

# Migraine strikes study: factors in patients' decision to treat early

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**Abstract** To describe factors associated with early treatment of migraine, and to examine reasons patients do not treat early, this cross-sectional observational study email-recruited migraineurs  $\geq 18$ -years-old who were currently prescribed acute migraine medication. Within 24 h of migraine resolution, eligible patients completed an online migraine strikes questionnaire which addressed pain severity, associated symptoms, and other variables including reasons for not treating early. Results reported were descriptive. Among 1,044 evaluable patients, early treatment was significantly associated with several factors such as leisure activity at onset (OR 1.32,  $P = 0.010$ ), photophobia (OR 1.39,  $P = 0.013$ ), diagnosis of migraine with aura (OR 1.36,  $P = 0.004$ ), and other factors. Among 840 patients who reported wanting to treat earlier desire to reserve medication for a severe migraine was the most common reason given for not doing so (51.2%). Overcoming these factors may facilitate earlier migraine treatment.

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## Abbreviations

MIST Migraine strikes study  
IRB Institutional Review Board  
CHS Consumer Health Sciences International  
OR Odds ratio  
SD Standard deviation

## Introduction

Migraine is a disabling disorder which affects about 30 million people in the United States [1]. Much research has been reported on the risk factors, triggers, premonitory symptoms, and concomitant symptoms associated with migraine attacks, such as nausea, photophobia, and visual disturbances [2–7]. Clinical and observational data from patients taking triptans have consistently demonstrated the benefits of treating early (i.e., at the onset of pain) [8–13], but despite this evidence, 69% of migraineurs report that they would not treat their migraine pain as soon as they feel pain [14]. In addition to issues regarding efficacy and potential side effects of triptans, other factors may affect patients' ability or willingness to treat early. This study investigated other such external environmental factors which may influence patients' decision to treat early, and factors which may prevent patients from treating a migraine as early as they desire.

## Methods

### Study design

This cross-sectional observational survey study [migraine strikes study (MIST)] was conducted from November to

December 2006. A central Institutional Review Board (IRB) (ESSEX IRB, Lebanon, NJ) approved the study protocol, survey instrument, and the statement of informed consent. Consumer Health Sciences International (CHS), a contract research organization, provided each patient with full and adequate information about the objective and procedures of the study. Compensation was provided by the Lightspeed Consumer Panel to participants in the form of ceremonial “points,” which patients were eligible to redeem at the panel’s website for various retail products such as online gift certificates, music downloads, and kitchen appliances.

### Patients and procedures

To be eligible for the study, patients had to be at least 18-years-old and fluent in English. Patients had to have been diagnosed with migraine (with or without aura) by a physician, and had to have a current prescription for acute migraine medication(s). Patients were contacted via the internet to participate in the study. In an initial invitation email circular, patients were informed about the purpose and design of the study. If patients experienced a migraine attack within 7 days after they received the invitation email, they were invited to report their migraine experience within 24 h of its resolution. Patients accessed a password-protected web link attached in the initial email circular. Those who gave consent to participate were allowed to proceed to the migraine strikes questionnaire (Electronic supplementary Appendix 1).

In the migraine strikes questionnaire, participants reported circumstances of the migraine attack that occurred within the past 24 h, such as the time and location in which the migraine occurred, and details about any therapy the patient used to treat the migraine. Information about migraine and other headache history was also collected. Consumer Health Sciences International fielded the study by setting up data programming for the migraine strikes questionnaire, tracking and monitoring patient’s compliance with completing the questionnaire, and sending email reminders and thank you notes to participants. Consumer Health Sciences International collected the data, which was accessible only to research team members. Upon stripping the data of all patient-identifying information, CHS provided the sponsor (Merck and Co., Inc.) with a cumulative data base in SAS format, which contained all information on headache experience for the migraine strikes questionnaire.

### Statistical methods

To assess the factors associated with early treatment patterns, questions evaluated included pain severity and

associated symptoms, activities at onset of migraine, timing and selection of medication, physician-level variables, and co-morbid headache diagnoses. Logistic regression was used to identify factors associated with early treatment; adjustments were made for covariates. Chi-square and Student’s *t* tests were used for univariate analysis, where appropriate, and a binary logistic regression model using backward elimination was used for multivariate analyses. The dependent variable was “Treat early” (defined as treating within 1 h of headache onset), and candidate independent variables were those determined to be clinically relevant and/or which had a trend toward significance ( $P < 0.1$ ) on univariate analysis.

To assess reasons for not treating early even when desiring to do so, data were collected for questions about whether the attack was treated when desired (“Did you want to take your medication earlier than you actually did?”), factors that may have prevented earlier treatment (“What prevented you from taking the medication sooner?”), physician specialty (“Are you currently seeing any of the following physicians for your headaches?”), physician education regarding early treatment (“Has your physician ever instructed or advised you to take your migraine medications ‘early’ when the pain is still ‘mild’?”) and satisfaction with pain relief (“How satisfied were you with the pain relief you achieved with the medication you took for this migraine attack?”).

Descriptive statistics were used to examine factors potentially hindering earlier treatment and Chi-square tests were used to examine univariate associations.

## Results

### Early treatment

Table 1 shows patient demographics and baseline characteristics. Of the 2,001 migraineurs who participated (mean age 42.7, 74.2% female), 1,856 (92.8%) reported at least one associated symptom (nausea, vomiting, photophobia, or phonophobia) at headache onset during their attack, providing supporting evidence that participants were correct in their ascertainment of migraine. Of the 1,752 participants who provided information on treatment timing, 1,044 treated their migraine early (i.e., within 1 h of headache onset) (59.6%).

Univariate analysis (Table 2) showed that factors significantly positively associated with treating early included increasing age, male gender, doing something for fun/leisure at onset, presence of photophobia, diagnosis of migraine with aura, physician advice about early treatment, and regular adherence to physician’s instructions. Patients were significantly less likely to treat early if they

**Table 1** Patient demographics and baseline characteristics

Baseline characteristics	<i>N</i> = 2,001
Mean age, years (SD)	42.7 (11.7)
Female (%)	74.2
Associated symptoms (%)	
Photophobia	81.0
Phonophobia	77.7
Nausea	58.4
Vomiting	11.7
At least one of the above	92.8
Initial treatment chosen (%)	
None	0.0
Over-the-counter (OTC)	12.6
Triptan	62.3
Other prescription	25.1
Age at first migraine, years (SD)	23.2 (11.3)
Age at diagnosis, years (SD)	27.1 (11.0)
Migraine type (%)	
With aura	44.1
Without aura	55.9
General migraine severity (%)	
Mild	2.9
Moderate	42.1
Severe	55.0
Migraines per month (%)	
≤2	34.8
3–4	25.0
5–8	19.5
≥9	20.7
Employment status (%)	
Full-time	48.2
Part-time	12.4
Student or unemployed	39.4
Education level (%)	
High school or less	17.5
Some college	38.8
College or graduate degree	43.7
Prescription drug coverage (%)	
Yes	87.4
No	12.6
Other headache type	
Tension-type	79.4
Cluster	36.4
Chronic daily (>15/month)	33.6
Sinus	66.6

*SD* standard deviation

were at work or school at the time of migraine onset, or if they had co-morbid tension-type and/or chronic daily headache.

**Table 2** Univariate analysis: early treatment

Demographic characteristics	Treat early (%)
<i>N</i> = 1,752	
Age	
<30, <i>n</i> = 293	52.9
30–39, <i>n</i> = 469	56.3
40–49, <i>n</i> = 515	59.8
50–59, <i>n</i> = 339	64.3
≥60, <i>n</i> = 136	72.8
<i>P</i> -value	<0.001
Gender	
Female, <i>n</i> = 1,291	58.0
Male, <i>n</i> = 461	64.0
<i>P</i> -value	0.025
Employment status	
Full-time, <i>n</i> = 847	60.1
Part-time, <i>n</i> = 216	55.1
Student or unemployed, <i>n</i> = 689	60.4
<i>P</i> -value	0.353
Education level	
High school degree or less, <i>n</i> = 305	57.1
Some college, <i>n</i> = 681	59.5
College graduate, <i>n</i> = 766	60.7
<i>P</i> -value	0.544
Prescription drug insurance	
Yes, <i>n</i> = 1,551	60.2
No, <i>n</i> = 201	54.7
<i>P</i> -value	0.135
When your migraine began, were you...?	
At work or school?	
Yes, <i>n</i> = 248	52.0
No, <i>n</i> = 1,504	60.8
<i>P</i> -value	0.009
Doing something for fun or leisure?	
Yes, <i>n</i> = 676	63.3
No, <i>n</i> = 1,076	57.3
<i>P</i> -value	0.012
In a private place?	
Yes, <i>n</i> = 1,256	60.4
No, <i>n</i> = 496	57.7
<i>P</i> -value	0.302
A critical member of the task at hand?	
Yes, <i>n</i> = 779	58.3
No, <i>n</i> = 973	60.6
<i>P</i> -value	0.318
Doing something as part of your daily routine?	
Yes, <i>n</i> = 1,316	59.6
No, <i>n</i> = 436	59.6
<i>P</i> -value	0.963
Associated symptoms	

**Table 2** continued

Demographic characteristics	Treat early (%)
Nausea	
Yes, <i>n</i> = 1,042	60.4
No, <i>n</i> = 710	58.5
<i>P</i> -value	0.423
Vomiting	
Yes, <i>n</i> = 212	57.6
No, <i>n</i> = 1,540	59.9
<i>P</i> -value	0.518
Photophobia	
Yes, <i>n</i> = 1,428	61.1
No, <i>n</i> = 324	53.1
<i>P</i> -value	0.008
Phonophobia	
Yes, <i>n</i> = 1,364	60.1
No, <i>n</i> = 388	57.7
<i>P</i> -value	0.398
Medication	
First medication used	
Triptan, <i>n</i> = 1,091	60.1
Non-triptan prescription, <i>n</i> = 440	60.2
OTC, <i>n</i> = 221	55.7
<i>P</i> -value	0.444
Migraine characteristics	
Migraine type	
With aura, <i>n</i> = 781	63.8
Without aura, <i>n</i> = 971	56.2
<i>P</i> -value	0.001
Migraines per month	
≤2, <i>n</i> = 593	59.4
3–4, <i>n</i> = 439	59.7
5–8, <i>n</i> = 352	61.7
≥9, <i>n</i> = 368	52.9
<i>P</i> -value	0.782
General migraine severity	
Mild, <i>n</i> = 40	60.0
Moderate, <i>n</i> = 714	59.8
Severe, <i>n</i> = 464	59.4
<i>P</i> -value	0.986
Presence of prodromal symptoms	
Yes, <i>n</i> = 942	58.6
No, <i>n</i> = 717	61.5
Do not know, <i>n</i> = 93	54.8
<i>P</i> -value	0.309
Other headache type	
Tension-type	
Yes, <i>n</i> = 1,384	57.7
No, <i>n</i> = 368	66.9
<i>P</i> -value	0.001

**Table 2** continued

Demographic characteristics	Treat early (%)
Cluster	
Yes, <i>n</i> = 646	60.4
No, <i>n</i> = 1,106	59.1
<i>P</i> -value	0.610
Chronic daily (>15/month)	
Yes, <i>n</i> = 583	54.6
No, <i>n</i> = 1,169	62.1
<i>P</i> -value	0.002
Sinus	
Yes, <i>n</i> = 1,153	58.5
No, <i>n</i> = 599	61.8
<i>P</i> -value	0.180
Physician-related variable	
Physician specialty	
Primary care, <i>n</i> = 1,260	750 (59.5)
Specialist, <i>n</i> = 403	245 (60.8)
Others, <i>n</i> = 89	49 (55.1)
<i>P</i> -value	0.605
Physician advisement regarding treat early	
Yes, <i>n</i> = 1,447	889 (61.4)
No, <i>n</i> = 305	155 (50.8)
<i>P</i> -value	<0.001
Regular adherence to physician's instructions	
Rarely/sometimes, <i>n</i> = 343	146 (42.6)
Most of the time/always, <i>n</i> = 1,361	871 (64.0)
<i>P</i> -value	<0.001

After adjusting for age, gender, and pain severity, multivariate analysis showed that early treatment was significantly positively associated with leisure activity at onset [odds ratio (OR) 1.32,  $P = 0.010$ ], photophobia (OR 1.39,  $P = 0.013$ ), diagnosis of migraine with aura (OR 1.36,  $P = 0.004$ ), prior early treatment instruction by a physician (OR 1.75,  $P < 0.001$ ), regular adherence to physicians' instructions (OR 2.31,  $P < 0.001$ ). Early treatment was significantly negatively associated with co-morbid tension and/or chronic daily headaches (OR 0.68,  $P = 0.004$  and OR 0.78,  $P = 0.022$ , respectively) (Table 3). Being at work or school at onset did not retain a significant association with early treatment in the multivariate analysis.

#### Reasons for not treating earlier

Of the 2,001 migraineurs who completed the survey, 840 (42.0%) reported willingness to treat their migraine earlier. Among the 764 patients who wanted to treat earlier and who also provided information on treatment timing, 379 (49.6%) treated within 1 h of headache onset, compared with 67.3% of patients who did not want to treat

**Table 3** Multivariate analysis: early treatment

Variable	Adjusted OR	95% CI	P-value
Age (continuous)	1.02	1.01–1.03	<0.001
Female	0.81	0.64–1.02	0.071
Pain severity at onset (none, mild, moderate, severe)	0.89	0.77–1.02	0.096
Leisure activity at onset	1.32	1.07–1.62	0.010
Photophobia	1.39	1.07–1.81	0.013
Migraine with aura (vs. all others)	1.36	1.10–1.67	0.004
Tension headaches	0.68	0.53–0.89	0.004
Chronic daily headaches	0.78	0.63–0.96	0.022
Physician early treatment instruction	1.75	1.33–2.30	<0.001
Regular adherence to physician's instructions (most of the time/always vs. rarely/sometimes)	2.31	1.80–2.96	<0.001

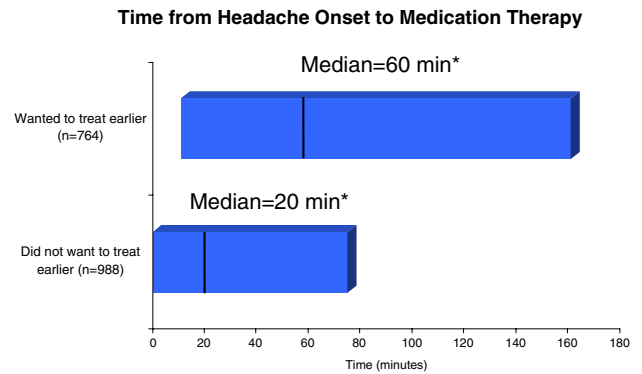
OR odds ratio

earlier ( $P < 0.001$ ). Of those who desired earlier treatment, the median time to treatment was 60 min, compared with 20 min among patients who did not want to treat earlier ( $P < 0.001$ ) (Fig. 1). The most commonly stated reason for not treating when wanted was the desire to reserve medication for a severe migraine (51.2%). Other reasons included not having medication on hand (34.9%), health plan quantity limit on drugs (27.0%), inability to swallow because of nausea (18.7%), not having access to fluid (17.3%), and not having privacy (13.5%) (Fig. 2).

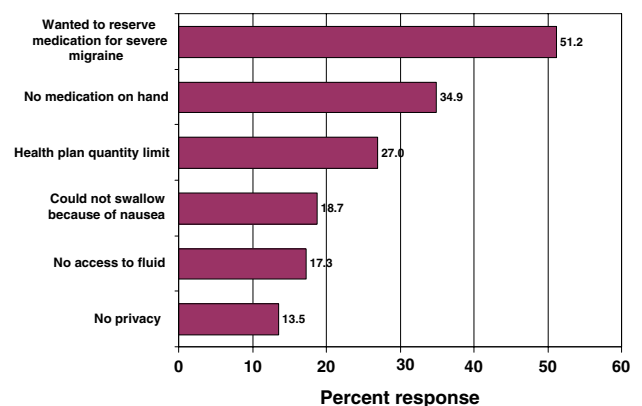
Desire to treat earlier was not significantly associated with physician education regarding early treatment; 82.1% among those desiring to treat early reported having been educated about early treatment by their physician versus 80.3% among those who did not want to treat earlier ( $P = 0.293$ ). Likewise, between-group differences were not significant based on physician specialty (71.4 vs. 70.8% seeing a primary care physician,  $P = 0.760$ ; 22.7 vs. 22.1% seeing a headache specialist,  $P = 0.750$ ; and 5.8 vs. 7.1% seeing other or no physician,  $P = 0.273$ ). Desire to treat earlier was associated with dissatisfaction with pain relief (18.6 vs. 14.3%,  $P = 0.015$ ).

**Discussion**

Early treatment of migraine has been shown to be particularly beneficial compared with treating >1 h after onset of pain, but it is known that not all patients take advantage of this benefit. To elucidate the possible reasons, which might then indicate paths forward in terms of helping patients maximize the benefit of migraine treatment, data from this



**Fig. 1** Time from headache onset to first dose of medication.\*  $P < 0.001$  for difference between medians



**Fig. 2** Factors preventing early treatment among those who sought it ( $n = 840$ )

questionnaire were assessed to answer two main questions about early treatment among a sample population of migraineurs. First, the analysis assessed what proportion of patients treated their headache within 1 h of onset; second, among those who did not treat their migraine as early as they wanted to, the data were evaluated to help determine why not. Within 24 h of resolution of a headache, patients reported the circumstances of the migraine attack, including their physical location and time when the migraine occurred, their activities at migraine onset, and medication use. Patients also provided information on their personal migraine history and its treatment, presence of migraine-associated symptoms, and current headache frequency and severity.

The analysis found that more than half (approximately 60%) of patients treated their headache within an hour of its onset; thus, about 40% of patients waited more than an hour after the onset of pain to take therapy for the migraine. These results are in accord with those of Gallagher et al. [15], who also reported that prescription medications were delayed in 40% of migraine episodes, and Foley et al. [14],

who reported that migraine medications were delayed by 49% of patients. These findings clearly indicate a need to address potential reasons for delays in treatment, in order to ensure that as many patients as possible are able to optimize their use of treatment.

To obviate unwanted delays, it is useful to understand specific reasons that patients, who may indeed know that early treatment is beneficial, nevertheless may not be taking their medication as early as possible. About 42% of patients indicated that they wanted to treat their migraine earlier than they actually did. Of those who expressed desire for earlier treatment, only about half treated their most recent migraine within an hour. The desire to reserve medication for a severe migraine was the most common reason given for delaying treatment, reported in fully half the patients who wanted to treat earlier. The next most common reason, reported in one-third of patients, was not having the medication on hand, and about one quarter of the patients said that their health plan quantity limit on drugs prevented them from treating as early as they wanted; additional reasons included nausea interfering with the ability to swallow, lack of access to fluid, and lack of privacy.

These results are in general agreement with the small amount of prior work that has previously been done in this area. In the aforementioned survey by Gallagher et al. [15], the authors reported that the most common reasons for delaying prescription medication use were medication access issues, limited numbers of pills, difficulties in functioning, and concerns about adverse events. Interestingly, Gallagher did not report on what we found to be the most commonly reported reason for delay: the desire to reserve medications for severe migraine. This commonly cited reason for treatment delay was also observed by Foley et al. [14]. Of patients who reported delayed treatment, 70% cited wanting to wait and see if the attack was really a migraine attack as a reason for the delay, and 46% cited wanting to take medication only for a severe attack.

Despite the observed high rate of reported migraine-associated symptoms at headache onset, we observed that patients with other co-morbid primary headaches were more likely to delay treatment. Epidemiologic research has shown that up to 90% of migraine patients also suffer from tension-type headache [16] and migraine and tension-type headaches share many important similarities [17]. To optimize migraine care, physicians should routinely educate their patients about early migraine symptoms, particularly for patients recently diagnosed with migraine, in addition to prescribing appropriate medications. Both Gallagher and Foley also found concern about medication side effects as a factor in treatment delay, reported by 15 and 37%, respectively. Our study did not directly explore fear of side effects as a potential reason for delaying treatment.

Some of the stated reasons for treatment delay can be addressed with practical adjustments, such as carrying medication when leaving home. Alternative formulations (e.g., rapidly dissolving tablet, nasal spray) can be considered in patients prone to migraine-associated nausea or who are frequently on the go and may not have continuous access to water or other liquids. However, solutions to the most commonly reported obstacles are not straightforward. For example, in patients with other types of headaches and/or chronic daily headache, the advantages and disadvantages of early treatment must be carefully weighed, bearing in mind that frequent use of certain acute migraine medications may predispose to medication overuse headache and chronic migraine [18].

Several factors act as limitations on the analysis of reasons for delayed treatment. It is possible that the retrospective desire to treat earlier may be influenced by severity of headache pain and/or any associated symptoms the patient may have experienced. Thus, the wish itself to treat earlier may not have emerged until after the first hour of migraine. Moreover, the survey does not account for the fact that reasons for not treating may vary by attack, within the same patient. For example, on two different occasions in which a migraine begins, a patient may have considerably easier access to medication in one situation versus the other. In addition, other practical considerations that could interfere with timely treatment may not have been captured by this survey.

In summary, a large proportion of migraine patients did not treat their headache within the first hour of headache onset. The study found that the most common reasons for the delay in treatment were (1) a wish to reserve the medication for a severe migraine, and (2) lack of easy access to the medication. Finding ways to overcome these and other practical obstacles preventing patients from medicating early may help a greater number of patients to relieve their migraines faster.

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**Conflict of interest** Drs. Golden and Hu are employees of Merck and Co., Inc., and may own stock or stock options in the company. Dr. Evans was an employee of Merck during the conduct of this trial and the writing of this manuscript, and may own stock in the company.

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