

Migraine in the Emergency Department: A Prospective Multinational Study of Patient Characteristics, Management, and Outcomes

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Keywords

Migraine disorders · Emergency department · Epidemiology · Neuroimaging · Therapeutics

Abstract

Background and Aim: Migraine headache is commonly diagnosed in emergency departments (ED). There is relatively little real-world information about the epidemiology, investigation, management, adherence to therapeutic guidelines

and disposition of patients treated in ED with a final diagnosis of migraine. The primary aim of the current study is to get a snapshot of assessment and management patterns of acute migraine presentations to the different settings of EDs with a view to raise awareness. **Methods:** This is a planned sub-study of a prospective study conducted in 67 health services in 10 countries including Australia, New Zealand, Southeast Asia, Europe, and the UK investigating the epidemiology and outcome of adult patients presenting to ED with nontraumatic headache. Outcomes of interest for this study are demographics, clinical features (including severity), patterns of investigation, treatment, disposition, and outcome of patients diagnosed as having migraine as their final ED diagnosis. **Results:** The cohort comprises 1,101 patients with a mean age of 39 years (SD \pm 13.5; 73.7% [811]) were female. Most patients had had migraine diagnosed previously (77.7%). Neuroimaging was performed in 25.9% with a very low diagnostic yield or significant findings (0.07%). Treatment of mild migraine was in accordance with current guidelines, but few patients with moderate or severe symptoms received recommended treatment. Paracetamol (46.3%) and nonsteroidal anti-inflammatory drugs (42.7%) were the most commonly prescribed agents. Metoclopramide (22.8%), ondansetron (19.2%), chlorpromazine (12.8%), and prochlorperazine (12.8%) were also used. **Conclusions:** This study suggests that therapeutic practices are not congruent with current guidelines, especially for patients with severe symptoms. Efforts to improve and sustain compliance with existing management best practices are required.

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Introduction

Headaches account for 1–3% of all emergency department (ED) visits, of which migraine is the most common discrete primary headache disorder diagnosed [1, 2]. Migraine is the leading cause of disability worldwide among people below the age of 50 years [3, 4]. Despite this, it has been suggested that migraine continues to be one of the most neglected and badly managed medical disorders [3, 5, 6]. The role of ED is primarily in abortive management, but there may be some role for recommending or referring patients for initiation of preventive therapy [7].

Migraine headaches can exhibit similar clinical features to potentially life-threatening conditions, such as infectious and inflammatory conditions, vascular pathologies (including subarachnoid hemorrhage), and space-occupying lesions. They typically lack specific neurologic

signs [8, 9]. This can make accurate diagnosis challenging. Diagnostic practices and acute management pathways may vary both between and within countries, depending, in part on individual hospital treatment pathways. Several regional and international guidelines exist for the assessment and management of acute migraine attacks [10–12]. They are broadly similar. The adherence to such guidelines, especially across geographical regions has not been well described. We embarked on the Headache in Emergency Departments (HEAD) study to understand the epidemiology of atraumatic headache in the EDs of ten countries. The aim of this planned sub-study is to describe the real-world demographics, clinical features, investigations, treatment, and outcome of patients with an ED final diagnosis of migraine.

Materials and Methods

This was a planned sub-study of a prospective multicentre observational study conducted over one calendar month in 2019 (for most sites March 2019), the HEAD study. It includes patients coded in the HEAD study cohort as having migraine as their final ED diagnosis.

For the parent study, participants were adult patients (aged \geq 18 years) with nontraumatic headache as their presenting complaint [13]. 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 a main complaint. Determination of whether headache was a primary complaint was at the discretion of the local researcher based on all available data.

Qualifying adult patients presenting during the study period were identified from ED data management systems. Patients were identified prospectively but, depending on on-site resources, some data were collected retrospectively.

Data collected included demographics, 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 REDCap electronic data capture tools hosted at the Joseph Epstein Centre for Emergency Medicine Research (Melbourne, Australia). For the majority of sites, the data were collected in March 2019, with some minor variations following delays in ethical/governance approval. Outcomes of interest for this study are demographics, clinical features, patterns of investigation, treatment, disposition and outcome of patients diagnosed with migraine as their final ED diagnosis.

Data analyses were predominantly descriptive (counts and proportions with confidence intervals where appropriate). It was undertaken using Stata v15 (College Station, TX, USA).

The lead ethics approval was by 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,

Table 1. Demographic features, past medical history, regular medications, disposition and re-attendances

Variable	Result (total N = 1,101)	Missing data
Age, years		
Mean (SD)	39.0 (±13.5)	0
Median (IQR)	37 (28–48)	
Gender (female)	811, 73.7 (71.0–76.2)	0
Pregnancy among female patients	28, 3.5 (2.4–5.0)	0
Referral by a doctor	160, 14.5 (12.6–16.7)	0
Conveyed by ambulance	200, 18.2 (16.0–20.6)	0
Triage category		
Immediate	4, 0.4 (0.1–0.9)	
Urgent	587, 53.3 (50.4–56.3)	0
Nonurgent	510, 46.3 (43.4–49.3)	
Duration of symptoms		
<24 h	551, 50.1 (47.1–53.0)	
1–3 days	248, 22.5 (20.1–25.1)	16
>3 days	286, 26.0 (23.5–28.7)	
Any past medical history	829, 75.3 (72.7–77.8)	0
Migraine	643, 77.7 (74.7–80.4)	1
Recurrent headache (excluding migraine)	129, 15.9 (13.5–18.5)	16
Tension headache	17, 2.1 (1.3–3.3)	16
Cluster headache	6, 0.7 (0.3–1.6)	15
Any regular medications taken	376, 34.2 (31.4–37.0)	0
Triptan	133, 35.8 (31.1–40.9)	5
Beta-blockers	48, 13.0 (9.9–16.9)	7
Tricyclic antidepressants	44, 11.9 (8.9–15.6)	5
Long-term codeine preparations	24, 6.4 (4.3–9.4)	3
Topiramate	22, 6.0 (3.9–8.9)	6
Anticoagulants	17, 4.6 (2.9–7.3)	6
Candesartan	11, 3.0 (1.6–5.3)	6
Botulinum toxin	10, 2.7 (1.5–5.0)	6
Pizotifen	6, 1.6 (0.7–3.6)	6
Sodium valproate	4, 1.1 (0.4–2.9)	6
Verapamil	1, 0.3 (0.04–1.9)	6
Other opioids	33, 8.9 (6.4–12.3)	7
Disposition		
Home from ED	709, 64.4 (61.5–67.2)	
Home from ED observation unit	321, 29.2 (26.5–31.9)	0
Admitted	70, 6.4 (5.1–8.0)	
Death	1, 0.09 (0.01–0.6)	
Reattendance within 72 h of discharge from ED	42, 4.1 (3.0–5.5)	
Migraine	28	
Benign primary headache	2	
Musculoskeletal headache	1	
Tension headache	1	
Subarachnoid hemorrhage	1	73
Viral meningitis	1	
Bacterial meningitis	1	
Stroke	1	
Intracranial hypertension	1	
Posterior reversible encephalopathy syndrome	1	
Unrelated conditions	4	

Data presented as N, % (95% confidence intervals) unless otherwise stated. ED, emergency department.

Table 2. Clinical features

Symptoms, <i>n</i> , % (95% CI)	Result (total <i>N</i> = 1,101)	Missing data
Onset of symptoms		
Gradual	633, 57.5 (54.5–60.4)	
Sudden or thunderclap (instant peak)	147, 13.4 (11.5–15.5)	0
Peak intensity <1 h	130, 11.8 (10.0–13.9)	
Unknown	191, 17.4 (15.2–19.7)	
Location of headache		
Generalized	490, 44.6 (41.6–47.5)	
Unilateral	479, 43.6 (40.6–46.5)	0
Unclear	131, 11.9 (10.1–14.0)	
Worst headache ever	147, 13.4 (11.5–15.5)	0
Severity		
Mild (pain score ≤3)	129, 11.7 (9.9–13.8)	
Moderate (pain score 4–7)	447, 40.6 (37.7–43.5)	0
Severe (pain score >7)	392, 35.6 (32.8–38.5)	
Unclear	133, 12.1 (10.3–14.1)	
Reported neck pain or stiffness	189, 17.2 (15.0–19.5)	0
Nausea or vomiting	663, 60.2 (57.3–63.1)	0
Syncope or loss of consciousness	23, 2.1 (1.4–3.1)	0
Reported photophobia	471, 42.8 (39.9–45.7)	0
New limb weakness (current/transient)	49, 4.5 (3.4–5.8)	0
New limb paraesthesia (current/transient)	100, 9.1 (7.5–10.9)	0
New speech difficulty (current/transient)	45, 4.1 (3.1–5.4)	0
New visual disturbance (current/transient)	244, 22.2 (19.8–24.7)	0
Subjective fever or rigors	49, 4.5 (3.4–5.8)	0
Reported rash	4, 0.4 (0.1–1.0)	0
Clinical examination		
Pulse rate, beats per min, median (IQR)	80 (70–87)	8
Systolic blood pressure, mm Hg, median (IQR)	129 (115–140)	9
Temperature, °C, median (IQR)	36.5 (36.2–36.8)	117
Glasgow Coma scale score		
15	988, 98.5 (97.5–99.1)	98
13–14	15, 1.5 (0.8–2.3)	
Confusion on examination	8, 0.7 (0.4–1.4)	0
Meningism on examination	12, 1.1 (0.6–1.9)	0
Limited neck flexion on examination	16, 1.5 (0.9–2.4)	0
New neurological signs on examination	32, 2.9 (2.1–4.1)	0
New visual defects on examination	19, 1.7 (1.1–2.7)	0

the study was conducted under waiver of consent. Patient consent was required in a few jurisdictions including the UK, where an opt-out consent approach was used, and approval obtained through the Health Research Authorization following application and review by committee (REC reference: 19/SW/0089). The study was registered with Australia and New Zealand Clinical Trials Registry (trial number 376695).

Results

A total of 4,536 patients presenting with headache were included in the parent study across 67 hospital groups (74 EDs) in 10 countries (Australia 28, New Zea-

land 9, Turkey 9, UK 7, Singapore 4, Belgium, 4, France 3, Romania 1, Hong Kong 1, and Israel 1). For hospitals that provided caseload data, headache patients accounted for 1% of ED caseload (95% CI 1.0–1.1%). Migraine was the final diagnosis in 1,101 (24.3%) of patients.

The proportion of ED headache patients diagnosed with migraine varied between 18.0% and 32.2% of all patients presenting with headache in countries that contributed to at least 100 patients to the study (i.e., Australia, Turkey, New Zealand, Singapore, the UK, and France) (online suppl. Table A; for all online suppl. material, see www.karger.com/doi/10.1159/000520548).

Table 3. Investigations

Imaging modality	Results, N, % (95% CI)
Head CT performed	285, 25.9 (23.4–28.6)
Head CT angiography performed	42, 3.8 (2.8–5.1)
MRI brain performed	22, 2.0 (1.3–3.0)
Lumbar puncture performed	23, 2.1 (1.4–3.1)

CT, computed tomography.

Demographic features, past medical history, regular medication, disposition, and reattendance within 48 h are shown in Table 1. The median age was 37 (interquartile range 28–48) years. Females constituted 73.7% of patients, 3.5% of whom were pregnant.

58.4% (643/1,101) had a previous migraine diagnosis. Half (50.1%) presented to ED within 24 h of symptom onset. Over a third (34.2%) of patients were taking chronic medications, of which 35.8%, 13.0%, and 11.9% were taking triptans, β -blockers, and tricyclic antidepressants, respectively. The majority were either directly discharged from the ED (64.4%) or from the ED observation unit (29.2%).

Clinical features and severity are shown in Table 2. Most patients presented with gradual onset of headache (57.5%) that was either generalized (44.6%) or unilateral (43.6%) in location and of moderate (40.6%) to severe (35.6%) pain (Table 2). Predominant symptoms were nausea or vomiting (60.2%), photophobia (42.8%), and patient report of current or transient new visual disturbance (22.2%). Neurological signs on clinical examination were uncommon.

Investigations are shown in Table 3. Head computed tomography (CT) was performed in about one quarter (25.9%) of patients. In 2 cases, CT raised suspicion of a vascular abnormality which was excluded on further testing. There was significant variation in the proportion of head CT performed among different countries ($p < 0.001$) (online suppl. Table B). Lumbar puncture was performed infrequently (2.1%), and none were diagnostic.

Self-administered and ambulance-initiated treatment is shown in Table 4. Common prehospital medications that were self-administered by patients include paracetamol (64.7%), nonsteroidal anti-inflammatory drugs (NSAIDs) (32.8%), triptans (18.9%), and codeine (14.0%) (Table 4). Among the 200 (18.2%) patients conveyed to hospital by ambulance, antiemetics (64.6%), paracetamol (35.9%), fentanyl (32.3%), and intravenous morphine (14.2%) were most frequently given by paramedics.

Table 4. Medications taken prehospital

Medications	N, % (95% CI)	Missing data
Self-administered	542, 49.2 (46.3–52.1)	0
Paracetamol	348, 64.7 (60.5–68.6)	4
Aspirin	40, 7.5 (5.5–10.0)	6
NSAID (nonaspirin)	176, 32.8 (28.9–36.9)	5
Codeine	75, 14.0 (11.3–17.2)	6
Triptan	101, 18.9 (15.8–22.4)	7
Oxycodone	25, 4.7 (3.2–6.8)	8
Tramadol	21, 3.9 (2.6–6.0)	8
Other opioids	10, 1.9 (1.0–3.5)	8
Antiemetic	53, 9.9 (7.6–12.7)	6
Other medications	37, 6.9 (5.1–9.4)	8
Ambulance prehospital (N = 200)	131, 65.5 (58.6–71.8)	12
Paracetamol	46, 35.9 (28.0–44.7)	3
Aspirin	3, 2.4 (0.8–7.2)	4
NSAID (nonaspirin)	5, 3.9 (1.6–9.2)	4
Triptan	2, 1.6 (0.4–6.1)	3
Oxycodone	1, 0.8 (0.1–5.5)	4
Fentanyl	41, 32.3 (24.6–41.0)	4
Oramorph	1, 0.8 (0.1–5.5)	4
Intravenous morphine	18, 14.2 (9.1–21.5)	4
Other opioids	2, 1.6 (0.4–6.1)	3
Antiemetic	84, 64.6 (55.9–72.4)	1
Methoxyflurane	14, 10.9 (6.5–17.6)	2
Other medications	3, 2.4 (0.8–7.2)	4

NSAID, nonsteroidal anti-inflammatory drugs.

Pharmacological treatment in ED is shown in Table 5. 84.9% of patients received medications for their headache. Paracetamol (46.3%) and NSAIDs (42.7%) were the most commonly. Metoclopramide (22.8%), ondansetron (19.2%), chlorpromazine (12.8%), and prochlorperazine (12.8%) were also used. Chlorpromazine was only used in Australia and New Zealand. Over two-thirds (67.2%) of patients received intravenous fluids. Rescue medications (given >30 min after initial treatment) were required in 41.3% of patients. Almost a third (30.6%) received chlorpromazine as second-line therapy. Of the 437 patients who presented within 24 h of headache onset (39.7%) and reported moderate or severe headache, only 88 (20%) received initial treatment with a triptan or phenothiazine.

Discussion/Conclusion

Almost a quarter of patients in the HEAD study who presented with atraumatic headache were ultimately classified at ED discharge as having migraine, underscoring

Table 5. Initial treatment in ED

	Total, <i>n</i> , %	Oral	Parenteral	Missing data
Initial treatment				
Any medication given to treat headache, <i>n</i> , %	935, 84.9 (82.7%–86.9%)			0
Medications after initial clinical assessment,* <i>n</i> , %	854, 91.3 (89.4%–93.0%)			0
Paracetamol, <i>n</i> , %	390, 46.3	334	56	11
Aspirin, <i>n</i> , %	96, 11.5	95	1	17
NSAID (nonaspirin), <i>n</i> , %	359, 42.7	191	168	14
Opioids, <i>n</i> , %				
Codeine containing medication	83, 9.9	78	5	19
Oxycodone	70, 8.4	69	1	17
Pethidine/meperidine	1, 0.1	0	1	20
Other opioid	57, 6.8	26	31	20
Triptan	36, 4.3	24	12	19
Chlorpromazine	107, 12.8	4	103	20
Prochlorperazine	109, 12.8	24	85	5
Droperidol/haloperidol	11, 1.3	4	7	20
Metoclopramide	191, 22.8	49	142	18
Ondansetron	160, 19.2	111	49	20
Corticosteroid	12, 1.4	5	7	20
Antibiotic/antiviral agent	4, 0.5	3	1	20
Other initial treatments,* <i>n</i> , %	313, 28.4 (25.8%–31.2%)			0
Oxygen, <i>n</i> , %	13, 4.2 (2.4%–7.0%)			0
IV fluids, <i>n</i> , %	211, 67.2 (61.8%–72.2%)			0
Follow-up treatment >30 min after initial treatment				
Any medications given to treat headache, <i>n</i> , %	385, 41.3 (38.1%–44.5%)			2
Paracetamol	144, 36.7	122	22	3
Aspirin	42, 11.0	42	0	3
NSAID (nonaspirin)	100, 26.1	77	23	2
Codeine	27, 7.1	26	1	3
Triptan	27, 7.1	23	4	3
Pethidine	1, 0.3	0	1	3
Other opioid	34, 8.9	13	21	3
Oxycodone	45, 11.8	45	0	3
Chlorpromazine	117, 30.6	10	107	2
Metoclopramide	56, 14.7	21	35	3
Ondansetron	61, 16.0	34	27	3
Prochlorperazine	60, 15.7	10	50	2
Droperidol/haloperidol	8, 2.1	2	6	3
Ergot alkaloids	0	0	0	3

ED, emergency department; NSAID, nonsteroidal anti-inflammatory drug. * More than one medication is possible.

the high prevalence of this condition [14]. The epidemiology of patients diagnosed with migraine in our study cohort is congruent with a previous large study in the USA where the predominant age-group was between 30 and 39 years, with female to male ratio of 3:1 [15]. A non-negligible proportion of females (3.5%) in our study were pregnant at the time of ED presentation, stressing the need for emergency physicians to be well aware of the

principles of acute migraine management in the context of pregnancy [16, 17].

In our cohort, the classification as migraine was mostly in line with the International Classification of Headache Disorders-3 criteria for both variants with and without aura [18]. A high proportion of patients had recognized migraine features such as location (unilateral), severity (moderate to severe intensity), symptoms (nau-

sea, vomiting, and photophobia), and aura (especially visual disturbance) [7]. The fact that 58.4% (643/1,101) of migraineurs were previously diagnosed to have suffered from migraine probably contributed to diagnostic considerations in the ED since migraine is a disorder of recurrent attacks.

Neuroimaging is not recommended in most instances, unless there are abnormal neurological findings on clinical examination, sudden severe headache or red flag features that do not fit into the diagnosis of migraine [19]. Our data could be interpreted to suggest overperformance of head CT (25.9%) and magnetic resonance imaging (2.0%) despite the known very low yield among migraineurs. That said, about 20% of patients did not have a confirmed prior diagnosis of migraine and a similar proportion had concerning clinical features so a cautious approach to ruling out a serious cause is probably justified. When comparing countries and regions, there were significant differences in the proportion of head CT performed, ranging from 14.2% (Singapore) to 50.0% (France) (online suppl. Table B). This study was not designed to explore reasons for this variation in practice. It could be postulated that issues such as structure of the health system, reimbursement and financing mechanisms, the medicolegal environment and health-seeking behaviors could vary between countries and contribute to this variation in practice. Alternatively, it may be due, in part, to random variation as the number of patients diagnosed with migraine in some countries was very low.

A possible approach to neuroimaging in patients with migraine is using the so-called SNNOOP10 list of flag items to screen for secondary headaches [20] (online suppl. Table C). These have been shown to have high negative predictive value [21]. They have not however been validated in a large ED cohort of patients with headache.

Abortive or symptomatic treatment of migraine remains the cornerstone of therapy in the ED [7]. Stratified treatment strategies based on the severity of the episode have been shown to be more effective than a step-care approach [22, 23]. An initial single large dose of medication given early during the headache has been demonstrated to be more effective than small, repeated doses [24]. Generally, simple analgesics such as paracetamol and NSAIDs are considered first-line agents for mild attacks due to the superior cost and side effect profile compared to migraine-specific medications [23]. In our cohort, very few patients had mild headache. In moderate to severe attacks, triptans combined with NSAIDs and an antiemetic

agent (to treat nausea and assist absorption) or use of a phenothiazine such as chlorpromazine or prochlorperazine is suggested [25, 26]. These were prescribed infrequently (Table 5). When coupled with the finding that about half of patients have taken some analgesia before attending ED and the high proportion of patients requiring rescue therapy (>40%), this suggests that suboptimal treatment in ED is common and strengthens the case for stratified therapy based on severity and appropriate initial dosing [27, 28].

The proportion of patients treated with opiates in concerning. Opiates have been shown to be less effective than alternative agents and carry the risks of addiction (Dodson). Opiate use for treatment of headache more generally has been challenged. Despite this, their use is common (Pettat). Interestingly, although ergot alkaloids have been suggested for treatment of status migrainosus none were used as initial or rescue therapy in our patient population [29].

It is important where possible to avoid medication overuse headache or analgesic rebound headache. The risk is highest with opioids, moderate with triptans, and lowest with NSAIDs [27, 28, 30]. The number of patients with migraine in our study on regular triptans, codeine, and other opioid medications and who self-administered similar class of drugs, use of fentanyl and morphine in ambulances, and use of opioids in the ED may warrant further investigation to gain further insight into the potential risk of medication overuse headache.

The strengths of this sub-study include the size of the cohort and the incorporation of broad geographical regions in different continents, allowing some inferences in clinical practice related to variation in health care systems to be made. We were able to establish face validity of our methodology as the demographics of migraine patients in our cohort closely resembles previous epidemiological studies from the USA. The limitations include the cross-sectional nature of this study may introduce confounding issues that could lead to bias and subsequent misinterpretation [30, 31]. Information on discharge pain score, recurrence, and number of episodes of headaches as well as dose and timing of treatment were not collected. The number of cases from certain participating countries is very low, which could have led to imprecise estimates, although we attempted to circumvent this issue by only considering regions that contributed significant to the dataset in between country analyses. The diagnosis of migraine was made by the treating clinician and not confirmed independently. It is possible that some cases were miscoded; this is the nature of ED practice.

Conclusion

Migraine is one of the commonest neurological conditions in the ED. This study suggests that therapeutic practices are not congruent with current guidelines, especially for patients with severe symptoms. Efforts to improve and sustain compliance with existing management best practices are required urgently.

Acknowledgments

HEAD study group (Appendix, published as online suppl. material).

Statement of Ethics

This study was conducted in accordance with the World Medical Association Declaration of Helsinki. The lead ethics approval was by 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 including the UK, where an opt-out consent approach was used, and approval obtained through the Health Research Autho-

rization following application and review by committee (REC reference: 19/SW/0089). The study was registered with Australia and New Zealand Clinical Trials Registry (trial number 376695).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

T.W., A.M.K., K.H.C., and W.S.K. conceived the idea of the HEAD study. T.W., A.M.K., W.S.K., K.H.C., F.B.K., G.K., M.A.K., S.K., C.A.G., T.R., D.H., and S.L. developed the concept further through a series of international teleconferences and agreed on the main study protocol that was drafted by A.M.K. T.W. drafted the original manuscript. All the authors contributed with revisions and agreed with final submission version.

Data Availability Statement

Data are available from the corresponding author upon reasonable request.

References

- 1 Doretti A, Shestaritc I, Ungaro D, Lee J-I, Lympopoulos L, Kokoti L, et al. Headaches in the emergency department: a survey of patients' characteristics, facts and needs. *J Headache Pain*. 2019;20(1):100.
- 2 Burch R, Rizzoli P, Loder E. The prevalence and impact of migraine and severe headache in the United States: updated age, sex, and socioeconomic-specific estimates from government health surveys. *Headache*. 2021;61(1):60–8.
- 3 Wijeratne T, Grisold W, Dodick D, Carroll W. World Brain Day 2019: migraine, the painful truth. *Lancet Neurol*. 2019;18(10):914.
- 4 Steiner TJ, Stovner LJ, Vos T, Jensen R, Katsarava Z. Migraine is first cause of disability in under 50s: will health politicians now take notice? *J Headache Pain*. 2018;19(1):17.
- 5 GBD 2016 Headache Collaborators. Global, regional, and national burden of migraine and tension-type headache, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol*. 2018;17(11):954–76.
- 6 Rao GN, Kulkarni GB, Gururaj G, Stovner LJ, Steiner TJ. The burden attributable to headache disorders in India: estimates from a community-based study in Karnataka State. *J Headache Pain*. 2015;16:94.
- 7 Tepper SJ. Acute treatment of migraine. *Neurol Clin*. 2019;37(4):727–42.
- 8 Cady R, Dodick DW. Diagnosis and treatment of migraine. *Mayo Clin Proc*. 2002;77(3):255–61.
- 9 Dodick DW. Migraine. *Lancet*. 2018;391(10127):1315–30.
- 10 Evers S, Afra J, Frese A, Goadsby PJ, Linde M, May A, et al. EFNS guideline on the drug treatment of migraine: revised report of an EFNS task force. *Eur J Neurol*. 2009 Sep;16(9):968–81.
- 11 Worthington I, Pringsheim T, Gawel MJ, Gladstone J, Cooper P, Dilli E, et al. Canadian Headache Society Guideline: acute drug therapy for migraine headache. *Can J Neurol Sci*. 2013 Sep;40(5 Suppl 3):S1–80.
- 12 Lanteri-Minet M, Valade D, Geraud G, Lucas C, Donnet A. Revised French guidelines for the diagnosis and management of migraine in adults and children. *J Headache Pain*. 2014 Jan 8;15(1):2.
- 13 Kelly AM, Kuan WS, Chu K, Kinnear FB, Keijzers G, Karamercan M, et al. Epidemiology, investigation, management and outcome of Headache In Emergency Departments, (HEAD Study): an Multinational Observational Cohort Study. *Headache*. 2021. Epub ahead of print.
- 14 Lipton RB, Diamond S, Reed M, Diamond ML, Stewart WF. Migraine diagnosis and treatment: results from the American Migraine Study II. *Headache*. 2001 Jul–Aug;41(7):638–45.
- 15 Lipton RB, Bigal ME, Diamond M, Freitag F, Reed ML, Stewart WF; AMPP Advisory Group. Migraine prevalence, disease burden, and the need for preventive therapy. *Neurology*. 2007;68(5):343–9.
- 16 Saldanha IJ, Cao W, Bhuma MR, Konnyu KJ, Adam GP, Mehta S, et al. Management of primary headaches during pregnancy, postpartum, and breastfeeding: a systematic review. *Headache*. 2021 Jan;61(1):11–43.
- 17 Allais G, Castagnoli Gabellari I, Airola G, Schiapparelli P, Terzi MG, Mana O, et al. Is migraine a risk factor in pregnancy? *Neurol Sci*. 2007;28(Suppl 2):S184–7.
- 18 Headache Classification Committee of the International Headache Society (IHS). Headache Classification Committee of the International Headache Society (IHS) The international classification of headache disorders, 3rd edition. *Cephalalgia*. 2018 Jan;38(1):1–211.
- 19 Evans RW, Burch RC, Frishberg BM, Marmura MJ, Mechtler LL, Silberstein SD, et al. Neuroimaging for migraine: the American Headache Society systematic review and evidence-based guideline. *Headache*. 2020 Feb;60(2):318–36.

- 20 Do TP, Remmers A, Schytz HW, Schankin C, Nelson SE, Obermann M, et al. Red and orange flags for secondary headaches in clinical practice: SNNOP10 list. *Neurology*. 2019; 92(3):134–44.
- 21 Wongtanarasarin W, Wittayachamnankul B. Clinical availability of SNOOP4 in acute non-traumatic headache patients admitted to the emergency department. *Hong Kong J Emerg Med*. 2020:102490792092868.
- 22 Lipton RB, Stewart WF, Stone AM, Láinez MJ, Sawyer JP; Disability in Strategies of Care Study group. Stratified care vs step care strategies for migraine: the Disability in Strategies of Care (DISC) Study—a randomized trial. *JAMA*. 2000 Nov 22–29;284(20): 2599–605.
- 23 Marissa Lagman-Bartolome A, Lay C. The traffic light of headache: simplifying acute migraine management for physicians and patients using the Canadian Headache Society guidelines. *Headache*. 2019 Feb;59(2):250–2.
- 24 Silberstein SD. Practice parameter: evidence-based guidelines for migraine headache (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*. 2000 Sep 26;55(6):754–62.
- 25 Becker WJ. Acute migraine treatment in adults. *Headache*. 2015 Jun;55(6):778–93.
- 26 Holdgate A, Kelly AM. [Emergency care evidence in practice series: management of acute migraine](#). 2006. Emergency Care Community of Practice. National Institute of Clinical Studies.
- 27 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(4):e2439.
- 28 Pettat RAF, Kamona S, Chu K, Sweeny A, Keijzers G, Kelly AM, et al. The Headache in Emergency Departments (HEAD) Study: opioid prescribing in patients presenting with headache: a Multicentre Observational Study. *Headache*. 2021;61(9):1387–1402.
- 29 Rozen TD. Emergency department and inpatient management of status migrainosus and intractable headache. *Continuum*. 2015 Aug; 21(4 Headache):1004–17.
- 30 Diener HC, Limmroth V. Medication-overuse headache: a worldwide problem. *Lancet Neurol*. 2004 Aug;3(8):475–83.
- 31 Sedgwick P. Ecological studies: advantages and disadvantages. *BMJ*. 2014 May 2;348: g2979.