

#### Migraine care challenges and strategies in US uninsured and underinsured

#### adults: A narrative review, Part 2

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#### Abstract:

**Objective:** To review the challenges and potential solutions in treatment options for quality migraine care in adult patients who are under or uninsured.

**Background:** The Affordable Care Act has improved access to health care for many, however those who are underserved continue to face treatment disparities and have inadequate access to appropriate migraine management.

Methods: This manuscript is the second of a two-part narrative review which was performed after a series of discussions within the Underserved Populations in Headache Medicine Special Interest Section meetings of the American Headache Society. Literature was reviewed for key concepts underpinning conceptual boundaries and a broad overview of the subject matter. Published guidelines, state-specific Medicaid websites, headache quality measurement sets, literature review and expert opinion were used to tailor suggested treatment options and therapeutic strategies. In this second part of our narrative review, we explored migraine care strategies and considerations for underserved and vulnerable adult populations with migraine.

**Results:** Although common, migraine remains untreated, particularly among those of low socioeconomic status. Low socioeconomic status may play an important role in the disease progression, prescription of hazardous medications such as opioids, outcomes and quality of life of patients with migraine and other

headache disorders. There are some evidence-based and guideline supported treatment options available at low cost which include prescription medications and supplements, though approved devices are costly. Resources available online and simple non-pharmacological strategies may be particularly useful in the underserved migraine population.

**Conclusions:** We identified and discussed migraine treatment barriers that affect underserved populations in the US and summarized practical, cost-effective strategies to surmount them. However, more research is needed to identify the best cost effective measures for migraine management in underserved and vulnerable patients who are uninsured or underinsured.

#### Introduction

In part one of this review, we described the methodology which led to the execution of this narrative review by the Underserved Populations in Headache Medicine special interest section of the American Headache Society, followed by an exploration of the epidemiology of the underserved population with migraine as well as the challenges in managing patients who are at a disadvantage in this context. In part two, using the same narrative methodology we specifically address management considerations of the underserved population with migraine. There are three approaches generally considered in migraine treatment. These approaches include abortive (acute), prophylactic (preventive), and non-pharmacological (i.e. lifestyle, behavioral changes) treatments and

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modalities. In this section we will explore each therapeutic group with special considerations and suggestions for underserved, vulnerable and underinsured adult populations.

#### **Treatment Considerations and Options**

#### **Acute (Abortive) Treatment of Migraine in the Underserved Population**

The goals of acute migraine therapy in the underserved population are the same as the goals for the general population at large who suffer with migraine (Table 1).(1) There are several challenges in meeting these goals in the underserved as outlined in part one of this manuscript. An important consideration for populations with migraine who have low socioeconomic status is the risk of developing chronic migraine in association with medication overuse that can occur with acute medications. At least two-thirds of people with medication overuse headache (MOH) have migraine as their primary headache disorder. (2) The sociodemographic profile of the MOH population with chronic migraine is characterized by a higher proportion of women, a lower education level, and a higher level of unemployment as compared to those with episodic migraine. (3)

Most all of the group 1 (proven, pronounced statistical and clinical benefit) medications recommended in the 2000 AAN practice parameter and the Level A (established as effective based on available evidence) medications listed by the American Headache Society Guidelines Committee are substances that can be

associated with MOH in susceptible persons. (4) Prochlorperazine IV (Group 1, Level B) is the only exception. (1, 5) Although relatively inexpensive medications, butalbital-containing products and opioids may lead to the development of MOH in the medically underserved as readily as in the general migraine population. Opioid use has been associated with lower annual household income when compared to nonusers and opioid users are less likely to be currently married or employed. (6) It is possible that increased use of opioids in the underserved population particularly elevates the risk of MOH. In addition, opioids and butalbital-containing medications may be more forceful drivers of MOH. (4) In our experience, unlike triptans, practitioners prescribing opioids and butalbital-containing compounds typically do not face quantity limits which may lead to more frequent use and place such patients at a higher risk of medication overuse. Therefore, the use of butalbital-containing products and opioids should be limited or avoided in the underserved with migraine.

Similar to the general population, patients in underserved and vulnerable populations with migraine need a formal management plan in which appropriate therapeutic goals and realistic patient expectations are set. Potential barriers to management plans in underserved/vulnerable populations may include a lack of formal education and low literacy. Persons with less education may be more concrete in their thinking operations and may have trouble thinking beyond the current state to plan for future events.(7) It is important to ensure understanding of the goal(s) of successful abortive treatment. These goals may include decreasing and eliminating the use of poorly tolerated, ineffective or unwanted

acute medications. Thus, clinical guidelines may provide practitioners with a good starting point to initiate appropriate treatment options. Another goal of an abortive plan may be to reduce the management of non-emergent headache attacks in the emergency department (ED). (8) One multicenter study has shown that opioids are ordered for acute migraine treatment in 12.3% of academic medical center visits, 40.9% of urban ED visits, and 68.6% of community ED visits.(9) ED management often includes non-migraine specific medications and opioids.

The 2000 AAN practice parameter for migraine recommends meeting the goal of acute management by using migraine specific agents (triptans and DHE) for patients with moderate to severe migraine or poor non-steroidal anti-inflammatory drug (NSAID) responders. (1) These medications have proven efficacy. Unfortunately, some may cost in excess of \$12 per dose and are strictly limited in monthly quantity on many Medicaid plans.(10) Oral NSAIDs and combination analgesics with caffeine are considered reasonable first-line treatment choices for mild to moderate migraine attacks or severe attacks, which have previously responded to NSAIDs. Many generic NSAIDs are covered on Medicaid plans. Ibuprofen and naproxen are often included in reduced cost cash pay formularies (see Table 2). Acetaminophen, which was considered clinically ineffective per the 2000 AAN practice parameter has been elevated to a Level A for non-incapacitating attacks in more recent AHS guidelines.(5)

Acetaminophen, in combination with acetylsalicylic acid and caffeine, may be more effective in severe migraine headache attacks. (11)

Gleaning from the list of medications in Group 2 (moderate statistical and clinical benefit) and Level B (probably effective) are the NSAIDs flurbiprofen PO, ketoprofen PO and ketorolac IV/IM. Dopamine antagonists prochlorperazine IV/IM, chlorpromazine IV, metoclopramide IV and prochlorperazine 25 mg PR are also Group 2 and Level B agents. (1, 5) These are abortive medications with low risk of causing MOH. Attempting oral use of dopamine antagonists alone or in combination for analgesia has not been rigorously studied but may be reasonable as they often appear on low cost formularies and have antiemetic effects. (12, 13) Promethazine has the lowest risk of extrapyramidal side effects, as it is a weak dopamine antagonist which has strong anticholinergic and antihistaminic effects, though studies specifically in migraine are lacking.

Two antihistamines may be used as adjuvant medications to dopamine antagonists to prevent akathisia. Hydroxyzine possesses anxiolytic qualities and has been studied for use in pain alone and with DHE in migraine. (14, 15)

Diphenhydramine is frequently used as a parenteral adjunct for migraine treatment in the ED, though study results have been mixed.(16-21) Neither drug is listed in the AHS guidelines or the 2000 AAN practice parameter.

Finally, baclofen is a GABA receptor agonist used to treat spasticity. A few studies have been conducted using it in the treatment of migraine or pain.(22-24) Baclofen is often listed on the low cost cash formularies and may be considered as an acute medication for migraine in our experience and in the limited literature reports. Again, neither the AAN practice parameter nor the AHS

guidelines evaluated this medication because of a low quality of evidence. (See Table 2)

### Prophylactic (Preventive) treatment of Migraine in the Underserved Population

Migraine is undertreated with prophylactic medication in the US population as a whole. Of those who receive prophylaxis, prophylactic medications with low quality evidence are prescribed to just over one-fourth of patients with migraine.(25) In fact, it is almost twice as likely that people with migraine will only receive prophylactic medications with low-quality evidence as it is that they will receive prophylactic medications with only high-quality evidence.(25) We will review the goals of prophylactic or preventive agents in migraine, the considerations for their use, and tips to optimizing preventive therapies in this section of the manuscript. Some natural supplements and complementary agents have high-level evidence as migraine prophylactic agents and they will be discussed in a subsequent section.

The goals of preventive or prophylactic agents usually include one or more of the following: 1) reduce frequency of headache attacks, 2) reduce duration of headache attacks, 3) reduce the number of days of headache, 4) reduce the use/need of abortive medications, and 5) improve quality of life.(26, 27) Prophylaxis may also help to reduce the associated symptoms of migraine as

well as the interictal burden. Prevention should be offered to those with migraine reporting 6 or more headache days per month, 4 or more headache days with at least some impairment, or 3 or more headache days with severe impairment or requiring bed rest, and should be considered in patients with 4 or 5 migraine days per month with normal functioning, 3 migraine days with some impairment, or 2 migraine days with severe impairment.(27) Patients should be informed that it may take approximately 12 weeks at an effective, appropriate dose of the prophylactic agent before results are seen and goals are realized. Counseling of prophylaxis may be very important to maximize adherence and avoid early prophylactic discontinuation (i.e. after 2-3 weeks of taking agent) due to "lack of response" as an adequate trial is necessary. Initiation of therapies at the lowest effective dose is recommended with slow titration until clinical benefits are realized without untoward effects or limited by untoward effects. Overuse of abortive medications should be avoided. Comorbid conditions and coexisting illnesses should be considered when prescribing medications. Headache diaries or calendars may be very helpful in patient management and are available at very little or no cost to patients. As mentioned previously, these recommendations are time consuming to implement in the clinical setting and underserved populations with migraine may not be well positioned to receive them because of poor access to care or low educational levels.

The American Academy of Neurology Headache Quality Measure Set (AAN-HQMS) recommended guideline prophylactic medications for episodic

migraine: level A are divalproex/sodium valproate 400-1500mg/daily, topiramate 25-200mg, propranolol 80-240mg, metoprolol 47.5-200mg and timolol 10-15mg BID. Frovatriptan can be tried for short-term prophylaxis of menstrual related migraine (MRM).(26) Although frovatriptan has level A evidence for the prophylactic treatment of MRM, other triptans (e.g. zolmitriptan, sumatriptan, rizatriptan) have also been shown to be effective. A generic or lower cost triptan (e.g. naratriptan 1mg/d for six days, or zolmitriptan 2.5mg BID/TID for five days (level B), sumatriptan 25mg TID for five days) may provide an effective low cost alternative for the prophylaxis of MRM; however, such use often exhausts the monthly triptan allotment by insurance coverage including Medicaid.(28, 29)

Level B prophylactic recommendations include amitriptyline 25-150mg/daily, venlafaxine 75-225mg, atenolol 100mg daily, nadolol, NSAIDs (fenoprofen 200-600mg, ibuprofen 200mg BID, ketoprofen 50mg TID, naproxen 250-500mg daily, naproxen sodium 550mg BID) histamine 1-10ng subcutaneously twice a week and bisoprolol 5-10mg daily. (26) NSAIDs may have a protective effect when used 5-10 days per month, however taken ≥10 days per month, NSAIDs may increase the risk of medication overuse headache.(4, 26) State-specific Medicaid program websites can be helpful for identifying low cost, coverage status and other useful information about high quality prophylactic medications for underinsured within individual states.(26, 30, 31) (See Table 3)

#### Natural supplements/Nutraceuticals:

Several supplements are used to reduce the frequency and associated symptoms of migraine. Some of these may be prescribed and others purchased over the counter. Evidenced-based guidelines rate magnesium, riboflavin and feverfew as probably effective while co-enzyme Q10 is rated as possibly effective. (30) Petasites, or Butterbur, has been rated as effective, however there is current controversy over its safety. It is often falsely believed that natural supplements are without side effects, however, this is not always the case and requires counseling to patients in the same manner as prescription preventive therapies. We will explore some of the uses as well as potential adverse effects of natural supplement use in migraine.

Magnesium may be particularly effective for patients with migraine aura and those with menstrual migraines.(29, 32-34) Different formulations exist but the chelated forms are better tolerated. Magnesium citrate has been shown to be more bioavailable than magnesium oxide (35). Magnesium glycinate also appears to be highly bioavailable. The recommended doses are 400 to 600 mg daily depending on tolerability.(36, 37) Side effects include softening of stool or diarrhea.

Several studies support use of riboflavin (vitamin B2) for migraine prevention. The recommended doses are up to 400 mg a day in adults. Side effects include bright yellow discoloration of the urine, frequent urination and less commonly diarrhea.(38)

Although preparations of feverfew vary widely, MIG-99, a specific feverfew CO2-extract, has been shown to be safe and effective at 6.25mg TID. Side effects may include gastrointestinal upset, mouth ulcers and a "post-feverfew syndrome of joint aches". (39, 40)Dosing of co-enzyme Q10 for adults is 300 mg once a day. Side effects, although appearing rarely, can include gastrointestinal upset and skin allergies.(41, 42)

Although the level of evidence varies, other natural supplements such a thioctic acid 600mg/day (for migraine prophylaxis), vitamin E 400IU for 5 days (for menstrual migraine prophylaxis), and ginko biloba (for prophylaxis of migraine aura) may be helpful in migraine and its associated symptoms in select populations. (43-47)

Cost may also be a concern with supplements since they are not generally covered by insurers. For example, Co-enzyme Q10 and Butterbur can be costly. However, magnesium, riboflavin and feverfew are readily purchased in a health food store or pharmacy and are relatively inexpensive. Vitamin E use for menstrual or menstrual-related migraine as described above is also relatively inexpensive. Patients may be encouraged to browse online for the best value (price, quantity and quality). It is important to note that the US Food and Drug Administration does not regulate natural supplements.

#### **Chronic Migraine Prophylaxis**

Expert consensus supports the use of migraine preventive strategies considered effective for episodic migraine in chronic migraine. Topiramate has also been

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shown to be effective specifically for chronic migraine.(48) Topiramate is available in a generic form in the US. Currently, onabotulinumtoxinA is effective and the only US-FDA approved treatment for chronic migraine. (49-53) It has been shown to be cost-effective in patients with chronic migraine and may decrease ED utilization and hospitalizations. Treatment with onabotulinumtoxinA may result in overall health cost savings and increase quality of life for patients with chronic migraine. (54, 55) Although we have found this treatment to be partially covered in some Medicaid programs, the proportion that remains for patients to cover may be an expense that presents an economic barrier for patients to receive treatment. Insurance authorization and a step-wise approach are required for most insurances to limit cost despite the lack of evidence-based justification for this strategy. However, the reduction in headache-related health care utilization among adults with chronic migraine treated with onabtulinumtoxinA as compared to oral migraine prophylactic medications suggest a potential benefit from earlier initiation. (56) In addition, this therapy does not feature any concerns about adherence because of practitioner administration and the long therapeutic benefit over a 3 month period.

#### Devices:

Newer devices and products that have demonstrated some evidence for efficacy in headache disorders are emerging. Two devices have recently been FDA approved and have come to market for the care of migraine in the US; a transcutaneous supraorbital neurostimulation device, Cefaly®, and a single pulse

transcranial magnetic stimulator, SpringTMS®. (57-60) However their costs may be prohibitive in this population. The Cefaly device was the first FDA approved device for the prophylactic treatment of migraine and is now approved for acute attack treatment as well. However, this device and its accessories are not covered by most insurances and out-of-pocket cost are usually around \$375.00 USD. The SpringTMS® device has been FDA approved for the acute treatment of migraine with aura and for migraine prophylaxis.(61) The cost to rent this device is \$250.00 USD per month billed in 3 month increments and an initial shipping fee of \$50.00 USD. In our clinical practice, we have not found these costs to be routinely covered by insurances. To the authors' knowledge, neither device company currently have programs in place to help care for underinsured populations.

#### Low/Non-cost Non-pharmacological treatment modalities

Migraine may be best managed in a multi-modal fashion.(62, 63) In addition to medication, non-pharmacological approaches can be employed.(64) These modalities include lifestyle changes, stress management, use of heat or cold, and addressing migraine comorbidities that contribute to its chronification.(63, 65) Information about complementary treatments as well as methods for addressing these factors can be low-cost or free and include patient education as well as resources patients can access themselves. Finally, the

engagement of other health professionals can be useful in addressing the burden of migraine.(62)

Other Alternative treatments: Acutely, many patients find heat or cold packs, a hot shower or a combination of these beneficial in dampening down the pain of migraine or tension-type headache.(66) Some patients find topical treatments such as herbal balms with small amounts of menthol or camphor (one of the main components of *Tanacetum parthenium*) applied to the temples, forehead or base of the neck helpful.(67, 68) Inhalation of lavender essential oil for 15 minutes may be helpful for some patients with migraine. (69) Deep relaxation, diaphragmatic breathing and cognitive behavioral techniques to adapt behavioral responses to pain can also be useful. (70, 71) Mindfulness and meditation may also be helpful.(65, 72, 73) Teaching these techniques is simple and there are multiple online resources for downloadable exercises easily found via internet search engines (e.g. search term = "downloadable deep relaxation and breathing techniques"). Avoidance of migraine triggers is also recommended.(74) Trigger management apps, online educational resources and patient support organizations may be considered to supplement headache management. Most public libraries have computers and Internet services that can be readily accessed by patients who do not have computers or Internet access at home.

<u>Lifestyle and other health factors</u>: Chronification of migraine has been associated with stressful life events, medication overuse, obesity, sleep

disturbance, depression and caffeine overuse.(75, 76) Modifying these risk factors can be as important as medication initiatives and can directly improve patient outcomes. Additionally, sleep, diet, exercise and hydration all seem to play a role in migraine. Limited resources can be a barrier to addressing these but patient education and engagement of other health care professionals can be employed at low or no cost. Table 3 outlines many of these aspects and contains simple recommendations for the patient that can be readily integrated into patient care.

#### Other Conditions and Considerations:

Medication Overuse: Educating patients about medication overuse and its contribution to headache chronification should be considered a foundation for discussing acute treatments. Limiting acute treatments to 2-3 days per week or less can be the first step towards improving outcomes and will enhance the patient's response to preventatives.

<u>Depression</u>: Identification of depression historically has been time consuming leading to under diagnosis of this disorder.(77) However, a simple self-administered screening tool such as the PHQ-9 can be used to identify those with depression which may be useful in the management of underserved populations who have limited access to behavioral health professionals.(77) In addition to anti-depressant medications that can dovetail as headache prevention

agents, referral to a clinic social worker may provide the additional needed therapy at low or no cost.

Use of Other Healthcare Professionals: Primary care physicians most commonly treat patients with migraine, although universal awareness of migraine guidelines is lacking. (78) Patients should be referred to neurologists when migraine is refractory to treatments, associated with a high degree of disability, or have atypical symptoms. Referral to headache subspecialists or integrative headache care centers are often effective for chronic or treatment refractory migraine cases (62) but such specialists are often aggregated in selected geographic areas(79) or lacking in many states entirely(80). In a clinic setting, referrals to in-house healthcare professionals can be employed to reduce other comorbidities. Many Medicaid Clinics have a nutritionist consultation service. Using this resource can help patients in weight reduction and in learning healthy eating habits. Additionally, clinic social workers can help in addressing mood disorders, teach cognitive behavioral techniques and other coping strategies to deal with pain as well as to reduce stress. They also can be a referral source for help in other areas of the patient's life to reduce stress, such as city or state legal or housing resources and protective services (Table 4). Given that temporomandibular disorders (TMD) are comorbid with migraine and are a risk factor for migraine progression (81-88), it may be helpful if people with migraine and comorbid TMD are referred to a dentist trained in orofacial pain to manage the TMD aspect of the patient's pain.(86)

#### Adherence

Studies investigating adherence to migraine management are limited but increasing in recent years; it is a major topic of concern for the underserved with migraine. In reviewing the literature, description of adherence has been either vague or relied on self-report, and there has been no recommendation on how to improve adherence in patients with recurrent migraine. Ramsey et al. published a systematic review that showed overall compliance to treatment, including those considered non-pharmacological, ranged from 25-95%, but there is little demographic information that addresses or explains these differences.(89) One study showed no significant difference in medication compliance between African-American and Caucasian patients with migraine. (90) However, African-Americans and young patients were less likely to return for follow-up appointments. In the same study, socioeconomic status influenced adherence among Caucasians but not among African-Americans. There does appear to be specific management recommendations where patients are likely to be adherent, such as, once daily dosing over twice daily dosing(91) and the use of a multidisciplinary approach with frequent encounters between provider and patient. (92) Furthermore, those who practice regular aerobic exercise tend to adhere more than those who are instructed on healthy habits and practice relaxation techniques.(92) In general, adherence remains a concern for patients with migraine as those who adhere with consistent management, whether pharmaceutical, behavioral or lifestyle modification, tend to have overall

improvement of headache related outcomes (lower headache frequency and disability scores).(63, 93)

#### **Summary & General Approach to the Underserved Population:**

In summary, multiple barriers exist in providing optimal headache care to underinsured, uninsured and Medicaid populations. Greater awareness and a systematic approach may reduce the impact of the headache burden, which disproportionately afflicts underserved communities.

There are several options to optimize migraine care in adult patients who are uninsured or underinsured. This manuscript examines some potential non-opioid solutions to comprehensive care for underserved populations, however may not be all-inclusive. Although opioids and butalbital-containing compounds are often covered by Medicaid or offered at a very low cost for patients to receive, practitioners should avoid them as much as possible in this population. Opioid use for migraine is associated with more severe headache-related disability, symptomology, comorbidities (depression, anxiety, and cardiovascular disease and events) and greater need to see health care providers. (6) Opioids are not a substitute for a comprehensive headache treatment plan. Caution is also advised with the use of butalbital-containing medications as these combination medications can lead to medication overuse headache with only five days of use per month for three months.(94) Providers are encouraged to actively seek safer alternatives. Counseling, abortive therapies with limits,

prophylaxis and non-pharmacological modalities as appropriate may be the constituents of a comprehensive migraine treatment plan.

Finally, newer products demonstrating efficacy and safety in the treatment of migraine and other headache disorders are emerging, including for the first time biological therapies. Monoclonal antibodies to calcitonin gene-related peptide and its receptor appear to be a promising preventive treatment for migraine and chronic migraine(95, 96) and are likely to come to the market in 2018. In an analogous situation with another neurological disorder, the US has witnessed increased costs with disease-modifying therapies (DMT) for the treatment of multiple sclerosis. DMT costs have skyrocketed beyond inflation over the last several years and are currently 2 to 3 times higher in the US than in other comparable countries, generating concern within the neurology community. (97, 98) It is our hope that technological, pharmaceutical and other industries consider as well as implement plans to make their emerging headache therapies including biological drugs and devices accessible to underserved and underinsured populations.

#### **Limitations**

There are inherent limitations in this 2-part narrative review. The authors undertook this review because of the paucity of research on this particular topic and therefore may be subject to bias. This manuscript does not address all social determinants that are likely to play a role in the headache health of underserved and underinsured populations (e.g. cultural considerations,

environments/community, transportation, etc.). A multi-collaborative systematic approach may be needed to address these concerns of underserved and vulnerable populations. Although many of our recommendations are derived from recently published guidelines, some are not and the body of evidence varies. Quality headache care is needed for these vulnerable populations. In addition, telemedicine is becoming more widely used for neurological conditions and may be a mechanism to address barriers to care, provide medical consultation, and may provide cost-saving alternatives for underserved and underinsured populations in headache medicine.(99, 100)

More research is needed to explore mechanisms to improve quality care, decrease gaps in care, investigate low cost therapies, balance cost and policy with medical innovation, and address headache care inequities of underserved, vulnerable, underinsured and uninsured populations.

#### **Conclusion:**

Migraine is a common, undertreated, and underdiagnosed disorder which is even more prevalent and may have a worse course among those with a low socioeconomic status. Moreover, a number of individual, societal and healthcare barriers negatively influence underinsured and uninsured migraine sufferers.

Low socioeconomic status may play an important role in the disease progression, characteristics, outcome and quality of life of patients with migraine and other headache disorders. Research is needed to identify the best cost-effective measures for migraine management especially during this period of rapidly

changing healthcare policies and medical innovation. Although cost remains an issue, conscientious comprehensive headache treatment plans are valuable, available, and may be needed to improve patient outcomes in the underinsured and uninsured.

#### References:

- 1. Silberstein SD. Practice parameter: Evidence-based guidelines for migraine headache (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2000;55(6):754-62.
- 2. Diener HC, Dalhof CGH. Headache associated with chronic use of substances. In: Olesen J, Tfelt-Hansen P, Welch KMA, editors. The Headaches. 2nd ed. Philadelphia, PA: Lippincott, Williams and Wilkins; 1999. p. 671-878.
- 3. Ferrari A, Leone S, Vergoni AV, Bertolini A, Sances G, Coccia CPR, et al. Similarities and Differences Between Chronic Migraine and Episodic Migraine. Headache. 2007;47(1).
- 4. Bigal ME, Serrano D, Buse D, Scher A, Stewart WF, Lipton RB. Acute Migraine Medications and Evolution From Episodic to Chronic Migraine: A Longitudinal Population-Based Study. Headache: The Journal of Head and Face Pain. 2008;48(8):1157-68.
- 5. Marmura MJ, Silberstein SD, Schwedt TJ. The Acute Treatment of Migraine in Adults: The American Headache Society Evidence Assessment of Migraine Pharmacotherapies. Headache: The Journal of Head and Face Pain. 2015;55(1):3-20.
- 6. Buse DC, Pearlman SH, Reed ML, Serrano D, Ng-Mak DS, Lipton RB. Opioid use and dependence among persons with migraine: results of the AMPP study. Headache. 2012;52(1):18-36.
- 7. Weinrich SP, Boyd MD, Herman J. Tool adaptation to reduce health disparities. . In: Frank-Stromberg M, Olsen SJ, editors. Instruments for Clinical Health-care Research. 3rd ed. Sudbury, MA: Jones and Bartlett, Inc; 2004. p. 20-30.
- 8. Winter AC, Berger K, Buring JE, Kurth T. Associations of socioeconomic status with migraine and non-migraine headache. Cephalalgia. 2011;32(2):159-70.
- 9. Young N, Silverman D, Bradford H, Finkelstein J. Multicenter prevalence of opioid medication use as abortive therapy in the emergency department treatment of migraine headaches. Am J Emerg Med. 2017.
- 10. Minen MT, Lindberg K, Langford A, Loder E. Variation in Prescription Drug Coverage for Triptans: Analysis of Insurance Formularies. Headache. 2017;57(8):1243-51.
- II. Goldstein J, Hagen M, Gold M. Results of a multicenter, double-blind, randomized, parallel-group, placebo-controlled, single-dose study comparing the fixed combination of acetaminophen, acetylsalicylic acid, and caffeine with ibuprofen for acute treatment of patients with severe migraine. Cephalalgia. 2014;34(13):1070-8.
- 12. Ashkenazi A, Silberstein SD. The evolving management of migraine. Current Opinion in Neurology. 2003;16(3):341-5.
- 13. Schulman EA, Dermott KF. Sumatriptan Plus Metoclopramide in Triptan-Nonresponsive Migraineurs. Headache: The Journal of Head and Face Pain. 2003;43(7):729-33.
- 14. Bellville JW, Dorey F, Capparell D, Knox V, Bauer RO. Analgesic Effects of Hydroxyzine Compared to Morphine in Man. The Journal of Clinical Pharmacology. 1979;19(5-6):290-6.

- 15. Carleton SC, Shesser RF, Pietrzak MP, Chudnofsky CR, Starkman S, Morris D, et al. Double-Blind, Multicenter Trial to Compare the Efficacy of Intramuscular Dihydroergotamine Plus Hydroxyzine Versus Intramuscular Meperidine Plus Hydroxyzine for the Emergency Department Treatment of Acute Migraine Headache. Annals of Emergency Medicine. 1998;32(2):129–38.
- 16. Friedman BW, Cabral L, Adewunmi V, Solorzano C, Esses D, Bijur PE, et al. Diphenhydramine as Adjuvant Therapy for Acute Migraine: An Emergency Department-Based Randomized Clinical Trial. Ann Emerg Med. 2016;67(1):32-9 e3.
- 17. Friedman BW, Cisewski DH, Holden L, Bijur PE, Gallagher EJ. Age But Not Sex Is Associated With Efficacy and Adverse Events Following Administration of Intravenous Migraine Medication: An Analysis of a Clinical Trial Database. Headache. 2015;55(10):1342-55.
- 18. Friedman BW, Hochberg M, Esses D, Bijur PE, Corbo J, Paternoster J, et al. A clinical trial of trimethobenzamide/diphenhydramine versus sumatriptan for acute migraines. Headache. 2006;46(6):934-41.
- 19. Kostic MA, Gutierrez FJ, Rieg TS, Moore TS, Gendron RT. A prospective, randomized trial of intravenous prochlorperazine versus subcutaneous sumatriptan in acute migraine therapy in the emergency department. Ann Emerg Med. 2010;56(1):1-6.
- 20. Swidan SZ, Lake AE, 3rd, Saper JR. Efficacy of intravenous diphenhydramine versus intravenous DHE-45 in the treatment of severe migraine headache. Curr Pain Headache Rep. 2005;9(1):65-70.
- 21. Friedman BW, Irizarry E, Solorzano C, Latev A, Rosa K, Zias E, et al. Randomized study of IV prochlorperazine plus diphenhydramine vs IV hydromorphone for migraine. Neurology. 2017.
- 22. Freitag FG. Preventative Treatment for Migraine and Tension-Type Headaches. CNS Drugs. 2003;17(6):373-81.
- 23. Fromm GH. Baclofen as an adjuvant analgesic. Journal of Pain and Symptom Management. 1994;9(8):500-9.
- 24. Hering-Hanit R. Baclofen for prevention of migraine. Cephalalgia. 1999;19(6):589-92.
- 25. Charleston IV L, Burke JF. Do racial/ethnic disparities exist in recommended migraine treatments in US ambulatory care? Cephalalgia. 2017;333102417716933.
- 26. American Academy Of Neurology. Headache Quality Measurement Set. [Accessed January 15, 2015]. Available from:
- https://www.aan.com/uploadedFiles/Website Library Assets/Documents/3.Practice Management/2. Quality Improvement/1.Quality Measures/1.All Measures/2014%209%20%208%20REVISED%20AA N%20Headache%20Measurement%20Set.pdf
- 27. Lipton RB, Bigal ME, Diamond M, Freitag F, Reed ML, Stewart WF, et al. Migraine prevalence, disease burden, and the need for preventive therapy. Neurology. 2007;68(5):343-9.
- 28. Nierenburg Hdel C, Ailani J, Malloy M, Siavoshi S, Hu NN, Yusuf N. Systematic Review of Preventive and Acute Treatment of Menstrual Migraine. Headache. 2015;55(8):1052-71.
- 29. Maasumi K, Tepper SJ, Kriegler JS. Menstrual Migraine and Treatment Options: Review. Headache. 2017;57(2):194-208.
- 30. Holland S, Silberstein SD, Freitag F, Dodick DW, Argoff C, Ashman E. Evidence-based guideline update: NSAIDs and other complementary treatments for episodic migraine prevention in adults: Report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. Neurology. 2012;78(17):1346-53.
- 31. Nebraska Medicaid: Magellan Medicaid Administration, Inc; [Drug Lookup-Search]. Available from:
- https://druglookup.fhsc.com/druglookupweb/pages/unsecured/druglookup/drugSearch.jsf.
- 32. Facchinetti F, Sances G, Borella P, Genazzani AR, Nappi G. Magnesium prophylaxis of menstrual migraine: effects on intracellular magnesium. Headache. 1991;31(5):298-301.

- 33. Chiu HY, Yeh TH, Huang YC, Chen PY. Effects of Intravenous and Oral Magnesium on Reducing Migraine: A Meta-analysis of Randomized Controlled Trials. Pain Physician. 2016;19(1):E97-112.
- 34. Bigal ME, Bordini CA, Tepper SJ, Speciali JG. Intravenous magnesium sulphate in the acute treatment of migraine without aura and migraine with aura. A randomized, double-blind, placebo-controlled study. Cephalalgia. 2002;22(5):345-53.
- 35. Lindberg JS, Zobitz MM, Poindexter JR, Pak CY. Magnesium bioavailability from magnesium citrate and magnesium oxide. J Am Coll Nutr. 1990;9(1):48-55.
- 36. Pfaffenrath V, Wessely P, Meyer C, Isler HR, Evers S, Grotemeyer KH, et al. Magnesium in the prophylaxis of migraine—a double-blind placebo-controlled study. Cephalalgia. 1996;16(6):436-40.
- 37. Koseoglu E, Talaslioglu A, Gonul AS, Kula M. The effects of magnesium prophylaxis in migraine without aura. Magnes Res. 2008;21(2):101-8.
- 38. Schoenen J, Jacquy J, Lenaerts M. Effectiveness of high-dose riboflavin in migraine prophylaxis. A randomized controlled trial. Neurology. 1998;50(2):466-70.
- 39. Diener HC, Pfaffenrath V, Schnitker J, Friede M, Henneicke-von Zepelin HH. Efficacy and safety of 6.25 mg t.i.d. feverfew CO2-extract (MIG-99) in migraine prevention a randomized, double-blind, multicentre, placebo-controlled study. Cephalalgia. 2005;25(11):1031-41.
- 40. Pfaffenrath V, Diener HC, Fischer M, Friede M, Henneicke-von Zepelin HH, Investigators. The efficacy and safety of Tanacetum parthenium (feverfew) in migraine prophylaxis--a double-blind, multicentre, randomized placebo-controlled dose-response study. Cephalalgia. 2002;22(7):523-32.
- 41. Rozen TD, Oshinsky ML, Gebeline CA, Bradley KC, Young WB, Shechter AL, et al. Open label trial of coenzyme Q10 as a migraine preventive. Cephalalgia. 2002;22(2):137-41.
- 42. Hershey AD, Powers SW, Vockell AL, Lecates SL, Ellinor PL, Segers A, et al. Coenzyme Q10 deficiency and response to supplementation in pediatric and adolescent migraine. Headache. 2007;47(1):73-80.
- 43. Charleston L, Holland S, Silberstein SD, Freitag F, Dodick DW, Argoff C. Evidence-based guideline update: NSAIDs and other complementary treatments for episodic migraine prevention in adults: Report of the quality standards subcommittee of the American Academy of Neurology and the American Headache Society. Neurology. 2012;79(12):1301-2.
- 44. Magis D, Ambrosini A, Sandor P, Jacquy J, Laloux P, Schoenen J. A randomized double-blind placebo-controlled trial of thioctic acid in migraine prophylaxis. Headache. 2007;47(1):52-7.
- 45. Ziaei S, Kazemnejad A, Sedighi A. The effect of vitamin E on the treatment of menstrual migraine. Med Sci Monit. 2009;15(1):CR16-9.
- 46. Allais G, D'Andrea G, Maggio M, Benedetto C. The efficacy of ginkgolide B in the acute treatment of migraine aura: an open preliminary trial. Neurol Sci. 2013;34 Suppl 1:S161-3.
- 47. D'Andrea G, Bussone G, Allais G, Aguggia M, D'Onofrio F, Maggio M, et al. Efficacy of Ginkgolide B in the prophylaxis of migraine with aura. Neurol Sci. 2009;30 Suppl 1:S121-4.
- 48. Diener HC, Bussone G, Van Oene JC, Lahaye M, Schwalen S, Goadsby PJ, et al. Topiramate reduces headache days in chronic migraine: a randomized, double-blind, placebocontrolled study. Cephalalgia. 2007;27(7):814-23.
- 49. Silberstein SD, Dodick DW, Aurora SK, Diener HC, DeGryse RE, Lipton RB, et al. Per cent of patients with chronic migraine who responded per onabotulinumtoxinA treatment cycle: PREEMPT. J Neurol Neurosurg Psychiatry. 2015;86(9):996-1001.
- 50. Aurora SK, Winner P, Freeman MC, Spierings EL, Heiring JO, DeGryse RE, et al. OnabotulinumtoxinA for treatment of chronic migraine: pooled analyses of the 56-week PREEMPT clinical program. Headache. 2011;51(9):1358-73.
- 51. Diener HC, Dodick DW, Aurora SK, Turkel CC, DeGryse RE, Lipton RB, et al. OnabotulinumtoxinA for treatment of chronic migraine: results from the double-blind, randomized, placebo-controlled phase of the PREEMPT 2 trial. Cephalalgia. 2010;30(7):804-14.

52. Aurora SK, Dodick DW, Turkel CC, DeGryse RE, Silberstein SD, Lipton RB, et al. OnabotulinumtoxinA for treatment of chronic migraine: results from the double-blind, randomized, placebo-controlled phase of the PREEMPT 1 trial. Cephalalgia. 2010;30(7):793-803. 53. Dodick DW, Turkel CC, DeGryse RE, Aurora SK, Silberstein SD, Lipton RB, et al. OnabotulinumtoxinA for treatment of chronic migraine: pooled results from the double-blind, randomized, placebo-controlled phases of the PREEMPT clinical program. Headache. 2010;50(6):921-36.

- 54. Batty AJ, Hansen RN, Bloudek LM, Varon SF, Hayward EJ, Pennington BW, et al. The cost-effectiveness of onabotulinumtoxinA for the prophylaxis of headache in adults with chronic migraine in the UK. J Med Econ. 2013;16(7):877-87.
- 55. Rothrock JF, Bloudek LM, Houle TT, Andress-Rothrock D, Varon SF. Real-world economic impact of onabotulinumtoxinA in patients with chronic migraine. Headache. 2014;54(10):1565-73.
- 56. Hepp Z, Rosen NL, Gillard PG, Varon SF, Mathew N, Dodick DW. Comparative effectiveness of onabotulinumtoxinA versus oral migraine prophylactic medications on headacherelated resource utilization in the management of chronic migraine: Retrospective analysis of a US-based insurance claims database. Cephalalgia. 2016;36(9):862-74.
- 57. Diener HC, Charles A, Goadsby PJ, Holle D. New therapeutic approaches for the prevention and treatment of migraine. Lancet Neurol. 2015;14(10):1010-22.
- 58. Lipton RB, Dodick DW, Silberstein SD, Saper JR, Aurora SK, Pearlman SH, et al. Single-pulse transcranial magnetic stimulation for acute treatment of migraine with aura: a randomised, double-blind, parallel-group, sham-controlled trial. Lancet Neurol. 2010;9(4):373-80.
- 59. Magis D, Sava S, d'Elia TS, Baschi R, Schoenen J. Safety and patients' satisfaction of transcutaneous supraorbital neurostimulation (tSNS) with the Cefaly(R) device in headache treatment: a survey of 2,313 headache sufferers in the general population. J Headache Pain. 2013;14:95.
- 60. Schoenen J, Vandersmissen B, Jeangette S, Herroelen L, Vandenheede M, Gerard P, et al. Migraine prevention with a supraorbital transcutaneous stimulator: a randomized controlled trial. Neurology. 2013;80(8):697-704.
- 61. More Information on eNeura SpringTMS migraine treatment device [Available from: <a href="http://www.eneura.com/Clinical%20papers/LBL">http://www.eneura.com/Clinical%20papers/LBL</a> 0085 REVD.pdf.
- 62. Diener HC, Gaul C, Jensen R, Gobel H, Heinze A, Silberstein SD. Integrated headache care. Cephalalgia. 2011;31(9):1039-47.
- 63. Lemstra M, Stewart B, Olszynski WP. Effectiveness of multidisciplinary intervention in the treatment of migraine: a randomized clinical trial. Headache. 2002;42(9):845-54.
- 64. Probyn K, Bowers H, Mistry D, Caldwell F, Underwood M, Patel S, et al. Non-pharmacological self-management for people living with migraine or tension-type headache: a systematic review including analysis of intervention components. BMJ Open. 2017;7(8):e016670.
- 65. Wells RE, Burch R, Paulsen RH, Wayne PM, Houle TT, Loder E. Meditation for migraines: a pilot randomized controlled trial. Headache. 2014;54(9):1484-95.
- 66. Sprouse-Blum AS, Gabriel AK, Brown JP, Yee MH. Randomized controlled trial: targeted neck cooling in the treatment of the migraine patient. Hawaii J Med Public Health. 2013;72(7):237-41.
- 67. Dussor G, Cao YQ. TRPM8 and Migraine. Headache. 2016;56(9):1406-17.
- 68. Vegh K, Riethmuller E, Toth A, Alberti A, Beni S, Balla J, et al. Convergence chromatographic determination of camphor in the essential oil of Tanacetum parthenium L. Biomed Chromatogr. 2016;30(12):2031-7.
- 69. Sasannejad P, Saeedi M, Shoeibi A, Gorji A, Abbasi M, Foroughipour M. Lavender essential oil in the treatment of migraine headache: a placebo-controlled clinical trial. Eur Neurol. 2012;67(5):288-91.

- 70. Andrasik F, Buse DC, Grazzi L. Behavioral medicine for migraine and medication overuse headache. Curr Pain Headache Rep. 2009;13(3):241-8.
- 71. D'Souza PJ, Lumley MA, Kraft CA, Dooley JA. Relaxation training and written emotional disclosure for tension or migraine headaches: a randomized, controlled trial. Ann Behav Med. 2008;36(1):21-32.
- 72. Grazzi L, Sansone E, Raggi A, D'Amico D, De Giorgio A, Leonardi M, et al. Mindfulness and pharmacological prophylaxis after withdrawal from medication overuse in patients with Chronic Migraine: an effectiveness trial with a one-year follow-up. J Headache Pain. 2017;18(1):15.
- 73. Bakhshani NM, Amirani A, Amirifard H, Shahrakipoor M. The Effectiveness of Mindfulness-Based Stress Reduction on Perceived Pain Intensity and Quality of Life in Patients With Chronic Headache. Glob J Health Sci. 2015;8(4):142-51.
- 74. Pryse-Phillips WE, Dodick DW, Edmeads JG, Gawel MJ, Nelson RF, Purdy RA, et al. Guidelines for the nonpharmacologic management of migraine in clinical practice. Canadian Headache Society. CMAJ. 1998;159(1):47-54.
- 75. Bigal ME, Lipton RB. Modifiable risk factors for migraine progression. Headache. 2006;46(9):1334-43.
- 76. Bigal ME, Lipton RB. Migraine Chronification. Current Neurology and Neuroscience Reports. 2011;11(2):139-48.
- 77. Kroenke K, Spitzer RL, Williams JBW. The PHQ-9. J Gen Intern Med. 2001;16(9):606-13.
- 78. Minen MT, Loder E, Tishler L, Silbersweig D. Migraine diagnosis and treatment: A knowledge and needs assessment among primary care providers. Cephalalgia. 2016;36(4):358-70.
- 79. Rizzoli P, Weizenbaum E, Loder T, Friedman D, Loder E. The evolution and geographic distribution of headache medicine fellowship programs and graduates: an observational study. Headache. 2014;54(10):1591-600.
- 80. Mauser ED, Rosen NL. So many migraines, so few subspecialists: analysis of the geographic location of United Council for Neurologic Subspecialities (UCNS) certified headache subspecialists compared to United States headache demographics. Headache. 2014;54(8):1347-57.
- 81. Goncalves DAG, Bigal ME, Jales LCF, Camparis CM, Speciali JG. Headache and Symptoms of Temporomandibular Disorder: An Epidemiological Study. Headache. 2010;50(2):231-41.
- 82. Grossi DB, Lipton RB, Bigal ME. Temporomandibular disorders and migraine chronification. Curr Pain Headache R. 2009;13(4):314-8.
- 83. Plesh O, Noonan C, Buchwald DS, Goldberg J, Afari N. Temporomandibular Disorder-Type Pain and Migraine Headache in Women: A Preliminary Twin Study. J Orofac Pain. 2012;26(2):91-8.
- 84. Stuginski-Barbosa J, Macedo HR, Bigal ME, Speciali JG. Signs of Temporomandibular Disorders in Migraine Patients: A Prospective, Controlled Study. Clin J Pain. 2010;26(5):418-21.
- 85. Franco AL, Goncalves DAG, Castanharo SM, Speciali JG, Bigal ME, Camparis CM. Migraine is the Most Prevalent Primary Headache in Individuals with Temporomandibular Disorders. J Orofac Pain. 2010;24(3):287-92.
- 86. Goncalves DAG, Camparis CM, Speciali JG, Castanharo SM, Ujikawa LT, Lipton RB, et al. Treatment of Comorbid Migraine and Temporomandibular Disorders: A Factorial, Double-Blind, Randomized, Placebo-Controlled Study. J Orofac Pain. 2013;27(4):325-35.
- 87. Goncalves DAG, Camparis CM, Speciali JG, Franco AL, Castanharo SM, Bigal ME. Temporomandibular Disorders Are Differentially Associated With Headache Diagnoses A Controlled Study. Clin J Pain. 2011;27(7):611-5.
- 88. Goncalves DAG, Speciali JG, Jales LCF, Camparis CM, Bigal ME. Temporomandibular Symptoms, Migraine, and Chronic Daily Headaches in the Population. Neurology. 2009;73(8):645-6.
- 89. Ramsey RR, Ryan JL, Hershey AD, Powers SW, Aylward BS, Hommel KA. Treatment adherence in patients with headache: a systematic review. Headache. 2014;54(5):795-816.

90. Heckman BD, Ellis G. Preventive medication adherence in African American and Caucasian headache patients. Headache. 2011;51(4):520-32.

91. Kroon Van Diest AM, Ramsey R, Aylward B, Kroner JW, Sullivan SM, Nause K, et al. Adherence to Biobehavioral Recommendations in Pediatric Migraine as Measured by Electronic Monitoring: The Adherence in Migraine (AIM) Study. Headache. 2016;56(7):1137-46.

92. Gaul C, van Doorn C, Webering N, Dlugaj M, Katsarava Z, Diener HC, et al. Clinical outcome of a headache-specific multidisciplinary treatment program and adherence to treatment recommendations in a tertiary headache center: an observational study. J Headache Pain. 2011;12(4):475-83.

93. Katic BJ, Rajagopalan S, Ho TW, Chen YT, Hu XH. Triptan persistency among newly initiated users in a pharmacy claims database. Cephalalgia. 2011;31(4):488-500.

94. Bigal ME, Lipton RB. Excessive acute migraine medication use and migraine progression. Neurology. 2008;71(22):1821-8.

95. Tso AR, Goadsby PJ. Anti-CGRP Monoclonal Antibodies: the Next Era of Migraine Prevention? Curr Treat Options Neurol. 2017;19(8):27.

96. Schuster NM, Rapoport AM. Calcitonin Gene-Related Peptide-Targeted Therapies for Migraine and Cluster Headache: A Review. Clin Neuropharmacol. 2017;40(4):169-74.

97. Hartung DM, Bourdette DN, Ahmed SM, Whitham RH. The cost of multiple sclerosis drugs in the US and the pharmaceutical industry: Too big to fail? Neurology. 2015;84(21):2185-92.

98. Murray TJ, Brown MG. Escalating MS drug costs in the US: Puzzling, troubling, and suspicious. Neurology. 2015;84(21):2105-6.

99. Larner AJ. Teleneurology: an overview of current status. Pract Neurol. 2011;11(5):283-8.

100. Muller KI, Alstadhaug KB, Bekkelund SI. Acceptability, Feasibility, and Cost of Telemedicine for Nonacute Headaches: A Randomized Study Comparing Video and Traditional Consultations. J Med Internet Res. 2016;18(5):e140.

101. Addicott MA, Yang LL, Peiffer AM, Burnett LR, Burdette JH, Chen MY, et al. The effect of daily caffeine use on cerebral blood flow: How much caffeine can we tolerate? Hum Brain Mapp. 2009;30(10):3102-14.

102. Bigal ME, Rapoport AM, Sheftell FD, Tepper SJ, Lipton RB. Transformed migraine and medication overuse in a tertiary headache centre--clinical characteristics and treatment outcomes. Cephalalgia. 2004;24(6):483-90.

103. Breslau N, Lipton RB, Stewart WF, Schultz LR, Welch KM. Comorbidity of migraine and depression: investigating potential etiology and prognosis. Neurology. 2003;60(8):1308-12.

104. Rasmussen BK. Migraine and tension-type headache in a general population: precipitating factors, female hormones, sleep pattern and relation to lifestyle. Pain. 1993;53(1):65-72.

105. Scher Al, Stewart WF, Ricci JA, Lipton RB. Factors associated with the onset and remission of chronic daily headache in a population-based study. Pain. 2003;106(1-2):81-9.

106. Varkey E, Cider A, Carlsson J, Linde M. A study to evaluate the feasibility of an aerobic exercise program in patients with migraine. Headache. 2009;49(4):563-70.

107. Wöber C, Wöber-Bingöl Ç. Triggers of migraine and tension-type headache. Handbook of Clinical Neurology: Elsevier BV; 2010. p. 161-72.

108. Guidetti V. Sleep and headaches. In: Wuidetti V, Sillanpaa M, Russell G, Winner P, editors. Headache and migraine in childhood and adolescence. London: Martin Dunitz; 2002. p. 417-31.

109. C.C. B, Estemalik E. Preventative Treatment of Episodic Migraine. In: Tepper SJ, Tepper DE, editors. The Cleveland Clinic Manual of Headache Therapy 2nd ed: Springer; 2014. p. 161-78.

Table 1: 2000 AAN Practice Parameter: Acute treatment goals (1)

- 1. Treat attacks rapidly and consistently without recurrence.
- 2. Restore the patient's ability to function.
- 3. Minimize the use of back-up and rescue medicines.
- 4. Optimize self-care and reduce subsequent use of resources.
- 5. Be cost effective for overall management.
- 6. Have minimal or no adverse events.

Table 2:

Acute Medications for Migraine Covered by Nebraska Medicaid (1, 5, 16, 26, 30, 31))

Acute Medication	Formulation/strength		Prior	Medicaid State
		Preferred	Authorization	Maximum
		Drug	required	Allowable cost
Level A/Group 1				
1buprofen	600,	preferred		\$0.04821
	800 mg tab			\$0.05695
Naproxen	375,	preferred		\$0.05360
	500 Mg tab			\$0.06499
Diclofenac	50 mg tab	preferred		\$0.27500
Diclofenac	50 mg powder pack	Non-	PA required	N/A
C	50	preferred		¢0.00402
Sumatriptan	50,	preferred		\$0.69182
71	100 mg tab	C 1		\$0.71020
Rizatriptan	5,	preferred		\$0.96033
	10 mg tab			\$1.26038
Rizatriptan	5,			\$1.56000
	10 mg ODT	preferred		\$1.75647
Level B/Group II				
Flurbiprofen	50,	preferred		
	100 mg tabs			\$0.43027
Ketoprofen	50,	Non-		\$0.38605
	75 mg tab	preferred		\$0.49982
Codeine/APAP	30/300 mg tab	preferred		\$0.50960
Promethazine	25 mg suppository	preferred		\$8.74317

Headache

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Uncategorized				
Baclofen	10 mg tab	preferred		\$0.20932
Prednisone	10,	Preferred		\$0.15689
	20 mg tab			\$0.18760
Dexamethasone	4 mg tab	N/A	N/A	N/A
Prochlorperazine	5,	preferred		\$0.06700
	10 mg tab			\$0.07370
Metoclopramide	10 mg tab	preferred		\$0.04020
Haloperidol	1, 2, 5 mg tab	preferred		\$0.38860, \$0.54873,
				\$0.83951
Promethazine	25 mg tab	preferred		\$7.30639

https://druglookup.fhsc.com/



High Quality (Level A or B) Prophylactic Medications for Migraine Covered by Nebraska's Medicaid(26, 30, 31)

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Prophylactic Medications	Formulation/Strength	Preferred Drug	Prior Authorization	Medicaid State Maximum
			Required	Allowable Cost
Level A				
DIVALPROEX	250MG TAB	N/A	N/A	\$0.09380
SODIUM				
TOPIRAMATE	25 MG TABLET	Preferred	N/A	\$0.03815
PROPRANOLOL	80MG TAB	Preferred	N/A	\$0.50649
METOPROLOL	50 MG TAB	Preferred	N/A	\$0.37520
SUCC ER				
TIMOLOL	10 MG TABLET	Non-preferred	N/A	N/A
MALEATE				
BISOPROLOL	5 MG TAB	Non-preferred	PA required	\$0.44533
FUMARATE				
Level B				
AMITRIPTYLINE	25 MG TAB	N/A	N/A	\$0.32160
HCL				
VENLAFAXINE	75 MG TABLET	Preferred	N/A	\$0.25366
HCL				
ATENOLOL	100 MG TABLET	Preferred	N/A	\$0.03279
NADOLOL	40 MG TABLET	Non-preferred	PA required	\$2.21100
IBUPROFEN	200 MG CAPLET	Preferred	N/A	\$0.02500



KETOPROFEN	50 MG CAPSULE	Non-Preferred	PA required	\$0.38605
NAPROXEN	250 MG TABLET	Preferred	N/A	\$0.04020
NAPROXEN	550 MG TAB	Non-Preferred	PA required	\$2.12179
SODIUM				

Table 4:

#### Low cost behavioral and lifestyle recommendations for headache

#### management

		I
Lifestyle Factor	Recommendation	References (101-109)
Hydration	Drink 6-8 cups of water a day	Wöber, Christian, and Çiçek Wöber-Bingöl. "Triggers of Migraine and Tension-type Headache." <i>Handbook of</i> <i>Clinical Neurology Headache</i> (2010): 161-72.
Sleep	Encourage good sleep hygiene and a regular waking time daily	Rasmussen BK. Migraine and tension-type headache in a general population: precipitating factors, hormones, sleep patterns and relation to lifestyle. Pain April 1993. Vol 53(1):65-72. (Guidetti V. Sleep and headaches. In: Wuidetti V, Sillanpaa M, Russell G, Winner P, eds. Headache and migraine in childhood and adolescence. London: Martin Dunitz 2002:417-31.)
Caffeine	Limit caffeine to 8oz a day	Tepper, Stewart J., and Deborah E. Tepper. "Preventative Treatment of Episodic Migraine." The Cleveland Clinic Manual of Headache Therapy (2014): 161-78.  Addicott, Merideth A. et al. "The Effect of Daily Caffeine Use on Cerebral Blood Flow: How Much Caffeine Can We Tolerate?" Human brain mapping 30.10 (2009): 3102–3114. PMC.
Exercise	Regular exercise of at least 3 times a week for 20 minutes or more. Free or low-cost gyms are in many cities and towns. Online exercise programs are also available.	Varkey, Emma, Asa Cider, Jane Carlsson, and Mattias Linde. "A Study to Evaluate the Feasibility of an Aerobic Exercise Program in Patients With Migraine."

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		Headache: The Journal of Head and Face Pain 49.4 (2009): 563- 70.
Diet	Eat meals on regular basis. Don't skip meals. Avoid processed foods. Avoid their known triggers. Refer to nutritionist for help in weight loss.	A. I. Scher, W. F. Stewart, J. A. Ricci, and R. B. Lipton, "Factors associated with the onset and remission of chronic daily headache in a population-based study," Pain, vol. 106, no. 1-2, pp. 81–89, 2003.
Stress Reduction	Encourage enhancing activities ranging from exercise/sports to meditation and mindfulness. Cognitive Behavioral Techniques can also be useful. Online resources exist. Referral to clinic social worker.	Breslau, N., R. B. Lipton, W. F. Stewart, L. R. Schultz, and K. M.a. Welch. "Comorbidity of Migraine and Depression: Investigating Potential Etiology and Prognosis." Neurology 60.8 (2003): 1308-312.
Medication Overuse	Discuss limits on acute treatments to no more than 2-3 days a week.	Bigal, ME, AM Rapoport, FD Sheftell, SJ Tepper, and RB Lipton. "Transformed Migraine and Medication Overuse in a Tertiary Headache Centre - Clinical Characteristics and Treatment Outcomes." Cephalalgia 24.6 (2004): 483- 90.

#### **Headache** Author Declaration Form

#### Statement of Authorship

Thank you for your submission to *Headache - the journal of head and face pain*. The Journal now conforms to guidelines regarding transparency of authorship as outlined in the Uniform Requirements for Manuscripts Submitted to Biomedical Journals: Writing and Editing for Biomedical Publication produced by the International Committee of Medical Journal Editors.

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uninsured and under-insured adults: A narrative review

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Please list names of authors who have participated in each category:

Category 1:

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