VA/DoD Clinical Practice Guidelines

THE PRIMARY CARE MANAGEMENT OF HEADACHE

Provider Summary

Version 1.0 | 2020

VA/DoD CLINICAL PRACTICE GUIDELINE FOR THE PRIMARY CARE MANAGEMENT OF HEADACHE

Department of Veterans Affairs

Department of Defense

Provider Summary

QUALIFYING STATEMENTS

The Department of Veterans Affairs and the Department of Defense guidelines are based upon the best information available at the time of publication. They are designed to provide information and assist decision making. They are not intended to define a standard of care and should not be construed as one. Neither should they be interpreted as prescribing an exclusive course of management.

This Clinical Practice Guideline is based on a systematic review of both clinical and epidemiological evidence. Developed by a panel of multidisciplinary experts, it provides a clear explanation of the logical relationships between various care options and health outcomes while rating both the quality of the evidence and the strength of the recommendation.

Variations in practice will inevitably and appropriately occur when clinicians take into account the needs of individual patients, available resources, and limitations unique to an institution or type of practice. Every healthcare professional making use of these guidelines is responsible for evaluating the appropriateness of applying them in the setting of any particular clinical situation.

These guidelines are not intended to represent Department of Veterans Affairs or TRICARE policy. Further, inclusion of recommendations for specific testing and/or therapeutic interventions within these guidelines does not guarantee coverage of civilian sector care. Additional information on current TRICARE benefits may be found at www.tricare.mil or by contacting your regional TRICARE Managed Care Support Contractor.

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Introduction

The Department of Veterans Affairs (VA) and Department of Defense (DoD) Evidence-Based Practice Work Group (EBPWG) was established and first chartered in 2004, with a mission to advise the Health Executive Committee (HEC) "…on the use of clinical and epidemiological evidence to improve the health of the population…" across the Veterans Health Administration (VHA) and Military Health System (MHS), by facilitating the development of clinical practice guidelines (CPGs) for the VA and DoD populations.[1] This CPG is intended to provide healthcare providers with a framework by which to evaluate, treat, and manage the individual needs and preferences of patients with headache, thereby leading to improved clinical outcomes.

Consequently, a recommendation to create the VA/DoD CPG for the Primary Care Management of Headache (VA/DoD Headache CPG) was initiated in 2018. The CPG includes objective, evidence-based information on the diagnosis and management of headache. It is intended to assist primary care providers (PCPs) in all aspects of patient care, including assessment, treatment, and follow-up. The system-wide goal of evidence-based guidelines is to improve the patient's health and well-being by guiding health providers who are caring for patients with headache along management pathways that are supported by evidence. The expected outcome of successful implementation of this guideline is to:

- Assess the individual's condition and determine, in collaboration with the patient, the best treatment method
- Optimize health outcomes and improve quality of life
- Minimize preventable complications and morbidity
- Emphasize the use of patient-centered care (PCC)

Recommendations

The following recommendations were made using a systematic approach considering four domains as per the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach as detailed in the section on Methods and Appendix B in the full text Headache CPG. These domains include: confidence in the quality of the evidence, balance of desirable and undesirable outcomes (i.e., benefits and harms), patient or provider values and preferences, and other implications, as appropriate (e.g., resource use, equity, acceptability).

Topic	Sub-topic	#	Recommendation[a]	Strength[b]
Screening and Healthcare Settings		1.	We suggest providers assess the following risk factors for medication overuse headache in patients with headache: • Medication use: frequent use of anxiolytics, analgesics, or sedative hypnotics • Physical inactivity • Self-reported whiplash • History of anxiety or depression with or without musculoskeletal complaints and/or gastrointestinal complaints • Sick leave of greater than two weeks in the last year • Smoking	Weak for
		2.	There is insufficient evidence to recommend for or against any specific strategy or healthcare setting for the withdrawal of medication in the treatment of medication overuse headache.	Neither for nor against
Non-pharmacologic Therapy		3.	We suggest physical therapy for the management of tension-type headache.	Weak for
		4.	We suggest aerobic exercise or progressive strength training for the management of headache.	Weak for
		5.	We suggest mindfulness-based therapies for the treatment of headache.	Weak for
		6.	We suggest education regarding dietary trigger avoidance for the prevention of migraine.	Weak for
		7.	We suggest non-invasive vagus nerve stimulation for the acute treatment of episodic cluster headache.	Weak for
		8.	There is insufficient evidence to recommend for or against acupuncture for the treatment of headache.	Neither for nor against
		9.	There is insufficient evidence to recommend for or against dry needling for the treatment of headache.	Neither for nor against
		10.	There is insufficient evidence to recommend for or against pulsed radiofrequency or sphenopalatine ganglion block for the treatment of headache.	Neither for nor against
		11.	There is insufficient evidence to recommend for or against cognitive behavioral therapy or biofeedback for the treatment of headache.	Neither for nor against
		12.	There is insufficient evidence to recommend for or against an elimination diet based on immunoglobulin G antibody test results for the prevention of headache.	Neither for nor against
		13.	There is insufficient evidence to recommend for or against the following for headache: • Transcranial magnetic stimulation • Transcranial direct current stimulation • External trigeminal nerve stimulation • Supraorbital electrical stimulation	Neither for nor against

Topic	Sub-topic	#	Recommendation[a]	Strength[b]
Pharmacotherapy	*a. Migraine – Preventive*	14.	We recommend candesartan or telmisartan for the prevention of episodic or chronic migraine.	Strong for
		15.	We suggest erenumab, fremanezumab, or galcanezumab for the prevention of episodic or chronic migraine.	Weak for
		16.	We suggest lisinopril for the prevention of episodic migraine.	Weak for
		17.	We suggest oral magnesium for the prevention of migraine.	Weak for
		18.	We suggest topiramate for the prevention of episodic migraine.	Weak for
		19.	We suggest propranolol for the prevention of migraine.	Weak for
		20.	We suggest onabotulinumtoxinA injection for the prevention of chronic migraine.	Weak for
		21.	We suggest against abobotulinumtoxinA or onabotulinumtoxinA injection for the prevention of episodic migraine.	Weak against
		22.	There is insufficient evidence to recommend for or against gabapentin for the prevention of episodic migraine.	Neither for nor against
		23.	There is insufficient evidence to recommend for or against nimodipine or nifedipine for the prevention of episodic migraine.	Neither for nor against
		24.	There is insufficient evidence to recommend for or against coenzyme Q10, feverfew, melatonin, omega-3, vitamin B2, or vitamin B6 for the prevention of migraine.	Neither for nor against
		25.	There is insufficient evidence to recommend for or against combination pharmacotherapy for the prevention of migraine.	Neither for nor against
	b. Migraine – Abortive	26.	We recommend sumatriptan (oral or subcutaneous), the combination of sumatriptan/naproxen, or zolmitriptan (oral or intranasal) for the acute treatment of migraine.	Strong for
		27.	We suggest frovatriptan or rizatriptan for the acute treatment of migraine.	Weak for
		28.	We suggest triptans instead of opioids or non-opioid analgesics to lower the risk of medication overuse headache for the acute treatment of migraine.	Weak for
		29.	We suggest ibuprofen, naproxen, aspirin, or acetaminophen for the acute treatment of migraine.	Weak for
		30.	We suggest greater occipital nerve block for the acute treatment of migraine.	Weak for
		31.	We suggest intravenous magnesium for the acute treatment of migraine.	Weak for
	c. Tension-type Headache – Preventive	32.	We suggest amitriptyline for the prevention of chronic tension-type headache.	Weak for
		33.	We suggest against botulinum/neurotoxin injection for the prevention of chronic tension-type headache.	Weak against
	d. Tension-type Headache – Abortive	34.	We suggest ibuprofen (400 mg) or acetaminophen (1,000 mg) for the acute treatment of tension-type headache.	Weak for

Topic	Sub-topic	#	Recommendation[a]	Strength[b]
Pharmacotherapy (cont.)	*e. Cluster Headache – Preventive*	35.	We suggest galcanezumab for the prevention of episodic cluster headache.	Weak for
	f. Cluster Headache – Abortive	36.	There is insufficient evidence to recommend for or against any particular medication for the acute treatment of cluster headache.	Neither for nor against
	g. Headache – Preventive	37.	There is insufficient evidence to recommend for or against oxygen therapy for the acute treatment of primary headache.	Neither for nor against
		38.	There is insufficient evidence to recommend for or against valproate for the prevention of headache.	Neither for nor against
		39.	There is insufficient evidence to recommend for or against fluoxetine or venlafaxine for the prevention of headache.	Neither for nor against
	h. Headache – Abortive	40.	We suggest against intravenous ketamine for the acute treatment of headache.	Weak against
		41.	There is insufficient evidence to recommend for or against intravenous metoclopramide, intravenous prochlorperazine, or intranasal lidocaine for the acute treatment of headache.	Neither for nor against
	i. Secondary Headache – Abortive	42.	There is insufficient evidence to recommend for or against prescription or non-prescription pharmacologic agents for the treatment of secondary headache.	Neither for nor against

[a] For more information regarding regarding the scope of the CPG, please refer to Scope of this Clinical Practice Guideline in the full text Headache CPG

[b] For additional information, please refer to Grading Recommendations in the full text Headache CPG

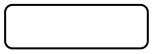
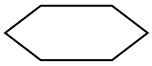
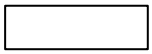
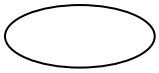
* The category for all recommendations is *Reviewed*, *New-added*. For additional information on recommendation categories, please refer to Recommendation Categorization and Appendix B in the full text Headache CPG

Algorithm

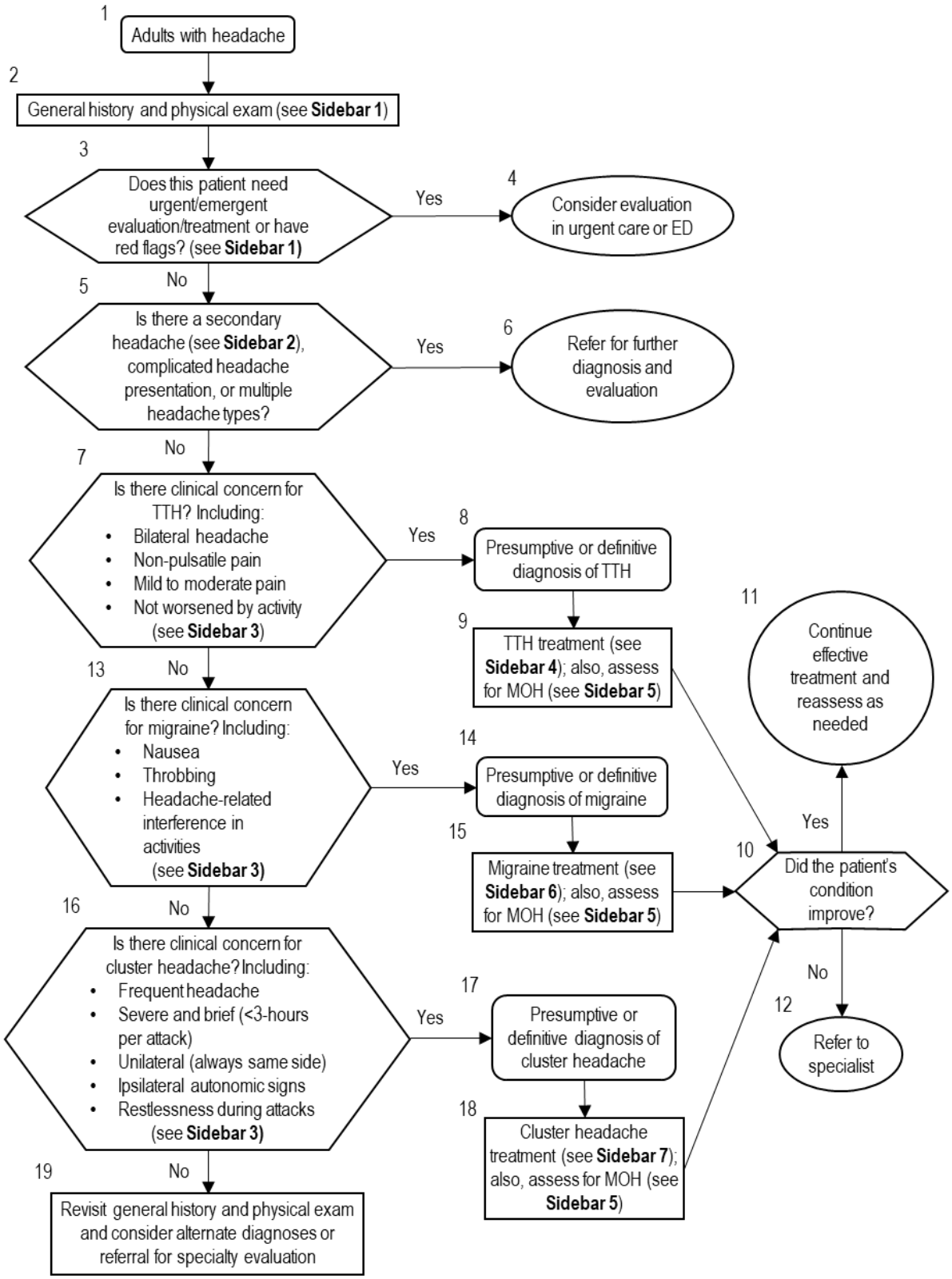
This CPG's algorithm is designed to facilitate understanding of the clinical pathway and decision-making process used in the management of headache. This algorithm format represents a simplified flow of the management of patients with headache and helps foster efficient decision making by providers. It includes:

- An ordered sequence of steps of care
- Recommended decision criteria
- Decisions to be considered
- Actions to be taken

The algorithm is a step-by-step decision tree. Standardized symbols are used to display each step, and arrows connect the numbered boxes indicating the order in which the steps should be followed.[2] Sidebars provide more detailed information to assist in defining and interpreting elements in the boxes.

Shape	Description
	Rounded rectangles represent a clinical state or condition
	Hexagons represent a decision point in the guideline, formulated as a question that can be answered "Yes" or "No"
	Rectangles represent an action in the process of care
	Ovals represent a link to another section within the guideline

Module A: Evaluation and Treatment of Headache



Abbreviations: ED: emergency department; MOH: medication overuse headache; TTH: tension-type headache

Sidebar 1: General History and Physical Exam

Headache history

- Frequency
- Character
- Onset
- Location
- Duration
- Exacerbating factors
- Relieving factors
- Prodrome/aura
- Associated symptoms
- Jaw symptoms
- Neck symptoms
- Visual deficits/changes
- Dizziness/imbalance
- Current medications, abortive dose and frequency per month, prophylactic dose
- Prior medication trials
- Hydration
- Meals
- Caffeine
- Sleep
- Exercise
- Nicotine/stimulant use
- Other comorbid conditions that may contribute to or exacerbate headaches
- Risk factors for MOH
- History of trauma to the head and/or neck

Red flags SNOOP(4)E [3]

- Systemic symptoms, illness, or condition (e.g., fever, chills, myalgias, night sweats, weight loss or gain, cancer, infection, giant cell arteritis, pregnancy or postpartum, or an immunocompromised state – including HIV)
- Neurologic symptoms or abnormal signs (e.g., confusion, impaired alertness or consciousness, changes in behavior or personality, diplopia, pulsatile tinnitus, focal neurologic symptoms or signs, meningismus, or seizures ptosis, proptosis, pain with eye movements)
- Onset (e.g., abrupt or "thunderclap" where pain reaches maximal intensity immediately or within minutes after onset; first ever, severe, or "worst headache of life")
- Older onset (age ≥50-years)
- Progression or change pattern (e.g., in attack frequency, severity, or clinical features)
- Precipitated by Valsalva (e.g., coughing or bearing down)
- Postural aggravation
- Papilledema
- Exertion

Examination

- Cranial nerves (including funduscopic exam)
- Cervical spine and surrounding musculature (palpation, ROM, Spurling's)
- Temporomandibular joint (palpation, ROM, symmetry, jaw claudication)
- Pericranial muscle palpation
- General neurologic (upper extremities reflexes, sensation, strength, UMN, pathologic reflexes)
- Temporal artery palpation (tenderness, cord-like artery, or lack of pulse)
- Blood pressure

Standardized headache assessments:

- MIDAS [4]
- HIT-6 [5]
- MSQL [6]

Abbreviations: HIT-6: Headache Impact Test, 6th edition; HIV: human immunodeficiency virus; MIDAS: Migraine Disability Assessment Test; MOH: medication overuse headache; MSQL: Migraine-Specific Quality of Life questionnaire; ROM: range of motion; SNOOP(4)E: Systemic, Neurologic symptoms, Onset sudden, Onset after 50, Pattern change, Precipitated, Postural, Papilledema, Exertion; UMN: upper motor neuron

Sidebar 2: Criteria for Determining Primary Versus Secondary Headache Disorders

Initial evaluation of headache should be targeted at determining if there is a secondary cause for the headache or if the diagnosis of a primary headache disorder is appropriate. Emergent evaluation should be considered based on red flag features. In general, a secondary headache can be diagnosed if the headache is new and occurs in close temporal relation to another disorder that is known to cause headache. It can also be diagnosed when a pre-existing headache disorder significantly worsens in close temporal relation to a causative disorder in which case both the primary and secondary headache diagnoses should be given. ICHD-3 diagnostic criteria are below.[7]

General diagnostic criteria for secondary headaches:

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

The secondary headaches include: headache attributed to trauma or injury to the head and/or neck, cranial or cervical vascular disorder, non-vascular intracranial disorder, a substance or its withdrawal, infection, disorder of homeostasis, disorder of the cranium, neck, eyes, ears, nose, sinuses, teeth, mouth, other facial or cervical structure, or psychiatric disorder

Abbreviations: ICHD-3: International Classification of Headache Disorders, 3rd edition

Sidebar 3: Primary Headache Disorders Criteria*				
		Tension-type headache[a]	**Migraine headache[b]**	**Cluster headache[c]**
Attack duration and frequency	Duration	30-minutes – 7-days	4 – 72 hours	15 – 180 minutes
	Frequency	Variable	Variable	Once every other day to eight per day; often occurring at the same time of day
Headache characteristics	Severity	Mild to moderate	Moderate to severe	Severe or very severe
	Location	Bilateral	Unilateral	Unilateral orbital, supraorbital, and/or temporal
	Quality	Pressing or tightening, non-pulsating	Throbbing or pulsating	Stabbing, boring
	Aggravated by routine physical activity	Not aggravated by routine activity	Aggravated by routine activity	Causes a sense of agitation or restlessness; routine activity may improve symptoms
Associated features	Photophobia and phonophobia	Can have one but not both	Both	Variably present
	Nausea and/or vomiting	Neither	Either or both	May be present
Other features	Autonomic features	None	May occur, but are often subtle and not noticed by the patient	Prominent autonomic features ipsilateral to the pain (see Appendix A in full text Headache CPG)

[a] A diagnosis of TTH requires at least 10 headache attacks lasting 30-minutes to 7-days with at least two defining characteristics (i.e., bilateral location, non-pulsating quality, mild to moderate intensity, not aggravated by routine physical activity), and both of the associated features (i.e., no nausea or vomiting; either photophobia or phonophobia, but not both). If headaches fulfill all but one of the TTH criteria (e.g., having both photophobia and phonophobia), the diagnosis would be probable TTH.

[b] A diagnosis of migraine requires at least five attacks lasting 4 – 72 hours with at least two defining headache characteristics (i.e., unilateral, throbbing/pulsating, moderate or severe intensity, aggravated, or caused by routine physical activity) and at least one associated feature (i.e., nausea and/or vomiting and both photophobia and phonophobia). If headaches fulfill all but one of the migraine criteria (e.g., photophobia or phonophobia but not but photophobia and phonophobia), the diagnosis would be probable migraine.

[c] A diagnosis of cluster headache requires at least five attacks of severe to very severe unilateral orbital, supraorbital, and/or temporal pain lasting 15 – 180 minutes and occurring once every other day to no more than eight times a day. Either or both autonomic features and a feeling of restless/agitation are required.

* There are definitions for probable TTH, probable migraine, or probable cluster headache where patients may not fulfill all criteria listed above. The Work Group suggests that providers should not withhold therapy when patients do not meet all criteria listed for TTH, migraine, or cluster headache (i.e., are diagnosed with probable TTH, probable migraine, or probable cluster headache).[7] Providers should continually reassess patients during therapy (see Box 19 in Module A).

Sidebar 4: Treatment Options for Tension-type Headache[a, b]		
Type	**Treatment**	**Notes**
Non-pharmacologic Therapy – Preventive	Physical therapy↑	• "Physical therapy" refers to a range of interventions carried out by licensed physical therapists, including manual therapy, therapeutic exercise, strength and endurance training, self-management training, and adjunctive modalities
Pharmacotherapy – Preventive	Amitriptyline↑	• Accessible for general practitioners to prescribe, inexpensive, and may help with patients who suffer from insomnia. Side effects include dry mouth, dry eyes, weight gain, sedation, dizziness, blurred vision, GI distress, and nausea
	Botulinum toxin/ neurotoxin↓	• Evidence suggests intervention is ineffective for preventing chronic TTH
Pharmacotherapy – Abortive	Ibuprofen 400 mg or acetaminophen 1,000 mg↑	• Evidence suggests a statistically significant between-group difference for acetaminophen 1,000 mg versus placebo, favoring acetaminophen

[a] For the full recommendation language, see Recommendations

[b] Sidebar 8 presents additional treatment options for general headache

Abbreviations: GI: gastrointestinal; mg: milligrams; TTH: tension-type headache

↑ Indicates a "Weak for" recommendation strength; ↓ indicates a "Weak against" recommendation strength

Sidebar 5: Common Medications and their Association with MOH	
MOH Type	**Medication Overuse Frequency**
Acetaminophen overuse	≥15-days/month for >3-months
NSAID overuse	
Other non-opioid analgesic overuse	
Triptan overuse	≥10-days/month for >3-months
Ergotamine overuse	
Opioid overuse	≥10-days/month for >3-months
Combination-analgesic overuse	

Abbreviations: MOH: medication overuse headache; NSAID: nonsteroidal anti-inflammatory drug

Sidebar 6: Treatment Options for Migraine Headache[a, b]		
Type	**Treatment**	**Notes**
Pharmacotherapy – Preventive	AbobotulinumtoxinA and onabotulinumtoxinA↓	• Not FDA approved or effective for prevention of episodic migraine
	Candesartan or telmisartan↑↑	• Applies to episodic and chronic migraine
	Combination pharmacotherapy↔	• Evidence was very low quality for the use of combinations of more than one pharmacotherapeutic agent for prevention of migraine
	Erenumab, fremanezumab, or galcanezumab↑	• Applies to episodic and chronic migraine • FDA approved and effective for prevention of migraine
	Gabapentin↔	• Applies to episodic migraine • Not FDA approved or effective for prevention of migraine
	Lisinopril↑	• Applies to episodic migraine only
	Magnesium, oral↑	• Oral magnesium formulations varied in the evidence, including magnesium sulfate, magnesium 2-propyl valerate, and magnesium oxide
	Nimodipine or nifedipine↔	• Applies to episodic migraine only
	Nutraceuticals: CoQ10, feverfew, melatonin, omega-3, vitamin B2, vitamin B6↔	• Evidence suggests small but somewhat inconsistent benefits in reducing migraine frequency, which slightly outweighed potential harms, such as dose variability in supplements, and some specific harms, such as post-feverfew syndrome or vitamin B6 neurotoxicity in high, sustained doses
	OnabotulinumtoxinA↑	• Applies to chronic migraine only • FDA approved and effective for prevention of chronic migraine
	Propranolol↑	• FDA approved for prevention of migraine
	Topiramate↑	• Applies to episodic migraine only • FDA approved and effective for prevention of migraine
	Valproate↔	• Applies to episodic and chronic migraine • FDA approved and effective for prevention of migraine
Pharmacotherapy – Abortive	Frovatriptan or rizatriptan↑	• FDA approved and effective for treatment of migraine
	GON block↑	• Evidence suggests improvement of pain intensity
	Ibuprofen, naproxen, aspirin, or acetaminophen↑	• FDA approved and effective for treatment of migraine
	IV magnesium↑	• Evidence suggests pain reduction with minimal risks
	Sumatriptan, sumatriptan/naproxen, or zolmitriptan↑↑	• Sumatriptan alone and in combination with naproxen are FDA approved and effective for prevention of migraine • Zolmitriptan is FDA approved and effective for treatment of migraine
	Triptans↑	• Triptans alone and in combination with naproxen are FDA approved and effective for treatment of migraine

[a] For the full recommendation language, see Recommendations

[b] Sidebar 8 presents additional treatment options for general headache

Abbreviations: CoQ10: coenzyme Q10; FDA: U.S. Food and Drug Administration; GON: greater occipital nerve block; IV: intravenous

↑↑ Indicates a "Strong for" recommendation strength; ↑ indicates a "Weak for" recommendation strength; ↓ indicates a "Weak against" recommendation strength; ↔ indicates a "Neither for nor against" recommendation strength

Sidebar 7: Treatment Options for Cluster Headache[a, b]		
Type	**Treatment**	**Notes**
Non-pharmacologic Therapy – Abortive	Non-invasive vagus nerve stimulation↑	• For episodic cluster headache only
Pharmacotherapy – Prevention	Galcanezumab↑	• FDA approved and effective for episodic cluster headache only
	Lovastatin#	• For episodic and chronic cluster headache
	Pravastatin#	• For episodic and chronic cluster headache
Pharmacotherapy – Abortive	Oxygen therapy↔	• For episodic cluster headache only
	Pharmacotherapy for acute treatment↔	• Evidence is limited for specific pharmacotherapy for acute treatment of cluster headache
	Sumatriptan SQ (not oral)#	• For episodic and chronic cluster headache
	Zolmitriptan nasal spray#	• FDA approved and effective for episodic and chronic cluster headache

[a] For the full recommendation language, see Recommendations

[b] Sidebar 8 presents additional treatment options for general headache

Abbreviations: FDA: U.S. Food and Drug Administration; SQ: subcutaneous

↑ Indicates a "Weak for" recommendation strength; ↔ indicates a "Neither for nor against" recommendation strength;
# indicates the treatment was "Not reviewed" in the CPG's evidence review

Sidebar 8: Treatment Options for Headache in General[a]		
Type	**Treatment**	**Notes**
Non-pharmacologic Therapy	Acupuncture↔	• Evidence suggests small or inconsistent benefits for migraine and TTH in comparison to sham acupuncture • No statistically significant differences when compared to beta-blockers, valproic acid, or CCBs, which are also reviewed in this CPG
	Aerobic exercise/ progressive strength training↑	• Evidence suggests aerobic exercise and progressive strength training decreases headache frequency
	CBT or biofeedback↔	• Although CBT and biofeedback are commonly used, there was insufficient evidence in this CPG's systematic evidence review to support a recommendation
	Dietary trigger education↑	• While the evidence regarding dietary trigger avoidance is limited, it is reasonable to offer patient education regarding diet modification to decrease the frequency and/or severity of their migraine headache
	Dry needling↔	• Evidence of dry needling compared to no treatment was limited
	Elimination-based diet testing↔	• There was insufficient evidence in this CPG's systematic evidence review to support a recommendation
	Mindfulness-based therapy↑	• Improved outcomes of headache frequency and other potential benefits outweigh the harms with this relatively low-risk activity
	Neuromodulation↔	• There was insufficient evidence in this CPG's systematic evidence review to support a recommendation • Some patients experienced headache following treatment
	Pulsed radiofrequency or SPG↔	• There was insufficient evidence in this CPG's systematic evidence review to support a recommendation • Feasibility and acceptability limit these interventions
Pharmacotherapy – Preventive	Fluoxetine or venlafaxine↔	• There was insufficient evidence in this CPG's systematic evidence review to support a recommendation
Pharmacotherapy – Abortive	IV ketamine↓	• Further research should be conducted before administering to patients with headache
	IV metoclopramide, IV prochlorperazine, or intranasal lidocaine↔	• There was insufficient evidence in this CPG's systematic evidence review to support a recommendation

[a] For the full recommendation language, see Recommendations

Abbreviations: CBT: cognitive behavioral therapy; CCB: calcium channel blockers; CPG: Clinical Practice Guideline; IV: intravenous; SPG: sphenopalatine ganglion; TTH: tension-type headache

↑ Indicates a "Weak for" recommendation strength; ↓ indicates a "Weak against" recommendation strength; ↔ indicates a "Neither for nor against" recommendation strength

Pharmacotherapy

Table 1. Prevention Dosing Information

Type	Drug	Initial Dose	Usual Range	Comments
Beta-adrenergic antagonists	Atenolol (Tenormin®)	50 mg/day	50 – 200 mg/day	• Dose should be titrated and maintained for at least three months before assessment of response
	Metoprolol (Toprol®, Toprol XL®)	100 mg/day in divided doses	100 – 200 mg/day in divided doses	• Dose short-acting four times a day and long-acting two times a day • Available as extended release • Dose should be titrated and maintained for at least three months before assessment of response
	Nadolol (Corgard®)	40 – 80 mg/day	80 – 240 mg/day	• Dose should be titrated and maintained for at least three months before assessment of response
	Propranolol (Inderal®, Inderal® LA)	40 mg/day in divided doses	40 – 160 mg/day in divided doses	• Dose short-acting 2 – 3 times a day and long-acting 1 – 2 times a day • Available as extended release • Dose should be titrated and maintained for at least three months before assessment of response
	Timolol (Blocadren®)	20 mg/day in divided doses	20 – 60 mg/day in divided doses	• Dose should be titrated and maintained for at least three months before assessment of response
Antidepressants	Amitriptyline (Elavil™)	10 mg at bedtime	20 – 50 mg at bedtime	• Use slow titration to reduce sedation
	Venlafaxine (Effexor®, Effexor-XR®)	37.5 mg/day	75 – 150 mg/day	• Available as extended release • Increase dose after one week
Anticonvulsants	Topiramate (Topamax®)	25 mg/day	50 – 200 mg/day in divided doses	• As effective as amitriptyline, propranolol, or valproate • Increase by 25 mg/week
	Valproic acid/ divalproex sodium (Depakene®, Depakote®, Depakote ER®)	250 – 500 mg/ day in divided doses, or daily for extended release	500 – 1,500 mg/day in divided doses, or daily for extended release	• Monitor levels if compliance is an issue

Type	Drug	Initial Dose	Usual Range	Comments
Calcitonin Gene-related Peptide Inhibitors	Eptinezumab-jjmr (Vyepti™)	100 mg IV every 3 months	up to 300 mg IV every 3 months	• May contain polysorbate 80 (also known as Tweens), which can cause hypersensitivity reactions
	Erenumab-aooe (Aimovig®)	70 mg SQ monthly	70 – 140 mg SQ monthly	• May cause constipation, packaging may contain latex
	Fremanezumab-vfrm (Ajovy®)	225 mg SQ monthly	225 mg SQ monthly or 675 mg SQ every 3 months	• May contain polysorbate 80 (also known as Tweens), which can cause hypersensitivity reactions
	Galcanezumab-gnlm (Emgality®)	120 mg SQ monthly (migraine), 300 mg SQ (cluster)	Can use 240 mg loading dose for migraine, use in cluster should continue monthly until end of cluster period	• May contain polysorbate 80 (also known as Tweens), which can cause hypersensitivity reactions
Nonsteroidal Anti-inflammatory Drugs	Ibuprofen (Motrin®)	400 – 1,200 mg/ day in divided doses	Same as initial dose	• Use intermittently, such as for menstrual migraine prevention; daily or prolonged use may lead to medication overuse headache and is limited by potential toxicity
	Ketoprofen (Orudis®)	150 mg/day in divided doses	Same as initial dose	• Use intermittently, such as for menstrual migraine prevention; daily or prolonged use may lead to medication overuse headache and is limited by potential toxicity
	Naproxen sodium (Aleve®, Anaprox®)	550 – 1,100 mg/ day in divided doses	Same as initial dose	• Use intermittently, such as for menstrual migraine prevention; daily or prolonged use may lead to medication overuse headache and is limited by potential toxicity
Triptans	Frovatriptan (Frova®)	2.5 mg/day or 5 mg/day in divided doses	Same as initial dose	• Taken in the perimenstrual period to prevent menstrual migraine
	Naratriptan (Amerge®)	2 mg/day in divided doses	Same as initial dose	• Taken in the perimenstrual period to prevent menstrual migraine
	Zolmitriptan (Zomig®)	5 – 7.5 mg/day in divided doses	Same as initial dose	• Taken in the perimenstrual period to prevent menstrual migraine
Miscellaneous	Histamine (Histatrol®)	1 – 10 mg two times/week	Same as initial dose	• May cause transient itching and burning at injection site
	Magnesium	400 mg/day	800 mg/day in divided doses	• May be more helpful in migraine with aura and menstrual migraine
	MIG-99 (feverfew)	10 – 100 mg/day in divided doses	Same as initial dose	• Withdrawal may be associated with increased headaches
	Petasites	100 – 150 mg/ day in divided doses	150 mg/day in divided doses	• Use only commercial preparations, plant is carcinogenic
	Riboflavin	400 mg/day in divided doses	400 mg/day in divided doses	• Benefit only after 3 months

Abbreviations: ER: extended release; LA: long acting; mg: milligrams; SQ: subcutaneously; XL: extended release; XR: extended release

Table 2. Abortive Dosing Information

Type	Drug	Dose	Comments
Analgesics	Acetaminophen (Tylenol®)	1,000 mg at onset; repeat every 4 – 6 hours as needed	• Maximum daily dose is 4 g
	Acetaminophen 250 mg/ aspirin 250 mg/caffeine 65 mg (Excedrin® Migraine)	2 tablets at onset and every 6-hours	• Available OTC as Excedrin® Migraine
Nonsteroidal Anti-inflammatory Drugs	Aspirin	500 – 1,000 mg every 4 – 6 hours	• Maximum daily dose is 4 g
	Diclofenac (Cataflam®, Voltaren®)	50 – 100 mg at onset; can repeat 50 mg in 8-hours	• Avoid doses >150 mg/day
	Ibuprofen (Motrin®)	200 – 800 mg every 6-hours	• Avoid doses >2.4 g/day
	Naproxen sodium (Aleve®, Anaprox®)	550 – 825 mg at onset; can repeat 220 mg in 3 – 4 hours	• Avoid doses >1.375 g/day
Ergotamine Tartrate	Oral tablet (1 mg) with caffeine 100 mg (Cafergot®)	2 mg at onset; then 1 – 2 mg every 30-minutes as needed	• Maximum dose is 6 mg/day or 10 mg/ week • Consider pretreatment with an antiemetic
	Sublingual tablet (2 mg) (Ergomar®)	2 mg SL at the first sign of an attack. Then, 2 mg SL after 30 minutes if needed. If the additional dose is well tolerated, the initial dose may be increased at the next attack, up to a maximum initial dose of 4 mg ergotamine.	• Do not exceed 3 tablets (6 mg ergotamine)/24-hours per any 1 attack
	Rectal suppository (2 mg) with caffeine 100 mg (Cafergot®, Migergot®)	Insert 1/2 to 1 suppository at onset; repeat after 1-hour as needed	• Maximum dose is 4 mg/day or 10 mg/ week • Consider pretreatment with an antiemetic
Dihydroergotamine	Injection 1 mg/mL (D.H.E. 45®)	0.25 – 1 mg at onset IM, IV, or subcutaneous; repeat every hour as needed	• Maximum dose is 3 mg/day or 6 mg/ week
	Nasal spray 4 mg/mL (Migranal®)	One spray (0.5 mg) in each nostril at onset; repeat sequence 15-minutes later (total dose is 2 mg or four sprays)	• Maximum dose is 3 mg/day • Prime sprayer four times before using • Do not tilt head back or inhale through nose while spraying • Discard open ampules after 8-hours
Triptans	Zolmitriptan (Zomig®)	5 – 7.5 mg/day in divided doses Same as initial dose	• Taken in the perimenstrual period to prevent menstrual migraine
	Almotriptan (Axert®)	6.25 or 12.5 mg at onset; can repeat after 2-hours if needed	• Optimal dose is 12.5 mg • Maximum daily dose is 25 mg
	Eletriptan (Relpax®)	20 or 40 mg at onset; can repeat after 2-hours if needed	• Maximum single dose is 40 mg • Maximum daily dose is 80 mg

Type	Drug	Dose	Comments
Triptans (cont.)	Frovatriptan (Frova®)	2.5 or 5 mg at onset; can repeat in 2-hours if needed	• Optimal dose 2.5 – 5 mg • Maximum daily dose is 7.5 mg (three tablets)
	Sumatriptan (Imitrex®) injection	6 mg subcutaneous at onset; can repeat after 1-hour if needed	• Maximum daily dose is 12 mg
	Naratriptan (Amerge®)	1 or 2.5 mg at onset; can repeat after 4-hours if needed	• Optimal dose is 2.5 mg • Maximum daily dose is 5 mg
	Zolmitriptan nasal spray	5 mg (one spray) at onset; can repeat after 2-hours if needed	• Maximum daily dose is 10 mg/day
	Sumatriptan nasal spray	5, 10, or 20 mg at onset; can repeat after 2-hours if needed	• Optimal dose is 20 mg • Maximum daily dose is 40 mg • Single-dose device delivering 5 or 20 mg • Administer one spray in one nostril
	Zolmitriptan oral tablets	2.5 or 5 mg at onset as regular or orally disintegrating tablet; can repeat after 2-hours if needed	• Optimal dose is 2.5 mg • Maximum dose is 10 mg/day
	Sumatriptan oral tablets	25, 50, 85, or 100 mg at onset; can repeat after 2-hours if needed	• Optimal dose is 50 – 100 mg • Maximum daily dose is 200 mg • Combination product with naproxen, 85 mg/500 mg
	Rizatriptan (Maxalt®, Maxalt-MLT®)	5 or 10 mg at onset as regular or orally disintegrating tablet; can repeat after 2-hours if needed	• Optimal dose is 10 mg • Maximum daily dose is 30 mg • Onset of effect is similar with standard and orally disintegrating tablets • Use 5 mg dose (15 mg/day maximum) in patients receiving propranolol
Calcitonin Gene Related Peptides Inhibitors	Rimegepant (Nurtec™)	75 mg orally disintegrating tablet	• 75 mg per day, doses should not be more frequent than ≥48-hours • Avoid strong CYP3A4 inhibitors, strong or moderate CYP3A4 inducers, p-glycoprotein inhibitors
	Ubrogepant (Ubrelvy®)	50 – 100 mg as a single dose, may repeat in ≥2-hours	• Up to 200 mg/24-hours, contraindicated with CYP3A4 inhibitors, dose adjustment in moderate renal impairment and severe (Child Pugh Class C) hepatic impairment
Selective Serotonin 1F Receptor Agonist	Lasmidtan (Reyvow™)	50 mg, maximum of one dose per 24-hours	• 50 – 200 mg per 24-hours as a single dose • Is a Schedule V drug, may not drive for 8-hours after dose

Type	Drug	Dose	Comments
Miscellaneous	Metoclopramide (Reglan®)	10 mg IV at onset	• Useful for acute relief in the office or ED setting
	Prochlorperazine (Compazine®)	10 mg IV or IM at onset	• Useful for acute relief in the office or ED setting

Abbreviations: CYP3A4: cytochrome P450 3A4; D.H.E.: dihydroergotamine; ED: emergency department; IM: intramuscular; IV: intravenous; mg: milligrams; mL: milliliters; OTC: over-the-counter

Scope of the CPG

Regardless of setting, any patient in the VA and DoD healthcare system should ideally have access to the interventions that are recommended in this guideline after taking into consideration the patient's specific circumstances.

Guideline recommendations are intended to be patient centered. Thus, treatment and care should consider a patient's needs and preferences. Effective, open communication between healthcare professionals and the patient is essential and should be supported by evidence-based information tailored to the patient's needs. Use of an empathetic and non-judgmental approach facilitates discussions sensitive to gender, culture, ethnic, and other considerations. The information that patients are given about treatment and care should be culturally appropriate and available to people with limited literacy skills. Treatment information should also be accessible to people with additional needs such as physical, sensory, or learning disabilities. Family and caregiver involvement should be considered, if appropriate.

This CPG is designed to assist providers in managing or co-managing patients with headache. Moreover, the patient population of interest for this CPG is patients with headache who are eligible for care in the VA and DoD healthcare delivery systems and those who are in the community receiving care from community-based clinicians. It includes Veterans as well as deployed and non-deployed active duty Service, Guard, and Reserve Members and their dependents.

Methods

The methodology used in developing the 2020 CPG follows the *Guideline for Guidelines*, an internal document of the VA and DoD EBPWG.[8] The *Guideline for Guidelines* can be downloaded from http://www.healthquality.va.gov/policy/index.asp. The guideline development process for the 2020 CPG consisted of the following steps: formulating and prioritizing evidence (KQs); convening patient focus groups; conducting the systematic review; convening a face-to-face meeting with the CPG Champions and Work Group members; and drafting and submitting a final CPG on the primary care management of headache to the VA/DoD EBPWG.

The Champions and Work Group used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) system to assess the quality of the evidence base and assign a grade for the strength for each recommendation. The GRADE system uses the following four domains to assess the strength of each recommendation: balance of desirable and undesirable outcomes; confidence in the quality of the evidence; patient or provider values and preferences; other implications, as appropriate (e.g., resource use, equity).[9] Using this system, the Champions and Work Group determined the relative strength of

each recommendation (strong or weak). A strong recommendation indicates that the Work Group is highly confident that the desirable effects of an intervention outweigh undesirable effects. If the Work Group is less confident that the desirable effects of an intervention outweigh undesirable effects, they give a weak recommendation. It is important to note that the GRADE terminology used to indicate the confidence in the desirable effects of an intervention (i.e., strong versus weak) should not be confused with the clinical importance of the recommendation. A weak recommendation may be just as important to the clinical care of a patient as a strong recommendation.

Occasionally, instances may occur when the Work Group feels there is insufficient evidence to make a recommendation for or against a particular therapy or preventive measure. This can occur when there is an absence of studies on a particular topic that met evidence review inclusion criteria, studies included in the evidence review report conflicting results, or studies included in the evidence review report inconclusive results regarding the desirable and undesirable outcomes.

Using these elements, the grade of each recommendation is presented as part of a continuum:

- Strong for (or "We recommend this option …")
- Weak for (or "We suggest this option …")
- No recommendation for or against (or "There is insufficient evidence …")
- Weak against (or "We suggest against this option …")
- Strong against (or "We recommend against this option …")

The grade of each recommendation made in the 2020 CPG can be found in the section on Recommendations. Additional information regarding the use of the GRADE system can be found in Appendix B in the full text Headache CPG.

The Work Group developed both new and updated recommendations based on the evidence review conducted for the priority areas addressed by the KQs. A set of recommendation categories was adapted from those used by the National Institute for Health and Care Excellence (NICE).[10,11] The categories and definitions can be found in Table 3.

Table 3. Recommendation Categories and Definitions*

Evidence Reviewed*	Recommendation Category	Definition
Reviewed	New-added	New recommendation following review of the evidence
	New-replaced	Recommendation from previous CPG that has been carried over to the updated CPG that has been changed following review of the evidence
	Not changed	Recommendation from previous CPG that has been carried forward to the updated CPG where the evidence has been reviewed but the recommendation is not changed
	Amended	Recommendation from previous CPG that has been carried forward to the updated CPG where the evidence has been reviewed and a minor amendment has been made
	Deleted	Recommendation from previous CPG that has been removed based on review of the evidence

Evidence Reviewed*	Recommendation Category	Definition
Not reviewed	Not changed	Recommendation from previous CPG that has been carried forward to the updated CPG, but for which the evidence has not been reviewed
	Amended	Recommendation from previous CPG that has been carried forward to the updated CPG where the evidence has not been reviewed and a minor amendment has been made
	Deleted	Recommendation from previous CPG that has been removed because it was deemed out of scope for the updated CPG

* Adapted from the NICE guideline manual (2012) [10] and Garcia et al. (2014) [11]

Abbreviation: CPG: Clinical Practice Guideline

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Patient-centered Care

VA/DoD CPGs encourage clinicians to use a patient- (and family-) centered care (PCC) approach that is individualized based on patient needs, characteristics, and preferences. Regardless of setting, all patients in the healthcare system should be able to access evidence-based care appropriate to that patient. When properly executed, PCC may decrease patient anxiety, increase trust in clinicians, and improve treatment adherence.[12,13] Improved patient-clinician communication and a PCC approach conveys openness and supports disclosure of current and future concerns.

As part of the PCC approach, clinicians should engage patients in shared decision making (SDM) to review the outcomes of previous healthcare experiences with the patients who are living with headache. They should ask each patient about any concerns he or she has or barriers to high quality care he or she might experience. Lastly, they should educate the patient on the actions that need to be taken and any decisions that need to be made and should involve the individual in decision making regarding management of headache.

Shared Decision Making

Throughout the VA/DoD CPG, the authors encourage clinicians to focus on SDM. The SDM model was introduced in *Crossing the Quality Chasm,* an Institute of Medicine (IOM) (now called the National Academy of Medicine [NAM]) report, in 2001.[14] It is readily apparent that patients, together with their clinicians, make decisions regarding their plan of care and management options. Clinicians must be adept at presenting information to their patients regarding individual treatments, expected outcomes, and levels and/or locations of care. Clinicians are encouraged to use SDM to individualize treatment goals and plans based on patient capabilities, needs, goals, and preferences.

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Access to the full guideline and additional resources are available at the following link:
https://www.healthquality.va.gov/guidelines/Pain/headache/