



Published in final edited form as:

Headache. 2019 February ; 59(2): 289–297. doi:10.1111/head.13438.

## Cognitive Behavioral Therapy for Pediatric Headache and Migraine: Why to Prescribe and What New Research is Critical for Advancing Integrated Biobehavioral Care

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### Abstract

**Purpose of Review:** To highlight current evidence supporting the prescription of cognitive behavioral therapy (CBT) as part of first-line preventive treatment for children and adolescents with headache and discuss a research strategy aimed at: 1. understanding how and why CBT works, and 2. developing effective and efficient approaches for integrating CBT into headache specialty, neurology, and primary care settings.

**Recent Findings:** Although preventive medications for pediatric headache and migraine are commonly prescribed, recent meta-analyses and an NIH-funded, multi-center clinical trial suggest that the effect of pill-taking therapies may be mostly due to a placebo effect. These findings have led to greater consideration of prescription of non-pharmacological therapies as first-line interventions (either alone or in combination with pill-based therapy). A literature that extends back to the 1980's and includes recent clinical trials and meta-analyses demonstrates that CBT decreases headache frequency and related disability in youth with headache and migraine and has a favorable benefit to risk profile with almost no negative side effects.

**Summary:** CBT has been repeatedly demonstrated as effective in treating pediatric headache and migraine. As such, it should be considered as part of first-line preventive treatment for pediatric headache (either alone or in combination with a pill-based therapy). We need to better understand how this therapy works and what makes it distinct (if anything) from the placebo effect. What we need to achieve is empirical support for efficient access to this evidence-based treatment and

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Conflict of Interest Statement: Dr. Powers receives support for research from the National Institutes of Health, Migraine Research Foundation, and National Headache Foundation.

clarity on how to match the intensity of non-pharmacological intervention to the needs of our patients at the time they present for care.

### Keywords

migraine prevention; psychological interventions; evidence-based care; children; adolescents; pain; placebo effect

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## Introduction

Headache and migraine are prevalent chronic health conditions among youth,<sup>1-3</sup> with migraine itself affecting approximately 10 percent of school-aged children and adolescents<sup>4</sup> and up to 1 in 4 young women.<sup>5</sup> Headache commonly leads to significant functional disability in home, school, and social settings for affected youth, including frequently missing days of school or functioning at less than half of typical productivity while at school due specifically to headache.<sup>6,7</sup> Onset of headache and migraine typically occurs in early to mid-adolescence,<sup>8</sup> with the majority of affected children and adolescents continuing to experience headache well into adulthood.<sup>5</sup> Given the significant disability and recurrent trajectory associated with pediatric onset headache disorders, it is imperative to understand treatments that are effective for treating headache and migraine among youth. As such, the current review presents evidence of treatments that have demonstrated effectiveness for management of pediatric headache and migraine and discusses critical new research to advance understanding of and access to biobehavioral care.

## The current state of evidence for prescription preventive medication therapy

Preventive medications are often recommended and prescribed by headache specialists as first-line treatments for recurrent headache and migraine (i.e., occurring twice a week or more) in children and adolescents.<sup>9-12</sup> Practice decisions are primarily influenced by inferring findings from adult migraine trials to children and adolescents. Several medications are commonly used for prevention in youth, including antidepressants (e.g., amitriptyline) and antiepileptics (e.g., topiramate).<sup>12,13</sup> The only FDA approved medicine for headache prevention in adolescents 12 to 17 years of age is topiramate; no medicines are approved for use under age 12. Flunarizine, a drug not available in the United States, was described in a American Academy of Neurology practice parameter statement from 2004 as probably effective for migraine prevention in youth > 12 years of age.<sup>14</sup>

Recent reviews and meta-analyses raise concerns about the evidence base supporting prescription medications in youth with headache and migraine.<sup>13,15</sup> Specifically, a 2017 meta-analysis of the four available randomized clinical trials of topiramate aggregated 465 participants (329 receiving topiramate and 136 placebo pill).<sup>16</sup> Compared to placebo, the medicine did not lead to a decrease in headache days (measured both as absolute reduction in days with headache as well as proportion with a relative reduction in headache days of 50% or greater). The analysis did suggest that disability, as measured by the pediatric migraine disability scale (PedMIDAS), was reduced more by topiramate than placebo pill.

Disability was only measured in 2 of the 4 randomized trials, and a total of 205 participants were available for the analyses. Another meta-analysis was conducted in 2013 and included 21 trials of pharmacologic preventive treatment for pediatric headache (13 placebo controlled studies and 10 active comparative trials [of which 2 also included placebo]).<sup>17</sup> Twenty trials focused on episodic migraine and 1 on chronic daily headache. No studies focused on chronic migraine or tension headache. Medications included topiramate, valproate, trazodone, propranolol, flunarizine, fluoxetine, pizotifen, dihydroergotamine, aspirin, cinnarizine, and clonidine. Trial quality was typically low, with a few exceptions (2 of 3 trials of topiramate, 1 of 3 valproate, 1 of 5 flunarizine, and 1 of 1 pizotifen). Only 4 of the studies included intention-to-treat analyses; yet, the average withdrawal rate was 10% (range: 5–26%). This meta-analysis concluded that there was limited evidence for trazodone (1 trial) and topiramate (2 trials) as a preventive treatment for episodic migraine. For the other medications, there was no evidence of benefit relative to placebo. Also notable for clinicians, this comprehensive review of trials up to 2012 suggested that the notably few clinical trials, and even fewer of high rigor and reproducibility, did not make firm conclusions possible. One sign of the need for many more studies is that Cochrane reviews of these treatments have not been initiated in the past decade, possibly because of the dearth of well-designed clinical trials and relatively little data from which to assess efficacy. At present, an updated practice parameter document from the American Academy of Neurology is undergoing public comment. This update will likely be published in 2019, and the draft paper's preliminary conclusions are consistent with the findings from the most recent meta-analyses described above.

Since 2012, a NIH-funded, multi-center trial, the Childhood and Adolescent Migraine Prevention Trial (CHAMP Study), was conducted. Amitriptyline, topiramate, and placebo were compared over a 24-week period. These medications were chosen because at the time the trial was designed, pediatric headache specialists reported these were the two most common prescriptions made in practice. The CHAMP study found no significant between-group differences in headache days or headache-related disability. Of note, this trial was designed to compare each drug to placebo as well as comparing the two drugs in a comparative effectiveness approach. A clinically meaningful primary endpoint of 50% or greater reduction in headache days was used. It was predicted, based on the few available pediatric trials (and recent adult trials of pill- and injection-based therapies), that the placebo effect would lead to half of participants having a 50% or greater reduction in headache days (and an impact of up to 60% responders to placebo was considered in the determination of the trial sample size and power calculations; see online appendix materials to the trial report in the New England Journal of Medicine<sup>18</sup> Supplemental Materials link<sup>19,20</sup> Clinical database knowledge from the Cincinnati Children's Headache Center for amitriptyline<sup>10</sup> and three prior studies of topiramate<sup>12,16,17</sup> led to the prediction that 70 to 85% of participants would show a 50% or greater reduction in headache days when taking these frequently prescribed preventive medications over a 6-month time period. The results of the trial, which was stopped early due to futility, supported the assumed placebo effect but did not support the predicted level of improvement that could be attributed to either amitriptyline or topiramate. Participants who received amitriptyline or topiramate had significantly more negative side effects when compared to participants taking placebo. Thus, not only were the

medications not outperforming placebo, they were found to provide more potential harm than benefit. Obviously, more research is needed to inform practice. In 2018, a class of new migraine preventive agents (anti-CGRP drugs) is in the planning stages for initial efficacy clinical trials in youth. These studies are being designed with the notable placebo effect in mind. Results will likely be available in the coming few years.

In trials of adults with headache<sup>21,22</sup> and youth with chronic migraine,<sup>2</sup> evidence does support the prescription of a combination of cognitive behavioral therapy (CBT) with a pill-based therapy. Specific to pediatrics, the combination of CBT with the medication amitriptyline was superior to taking amitriptyline and receiving headache education and equal attention from a therapist over the course of a 5-month study and then a one-year follow-up period.<sup>2,23,24</sup> CBT + amitriptyline led to 66% of participants experiencing a 50% or greater reduction in headache days at the 5-month trial endpoint, and 86% met this responder status at the 1-year follow-up. Notably, the positive impact of combined treatment was seen early in the course of therapy, and a clinically meaningful proportion of the participants achieved benefit to the level of headache days being reduced to one or less per week (from a baseline of 5 per week).<sup>24</sup> Replication of these findings and extension to other pediatric headache populations would strengthen confidence in this higher-intensity therapeutic regimen, but at present it appears that pill-based therapies are more effective when combined with evidence-based non-pharmacological treatment.

These results suggest that turning pediatric migraine treatment efforts towards non-pharmacological interventions, such as CBT, may be a more optimal approach to care. This reconsideration of first-line therapy is supported by the fact that the evidence base for CBT is more robust than what we have at present for pill-based therapies in pediatric patients. A recent Cochrane Review highlights our current understanding of how psychological treatments impact pediatric pain, and the majority of trials reviewed involved pediatric headache and migraine.<sup>25</sup>

## The current state of evidence for psychological therapies

The most commonly used and evaluated psychological treatment for migraine is CBT. CBT strategies for headache and migraine management typically include psychoeducation on the gate control theory of pain, deep diaphragmatic breathing, progressive muscle relaxation, guided imagery, activity pacing, cognitive modification, distraction/pleasant activities, problem-solving, and cued relaxation.<sup>2,25,26</sup> Biofeedback is frequently used during teaching of relaxation strategies to provide patients with visual data on the physiological changes that occur in their body (i.e., decreased heart rate, muscle tension) as a result of using relaxation skills, and is supported as an effective treatment within the pediatric migraine literature.<sup>2,27</sup> Parents/caregivers are often included in this treatment approach and learn ways to support skills-practice by youth and reinforce adaptive coping behaviors. The majority of trials have investigated a package of these various interventions, and few single component trials or dismantling research designs have been employed to date. The primary goals of CBT packages for headaches is to teach patients how to utilize coping skills for headache pain management as it occurs, to prevent headaches through regular use of coping skills, and to alleviate related disability and/or comorbid symptoms of anxiety and depression.<sup>28</sup>

There is a strong and growing body of evidence demonstrating the effectiveness of psychological approaches, primarily CBT, for treating pediatric headache and migraine. The 2014 Cochrane review showed that across 20 studies, pain ratings following psychological treatments (10 CBT, 10 behavioral strategies only) decreased for 56% of youth with headache compared to 22% in the control groups.<sup>27</sup> Three of these trials evaluated functional disability related to headache, and showed decreases in headache related disability ratings post-psychological treatments; two of these studies explored functional disability at a follow-up point months after treatment and found that disability was still reduced at this follow-up point.

A recent meta-analysis from 2017 reviewed studies evaluating the effectiveness of CBT in the treatment of pediatric headache and migraine for patients under the age of 19.<sup>29</sup> For this review, clinically significant improvement in headaches was identified as a 50% or greater reduction in headache frequency, and included long-term follow-up data (≥ 3 months post-final CBT session). Odds ratios were found to be 9.11 (95% CI: 5.01 to 16.58,  $P < .001$ ) post-treatment and 9.18 (95% CI: 5.69 to 14.81,  $P < .001$ ) at follow-up. Results from this review of 14 RCTs overwhelmingly support CBT as an effective form of treatment for pediatric headache conditions as compared to placebo, waitlist or medication, producing clinically significant improvement in headache frequency. Studies with available follow-up data also suggest that headache frequency reductions were maintained long-term. The majority of the studies within this review that explored CBT alone in comparison to a waitlist control showed that CBT alone was effective in creating a clinically significant improvement in headache frequency for the majority of participants, consistently outperforming the control groups. Of note, some of these studies demonstrated improvements in headaches using computerized/web-based versions of CBT<sup>30,31</sup> and versions of CBT using relaxation training and biofeedback only.<sup>32,33</sup>

In the Cognitive Behavioral Therapy (CBT) plus Amitriptyline Study, 10- to 17-year-olds with chronic migraine participated in 8 weekly CBT appointments and 2 monthly booster sessions (including treatment components described above).<sup>2</sup> Results showed that headache frequency and disability both decreased for a significant portion of participants receiving CBT plus Amitriptyline (CBT+A). Specifically, youth in the CBT+A group reported headache days per month decreased by 11.5 days compared to a 6.8 day decrease for youth in the receiving headache education plus amitriptyline (HE+A) group. Headache-related disability (as indicated by Pediatric Migraine Disability Scores; PedMIDAS) decreased by 52.7 points for the CBT+A group versus 38.6 points for the HE+A group. These improvements were maintained through one-year follow-up, with 72% of the CBT+A group experiencing one or fewer headaches per week (versus 5 or more at baseline) compared to 52% of the HE+A group.<sup>34</sup> Adherence to treatment was also demonstrated, as Participants in the CBT+A group were found to regularly attend treatment sessions and engage in home practice of the skills they were taught.<sup>23</sup>

Some of the available studies of CBT have measurable and defined methodological challenges, but more recent trials have met published standards for conduct of behavioral intervention trials and have been included in high impact medical journals.<sup>25,29,35-37</sup> More research focused on headache populations yet to be examined would further strengthen the

potential reach of psychological treatments such as CBT (e.g., post concussive headache, new daily persistent headache, patients who do not benefit from drug and/or device-based treatments, constant headache for more than 3 months). And, as for pharmacological and device trials, additional non-pharmacological trials conducted with a high level of rigor, reproducibility, and clinical relevance are needed to increase the evidence base and allow for the firm conclusions that clinicians are seeking to inform care.

Although research suggests that CBT is an effective form of treatment for pediatric headache, it is important to note that CBT may not be an optimal treatment strategy for some patients. CBT and behavioral strategies, without more extensive parental involvement, are often not appropriate as a sole intervention for rather young patients, as younger children can struggle to implement both behavioral and cognitive strategies delivered in CBT. Despite such a limitation, given that pediatric headache is not as common in very young patients, CBT would remain an option for most pediatric headache patients. Other limitations of CBT include required willingness of patients to participate in treatment and use of skills learned outside of therapy sessions, and patients must be cognitively able to participate in therapy (often precluding use of CBT in patients with cognitive delays or disabilities). It is true that the stigma of mental health and access to appropriate and evidence-based care can be a barrier; however, this is not reason to avoid these recommendations for patients. It is important to advocate for and find ways to make sound interventions with minimal side effects accessible and acceptable to people who suffer from pain disorders such as migraine. 38–42

At present, the number of trials, strength of evidence, and replication of findings is greater for psychological therapies in pediatric headache than prescription medications, device-based treatments, and nutraceuticals.<sup>43–45</sup> As always, we know less than we need to know to optimally care for patients and families, and the primary way forward is to conduct more (and more rigorous and clinically relevant) investigations. This includes striving to perform implementation science experiments within the context of headache specialty care, neurology practices, and primary care settings. *But, today, we should pursue care based on the evidence-base we have that is specific to children and adolescents.*

## **A research strategy for pediatric headache and migraine going forward:**

### **1. Understanding how and why therapies that positively impact youth with headache and migraine work**

Mechanistic investigations are designed to understand a biological or behavioral process, the pathophysiology of a disease, or the mechanism of action of an intervention. Such science is needed to advance our understanding of why youth with headache and migraine benefit from different treatments including psychological therapies, medications, or a combination of therapies. Research technologies such as genetics and genomics, application of bioinformatics, functional brain imaging, and pain processing assessments such as quantitative sensory testing and the conditioned pain modulation paradigm offer much for the pursuit of this scientific knowledge that has great promise for translation into practice.<sup>46–50</sup> A recently funded NIH project (1R01NS101321–01A1) will provide a better understanding of how and why youth with migraine get better when they receive CBT,

placebo pill, or amitriptyline therapy.<sup>51</sup> This mechanistic trial will be one of the first in pediatric migraine patients to use brain imaging and quantitative sensory testing pre- and post-intervention to discover changes that occur due to a given treatment and test if there are distinct changes for each of the 3 tested therapies (CBT, amitriptyline, placebo). Genetic and genomic analyses of the CHAMP Study sample are currently being conducted with support from the NIH and the Migraine Research Foundation. In future research, incorporation of other possible mechanisms of action for a treatment will be important as well. Such possible mechanisms include psychological (e.g., expectation for improvement), behavioral (e.g., adherence), cognitive (e.g., catastrophizing), and/or parent and family variables (e.g., reinforcement of pain behaviors). It is only with more research such as these ongoing investigations and other future trials that have a mechanistic focus, that we will understand the distinct effects of our therapies (and any overlapping/common mechanisms of change) and then be able to empirically derive algorithms that help with prediction of which treatments (or order or combination of therapies) will work best for which children and adolescents. In this way, we aspire to not only improve upon the available evidence base for clinicians and families, but to realize the promise of individualized or precision medicine in the field of headache medicine (especially for pediatric patients as effective and durable early intervention could prevent suffering and enhance quality of life over decades for such patients).

## **2. Consideration of and strategies for addressing barriers to accessing pharmacological and non-pharmacological treatments**

There is a widely available system for access to medications in the United States. However, barriers can exist when the evidence base is inconsistent or limited (e.g., absence of FDA approval for a drug; concerns raised when insurance policies include reviews for medical need) and/or the cost of a treatment is large (e.g., coverage policies that suggest failure of less expensive treatments prior to potential authorization of a more costly drug; increased cost to patients for non-generic medications; greater oversight and review of medications not included on an insurance plan's formulary; lack of evidence that newer and/or more expensive drugs are superior to available generic or earlier developed medications). Once a medication is obtained, regular adherence (often on a daily or multiple times per day basis) is prescribed. For both pharmacological and non-pharmacological therapies, adherence requires time and adds burden to the flow of everyday activities. Thus, adherence is often less than optimal resulting in higher health care costs, and can be improved with behavioral intervention (e.g., eHealth applications that remind patients to take medicine or attend appointments, reminder phone calls ahead of appointments, therapy itself addressing adherence to medications).<sup>52,53</sup> It is important to consider that while access to obtaining prescription medication is supported by a robust health care system in the United States, the act of adhering to a daily treatment produces a number of barriers (e.g., time, costs and co-payments, knowledge deficits, side effects, motivational challenges, multiple living environments and family communication challenges). In practice, while barriers may exist, access to a pill-based therapy is most often better than for non-pharmacological treatments at present. But adherence challenges are often similar.<sup>28,53</sup>

There is a less developed system available to patients who are seeking psychological care in the United States, and access to care is a major concern to health care providers and patients with chronic pain.<sup>38,41</sup> Of note, barriers to treatment have been reported as a reason for patients and/or parents declining participation in psychological treatments among youth with chronic pain such as headache.<sup>54,55</sup> Such reported barriers include time required to attend repeated sessions and travel to sessions, cost of attendance for transportation to sessions and co-payments, and living too far away from centers that deliver non-pharmacological treatment. The CBT+A study did have a high rate of adherence to treatment attendance and use of CBT skills in home and school settings; however, there was still a notable rate of refusal to participate in the study, with some patients who opted not to participate citing extensive treatment burden as the reason.<sup>2</sup> Further, some patients may be unwilling to participate in CBT based on a lack of acceptability of engaging in psychological treatment as a result of stigma against mental health diagnoses and treatment, which is a larger, societal level barrier that cannot be ignored and requires advocacy and public health education. Regardless, it seems that those patients that are able and willing to participate can and do. Yet there are a large number of patients that do not participate due to barriers to treatment. Accordingly, it is important to focus on improving access and availability of trained care providers as well as novel research efforts focused on finding ways to streamline interventions and minimize treatment burden; thereby increasing accessibility and feasibility of treatment for a larger number of pediatric headache and migraine patients.

### **Increasing accessibility and feasibility of CBT for pediatric headache and migraine: Where do we go from here?**

Understanding key mechanisms of change within a multi-component treatment is necessary to create a streamlined CBT for pediatric migraine. There are numerous ways to investigate mechanisms of change within CBT, including dismantling studies that evaluate each individual treatment component of CBT to determine which produce the most clinical benefit (in this case decrease in head pain and/or increased ability to function with pain). To our knowledge, there have been no dismantling studies of CBT components for pediatric migraine, as all studies evaluating the effectiveness of CBT include an entire treatment package as one.

Another approach to learning ways to streamline CBT is to solicit feedback from patients and families who have completed CBT in order to learn specific aspects of treatment they found to be most helpful. A recent qualitative study obtained such data by exploring feedback from pediatric migraine patients and their parents who participated in CBT for headache approximately 12–24 months prior to being interviewed.<sup>26</sup> Patients and parents indicated finding CBT to be helpful overall in reducing headache frequency and disability. Patients also reported that the mind and body portions of the treatment package, including deep diaphragmatic breathing, progressive muscle relaxation, and guided imagery, were the most essential skills learned in CBT for headache management. Most families reported attending fewer CBT sessions (average of 3–4) than the traditional 8 sessions reported in randomized clinical trials.<sup>2</sup> Additionally, some families did not believe CBT needed to be delivered by a psychologist to be effective; however, parents did believe it needed to be delivered by allied health professionals rather than a parent or caregiver. Collectively, patient



and parent feedback suggests that a shortened version of CBT, focusing largely on mind and body relaxation skills, may help to increase feasibility of treatment, decreasing costs of treatment (due to fewer treatment sessions and less travel costs), while maintaining treatment effectiveness for pediatric headache.

In addition to shortening the duration of CBT for headache treatment, consideration should also be given to where the treatment is provided. For example, patients and parents who participate in CBT for headache are often referred for this treatment by neurologists during clinic visits. Thus, introducing CBT mind and body skills training during these same clinic visits may help to reduce additional barriers to treatment by eliminating extra travel time and costs for additional CBT appointments scheduled at other times. Home practice of skills could then be supported via mHealth approaches and/or with parent involvement. This same model could also be applied to primary care settings, where pediatric patients are seen by their pediatricians for ongoing concern with headache and migraine.

While the idea of delivering CBT directly in clinics seems like a promising method for increasing accessibility of treatment while decreasing costs for patients and families, consideration of provider availability is necessary. Psychologists are largely the deliverers of CBT for pediatric headache, yet they are not physically practicing in all headache specialty or primary care clinics. As such, it may be worth considering other allied health providers, such as nurses already present in such clinics, as possible means for introducing CBT. With additional training, such health professionals already integrated into clinics may be ideal providers of streamlined CBT for pediatric migraine patients as part of routine clinical care to reduce barriers to treatment for patients and families. Indeed, based upon a poll of members, there is interest expressed by physicians in the AHS Pediatrics and Adolescent Section in learning how to introduce and prescribe relaxation skills during initial clinic visits with families. So, headache specialists, neurologists, and primary care providers could also help to deliver this evidence-based treatment. This approach, as well as streamlined versions of CBT, warrant further investigation to determine both feasibility and effectiveness. While this approach may be a way to increase accessibility of CBT treatment, it is important to note that clinic settings that are rather busy and limited in personnel may have some difficulty implementing such procedures without innovative implementation science being conducted to find ways to deliver evidence-based, non-pharmacologic therapies. But, importantly, challenges of time in clinical practice can be addressed with innovative science and commitment to optimizing outcomes from the care provided in a health care system.

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Finally, efforts should also be directed towards exploring options of alternative methods of CBT delivery, beyond traditional face-to-face interventions. Exploration of eHealth/mHealth and web-based treatment delivery is particularly timely given the reliance on technology by youth. Further, electronic methods of CBT delivery would eliminate barriers of travel time and reduce the cost of care. A recent study explored an internet-delivered CBT for pediatric chronic pain, including headache, and found the components of treatment similar to face-to-face interventions (psychoeducation, mind and body relaxation skills, cognitive skills).<sup>55</sup> Biofeedback was the primary aspect of CBT that was not used in the web-based intervention, because of equipment necessary for completing biofeedback that patients

would not have. Qualitative data from patients and parents who participated in this internet-delivered version of CBT for chronic pain indicates that, similar to the qualitative data from patients who completed face-to-face CBT, relaxation skills were a core component of their treatment success. The majority of patients who participated in this web-based CBT also reported 50% or greater reductions in headache frequency from treatment. Collectively, these results suggest that internet delivered CBT for pediatric migraine may be another avenue for increasing treatment accessibility.

Overall, a number of changes in our health care system, novel research efforts, and better understanding of how to best predict which patients will benefit from different intensities of care are needed to advance the use of evidence-based non-pharmacological therapies for chronic pain. For example, consideration could be given to evaluating and comparing different ways of delivering CBT, including self-directed web-based learning, introduction to treatment and support from an allied health care professional (e.g., nurse), brief outpatient care by a psychologist, and more extensive therapy that includes CBT as well as attention to co-morbidities (e.g., sleep problems, adherence challenges, anxiety and/or depression, family conflict, obesity or other chronic illnesses, and/or other co-occurring pain conditions). National efforts in the United States are calling for urgency in addressing these critical issues to enhance the quality of life for people with pain conditions such as headache and migraine.<sup>38,41</sup>

## Conclusions

Despite medications often being considered as the first-line treatments for pediatric headache and migraine, research to date (as highlighted throughout this review) suggests that this may not be at present the most evidence-based approach. The more robust evidence at present supports prescription of cognitive behavioral therapy (either alone or in combination with a pill-based therapy such as low-dose amitriptyline [to minimize side effects]). Based on this recommendation for first-line therapy to prevent headache/migraine in youth, research efforts should be aimed at understanding how and why CBT works to allow for development of more streamlined and efficient forms of CBT that can be implemented in headache specialty, neurology, and primary care settings.

## Acknowledgements:

We would like to thank Drs. Marielle Kabbouche and Joanne Kacperski for reviewing this manuscript and providing helpful suggestions. We would also like to acknowledge the team science, care, and training approach of the Cincinnati Children's Headache Center group and the contributions they make every day to improve the lives of children, adolescents, young adults, and their families who are coping with migraine and headache.

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**Key Conclusions:**

- Commonly prescribed preventive medications for pediatric headache and migraine are no more effective than placebo and have negative side effects
- Lack of medication effectiveness suggests non-pharmacological interventions may be a better approach
- Cognitive behavioral therapy (CBT) has demonstrated effectiveness for treatment of pediatric headache and migraine
- Future research should explore our understanding of how and why CBT produces clinically meaningful benefit and continue to provide data on ways to increase accessibility of CBT for pediatric migraine and headache patients and families