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RESEARCH SUBMISSIONS

The Headache in Emergency Departments study: Opioid prescribing in patients presenting with headache. A multicenter, cross-sectional, observational study

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Abstract

Objective: To describe the patterns of opioid use in patients presenting to the emergency department (ED) with nontraumatic headache by severity and geography.

Background: International guidelines recognize opioids are ineffective in treating primary headache disorders. Globally, many countries are experiencing an opioid crisis. The ED can be a point of initial exposure leading to tolerance for patients. More geographically diverse data are required to inform practice.

Methods: This was a planned, multicenter, cross-sectional, observational substudy of the international Headache in Emergency Departments (HEAD) study. Participants were prospectively identified throughout March 2019 from 67 hospitals in Europe, Asia, Australia, and New Zealand. Adult patients with nontraumatic headache were included as identified by the local site investigator.

Results: Overall, 4536 patients were enrolled in the HEAD study. Opioids were administered in 1072/4536 (23.6%) patients in the ED, and 386/3792 (10.2%) of discharged patients. High opioid use occurred prehospital in Australia (190/1777, 10.7%) and New Zealand (55/593, 9.3%). Opioid use in the ED was highest in these countries (Australia: 586/1777, 33.0%; New Zealand: 221/593, 37.3%). Opioid prescription on discharge was highest in Singapore (125/442, 28.3%) and Hong Kong (12/49, 24.5%). Independent predictors of ED opioid administration included the following: severe headache (OR 4.2, 95% CI 3.1–5.5), pre-ED opioid use (OR 1.42, 95% CI 1.11–1.82),

Abbreviations: 95% CI, ninety-five percent confidence interval; ED, emergency department; HEAD, Headache in Emergency Departments; OR, odds ratio.

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and long-term opioid use (OR 1.80, 95% CI 1.26–2.58). ED opioid administration independently predicted opioid prescription at discharge (OR 8.4, 95% CI 6.3–11.0). **Conclusion:** Opioid prescription for nontraumatic headache in the ED and on discharge varies internationally. Severe headache, prehospital opioid use, and long-term opioid use predicted ED opioid administration. ED opioid administration was a strong predictor of opioid prescription at discharge. These findings support education around policy and guidelines to ensure adherence to evidence-based interventions for headache.

KEYWORDS
analgesia, emergency medicine, opioid, overuse, primary headache disorder

INTRODUCTION

Primary headache disorders affect more than two billion people globally.[1] They are a leading cause of disability among those under 50 years of age, with associated economic costs.[2] Patients with a primary complaint of headache comprise approximately 1%–2% of total presentations to emergency departments (EDs) worldwide.[3] Primary, self-limiting headaches include conditions such as tension-type headache, migraine, and cluster headache. Although they may be debilitating, they are not life-threatening, and patients are usually discharged home.[4] Serious underlying causes such as intracranial hemorrhage, space occupying lesion, and infection must be considered but are infrequent overall.[5]

A rise in opioid use has been recognized as a significant public health concern worldwide, with associated negative health and societal impacts.[6] Opioid prescriptions in EDs and hospitals can be inappropriate and can lead to misuse and dependency.[7,8] Opioid prescribing in primary headache disorders is not evidence-based and increases the risk of medication-overuse headaches. In migraine, it has been recognized as ineffective, potentially habit forming, and inferior to nonopioid options.[9–11] Treatment of primary headache with opioids is not recommended by any national or international guidelines.

There is a recognized practice variation in the treatment of headache at both local and international levels.[10,12] Variation can depend on demographic, clinical, geographical, and provider variables. Understanding the reasons for such variation can lead to better overall patient care.[13] Although several guidelines exist on the assessment and management of primary headache disorders, there is a lack of consensus on the best treatment.[12,14,15] Some guidelines

focus on the treatment of undifferentiated headache, whereas others reference specific treatments for a particular diagnosis.[14,15]

The overarching aims of the Headache in Emergency Departments (HEAD) study are to provide further insight regarding current practice, inform relevant guidelines, and explore the evidence–practice relationship in the treatment of headaches. This study aims to describe opioid use prehospital, in the ED, and at discharge, and to evaluate which geographic, demographic, clinical, and provider variables were associated with more frequent opioid presecription.[16,17] We hypothesized that there would be a variation by country in the treatment of adult patients with headache.

METHODS

Study design and setting

This was a preplanned, cross-sectional substudy of the HEAD multicenter observational study, with data collection over one calendar month in March 2019 for most participating hospitals. The study was coordinated at Joseph Epstein Centre for Emergency Medicine Research, Melbourne, Australia. Participating sites included 67 hospitals in Australia, New Zealand, Hong Kong, Singapore, the United Kingdom, Israel, Turkey, France, Belgium, and Romania. The study protocol was approved by the Melbourne Human Research Ethics Committee (HREC/43148/MH-2018). Subsequent ethical approval was obtained at each participating site, with appropriate waiver of consent at most sites. Patient consent was required in Queensland, Australia. In the United Kingdom, an opt-out consent approach was used, approved through the Health Research Authorization (REC reference 19/SW/0089). The study was registered with the Australia and New Zealand Clinical Trials Register (No. 376695, ID ACTRN12619000094178).

Participants and recruitment

Adult patients (≥18 years) with nontraumatic headache were included, based on a review of the local patient data management systems by the site investigator. Patients were identified prospectively; in some instances, data were collected retrospectively. Patients were excluded if there was a history of trauma within 48 h of presentation, if headache was not the main presenting complaint, if they were re-presenting with the same symptoms, were interhospital transfers, or if medical records were missing. Participating institutions were instructed to include all eligible patients within the enrolment period. No formal sample size calculation was undertaken due to the descriptive nature of the study.

Outcomes

Primary outcomes of interest were administration of opioids prehospital, opioid prescription in the ED, and opioid prescription at discharge. "Administration of opioid" was defined by documentation of opioid prescription prehospitally, in the ED, or at discharge. Data included demographic, geographic, and clinical factors such as country, age, sex, mode of arrival, referral, triage category in the ED, severity of headache, duration of symptoms, and patient disposition from the ED. Headache severity was defined as mild (pain score 0–3), moderate (4–7), or severe (8–10). Opioid use was classified as use of an opioid or opioid-related substance including oxycodone, codeine, fentanyl, morphine, hydromorphone, tramadol, and pethidine. The variable "history of long-term opioid use" was defined as documentation of chronic opioid use in the medical record. The ED discharge diagnosis by the treating clinician was used.

Data collection

Demographics, clinical details, investigations, treatments, disposition, and outcomes were collected at each site by local researchers and entered into an online database (REDCap). The data collection form is included as an Appendix S1.

Statistical analyses

Descriptive (counts and proportions with 95% confidence intervals [95% CI] wherever appropriate) and univariate inferential statistics were produced using SPSS v26 (IBM Corp., Armonk, NY). Normality of continuous variables was assessed through visualizing the histogram and Q-Q plot, as well as by the Kolmogorov–Smirnov test of normality. Medians and interquartile ranges (IQRs) were produced for not normally distributed continuous variables. The chi-squared test or chi-squared test for trend was used to evaluate the factors associated with opioid use, along with odds ratios (ORs) and 95% CI. Two-tailed testing was applied to all inferential tests, and a p-value of <0.05 was considered statistically significant. As Australia contributed the largest proportion of patients, it was used as the reference group for categorical comparisons. For proportions of opioid use by country, 95% CIs were calculated using the open-source software OpenEpi and the Wilson-score method.[18]

Multilevel logistic regression analysis was performed using Stata v16 (StataCorp, College Station, TX). Multilevel modeling was used because the data have a hierarchical structure with patients nested within hospitals, and hospitals within countries. The multilevel model accounted for the nonindependence of data units within clusters. Preliminary analyses using an intercept-only model confirmed that country variance was greater than zero indicating variation in opioid use across countries. Two models were built: one with ED opioid use as the binary outcome and the other with discharge prescription of opioid as the binary outcome. Any variable that was univariately associated with the binary outcome was entered into the respective model as a fixed effect. Country and hospital were entered as random effects. Missing data (e.g., oxycodone administered in the ED) were recorded as a negative response (i.e., oxycodone note administered). The analysis provided an overall average measure of ED opioid use and opioid prescription at discharge across countries. Furthermore, the analyses provided an estimation of variations between

TABLE 1 Distribution of demographics and selected clinical features by country

Country	#Missing	All		Australia		New Zealand		Hong Kong		Singapore		France		United Kingdom		Israel		Belgium		Turkey		Romania	
		n = 4536 (100%)		*n* = 1777 (39%)		*n* = 593 (13%)		*n* = 64 (1.4%)		*n* = 578 (13%)		*n* = 115 (2.5%)		*n* = 276 (6.1%)		*n* = 12 (0.3%)		*n* = 70 (1.5%)		*n* = 982 (22%)		*n* = 69 (1.5%)	
Age (years)	**0**																						
Median (years), IQR		41 (29–55)		43 (30–57)		43 (29–57.5)		47.5 (37–64.75)		36 (26–51)		35 (26–49)		39.5 (30–55)		34.5 (30.25–48.25)		35.5 (29–46.25)		40.0 (31–52)		41 (30.5–53.5)	
		n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Sex F, *n* (%)	**2**	2907	64.1	1238	69.7	400	67.5	47	73.4	258	44.6	76	66.1	166	60.1	9	75.0	50	71.4	616	62.7	47	68.1
Mode of arrival	**0**																						
Self		3635	80.1	1259	70.8	440	74.2	53	82.8	556	96.2	81	70.4	202	73.2	12	100.0	68	97.1	914	93.1	50	72.5
Ambulance		791	17.4	457	25.7	146	24.6	11	17.2	21	3.6	30	26.1	72	26.1	0	0.0	1	1.4	35	3.6	18	26.1
Other		110	2.4	61	3.4	7	1.2	0	0.0	1	0.2	4	3.5	2	0.7	0	0.0	1	1.4	33	3.4	1	1.4
Severity	**617**																						
Mild		815	18.0	232	13.1	58	9.8	2	3.1	147	25.4	25	21.7	35	12.7	1	8.3	8	11.4	296	30.1	11	15.9
Moderate		1869	41.2	661	37.2	200	33.7	0	0.0	266	46.0	41	35.7	123	44.6	6	50.0	28	40.0	493	50.2	51	73.9
Severe		1235	27.2	576	32.4	226	38.1	0	0.0	127	22.0	39	33.9	88	31.9	5	41.7	26	37.1	141	14.4	7	10.1
Unknown		617	13.6	308	17.3	108	18.2	62	96.9	38	6.6	10	8.7	30	10.9	0	0.0	8	11.4	52	5.3	0	0.0
Referral	**0**																						
Self		3748	82.6	1440	81.0	488	82.3	63	98.4	465	80.4	67	58.3	242	87.7	3	25.0	62	88.6	854	87.0	64	92.8
GP/other		788	17.4	337	19.0	105	17.7	1	1.6	113	19.6	48	41.7	34	12.3	9	75.0	8	11.4	128	13.0	5	7.2
Triage category	**0**																						
Immediate		77	1.7	3	0.2	9	1.5	0	0.0	6	1.0	2	1.7	1	0.4	0	0.0	0	0.0	52	5.3	4	5.8
Urgent		2294	50.6	1095	61.6	422	71.2	8	12.5	201	34.8	78	67.8	183	66.3	2	16.7	25	35.7	218	22.2	62	89.9
Nonurgent		2165	47.7	679	38.2	162	27.3	56	87.5	371	64.2	35	30.4	92	33.3	10	83.3	45	64.3	712	72.5	3	4.3
History of any head complaint (known past history)	**0**																						
Yes		2583	56.9	1195	67.2	377	63.6	47	73.4	178	30.8	55	47.8	175	63.4	6	50.0	61	87.1	455	46.3	34	49.3
No		1953	43.1	582	32.8	216	36.4	17	26.6	400	69.2	60	52.2	101	36.6	6	50.0	9	12.9	527	53.7	35	50.7
History of long-term codeine/opioid use	**0**																						
Yes		165	3.6	102	5.7	34	5.7	0	0.0	2	0.3	3	2.6	20	7.2	0	0.0	3	4.3	1	0.1	0	0.0
No		4371	96.4	1675	94.3	559	94.3	64	100.0	576	99.7	112	97.4	256	92.8	12	100.0	67	95.7	981	99.9	69	100.0

Note: Bold indicates missing data.

TABLE 2 Distribution of medications administered prehospital, in the emergency department (ED), and at discharge by country

		All		Australia		New Zealand		Hong Kong		Singapore		France		United Kingdom		Israel		Belgium		Turkey		Romania	
		n = 4536 (100%)		*n* = 1777 (39%)		*n* = 593 (13%)		*n* = 64 (1.4%)		*n* = 578 (13%)		*n* = 115 (2.5%)		*n* = 276 (6.1%)		*n* = 12 (0.3%)		*n* = 70 (1.5%)		*n* = 982 (22%)		*n* = 69 (1.5%)	
Country	**#Missing**	***n***	**%**	***n***	**%**	***n***	**%**	***n***	**%**	***n***	**%**	***n***	**%**	***n***	**%**	***n***	**%**	***n***	**%**	***n***	**%**	***n***	**%**
Medications taken pre-ED by patient, *n* (%)																							
Any		1608	35.4	765	43.1	266	44.9	0	0.0	138	23.9	67	58.3	119	43.1	7	58.3	56	80.0	165	16.8	25	36.2
Paracetamol		1137	25.1	538	30.3	201	33.9	0	0.0	110	19.0	53	46.1	91	33.0	4	33.3	41	58.6	89	9.1	10	14.5
Aspirin		95	2.1	59	3.3	7	1.2	0	0.0	2	0.3	0	0.0	5	1.8	1	8.3	3	4.3	15	1.5	3	4.3
NSAIDs		537	11.8	242	13.6	99	16.7	0	0.0	25	4.3	16	13.9	35	12.7	1	8.3	23	32.9	83	8.5	13	18.8
Opioids		289	6.4	190	10.7	55	9.3	0	0.0	4	0.7	9	7.8	21	7.6	0	0.0	3	4.3	3	0.3	4	5.8
Antiemetic		101	2.2	62	3.5	26	4.4	0	0.0	1	0.2	1	0.9	3	1.1	0	0.0	0	0.0	7	0.7	1	1.4
Triptan		131	2.9	68	3.8	27	4.6	0	0.0	3	0.5	6	5.2	12	4.3	0	0.0	7	10.0	8	0.8	0	0.0
Others		108	2.4	46	2.6	14	2.4		0.0	12	2.1	2	1.7	9	3.3	3	25.0	8	11.4	3	0.3	11	15.9
None		2928	64.6	1012	56.9	327	55.1	64	100.0	440	76.1	48	41.7	157	56.9	5	41.7	14	20.0	817	83.2	44	63.8
Medications given pre-ED by a paramedic, *n* (%) for 791 ambulance arrivals																							
Any		347	44.0	245	53.6	72	50.0	0	0.0	0	0.0	2	6.7	19	26.4	0	0.0	0	0.0	2	5.7	7	38.9
Paracetamol		140	17.7	97	21.2	30	20.8	0	0.0	0	0.0	2	6.7	11	15.3	0	0.0	0	0.0	0	0.0	0	0.0
Aspirin		10	1.3	7	1.5	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	2.9	1	5.6
NSAIDs		20	2.5	4	0.9	12	8.3	0	0.0	0	0.0	0	0.0	2	2.8	0	0.0	0	0.0	0	0.0	2	11.1
Triptan		2	0.3	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Opioids		125	15.8	88	19.3	32	22.2	0	0.0	0	0.0	2	6.7	3	4.2	0	0.0	0	0.0	0	0.0	0	0.0
Antiemetic		198	25.1	156	34.1	32	22.2	0	0.0	0	0.0	1	3.3	8	11.1	0	0.0	0	0.0	1	2.9	0	0.0
Methoxyflurane		29	3.7	23	5.0	6	4.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Others		17	2.2	9	2.0	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	6	33.3
None		402	51.0	188	41.1	68	47.2	11	100.0	21	100.0	28	93.3	42	58.3	0	0.0	1	100.0	32	91.4	11	61.1
Not documented		40	5.1	24	5.3	4	2.8	0	0.0	0	0.0	0	0.0	11	15.3	0	0.0	0	0.0	1	2.9	0	0.0
Medications prescribed in the ED, *n* (%)																							
Any	1	3449	76.0	1464	82.4	480	80.9	20	31.3	339	58.7	80	69.6	140	50.7	7	58.3	51	72.9	808	82.3	60	87.0
Paracetamol		1933	42.6	1016	57.2	336	56.7	9	14.1	158	27.3	58	50.4	84	30.4	0	0.0	36	51.4	200	20.4	36	52.2
NSAIDs		1641	36.2	605	34.0	188	31.7	3	4.7	127	22.0	21	18.3	23	8.3	1	8.3	32	45.7	617	62.8	24	34.8
Aspirin		222	4.9	185	10.4	10	1.7	0	0.0	0	0.0	0	0.0	27	9.8	0	0.0	0	0.0	0	0.0	0	0.0
Opioids[a]		1072	23.6	586	33.0	221	37.3	7	10.9	132	22.8	22	19.1	52	18.8	1	8.3	13	18.6	38	3.9	0	0.0
Oxycodone		371	8.2	363	20.4	5	0.8	0	0.0	0	0.0	1	0.9	1	0.4	0	0.0	0	0.0	1	0.1	0	0.0
Codeine		395	8.7	169	9.5	158	26.6	0	0.0	19	3.3	4	3.5	30	10.9	0	0.0	1	1.4	14	1.4	0	0.0

(Continues)

TABLE 2 (Continued)

Country	#Missing	All		Australia		New Zealand		Hong Kong		Singapore		France		United Kingdom		Israel		Belgium		Turkey		Romania	
		n = 4536 (100%)		*n* = 1777 (39%)		*n* = 593 (13%)		*n* = 64 (1.4%)		*n* = 578 (13%)		*n* = 115 (2.5%)		*n* = 276 (6.1%)		*n* = 12 (0.3%)		*n* = 70 (1.5%)		*n* = 982 (22%)		*n* = 69 (1.5%)	
		n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Pethidine		13	0.3	2	0.1	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	10	1.0	0	0.0
Other opioid		405	8.9	129	7.3	78	13.2	7	10.9	114	19.7	17	14.8	27	9.8	1	8.3	12	17.1	20	2.0	0	0.0
Antiemetic		1384	30.5	707	39.8	244	41.1	7	10.9	151	26.1	11	9.6	50	18.1	2	16.7	4	5.7	196	20.0	12	17.4
Triptan		85	1.9	41	2.3	12	2.0	0	0.0	5	0.9	3	2.6	9	3.3	0	0.0	4	5.7	11	1.1	0	0.0
Chlorpromazine		311	6.9	264	14.9	47	7.9	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Corticosteroids		89	2.0	53	3.0	17	2.9	0	0.0	2	0.3	1	0.9	2	0.7	0	0.0	1	1.4	11	1.1	2	2.9
Ergot alkaloids		6	0.1	1	0.1	0	0.0	0	0.0	4	0.7	0	0.0	1	0.4	0	0.0	0	0.0	0	0.0	0	0.0
Antibiotic or antiviral		48	1.1	19	1.1	23	3.9		0.0	2	0.3		0.0	1	0.4	0	0.0	2	2.9	1	0.1	0	0.0
Others		391	8.6	151	8.5	41	6.9	5	7.8	40	6.9	28	24.3	31	11.2	4	33.3	17	24.3	40	4.1	34	49.3
IV fluids		294	6.5	190	10.7	60	10.1	0	0.0	13	2.2	1	0.9	10	3.6	0	0.0	4	5.7	15	1.5	1	1.4
None		1086	23.9	313	17.6	113	19.1	44	68.8	239	41.3	35	30.4	135	48.9	5	41.7	19	27.1	174	17.7	9	13.0
Patient disposition, *n* (%)																							
Home from the ED via observation unit		984	21.7	559	31.5	94	15.9	4	6.3	20	3.5	7	6.1	39	14.1	1	8.3	13	18.6	243	24.7	4	5.8
Home from the ED		2808	61.9	899	50.6	365	61.6	45	70.3	422	73.0	93	80.9	164	59.4	11	91.7	51	72.9	707	72.0	51	73.9
Admit ward		633	14.0	276	15.5	119	20.1	11	17.2	131	22.7	14	12.2	63	22.8	0	0.0	5	7.1	14	1.4	0	0.0
Admit critical care		33	0.7	12	0.7	4	0.7	0	0.0	4	0.7	0	0.0	2	0.7	0	0.0	1	1.4	10	1.0	0	0.0
Transfer		63	1.4	22	1.2	9	1.5	1	1.6	0	0.0	1	0.9	8	2.9	0	0.0	0	0.0	8	0.8	14	20.3
Unknown		10	0.2	7	0.4	0	0.0	3	4.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Died in the ED		1	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Theater		3	0.1	1	0.1	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Interventional radiology		1	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Medications prescribed at discharge, *n* = 3792 (patients discharged from the ED or ED observation unit)																							
Any	0	1555	41.0	314	21.5	252	54.9	47	95.9	412	93.2	68	68.0	35	17.2	2	16.7	47	73.4	344	36.2	34	61.8
Paracetamol		902	23.8	94	6.4	169	36.8	33	67.3	283	64.0	46	46.0	4	2.0	0	0.0	38	59.4	217	22.8	18	32.7
NSAIDs		625	16.5	62	4.3	114	24.8	21	42.9	213	48.2	25	25.0	5	2.5	1	8.3	34	53.1	135	14.2	15	27.3
Aspirin		47	1.2	29	2.0	6	1.3	1	2.0	2	0.5	1	1.0	3	1.5	0	0.0	1	1.6	0	0.0	4	7.3
Opioids[a]		386	10.2	99	6.8	73	15.9	12	24.5	125	28.3	20	20.0	14	6.9	0	0.0	4	6.3	29	3.1	10	18.2
Oxycodone		36	0.9	35	2.4	0	0.0	0	0.0	0	0.0	1	1.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

(Continues)

TABLE 2 (Continued)

Country	#Missing	All		Australia		New Zealand		Hong Kong		Singapore		France		United Kingdom		Israel		Belgium		Turkey		Romania	
		n = 4536 (100%)		*n* = 1777 (39%)		*n* = 593 (13%)		*n* = 64 (1.4%)		*n* = 578 (13%)		*n* = 115 (2.5%)		*n* = 276 (6.1%)		*n* = 12 (0.3%)		*n* = 70 (1.5%)		*n* = 982 (22%)		*n* = 69 (1.5%)	
		n	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%
Codeine		221	5.8	57	3.9	64	13.9	1	2.0	43	9.7	6	6.0	14	6.9	0	0.0	1	1.6	29	3.1	6	10.9
Tramadol		113	3.0	5	0.3	7	1.5	8	16.3	82	18.6	4	4.0	0	0.0	0	0.0	3	4.7	0	0.0	4	7.3
Other opioid		21	0.6	4	0.3	3	0.7	4	8.2	0	0.0	9	9.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
Antiemetic		312	8.2	89	6.1	83	18.1	11	22.4	124	28.1	2	2.0	1	0.5	0	0.0	1	1.6	1	0.1	0	0.0
Triptan		63	1.7	21	1.4	12	2.6	2	4.1	6	1.4	5	5.0	4	2.0	0	0.0	2	3.1	11	1.2	0	0.0
Steroids		20	0.5	7	0.5	8	1.7	1	2.0	0	0.0	0	0.0	2	1.0	0	0.0	1	1.6	1	0.1	0	0.0
Ergot alkaloids		20	0.5	0	0.0	1	0.2	0	0.0	19	4.3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Others		172	4.5	42	2.9	25	5.4	17	34.7	45	10.2	12	12.0	7	3.4	1	8.3	9	14.1	2	0.2	12	21.8
Antibiotic, antiviral		109	2.9	26	1.8	29	6.3	4	8.2	18	4.1	6	6.0	4	2.0	0	0.0	1	1.6	20	2.1	1	1.8
None		2237	59.0	1144	78.5	207	45.1	2	4.1	30	6.8	32	32.0	168	82.8	10	83.3	17	26.6	606	63.8	21	38.2

[a]Patients may have received more than one opioid.

countries and an exploration of independent predictors of opioid use, after adjusting for other predictors.

RESULTS

We enrolled 4536 patients. 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 (Table 1). "Benign headache" (nonmigraine primary, tension-type, musculoskeletal, and cluster) accounted for almost half of the cases, 2058/4536 (45.4%). Headache was classified as migraine in a further 1101/4536 (24.3%). Life-threatening headache disorder was found in 323/4536 (7.1%) patients, of which subarachnoid hemorrhage, stroke, neoplasm, non-subarachnoid hemorrhage intracranial hemorrhage/hematoma, and meningitis accounted for about 1% each. Detailed ED caseload data were available for 62 hospitals. Patients with headache accounted for 1% (95% CI 1.0%–1.1%) of available ED caseload data.

The median patient age was 41 (IQR 29–55) years, and females accounted for 2907/4536 (64.1%) patients (Table 1). A small number of patients reported long-term opioid use (3.6%). The most common mode of arrival to the ED was self-presentation (80.1%) (Table 1). Patients were most likely to present with a moderate pain score for their headache (41.2%). More than a quarter of patients reported headache pain as severe (27.2%) (Table 1). In total, 2808/4536 (61.9%) patients were discharged directly from the ED, and a further 984/4536 (21.7%) patients were discharged from the ED observation or short-stay unit (Table 2). There were 633/4536 (14.0%) patients admitted to an inpatient ward, with a small number admitted to critical care, operating theater, or transferred to a referral hospital (Table 2).

Opioid administration prehospital, in ED, and discharge

Prior to ED presentation, 289/4536 (6.4%) patients reported self-administration of opioids at home (Table 2). There were 791 patients transferred to the hospital by ambulance, and of these, opioids were administered in 125 (15.8%) (Table 2). In the ED, 1072/4536 (23.6%, 95% CI 22.4–24.9) patients received an opioid including oxycodone (8.2%), codeine (8.7%), pethidine (0.3%), and the composite other opioids (8.9%). Of the patients discharged either directly from the ED or from the ED short-stay unit, 386/3792 (10.2%, 95% CI 9.3–11.2) received a prescription for opioids, including oxycodone (0.9%), codeine (5.8%), tramadol (3.0%), or the composite "other opioid" (0.6%) (see Tables 2 and 3).

Geographical variation in opioid administration

There was a variation in opioid use by country prehospital, in the ED, and at discharge, presented in Table 2 and Figure 1. Patients in Australia and New Zealand self-administered opioids prior to ED

TABLE 3 Opioid use per 100 patients with headache, by country and timing of opioid use/prescription

Country	Pre-ED (self-administered), all patients	In ambulance, all patients arriving by ambulance ($n = 791$)	In the ED, all patients	At discharge, all discharged from the ED or ED observation unit ($n = 3792$)
	Proportion (95% CI)	Proportion (95% CI)	Proportion (95% CI)	Proportion (95% CI)
Australia ($n = 1777$)	10.7 (9.4–12.2)	19.3 (15.9–23.1)	33.0 (30.8–35.2)	6.8 (5.6–8.2)
New Zealand ($n = 593$)	9.3 (7.2–11.9)	22.2 (16.2–30.0)	37.3 (33.5–41.2)	15.9 (12.8–19.5)
Hong Kong ($n = 64$)	0.0 (0.0–5.7)	0.0 (0.0–25.9)	10.9 (5.4–20.9)	24.5 (14.6–38.1)
Singapore ($n = 578$)	0.69 (0.27–1.77)	0.0 (0.0–15.5)	22.8 (19.6–26.4)	28.3 (24.3–32.7)
France ($n = 115$)	7.8 (4.2–14.2)	6.7 (1.8–21.3)	19.1 (13.0–27.3)	20.0 (13.3–28.9)
United Kingdom ($n = 276$)	7.7 (5.0–11.3)	4.2 (1.4–11.6)	19.9 (15.6–25.0)	6.9 (4.2–11.2)
Israel ($n = 12$)	0.0 (0.0–24.3)	[a]	8.3 (1.5–35.4)	0.0 (0.0–24.3)
Belgium ($n = 70$)	4.3 (1.5–11.9)	0.0 (0.0–79.8)	18.6 (11.2–29.2)	6.3 (2.5–15.0)
Turkey ($n = 982$)	0.31 (0.10–0.89)	0.0 (0.0–9.9)	3.9 (2.8–5.3)	3.1 (2.1–4.4)
Romania ($n = 69$)	5.8 (2.3–14.0)	0.0 (0.0–17.6)	0.0 (0.0–5.3)	18.2 (10.2–30.3)
All above ($n = 4536$)	6.4 (5.7–7.1)	15.8 (13.4–18.5)	23.6 (22.4–24.9)	10.2 (9.3–11.2)

[a]There were no ambulance arrivals in the Israel sample.

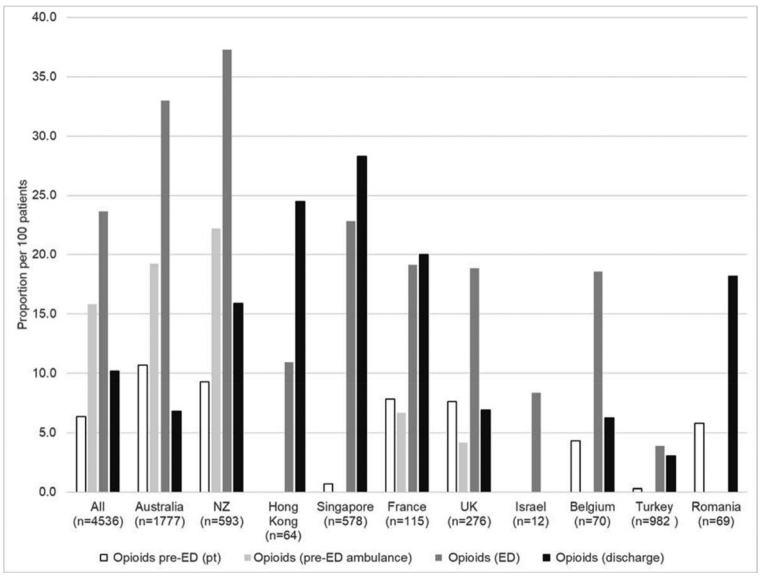

FIGURE 1 Opioids taken or given by country pre-ED (patient), pre-ED (ambulance), in the ED, and at discharge. ED, emergency department; NZ, New Zealand; pt, patient; UK, United Kingdom

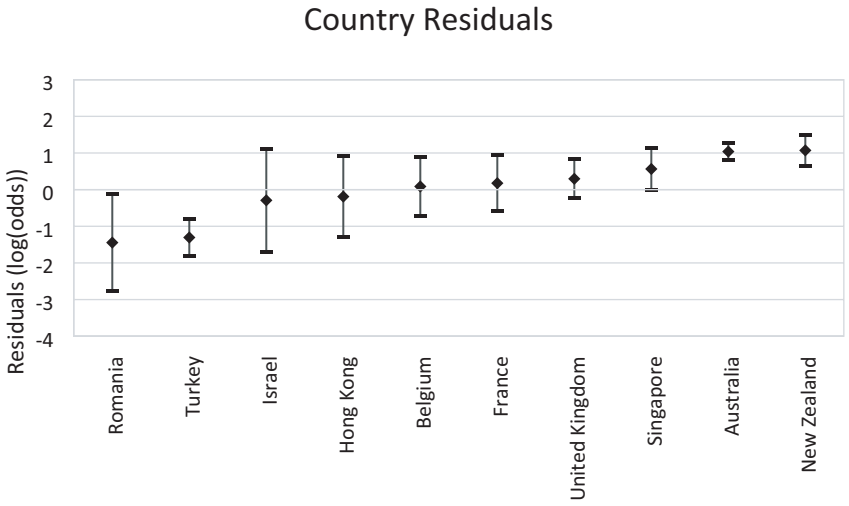

FIGURE 2 Plot of country residuals derived from the multilevel logistic regression modeling of emergency department (ED) opioid use with country and hospital included as random effects in an intercept-only model. The residual is the deviation of a country's log-odds for any ED opioid use from the overall average across all countries. The average country has a residual of zero. The vertical lines are 95% confidence intervals. The residuals were greater for New Zealand and Australia indicating that they used more opioids in the ED than the average country. Likewise, Romania and Turkey used less opioids than the average country

TABLE 4 Factors univariately associated with opioid prescription in the emergency department (ED) and at discharge

	In the ED ($n = 4534$)						At discharge (discharge home from the ED/EDU only $n = 3792$)					
	Opioid used		Opioid not used				Opioid used		Opioid not used			
Characteristic	*n*	%	*n*	%	*p*-value	OR (95% CI)	*n*	%	*n*	%	*p*-value	OR (95% CI)
N	1072	23.6	3462	76.4			386	10.2	3406	89.8		
Country					<0.001						<0.001	
Australia	586	33.0	1191	67.0		1.00 (ref.)	99	6.8	1359	93.2		1.00 (ref.)
New Zealand	221	37.3	372	62.7		1.21 (1.00–1.47)	73	15.9	386	84.1		2.60 (1.88–3.59)
Hong Kong	7	10.9	57	89.1		0.250 (0.113–0.551)	12	24.5	37	75.5		4.5 (2.3–8.8)
Singapore	132	22.8	446	77.2		0.60 (0.48–0.75)	125	28.3	317	71.7		5.4 (4.0–7.2)
France	22	19.1	93	80.9		0.48 (0.30–0.77)	20	20	80	80		3.43 (2.02–5.84)
United Kingdom	52	18.8	224	81.2		0.47 (0.34–0.65)	14	6.9	189	93.1		1.02 (0.57–1.82)
Israel	1	8.3	11	91.7		0.185 (0.024–1.435)	0	0	12	100		0.000 (0.000–IND)
Belgium	13	18.6	57	81.4		0.46 (0.25–0.85)	4	6.3	60	93.8		0.92 (0.33–2.57)
Turkey	38	3.9	944	96.1		0.082 (0.058–0.115)	29	3.1	921	96.9		0.43 (0.28–0.66)
Romania	0	0	69	100		0.000 (0.000–IND)	10	18.2	45	81.8		3.05 (1.49–6.24)
Age group					0.075	Trend					0.620	Trend
18–29 years	243	20.9	921	79.1		1.00 (ref.)	106	10.1	947	89.9		1.00 (ref.)
30–59 years	625	24.8	1891	75.2		1.25 (1.06–1.48)	227	10.6	1921	89.4		1.06 (0.83–1.35)
60+ years	204	23.8	652	76.2		1.19 (0.96–1.47)	53	9	538	91		0.88 (0.62–1.24)
Sex					0.594						0.070	
Male	377	23.2	1250	76.8		0.97 (0.87–1.08)	153	11.4	1191	88.6		1.00 (ref.)
Female	694	23.9	2213	76.1		1.00 (ref.)	233	9.5	2213	90.5		0.82 (0.66–1.02)
Pain score					<0.001	Trend					<0.001	Trend
Mild	77	9.4	738	90.6		1.00 (ref.)	45	6.3	667	93.7		1.00 (ref.)
Moderate	381	20.4	1488	79.6		2.45 (1.89–3.18)	174	10.7	1455	89.3		1.77 (1.26–2.49)
Severe	477	38.6	758	61.4		6.0 (4.6–7.8)	117	12.3	835	87.7		2.08 (1.45–2.97)
Unclear	137	22.2	479	77.8		Excluded	50	10	449	90		Excluded
Referral					0.055						0.716	
Self	865	23.1	2883	76.9		1.00 (ref.)	327	10.3	2861	89.7		1.00 (ref.)
GP/other	207	26.3	581	73.7		1.19 (1.00–1.42)	59	9.8	545	90.2		0.95 (0.71–1.27)
Mode of arrival					<0.001						0.112	
Self	788	21.7	2847	78.3		1.00 (ref.)	329	10.5	2796	89.5		1.00 (ref.)

(Continues)

TABLE 4 (Continued)

	In the ED ($n = 4534$)						At discharge (discharge home from the ED/EDU only $n = 3792$)					
	Opioid used		Opioid not used				Opioid used		Opioid not used			
Characteristic	*n*	%	*n*	%	*p*-value	OR (95% CI)	*n*	%	*n*	%	*p*-value	OR (95% CI)
Ambulance	257	32.5	534	67.5		1.74 (1.47–2.06)	48	8.3	527	91.7		0.77 (0.56–1.06)
Other	27	24.5	83	75.5		Excluded	9	9.8	83	90.2		Excluded
Triage category					<0.001	Trend					0.671	Trend
Immediate	12	15.6	65	84.4		0.94 (0.51–1.77)	3	7.7	36	92.3		0.76 (0.23–2.48)
Urgent	706	30.8	1588	69.2		2.27 (1.97–2.63)	185	10.5	1573	89.5		1.07 (0.86–1.32)
Nonurgent	354	16.4	1811	83.6		1.00 (ref.)	198	9.9	1797	90.1		1.00 (ref.)
Any prehospital opioid					<0.001						0.109	
Yes	172	42.8	230	57.2		2.69 (2.18–3.32)	42	12.7	288	87.3		1.32 (0.94–1.86)
No	900	21.8	3234	78.2		1.00 (ref.)	344	9.9	3118	90.1		1.00 (ref.)
Any ED opioid											<0.001	
Yes	Not applicable						219	27.2	587	72.8		6.3 (5.1–7.8)
No							167	5.6	2819	94.4		1.00 (ref.)
History of any head complaint					<0.001						0.048	
Yes	399	20.4	1554	79.6		1.00 (ref.)	196	9.3	1909	90.7		0.81 (0.66–1.00)
No	673	26.1	1910	73.9		1.37 (1.19–1.58)	190	11.3	1497	88.7		1.00 (ref.)
History of opioid long term					<0.001						0.276	
Yes	75	45.5	90	54.5		2.82 (2.06–3.86)	16	13.1	106	86.9		1.35 (0.77–2.30)
No	997	22.8	3374	77.2		1.00 (ref.)	370	10.1	3300	89.9		1.00 (ref.)
Duration of symptoms					<0.001						<0.001	
<24 h	425	20.6	1635	79.4		1.00 (ref.)	118	6.6	1677	93.4		1.00 (ref.)
1–3 days	237	23.2	784	76.8		1.16 (0.97–1.39)	85	9.9	775	90.1		1.56 (1.17–2.09)
>3 days	398	28.7	987	71.3		1.55 (1.33–1.82)	176	16.2	910	83.8		2.75 (2.15–3.52)
Unknown	12	17.1	58	82.9		Excluded	7	13.7	44	86.3		Excluded

TABLE 5 Multilevel logistic regression analysis modeling emergency department (ED) opioid use as the binary outcome, country, and hospital as the random effects, and predicators as the fixed effects (n = 4536)

Predictors	Adjusted OR	95% CI	*p*-value
Headache severity			
Mild (reference)	1.00		
Moderate	2.31	1.75–3.05	<0.001
Severe	4.17	3.14–5.54	<0.001
Unknown	1.85	1.35–2.54	0.002
Any opioid long term			
No (reference)	1.00		
Yes	1.80	1.26–2.58	0.001
Any opioid pre-ED[a]			
No (reference)	1.00		
Yes	1.42	1.11–1.82	0.006
Mode of arrival			
Ambulance (reference)	1.00		
Self	1.02	0.84–1.24	0.823
Others	1.31	0.70–2.45	0.393
Triage category			
Nonurgent (reference)	1.00		
Urgent	1.48	1.24–1.76	<0.001
Immediate	1.34	0.64–2.84	0.439
Prior history of headache			
No (reference)	1.00		
Yes	1.04	0.82–1.34	0.726
Random effect			
Country variance	0.66	0.18–2.42	
Hospital variance	0.37	0.21–0.66	
Intraclass correlation			
Country	0.152	0.046–0.399	
Hospital	0.238	0.118–0.422	

Note: In a regression analysis, the outcome variable is modeled as a linear combination of its predictor variables. In a multilevel regression, the intercept of the regression line is allowed to vary across clusters, that is, hospitals and countries. This variability is reflected by the country and hospital variances reported in the table.

The multilevel model shows that there is greater variation in "ED opioid use" between countries than between hospitals (country variance greater than hospital variance). The analysis provided an intraclass correlation (ICC), which is a measure of the correlation between patient outcomes within a cluster. The results show that there is greater correlation in "ED opioid use" within hospitals than within countries (hospital ICC greater than country ICC).

[a]Given by paramedics or self-administered by the patient.

attendance more frequently than in other countries. Of those patients arriving by ambulance (n = 791), patients in Australia (19.3%, 95% CI 15.9–23.1) and New Zealand (22.2%, 95% CI 16.2–30.0) had the highest rates of opioid administration. In the ED, patients in New Zealand (37.3%, 95% CI 33.5–41.2) and Australia (33.0%, 95% CI 30.8–35.2) were more likely to receive opioids than those in other countries. The proportion of patients receiving opioid discharge prescriptions was highest in Singapore (28.3%, 95% CI 24.3–32.7), Hong Kong (24.5%, 95%CI 14.6–38.1), and France (20.0%, 95% CI 13.3–28.9) (see Table 3).

Univariate analysis, factors associated with opioid administration

Table 4 details the factors univariately associated with opioid prescription in the ED and at discharge. Patients in New Zealand were most likely to receive opioids in the ED (37.3%, OR 1.21, 95% CI 1.00–1.47). In other countries, patients were significantly less likely to receive opioids compared with Australia. OR ranged from 0.082 in Turkey, 0.47 and 0.48 in the United Kingdom and France to 0.60 in Singapore. Patients with a moderate or severe pain score were also more likely to receive opioids than those with a mild pain score (OR 2.45, 95% CI 1.89–3.18 for moderate and OR 6.0, 95% CI 4.6–7.8 for severe compared with mild, respectively).

Arrival by ambulance was associated with opioid administration in the ED (OR 1.74, 95% CI 1.47–2.06). Overall, patients who received prehospital opioid, either self-administered or with paramedics, were more likely to receive opioids in the ED (OR 2.69, 95% CI 2.18–3.32). A history of long-term opioid use was also associated with an increased likelihood of receiving opioids in the ED (OR 2.82, 95% CI 2.06–3.86). At discharge, patients in France (OR 3.43, 95% CI 2.02–5.84), New Zealand (OR 2.60, 95% CI 1.88–3.59), and Singapore (OR 5.4, 95% CI 3.0–7.2) were more likely to receive opioids than patients in Australia. Prescription of an opioid in the ED was associated with opioid prescription at discharge (OR 6.3, 95% CI 5.1–7.8).

Multilevel logistic regression

The proportion of patients receiving an opioid in the ED was 18.1% (95% CI 10.8–25.3), as calculated from the multilevel logistic regression analysis using an intercept-only model with country and hospital as the random effects. There was a variation in opioid use in the ED between countries (Figure 2, Table 5). Independent predictors of ED opioid administration were severe headache (OR 4.17, 95% CI 3.14–5.54 compared with mild), pre-ED opioid use (OR 1.42, 95% CI 1.11–1.82), and long-term opioid use (OR 1.80, 95% CI 1.26–2.58) (Table 5). Patients self-presenting and prior history of headache were not statistically significant predictors after adjustment for the aforementioned variables.

The proportion of patients prescribed an opioid at discharge was 14.2% (95% CI 7.4–21.0) from a separate regression analysis using an intercept-only model with country and hospital as the random effects. There was a variation in opioid prescribing at discharge between countries (Figure 3, Table 6). Any opioid use in the ED was the statistically significant predictor of opioid prescription at discharge (OR 8.4, 95% CI 6.3–11.0) (Table 6).

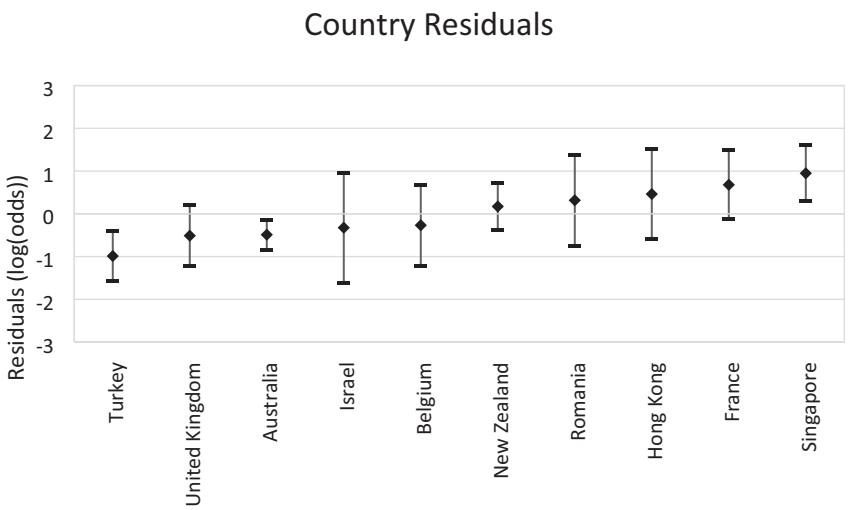

FIGURE 3 Plot of country residuals derived from the multilevel logistic regression modeling of opioid prescribed at discharge with country and hospital included as random effects in an intercept-only model. The residual is the deviation of a country's log-odds for opioid prescribed at discharge compared with the average country with a residual of zero. The vertical lines are 95% confidence interval

DISCUSSION

This study described the use of opioids prehospital, in the ED and at discharge for patients presenting to the ED with nontraumatic headache. Opioid use prehospital, during ambulance transfer, and in the ED was more common in patients from Australia and New Zealand. Overall opioid use in the ED was high, with 23.6% of patients receiving an opioid at some stage during their stay in the ED. At discharge, patients from France, New Zealand, and Singapore were more likely to receive an opioid prescription.

The overall rate of opioid use in this study was similar to that observed in the existing literature.[5] However, there was a significant variation between the countries involved in the study. Australia and New Zealand had the highest ED opioid use (33.0% and 37.3%, respectively) compared with other countries. In Australia, 20.4% of patients received oxycodone in the ED. Oxycodone is a commonly prescribed drug in Australia, being less common in the United Kingdom and Europe.[19] In this study, most countries, including New Zealand, favored codeine use over oxycodone. Codeine regulations were introduced in Australia in 2018, restricting over-the-counter use, possibly likely explaining the lower rates of codeine use.

Patients presenting with a severe headache (pain score 8–10) were more likely to receive opioids in the ED. In the regression analysis, long-term opioid use and opioid use pre-ED (self- and ambulance-administered) were, along with headache severity, independently associated with a higher ED opioid prescription rate (Figure 2, Table 5). Headache severity is a common way of classifying a headache on arrival to the ED, prior to a clear diagnosis being made. The fact that severity is associated with opioid prescription is important, as many self-limiting headaches can be severe. Nonetheless, it is recognized that opioid use may be a suboptimal therapeutic choice in these cases.[20] Although clinicians want to decrease pain levels, the risk of dependency and lack of evidence for the use of opioids need to be considered in this decision.

The diagnosis of primary headache disorder includes several diagnoses that have differing management, for example, migraine, tension-type headache, and cluster headache. Although headache severity can guide initial therapy, diagnosis alters subsequent management including selection of medication. It is recognized that those presenting with a severe headache may receive "stronger" medications, that is, opioids, especially when diagnostic uncertainty exists.[12,21] For example, a patient presenting with a severe headache might receive opioids with the ambulance or on arrival to the ED, prior to the diagnosis of migraine being made. Results from this study demonstrated that receiving opioids prehospital was associated with an increased likelihood of opioid administration in the hospital. As such, *formulating* a working diagnosis may inform better evidence-based strategies, with other modalities gaining attention for undifferentiated severe headaches, such as the inexpensive, minimally invasive, and nonaddictive sphenopalatine ganglion block.[22]

A recognition that opioids are more likely to be prescribed for severe headache is important for patients, as education may aid in reducing opioid prescriptions in this cohort. Even if a patient classifies his or her symptoms as severe, a considered approach to analgesic options should be taken, with the patient involved in the decision to avoid an opioid wherever possible and appropriate. Although a patient may classify his or her symptoms as severe, this does not necessarily mean he or she wants or needs opioids. Coupled with an awareness of the habit-forming nature of these drugs, this could reduce the overall usage of opioids. A shared approach to decision-making may avoid unnecessary and potentially harmful care.[23,24]

The rate of ambulance-administered opioids (16%) indicates a potential avenue for opioid reduction in headache presentations. However, as with the initial assessment in the ED, it is often difficult to form a clear diagnosis prehospital, and paramedics are likely to initiate treatments based on symptom severity. Nonetheless, knowledge of the epidemiology of prehospital headache presentations from our data set, where prehospital prescription is associated with ED prescription, would support rationalization of prehospital opioid use.

The United States is currently experiencing an opioid crisis, and opioid use has increased in countries throughout Europe.[25,26] It is recognized that the ED is a potential location for patients to become exposed to, and subsequently reliant on, opioid-containing medications.[27–30] Wherever possible, and wherever clinically appropriate, opioid prescribing should be avoided, as is the case in self-limiting

TABLE 6 Multilevel logistic regression analysis modeling opioid prescription on discharge from the emergency department (ED) as the binary outcome, country, and hospital as the random effects, and predicators as the fixed effects (n = 4536)

Predictors	Adjusted OR	95% CI	*p*-value
Any ED opioid use			
No (reference)	1.00		
Yes	8.4	6.3–11.0	<0.001
Headache severity			
Mild (reference)	1.00		
Moderate	1.57	1.06–2.33	0.024
Severe	1.43	0.93–1.95	0.105
Unknown	1.33	0.80–2.23	0.272
Any opioid long term			
No (reference)	1.00		
Yes	1.07	0.56–2.03	0.832
Any opioid pre-ED[a]			
No (reference)	1.00		
Yes	1.49	0.97–2.29	0.067
Mode of arrival			
Ambulance	1.00		
Self	1.38	0.95–2.00	0.091
Others	1.87	0.73–4.81	0.191
Prior history of headache			
No (reference)	1.00		
Yes	1.08	0.75–1.58	0.701
Random effect			
Country variance	0.85	0.25 – 2.93	
Hospital variance	0.62	0.29–1.34	
Intraclass correlation			
Country	0.179	0.06–0.43	
Hospital	0.31	0.17–0.49	

Note: In a regression analysis, the outcome variable is modeled as a linear combination of its predictor variables. In a multilevel regression, the intercept of the regression line is allowed to vary across clusters, that is, hospitals and countries. This variability is reflected by the country and hospital variances reported in the table.

The multilevel model shows that there is greater variation in "opioid prescription on discharge from the ED" between countries than between hospitals (country variance greater than hospital variance). The analysis provided an intraclass correlation (ICC), which is a measure of the correlation between patient outcomes within a cluster. The results show that there is greater correlation in "opioid prescription on discharge from the ED" within hospitals than within countries (hospital ICC greater than country ICC).

[a]Given by paramedics or self-administered by the patient.

headaches. This has the dual benefit of reducing the overall risk of opioid dependence in opioid-naïve patients, and offering superior, evidence-based therapy, particularly in conditions such as migraine and tension-type headache.

The results of this study are of interest to the geographical areas included and may serve as a useful comparison for other regions, such as in North America. The finding of relatively high opioid administration prehospital, and of high levels of opioid prescription in the ED, as well as at discharge for patients with headache reinforces concerns around inappropriate prescribing of opioids. The rate of opioid prescription in this study was similar to other studies.[31,32]

In this study, there was a practice variation in prescribing of opioids for headache based on the country. Given the potential harms of opioid use, and a consensus that primary headache disorders (and in particular migraine) can be treated without using these drugs, an effort should be made to reduce opioid use. Education should include rationalizing prehospital opioid delivery, as well as opioid use in the ED, with the knowledge that a prehospital reduction may reduce overall use in the ED. It should also be recognized that a headache classified as severe does not necessitate opioid use. Many patients with self-limiting headaches will report their symptoms as severe and may not want or need opioids if involved in decisions around care.

LIMITATIONS

As a "snapshot" observational study design over the course of a single calendar month, the study was potentially open to issues of confounding and convenience sampling. There were low patient numbers enrolled in some countries, making the overall interpretation of comparison by country more challenging. A reliance on routine data collection without formal follow up limited data completeness. With the exception of Queensland and the United Kingdom where some form of consent was required, institutions were instructed to include all eligible patients during the enrolment period. There was not the resource to allow verification, which would have the potential to introduce selection bias. Nonetheless, there were a high number of participating patients, and 1% of presentations in our study were for headache, consistent with the literature.[3]

It is possible that prehospital opioid was administered for reasons other than pain. There was no posttreatment pain score; thus, comparison of the effectiveness of different analgesics could not be conducted. Route of administration was not considered. It is acknowledged that drug prescriptions may have been related to another secondary condition, although prescribed analgesia was likely intended to treat the primary complaint of headache. This was a pragmatic, real-world study. Because of resource limitations, interrater reliability was outside of the scope of the paper.

Although most patients were recruited prospectively, some data were collected retrospectively. Although it was intended to include all eligible consecutive patients, we cannot quantify the proportion of potentially eligible patients who were not included. Several criteria in the data collection were reliant on clinician and researcher classification, including diagnosis, severity, and presenting symptoms. Nonetheless, headache is often a clinical diagnosis, without supporting investigation, and symptom

classification is often subjective and is based on patient experience. In this study, all opioids were combined, regardless of the route of administration; this could be an area for investigation in future studies. We acknowledge other variables as nonmeasured possible confounders and areas for future research: prescriber (an ED clinician, a neurologist, etc.), ineffective first-line medication, duration of headache, comorbidities, and presence of clear guidelines in a particular hospital or country.

CONCLUSIONS

Opioid prescription for primary headache disorders in the ED varies internationally, with Australia and New Zealand having the highest use. Prescription patterns varied across other countries. Severe headache, pre-ED opioid use, and long-term opioid use were independent predictors of ED opioid administration, and ED opioid administration was a predictor of opioid prescription at discharge. These findings highlight the importance of identifying strategies to reduce this evidence–practice gap as a matter of priority.

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CONFLICT OF INTEREST

All authors declare no real or potential conflict of interest to exist regarding this research paper.

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SUPPORTING INFORMATION

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

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