

Frequent Headaches: Evaluation and Management

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Most frequent headaches are typically migraine or tension-type headaches and are often exacerbated by medication overuse. Repeated headaches can induce central sensitization and transformation to chronic headaches that are intractable, are difficult to treat, and cause significant morbidity and costs. A complete history is essential to identify the most likely headache type, indications of serious secondary headaches, and significant comorbidities. A headache diary can document headache frequency, symptoms, initiating and exacerbating conditions, and treatment response over time. Neurologic assessment and physical examination focused on the head and neck are indicated in all patients. Although rare, serious underlying conditions must be excluded by the patient history, screening tools such as SNNOOP10, neurologic and physical examinations, and targeted imaging and other assessments. Medication overuse headache should be suspected in patients with frequent headaches. Medication history should include nonprescription analgesics and substances, including opiates, that may be obtained from others. Patients who overuse opiates, barbiturates, or benzodiazepines require slow tapering and possibly inpatient treatment to prevent acute withdrawal. Patients who overuse other agents can usually withdraw more quickly. Evidence is mixed on the role of medications such as topiramate for patients with medication overuse headache. For the underlying headache, an individualized evidence-based management plan incorporating pharmacologic and nonpharmacologic strategies is necessary. Patients with frequent migraine, tension-type, and cluster headaches should be offered prophylactic therapy. A complete management plan includes addressing risk factors, headache triggers, and common comorbid conditions such as depression, anxiety, substance abuse, and chronic musculoskeletal pain syndromes that can impair treatment effectiveness. Regular scheduled follow-up is important to monitor progress. (*Am Fam Physician*. 2020;101(7):419-428. Copyright © 2020 American Academy of Family Physicians.)

Patients with increasingly frequent headaches can develop disabling symptoms. Biochemical, metabolic, and other changes induced by frequent headaches and/or medication are thought to cause central sensitization and neuronal dysfunction that results in inappropriate response to innocuous stimuli, lowered thresholds to trigger pain response, exaggerated response to stimuli, and persistence of pain after removal of inciting factors.¹⁻⁴ Together, these changes result in increasingly frequent—and often daily—headache and related symptoms. Each year, 3% to 4% of patients with episodic migraine or tension-type headaches (TTH) escalate to chronic forms.^{5,6}

An estimated 2% to 4% of U.S. adults have chronic headaches, and more than 30% of these report daily symptoms.⁶⁻⁸

Additional content at <https://www.aafp.org/afp/2020/0401/p419.html>.

CME This clinical content conforms to AAFP criteria for continuing medical education (CME). See CME Quiz on page 391.

Author disclosure: No relevant financial affiliations.

Once central sensitization occurs, headaches are difficult to treat and cause substantial morbidity. The mean annual cost of chronic migraine (including lost productivity and medical care) is more than three times the cost of episodic migraine (approximately \$8,250 vs. \$2,650).^{9,10} This article aims to assist physicians in identifying patients at risk of escalating to chronic headache and presents an approach to preventing such escalation. Although the literature focuses on migraine, the approach is applicable to other types of headache.

Risk Factors for Escalation from Episodic to Chronic Headache

Identifying patients with risk factors for escalating from episodic to chronic headaches can help physicians and patients be alert for early signs of escalation and aware of the need to address modifiable risk factors, especially medications.

The strongest predictive factors for headache progression are frequent headache episodes at baseline and medication overuse¹¹ (*Table 1*^{2,7,8,11}). Definitions of chronic migraine and TTH specify that symptoms be present on at least

TABLE 1

Risk Factors for Escalation of Episodic Migraine to Chronic Migraine

Risk factor	Odds ratio (95% CI)	Comments
Headache days per month*		—
0 to 4	1.00 (referent)	
5 to 9	7.6 (2.2 to 26.1); <i>P</i> = .001	
10 to 15	25.4 (7.6 to 84.5); <i>P</i> = .001	
Medication overuse*†		—
Opioids	4.4 (0.3 to 59.7)	
Triptans	3.7 (0.8 to 16.4)	
Ergotamines	2.9 (0.4 to 23.0)	
Analgesics	2.7 (0.6 to 11.7)	
Obesity (BMI > 30 kg per m ²)	5.53 (1.4 to 21.8)	May explain other associations (e.g., sleep disorders)
Diabetes mellitus	3.34 (0.96 to 12.3); <i>P</i> = .059	Not significant after adjusting for BMI and baseline headache frequency
Arthritis	3.29 (1.03 to 10.5); <i>P</i> < .05	Not significant after adjusting for BMI and baseline headache frequency
Head or neck injury	Males: 3.3 (1.0 to 19.8) Females: 2.4 (1.0 to 10.8)	No relationship with severity or time since injury

BMI = body mass index.

*—Highly significant in multivariate analysis adjusting for other variables.

†—Use of any headache medication on 10 or more days per month.

Information from references 2, 7, 8, and 11.

15 days per month, but central sensitization may occur at lower frequencies.⁵ Migraine may have a threshold for central sensitization of four episodes per month.¹¹ Symptoms predictive of migraine escalation are pulsating quality, severe pain, photophobia, phonophobia, and attacks lasting longer than 72 hours.¹² Long attack duration and nausea are predictive of development of chronic TTH.¹³ Cutaneous allodynia is strongly associated with chronification and may be a marker of central sensitization.^{13,14} The highest medication-associated risk is with opioids, followed by triptans, ergotamines, and nonopioid analgesics.^{7,11}

Chronic pain, especially musculoskeletal pain, and obesity are strongly associated with chronification.¹⁵ Associations with snoring, sleep disorders, diabetes mellitus, and arthritis lose significance when controlling for body mass index and headache frequency.¹¹ Several psychiatric conditions (e.g., major depressive disorder, bipolar disorder,

anxiety) are associated with headache frequency and disability. It is unclear if these are risk factors or comorbidities, or if they share etiologies with chronic headaches.^{6,16} Stressful life events are associated with increasing headache frequency, especially in middle age.¹⁷

Approach to the Patient with Frequent Headaches

An algorithm for the evaluation of patients with frequent headaches is presented in *Figure 1*.

Clarify Headache Type and Pattern

A full assessment to clarify headache frequency, type, and severity takes time, but it is an investment in successful management and may avoid multiple patient visits and requests for medication (*Table 2*).¹⁸⁻²¹ Every effort should be made to accurately diagnose each headache using criteria from the International Headache Society (*eTables A through E*) that define different primary (e.g., migraine, TTH, cluster headaches) and secondary headaches (e.g., those due to trauma, vascular malformations, infection, or cerebrospinal fluid pressure disorders). Individual patients may not completely match criteria for a specific

headache diagnosis and may have more than one type of headache.⁵ The POUND mnemonic can be useful in the diagnosis of migraine^{22,23} (*Table 3*²²).

History. As headaches become more frequent, patients often have difficulty recalling details. A headache diary can help document date, duration, symptoms, treatment, and outcome of each headache episode, in addition to suspected triggers or other patient observations.^{18-21,24,25} Patients with migraine are often hyperresponsive to causes of secondary headaches.⁵ A diary may identify an overlooked cause of secondary headaches or a recurrent trigger for migraine episodes.

The history should cover the patient's typical headaches as well as recent changes. The current headache diagnosis may be inaccurate, incomplete, or undergoing transition. In studies, migraine was the correct diagnosis in 82% of patients previously diagnosed with nonmigraine headaches

Recommendations from the Choosing Wisely Campaign

Recommendation	Sponsoring organization
Do not recommend prolonged or frequent use of over-the-counter pain medications for headache.	American Headache Society
Do not prescribe opioid or butalbital-containing medications as first-line treatment for recurrent headache disorders.	American Headache Society
Do not perform neuroimaging studies in patients with stable headaches that meet criteria for migraine.	American Headache Society
Do not perform computed tomography imaging for headache when magnetic resonance imaging is available, except in emergency settings.	American Headache Society

Source: For more information on the Choosing Wisely Campaign, see <https://www.choosingwisely.org>. For supporting citations and to search Choosing Wisely recommendations relevant to primary care, see <https://www.aafp.org/afp/recommendations/search.htm>.

and in 88% of patients diagnosed with sinus headaches.^{26,27} Patients often describe more than one type of headache. More than 80% of those with confirmed migraine also have TTH, and patients with any primary headache may develop superimposed secondary headaches.²⁸

The history may detect symptoms of progression to chronic headache. Patients who develop chronic migraine typically report progressively frequent bilateral frontotemporal TTH-type symptoms with superimposed full-blown migraine attacks. Sleep and emotional disturbances are common.^{12,29} Patients developing chronic TTH or medication overuse headaches (MOH) often have nonspecific headaches.

Physical Examination. Between headache episodes, physical examination is usually normal in patients with frequent migraine, TTH, and other primary headaches. Guidelines recommend neurologic assessment and physical examination of the head and neck, focusing on any potential source of secondary headaches (Table 2).¹⁸⁻²¹

Imaging. Guidelines recommend magnetic resonance imaging with and without contrast in patients with trigeminal autonomic cephalalgias (e.g., cluster headache, paroxysmal hemicrania, hemicrania continua, short-lasting neuralgiform headache), headaches with new features or neurologic deficits, or suspected intracranial abnormality.³⁰⁻³² The American College of Radiology recommendations can help guide imaging for various headache presentations, headaches in specific locations (e.g., base of skull, orbit, sinuses), and investigation of specific conditions, and imaging

in older adults, pregnant women, and patients with cancer or other immunocompromising condition.³²

Decisions about imaging in patients with increasingly frequent migraine or TTH are challenging.^{18-21,24,30-32} U.S. headache guidelines recommend magnetic resonance imaging with and without contrast for patients with progressively worsening headaches over weeks to months because of the remote possibility of subdural hematoma, hydrocephalus, tumor, or another progressive intracranial lesion.¹⁸ Nevertheless, without neurologic

FIGURE 1

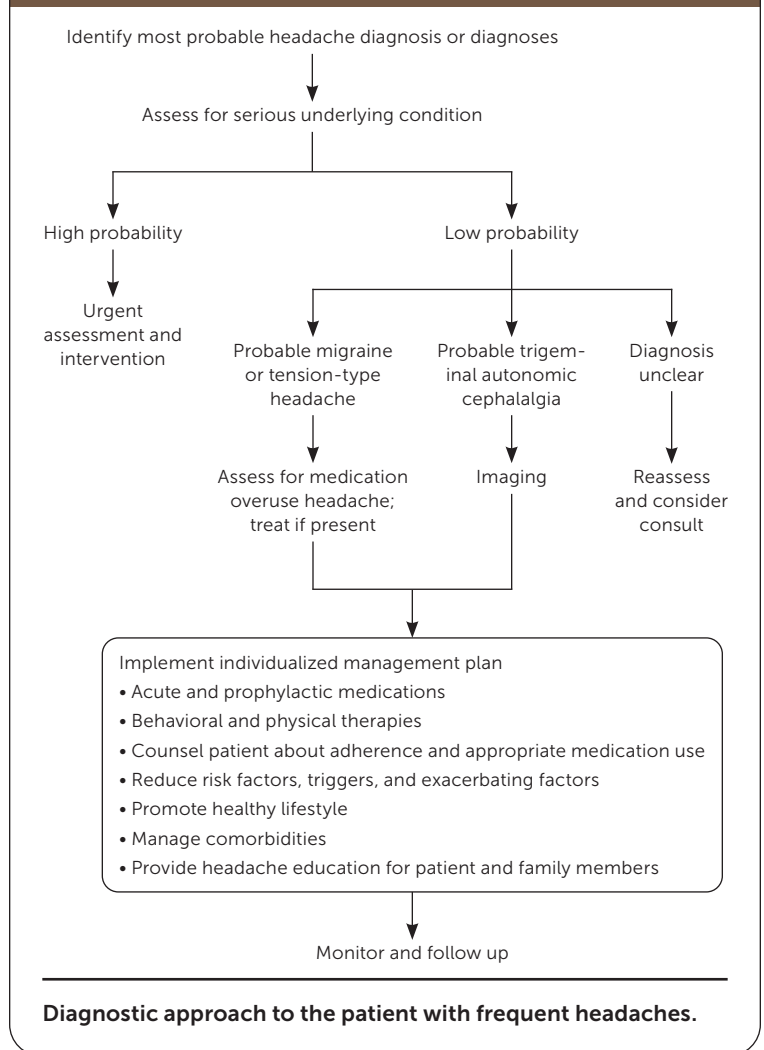


TABLE 2

Assessment of Patients with Frequent Headache

Headache history

- Associated symptoms (especially nausea, vomiting, fatigue, photo- or phonophobia, head or neck tenderness, autonomic symptoms, or allodynia)
- Beliefs about cause, appropriate management, and prognosis; goals for management
- Coping mechanism, effects on quality of life, and support system
- Duration of episodes
- Exacerbating and relieving factors (e.g., activity, light and noise avoidance, sleep)
- Frequency of episodes and change in pattern
- Intensity of pain (1 to 10 scale)
- Medications used and effectiveness (name and dosage for all prescription and nonprescription medications)
- Pain location
- Pattern and rate of onset, peaking, and resolution of symptoms
- Precipitating or associated events (triggers, prodromes)
- Previous assessments, diagnoses, and treatments
- Quality of pain (e.g. throbbing, pulsating, squeezing, splitting)

Additional history

- Evidence of common comorbidities (e.g., depression, anxiety, posttraumatic stress disorder, substance or alcohol misuse, chronic pain)
- Risk factors for conversion to chronic headache (Table 1)
- Signs or symptoms of serious secondary headache (Table 4)

Physical examination

- General impression, vital signs (pulse, blood pressure, temperature)
- Head: temporal artery firmness/tenderness (in older patients), sinus tenderness
- Neck: posture, range of motion, muscle tenderness
- Neurologic: general assessment of mental status; cranial nerve examination, including fundoscopy; pupils; eye movements; visual fields; facial power and sensation; soft palate and tongue movements; limb power; tone; coordination; reflexes; gait, including heel-toe walking (tandem gait); plantar responses
- Other assessments as indicated by symptoms, medical history, or risk factors

Diagnostic testing

- Imaging: not recommended unless patient has red flag symptoms (Table 4), trigeminal autonomic cephalalgias, or atypical headache, or to diagnose specific suspected underlying disorder
- Laboratory testing as indicated to identify underlying condition in patients with secondary headache (e.g., erythrocyte sedimentation rate for temporal arteritis)

Other assessments

- Headache diaries
- Measures of headache effects and disability (e.g., Headache Impact Test*) to assess quality of life and track progress
- Screening tools for comorbidities (e.g., Patient Health Questionnaire-9 for depression†, CAGE questionnaire for alcohol use‡)

*—Available at http://www.migraineresourcenetwork.com/images/assessment_tools/HIT-6.pdf.
 †—Available at <https://www.mdcalc.com/phq-9-patient-health-questionnaire-9>.
 ‡—Available at <https://www.mdcalc.com/cage-questions-alcohol-use>.

Information from references 18–21.

findings, relevant results from neuroimaging are reported in less than 1% of patients who have frequent episodic migraine.²³ Other imaging modalities such as positron emission tomography, single-photon emission computed tomography, electroencephalography, and transcranial Doppler ultrasonography are not recommended in patients with frequent headaches.³¹

RULE OUT SERIOUS UNDERLYING CONDITIONS

Serious pathologic conditions are uncommon causes of frequent headaches, but they must be considered, even in patients with confirmed primary headaches. Expert groups list different red flag warning features. The SNNOOP10 mnemonic describes symptoms that should raise suspicion for serious underlying pathology in patients with headache (Table 4).³³ The probability of a significant lesion is most strongly associated with cluster-type headache symptoms, abnormal neurologic examination, poorly defined headache, and headaches associated with aura, the Valsalva maneuver, or exertion.²³

ASSESS FOR MEDICATION OVERUSE

Addressing medication overuse may be the most important intervention for increasingly frequent headaches.^{18–21,34} About 30% to 50% of patients who develop chronic headaches have MOH,^{6,8,35,36} which is defined as headache on 15 or more days per month in a patient with preexisting primary headache, developing as a consequence of regular overuse of acute or symptomatic headache medication for more than three months.⁵ Overuse is defined as 15 or more days per month for nonopioid analgesics and 10 or more days per month for ergotamines, triptans, opioids, and combinations of drugs from more than one class.⁵ MOH usually resolves after stopping overuse, but this is no longer

required for diagnosis.⁵ MOH develops almost exclusively in patients with migraine or TTH. Nonopioid analgesics are the most commonly implicated medications because of their widespread use in headache treatment; however, triptans are an increasingly common cause of MOH in the United States. The estimated mean critical dose and duration of use for triptans are 18 doses per month and 1.7 years, compared with 114 doses per month and 4.8 years for simple analgesics.³⁷ Although not recommended and less commonly used for headache, opioids present the greatest risk of MOH and the most difficult type to treat.^{35,36}

MOH has no classic features. Symptoms vary among patients and over time. Patients often describe insidious onset of increasingly frequent headaches on awakening or early in the day. Headaches are of variable quality, intensity, and location. Neck pain is common, and autonomic and vasomotor symptoms such as rhinorrhea, nasal stuffiness, and vasomotor instability are reported.^{35,36} Patients with MOH often have sleep disturbances and psychiatric disorders, especially depression, anxiety, and obsessive-compulsive disorder. These disorders usually predate MOH and may contribute to the progression to chronic headaches.^{35,36,38} Diagnosing MOH depends on an accurate and detailed medication history. Patients may underestimate their use of nonprescription analgesics or be unwilling to disclose opiate use. Screening with the questions “Do you take a treatment for attacks more than 10 days per month?” and “Is this intake on a regular basis?” is reported to be 95.2% sensitive and 80% specific for MOH in patients with frequent migraines.³⁹ The single-question drug screen (“How many times in the past year have you used an illegal drug or used a prescription medication for nonmedical reasons?”) is reported to be 100% sensitive and 74% specific for detection of a drug use disorder in the family medicine setting.³⁴

The optimal strategy for medication withdrawal is unclear. Guidelines stress that treatment should be individualized, incorporating patient education, supportive resources, and nonpharmacologic therapies, especially in patients with associated stress and chronic pain conditions. Patient education is crucial.^{18-20,35} In one study, 76% of patients with MOH were no longer overusing medications and 42% no longer had chronic headache 18 months after being provided information but no other specific treatment.⁴⁰ Evidence on the effectiveness of abrupt vs. tapered withdrawal

is inconsistent.⁴¹⁻⁴³ Rapid outpatient withdrawal is generally recommended for nonopioid analgesics (including nonsteroidal anti-inflammatory drugs, acetaminophen, and aspirin), ergotamines, and triptans. Inpatient tapered withdrawal is recommended for patients taking opiates, barbiturates, or benzodiazepines; those with significant comorbidities; and those in whom previous outpatient withdrawal was ineffective.^{18-20,35,41} Recommendations about pharmacologic treatment for MOH are limited by study quality, limited follow-up, poor compliance with study medications, and difficulty controlling for other factors in treatment, especially patient education

and support during withdrawal.^{35,42,43} All studies have been conducted on patients with MOH and chronic migraine; no guidelines are available for other patients with MOH. European guidelines state that topiramate (Topamax), 100 to 200 mg per day, is probably effective in MOH, and that corticosteroids (at least 60 mg per day) and amitriptyline (up to 50 mg per day) are possibly effective.⁴¹ A 2019 review found two studies reporting significant therapeutic advantage over placebo for topiramate, and one study each for onabotulinumtoxin A (Botox) and valproate (Depacon).³⁵

In about 75% of patients with MOH, discontinuing the overused medication results in reversion to episodic migraine or TTH; however, the relapse rate is about 30% per year.⁴¹ Effective treatment for the underlying headache and close follow-up are essential to prevent the patient from reverting to MOH.

DEVELOP A HEADACHE MANAGEMENT PLAN

Achieving prolonged symptom-free periods may be initially unrealistic, but progress in breaking the escalating pattern of frequent headaches enables the patient and physician to focus on developing the most effective plan to manage episodic headaches and prevent recurrent escalation. Before initiating a management plan, the clinical features should be reviewed to verify the probable headache diagnosis, confirm the absence of significant underlying conditions, and identify comorbidities that could complicate management. Consultation with a neurologist is recommended if a primary headache diagnosis cannot be confirmed, red flag symptoms are detected, or headaches do not improve with appropriate treatment.¹⁸

A comprehensive management plan requires pharmacologic and nonpharmacologic interventions, attention

TABLE 3

POUND Mnemonic for the Diagnosis of Migraine

- Pulsating or throbbing pain
- One-day average duration
- Unilateral location
- Nausea or vomiting
- Disabling

Note: Probability of migraine in a primary care patient is 92% when 4 POUND symptoms are present; 64% with 3 symptoms; and 17% with fewer than 3.

Adapted with permission from Ebell MH. Diagnosis of migraine headache. Am Fam Physician. 2006;74(12):2088.

TABLE 4

SNNOOP10 Mnemonic for Red Flag Symptoms in Patients with Headache

Sign or symptom	Potential cause of headache
Systemic symptoms (e.g., fever, rash, myalgia, weight loss)	Intracranial infection or nonvascular condition; carcinoid tumor, pheochromocytoma
Neoplasm diagnosis (current or history)	Brain neoplasm or metastasis
Neurologic deficit or dysfunction (e.g., focal deficits, seizure, cognitive or consciousness changes)	Intracranial disorder
Onset sudden or abrupt*	Subarachnoid hemorrhage, cranial or cervical vascular lesion
Older age (> 50 years)	Giant cell arteritis, cervical or intracranial lesions
Painful eye plus autonomic features	Posterior fossa; pituitary, cavernous sinus, or ophthalmic condition; Tolosa-Hunt syndrome
Painkiller overuse or new medication	Medication overuse headache, medication adverse effect or incompatibility
Papilledema	Intracranial condition, intracranial hypertension
Pathology of immune system	HIV or opportunistic infection
Pattern: new headache or change in pattern of established headache	Intracranial condition
Position exacerbates or relieves pain	Intracranial hypotension or hypertension
Posttraumatic onset (acute or chronic)	Subdural hematoma, vascular condition
Precipitated by sneezing, coughing, or exercise	Posterior fossa or Arnold-Chiari malformation
Pregnancy or puerperium	Cranial or cervical vascular condition, hypertension/preeclampsia, cerebral sinus thrombosis, epidural-related headache
Progressive and atypical presentation	Nonvascular intracranial condition

*—Recurrent “thunderclap” headaches suggest reversible cerebral vasoconstriction syndrome.

Adapted with permission from Do TP, Remmers A, Schytz HW, et al. Red and orange flags for secondary headaches in clinical practice: SNNOOP10 list. *Neurology*. 2019;92(3):136.

to inciting and exacerbating factors, advice on healthy lifestyle, attention to comorbid conditions, and education for patients and family members on headache management.¹⁸⁻²⁰

Patients with frequent headaches require both prophylactic and acute pharmacologic treatment.¹⁸⁻²¹ Evidence-based reviews and guidelines provide a basis for selecting medications for individual patients (*Table 5*).^{20,44-53} Considerations include effectiveness, pharmacokinetics, medical history, coexisting conditions, adherence, tolerance of adverse effects, cost and insurance considerations, and patient beliefs about the selected agent.²¹ Patients with a history of MOH with one agent should be prescribed an alternative agent with a lower risk of overuse. Coexisting conditions, especially depression and anxiety, may impair adherence and are associated with poorer outcomes. Medications for headache prophylaxis may be helpful in treating comorbid conditions (e.g., amitriptyline for depression or chronic pain, propranolol for hypertension).

Guidelines stress that behavioral and physical therapies should be integrated with pharmacologic treatment of frequent headaches, but patient access may be limited, and evidence-based guidance is sparse.^{18-20,53} For migraine, relaxation training with or without thermal biofeedback, electromyographic biofeedback, and cognitive behavior therapy were strongly recommended by the U.S. Headache Consortium based on evidence from consistent findings in randomized controlled trials.⁵³ Other guidelines recommend stress management and acupuncture. European guidelines for TTH recommend electromyographic biofeedback based on a meta-analysis of 53 studies.⁴⁷ Cognitive behavior therapy, relaxation training, physical therapy, and acupuncture were given lower-grade recommendations because of lack of conclusive evidence of effectiveness.⁴⁷ Patient adherence is a major barrier to behavioral treatments. Key factors in adherence are negative attitudes and beliefs, lack of motivation, poor awareness of triggers, external locus of control, poor self-efficacy, low levels of pain acceptance, and maladaptive coping styles.⁵⁴ Self-management interventions such as cognitive behavior therapy, mindfulness, and education are more effective than usual care in reducing pain intensity, mood- and headache-related disability, but they may not reduce the frequency of migraine or TTH.⁵⁵

Guidelines stress addressing the role of lifestyle issues such as poor sleep, lack of exercise, smoking, obesity, and caffeine use in triggering and exacerbating headaches, but the impact of these factors has not been quantified.

ENSURE FOLLOW-UP

Regularly scheduled follow-up is necessary to monitor the patient’s headache pattern and make adjustments to the management plan. Patients should be instructed to report signs of reescalation of primary headaches, development of MOH, or red flags for developing serious secondary headaches. Factors associated with recurrent escalation of episodic headache are not clear, but poor prognosis in patients with chronic headache is associated with psychosocial factors, anxiety, mood disorders, poor sleep, stress, and low headache management self-efficacy. Based on lower-quality studies, other factors such as higher patient expectations, older age, older age at onset, headache frequency and intensity, BMI, disability scores, and unemployment are inconsistently predictive of treatment response.⁵⁶

Several innovative medications are becoming available for prevention and acute treatment of migraine but have not yet been incorporated into evidence-based guidelines. Although these are valuable additions to migraine treatment, it is important to reconsider the diagnosis, screen for MOH, and address factors that could be driving headache escalation before prescribing new and expensive agents. The current expert consensus supports the use of small-molecule calcitonin gene-related peptide (CGRP) receptor antagonists (ubrogepant [Ubrovelvy] and rimegepant [Nurtec], both of which were recently approved by the U.S. Food and Drug Administration) and the selective 5-hydroxytryptamine receptor 1F agonist lasmiditan (Reyvow) for

TABLE 5

Pharmacologic Options for Treatment and Chemoprophylaxis of Primary Headache

Headache type	Acute treatments	Chemoprophylaxis*
Migraine	Acetaminophen, 1,000 mg	Amitriptyline, 10 to 150 mg at bedtime
	Acetaminophen/aspirin/caffeine, 500 mg/500 mg/130 mg	Atenolol, 50 to 200 mg daily
	Almotriptan, 12.5 mg	Candesartan (Atacand), 16 mg daily
	Aspirin, 900 to 1,000 mg	Divalproex (Depakote), 250 to 750 mg twice daily
	Eletriptan (Relpax), 20 to 80 mg	Metoprolol, 50 to 100 mg twice daily
	Frovatriptan (Frova), 2.5 mg	Nadolol (Corgard), 80 to 160 mg daily
	Ibuprofen, 200 to 400 mg	Nortriptyline (Pamelor), 10 to 100 mg at bedtime
	Naproxen, 500 to 825 mg	Propranolol, 40 to 160 mg twice daily
	Naratriptan (Amerge), 1 to 2.5 mg	Topiramate (Topamax), 25 to 200 mg daily
	Rizatriptan (Maxalt), 5 to 10 mg	Valproate (Depacon), 400 to 1,500 mg daily
Tension	Sumatriptan (Imitrex), 25 to 100 mg orally, 10 to 20 mg intranasally, or 4 to 6 mg subcutaneously	
	Sumatriptan/naproxen (Treximet), 85 mg/500 mg	
	Zolmitriptan (Zomig), 2.5 mg orally or 2.5 to 5 mg intranasally	
	Acetaminophen, 1,000 mg	Amitriptyline, 10 to 75 mg at bedtime
	Aspirin, 500 to 1,000 mg	Nortriptyline, 10 to 100 mg at bedtime
	Diclofenac, 12.5 to 25 mg	
Cluster	Ibuprofen, 200 to 800 mg	
	Ketoprofen, 25 mg	
	Naproxen, 375 to 550 mg	
Cluster	Oxygen 100%, 7 to 12 L per minute for 15 minutes	Civamide (not available in the United States), 100 mcg intranasally
	Sumatriptan, 6 mg subcutaneously	Lithium, 900 to 1,200 mg daily
	Zolmitriptan, 5 mg intranasally	Verapamil, 240 to 960 mg daily
Rare primary headaches	May respond to indomethacin	—

Note: All medications are administered orally unless noted otherwise. Medication guidelines are based on highest-grade evidence-based recommendations.^{20,44-53}

*—2016 U.S. and 2018 European guidelines state that onabotulinumtoxinA (Botox) is effective for decreasing the number and severity of headaches in patients with established chronic migraine, is probably effective for improving health-related quality of life in patients with established chronic migraine, and is ineffective for and should not be offered to patients with episodic migraine.^{52,53}

Information from references 20 and 44-53.

FREQUENT HEADACHES

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	Evidence rating	Comment
Physicians should conduct a complete assessment in patients with frequent or increasing headaches—even in those with long-standing headaches—because a new headache type may have developed or the current diagnosis may be inaccurate. ^{18-21,26,27}	C	Expert consensus and several diagnostic studies showing high rates of misdiagnosis of headache, especially migraine and sinus headaches
Neuroimaging is indicated in patients with headaches with new features or neurologic deficits, trigeminal autonomic cephalalgias, or suspected intracranial abnormality. ^{18-21,30-32}	C	Expert consensus based on concerns that intracranial conditions can mimic unilateral autonomic symptoms of trigeminal autonomic cephalalgias
All patients with frequent or increasing headaches should be assessed for medication overuse. ^{18-21,34}	C	Expert consensus based on multiple observational studies showing that at least 30% to 50% of patients with chronic headache have medication overuse headache
Prophylactic and acute therapy should be offered to patients with frequent migraine, tension-type, cluster, or other primary headache. ^{18-21,44-52}	C	Expert consensus based on studies and meta-analyses supporting the effectiveness of prophylactic and acute therapy in reducing the number and severity of headache episodes
Nonpharmacologic therapies such as relaxation with or without biofeedback, cognitive behavior therapy, acupuncture, and physical therapy should be incorporated in management strategies for frequent headaches. ^{18-20,47,53}	C	Expert consensus supporting biofeedback in the treatment of tension-type headache (meta-analysis) and few studies supporting benefits of other modalities

A = consistent, good-quality patient-oriented evidence; **B** = inconsistent or limited-quality patient-oriented evidence; **C** = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to <https://www.aafp.org/afpsort>.

treatment of acute migraine in patients who have documented nonresponse to or intolerance of at least two oral triptans. Validated outcome questionnaires, such as the Migraine-Treatment Optimization Questionnaire, Migraine Assessment of Current Therapy, or Functional Impairment Scale, are recommended to document eligibility for therapy and to monitor outcomes.

Emerging treatments for migraine prophylaxis include monoclonal antibodies to the CGRP receptor (erenumab [Aimovig]) and CGRP ligands (fremanezumab [Ajovy], galcanezumab [Emgality], and eptinezumab). Other agents and oral forms are in development. Indications for use require confirmed diagnosis of frequent or chronic migraine plus inability to tolerate or inadequate response to an adequate trial of at least two prophylactic agents with established effectiveness, such as topiramate, metoprolol, divalproex (Depakote), or amitriptyline. After three to six months, therapy should be continued only if headache days per month have been reduced by 50% or significant improvement can be documented on a validated outcome measure, such as the Migraine Disability Assessment, the six-item Headache Impact Test, or the Migraine Physical Function Impact Diary.

Data Sources: Multiple PubMed searches were completed using the key words headache, frequent headache, and chronic headache. Information from Essential Evidence Plus was incorporated in literature searches. Guidelines and expert recommendations from the American Academy of Neurology, Institute for Clinical Systems Improvement, Scottish Intercollegiate Guidelines Network, American Headache Society, U.S. Headache Consortium, and European Federation of Neurologic Societies were also searched. The bibliographies of relevant articles were reviewed to identify any primary sources missed in the original searches. Search dates: November 2018 and January 2019.

Editor's Note: Dr. Walling is an associate editor for *American Family Physician*.

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eTABLE A

Diagnostic Criteria for Migraine**Acute (episodic)**

- A. At least 5 attacks fulfilling criteria B to D
- B. Attacks last 4 to 72 hours (when untreated or unsuccessfully treated)
- C. At least 2 of the following:
 - 1. Unilateral location
 - 2. Pulsating quality
 - 3. Moderate or severe pain intensity
 - 4. Aggravated by or causing avoidance of routine physical activity
- D. During headache, at least 1 of the following:
 - 1. Nausea and/or vomiting
 - 2. Photophobia and phonophobia
- E. Not better accounted for by another ICHD-3 diagnosis

Chronic

- A. Headache (migraine or tension-type) on ≥ 15 days per month for > 3 months, and fulfilling criteria B and C
- B. At least 5 attacks fulfilling criteria B to D for acute migraine and/or both of the following:
 - 1. At least 1 of the following fully reversible aura symptoms:
 - a. Visual
 - b. Sensory
 - c. Speech and/or language
 - d. Motor
 - e. Brain stem
 - f. Retinal
 - 2. At least 3 of the following:
 - a. At least 1 aura symptom spreads gradually over ≥ 5 minutes
 - b. At least 2 aura symptoms occur in succession
 - c. Each aura symptom lasts 5 to 60 minutes
 - d. At least 1 aura symptom is unilateral
 - e. At least 1 aura symptom is positive
 - f. The aura is accompanied or followed within 60 minutes by headache
- C. On ≥ 8 days per month for > 3 months, fulfilling any of the following:
 - 1. Criteria C and D for acute migraine
 - 2. Criteria B1 and B2 for chronic migraine
 - 3. Believed by the patient to be migraine at onset and relieved by a triptan or ergotamine
- D. Not better accounted for by another ICHD-3 diagnosis

ICHD-3 = International Classification of Headache Disorders, 3rd ed.

Information from Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd ed. Cephalalgia. 2018;38(1):1-211.

eTABLE B

Diagnostic Criteria for Tension-Type Headache

Infrequent episodic

- A. At least 10 episodes occurring on < 1 day per month on average (< 12 days per year) and fulfilling criteria B to D
- B. Lasting 30 minutes to 7 days
- C. At least 2 of the following:
 1. Bilateral location
 2. Pressing or tightening (nonpulsating) quality
 3. Mild or moderate intensity
 4. Not aggravated by routine physical activity
- D. Both of the following:
 1. No nausea or vomiting
 2. Photophobia or phonophobia (but not both)
- E. Not better accounted for by another ICHD-3 diagnosis*

Frequent episodic

At least 10 episodes occurring on 1 to 14 days per month on average for > 3 months (≥ 12 and < 180 days per year) and fulfilling criteria B to E for infrequent episodic tension-type headache

Chronic

- A. Headache occurring on ≥ 15 days per month on average for > 3 months (≥ 180 days per year) and fulfilling criteria B to D
- B. Lasting hours to days, or unremitting
- C. Fulfilling criteria C and E for infrequent episodic tension-type headache
- D. Both of the following:
 1. Neither moderate nor severe nausea, nor vomiting
 2. No more than 1 of the following:
 - a. Photophobia
 - b. Phonophobia
 - c. Mild nausea

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*—When headache fulfills criteria for both probable migraine and tension-type headache, tension-type headache should be diagnosed.

Information from Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd ed. Cephalalgia. 2018;38(1):1-211.

Diagnostic Criteria for Trigeminal Autonomic Cephalalgias

Cluster headache

Episodic

- A. At least 5 attacks fulfilling criteria B to D
- B. Severe unilateral orbital, supraorbital, or temporal pain lasting 15 to 180 minutes (untreated)
- C. Either or both of the following:
 1. At least 1 of the following, ipsilateral to the headache:
 - a. Conjunctival injection or lacrimation
 - b. Nasal congestion or rhinorrhea
 - c. Eyelid edema
 - d. Forehead and facial sweating
 - e. Miosis or ptosis
 2. Restlessness or agitation
- D. Occurring from every other day up to 8 times per day
- E. At least 2 cluster periods lasting from 7 days to 1 year (untreated) and separated by pain-free remission periods of ≥ 3 months
- F. Not better accounted for by another ICHD-3 diagnosis

Chronic

- A. Attacks fulfilling criteria A to D for episodic cluster headache
- B. Occurring for ≥ 1 year without a remission period, or with remissions lasting < 3 months

Paroxysmal hemicrania

Episodic

- A. At least 20 attacks fulfilling criteria B to E
- B. Severe unilateral orbital, supraorbital, or temporal pain lasting 2 to 30 minutes
- C. Either or both of the following:
 1. At least 1 of the following, ipsilateral to the headache:
 - a. Conjunctival injection or lacrimation
 - b. Nasal congestion or rhinorrhea
 - c. Eyelid edema
 - d. Forehead and facial sweating
 - e. Miosis or ptosis
 2. Restlessness or agitation
- D. Occurring > 5 times per day
- E. Prevented absolutely with therapeutic doses of indomethacin (150 to 225 mg per day)
- F. At least 2 bouts lasting 7 days to 1 year (untreated) and separated by pain-free remission periods of ≥ 3 months
- G. Not better accounted for by another ICHD-3 diagnosis

Chronic

- A. Attacks fulfilling criteria A to E for paroxysmal hemicrania
- B. Occurring ≥ 1 year without a remission period, or with remissions lasting < 3 months

Short-lasting unilateral neuralgiform headache

Episodic

- A. At least 20 attacks fulfilling criteria B to D
- B. Moderate or severe unilateral pain with orbital, supraorbital, temporal, or other trigeminal distribution, lasting 1 second to 10 minutes and occurring as single stabs, series of stabs, or in a sawtooth pattern
- C. At least 1 of the following, ipsilateral to the pain:
 1. Either conjunctival injection and lacrimation (in short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing) or conjunctival injection or lacrimation (in short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms)
 2. Nasal congestion or rhinorrhea
 3. Eyelid edema
 4. Forehead and facial sweating
 5. Miosis or ptosis
- D. Occurring ≥ 1 time per day
- E. At least 2 bouts lasting 7 days to 1 year (untreated) and separated by pain-free remission periods of ≥ 3 months
- F. Not better accounted for by another ICHD-3 diagnosis

Chronic

- A. Attacks fulfilling criteria A to D for episodic short-lasting unilateral neuralgiform headache
- B. Occurring for ≥ 1 year without a remission period, or with remissions lasting < 3 months

Hemicrania continua

Remitting

- A. Unilateral headache fulfilling criteria B to D
- B. Present for > 3 months, with exacerbations of moderate or greater intensity
- C. Either or both of the following:
 1. At least 1 of the following, ipsilateral to the headache:
 - a. Conjunctival injection or lacrimation
 - b. Nasal congestion or rhinorrhea
 - c. Eyelid edema
 - d. Forehead and facial sweating
 - e. Miosis or ptosis
 2. Restlessness or agitation, or aggravation of the pain by movement
- D. Responds absolutely to therapeutic doses of indomethacin (150 to 225 mg per day)
- E. Not better accounted for by another ICHD-3 diagnosis

Unremitting

- A. Headache fulfilling criteria A to E for remitting hemicrania continua
- B. Daily and continuous for ≥ 1 year without remission periods of ≥ 24 hours

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Information from Headache Classification Committee of the International Headache Society (IHS). *The International Classification of Headache Disorders, 3rd ed.* Cephalalgia. 2018;38(1):1-211.

eTABLE D

Diagnostic Criteria for Other Primary Headache Disorders

Primary cough headache

- A. At least 2 episodes fulfilling criteria B to D
- B. Brought on by and occurring only in association with coughing, straining, and/or other Valsalva maneuver
- C. Begins moments after the stimulus and reaches peak intensity almost immediately
- D. Lasting 1 second to 2 hours
- E. Not better accounted for by another ICHD-3 diagnosis

Primary exercise headache

- A. At least 2 headache episodes fulfilling criteria B and C
- B. Brought on by and occurring only during or after strenuous physical exercise
- C. Lasting < 48 hours
- D. Not better accounted for by another ICHD-3 diagnosis

Primary headache associated with sexual activity

- A. At least 2 episodes of pain in the head and/or neck fulfilling criteria B to D
- B. Brought on by and occurring only during sexual activity
- C. Either or both of the following:
 - 1. Increasing intensity with increasing sexual excitement
 - 2. Abrupt explosive intensity just before or with orgasm
- D. Lasting 1 minute to 24 hours with severe intensity or up to 72 hours with mild intensity
- E. Not better accounted for by another ICHD-3 diagnosis

Primary thunderclap headache

- A. Severe pain fulfilling criteria B and C
- B. Abrupt onset with maximal intensity in < 1 minute
- C. Lasting for ≥ 5 minutes
- D. Not better accounted for by another ICHD-3 diagnosis

Cold-stimulus headache

- A. At least 2 acute headache episodes fulfilling criteria B and C
- B. Brought on by and occurring only during application of an external cold stimulus to the head
- C. Resolving within 30 minutes after removal of the cold stimulus
- D. Not better accounted for by another ICHD-3 diagnosis

External-pressure headache

- A. At least 2 episodes of headache fulfilling criteria B to D
- B. Brought on by and occurring within 1 hour during sustained external pressure (compression or traction) of the forehead or scalp
- C. Maximal intensity at the site of external pressure
- D. Resolving within 1 hour after external pressure is relieved
- E. Not better accounted for by another ICHD-3 diagnosis

Primary stabbing headache

- A. Pain occurring spontaneously as a single stab or series of stabs and fulfilling criteria B and C
- B. Each stab lasts up to a few seconds
- C. Stabs recur with irregular frequency, from 1 to many per day
- D. No cranial autonomic symptoms
- E. Not better accounted for by another ICHD-3 diagnosis

Nummular headache

- A. Continuous or intermittent pain fulfilling criterion B
- B. Felt exclusively in an area of the scalp, with all of the following:
 - 1. Sharply contoured
 - 2. Fixed size and shape
 - 3. Round or elliptical
 - 4. 1 to 6 cm in diameter
- C. Not better accounted for by another ICHD-3 diagnosis

Hypnic headache

- A. Recurrent attacks fulfilling criteria B to E
- B. Developing only during sleep, and causing waking
- C. Occurring on ≥ 10 days per month for > 3 months
- D. Lasting 15 minutes to 4 hours after waking
- E. No cranial autonomic symptoms or restlessness
- F. Not better accounted for by another ICHD-3 diagnosis

New daily persistent headache

- A. Persistent headache fulfilling criteria B and C
- B. Distinct and clearly remembered onset, with pain becoming continuous and unremitting within 24 hours
- C. Present for > 3 months
- D. Not better accounted for by another ICHD-3 diagnosis

Note: Presentation of the headache disorders in this table may be difficult to differentiate from serious causes of secondary headache (e.g., subarachnoid hemorrhage, Arnold-Chiari malformation, intracranial lesions). See eTable E.

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eTABLE E

Diagnostic Criteria for Secondary Headaches

General definition

- A. Any headache fulfilling criterion C
- B. Another disorder scientifically documented to cause headache has been diagnosed
- C. Evidence of causation demonstrated by at least 2 of the following:
 - 1. Headache has developed in temporal relation to the onset of the presumed causative disorder
 - 2. Either or both of the following:
 - a. Headache has significantly worsened in parallel with worsening of the presumed causative disorder
 - b. Headache has significantly improved in parallel with improvement of the presumed causative disorder
 - 3. Headache has characteristics typical for the causative disorder
 - 4. Other evidence of causation exists
- D. Not better accounted for by another ICHD-3 diagnosis

Diagnostic categories

Headache attributed to:

- Cranial and/or cervical vascular disorder (e.g., cerebral ischemia, hemorrhage, thrombosis, arteritis, vascular malformations, reversible cerebral vasoconstriction syndrome, carotid and vertebral artery conditions)
- Disorder of homeostasis (e.g., hypoxia, hypercapnia, hypertension, fasting, dialysis, hypothyroidism, cardiac conditions)
- Disorder of the cranium, neck, eyes, ears, nose, sinuses, teeth, mouth, or other facial or cranial structure (e.g., glaucoma, sinus conditions, cervical radiculopathy, temporomandibular disorder)
- Infection (e.g., acute and nonacute intracranial and systemic infections)
- Nonvascular intracranial disorder (e.g., increased or decreased cerebrospinal fluid pressure, inflammatory conditions, neoplasia, seizure, type 1 Chiari malformation)
- Psychiatric disorder (e.g., somatization or psychotic disorder)
- Trauma or injury to the head and/or neck (e.g., acute or persistent headaches related to injury or trauma)
- Use of or withdrawal from a substance (e.g., carbon monoxide, nitrous oxide, histamine, alcohol, cocaine)

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