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Research Submission

Unmet Acute Treatment Needs From the 2017 Migraine in America Symptoms and Treatment Study

Richard B. Lipton, MD; Sagar Munjal, MD, MS; Dawn C. Buse, PhD; Aftab Alam, MBBS, MS, MBA; Kristina M. Fanning, PhD; Michael L. Reed, PhD; Todd J. Schwedt, MD; David W. Dodick, MD

Objectives.—To characterize unmet treatment needs in a sample of Migraine in America Symptoms and Treatment (MAST) Study participants using oral, acute prescription migraine medications.

Background.—The MAST Study is a 2017 study of U.S. adults with migraine that profiles current treatment patterns and identifies and quantifies unmet treatment needs.

Methods.—Cross-sectional data from an online survey of US adults meeting ICHD-3 beta criteria for migraine. For inclusion in this paper, respondents self-reported a history of 3 or more monthly headache days (MHDs) in the past 3 months and at least 1 MHD in the past 30 days, and current use of orally administered acute prescription medication for headache. Three domains of unmet need were identified: inadequate treatment response (ie, inadequate 2-hour pain freedom, recurrence within 24 hours of initial relief), demanding attack characteristics (rapid onset of attack, headache associated with sleep), and unique patient characteristics (opioid or barbiturate overuse, cardiovascular comorbidity). Sociodemographics, oral medication use, and coexisting conditions and symptoms (ie, level of treatment optimization, psychological symptoms, attack-related cutaneous allodynia, and migraine symptom severity) were assessed for each domain and by the number of unmet need domains.

Results.—Overall, 15,133 respondents met inclusion criteria, 26.0% (3930/15,133) reported current use of oral acute prescription medication to treat headache. Eligible participants had a mean age of 45.0 years, 73.6% [2892/3930] were women and 81.1% [3186/3930]) were White. A total of 95.8% (3765/3930) of respondents had at least 1 unmet acute treatment need; 89.5% (3516/3930) reported demanding attack characteristics, 74.1% (2912/3930) reported inadequate treatment response, and 16.1% (634/3930) presented with unique patient characteristics. Common areas of unmet need were rapid headache onset (65.3% [2567/3930]), moderate to severe disability (55.6% [2187/3930]), inadequate 2-hours pain freedom (49.0% [1892/3930]), and headache recurrence within 24 hours (38.0% [1493/3930]). An increasing number of unmet treatment need domains was associated with worsening psychological symptoms, attack-related cutaneous allodynia and migraine symptom severity.

Conclusion.—Nearly all MAST Study respondents using acute oral prescription medications for migraine reported at least 1 unmet treatment need. As unmet needs increased, so did coexisting conditions and symptom severity.

Key words: migraine, epidemiology, acute treatment, unmet needs

Abbreviations: ASC-12 Allodynia Symptom Checklist, BMI body mass index, CV cardiovascular, ED/UC emergency department or urgent care, ICHD International Classification of Headache Disorders, MAST Migraine in America: Symptoms and Treatment, MIDAS Migraine Disability Assessment, MSSS Migraine Symptom Severity Scale, m-TOQ6 Migraine Treatment Optimization Questionnaire, MHD monthly headache day, NSAID nonsteroidal anti-inflammatory drugs, OTC over-the-counter, PHQ-4 Patient Health Questionnaire, U.S. United States

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From the Saul R. Korey Department of Neurology, Montefiore Medical Center, Albert Einstein College of Medicine, Bronx, NY, USA (R.B. Lipton and D.C. Buse); Promius Pharma, Princeton, NJ, USA (S. Munjal and A. Alam); Vedanta Research, Chapel Hill, NC, USA (K.M. Fanning and M.L. Reed); Mayo Clinic Arizona, Scottsdale, AZ, USA (T.J. Schwedt and D.W. Dodick).

Address all correspondence to R.B. Lipton, The Saul R. Korey Department of Neurology, Montefiore Medical Center, Albert Einstein College of Medicine, 1225 Morris Park Avenue, Van Etten Building, Room 3C-12, Bronx, NY 10461, USA, email: Richard.Lipton@einstein.yu.edu

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INTRODUCTION

Migraine is a painful, disabling headache condition that affects more than 1 billion people worldwide[1] and between 38 million[2,3] and 47 million[1] people in the United States with recurrent attacks of moderate to severe headache that are typically unilateral, pulsating, aggravated by routine physical activity, and variably associated with nausea, vomiting, photophobia, and phonophobia.[4] Disability associated with migraine is common, and affected individuals have been shown to experience substantially impaired performance in professional and academic settings and negative effects on social activities.[2,3,5] Due to its high prevalence and adverse effects on health-related quality of life,[6] migraine is among the most common reasons for consulting a medical professional.[7-9] The professionals most likely to be consulted are primary care providers,[7-10] and the majority of consulting headache patients remain in primary care; only a minority receive treatment from specialists and an even smaller number at specialty headache centers.[10]

Patterns of diagnosis and treatment of migraine have been studied in population and clinic-based studies.[3,11,12] Evidence-based medications for acute use include both over-the-counter (OTC) and prescription medications, and they can be grouped into 5 widely used drug classes: serotonin 5-HT_{1B-1D} receptor agonists (ie, triptans), nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, barbiturate-containing analgesics, and ergot alkaloids.[13,14] Antiemetics, muscle relaxants, simple analgesics, analgesic combinations, neurostimulators devices, and behavioral treatments may also be used as acute treatments.

Surveys of patient attitudes about acute migraine medications indicate that the most important attributes are rapid onset of pain relief, complete pain

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relief, few or no side effects, and no headache recurrence.[15-19] Previous research into unmet needs among individuals with migraine has shown that nearly 40% are dissatisfied.[20] The most common complaints about acute treatment are that pain relief takes too long or is inconsistent, that pain recurs, or that medication leads to side effects.[21] Poorly optimized acute treatment of patients with episodic migraine is associated with an increased risk they will develop chronic migraine.[22] Other analyses of unmet needs have shown that, among persons with episodic migraine, 25% or fewer receive minimally appropriate medical care, which includes consultation, diagnosis, and evidence-based treatment.[21,23,24] Although a number of unmet needs have been identified and described individually, and prior analyses have generally associated unmet needs with outcomes in clinical practice, no population study has simultaneously evaluated a broad range of unmet treatment needs and explored the relationship of the number of unmet needs to treatment outcomes. Understanding and describing these unmet needs is likely to suggest opportunities for improving outcomes.

The Migraine in America Symptoms and Treatment (MAST) Study is a 2017 study of US adults with migraine. MAST profiles persons with migraine and current treatment patterns and identifies and quantifies unmet treatment needs. The objectives of the current analysis were to characterize and quantify unmet treatment needs among persons with migraine and to provide clinicians with resources for identifying unmet needs and medical strategies for addressing them.

METHODS

Ethics.—The MAST Study protocol was reviewed by Ethical and Independent Review Services (Independence, MO), which granted an exemption from the requirements of federal regulation 45 CFR 46.101(b)(2) and certified the exemption status of the MAST Study (#16106-01) on 31 August 2016. Volunteer study respondents were provided with a description of the study; they were asked to confirm their interest in participating and electronically signify informed consent. A small monetary incentive was given to respondents who completed the survey. All authors had full access to all data and can take responsibility for the integrity of the analyses.

Design.—The MAST Study is a cross-sectional and longitudinal Web-based study of U.S. adults who met migraine symptom criteria and experienced 1 or more recent attacks. Detailed study methods have been previously published.[25] In brief, respondents were selected from an online research panel (Research Now, Plano, TX) and stratified sampling was used to identify a baseline cohort that was comparable to the total U.S. population (±5% of 2015 Census data) for sex, age, household income, race, marital status, and Census region.

Respondent recruitment was implemented from October 2016 to January 2017 and included the validated American Migraine Study/American Migraine Prevalence and Prevention study diagnostic migraine screening module to assess modified International Classification of Headache Disorders, 3rd edition beta (ICHD-3 beta) migraine criteria.[2,26-29] (The most recent edition, ICHD-3,[4] was not used because it had not been published at the time of the study.) This module has sensitivities of 100% and 91% for episodic migraine and chronic migraine, respectively, and specificities of 82% and 80% for episodic migraine and chronic migraine, respectively.[11,30]

Analysis Sample.—Respondents with a self-reported history of 3 or more monthly headache days (MHDs) in the past 3 months and at least 1 MHD in the past 30 days were included in the total MAST Study sample. The present analysis examines the subset of respondents who reported current use of orally administered acute prescription medications to treat headache with or without OTC medication. Respondents using nonoral acute medication (ie, intranasal or parenteral formulations) were excluded.

Data Integrity.—Completed surveys were subjected to a series of quality checks to eliminate unreliable responses. At the beginning and end of the survey, respondents were asked to provide their sex and date of birth, and individuals who provided inconsistent responses were eliminated. The mean time to survey completion was also used as a quality check, and respondents who finished faster than 2 standard deviations (SDs) from the mean time were excluded. Respondents who provided undifferentiated or pattern-based responses (eg, selecting all listed options or the same option consistently), as well as those who provided

incorrect responses to specific requests (eg, please enter the number 23 in the box below) after receiving online prompts were also excluded.

Assessments.—The MAST Study baseline assessment included validated instruments and original questions that were developed through patient focus groups, literature review, consensus opinion from expert clinicians working in tertiary headache centers and co-authors on this report. Respondent age (years); sex (male or female); total annual household income (<$25,000 to ≥$100,000); race (White or non-White); marital status (yes or no); education (<4-year college degree or ≥4-year college degree); employment status (full- or part-time employment); health insurance status (yes vs no) were obtained from single self-reported survey items. Body mass index (BMI) was calculated in the usual manner[31] and categorized as underweight (<18.5), normal weight (18.5-24.9), overweight (25.0-29.9), or obese (≥30.0). Smoking status was assessed by asking respondents about current and lifetime smoking history. Migraine attack frequency was measured by MHDs, which were calculated by asking how many days over the past 3 months respondents had been affected by headache for any part or the whole of the day and dividing the result by 3.

Unmet Treatment Needs.—The acute treatment needs item set was initially developed from a review of related literature and from discussions with clinician experts in migraine management. These items were reviewed with migraine patients in multiple focus group settings and refined as necessary to match patient experience and linguistic preferences. Further testing and refinement of the item set was implemented prior to initiating data collection. This process resulted in 11 items related to either inadequate treatment response or demanding attack characteristics that were queried over the prior 3 months. Respondents were asked to rate each item as occurring never, rarely, less than half the time, half the time or more, or all or nearly all of the time. Unmet treatment need on these variables was assigned when items were reported as occurring half the time or more or all or nearly all of the time.

Four additional unmet treatment needs were included in this analysis. Migraine-related disability was assessed with the 5-item Migraine Disability Assessment (MIDAS) questionnaire,[32] a 5-item scale assessing missed and reduced productivity days at work, school, or home during the previous 3 months due to headache. Items were summed and grouped to identify disability by 4 grades: little or no (score of 0-5), mild (score of 6-10), moderate (score of 11-20), and severe (score of ≥21); the present analysis used the cut point of at least 11 to indicate moderate-to-severe disability.

Because the use of opioid and barbiturate medications is generally considered inappropriate for management of migraine,[14] the use of either class of drugs on 10 or more days per month was considered an unmet need. The use of emergency department or urgent care (ED/UC) in the past 6 months for migraine was judged to be a sign of unmet needs, as well as the opportunity to improve treatment. Finally, the presence of CV risk factors can limit treatment options[33] and thus was considered an unmet treatment need. Respondents were asked if they have or have ever had angina/heart disease (chest pain with exertion); circulation problems (peripheral artery disease); heart attack (myocardial infarction); high cholesterol; hypertension; pulmonary vascular disease; and stroke or transient ischemic attack. Respondents were asked to select all applicable conditions and were considered to have CV risk if they endorsed any of them.

Based on item face validity and expert clinician judgment, these 15 unmet needs were organized into 3 domains and 11 subdomains. The first domain, inadequate treatment response, was assigned 5 subdomains: inadequate 2-hour pain freedom; recurrence within 24 hours of initial relief; treatment-related nausea (oral medications cause nausea and oral medications worsen nausea); delay taking treatment out of fearing side effects; and ED/UC use for headache. The second domain, demanding attack characteristics, was assigned 4 subdomains: rapid onset of attack (come on very rapidly and peak in less than 30 minutes), headache associated with sleep (awaken from sleep and awaken normally with a severe headache); nausea affects treatment (makes it difficult/impossible to take oral medication and makes oral medications less effective); and disability (MIDAS ≥ 11). The third domain, unique patient characteristics, was assigned based on 2 subdomains: opioid or barbiturate overuse and CV

comorbidity. These patient characteristics are important because they impact the (1) risk of disease progression and (2) the recommended treatment options. The 3 domains described above formed the basis of the current analysis of unmet treatment need among this population sample of persons with migraine using acute oral medications.

Coexisting Conditions and Symptom Measures.—We explored the associated impact or burden of unmet treatment needs by looking at the level of treatment optimization and 3 respondent characteristics (psychological symptoms, cutaneous allodynia, and migraine symptom severity).

Acute treatment optimization was evaluated with the Migraine Treatment Optimization Questionnaire (m-TOQ6).[34,35] Functional ability, pain freedom within 2 hours of treatment, sustained relief, and tolerability were queried. Respondent answers of never, rarely, less than half the time, and half the time or more were assigned respective scores of 0, 0, 1, and 2. Total scores were calculated by summing these responses, and based on total score, respondents were classified as having very poor (0), poor (1-5), moderate (6-7), or maximum (8) treatment optimization.[22] A collapsed score of 0-5 was used here to indicate poor or very poor treatment optimization.

The presence of psychological symptoms was based on 2-week recall and measured with the Patient Health Questionnaire (PHQ-4),[36] a 4-item depression and anxiety screener with responses including not at all (0), several days (1), more than half the days (2), and nearly every day (3). Total score was calculated by adding the scores for the 4 items, yielding a score range from 0 to 12. Symptom scores of 0-2 were considered none, 3-5 were mild, 6-8 were moderate, and 9-12 were severe. A dichotomous cut score of 6 or more (moderate or severe) was used to indicate the presence of clinically significant psychological symptoms.

The presence of cutaneous allodynia (defined as increased pain or an unpleasant sensation on the skin during a migraine attack) was determined with the 12-item Allodynia Symptom Checklist (ASC-12).[37] Possible responses to each item were does not apply to me, never, rarely, less than half the time, and half the time or more. Scores on the ASC-12 range from 0 to 24, and a score of at least 3 signified the presence of cutaneous allodynia.

Migraine symptom severity was measured with the Migraine Symptom Severity Scale (MSSS), which evaluates migraine pain and associated symptoms by assigning scores between 0 and 3 for 7 headache features (unilateral pain, pulsating pain, pain with moderate to severe intensity, pain made worse by routine activity, nausea, photophobia, and phonophobia), yielding a score range of 0-21. On the MAST survey instrument, response options were never (0), rarely (1), less than half the time (2), half the time or more (3), or all or nearly all the time (3). MSSS was evaluated as a continuous score.

Statistical Analysis.—All analyses were performed using IBM SPSS Statistics Version 24.0 (IBM, Armonk, NY, USA; 2011), with the aim of summarizing sociodemographics, headache features, attack characteristics, and treatment response for a sample of oral acute medication users and by unmet need domain. Percentages were calculated for all variables except for respondent age, BMI, symptom severity (MSSS), and MHDs, for which means and SDs were calculated. All percentages are based on total sample of respondents in the analysis. Respondents could be included in more than 1 treatment need domain, hence statistical comparisons were not implemented among domains. However, we did test for the impact of increasing domain endorsement and hypothesized that respondents would report greater burden as the number of unmet need domains increased. Chi-square test for trend and one-way analysis of variance were conducted a priori to compare respondents presenting with 0, 1, 2, or 3 unmet need domains. One-tailed Chi-square testing and 2-tailed analysis of variance testing was implemented using $P < .05$ as the criteria for significance. Missing data were minimal and were, therefore, not imputed.

Data Availability.—Data used for the analyses in this article are available by request.

RESULTS

Respondents.—Of the 15,133 MAST Study respondents initially eligible for analysis, 26.0% (n = 3930) reported current use of orally administered acute prescription medication with or without an OTC medication to treat headache. The remaining 74% of respondents reported no current acute

Table 1.—Sociodemographics, Medication Use, and Coexisting Conditions and Symptoms among MAST Study Respondents by Unmet Need Domain

	Total	Inadequate Treatment Response†	Demanding Attack Characteristics†	Unique Patient Characteristics†
Total within each unmet need domain, n (%)	3930 (100)	2912 (74.1)	3516 (89.5)	634 (16.1)
Sociodemographics				
Age, mean (SD), *y*	45 (13.5)	44 (13.1)	45 (13.4)	48 (13.5)
Women, n (%)	2892 (73.6)	2164 (74.3)	2607 (74.1)	392 (61.8)
Body mass index, mean (SD), kg/m^2	28.3 (7.8)	28.4 (7.9)	28.4 (7.9)	28.8 (8.6)
Household income >$50,000, n (%)	2592 (66)	1871 (64.3)	2295 (65.3)	395 (62.3)
White, n (%)	3186 (81.1)	2349 (80.7)	2853 (81.1)	503 (79.3)
Married, n (%)	2240 (57)	1651 (56.7)	2002 (56.9)	386 (60.9)
≥4-year college degree, n (%)	2300 (58.5)	1687 (57.9)	2021 (57.5)	321 (50.6)
Employed (full/part-time), n (%)	2694 (68.5)	2002 (68.8)	2385 (67.8)	359 (56.6)
Health insurance, n (%)	3706 (94.3)	2735 (93.9)	3313 (94.2)	595 (93.8)
Current smoker, n (%)	533 (13.6)	422 (14.5)	497 (14.1)	150 (23.7)
MHD, mean (SD)	6.9 (6.8)	7.6 (7.2)	7.3 (7.0)	10.2 (8.5)
Oral medication use, n (%)				
Triptan	1808 (46)	1285 (44.1)	1638 (46.6)	174 (27.4)
Rx NSAID	1439 (36.6)	1118 (38.4)	1290 (36.7)	251 (39.6)
Ergot alkaloid	31 (.8)	25 (.9)	28 (.8)	6 (.9)
Opioid	1299 (33.1)	1036 (35.6)	1190 (33.8)	414 (65.3)
Barbiturate	440 (11.2)	343 (11.8)	405 (11.5)	130 (20.5)
At least 1 OTC for headache	2603 (66.2)	1960 (67.3)	2312 (65.8)	391 (61.7)
Coexisting conditions and symptoms				
Poor/very poor treatment optimization,‡ n (%)	1483 (37.7)	1373 (47.1)	1409 (40.1)	331 (52.2)
Psychological symptoms,§ n (%)	1011 (25.7)	869 (29.8)	968 (27.5)	249 (39.3)
Cutaneous allodynia,¶ n (%)	1827 (46.5)	1486 (51)	1735 (49.3)	366 (57.7)
Symptom severity,†† mean (SD)	17.7 (2.7)	17.9 (2.6)	17.9 (2.6)	18.1 (2.5)

†The 3 domains of unmet need are not mutually exclusive.
‡Assessed by the Migraine Treatment Optimization Questionnaire.
§Assessed by the Patient Health Questionnaire 4-item Depression and Anxiety Screener.
¶Assessed by the Allodynia Symptom Checklist.
††Assessed by the Migraine Symptom Severity Scale.
MAST = Migraine in America Symptoms and Treatment; MHD = monthly headache day; NSAID = nonsteroidal anti-inflammatory drug; OTC = over-the-counter.

treatment (6.5%, n = 989); or exclusive use of OTCs (62.4%, n = 9443); or use of injectable, nasal, or topical acute medication (5.1%, n = 771).

Sociodemographics and Sample Disposition.— Respondents had a mean (SD) age of 45 (13.5) years. A total of 73.6% were women, and 81.1% were White. As shown in Table 1, most were married (57%), had at least a 4-year college degree (58.5%), and were employed full- or part-time (68.5%). Two thirds (66.2%) of the sample used OTC medication, 46% reported the use of a triptan, 36.6% a prescription NSAID, and 33.1% an opioid medication. Less than 1% reported using an ergot alkaloid. Poor or very poor treatment optimization occurred among 37.7% of the sample (based on mTOQ), psychological symptoms (from the PHQ-4) were present is 25.7%, ictal cutaneous allodynia (from the ASC-12) was present in 46.5%, and the mean symptom severity (from the MSSS) was 17.7 (SD 2.7).

While respondents meeting study criteria for unmet needs in the domains of inadequate treatment response and demanding attack characteristics were demographically similar (Table 1), respondents with unique patient characteristics were somewhat older and less likely to be women, less likely to have a 4-year college degree,

less likely to be employed full- or part-time, more likely to be a smoker, report more monthly headache days, report more opioid use (partially explained by opioid and barbiturate overuse being part of the criteria that defined the group) and less triptan and OTC use, and were more likely to report poor/very poor treatment efficacy, psychological symptoms, and cutaneous allodynia. The pattern of medication use was similar for the inadequate treatment response and demanding attack characteristics groups; however, those in the inadequate treatment response group had a higher rate of poor/very poor treatment response (47.1% vs 40.1%). Rates of psychological symptoms, cutaneous allodynia and mean symptom severity were comparable between these 2 groups (Table 1).

Table 2 shows the sociodemographics, oral medication use, and coexisting conditions and symptoms by the number of unmet needs endorsed. Overall significant differences across the number of unmet needs were detected for sex, and those with 3 or more

Table 2.—Sociodemographics, Oral Medication Use, and Coexisting Conditions and Symptoms among MAST Study Respondents by the Number of Unmet Need Domains

	Number of Unmet Need Domains					
	0	1	2	3	Chi† for Trend	*P* Value
Total by unmet need domain frequency, n (%)	167 (4.2)	986 (25.1)	2255 (57.4)	522 (13.3)	–	–
Sociodemographics						
Age, mean (SD), *y*	48 (14.7)	46 (14.0)	44 (13.0)	47 (13.4)	17.636‡	<.001
Female, n (%)	113 (67.7)	727 (73.7)	1720 (76.3)	332 (63.6)	2.913	<.001
Body mass index, mean (SD), kg/m^2	27.6 (6.1)	27.7 (7.1)	28.4 (8.0)	28.9 (8.5)	3.341‡	.018
Household income >$50,000, n (%)	126 (75.4)	694 (70.4)	1449 (64.3)	323 (61.9)	26.595	<.001
White, n (%)	142 (85)	795 (80.6)	1837 (81.5)	412 (78.9)	1.680	.195
Married, n (%)	97 (58.1)	559 (56.7)	1272 (56.4)	312 (59.8)	.430	.512
≥4-year college degree, n (%)	111 (66.5)	609 (61.8)	1320 (58.5)	260 (49.8)	22.110	<.001
Employed (full/part-time), n (%)	119 (71.3)	704 (71.4)	1571 (69.7)	300 (57.5)	20.769	<.001
Health insurance, n (%)	157 (94)	944 (95.7)	2116 (93.8)	489 (93.7)	1.779	.182
Current smoker, n (%)	15 (9.0)	99 (10.0)	287 (12.7)	132 (25.3)	52.387	<.001
MHD, mean (SD)	3.2 (2.8)	4.6 (4.6)	7.2 (6.8)	10.9 (8.5)	126.950‡	<.001
Oral medication use, n (%)						
Triptan	69 (41.3)	525 (53.2)	1070 (47.5)	144 (27.6)	46.097	<.001
NSAID	57 (34.1)	318 (32.3)	851 (37.7)	213 (40.8)	11.459	.001
Ergot alkaloid	2 (1.2)	5 (.5)	18 (.8)	6 (1.1)	.689	.407
Opioid	39 (23.4)	231 (23.4)	678 (30.1)	351 (67.2)	209.736	<.001
Barbiturate	11 (6.6)	92 (9.3)	225 (10.0)	112 (21.5)	38.090	<.001
At least 1 OTC for headache	115 (68.9)	635 (64.4)	1531 (67.9)	322 (61.7)	.464	.496
Coexisting conditions and symptoms						
Poor/very poor treatment optimization,§ n (%)	10 (6.0)	143 (14.5)	1020 (45.2)	310 (59.4)	424.280	<.001
Psychological symptoms,¶ n (%)	9 (5.4)	145 (14.7)	630 (27.9)	227 (43.5)	188.395	<.001
Cutaneous allodynia,†† n (%)	29 (17.4)	331 (33.6)	1145 (50.8)	322 (61.7)	184.387	<.001
Symptom severity,‡‡ mean (SD)	15.4 (3.0)	17.1 (2.8)	17.9 (2.6)	18.4 (2.3)	77.850‡	<.001

†Chi-square test for trend among respondents with 0, 1, 2, or 3 unmet need domains.
‡Analysis of variance.
§Assessed by the Migraine Treatment Optimization Questionnaire.
¶Assessed by the Patient Health Questionnaire 4-item Depression and Anxiety Screener.
††Assessed by the Allodynia Symptom Checklist.
‡‡Assessed by the Migraine Symptom Severity Scale.
MAST = Migraine in America Symptoms and Treatment; MHD = monthly headache day; NSAID = nonsteroidal anti-inflammatory drug; OTC = over-the-counter.

Table 3.—MAST Study Respondents Reporting Unmet Needs Associated With Inadequate Treatment Response, Demanding Attack Characteristics, and Unique Patient Characteristics

Unmet Needs Domains and Subdomains	N = 3930 n (%)
Inadequate treatment response domain	2912 (74.1)
Inadequate 2-hours pain freedom	1892 (48.1)
Recurrence within 24 hours of initial relief	1493 (38.0)
Treatment-related nausea (net)	599 (15.2)
Oral medications cause nausea	481 (12.2)
Oral medications worsen nausea	466 (11.9)
Delay taking treatment out of fearing side effects	835 (21.2)
ED/UC use for headache	515 (13.1)
Demanding attack characteristics domain	3516 (89.5)
Rapid onset of attack (net)	2567 (65.3)
Come on very rapidly	2076 (52.8)
Peak in less than 30 minutes	1981 (50.4)
Headache associated with sleep (net)	1954 (49.7)
Awaken from sleep	1150 (29.3)
Awaken normally with a severe headache	1609 (40.9)
Nausea affects treatment (net)	933 (23.7)
Makes it difficult/impossible to take oral medication	646 (16.4)
Makes oral medications less effective	609 (15.5)
Disability (MIDAS >11)	2187 (55.6)
Unique patient characteristics domain	634 (16.1)
Opioid or barbiturate overuse†	319 (8.1)
Cardiovascular comorbidity	377 (9.6)

†10 or more days per month.
ED/UC = emergency department or urgent care; MAST = Migraine in America Symptoms and Treatment; MIDAS = Migraine Disability Assessment.

unmet needs had the lowest proportion of women ($P < .001$). The proportion of respondents with a household income of $50,000 or more, at least a 4-year college degree, and full- or part-time employment decreased as the number of unmet needs increased ($P < .001$). Rates of smoking, cutaneous allodynia, psychological symptoms, mean MSSS, poor/very poor treatment optimization, and mean MHDs all trended upward as the number of unmet needs increased ($P < .001$). The trend of reported use for triptans decreased with increasing unmet needs ($P < .001$), while the trend for use of NSAIDs, opioids, and barbiturates increased ($P < .001$ for both) (Table 2).

In the total sample, 4.2% of respondents had no unmet needs, and 95.8% of respondents had at least 1 unmet need (Table 2). A total of 74.1% reported unmet needs related to inadequate treatment response, 89.5% had demanding attack characteristics and 16.1% had unique patient characteristics. The most common areas of unmet need associated with treatment response were inadequate 2-hours pain freedom (48.1%), recurrence within 24 hours of initial relief (38%), and delay taking treatment due to fear side effects (21.2%), as presented in Table 3, whereas the most common attack-related unmet needs included rapid onset (65.3%) and disability (55.6%). Relative to the other domains, patient-related unmet needs were less common; the use of opioids or barbiturates overuse (8.1%) and presence of CV comorbidity (9.6%) were reported by small but substantial proportions of respondents.

Table 4 displays the cross-section between the subdomains of unmet need in respondents meeting criteria for 1 subdomain given that they endorsed another subdomain. For example, respondents with recurrence of pain within 24 hours of initial relief were more likely to report headache associated with sleep (64.8%) than those without recurrence within 24 hours of initial relief (40.0%). Respondents with treatment-related nausea were far more likely to have attack-related nausea (75.2%) than those without treatment-related nausea (16.8%), and those with barbiturate/opioid overuse were more likely to report recurrence within 24 hours of initial relief (61.9% vs 36.6%) than respondents without barbiturate/opioid overuse.

DISCUSSION

Prior work[23] from the 2009 American Migraine Prevalence and Prevention study assessed barriers to optimal migraine care among a population sample of persons with episodic migraine reporting at least some (mild) headache-related disability. Fewer than half (45.5%) of study participants had consulted a provider for headache in the prior year. Predictors of consulting were having health insurance, disability, and symptom severity. Consulting a provider often led to a medical diagnosis of migraine (86.7%) and a majority (66.7%) with a diagnosis were using migraine specific acute treatment. However, only 26.3% of this sample traversed all 3 steps and were using migraine specific acute treatment.[23] A second more recent

Table 4.—Cross Section of Unmet Treatment Needs: Percentage of Respondents Within Each Subdomain Reporting the Presence (Yes) or Absence (No) of the Other Subdomains of Unmet Need

	Unmet Needs Domains																					
	Inadequate Treatment Response										Demanding Attack Characteristics								Unique Patient Characteristics			
	Inadequate Pain Freedom†		24-hours Recurrence‡		Nausea-T§		Fear of SE¶		ED/UC		Rapid Onset of Attack		Sleep-Associated		Nausea-A††		Disability‡‡		Barbiturate/ Opioid Overuse§§		CV¶¶	
	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y	N	Y
	1971	1892	2371	1493	3127	599	3024	835	3415	515	1363	2567	1976	1954	2557	933	1743	2187	36111	319	3553	377
Inadequate pain freedom†	0	100	43.4	57.1	48.8	52.0	48.9	49.4	47.7	57.4	51.1	47.8	46.5	51.5	48.7	53.8	40.5	55.7	48.3	57.0	48.4	54.7
24-hour recurrence‡	32.3	45.2	0	100	35.2	56.8	34.5	53.8	36.5	52.8	28.9	43.8	27.0	50.5	33.9	53.5	25.8	48.8	36.6	61.9	37.5	49.5
Nausea-T§	15.2	17.0	11.3	23.5	0	100	10.2	37.5	13.7	31.4	9.7	19.5	8.7	23.5	5.7	47.6	11.9	19.3	14.7	31.6	15.4	22.8
Fear of SE¶	21.2	21.6	16.1	29.7	16.1	50.3	0	100	19.7	34.3	17.1	24.1	15.8	27.5	14.9	41.3	17.1	25.2	21.0	28.5	21.4	24.0
ED/UC	10.9	15.3	10.0	17.8	10.9	26.0	11.0	20.8	0	100	8.4	15.6	9.1	17.1	9.9	24.7	8.0	17.2	11.7	28.5	12.0	23.3
Rapid onset of attack	66.7	63.7	59.8	74.1	62.8	79.1	63.2	72.6	63.4	77.9	0	100	58.7	72.1	62.1	76.0	58.8	70.5	64.1	78.7	64.0	77.5
Sleep-associated	47.2	52.2	40.0	64.8	45.3	72.6	45.9	63.2	47.4	65.0	40.1	54.9	0	100	44.0	66.8	41.3	56.5	48.4	64.6	49.3	53.8
Nausea-A††	24.7	28.7	20.3	36.3	16.8	75.2	20.0	50.1	23.4	47.6	18.8	30.9	17.8	35.7	0	100	20.3	31.6	25.1	43.5	25.7	36.6
Disability‡‡	48.5	63.4	46.5	70.5	54.0	67.4	53.4	65.1	53.0	73.0	47.3	60.1	48.2	63.2	53.1	67.2	0	100	53.3	82.8	54.4	67.1
Barbiturate/opioid overuse§§	6.8	9.5	5.1	13.1	6.8	16.4	7.5	10.8	6.7	17.7	5.0	9.8	5.7	10.5	6.6	14.0	3.2	12.1	0	100	7.2	16.4
CV¶¶	8.5	10.7	7.8	12.2	8.9	13.7	9.2	10.5	8.5	17.1	6.2	11.4	8.8	10.4	8.1	12.9	7.1	11.6	8.7	19.4	0	100

†Inadequate 2-hour pain freedom.
‡Recurrence within 24 hours of initial relief.
§Treatment-related nausea.
¶Delay taking treatment out of fearing side effects.
††Attack-related nausea.
‡‡MIDAS score >11.
§§10 or more days per month.
¶¶Cardiovascular comorbidity.
CV = cardiovascular; ED/UC = use of emergency department or urgent care; N = no; Y = yes.

study[24] utilized data from the Chronic Migraine Epidemiology and Outcomes study to explore barriers to care in a similar manner for persons with chronic migraine. The predictors of provider consultation were similar and 40.8% had done so in the prior year, however, only 24.6% received an accurate diagnosis. Although 44% of those with a diagnosis were receiving migraine-specific acute treatment and preventive treatment, the number of chronic migraine respondents who consulted, were diagnosed, and received appropriate care was only 4.5%.[24]

The current analysis extends this earlier work on barriers to care by broadly characterizing unmet treatment needs among those who use acute oral medications and examining the frequency and precise nature of individual unmet needs as well as expert clinician-defined domains of unmet need and their associated conditions and symptoms. The overwhelming majority of participants (95.8%) had at least 1 area of unmet need. Attack-related unmet needs were reported by nearly 90% of respondents, and unmet needs related to inadequate treatment response were experienced by 3 quarters of the sample (74.1%). The most common areas of unmet need were in the attack-related and treatment response domains, in particular rapid onset of attack (65.3% of respondents), headache related disability (55.6%), headache associated with sleep (49.7% inadequate 2-hour pain freedom (48.1%), and recurrence within 24 hours of initial relief (38%). The occurrence of rapid attack onset is high in this sample of oral medication users and might be even more common in the broader population of persons with migraine who may use non-oral forms of medication. Subcutaneously administered sumatriptan might, if more widely used, help to reduce the burden of this attack-related unmet need.

Only 4.2% of the analysis sample did not report a treatment need in 1 of the studied domains, while 25.1% reported 1 unmet need, 57.4% reported 2 unmet needs, and 13.3% reported unmet needs in all 3 domains. As reported in Table 2, respondents who reported an increasing number of unmet treatment need domains were found to have significantly less treatment optimization. This finding was somewhat expected because some of the unmet needs explored herein overlap with domains captured by the mTOQ assessment tool. However, the item sets are sufficiently different and the pattern of findings further supports the need for more effective acute treatments and optimized treatment approaches. This overarching and abiding unmet need – for better orally administered acute treatments and ways of using them – is confirmed by the present finding that, as the number of domains with unmet needs increased from none to 3, triptan use dropped by more than one third, while opioid and barbiturate usage nearly tripled. That these agents are associated with habituation, addiction, medication overuse headache, and disease progression further underscores the clinical urgency. An increasing number of unmet treatment need domains was also associated with statistically significant worsening of psychological symptoms (increasing PHQ-4 score) as well as higher cutaneous allodynia symptom scores and higher levels of reported migraine symptom severity. These results make intuitive sense and provide further face validity for the domains studied here and the importance of better management and therapeutic alternatives for the acute management of migraine and associated symptoms.

The frequency and wide distribution of unmet need in migraine demonstrated by the descriptive analysis suggests many potential management strategies (Table 5).[13,14] Unmet needs related to the 4 subdomains grouped under demanding attack characteristics include known predictors of acute treatment failure, such as rapid attack onset (65.3% of respondents), headache associated with sleep disturbance (49.7%), nausea that effects treatment or treatment efficacy (23.7%), and migraine-related disability[23,38] (55.6%). Unmet needs associated with the 5 subdomains grouped under inadequate treatment response included inadequate pain freedom (48.1% of respondents), recurrence within 24 hours of initial relief (38.0%), nausea induced or worsened by treatment (15.2%), medication delay due to fear of side effects (21.2%), and ED/UC use (13.1%). Relative to the other domains, the 2 unique patient-related subdomains – overuse of opioids or barbiturate-containing analgesics (8.1%) and presence of 1 or more CV conditions or events (leading to contraindications to triptan

Table 5.—Medical Strategies for Managing Inadequate Treatment Response, Demanding Attack Characteristics, and Unique Patient Characteristics Associated With the Acute Treatment of Migraine

Inadequate Treatment Response	
Inadequate 2-hours pain freedom	Ensure agent is administered while pain is mild
	Select a rapid onset or more effective agent[13,14]
	Consider nonoral formulations[13,14]
Recurrence within 24 hours of initial relief	Select long half-life products[13,14]
	Consider combining acute treatments at time of administration (eg, triptan plus long-acting NSAID)
Treatment-related nausea	Consider nonoral formulations[13,14]
	Add antiemetic medication[13,14]
Delay treatment due to side effect concerns	Chose more tolerable acute treatments[13,14]
	Consider preventive treatment options (pharmacologic, behavioral, neurostimulators)[13,14]
ED/UC use for headache	Provide a rescue treatment plan for acute treatment failures[13,14]
	Consider preventive treatment options (pharmacologic, behavioral, neurostimulators) [13,14]
Demanding attack characteristics	
Rapid onset of attack	Treat early with rapid-onset oral[13,14]
	Consider nonoral formulations[13,14]
Sleep-related onset	Consider nonoral formulations[13,14]
	Consider prevention[13,14]
Attack-related nausea	Treat with antiemetic[13,14]
	Consider nonoral formulations[13,14]
Disability†	Treat early while pain intensity is mild[13,14]
	Consider nonoral formulations[13,14]
	Consider preventive treatment options (pharmacologic, behavioral, neurostimulators)[13,14]
Unique patient characteristics	
Barbiturate/opioid overuse‡	Withdraw inappropriate medication[13,14]
	Add behavioral treatment for medication withdrawal
	Replace with another class of acute treatment[13,14]
	Consider preventive treatment options (pharmacologic, behavioral, neurostimulators)[13,14]
CV contraindications	Select drugs without cardiovascular adverse effects[13,14]
	Consider behavioral treatment options[13,14]

†MIDAS score >11.
‡10 or more days per month.
CV = cardiovascular; ED/UC = emergency department or urgent care.

use) (9.6%) – were less common sources of unmet need but were still reported by a significant proportions of respondents. When considering the recommendations listed in Table 5, providers should keep in mind that treatment plans must be tailored to the needs of individual patients.

As in previous studies evaluating patterns of medication usage for migraine,[3,11] almost two thirds (62.4%) of MAST Study respondents in this analysis reported exclusive use of OTCs. These agents can be effective for the treatment of mild, infrequent migraine attacks, but the likelihood of poor treatment optimization is high with OTC agents alone. The possibility of better acute treatment optimization by incorporating or switching to migraine-specific agents or considering preventive, device, and behavioral treatments should be explored.

The current MAST Study analysis has strengths and limitations. Because the demographic profile of the study population aligns with U.S. Census data, our findings should be generalizable to the population of persons with migraine using oral medications; generalizability may be limited by the slight distinction between MAST study respondents (ie, ≥3 MHDs in the past 3 months during screening and ≥1 MHD in the past 30 days) and the broader migraine population with no attack frequency criteria. In the current analysis we have not stratified the sample by episodic and chronic migraine and the authors acknowledge that this might provide further insights into the relative importance of unmet treatment needs in these distinct populations and warrants further study. The use of self-reported outcomes is also a limitation that may have led to overreporting of poor treatment response,

Table 6.—Measuring Optimization of and/or Satisfaction With Acute Medications

Scale	Notes
Migraine Assessment of Current Therapy (Migraine-ACT)[39]	Self-response questionnaire containing 4 dichotomous (yes/no) items pertaining to headache impact, global assessment of relief, consistency of response, and emotional response
Migraine Therapy Assessment Questionnaire (MTAQ)[40]	A 9-item questionnaire that identifies suboptimal treatment in 3 domains: economic burden, knowledge/behavior/ treatment satisfaction, and migraine control
Migraine Treatment Optimization Questionnaire (mTOQ)[35]	Assesses acute treatment optimization and suggests strategies for improvement in any areas highlighted as deficient
Headache Under-Response to Treatment Questionnaire (HURT)[41]	An 8-item, self-administered questionnaire addressing headache frequency, disability, medication use and effect, perceptions of headache control, and knowledge of diagnosis; provides guidance on appropriate actions toward treatment optimization

as negative outcomes may be more easily recalled than positive outcomes. The evaluation of the CV health of MAST Study respondents may have been strengthened by including all events, conditions, and risk factors that are contraindications to triptan usage. Validated instruments were used where possible, but the 11 unmet need items were derived from migraine patient interviews and expert clinician guidance. These items were tested for meaning and linguistic clarity with patients prior to use but more rigorous psychometric item development would enhance the validity of our findings. Because they were not mutually exclusive, differences between the respondents in each domain and their potential impact on outcomes could not be evaluated statistically. However, we did explore differences among respondents with none of the studied unmet needs, as well as those with unmet needs in 1, 2, or all 3 domains. We found that clinically significant depression and anxiety symptoms, as well as attack-related cutaneous allodynia, and rates of poor/very poor treatment optimization increased with increases in the number of unmet treatment domains that were endorsed.

These findings highlight the importance of assessing patient history, preferences, and needs both at the initiation of a treatment plan as well as for ongoing management. See Table 5 for a list of suggestions for optimizing acute treatment and addressing unmet needs.[13,14] One approach to assessing and optimizing the treatment of headache diseases is the use of headache diaries. In addition, several instruments have been designed to measure optimization of and/or satisfaction with acute and preventive medications (Table 6).[35,39-41]

CONCLUSIONS

MAST Study respondents using acute oral prescription migraine treatments were generally similar to the total MAST sample, and at least 1 unmet need was reported by nearly all respondents. Unmet needs related to attack characteristics and treatment response were most frequently observed. Understanding unmet treatment needs with orally administered acute medications can be a useful framework for designing clinical trials, developing new treatments, optimizing treatment plans, and improving acute treatment outcomes for people with migraine.

STATEMENT OF AUTHORSHIP

Category 1

(a) Conception and Design
Richard B. Lipton, Sagar Munjal, Aftab Alam, Dawn C. Buse, Kristina M. Fanning, Michael L. Reed, Todd J. Schwedt, David W. Dodick

(b) Acquisition of Data
Michael L. Reed

(c) Analysis and Interpretation of Data
Richard B. Lipton, Michael L. Reed, Kristina M. Fanning

Category 2

(a) Drafting the Manuscript
Richard B. Lipton, Michael L. Reed, Kristina M. Fanning

(b) Revising It for Intellectual Content
Richard B. Lipton, Sagar Munjal, Aftab Alam, Dawn C. Buse, Kristina M. Fanning, Michael L. Reed, Todd J. Schwedt, David W. Dodick

Category 3

(a) Final Approval of the Completed Manuscript
Richard B. Lipton, Sagar Munjal, Aftab Alam, Dawn C. Buse, Kristina M. Fanning, Michael L. Reed, Todd J. Schwedt, David W. Dodick

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