


**Speaker Name**

Title

Affiliation

City, State

#HeadacheEdu

AMERICAN HEADACHE SOCIETY




# Grand Rounds in Headache Medicine

## Program Date

#HeadacheEdu

AMERICAN HEADACHE SOCIETY

The **Resident Education for the Assessment and Care of Headache** program is supported by an unrestricted educational grant from Eli Lilly to the American Headache Society®.

Additional support has been provided by Miles for Migraine.

# Disclosure Statement

Insert COIs

# REACH Curriculum Developers

| | |
|---|---|
| **Course Co-Directors** | |
| Rashmi Halker Singh, MD, FAHS | Mayo Clinic, Arizona |
| Matthew Robbins, MD, FAHS | Weill Cornell Medicine |
| Noah Rosen, MD, FAHS | Zucker School of Medicine at Northwell Health |
| **REACH Program Committee** | |
| Jessica Ailani, MD, FAHS | Georgetown University Hospital |
| Cynthia Armand, MD | Albert Einstein College of Medicine |
| Rebecca Burch, MD, FAHS | University of Vermont |
| Antonia Teruel Castellon, DMD, MS, PhD | Head Pain Institute Scottsdale |
| Andrew Charles, MD, FAHS | University of California Los Angeles |
| María F. Hernández Nuño de la Rosa, DDS, MS | Harvard School of Dental Medicine |
| Morris Levin, MD, FAHS | UCSF Headache Center |
| Stephanie Nahas, MD, FAHS | Thomas Jefferson University |
| Marcela Romero Reyes DDS, PhD, FAHS | University of Maryland School of Dentistry |
| Lauren Strauss, DO, FAHS | Wake Forest Baptist Health Center |
| Stewart Tepper, MD, FAHS | Geisel School of Medicine at Dartmouth |
| Juliana VanderPluym, MD, FAHS | Mayo Clinic Phoenix |
| David Watson, MD, FAHS | West Virginia University School of Medicine |
| Niushen Zhang, MD | Stanford University |
| **For the AHS** | |
| Hayley Swiderski (Executive/Program Management) | |
| Christopher Caiazza (Content Development/Presentation Design) | |

# Learning Objectives

At the conclusion of this program, participants should be able to:

- Discuss the many rewards of the practice of Headache Medicine
- Appraise the impact of migraine on the population and individual levels, including those more vulnerable
- Identify key brain structures and pain generators involved in primary and common secondary headache conditions
- Accurately diagnose patients presenting with head pain
- Personalize treatment plans using evidence-based therapies
- Describe several advocacy initiatives in Headache Medicine

# Overview

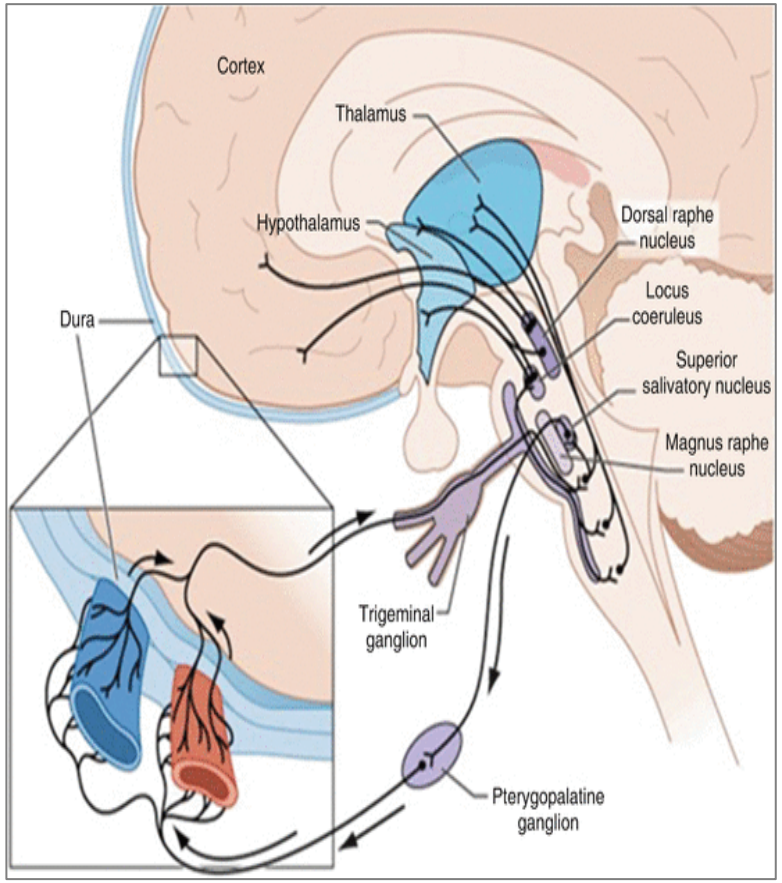
- Headache Medicine: A Rewarding Career
- Anatomy and Pathophysiology
- Diagnosis
- Treatment
- Advocacy

# Overview

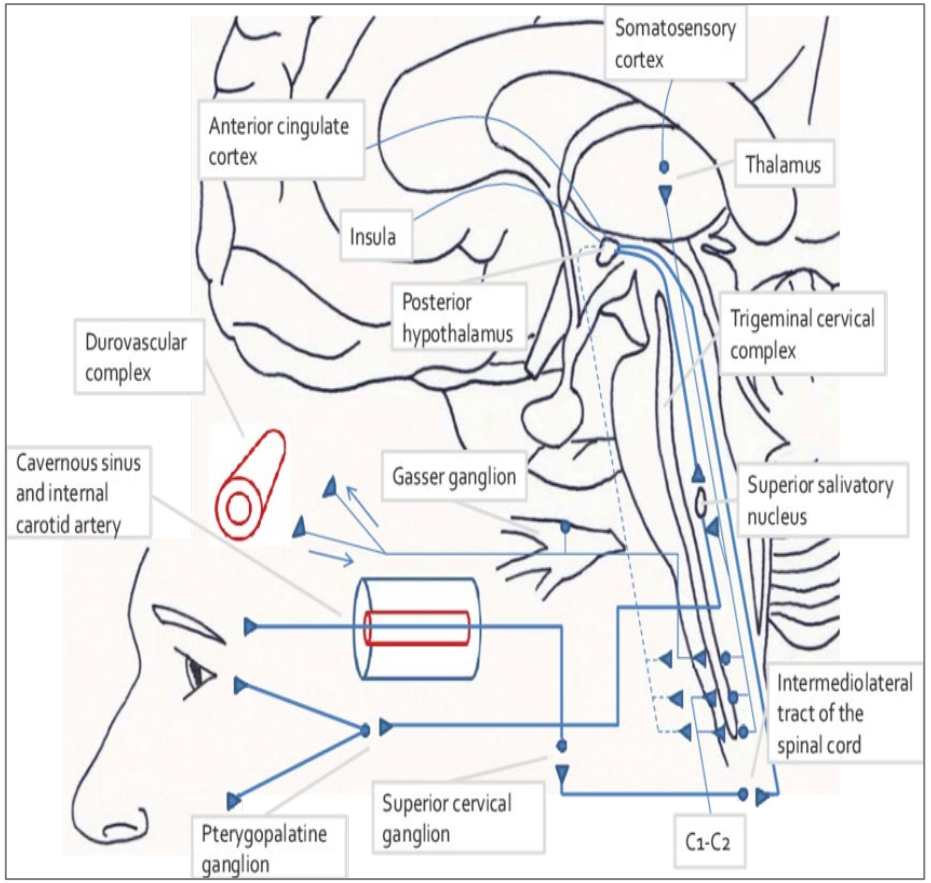
- **Headache Medicine: A Rewarding Career**
- Anatomy and Pathophysiology
- Diagnosis
- Treatment
- Advocacy

# Stay Current With Advanced Brain Science

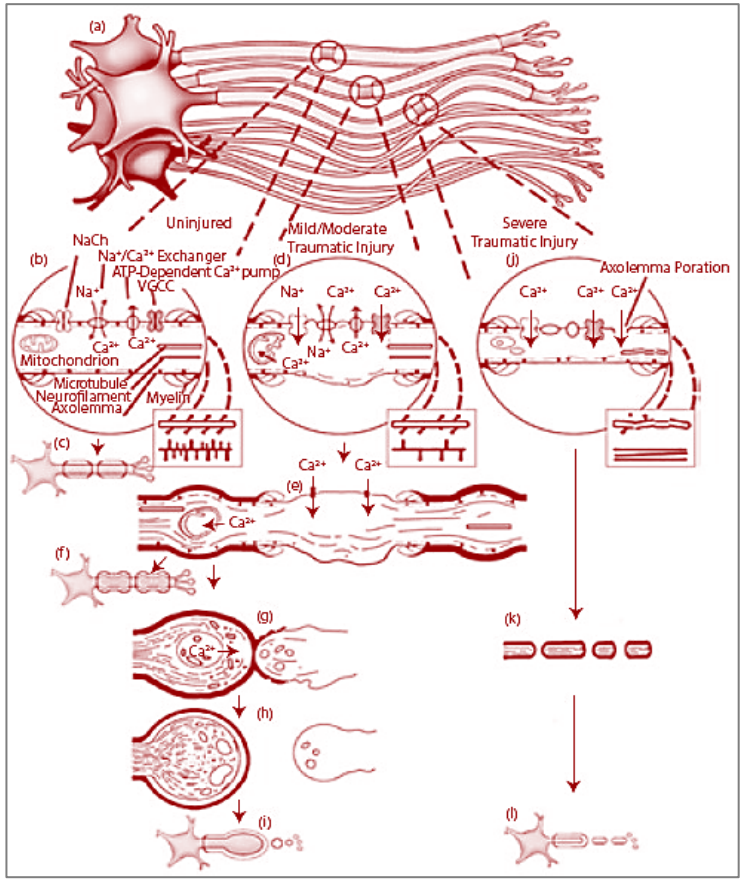
## Migraine



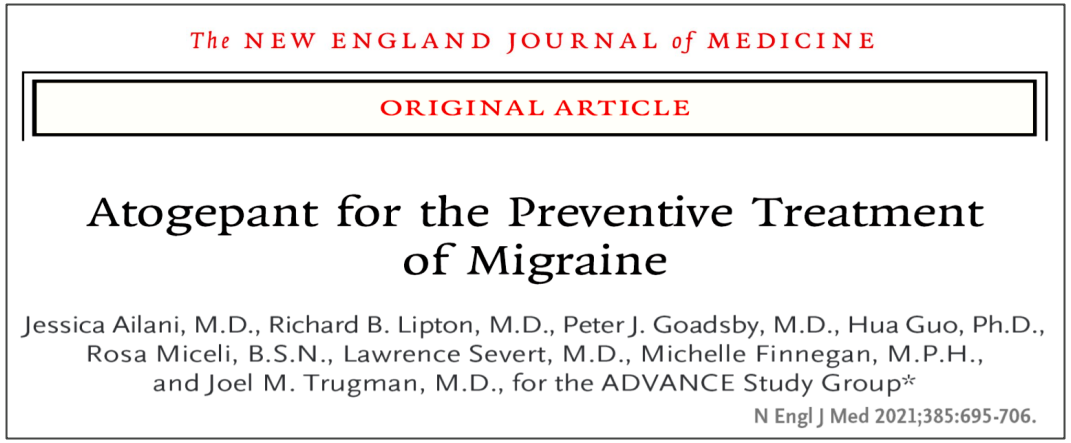

## Trigeminal Autonomic Cephalalgias




## Traumatic Brain Injury



# Conduct Groundbreaking Research



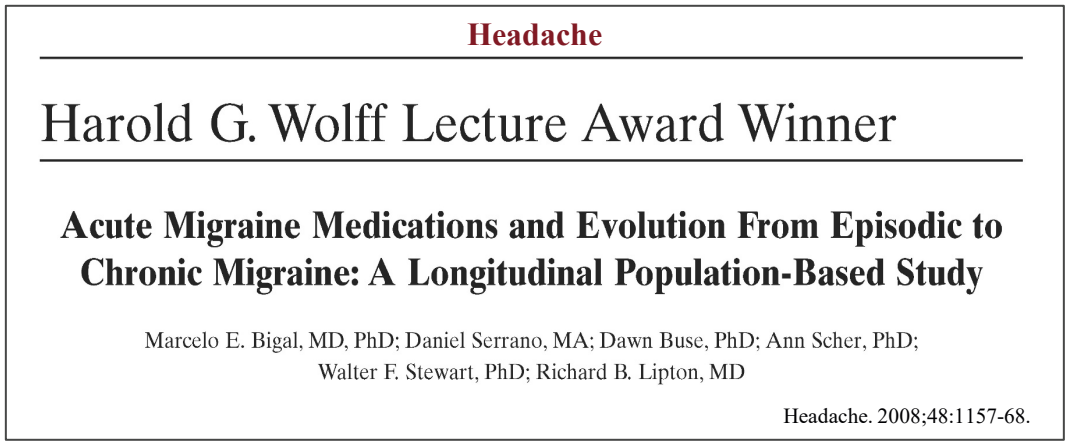
The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Atogepant for the Preventive Treatment of Migraine

Jessica Ailani, M.D., Richard B. Lipton, M.D., Peter J. Goadsby, M.D., Hua Guo, Ph.D., Rosa Miceli, B.S.N., Lawrence Severt, M.D., Michelle Finnegan, M.P.H., and Joel M. Trugman, M.D., for the ADVANCE Study Group*

N Engl J Med 2021;385:695-706.



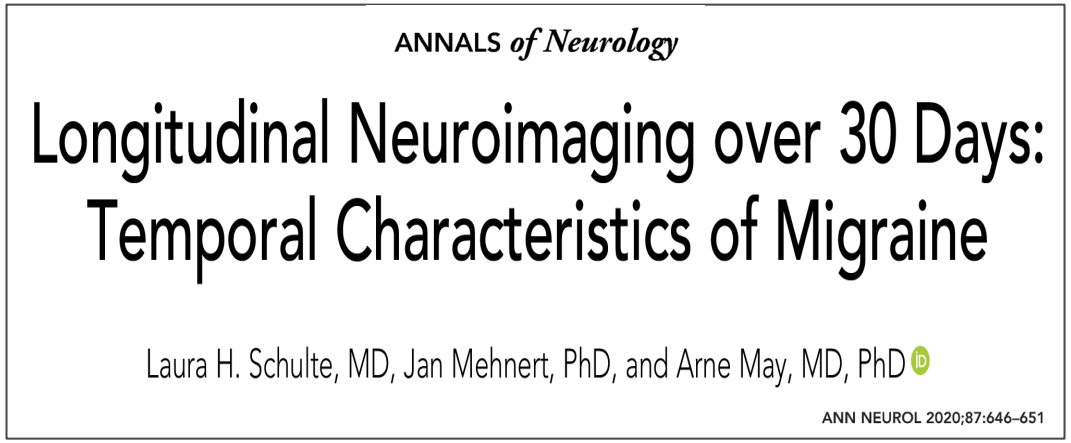
Headache

Harold G. Wolff Lecture Award Winner

## Acute Migraine Medications and Evolution From Episodic to Chronic Migraine: A Longitudinal Population-Based Study

Marcelo E. Bigal, MD, PhD; Daniel Serrano, MA; Dawn Buse, PhD; Ann Scher, PhD; Walter F. Stewart, PhD; Richard B. Lipton, MD

Headache. 2008;48:1157-68.

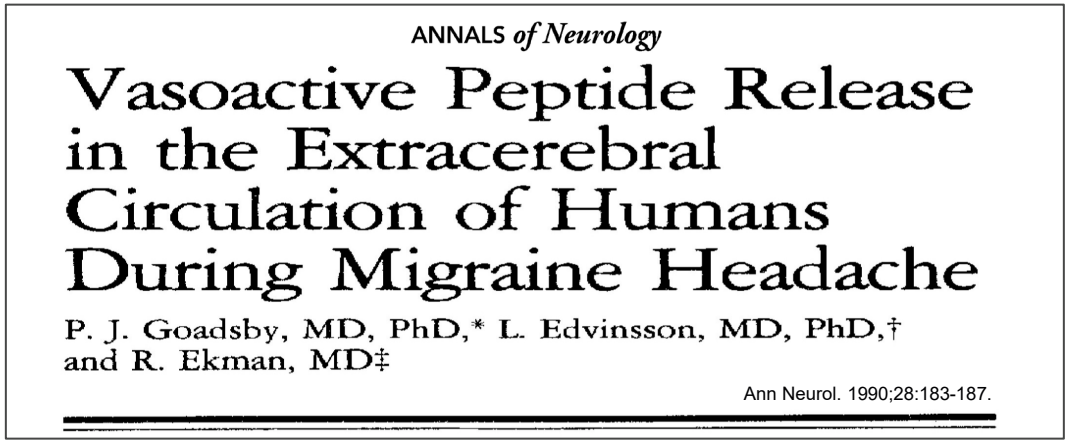


ANNALS *of Neurology*

## Longitudinal Neuroimaging over 30 Days: Temporal Characteristics of Migraine

Laura H. Schulte, MD, Jan Mehnert, PhD, and Arne May, MD, PhD

ANN NEUROL 2020;87:646–651



ANNALS *of Neurology*

## Vasoactive Peptide Release in the Extracerebral Circulation of Humans During Migraine Headache

P. J. Goadsby, MD, PhD,* L. Edvinsson, MD, PhD,† and R. Ekman, MD‡

Ann Neurol. 1990;28:183-187.

# Use New, Emerging, and Hands-on Treatments



CGRP-targeting therapies




Neuromodulation



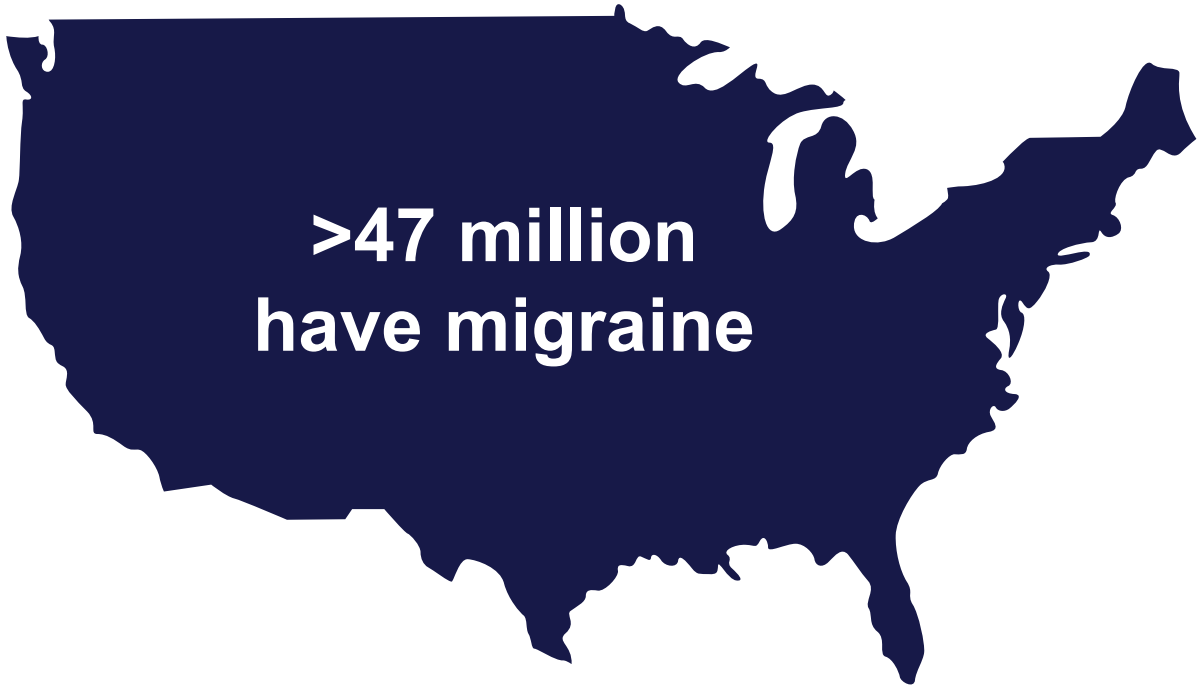
OnabotulinumtoxinA

Image courtesy of The Johns Hopkins University, The Johns Hopkins Hospital, and Johns Hopkins Health System.

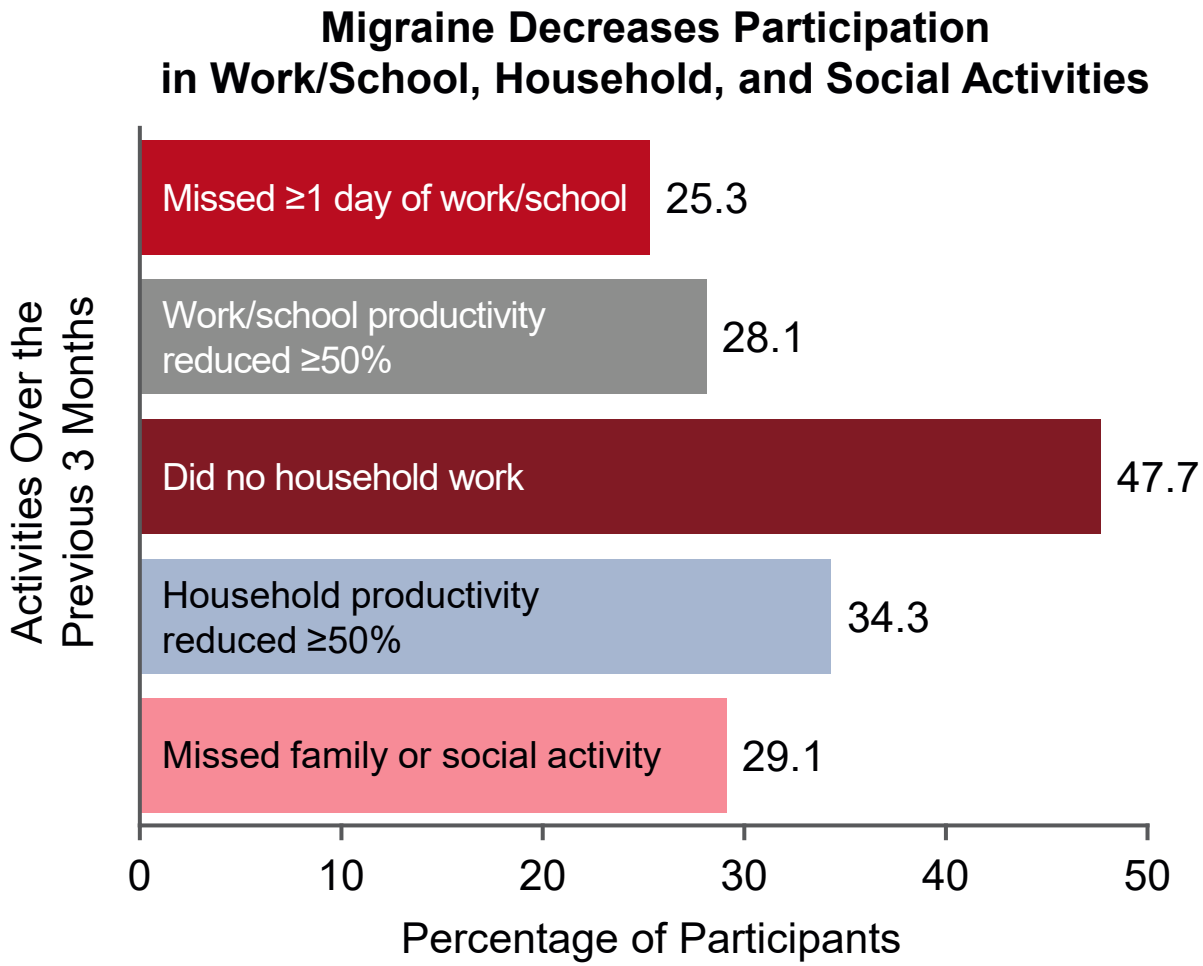
#HeadacheEdu

*Pain Med*. 2015;16:1827-1834; *Curr Pain Headache Rep. 2021;*25:71.

# Treat Highly Prevalent and Disabling Conditions




Most people (54%) have severe impairment



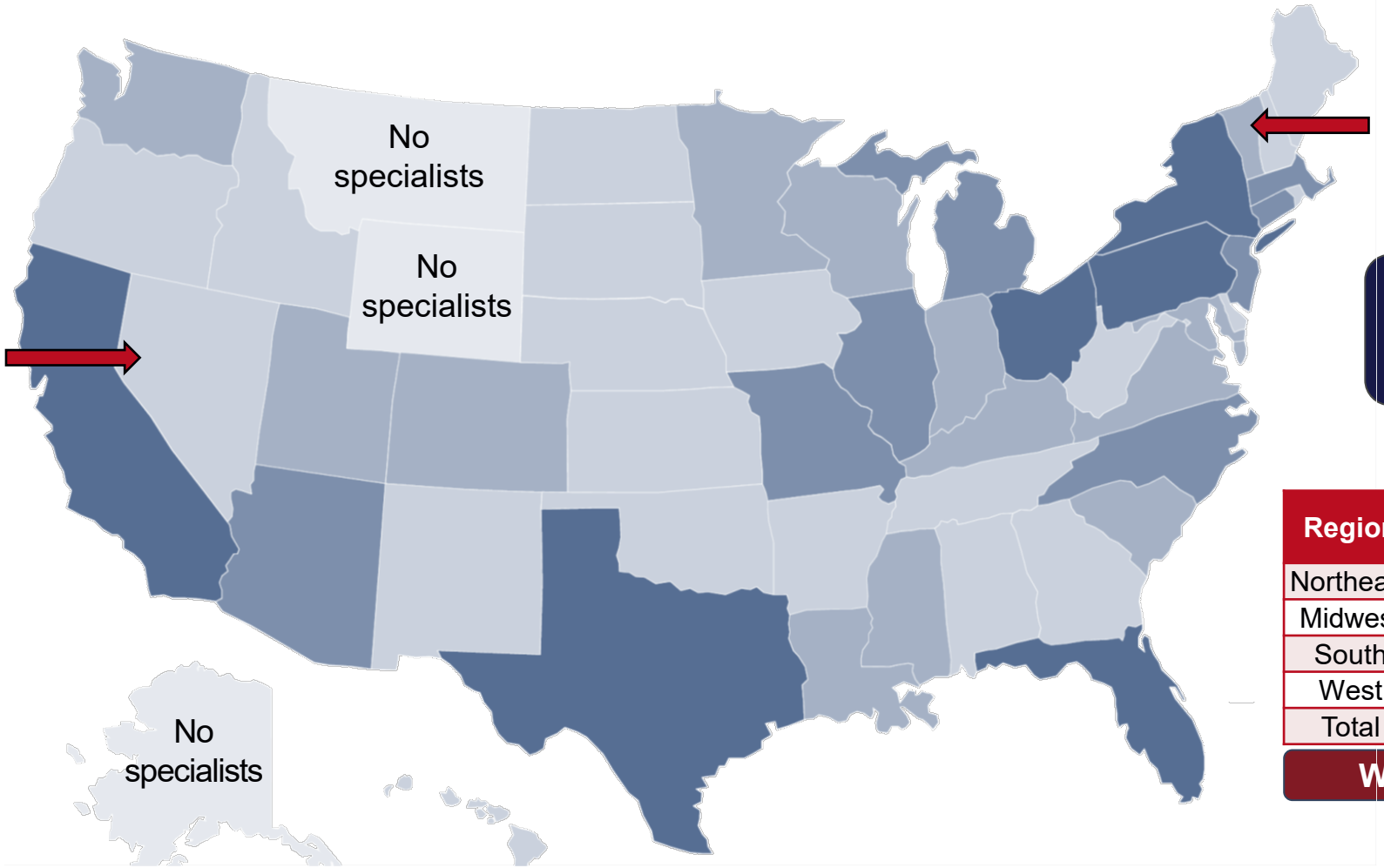

#HeadacheEdu

*Lancet Neurol*. 2018;17:954-976; *Neurology*. 2007;68:343-349.

AMERICAN HEADACHE SOCIETY

# Help Underserved US Patient Populations

**Ratio of US Headache Specialists to Adults with Migraine = 1:59,000**




**Nevada**
1:401,000

**Vermont**
1:13,000

**Wide Range of Specialists**
California, New York = 64
Alaska, Montana, Wyoming = 0

| Region | Specialists | Migraine Population | Specialist Ratio |
|---|---|---|---|
| Northeast | 186 | 6,450,129 | 34,678 |
| Midwest | 165 | 9,075,768 | 55,005 |
| South | 208 | 15,556,189 | 74,789 |
| West | 133 | 10,013,856 | 75,292 |
| Total | 692 | 41,095,943 | 59,387 |

**West and South >2x Northeast**

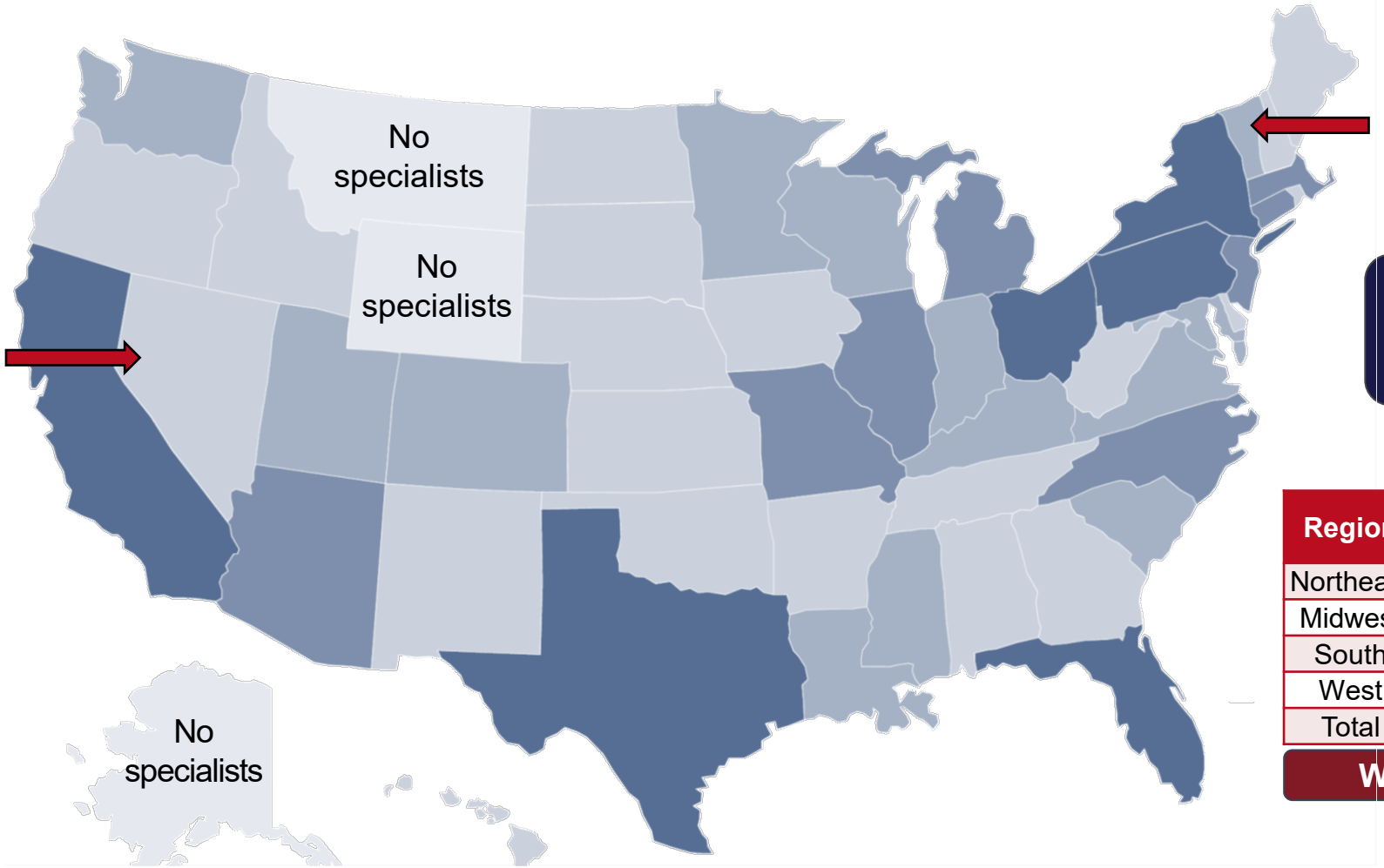
#HeadacheEdu

*Headache.* 2022;00:1-15.

AMERICAN HEADACHE SOCIETY

# Help Underserved US Patient Populations

**Ratio of US Headache Specialists to Adults with Migraine = 1:59,000**




**Nevada**
1:401,000

**Vermont**
1:13,000

**Wide Range of Specialists**
California, New York = 64
Alaska, Montana, Wyoming = 0

| Region | Specialists | Migraine Population | Specialist Ratio |
|---|---|---|---|
| Northeast | 186 | 6,450,129 | 34,678 |
| Midwest | 165 | 9,075,768 | 55,005 |
| South | 208 | 15,556,189 | 74,789 |
| West | 133 | 10,013,856 | 75,292 |
| Total | 692 | 41,095,943 | 59,387 |

**West and South >2x Northeast**

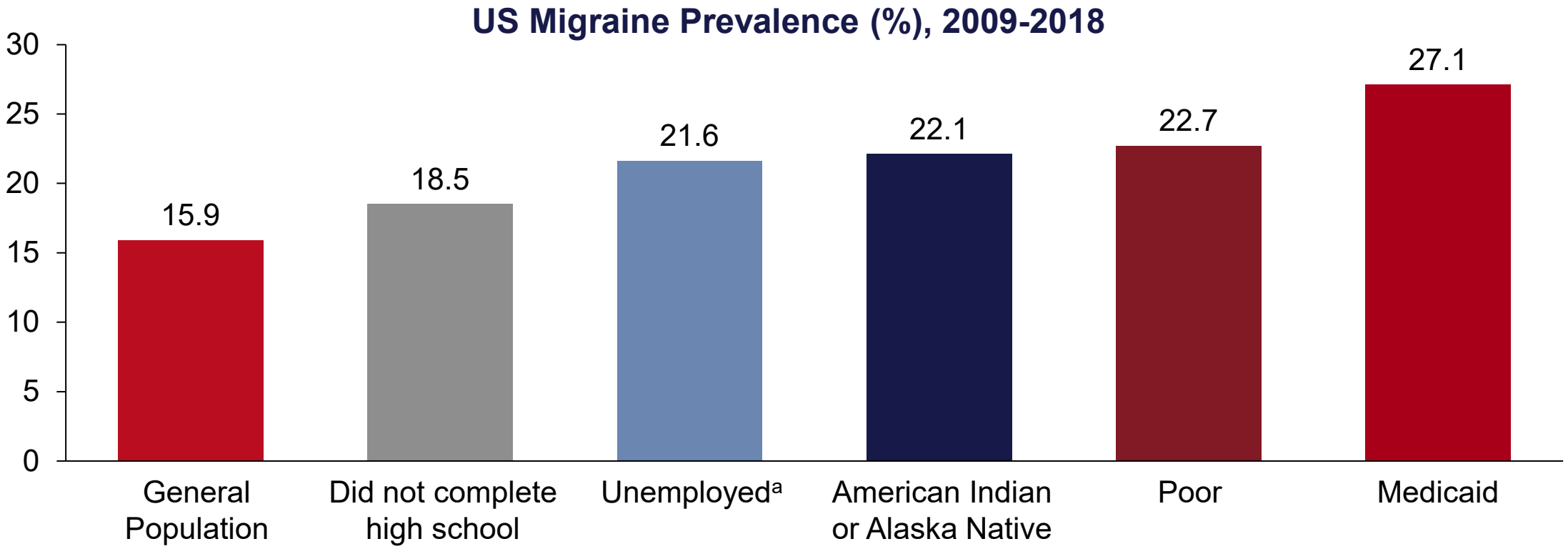
#HeadacheEdu

*Headache.* 2022;00:1-15.

AMERICAN HEADACHE SOCIETY

# Address Disparities Where Risk is Highest

Risk of migraine is elevated among members of socially, economically, and educationally disadvantaged groups




[a]Only previously employed individuals



*Headache.* 2021;61:60-68.

# Assist Underserved Communities Worldwide

**Migraine affects 1.1 billion people — mostly women aged 25 to 44**



- **Asia Oceania** — scarcity of clinical guidelines, subspecialty training, dedicated headache clinics
- **Africa** — mainly affects working-age adults. . .disability has wider socioeconomic implications
- **Latin America** — significant burden due to high disability and resource use coupled with inadequate treatment practice
- **United States** — highest burden among individuals from historically disadvantaged groups

#HeadacheEdu

*Cephalalgia*. 2021;41:1348-1358; *J Neurol Sci*. 2014;342:1-15; *Value Health Reg Issues*. 2019;S62;562 (PND17).

AMERICAN HEADACHE SOCIETY

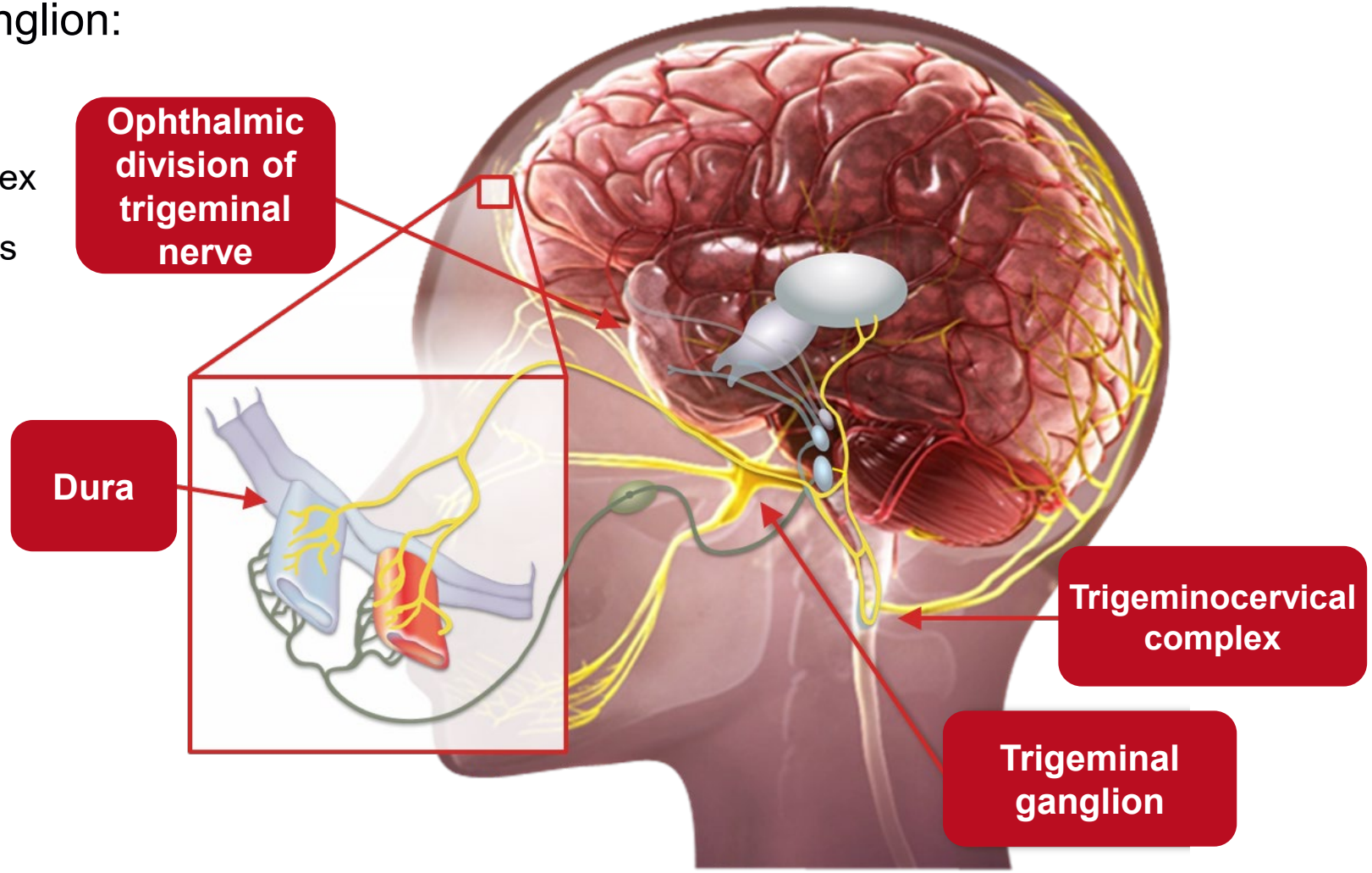
# Overview

- Headache Medicine: A Rewarding Career
- **Anatomy and Pathophysiology**
- Diagnosis
- Treatment
- Advocacy

# The Trigeminovascular System Plays a Key Role in Migraine

- Projections from the trigeminal ganglion:
  - Innervate the meninges and intracranial arteries
  - Converge in the trigeminocervical complex
  - Release neurotransmitters/neuropeptides (eg, calcitonin gene-related peptide)

- The trigeminocervical complex
  - Located in brain stem and upper cervical spinal cord
  - Connected to key brain centers
  - Activation crucial for migraine headache

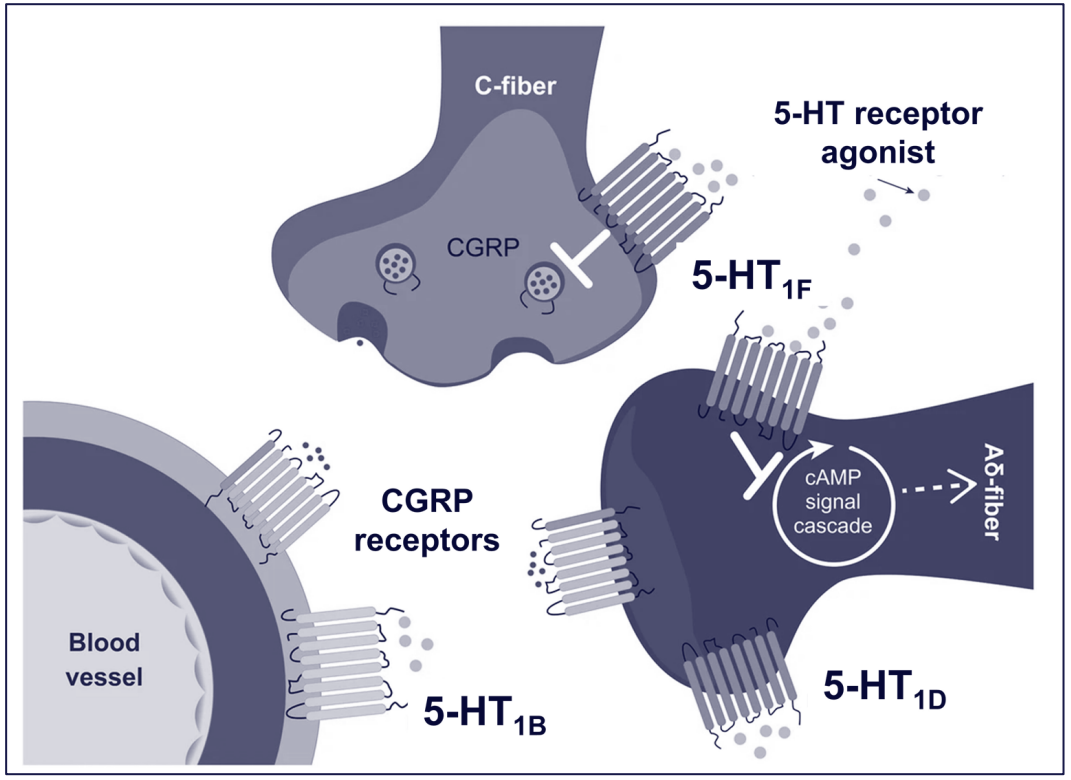





*Physiol Revs*. 2017;97:553-622

# Serotonin Receptors: Targets for Acute Migraine Treatment

| Receptor | Location | Primary Activity |
|---|---|---|
| 5-$HT_{1D}$/5-$HT_{1F}$ | Trigeminal terminals | Inhibit release of CGRP |
| 5-$HT_{1B}$ | Blood vessels | Vasoconstrictor |
| 5-$HT_{1F}$ | Central nervous system | Inhibit release of serotonin, norepinephrine, acetylcholine |




#HeadacheEdu

*Cent Nerv Syst Agents Med Chem*. 2012;12:241-9; *J Headache Pain*. 2020;21:71.

# Neuropeptides in Migraine

Numerous Distinct Molecules Identified

| Neuropeptide Gene Family | Candidate in Migraine |
|---|---|
| CGRP | CGRP |
| Glucagon/secretin | PACAP |
| F- and Y-amides | Neuropeptide Y |
| Tachykinins | Substance P |
| Tensins | Angiotensin |
| Corticotropin-releasing hormone-related | CRH |
| Adipose neuropeptides | Adiponectin |
| Orexin | Orexin receptor 1 (OXR1)<br>Orexin receptor 2 (OXR2) |

CGRP, calcitonin gene-related peptide; PACAP, pituitary adenylate cyclase-activating polypeptide

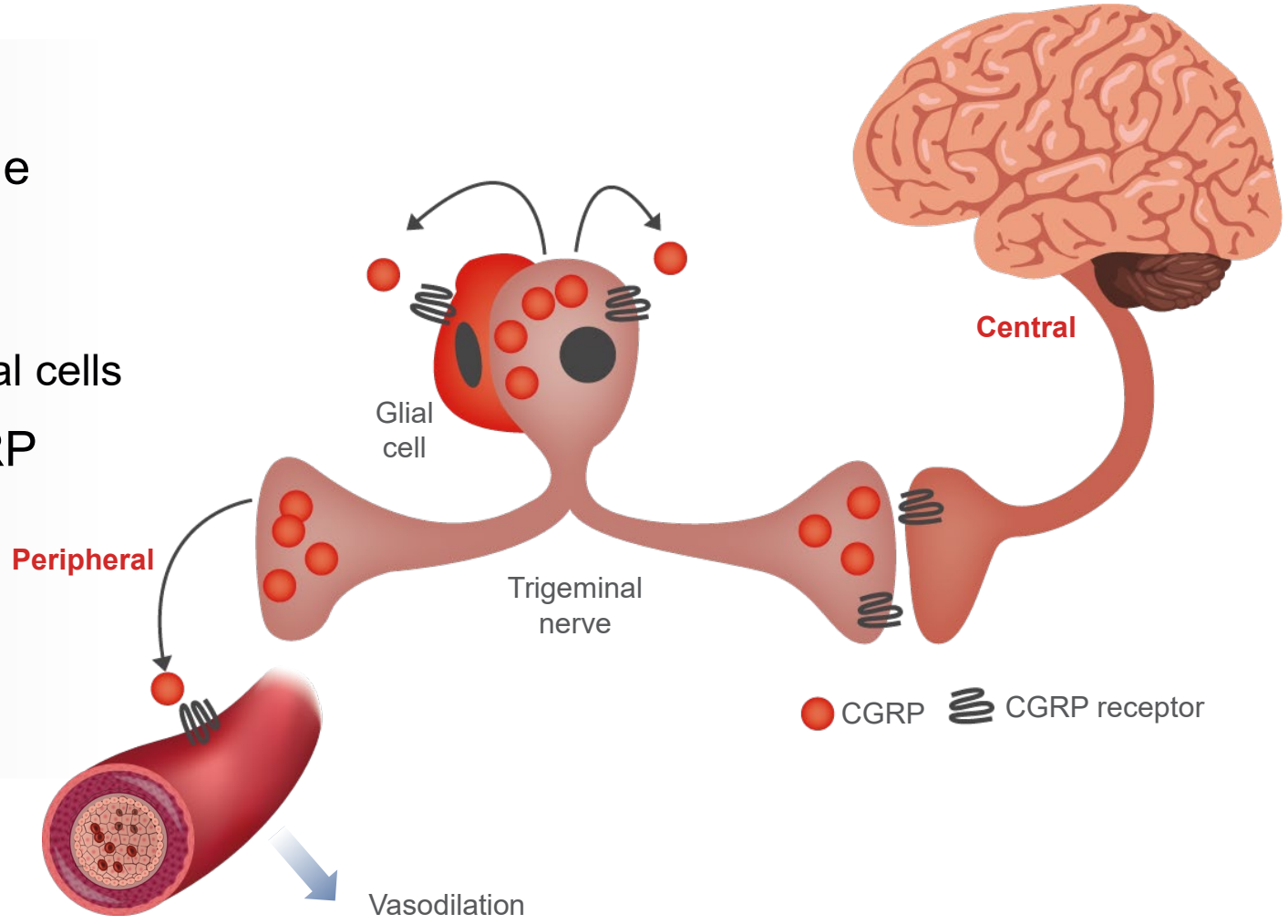


*Headache*. 2017;57:37-46.

# Role of CGRP in Migraine

- Widely expressed in CNS and PNS; expressed in 35–50% of neurons in the trigeminal ganglia
  - CGRP in C fibers
  - CGRP receptor in in Aδ fibers and glial cells
- Trigeminal system activated and CGRP released during migraine headache
- CGRP plays a role in vasodilation, inflammation, pain, and central activation of the brain

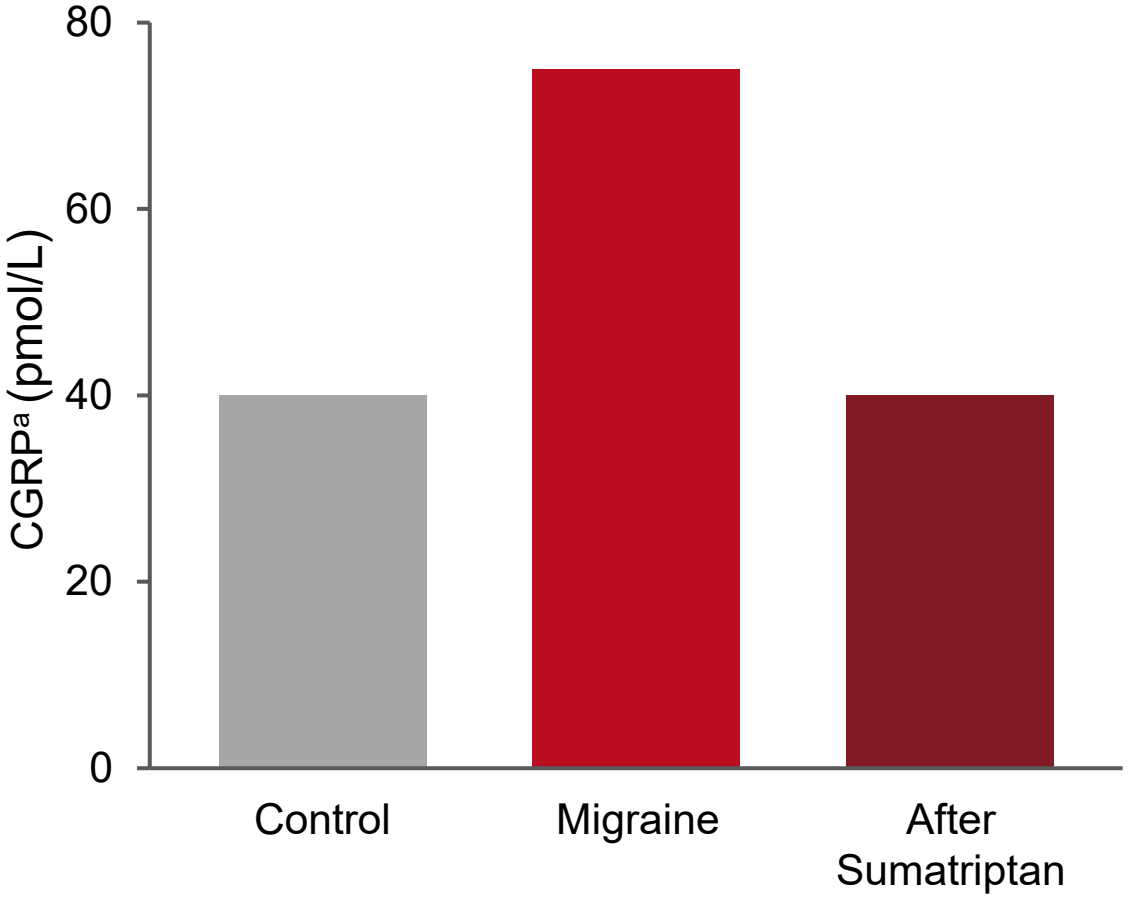
PNS, peripheral nervous system




#HeadacheEdu

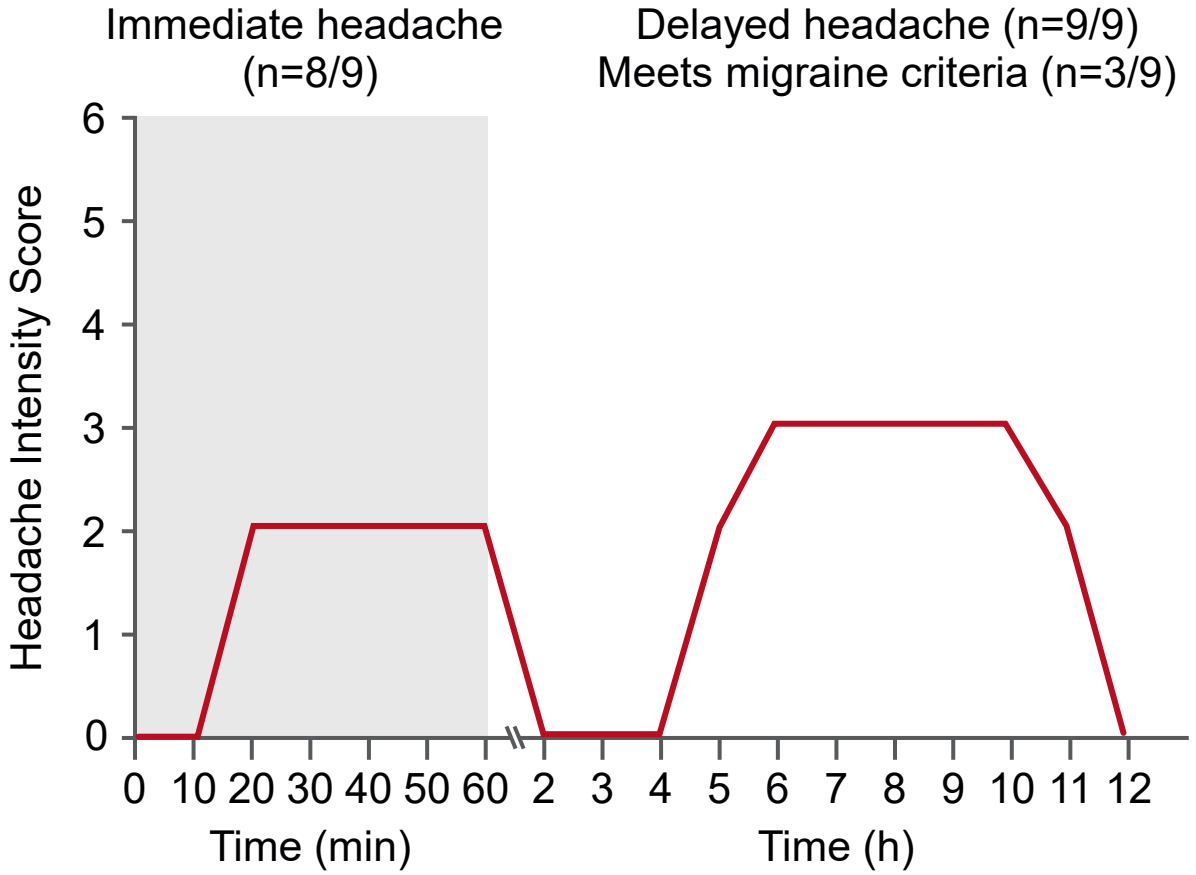
*J Pain.* 2013;14:1289-1303; *Neurotherapeutics*. 2010;7:164-175.

# Plasma CGRP Levels[a] Are Elevated During Migraine and Return to Normal After Treatment




[a]Measured from external jugular blood

# CGRP Infusion Triggers Immediate and Delayed Headache




#HeadacheEdu

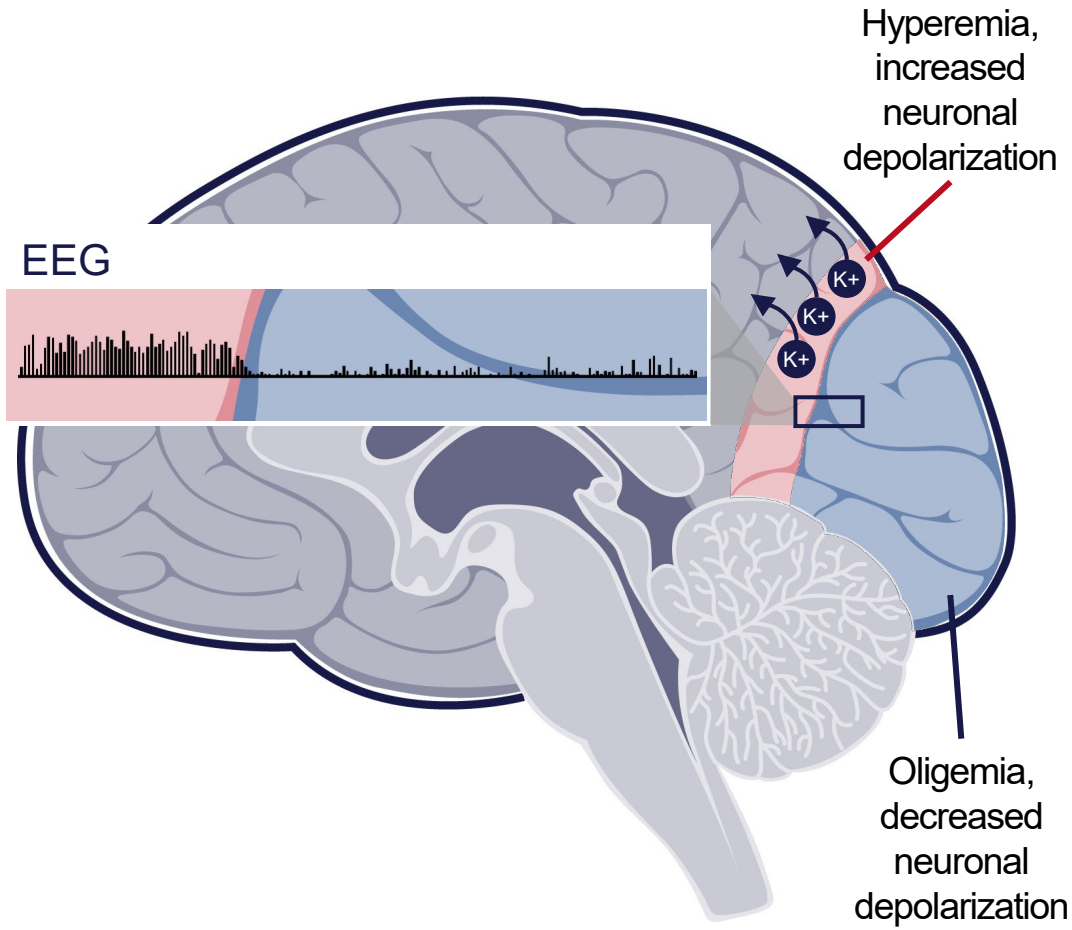
*Ann Neurol*. 1990;28:183–187; *Ann Neurol*. 1993;33:48–56; *Cephalalgia*. 2002;22:54–61.

AMERICAN HEADACHE SOCIETY

# Cortical Spreading Depression — Neurophysiological Correlate of Migraine

- First described by Aristides Leão in 1944
  - Slowly (2-6 mm/min) propagating wave of depolarization in neuronal and glial cell membranes
  - Followed by inhibition of cortical activity for up to 30 minutes
  - Coincides with the initiation and progression of aura

- Associated with:
  - Wave of hyperemia, increased neuronal depolarization
  - Cortical oligemia, decreased neuronal depolarization




*J Neurophysiol*. 1944;7:359-390; *Headache*. 2018;58:4-16.

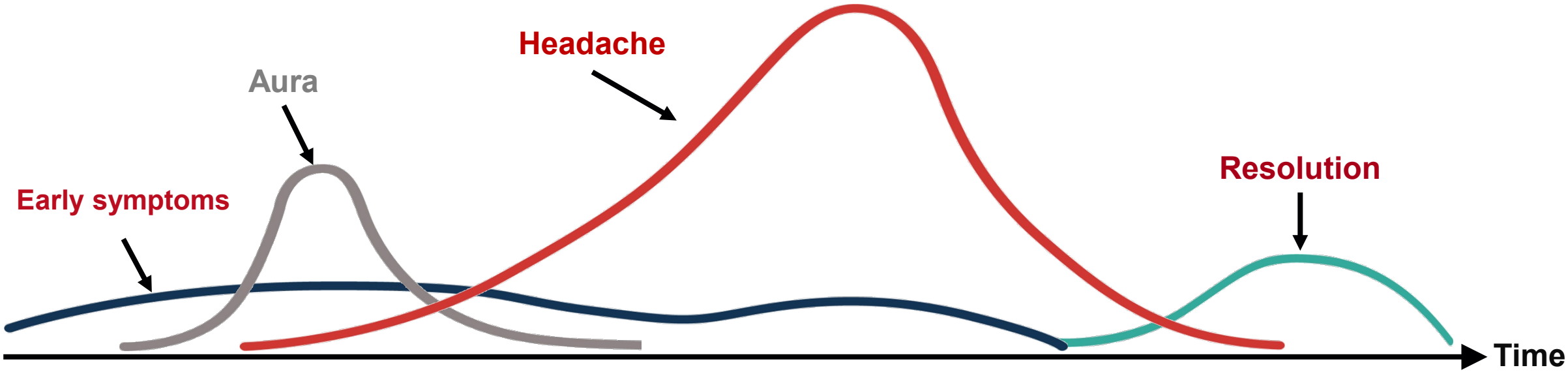
#HeadacheEdu

# Cortical “Waves” in Migraine



Video courtesy of AA Parsons

# Phases of a Migraine Attack




**Premonitory symptoms**

Mood change
Fatigue
Cognitive changes
Food craving
Yawning
Neck Stiffness

**Headache**

Throbbing pain
Nausea
Photophobia
Phonophobia
Osmophobia

**Postdrome**

Fatigue
Cognitive changes
Neck stiffness

#HeadacheEdu

*Drugs*. 2018;78:411-437.

# The Genetics of Migraine

ARTICLES
https://doi.org/10.1038/s41588-021-00990-0
nature genetics
OPEN
*Nat Genet*. 2022;54:152-160.

**Genome-wide analysis of 102,084 migraine cases identifies 123 risk loci and subtype-specific risk alleles**

## More than 100 loci associated with migraine

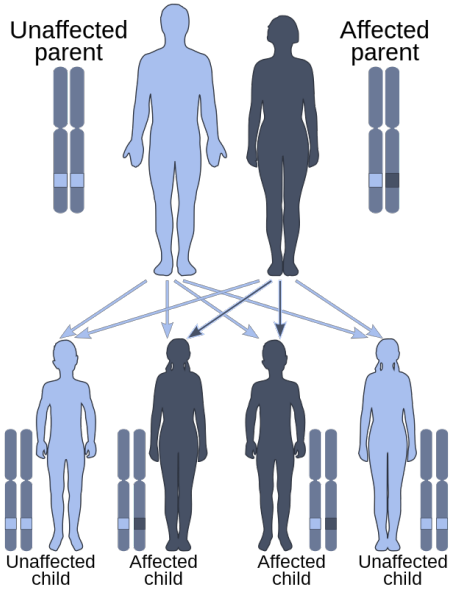
- Enriched in vascular and central nervous system tissue and cell types
- Confirms involvement of neurovascular mechanisms in migraine pathophysiology

## Multiple rare, monogenic forms identified

| Disorder | Causal gene/s |
|---|---|
| Familial Hemiplegic Migraine | CACNA1A, ATP1A2, SCN1A |
| Mendelian Migraine with Aura | KCNK18 |
| Episodic Ataxia type 2 | CACNA1A |
| Spinocerebellar Ataxia type 6 | CACNA1A |
| FASPS | CSNK1D |
| ROSAH syndrome | ALPK1 |
| Paroxysmal dyskinesia disorders | PRRT2, PNKD, SLC1A3 |
| CADASIL | NOTCH3 |
| COL4A1/A2 disorders | COL4A1, COL4A2 |
| RVCL | TREX1 |

FASPS, familial advanced sleep-phase syndrome; ROASH, retinal dystrophy, optic nerve edema, anhidrosis, splenomegaly, headache; CADASIL, cerebral autosomal dominant arteriopathy subcortical infarcts with leukoencephalopathy; Retinal vasculopathy with cerebral leukodystophy

## Autosomal dominant inheritance




- If 1 parent has migraine, 50% chance of children having migraine
- If both parents have migraine, 75% chance of children having migraine

#HeadacheEdu

*Nat Genet*. 2022;54:152-160; *J Headache Pain*. 2019; 20:72.

AMERICAN HEADACHE SOCIETY

# Overview

- Headache Medicine: A Rewarding Career
- Anatomy and Pathophysiology
- **Diagnosis**
- Treatment
- Advocacy

# Headache Classification

## The Primary Headaches

- Migraine
- Trigeminal autonomic cephalalgias
- Tension-type headache
- Other

## The Secondary Headaches

- Trauma or injury to the head and/or neck
- Cranial and/or cervical vascular disorder
- Nonvascular intracranial disorder
- Substance or its withdrawal
- Infection
- Disorder of homoeostasis
- Disorders of the cranium, neck, eyes, ears, nose, sinuses, teeth, mouth, or other facial or cervical structure
- Psychiatric disorder

## Painful Cranial Neuropathies, Other Facial Pain, and Other Headaches

- Painful lesions of the cranial nerves and other facial pain
- Other headache disorders



*Cephalalgia*. 2018;38:1-211.

# Steps to Diagnosis of a Headache Disorder

Rule out secondary headache

Headache History and Examination

**Questions for a Headache History**

- Since when?
- Where in the head?
- How often?
- How long?
- How severe?
- What type of pain?
- Other symptoms?
- Aura?
- How many types?
- Family history?



*J Headache Pain*. 2007;8:263–272.; *Adv Stud Med*. 2003;3:550-555.

# Physical and Neurologic Examinations: Patients Presenting With Headache

| Vitals |
| --- |
| Blood pressure |
| Temperature |
| Body mass index |

| Head and Neck |
| --- |
| Neck range of motion/provocative maneuvers |
| Palpate: |
| Extracranial nerves |
| TMJs |
| Temporal arteries (age 50+) |
| Pericranial and paraspinal muscles |
| Paranasal sinuses |

| Focused Neurologic Examination |
| --- |
| **Talk** to patients—mental status |
| **Cranial nerves** |
| Fundi |
| Visual fields |
| Ocular motility |
| Masseter muscle bulk |
| Facial sensation and symmetry |
| Palate/tongue |
| **Reflexes** |
| Tendon stretch reflexes |
| Plantar responses |
| **Watch them walk** |
| Other as needed |

# Steps to Diagnosis of a Headache Disorder

Rule out secondary headache

Headache History and Examination

Red Flags

Green Flags

- Since when?
- Where in the head?
- How often?
- How long?
- How severe?
- What type of pain?
- Other symptoms?
- Aura?
- How many types?
- Family history?

#HeadacheEdu

*J Headache Pain*. 2007;8:263–272.; *Adv Stud Med*. 2003;3:550-555; *Headache*. 2021;61:300-309.

AMERICAN HEADACHE SOCIETY

# Screen for Red Flags With "SNOOP"



**Suggest headaches are secondary and need further investigation**

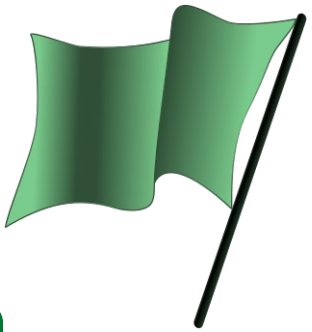
- **S** Systemic symptoms or risk factors (fever, weight loss, myalgias, HIV, cancer, pregnancy)
- **N** Neurologic exam (papilledema, focal deficit, confusion, seizures)
- **O** Onset (sudden/thunderclap)
- **O** Older (new or progressive headache, especially over 50 years)
- **P** Pattern change (new symptoms in previously stable pattern)
- **P** Precipitants (Valsalva, position change, sexual activity)
- **P** Pregnancy and postpartum

#HeadacheEdu

*Adv Stud Med*. 2003;3:550-555.

AMERICAN HEADACHE SOCIETY

# Screen for Green Flags



**Indicate headaches are more likely to be primary than secondary**

1. The current headache has been present since childhood.
2. The headache occurs in temporal relationship with the menstrual cycle.
3. The patient has headache-free days.
4. Close family members have the same headache phenotype.
5. Headache occurred or stopped more than 1 week ago.

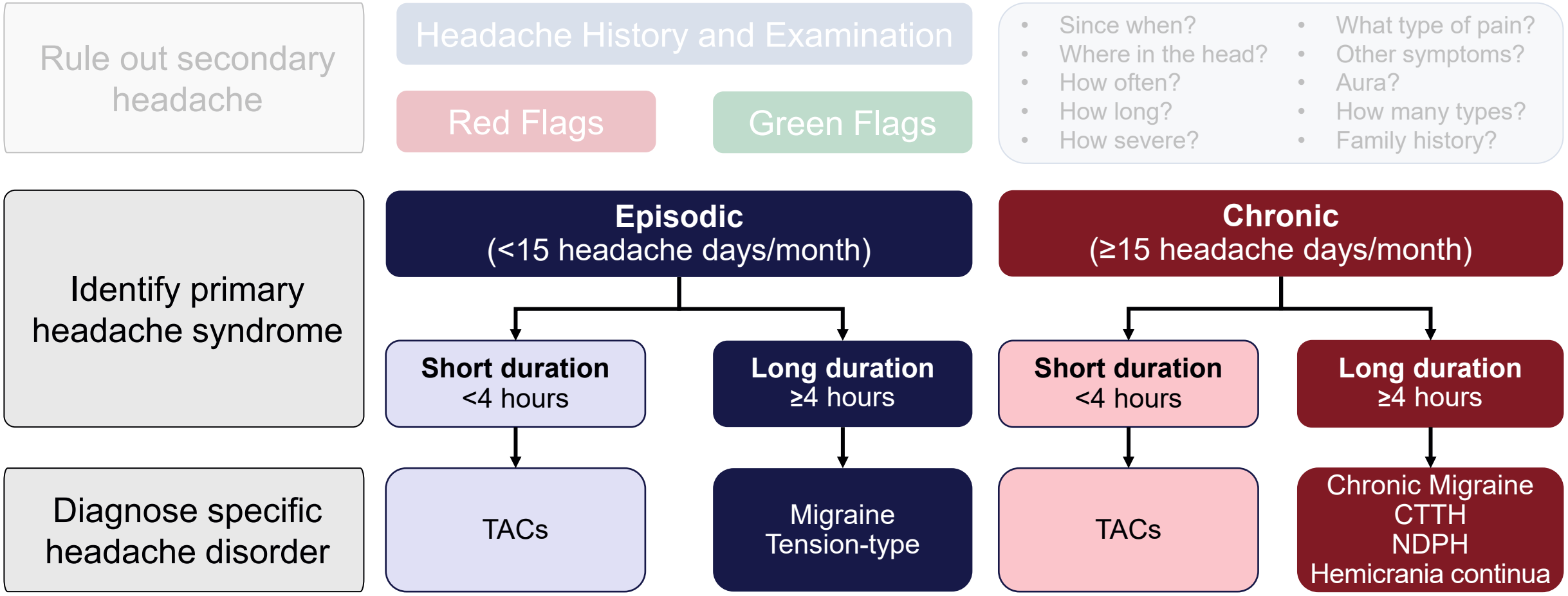
- Must also investigate **Red Flags**
- If red and green flags are both present, suspect secondary headache

#HeadacheEdu

*Headache*. 2021;61:300-309.

AMERICAN HEADACHE SOCIETY

# Steps to Diagnosis of a Headache Disorder




TACs (trigeminal autonomic cephalalgias) include cluster headache, paroxysmal hemicrania, short-lasting unilateral neuralgiform headache attacks, and hemicrania continua. CTTH, chronic tension-type headache; NDPH, new daily persistent headache.

#HeadacheEdu

*J Headache Pain*. 2007;8:263–272.; *Adv Stud Med*. 2003;3:550-555; *Headache*. 2021;61:300-309.

AMERICAN HEADACHE SOCIETY

# ICHD-3 Diagnostic Criteria: Migraine and Tension-type Headache

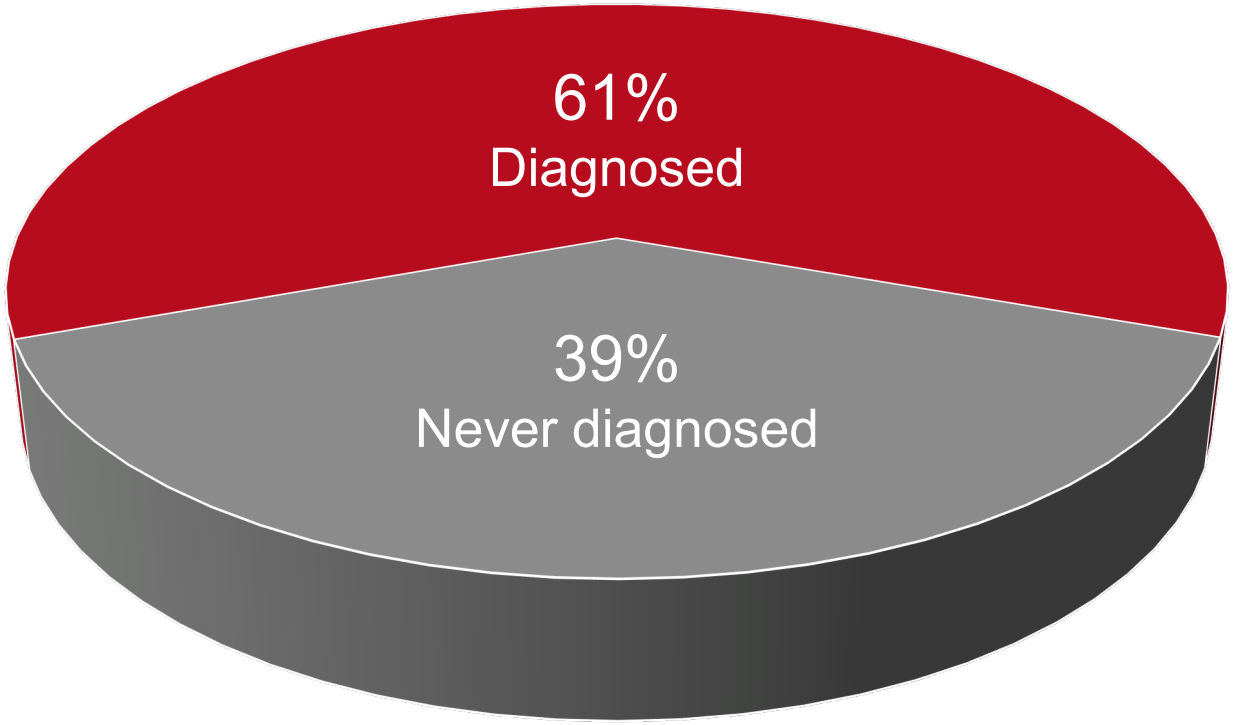
| Parameter | Migraine | Tension-type Headache |
|---|---|---|
| Frequency | Variable | Variable |
| Duration[a] | 4–72 hours[b] | 30 minutes–7 days |
| Location | Unilateral (40% bilateral) | Bilateral |
| Description | Pulsating (50% non-pulsating) | Pressing/tightening (non-pulsating) |
| Intensity | Moderate-severe | Mild-moderate |
| Effect of routine physical activity | Aggravated by or cause avoidance of | Not aggravated by |
| Nausea or vomiting | Yes | No |
| Photophobia or phonophobia | One or both | No more than one |
| Aura | Yes (~30% of patients) | No |

[a]Untreated or unsuccessfully treated
[b]2–72 hours in children

#HeadacheEdu

*Cephalalgia*. 2018;38:1-211.

# Many People With Migraine Remain Undiagnosed




About half of those with migraine (51%) have consulted a medical professional within the past year

#HeadacheEdu

*Headache*. 2022;62:122-140.

# Neurologic Conditions That Mimic Migraine Aura

| | Migraine aura | Transient ischemic attack | Seizure | Transient focal neurological episode |
|---|---|---|---|---|
| **Demographics** | Younger age; F>M | Older age; M>F; vascular risk factors | Any | Older age; +/- cognitive impairment |
| **Associated headache** | 95% – usually follows the aura | 30% – usually ictal | 20% – usually post-ictal | No/mild pain |
| **Neurological features** | Positive and negative features | Negative features that fit a cerebral vascular pattern | Positive features early, sometimes post-ictal negative features | Positive and negative symptoms; may not have a clear spreading pattern |
| **Onset** | Slow spread of symptoms, each lasting 5–60 min; premonitory phase common | Abrupt onset; gradual offset; no premonitory phase | Abrupt onset; premonitory phase common | Seconds to minutes; no premonitory phase |
| **Duration** | Aura <1 h; headache 4–72h | Neurological symptoms >10 min, <1 h | <2 min | 10-30 min, may [illegible] hours |
| **Recurrence** | Common over years | | | |
| **Loss of consciousness** | Very rare | | | |
| **Associated symptoms** | Nausea, photophobia, phonophobia | | | focal [illegible] sia |

Presence of positive features in migraine aura distinguishes it from TIA

Presence of negative features in migraine aura distinguishes it from seizure

No headache distinguishes it from migraine aura, TIA, and seizure

TIA, transient ischemic attack

#HeadacheEdu

*Adv Stud Med*. 2005;5:S658–S665; *Pract Neurol*. 2014;14:23-31; *Arq Neuropsiquiatr*. 2020;78(1):56-57.

AMERICAN HEADACHE SOCIETY

# Discussion Points to Refine Migraine Diagnoses

**Determine headache frequency**

Days with headache in the last month

+

Days without headache of any intensity

- Discuss unaccounted for days
- Distinguish between attacks and headache days

9 attacks, each lasting 1-3 days = **20 headache days**

| S | M | T | W | T | F | S |
|---|---|---|---|---|---|---|
| | | | | 1 1 | 2 1 | 3 1 |
| 4 | 5 2 | 6 2 | 7 2 | 8 | 9 3 | 10 3 |
| 11 | 12 4 | 13 4 | 14 | 15 | 16 | 17 |
| 18 5 | 19 5 | 20 5 | 21 | 22 6 | 23 6 | 24 |
| 25 7 | 26 7 | 27 | 28 8 | 29 8 | 30 | 31 9 |

Diagnosis: Chronic Migraine

#HeadacheEdu

AMERICAN HEADACHE SOCIETY

# Conditions That Are Comorbid With Migraine



Myocardial infarction
Angina
Stroke
Hypertension/hypotension
Raynaud's phenomenon
Patent foramen ovale



Epilepsy
Essential tremor
Restless leg syndrome
Vestibular disorders
Bell's palsy



Depression
Anxiety
Panic disorder
Bipolar disorder



Snoring/sleep apnea
Asthma/allergy
Nonheadache chronic pain
Irritable bowel syndrome

#HeadacheEdu

*J Headache Pain*. 2020;21:23.

AMERICAN HEADACHE SOCIETY

# Overview

- Headache Medicine: A Rewarding Career
- Anatomy and Pathophysiology
- Diagnosis
- **Treatment**
- Advocacy

# Goals of Acute Treatment Reflect Patient Preferences

Rapid, consistent freedom from pain and associated symptoms without recurrence

Restored ability to function

Minimal need for repeat dosing or rescue medications

Optimal self-care and reduced subsequent use of resources[a]

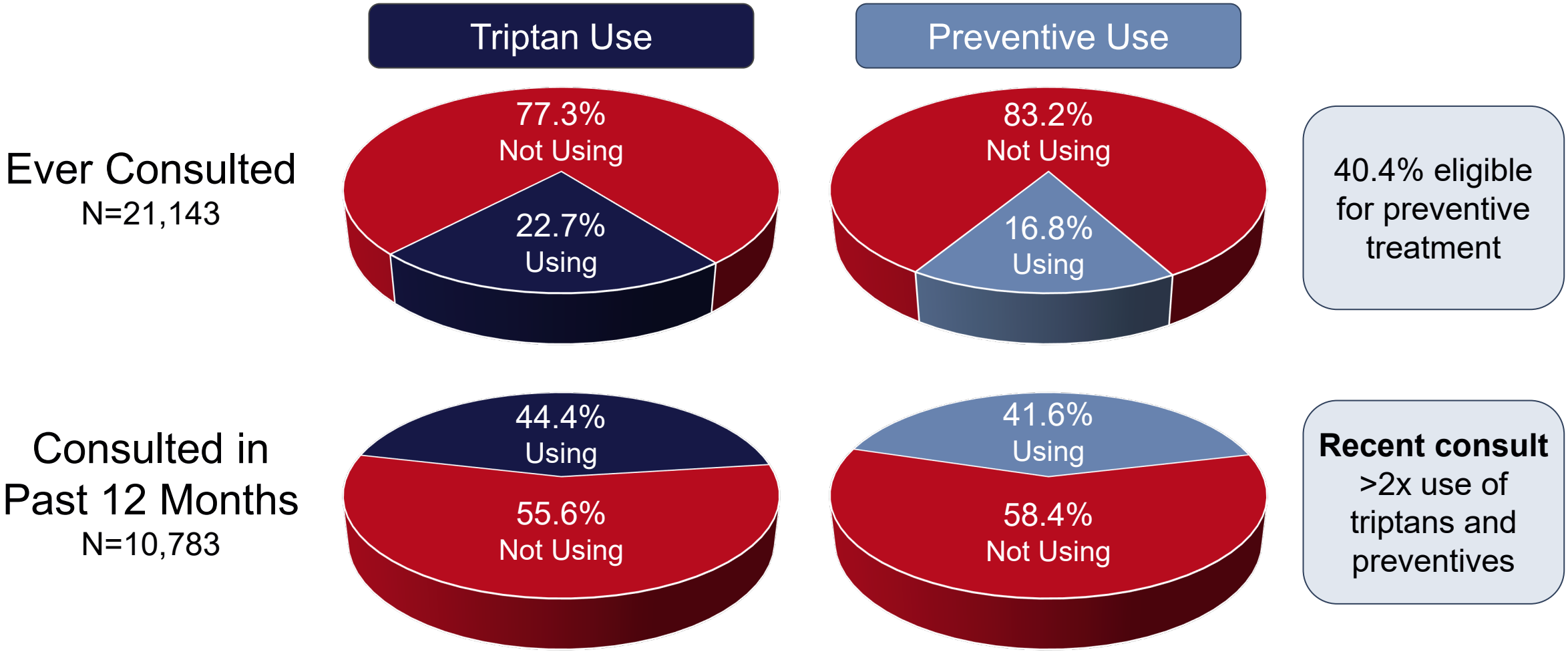
Minimal or no AEs

[a]ER visits, diagnostic imaging, office visits



*Headache*. 2021;59:1-19.

# Most People Consulting for Migraine Do Not Receive Optimal Care




#HeadacheEdu

*Headache*. 2022;62:122-140.

AMERICAN HEADACHE SOCIETY

# Medications for the Acute Treatment of Migraine

| Established Efficacy[a] | Probably Effective |
|---|---|
| **Migraine-specific** | **Migraine-specific** |
| Triptans | |
| Ergotamine | Other forms of dihydroergotamine |
| Gepants | |
| Lasmiditan | |
| **Nonspecific** | **Nonspecific** |
| NSAIDs: aspirin, diclofenac, ibuprofen, naproxen | NSAIDs: flurbiprofen, ketoprofen, IV and IM ketorolac |
| Combination analgesic: acetaminophen+aspirin+caffeine | IV magnesium[b] |
| | Isometheptene-containing compounds |
| | Antiemetics: chlorpromazine, droperidol, metoclopramide, prochlorperazine, promethazine |

DHE, dihydroergotamine; IV, intravenous; IM, intramuscular; NSAID, nonsteroidal anti-inflammatory drug

[a]Consider neuromodulation if patients prefer nondrug treatments or if drug treatment is ineffective, intolerable, or contraindicated.

[b]In migraine with aura

#HeadacheEdu

*Headache*. 2021;59:1-19.

AMERICAN HEADACHE SOCIETY

# Pharmacology of Oral Triptans

| Agent | $T_{max}$ (hours) | $t_{½}$ (hours) |
|---|---|---|
| Almotriptan | 1-3 | 3-4 |
| Eletriptan | 1.5 | 4 |
| Frovatriptan | 2-4 | 26 |
| Naratriptan | 2-3 | 6 |
| Rizatriptan | 1-1.5 | 2-3 |
| Sumatriptan | 2-2.5 | 2.5 |
| Zolmitriptan | 1.5 | 3 |

Oral triptan treatments may be suboptimal because of $T_{max}$

#HeadacheEdu

*Arch Neurol*. 2001;58:1056–1058.

AMERICAN HEADACHE SOCIETY

# Nonoral Options for Acute Treatment

## Pharmacologic

- **Sumatriptan**
  - 3, 4, or 6 mg subcutaneous
  - Nasal spray and powder
- **Zolmitriptan**
  - 2.5 and 5 mg nasal spray
- **Ketorolac**
  - Nasal spray
  - Intramuscular
- **Dihydroergotamine**[a]
  - Subcutaneous
  - Nasal spray
- **Antiemetics**[b]
  - Prochlorperazine
  - Promethazine

[a]Add an antiemetic for refractory headaches
[b]Suppositories for headache and nausea

## Nonpharmacologic

- **Neuromodulation**
  - Electrical trigeminal nerve stimulation (eTNS)
  - Single-pulse transcranial magnetic stimulation (sTMS)
  - Noninvasive vagus nerve stimulation(nVNS)
  - Remote electrical neuromodulation (REN)
  - Combined occipital and trigeminal nerve stimulation (eCOT-NS)

#HeadacheEdu

*Headache*. 2021;59:1-19; *Expert Rev Med Devices*. 2021;18:333-342.

AMERICAN HEADACHE SOCIETY

# Criteria for Initiating Treatment With Gepants, Ditans, or Neuromodulatory Devices

**Use is appropriate when ALL of the following are met:**

A. Prescribed by a licensed medical provider
B. Patient is ≥18 years of age[a]
C. ICHD-3 migraine with aura, without aura, or chronic migraine
D. Either
   a. Contraindications to or inability to tolerate triptans[b]
   b. Inadequate response ≥2 oral triptans measured by EITHER:
      i. Validated acute treatment patient reported outcome questionnaire (mTOQ, Migraine-ACT, PPMQ-R, FIS, PGIC)
      ii. Clinician attestation

ICHD, International Classification of Headache Disorders; mTOQ, Migraine Treatment Optimization Questionnaire; Migraine-ACT, Migraine Assessment of Current Therapy; PPMQ-R, Patient Perception of Migraine Questionnaire-Revised; FIS, Functional Impairment Scale; PGIC, Patient Global Impression of Change

[a]Three neuromodulatory devices (nVNS, REN, sTMS) have also received clearance for the treatment of patients aged 12 to 17 years.

[b]Gepants, ditans, and neuromodulatory devices may be considered



*Headache*. 2021;59:1-19.

# Medication Overuse — Thresholds in the Treatment of Migraine

**Thresholds for medication overuse in patients with migraine**

| Days of use per month | Drug class |
|---|---|
| >10 | Triptans<br>Opioids<br>Combination analgesics[a]<br>Ergot alkaloids |
| >15 | Acetaminophen<br>Aspirin<br>Nonsteroidal anti-inflammatory drugs |

[a]Nonopioid analgesics; opioids, butalbital, and/or caffeine.

**Assess total exposure —**
**Use of multiple medications may constitute overuse when no single drug exceeds thresholds**

#HeadacheEdu

*Cephalalgia*. 2018;38:1-211.

# Goals of Migraine Prevention

## Reduce

- Attack frequency, severity, duration, and disability
- Reliance on acute treatment
- Overall cost of treatment
- Distress and psychological symptoms

## Improve

- Response to acute treatment
- Functional ability
- Health-related quality of life

## Enable

- Self-management

**Benefits Occur Over Time**




#HeadacheEdu

*Headache.* 2021;59:1-19.

# General Principles of Migraine Prevention

Determine appropriate starting dose or stimulation parameters

- Low dose, increase slowly (non-specific oral medications)
- Optimal dose/parameters at onset (anti-CGRP, neuromodulation)

Allow enough time on an adequate dose (2–3 months)

Monitor medication usage

- Avoid overuse of acute medications
- Limit/Eliminate drugs with interaction potential

#HeadacheEdu

*Headache.* 2021;59:1-19.

AMERICAN HEADACHE SOCIETY

# General Principles of Migraine Prevention *cont.*

## Evaluate preventive therapy

- Use calendar/diary
- Consider taper/discontinue if controlled at 6 months

## Manage communications

- Ask about patient preference
- Discuss contraception

## Optimize medication use

- Best efficacy
- Fewest AEs



*Headache.* 2021;59:1-19.

# Preventive Treatments for Migraine[a]

| Established Efficacy[b] | | |
|---|---|---|
| **Oral** | **Parenteral** | **Nonpharmacologic** |
| Candesartan | Eptinezumab | e-TNS |
| Divalproex sodium | Erenumab | sTMS |
| Frovatriptan[d] | Fremanezumab | nVNS |
| Metoprolol | Galcanezumab | |
| Propranolol | OnabotulinumtoxinA[e] | |
| Timolol | | |
| Topiramate | | |
| Valproate sodium | | |
| Atogepant[g] | | |
| Rimegepant[g] | | |

| Probably Effective[c] | |
|---|---|
| **Oral** | **Parenteral** |
| Amitriptyline | OnabotulinumtoxinA + CGRP mAb[e,f] |
| Atenolol | |
| Lisinopril | |
| Memantine | |
| Nadolol | |
| Venlafaxine | |

CGRP, calcitonin gene-related peptide; mAb, monoclonal antibody; e-TNS, external trigeminal nerve stimulation,; sTMS, single-pulse transcranial magnetic stimulation; nVNS, noninvasive vagus nerve stimulation. [a]The decision to prescribe preventive therapy in women who are pregnant or of childbearing age should be based on the needs of individual patients and available safety data; [b]Two or more Class I trials based on American Academy of Neurology evidence classification; [c]One Class I or 2 Class II trials based on American Academy of Neurology (AAN) evidence classification; [d]Short-term prevention of menstrual-related migraine; evaluated and rejected by the FDA for this indication; [e]Prevention of chronic migraine; [f]One Class IV trial based on AAN evidence classification; [g]Episodic migraine only.



*Headache*. 2021;59:1-19.

# Criteria for Initiating Preventive Treatment With CGRP mAbs or Gepants

**Use is appropriate when ALL of the following are met:**

A. Prescribed by a licensed medical provider

B. Patient is ≥18 years of age

C. ICHD-3 migraine with or without aura (4-14 monthly migraine days) or chronic migraine AND:

   a. Poor tolerability or inadequate response to an 8-week trial of ≥2 preventive treatments[a]

   b. At least moderate disability

   c. ≥2 quarterly injections of onabotulinumtoxinA[b]

CGRP, calcitonin gene-related peptide;AAN-AHS, American Academy of Neurology-American Headache Society

[a]With attestation by the prescribing clinician about medical risk, a trial of 2 established therapies may not be required

[b]Chronic migraine only



*Headache*. 2021;59:1-19.

# Behavioral Therapies for Migraine

## Biofeedback



## CBT



## Relaxation Training






- Supported by data
- Endorsed in US Headache Consortium guidelines
- Have long-lasting benefits
- Effective at all life stages
- Can be stand alone or combined with other therapies

#HeadacheEdu

*Neurology*. 2000;55:754-762; *Headache*. 2021;59:1-19.

AMERICAN HEADACHE SOCIETY

# Procedures Commonly Performed by Neurologists

| Procedure | Treatment type | Injection frequency | Evidence highlights |
|---|---|---|---|
| OnabotulinumtoxinA | Preventive | Every 12 weeks | • RCTs: chronic migraine, sleep-related bruxism<br>• Observational: NDPH, chronic posttraumatic headache, nummular headache, trigeminal neuralgia |
| Peripheral nerve blocks | Acute, short-term preventive | Single or every 2 weeks[a] | • RCTs: migraine, cluster headache<br>• Observational: pediatric, pregnant, and geriatric populations |
| Trigger point injections | Acute, short-term preventive | Single or every 2 weeks[a] | RCTs: tension-type headache |
| Sphenopalatine ganglion blocks | Acute, short-term preventive | Single or twice weekly[a] | RCTs: chronic migraine, acute headache in ED |

[a]Or longer intervals as needed

#HeadacheEdu

*Continuum (Minneap Minn)*. 2021;27(3, Headache):732-745.

AMERICAN HEADACHE SOCIETY

# Neuromodulation: Nonpharmacologic Options for Acute and Preventive Treatment

Acute/Preventive



External trigeminal nerve stimulation

Available Without a Prescription

Acute/Preventive



Single-pulse transcranial magnetic stimulation

Acute/Preventive



Noninvasive vagus nerve stimulation

Acute



Remote electrical neurostimulation

Acute



Noninvasive combined occipital and trigeminal nerve stimulation

#HeadacheEdu

*Headache*. 2019;59 Suppl 2:33-49; *Expert Rev Med Devices*. 2021;18:333-342.

AMERICAN HEADACHE SOCIETY

# Overview

- Headache Medicine: A Rewarding Career
- Anatomy and Pathophysiology
- Diagnosis
- Treatment
- **Advocacy**

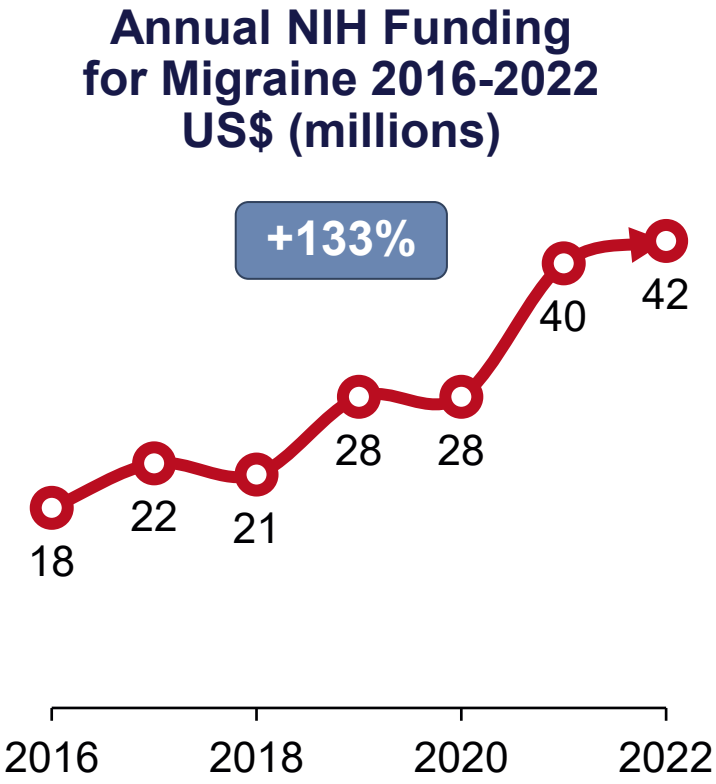
# Advocacy — An Engine of Research




- Walk/run events to support fellowship programs in Headache Medicine
- Adult/family education, social programs, and support groups

HEADACHE on the HILL

- Annual advocacy event in Washington, DC
- Clinicians, research scientists, and patient advocates involved in Headache Medicine
- Visit representatives from as many states/congressional districts as possible




#HeadacheEdu

AMERICAN HEADACHE SOCIETY

# The Voice of Migraine

"Every day is a new chance — a new chance for a pain-free day, a new chance for a cure to be discovered. . .We always have high hopes for a better tomorrow."

Gabrielle V.






# Questions?

#HeadacheEdu

AMERICAN HEADACHE SOCIETY




RESIDENT EDUCATION FOR THE ASSESSMENT AND CARE OF HEADACHE

# Thank You!

#HeadacheEdu

AMERICAN HEADACHE SOCIETY

# Pediatric

(optional)

# Primary Headaches Are Among the Most Common Disorders of Childhood

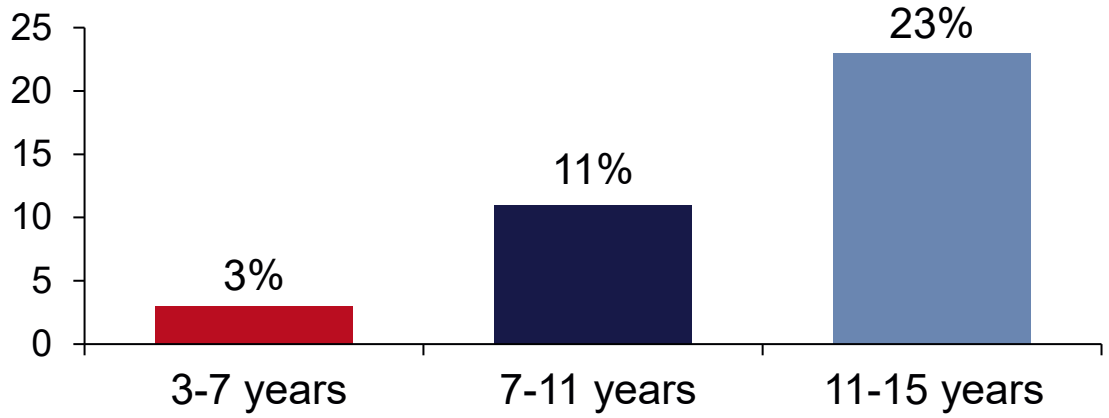
- Migraine and tension-type headache are the most common diagnoses
- Most knowledge is based on clinical observation and estimates from studies of adults
- Treatment decisions must account for age, family structure, culture and beliefs, headache diagnosis, and disability
- Multidisciplinary treatment plans — counseling, education, and reassurance combined with medication and non-drug approaches — appear to be optimal

# Migraine in Pediatric Populations: Prevalence and Disability

**Affects 1 in 11 Children**



**Migraine Prevalence Age 3-15 Years**




**Migraine**

The leading cause of disability in people aged 15 to 49 years

**Children and Adolescents With Migraine**

- Miss more school days
- Perform more poorly in school
- Have decreased family/social interaction
- Experience lower quality of life

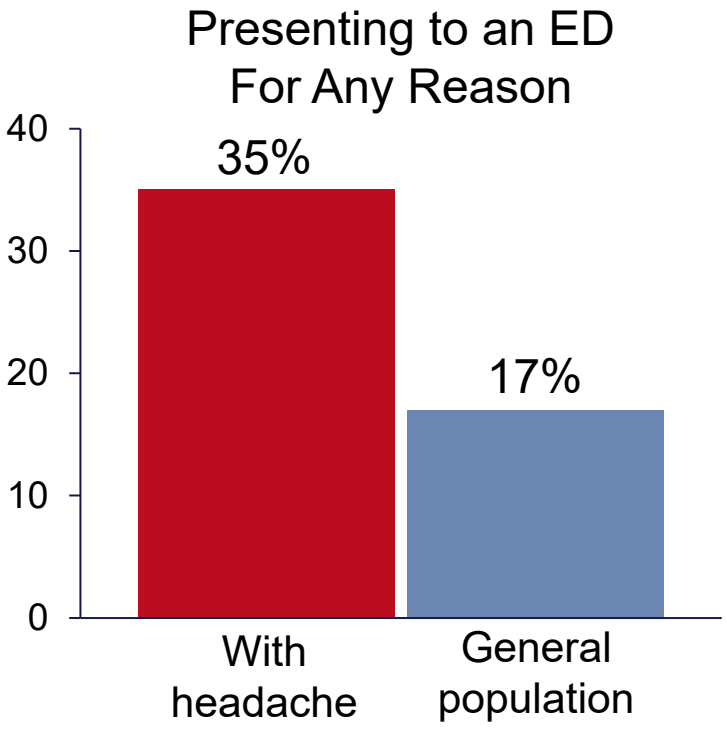
#HeadacheEdu

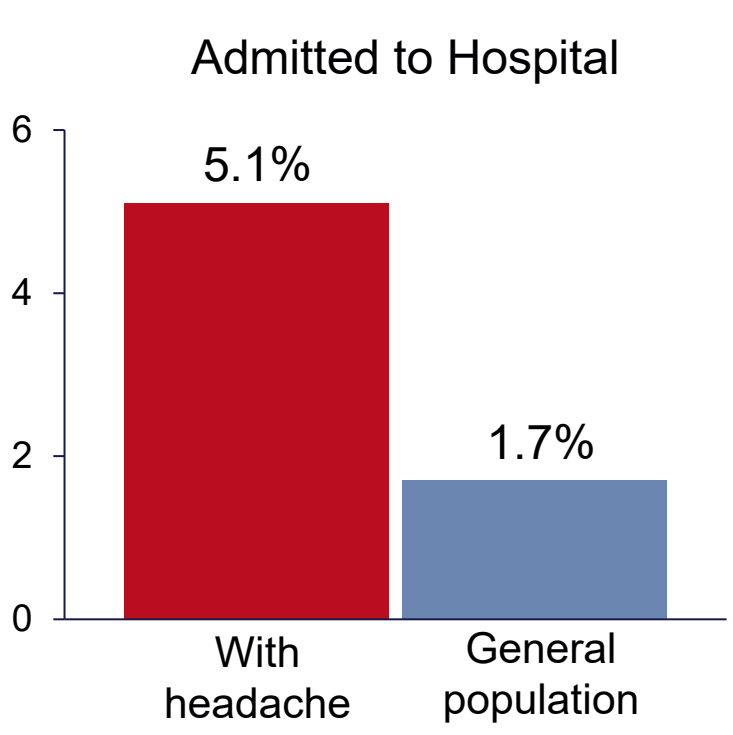
*Curr Pain Headache Rep*. 2013;17:341; *Neurology*. 2002;59:490-498; *Lancet*. 2017;390(10100):1211-1259; *J Headache Pain*. 2018;19:17; *JAMA Pediatr*. 2021;175:522-524; *Pediatrics*. 2003;112(1 Pt 1):e1-e5.

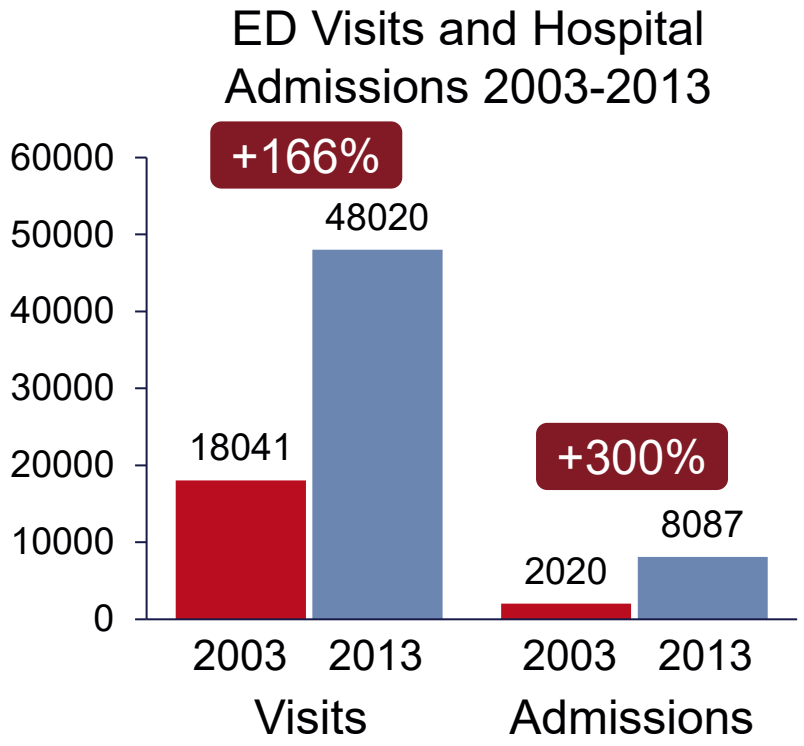
AMERICAN HEADACHE SOCIETY

# Emergency Consultation for Migraine Among Children and Adolescents

Headaches account for approximately 0.9% to 2.6% of ED visits among youth — the third most common cause of consultation




#HeadacheEdu

*J Pediatr*. 2014;165:376-382; *Pediatrics*. 2013;132:e1173-1183; *Pediatr Neurol*. 2018;89:19-25.

AMERICAN HEADACHE SOCIETY

# Distinguishing Features of Migraine in Children and Adolescents

| Pain | |
|---|---|
| More often bilateral than in adults | Unilateral pain usually emerges in older adolescents/young adults |
| Usually frontotemporal | Other locations may suggest diagnostic caution |
| **Associated Symptoms** | |
| Photophobia and phonophobia | May be inferred from behavior in the youngest patients |
| Less typical bilateral visual symptoms | May be an aura |





*Cephalalgia*. 2018;38:1-211.

# Pediatric and Adolescent Migraine Screen (PAMS): 3-Question Migraine Screener

| Younger Than 12 Years | 12 to 18 Years |
|---|---|
| 1. Would you rate the pain from your headache as bad or very bad? | 1. Would you rate the pain from your headache as moderate or severe? |
| 2. Does your head feel like it is pounding? | 2. Does your head feel like it is throbbing? |
| 3. Does your headache get worse when you run, walk, or play? | 3. Did you ever skip a school day, a sports event, or other fun activity because your head hurt too much? |

Children with history of similar headaches who answer **"Yes"** to **any of the above** questions are likely to have migraine.

Adapted with permission from Cincinnati Children's Hospital. https://www.cincinnatichildrens.org/service/h/headache-center/pams

# Episodic Syndromes Associated with Migraine in Children

| Syndrome | Features recurrent episodes of: |
|---|---|
| Recurrent gastrointestinal disturbance | Abdominal pain and/or discomfort, nausea and/or vomiting, occurring infrequently, chronically, or at predictable intervals |
| Cyclic vomiting syndrome | Intense nausea and vomiting, usually stereotypical in the individual and with predictable timing; may be associated with pallor and lethargy |
| Abdominal migraine | Moderate to severe midline abdominal pain, associated with vasomotor symptoms, nausea, and vomiting, lasting 2–72 hours, with no headache |
| Benign paroxysmal vertigo | Vertigo occurring without warning and resolving spontaneously in otherwise healthy children |
| Benign paroxysmal torticollis | Head tilt to one side, perhaps with slight rotation, that remit spontaneously; occurs in infants and small children, with onset in the first year |
| Infantile colic | Irritability, fussing, or crying from birth to 4 months, with episodes lasting for 3 hours/day and occurring on 3 days/week for 3 weeks |

Conditions that may co-occur

- Motion sickness
- Periodic sleep disorders (eg, walking, talking, night terrors, bruxism)



*Cephalalgia*. 2018;38:1-211.

# Imaging in Headache Disorders

Choosing Wisely®

Don’t perform neuroimaging studies in patients with **stable headaches** that meet criteria for **migraine**

Don’t perform **CT imaging** for headache when **MRI is available**, except in **emergency settings** (eg, acute bleed)

AMERICAN HEADACHE SOCIETY®

There is **no necessity** to do neuroimaging in patients with **headaches consistent with migraine** with a **normal neurologic examination** and **no atypical features or red flags**

ACR® AMERICAN COLLEGE OF RADIOLOGY

Appropriateness Criteria Headache — good resource for image selection in **specific clinical scenarios**

# Patient and Family/Caregiver Education: Key Points to Cover

**We know the cause!**

Migraine is a neurologic disorder

Describe basic physiology

**Approach to treatment is 3-pronged**

- Wellness/Headache Hygiene
- Acute treatment
- Preventive treatment

**Set appropriate goals for treatment**



#HeadacheEdu

AMERICAN HEADACHE SOCIETY

# Healthy Habits for Migraine Disease

| Intervention | Recommendation |
|---|---|
| Hydration | At least 64 oz of water per day, consider water note for school, extra hydration during sports/physical activity |
| Diet | No skipping meals, avoid periods of fasting. May need snacks at school. May need note for school lunch accommodations |
| Sleep | Quantity: enough sleep for age (8-12 hours)<br>Quality: rule out OSA, turn off TVs/music during sleep<br>Consistency: create a routine with a regular sleep schedule even for weekends |
| Physical Activity | AAP recommends 1 hour of physical activity daily |
| Caffeine | AAP advises no caffeine below age 12 |

# Behavioral Therapies for Migraine

## Biofeedback



## CBT



## Relaxation Training






- Supported by data
- Endorsed in US Headache Consortium guidelines
- Have long-lasting benefits
- Effective at all life stages
- Can be stand alone or combined with other therapies

#HeadacheEdu

*Neurology*. 2000;55:754-762.

AMERICAN HEADACHE SOCIETY

# AAN/AHS Guideline: Acute Treatment of Migraine in Children and Adolescents

## NSAIDs

Ibuprofen 10 mg/kg

## Triptans

- Sumatriptan/naproxen OT 10/60 mg, 30/180 mg, 85/500 mg (≥12 y/o)
- Zolmitriptan NS 5 mg (≥6 y/o)
- Sumatriptan NS 20 mg
- Rizatriptan ODT 5 mg or 10 mg (≥6 y/o)
- Almotriptan OT 6.25 mg or 12.5 mg (≥12 y/o)

For relief of GI symptoms, consider adding:

## Antiemetics

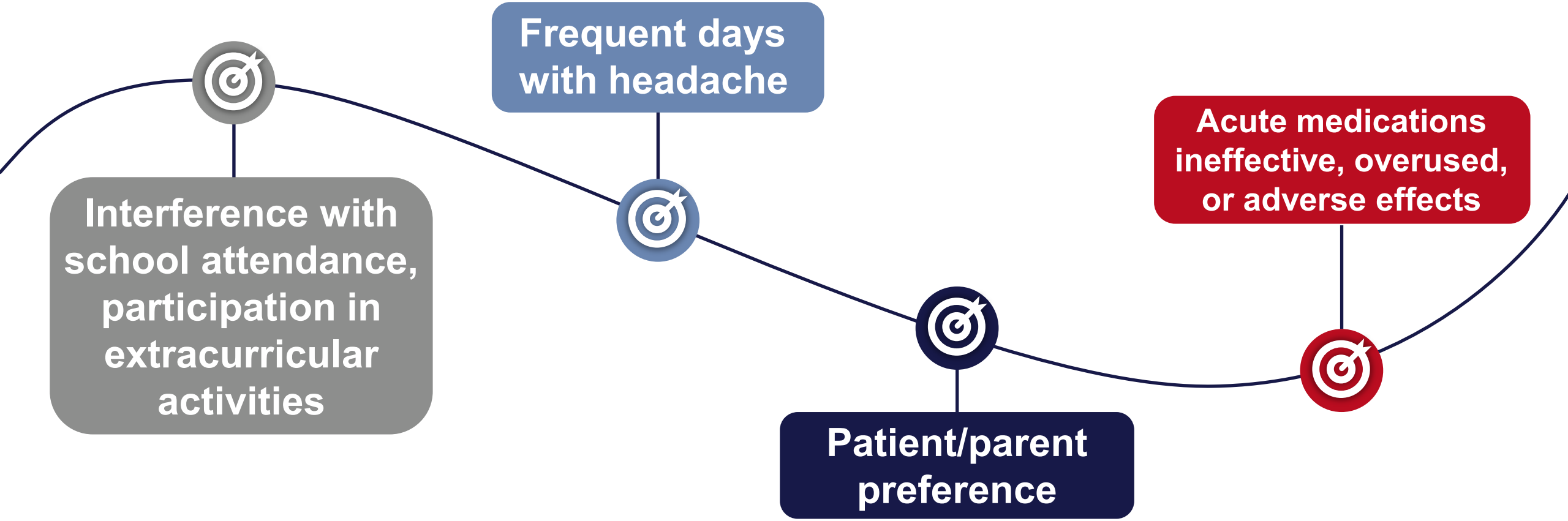
- Ondansetron 0.1 mg/kg
- Prochlorperazine 0.1 mg/kg
- Promethazine 0.25-1 mg/kg

#HeadacheEdu

*Neurology*. 2019;93:487-499;

AMERICAN HEADACHE SOCIETY

# When to Prescribe Preventive Therapy




*Neurology*. 2000;55:754-62; *Neurology*. 2001;57:2034-2039.

#HeadacheEdu

# AAN/AHS Migraine Prevention Guidelines

| Lifestyle | |
|---|---|
| Poor sleep | Poor diet or hydration |
| Overweight, lack of exercise | Screen for depression or mood issues |
| Caffeine/alcohol/tobacco use | |

| Medications | |
|---|---|
| Topiramate | Propranolol |
| Amitriptyline + CBT | |

CBT, Cognitive Behavioral Therapy

Counsel on Limitations
and Potential Adverse Effects

#HeadacheEdu

*Neurology*. 2019;93:500-509.

AMERICAN HEADACHE SOCIETY

# Preventative Nutraceuticals

| Agent | Daily Dose | Notes |
|---|---|---|
| Riboflavin (vitamin B2) | 400 mg | Urine discoloration |
| Magnesium | 400 mg – 600 mg | Diarrhea; chelated forms better tolerated |
| Coenzyme Q10 | 300 mg | Most expensive |
| Feverfew | 50 mg – 300 mg | Low-quality evidence |
| Melatonin | 3 mg | Conflicting evidence |

Note: Petasites/Butterbur not currently recommended due to concerns about liver toxicity

#HeadacheEdu

*Neurology*. 2012;78:1346-53; *Medicine (Baltimore)*. 2019;98(3):e14099; *Headache*. 2016;56:1257-66.

AMERICAN HEADACHE SOCIETY

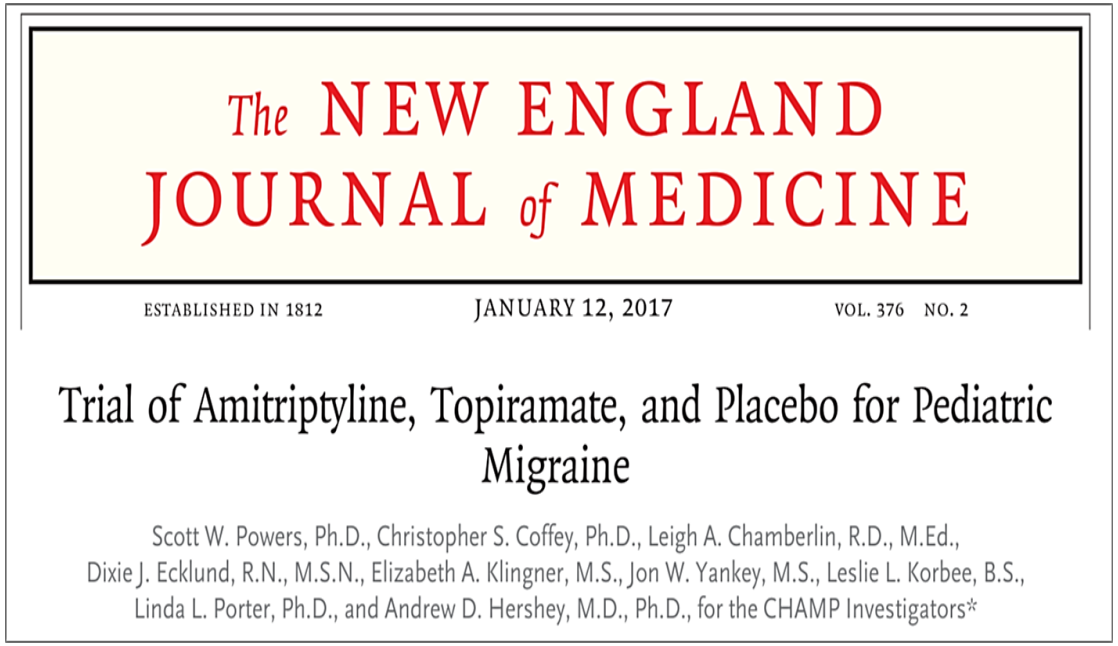
# Which Medications Can Be Used To Prevent Migraine Attacks in Pediatric Patients?

## Childhood and Adolescent Migraine Prevention (CHAMP) Trial

**Design**
Randomized, double-blind, placebo-controlled 24-week trial

**Subjects**
Children and adolescents, age 8 to 17

**Primary efficacy outcome**
Reduction of ≥50% in headache days
(28-day baseline vs last 28 days of the trial)




## No significant differences from placebo over the 24-week study period



*N Engl J Med.* 2017;376:115-124.

# CHAMP: Lessons Learned

| | |
|---|---|
| 1 | Neither of two preventive medications for pediatric migraine was more effective than placebo in reducing the number of headache days[1] |
| 2 | Prevention medication for pediatric migraine might be reexamined[1] |
| 3 | Most (~60%) pediatric patients will improve with[2]:<br>• Lifestyle management counseling (eg, sleep, exercise, hydration, caffeine, and avoidance of meal skipping)<br>• Acute therapy with nonsteroidal anti-inflammatory drugs or triptans, the latter of which are approved for use in patients aged ≥6 years<br>• A preventive treatment with evidence of efficacy |

CHAMP, Childhood and Adolescent Migraine Prevention

#HeadacheEdu

*N Engl J Med.* 2017;376:115-124; *Continuum (Minneap Minn)*. 2018;24(4, Headache):1108-1136.

AMERICAN HEADACHE SOCIETY

# Use of CGRP mAbs in Children and Adolescents With Migraine

| Indications | Contraindications | Monitoring |
|---|---|---|
| ≥8 headache days per month | Disturbed blood-brain barrier[b] | Pubertal status |
| PedMIDAS score ≥30 | Severe cardiovascular disease, stroke | Bone health, consider checking Vitamin D status |
| Failure of ≥2 preventive therapies[a] | Pregnancy, planned pregnancy, or breastfeeding | Linear growth |
| Postpubertal adolescent or prepubertal child (selected cases) | | Weight/Body mass index |
| | | Infections |
| | | Pregnancy status |

PedMIDAS, Pediatric Migraine Disability Assessment scale
[a]Pharmacologic, nutraceutical, and/or nonpharmacologic
[b]For example, recent history of meningitis, recent neurosurgery

#HeadacheEdu

*Headache*. 2018;58:1658-69; *Neurology*. 2001;57:2034-2039.

AMERICAN HEADACHE SOCIETY

# Neuromodulation: Acute and Preventive Treatment for Patients Aged 12 and Older

Acute/Preventive



Noninvasive vagus nerve stimulation

Acute/Preventive



Single-pulse transcranial magnetic stimulation

Acute



Remote electrical neurostimulation

#HeadacheEdu

*Headache*. 2019;59 Suppl 2:33-49; *Expert Rev Med Devices*. 2021;18:333-342.

AMERICAN HEADACHE SOCIETY