4% of patients (95% CI: 1.1%–1.8%). Some

TABLE 1 Patient characteristics

Variable	Result (total *N* = 4536)		Missing data
	N, %	IQR/95% CI	
Age (years)	41	29–55	0
Age >50 years	1451, 32%	30.7%–33.4%	0
Sex (male)	1627, 35.9%	35.4%–37.3%	1
Duration of symptoms			70
<24 h	2060, 45.4%	44.0%–46.9%	
1–3 days	1021, 22.5%	21.3%–23.8%	
>3 days	1385, 30.5%	29.2%–31.9%	
Referral by a doctor	788, 17.4%	16.3%–18.5%	0
Arrival by ambulance	791, 17.4%	16.4%–18.6%	0
Triage category			0
Immediate	77, 1.7%	1.4%–2.1%	
Urgent	2294, 50.6%	49.1%–52.0%	
Nonurgent	2165, 47.7%	46.3%–49.2%	

Note: Data are reported as median (interquartile range) or *N*, % (95% confidence interval). 95% CI were estimated using http://vassarstats.net/prop1.html Method Wilson, no continuity correction.

patients (35.5%, 95% CI: 34.1%–36.9%) had taken medication before attending the ED, the most common being paracetamol (70.7%, 95% CI: 68.4%–72.9%) and nonsteroidal anti-inflammatory drugs (NSAIDs) (38.1%, 95% CI: 35.8%–40.5%).

Clinical features

More than half (54.8%, 95% CI: 53.4%–53.6%) of the patients had gradual onset of symptoms (Table 2). "Thunderclap onset headache" accounted for 14.2% of cases (95% CI: 13.2%–15.3%), with a further 8.1% of patients (95% CI: 7.3%–8.9%) reporting peak intensity within 1 h on headache onset. Pain was rated as severe (pain score >7) in 27.2% (95% CI: 26.0%–28.5%). Nausea and/or vomiting was present in 40.7% of patients (95% CI: 39.2%–42.1%). New neurological findings on examination were uncommon (3.2%, 95% CI: 2.8%–3.8%). An extended report of the clinical features is available in Online Appendix 4.

Investigations

Investigations are summarized in Table 3. Overall, 36.6% of patients (95% CI: 35.2%–38.0%) underwent noncontrast head CT, of which 9.9% showed important pathology (95% CI: 8.6%–11.5%). MRI was performed in 3.3% of cases (95% CI: 2.9%–3.9%), whereas 4.8% (95% CI: 4.2%–5.5%) underwent CT angiography (CTA). There was considerable variation in CT rates by country, ranging from 15.9% in Romania to 75.0% in Israel ($p < 0.001$, omnibus chi-squared, Online Appendix 5 and Online Figures 1 and 2). A plot of CT scan rate versus the proportion of scans with serious pathology is shown in Figure 1. Lumbar puncture was performed in 3.8% of patients (95% CI: 3.3%–4.4%) and of these, 67.3% (95% CI: 59.9%–73.8%) were reported as normal and another 11.1% (95% CI: 7.2%–16.7%) were inconclusive. On multilevel binary logistic regression analysis with country and hospital modeled as random effects, there was greater variation between hospitals than between countries for rates of CT scan but conversely greater variation between countries than between hospitals for lumbar puncture (Online Appendices 6 and 7). Fundoscopy was performed infrequently (7.4%, 95% CI: 6.7%–8.2%), of which 88.4% (95% CI: 84.5%–91.4%) were normal.

Diagnosis, treatment, and outcome

There was a wide variety of diagnoses made in the ED (Table 4). Nonmigraine benign headache (primary, nonmigraine, tension-type, musculoskeletal, cluster) accounted for almost half of the cases (45.4%, 95% CI: 43.9%–46.8%). Headache was classified as migraine in a further 24.3% (95% CI: 23.0%–25.5%). A serious secondary cause for headache was found in 7.1% of patients (95% CI: 6.4%–7.9%), of which SAH, stroke, neoplasm, non-SAH intracranial hemorrhage/hematoma, and meningitis accounted for about 1% each.

Seventy-six percent of patients were treated with medication in the ED (95% CI: 74.8%–77.3%). The most commonly administered initial medications were paracetamol (34.7%, 95% CI: 33.4%–36.1%) followed by NSAIDs, including aspirin (33.2%, 95% CI: 31.9%–34.6%). Opioids were administered in 18.3% of cases (95% CI: 17.3%–19.5%). Antiemetics (prochlorperazine, metoclopramide, or ondansetron) were administered in 27.5% of cases (95% CI: 26.1%–29.0%). Triptans were used rarely (1%, 95% CI: 0.8%–1.4%). Rescue medication was administered to 27.5% of patients (95% CI: 26.1%–29.0%) who had received an initial therapy, of whom 38.0% received opioids (95% CI: 35.0%–41.2%) (Table 5 and Online Appendix 8).

In terms of disposition, the vast majority of participants were discharged home either directly from the ED or from an ED observation unit (3792/4526, 83.8%, 95% CI: 82.7%–84.8%). A total of 633 (14%, 95% CI: 13.0%–15.0%) patients were admitted to a noncritical care ward, whereas a further 33 (0.7%, 95% CI: 0.5%–1.0%) were admitted to a critical care unit. Only three patients (0.07%, 95% CI: 0.02%–0.2%) were transferred directly from the ED to an operating theater, and one (0.02%, 95% CI: 0%–0.1%) proceeded directly to interventional radiology. Eleven patients died in the ED or during their index hospital visit (0.2%, 95% CI: 0.1%–0.4%).

Imaging availability and contribution to ED caseload

Sixty-four sites provided data on imaging availability. Regarding CT availability, 62 hospitals reported 24/7 availability (96.9%, 95% CI: 89.3%–99.1%), with one hospital having CT available in office hours only and one on call. Regarding MRI availability, 36 hospitals reported that an MRI could be obtained 24/7 (56.3%, 95% CI: 44.1%–67.7%) but there were a variety of limitations on after-hours MRI. Nineteen hospitals reported office hours MRI only (29.7%, 95% CI: 19.9%–41.8%), and eight had no onsite MRI compatibility (12.5%, 95% CI: 6.5%–22.8%).

Sixty-two hospitals provided detailed ED caseload data (covering 3728 enrolled patients, 82%). Overall, headache patients accounted for 1% of ED caseload (3728/352,514, 95% CI: 1%–1.1%). The proportion of ward admissions attributable to headache is 0.84% (640/76,379, 95% CI: 0.78%–0.91%). Headache accounted for 1% of critical care admissions (37/3639, 95% CI: 0.7%–1.4%).

DISCUSSION

This study describes the clinical characteristics, epidemiology, and outcome of a large international cohort of patients presenting to the ED with nontrauma-related headache as their main presenting symptom. The primary role of the ED physician is to exclude serious pathology.[21] The so-called "red flags" have been described to help identify secondary headaches.[22] These include systemic symptoms including fever; a history of neoplasm; neurologic deficit (including decreased consciousness); sudden or abrupt onset; older age (onset after 65 years); pattern change or recent onset of new headache; positional headache,

TABLE 2 Clinical features

Clinical features	Present (total $N = 4536$)		Serious secondary cause identified ($N = 323$)	Serious secondary cause not identified ($N = 4213$)	p value for comparison of proportion with serious secondary cause identified
	N, %	95% CI			
Onset of symptoms					
Gradual	2486, 54.8%	53.4%–56.3%	153, 6.2%	2333, 93.8%	$p < 0.001$[a]
Sudden or thunderclap (instant peak)	644, 14.2%	13.2%–15.3%	72, 11.2%	572, 88.8%	
Peak intensity <1 h	366, 8.1%	7.3%–8.9%	24, 6.6%	342, 93.4%	
Unknown	1040, 22.9%	21.7%–24.2%	74, 7.1%	966, 92.9%	
Head trauma within the last week	111, 2.5%	2.0%–2.9%	11, 9.9%	100. 90.1%	$p = 0.332$
Location of headache					
Generalized	2597, 57.3%	55.8%–58.7%	195, 7.5%	2402, 92.5%	$p = 0.018$[a]
Unilateral	1290, 28.4%	27.2%–29.8%	70, 5.4%	1220, 94.6%	
Unclear	649, 14.3%	13.3%–15.3%	58, 9.0%	591, 91.0%	
Worst headache ever	582, 12.8%	11.9%–13.8%	66, 11.3%	516, 88.7%	$p < 0.0001$
Severity					
Mild (pain score ≤3)	815, 18%	16.9%–19.1%	42, 5.2%	773, 94.8%	$p = 0.671$[a]
Moderate (pain score 4–7)	1869, 41.2%	39.8%–42.6%	109, 5.8%	1760, 94.2%	
Severe (pain score >7)	1235, 27.2%	26.0%–28.5%	120, 9.7%	1115, 90.3%	
Unclear	617, 13.6%	12.6%–14.6%	52, 8.4%	565, 91.6%	
Reported neck pain or stiffness	756, 16.7%	15.7%–17.8%	74, 9.8%	682. 90.2%	$p = 0.002$
Nausea or vomiting	1844, 40.7%	39.2%–42.1%	155, 8.4%	1689, 91.6%	$p = 0.005$
Syncope or loss of consciousness	136, 3%	2.5%–3.5%	30, 22.1%	106, 77.9%	$p < 0.0001$
Reported photophobia	940, 20.7%	19.6%–21.9%	73, 7.8%	867, 92.2%	$p = 0.388$
Reported new limb weakness (current/transient; unilateral or bilateral)	201, 4.4%	3.9%–5.1%	41, 20.4%	160, 79.6%	$p < 0.0001$
Reported new limb paresthesia (current/transient; unilateral or bilateral)	268, 5.9%	5.3%–6.6%	29, 10.8%	239, 89.2%	$p = 0.015$
Reported new speech difficulty (current/transient)	152, 3.4%	2.9%–3.9%	42, 27.6%	110, 72.4%	$p < 0.0001$
New visual disturbance (current/transient)	600, 13.2%	12.3%–14.3%	62, 10.3%	538, 89.7%	$p = 0.001$
Subjective fever or rigors	406, 9%	8.2%–9.8%	42, 10.3%	364, 89.7%	$p = 0.008$
Reported rash	56, 1.2%	1.0%–1.6%	7, 12.5%	49, 87.5%	$p = 0.115$

TABLE 2 (Continued)

Clinical examination	Present (*N*, %, total *N* = 4536)	95% CI			
Pulse rate >110 beats per min	149, 3.3%	2.8%–3.9%	17, 11.4%	132, 88.6%	$p = 0.037$[a]
Missing data	41		4		
Systolic BP > 160 mm Hg	540, 12.7%	11.2%–13.1%	87, 16.1%	453, 83.9%	$p < 0.0001$[a]
Systolic BP < 90 mm Hg	8, 0.2%	0.1%–0.4%	1, 12.5%	7, 87.5%	$p = 0.555$[a]
Missing BP data	63		4		
Temperature >38°C	104, 2.6%	2.2%–3.2%	21, 20.2%	83. 79.8%	$p < 0.001$[a]
Missing data	588		36		
Glasgow Coma Score					
15	3921, 98.0%	97.6%–98.4%	265, 6.8%	3656, 93.2%	$p = 0.003$[a]
13–14	62, 1.6%	1.2%–2.0%	25, 40.3%	37, 59.7%	
<13	16, 0.4%	0.3%–0.7%	13, 81.3%	3, 18.7%	
Missing data	537		20		
Rash on examination	70, 1.5%	1.2%–1.9%	10, 14.3%	60, 85.7%	$p = 0.019$
Confusion on examination	68, 1.5%	1.2%–1.9%	27, 39.7%	41, 60.3%	$p < 0.0001$
Meningism on examination	63, 1.4%	1.1%–1.8%	26, 41.3%	37, 58.7%	$p < 0.0001$
Limited neck flexion on examination	90, 2%	1.6%–2.4%	10, 11.1%	80, 88.9%	$p = 0.137$
New neurological signs on examination	147, 3.2%	2.8%–3.8%	50, 34.0%	97, 66.0%	$p < 0.0001$

Note: 95% CI were estimated using http://vassarstats.net/prop1.html; Method Wilson, no continuity correction.

[a]Excludes unknown/unclear/missing data.

TABLE 3 Investigations

Investigations (*N*, %)	Total sample 4536		Missing data/not taken
	N, %	95% CI	
Lumbar puncture performed	171, 3.8%	3.3%–4.4%	0
Normal	115, 67.3%	59.9%–73.8%	0
Suggestive of infection	27, 15.8%	11.1%–22%	0
Suggestive of subarachnoid hemorrhage	5, 2.9%	1.3%–6.7%	0
Suggestive of raised intracranial pressure	5, 2.9%	1.3%–6.7%	0
Inconclusive	19, 11.1%	7.2%–16.7%	0
Head CT performed	1661, 36.6%	35.2%–38.0%	0
Normal	1366, 82.2%	80.3%–84.0%	
Subarachnoid hemorrhage	31, 1.9%	1.3%–2.6%	
Other bleed	61, 3.7%	2.9%–4.7%	
Abscess or intracranial infection	2, 0.1%	0.03%–0.4%	
Neoplasm	35, 2.1%	1.5%–2.9%	
Stroke	16, 1%	0.6%–1.6%	
Sinusitis	40, 2.4%	1.8%–3.3%	
Suggestive of intracranial hypertension	2, 0.1%	0.03%–0.4%	
Venous thrombosis (acute or chronic)	7, 0.4%	0.2%–0.9%	
Vascular abnormality without acute complication (including aneurysm)	10, 0.6%	0.3%–1.1%	
Hydrocephalus	1, 0.06%	0.01%–0.3%	
Other (including chronic changes, extracranial findings)	90, 5.4%	4.4%–6.6%	
Combined acute clinically important abnormality (excluding sinusitis and other)	165, 9.9%	8.6%–11.5%	
MRI performed	151, 3.3%	2.9%–3.9%	0
Normal	89, 58.9%	51.0%–66.5%	
Intracranial bleed	3, 2%	0.7%–5.7%	
Abscess	1, 0.7%	0.1%–3.7%	
Neoplasm	16, 10.6%	6.6%–16.5%	
CT angiography performed	219, 4.8%	4.2%–5.5%	0
Normal	158, 72.1%	65.9%–77.7%	
Aneurysm with bleed	19, 8.7%	5.6%–13.2%	
Aneurysm without bleed	8, 3.7%	1.9%–7%	
Arterial dissection	3, 1.4%	0.5%–4.0%	
CT plus MRI	114, 2.5%	2.1%–3.0%	
CT plus CTA	196, 4.3%	3.8%–5.0%	

Note: 95% CI were estimated using http://vassarstats.net/prop1.html Method Wilson, no continuity correction. Note patients may have had more than one investigation and investigations may have been sequential.

Abbreviations: CT, computed tomography; MRI, magnetic resonance imaging.

precipitated by sneezing, coughing, or exercise; papilledema, progressive headache and atypical presentations; pregnancy or puerperium; painful eye with autonomic features; posttraumatic onset of headache; pathology of the immune system such as HIV; and painkiller overuse or new drug at onset of headache.[22] Severe, persistent headache that rapidly reaches maximum intensity has been associated with SAH, vascular dissections, venous sinus thrombosis, and reversible cerebral vasoconstriction syndromes.[23,24] Our results suggest that these features are common (sudden onset 14.2%, severe pain 27.2%, worst headache ever 12.8%). A serious secondary cause for headache was found in 7.1% of cases. Less than 10% of patients reporting severe headache were found to have a serious secondary cause, challenging the validity of this "red flag" in isolation. This highlights the diagnostic challenge faced in the ED by patients with nontraumatic headache, which is further supported by the myriad of possible diagnoses we identified to explain this primary symptom (Table 4).

Extensive diagnostic workup and imaging in the ED are generally not required for the majority of patients presenting with headache.[10]

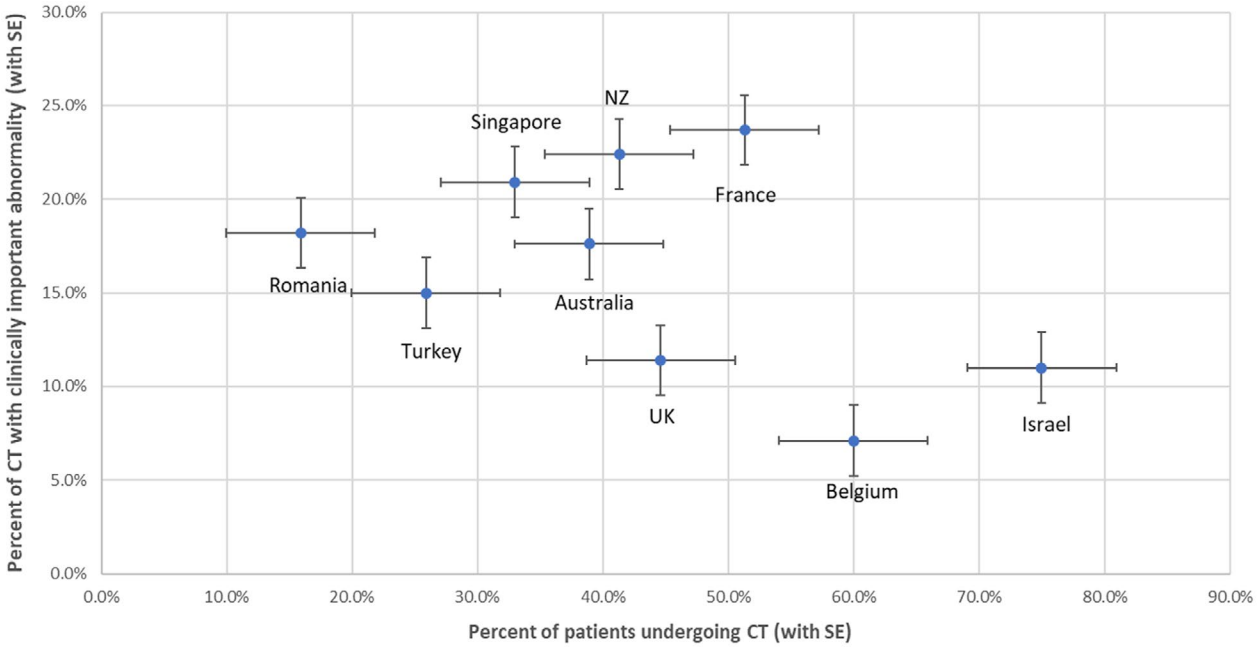

FIGURE 1 CT rate versus proportion of CT with clinically important abnormality by country [Color figure can be viewed at wileyonlinelibrary.com]

Imaging tests, typically head CT, are warranted in those presenting with high-risk features.[25] Several decision analyses have been formulated to rationalize the use of head CT.[26,27] That said, imaging can fail to diagnose serious secondary causes such as meningitis.

Fundoscopic examination has been proposed to assist in the determination of head CT requirement. A very low number of patients in our cohort underwent fundoscopy (7.4%). This suggests that fundoscopy is no longer a standard test in the ED. Reasons for this might include lack of training, resources or time, the ED environment, lack of confidence in the test, and ready availability of neuroimaging.[28] Research also suggests that fundoscopy in the ED is inaccurate for detection of some serious conditions.[29] In the research team's experience, fundoscopy has little influence on decision-making regarding investigation and treatment. In the wake of the COVID-19 pandemic and the close proximity required for this test, fundoscopy may be considered a high-risk procedure and inadvisable. In the future, portable retinal cameras in the ED may change the way that patients with headache are assessed. They have been shown to impact diagnostic accuracy in the ED with headaches and common neurological symptoms.[30,31]

Despite availability of guidelines, the possibility of missing a serious diagnosis may lead to the performance of noncontrast head CT scans in a relatively high proportion of ED patients with headache. Previous research found head CT to be negative in more than 90% of patients with headache suspected to have SAH as an indication for the scan.[32] Our data suggest a similar trend with overall 82.2% of head CT scans found to be normal. However, considerable variations in proportions of positive CT abnormalities (range from 7.1% to 34.3%) exist between different regions of our study cohort. There is no accepted definition of an "acceptable" yield for head CT. Our study was not designed to explore reasons for any variation in head CT rates, but this is a question worthy of further research. If neuroimaging is overused it comes with considerable cost to the system, radiation, and inconvenience for patients. Guidelines do not seem to be effective in managing neuroimaging use and, at least theoretically, could increase the use of CT. Further research to better define the best balance between the rate of neuroimaging and missing serious diagnosis is needed. Other strategies such as empowering patients with knowledge regarding unwarranted testing may also be useful as part of a shared decision-making approach.[33]

Although over one-third of patients were referred by their primary care physicians (17.4%) or arrived by ambulance (17.4%), only 1.7% were triaged to immediate care in the ED (by relevant national triage scales). High numbers of ambulatory patients could contribute to overcrowding, unnecessary testing, and increased cost.[34] That said, 7.1% of patients were found to have a serious secondary cause for headache, 27% reported severe pain, and 40% reported nausea or vomiting that precluded oral analgesia. The yield of a serious secondary cause is only marginally less than that for major adverse events in patients with chest pain.[35] Whether some headache patients could be treated in an ambulatory care area rather than the ED is worthy of further evaluation.

Working diagnosis and severity of symptoms generally guide the types of medication prescribed.[36] Paracetamol and NSAIDs were the most commonly administered medications during our study, in line with almost 60% of patients reporting mild to moderate severity of headache. Of interest was the frequent use of opioids in our cohort (17.6%), which are associated with a high risk of medication overuse headache. Our study was not designed to determine whether opioid prescription was appropriate; however, overuse of opioids for headache in EDs has been suggested to

TABLE 4 Emergency department (ED) diagnosis

ED diagnosis (total sample 4536)	Number, %	Percent (95% CI)
Presumed primary nonmigraine headache (not otherwise classified)	1598, 35.2%	33.9%–36.6%
Migraine	1101, 24.3%	23.0%–25.5%
Tension-type headache	317, 7.0%	6.3%–7.8%
Viral illness (nonmeningitis)	204, 4.5%	3.9%–5.1%
Sinusitis	141, 3.1%	2.6%–3.7%
Post traumatic headache	76, 1.7%	1.3%–2.1%
Musculoskeletal	72, 1.6%	1.2%–2.0%
Cluster headache	71, 1.6%	1.3%–2.0%
Stroke/TIA		
All	68, 1.5%	1.2%–1.9%
Stroke	50, 1.1%	0.8%–1.5%
TIA	18, 0.4%	0.3%–0.6%
Hypertension		
All	64, 1.4%	1.1%–1.8%
Hypertension crisis/ urgency/malignant hypertension	11, 0.2%	0.1%–0.4%
Pregnancy-related hypertension	5, 0.1%	0.05%–0.3%
Hypertension-other	48, 1.1%	0.8%–1.4%
Non-SAH intracranial hemorrhage/hematoma	57, 1.3%	1%–1.6%
Meningitis (all)		
All	48, 1.1%	0.8%–1.4%
Viral	40, 0.9%	0.7%–1.2%
Bacterial	3, 0.07%	0.02%–0.2%
Unknown	5, 0.1%	0.05%–0.3%
Subarachnoid hemorrhage	44, 1.0%	0.7%–1.3%
Neoplasm	43, 1.0%	0.7%–1.3%
Trigeminal neuralgia/cranial neuralgia	34, 0.8%	0.5%–1.1%
Noncranial sepsis (e.g., pneumonia, UTI, tonsillitis, etc.)	32, 0.7%	0.5%–1%
Intracranial hypertension	27, 0.6%	0.4%–0.9%
Vertigo/BPPV	23, 0.5%	0.3%–0.8%
Post lumbar puncture headache	13, 0.3%	0.2%–0.5%
Ventriculoperitoneal shunt issues	12, 0.3%	0.2%–0.5%
Temporal arteritis	11, 0.2%	0.1%–0.4%
Dental cause	10, 0.2%	0.1%–0.4%
Anxiety or psychogenic	9, 0.2%	0.1%–0.4%
Alcohol-related hangover	8, 0.2%	0.09%–0.4%
Post coital headache	8, 0.2%	0.09%–0.4%
Aneurysm/vascular malformation	8, 0.2%	0.09%–0.4%
Toxicity	6, 0.1%	0.06%–0.3%
Hyponatremia	6, 0.1%	0.06%–0.3%
Herpes zoster of head and neck	6, 0.1%	0.06%–0.3%
Encephalitis	6, 0.1%	0.06%–0.3%
Vascular dissection	4, 0.09%	0.04%–0.2%
Hydrocephalus	4, 0.09%	0.04%–0.2%
Seizure	3, 0.07%	0.02%–0.2%
Analgesia overuse syndrome	2, 0.04%	0.01%–0.2%
Glaucoma	2, 0.04%	0.01%–0.2%
Cerebral abscess	1, 0.02%	0%–0.1%
Other	157, 3.5%	3.0%–4.0%
Unclear	240, 5.3%	4.7%–6%
Aggregate nonmigraine benign cause	2058, 45.4%	43.9%–46.9%
Aggregate serious secondary cause	323, 7.1%	6.4%–7.9%

Note: 95% CI were estimated using http://vassarstats.net/prop1.html Method Wilson, no continuity correction.

Abbreviations: BPPV, benign paroxysmal positional vertigo; SAH, subarachnoid hemorrhage; TIA, transient ischemic attack; UTI, urinary tract infection.

have negative effects.[37] Overprescription has been attributed to factors including lack of physician education.[38] The current opioid crisis has prompted heightened interest in curbing inappropriate use including tightening of regulations through government legislations.[39,40]

The proportion of patients reporting the so-called thunderclap onset headache in our study cohort who had a final diagnosis of SAH is significantly lower than previously reported. Some studies have reported that up to 40% of patients with this symptom have a SAH.[41] The difference may lie in study design including selection bias toward patients admitted to specialist units with suspected SAH. It could also represent under-investigation in the ED. This study was not designed to address this issue.

The finding that only 27% of patients reporting new speech difficulty had a serious secondary cause for their headache identified might seem surprising. In fact, only 15 (15/152; 9.9%, 95% CI: 6.1%–15.7%) had speech deficit identified on examination. Of these, 66.7% (10/15; 95% CI: 41.7%–84.8%) had a serious secondary cause identified. This highlights that there is sometimes a mismatch between people's perception of their symptoms and objective clinical findings. This is consistent with the finding that 66.7% of patients with new neurological signs on examination had a serious secondary cause for their headache identified in the ED. It is also possible that a serious secondary cause was identified after the ED phase of care.

The finding that viral meningitis was more common than bacterial meningitis is also noteworthy. It may reflect high immunization rates in the participating countries.

TABLE 5 Initial treatment

Initial treatment—within 30 min of medical assessment (total sample 4536)					
Any medication given	**3449, 76.0% (74.8%–77.3%)**				**Missing data**
Note: More than one medication is possible	**Total (*N*, %, 95% CI)**	**95% CI**	**Oral**	**Parenteral (IM/IV)**	**1**
Paracetamol	1575, 34.7%	33.4%–36.1%	1275	300	
Aspirin	141, 3.1%	2.6%–3.7%	140	1	
NSAID (non-aspirin)	1367, 30.1%	28.8%–31.5%	634	733	
Any opioid	832, 18.3%	17.3%–19.5%			
Codeine-containing medication	298, 6.6%	5.9%–7.3%	285	14	
Oxycodone	231, 5.1%	4.5%–5.8%	228	3	
Pethidine/meperidine	8, 0.2%	0.09%–0.4%	2	6	
Other opioid	295, 6.5%	5.8%–7.3%	101	194	
Triptan	48, 1.0%	0.8%–1.4%	32	16	
Chlorpromazine	145, 3.2%	2.7%–3.8%	11	134	
Prochlorperazine	282, 6.2%	5.6%–7%	66	216	
Droperidol/haloperidol	22, 0.5%	0.3%–0.7%	6	16	
Metoclopramide	451, 9.9%	9.1%–10.8%	101	350	
Ondansetron	412, 9.1%	8.3%–10%	281	131	
Ergots	5, 0.1%	0.05%–0.3%	5	0	
Corticosteroid	38, 0.8%	0.06–1.1%	12	26	
Antibiotic/antiviral agent	62, 1.4%	1%–1.8%	19	43	
Other treatments					
Oxygen	54, 1.2%	0.09%–1.6%			
Acupuncture	1, 0.02%	0%–0.1%			
IV fluids	548, 12.1%	11.2%–13.1%			

Note: 95% CI were estimated using http://vassarstats.net/prop1.html Method Wilson, no continuity correction.

LIMITATIONS

Our study has several strengths. We report the real-world snapshot on what is happening to EDs around the world. The large sample size across wide-ranging geographical regions with different health-care systems provides a valuable insight into the international variations in patient characteristics and clinical practice. Sites participating included small regional hospitals, metropolitan general hospitals, and tertiary referral centers and thus are likely to be representative of hospitals in the countries studied. The incidence rates of serious secondary cause of headaches are consistent with previous studies, suggesting face validity to our methodology.[32] We specifically designed the standardized case report form to include as much subjective and objective data related to headache as possible, to allow assessment of presenting symptoms, signs, and investigations for diagnostic importance.

There are some limitations that should be considered in interpreting the results. The classification of headache as the main symptom and ED diagnosis were based on clinician judgment. This has been shown to be difficult to classify accurately in the ED.[42] Although patients were identified prospectively, some data were collected retrospectively with the inherent risks that imposes, including missing data for some items such as prehospital medication use.[42] With the exception of some Queensland sites and the United Kingdom where some form of consent was required, participating institutions were instructed to include all patients presenting with headache within the enrolment period. Resources did not allow verification of this. That said, given the high number of participating patients, it is unlikely that missed patients at individual EDs would have introduced systematic bias. We chose to exclude patients representing with the same headache as a recent episode. We are aware that there are arguments for and against this approach. Including them could have inflated the numbers and characteristics of patients with benign headache. Excluding them runs the risk of missing patients with a different final diagnosis. We felt that the former risk had potentially greater risk to data validity and utility. The wide variation in reporting (e.g., 12 patients in Israel vs. 1777 patients in Australia) made certain comparisons between countries difficult or inappropriate and will have skewed results toward practice in the countries with higher patient numbers. The design of the study and resource limitations precluded assessment of inter-rater reliability of data collection. We are unable to quantify the proportion of missing records; however, in similar studies, it has been found to be low, ≤1%. This is unlikely to have significantly biased the results. Diagnosis was as determined by the ED physician at the end of the ED phase of care.

It is possible that some patients may have had further investigations after the ED phase of care (particularly those transferred to another hospital for further imaging and specialist consultation). This may have identified an alternative diagnosis. Similarly, the nature of ED practice precludes validation of diagnoses. Some cases of serious secondary headache may have been missed, resulting in underestimation of its prevalence. We were unable to capture these. The hospitals were mostly located in developed countries, so findings may not be generalizable to the developing world.

CONCLUSION

Diagnosis and management of headache in the ED is challenging. About 1 in 14 patients (7.1%) has a serious secondary cause for their headache identified in the ED. There is wide variation in the use of neuroimaging and treatments. Further work is needed to understand the variation in practice and to better inform international guidelines regarding emergent neuroimaging and treatment.

CONFLICT OF INTEREST

On behalf of all authors, I declare no known real or potential conflicts of interest to exist regarding this research article.

ETHICAL APPROVAL

Lead ethics approval was obtained from the Melbourne Health Human Research Ethics Committee (HREC/43148/MH-2018). Ethics approval was subsequently obtained for each participating site according to local institutional requirements. In most jurisdictions, the study was conducted under waiver of consent. Patient consent was required in a few jurisdictions. In some Queensland sites, formal consent was required. This was verbal. In the United Kingdom, an opt-out consent approach was used, and approval obtained through the Health Research Authorisation following application and review by a committee (reference: 19/SW/0089).

INSTITUTIONAL REVIEW BOARD APPROVAL

Institutional Review Board approval was granted by Melbourne Health HREC.

AUTHOR CONTRIBUTIONS

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CLINICAL TRIALS REGISTRATION NUMBER

The study was registered with the Australia and New Zealand Clinical Trials Register (trial number 376695).

REFERENCES

1. Wijeratne T, Grisold W, Dodick D, Carroll W. World brain day 2019: migraine, the painful truth. *Lancet Neurol*. 2019;18:914.
2. Chu KH, Howell TE, Keijzers G, et al. Acute headache presentations to the emergency department: a statewide cross-sectional study. *Acad Emerg Med*. 2017;24:53-62.
3. National Center for Health Statistics. *Ambulatory Health Care Data*. 2017. Accessed December 11, 2020. https://www.cdc.gov/nchs/ahcd/new_ahcd.htm
4. Doretti A, Shestaritc I, Ungaro D, et al. Headaches in the emergency department—a survey of patients' characteristics, facts and needs. *J Headache Pain*. 2019;20:100-106.
5. Goldstein JN, Camargo CA, Pelletier AJ, Edlow JA. Headache in United States emergency departments: demographics, work-up and frequency of pathological diagnoses. *Cephalalgia*. 2006;26:684-690. Accessed May 2021. https://ichd-3.org/
6. Torelli P, Campana V, Cervellin G, Manzoni GC. Management of primary headaches in adult Emergency Departments: a literature review, the Parma ED experience and a therapy flow chart proposal. *Neurol Sci*. 2010;31:545-553.
7. Evans RW, Burch RC, Frishberg BM, et al. Neuroimaging for migraine: the American Headache Society systematic review and evidence-based guideline. *Headache*. 2020;60:318-336.
8. Australasian College for Emergency Medicine. *Guidelines on Diagnostic Imaging*. G126, July 2012. Accessed March 2019. https://acem.org.au/getmedia/b7f67701-7e80-4e06-b87e-9193310415b0/Guidelines-for-Diagnostic-Imaging-Jul-12-v01.aspx
9. American College for Emergency Physicians. Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with acute headache. *Ann Emerg Med*. 2019;74:e41-e74.
10. Vinson DR, Hurtado TR, Vandenberg JT, Banwart L. Variations among emergency departments in the treatment of benign headache. *Ann Emerg Med*. 2003;41:90-97.
11. Shao E, Hughes J, Eley R. The presenting and prescribing patterns of migraine in an Australian emergency department: a descriptive exploratory study. *World J Emerg Med*. 2017;8:170-176.
12. Colman I, Rothney A, Wright SC, Zilkalns B, Rowe BH. Use of narcotic analgesics in the emergency department treatment of migraine headache. *Neurology*. 2004;62:1695-1700.
13. Dasgupta N, Beletsky L, Ciccarone D. Opioid crisis: no easy fix to its social and economic determinants. *Am J Public Health*. 2018;108:182-186.
14. Dodson H, Bhula J, Eriksson S, Nguyen K. Migraine treatment in the emergency department: alternatives to opioids and their effectiveness in relieving migraines and reducing treatment times. *Cureus*. 2018;10:e2439.

15. Ferguson C, College of Emergency Medicine. *Guideline for the Management of Lone Acute Severe Headache*. 2009. Accessed March 2019. https://www.rcem.ac.uk/docs/College%20Guidelines/5z31.%20Lone%20acute%20severe%20headache%20-%20(Flowchart)%20(Dec%202009).pdf
16. National Institute for Health and Care Excellence. *Headaches in Over 12s: Diagnosis and Management*. 2015. Accessed January 12, 2021. https://www.nice.org.uk/guidance/cg150
17. Perry JJ, Sivilotti MLA, Sutherland J, et al. Validation of the Ottawa Subarachnoid Hemorrhage Rule in patients with acute headache. *CMAJ*. 2017;189:E1379-E1385.
18. Orr SL, Friedman BW, Christie S, et al. Management of adults with acute migraine in the emergency department: the American Headache Society evidence assessment of parenteral pharmacotherapies. *Headache*. 2016;6:911-940.
19. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009;42:377-381.
20. Friedman BW, Grosberg BM. Diagnosis and management of the primary headache disorders in the emergency department setting. *Emerg Med Clin North Am*. 2009;27:71-87.
21. Do TP, Remmers A, Schytz HW, et al. Red and orange flags for secondary headache in clinical practice—the SNNOOP10 list. *Neurology*. 2019;92:134-144.
22. Raam R, Tabatabai RR. Headache in the emergency department: avoiding misdiagnosis of dangerous secondary causes, an update. *Emerg Med Clin North Am*. 2021;39:67-85.
23. Ducros A, Bousser MG. Thunderclap headache. *BMJ*. 2013;346:e8557.
24. Perry JJ, Eagles D, Clement CM, et al. An international study of emergency physicians' practice for acute headache management and the need for a clinical decision rule. *CJEM*. 2009;11:516-522.
25. McCormack RF, Hutson A. Can computed tomography angiography of the brain replace lumbar puncture in the evaluation of acute-onset headache after a negative noncontrast cranial computed tomography scan? *Acad Emerg Med*. 2010;17:444-451.
26. Perry JJ, Stiell IG, Sivilotti MLA, et al. High risk clinical characteristics for subarachnoid haemorrhage in patients with acute headache: prospective cohort study. *BMJ*. 2010;341:c5204.
27. Dalay S, Umar F, Saeed S. Fundoscopy: a reflection upon medical training? *Clin Teach*. 2013;10:103-106.
28. Mackay DD, Garza PS, Bruce BB, et al. The demise of direct ophthalmoscopy: a modern clinical challenge. *Neurol Clin Pract*. 2015;5:150-157.
29. Bruce BB, Bidot S, Hage R, et al. Fundus photography vs. ophthalmoscopy outcomes in the emergency department (FOTO-ED) phase III: web-based, in-service training of emergency providers. *Neuroophthalmology*. 2018;42:269-274.
30. Dunn HP, Teo KZ, Smyth JW, et al. Using non-mydriatic fundus photography to detect fundus pathology in Australian metropolitan emergency departments: a prospective prevalence and diagnostic accuracy study. *Emerg Med Australas* 2021;33:302-309.
31. Carpenter CR, Hussain AM, Ward MJ, et al. Spontaneous subarachnoid hemorrhage: a systematic review and meta-analysis describing the diagnostic accuracy of history, physical examination, imaging, and lumbar puncture with an exploration of test thresholds. *Acad Emerg Med*. 2016;23:963-1003.
32. Callaghan BC, Kerber KA, Pace RJ, Skolarus LE, Burke JF. Headaches and neuroimaging: high utilization and costs despite guidelines. *JAMA Intern Med*. 2014;174:819-821.
33. Luciani M, Negro A, Spunatrelli V, Bentivegna E, Martelletti P. Evaluating and managing severe headache in the emergency department. *Expert Rev Neurother*. 2021;21:277-285.
34. Body R, Morris N, Reynard C, Collinson PO. Comparison of four decision aids for the early diagnosis of acute coronary syndromes in the emergency department. *Emerg Med J*. 2020;37:8-13.
35. Robblee J, Grimsrud KW. Emergency department and inpatient management of headache in adults. *Curr Neurol Neurosci Rep*. 2020;20:7.
36. Miller J, Koons L, Longyhore D. Opioid free treatment algorithm for ED headache management: effect on revisit rate. *Am J Emerg Med*. 2020;38:28-32.
37. Minen MT, Tanev K, Friedman BW. Evaluation and treatment of migraine in the emergency department: a review. *Headache*. 2014;54:1131-1145.
38. Volkow ND, Collins FS. The role of science in addressing the opioid crisis. *N Engl J Med*. 2017;377:391-394.
39. Jones MR, Novitch MB, Sarrafpour S, et al. Government legislation in response to the opioid epidemic. *Curr Pain Headache Rep*. 2019;23:40.
40. Friedman BW, Hochberg ML, Esses D, et al. Applying the International Classification of Headache Disorders to the emergency department: an assessment of reproducibility and the frequency with which a unique diagnosis can be assigned to every acute headache presentation. *Ann Emerg Med*. 2007;49:409-419, 419.e1-9.
41. Linn FHH, Rinkel GJE, Algra A, et al. Headache characteristics in subarachnoid haemorrhage and benign thunderclap headache. *J Neurol Neurosurg Psychiatry*. 1998;65:791-793.
42. Gilbert EH, Lowenstein SR, Koziol-McLain J, Barta DC, Steiner J. Chart reviews in emergency medicine research: where are the methods? *Ann Emerg Med*. 1996;27:305-308.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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APPENDIX A

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