Underdiagnosed and undertreated

A closer look at some of the facts and the lives affected
INTRODUCTION

A population not clearly defined

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An evolution of classification

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DIAGNOSIS

A challenging condition for both diagnosis and management

Awareness of migraine has increased over the past 2 decades with the availability of standardized diagnostic criteria, effective treatments, publication of treatment guidelines, and large-scale studies. There are several subtypes of migraine diagnosis. The newest subtype, Chronic Migraine, was officially introduced in The International Classification of Headache Disorders, Second Edition (ICHD-2). Despite awareness and new classifications, there remains a significant portion of underdiagnosed migraine and Chronic Migraine patients. An accurate and complete diagnosis is a key factor in the effective management of these patients. It is the foundation for not only individualized treatment, but also patient education and the establishment of realistic expectations.

About this review
This review will provide a brief overview of some of the diagnostic and management challenges in migraine and Chronic Migraine, especially as new population-based data shed light on prevalence, burden, and treatment patterns.

Table 1. Classification of Headache Disorders
Adapted from The International Classification of Headache Disorders, Second Edition.

<table>
<thead>
<tr>
<th>Primary Headache</th>
<th>Secondary Headache</th>
</tr>
</thead>
<tbody>
<tr>
<td>Migraine</td>
<td>Headache attributed to an underlying cause (such as medication overuse)</td>
</tr>
<tr>
<td>Migraine without aura</td>
<td>Tension-type headache (and other trigeminal autonomic cephalalgias)</td>
</tr>
<tr>
<td>Migraine with aura</td>
<td>Cluster headache (and other trigeminal autonomic cephalalgias)</td>
</tr>
<tr>
<td>Childhood precursors to migraine</td>
<td>Other primary headaches</td>
</tr>
<tr>
<td>Retinal migraine</td>
<td></td>
</tr>
<tr>
<td>Complications of migraine, including Chronic Migraine</td>
<td></td>
</tr>
<tr>
<td>Probable migraine</td>
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</tr>
</tbody>
</table>

About this study
Approximately 12% of the population suffers from migraine according to the American Migraine Prevalence and Prevention (AMPP) Study, which assessed data from 162,576 survey respondents aged 12 years or older. All headache disorders, like migraine, are classified into 2 major groups, and then subdivided into several diagnoses and subtypes. Table 1 below outlines the major groups, including migraine and its 6 subtypes. ICHD-2 identified the newest subtype, Chronic Migraine, which is defined by the frequency of headache days.

Based on findings from a recent publication summarizing global prevalence rates, there are approximately 3.2 million Americans, mostly women, suffering from Chronic Migraine. This was determined by taking the publication’s Chronic Migraine prevalence rate and applying it to 2010 US population estimates for those 18 or more years of age (n = 234,504,070). Few of these patients are properly diagnosed according to AMPP data. By analyzing data for a subset of 520 Chronic Migraine patients, Bigal and colleagues found that approximately 80% had not received a diagnosis of Chronic Migraine. When the frequency of headaches increases, the differential diagnosis can be challenging. Figure 1 on the next page reviews an algorithm for the differential diagnosis of frequent (ie, chronic) headache.
When the number of headache days equals or exceeds 15 per month, the diagnosis falls into the spectrum of chronic daily headache (CDH) disorders. Chronic Migraine is defined by 15 or more days of headache per month, with each headache lasting 4 hours or longer and 8 or more of those days being migraine or probable migraine. As discussed previously, Chronic Migraine is underdiagnosed. Common misdiagnoses reported by Dodick are tension-vascular headache or mixed headache. Based on a few studies, in the specialty-clinic setting Chronic Migraine is the most common diagnosis for CDH patients.

Chronic daily headache
≥ 15 headache days a month with a duration ≥ 4 hours for at least 3 consecutive months

≥ 8 days a month of migraine or probable migraine (ie, use of migraine-specific acute medications)

Continuous unilateral pain with autonomic features and an indomethacin response

Clear onset as a daily syndrome

Pain and associated symptom profile

**Chronic Migraine**

**Hemicrania continua**

**New daily persistent headache**

**Chronic tension-type headache**

In 1982, Dr. Mathew first proposed the concept of transformed migraine to describe the highly burdened patients whose migraines transformed into daily or near-daily occurrences. After decades of discussion, the Second International Headache Classification Committee formally introduced Chronic Migraine in 2004. Very few patients fit these original diagnostic criteria. The criteria were revised in 2006 and have since been used in clinical trials. The formal guidelines can be difficult to implement in clinical practice, and thus alternative simplified classifications have been proposed for Chronic Migraine.

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Headache ≥ 15 days/month for ≥ 3 months with ≥ 5 prior migraine attacks</td>
<td>Headache on ≥ 15 days/month and greater than 4 hours per day</td>
</tr>
<tr>
<td>On ≥ 8 days/month headache fulfills the criteria for migraine</td>
<td>AND</td>
</tr>
<tr>
<td>Not attributed to another causative disorder</td>
<td>Current or prior diagnosis of migraine</td>
</tr>
<tr>
<td>Without medication overuse headache as defined in section 8.2 of The International Classification of Headache Disorders, Second Edition (ICHD-2)</td>
<td>AND</td>
</tr>
<tr>
<td>With or without medication overuse</td>
<td>With or without medication overuse</td>
</tr>
</tbody>
</table>
PATIENT PROFILES

Important similarities, striking differences

Most migraine patients are women who tend to be overweight (mean BMI 29.2-29.9) and in their late 40s. However, beyond demographics, there are striking differences between the 2 groups of migraine patients. The data below, gathered from several studies, highlight these differences between episodic and chronic migraineurs.

### Abbreviations:
- CM: Chronic Migraine
- EM: Episodic Migraine

<table>
<thead>
<tr>
<th>The Episodic Migraine (14 or fewer headache days/month)</th>
<th>The Chronic Migraine (15 or more headache days/month)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• 1 in 10 occupationally disabled (P &lt; .001)(^a) (^b)</td>
<td></td>
</tr>
<tr>
<td>• 17% to 25% suffer depression (P &lt; .001)(^a) (^b)</td>
<td></td>
</tr>
<tr>
<td>• &lt; 1 PCP consultation in the past 12 months for severe headache (P ≤ .001)(^a) (^b)</td>
<td></td>
</tr>
</tbody>
</table>
| • Medications used\(^c\):
  - 78% over-the-counter (P = .05)\(^c\)
  - 42% prescription (P < .001)\(^c\)
  - 4% no treatment (P = .03)\(^c\)
  - 35% prophylactic treatment currently or past (P ≤ .001)\(^c\)
  - 5% medication overuse (P ≤ .001)\(^c\) |
| • Over a 3-month period:
  - ≥ 12% experience ≥ 5 days of reduced productivity at school or work\(^c\)
  - 9.5% miss ≥ 5 days of family activities\(^c\)
  - ≥ 13-hour average headache duration with medication; ≥ 39 hours, without medication\(^c\) |
| • $1757 cost per patient/year (based on 2006 dollars)\(^c\) \(^d\) |

| • 1 in 5 occupationally disabled (P < .001)\(^a\) \(^b\) |
| • 30% to 41% suffer depression (P ≤ .001)\(^a\) \(^b\) |
| • 2.5 PCP consultations in the past 12 months for severe headache (P ≤ .001)\(^a\) \(^b\) |
| • Medications used\(^c\):
  - 74% over-the-counter (P = .05)\(^c\)
  - 57% prescription (P ≤ .001)\(^c\)
  - 2% no treatment (P = .03)\(^c\)
  - 49% prophylactic treatment currently or past (P ≤ .001)\(^c\)
  - 13% medication overuse (P ≤ .001)\(^c\) |
| • Over a 3-month period:
  - ≥ 34% experience ≥ 5 days of reduced productivity at school or work\(^c\)
  - ≥ 37% miss ≥ 5 days of family activities\(^c\) |
| • ≥ 24-hour average headache duration with medication; ≥ 65 hours, without medication\(^c\) |
| • $7750 cost per patient/year (based on 2006 dollars)\(^c\) \(^d\) |

### Published Data (2009) from the AMPP study.
Analysis included 7437 respondents with CM and 8768 with EM. Mean per-person annual total costs, including direct and indirect costs.

### In-press data from the International Burden of Migraine Study (IBMS).
Analysis from a cross-sectional web survey of 499 respondents with CM and 8227 with EM.

### Presented data (2006) from the AMPP study.
Analysis included 1226 respondents with CM and 2520 with EM.

### Published data (2008) from the AMPP study.
Analysis included 655 survey respondents with CM and 9494 with EM.

### Presented data (2006) from the AMPP study.
Analysis included 359 survey respondents with CM and 7437 with EM. Mean per-person annual total costs, including direct and indirect costs.

### Important similarities, striking differences

- In a study of headache frequency, severity, and associated impairment, 55% of doctor-patient pairs (n = 60) were misaligned on their interpretation of headache frequency. Confirmed migraine frequency in days rather than attacks can provide critical insight and lead to a more accurate diagnosis.

### Shifting the conversation from attacks to days

The assessment of headache frequency, severity, and associated impairment is key to determining optimal treatment, and can be assessed only through dialogue with the patient. A recent study analyzing in-office discussions between migraine patients and healthcare providers found that focusing on the number of migraine attacks versus migraine days could cause healthcare professionals to underestimate the number of days per month that a patient suffers from migraine. The study found that 55% of doctor-patient pairs (n = 60) were misaligned on their interpretation of headache frequency. Confirming migraine frequency in days rather than attacks can provide critical insight and lead to a more accurate diagnosis.

A migraine diary may help facilitate better communication between the physician and patient, and assist the physician in making a more accurate diagnosis. There are a number of these diaries available to download online.

**Communincation**

**55% of doctor-patient pairs were misaligned on their interpretation of headache frequency**

Lipton et al. J Gen Intern Med. 2008. 25

**Migraine diaries help facilitate communication to make an accurate diagnosis**

Download patient migraine diaries at www.MyChronicMigraine.com
TREATMENT

Patients have options

Because migraine patients can have severe and disabling attacks, acute and prophylactic treatments are often required. Table 2 reviews the available options by class to help control and prevent migraine. While these medications may be used in clinical practice, please note indications approved by the FDA may vary.

Available, but underutilized

A survey showed nearly all migraine patients treat their typical migraine attacks with acute medications. Data from the AMPP study show 13% of migraine patients (n = 162,576) currently receive prophylactic treatment. General principles of management from the American Academy of Neurology (AAN) include creating a formal and individualized management plan, which takes into consideration patient factors such as response to, and tolerance for, specific medications. Patient preference is also a factor in deciding whether to start certain treatments.

According to an evidence-based-review report:

Patient preference is a factor in deciding whether to start certain therapies

ADHERENCE

A challenge over time

Poor compliance is a common problem with many daily medications. In migraine, poor compliance may lead to disability and reduced quality of life. Gallagher and Kunkel in 2003 studied the factors contributing to poor compliance in a survey of a representative sample of 1160 migraine patients who were taking prescription medications. Their analysis showed 2 out of 3 (67%) survey respondents had delayed or avoided their prescription medication due to concerns over adverse effects.

Other researchers have more recently looked at compliance rates in even larger samples of migraine patients, using claims data:

- Yaldo and colleagues (2008) looked at 12,783 patients on prophylaxis in the HealthCore Integrated Research Database
  - At 2 months, analyses showed fewer than half of these patients remained compliant
- Berger and colleagues (2009) looked at 5187 prophylaxis episodes from the Medstat Health and Productivity Database
  - At 6 months, analyses found that 15% to 28% of migraine patients were compliant to their daily prophylaxis (SSRI or TCA)

Abbreviations: SSRI, selective serotonin reuptake inhibitor; TCA, tricyclic antidepressant.

*Prophylaxis episodes = 1-year data per patient, consisting of 6 months of pretreatment and 6 months of follow-up.
SUMMARY

Recognition and relief

Migraine and Chronic Migraine remain underdiagnosed despite progress in classifications. As discussed earlier, 80% of Chronic Migraine patients are not properly diagnosed. Communication between frustrated migraine patients and their physicians is often incomplete, but tools like a migraine diary may provide details about the frequency, duration, and severity of headache attacks. With this important information in hand, physicians can follow established criteria to classify migraine patients.

An accurate and complete diagnosis is a critical factor for effective management. It not only helps guide treatment decisions, but it can also help patients understand their condition and subsequently set realistic expectations. Experts suggest this helps engage patients in their own care, which in turn facilitates management. Patients have both acute and prophylactic medication options for migraine. Because compliance can be a common problem, openly discussing treatment options is part of the patient-physician collaboration. The physician should help the patient weigh the risk-to-benefit profile of each potential treatment choice.

Key points in summary:

- Migraine and its subtypes are underdiagnosed
- Tools like a migraine diary can help facilitate patient-physician communication and diagnosis
- Accurate diagnosis is a critical factor for success with treatment
- Patients should be educated to understand their specific condition, treatment options, realistic goals, and risk-to-benefit ratio

Working together as a team, migraine patients and their physicians can work toward greater recognition of the problem and find a realistic level of relief.