IHE INSTITUTE OF HEALTH ECONOMICS ALBERTA CANADA

TOP Toward Optimized Practice

Ambassador Program Guideline for Management of Primary Headache in Adults, 2nd Edition

Background Document

Supporting documents and process description

July 2017

Abbreviations

All abbreviations that have been used in this document are listed here unless the abbreviation is well known, has been used only once, or has been used only in tables or appendices, in which case the abbreviation is defined in the figure legend or in the notes at the end of the table.

AGREE	Appraisal of Guidelines for Research and Evaluation
AHS	Alberta Health Services
Alberta CPG	*Alberta Clinical Practice Guideline for Management of Primary Headache in Adults*
CADTH	Canadian Agency for Drugs and Technologies in Health
CPG	clinical practice guideline
CS	case series study
DALY	disability-adjusted life-year
EO	expert opinion
G	guideline
G1 to G11	seed guidelines
GDG	Guideline Development Group
GLIA	GuideLine Implementability Appraisal
GUC	Guideline Update Committee
HTA	health technology assessment
IHE	Institute of Health Economics
IHS	International Headache Society
MA	meta-analysis
NA	not applicable
NR	Nonsystematic/narrative review
NRCS	nonrandomized comparative study
NRT	non-randomized trial
NSAID	non-steroidal anti-inflammatory drug
qSR	quasi-systematic review
RCT	randomized controlled trial
SC	Steering Committee
SR	systematic review
TOP	Toward Optimized Practice
US FDA	United States Food and Drug Administration

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SCOPE OF THIS DOCUMENT

This background document outlines the methods used to update the *Alberta Clinical Practice Guideline for Management of Primary Headache in Adults*, which was produced as part of the Alberta Ambassador Guideline Adaptation Program.

This document should be cited as: Institute of Health Economics (IHE). *Ambassador Program guideline for management of primary headache in adults, 2nd Edition: Background document*. Edmonton (AB): Institute of Health Economics; 2017. Available from: *http://www.ihe.ca/research-programs/hta/aagap/headache*.

The citation for the background document describing the methods and process used to create the 1st Edition of this guideline is as follows: Institute of Health Economics (IHE). *Ambassador Program guideline for management of primary headache in adults: Background document*. Edmonton (AB): Institute of Health Economics; 2013. Available from: *http://www.ihe.ca/download/ambassador_headache_final_100_pager.pdf*.

ABOUT THE *ALBERTA CPG*

This section contains the following information about the *Alberta Clinical Practice Guideline for Management of Primary Headache in Adults*, 2nd Edition:

- ✓ Purpose, objectives, and target users
- ✓ Multidisciplinary committees involved in its development
- ✓ Type and location of guideline and companion documents available to clinicians and patients
- ✓ Conflict of interest, funding, and editorial independence
- ✓ Terms of use

Purpose

The purpose of the 2nd edition of the *Alberta Clinical Practice Guideline for Management of Primary Headache in Adults* (herein referred to as the *Alberta CPG*) is to help Alberta clinicians make evidence-informed decisions about the care of adult patients (18 years of age or older) with headache. The guideline was written to provide healthcare professionals in community practice and patients in Alberta with guidance about the prevention, diagnosis, evaluation, management, and treatment of headache.

It is expected that providing relevant, up-to-date information to assist primary care practitioners in the prevention, diagnosis, evaluation, management, and treatment of headache will allow more patients to be competently managed in the primary care setting and decrease unnecessary referrals to increasingly overburdened specialists.

Objectives

The primary objectives are to:

- increase the use of evidence-informed approaches to the prevention, assessment, diagnosis, and treatment of headache for patients in primary care;
- promote appropriate specialist referrals and use of diagnostic tests in patients with headache;
- provide guidance on the parenteral pharmacological treatment of refractory migraine attacks for use in appropriate settings where parenteral medications can be safely administered; and
- encourage patients to engage in appropriate self-management.

Target Users

The guideline is intended to be used by any healthcare provider (e.g., family physician, physical therapist, occupational therapist, nurse, nurse practitioner, pharmacist, psychologist, or chiropractor) in a primary care setting who is responsible for the care of patients with headache.

Multidisciplinary Participation

Two multidisciplinary committees were involved in the development of the *Alberta CPG*, 2nd Edition:

- The Steering Committee (SC) guided the collection and collation of research material, provided operational oversight, and acted as a secretariat to the Guideline Update Committee (GUC).
- The GUC reviewed the 1st Edition of the *Alberta CPG* and revised the recommendations, where necessary, to reflect current research in the management of headache.

A Research Team of health technology assessment (HTA) researchers with methodological expertise from the Institute of Health Economics (IHE) assisted the SC and the GUC in developing the *Alberta CPG*, 2nd Edition. The profile of each committee participant is listed in *Appendix A*. A flow diagram of the development process for the *Alberta CPG*, 2nd Edition, and an outline of the roles and activities of each of the committees are provided in *Appendix B*.

Guideline and Companion Documents

The *Alberta CPG*, 2nd Edition and its companion documents are hosted by Toward Optimized Practice (TOP), the program responsible for provincial CPGs, on its website (*www.topalbertadoctors.org/cpgs/*). The *Alberta CPG*, 2nd Edition, was posted on the TOP website on 20 December 2016. Additional companion documents are hosted by or linked to on the IHE on the Ambassador Program website (*www.ihe.ca/research-programs/hta/aagap/headache*).

For clinicians

1. Guideline
   a) *Guideline for Primary Care Management of Headache in Adults*, 2nd Edition
   b) *Quick Reference* (algorithm, medication table, and key messages), 2nd Edition
2. Practice tools
   a) *Headache History Guide* (in *Appendix F: Resources and Tools* of *Alberta CPG*, 2nd Edition)
   b) *Headache Diary Sheets* (long and short form)
   c) Headache disability measurement tools:
      - *Headache Impact Test* (*HIT-6*). Available at: *http://www.headaches.org/2007/11/16/headache-management-tools-hit/*
      - *Migraine Disability Assessment Scale* (*MIDAS*). Available at: *http://www.headaches.org/wp-content/uploads/2015/01/MIDAS.pdf?7a7d37*
3. *2017 Canadian Guideline for Opioids for Chronic Non-Cancer Pain*. Hamilton (ON): Michael G. DeGroote National Pain Centre at McMaster University; 2017. Available at: *http://nationalpaincentre.mcmaster.ca/guidelines.html*
4. Instructional YouTube videos:
   a) *Temporomandibular and neck exam*. Available at: *https://youtu.be/QirMbworS10*
   b) *Neurological exam*. Available at: *https://www.youtube.com/watch?v=fgwN1P5PDaA*

5. *HeadachePro* pathway tool, app developed by Alberta Health Services (AHS) and based on *Alberta CPG*, 2nd Edition. Available at: *https://headachepro.albertahealthservices.ca/*
6. *Ambassador Program Guideline for Primary Care Management of Headache in Adults, 2nd Edition: Background Document* (supporting documents and process description)
7. *Ambassador Program Guideline for Primary Care Management of Headache in Adults: Background Document* (supporting documents and process description for 1st Edition)

For patients

1. Patient information sheets:
   a. *What You Should Know About Your Headache*
   b. *What You Should Know About Headache Self-Management*
   c. *What You Should Know About Your Migraine Headache*
   d. *What You Should Know About Migraine Preventive Medications*
   e. *What You Should Know About Your Tension-Type Headache*
   f. *What You Should Know About Your Medication-Overuse Headache*
   g. *What You Should Know About Your Headache During Pregnancy and Breastfeeding* (new for 2nd Edition)
2. Patient information brochure (new for 2nd Edition): *What You Should Know About Your Headache – Learn more about headache types, triggers, and treatments, when to get help, and how to help yourself*
3. *Food Triggers, Caffeine, and Migraine Attacks* information sheet

Conflict of Interest

All GUC, SC, Research Team, and invited clinical experts who were not members of the GUC completed a declaration of competing interest using a standard form (see *Appendix S*). Competing interest was considered to be financial or nonfinancial interest, either direct or indirect, that could affect the recommendations contained in the *Alberta CPG*.

Two members of the GUC declared competing interests (see *Appendix S*). However, the collaborative nature of the CPG development process, which involved a large, multidisciplinary GUC and invited clinical experts led by two co-chairs, ensured that these interests had no influence on the design, data analysis, formulation, or content of the guideline.

Funding and Editorial Independence

Alberta's HTA program was established under the Health Research Collaboration Agreement between the IHE and the Alberta Ministry of Health. Funding for this initiative was provided by Alberta Health.

Alberta Health Services (AHS), Calgary Zone, provided clinical leadership and in-kind contributions.

The above-mentioned funders had no influence on the recommendations contained in the final *Alberta CPG*, 2nd Edition.

Legal aspects

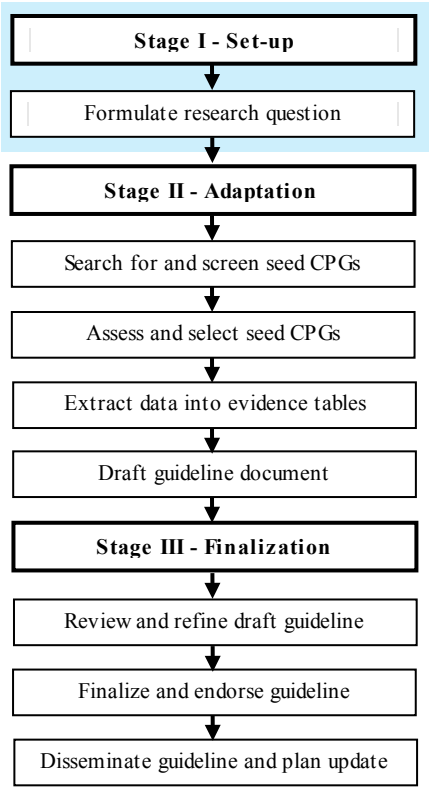
TOP, the program responsible for provincial guidelines, hosts the *Alberta CPG*, 2nd Edition, and possesses the associated legal and intellectual property rights.

The *Alberta CPG*, 2nd Edition, was posted on the TOP website on 20 December 2016 (*www.topalbertadoctors.org/cpgs/10065*).

Terms of Use

STAGE I: SET-UP

BACKGROUND AND PLANNING



This section contains the following information:

- ✓ Overview of the Ambassador Program – its genesis and establishment
- ✓ Development of the *Alberta CPG* (1st Edition)
- ✓ Set-up of the *Alberta CPG* update process
- ✓ About headache – the epidemiology and disease burden, as well as the knowledge gaps identified among primary care practitioners regarding its management

Overview of the Ambassador Program

The Alberta HTA Ambassador Program is a knowledge translation strategy that was trialled in Alberta, Canada in 2004-2005. The first phase of the program (the Ambassador Pilot Project), completed in 2005, used clinical opinion leaders to present evidence to healthcare providers on various treatments for chronic pain.[1-4] Funding for the Ambassador Pilot Project was provided by a capacity-building grant from the Canadian Agency for Drugs and Technologies in Health (CADTH; formerly known as the Canadian Coordinating Office for Health Technology Assessment). The success of the initial Ambassador Program led to additional funding from Alberta Health to expand the scope of the project.

The second phase of the program started in 2006 and focused on developing evidence-based, Alberta-specific CPGs for the management of two conditions: low back pain and headache. This second iteration of the Ambassador Program built on the Ambassador Pilot Project, with the aims of:

- collaborating with local champions to develop locally adapted CPGs for low back pain and headache, in order to guide clinicians through a sequential process of determining the clinically appropriate treatment options available in their region;
- supporting local networks in disseminating the CPGs to clinicians in Alberta;
- updating and maintaining the Ambassador Program website (*www.ihe.ca/research-programs/hta/aagap*) as a resource for clinicians and patients;
- designing and implementing an appropriate approach for evaluating the impact of the CPGs; and
- exploring strategies for engaging the public in HTA research transfer on the topics of low back pain and headache management.

Development of the *Alberta CPG* (1st Edition)

The Ambassador Program began developing the 1st Edition of the *Alberta CPG* in March 2010. This involved adapting six CPGs on headache into a single guideline for primary care practitioners that spanned the continuum of care from prevention and diagnosis through to treatment of migraine headache, tension-type headache, medication overuse headache, cluster headache, and other headache disorders. The process used to produce the 1st Edition of the *Alberta CPG* has been described in more detail elsewhere.[5,6]

Briefly, the following three multidisciplinary committees were formed comprising participants with clinical, research, and dissemination expertise (see *Appendix C* for profiles of each of the committee participants).

- The SC provided project leadership, guided the collection and collation of research material, provided operational and fiscal oversight, and acted as a secretariat to the Guideline Development Group (GDG) and the Advisory Committee. The SC was responsible for finalizing and signing off on the guideline.
- The Advisory Committee provided general project oversight, advised the SC on strategic matters, and provided linkages to appropriate stakeholders.
- The multidisciplinary GDG constructed the CPG.

A Research Team consisting of HTA researchers assisted the SC and GDG by selecting and appraising the published guidelines, preparing background documents, tracking decision points, and helping to write the final guideline. The GDG reviewed all of the background materials (the six seed guidelines and their companion documents, the evidence inventory tables, and the quality appraisal scores) and drafted an Alberta-specific guideline during 13 half-day meetings (one face-to-face and 12 via WebEx teleconference) over a 23-month period.[5,6]

The final guideline was posted on the TOP website in July 2012. The guideline was also listed on the Canadian Medical Association (CMA) Infobase (July 2012) and the United States Department of Health and Human Services National Guideline Clearinghouse (NGC) (January 2013) websites.

Set-Up and Planning of the *Alberta CPG* (2nd Edition) Update Process

TOP, the program responsible for provincial guidelines, and HTA researchers from the IHE were responsible for updating the scientific content of the *Alberta CPG*. The *Alberta CPG* was developed using a hybrid process involving adaptation of seed guidelines supplemented with evidence from published systematic reviews as required. Published literature indicates that the median life span of a de novo guideline is about five years from publication and that updated guidelines have an even shorter life span.[7-9] To maintain the currency of the *Alberta CPG*, a scoping search of the medical literature is conducted annually. An update of the CPG is considered necessary when at least two new guidelines of good quality (or updates of previously reviewed seed guidelines) are identified.

An update search was conducted in November 2014. On 15 December 2014, the SC met to discuss whether an update of the *Alberta CPG* was required. A summary of the key discussion points follows:

- The scoping search of the medical literature identified new published guidelines and updates of seed guidelines. Participants reviewed the new guidelines and their quality scores, as well as the list of excluded guidelines.

- At least two new guidelines of good quality had been published since the launch of the 1st Edition of the *Alberta CPG*, so it was decided to update the guideline.
- Participants emphasized the need to survey stakeholders for new interventions not included in the 1st Edition of the *Alberta CPG*.
- It was noted that an updated *Alberta CPG* would dovetail with initiatives by the Council of the Federation examining the appropriateness of diagnostic imaging in patients with low back pain, headache, or minor head injuries.

The SC subsequently met several times over the period from March to May 2015 to discuss the logistics and approach for updating the *Alberta CPG*, including recruiting new members for the GUC and involving patients and lay people in the update process.

An online survey was created (one for patients and one for clinicians) to inquire about new interventions not currently included in the *Alberta CPG*. The survey was emailed to former GDG and Advisory Committee members (n=54) on 19 November 2014. Hard copies of the survey were also distributed in January 2015 to patients at the South Health Campus Headache Clinic in Calgary. Twenty participants answered the clinician survey, listing six new interventions. From the 55 completed patient surveys, eight new interventions were added. Another seven interventions were proposed by members of the GUC.

About Headache – Epidemiology and Disease Burden

Headache disorders are usually classified as primary or secondary. Primary headache disorders have no identifiable cause, whereas secondary headache disorders are associated with an identified pathological cause, such as an infection, a brain tumour, or a stroke.[10]

Although headache disorders are prevalent worldwide, the intermittent nature of some of these disorders makes it difficult to estimate their incidence and prevalence.[11-13] Globally, 46% of the adult population has an active headache disorder, 20% has tension-type headache, 15% has migraine, and 3% has chronic daily headache.[13,14] The mean one-year prevalence of migraine in adults is between 4 and 15% across the World Health Organization regions and 11% in the Americas.[15] The majority of people with tension-type headache experience pain on one day a month or less, which is classified as infrequent episodic tension-type headache. However, 18 to 37% of sufferers have tension-type headache several times a month and 10 to 25% have it weekly; 1 to 3% of sufferers have chronic tension-type headache.[16,17] Approximately 3 to 5% of individuals with episodic headache progress to chronic daily headache.[18,19] Medication-overuse headache, a potentially treatable and preventable disorder, is common among individuals with chronic daily headache and may affect up to 5% of some adult populations.[13,17] In the general population, the life-time prevalence is 66% for headache, 14 to 16% for migraine, 46 to 78% for tension-type headache, and 0.06 to 0.3% for cluster headache.[10,13,19]

Studies conducted in Canada, France, Germany, and the United States, show that migraine prevalence is affected by age, gender, and socioeconomic factors. Migraine is most prevalent in individuals aged between 25 and 55 years, with the highest prevalence occurring during the peak productive years (30 to 49 years of age).[10,12,20-23] Women are more likely to experience migraine than men, particularly between the ages of 40 and 45 years when the female to male ratio reaches its zenith at 3.3:1.[12,19,23] In the United States, Caucasians are more likely to suffer migraines than those of African or Asian descent,[10,12,19-23] as are individuals with the lowest relative household incomes.[10,12,20-23]

In 1994, the prevalence of migraine among Canadians was 8% for men and 25% for women.[24] A national telephone survey of 1,210 Canadian women conducted in 2005 found that the prevalence of migraine in this population was relatively unchanged at 26%.[25] In 2010/11, 5% of men and 12% of women in Canada reported that they had been diagnosed with migraine, which corresponds to 2.7 million Canadians (8%).[26] This prevalence, which is lower than the range reported for diagnosed migraine in the United States (12 to 23%), is likely an underestimate because many migraineurs do not seek professional help and would not receive a diagnosis. The regional migraine prevalence across Canada varied from 6.8% in Quebec to 9.5% in Manitoba; the prevalence in Alberta was 8.7%.[26]

Because of its chronic nature, migraine is associated with high levels of emotional distress and disability, as well as impaired quality of life for the affected individuals, their families, and society as a whole.[10,12,19,22,27-30] According to the 2013 Global Burden of Disease Study, migraine is the sixth highest cause of disability worldwide and, when combined with medication-overuse headache (ranked 18th), headache disorders are placed third among the causes of years of life lost to disability worldwide.[31,32]

Emerging evidence indicates that, in some patients, migraine may be a chronic progressive disorder that is characterized by an escalating frequency of headache attacks.[18,23] Approximately 60% of migraineurs have one or more headache attacks per month.[21,29] Moderate or severe pain is experienced by approximately 90% of migraineurs, with 75% reporting impaired function and 33% requiring bed rest during their attacks.[21] Similar rates of significant debilitation are reflected in Canadian data.[29,23,26] More than 70% of Canadian migraine sufferers experience impairments in interpersonal relationships,[23] and 97% of women from a 2005 Canadian survey reported at least one psychosocial impact resulting from migraines (such as lack of control over their lives, missed days at work or family activities, or lack of understanding or cynicism from those around them).[25]

In general, headache accounts for about 20% of absences due to sickness,[11] with migraine being a major cause of absenteeism and decreased work productivity.[10,27,28,30] A 2005 survey found that, on average, Canadian women experienced at least partial incapacitation on almost 21 days a year due to migraine.[25] The 2013 Global Burden of Disease Study found that migraine and medication-overuse headache accounted for nearly 29 million and 9.8 million years lived with disability, respectively. In terms of disability-adjusted life-years (DALYs), migraine causes nearly 400 DALYs per 100,000 people worldwide, with medication-overuse headache contributing 138 DALYs.[31]

Despite their evident clinical, economic, and social burden, headache disorders (and migraine in particular) have historically been under-diagnosed and undertreated.[10,20-23,27,29,33] Many migraineurs, even those with disabling headaches, have never consulted a physician for their problem. Vast amounts of over-the-counter medications are taken for headache disorders,[10,17] and treatment is often suboptimal and characterized by low compliance.[33] More than one in four migraineurs are candidates for preventive therapy. However, although most migraine sufferers use acute treatment to relieve their headaches, a substantial number of people who might benefit from prophylactic therapy do not receive it.[12,21]

Prompt diagnosis and effective treatment, in conjunction with better information and education for patients and health professionals, are essential for improving the management of headache and migraine in primary care.[29,34]

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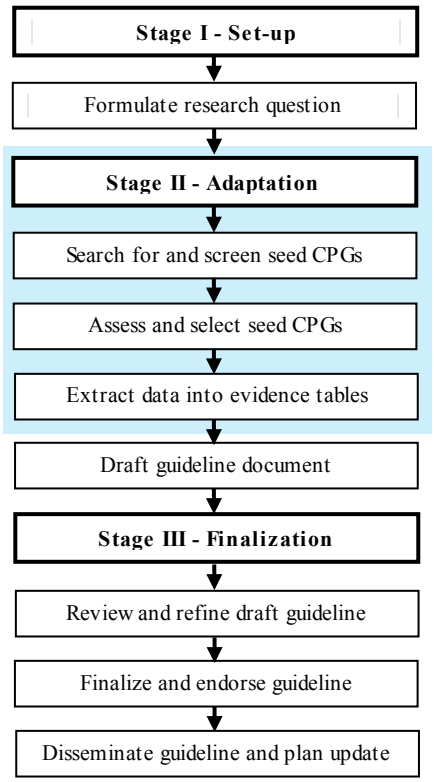
STAGE II: ADAPTATION

IDENTIFYING, SELECTING, AND APPRAISING THE SEED GUIDELINES



This section contains the following information:

- ✓ Rationale for choosing an adaptation approach over de novo guideline production
- ✓ Search strategy used to identify the seed guidelines
- ✓ Criteria used to select the seed guidelines
- ✓ Method and results of the critical appraisal of the selected guidelines and systematic review evidence

Rationale

CPGs are systematically developed statements that assist practitioners and patients in choosing appropriate interventions for specific clinical situations.[1] The creation of CPGs can take different approaches that range from de novo development to adopting or adapting existing guidelines. The development and adaptation of CPGs are processes that necessitate extensive resources and expertise to ensure high quality outcomes.[2]

The CPG adaptation process encompasses a variety of options, from accepting the entire guideline and its recommendations to partial acceptance of some of the guideline recommendations or its companion documents, with or without modification. For example, the Guidelines Advisory Committee[3] in Ontario, Canada, endorses guidelines based primarily on the methodological rigour of their development process, the quality of the linkage between evidence and recommendations for best clinical practice, and their applicability to the local context. In contrast, the COMPUS[4] program of CADTH unbundles existing guidelines, reviews and updates the pertinent evidence, and constructs a new guideline with input from a panel of experts.

The adaptation process takes advantage of existing high quality CPGs while also allowing guideline developers to modify the guideline to meet the needs, priorities, legislation, policies, and resources of a targeted setting.[2] Adapting pre-existing guidelines offers the advantages of reduced duplication, decreased resource commitment, increased efficiency, and enhanced local uptake. Adaptation may be applied to only one guideline or multiple guidelines.

Preliminary literature and consultation with clinical experts in Alberta revealed the existence of an important body of CPGs on headache disorders that could be adapted to meet local needs, thereby avoiding unnecessary duplication of effort in developing a guideline from scratch. In addition, it was thought that the adaptation approach would capitalize on the heightened interest and receptivity of local users generated by the Ambassador Pilot Project, thereby allowing the production of a CPG that was more tailored and relevant to the Alberta context.

Thus, the second phase of the Ambassador Program aimed to adapt and contextualize good quality international and national guidelines on the management of headache disorders in the primary care setting to the provincial healthcare system.

Identifying Seed Guidelines

Inclusion criteria

Guidelines

Guidelines ("seed" guidelines) were included if they focused on the diagnosis, conservative nonsurgical treatment, or prevention of primary headache and were designed for use in primary healthcare settings by physicians, physical therapists, chiropractors, occupational therapists, nurses, community-based nurses, pharmacists, mental health professionals, and other healthcare providers who treat patients with headache.

Only CPGs formulated in countries with developed market economies were included since the health status, cultural norms, access to health care, and disease burden of individuals from countries with transitional or developing economies were likely to be too different from those in Canada to be clinically relevant. Countries deemed to have developed economies, as defined by the United Nations, were Australia, Canada, Japan, New Zealand, the United States, and European countries (except for those with transition economies).[5]

Patient group

Patients included individuals who were 18 years of age or older. Guidelines that referred to adult patients or focused on headache in pregnant women without providing a specific age range were also included on the basis that the majority of the populations in these guidelines were likely to be at least 18 years of age.

Condition

For guidelines on treatment and diagnosis, only those that used the diagnostic criteria developed by the International Headache Society[6] were included.

Guidelines were included if they dealt with the prevention, diagnosis and investigation, and treatment of primary headache that is not related to or caused by another disorder. These headache types include migraine, tension-type, and cluster headache, as well as other primary headaches (thunderclap headache, hemicranias continua, new daily-persistent headache). Other trigeminal autonomic cephalalgias, such as chronic paroxysmal hemicranias and short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) or cranial autonomic features (SUNA), were excluded because of their low incidence.

Guidelines on medication-overuse headache (secondary headache) were also included because this headache type is typically present in a subgroup of patients with primary headache who have over-medicated. Cervicogenic headaches (secondary headache) were also included because a significant number of patients present to primary care physicians with this malady. Headache related with temporomandibular disorder is briefly discussed. However, other secondary headaches related to a causative disorder, such as trauma or infection, were excluded.

Exclusion criteria

Guidelines were excluded that focused on diagnostic techniques, interventions, or treatments applied in the emergency department or inpatient setting (e.g., surgical treatments).

Also excluded were guidelines focused on children or adolescents, or patients with specific causes for headache, such as head or neck trauma (except for cervicogenic headache), cranial or cervical vascular disorders, non-vascular intracranial disorders (e.g., neoplasm or idiopathic intracranial hypertension), use of a substance or its withdrawal (except for secondary medication-overuse headache), temporomandibular joint disorder, infection, disorders of homeostasis, psychiatric disorders, or disorders or lesions of the cranium, neck, eyes, ears, nose, sinuses, teeth, mouth, or other facial or cranial structures.

Literature search strategies

For the 1st Edition of the *Alberta CPG*, a preliminary systematic literature search was conducted to identify relevant guidelines published in English between January 2000 and April 2006. The search was further refined and updates were conducted in April 2009, October 2009, August 2010, and May 2011.

For the 2nd Edition of the *Alberta CPG*, a systematic literature search was conducted to identify relevant guidelines published in English from May 2011 (date of the last update search for the 1st Edition) to November 2014 (see *Table 1*). The date restriction was applied to ensure that the guidelines collected were current and clinically relevant. Relevant websites were also checked for updates or revisions to previously included seed guidelines.

Medical Subject Headings (MeSH) relevant to this topic are: *Headache*, *Headache disorders*.

TABLE 1: Search strategy used to identify relevant headache seed guidelines

Database/Website	Date Searched	Search Terms
PubMed *www.pubmed.gov*	30 November 2014	("Headache"[MeSH] OR "Headache Disorders"[MeSH] Limits: Entrez Date from 2011/03/11, Practice Guideline, Guideline) OR ((Headache* OR migraine*) AND (inprocess[sb] OR publisher[sb]) AND (guideline* OR "clinical decision" OR "clinical pathway"))
EMBASE Licensed Resource (OVID Interface)	30 November 2014	1 (headache$ OR migraine$ OR hemicrania$ OR cephalgia$ OR cephalalgia$ OR sunct).ti. 2 *"headache AND facial pain"/ OR *chronic paroxysmal hemicrania/ OR *cluster headache/ OR *drug induced headache/ OR *headache/ OR *hypnic headache/ OR *primary headache/ OR *postdural puncture headache/ OR *sinus headache/ OR *sunct syndrome/ OR *vascular headache/ OR exp *chronic daily headache/ OR exp *migraine/ OR exp *tension headache/ OR exp *trigeminal autonomic cephalalgia/ 3 1 OR 2 4 practice guideline/ AND (guideline$ OR recommendation$).ti,ab. 5 (consensus statement OR practice parameter).ti. 6 (guideline$ OR recommendation$).ti. 7 OR/4-6 8 3 AND 7

Database/Website	Date Searched	Search Terms
		9 limit 8 to yr="2011 -Current" 10 limit 9 to English language
PsycINFO	30 November 2014	1 exp headache/ 2 (headache$ OR migraine$ OR hemicrania$ OR cephalgia$ OR cephalalgia$ OR sunct).ti. 3 1 OR 2 4 treatment guidelines/ 5 (guideline$ OR recommendation$ OR consensus statement OR practice parameter).ti. 6 4 OR 5 7 3 AND 6 8 limit 7 to (English language and yr="2011 -Current")
AMA Clinical Practice Guidelines *www.topalbertadoctors.org/cpg.html*	30 November 2014	Browsed list of guidelines
CMA infobase *www.cma.ca/index.cfm/ci_id/54316/la_id/1.htm*	30 November 2014	headache; headaches; migraine; migraines; cephalgia head pain
National Guidelines Clearinghouse *www.guideline.gov/*	30 November 2014	Disease/Condition > Diseases > Nervous System Diseases > Central Nervous System Diseases > Brain Diseases > Headache Disorders Sort Order: Publication date
New Zealand Guidelines Group *www.nzgg.org.nz*	30 November 2014	headache OR migraine OR headaches OR migraines
Scottish Intercollegiate Guidelines Network *www.sign.ac.uk*	30 November 2014	Browsed list of guidelines
Guidelines Advisory Committee *www.gacguidelines.ca/index.cfm*	30 November 2014	Browsed list of guidelines
Institute for Clinical Systems Improvement *www.icsi.org/guidelines_and_more/*	30 November 2014	Browsed health care guidelines by topic
NICE *www.nice.org.uk/guidance/index.jsp?status=3&d-16544-p=1&action=byType&type=2*	30 November 2014	Browsed list of published clinical guidelines under headache
Guidelines International Network *www.g-i-n.net/*	5 December 2014	“headache”
Google *www.google.ca*	30 November 2014	"practice guideline" OR "clinical guidelines" headache OR migraine limited to PDFs and English pages

Database/Website	Date Searched	Search Terms
Websites *(selected based on relevance to the condition or sources of interest identified by the original search)*		
American Academy of Family Physicians *www.aafp.org/online/en/home.html*	30 November 2014	Headache AND guideline
American Academy of Neurology *www.aan.com/go/practice/guidelines*	30 November 2014	Guideline search by topic: headache.
American Academy of Pain Medicine *http://www.painmed.org/clinical_info/guidelines.html*	30 November 2014	Browsed clinical guidelines section
American College of Physicians *www.acponline.org/clinical_information/guidelines/current/*	30 November 2014	Browsed list of current guidelines
American Headache Society *www.americanheadachesociety.org/professionalresources/ProfessionalResourcesHeadacheInformationforClinicians.asp*	30 November 2014	Browsed list of links to practice parameters, guidelines and classification
American Pain Society *www.ampainsoc.org/pub/cp_guidelines.htm*	30 November 2014	Browsed list of clinical practice guidelines
Canadian Headache Society *www.headachenetwork.ca/*	30 November 2014	Guideline; guidelines
International Headache Society *www.i-h-s.org/frame_non_members.asp*	30 November 2014	Reviewed lists of guidelines
German Migraine and Headache Society *www.dmkg.de/allg/e_intro.html*	30 November 2014	Website in German, so no guidelines found. The other language Embase results that were excluded from this search contained many references by this group.
National Headache Foundation *www.headaches.org/*	30 November 2014	Guideline; guidelines
Registered Nurses' Association of Ontario *www.rnao.org/Page.asp?PageID=1212&SiteNodeID=155&BL_ExpandID=*	30 November 2014	Browsed list of guidelines and factsheets

Notes: Publication date limit was from May 2011 onward. The * and $ symbols are truncation characters that retrieve possible suffix variations of the root word; e.g., surg* retrieves surgery, surgical, surgeon, etc. In databases accessed via the OVID platform, the truncation character is $. Semicolons are used to separate search terms that were searched separately.

In cases where additional information was required by the GUC to finalize a recommendation, the database developed for the Ambassador Pilot Project, known as the IHE Database (updated to May 2015), was searched for systematic reviews focused on specific interventions for headache that were published in English and had a search end date no earlier than January 2008. The search end date restriction was applied to ensure that the systematic reviews included research that had been published within the last seven years (generally, the median shelf life of a systematic review is seven years[7]). The search strategy for the systematic reviews in this database is outlined in *Table 2* below.

Medical Subject Headings (MeSH) relevant to this topic are: *Headache*, *Headache disorders*, *Migraine*, *Migraine disorders*.

TABLE 2: Search strategy used to identify relevant systematic reviews for the IHE Database

Database/Website	Date Searched	Search Terms
The Cochrane Library *www.thecochranelibrary.com*	20 May 2015	headache* OR migraine* OR hemicrania* OR cephalgia* OR cephalalgia* OR sunct in Record Title or Keywords, from 2010
PubMed *www.pubmed.gov*	20 May 2015	1. Search "Headache Disorders"[MeSH] OR "Headache"[MeSH] Filters: Publication date from 2010/10/20 to 2015/12/31; English 2. ((headache OR headaches OR migraine OR migraines OR cephalgia* OR cephalalgia* OR hemicrania* OR SUNCT) AND (inprocess[sb] OR publisher[sb] OR pubmednotmedline[sb])) Filters:Publication date from 2010/10/20 to 2015/12/31; English 3. (headache[ti] OR headaches[ti] OR migraine[ti] OR migraines[ti] OR cephalgia*[ti] OR cephalalgia*[ti] OR hemicrania*[ti] OR SUNCT[ti] OR head pain*[ti]) Filters: Publication date from 2010/10/20 to 2015/12/31; English 4. Search (search[tiab] OR meta-analysis[Publication Type] OR MEDLINE[tiab] OR (systematic[tiab] AND review[tiab])) 5. (#1 OR #2 OR #3) AND #4 6. #5 Limits: All Child: 0-18 years 7. #5 Limits: All Adult: 19+ years 8. #5 NOT (#6 NOT #7) 9. (child*[ti] OR pediatric*[ti] OR paediatric*[ti] OR adolescen*[ti] OR school*[ti] OR teen*[ti] OR juvenile*[ti]) NOT adult*[ti] 10. #8 NOT #9
CRD Databases (HTA, DARE, NHS EED) *www.york.ac.uk/inst/crd/crddatabases.htm*	20 May 2015	1. MeSH DESCRIPTOR Headache EXPLODE ALL TREES 2. MeSH DESCRIPTOR Headache Disorders EXPLODE ALL TREES 3. (headache* OR migraine* OR cephalgia* OR cephalalgia* OR hemicrania* OR SUNCT):TI 4. #1 OR #2 OR #3 5. * From 2010 to 2015 6. #4 AND #5

Database/Website	Date Searched	Search Terms
EMBASE Licensed Resource (OVID Interface)	20 May 2015	1. (headache$ OR migraine$ OR hemicrania$ OR cephalgia$ OR cephalalgia$ OR sunct).ti. 2. *"headache AND facial pain"/ OR *chronic paroxysmal hemicrania/ OR *cluster headache/ OR *drug induced headache/ OR *headache/ OR *hypnic headache/ OR *primary headache/ OR *postdural puncture headache/ OR *sinus headache/ OR *sunct syndrome/ OR *vascular headache/ OR exp *chronic daily headache/ OR exp *migraine/ OR exp *tension headache/ OR exp *trigeminal autonomic cephalalgia/ 3. meta-analys$.mp OR search$.tw. OR review.pt. 4. (1 OR 2) AND 3 5. ((child$ OR pediatric$ OR paediatric$ OR adolescent$ OR school$ OR teen$ OR juvenile$) NOT adult$).jw,ti. 6. (4 NOT 5) 7. ("201042" OR "201043" OR "201044" OR "201045" OR "201046" OR "201047" OR "201048" OR "201049" OR 20105$ OR 2011$ OR 2012$ OR 2013$ OR 2014$ OR 2015$).em. 8. 6 AND 7 9. limit 8 to English language *Note*: The * before the subject headings in this search limits the search to records where the subject heading is considered by the indexer to be one of the foci of the article.
Web of Science Licensed Resource (ISI Interface)	20 May 2015	#1: TI=((headache* OR migraine* OR cephalgia* OR cephalalgia* OR hemicrania* OR SUNCT) AND TS=("systematic review" OR metaanalys* OR "systematically reviewed" OR meta-analys*)) #2: TS=(child* OR pediatric* OR paediatric* OR juvenile* OR teen* OR adolescen* OR school*) NOT TS=adult* #3: #1 NOT #2 DocType=All document types; Language=English; Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=2010-2015
CINAHL Licensed Resource (OVID Interface)	20 May 2015	S1. (MH Headache+ AND (TI meta analy* OR AB meta analy* OR MH meta analysis OR TX metaanalys* OR MH systematic review OR PT review OR PT systematic review)) S2. (TI (migraine* OR headache* OR cephalgia* OR cephalalgia* OR hemicrania* OR SUNCT) AND TX (meta analy* OR metaanalys* OR systematic review)) S3. S1 OR S2 S4. Limit S3 to Age Groups: Fetus, Conception to Birth, Infant, Newborn 0-1 month, Infant, 1-23 months, Child, Preschool 2-5 years, Child, 6-12 years, Adolescence, 13-18 years S5. S4 NOT (S4 AND MW Adult) S6. (S3) NOT (S5)

Database/Website	Date Searched	Search Terms
		Limiters -Published Date: 20100101-20151231; Language: English
Library Catalogues		
Proquest Dissertations and Theses Full Text Licensed Resource (Proquest Interface)	5 June 2015	Headache* OR migraine*
Government		
Alberta Health *www.health.gov.ab.ca*	5 June 2015	headache OR migraine systematic-review OR meta-analysis
Health Canada (site searched with Google)	5 June 2015	"systematic review" | "meta analysis" migraine OR headache site:hc-sc.gc.ca Date: past year
HTA Agencies/Coverage Agencies		
INESS *www.inesss.qc.ca/en/home.html*	8 June 2015	Headache; headaches; migraine; migraines
CADTH *www.cadth.ca/index.php/en/hta/reports-publications/search*	8 June 2015	Headache; headaches; migraine; migraines
ICES *www.ices.on.ca/*	8 June 2015	Headache; headaches; migraine; migraines
HTA at McGill *www.mcgill.ca/tau/*	8 June 2015	Browsed list
OHTAC *www.hqontario.ca/evidence/publications-and-ohtac-recommendations/ontario-health-technology-assessment-series*	8 June 2015	Browsed list
NICE (UK) Evidence Search *www.evidence.nhs.uk/*	8 June 2015	Headache; headaches; migraine; migraines
NIHR HTA *www.nets.nihr.ac.uk/programmes/hta*	8 June 2015	Searched projects and HTA journal for "Headache; headaches; migraine; migraine"
BlueCrossBlue Shield Technology Assessments *www.bcbs.com/blueresources/tec/vols/*	10 June 2015	Browsed list of TEC assessments

Database/Website	Date Searched	Search Terms
Aetna Clinical Policy Bulletins *www.aetna.com/about/cov_det_policies.html*	10 June 2015	Headache; migraine
Agency for Healthcare Research and Quality (AHRQ) *www.ahrq.gov/research/findings/evidence-based-reports/index.html*	10 June 2015	Headache; migraine
Internet Search Engine		
Google *www.google.ca*	10 June 2015	headache OR migraine systematic-review OR meta-analysis -pubmed -bmj
TRIP Database *www.tripdatabase.com*	11 June 2015	(title:headache OR migraine) from:2010 to:2015

Notes: The * and $ symbols are truncation characters that retrieve possible suffix variations of the root word; e.g., surg* retrieves surgery, surgical, surgeon, etc. In databases accessed via the OVID platform, the truncation character is $. Semicolons are used to indicate terms that were searched separately.

"Do Not Know" Recommendations, New Interventions, and Medication Table

The IHE Database was searched to identify recently published systematic reviews on:

- interventions proposed by stakeholders (the SC, the GUC, members of the former GDG and Advisory Committee [1st Edition], and others) that were considered important by the GUC, but which were not covered in the 1st Edition of the *Alberta CPG*, or in the new seed guidelines – these included: craniosacral therapy, self-management, and aerobic exercise for migraine; occipital nerve stimulation for chronic migraine; gabapentin for episodic migraine prophylaxis; massage for migraine and tension-type headache; selective serotonin reuptake inhibitors (SSRIs); and trigger point injection;
- recommendations from the 1st Edition of the *Alberta CPG* that were sourced from a seed guideline but are no longer listed in subsequent updates of the seed guideline and are not supported by another new seed guideline – this applied to the recommendation on hypnotherapy; and
- all of the drugs listed in the medication table from the 1st Edition of the *Alberta CPG*.

Selecting the Seed Guidelines

The initial selection of guidelines was made by one reviewer and double-checked by a second reviewer. Guidelines were excluded that, on the basis of their abstract, clearly did not meet the inclusion criteria. Copies of the full text of potentially eligible guidelines were retrieved. In some cases, closer examination of the full text revealed that the guideline did not meet the inclusion criteria. Consequently, these papers were excluded (see *Appendix D*). When a single guideline development group had published more than one guideline, only the most recent version was used.

From the 47 relevant guidelines identified by the search strategy, the IHE Research Team, in consultation with one GUC co-chair, compiled a final shortlist of 11 potential seed guidelines.

Critically Appraising the Seed Guidelines

The included guidelines were assessed with respect to various aspects of methodology and reporting using the Appraisal of Guidelines for Research and Evaluation (AGREE) II instrument[8,9] (*note*: the original AGREE tool was used in the 1st Edition of the *Alberta CPG*[10,11]). The AGREE instrument is an internationally developed, generic tool that is validated, transparent, and widely accepted, with satisfactory reliability for most domains. The instrument has 23 key items organized into the following six domains:

- *Scope and Purpose* (items 1 to 3) reflects the overall aim of the CPG, the specific health question(s), and the target population.
- *Stakeholder Involvement* (items 4 to 6) refers to the extent to which the guideline was developed by the appropriate stakeholders and represents the views of intended users.
- *Rigour of Development* (items 7 to 14) is the process used to gather and synthesize the evidence, and the methods used to formulate the recommendations and to update them.
- *Clarity of Presentation* (items 15 to 17) assesses the language, structure, and format of the CPG.
- *Applicability* (items 18 to 21) refers to the likely barriers to and facilitators of implementation, strategies to improve guideline uptake, and the resource implications of applying the guideline.
- *Editorial Independence* (items 22 to 23) indicates the independence of the recommendations from possible conflict of interest.

The tool is accompanied by a detailed User Guide that explains how to score the 23 items.[9] Each guideline is assessed by at least two (ideally four) appraisers using a seven-point scale (ranging from 7 = "strongly agree" to 1 = "strongly disagree") to rate each of the 23 items. These scores are then combined for each of the six domains and converted into standardized domain scores as per the following formula:

$$\text{Standardized domain score (\%)} = \frac{\text{obtained score} - \text{minimum possible score}}{\text{maximum possible score} - \text{minimum possible score}} \times 100$$

The six domain scores are independent and cannot be combined into a single score. Instead, appraisers can provide an overall assessment of the guideline according to the following categories:

- Overall quality using a seven-point scale (ranging from 7 = "highest possible quality" to 1 = "lowest possible quality")
- Inclination to recommend the guideline for use ("yes", "yes with modifications", or "no")

The Research Team modified the original AGREE tool[10] (and subsequently AGREE II) to reduce the ambiguity and subjectivity associated with item scoring, and to enable the differentiation of good quality guidelines from poor quality guidelines (see *Appendix E*). Three modifications were made:[12]

1. A detailed set of instructions, or dictionary, based on the AGREE II User Guide,[9] was constructed using logical operators (AND, OR, NOT) to quantify what constitutes a score

of 4, 3, 2, or 1 for each of the 23 items (for consistency and ease of scoring, the four-point scale from the original AGREE instrument was used instead of the new seven-point scale).

2. Seven "essential" criteria were identified for categorizing guidelines as good, moderate, or poor quality:[13]
    - Item 8: Systematic search conducted
    - Item 10: Methods used to formulate recommendations described
    - Item 12: Link between recommendations and evidence
    - Item 13: External review by experts
    - Item 15: Specific, unambiguous recommendations
    - Item 22: Editorially independent from funder
    - Item 23: Conflicts of interest reported

The average quality score (maximum possible of 28 [7 × 4]) was then rated as:

- *good* – a score of 22 to 28
- *average* – a score of 15 to 21
- *poor* – a score of 0 to 14

Two reviewers undertook seed guideline quality assessments independently, and discussed the dictionary with respect to the interpretation of questions prior to assessing the guidelines. To minimise coding bias, reviewers discussed any items where the scores differed by at least two points.

At a meeting on 25 March 2015, the SC discussed and approved the AGREE II modifications and the results obtained after applying the tool to the included seed guidelines. The results were subsequently presented to the GUC on 25 May 2015.

Critically Appraising the Systematic Reviews on New Interventions

The quality of each systematic review was assessed independently by two reviewers with respect to various aspects of methodology and reporting using an in-house quality appraisal checklist adapted from a number of sources (*Appendix F*). The checklist was operationalized by constructing a dictionary that explained each criterion. The reviewers discussed the dictionary with respect to the interpretation of questions prior to assessing the reviews. Any disagreements in scoring were resolved by discussion until consensus was reached. The systematic reviews were rated according to six essential quality criteria as good, average, or poor. Critical appraisal results for all of the included reviews are tabulated in *Appendix G*. Although the results of the quality appraisal were examined by the SC, interventions with poor-quality systematic review evidence were not excluded from the *Alberta CPG*.

Extracting Data

Two reviewers extracted guideline information into standardized evidence inventory tables that were developed a priori. However, duplicate data extraction and cross-checking were not performed. The evidence inventory tables included guideline profile information (title, country, intervention category; e.g., diagnosis, prophylaxis, pharmaceutical or non-pharmaceutical treatment), the recommendations, a list of the number and types of studies referenced by the guideline to support its recommendations, and the strength of recommendation grades assigned by the seed guidelines.

Only seed guideline recommendations that were not included or disagreed with those in the 1st Edition of the *Alberta CPG*, or provided additional information beyond what was in the *Alberta CPG*, were listed in the evidence inventory tables. Discordant recommendations among guidelines were highlighted within the table. Any recommendations on the use of parenteral pharmacological treatments for refractory migraine attacks were also extracted so that guidance could be provided for situations where primary care practitioners may be required to administer such treatments.

Additional research evidence and information was required, particularly when recommendations were overlapping, discordant, or absent. These supplementary requests by the GUC or its Subcommittees, named "parking lot" items, necessitated examination of the individual studies cited by the seed guideline(s) or of other research evidence, i.e., systematic reviews on headache with a search end date of January 2008 onwards identified by a supplementary literature search of the IHE Database (for details, see *Table 2*). Only systematic reviews that focused on adults and used diagnostic criteria developed by the International Headache Society were considered. An article was deemed to be a systematic review if it met all of the following criteria as defined by Cook et al. (1997):[14]

- focused clinical question;
- explicit search strategy;
- use of explicit, reproducible, and uniformly applied criteria for article selection;
- critical appraisal of the included studies; and
- qualitative or quantitative data synthesis.

The information abstracted from studies referenced by the seed guidelines or identified by a supplementary literature search of the IHE Database included (to the level of detail sufficient to allow an informed decision): objectives, studies reviewed, funding, inclusion and exclusion criteria, interventions, outcome measures, and relevant results and conclusions. If a potentially relevant systematic review lacked adequate detail to determine whether the target population, type of headache, or intervention was relevant, then the primary studies referred to in the review were retrieved for closer examination, when requested by the GUC or its Subcommittees. When required, the authors of the systematic review were also contacted by the Research Team to obtain further information.

If a systematic review included multiple interventions or conditions, only the results and conclusions related to the intervention or condition of interest were extracted. The primary studies included in these reviews were not disaggregated into the various component conditions or interventions, nor were any additional analyses conducted by the Research Team (e.g., appraising the quality of primary studies or conducting supplementary meta-analyses).

When no systematic review was available for a specific intervention, information was considered from the most recent quasi-systematic review(s) (defined as a review that did not critically appraise the included studies) or narrative review(s) (defined as a review that did not use a search strategy or critically appraise the included studies) listed in the IHE Database of systematic reviews. The information abstracted from quasi-systematic or narrative reviews (referenced by seed guidelines or identified in the supplementary literature search) was less comprehensive than for systematic reviews and only included a summary of the relevant results and conclusions.

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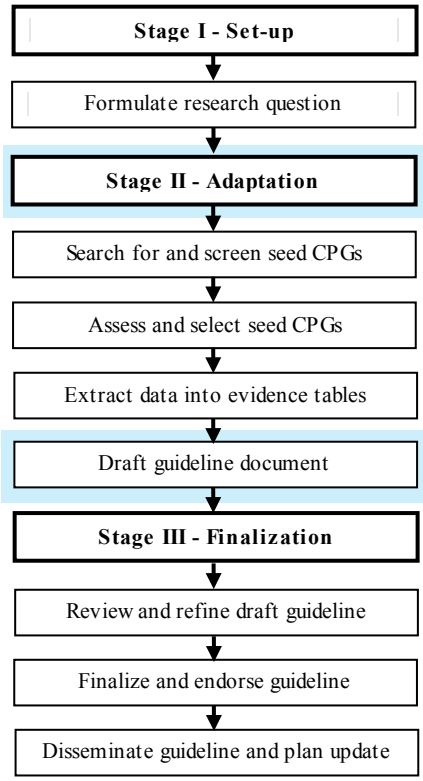
STAGE II: ADAPTATION

GUIDELINE DEVELOPMENT PROCESS



This section contains the following information:

- ✓ Multidisciplinary process used to adapt the seed guidelines
- ✓ Rationale and process for developing and classifying the recommendations as "Do", "Do Not Do" (not recommended), and "Do Not Know"
- ✓ Limitations of the guideline development process

General Process

Guidelines reviewed

A flow diagram of the guideline development process is provided in *Appendix B* (*Figure B.2*). Eleven relevant new guidelines met the predefined inclusion criteria (see *Appendix D* and *Appendix H*). The modified AGREE tool was used to appraise the quality of all potentially eligible seed guidelines. Results were reviewed by the two co-chairs of the GUC on 15 December 2014. One updated guideline (G3) and three new guidelines were excluded due to their poor quality rating (see *Appendix D* and *Appendix I*). This decision, as well as the quality appraisal results for all of the potentially eligible seed guidelines, was presented to the GUC on 25 May 2015. Thus, seven guidelines (five new guidelines and six, including two updated guidelines, from the previous edition) were used in the adaptation process and were included in the *Alberta CPG*, 2nd Edition (*Appendix H*). The new guidelines focused on: migraine (G7); episodic migraine (G8); migraine, tension-type, and cervicogenic headache (G9); primary headaches (migraine, tension-type headache, cluster headache, other trigeminal autonomic cephalalgias) (G10); and migraine, tension-type, and cluster headache (G11) (see *Appendix H*). The references for the included guidelines, together with their AGREE scores and evidence inventory tables, were provided to the GUC.

See *Appendix I* for the AGREE II critical appraisal results (standardized domain scores and average quality scores based on the seven essential criteria) for the six original seed guidelines from the 1st Edition, the seven new seed guidelines, and the four excluded guidelines. Evidence inventory tables for all seven seed guidelines were produced for the GUC (see *Appendix J*).

Update protocol

There is no published information on how to deal with "old" evidence in subsequent iterations of an updated guideline developed using an adaptation process. Since recommendations differ in terms of their need for review, partial updating of a guideline may be just as effective as, and more efficient than, full updating when there is an ongoing monitoring system.[1] To streamline the update process and avoid the wholesale, and unnecessary, review of the entire *Alberta CPG* every two years, a

systematic protocol was devised for conducting sequential partial updates of the *Alberta CPG* (see *Table 3* below). This focused the limited available resources on reviewing only those recommendations that truly required updating. Therefore, in addition to reviewing five new and two updated guidelines, the present *Alberta CPG* update involved: a) updating 12 "Do Not Know" recommendations from the 1st Edition; b) reviewing evidence on new interventions that were not included in the *Alberta CPG* to date; and c) checking drug alerts from Health Canada and the United States Food and Drug Administration (US FDA) for changes in medication availability and safety.

TABLE 3: Ambassador Program guideline update protocol

Timeline	Process Details
Annually	Scan literature for new seed guidelines according to TOP requirements Update triggered when there are at least two new seed guidelines of good quality as judged by the AGREE tool[2] (can include new seed guidelines or updates of previously reviewed guidelines) containing recommendations suggesting that the Alberta guidance needs to be updated
After two years (quadrennially thereafter) [the focus of the present update]	Update "Do Not Know" recommendations by searching for recently published systematic reviews
	Update medication table by searching for recently published systematic reviews for all drugs listed therein
	Update any existing recommendations sourced from a seed guideline that are no longer listed in subsequent updates of the seed guideline and are not supported by another new seed guideline
	Survey stakeholders to identify new interventions of interest that are not included in the current edition of the *Alberta CPG*
	Check Health Canada and US FDA drug alerts for changes in medication availability and safety
	Extract recommendations from selected seed guidelines that: • are not included in the current edition of the *Alberta CPG* • disagree with recommendations in the current edition of the *Alberta CPG* • provide additional information beyond what is in the current edition of the *Alberta CPG*
After four years (quadrennially thereafter)	Update old* recommendations that are based on expired evidence by searching for recently published systematic reviews
	Update "Do" and "Do Not Do" recommendations that are based on EO (GDG/GUC) evidence by searching for recently published systematic reviews
	Update any existing recommendations sourced from a seed guideline that are no longer listed in subsequent updates of the seed guideline and are not supported by another new seed guideline
	Survey stakeholders to identify new interventions of interest that are not included in the current edition of the *Alberta CPG*
	Check Health Canada and US FDA drug alerts for changes in medication availability and safety
	Extract recommendations from selected seed guidelines that: • are not included in the current edition of the *Alberta CPG* • disagree with recommendations in the current edition of the *Alberta CPG* • provide additional information beyond what is in the current edition of the *Alberta CPG*

*More than 7 years from search end date of seed guideline to current date[3]

AGREE: Appraisal of Guidelines for Research and Evaluation; EO: expert opinion; GDG: Guideline Development Group; GUC: Guideline Update Committee; TOP: Toward Optimized Practice; US FDA: United States Food and Drug Administration

In following this protocol, it was decided that, rather than removing the outdated seed guidelines from the *Alberta CPG*, the information would be updated according to the protocol in *Table 3* above and the references for the older guidelines would be cited alongside those for the newer evidence, unless the two sets of evidence were discordant.

Committees

The inaugural face-to-face GUC meeting was held in Calgary on 25 May 2015. The GUC comprised former members, including the two co-chairs of the GDG, and other invited specialists in headache management. The GUC reviewed the results of the survey for new interventions and all of the documents for the new seed guidelines (the guidelines plus their companion documents, evidence inventory tables, and AGREE scores). To expedite the recommendation review process, four topic-specific GUC subcommittees were formed: 1) the Rehabilitation Subcommittee; 2) the Interventional Therapies Subcommittee; 3) the Parenteral Therapies Subcommittee; and 4) the Office-Based Pharmacy Subcommittee. The subcommittees each had two chairpersons (one was always a GUC co-chair) and included one HTA researcher and at least one volunteer from the GUC with relevant expertise. The Parenteral Therapies Subcommittee included invited clinical experts who were not members of the GUC (one pharmacist and one physician). Recommendations were assigned by the GUC and SC to the appropriate subcommittees for discussion and deliberation.

Formulating recommendations

To simplify the task of reviewing the new research evidence, only those recommendations that were discordant with or contained more information than the *Alberta CPG*, or that were new (i.e., were not included in the 1st Edition of the *Alberta CPG*), were tabulated in the evidence inventory tables (see *Appendix J*). The recommendations from the 1st Edition of the *Alberta CPG* were listed for reference alongside the new evidence, where applicable. Evidence inventory tables for the guidelines in the 1st Edition of the *Alberta CPG* can be found in Appendix G of the background document for that guideline.[4]

The four subcommittees reviewed the evidence inventory tables and drafted new or revised recommendations via email and during half-day meetings via WebEx: the Rehabilitation Subcommittee had three meetings, on 12 August, 14 October, and 18 November 2015; the Interventional Therapies Subcommittee had one meeting, on 7 October 2015; the Parenteral Therapies Subcommittee had one meeting, on 2 September 2015; and the Office-Based Pharmacy Subcommittee had two meetings, on 28 October and 11 December 2015. Each of the subcommittee meetings was guided by both co-chairs. Consensus-based decisions made by the subcommittees were presented to the GUC for final approval during two half-day WebEx meetings, held on 7 March and 21 March 2016.

The agenda and all documents were provided in advance for each meeting, and participants had the option of joining the meetings via telephone if they could not attend the face-to-face meeting in-person or use the WebEx conferencing system. Each of the subcommittee meetings was guided by both co-chairs. Frequent "roundtables" were conducted during each meeting to ensure that all participants had a voice in the proceedings, and process reviews were instigated at strategic points throughout. All final decisions were made by consensus.

In three subcommittees (Interventional Therapies, Parenteral Therapies, and Office-Based Pharmacy), one co-chair (a neurologist with expertise in headache management) created "straw dog" recommendations based on the seed guideline recommendations prior to the subcommittee

discussions. These, along with the relevant evidence inventory tables, were then reviewed at the subcommittee meetings. After the meetings, the same co-chair refined or reworded recommendations based on the feedback received from participants. This additional work by the co-chair served to focus discussion and promote consensus on recommendation wording.

Additional evidence was required when uncertainties or disagreements arose regarding interpretation of the evidence from the seed guidelines or when new interventions that were not included in the seed guidelines or the 1st Edition of the *Alberta CPG* were considered. These requests by the GUC or subcommittees, named "parking lot" items, encompassed the examination of individual research studies cited by the seed guidelines as well as additional systematic reviews on headache published between January 2008 and May 2015 identified by a supplementary literature search of the IHE Database (see *Table 2*). The parking lot items were referred for further analysis to the relevant subcommittees. In addition, per the update protocol (see *Table 3*), recently published systematic reviews from the IHE Database were also sought to update: the "Do Not Know" recommendations and medication table entries from the *Alberta CPG*, 1st Edition; and any existing recommendations sourced from a seed guideline that are no longer listed in subsequent updates of the seed guideline and are not supported by another new seed guideline. Occasionally, new recommendations were generated from parking lot item discussions. These included the following:

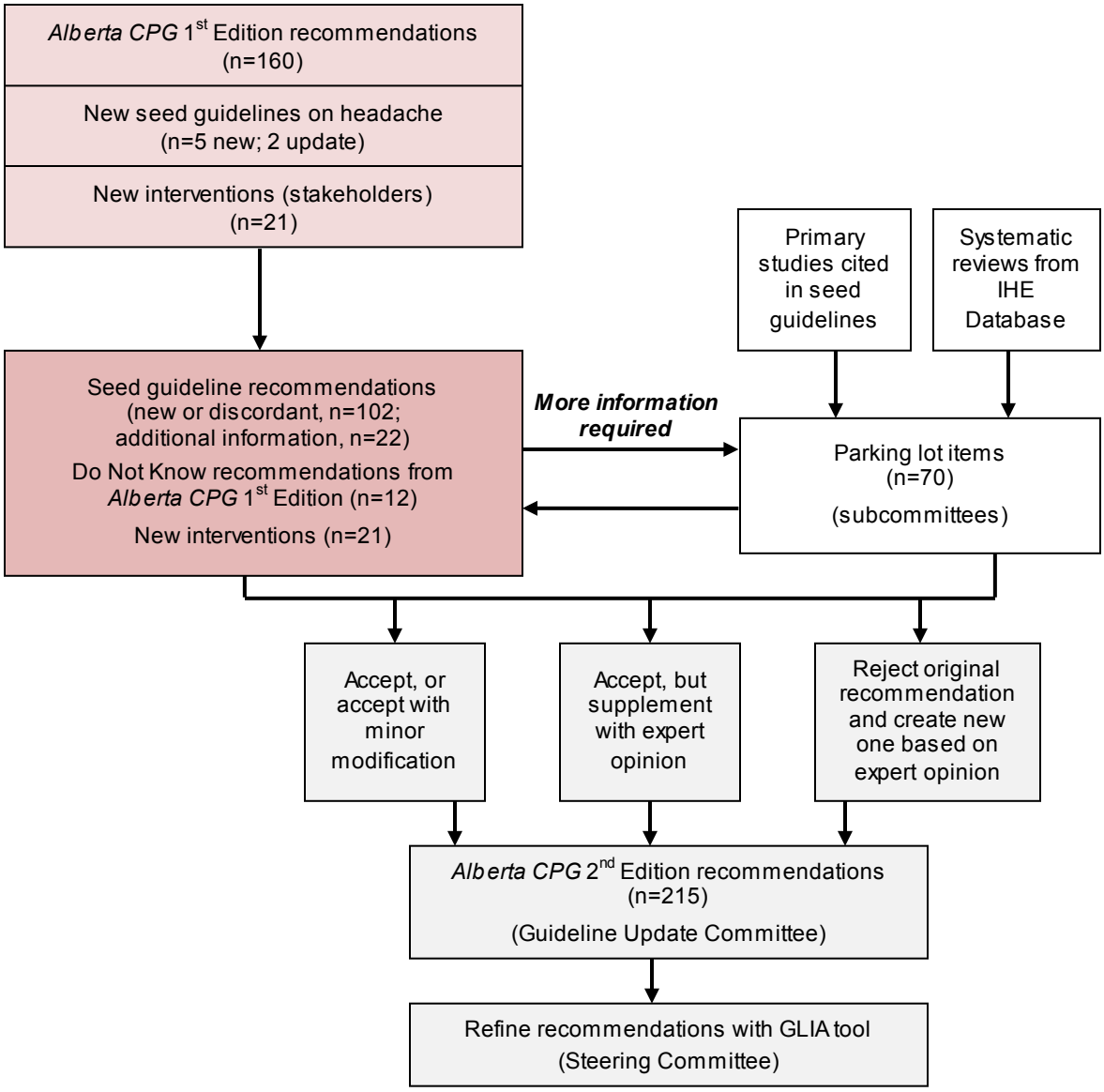
- occipital nerve blockade for cluster headache
- persistent headache attributed to head trauma
- intranasal lidocaine for migraine headache
- ketorolac for acute migraine
- angiotensin-converting-enzyme (ACE) inhibitors during pregnancy
- dimenhydrinate during pregnancy
- sumatriptan for migraine during pregnancy
- intravenous ketorolac for refractory migraine

See *Appendix K* for information about the parking lot items and other miscellaneous requests made by the GUC, subcommittees, and SC, the deliberations of the subcommittees, and the dates when the actions and final approval of the recommendations took place.

The GUC identified 70 parking lot items (see *Figure 1*). After they had reviewed the additional evidence and subcommittee deliberations, redundant recommendations were subsequently incorporated into other recommendations or removed (see *Appendix K*). Parking lot items included existing "Do Not Know" recommendations (1st Edition), new interventions that were not included in the 1st Edition of the *Alberta CPG*, and queries about revised or new recommendations from the GUC or the four subcommittees. Three new recommendations were generated from parking lot item discussions alone rather than from seed guidelines or proposals from stakeholders. A summary table of the revisions made to the *Alberta CPG* for the 2nd Edition is available in *Appendix L*.

A sample of a parking lot item document prepared by the Research Team for discussion in a subcommittee meeting is provided in *Appendix M*. Other parking lot item documents are available upon request.

FIGURE 1: Process of formulating recommendations and resolving parking lot items



To keep track of the deliberations relating to the formulation of the *Alberta CPG* recommendations, the SC and the Research Team developed an internal document for each subcommittee that included the original wording of each recommendation from the seed guidelines, discussions undertaken and decisions made by the subcommittees, revisions of each draft recommendation, and the evidence source for each recommendation. These documents were continuously updated throughout the guideline development process, and abridged versions were provided to the GUC at each meeting. A sample of these documents is provided in *Appendix N*.

The SC and the Research Team added harm statements to some recommendations, where appropriate; these were sourced from the original seed guideline recommendations, from elsewhere in the seed guidelines, or from a systematic review identified from a supplementary literature search required by the GUC, or were created by the GDG or GUC based on their collective professional

opinion. The lack of a harm statement for some recommendations indicates an absence of adverse event information in the seed guidelines, not an absence of adverse events for the intervention itself. Harm statements were added to the following new or updated recommendations on the management of migraine:

- *acute pharmacological therapy*: butalbital
- *pharmacological prophylaxis*: topiramate, divalproex, candesartan, lisinopril, and non-steroidal anti-inflammatory drugs
- *parenteral treatment of refractory migraine*: subcutaneous sumatriptan; intravenous metoclopramide, prochlorperazine, chlorpromazine, dihydroergotamine mesylate, and steroids

The medication tables provided in the 1st Edition of the *Alberta CPG* for acute (symptomatic) and prophylactic treatment of migraine were adapted from two seed guidelines (G1 and G6) and other various sources[5-8] by two pharmacists from the GDG and one co-chair (a neurologist with expertise in headache management). The Office-Based Pharmacy Subcommittee reviewed and updated the medication tables with information from the new seed guidelines G7 and G8. Also, the Parenteral Therapies Subcommittee created a new table on parenteral treatment of refractory migraine, adapted from seed guidelines (G1d, G10, G11) and the *Compendium of Pharmaceuticals and Specialties*.[8] The drug alerts from Health Canada and the US FDA were also checked for changes in medication availability and safety.

The algorithm in the 1st Edition for headache diagnosis, prophylactic and acute medications for migraine, pharmacological therapy for tension-type headache (episodic and chronic), medication-overuse headache, and cluster headache was reviewed for consistency with the new and revised recommendations. The GUC decided to discontinue the 8-page guideline summary from the 1st Edition because most clinicians use the main guideline and the 2-page summary (algorithm and medication tables). However, the practice points from the 8-page summary, which the SC considered useful, were added to the updated 2-page summary guideline in the 2nd Edition.

Rationale and Process for Developing Recommendations

Each recommendation from the *Alberta CPG* was sourced from one or multiple seed guidelines and was accepted, supplemented, or changed as follows:

- Accepted, or accepted with minor modification (e.g., wording)
- Accepted, but supplemented with expert opinion
- Additional information retrieved/considered:
    - accepted/changed original recommendation based only on studies included in seed guidelines
    - accepted/changed original recommendation based on additional evidence from systematic review literature search
    - supplemented additional evidence with expert opinion

In wording the recommendations, the GUC, subcommittees, SC, and Research Team considered the GuideLine Implementability Appraisal (GLIA) tool,[9,10] which is designed for appraising the implementability of CPGs. It explores different dimensions of individual recommendations, such as

decidability, executability, effect on process of care, presentation and formatting, measurable outcomes, apparent validity, novelty/innovation, flexibility, and computability. The SC and Research Team met several times over the period from May to August 2016 to refine the wording of recommendations. The final version of the recommendations was reviewed by the GUC via an online survey in August 2016.

In the *Alberta CPG*, the type of evidence (evidence source) referenced by the seed guideline(s) in support of the original recommendation was represented in several possible ways, as follows (note that some evidence types are not listed because not all study designs were cited by the seed guidelines):

- Systematic review (SR), as cited by the seed guideline(s) or identified by the search for supplementary literature that was required by the GDG (1st Edition) or GUC (2nd Edition). The literature search spanned the period between January 2000 and October 2010 for the 1st Edition of the guideline, and between January 2008 and May 2015 for the 2nd Edition.
- Quasi-systematic review (qSR): A review with a systematic search strategy that does not include a critical appraisal of the included studies.
- Randomized controlled trial (RCT), as cited by the seed guideline(s).
- Non-randomized comparative study (NRCS), as cited by the seed guideline(s).
- Case series (CS), as cited by the seed guideline(s).
- Guideline (G), as cited by the seed guideline.
- Nonsystematic/narrative review (NR): An evidence synthesis, consensus statement, or report that does not include either a systematic search strategy or a critical appraisal of the included studies.
- Expert opinion (EO), as cited by the seed guideline, when no evidence was provided by the seed guideline in support of the recommendation.
- EO (GDG) or EO (GUC): After examining the individual studies cited by the seed guideline(s), additional SRs on headache as identified by a supplementary literature search spanning from January 2008 to May 2015, or other references nominated by the GDG or GUC members, or when no evidence from SRs was found on an intervention, the original recommendation was rejected and or a new recommendation was drafted based on the collective EO of the GDG or GUC.

For evidence cited by the seed guideline(s), only the highest level of evidence was listed. For example, when the evidence cited by a seed guideline was from SRs and studies of other design (i.e., qSR, RCT, NRCS, CS, G, or NR) only SR was listed as the source. When no SR was referenced in the seed guideline, the evidence source was indicated in the following order: qSR, RCT, NRCS, CS, G, NR, EO. The same classification for the evidence source was applied when multiple seed guidelines were used to inform one recommendation.

Each recommendation in the *Alberta CPG* came from one or more seed guideline(s), was based on evidence from SRs or qSRs from the IHE Database, or was created by the GDG (1st Edition) or GUC (2nd Edition), based on their collective professional opinion and an analysis of relevant evidence. Recommendations that used SRs from the IHE Database in their evidence source, together with the relevant SR citations, are listed in *Appendix O*.

The background statements in the *Alberta CPG* were derived from the seed guidelines, or were created by the GDG or GUC based on their collective professional opinion and an analysis of relevant SRs or other published evidence provided by the GDG that was not captured in the IHE Database.

In cases where *Alberta CPG* recommendations were sourced from a seed guideline but are no longer listed in subsequent updates of that seed guideline, the original citations were removed only if, in the update process, a new recommendation was developed by the GUC based on evidence from a new seed guideline that would constitute a change of recommendation category (e.g., from "Do" to "Do Not Do"), or if the older recommendation is supported by newer research evidence of a higher evidence level (e.g., from other seed guidelines or an SR from the IHE Database).

Classification of Recommendations

Although one average-quality and 10 good-quality guidelines informed the 2nd Edition of the *Alberta CPG* (see *Appendix I*), the AGREE tool could not verify the validity of the guideline recommendations and the underlying evidence, or reconcile differences in evidence rating scales. In addition, the seed guidelines were inconsistent in how they rated the quality of the evidence and the strength of the recommendations. Also, because of time constraints, the Ambassador Program guideline adaptation process could not unbundle the seed guidelines to review all of the research evidence cited by the guidelines to support their recommendations. Therefore, a process was developed to ensure a standardized definition of the final guideline recommendations in the *Alberta CPG* (i.e., what constituted a "Do", "Do Not Do", or "Do Not Know" recommendation), systematically meld the seed guidelines' recommendations into consistently worded recommendations, and display the source (e.g., seed guideline(s), expert opinion) of the final recommendations in a transparent and systematic way (see *Appendix P*).

In the *Alberta CPG*, the recommendations are categorized into three groups: "Do", "Do Not Do" (i.e., not recommended), and "Do Not Know" (see *Table 4* below); more details on the recommendation categories are available in *Appendix Q*.

TABLE 4: Definitions for recommendation categories

Recommendation Category	Definition
Do ✓	The GDG or GUC accepted the original recommendation, which provided a prescriptive direction to perform the action or used the term "effective" to describe it. The GDG or GUC supplemented a recommendation or created a new one based on their collective professional opinion, which supported the action. A supplementary literature search found at least one systematic review presenting consistent evidence to support the action.
Do not do ✗	The GDG or GUC accepted the original recommendation, which provided a prescriptive direction "not" to perform the action, or used the term "ineffective" to describe it, or stated that the evidence does "not support" it. The GDG or GUC supplemented a recommendation, or created a new one based on their collective professional opinion, which did not support the action. A supplementary literature search found at least one systematic review presenting consistent evidence that did not support the action.
Do not know ?	The GDG or GUC accepted the original recommendation, which did not recommend for or against the action, or stated that there was "no evidence," "insufficient or conflicting evidence," or "no good evidence" to support its use. The GDG or GUC supplemented a recommendation or created a new one based on their collective professional opinion, which was equivocal with respect to supporting the action. A supplementary literature search found either no systematic reviews ("insufficient evidence to recommend for or against") or at least one systematic review presenting conflicting or equivocal results or stating that the evidence in relation to the action was "limited," "inconclusive," "inconsistent," or "insufficient" ("inconclusive evidence to recommend for or against").

Limitations of the Guideline Development Process

Using seed guidelines minimized resource commitment, and the expedited development process ensured the continued engagement of clinical experts. Stakeholder buy-in was also fostered by the contextualization process. However, the following challenges were identified:

- The AGREE tool identified well-developed and reported guidelines, but could not verify the validity of the recommendations and the underlying evidence, or reconcile differences in evidence rating scales.
- Clinical judgement was needed for overlapping, discordant, or absent recommendations.
- The strength and quality of the underlying empirical evidence was not formally assessed and could not be defined by terms such as *good*, *fair*, *poor*, *insufficient*, or *conflicting*, which made categorizing the strength and type of recommendations problematic.
- Faith in the process can be undermined by the fear of using inferior seed guidelines.
- Recently published evidence is not necessarily incorporated.
- Not all recommended treatment options are available in all communities, nor are all treatment options necessarily covered by CPGs.

Updating an adapted guideline posed the following additional challenges, which became apparent during the revision process:

- How to efficiently extract information from the new seed guidelines into evidence tables without duplicating previous effort: only new or discordant recommendations were extracted from the additional seed guidelines.
- How to incorporate new seed guideline information, while preserving the accumulated knowledge from previous guidelines whose publication dates would otherwise render them obsolete: original citations were retained, new guideline references were added when the guideline supported the original recommendation, and any changes to original recommendations were highlighted within the updated guideline.
- How to incorporate new interventions and revise recommendations rated as "Do Not Know" in the original *Alberta CPG* that are not addressed by the new seed guidelines: search for and appraise any systematic review evidence on the interventions and use ad hoc subcommittees to deliberate on the additional information.
- How to form a streamlined, multidisciplinary GDG/GUC that maximizes local relevance and buy-in, but is also efficient: ensure continuity by using the same experienced GDG/GUC chair, SC, and Research Team, together with a smaller GUC comprising some of the original GDG who are familiar with the adaptation process; ration expertise wisely; clearly outline the process and responsibilities of all participants upfront; and use topic-specific subcommittees of the GUC to review research evidence and recommendations.

References

Note: The references for the seed guidelines (G1 to G11) are available in *Appendix H*.

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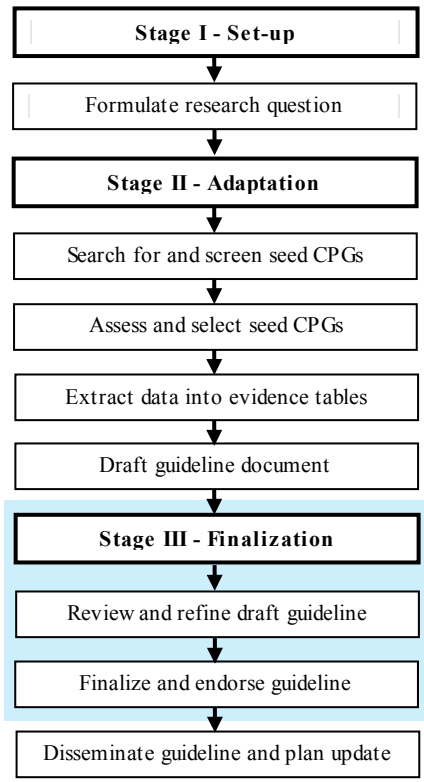
STAGE III: FINALIZATION



REVIEWING, EVALUATING, AND ENDORSING THE *ALBERTA CPG*

This section contains the following information:

- ✓ Process used to review the *Alberta CPG*, 2nd Edition
- ✓ Evaluation of the *Alberta CPG*
- ✓ Key review criteria for assessing the impact of the *Alberta CPG*

Reviewing the *Alberta CPG*

The 1st Edition of the *Alberta CPG* (quick reference algorithm and medication tables, main guideline, and companion documents) was reviewed by various stakeholders; family physicians with experience and interest in headache management and members of the GDG reviewed the quick reference algorithm and medication tables, main guideline, and companion documents, and lay people and patients with headache conditions reviewed the patient information sheets. The SC and Research Team collated all feedback and incorporated it, where possible, into the *Alberta CPG*. All changes were subsequently presented to the GDG. Further details are available in the background document for the 1st Edition of this guideline.[1]

For the 2nd Edition of the *Alberta CPG*, the GUC and subcommittee members were asked to provide feedback on the clarity of the recommendations, particularly the new and revised sections of the guideline, and their implementability within primary care practice in Alberta. The respondents included four family physicians, one pharmacist, and one registered nurse. A sample of the web-based survey form and the responses received are provided in *Appendix R* (Figure R.1 and Tables R.1 and R.2).

The existing patient information sheets were updated by the SC to match updates to the guideline. The draft patient information sheets were then reviewed by the IHE Lay Advisory Committee on 22 April 2016. A sample of the feedback received from the committee is provided in *Appendix R* (Table R.3). The SC reviewed the committee's feedback, the majority of which was incorporated into the final versions of the patient materials. The revisions included streamlining the document formats and simplifying the wording. A new patient information sheet (*What you should know about your headache during pregnancy and breastfeeding*) and 23-page brochure (*What you should know about your headache*) were also created. The final version of the brochure was reviewed by patients from the Calgary Headache Assessment & Management Program in January/February 2017. Patients were provided with a copy of the brochure, a feedback form (which included questions about wording and what other useful information could be added for patients), and a stamped envelope. Two feedback forms were returned, after the guideline and companion materials had been published on

the TOP and IHE websites. Any future editions of the materials will take this feedback into account. A selection of all the comments received is provided in *Appendix R* (Table R.4).

The *Alberta CPG*, 2nd Edition was endorsed by the TOP program, which is funded under the Master Agreement between the Alberta Medical Association (AMA), AHS, and Alberta Health. TOP is administered by the AMA.

Evaluation Strategy

The key review criteria established in the dissemination and implementation plan[2] for the 1st Edition of the *Alberta CPG* are applicable to the 2nd Edition. The key evaluation question is: *Did the dissemination and implementation (KT) strategy work?* The objective of the KT strategy was "to positively inform and influence the treatment of headache pain: that is, encourage and support adherence to the CPG." The Canadian Academy of Health Sciences (CAHS)[3] notes the following five broad types of long-term impacts of research:

- Advancing knowledge
- Capacity-building
- Informing decision-making
- Health impacts
- Broad economic and social impacts

The indicators and metrics used to measure effect should be appropriate (valid, relevant, transparent), feasible (cost, timelines), and well matched to the specific project under evaluation. Potential evaluation questions and metrics for evaluating the impact of the *Alberta CPG* are listed below.

Advancing knowledge

This refers to measures of research quality, activity, outreach, and structure.

- **Question**: Have we influenced the science around guideline development?
- **Indicators/Metrics**: Presentations and publications
    - Number of presentations given by SC or GDG or GUC members; particularly on the process of developing the guidelines, such as the use of the AGREE tool and the ADAPTE framework
    - Publication counts in highly cited publications

Capacity-building

This refers to personnel, additional research activity funding, and infrastructure. Typically, this encompasses the number of research students engaged in projects and, for organizations, the level of additional research funding. It can also include aspirational indicators such as receptor capacity.

- **Questions**:
    - Did we receive any other research funding?
    - Did we improve receptor and absorptive capacity?
- **Indicators/Metrics**:

- Number of collaborations (informed through the process evaluation)
- Other research dollars leveraged

Informed decision-making

This refers to health-related decision-making, research-related decision-making, health products/industry decision-making, and general public decision-making.

- **Questions**:
  - Were we successful at making our key audiences aware of the guidelines?
  - Are people using the guideline to inform their decision-making?
- **Indicators/Metrics**:
  - Bibliometrics
    - Publication in key audience publications
    - Publication counts in highly cited publications
  - Website diagnostics
    - Hits on website
    - Average time spent on website
    - Number of pages viewed on website
    - Downloaded material (e.g., patient information sheet) and relative download rate compared with discipline benchmark
    - Downloads to PDAs
  - Mentions in patient organization communication vehicles
    - Recommended/referred to by related public campaigns
    - Links posted on other national and international guideline sites
    - Cited in public policy documents (e.g., the Primary Care Network newsletter)
    - Surveys of sample groups of primary care providers (separate research project – see below)

Health impacts

This refers to health status, determinants of health, and system changes.

- **Question**: Where primary providers and patients adhere to the guidelines, is there a positive impact on health status and health system indicators?
- **Indicators/Metrics**:
  - Desirable changes in physician behaviour include the following:
    - Assessment of red flags
    - Increased provision of appropriate education and reassurance to patients
    - Reduction of inappropriate recommendations regarding neuroimaging, electroencephalography, or sinus and cervical spine x-rays

        - Increase in appropriate prescribing for behavioural therapies
        - Reduction of inappropriate prescribing of pharmacological therapies
        - Increase in appropriate prescribing of patient self-management programs
    - Evaluation of social media tools

Broad economic and social impacts

This refers to activity, commercialization, health benefit, well-being, and social benefit indicators.

- **Question**: Have the guidelines generated any spin-off activity or products?
- **Indicators/Metrics**: To be determined

References

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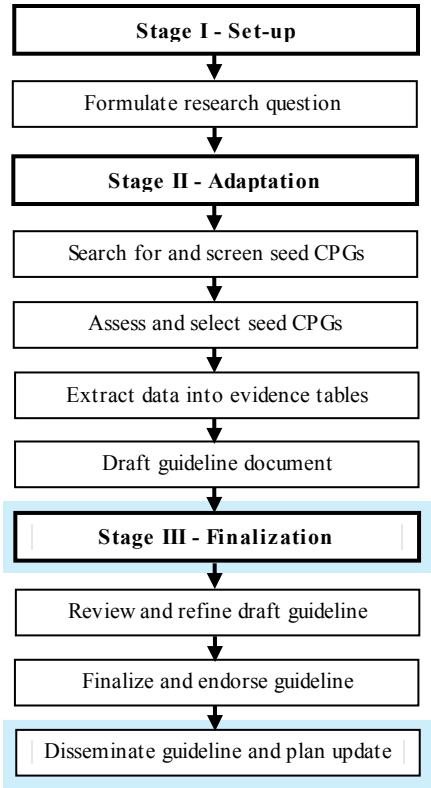
STAGE III: FINALIZATION

DISSEMINATING, IMPLEMENTING, AND UPDATING THE *ALBERTA CPG*



This section contains the following information:

- ✓ Potential organizational barriers to implementing the *Alberta CPG*
- ✓ Plan for disseminating and implementing the *Alberta CPG* within Alberta
- ✓ Process for updating the *Alberta CPG*

Potential Barriers to Guideline Uptake and Implementation

Information on potential barriers to appropriately managing chronic pain and to the uptake of CPGs was obtained from surveys conducted in 2006, 2007, 2009 and 2012 as part of the Ambassador Program. Further details are available in the background document for the 1st Edition of the *Alberta CPG*.[1] The barriers listed in *Figure 2* and *Table 5* are also applicable to the 2nd Edition of the *Alberta CPG*.

The updated recommendations in the 2nd Edition of the *Alberta CPG* were reviewed by members of the GUC and subcommittees. Feedback via a web-based form, which included questions about the potential barriers to implementing the recommendations, was received from four family physicians, one pharmacist, and one registered nurse. A sample of the web-based survey form and the responses are provided in *Appendix R*.

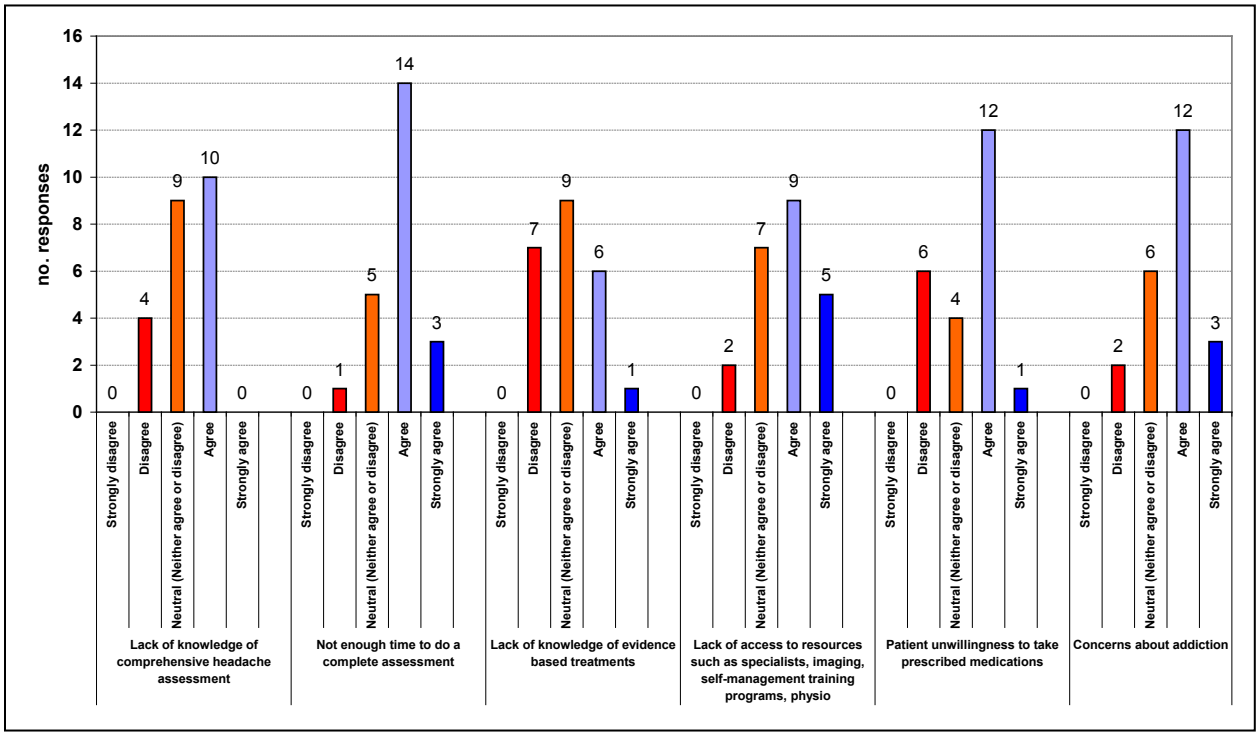
Key actors

A dissemination and implementation plan[2] was developed for the 1st Edition of the *Alberta CPG*. This document included a section on the state of practice and knowledge as well as barriers to change, grouped by audience. The plan also identified the key actors in the dissemination and implementation process:

Physicians and other healthcare providers

Literature on physician compliance with CPGs[3] suggests that guideline adherence is affected by a complex interplay of factors that influence practitioner knowledge, attitudes, and behaviours. Many determinants, such as regulatory decisions, allocation of resources, and availability of treatment options, are out of the practitioner's control.

FIGURE 2: Perceived barriers to providing the best care possible to patients with headache (n=23 family physicians)



Source: [1]

Patients

Patient preferences can be a significant barrier to guideline adherence. Patients often present to practitioners with preconceived notions about the management of their condition and outdated knowledge about treatments. Consequently, they often look for a specific cause for their pain and expect rapid resolution of the problem.

From a physician's perspective, agreement with guideline recommendations is a basic but not sufficient precondition for guideline implementation. Physicians may agree with the guideline content but believe that guideline stipulations are not congruent with patient wishes.[4]

Public

The public is an audience for the *Alberta CPG*, but the public can also be seen as a strategy to support dissemination and implementation with other decision-makers in the healthcare system. The general public can understand scientific material, but need assistance in extracting meaning and relevance, and an explanation of the significance of limitations is required. Therefore, any effective strategy for communicating with the general public requires a sustained effort and is likely to be very costly.

It is useful to gauge public reaction to population-based campaigns through focus groups before developing materials. In large media campaigns, it is difficult to tailor media messages for particular subgroups that are at different stages of readiness. Therefore, key messages should be built on a social marketing-based knowledge translation strategy.

Government

Government representation and involvement has been part of the Ambassador Program from its inception. These representatives are in the best position to inform the dissemination and implementation of the *Alberta CPG* within government and within the Primary Care Networks.

Professional associations and colleges

Professional associations and colleges are an important means of facilitating communication with allied health professionals. They are also an audience in their own right, as the *Alberta CPG* might or might not align with their own profession-specific guidelines.

Health regions and provincial authorities

Clinicians from AHS have participated in the development of the *Alberta CPG* and senior AHS administrators are members of the AC. This linkage will capitalize on the considerable experience and multiple communication channels available within AHS, enabling the dissemination and implementation of the *Alberta CPG* throughout AHS and to community based clinicians and the public.

Insurers and others

The interest in the *Alberta CPG* within this audience group will vary according to their specific involvement with the guideline. The intensity of dissemination and implementation within these groups will vary accordingly.

Dissemination and Implementation Plan

The *Alberta CPG* dissemination plan includes five main strategies to manage barriers:

- Develop patient support materials (information sheets, website, brochure).
- Involve partners:
  - TOP, to launch the guideline; and
  - GUC members, to champion the CPG in their regions.
- Facilitate access to the *Alberta CPG* on the TOP website from provincial, national, and international associations and organizations.
- Contact and connect with important stakeholders such as Alberta Health, AHS, and the Primary Care Networks.
- Promote the CPG to professionals through different channels such as workshops, teaching support for continuing medical education (CME) in faculties of medicine (University of Calgary and University of Alberta), rural CME sessions, videoconferences, webinars, participation at conferences and other professional meetings, and publication in professional newsletters and peer-reviewed Canadian and international journals.

Dissemination of the *Alberta CPG* has included peer-reviewed publications, conference presentations, workshops, and inclusion in academic curricula, as well as the following activities:

- Listing on the Canadian Medical Association (CMA) Infobase and the United States Department of Health and Human Services National Guideline Clearinghouse (NGC).

- Alignment with Choosing Wisely Canada's national recommendations on neuroimaging and prescription of analgesics for patients with headache (available from *www.choosingwiselycanada.org/recommendations/headache/*).
- Development of the HeadachePro clinical pathway app by AHS (available from *headachepro.albertahealthservices.ca/*).

Update Process

For guidelines to remain valid and relevant, TOP, the program responsible for provincial guidelines, requires that guidelines be reviewed annually and updated every two years, if necessary.

The GUC was established to be responsible for the ongoing review and maintenance of the *Alberta CPG*. The committee includes former members of the GDG (1st Edition of the *Alberta CPG*) and new members (added in the 2nd Edition of the *Alberta CPG*) with expertise in the field. Technical support is provided by HTA researchers from the IHE. The task of the GUC is to ensure that the currency of the *Alberta CPG* is maintained over time.

The timelines and process details for the sequential updating of the *Alberta CPG* are listed in *Table 3*. An update is triggered when at least two new guidelines (or updates of previously reviewed seed guidelines) of good quality, as judged by the modified AGREE tool, are identified that contain recommendations suggesting that the *Alberta CPG* needs to be updated.

TOP and HTA researchers from the IHE will co-lead any future updates of the scientific content of the *Alberta CPG*.

TABLE 5: Potential barriers to the use of care pathways, chronic pain and headache management, and implementing the *Alberta CPG* recommendations

Potential Barriers to the Use of Care Pathways[5] (Survey, 2006)	Potential Barriers to Chronic Pain and Headache Management[4] (Surveys, 2007 and 2009)	Potential Barriers to Implementing the *Alberta CPG* Recommendations (Focus Group, 2012)
Guideline/pathway factors		
Not available in form and format needed Not practical; too rigid Lack of satisfaction with the initial guideline or pathway Multiple contradictory pathways No obvious benefit to patients Unsure of its quality Developed with little input from physicians Variation in interpretation across clinicians and cases	Access to guidelines Access to a simple algorithm to sort through different chronic pain models	Not practical, too rigid Too lengthy to use on a regular basis—more like a reference document Lack of a tabular summary of treatment options
Practice environment/organizational barriers		
No institutional support Lack of time to use care pathways in the clinical setting Challenge of allocating time for informing staff of new materials Lack of staff availability Lack of communication, e.g., between departments Lack of networking The regional service model does not support the use of care pathways	Accessibility to resources, such as pain management specialists, diagnostic imaging, self-management training programs, and physiotherapy programs Accessibility to alternative and effective non-drug treatment modalities such as mind/body work, e.g., yoga, tai chi, exercise programs, and nutrition considerations (especially for migraine) Poor understanding of, and support for, a holistic mind-body view of chronic pain, and appropriate alternative treatment approaches (e.g., craniosacral therapy, visceral release therapy, myofascial release therapy, acupuncture) in conjunction with emotional/psychological support Lack of communication mechanisms between the various disciplines managing the patient Lack of time to do a complete assessment	Lack of time to use the CPG in the clinical setting

Potential Barriers to the Use of Care Pathways[5] (Survey, 2006)	Potential Barriers to Chronic Pain and Headache Management[4] (Surveys, 2007 and 2009)	Potential Barriers to Implementing the *Alberta CPG* Recommendations (Focus Group, 2012)
Educational environment/knowledge barriers		
Lack of awareness about relevant pathways Pathways not compatible with practitioner values/ experience Inconsistent interpretation and use of care pathways across clinicians and cases	Poor understanding of and support for a holistic mind-body view of chronic pain and appropriate alternative treatment approaches Lack of knowledge of evidence-based treatments	
Healthcare environment		
Lack of resources (infrastructure/information technology to support use of care pathways, funding, staff) Cumbersome approval process for pathways	Limited resources (staff, funding for rehabilitation programs)	Lack of infrastructure and information technology to support the use of CPG
Practitioner factors		
Lack of time and/or other resources (electronic records, information technology resources) Resistance of clinicians to trying new approaches and lack of physician buy-in Lack of interest in education Lack of awareness Lack of competence No obvious benefit to practice Pain management is directed by a doctor, not by a pathway Information overload	Concern about patient drug-taking behaviour (e.g., abuse, addiction) Physician prescribing practices: family physicians frequently are not following current professional medical standards (e.g., may under-/over-medicate, or medicate in a substandard fashion) Accurate diagnosis and subsequent appropriate treatment Lack of information and cohesiveness among health professionals when managing a patient with chronic pain Poor understanding of, and support for, a holistic mind-body view of chronic pain and appropriate alternative treatment approaches Lack of knowledge of comprehensive headache assessment	Information overload

Potential Barriers to the Use of Care Pathways[5] (Survey, 2006)	Potential Barriers to Chronic Pain and Headache Management[4] (Surveys, 2007 and 2009)	Potential Barriers to Implementing the *Alberta CPG* Recommendations (Focus Group, 2012)
Patient factors		
Difficulties in reconciling patient preferences with pathway recommendations Patient complexity, multiple concerns	Patient willingness to accept recommendations for management instead of focusing on cure Patient engagement and compliance with learning self-management techniques Patient noncompliance with self-care as advised Patient unwillingness to take prescribed medications Ability to override physician opinion if current treatment does not seem to work Self-diagnosis, self-treatment, and use of non-prescription medications General misinformation among patients about chronic pain, especially back pain Patients with special conditions (e.g., dementia)	

References

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APPLICABILITY OF THE *ALBERTA CPG* – ECONOMIC/COST IMPLICATIONS

This section contains the following information:

- ✓ Economic burden of headache pain
- ✓ Economic implications of recommendations reported in the seed guidelines
- ✓ Potential resource implications of the *Alberta CPG*

General Aspects

Migraine is associated with high levels of emotional distress and disability, as well as impaired quality of life for the affected individuals, their families, and society as a whole.[1] The economic impact of migraine can be assessed in terms of direct medical costs and indirect (productivity loss) costs.

Direct costs include medical care costs associated with inpatient and outpatient visits, prescription drug claims, laboratory and diagnostic services, management of side effects, and family costs.[1] Migraine is often associated with comorbid conditions such as psychiatric disorders (anxiety and depression), asthma, and epilepsy. Consequently, estimates of the economic burden of migraine often include the costs of managing these comorbid conditions.[1] However, the direct medical costs represent only a fraction of the overall cost of the disease to society. Indirect costs attempt to capture these other economic effects, which include the cost of missed work days and impaired work performance, unemployment or underemployment because of migraine, short-term disability, the burden experienced between migraine attacks, and time lost due to caring for family members with migraine.[1]

In general, headache accounts for about 20% of absences due to sickness,[2] with migraine being a major cause of absenteeism and decreased work productivity.[3-6] A 2005 survey found that, on average, Canadian women experienced at least partial incapacitation on almost 21 days a year due to migraine.[7] The 2013 Global Burden of Disease Study found that migraine and medication-overuse headache accounted for nearly 29 million and 9.8 million years lived with disability, respectively. In terms of DALYs, migraine causes nearly 400 DALYs per 100,000 people worldwide, with medication-overuse headache contributing 138 DALYs.[8]

Emerging evidence indicates that migraine may be a chronic progressive disorder characterized by escalating frequency of headache attacks (transformed migraine).[9] In the United States, the average annual total costs (including direct and indirect costs) for patients with transformed migraine were at least four times higher than for individuals whose migraine frequency remained unchanged, owing to increased health care utilization, more visits to primary care physicians, neurologist or headache specialists, pain clinics, and emergency rooms, as well as more time missed at work.[9] Tension-type headache is also a costly disorder to society because of its high prevalence.[10]

A general belief exists that medical care is based on scientific evidence and that clinical decisions about the assessment, diagnosis, treatment, and management of a particular condition should also be evidence-based. However, professionals often have their own specific clinical opinions that affect the use of medical services and also their costs. Despite its evident clinical, economic, and social burden, migraine has historically been under-diagnosed and undertreated, and treatment is often

suboptimal and characterised by low compliance.[11] Adherence to CPGs may assist practitioner and patient decisions on appropriate health care and may also improve practice and reduce costs.

Economic Implications Reported in the Seed Guidelines

Formal economic evaluations or cost analyses were not performed or included in any of the new seed guidelines. The following statements were made in the seed guidelines regarding the economic implications of their recommendations:

- Overall cost is a consideration when prescribing medications; cost may influence compliance, especially long-term (G1c).
- "Stratified care" is likely to be the most effective acute treatment approach and has been shown to be cost-effective (G7).
- For patients without significant nausea, regular oral tablets, orally disintegrating tablets, nasal sprays, and injections are all appropriate options. The injection formulation has the greatest efficacy, but has higher cost and more discomfort (G7).
- Medication cost has not been directly considered in the recommendations in this guideline, although it is considered to some extent in the "combined acute medication treatment approach". In this approach, unless the patient has severe attacks and fits into the "stratified care" approach, less expensive non-steroidal anti-inflammatory drugs are tried before a triptan is chosen (if necessary) as the patient's primary acute medication (G7).
- A disadvantage of triptans is their relatively high cost compared with other acute therapies; however, generic versions of triptans are now available at a slightly lower cost (G7).
- The cost of ergotamine is much lower than that of triptans, and it may be an option in selected patients who do not respond to triptans or who are unable to pay for triptans (G7).
- Patient preference may also include considerations of cost, and cost may be a societal consideration as well. However, it must be kept in mind that most of the costs associated with migraine are indirect costs related to missed work and other activities, and these are often much larger than the direct costs which include medication costs (G7).
- When recommending an acute migraine medication, medication cost is among the factors to be considered. Although cost is an important factor, less expensive but also less effective medications may result in increased indirect costs (e.g., missed work), and therefore greater overall costs given that the indirect costs of migraine are much greater than the direct costs (G7).
- Potential effects of these guidelines on the need for additional resources include:
    - a potential increase in triptan use as compared to the less expensive codeine-containing analgesics, which are commonly used or overused in Canada. It is possible that this might increase the overall costs of drugs used for migraine, but as the triptans are more effective than the combination analgesics for most patients, the indirect costs of migraine such as missed work should be reduced much more.
    - a reduction in the prevalence of medication-overuse headache, a condition which imposes a huge economic and social burden on patients and society (G7).
- If prophylactic medications are prescribed more frequently than in the past for patients with migraine as a result of these guidelines, this has the potential to increase demand on

physician offices and to increase prophylactic drug costs. On the other hand, several studies have shown that migraine drug prophylaxis reduces the cost of symptomatic medications significantly, so that the overall drug costs may be unchanged, reduced, or affected less than might be expected (G8).

- The costs of using onabotulinum toxin type A for chronic migraine are comparable to administering topiramate 100 mg for 3 months and lower than using topiramate for 4 months (G10).
- Reducing office visits, emergency department visits, and inpatient admissions for uncontrolled headache syndromes, along with reducing unnecessary tests and procedures for headache diagnosis, is likely to reduce total costs of care even if there are more visits for diagnosis of headache and increased costs for headache-specific drugs (G11).
- Use of computed tomography scanning for diagnosis in patients with headache is costly and unrewarding (G11).
- The monthly cost of gonadotropin-releasing hormone agonist therapy is about 10 times the cost of conventional hormone therapy (G11).
- The clinician-patient relationship plays a key role in improving adherence. Clinicians should ask patients open-ended, non-threatening questions regularly to assess adherence. Questions that probe for factors that contribute to non-adherence could include those surrounding adverse reactions, misunderstandings of treatment, depression, cognitive impairment, complex regimens, and financial constraints.

Economic implications reported in seed guidelines included in the previous edition of the *Alberta CPG* can be found in the relevant background document.[12]

Resource Implications of the *Alberta CPG*

The updated recommendations were reviewed by members of the GUC and subcommittees with respect to implementing the *Alberta CPG*, including resource implications. Feedback was received from four family physicians, one pharmacist, and one registered nurse. A sample of the web-based survey form and the responses received are provided in *Appendix R* (Figure R.1 and Table R.2, respectively).

Because of time and resource constraints, a formal cost analysis or economic evaluation of the impact of the *Alberta CPG* was not conducted. Nevertheless, information derived from such analyses (e.g., cost of implementation of multidisciplinary treatment programs, cost of unnecessary imaging tests) is important and useful in the decision-making process. Studies to address the resource implications of the *Alberta CPG* are planned for the future.

References

Note: References for the seed guidelines (G1 to G11) are available in *Appendix H*.

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APPENDIX A: Participants in the Update Process for the *Alberta CPG*, 2nd Edition

TABLE A.1: Guideline Update Committee – Active members

Zone	City/Site	Affiliation, Discipline, Area of Expertise
Calgary	Calgary[‡§‖]	**Werner Becker MD, BSc, FRCP(C), Co-Chair** Professor, Department of Clinical Neurosciences, University of Calgary Neurology
	Calgary[†]	**Paul Taenzer BSc, PhD, RPsych, Co-Chair** Psychologist, Consultant, University of Calgary Psychology, pain management
	Calgary[‖]	MD, CCFP, FCFP Associate Professor Emeritus, Department of Family Medicine, University of Calgary Primary care
	Calgary[‖]	MD, CCFP Private community physician Primary care
	Calgary	MD, FRCPC (Neurology), DABPN Clinical Assistant Professor, Division of Neurology, Department of Clinical Neurosciences, University of Calgary Neurology
	Calgary[†]	MD, DO, CCFP Consultant, Family physician, Chronic Pain Centre, Alberta Health Services Musculoskeletal chronic pain management
	Calgary[†]	BSc PT, BPE Physical therapist, Chronic Pain Centre, Alberta Health Services Manual therapy, acupuncture, intramuscular stimulation, therapeutic exercise
	Calgary[†‡]	MD, CCFP, FCFP, Consultant, Chronic Pain Centre, Alberta Health Services Family medicine
	Calgary	PhD Psychologist, Alberta Health Services Psychology, chronic pain, chronic headache
	Calgary*[‖]	MD, FRCPC (Neurology), CSCN Diplomate, BSc Clinical Assistant Professor, Division of Neurology, Department of Clinical Neurosciences, University of Calgary Neurology
	Calgary*[†]	MScOT Occupational therapist, Calgary Headache Assessment & Management Program (CHAMP), Alberta Health Services Rehabilitation/physiotherapy
	Calgary[‡‖]	MD, CCFP Medical Director, Chronic Pain Centre, Alberta Health Services Family medicine, chronic pain management
	Calgary[‖]	RN Clinic Coordinator, Calgary Headache Assessment & Management Program (CHAMP), Alberta Health Services Pain management, headache

Zone	City/Site	Affiliation, Discipline, Area of Expertise
	Calgary*	RN Chronic Pain Centre, Alberta Health Services Pain management
Central	Sylvan Lake§	BSc, MSc, MD, CCFP, FCFP Director of Rural and Regional Health, University of Alberta Physician, Sylvan Family Health Centre Family medicine, medical education
Edmonton	Edmonton‖	BScPharm Clinical Pharmacist, Alberta Health Services Pharmacy, pain management
	Edmonton	BScMLS, MHSA Director, Health Technology Assessment (HTA), Institute of Health Economics HTA, research
	Edmonton*‡	MD, FRCPC Professor, Radiology & Diagnosis Imaging, University of Alberta Neuroimaging
	Edmonton†	BSc, DC, MSc, PhD Professor, University of Alberta Spine function
	Edmonton	BA (Hons), MD Associate Dean, Community Engagement Professor, Department of Family Medicine, University of Alberta Family medicine
South	Lethbridge‖	MD, FCFP Family physician, Chinook Regional Hospital Practice limited to chronic pain management

*Members who were not part of the GDG for the 1st Edition of the guideline
†Members who participated in the Rehabilitation Subcommittee
‡Members who participated in Interventional Therapies Subcommittee
§Members who participated in the Parenteral Therapies Subcommittee
‖Members who participated in the Office-Based Pharmacy Subcommittee
Note: Occasionally a representative from Alberta Health was invited to attend GUC or SC meetings, as needed, to update participants on government initiatives.

TABLE A.2: Additional subcommittee members

Zone	City/Site	Affiliation, Discipline, Area of Expertise
Calgary	Calgary*†	BSc Pharm, ACPR Chronic Pain Centre, Alberta Health Services, Calgary, Alberta Pharmacy, pain management
North	Hinton*†	BSc (Hons), MD, CCFP Family physician, Hinton Medical Clinic Family medicine

*Members who were not part of the GDG for the 1st Edition of the guideline
†Members who participated in the Parenteral Therapies Subcommittee

The following individual withdrew from the GDG because of time constraints and/or workload issues.

TABLE A.3: Guideline Update Committee – Resigned member

Zone	City/Site	Affiliation, Discipline, Area of Expertise
Edmonton	Edmonton	BSc, BScOT Clinic Director, LifeMark Health Institute, LifeMark Chronic pain

TABLE A.4: Guideline Update Committee – Ex-officio members

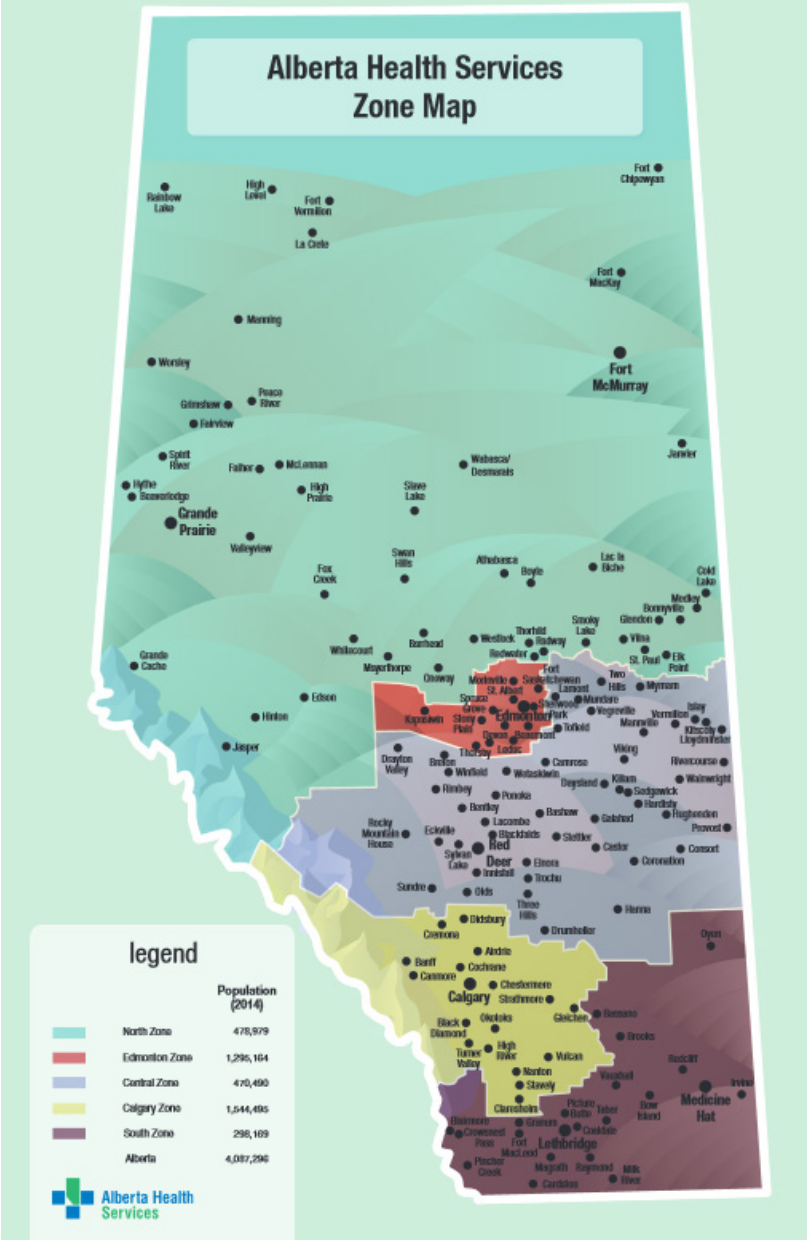
Zone	City/Site	Affiliation, Discipline, Area of Expertise
Calgary	Calgary	MSc Director, Clinical Epidemiology Health Technology Assessment & Innovation, Alberta Health Services Systematic reviews, evidence-based research, guideline development
Edmonton	Edmonton	MSc Program Director, Toward Optimized Practice

TABLE A.5: Steering Committee and Research Team members

Zone	City/Site	Name	Affiliation, Discipline, Area of Expertise
Calgary	Calgary	**Werner Becker*‡‖¶#** Co-Chair of the Guideline Update Committee and Steering Committee	MD, BSc, FRCP(C) Professor, Department of Clinical Neurosciences, University of Calgary Neurology
	Calgary	**Paul Taenzer*‡§** Co-Chair of the Guideline Update Committee and Steering Committee	BSc, PhD, RPsych Psychologist, Consultant, University of Calgary Psychology, pain management
Edmonton	Edmonton	Christa Harstall*‡	BScMLS, MHSA Director, Health Technology Assessment (HTA), Institute of Health Economics HTA, research
	Edmonton	Carmen Moga†‡‖#	MD, MSc Principal Research Lead, HTA, Institute of Health Economics HTA, methodologist
	Edmonton	Ann Scott†‡§¶	BSc (Hons), PhD Principal Research Lead, HTA, Institute of Health Economics HTA, methodologist
	Edmonton	Kimberly Pinnick Broderick*	BSc, MHA Project Coordinator (November 2014 to January 2015), Institute of Health Economics
	Edmonton	Stefanie Kletke*‡§‖¶#	BSc, BA (Hons), MA Project Coordinator (from February 2015), Institute of Health Economics
Other Members of the Research Team			
Edmonton	Edmonton	Dagmara Chojecki	MLIS Information Specialist, Institute of Health Economics

*Steering Committee members
†Research Team members
‡Members who participated in the Guideline Update Committee meetings
§Members who participated in the Rehabilitation Subcommittee
‖Members who participated in the Interventional Therapies Subcommittee
¶Members who participated in the Parenteral Therapies Subcommittee
#Members who participated in the Office-Based Pharmacy Subcommittee

FIGURE A.1: Multidisciplinary Guideline Update Committee and subcommittee participation from the Alberta Health Services zones (active members)



Source: *www.albertahealthservices.ca/ahs-map-ahs-zones.pdf*

Edmonton Zone: family physician (1), pharmacist (1), chiropractor (1), radiologist (1), health technology assessment researcher (1)

Central Zone: family physician (1)

Calgary Zone: family physician (4), osteopathic physician (1), specialist physicians (neurologists) (3), psychologists (2), registered nurse (2), physical therapist (1), pharmacist (1*), occupational therapist (1)

North Zone: family physician (1*)

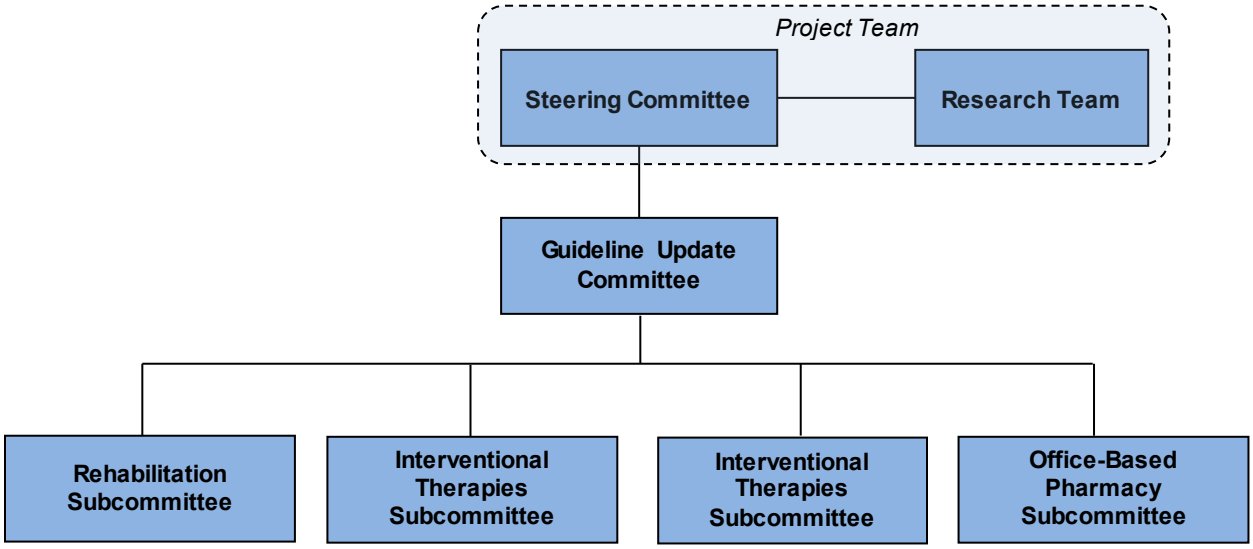
South Zone: family physician (1)

*Members who were not part of the Guideline Update Committee

APPENDIX B: *Alberta CPG* Update Process – Roles and Activities

A streamlined, multidisciplinary, collaborative process was utilized for the guideline updating process to ensure that expertise was rationed wisely and efficiently (see Figure B.1).

FIGURE B.1: Relationships among the committees in the guideline update process



Project Team

The Project Team comprised the combined membership of the SC and the Research Team. The Project Team provided project oversight, identified areas for methodological development, and implemented efficient tracking tools. The Project Team was also responsible for the final editing of the guideline recommendations.

Steering Committee (SC)

Role

- Had the authority and responsibility for the development, implementation, monitoring, and reporting of the project
- Provided guidance to the Research Team
- Provided operational and fiscal oversight
- Acted as a secretariat to the GUC
- Wrote or revised guideline recommendations, based on GUC and subcommittee deliberations, for subsequent reassessment by the GUC
- Was responsible for the final decisions regarding the wording of the guideline recommendations

Membership

- Clinical ambassador, HTA expert, members of the Research Team, and project coordinator

The committee met by WebEx monthly, or more often as required.

Guideline Update Committee (GUC)

Role

- Had the authority and responsibility for developing and revising guideline recommendations
- Reviewed and revised the guideline recommendations, including those prepared by four subcommittees, and companion documents to reflect advances in the research evidence regarding the assessment and management of headache, and considered recommendations related to treatments and interventions that would potentially benefit primary care in Alberta and were not included in the 1st Edition of the *Alberta CPG*
- Worked in subcommittees to analyze supplementary research evidence and draft recommendations

Membership

- Multidisciplinary group of primary care practitioners (i.e., nine family physicians, one occupational therapist, two pharmacists, one chiropractor, one radiologist, two neurologists, one physical therapist, two psychologists, and two nurses) – most of whom were members of the GDG that developed the previous edition of the guideline – SC members, and Research Team members
- Led by two co-chairs who attended the WebEx meetings as well as the subcommittee meetings

The GUC had an inaugural face-to-face meeting at the beginning of the update process and also met twice via WebEx to assess and formulate the recommendations prepared by the subcommittees. Some discussions were also conducted by e-mail.

Subcommittees

Role

- Reviewed, revised, and drafted guideline recommendations in the following areas of expertise, as directed by the GUC: 1) rehabilitation therapies; 2) interventional therapies; 3) parenteral therapies; 4) office-based pharmacy
- Considered and assessed recommendations from the seed guidelines that were new to or discordant with the 1st Edition of the *Alberta CPG*
- Assessed background materials prepared by the Research Team and reviewed research evidence to reach a consensus on assigned questions, the decisions on which were then presented by the chairs of the subcommittees to the GUC for approval

Membership

- Subcommittees had two chairpersons (one of which a GUC co-chair) and comprised one HTA researcher and at least one volunteer from the GUC with relevant expertise, as well as invited experts who were not members of the GUC, when required

The subcommittees conferred via WebEx or email to analyze supplementary research evidence and draft recommendations before presenting them to the GUC.

Research Team

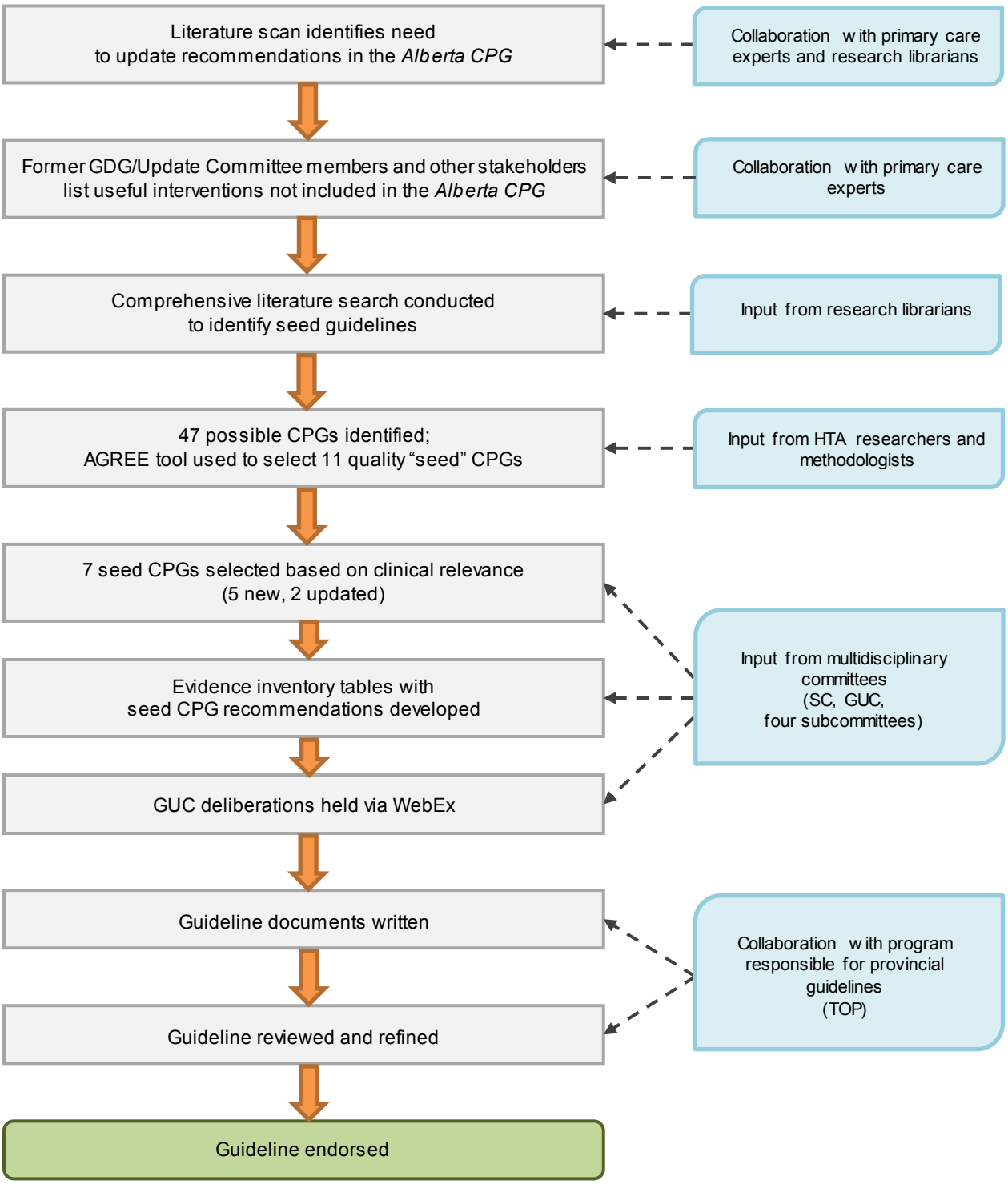
Role

The Research Team played multiple roles and served various functions in the guideline update process, including the following:

- selection and critical appraisal of published guidelines
- preparation of background documents and evidence inventory tables, and development of a system for tracking decision points
- active leadership and participation on all committees
- presentation of relevant research information to the GUC and subcommittees
- co-chairing of subcommittee discussions on selected interventions
- preparation and condensation of all the materials to expedite the review by the GUC
- participation in the process of writing the guideline documents

Figure B.2 below outlines the guideline update process.

FIGURE B.2: *Alberta CPG* update process and involvement of stakeholders, experts, and committee members



APPENDIX C: Participants in the Development Process for the *Alberta CPG*, 1st Edition

TABLE C.1: Guideline Development Group – Active members

Zone	City/Site	Affiliation, Discipline, Area of Expertise
Calgary	Calgary	**Werner Becker MD, BSc, FRCP(C) (Co-Chair)** Professor, Department of Clinical Neurosciences, University of Calgary Neurology
	Calgary	**Paul Taenzer BSc, PhD, RPsych (Co-Chair)** Adjunct Clinical Assistant Professor, Faculty of Medicine, University of Calgary Psychology, pain management
	Calgary	MD, CCFP, FCFP Associate Professor Emeritus, Department of Family Medicine, University of Calgary Primary care
	Calgary	MD, CCFP Private community physician Primary care
	Calgary	MD, FRCPC (Neurology), DABPN Clinical Assistant Professor, Division of Neurology, Department of Clinical Neurosciences, University of Calgary Neurology
	Calgary	MD, DO, CCFP, Consultant Chronic Pain Centre, Alberta Health Services Musculoskeletal chronic pain management
	Calgary	BSc PT, BPE Chronic Pain Centre, Alberta Health Services College of Physical Therapists of Alberta, Canadian Physiotherapy Association Manual therapy, acupuncture, intramuscular stimulation, therapeutic exercise
	Calgary	MD, CCFP, FCFP, Consultant Chronic Pain Centre, Alberta Health Services Family medicine
	Calgary	PhD Alberta Health Services Psychology, chronic pain, chronic headaches
	Calgary	MD, CCFP Medical Director, Chronic Pain Centre, Alberta Health Services Family medicine, chronic pain management
	Calgary	Registered Nurse Clinic Coordinator, Calgary Headache Assessment & Management Program (CHAMP), Alberta Health Services Pain management, headache
Central	Sylvan Lake	BSc, MSc, MD, CCFP, FCFP Director of Rural and Regional Health, University of Alberta Physician, Sylvan Family Health Centre Family medicine, medical education
	Wainwright	MD, BSc Physician Family medicine

Zone	City/Site	Affiliation, Discipline, Area of Expertise
Edmonton	Edmonton	BScPharm Clinical Pharmacist, Alberta Health Services Pharmacy, pain management
	Edmonton	BScMLS, MHSA Director Health Technology Assessment (HTA), Institute of Health Economics Health technology assessment, systematic reviews
	Edmonton	BSc, DC, MSc, PhD Associate Professor, Canada Research Chair in Spinal Function, University of Alberta Spinal biomechanics
	Edmonton	BA (Hons), MD Associate Dean, Community Engagement Professor, Department of Family Medicine, University of Alberta Family medicine
	Edmonton	BSc, BScOT Clinic Director, LifeMark Health Institute Chronic pain
	Edmonton	MD, MSc, CCFP Undergraduate Program Director Assistant Professor, University of Alberta Family medicine
South	Lethbridge	MD, FCFP Family physician, Chinook Regional Hospital Practice limited to chronic pain management
	Medicine Hat	BScPT Physical Therapist, Medicine Hat Regional Hospital, Alberta Health Services Chronic pain, physiotherapy

The following individual withdrew from the GDG because of time constraints and/or workload issues.

TABLE C.2: Guideline Development Group – Resigned member

Zone	City/Site	Affiliation, Discipline, Area of expertise
Calgary	Calgary	BSP, MBA Chronic Pain Centre, Alberta Health Services Clinical pharmacy

TABLE C.3: Guideline Development Group – Ex-officio members

Zone	City/Site	Affiliation, Discipline, Area of Expertise
Calgary	Calgary	MSc Director, Clinical Epidemiology, Health Technology Assessment & Innovation, Alberta Health Services Systematic reviews, evidence-based research, guideline development
Edmonton	Edmonton	MSc Director Knowledge Transfer Initiatives, Alberta Innovates – Health Solutions Knowledge transfer

Zone	City/Site	Affiliation, Discipline, Area of Expertise
	Edmonton	MD, MSc Research Associate HTA, Institute of Health Economics Health technology assessment, methodologist
	Edmonton	BSc (Hons), PhD Research Associate HTA, Institute of Health Economics Health technology assessment, methodologist
	Edmonton	Staff from Charis Management Consulting, Inc. and the Institute of Health Economics Project coordinator

TABLE C.4: Steering Committee and Research Team members

Zone	City/Site	Name	Affiliation, Discipline, Area of expertise
Calgary	Calgary	**Werner Becker*‡** Co-Chair of the GDG and the SC	MD, BSc, FRCP(C) Professor, Department of Clinical Neurosciences, University of Calgary Neurology
	Calgary	**Paul Taenzer*‡** Co-Chair of the GDG and the Advisory Committee	BSc, PhD, RPsych Adjunct Clinical Assistant Professor, Faculty of Medicine, University of Calgary Psychology, pain management Project manager
Edmonton	Edmonton	Christa Harstall*†‡ Co-Chair of the SC and the Advisory Committee	BScMLS, MHSA Director Health Technology Assessment (HTA), Institute of Health Economics Health technology assessment, systematic reviews Project manager
	Edmonton	Carmen Moga†‡	MD, MSc Research Associate HTA, Institute of Health Economics Health technology assessment, methodologist
	Edmonton	Ann Scott†‡	BSc (Hons), PhD Research Associate HTA, Institute of Health Economics Health technology assessment, methodologist
	Edmonton	Various#	Staff from Charis Management Consulting, Inc. and the Institute of Health Economics Project Coordinator
Other Members of the Research Team			
Edmonton	Edmonton	Dagmara Chojecki	MLIS Information Specialist, Institute of Health Economics

*SC members

†Research Team members

‡Members who participated at the GDG videoconference meetings

#Owing to staffing issues, six different people filled this role over the course of the project, including a member of the Research Team

TABLE C.5: Advisory Committee members

Name	Affiliation, Discipline
Christa Harstall (Chair)	Director, Health Technology Assessment, Institute of Health Economics
Paul Taenzer (Chair)	Adjunct Clinical Assistant Professor, Faculty of Medicine, University of Calgary
Michael Aherne	Director of Initiative Development, Pallium Project
Donna Angus	Director, Knowledge Transfer Initiatives, Alberta Innovates – Health Solutions
JoAnne Beckie	Alberta Health Services
Werner Becker	Professor, Department of Clinical Neurosciences, University of Calgary Alberta Health Services, Calgary
Joan Berezanski	Executive Director, Clinical Advisory and Research Branch, Alberta Health
Robyn Blackadar	Executive Director, Knowledge Management, Quality Practice and Partnerships, Alberta Health
Angela Estey	Executive Director Chronic Disease, Specialty Linkages (Children & Adults), Alberta Health Services
Sharon Habermann	Alberta Health Services
Rob Hauptman	Pain Society of Alberta
Sheila Kelly	Manager, Regional Pain Program, Alberta Health Services
Gordon Mackie	Canadian Headache Society
Blair MacKinnon	Dissemination Coordinator, Primary Care Unit, Alberta Health
June Norris	Manager, Allied Health Operations Public Health, Primary Care and Chronic Disease Management Alberta Health Services
John Parboosingh	Professor Emeritus, University of Calgary Consultant, Community Learning, PEAK Project
Douglas Perry	Senior Provincial Clinical Advisor, Clinical Advisory & Research Branch, Alberta Health
Saifee Rashiq	Associate Professor, Director Division of Pain Medicine, Department of Anesthesiology and Pain Medicine, University of Alberta
Don Schopflocher	Associate Professor & Research Statistician, Faculty of Nursing, University of Alberta
Chris Spanswick	Pain Medicine/Medical Leader, Alberta Health Services Assistant Professor, Department of Anaesthesia, University of Calgary
Doug Stich	Program Director, Toward Optimized Practice
Susan Ulan	Senior Medical Advisor, College of Physicians & Surgeons of Alberta
Barry Ulmer	Executive Director, Chronic Pain Association of Canada
Richard Ward	President, Alberta College of Family Physicians

Name	Affiliation, Discipline
Susan Williams	Assistant Deputy Minister, Health Policy and Service Standards Divisions, Alberta Health
Paul Woods	Alberta College of Family Physicians
Michele Zielinski	Executive Director, Clinical Practice Improvement: Quality Performance Improvement, Alberta Health Services

TABLE C.6: Advisory Committee – Ex-officio members

Name	Affiliation, Discipline
Egon Jonsson	PhD, Professor School of Public Health, University of Alberta Community Health Sciences, University of Calgary Executive Director & CEO, Institute of Health Economics
Various	Staff from Charis Management Consulting, Inc. and the Institute of Health Economics Project coordinator

APPENDIX D: Excluded Guidelines

TABLE D.1: Summary of excluded guidelines

Publication	Reason for exclusion
American College of Radiology (ACR). *ACR Appropriateness Criteria®: Headache*. Reston (VA): American College of Radiology; 2013. Available from: acsearch.acr.org/docs/69482/Narrative/ (accessed 8 April 2017).	Target population (adult) not stated
Armstrong C. American Academy of Neurology and American Headache Society. AAN/AHS update recommendations for migraine prevention in adults. *American Family Physician* 2013;87(8):584-5.	Summary of G1
BlueCross BlueShield of Tennessee, Inc. *Clinical practice guideline. Migraine headache*. 2013. Available from: www.bcbst.com/providers/hcpr/ANN_Practice_Parameter_Migraine_Headache.pdf (accessed 8 April 2017).	Not a guideline
Canadian Association of Radiologists. *Diagnostic imaging referral guidelines - Section A: Central nervous system*. Ottawa: Canadian Association of Radiologists; 2012. Available from: www.car.ca/uploads/standards%20guidelines/car-referralguidelines-a-en-20120927.pdf (accessed 8 April 2017).	Did not use International Headache Society (IHS) diagnostic criteria
Donnet A, Demarquay G, Ducros A, Geraud G, Giraud P, Guegan-Massardier E, et al. French guidelines for diagnosis and treatment of cluster headache (French Headache Society). *Revue Neurologique* 2014;170(11):653-70.	Not available in English
Dougherty C, Silberstein SD. Providing care for patients with chronic migraine: Diagnosis, treatment, and management. *Pain Practice* 2014;15(7):688-92.	Not a guideline
Estemalik E, Tepper S. Preventive treatment in migraine and the new US guidelines. *Neuropsychiatric Disease and Treatment* 2013;9:709-20.	Not a guideline
Evers S, Goadsby P, Jensen R, May A, Pascual J, Sixt G, et al. Treatment of miscellaneous idiopathic headache disorders (Group 4 of the IHS classification) -- report of an EFNS task force. *European Journal of Neurology* 2011;18(6):803-12. *Note: Included patients with headache disorders classified as the so-called group 4 headaches in the second edition of the International Classification of Headache Disorders (ICHD-II).*	Target population (adult) not stated
Evers S, Jensen R, European Federation of Neurological Societies. Treatment of medication overuse headache--guideline of the EFNS headache panel. *European Journal of Neurology* 2011;18(9):1115-21.	Target population (adult) not stated
Fontebasso M. Current recommended diagnosis and management of headache. *Prescriber* 2013;24(20):15-26.	Not a guideline
Freitag FG, Schloemer F. Medical management of adult headache. *Otolaryngologic Clinics of North America* 2014;47(2):221-37.	Not a guideline
Harrison DD, Siskin LA, Betz JW, editor(s). *Best practices & practice guidelines*. Arlington (VA): International Chiropractors Association (ICA); 2013.	Did not use IHS diagnostic criteria Target population (adult) not stated
Hicks JK, Swen JJ, Thorn CF, Sangkuhl K, Kharasch ED, Ellingrod VL, et al. Clinical Pharmacogenetics Implementation Consortium guideline for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants. *Clinical Pharmacology and Therapeutics* 2013;93(5):402-8.	Not relevant

Publication	Reason for exclusion
Holdgate A, Kelly AM. *Emergency Care Evidence in Practice series: Management of acute migraine*. Canberra, Australia: Emergency Care Community of Practice, National Institute of Clinical Studies; 2006. Available from: *www.nhmrc.gov.au/_files_nhmrc/file/nics/material_resources/Management%20of%20acute%20migraine%20colour.pdf* (accessed 8 April 2017).	Did not use IHS diagnostic criteria Target population (adult) not stated Focused on treatment in the emergency room
Illinois Department of Healthcare and Family Services. *Migraine prophylaxis considerations. An educational update for providers*. Chicago (IL): University of Illinois at Chicago College of Pharmacy Chicago Rockford; 2014.	Not a guideline
Kaiser Permanente Ohio. *Headache*. 2011. Available from: *www.providers.kaiserpermanente.org/info_assets/cpp_oh/oh_headache_012011.pdf* (accessed 8 April 2017).	Did not use IHS diagnostic criteria
Kwinana Medical Centre, Leda Medical Centre, Coolbellup Medical Centre, Aubin Grove Medical Centre. *Nurse practitioner, primary health care clinical practice guideline*. 2011. Available from: *www.nursing.health.wa.gov.au/docs/career/np/coolbalup/Headache.pdf* (accessed 8 April 2017).	Not a guideline
Lecchi M, D'Alonz L, Negro A, Martelletti P. Pharmacokinetics and safety of a new aspirin formulation for the acute treatment of primary headaches. *Expert Opinion on Drug Metabolism & Toxicology* 2014;10(10):1381-95.	Expert opinion recommendations Target population (adult) not stated
Loder E, Burch R, Rizzori P. The 2012 AHS/AAN guidelines for prevention of episodic migraine: A summary and comparison with other recent clinical practice guidelines. *Headache* 2012;52(6):930-45.	Not a guideline
MacGregor A. Frovatriptan in the treatment of menstrually related migraine: Evidence from late trials and current recommendations. *Journal of the Neurological Sciences* 2013;333:e501.	Not a guideline (Conference abstract)
MacGregor EA. Headache in pregnancy. *Continuum* 2014;20(1):128-47.	Not a guideline
Marmura MJ, Silberstein SD, Ailani J. Evidence-based guideline of the American headache society: A report on the pharmacologic treatment of acute migraine in adults. *Cephalalgia* 2013;33.	Conference abstract
Martelletti P, Rigmor JH, Antal A, Arcioni R, Brighina F, de Tommaso M, et al. Neuromodulation of chronic headaches: Position statement from the European Headache Federation. *Journal of Headache and Pain* 2013;14:86.	Did not use IHS diagnostic criteria Target population (adult) not stated
Migraine prevention: techniques are available, but underutilized. New guidelines emphasize ways to reduce the number of migraine attacks. *Duke Medicine Health News* 2012;18(7):6-7.	Not a guideline
National Clinical Guideline Centre. *Headaches: diagnosis and management of headaches in young people and adults*. London (UK): National Institute for Health and Clinical Excellence (NICE); 2012. Available from: *www.nice.org.uk/guidance/CG150* (accessed 8 April 2017).	All recommendations apply to adults and young people aged 12 years and over unless specifically stated otherwise in the recommendation Some of the recommendations have notes about medications that are not indicated in populations <18 years of age

Publication	Reason for exclusion
National Imaging Associates (NIA), Inc. *2014 NIA radiology standard clinical guidelines*. Columbia (MD): National Imaging Associates; 2014. Available from: *www.niahealthcare.com/media/629554/2014-nia-radiology-clinical-guidelines.pdf* (accessed 8 April 2017).	Did not use the IHS diagnostic criteria Target population (adult) not stated
Patel ZM, Kennedy DW, Setzen M, Poetker DM, Delgaudio JM. "Sinus headache": Rhinogenic headache or migraine? An evidence-based guide to diagnosis and treatment. *International Forum of Allergy and Rhinology* 2013;3(3):221-30.	Systematic review and guidelines on a headache type that is not a focus for the Alberta guideline
Pearlman SH, Dodick DW. Therapeutic guidelines for headache. *Handbook of Clinical Neurology* 2010;97(C).	Not a guideline
Ravishankar K, Chakravarty A, Chowdhury D, Shukla R, Singh S. Guidelines on the diagnosis and the current management of headache and related disorders. *Annals of Indian Academy of Neurology* 2011;14(Suppl 1):S40-S59.	Target population (adult) not stated Pertains to the Indian setting
Schwedt TJ. Chronic migraine. *BMJ*;2014;348:g1416.	Not a guideline
Swiss Headache Society. *Céphalées et algies facials. Recommandations thérapeutiques 2012*. Available from: *www.ihs-headache.org/binary_data/1474_swiss-french-guidelines-2012.pdf* (accessed 8 April 2017).	French language; does not include a summary in English language Target population (adult) not stated
Tassorelli C, Jensen R, Allena M, De Icco R, Sances G, Katsarava Z, et al. A consensus protocol for the management of medication-overuse headache: Evaluation in a multicentric, multinational study. *Cephalalgia* 2014;34(9):645-55.	Not a guideline
Thorson D, Biewen P, Bonte B, Epstein H, Haake B, Hansen C, et al. *Acute pain assessment and opioid prescribing protocol*. Bloomington (MN): Institute for Clinical Systems Improvement; 2014. Available from: *crh.arizona.edu/sites/default/files/u35/Opioids.pdf* (accessed 8 April 2017).	Not relevant
Work Loss Data Institute. *Head (trauma, headaches, etc., not including stress & mental disorders)*. Encinitas (CA): Work Loss Data Institute; 2013.	Did not use IHS diagnostic criteria

HIS: International Headache Society

Note: References for the seed guideline G1 is available in *Appendix H*.

TABLE D.2: Summary of guidelines excluded after reviewing the AGREE quality appraisal results (Steering Committee meeting, 25 March 2015)

Publication, Type of headache, Target population, Setting Intended users, Focus, Clinical algorithm	Reason for exclusion
E1 National Institute for Health and Care Excellence (NICE). *Botulinum toxin type A for the prevention of headaches in adults with chronic migraine. NICE technology appraisal guidance 260*. London (UK): NICE; 2012.Available from: *www.nice.org.uk/guidance/ta260/resources/guidance-botulinum-toxin-typea-for-the-prevention-of-headaches-in-adults-with-chronic-migraine-pdf* (accessed 8 April 2017). **Type of headache:** Chronic migraine **Target population:** Adults **Setting:** Secondary (specialist) **Intended users:** Neurologists, other physicians **Focus:** Prophylaxis/treatment **Clinical algorithm:** Not available	Low score on AGREE II tool (average quality); low score on AGREE II domain rigour of development Not technically a guideline
E2 Bendtsen L, Birk S, Kasch H, Aegidius K, Sorensen PS, Thomsen LL, et al. Reference programme: Diagnosis and treatment of headache disorders and facial pain. Danish Headache Society, 2nd Edition, 2012. *Journal of Headache and Pain* 2012;13(Suppl 1):S1-29. **Type of headache:** Primary headaches (migraine, tension-type headache, cluster headache, medication overuse headache) **Target population:** Adults and children **Setting:** Primary, secondary (specialist), and tertiary (hospital) care **Intended users:** Any physician, other healthcare professionals who see patients with headache (general practitioners, junior physicians in training, neurologists, pediatricians), public sector decision-makers **Focus:** Diagnosis, treatment **Clinical algorithm:** Organization diagram	Low score on AGREE II tool (average quality); low score on AGREE II domain rigour of development
E3 Unity Health Insurance affiliated with University of Wisconsin Health. *Migraine assessment and treatment in a primary care setting – adult – clinical practice guideline*. Madison (WI): University of Wisconsin Hospitals and Clinics Authority; 2013. Available from: *unityhealth.com/docs/default-source/docs/clinicalguidelinesadultmigraineinprimarycare.pdf?sfvrsn=2* (accessed 8 April 2017). **Type of headache:** Migraine **Target population:** Adults (18 years of age and older) **Setting:** Primary setting **Intended users:** Primary care physicians, advanced practice nurses, physician assistants **Focus:** Diagnosis, treatment, monitoring, prophylaxis **Clinical algorithm:** Available	Low score on AGREE II tool (poor quality); low scores on AGREE II domains: rigour of development, applicability, and editorial independence

Publication, Type of headache, Target population, Setting Intended users, Focus, Clinical algorithm	Reason for exclusion
G3 - Update Lanteri-Minet M, Valade D, Geraud G, Lucas C, Donnet A. Revised French guidelines for the diagnosis and management of migraine in adults and children. *Journal of Headache and Pain* 2014;15:2. **Type of headache**: Migraine (including menstrual migraine, migraine in pregnancy, migraine and oral contraception, migraine and menopause) **Target population**: Adults (aged 18 to 65 years) and children (aged 5 to 17 years) presented separately **Setting**: Not stated **Intended users**: General practitioners, specialists, pharmacists **Focus**: Diagnosis, treatment, management, prophylaxis **Clinical algorithm**: Not available	Low score on AGREE II tool (average quality); low scores on AGREE II domains: rigour of development and editorial independence Recommendations not linked with the research evidence

AGREE: Appraisal of Guidelines for Research and Evaluation

Note: Guidelines are not presented in any specific order. The identifiers (E1, E2, etc.) have been randomly assigned for the purpose of organization only. Excluded guidelines for the 1st of the *Alberta CPG* can be found in the background document available from: *www.ihe.ca/research-programs/hta/aagap/headache*.

APPENDIX E: Modifications Made to the AGREE II Tool

Examples of the detailed instructions constructed using logical operators (AND, OR, NOT) for the AGREE II tool items are listed below.

Item 7 – Systematic methods used to search for evidence

Information about the search terms used, sources consulted, and date limits of the literature searches should be provided.

4 – All three elements (search terms, sources, date limits) reported
3 – Two elements reported
2 – Unclear or one element reported
1 – Information about the methods used to search for evidence is not provided

Item 16 – Different management options presented

4 – Different management options were considered to be adequately presented if the comparators for each intervention were stated in the guideline (e.g., sumatriptan is more effective than naratriptan in patients with migraine)
3 – The comparators were stated for only some of the interventions
2 – Unclear
1 – The comparators for the interventions were not stated

Item 18 – Facilitators and barriers discussed

4 – Not applicable, or facilitators and barriers discussed and required changes are outlined
3 – Facilitators and barriers mentioned but required changes are not outlined
2 – Unclear
1 – Facilitators and barriers not discussed

Source: Scott NA, Moga C, Harstall C. Making the AGREE tool more user friendly: The feasibility of a user guide based on Boolean operators. *Journal of Evaluation in Clinical Practice* 2009;15(6):1061-1073.

APPENDIX F: Systematic Review Quality Assessment Checklist

(*Note*: Adapted from various sources[1-4])

This checklist contains six quality subsections (grey sections) that, according to the literature, reflect aspects considered essential for a good quality systematic review.[1-4] If desired, the scores obtained for these six subsections can be used to categorize the review as good, average, or poor quality according to the number of criteria met. This additional categorization is optional. The rating system is flexible in that other criteria can be substituted for some or all of the six criteria in accordance with the priorities and opinions of the assessors.

Study Question

The research question should be established a priori.

- *Reported*: The objectives of the review are clearly stated in the abstract, introduction, or methods.
- *Partially reported*: The objectives of the review are stated in:
  - the abstract, introduction, or methods, but are vague or unclear; or
  - a section of the report other than the abstract, introduction, or methods.
- *Not reported*: The objectives are not stated in any section of the review.

Inclusion/Exclusion Criteria

The participants, interventions, outcome measures, and types of studies considered for analysis should be established a priori.

- *Reported*: All four elements (participants, interventions, outcome measures, types of studies) are reported in the abstract, introduction, or methods section of the review.
- *Partially reported*: Only three of the four elements are reported in the abstract, introduction, or methods section.
- *Not reported*:
  - Less than three of the four elements are reported in the abstract, introduction, or methods section; or
  - the first mention of any of these elements occurs in the results section.

Search Strategy

<u>Electronic databases</u>

- *Reported*: At least one electronic database was searched and the names of the databases are provided.
- *Partially reported*: At least one electronic database was searched but the names are not provided.
- *Not reported*: Electronic databases were not searched or are not mentioned in the review.

Quality subsection 1: At least MEDLINE and one other relevant literature database

- *Yes*: MEDLINE and one other relevant literature database were searched.
- *Unclear*: It was unclear whether MEDLINE and one other relevant literature database were searched because a complete list of all the electronic databases searched is not provided.
- *No:*
  - The review stated that neither MEDLINE nor another relevant literature database was searched;
  - neither MEDLINE nor another relevant literature database is mentioned in the complete list of electronic databases searched; or
  - only one of the two databases (MEDLINE or one other relevant database) was searched.

Other sources

- *Reported*: At least one additional resource or method, other than searching electronic databases, was used to identify relevant literature (e.g., pearling or review of reference lists in retrieved articles, hand-searching of journals).
- *Partially reported*: Other resource or methods were used but details are not provided.
- *Not reported*: The review did not use other resource or methods to identify relevant literature or does not mention them.

Data Extraction

Data extraction method

- *Reported*: The data extraction process is described.
- *Partially reported*: A data extraction process is mentioned but no details are provided.
- *Not reported*: A data extraction process was not used or described.

Quality subsection 2: Standardized method

- *Yes*: The data categories extracted are listed or the use of a standardized data extraction form is mentioned.
- *Unclear*: The review states that a formal or structured data extraction process was used but does not list the data categories extracted or mention the use of a standardized data extraction form.
- *No*: The data categories extracted are not listed or the use of a standardized data extraction form is not mentioned.

Quality subsection 3: Independent data extraction by at least two reviewers

- *Yes*: Data were extracted independently by at least two reviewers.
- *Unclear*: The number of reviewers who extracted data is not stated.
- *No*: Details of data extraction were not provided or:
  - data were extracted by only one reviewer;
  - data were extracted by one reviewer and checked by another; or
  - the review had only one author and the number of reviewers who extracted data is not stated.

Quality Assessment

Criteria used to assess the validity of included studies

- *Reported*: A quality assessment tool or checklist was used and details are provided (e.g., name or source).
- *Partially reported*: A quality assessment tool or checklist was used but no details are provided.
- *Not reported*:
  - A quality assessment tool or checklist was not used or mentioned; or
  - studies were only categorized according to a level of evidence hierarchy.

Quality subsection 4: Independent quality assessment by at least two reviewers

- *Yes*: The quality of the included studies was assessed independently by at least two reviewers.
- *Unclear*: The number of reviewers who appraised study quality is not stated or study quality assessed independently by at least two reviewers for only some of the studies.
- *No*: Studies were assessed by:
  - only one reviewer;
  - one reviewer and checked by another;
  - the review had only one author and the number of reviewers who assessed the study quality is not stated.

Inter-rater agreement

- *Reported*: The review mentions that a consensus method was used or provides a statement of the degree of difference/equivalence between the reviewers or a statistical measure of inter-rater agreement.
- *Partially reported*: The review mentions that inter-rater agreement was measured but does not provide a statement of the degree of difference/equivalence or a statistical measure of inter-rater agreement.

- *Not reported*: The review does not provide any information on inter-rater agreement.

Data Analysis/Synthesis

Only ONE of the three methods for data analysis/synthesis can be assessed. Select the data analysis type according to the definitions below. Only score the quality subsection that pertains to the particular data analysis method used in the review.

Qualitative review

A narrative summary of the study results with no pooling of results or statistical analysis, other than what was provided in the original studies.

Quality subsection 5a: Study quality used in analysis or discussion of study results

- *Yes*: Results of the included studies are discussed or analyzed in terms of their quality.
- *Unclear*:
  - Study quality was assessed but is either not used at all or is only used to analyze some of the included studies.
  - The review mentions selective inclusion of "quality" studies, but without further assessment of their quality (e.g., only RCTs were included but the robustness of their execution was not assessed).
- *No*:
  - The results of the included studies are not discussed or analyzed in terms of their quality.
  - Study quality was not assessed.

Semi-quantitative review

Incorporates a statistical analysis of individual studies without pooling the results (e.g., relative risks calculated for individual study outcomes) or pooling of results using only descriptive statistics (e.g., median, mean, mode, frequency).

Quality subsection 5b: Confidence interval/measures of dispersion reported

- *Yes*: Confidence intervals or measures of dispersion (range, standard deviation, standard error of the mean) are reported for all relevant analyses.
- *Unclear*:
  - Confidence intervals or measures of dispersion are only reported for some of the relevant analyses.
  - Confidence intervals are reported for all relevant analyses, but the level of confidence is not specified (e.g., unclear whether 95% or 99% confidence intervals were calculated).
  - Measures of dispersion are reported for all relevant analyses but the type is not specified (e.g., standard deviation or standard error).
- *No*: Confidence intervals or measures of dispersion are not reported.

Meta-analysis

A pooled effect estimate is calculated for at least two studies. Reviews that contain a meta-analysis of some studies and a qualitative analysis of the remaining studies are considered a "meta-analysis."

Quality subsection 5c: Precision of results reported

- *Yes*: Confidence intervals are reported for all pooled effect estimates.
- *Unclear*:
  - Confidence intervals are reported for some but not all pooled effect estimates.
  - Confidence intervals are reported for all pooled effect estimates but the level of confidence is not specified (e.g., unclear whether 95% or 99% confidence intervals were calculated).
- *No*: Confidence intervals are not reported.

Quality subsection 5d: Test of study heterogeneity conducted

- *Yes*: A statistical analysis of study heterogeneity is reported for all pooled studies.
- *Unclear*:
  - A statistical analysis of study heterogeneity is reported for some but not all pooled studies.
  - Heterogeneity was examined visually or a statistical analysis of study heterogeneity is reported for all pooled studies, but the type of model used is not specified (e.g., fixed-effect or random-effects).
- *No*: A statistical analysis of study heterogeneity was not conducted.

Test for publication bias

- *Reported*: Publication bias was analyzed or a reason provided for why it was not.
- *Partially reported*:
  - The review mentions analyzing publication bias but does not present the results.
  - The review mentions publication bias but does not provide a formal analysis.
  - The review states that publication bias was not analyzed but does not explain why.
- *Not reported*: There was no mention of analyzing publication bias.

Concluding Section

Potential methodological limitations/advantages

- *Reported*: The methodological limitations or advantages of the review (not of the evidence base) are described in a separate section or paragraph.
- *Partially reported*: The description of the methodological limitations or advantages of the review is cursory (e.g., a single sentence or no separate paragraph or section).
- *Not reported*: There is no mention of the potential methodological limitations or advantages of the review; only the limitations or advantages of the evidence base are described

Clinical application of results

The clinical application of results is considered adequate if all of the following four elements are present in the concluding section (includes discussion) or statement of the review: treatment, treatment effect, patient group, and comparator.

- *Reported*: All four elements are present.
- *Partially reported*: Only three of the four elements are present.
- *Not reported*: Less than three of the four elements are present.

Incorporation of methodological quality

The review should take into account the methodological quality of the included studies when formulating the conclusions.

- *Reported*: The methodological quality of the included studies is mentioned in the concluding section (includes discussion) or statement of the review.
- *Partially reported*: The study types, as designated by a level of evidence hierarchy category, are mentioned in the concluding section (includes discussion) or statement of the review, but not the quality of the studies.
- *Not reported*: The methodological quality of the included studies is not mentioned in the concluding section (includes discussion) or statement of the review.

Quality subsection 6: Conclusions supported by results

- *Yes*: The conclusions drawn by the authors of the review are supported by the evidence presented in the results section.
- *Unclear*: Some, but not all, of the conclusions drawn by the authors of the review are supported by the evidence presented in the results section.
- *No*: The conclusions drawn by the authors of the review are not supported by the evidence presented in the results section.

Conflict of Interest and Funding

Conflict of interest

- *Reported*: A statement of conflict of interest (if any) is provided.
- *Partially reported*: A conflict of interest is mentioned but details are not provided.
- *Not reported*: A statement of conflict of interest (if any) is not provided.

Sources of funding

- *Reported*:
  - Funding sources are mentioned; or
  - the review was developed without external funding (e.g., authors employed by a university or volunteered time to produce a Cochrane Review).
- *Partially reported*: External funding is mentioned but details are not provided.
- *Not reported*: Funding sources are not mentioned.

Optional Quality Rating System

The quality of systematic reviews can be assessed according to how well their methods exclude bias and confounding by examining: the search strategy used; how the data extraction, quality assessment of the included studies, and data analysis/synthesis were conducted, and; whether the conclusions of the review match the results. Thus, the quality of the review can be rated numerically with respect to the six quality subsections (grey boxes above) as follows.

- ***Good*** – six criteria met, or five criteria met and one criterion "unclear"
- ***Average*** – one criterion not met, or one criterion not met and one criterion "unclear," or two criteria "unclear"
- ***Poor*** – at least two criteria not met

N.B. For a criterion to have been "met," it must be scored as "yes" (✓). For meta-analyses, the two applicable quality subsections (5c and 5d) are counted as a single quality criterion. Therefore, to meet the fifth quality criterion for meta-analyses, both 5c and 5d must be scored as "yes" (✓).

References (Appendix F)

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2. Aggressive Research Intelligence Facility – University of Birmingham. *ARIF critical appraisal checklist*. Birmingham: University of Birmingham; 2002.
3. University of Alberta. Evidence based medicine tool kit. Available from: *www.ebm.med.ualberta.ca* (accessed 16 April 2017).
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APPENDIX G: Quality Assessment Results for Systematic Reviews of New Interventions

TABLE G.1: Critical appraisal results for systematic reviews of new interventions

Review Characteristic	Exercise	Craniosacral therapy	Trigger point therapy		Lifestyle factors	Massage	Self-management		ONS	Gabapentin	SSRIs
	Baillie et al. (2014)[1]	Ernst (2012)[2]	France et al. (2014)[3]	Kim et al. (2012)[4]	Ornello et al. (2015)[5]	Wanderly et al. (2014[6]	Hundert et al. (2014)[7]	Kindelan-Calvo et al. (2014)[8]	Chen et al. (2015)[9]	Linde et al. (2013)[10]	Banzi et al. (2015)[11]
Study question established a priori	●	●	●	●	●	●	●	●	●	●	●
Inclusion/exclusion criteria	●	●	●	◐	●	●	●	●	●	●	●
Search strategy											
Electronic databases	●	●	●	●	●	●	●	●	●	●	●
1. At least MEDLINE and one other relevant literature database	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓
Other sources	●	●	●	○	●	○	○	○	●	●	●
Data extraction											
Data extraction method	●	◐	◐	◐	●	●	●	●	●	●	●
2. Standardized method	✓	?	X	X	✓	✓	✓	?	✓	✓	✓
3. Independent data extraction by at least two reviewers	?	X	✓	✓	?	✓	X	✓	X	✓	✓
Quality assessment											
Criteria used to assess the validity of included studies	●	●	●	●	●	●	●	●	●	●	●
4. Independent quality assessment by at least two reviewers	✓	X	✓	✓	?	?	X	✓	X	?	✓

Review Characteristic	Exercise	Craniosacral therapy	Trigger point therapy		Lifestyle factors	Massage	Self-management		ONS	Gabapentin	SSRIs
	Baillie et al. (2014)[1]	Ernst (2012)[2]	France et al. (2014)[3]	Kim et al. (2012)[4]	Ornello et al. (2015)[5]	Wanderly et al. (2014[6]	Hundert et al. (2014)[7]	Kindelan-Calvo et al. (2014)[8]	Chen et al. (2015)[9]	Linde et al. (2013)[10]	Banzi et al. (2015)[11]
Inter-rater agreement for quality assessment	●	○	●	●	○	○	N/A	●	○	●	●
Data analysis/synthesis											
Qualitative review	●	●	●	N/A	N/A	●	●	N/A	N/A	N/A	N/A
5a. Study quality used in analysis or discussion of study results	✓	✓	✓	N/A	N/A	✓	✓	N/A	-	-	-
Semi-quantitative review	N/A	N/A	N/A	●	N/A	N/A	N/A	N/A	N/A	N/A	N/A
5b. Confidence interval/ measures of dispersion reported	N/A	N/A	N/A	✓	N/A	N/A	N/A	N/A	-	-	-
Meta-analysis	N/A	N/A	N/A	N/A	●	N/A	N/A	●	●	●	●
5c. Precision of results reported	N/A	N/A	N/A	N/A	✓	N/A	N/A	✓	✓	✓	✓
5d. Test of study heterogeneity conducted	N/A	N/A	N/A	N/A	✓	N/A	N/A	✓	✓	✓	✓
Test for publication bias	○	◐	○	○	○	○	N/A	●	●	◐	○
Concluding section											
Potential methodological limitations/advantages	○	●	○	●	●	○	●	●	●	●	○
Clinical application of results	◐	◐	◐	●	●	◐	●	◐	●	●	●
Incorporation of methodological quality	●	●	●	●	●	●	●	●	●	●	●
6. Conclusions supported by results	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓

Review Characteristic	Exercise	Craniosacral therapy	Trigger point therapy		Lifestyle factors	Massage	Self-management		ONS	Gabapentin	SSRIs
	Baillie et al. (2014)[1]	Ernst (2012)[2]	France et al. (2014)[3]	Kim et al. (2012)[4]	Ornello et al. (2015)[5]	Wanderly et al. (2014[6]	Hundert et al. (2014)[7]	Kindelan-Calvo et al. (2014)[8]	Chen et al. (2015)[9]	Linde et al. (2013)[10]	Banzi et al. (2015)[11]
Conflict of interest and funding											
Conflict of interest	●	●	●	●	●	○	●	●	●	●	●
Sources of funding	●	●	●	●	●	●	●	●	●	●	●
Rating											
Six criteria (see grey rows above)	5/6 Good	3/6 Poor	5/6 Average	5/6 Average	4/6 Average	5/6 Good	4/6 Poor	5/6 Good	4/6 Poor	5/6 Good	6/6 Good

Key for quality of reporting: Reported = ●; Partially reported = ◐; Not reported = ○; Not applicable = N/A
Key for quality of review (grey sections of table): Yes = ✓; No = **X**; Unclear = **?**
ONS: occipital nerve block; SSRI: selective serotonin reuptake inhibitor

References (Appendix G)

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APPENDIX H: Included Seed Guidelines

Note that the guidelines are not presented in the below table in any specific order. The G1, G2, etc., identifiers were randomly assigned for the purpose of organization only.

TABLE H.1: Summary of included seed guidelines

Guideline Country	Type of Headache, Definition; Target Population; Setting; Intended Users; Focus	Source Database Clinical Algorithms
G1 **USA** 469 references	**Type of headache**: Migraine **Target population**: Adults **Setting**: Primary care **Intended users**: Not stated **Focus**: Diagnostic testing (primarily neuroimaging studies), pharmacological management of acute attacks, migraine-preventive drugs, and behavioural and physical treatments	**Source:** Google **Clinical algorithm**: Available
G1 - Update **USA** G1: 469 references G1-update: 130 references	**Type of headache**: Migraine **Target population**: Adults **Setting**: Primary care **Intended users**: Advanced practice nurses, nurses, physician assistants, physicians **Focus**: Diagnostic testing (primarily neuroimaging studies) (2000 Edition), pharmacological treatment for acute migraine and episodic migraine-preventive drugs (including non-steroidal anti-inflammatory drugs and other complementary treatments)	**Source**: Google **Clinical algorithm**: Not available
G2 **Europe** 193 references (excluding references for pregnant women and children)	**Type of headache**: Migraine **Target population**: Age not stated (has a separate section that briefly discusses children and adolescents) **Setting**: Not stated **Intended users**: Not stated **Focus**: Drug treatment	**Source**: PubMed **Clinical algorithm**: Not available
G3 **France** 51 references on adults (total references 59) *Note*: Article publication summarizes the guideline; entire guideline is available in French	**Type of headache**: Migraine **Target population**: Adults (aged 18 to 65 years) and children (aged 5 to 17 years) presented separately **Setting**: Not stated **Intended users**: General practitioners, specialists, pharmacists **Focus**: Diagnosis and management	**Source**: PubMed **Clinical algorithm**: Not available

Guideline Country	Type of Headache, Definition; Target Population; Setting; Intended Users; Focus	Source Database Clinical Algorithms
G4 **United Kingdom** 275 references	**Type of headache**: Migraine, tension-type headache, trigeminal autonomic cephalalgias, medication-overuse headache **Target population**: Adults **Setting**: Primary and secondary care **Intended users**: General practitioners, community pharmacists, patients with headache, opticians, dental practitioners **Focus**: Diagnosis and management	**Source**: United Kingdom National Library for Health Guidelines **Clinical algorithm**: Not available
G5 **Europe** 143 references	**Type of headache**: Cluster headache and the other trigeminal autonomic cephalalgias **Target population**: Age not stated **Setting**: Not stated **Intended users**: Physicians **Focus**: Prevention, management, and treatment	**Source**: PubMed **Clinical algorithm**: Not available
G5 - Update **Europe** 141 references	**Type of headache**: Cluster headache and the other trigeminal autonomic cephalalgias **Target population**: Age not stated **Setting**: Not stated **Intended users**: Physicians **Focus**: Prevention, management, and treatment	**Source**: PubMed **Clinical algorithm**: Not available
G6 **Europe** 129 references	**Type of headache**: Tension-type headache **Target population**: Adults **Setting**: Not stated **Intended users**: Clinical neurologists, other healthcare professionals and healthcare providers **Focus**: Drug treatment	**Source**: PubMed **Clinical algorithm**: Not available
New G7 **Canada** 309 references	**Type of headache**: Migraine **Target population**: Adults **Setting**: Primary and secondary care **Intended users**: Family physicians, specialists, other health professionals, patients with migraine and their families **Focus**: Treatment	**Source**: PubMed, Google **Clinical algorithm**: Not available
New G8 **Canada** 145 references	**Type of headache**: Episodic migraine **Target population**: Adults **Setting**: Primary care **Intended users**: Family physicians, specialists, other health professionals, patients with migraine and their families **Focus**: Prophylaxis	**Source**: PubMed, Google **Clinical algorithm**: Available
New G9 **Canada** 60 references	**Type of headache**: Migraine, tension type headache, cervicogenic headache **Target population**: Adults **Setting**: Not stated **Intended users**: Chiropractors, occupational therapists, physical therapists, physicians **Focus**: Treatment, management	**Source**: Google **Clinical algorithm**: Available

Guideline Country	Type of Headache, Definition; Target Population; Setting; Intended Users; Focus	Source Database Clinical Algorithms
New **G10** **Italy** 471 references	**Type of headache**: Primary headaches (migraine, tension-type headache, cluster headache, other trigeminal autonomic cephalgias, other: headache management in pregnancy and lactation, headache management in the elderly) **Target population**: Adults **Setting**: Not stated (nonemergency and emergency department) **Intended users**: Not stated **Focus**: Treatment, prevention	**Source**: PubMed, Google **Clinical algorithm**: Not available
New **G11** **USA** 140 references	**Type of headache**: Migraine, tension-type headache, cluster headache **Target population**: Patients 12 years of age and older, adolescents 12 to 17 years are presented separately **Setting**: Primary, secondary, tertiary care **Intended users**: Advanced practice nurses, allied health personnel, healthcare providers, health plans, hospitals, managed care organizations, nurses, family practice, physicians, internal medicine, neurologists, physician assistants **Focus**: Diagnosis, evaluation, management, prevention, treatment	**Source**: Google **Clinical algorithm**: Available

References (included seed guidelines)

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  - **G1a**: Silberstein SD for the US Headache Consortium. *Practice parameter: Evidence-based guidelines for migraine headache (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology*. St. Paul (MN): American Academy of Neurology; 2000. Available from: *www.neurology.org/content/55/6/754.full.pdf* (accessed 8 April 2017). (Note: Superseded by guidelines G1b to G1d listed below.)
  - **G1b**: 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.
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  - **G1c**: Silberstein SD, Holland S, Freitag F, Dodick DW, Argoff C, Ashman E. Evidence-based guideline update: pharmacologic treatment 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):1337-45.
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- **G2 (Europe)**: Evers S, Afra J, Frese A, Goadsby PJ, Linde M, May A, et al. EFNS guideline on the drug treatment of migraine--revised report of an EFNS task force. *European Journal of Neurology* 2009;16(9):968-81.
  - Information about the task force and methods: Brainin M, Barnes M, Baron JC, Gilhus NE, Hughes R, Selmaj K, et al. Guidance for the preparation of neurological management guidelines by EFNS scientific task forces--revised recommendations 2004. *European Journal of Neurology* 2004;11(9):577-81.
- **G3 (France)**: Géraud G, Lantéri-Minet M, Lucas C, Valade D; French Society for the Study of Migraine Headache (SFEMC). French guidelines for the diagnosis and management of migraine in adults and children. *Clinical Therapeutics* 2004;26(8):1305-18.
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- **G5 (Europe)**
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- *Note*: Adult population not stated (a separate section on children was available in the 2006 edition, but was not available in the 2011 edition).

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- **G11 (USA)**: Beithon J, Gallenberg M, Johnson K, Kildahl P, Krenik J, Liebow M, et al. *Diagnosis and treatment of headache*. Bloomington (MN): Institute for Clinical Systems Improvement; 2013. Available from: *www.icsi.org/guidelines__more/catalog_guidelines_and_more/catalog_guidelines/catalog_neurological_guidelines/headache/* (accessed 4 April 2017).
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APPENDIX I: Critical Appraisal Results (Modified AGREE II Tool)

TABLE I.1: Standardized domain scores AGREE II (%) – Included seed guidelines

AGREE Domain*	G1† *Migraine*		G2 *Migraine*	G3 *Migraine*	G4 *Various*	G5 *Cluster*		G6 *Tension-type*	New G7 *Migraine*	New G8 *Migraine*	New G9 *Various*	New G10 *Various*	New G11 *Various*
	(a)	(b)	(c)	(d)	(e)	(f)		(g)	(h)	(i)	(j)	(k)	(l)
	D/M/ P/T	P/T	M/T	D/M/P/T	D/E/M/ T/P	M/P/T		P/T	T	P	M/T	P/T	D/M/T
Scope and purpose	**100**	72	78	**100**	**100**	78	39	83	89	83	83	83	83
Stakeholder involvement	38	44	38	42	75	38	56	50	**100**	**100**	67	28	**100**
Rigour of development	67	**100**	83	81	76	83	81	79	92	92	79	63	94
Clarity and presentation	**100**	**100**	75	96	**100**	71	**100**	75	**100**	**100**	**100**	**100**	94
Applicability	50	46	33	67	67	6	17	0	**100**	**100**	67	63	96
Editorial independence	50	**100**	**100**	67	92	**100**	**100**	**100**	**100**	**100**	92	58	**100**

Focus: D = diagnosis; E = evaluation; M = management; P = prophylaxis; T = treatment

Type of headache: (a) 1st Edition: migraine; (b) Update: acute migraine, episodic migraine; (c) migraine; (d) migraine; (e) migraine, tension-type headache, cluster headache, other primary headaches; (f) 1st Edition and update: cluster headache and the other trigeminal autonomic cephalalgias; (g) tension-type headache; (h) acute migraine; (i) episodic migraine; (j) migraine, tension-type headache, cervicogenic headache; (k) primary headaches: migraine, tension-type headache, cluster headache, other trigeminal autonomic cephalalgias, other (headache management in pregnancy and lactation, headache management in the elderly); (l) migraine, tension-type headache, cluster headache

*The quality assessments were undertaken independently by two reviewers.

†References for the seed guidelines are available in *Appendix H*.

AGREE: Appraisal of Guidelines for Research and Evaluation

TABLE I.2: Standardized domain scores AGREE II (%) – Guidelines excluded by the Steering Committee

AGREE Domain*	E1† *Migraine*	E2 *Various*	E3 *Migraine*	G3 - Update *Migraine*
	(a)	(b)	(c)	(d)
	P/T	D/T	D/P/T	D/M/P/T
Scope and purpose	72	67	89	83
Stakeholder involvement	61	61	50	78
Rigour of development	50	29	31	27
Clarity and presentation	100	89	67	94
Applicability	96	83	46	50
Editorial independence	100	67	17	67

Focus: D = diagnosis; M = management; P = prophylaxis; T = treatment

Type of headache: (a) chronic migraine–treatment with botulinum toxin type A; (b) primary headaches: migraine, tension-type headache, cluster headache, medication-overuse headache; (c) migraine; (d) acute migraine including menstrual migraine, migraine in pregnancy, migraine and oral contraception, migraine and menopause

*The quality assessments were undertaken independently by two reviewers.

†References for the excluded guidelines are available in *Appendix D, Table D.2*.

AGREE: Appraisal of Guidelines for Research and Evaluation

TABLE I.3: Average quality score based on seven designated quality criteria – Included seed guidelines

Rating	G1† *Migraine*		G2 *Migraine*	G3 *Migraine*	G4 *Various*	G5 *Cluster*		G6 *Tension -type*	New G7 *Migraine*	New G8 *Migraine*	New G9 *Various*	New G10 *Various*	New G11 *Various*
	(a)	(b)	(c)	(d)	(e)	(f)		(g)	(h)	(i)	(j)	(k)	(l)
	D/M/ P/T	P/T	M/T	D/M/P/T	D/E/M/ T/P	M/P/T		P/T	T	P	M/T	P/T	D/M/T
Main score	23	28	26.5	24.5	25.5	26	26	25.5	27	27	25.5	20	27.5
Quality rating*	Good	Good	Good	Good	Good	Good	Good	Good	Good	Good	Good	Average	Good

Focus: D = diagnosis; E = evaluation; M = management; P = prophylaxis; T = treatment

Type of headache: (a) 1st Edition: migraine; (b) Update: acute migraine, episodic migraine; (c) migraine; (d) migraine; (e) migraine, tension-type headache, cluster headache, other primary headaches; (f) 1st Edition and update: cluster headache and the other trigeminal autonomic cephalalgias; (g) tension-type headache; (h) acute migraine; (i) episodic migraine; (j) migraine, tension-type headache, cervicogenic headache; (k) primary headaches: migraine, tension-type headache, cluster headache, other trigeminal autonomic cephalalgias, other (headache management in pregnancy and lactation, headache management in the elderly); (l) migraine, tension-type headache, cluster headache

*Guidelines were rated independently by two reviewers on how well their methods excluded bias by examining the search strategy used, how the recommendations were formulated and presented, whether the recommendations were directly linked to the evidence, the external review process, and whether conflicts of interest and funding sources were reported. The average quality rating score (maximum possible score is 28 [7 × 4]) for these criteria is derived by dividing the sum of the scores given by each reviewer by the number of reviewers. The guideline is then rated as follows:

- *Good* – average score of 22 to 28
- *Average* – average score of 15 to 21
- *Poor* – average score 0 to 14

†References for the seed guidelines are available in *Appendix H*.

TABLE I.4: Average quality score based on seven designated quality criteria – Excluded seed guidelines

Rating	E1† *Migraine*	E2 *Various*	E3 *Migraine*	G3 - Update *Migraine*
	(a)	(b)	(c)	(d)
	P/T	D/T	D/P/T	D/M/P/T
Main score	21	16	12	15.5
Quality rating*	Average	Average	Poor	Average

Focus: D = diagnosis; M = management; P = prophylaxis; T = treatment

Type of headache: (a) chronic migraine–treatment with botulinum toxin type A; (b) primary headaches: migraine, tension-type headache, cluster headache, medication-overuse headache; (c) migraine; (d) acute migraine including menstrual migraine, migraine in pregnancy, migraine and oral contraception, migraine and menopause

*Guidelines were rated independently by two reviewers on how well their methods excluded bias by examining the search strategy used, how the recommendations were formulated and presented, whether the recommendations were directly linked to the evidence, the external review process, and whether conflicts of interest and funding sources were reported. The average quality rating score (maximum possible score is 28 [7 × 4]) for these criteria is derived by dividing the sum of the scores given by each reviewer by the number of reviewers. The guideline is then rated as follows:

- *Good* – average score of 22 to 28
- *Average* – average score of 15 to 21
- *Poor* – average score 0 to 14

†References for the excluded guidelines are available in *Appendix D, Table D.2*.

APPENDIX J: Inventory of Recommendations from New Seed Guidelines

Note: References for the seed guidelines are available in *Appendix H*. Evidence inventory tables for the guidelines common to the 1st edition of the *Alberta CPG* can be found in Appendix E of the background documents for that edition (available from: *www.ihe.ca/research-programs/hta/aagap/headache*).

In navigating the tables, please note the following.

1. The recommendations are grouped as follows:
    - Acute Migraine Pharmacological Interventions
        - Table J.1a – Acute migraine – General principles
        - Table J.1b – Acute migraine – Pharmacological interventions
        - Table J.1c – Approach to the individual patient/pharmacological acute migraine treatment strategies
        - Table J.1d – Menstrual migraine – Advice and diagnosis
        - Table J.1e – Migraine – Acute treatment in pregnancy and lactation
        - Table J.1f – Perimenopausal or menopausal migraine – Hormone and pharmacological therapy
    - Migraine Prophylaxis
        - Table J.2a – Episodic migraine prevention/migraine prophylaxis – General considerations
        - Table J.2b – Episodic migraine prevention/migraine prophylaxis – Pharmacological interventions
        - Table J.2c – Approach to the individual patient/prophylactic drug treatment strategies based on the clinical setting
        - Table J.2d – Migraine prophylaxis – Menstrual migraine
        - Table J.2e – Migraine prophylaxis – Pregnancy and lactation
    - Migraine Non-Pharmacological Interventions
        - Table J.3a – Migraine – Non-pharmacological treatment
        - Table J.3b – Migraine – Non-pharmacological prophylaxis
    - Tension-Type Headache
        - Table J.4a – Tension-type headache – Pharmacological treatment
        - Table J.4b – Tension-type headache – Non-pharmacological treatment
        - Table J.4c – Tension-type headache – Pharmacological prophylaxis
    - Cluster Headache
        - Table J.5a – Cluster headache – Referral for surgery
        - Table J.5b – Cluster headache – Pharmacological prophylaxis
        - Table J.5c – Cluster headache in pregnancy and lactation – General statements

- Cervicogenic Headache
  - Table J.6 – Cervicogenic headache – Non-pharmacological treatment

2. The *Rating of Recommendation* column denotes the strength of the recommendation as stated by the seed guideline (see *Table J.7*).
3. The bolded integers in the columns under the *Supporting Evidence* (rightmost) section of the table represent the total number of discrete studies of that type cited by the guideline to support its recommendation. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.
4. The recommendations from the 1st Edition of the *Alberta CPG* are bolded in the tables. The nature of the recommendations from the new seed guidelines relative to the 1st Edition is noted in italics in the leftmost column as either providing *Additional information* or a *New recommendation*.
5. In cases where recommendations are discordant, a brief description of the disagreement is written in italics in the leftmost column under the relevant item name, and identified as a *Discordant recommendation*.

Item	Guideline/Country/Synopsis of Recommendations	Rating of Recommen-dation*	Supporting Evidence						
			SR/MA	NR	RCT	NRCS	CS	G	Other
Ergotamine derivatives	**TOP guideline** (p. 18) (Based on G4 (SR)) ★ **Ergotamine is not recommended for routine use in patients with acute migraine, although it may be helpful for selected patients where triptans are not an option.** *Because it is a vasoconstrictor, it should not be used in patients with cerebrovascular or cardiovascular disease.*	Not applicable	**1** [illegible]		**1** [illegible]				**1** [illegible]
Discordant recommendation (treatment length)	**G10 (Italy)** (p. S40) Ergotamine 2 mg qs + caffeine 200 mg rectal.	III		**2** [illegible]					
Opioids	**TOP guideline 1st edition** (p. 18) ★ (Based on CS (G4)) **Opioid analgesics and combination analgesics containing opioids (e.g., codeine) are not recommended for routine use for the treatment of migraine owing to their potential for causing medication overuse headache.** (Based on EO (GDG)) **Opioids may be necessary when other medications are contraindicated or ineffective, or as a rescue medication when the patient's usual medication has failed.** **For more information on the use of opioids for chronic non-cancer pain, consult the Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain endorsed by the College of Physicians and Surgeons of Alberta available at:** http://nationalpaincentre.mcmaster.ca/opioid/.	Not applicable					**1** [illegible]		
Codeine *New statement/ recommendation*	**G1c (USA)** (p. 11, 13) Codeine 30 mg PO is possibly effective for acute migraine treatment based on available evidence.	**Level C**	-						
Tramadol IV *New statement/ recommendation*	**G1c (USA)** (p. 11, 13) Tramadol IV 100 mg is possibly effective for acute migraine treatment based on available evidence.	**Level C**			**1** [illegible]				
Additional information	**G7 (Canada)** (p. Suppl. 3: 25) Oral opioids, including codeine, are not recommended for routine use in migraine, due to lack of evidence for superiority to standard drugs (NSAIDs and triptans), and the risk of dependence/abuse, potential for development of medication overuse headache, and the possibility of a withdrawal syndrome following discontinuation.	**Strong recommend-dation, low quality evidence**			**1** [illegible]				

Acute Migraine Pharmacological Interventions

TABLE J.1a: Acute migraine – General principles

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
General principles of acute migraine therapy *New statement/ recommendation*	**G7 (Canada)** (p. Suppl. 3: 6) 1. The response of the individual with migraine to a specific acute drug cannot be predicted with certainty. i) Several acute medication trials may be necessary before an appropriate acute medication is found for a specific patient. Some patients with attacks of varying severity may need access to more than one medication for successful migraine management. ii) A rescue plan should be discussed with patients with severe migraine attacks whose usual acute medication does not provide adequate headache relief consistently for every attack.	Not applicable	Expert consensus, based on a general literature review and expert opinion of the guideline development group (Background study cited: G[1])						
Early treatment of migraine attacks	**Alberta CPG** 1st Edition (p. 17) (Based on EO (GDG) ✓ **Advise patients to take their medication early in their migraine attack, where possible, to improve effectiveness. The strategy may not be appropriate for patients with frequent attacks who are at risk for medication overuse headache (see medication overuse recommendation). For patients with migraine with aura, it is usually advisable to take acute medication just as the headache phase is starting, rather than during the aura, although taking oral medication during the aura appears effective for many patients.**	Not applicable	Not applicable						
Additional information on taking medications while pain is still	**G7 (Canada)** (p. Suppl. 3: 6-7) 2. Patients should be advised to take acute medications as early as possible during their migraine attacks while pain is still mild, unless at risk for medication overuse headache.	Not applicable	Expert consensus based on a general literature review and expert opinion of the guideline development group (Background studies cited: NR[2]; Other[3])						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
mild *New statement/ recommendation*	**G7 (Canada)** (p. Suppl. 3: 7) 3. An appropriate treatment approach should be chosen i) When recommending an acute migraine medication, consideration should be given to attack severity ("stratified care" approach) and past response to medications. ii) If a "step care across attacks" approach is chosen, patients should be educated with regard to remaining available treatment options, to reduce the risk of patients becoming discouraged and no longer consulting for their headaches. iii) Although a "step care within an attack" approach may be suitable for some patients, patients should be advised that most acute medications are more effective if taken early in the migraine attack.	Not applicable	Expert consensus based on a general literature review and expert opinion of the guideline development group (Background studies cited: NR[4]; RCT[5]; G[6-8]; Other[9,10])						
New statement/ recommendation	**G7 (Canada)** (p. Suppl. 3: 8) 4. A suitable medication formulation should be chosen i) When choosing an acute migraine medication for a specific patient, consideration should be given to the clinical features of the attack including rate of increase of headache intensity and the presence of nausea and / or vomiting early in the attack, and an appropriate medication formulation should be chosen. Some patients may require more than one formulation.	Not applicable	Expert consensus based on a general literature review and expert opinion of the guideline development group (Background studies cited: SR[11]; NR[12-14,15-17]; RCT[18,19]; CS[20])						
New statement/ recommendation & Additional information on medication overuse	**G7 (Canada)** (p. Suppl. 3: 8) 5. Medication overuse needs to be avoided because of the risk of medication overuse headache i) When initiating treatment with acute migraine medications, the patient should be educated with regard to medication overuse headache. Patients should avoid use of ASA, NSAIDs and acetaminophen on more than 14 days per month, and use of triptans, ergots, opioids, or combination analgesics on more than 9 days a month. Patients taking different acute medications on different days should limit their total use of acute medications to 9	Not applicable	Expert consensus based on a general literature review and expert opinion of the guideline development group (Background studies cited: NR[21,22]; G[23,24])						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
New statement/ recommendation	days a month if one of their medications is a triptan, a combination analgesic, an ergotamine, or an opioid. ii) Patients should be advised to monitor their acute medication use if their attacks are frequent, preferably with a headache diary, in order to reduce the risk of medication overuse headache. iii) Pharmacological prophylaxis should be considered for patients with frequent migraine attacks who may be at risk of medication overuse.								
	G7 (Canada) (p. Suppl. 3: 8) 6. Two or more acute medications can be combined if necessary i) Although a single acute medication may relieve migraine attacks satisfactorily for many patients, others may benefit from taking more than one medication simultaneously (e.g., an NSAID with an anti-nauseant; an anti-nauseant with a triptan, or a triptan with an NSAID).	Not applicable	Expert consensus based expert opinion of the guideline development group						

*References for the seed guidelines are available in *Appendix H*.

†Refer to *Table J.7* for explanation of ratings.

‡The integers listed in the *Supporting Evidence* columns represent the total number of discrete studies. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.

ASA: acetylsalicylic acid; CS: case series study; G: guideline; NR: non-systematic/narrative review; NRCS: non-randomized comparative study; NSAID: nonsteroidal anti-inflammatory drug; RCT: randomized controlled trial; SR/MA: systematic review/meta-analysis

TABLE J.1b: Acute migraine – Pharmacological interventions

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
NSAIDs	**Alberta CPG 1st Edition** (p. 41) **MEDICATION TABLE STATEMENT** **To optimize response, use full dose but restrict to 14 days or less per month to avoid risk of medication overuse headache.**	Not applicable	Not provided						
Discordant recommendation (treatment length)	**G11 (USA)** (p. 30) Use of NSAIDs for acute treatment of headache for more than nine days per month is associated with an increased risk of chronic daily headache.	Not applicable	Not provided						
NSAIDs and acetaminophen	**Alberta CPG** 1st Edition (p. 17) (Based on RCT (G4) + SR (IHE Database)) ✓ **Acetylsalicylic acid 1,000 mg, ibuprofen 400 mg, and naproxen sodium 500 to 550 mg are recommended for acute treatment in patients with migraine of all severities.** **Acetaminophen 1,000 mg is recommended for acute treatment of migraine attacks of mild to moderate severity. Daily dosage should not exceed 4 grams per day to avoid liver dysfunction.** **If NSAIDs and/or acetaminophen are not effective by history or after a brief treatment trial, alternative medications (e.g., a triptan) should be tried.** ***NSAIDs can cause gastric irritation and bleeding and renal dysfunction.***	Not applicable	**1** 25		**7** 26-32				
Aspirin *Additional information*	**G11 (USA)** (p. 30) Use of aspirin for acute treatment of headache for more than 15 days is associated with an increased risk of chronic daily headache.	Not applicable	Not provided						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Additional information on dosage, combination of medications, harms	**G7 (Canada)** (p. Suppl. 3: 19) Acetylsalicylic acid (975 to 1,000 mg tablets or effervescent formulation), given with oral metoclopramide (10 mg) if nausea is present, is recommended for the acute treatment of migraine attacks of all severities.	**Strong recommendation, high quality evidence**	**2** 33,34						
	G7 (Canada) (p. Suppl. 3: 19-20) Ibuprofen (400 mg tablet or solubilized [liquid containing capsules] formulation) is recommended for the acute treatment of migraine attacks of all severities.	**Strong recommendation, high quality evidence**	**2** 35,36		**2** 37,38				
Additional information	Ibuprofen (400 mg) in solubilized formulation (liquid containing capsules) is recommended for the acute treatment of migraine attacks of all severities for patients desiring a faster onset of therapeutic effect as compared to the regular ibuprofen tablets.	**Strong recommendation, moderate quality evidence**							
	G7 (Canada) (p. Suppl. 3: 20) Naproxen sodium in immediate release formulation (500 or 550 mg; up to 825 mg, if needed and tolerated) is recommended for the acute treatment of migraine attacks of all severities. **The following, while not a recommendation, was mentioned in G7 regarding potential harm:** *Adverse events commonly associated with naproxen sodium were nausea, dizziness, dyspepsia and abdominal pain.*	**Strong recommendation, high quality evidence**	**1** 25						
	G7 (Canada) (p. Suppl. 3: 22-25) Acetaminophen (1,000 mg), alone or in combination with oral metoclopramide (10 mg), is recommended for the acute treatment of mild or moderate migraine attacks.	**Strong recommendation, high quality evidence**	**1** 39		**2** 32,40				
NSAIDs: Diclofenac/ diclofenac potassium	**G1d (USA)** (p. 10-11, 13) Diclofenac 50 and 100 mg is established as effective for acute migraine treatment based on available evidence.	**Level A**			**4** 41-44				

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
New statement/ recommendation	**G7 (Canada)** (p. Suppl. 3: 20-22) Diclofenac potassium (50 mg tablet or powder for oral solution) is recommended for the acute treatment of migraine attacks of all severities.	**Strong recommendation, high quality evidence**	**1** 45		**3** 41,43,44				
	Diclofenac potassium powder for oral solution (50 mg) is recommended for the acute treatment of migraine attacks of all severities for patients desiring a faster onset of therapeutic effect as compared to the diclofenac oral tablet formulation.	**Strong recommendation, moderate quality evidence**							
NSAIDs: Phenazone *New statement/ recommendation*	**G1d (USA)** (p. 10, 13) Phenazone 1,000 mg is possibly effective for acute migraine treatment based on available evidence.	**Level C**			**1** 46				
NSAIDs: Celecoxib *New statement/ recommendation*	**G1d (USA)** (p. 13) Evidence is conflicting or inadequate to support or refute the efficacy of celecoxib 400 mg for acute migraine. *Note*: No Class I or II studies exist for the use of celecoxib.	**Level U**	Not applicable						
Analgesics: Acetaminophen IV *New statement/ recommendation*	**G1d (USA)** (p. 10, 13) Acetaminophen IV 1,000 mg is possibly ineffective for acute migraine.	**Level C negative**			**1** 47				
Combination analgesics *New statement/ recommendation*	**G10 (Italy)** (p. S39) Acetaminophen 500 mg + acetyl salicylic acid 500 mg + caffeine suppository 130 mg for attacks of moderate intensity. Effective also in the treatment of menstrual migraine. **The following, while not a recommendation, was mentioned in G10 regarding potential harm:** *In the case of frequent migraine attacks, risk of abuse and headache chronification. Use should be limited to ≤10 days per month.*	Not stated		**1** 48					

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	For frequent migraine attacks: Indomethacin 25 mg + prochlorperazine 2 mg + caffeine oral 75 mg OR indomethacin 25-50 mg + prochlorperazine 4-8 mg + caffeine oral 75-150 mg **The following, while not a recommendation, was mentioned in G10 regarding potential harm:** *In the case of frequent migraine attacks, risk of abuse and headache chronification. Use should be limited to ≤10 days per month.*	I II			**2** 49,50				
Triptans	**Alberta CPG** 1st Edition (p. 17) (Based on SR (G3, G4)) ✓ **Oral triptans are recommended for acute treatment for all severities of migraine if previous attacks have not been controlled by simple analgesics. If a patient does not respond well to one triptan, a different triptan should be offered.**	Not applicable	**6** 51-56	**2** 57,58	**3** 28,59,60				**1** 61
Additional information on various triptans, administration, intensity of pain	**G7 (Canada)** (p. Suppl. 3: 13-18) Triptans (almotriptan, eletriptan, frovatriptan, naratriptan, rizatriptan, sumatriptan, and zolmitriptan) are recommended for the acute treatment of migraine attacks that are likely to become moderate or severe.	**Strong recommendation, high quality evidence**	**4** 11,51,5 4,55	**5** 17,62-65					
	If a patient does not respond well to one triptan or tolerates it poorly, other triptans should be tried over time in subsequent attacks. It is recommended that patients wait 24 hours before trying another triptan.	**Strong recommendation, high quality evidence**		**1** 66	**3** 67-69	**1** 70			
Additional information	**G7 (Canada)** (p. Suppl. 3: 18) Patients with migraine attacks that are usually moderate or severe in intensity should be advised to take triptans early during their migraine attacks while pain is mild (caution the patient regarding medication overuse headache).	**Strong recommendation, high quality evidence**			**6** 71-76	**1** 77			

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Antiemetics: Droperidol IV *New statement/ recommendation*	**G1d (USA)** (p. 10, 13) Droperidol IV 2.75 mg is probably effective for acute migraine treatment based on available evidence.	**Level B**			**1** 78				
Antiemectics: Ketorolac tromethamine *New statement/ recommendation*	**G1d (USA)** (p. 11, 13) Ketorolac tromethamine nasal spray is possibly ineffective for acute migraine.	**Level C negative**			**1** 79				
Dihydro-ergotamine	**Alberta CPG** 1st Edition (p. 18) (Based on RCT (G1, G3)) ✓ **Dihydroergotamine (DHE) by nasal spray or subcutaneous/intramuscular injection may be considered for patients who do not respond well to triptans.**	Not applicable			**5** 80-84				
Additional information on severity of pain	**G7 (Canada)** (p. Suppl. 3: 18) Dihydroergotamine (intranasal or subcutaneous self-injection) may be considered for the acute treatment of moderate or severe migraine attacks.	**Weak recommendation, moderate quality evidence**			**5** 80,82,84 -86				
Ergotamine derivatives	**Alberta CPG 1st** Edition (p. 18) (Based on G4 (SR)) × **Ergotamine is not recommended for routine use in patients with acute migraine, although it may be helpful for selected patients where triptans are not an option.** *Because it is a vasoconstrictor, it should not be used in patients with cerebrovascular or cardiovascular disease.*	Not applicable	**1** 52		**1** 59				**1** 61
Discordant recommendation (treatment length)	**G10 (Italy)** (p. S40) Ergotamine 2 mg oral + caffeine 200 mg rectal.	**III**		**2** 87,88					

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Opioids	**Alberta CPG** 1st Edition (p. 18) (Based on CS (G4)) ✗ **Opioid analgesics and combination analgesics containing opioids (e.g., codeine) are not recommended for routine use for the treatment of migraine owing to their potential for causing medication overuse headache.** (Based on EO (GDG)) **Opioids may be necessary when other medications are contraindicated or ineffective, or as a rescue medication when the patient's usual medication has failed.** **For more information on the use of opioids for chronic non-cancer pain, consult the Canadian Guideline for Safe and Effective Use of Opioids for Chronic Non-Cancer Pain endorsed by the College of Physicians and Surgeons of Alberta available at: http://nationalpaincentre.mcmaster.ca/opioid/.**	Not applicable					**1** 89		
Codeine *New statement/ recommendation*	**G1d (USA)** (p. 11, 13) Codeine 30 mg oral is possibly effective for acute migraine treatment based on available evidence.	**Level C**	Not provided						
Tramadol IV *New statement/ recommendation*	**G1d (USA)** (p. 11, 13) Tramadol IV 100 mg is possibly effective for acute migraine treatment based on available evidence.	**Level C**			**1** 90				
Additional information	**G7 (Canada)** (p. Suppl. 3: 25) Oral opioids, including codeine, are not recommended for routine use in migraine, due to lack of evidence for superiority to standard drugs (NSAIDs and triptans), and the risk of dependence/abuse, potential for development of medication overuse headache, and the possibility of a withdrawal syndrome following discontinuation.	**Strong recommendation, low quality evidence**			**1** 91				

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
New statement/ recommendation	**G7 (Canada)** (p. Suppl. 3: 25) Codeine containing combination analgesics may be considered for patients with moderate or severe migraine attacks when triptan and/or NSAIDs are ineffective or contraindicated, and for occasional use as rescue medication when the patient's regular medication has failed. Frequency of use should be closely monitored, preferably with use of headache diaries.	**Weak recommendation, low quality evidence**	Not provided						
Tramadol alone or in combination with acetaminophen *New statement/ recommendation*	**G7 (Canada)** (p. Suppl. 3: 25) Tramadol alone or in combination with acetaminophen is not recommended for routine use in migraine, due to lack of evidence for superiority to standard drugs (NSAIDs and triptans), and the risk of dependence/abuse, potential for development of medication overuse headache, and the possibility of a withdrawal syndrome following discontinuation.	**Strong recommendation, low quality evidence**			**1** 92				
Tramadol in combination with acetaminophen *New statement/ recommendation*	**G7 (Canada)** (p. Suppl. 3: 25-26) Tramadol in combination with acetaminophen may be considered for patients with moderate or severe migraine attacks when triptans and/or NSAIDs are ineffective or contraindicated, and for occasional use as rescue medication when the patient's regular medication has failed. Frequency of use should be closely monitored, preferably with use of headache diaries.	**Weak recommendation, moderate quality evidence**							
	The following, while not a recommendation, was mentioned in G7 regarding potential harm: *Tramadol use is associated with adverse effects such as central nervous system (CNS) depression and respiratory depression, dependence, withdrawal reactions, and the potential for abuse (less potential for abuse than opioids).* *Tramadol and acetaminophen combination treatment-related adverse events included nausea, dizziness, vomiting and somnolence.*	Not applicable		**1** 93	**1** 92				**2** 94,95

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	G1d (USA) (p. 11, 13) Tramadol 75 mg/acetaminophen 650 mg is probably effective for acute migraine treatment based on available evidence.	**Level B**			**1** 92				
Opioids: Butorphanol nasal spray *New statement/ recommendation*	**G7 (Canada)** (p. Suppl. 3: 25-26) Butorphanol nasal spray, although effective for acute migraine, should be avoided (except in exceptional circumstances) for the acute treatment of migraine, due to lack of evidence for superiority to standard drugs (NSAIDs and/or triptans), risk of dependence/abuse, potential for development of medication overuse headache, and the possibility of a withdrawal syndrome following discontinuation. When used, frequency of use should be closely monitored, preferably with use of headache diaries. **The following, while not a recommendation, was mentioned in G7 regarding potential harm:** *Butorphanol can produce unpleasant emotional sensations and dysphoria.*	**Strong recommendation, low quality evidence**		**1** 96	**2** 97,98				
Butalbital	**Alberta CPG** 1st Edition (p. 18) (Based on RCT (G1)) × **The use of butalbital-containing combination analgesics in migraine management should be avoided and limited to exceptional circumstances where other acute medications are contraindicated and/or ineffective. When used, they should be carefully monitored to avoid medication overuse (use on less than 10 days per month) and dependence.**	Not applicable			**1** 98				**1** 99
Additional information	**G7 (Canada)** (p. Suppl. 3: 26) Barbiturate (i.e., butalbital) containing combination analgesics should be avoided (except in exceptional circumstances) for the acute treatment of migraine, due to lack of evidence for superiority to standard drugs (NSAIDs and/or triptans), risk of dependence/abuse, potential for development of	**Strong recommendation, low quality evidence**		**1** 100	**2** 98,101				

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	medication overuse headache, and the possibility of a withdrawal syndrome following discontinuation of high doses.								
	The following, while not a recommendation, was mentioned in G7 regarding potential harm. *Butalbital-containing products are associated with significant adverse effects (e.g., sedation, intoxication similar to that produced by alcohol), risk of dependence, abuse potential, risk of medication-overuse headache with frequent use, and a severe withdrawal syndrome (including seizures) on discontinuation of high doses.*			**2** 100,102				**1** 1	**1** 103
Chlorpromazine IV *New statement/ recommendation*	**G1d (USA)** (p. 10, 13) Chlorpromazine IV 12.5 mg is probably effective for acute migraine treatment based on available evidence. Note: study conducted in emergency department.	**Level B**			**1** 104				
Chlorpromazine IM *New statement/ recommendation*	**G1d (USA)** (p. 13) Chlorpromazine IM 1mg/kg is possibly effective for acute migraine.	**Level C negative**	Not provided						
Prochlorperazine IV, IM, PR *(Listed in the medication table in Alberta CPG)*	**G1d (USA)** (p. 13) Prochlorperazine intravenous (IV) 10 mg, intramuscular (IM) 10 mg and PR 25 mg is probably effective for acute migraine treatment based on available evidence. **The following, while not a recommendation, was mentioned in G1 regarding potential harm:** *Metoclopramide and prochlorperazine share the common adverse event of drowsiness and sedation.*	**Level B**			**3** 105-107				
Adjunctive therapy *New statement/ recommendation*	**G11 (USA)** (p. 32) Clinicians may consider adjunctive therapy (singularly or in compatible combination) as a treatment option for headache as follows:	Not applicable	Not provided						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	• Caffeine minimum 65 mg by mouth. Caffeine should be added for intermittent, infrequent headache as a first choice when not contraindicated. The use of caffeine in patients with chronic daily headache is to be discouraged. Metoclopramide could be considered next. **The following, while not a recommendation, was mentioned in G11 regarding potential harm.** *Side effects are tremors and nausea.* • Metoclopramide 10 mg IV **The following, while not a recommendation, was mentioned in G11 regarding potential harm.** *Side effects are drowsiness and extrapyramidal symptoms.* • Prochlorperazine 5 mg to 10 mg IV or IM, or rectal suppository 25 mg **The following, while not a recommendation, was mentioned in G11 regarding potential harm.** *Side effects are drowsiness and extrapyramidal symptoms.* • Promethazine 25 mg IV over one minute, IM or rectal suppository **The following, while not a recommendation, was mentioned in G11 regarding potential harm.** *Side effects are drowsiness and extrapyramidal symptoms.*								
Intranasal lidocaine *New statement/ recommendation*	**G10 (Italy)** (p. S40) Intranasal lidocaine (0.4 mL 4% solution) for the treatment of migraine attacks and in the chronic, refractory migraine unresponsive to other treatments, with or without symptomatic drug overuse.	**III**		**1** 108	**2** 109,110				

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Steroids *New statement/ recommendation*	**G10 (Italy)** (p. S40) Dexamethasone IV 10 mg or prednisone 50 mg to 100 mg oral is recommended.	**III**	**2** 111,112		**3** 113-115				
Treatments recommended for moderate severity migraine (inhibits daily activities but is not incapacitating) *New statement/ recommendation*	**G11 (USA)** (p. 3) • Lidocaine 4% solution, 0.4 mL to 0.5 mL intranasally over 30 seconds (May cause burning or numbness in nose or pharynx.)	Not applicable			**1** 109				
	• Combination of isometheptene mucate (65 mg), dichloralphenazone (100 mg), and acetaminophen (325 mg): two by mouth at onset and then one every hour as needed. Not to exceed: 5 in 12 hours; two treatment days per week; or 40 capsules per month. **The following, while not a recommendation, was mentioned in G11 regarding potential harm.** *Side effects are drowsiness and dizziness. Contraindications include ischemic heart disease, severe renal disease, and ischemic cerebrovascular disease.*					**1** 116			
Treatments recommended for severe migraine (headache is incapacitating) *New statement/ recommendation*	**G11 (USA)** (p. 3) • Chlorpromazine (25 mg in 5 mL) injection or IV 0.1 mg/kg every 15 minutes (up to 3 doses, not to exceed 25 mg per dose) **The following, while not a recommendation, was mentioned in G11 regarding potential harm.** *Side effects are drowsiness and extrapyramidal symptoms. Contraindications include hypotension and previous adverse reaction.*	Not applicable			**2** 117,118				
	• Intramuscular ketorolac				**1** 119				
	• Intravenous magnesium sulfate				**1** 120				

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	• Intravenous valproate sodium						**2** 121,122		
Magnesium sulfate IV ($MgSO_4$) *New statement/ recommendation*	**G1d (USA)** (p. 10, 13) $MgSO_4$ IV 1-2 g is probably effective for acute migraine with aura treatment based on available evidence.	**Level B**			**2** 123,124				
Valproate IV *New statement/ recommendation*	**G1d (USA)** (p. 12, 13) Valproate IV 400 to 1000 mg is possibly effective for acute migraine treatment based on available evidence.	**Level C**					**2** 125,126		
	G10 (Italy) (p. S40) Valproic acid IV 300 mg to 800 mg has been demonstrated to be effective in the treatment of migraine attacks.	**III**	**1** 127						
Octreotide *New statement/ recommendation*	**G1d (USA)** (p. 11, 13) Octreotide SC 100 µg is probably ineffective for acute migraine.	**Level B negative**			**1** 128				
Migraine longer than 72 hour duration *New statement/ recommendation*	**G11 (USA)** (p. 32) It is recommended that the patient be hydrated prior to neuroleptic administration with 250 mL to 500 mL of 5% dextrose with 0.45% sodium chloride intravenously and advised of the potential for orthostatic hypotension and acute extrapyramidal side effects. The patient should be observed in a medical setting as clinically appropriate after administration of a neuroleptic and should not drive for 24 hours.	Not applicable	Not provided						
	Intravenous metoclopramide 10 mg IV should be given 15 minutes prior to each dihydroergotamine mesylate injection. Continue metoclopramide 10 mg IV every eight hours as needed for nausea. Begin dihydroergotamine mesylate (DHE) 2 mg in 1 L of normal saline at 42 mL/hour (no more than 2 mg/24				**1** 129 Metoclo-pramide	**2** 130,131 DHE	**2** 132,133 DHE		

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	hours). **The following, while not a recommendation, was mentioned in G11 regarding potential harm:** *Metoclopramide: Although uncommon, acute extrapyramidal side effects such as dystonia, jitteriness, and oculogyric crisis may occur.* *DHE: Side effects are nausea, vomiting, diarrhea, abdominal cramps, dizziness, paresthesia and leg pain, excessive anxiety, jitteriness, or dystonic reaction. Contraindicated in pregnancy, history of ischemic heart disease, history of Prinzmetal's angina, severe peripheral vascular disease, onset of chest pain following administration of test dose, within 24 hours of receiving any triptan or ergot derivative, elevated blood pressure, patients with hemiplegic or basilar-type migraines, or cerebrovascular disease.*								
	Clinicians should treat patients with migraine >72 hours who do not meet criteria for DHE, with chlorpromazine, intravenous valproate sodium, intravenous magnesium sulfate or prochlorperazine. **The following, while not a recommendation, was mentioned in G11 regarding potential harm.** *Chlorpromazine: Side effects are drowsiness and extrapyramidal symptoms. Contraindicated in patients with hypotension and previous adverse reaction.*				**5** 105,106, 117, 118,120		**2** 121,122		
	Clinicians should premedicate patients with diphenhydramine or benztropine who have migraine for > 72 hours, who do not meet criteria for DHE and who have a history of dystonic reaction.		Not provided						
	Dexamethasone (4 to 20 mg IM once per month) may be considered as a treatment of last resort and initiated only after careful consideration of the risks as they pertain to each individual. **The following, while not a recommendation, was mentioned in G11 regarding potential harm.** *Side effects are Cushingoid appearance.*					**1** 134			

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Treatment in the emergency setting *New statement/ recommendation*	**G10 (Italy)** (p. S50) In the Emergency Department (ED) acute treatment must be simple, based on a few drugs with a clear evidence of efficacy, administrable through rapid absorption routes (rectal, intramuscular or endovenous) and rapidly effective.	Not applicable					**1** 135		
NSAIDs	Among NSAIDs, ketorolac 60 mg administered intramuscularly, followed by a subsequent dose of 30 mg after 8 hours has been shown to be effective.				**1** 136	**1** 137	**1** 138		
ASA	Another first-choice treatment is ASA 1,000 mg with or without metoclopramide.			**1** 139					
Metamizole	Metamizole has been shown to be significantly more effective than placebo. **The following, while not a recommendation, was mentioned in G10 regarding potential harm.** *Its potential side effects should be taken into account including severe hypotension, agranulocytosis, and allergic reactions.*				**1** 140				
Dihydro-ergotamine	Positive data are available for dihydroergotamine 2 mg nasal spray or suppository, but it is less effective than sumatriptan.			**1** 88					
Sumatriptan	Subcutaneous, intranasal and rectal sumatriptan should be available in the ED and it may be particularly useful in migraine patients with nausea and/or vomiting.				**2** 141,142				**1** 143
Antiemetics	In the presence of nausea and vomiting 10 mg metoclopramide IM can be useful, even if occasional adverse events with this drug should be considered including sedation, akathisia, acute dystonic crises and other extrapyramidal symptoms such as stiff neck and oculogyric crises. Among the other antiemetics, ondansetron 4 to 8 mg IV may be used.			**1** 144 Metoclo-pramide					

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Prochlorperazine	Prochlorperazine has been shown to be more effective than placebo, metoclopramide and other agents in the symptomatic treatment of migraine attacks in the ED. In association with diphenhydramine, prochlorperazine has been shown to be more effective than sumatriptan and sodium valproate IV. **The following, while not a recommendation, was mentioned in G10 regarding potential harm.** *Its most frequent adverse event is sedation.*				**4** 105,142, 145,146				
Meperidine	Meperidine, an opioid analgesic, although effective, is not recommended by the group of experts.		Expert opinion of the guideline development group						
Benzodiazepines	Benzodiazepines (especially diazepam 5–10 mg, administered by IV) are useful in case of concomitant anxiety.		Expert opinion of the guideline development group						
Dexamethasone	In the status migrainosus and in the treatment of attack recurrence, dexamethasone 10 mg followed by a subsequent dose of 4 mg every 6 hours can be used.		**1** 111		**4** 114,147-150				

Note: Statements in italics relate to harm. These statements were sourced from the recommendations or from elsewhere in the seed guidelines.

*References for the seed guidelines are available in *Appendix H*.

†Refer to *Table J.7* for explanation of ratings.

‡The integers listed in the *Supporting Evidence* columns represent the total number of discrete studies. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.

ASA: acetylsalicylic acid; CS: case series study; ED: emergency department; G: guideline; IM: intramuscular; IV: intravenous; NR: non-systematic/narrative review; NRCS: non-randomized comparative study; NSAIDs: nonsteroidal anti-inflammatory drugs; PR: per rectum; RCT: randomized controlled trial; SC: subcutaneous; SR/MA: systematic review/meta-analysis

TABLE J.1c: Approach to the individual patient/pharmacological acute migraine treatment strategies

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Combined acute medication treatment approach *Additional information*	**G7 (Canada)** (p. Suppl. 3: 34-37; S65) i. Patients with severe attacks that often require bed rest: a. Should be given a triptan (with an anti-nauseant, if necessary), consistent with the stratified approach. b. Subcutaneous sumatriptan 6 mg may be the preferred triptan for severe attacks with early vomiting, or for severe attacks which do not respond to other triptan formulations. ii. Patients with less severe attacks and who have not had adequate trials of non triptans: a. Should be educated about acute treatment options. b. An anti-emetic (metoclopramide 10 mg or domperidone 10 mg) can be added to acute migraine medications if needed for nausea. c. A "step care across attacks" strategy as outlined below can be initiated with careful patient follow-up. ***Step 1***: ASA 1,000 mg, ibuprofen 400 mg, diclofenac potassium 50 mg, naproxen sodium 550 mg, or acetaminophen 1,000 mg if NSAID intolerant. For patients with relatively severe attacks (but not usually requiring bed rest), a triptan can be prescribed at the same time. The triptan can be used as a rescue medication by the patient as necessary if the NSAID or acetaminophen occasionally fails, or can be adopted as the patient's primary acute migraine medication if the NSAID or acetaminophen proves unhelpful (see step 2 below). ***Step 2***: For patients not responding well to NSAIDs, use a triptan as the primary medication for acute migraine therapy: a. At least three different triptans should be tried (in different attacks) if the response to the first triptan is not excellent. An excellent response is defined as pain free or almost pain free with the	Not applicable	Expert consensus, based on a targeted and general literature review and expert opinion of the guideline development group (Background studies cited: NR[151] RCT[91]; Other[152,153])						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	ability to resume usual activities at 2 h post-dose, and no significant side effects. b. A triptan should be used to treat approximately three separate migraine attacks before being judged effective or ineffective. c. Intranasal triptans which are partially absorbed through the nasal mucosa (e.g., zolmitriptan 5 mg) may be preferred to oral triptans for patients with nausea. It is important that patients administer them according to the product monograph to allow for maximum nasal drug absorption. d. Orally dissolving tablets (wafers) may be the preferred oral triptan for patients with nausea exacerbated by taking fluids. e. For patients with more than one migraine attack severity, providing medications from two different classes should be considered (e.g., a triptan and NSAID). ***Step 3***: For patients whose response to triptans remains inadequate because of incomplete relief or frequent treatment failure, an NSAID (e.g., naproxen sodium 500 to 550 mg) should be used simultaneously with their triptan. ***Step 4***: For patients with a good response to their triptan-NSAID combination therapy but who experience occasional treatment failure, consider the need for a rescue medication. Rescue medications can include additional NSAIDs (oral, rectal, or injectable with oral metoclopramide), prochlorperazine (oral, rectal), corticosteroids, and acetaminophen with tramadol or codeine (not for routine use; monitor frequency of use carefully). ***Step 5***: For patients who do not respond satisfactorily to an NSAID-triptan combination, the use of dihydroergotamine (nasal spray or self-injection), combined with oral metoclopramide (if needed), can be considered. ***Step 6***: Although not recommended for routine use								

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	in migraine, opioid analgesics (e.g., acetaminophen with codeine or tramadol) remain an option for patients without a satisfactory response to earlier treatment steps, but: a. their frequency of use should be closely monitored (using a headache diary). b. behavioural and pharmacological preventive treatment options should be explored. c. these medications are also a treatment option for patients with contraindications to vasoconstrictor drugs and who do not respond to NSAIDs.								
1. Mild-moderate attack strategies	**G7 (Canada)** a. Acetaminophen strategy (p. Suppl. 3: 37; 66) i. Acetaminophen is an effective option for acute migraine therapy for some patients with attacks of mild to moderate intensity.	Not applicable	Expert consensus, based on a targeted and general literature review and expert opinion of the guideline development group (Background studies cited: RCT[32,40,154,155]; Other[156])						
	b. NSAIDs strategy (p. Suppl. 3: 37-39, 66) i. NSAIDs (including ASA) are helpful for many patients with migraine. Although it cannot be predicted which NSAID will be best for a specific patient, pharmacokinetic differences between them should be considered when treatment recommendations are made. ii. For patients with migraine attacks that increase in intensity rapidly, diclofenac potassium powder for oral solution, effervescent ASA, and solubilized ibuprofen capsules have a rapid onset of action and may be particularly helpful. iii. For patients with migraine attacks that increase in intensity rapidly, diclofenac potassium tablets have the most rapid onset of action for tablet formulations of NSAIDs (note: diclofenac potassium powder for oral solution has a more rapid oral absorption than tablets). iv. The long plasma half-life of naproxen sodium may make it particularly helpful for patients with		Expert consensus, based on a targeted and general literature review and expert opinion of the guideline development group (Background studies cited: SR[25,33-36,39,45]; RCT[28,43,44]; Other[157])						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	prolonged migraine attacks.								
2. Moderate-severe attack or NSAID failure strategies	**G7 (Canada)** NSAID with triptan rescue strategy (p. Suppl. 3: 39, 66) For patients with relatively severe attacks (but not usually requiring bed rest), an NSAID can be tried (if not tried and failed previously), and a triptan can be prescribed at the same time. The triptan can be used as a rescue medication by the patient as necessary if the NSAID occasionally fails, or can be adopted as the patient's primary acute migraine medication if the NSAID proves unhelpful.	Not applicable	Expert consensus, based on a targeted and general literature review and expert opinion of the guideline development group						
	Triptan strategy (p. Suppl. 3: 39-44, 66) i. It should be recognized that the response of an individual patient to a specific triptan cannot be predicted with accuracy. Patients with a less than optimal response to their current triptan should be encouraged to try several other triptans in different migraine attacks to determine if they will obtain better relief. ii. Patients should be encouraged to take their triptan early in their attacks while pain is still mild, although caution may need to be exercised in patients with frequent attacks to avoid medication overuse. iii. For severe migraine attacks with early vomiting, the use of subcutaneous sumatriptan 6 mg should be considered. Zolmitriptan nasal spray 5 mg may be an alternative choice for some patients. These formulations should also be considered for all patients with severe nausea, particularly those who have nausea early in their attacks, and for attacks not responsive to oral triptan medications. iv. For patients with moderate or severe migraine attacks who require triptan therapy, and whose attacks build up rapidly in intensity, rizatriptan 10 mg tablets, eletriptan 40 mg tablets, zolmitriptan 5 mg nasal spray, and sumatriptan 6 mg SC injection		Expert consensus, based on a targeted and general literature review and expert opinion of the guideline development group (Background studies cited: SR[11,54,158-160]; NR[12-14,17,62,64,161-165]; RCT[80,166-175 176-182]; NRCS[20,183-189]; CS[190-192]; G[193,194]; Other[153,161,195-203])						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	should be considered. v. For patients with moderate or severe attacks who experience side effects on other triptans, almotriptan 12.5 mg tablets should be considered. vi. For patients who experience frequent headache recurrence on triptan therapy, the use of eletriptan 40 mg or frovatriptan 2.5 mg tablets should be considered, or the addition of naproxen sodium to the patient's current triptan. vii. For patients with nausea or vomiting who require an additional anti-emetic, metoclopramide, domperidone, or if necessary, prochlorperazine can be considered, to be taken with the triptan or triptan-NSAID combination. For patients on the triptan strategy with headache recurrence within 24 hours after successful acute treatment: i. When patients experience recurrence of a migraine headache attack after initial headache relief from a triptan, a second dose of the triptan should be recommended. ii. For patients who experience frequent headache recurrence on triptan therapy, the use of eletriptan, frovatriptan, or dihydroergotamine (DHE) should be considered instead of the patient's current triptan, or the addition of naproxen sodium to the patient's current triptan. For patients on the triptan strategy who have occasional treatment failure (but not often enough to move on to the triptan-NSAID combined strategy): i. When patients experience occasional triptan failure with headache persistence two hours after taking a triptan, a rescue medication from another drug class should be considered, as opposed to dosing again with their triptan. Timing of triptan use in patients with migraine with aura:								

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	i. Patients with migraine with aura should be advised to take their triptan at the onset of the pain phase, although triptan treatment during typical migraine aura is safe, and if patients find that treatment during the aura is effective, there is no reason to discourage this practice.								
3. Refractory migraine strategies *(These are patients who have not responded satisfactorily to NSAIDs and/or triptans)*	**G7 (Canada)** Triptan-NSAID combination strategy (p. Suppl. 3: 45; 67) i. For patients whose response to triptans alone is inadequate, an NSAID (e.g., naproxen sodium 500 to 550 mg) should be used simultaneously with their triptan. ii. For patients with nausea, or where poor drug absorption is suspected, oral metoclopramide 10 mg or domperidone 10 mg can be given with the triptan.	Not applicable	Expert consensus, based on a targeted and general literature review and expert opinion of the guideline development group (Background studies cited: RCT[174,204-207]; G[1])						
	Triptan-NSAID combination with rescue medication strategy (p. Suppl. 3: 45-50, 67) i. For patients with severe migraine attacks where their triptan or triptan-NSAID combination occasionally fails to provide adequate relief, a rescue plan should be discussed with the patient. This may include a rescue medication to be taken at home when their usual medication fails. ii. In providing a rescue medication, the patient needs to be carefully assessed, and the medication tailored as much as possible to the patient's needs. For parenteral formulations, careful patient training is essential, and consideration should be given as to whether the patient can safely administer the medication. iii. For many rescue medications, in particular opioids and dexamethasone, frequency of use should be carefully monitored to ensure patient safety, and in the case of opioids to avoid medication overuse headache, abuse, dependence and possible addiction.		Expert consensus, based on a targeted and general literature review and expert opinion of the guideline development group (Background studies cited: SR[39,111]; NR[151,208-214]; RCT[49,50,91,106,118,215-217]; NRCS[218]; CS[219]; G[1]; Other[220-222])						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	iv. Rescue medications that can be considered, either alone or in combination, include: – NSAIDs with or without an anti-emetic, including ketorolac 60 mg by IM self-injection and rectal indomethacin; – Dopamine antagonists including prochlorperazine suppositories; – Oral dexamethasone or another steroid, either as a single dose or a short steroid taper over several days; – Tramadol or codeine-containing combination analgesics (limit use to not more than nine days a month); – Other opioids (suggest limiting use to not more than seven days per month). v. Migraine attack preventive management options, both pharmacological and behavioural, should be considered for all patients where acute therapy is not adequately successful or the patient is at risk of medication overuse headache.								
	Dihydroergotamine strategy (p. Suppl. 3: 50-52; 67) i. Dihydroergotamine (DHE) by nasal spray [one spray (0.5 mg) in each nostril, repeated once after 15-30 minutes; maximum daily dose eight sprays) or self-injection (0.5-1 mg; maximum daily dose 3 mg) is an option for acute migraine therapy for patients who do not respond well to triptan-NSAID combination therapy (but not as a rescue therapy as it is also a vasoconstrictor). ii. DHE self-injection (SC or IM) requires individual patient training in safe injection techniques, but provides more reliable drug absorption than the intranasal route.		Expert consensus, based on a targeted and general literature review and expert opinion of the guideline development group (Background studies cited: NR[87,223-227]; NRCS[133,228,229]; CS[230-233]; G[1]; Other[234-237])						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
4. Vasoconstrictor unresponsive-contraindicated strategy	**G7 (Canada)** (p. Suppl. 3: 52-53; 67) i. For patients with contraindications to vasoconstrictors or who have proven unresponsive to vasoconstrictors (triptans, DHE, and/or ergotamine), acetaminophen, NSAIDs (including ASA), acetaminophen-NSAID-caffeine combinations, dopamine antagonists (e.g., prochlorperazine), occasional steroid use, and opioid-containing combination analgesics can be considered. ii. Consideration needs to be given to the safety of NSAIDs in patients with cardiovascular disease. Because of a relatively benign cardiovascular profile, naproxen sodium may be the NSAID of choice, if effective, for patients with cardiovascular disease, particularly in patients who require relatively frequent use. iii. If use of tramadol or codeine-containing combination analgesics is necessary, frequency of use should be carefully monitored and limited to use on 9 days a month or less. iv. If, in exceptional cases, use of strong opioids or barbiturate-containing analgesics is considered, their frequency of use should be carefully monitored to avoid medication overuse headache, dependence, abuse, and possible addiction. Use should be limited to not more than seven days per month. v. Behavioural treatment strategies and pharmacological prophylaxis may need to be maximized if a satisfactory pharmacological acute treatment cannot be established.	Not applicable	Expert consensus, based on a targeted and general literature review and expert opinion of the guideline development group (Background studies cited: NR[238]; RCT[239,240]; NRCS[241]; CS[242]; Other[243])						
5. Menstrual migraine strategy	**G7 (Canada)** (p. Suppl. 3: 53-54; 67) *Same as Alberta CPG*	-	-						
6. Migraine during pregnancy strategy	**G7 (Canada)** (p. Suppl. 3: 54-56; 67-68) See *Table J.1e*: Migraine - acute treatment in pregnancy and lactation	-	-						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
7. Migraine during lactation strategy	**G7 (Canada)** (p. Suppl. 3: 56; 68) See *Table J.1e*: Migraine - acute treatment in pregnancy and lactation	-	-						
Premonitory symptoms and migraine treatment	**G7 (Canada)** (p. Suppl. 3: 57) i. There is insufficient evidence to make recommendations regarding the treatment of migraine during the premonitory period. In selected patients with clear cut and reliable premonitory symptoms, a trial of a triptan with a long half-life (e.g., frovatriptan) in a pre-emptive fashion could be considered.	Not applicable	Expert consensus, based on a targeted and general literature review and expert opinion of the guideline development group (Background studies cited: NR[244,245]; RCT[246]; CS[247-251]; Other[252])						

*References for the seed guidelines are available in *Appendix H*.

†Refer to *Table J.7* for explanation of ratings.

‡The integers listed in the *Supporting Evidence* columns represent the total number of discrete studies. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.

ASA: acetylsalicylic acid; CS: case series study; DHE: dihydroergotamine; G: guideline; NR: non-systematic/narrative review; NRCS: non-randomized comparative study; NSAID: nonsteroidal anti-inflammatory drug; RCT: randomized controlled trial; SC: subcutaneous; SR/MA: systematic review/meta-analysis

TABLE J.1d: Menstrual migraine – Advice and diagnosis

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Headache record *New statement/ recommendation*	**G11 (USA)** (p. 38) Clinicians should advise women who meet criteria for menstrual-associated migraine to keep a continuous daily record of headache occurrence, severity, duration and menstrual flow for at least two months.	Not applicable	Not provided						
Diagnosis *New statement/ recommendation*	**G11 (USA)** (p. 7) *Menstrual only*: headache occurs exclusively 2 days before and first 2 days of menstrual cycle. *Associated but not limited to menstruation*: Occurs >6-8 days per month OR occurs ≥3 says/months when optimally treated and still debilitating	Not applicable	**1** 253	**1** 254				**1** 194	

*References for the seed guidelines are available in *Appendix H*.

†Refer to *Table J.7* for explanation of ratings.

‡The integers listed in the *Supporting Evidence* columns represent the total number of discrete studies. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.

CS: case series study; G: guideline; NR: non-systematic/narrative review; NRCS: non-randomized comparative study; RCT: randomized controlled trial; SR/MA: systematic review/meta-analysis

TABLE J.1e: Migraine – Acute treatment in pregnancy and lactation

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Migraine treatment in pregnancy	**Alberta CPG** 1st Edition (p. 26) **Background Statement** (Based on EO (GDG)) **NSAIDs are not teratogenic, but there is some suggestion that NSAIDs may cause an increased risk of spontaneous abortion during the first trimester. NSAIDs including acetylsalicylic acid also increase the risk of premature closure of the ductus arteriosus when used during the third trimester.** **Although there is evidence that sumatriptan does not increase the risk of congenital malformations, an increased risk cannot be completely ruled out. Use of sumatriptan in the second and third trimesters may lead to a slightly increased risk of atonic uterus and blood loss over 500 ml during delivery.** **Because of potential effects on the fetus, the use of migraine prophylactic drugs during pregnancy should be avoided, where possible. When used, the balance of risk and benefits should be carefully considered. Information on drug safety during pregnancy is constantly evolving. To determine the risk profile of a prophylactic drug during pregnancy, practitioners may find the "Motherisk" website helpful (http://www.motherisk.org/women/drugs.jsp). Further advice from Motherisk is available by telephone (416.813.6780).**	Not applicable	Expert opinion of the guideline development group						
	(Based on EO (G4)) × **Drugs for migraine should be avoided during pregnancy where possible.**		Based on the clinical experience of the guideline development group (Background studies cited: Other[61,255-258])						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	(Based on EO (G2)) × **Ergot alkaloids should not be used during pregnancy.**		Not provided						
	(Based on EO (G2, G4)) ✓ **When necessary, acetaminophen 1000 mg and metoclopramide 10 mg can be used for the treatment of migraine in pregnancy. As with any medication used during pregnancy, acetaminophen should be taken at the lowest effective dose for the shortest time necessary. The total daily dose should not exceed 4 grams.**		Based on the clinical experience of the guideline development group (Background studies cited: Other[61,255-258])						
	(Based on EO (GDG)) ✓ **Where analgesia beyond acetaminophen is needed, acetaminophen - codeine combination analgesics can be used in pregnancy.**		Guideline development group expert opinion						
	(Based on EO (G4)) ✓ **Ibuprofen 400 mg can be used for acute migraine attacks during the second trimester of pregnancy. All NSAIDs, including ibuprofen, should be avoided in the third trimester of pregnancy.**		Based on the clinical experience of the guideline development group (Background studies cited: Other[61,255-258])						
	(Based on EO (G2, G4)) ? **The risks associated with the use of sumatriptan during pregnancy appear to be minimal, but there is insufficient evidence to make a recommendation for or against the use of sumatriptan in pregnancy. Sumatriptan should not be used routinely in pregnancy, but may be considered for use when other medications have failed and the benefits outweigh the risks. There is much less information or experience available**		Based on the clinical experience of the guideline development group (Background studies cited: SR[259-261]; NR[262]; NRCS[263-265])						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	regarding the safety of the other triptans during pregnancy.								
Migraine during pregnancy strategy *Additional information & new statement/ recommendation* *[some of the recommendations are similar to recommendations from Alberta CPG]*	**G7 (Canada)** (p. Suppl. 3: 54-56; 67-68) i. Avoid use of medications during pregnancy if possible, especially during the first trimester, and consider use of non-pharmacologic strategies (e.g., trigger avoidance, relaxation exercises, etc.). ii. Acetaminophen is generally regarded as the safest analgesic for use during pregnancy. iii. Alternatives to acetaminophen when acetaminophen is not adequate that may be considered for use during pregnancy include acetaminophen plus codeine combination products (intermittent use). iv. Sumatriptan is also a potential option for acute migraine treatment in pregnancy, but is not recommended for routine use. There is significant evidence that the risks of sumatriptan use in pregnancy are minimal. It may be considered when migraine headaches are severe with significant disability and/or vomiting, other medications have failed during similar attacks, and the benefits appear to outweigh potential risks. There is much less information available regarding the safety of the other triptans during pregnancy; therefore, they should be avoided. v. NSAIDs (e.g., ibuprofen, naproxen sodium) should be used with caution during pregnancy (possible increased risk of spontaneous abortion in first trimester), and should be discontinued before week 32. vi. Because of the long-lasting effects of ASA on platelet function, other NSAIDs are preferred to ASA for use during pregnancy. vii. Metoclopramide has not been associated with birth defects, and may be used during pregnancy. Dimenhydrinate is considered relatively safe for use as an antiemetic during pregnancy (but there is no	Not applicable	Expert consensus, based on a targeted and general literature review and expert opinion of the guideline development group (Background studies cited: NR[87,266]; NRCS[267]; G[268]; Other[269])						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	controlled trial evidence for efficacy in migraine). Domperidone should be avoided, as there is a lack of data with regard to its use during pregnancy. viii. Ergot alkaloids are contraindicated during pregnancy.								
Migraine during lactation strategy *New statement/ recommendation*	**G7 (Canada)** (p. Suppl. 3: 56, 68) i. Acetaminophen is considered safe during lactation. ii. Ibuprofen is the NSAID of choice during breast feeding. Diclofenac, ketorolac, and naproxen are also considered compatible with breast feeding, but with less data. ASA should be avoided. iii. Sumatriptan is considered compatible with breast feeding. iv. Metoclopramide, domperidone, dimenhydrinate, and prochlorperazine are all considered safe in breastfeeding. v. If pain medication is necessary in a breastfeeding mother, the safest drugs are acetaminophen and the NSAIDs. If opioids are considered necessary: – Morphine is considered the opioid of choice if potent analgesia is required in breastfeeding mothers; – Codeine in occasional doses is considered generally safe, although serious toxicity has been reported in maternal ultra-fast metabolizers (caution if premature infant or neonate less than four weeks old); – Avoid codeine for long-term therapy because of its variable maternal metabolism, because multiple cases of neonatal toxicity have been reported, and more effective opioid choices are available; – Avoid high doses of opioids in breastfeeding women; – For all opioids, exercise particular caution if the breastfeeding infant is under one month old.	Not applicable	Expert consensus, based on a targeted and general literature review and expert opinion of the guideline development group (Background studies cited: G[268,270]; Other[271])						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Nausea treatment *New statement/ recommendation*	**G10 (Italy)** (p. S53) In the case of nausea or vomiting during attacks, domperidone is the best choice drug. The use of antiemetics and sedative phenotiazinic drugs is not recommended.	Not applicable		**2** 272,273					
Beta-blockers and steroids *New statement/ recommendation*	**G10 (Italy)** (p. S53) Beta-blockers could have toxic effects on the newborn and may be responsible for intrauterine growth retardation, hypoglycemia, bradycardia and respiratory depression. They are not recommended in women who present with migraine with aura during pregnancy; they can be used, on the contrary, during lactation. In unresponsive cases, dexamethasone or prednisone may be used.	Not applicable		**2** 274,275					

*References for the seed guidelines are available in *Appendix H*.

†Refer to *Table J.7* for explanation of ratings.

‡The integers listed in the *Supporting Evidence* columns represent the total number of discrete studies. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.

ASA: acetylsalicylic acid; CS: case series study; G: guideline; NR: non-systematic/narrative review; NRCS: non-randomized comparative study; NSAID: nonsteroidal anti-inflammatory drug; RCT: randomized controlled trial; SR/MA: systematic review/meta-analysis

TABLE J.1f: Perimenopausal or menopausal migraine – Hormone and pharmacological therapy

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Hormone therapy *New statement/ recommendation*	**G11 (USA)** (p. 40) Hormone therapy includes the following: – transdermal, transvaginal or oral estrogen – progestin if indicated – estrogen-containing contraceptives	Not applicable		**3** 276-278					
	G11 (USA) (p. 41) Clinicians should evaluate for vascular risk factors before prescribing estrogen containing contraceptives for treatment of migraine (risk factors for coronary artery disease, prior thromboembolic disease, migraine aura, smoking).			**1** 279		**1** 280		**1** 281	
	G11 (USA) (p. 40) Clinicians should not prescribe hormone therapy for perimenopausal or menopausal migraine treatment in patients who are pregnant or have unexplained bleeding.			**1** 282	**1** 283				**1** 284
Combination analgesics *New statement/ recommendation*	**G10 (Italy)** (p. S39) Acetaminophen 500 mg + acetyl salicylic acid 500 mg + caffeine suppository 130 mg is effective in the treatment of menstrual migraine.	Not stated		**1** 48					

*References for the seed guidelines are available in *Appendix H*.

†Refer to *Table J.7* for explanation of ratings.

‡The integers listed in the *Supporting Evidence* columns represent the total number of discrete studies. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.

CS: case series study; G: guideline; NR: non-systematic/narrative review; NRCS: non-randomized comparative study; RCT: randomized controlled trial; SR/MA: systematic review/meta-analysis

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Migraine Prophylaxis

TABLE J.2a: Episodic migraine prevention/migraine prophylaxis – General considerations

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Indications for migraine preventive medication	**Alberta CPG** 1st Edition (p. 19) (Based on EO (GDG)) ✓ **Consider migraine pharmacological prophylactic therapy in the following situations:** **1. Recurrent migraine attacks are causing significant disability despite optimal acute drug therapy.** **2. The frequency of acute medication use is approaching levels that place the patient at risk for medication overuse headache:** **Use of acute medication on 10 days a month or more for triptans, ergotamines, opioids, and combination analgesics.** **Use of acute medications on 15 days a month or more for acetaminophen and NSAIDs.** **3. Recurrent attacks with prolonged aura are occurring (hemiplegic migraine, basilar-type migraine, etc.).** **4. Contraindications to acute migraine medications are making symptomatic treatment of individual migraine attacks difficult.**	Not applicable	GDG expert opinion						
New statement/ recommendation & additional information	**G8 (Canada)** (p. Suppl. 2: 4-5) (*New*) iii. Migraine prophylaxis should be considered for patients with greater than three moderate or severe headache days a month when acute medications are not reliably effective, and for patients with greater than eight headache days a month even when acute medications are optimally effective because of the risk of medication overuse headache. iv. Migraine prophylaxis may be considered in some patients with relatively infrequent attacks according to patient preference and physician judgement, for	Not applicable	Expert consensus, based on a general literature review and expert opinion of the guideline development group (Background studies cited: G[1,2])						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	example in patients with hemiplegic migraine.								
Indications for migraine preventive medication *Discordant recommendation (timing)*	**G10 (Italy)** (p. S32) Symptomatic treatment of migraine attacks alone is recommended when attacks are non-disabling or, if disabling, they occur <4 days per month. Vice versa, a preventive treatment is recommended when disabling migraine attacks are ≥4 per month or, if <4 per month, in the case of poor response to a symptomatic treatment.	Not applicable	Not provided						
Prescribing a migraine preventive medication	**Alberta CPG** 1st Edition (p. 20-21) (Based on EO (G3, G4)) ✓ **1. Educate patients on the need to take the medication daily and according to the prescribed frequency and dosage.** **2. Ensure that patients have realistic expectations as to what the likely benefits of pharmacological prophylaxis will be. That is:** • **Headache attacks will likely not be abolished completely.** • **A reduction in headache frequency of 50% is usually considered worthwhile and successful.** • **It may take 4 to 8 weeks for significant benefit to occur.** • **If the prophylactic drug provides significant benefit in the first 2 months of therapy, this may increase further over several additional months of therapy.** **3. Evaluate the effectiveness of therapy through the use of patient diaries that record headache frequency, drug use, and disability levels.** **4. For most prophylactic drugs, initiate therapy with a low dose and increase the dosage gradually to minimize side effects.** **5. Increase the dose until the drug proves**	Not applicable	Based on the clinical experience of the guideline development group (Background studies cited: NR[3]; RCT[4]; CS[5,6]; G[7,8]; Other[9])						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	effective, until dose-limiting side effects occur, or a target dose is reached. **6. Provide an adequate drug trial. Unless side effects mandate discontinuation, continue the prophylactic drug for at least 6 to 8 weeks after dose titration is completed.** **7. Because migraine attack tendency fluctuates over time, gradual discontinuation of the drug should be considered for many patients after 6 to 12 months of successful prophylactic therapy, but preventive medications can be continued for much longer in patients who have experienced significant migraine-related disability.**								
New statement/ recommendation & additional information "When should migraine prophylactic therapy be stopped?"	**G8 (Canada)** (p. Suppl. 2: 5-6) i. A prophylactic medication trial should consist of at least two months at the target or optimal dose (or at the maximum tolerated dose if the usual target dose is not tolerated) before a prophylactic drug is considered ineffective. ii. A prophylactic medication is usually considered effective if migraine attack frequency or the number of days with headache per month is reduced by 50% or more, although lesser reductions in migraine frequency may be worthwhile, particularly if the drug is well tolerated. *(New)* iii. In addition to reduction in migraine attack frequency or in the number of days with headache per month, reductions in headache intensity and migraine-related disability need to be considered when judging the effectiveness of prophylactic therapy. iv. Patients on migraine prophylaxis require periodic reevaluation both to monitor potential side effects, and to assess efficacy. vi. After 6 to 12 months of successful prophylactic therapy, consideration should be given to tapering and discontinuing the prophylactic medication in many patients, although others may benefit from a much longer duration of prophylactic therapy. If headache	Not applicable	Expert consensus, based on a general literature review and expert opinion of the guideline development group (Background studies cited: RCT[4,10-14]; NRCS[15]; CS[16,17]; G[18])						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	frequency increases as the prophylactic drug dosage is reduced, the dosage can be increased again or the drug restarted if it has been discontinued.								
Treatment plan *Additional information*	**G11 (USA)** (p. 45) After 6 to 12 months, a gradual taper of prophylactic migraine treatment is recommended unless headaches become more frequent or more severe.	Not applicable	Not provided						
New statement/ recommendation on evaluation for acute medication overuse	**G8 (Canada)** (p. Suppl. 2: 6) When prophylactic drug therapy is started, the patient should also be evaluated for the presence of acute medication overuse, and cessation of medication overuse should be strongly encouraged to optimize the chances of success. Medication overuse is defined as use of opioids, combination analgesics, or triptans on ten days a month or more, or use of simple analgesics (acetaminophen, ASA, NSAIDs) on 15 days a month or more.	Not applicable	Expert consensus, based on a general literature review and expert opinion of the guideline development group (Background studies cited: RCT[19-23]; G[1,2])						

*References for the seed guidelines are available in *Appendix H*.

†Refer to *Table J.7* for explanation of ratings.

‡The integers listed in the *Supporting Evidence* columns represent the total number of discrete studies. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.

ASA: acetylsalicylic acid; CS: case series study; G: guideline; GDG: Guideline Development Group; NR: non-systematic/narrative review; NRCS: non-randomized comparative study; NSAID: nonsteroidal anti-inflammatory drug; RCT: randomized controlled trial; SR/MA: systematic review/meta-analysis

TABLE J.2b: Episodic migraine prevention/migraine prophylaxis – Pharmacological interventions

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
B-blockers: Nebivolol *New statement/ recommendation*	**G1c (USA)** (p. 1341-1342) Nebivolol is possibly effective and may be considered for migraine prevention. Dose tested: 5 mg/day	**Level C**			**1** 24				
Beta-blockers and tricyclics *New statement/ recommendation*	**G11 (USA)** (p. 45) A beta-blocker and tricyclic antidepressant may be more effective and produce fewer side effects in combination than a single drug at a higher dose from either class.	Not applicable	Not provided						
Antidepressants: Amitriptyline	**Alberta CPG** 1st Edition (p. 21-22) (Based on G1, G2, G4, EO (GDG)) ✓ **Amitriptyline is recommended for migraine prophylaxis:** • **Dosage range 10 mg to 100 mg daily.** • **To assist with tolerability, it should be started at a low dose (10 mg daily is recommended) with the dose being built up slowly (10 mg per week is recommended). The total daily dose is usually given at bedtime or an hour or two before bedtime.** • **May be preferred in patients with migraine and depression, tension-type headache, insomnia, or anxiety.** • **It is contraindicated in patients with angle-closure glaucoma.** ***Common side effects are dry mouth and sedation.***	Not applicable			**11** 13,25-34	**3** 25,35,36	**1** 37	**1** 38	**1** 39
Additional statement supporting the EO (GDG) statement highlighted above	**G10 (Italy)** (p. S42) A progressive increase in doses is recommended until maintenance doses are reached in order to reduce adverse events.	**I**	Not provided						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Additional information related to type of migraine (episodic) and dosage	**G8 (Canada)** (p. Suppl 2: 14) We recommend that clinicians offer amitriptyline 10 to 100 mg per day to eligible patients for episodic migraine prophylaxis, although an occasional patient may require and tolerate higher doses. (See glossary in *Table J.8* for definition of episodic migraine.)	**Strong recommendation, high quality evidence**	**1** 40		**6** 25-27,41-43				
Other tricyclic antidepressants *New statement/ recommendation*	**G8 (Canada)** (p. Suppl 2: 25) i. Imipramine, trimipramine, desipramine, clomipramine, and doxepin are not recommended for routine use for migraine prophylaxis.	Not applicable	Expert consensus, based on a general literature review and expert opinion of the guideline development group (Background study cited: NR[44])						
Antidepressants: Fluoxetine *New statement/ recommendation*	**G1c (USA)** (p. 1340, 1342) Evidence is conflicting or inadequate to support or refute the use of fluoxetine for migraine prevention. Dose tested: 20 mg/day	**Level U**			**4** 45-48				**1** 49
	G10 (Italy) (p. S43) Fluoxetine 10 mg to 40 mg os. **The following, while not a recommendation, was mentioned in G10 regarding potential harm.** *Can induce insomnia, fatigue, tremor, and epigastric pain. Selective serotonin reuptake inhibitors can interfere with 5HT$_1$ agonists.*	**III**			**2** 47,48				
Antiepileptics: Topiramate	**Alberta CPG** 1st Edition (p. 22) (Based on G4) ✓ **Topiramate 50 mg to 200 mg daily (usual target dose 100 mg daily) is recommended for migraine prophylaxis.** • **May be preferred in patients with obesity.** • **Should be started at a low daily dosage (25 mg), and the daily dosage should be increased slowly (25 mg each week or every two weeks).** • ***Can result in a number of side effects including paresthesias, cognitive problems, word finding difficulty, and weight loss.***	Not applicable	**1** 50	**1** 51	**9** 20,52-59			**1** 7	**1** 60

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	• ***Should be avoided in pregnant patients or those with angle-closure glaucoma.*** • ***Should be avoided or used with caution in patients with a history of renal calculi.***								
Additional information related to type of migraine (episodic) and dosage	**G8 (Canada)** (p. Suppl 2: 13-14) We recommend that clinicians offer topiramate to eligible patients for episodic migraine prophylaxis. We found high quality evidence that topiramate provides a reduction in migraine frequency, though side effects from treatment are common. Due to the high number of adverse events and withdrawals on the 200 mg dose of topiramate, and the high quality evidence for a therapeutic benefit on the 100 mg dose, the recommended target dosage of topiramate for migraine prophylaxis is 100 mg per day. As was done in the clinical trials, the dosage should be increased gradually.	**Strong recommendation, high quality evidence**			**14** 12,41,42, 55,57,61-69				
Antiepileptics: Divalproex sodium	**Alberta CPG** 1st Edition (p. 22) (Based on G4) ✓ **Divalproex sodium 750 mg to 1500 mg daily is recommended for migraine prophylaxis.** ***May be preferred in patients with comorbid depression.*** ***Should be avoided in women who are pregnant or of child bearing potential and patients with liver disease.*** ***Can result in a number of side effects including hair loss, tremor, and weight gain.*** ***Is associated with serious fetal malformations (neural tube defects).***	Not applicable	**1** 50		**2** 53,57			**1** 7	**1** 60
Additional information related to type of migraine (episodic), dosage, and drug administration in	**G8 (Canada)** (p. Suppl 2: 12-13) While there is high quality evidence that divalproex sodium 500 to 1500 mg per day is effective for episodic migraine prophylaxis, a weak recommendation was made based on the risk benefit profile of this medication for many patients.	**Weak recommendation, high quality evidence**			**4** 10,11,70,71				

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
women with child bearing potential	*Divalproex sodium often promotes weight gain and may cause reversible tremor and hair loss. It is usually avoided in women with child bearing potential. When considered for this patient group, it should be given with folic acid, and caution should be exercised with careful consideration of birth control status due to the potential risk for teratogenicity.*								
Antiepileptics: Gabapentin	**Alberta CPG** 1st Edition (p. 22) (Based on G4) ✓ **Gabapentin (900 to 2400 mg daily) is recommended for migraine prophylaxis.**	Not applicable			**1** 72				
Discordant recommendation with TOP and G8	**G1c (USA)** (p.1339, 1342) Evidence is conflicting or inadequate to support or refute the use of gabapentin for migraine prevention. Dose tested: 4-week titration phase to 2400 mg/day; 8-week maintenance phase	**Level U**			**1** 72	**2** 73,74			
Additional information related to type of migraine (episodic) and dosage	**G8 (Canada)** (p. Suppl 2: 13) We recommend that clinicians offer gabapentin at a target dose of at least 1200 mg per day to eligible patients for episodic migraine prophylaxis.	**Strong recommendation, moderate quality evidence**			**2** 72,75				
Antiepileptics: Oxcarbazepine *New statement/ recommendation*	**G1c (USA)** (p. 1339, 1343) Oxcarbazepine is possibly ineffective and may not be considered for migraine prevention. Dose tested: 1,200 mg/day	**Level C negative**			**1** 76				
Antiepileptics: Lamotrigin *New statement/ recommendation*	**G10 (Italy)** (p. S43) Lamotrigin 50 mg to 200 mg os in the treatment of high-frequency migraine attack with aura. It is ineffective in migraine without aura.	**III**			**1** 77		**3** 78-80		

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Dihydro-ergotamine *New statement/ recommendation*	**G10 (Italy)** (p. S42) Dihydroergotamine 10 mg/day (useful for intermittent or short-term prophylaxis) and dihyrdroergocryptine 20 mg/day can be taken as second-line treatments. **The following, while not a recommendation, was mentioned in G10 regarding potential harm.** *Dihydroergotamine: Do not use within 6 hours after triptan administration. Withdrawal could be associated with rebound headache.* *Dihyrdroergocryptine: Mild side effects. Withdrawal could be associated with rebound headache.*	**II**	**1** 81		**1** 82				
Vitamins, minerals and herbals: Butterbur	**Alberta CPG** 1st Edition (p. 23) (Based on RCT (G2)) ✓ **Butterbur (*Petasites hybridus*) 75 mg twice a day is recommended for migraine prophylaxis. They may have lower efficacy than drug prophylactics (expert opinion), but all have minimal side effects.**	Not applicable			**2** 30,34				
Additional information related to type of migraine (episodic) and use with caution	**G8 (Canada)** (p. Suppl 2: 23-24) We recommend that clinicians offer butterbur 75 mg twice daily to eligible patients for episodic migraine prophylaxis. The magnitude of benefit may be small, but side effects are minimal. Due to the contrary evidence presented in these two trials for the 50 mg dose, we recommend that 75 mg of butterbur twice daily be used for migraine prophylaxis. Caution: only commercially prepared products in which plant carcinogens and hepatotoxic alkaloids have been removed and which have been standardized to contain a minimum of 15% petasins are recommended. Patients should be cautioned against consuming the plant in any other form.	**Strong recommendation, moderate quality evidence**			**2** 30,34 Studies were meta-analyzed by G8 authors				
Vitamins, minerals and herbals: Feverfew	**Alberta CPG** 1st Edition (p. 23) (Based on G4) × **Feverfew is not recommended for migraine prophylaxis.**	Not applicable	**1** 83		**1** 84				

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Discordant recommendation	**G1b (USA)** (p. 1349-1350) MIC-99 (feverfew) is probably effective and should be considered for migraine prevention.	**Level B**			**6** 84-89	**1** 90			
	G10 (Italy) (p. S43) Feverfew 18.75 mg.	**III**	**2** 83,91						
Thiotic acid *New statement/ recommendation*	**G10 (Italy)** (p. S43) Thiotic acid 600 mg.	**III**			**1** 92				
Omega-3 *New statement/ recommendation*	**G1b (USA)** (p. 1349-1350) Evidence is inadequate or conflicting to support or refute the use of omega-3 polyunsaturated fatty acids for migraine prevention. Dose tested: 3 g BID	**Level U**			**1** 93				
Botulinum toxin A	**Alberta CPG** 1st Edition (p. 23) (Based on EO (GDG)) ✓ **OnabotulinumtoxinA (botulinum toxin A) 155 to 195 Units injected as per protocol every 3 months by clinicians experienced in its use for headache is recommended for prophylaxis of chronic migraine only (migraine with headache on more than 14 days a month).**	Not applicable	Guideline development group expert opinion						
Additional information on type of migraine pain (episodic)	**G8 (Canada)** (p. Suppl 2: 24) We recommend against providing botulinum toxin type A for the prophylaxis of episodic migraine in patients with less than 15 headache days per month. The evidence indicates that botulinum toxin type A is no better than placebo for the prophylaxis of migraine in such patients.	**Strong recommendation, high quality evidence**	**1** 94		**13** 22,94-105				
Additional information	**G10 (Italy)** (p. S41-42) The majority of controlled studies have not provided conclusive results in episodic migraine. Data supporting a significant efficacy of onabotulinumtoxinA have been obtained in patients with chronic migraine with or without symptomatic drug	**IV**			**3** 106-108				

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	overuse. Onabotulinum toxin A (injection every 12 weeks) has given a statistically significant clinical benefit in patients with chronic migraine.								
NSAIDs	**Alberta CPG** 1st Edition (p. 23) (Based on EO (GDG) × **NSAIDs are not recommended for migraine prophylaxis.**	Not applicable	Guideline development group expert opinion						
Discordant recommendations	**G1b (USA)** (p. 1348-1350) The following NSAIDs are probably effective and should be considered for migraine prevention: fenoprofen, ibuprofen, ketoprofen, naproxen, naproxen sodium.	**Level B**			**4** 32,33,109, 110	**5** 36,111-114			**1** 115
	The following NSAIDs are possibly effective and may be considered for migraine prevention: flurbiprofen, mefenamic acid.	**Level C**			**1** 116	**1** 117			
	Evidence is inadequate or conflicting to support or refute the use of aspirin and indomethacin for migraine prevention.	**Level U**			**2** 118,119	**3** 120-122			
Verapamil	**Alberta CPG** 1st Edition (p. 23) (Based on EO (GDG)) ? **There is insufficient evidence to recommend for or against the use of verapamil for migraine prophylaxis.**	**Not applicable**	Guideline development group expert opinion						
	G1c (USA) (p.1342) Evidence is conflicting or inadequate to support or refute the use of calcium-channel blockers: verapamil for migraine prevention.	**Level U**			**1** 123	**1** 124			**1** 125
Discordant recommendation with TOP and G1	**G8 (Canada)** (p. Suppl 2: 20) Although verapamil has long been used for migraine prophylaxis and generally has few side effects, the evidence that it is effective is very limited.	**Weak recommendation, low quality evidence**			**1** 123	**1** 124			

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Antithrombotics *New statement/ recommendation*	**G1c (USA)** (p.1342) Evidence is conflicting or inadequate to support or refute the use of antithrombotics: acenocoumarol, Coumadin, picotamide for migraine prevention.	**Level U**	Not reported						
Acetazolamide *New statement/ recommendation*	**G1c (USA)** (p.1342) Evidence is conflicting or inadequate to support or refute the use of acetazolamide for migraine prevention. Dose tested: 250 mg BID; AE: *paresthesias, asthenia*	**Level U**			**1** 126				
Cyclandelate *New statement/ recommendation*	**G1c (USA)** (p.1341-1342) Evidence is conflicting or inadequate to support or refute the use of cyclandelate for migraine prevention.	**Level U**			**6** 127-132				
Lisinopril *New statement/ recommendation*	**G10 (Italy)** (p. S43) Lisinopril 5 mg to 20 mg os is a second choice drug to be considered for patients with concomitant hypertension. **The following, while not a recommendation, was mentioned in G10 regarding potential harm.** *Contraindications are angioedema and bilateral stenosis of the renal artery. Adverse effects include asthenia, hypotension, dry cough, hyperkalemia, gastrointestinal disturbances and impotence.*	**III**	**1** 133		**1** 134		**1** 135		**1** 136
Methysergide *New statement/ recommendation*	**G10 (Italy)** (p. S43) Methysergide 2 mg to 8 mg. **The following, while not a recommendation, was mentioned in G10 regarding potential harm.** *Contraindications include glaucoma, arrhythmias, urinary retention and obesity. The most frequent side effects are somnolence, increase in appetite, weight gain, xerosthomia and constipation.*	**III**		**2** 137, 138					
	G8 (Canada) (p. Suppl 2: 26) i. Methysergide is an effective migraine prophylactic, but because of side-effects should only be used under specialist supervision.	Not applicable	Expert consensus, based on a general literature review and expert opinion of the guideline development group (Background study cited: G[139])						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Clonidine *New statement/ recommendation*	**G8 (Canada)** (p. Suppl 2: 25) i. Clonidine is not recommended for migraine prophylaxis.	Not applicable	Expert consensus, based on a general literature review and expert opinion of the guideline development group (Background study cited: G[18])						
Angiotensin receptor blockers & ACE inhibitors: Lisinopril *New statement/ recommendation*	**G1c (USA)** (p. 1339, 1342) Lisinopril is possibly effective and may be considered for migraine prevention. AE: *cough, dizziness, "tendency to faint"*	**Level C**			**1** 134				
	G8 (Canada) (p. Suppl 2: 20) Although lisinopril 20 mg daily is generally well tolerated, the evidence for effectiveness is limited and the magnitude of benefit in episodic migraine prophylaxis appears small.	**Weak recommendation, low quality evidence**			**1** 134				
Angiotensin receptor blockers & ACE inhibitors: Telmisartan *New statement/ recommendation*	**G1c (USA)** (p. 1339, 1343) Telmisartan is possibly ineffective and may not be considered for migraine prevention. Dose tested: 80 mg	**Level C negative**			**1** 140				
Estrogen *New statement/ recommendation*	**G1b (USA)** (p 1349-1350) Estrogen is possibly effective and may be considered for migraine prevention. Dose tested: estradiol 1.5 mg (gel patch applied to the upper thigh or arm); soy isoflavones (60 mg) + dong quai (100 mg) + black cohosh (50 mg)	**Level C**			**1** 141	**1** 142			
Histamine SC *New statement/ recommendation*	**G1b (USA)** (p 1348,1350) Histamine SC is probably effective and should be considered for migraine prevention. *Histamine SC was associated with transitory burning and itching at the injection site.* Dose tested: 1 to 10 ng two times/week)	**Level B**			**3** 69,143,144				

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Antihistamine cyproheptadine *New statement/ recommendation*	**G1b (USA)** (p 1348,1350) Antihistamine-cyproheptadine is possibly effective and may be considered for migraine prevention. Dose tested: 4 mg/day	**Level C**				**3** 145			
Montelukast *New statement/ recommendation (Note: also in G2 Europe 1st Ed.)*	**G1b (USA)** (p 1348,1350) Montelukast therapy is probably ineffective and should not be considered for migraine prevention. Dose tested: 20 mg	**Level B negative**			**1** 146				

Note: Statements in italics relate to harm. These statements were sourced from the recommendations or from elsewhere in the seed guidelines.

*References for the seed guidelines are available in *Appendix H*.

†Refer to *Table J.7* for explanation of ratings.

‡The integers listed in the *Supporting Evidence* columns represent the total number of discrete studies. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.

AE: adverse events; BID: twice daily; CS: case series study; EO: expert opinion; G: guideline; GDG: Guideline Development Group; NR: non-systematic/narrative review; NRCS: non-randomized comparative study; NSAID: nonsteroidal anti-inflammatory drug; RCT: randomized controlled trial; SC: subcutaneous; SR/MA: systematic review/meta-analysis

TABLE J.2c: Approach to the individual patient/prophylactic drug treatment strategies based on the clinical setting

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
1. First time strategies	**G8 (Canada)** a. Beta-blocker strategy (p. Suppl. 2: 30-32) Propranolol, nadolol, and metoprolol are good initial prophylactic drug choices for many patients with migraine.	Not applicable	Expert consensus, based on a general literature review and expert opinion of the guideline development group (Background study cited: G[18])						
Additional information on initial choice strategy	b. Tricyclic strategy (p. Suppl. 2: 32-33) Amitriptyline is a good initial migraine prophylactic drug. It may be particularly useful in patients with insomnia or associated tension-type headache.		Expert consensus, based on a general literature review and expert opinion of the guideline development group (Background studies cited: NR[44]; RCT[41]; G[18])						
2. Low side effect strategy *New statement/ recommendation (lisinopril) & additional information on strategy*	**G8 (Canada)** a. Low side effect drug strategy (p. Suppl. 2: 33) i. Candesartan and lisinopril have evidence for efficacy in migraine prophylaxis, and generally have few side effects, although each has only one controlled trial to date supporting its use. The target dose for candesartan is 16 mg daily, for lisinopril 20 mg daily. Candesartan is preferred because of fewer side effects, and because clinical experience with lisinopril is more limited. Given the limited data for efficacy and the limited clinical experience with both these drugs at this time, they should not be considered as substitutes for the more established drugs in the "First time strategy" under most circumstances.	Not applicable	Expert consensus, based on a general literature review and expert opinion of the guideline development group						
Additional information on strategy	b. Low side effect herbal / vitamin / mineral strategy (p. Suppl. 2: 33) Butterbur, riboflavin, magnesium, and co-enzyme Q have very few side effects, and are evidence based options for migraine prophylaxis. These compounds are felt to have only modest efficacy, and should not be considered substitutes for "First time" strategy drugs under most circumstances.		Expert consensus, based on a general literature review and expert opinion of the guideline development group						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
3. Increased body mass index strategy *Additional information on strategy, diabetic patients, starting dose*	**G8 (Canada)** (p. Suppl. 2: 34) i. Topiramate is a migraine prophylactic drug which, because of its propensity to promote weight loss, is particularly useful in patients who are overweight, in patients who are particularly concerned about weight gain, and in patients with co-existent illnesses which might be exacerbated by weight gain (i.e. diabetes). ii. Topiramate should be started at a low dose (15 or 25 mg daily), and the daily dose should be increased slowly (by 15 mg every week or 25 mg every two weeks) in order to improve drug tolerability.	Not applicable	Expert consensus, based on a general literature review and expert opinion of the guideline development group (Background studies cited: RCT[41,147])						
4. Hypertension strategy *New statement/ recommendation & additional information on strategy, targeted population, medical co-morbidities, combination therapy*	**G8 (Canada)** (p. Suppl. 2: 34) i. For patients with hypertension and migraine, refer to the Canadian Hypertension Education Program's (CHEP) clinical practice recommendations which are updated annually and can be found at www.hypertension.ca. The following recommendations for managing patients with both migraine and hypertension have been reviewed with CHEP and are consistent with those evidence based recommendations. The specific angiotensin receptor blockers and angiotensin converting enzyme inhibitors listed below are those with evidence for efficacy in migraine prophylaxis. ii. Simplification of medical regimens is known to improve adherence, and the use of the same medication for both migraine and hypertension may reduce the potential for drug side effects and interactions. Recommended options are: – Propranolol, nadolol, or metoprolol (for patients under age 60). (Some other beta-blockers may also be effective, but have not been reviewed in this guideline.); – Candesartan (Candesartan has also demonstrated efficacy for patients with isolated systolic hypertension); – Lisinopril (ACE inhibitors have been found to	Not applicable	Expert consensus, based on a general literature review and expert opinion of the guideline development group						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	be less effective for lowering blood pressure as monotherapy in patients of African (black) origin). iii. Combination therapy is often required to achieve blood pressure targets. For patients requiring additional medication for blood pressure control, adding a thiazide diuretic and / or a calcium channel blocker to one of the above medications is indicated (combinations of beta blockers and nondihydropyridine calcium channel blockers like verapamil should be avoided due to the risk of heart block). iv. If adequate migraine prophylaxis is not achieved and the blood pressure is at target, other migraine prophylactic medications may be added.								
5. Depression/ anxiety strategy *New statement/ recommendation & additional information on strategy, SSRI medication*	**G8 (Canada)** (p. Suppl. 2: 34-36) i. Because of the advantages of monotherapy (less potential for drug interactions and side effects), monotherapy with one of amitriptyline or venlafaxine should be considered in patients with anxiety and/or depression who require migraine prophylaxis. Experience with venlafaxine in migraine prophylaxis is limited. Nortriptyline may be an alternative although less evidence-based choice. ii. In some patients, particularly if good control is not achieved with monotherapy or if the patient is unable to tolerate adequate doses of the tricyclic, clinicians may need to treat the migraine and the anxiety and/or depression with separate medications. iii. If SSRI – tricyclic co-therapy is planned, sertraline should be considered because of less potential for drug interactions. Most other SSRIs, in particular fluoxetine, fluvoxamine, and paroxetine, have a greater potential for significant drug interactions with amitriptyline and nortriptyline. iv. Should be typically be avoided (flunarizine), or used with caution (topiramate) in patients with depression. Although traditionally beta-blockers have been considered to predispose to depression, more recent	Not applicable	Expert consensus, based on a general literature review and expert opinion of the guideline development group (Background studies cited: SR[148-150]; NR[151-156]; RCT[41,157]; CS[158-160]; G[139,161,162]; Other[163])						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	studies suggest that this is not the case.								
6. Additional monotherapy drug strategies *New statement/ recommendation & additional information on strategy, prophylactic drugs for chronic migraine* Almost the same information as in the Alberta CPG	**G8 (Canada)** (p. Suppl. 2: 36-37) i. Topiramate is a useful migraine prophylactic drug. Although used for first time prophylaxis by some clinicians, it is not included here in the "First time" strategies because of its side effect profile. An exception is when it is used as part of the increased body mass index strategy. ii. Divalproex sodium is a useful migraine prophylactic drug in patients when other prophylactic drugs have failed. Given its teratogenicity, it should generally be avoided in women with child bearing potential and if used, should only be used when the benefits are felt to outweigh the risks, and with appropriate contraception in place. iii. Gabapentin can be considered in patients when other prophylactics have failed. It has the advantage of few drug interactions. Evidence for efficacy is less strong than for some other prophylactics. iv. Flunarizine can be a useful prophylactic when other prophylactics have failed, but should be avoided in patients with a significant history of depression. Patients on flunarizine should be monitored for onset of depression. v. Pizotifen is an option for migraine prophylaxis when other drugs have failed. vi. Verapamil can be considered for migraine prophylaxis when other drugs have failed, but the quality of evidence for efficacy of verapamil is low. vii. Although onabotulinumtoxinA is useful in chronic migraine, on the basis of clinical trial results it is not recommended for patients with episodic migraine (14 headache days per month or less). viii. Based on their proven efficacy in episodic migraine, many of the prophylactic drugs listed in this guideline are also utilized in chronic migraine. However, with the exception of topiramate and	Not applicable	Expert consensus, based on a general literature review and expert opinion of the guideline development group						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	onabotulinumtoxinA, the evidence for most migraine prophylactic drugs for efficacy in chronic migraine is very limited.								
7. Refractory patient strategy *New statement/ recommendation on strategy*	**G8 (Canada)** (p. Suppl. 2: 37-38) i. The simultaneous use of more than one prophylactic drug may be of benefit in patients with migraine refractory to prophylactic monotherapy. ii. The following drug combinations may be useful in patients with refractory migraine, based primarily on non-randomized trials and clinical experience: beta-blockers and topiramate, beta-blockers and divalproex sodium, beta-blockers and amitriptyline, and amitriptyline and topiramate. iii. Patients requiring prophylactic polypharmacy should be considered for specialist referral. (See glossary in *Table J.8* for definitions of refractory migraine and failure of prophylactic medications.)	Not applicable	Expert consensus, based on a general literature review and expert opinion of the guideline development group (Background studies cited: NR[164,165]; RCT[42]; CS[166-168]; Other[169,170])						
8. Migraine during pregnancy strategy	**G8 (Canada)** (p. Suppl. 2: 38) See *Table J.2e:* Migraine prophylaxis - pregnancy and lactation	Not applicable	Not provided						
9. Migraine during lactation strategy	**G8 (Canada)** (p. Suppl. 2: 38-39) See *Table J.2e:* Migraine prophylaxis - pregnancy and lactation	Not applicable	Not provided						

*References for the seed guidelines are available in *Appendix H*.

†Refer to *Table J.7* for explanation of ratings.

‡The integers listed in the *Supporting Evidence* columns represent the total number of discrete studies. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.

ACE: angiotensin-converting-enzyme; CS: case series study; G: guideline; NR: non-systematic/narrative review; NRCS: non-randomized comparative study; RCT: randomized controlled trial; SR/MA: systematic review/meta-analysis; SSRI: selective serotonin reuptake inhibitor

TABLE J.2d: Migraine prophylaxis – Menstrual migraine

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Menstrual migraine Prophylactic treatment	**Background Statement** **Patients with severe perimenstrual migraine attacks who do not respond well to the conventional use of acute medications may be considered for standard migraine prophylaxis, particularly if they also have a significant number of migraine attacks at other times during the month. If their attacks are primarily perimenstrual, they may be considered for intermittent short-term monthly migraine prophylaxis if their menstrual periods are regular and predictable enough to allow for proper timing of medication administration. Although intermittent short-term prophylaxis has been done with hormonal agents and with naproxen, short-term prophylaxis with frovatriptan has some of the best evidence for efficacy and is generally well tolerated.**	Not applicable							
	Alberta CPG 1st Edition (p. 25) (Based on RCT (G4) + SR (IHE Database)) ✓ **For patients with refractory menstrual migraine headache, frovatriptan 2.5 mg twice a day can be considered, with frovatriptan administration starting 2 days before the anticipated onset of the menstrually associated migraine attack and continuing for a total of 6 days.**		**1** 171		**1** 172				
New statement/ recommendation & additional information on strategy	**G7 (Canada)** (p. Suppl. 3: 53-54; 67) ii. For patients with refractory menstrual migraine who have a sufficient migraine attack frequency to justify general prophylactic therapy, this may be the best option. iii. For selected patients with refractory menstrual migraine with predicable timing of menstrual cycles, short-term monthly prophylaxis can be considered. Among the available options (frovatriptan, zolmitriptan, naratriptan, and naproxen), frovatriptan 2.5 mg twice a	Not applicable	Expert consensus, based on a targeted and general literature review and expert opinion of the guideline development group (Background studies cited: SR[171]; NR[173-175]; RCT[113,172,176-185]; NRCS[142,186-190]; CS[191])						

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	day starting two days before menstruation onset and continuing for six days has the strongest evidence for efficacy. (*New*) iv. In selected patients, hormonal manipulation including estrogen supplementation around the time of menstruation, and continuous use of combination oral contraceptives can be considered but other treatment options should be tried first. If continuous use of combined oral contraceptives is being considered, contraindications and cautions for these (e.g., smoking, migraine aura) should be observed (see discussion with regard to migraine with aura above).								
Triptans *New statement/ recommendation*	**G1c (USA)** (p. 1342) Naratriptan and zolmitriptan are probably effective and should be considered for short-term prevention of menstrually associated migraine. Naratriptan: Dose tested 1mg; AE: *dizziness, chest pain, malaise* Zolmitriptan: Dose tested 2.5 BID/TID; AE: *asthenia, headache, dizziness, nausea*	**Level B**			**2** 182,192				
Hormone prophylaxis *New statement/ recommendation*	**G11 (USA)** (p. 39) Clinicians may consider hormone prophylaxis treatment with transdermal estradiol, estrogen-containing contraceptives, or gonadotropin-releasing hormone (GnRH) agonists with "add back" therapy for patients with menstrual associated migraine.	Not applicable		**2** 193,194		**1** 195	**3** 196-198		**1** 199

Note: Statements in italics relate to harm. These statements were sourced from the recommendations or from elsewhere in the seed guidelines.

*References for the seed guidelines are available in *Appendix H*.

†Refer to *Table J.7* for explanation of ratings.

‡The integers listed in the *Supporting Evidence* columns represent the total number of discrete studies. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.

AE: adverse events; BID: twice daily; CS: case series study; G: guideline; NR: non-systematic/narrative review; NRCS: non-randomized comparative study; RCT: randomized controlled trial; SR/MA: systematic review/meta-analysis TID – three times daily

TABLE J.2e: Migraine prophylaxis – Pregnancy and lactation

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Migraine during pregnancy	**Alberta CPG** 1st Edition (p. 27) × **Preventive drugs for migraine should be avoided during pregnancy where possible.** ✓ **Preventive drugs for migraine should be gradually discontinued prior to the commencement of a planned pregnancy or should be stopped as soon as possible during an unplanned pregnancy.** ✓ **When it is necessary to continue migraine prophylaxis during pregnancy, obtaining specialist advice should be considered.**	Not applicable	Guideline development group expert opinion						
New statement/ recommendation & additional information on strategy	**G8 (Canada)** (p. Suppl. 2: 38) i. Migraine drug prophylaxis is best avoided during pregnancy if at all possible. Strategies involving trigger management, maintenance of good hydration, regular meals, regular sleep and attention to other lifestyle factors should be considered. ii. Magnesium is considered the safest migraine prophylactic during pregnancy. iii. If migraine drug prophylaxis is necessary during pregnancy, the best choice is a beta-blocker (propranolol or metoprolol) or if these are contraindicated or ineffective, amitriptyline or nortriptyline.	Not applicable	Expert consensus, based on a targeted and general literature review and expert opinion of the guideline development group (Background studies cited: NR[200-206]; NRCS[207,208] G[209]; Other[210])						
Magnesium and beta-blockers *New statement/ recommendation*	**G10 (Italy)** (p. S53) Prophylactic drugs should not be used, or at least only rarely, during pregnancy. The only exceptions are magnesium and beta-blockers (propranolol, metoprolol in the second and third trimesters of pregnancy) for which there is no evidence of teratogenicity.	Not applicable		**2** 211,212					

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Migraine during lactation strategy *New statement/ recommendation*	**G8 (Canada)** (p. Suppl. 2: 38-39) i. Migraine prophylaxis should be avoided during breast feeding, if possible. ii. Magnesium and the beta-blockers (propranolol, metoprolol, and nadolol) are the preferred choices if migraine prophylaxis is necessary during lactation. iii. Amitriptyline and nortriptyline may be considered for prophylaxis during lactation if magnesium and beta-blockers are contraindicated or ineffective. iv. Although divalproex sodium is considered compatible with breastfeeding, it may be best avoided due to the possibility of pregnancy in this population.	Not applicable	Expert consensus, based on a targeted and general literature review and expert opinion of the guideline development group (Background studies cited: NR[203,211,213,214]; G[215])						

*References for the seed guidelines are available in *Appendix H*.

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‡The integers listed in the *Supporting Evidence* columns represent the total number of discrete studies. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.

CS: case series study; G: guideline; NR: non-systematic/narrative review; NRCS: non-randomized comparative study; RCT: randomized controlled trial; SR/MA: systematic review/meta-analysis

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Migraine Non-Pharmacological Interventions

TABLE J.3a: Migraine – Non-pharmacological treatment

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Spinal manipulation	**Alberta CPG** 1st Edition (p. 25) (Based on SR (G4, IHE Database)) **?** **There is insufficient evidence to make a recommendation for or against the use of spinal manipulation for migraine management.**	Not applicable	**2** 1,2						
Discordant recommendation	**G9 (Canada)** (p.280[a]; 5[b]) Spinal manipulation (defined as high velocity low amplitude thrusts delivered to the spine) is recommended for the management of patients with episodic or chronic migraine with or without aura (treatment frequency one to two times per week for 8 weeks). **The following, while not a recommendation, was mentioned in G9 with respect to potential harm:** *Soreness or increase in headaches after spinal manipulation (n=2) were reasons for treatment discontinuation (source: RCT[3]).*	**Evidence level: Moderate**	**1** 1		**2** 3,4				
Massage	**Alberta CPG** 1st Edition (p. 25) (Based on RCT (G4)) **?** **There is insufficient evidence to make a recommendation for or against the use of massage for migraine management.**	Not applicable			**1** 5				
Discordant recommendation	**G9 (Canada)** (p.280[a];.5[b]) Weekly massage therapy is recommended for reducing episodic migraine frequency and for improving affective symptoms potentially linked to headache pain (45-minute massage with focus on neuromuscular and trigger point framework of the back, shoulder, neck, and head).	**Evidence level: Moderate**			**1** 6				

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Lifestyle factors	**Alberta CPG** 1st Edition (p. 15) (Based on EO (GDG)) ✓ **Patients should be advised to adjust their lifestyle to avoid exacerbating their migraine (e.g., avoid missing meals; avoid dehydration; maintain adequate, regular sleep).** **A general exercise program should be considered part of comprehensive migraine management.**	Not applicable	Not reported						
Relaxation training, biofeedback, and cognitive behavioural therapy (CBT)	**Alberta CPG** 1st edition (p. 24) (Based on SR (G3, IHE Database)) ✓ **Psychological therapies, including relaxation training, biofeedback, and CBT (alone or in combination), are treatment options for motivated patients with migraine. These therapies are considered to be effective components of stress management training.** **Specific recommendations regarding which of these therapies to use for specific patients cannot be made.**	Not applicable	**3** 7-9	**1** 10					
Additional information	**G9 (Canada)** (p.280[a]; 5[b]) Multimodal multidisciplinary care (exercise, relaxation, stress and nutritional counseling, massage therapy) is recommended for the management of patients with episodic or chronic migraine. Refer as appropriate.	**Evidence level: Moderate**			**1** 5				
Exercise *New statement/ recommendation*	**G9 (Canada)** (p.280[a]; 5[b]) There are insufficient clinical data to recommend for or against the use of exercise alone or exercise combined with multimodal physical therapies for the management of patients with episodic or chronic migraine (aerobic exercise, cervical range of motion (CROM), or whole body stretching).	Not stated			**1** 11	**2** 12,13			

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Transcranial magnetic stimulation *New statement/ recommendation*	**G10 (Italy)** (p. S56) Transcranial magnetic stimulation.	**II**		**1** 14	**2** 15,16				
Greater occipital nerve blockade *New statement/ recommendation*	**G10 (Italy)** (p. S56) Greater occipital and supraorbital nerve blockade.	**III**			**1** 17		**1** 18		
Sleep therapies *New statement/ recommendation*	**G10 (Italy)** (p. S56) Sleep therapies.	**III**		**1** 19	**1** 20				

Note: Statements in italics relate to harm. These statements were sourced from the recommendations or from elsewhere in the seed guidelines.

*References for the seed guidelines are available in *Appendix H*.

†Refer to *Table J.7* for explanation of ratings.

‡The integers listed in the *Supporting Evidence* columns represent the total number of discrete studies. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.

CBT: cognitive behavioural therapy; CS: case series study; EO – expert opinion; G: guideline; GDG – guideline development group; NR: non-systematic/narrative review; NRCS: non-randomized comparative study; RCT: randomized controlled trial; SR/MA: systematic review/meta-analysis

TABLE J.3b: Migraine – Non-pharmacological prophylaxis

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Physiotherapy *New statement/ recommendation*	**G10 (Italy)** (p. S56) Physiotherapy	**III**	**1** 21		**1** 6		12		
Transcranial magnetic stimulation *New statement/ recommendation*	**G10 (Italy)** (p. S56) Transcranial magnetic stimulation	**III**		**1** 14			**1** 22		

*References for the seed guidelines are available in *Appendix H*.

†Refer to *Table J.7* for explanation of ratings.

‡The integers listed in the *Supporting Evidence* columns represent the total number of discrete studies. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.

CS: case series study; G: guideline; NR: non-systematic/narrative review; NRCS: non-randomized comparative study; RCT: randomized controlled trial; SR/MA: systematic review/meta-analysis

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Tension-Type Headache

TABLE J.4a: Tension-type headache – Pharmacological treatment

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Analgesics and NSAIDs *New statement/ recommendation*	**G10 (Italy)** (p. S45-47) **The following, while not a recommendation, was mentioned in G10 with respect to potential harm:** *An excessive and frequent use of combination analgesics for ≥10 days per month should be avoided because of the high risk of drug abuse, headache chronification, and drug-induced headache.*	Not applicable		**1** 1	**1** 2				
	Ketoprofen oral 50 mg to 100 mg is a first choice drug.	**II**			**2** 3,4				
	Lumiracoxib 200 mg to 400 mg	**II**	Not provided						
	Metamizol (dipyrone) oral 500 mg to 1,000 mg **The following, while not a recommendation, was mentioned in G10 with respect to potential harm:** *Potential risk of agranulocytosis >0.1% and of hypotension.*	**II**	**1** 5		**1** 6				
Combination analgesics *New statement/ recommendation*	Indomethacin 25 mg + prochlorperazine 2 mg + caffeine 75 mg oral	**II**			**1** 7				
	Acetaminophen 500 mg + codeine 30 mg oral **The following, while not a recommendation, was mentioned in G10 with respect to potential harm:** *Patients taking opiates should be informed about the risks entailed with an abrupt discontinuation and undergo a hospitalized drug discontinuation schedule. There is an addiction potential.*	**III**		**1** 1	**1** 2				
	Butalbital (50 to 150 mg) + propyphenazone (125 to 175 mg) + caffeine (25 to 75 mg) oral **The following, while not a recommendation, was mentioned in G10 with respect to potential harm:** *Patients taking barbiturates should be informed about the risks entailed with an abrupt discontinuation and undergo a hospitalized drug discontinuation schedule.*	**III**		**1** 1	**1** 2				

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
	There is an addiction potential.								
Peppermint with ethanol topical *New statement/ recommendation*	**G10 (Italy)** (p. S47) Promising results have been obtained with a topical preparation of peppermint oil 10 g and ethanol (90% to 100%).	**III**			**2** 8,9				
Tiger balm topical *New statement/ recommendation*	**G10 (Italy)** (p. S47) Tiger balm has been shown to have a modest but significant effect in inducing headache relief.	**III**			**1** 10				
Treatment in the emergency setting *New statement/ recommendation*	**G10 (Italy)** (p. S53) The group of experts suggests the use of NSAIDs, IM or IV, to obtain a more significant and rapid relief of pain.	Not applicable	Expert opinion of the guideline development group						
	Oral benzodiazepines can also be useful in the case of attacks of great intensity, particularly in patients with concomitant anxiety.		Expert opinion of the guideline development group						
	Metoclopramide IV has demonstrated a modest analgesic efficacy at the dosage of 10 mg.				**1** 11				
	The efficacy of chlorpromazine IV, at the dosage of 10 mg, in tension-type headache patients presenting to the emergency department has also been demonstrated. **The following, while not a recommendation, was mentioned in G10 with respect to potential harm:** *The most frequent adverse event is sedation, occasionally extrapyramidal symptoms or akathisia may occur.*				**1** 12				

Note: Statements in italics relate to harm. These statements were sourced from the recommendations or from elsewhere in the seed guidelines.

*References for the seed guidelines are available in *Appendix H*.

†Refer to *Table J.7* for explanation of ratings.

‡The integers listed in the *Supporting Evidence* columns represent the total number of discrete studies. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.

CS: case series study; G: guideline; IM: intramuscular; IV: intravenous; NR: non-systematic/narrative review; NRCS: non-randomized comparative study; NSAID: non-steroidal anti-inflammatory drug; RCT: randomized controlled trial; SR/MA: systematic review/meta-analysis

TABLE J.4b: Tension-type headache – Non-pharmacological treatment

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Mobilization *New statement/ recommendation*	**G9 (Canada)** (p. 280-281[a]; 5[b]) Low-load craniocervical mobilization (e.g. Resistance Exercise Systems, Thera-Band®) is recommended for longer term management of patients with episodic or chronic tension-type headaches (10 minutes, two times per day for 6 weeks, then at least two times per week for 6 months).	**Evidence level: Moderate**			**1** 13				
Spinal manipulation *New statement/ recommendation*	**G9 (Canada)** (p. 281[a]; 5[b]) Spinal manipulation cannot be recommended for the management of patients with episodic tension-type headache. Spinal manipulation following pre-manipulative soft tissue therapy provides no added benefit for reducing tension-type headaches.	**Evidence level: Moderate**	**4** 14-17		**1** 18				
	G9 (Canada) (p. 281[a]; 5[b]) A recommendation cannot be made for or against the use of spinal manipulation for patients with chronic tension-type headaches. **The following, while not a recommendation, was mentioned in G9 regarding potential harm.** *4.3% of subjects experienced neck stiffness after initial spinal manipulation that disappeared for all cases after the first 2 weeks of treatment (source RCT[19]).*		**4** 14-17		**1** 19				
Manual traction, connective tissue manipulation, Cyriax's mobilization *New statement/ recommendation*	**G9 (Canada)** (p. 281[a]; 5[b]) There is insufficient evidence to recommend for or against the use of manual traction, connective tissue manipulation, or Cyriax's mobilization for patients with episodic or chronic tension-type headaches.	Not reported	**1** 15		**4** 20-23				

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Exercise	**Alberta CPG** 1st Edition (p. 29) (Based on EO (GDG)) ✓ **A therapeutic exercise program, based on an assessment by an appropriately trained health professional, may be considered for patients with tension-type headache.**	Not applicable	Not applicable						
Physical therapy	**Alberta CPG** 1st Edition (p. 29) (Based on SR (G6)) ✓ **Physical therapy and acupuncture may be considered for patients with frequent tension-type headache.**	Not applicable	**7** 14,17,24 -28	**1** 29	**7** 13,18,19 ,21,23,3 0,31	**1** 32			**1** 33
Discordant recommendation	**G9 (Canada)** (p. 281[a]; 5[b]) There is insufficient evidence to recommend for or against the use of exercise/physical training for patients with episodic or chronic tension-type headaches.	Not reported	**1** 15		**4** 20-23				

Note: Statements in italics relate to harm. These statements were sourced from the recommendations or from elsewhere in the seed guidelines.

*References for the seed guidelines are available in *Appendix H*.

†Refer to *Table J.7* for explanation of ratings.

‡The integers listed in the *Supporting Evidence* columns represent the total number of discrete studies. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.

CS: case series study; G: guideline; GDG: Guideline Development Group; NR: non-systematic/narrative review; NRCS: non-randomized comparative study; RCT: randomized controlled trial; SR/MA: systematic review/meta-analysis

TABLE J.4c: Tension-type headache – Pharmacological prophylaxis

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Antidepressants *New statement/ recommendation*	**G10 (Italy)** (p. S47) Clomipramine 10 mg to 150 mg	**II**			**2** 34,35				
	Fluvoxamine 50 mg to 100 mg	**II**	**1** 36		**1** 37				
	Maprotilin 75 mg	**II**			**2** 38,39				
	Mianserin 30 mg to 60 mg	**II**			**2** 38,39				
Muscle relaxants *New statement/ recommendation*	**G10 (Italy)** (p. S47-48) Tizanidine oral 3 mg to 12 mg Especially useful in the case of pericranial muscle tenderness. **The following, while not a recommendation, was mentioned in G10 with respect to potential harm:** *Adverse effects include somnolence, dizziness, dry mouth, and asthenia.*	**II**			**2** 40,41				
	Cyclobenzaprine oral 10 mg	**III**							**1** 42
Benzodiazepines *New statement/ recommendation*	**G10 (Italy)** (p. S47) Diazepam 5 mg/day. Can be useful in cases of comorbid anxiety.	**II**				**2** 43,44			
	Alprazolam oral 0.75 mg/day	**III**			**1** 45				
Topiramate *New statement/ recommendation*	**G10 (Italy)** (p. S47) Topiramate oral 25 mg to 100 mg	**II**					**1** 46		

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Buspirone *New statement/ recommendation*	**G10 (Italy)** (p. S48) Buspirone 30 mg	**III**			**1** 47				
L-5-hydroxytryptophan *New statement/ recommendation*	**G10 (Italy)** (p. S48) L-5-hydroxytryptophan	**III**			**1** 48				

Note: Statements in italics relate to harm. These statements were sourced from the recommendations or from elsewhere in the seed guidelines.

*References for the seed guidelines are available in *Appendix H*.

†Refer to *Table J.7* for explanation of ratings.

‡The integers listed in the *Supporting Evidence* columns represent the total number of discrete studies. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.

CS: case series study; G: guideline; GDG: Guideline Development Group; NR: non-systematic/narrative review; NRCS: non-randomized comparative study; RCT: randomized controlled trial; SR/MA: systematic review/meta-analysis

References (Tables J.4a to J.4c)

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Cluster Headache

TABLE J.5a: Cluster headache – Referral for surgery

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Referral for surgery *New statement/ recommendation*	**G5b (Europe)** (p. 185) Surgical procedures are not indicated in most patients with cluster headache. Patients with intractable chronic cluster headache should be referred to centres with expertise in both destructive and neuromodulatory procedures to be offered all reasonable alternatives before a definitive procedure is conducted.	**C**					**9** 1-9		

*References for the seed guidelines are available in *Appendix H*.

†Refer to *Table J.7* for explanation of ratings.

‡The integers listed in the *Supporting Evidence* columns represent the total number of discrete studies. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.

CS: case series study; G: guideline; GDG: Guideline Development Group; NR: non-systematic/narrative review; NRCS: non-randomized comparative study; RCT: randomized controlled trial; SR/MA: systematic review/meta-analysis

TABLE J.5b: Cluster headache – Pharmacological prophylaxis

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Corticosteroids *New statement/ recommendation*	**G10 (Italy)** (p. S49 & S51) Prednisone 50 mg to 75 mg/day per os for 3 to 7 days then gradually decreased to stop within 10 days. **The following, while not a recommendation, was mentioned in G10 with respect to potential harm:** *Repeated use may, over time, induce severe adverse events.*	**II (episodic)** **IIIb (chronic)**					**3** 10-12		
Serotonin antagonists *New statement/ recommendation*	**G10 (Italy)** (p. S49 & S51) Methysergide: Start with the dosage of 2 mg/day per os in three administrations, gradually increase the dosage (every 3 to 7 days) to the dosage of 8 mg/day. Maximum 6 month treatment due to possible development of retroperitoneal and lung fibrosis. **The following, while not a recommendation, was mentioned in G10 with respect to potential harm:** *Side effects occur in 20% to 45% of patients. The most frequent include nausea, dizziness, stomach pain, restlessness, somnolence, and cramps.*	**IIIb**					**3** 13-15		
	Pizotifen: Start with the dosage of 1 mg/day per os, increase the dosage to a maximum of 2.5 mg, to be reached in 2 weeks.	**IIIa**			**1** 16				
Capsaicin *New statement/ recommendation*	**G10 (Italy)** (p. S50-51) Intranasal capsaicin 300 µg/day in the ipsilateral nostril repeatedly to obtain a complete desensitization.	**IIIa**				**2** 17,18			
Histamine sulfate *New statement/ recommendation*	**G10 (Italy)** (p. S49 & S51) Intravenous histamine sulfate diluted in saline or 5 %: 1st day: 2.75 mg in 250 mL; 2nd to 10th day: 11 mg in 500 mL. Starting flow rate of 10 mL/hour then 120 mL/hour.	**IIIa (chronic)**					**1** 19		

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Bridging treatment *New statement/ recommendation*	**G11 (USA)** (p. 36) Occipital nerve block is an option for bridging treatment to be administered simultaneously with maintenance prophylactic treatment after acute treatment has suppressed the initial attack.	Not stated		**2** 20,21	**1** 22		**2** 23,24	**1** 25	

Note: Statements in italics relate to harm. These statements were sourced from the recommendations or from elsewhere in the seed guidelines.

*References for the seed guidelines are available in *Appendix H*.

†Refer to *Table J.7* for explanation of ratings.

‡The integers listed in the *Supporting Evidence* columns represent the total number of discrete studies. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.

CS: case series study; G: guideline; NR: non-systematic/narrative review; NRCS: non-randomized comparative study; RCT: randomized controlled trial; SR/MA: systematic review/meta-analysis

TABLE J.5c: Cluster headache in pregnancy and lactation – General statements

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
General statement *New statement/ recommendation*	**G11 (USA)** (p. S54) Treatments to be preferred are oxygen, prednisone and verapamil. If verapamil cannot be used, gabapentin should be preferred as prophylactic treatment. The use of subcutaneous or intranasal sumatriptan should be limited as much as possible. During lactation, oxygen and sumatriptan may be used as symptomatic drugs and prednisone/prednisolone, verapamil and lithium for prophylaxis.	Not applicable		**1** 26			**1** 27		

*References for the seed guidelines are available in *Appendix H*.

†Refer to *Table J.7* for explanation of ratings.

‡The integers listed in the *Supporting Evidence* columns represent the total number of discrete studies. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.

CS: case series study; G: guideline; NR: non-systematic/narrative review; NRCS: non-randomized comparative study; RCT: randomized controlled trial; SR/MA: systematic review/meta-analysis

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Cervicogenic Headache

TABLE J.6: Cervicogenic headache – Non-pharmacological treatment

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Cervical spinal manipulation	**Alberta CPG** 1st Edition (p. 36) (Based on SR (G4, IHE Database)) ✓ **Cervical spinal manipulation, defined as the application of high velocity, low amplitude manual thrusts to the spinal joints slightly beyond the passive range of joint motion, may be considered in the management of patients with cervicogenic headache.**	Not applicable	**2** 1,2						
Additional information	**G9 Chiropractic (Canada)** (p. 282[a]; 5[b]) Spinal manipulation is recommended for the treatment of patients with cervicogenic headaches (two times per week for 3 weeks).	**Evidence level: Moderate**	**2** 1,3		**1** 4				
Cervical spine mobilization	**Alberta CPG** 1st Edition (p. 37) (Based on SR (G4, IHE Database)) ✓ **Cervical spine mobilization, defined as the application of manual force to the spinal joints within the passive range of joint motion that does not involve a thrust, may be considered in the management of patients with cervicogenic headache.**	Not applicable	**2** 1,2						
Additional information	**G9 Chiropractic (Canada)** (p. 282[a]; 5[b]) Joint mobilization is recommended for the treatment of patients with cervicogenic headaches (Maitland joint mobilization 8 to 12 treatments over 6 weeks).	**Evidence level: Moderate**	**2** 1,3		**1** 5				

Item	Guideline/Country/Synopsis of Recommendations*	Rating of Recommendation†	Supporting Evidence‡						
			SR/ MA	NR	RCT	NRCS	CS	G	Other
Exercise	**Alberta CPG** 1st Edition (p. 36) (Based on SR (IHE Database)) ✓ **Although there is insufficient evidence to recommend any specific exercise for the treatment of cervicogenic headache, a therapeutic exercise program based upon an assessment by an appropriately trained health professional may be considered.**	Not applicable	**2** 1,6						
Discordant recommendation	**G9 Chiropractic (Canada)** (p. 282[a]; 5[b]) Deep neck flexor exercises are recommended for the treatment of patients with cervicogenic headaches (two times daily over 6 weeks). There is no consistently additive benefit of combining deep neck flexor exercises and joint mobilization for cervicogenic headaches.	**Evidence level: Moderate**	**2** 1,3		**1** 5				

*References for the seed guidelines are available in *Appendix H*.

†Refer to *Table J.7* for explanation of ratings.

‡The integers listed in the *Supporting Evidence* columns represent the total number of discrete studies. Thus, when there are multiple publications for a single study, the integers are less than the number of references listed below them.

CS: case series study; G: guideline; NR: non-systematic/narrative review; NRCS: non-randomized comparative study; RCT: randomized controlled trial; SR/MA: systematic review/meta-analysis

References (Table J.6)

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TABLE J.7: Recommendation ratings used by the new seed guidelines

Rating	Definition
G1b, G1c (USA)	
Rating scheme for the strength of the recommendation	
A	Established as effective, ineffective or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.)*
B	Probably effective, ineffective or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population. (Level B rating requires at least one Class I study or two consistent Class II studies.)
C	Possibly effective, ineffective or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)
U	Data inadequate or conflicting; given current knowledge, treatment (test, predictor) is unproven.
*In exceptional cases, one convincing Class I study may suffice for an "A" recommendation if: 1) all criteria are met; 2) the magnitude of effect is large (relative rate improved outcome >5 and the lower limit of the confidence interval is >2).	
Rating scheme for the strength of the evidence	
Class I	A randomized, controlled clinical trial of the intervention of interest with masked or objective outcome assessment, in a representative population. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences. The following are also required: 1. Concealed allocation 2. Primary outcome(s) clearly defined 3. Exclusion/inclusion criteria clearly defined 4. Adequate accounting for dropouts (with at least 80% of enrolled subjects completing the study) and crossovers with numbers sufficiently low to have minimal potential for bias. 5. For non-inferiority or equivalence trials claiming to prove efficacy for one or both drugs, the following are also required*: i. The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or non-inferiority. ii. The standard treatment used in the study is substantially similar to that used in previous studies establishing efficacy of the standard treatment (e.g., for a drug, the mode of administration, dose and dosage adjustments are similar to those previously shown to be effective). iii. The inclusion and exclusion criteria for patient selection and the outcomes of patients on the standard treatment are comparable to those of previous studies establishing efficacy of the standard treatment. iv. The interpretation of the results of the study is based upon a per protocol analysis that takes into account dropouts or crossovers.
Class II	A randomized controlled clinical trial of the intervention of interest in a representative population with masked or objective outcome assessment that lacks one criteria i–v above or a prospective matched cohort study with masked or objective outcome assessment in a representative population that meets ii–v above. Relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.

Rating	Definition
Class III	All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome is independently assessed, or independently derived by objective outcome measurement.†
Class IV	Studies not meeting Class I, II or III criteria including consensus or expert opinion.
*Note that numbers 1–3 in Class I are required for Class II in equivalence trials. If any one of the three is missing, the class is automatically downgraded to Class III. †Objective outcome measurement: an outcome measure that is unlikely to be affected by an observer's (patient, treating physician, investigator) expectation or bias (e.g., blood tests, administrative outcome data).	
G1d (USA)	
Rating scheme for the strength of the recommendation	
A	Established as effective (or ineffective) for acute migraine (supported by at least two Class I studies).
B	Probably effective (or ineffective) for acute migraine (supported by at least one Class I study or two Class II studies).
C	Possibly effective (or ineffective) for acute migraine (supported by one Class II study or two consistent Class III studies).
U	Evidence is conflicting or inadequate to support or refute the use of the medication(s) for acute migraine.
Rating scheme for the strength of the evidence	
Class I	Randomized, controlled clinical trial in a representative population Masked or objective outcome assessment Relevant baseline characteristics are presented and substantially equivalent between treatment groups, or there is appropriate statistical adjustment for differences Also required: 1. Concealed allocation 2. Primary outcome(s) clearly defined 3. Exclusion/inclusion criteria clearly defined 4. Adequate accounting for dropouts (with at least 80% of enrolled subjects completing the study) and crossovers with numbers sufficiently low to have minimal potential for bias 5. For non-inferiority or equivalence trials claiming to prove efficacy for 1 or both drugs, the following are also required*: i. The authors explicitly state the clinically meaningful difference to be excluded by defining the threshold for equivalence or non-inferiority. ii. The standard treatment used in the study is substantially similar to that used in previous studies establishing efficacy of the standard treatment (e.g., for a drug, the mode of administration, dose and dosage adjustments are similar to those previously shown to be effective). iii. The inclusion and exclusion criteria for patient selection and the outcomes of patients on the standard treatment are comparable to those of previous studies establishing efficacy of the standard treatment. iv. The interpretation of the results of the study is based upon a per protocol analysis that takes into account dropouts or crossovers.

Rating	Definition
Class II	Cohort study meeting criteria i–v (see Class I) or a randomized, controlled clinical trial that lacks 1 or 2 criteria ii–v (see Class I) All relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences Masked or objective outcome assessment
Class III	Controlled studies (including well-defined natural history controls or patients serving as their own controls) A description of major confounding differences between treatment groups that could affect outcome Outcome assessment masked, objective, or performed by someone who is not a member of the treatment team
Class IV	Did not include patients with the disease Did not include patients receiving different interventions Undefined or unaccepted interventions or outcome measures No measures of effectiveness or statistical precision presented or calculable
*Note that numbers 1–3 in Class I are required for Class II in equivalence trials. If any one of the three is missing, the class is automatically downgraded to Class III.	
G5b (Europe)	
Rating scheme for the strength of the recommendation	
A	Established as effective, ineffective, or harmful: requires at least one convincing class I study or at least two consistent, convincing class II studies
B	Probably effective, ineffective, or harmful: requires at least one convincing class II study or overwhelming class III evidence
C	Possibly effective, ineffective, or harmful: rating requires at least two convincing class III studies
Rating scheme for the strength of the evidence	
Class I	An adequately powered prospective, randomized, controlled clinical trial with masked outcome assessment in a representative population or an adequately powered systematic review of prospective randomized controlled clinical trials with masked outcome assessment in representative populations. The following are required: i. randomization concealment; ii. primary outcome(s) is/are clearly defined; iii. exclusion/inclusion criteria are clearly defined; iv. adequate accounting for dropouts and crossovers with numbers sufficiently low to have minimal potential for bias; v. relevant baseline characteristics are presented and substantially equivalent among treatment groups or there is appropriate statistical adjustment for differences.
Class II	Prospective matched-group cohort study in a representative population with masked outcome assessment that meets i-v above or a randomized, controlled trial in a representative population that lacks one criteria i-v.
Class III	All other controlled trials (including well-defined natural history controls or patients serving as own controls) in a representative population, where outcome assessment is independent of patient treatment.
Class IV	Evidence from uncontrolled studies, case series, case reports, or expert opinion.

Rating	Definition	
G7, G8 (Canada)		
Levels of evidence, GRADE system		
High quality	The guideline authors are confident that the true effect lies close to the estimate given by the evidence available.	
Moderate quality	The guideline authors are moderately confident in the effect estimate, but there is a possibility it is substantially different.	
Low quality	The confidence in the effect estimate is limited. The true effect may be substantially different.	
Very low quality	The guideline authors have little confidence in the effect estimate.	
Recommendation grades *Note*: Only categories used in the guideline are shown)		
Recommendation grade	*Benefits vs. risks*	*Clinical implication*
Strong-high quality evidence	Benefits clearly outweigh risks and burdens for most patients	Can apply to most patients in most circumstances
Strong-moderate quality evidence	Benefits clearly outweigh risks and burdens for most patients	Can apply to most patients, but there is a chance the recommendation may change with more research
Strong-low quality evidence	Benefits clearly outweigh risks and burdens for most patients	Can apply to most patients, but there is a good chance the recommendations could change with more research
Weak-high quality evidence	Benefits are more closely balanced with risks and burdens for many patients	Whether a medication is used will depend upon patient circumstances
Weak-moderate quality evidence	Benefits are more closely balanced with risks and burdens for many patients	Whether a medication is used will depend upon patient circumstances, but there is less certainly about when it should be used
Weak-low quality evidence	Benefits are more closely balanced with risks and burdens	There is considerable uncertainty about when to use this medication
G9 (Canada)		
Rating scheme for the strength of the recommendation		
Strong	Consistent findings among ≥2 high-quality controlled trials	
Moderate	Consistent findings among ≥2 low-quality controlled trials and/or 1 high-quality controlled trial	
Limited	One low-quality controlled trial	
Conflicting	Inconsistent findings among multiple controlled trials	
G10 (Italy)		
Rating scheme for the strength of the recommendation		
Level I	Drugs with high efficacy supported by statistically significant data (evidence of at least two controlled, randomized studies versus placebo or versus active drugs of proven efficacy) or very high clinical benefit for patients (clinical effectiveness +++) and with no severe adverse events	
Level II	Drugs whose value of efficacy is statistically of lower significance compared to drugs of group I and with a less significant clinical benefit for patients (clinical effectiveness ++) and no severe adverse events	

Rating	Definition
Level III	Drugs showing efficacy from a statistical point of view but not from a clinical point of view (contrasting results or evidence is not conclusive). The drugs belonging to this group were further subdivided into two subgroups: i. Drugs with no severe adverse events; ii. Unsafe drugs or with complex indications for use (e.g., special diets) or important pharmacological interactions
Level IV	Drugs of proven efficacy but with frequent and severe adverse events or drugs whose efficacy has not been proven from a clinical or statistical point of view (no difference with respect to placebo). Drugs with unknown clinical patient benefit or statistical significance of efficacy (data unavailable or insufficient)
Scientific strength of evidence	
+++	The difference in the parameters of efficacy registered in studies compared with placebo or another active drug has a high level of significance ($p<0.01$; $p<0.001$; $p<0.0001$). Adverse events are rare or occasional and not severe.
++	The difference in the parameters of efficacy registered in studies reaches the minimum level of significance ($p<0.05$) or the minimum clinically significant level (difference in the parameters <15%)*.
+	The difference in the efficacy parameters between the study drug and placebo or another active drug is not statistically significant.
0	The drug is not efficacious or is characterized by severe adverse events.
*Even drugs for which the difference in the efficacy parameters compared with placebo or another active drug is higher than the minimum level of statistical significance, but have frequent, yet no severe adverse events are included in this group	

Note: References for the seed guidelines (G1, G2, etc.) are available in *Appendix H*.

GRADE: Grading of Recommendations Assessment, Development and Evaluation

TABLE J.8: Glossary of terms for interventions included in the inventory tables

Term	Definition
Episodic migraine	Episodic migraine is defined as migraine with headache on less than 15 days a month. (G8, Canada)
Failure of prophylactic medications	Failure of prophylactic medications is defined as failure of adequate trials of medications from at least two of the four main classes of prophylactic medications: beta-blockers, anticonvulsants, tricyclics, and calcium channel blockers. (G8, Canada)
Refractory migraine	Refractory migraine has been defined as migraine causing significant interference with function or quality of life despite optimal management of triggers and lifestyle factors, and adequate trials of acute and prophylactic medications. (G8, Canada)

Appendix K: Summary of Parking Lot Items

Recommendations accepted or rejected by the Guideline Update Committee (GUC) based on supplementary information reviewed and discussed in subcommittee meetings.

TABLE K.1: Diagnosis and investigation

Intervention*	Parking lot item(s) and other miscellaneous requests by the GUC; SC actions	Subcommittee meetings		Final decision by Subcommittee and GUC; Evidence source
		Review/discussion/ deliberation†‡	Expertise of participants	
Definition of elderly **Additional information**	7 October 2015. Subcommittee meeting. Review definition of elderly (define elderly) to add in the Urgent Red Flags: Need investigation and referral within hours to days recommendation (i.e., item #4).	19 December 2015 to 3 January 2016. Email correspondence Subcommittee co-chair. Reviewed results from published reports. Leave up to the treating physician whether the patient is elderly or not (biological age rather than chronological age).	Neurology HTA research	*7 March 2016.* Urgent red flags recommendation accepted by GUC as status quo; do not add a definition.
		7 January to 2 February 2016. Email correspondence of Subcommittee members. Reviewed results from published reports. The College of Family Physicians Canada does not define elderly. Do not define elderly in the guidance.	Interventional Therapies Subcommittee (see details in *Table K.6*)	
Headache diagnosis and investigation recommendations - *Alberta CPG* 1st Edition	7 October 2015. Subcommittee meeting. Review headache diagnosis and investigation recommendations and update where necessary. Wording refinements to be consistent with the updated International Headache Society guidelines.		Interventional Therapies Subcommittee (see details in *Table K.6*)	*7 March 2016.* Changes accepted by GUC.
Emergency red flags Neuroimaging and diagnosis in the outpatient setting Imaging in typical migraine Unexplained focal signs in the patient with headache Unusual headache precipitants Unusual aura symptoms Cluster headache and other uncommon primary headache syndromes Neuroimaging for patient reassurance Electroencephalography		7 October 2015. Subcommittee meeting. Status quo		

Intervention*	Parking lot item(s) and other miscellaneous requests by the GUC; SC actions	Subcommittee meetings		Final decision by Subcommittee and GUC; Evidence source
		Review/discussion/ deliberation†‡	Expertise of participants	
Urgent red flags		7 October 2015. Subcommittee meeting. • Keep first statement as is • Second statement: reverse order of C-reactive protein and erythrocyte sedimentation rate • Keep third statement as is • Fourth statement: change "brain CT imaging" to "neuroimaging"; consider defining elderly; add evidence source GUC		
Atypical headaches and changes in headache pattern		7 October 2015. Subcommittee meeting. Remove sentence "A non-contrast brain CT…".		
Late onset headache		7 October 2015. Subcommittee meeting. Change "non-contrast brain CT scan" to "neuroimaging". Reverse order of C-reactive protein and erythrocyte sedimentation rate.		
Post-traumatic headache **New recommendation** (proposed by Subcommittee members)	7 October 2015. Subcommittee meeting. Supplementary search for SRs on investigation/imaging for subacute post-trauma headache.	19 December 2015. No SR found; 30 reviews excluded.	Neurology HTA research	*7 March 2016*. Accepted by GUC as "Do Not Know". **Persistent Headache Attributed to Head Trauma** **EO (GUC)**
		3 January 2016. Email correspondence of Subcommittee co-chair: wordsmithing of recommendation.	Neurology	
		7 January 2016 to 2 February 2016. Email correspondence Subcommittee. Reviewed results from published reports. Approved adding recommendation as a "Do Not Know".	Interventional Therapies Subcommittee (see details in *Table K.6*)	

CPG: clinical practice guideline; CT: computed tomography; EO: expert opinion; GUC: Guideline Update Committee (see role and membership in *Appendix A* and *Appendix B*); HTA: health technology assessment; SC: Steering Committee; SR: systematic review

Parking lot item – Any activity that involved review of individual studies referenced in the seed guideline(s), systematic reviews published between January 2008 and May 2015, or other requests that were required by the GUC before a final decision could be made.

*Interventions were sourced from the *Alberta CPG*, 1st Edition, new seed guideline(s), stakeholder requests, or systematic reviews (IHE Database). They are listed in the same order in which they are written in the *Alberta CPG*. Original recommendations from the seed guidelines are listed in *Appendix J*. References for the seed guidelines are available in *Appendix H*.

†Detailed information on the searches conducted and on data extraction from studies is available upon request.

‡The number of SRs may vary if there were multiple publications of the same study.

TABLE K.2: Management of migraine headache

Intervention*	Parking lot item(s) and other miscellaneous requests by the GUC; SC actions	Subcommittee meetings		Final decision by Subcommittee and GUC; Evidence source
		Review/discussion/ deliberation[†‡]	Expertise of participants	
General approach to management				
Allergy headache **New recommendation**	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on allergy headache.	21 October 2015. No SR found; 5 reviews excluded. 28 October 2015. Subcommittee meeting. Only NRs found. Do not add to *Alberta CPG*; mention in the methods background document.	Office-Based Pharmacy Subcommittee (see details in *Table K.6*)	*7 March 2016*. GUC. Do not add to *Alberta CPG*.
Pharmacological interventions				
Ketorolac **New recommendation**	28 October 2015. Subcommittee meeting. Supplementary search for SRs on ketorolac for acute migraine.	1 June 2015. SC meeting. Ketorolac is available in Canada. Review to be determined by Subcommittee.	Neurology Psychology, pain management HTA research (2 participants)	*7 March 2016*. Accepted by GUC to add in the background statement.
		28 October 2015. Subcommittee meeting. Nasal spray is not commercially available but it can be made.	Office-Based Pharmacy Subcommittee (see details in *Table K.6*)	
		11 December 2015. Subcommittee meeting. No SR found; 7 reviews focusing on ketorolac parenteral (IV or IM) excluded. Mention NSAIDs (ketorolac) without evidence from SR in background statement for treatment of acute migraine.		
Intranasal lidocaine for migraine headache **New recommendation**	28 October 2015. Subcommittee meeting. Review two RCTs[1,2] on intranasal lidocaine for migraine headache cited by G10 and G11.	11 December 2015. Subcommittee meeting. The RCTs provide conflicting evidence: (1) positive outcome, questionable set-up[1]; (2) negative outcome, complicated/inapplicable patient groups[2]. The intervention is not widely used in Canada, but auto-injector is available in the US. Add as a "Do Not Know" recommendation.	Office-Based Pharmacy Subcommittee (see details in *Table K.6*)	*7 March 2016*. Accepted by GUC as "Do Not Know". **EO (GUC)**

Intervention*	Parking lot item(s) and other miscellaneous requests by the GUC; SC actions	Subcommittee meetings		Final decision by Subcommittee and GUC; Evidence source
		Review/discussion/ deliberation[†‡]	Expertise of participants	
Pharmacological prophylactic therapy				
Beta-blockers and tricyclic antidepressants for migraine prophylaxis **New recommendation**	28 October 2015. Subcommittee meeting. Supplementary search for SRs on combination therapy beta-blockers and tricyclic antidepressants for migraine prophylaxis.	11 December 2015. Subcommittee meeting. No SR found: 27 reviews excluded, majority did not report any results. There was no evidence cited in seed guideline. There is a concern of risks from the medications administered in combination, and risk versus benefit is not clear. Do not add to *Alberta CPG*.	Office-Based Pharmacy Subcommittee (see details in *Table K.6*)	*7 March 2016*. GUC. Do not add to *Alberta CPG*.
Antidepressants for migraine prophylaxis **Additional information**	28 October 2015. Subcommittee meeting. Supplementary search for SRs on selective serotonin reuptake inhibitors (SSRIs), serotonin norepinephrine reuptake inhibitors (SNRIs) (venlafaxine, duloxetine) and nortriptyline for migraine prophylaxis.	11 December 2015. Subcommittee meeting. One SR[3] on SSRIs found; 40 other publications excluded. Keep venlafaxine and nortriptyline as is in TOP (1st Edition); update evidence source in SSRIs recommendation.	Office-Based Pharmacy Subcommittee (see details in *Table K.6*)	*7 March 2016*. GUC. Accepted by GUC as status quo for venlafaxine, nortriptyline, and SSRIs. Update evidence source for SSRIs: **SR (G4, IHE Database)**
Gabapentin **(Do – *Alberta CPG* 1st Edition)** G4 (UK)	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on gabapentin for migraine prophylaxis.	25 May 2015. GUC meeting. It should probably be a "Do Not Know" or a "Do Not Do", not a "Do".	GUC	*21 March 2016*. Accepted by GUC as "Do Not Do". **SR (IHE Database)**
		21 October 2015. One SR[4] found; 22 reviews excluded.	HTA research	
		14 June 2015. Suggested changes made by neurologist (co-chair) from "Do" to "Do Not Do".	Neurology	
		28 October 2015. Subcommittee meeting. Evidence has changed – no support for any dose. Agreed to accept proposed changes.	Office-Based Pharmacy Subcommittee (see details in *Table K.6*)	
		7 March 2016. GUC meeting. Agreed with the category change; the changes should be highlighted in the final guideline with a brief description of why the change was made.	GUC	
		13 March 2016. Email correspondence of Subcommittee co-chair. Proposed further revisions.	Neurology	

Intervention*	Parking lot item(s) and other miscellaneous requests by the GUC; SC actions	Subcommittee meetings		Final decision by Subcommittee and GUC; Evidence source
		Review/discussion/ deliberation[†‡]	Expertise of participants	
Butterbur (*Petasites hybridus*) **(Do – *Alberta CPG* 1st Edition)** G1 (USA)	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on butterbur for migraine prophylaxis.	25 May 2015. GUC meeting. There are issues around knowing which preparations are safe; other countries have banned butterbur.	GUC	*21 March 2016*. Accepted by GUC as "Do Not Do". **EO (GUC)**
		14 June 2015. Suggested changes made by Subcommittee co-chair.	Neurology	
		21 October 2015. No SRs found; 20 reviews excluded.	HTA research	
		7 March 2016. GUC meeting. While there is evidence that the molecule itself is effective, many preparations don't have the active ingredient and/or are hepatotoxic. There is one preparation (Petadolex) that is prepared correctly; subcommittee decided to change recommendation to a "Do Not Do" for all preparations and to not mention Petadolex as an exception. Agreed that it could be too confusing to have qualifiers in recommendation to say that some but not other preparations are safe. Majority voted to change recommendation category and evidence source.	GUC	
OnabotulinumtoxinA (chronic migraine) **(Do – *Alberta CPG* 1st Edition)** EO (GDG)	31 May 2016. SC meeting. Check if PREEMPT study is referenced as evidence source in the seed guidelines. 28 October 2016. Review wording with GUC.	25 May 2015. GUC. Revise wording and evidence source, include statement about episodic migraine[†].	GUC	*7 March 2016*. Accepted by GUC as "Do Not Know". *31 May 2016*. SC split the recommendation as follows: "Do Not Do" for episodic migraine **SR (G8)** "Do" for chronic migraine **EO (GDG, GUC) + RCT (G8, G10)**
		14 June 2015. Suggested changes made by Subcommittee co-chair.	Neurology	
		May 2016. SC meeting and email correspondence. Separate into two recommendations: prophylaxis of episodic migraine: "Do Not Do"; chronic migraine: "Do". Add information and dosages per the PREEMPT protocol.[5-7] (See glossary in *Appendix J, Table J.8* for definition of episodic migraine.)	Neurology Psychology, pain management HTA research (2 participants)	

Intervention*	Parking lot item(s) and other miscellaneous requests by the GUC; SC actions	Subcommittee meetings		Final decision by Subcommittee and GUC; Evidence source
		Review/discussion/ deliberation†‡	Expertise of participants	
Verapamil **(Do Not Know – *Alberta CPG* 1st Edition)** EO (GDG) (also nominated by stakeholders)	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on verapamil for migraine prophylaxis.	28 October 2015. Subcommittee meeting. No SR found; *Alberta CPG* recommendation is consistent with new seed guidelines G1c and G8. Status quo; update evidence source.	Office-Based Pharmacy Subcommittee (see details in *Table K.6*)	*7 March 2016*. Accepted by GUC as status quo. **RCT (G1c, G8) + EO (GDG)**
Melatonin for migraine **New recommendation**	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on melatonin for migraine prophylaxis.	28 October 2015. Subcommittee meeting. No SR found; 7 reviews excluded. Melatonin is an area of interest/research; include as a "Do Not Know".	Office-Based Pharmacy Subcommittee (see details in *Table K.6*)	*7 March 2016*. Accepted by GUC as "Do Not Know". **EO (GUC)**
Non-pharmacological therapy				
Homeopathic therapy **(Do Not Do – *Alberta CPG* 1st Edition)** G2 (Europe) (also nominated by stakeholders)	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on homeopathic therapy for migraine prophylaxis.	21 October 2015. No SR found; 16 reviews excluded. 28 October 2015. Subcommittee meeting. SRs are inconclusive. Status quo.	HTA research Office-Based Pharmacy Subcommittee (see details in *Table K.6*)	*7 March 2016*. Accepted by GUC as status quo. **RCT (G2)**
Hyperbaric oxygen for acute treatment and prophylaxis **(Do Not Know – *Alberta CPG* 1st Edition)** RCT (G1) + SR (IHE Database)	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on hyperbaric oxygen.	14 October 2015. Subcommittee meeting. No SR found, only quasi-SRs. Status quo. Change insufficient to inconclusive for consistency with recommendation wording protocol.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. Accepted by GUC as status quo. **RCT (G1b) + SR (IHE Database)**
Normobaric oxygen for acute treatment **(Do Not Know – *Alberta CPG* 1st Edition)** EO (GDG)	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on normobaric oxygen.	14 October 2015. Subcommittee meeting. No SR found, only quasi-SRs. Status quo.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. Accepted by GUC as status quo. **EO (GDG)**

Intervention*	Parking lot item(s) and other miscellaneous requests by the GUC; SC actions	Subcommittee meetings		Final decision by Subcommittee and GUC; Evidence source
		Review/discussion/ deliberation[†‡]	Expertise of participants	
Spinal manipulation **(Do Not Know – *Alberta CPG* 1st Edition)** SR (G4, IHE Database) (also nominated by stakeholders)	25 May 2015. GUC face-to-face meeting. G9 has discordant recommendation based on two old RCTs. Review RCTs referenced in G9.[8,9]	8 August 2015: Email correspondence of Subcommittee co-chair. What else is in the two SRs that we used to generate the TOP recommendation?	Pain management and psychology HTA research	*21 March 2016*. Accepted by GUC as status quo. **SR (G4, G10, G11, IHE Database)**
		14 October 2015. Subcommittee meeting. Both RCTs were included in the two SRs cited by *Alberta CPG*. No changes to TOP recommendation. Change insufficient to inconclusive for consistency with recommendation wording protocol.	Rehabilitation Subcommittee (see details in *Table K.6*)	
Transcutaneous electrical nerve stimulation (TENS) **(Do Not Know – *Alberta CPG* 1st Edition)** SR (G4)	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on TENS.	14 October 2015. Subcommittee meeting. No SR found. Status quo. Change insufficient to inconclusive for consistency with recommendation wording protocol.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. Accepted by GUC as status quo. **SR (G4)**
Hypnotherapy **(Do Not Know – *Alberta CPG* 1st Edition)** RCT (G1)	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on hypnotherapy.	14 October 2015. Subcommittee meeting. No SR found. Status quo.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. Accepted by GUC as status quo. **RCT (G1)**
Acrylic splints **(Do Not Know – *Alberta CPG* 1st Edition)** EO (G4)	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on acrylic splints.	14 October 2015. Subcommittee meeting. No SR found, only NRs. Status quo; add intra-oral to clarify splint type.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. Accepted by GUC as status quo. **EO (G4)**
Massage **(Do Not Know – *Alberta CPG* 1st Edition)** RCT (G4) (also nominated by stakeholders)	25 May 2015. GUC face-to-face meeting. Review RCT cited in G9.[10]	14 October 2015. Subcommittee meeting. RCT reviewed. Status quo.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. Accepted by GUC as status quo. **RCT (G4)**

Intervention*	Parking lot item(s) and other miscellaneous requests by the GUC; SC actions	Subcommittee meetings		Final decision by Subcommittee and GUC; Evidence source
		Review/discussion/ deliberation[†‡]	Expertise of participants	
Transcranial magnetic stimulation **New recommendation**	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on transcranial magnetic stimulation.	14 October 2015. Subcommittee meeting. No SR found. Add as a "Do Not Know" recommendation; specify single-pulse and repetitive types.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. GUC. Accepted by GUC as "Do Not Know". **EO (GUC)**
Transcutaneous supraorbital nerve stimulation **New recommendation**	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on transcutaneous supraorbital nerve stimulation.	14 October 2015. Subcommittee meeting. No SR found. Add as a "Do Not Know" recommendation.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. GUC. Accepted by GUC as "Do Not Know". **EO (GUC)**
Invasive therapies				
Electrical peripheral nerve stimulation therapy **New recommendation** (nominated by stakeholders)	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on electrical peripheral nerve stimulation for migraine.	30 September 2015. One poor quality SR[11] found; 60 reviews excluded. 7 October 2015. Subcommittee meeting. Add to *Alberta CPG* as a background statement.	Interventional Therapies Subcommittee (see details in *Table K.6*)	*7 March 2016*. Accepted by GUC as a background statement.
Nerve surgery for migraine prophylaxis **New recommendation** (nominated by stakeholders)	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on nerve surgery for migraine prophylaxis.	30 September 2015. No SR was found; 16 reviews excluded. 7 October 2015. Subcommittee meeting. The intervention is not included in the seed guidelines, but is popular in the United States; however, the publications are widely criticized due to strong placebo effect. Include general background statement on decompression surgery of peripheral nerves in the face and scalp.	Interventional Therapies Subcommittee (see details in *Table K.6*)	*7 March 2016*. Accepted by GUC as a background statement.
		7 October 2015. Wordsmithing by Subcommittee co-chair. Reviewed by Subcommittee via email correspondence.	Neurology Interventional Therapies Subcommittee (see details in *Table K.6*)	

Intervention*	Parking lot item(s) and other miscellaneous requests by the GUC; SC actions	Subcommittee meetings		Final decision by Subcommittee and GUC; Evidence source
		Review/discussion/ deliberation†‡	Expertise of participants	
Occipital nerve blocks for migraine **New recommendation** (nominated by stakeholders)	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on greater occipital and supraorbital nerve blockade for acute treatment and prophylaxis of migraine.	30 September 2015. No SR was found; 14 reviews excluded. 7 October 2015. Subcommittee meeting. The intervention is used by specialists and some rural primary care physicians. Add to *Alberta CPG* as a "Do Not Know" recommendation for treatment (acute).	Interventional Therapies Subcommittee (see details in *Table K.6*)	*21 March 2016*. Accepted by GUC as "Do Not Know". **EO (GUC)**
		7 October 2015. Email correspondence. Refined wording.	Neurology Family medicine	
		7 March 2016. GUC meeting. Remove specialist sentence and prophylaxis part; keep only on acute. Do not include reference to instructional video as the recommendation is a "Do Not Know".	GUC	
		7 March 2016. Suggested changes made by Subcommittee co-chair.	Neurology	
Menstrual migraine – prophylactic treatment				
Hormone treatment - estradiol **New recommendation**	28 October 2015. Subcommittee meeting. Supplementary search for SRs on effectiveness and clinical dosages of transdermal estradiol for menstrual migraine, and estrogen therapy for the treatment of migraine and menstrual migraine prophylaxis.	11 December 2015. Subcommittee meeting. No SR found; 9 reviews excluded. Include in the background statement estradiol.	Office-Based Pharmacy Subcommittee (see details in *Table K.6*)	*7 March 2016*. Accepted by GUC as a background statement.
		2 January 2016 to 12 January. Email correspondence of Subcommittee co-chair. Wordsmithing of recommendation.	Neurology HTA research	
		11 February 2016 to 22 February 2016. Email correspondence of Subcommittee members. Reviewed/accepted wording refinements.	Office-Based Pharmacy Subcommittee (see details in *Table K.6*)	

Intervention*	Parking lot item(s) and other miscellaneous requests by the GUC; SC actions	Subcommittee meetings		Final decision by Subcommittee and GUC; Evidence source
		Review/discussion/ deliberation†‡	Expertise of participants	
Hormone treatment - continuous use of oral contraceptives **New recommendation**	25 May 2015. GUC face-to-face meeting. Questioned whether to add new statement from G7 on continuous use of oral contraceptives for prophylaxis of menstrual migraine.	28 October 2015. Subcommittee meeting. No SR found; 16 reviews excluded. Keep G7 recommendation as "Do".	Office-Based Pharmacy Subcommittee (see details in *Table K.6*)	*7 March 2016*. Accepted by GUC as "Do". **EO (G7, GUC)**
	14 June 2015. Email correspondence of Subcommittee co-chair. Supplementary search for SRs on efficacy and safety of continuous use of oral combined contraceptives for preventing menstrual migraine.	11 December 2015. Subcommittee meeting. Further wording refinements.		
Migraine treatment in pregnancy				
Angiotensin-converting enzyme (ACE) inhibitors during pregnancy **Additional information**	14 July 2016. SC meeting. Review information from Health Canada monographs, Society of Obstetricians and Gynaecologists of Canada, and others about ACE inhibitors and angiotensin receptor blockers (ARB) used during pregnancy.	14 July to 15 July 2016. Email correspondence of SC to review summary table prepared by Research Team. ACE inhibitors and ARB (i.e., candesartan, lisinopril) should be avoided during pregnancy or if planning pregnancy. Add this to candesartan and lisinopril recommendations for episodic migraine prophylaxis and the medication table. (See glossary in *Appendix J, Table J.8* for definition of episodic migraine.)	Neurology Psychology, pain management HTA research (2 participants)	*August 2016*. Additional information accepted by GUC.
Sumatriptan **(Do not know – *Alberta CPG* 1st Edition)** G2 (Europe) G4 (UK)	28 October 2015. Subcommittee meeting. Supplementary search for SRs on sumatriptan for migraine during pregnancy.	25 May 2015. GUC meeting. Use G7 (Canada) which cites Norwegian study[12] published in 2010. Change from a "Do Not Know" to a "Do". Change wording about risks to mirror G7: "The risks…appear to be minimal…".	GUC	*7 March 2016*. Accepted by GUC as "Do". **EO (G2, G4, G7)**
		6 June 2015. Suggested changes made by neurologist (co-chair).	Neurology HTA research	

Intervention*	Parking lot item(s) and other miscellaneous requests by the GUC; SC actions	Subcommittee meetings		Final decision by Subcommittee and GUC; Evidence source
		Review/discussion/ deliberation†‡	Expertise of participants	
		28 October 2015. Subcommittee meeting. No SR found; 28 reviews excluded. Agreed to accept the wordsmith and change from "Do Not Know" to "Do" recommendation.	Office-Based Pharmacy Subcommittee (see details in *Table K.6*)	
Antiemetics - dimenhydrinate **New recommendation** (suggested by SC)	1 June 2015. SC member suggested review and addition of dimenhydrinate to the *Alberta CPG* as it is commonly used.	11 January 2016 to 18 January 2016. Email correspondence between the co-chairs of the Subcommittee. Reviewed summary of searches results prepared by pharmacist. Adverse events have not been observed in animal studies. The risk of fetal abnormalities was not increased following maternal use of dimenhydrinate during any trimester of pregnancy. Dimenhydrinate may have an oxytocic effect if used during labor. There is no good evidence for dimenhydranate efficacy in migraine-related nausea.	Pharmacy Neurology HTA research	*7 March 2016*. Accepted by GUC as "Do Not Know". **EO (G7)**
Magnesium **New recommendation**	28 October 2015. Subcommittee meeting. Supplementary search for SRs on magnesium for migraine prophylaxis during pregnancy.	11 December 2015. Subcommittee meeting. Originally considered safe, but now more published on risks of high dose IV; the US FDA issued warning and changed to category D in May 2015. No SRs found; 31 excluded reviews. Include in the background statement.	Office-Based Pharmacy Subcommittee (see details in *Table K.6*)	*7 March 2016*. GUC. Do not add to *Alberta CPG*.
		2 January 2016. Email correspondence of Subcommittee co-chair. Since we recommend specialist advice if prophylaxis is considered during pregnancy, do not add in the *Alberta CPG*.	Neurology HTA research	
		11 January 2016 to 18 January 2016. Email correspondence of Subcommittee. Proposed change approved; do not add in the *Alberta CPG*.	Office-Based Pharmacy Subcommittee (see details in *Table K.6*)	

Intervention*	Parking lot item(s) and other miscellaneous requests by the GUC; SC actions	Subcommittee meetings		Final decision by Subcommittee and GUC; Evidence source
		Review/discussion/ deliberation[†‡]	Expertise of participants	
Parenteral treatment of refractory migraine (See glossary in *Appendix J, Table J.8* for definition of refractory migraine)				
Ketorolac IV **New recommendation** (proposed by Subcommittee)	27 August 2015. Email correspondence of Subcommittee chair & 2 September 2015. Subcommittee meeting. Supplementary search for SRs on IV doses for ketorolac since IV ketorolac 30 mg is used in the emergency department.	6 September to 16 September 2015. Email correspondence of Subcommittee. Recommendation drafted by Subcommittee chair. Checked with pharmacist that the 120 mg in 24 hours dose applies to both IM and IV administration. February 2016. Email correspondence of Subcommittee. Two SRs[13,14] with dosing information reviewed. Wording accepted by Subcommittee.	Parenteral Therapies Subcommittee (see details in *Table K.6*)	*7 March 2016*. Accepted by GUC as "Do". Added interval between doses. **RCT (G10) + SR (IHE Database) + EO (GUC)**
Prochlorperazine IV **(Listed in *Alberta CPG* 1st Edition medication table)** **New recommendation**	2 September 2015. Subcommittee meeting. Supplementary search for SRs on whether extrapyramidal side effects are more common with prochlorperazine.	6 September 2015. Email correspondence of Subcommittee co-chair. Recommendation drafted. February 2016. Email correspondence of Subcommittee. No SRs found on extrapyramidal side effects. Wording accepted by Subcommittee with addition of information on combining diphenhydramine and prochlorperazine.	Neurology Parenteral Therapies Subcommittee (see details in *Table K.6*)	*7 March 2016*. Accepted by GUC as "Do". Add maximum daily dose of 40 mg and move up in the recommendation list order. **RCT (G1d, G10) + EO (GUC)**
Diphenhydramine IV **New recommendation**	2 September 2015. Subcommittee meeting. Supplementary search for SRs on diphenhydramine with metoclopramide or any other drug administered in the emergency department for any headache type.	6 September 2015. Email correspondence of Subcommittee co-chair. Recommendation drafted. February 2016. Email correspondence of Subcommittee. One SR[15] reviewed that mentioned combining diphenhydramine with metoclopramide. Current wording accepted by Subcommittee with addition of dosing information.	Neurology Parenteral Therapies Subcommittee (see details in *Table K.6*)	*7 March 2016*. Accepted by GUC as "Do". **EO (G11, GUC)**
Ibuprofen IV **New recommendation** (suggested by Subcommittee chair)	27 August 2015. Email correspondence of Subcommittee co-chair. Supplementary search for SRs on IV ibuprofen since it is now available in Canada.	2 September 2015. Subcommittee meeting. No SR found. Do not add to *Alberta CPG*.	Parenteral Therapies Subcommittee (see details in *Table K.6*)	*7 March 2016*. GUC. Do not add to *Alberta CPG*.

Intervention*	Parking lot item(s) and other miscellaneous requests by the GUC; SC actions	Subcommittee meetings		Final decision by Subcommittee and GUC; Evidence source
		Review/discussion/ deliberation[†‡]	Expertise of participants	
Magnesium sulfate IV **New recommendation**	27 August 2015. Email correspondence of Subcommittee co-chair. Retrieve RCTs[16,17] cited by G1d and G11.	2 September 2015. Subcommittee meeting. Do not add to *Alberta CPG*.	Parenteral Therapies Subcommittee (see details in *Table K.6*)	*7 March 2016*. GUC. Do not add to *Alberta CPG*.
Steroids IV **New recommendation**	27 August 2015. Email correspondence of Subcommittee co-chair. Retrieve SRs[18,19] cited in G10 to clarify if they are about preventing headache recurrence or actually treating the headache (treatment may only be useful for preventing recurrence after initial treatment).	2 September 2015. Subcommittee meeting. Recommendation wording modified.	Parenteral Therapies Subcommittee (see details in *Table K.6*)	*7 March 2016*. GUC. Do not add to *Alberta CPG*.

ACE: angiotensin-converting enzyme; ARB: angiotensin receptor blocker; CPG: clinical practice guideline; EO: expert opinion; FDA: Food and Drug Administration; GDG: Guideline Development Group; GUC: Guideline Update Committee (see role and membership in *Appendix A* and *Appendix B*); HTA: health technology assessment; IM: intramuscular; IV: intravenous; NR: narrative review; NSAID: non-steroidal anti-inflammatory drug; RCT: randomized controlled trial; SC: Steering Committee; SNRI: serotonin-norepinephrine reuptake inhibitor; SR: systematic review; SSRI: selective serotonin reuptake inhibitor

Parking lot item – Any activity that involved review of individual studies referenced in the seed guideline(s), systematic reviews published between January 2008 and May 2015, or other requests that were required by the GUC before a final decision could be made.

*Interventions were sourced from the *Alberta CPG*, 1st Edition, new seed guideline(s), stakeholder requests, or systematic reviews (IHE Database). They are listed in the same order in which they are written in the *Alberta CPG*. Original recommendations from the seed guidelines are listed in *Appendix J*. References for the seed guidelines are available in *Appendix H*.

[†]Detailed information on the searches conducted and on data extraction from studies is available upon request.

[‡]The number of SRs may vary if there were multiple publications of the same study.

TABLE K.3: Management of tension-type headache

Intervention*	Parking lot item(s) and other miscellaneous requests by the GUC; SC actions	Subcommittee meetings		Final decision by Subcommittee and GUC; Evidence source
		Review/discussion/ deliberation†‡	Expertise of participants	
Cyclobenzaprine **New recommendation**	11 December 2015. Subcommittee meeting. Review one RCT[20] on cyclobenzaprine for TTH cited by G10.	2 January 2016 to 18 January 2016. Email correspondence of Subcommittee co-chair. The RCT was small and diagnostic criteria would not have been those in use today (International Headache Society). Add cyclobenzaprine as a background statement, not a recommendation.	Neurology HTA research	*7 March 2016*. GUC. Accepted background statement.
		11 February 2016 to 22 February 2016. Email correspondence of Subcommittee. Approved suggested action.	Office-Based Pharmacy Subcommittee (see details in *Table K.6*)	
Physical therapy and acupuncture **(Do – *Alberta CPG* 1st Edition)** SR (G6) (also nominated by stakeholders)	14 October 2015. Subcommittee meeting. Review SR cited by G9. Supplementary search for SRs on acupuncture and exercise for TTH.	18 November 2015. Subcommittee meeting. Reviewed SR cited by G9.[21] Reviewed two additional SRs.[22,23] Remove physical therapy from the *Alberta CPG* recommendation on physical therapy and acupuncture.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. Revision accepted by GUC. **SR (G6, G10)**
Spinal manipulation **New recommendation**	14 October 2015. Subcommittee meeting. Add as "Do Not Know" recommendation. Supplementary search for SRs on harms.	18 November 2015. Subcommittee meeting. Reviewed three SRs.[24-26] Do not add harms statement.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. Accepted by GUC as "Do Not Know". Add general statement about harms to background section. **SR (G9)**
Manual traction **New recommendation**	14 October 2015. Subcommittee meeting. Add as "Do Not Know" recommendation. Supplementary search for SRs on manual or machine traction for TTH. Check whether evidence cited by G9 only refers to manual traction.	18 November 2015. Subcommittee meeting. No SR found. Reviewed evidence from G9.[21,27-30] Add as "Do Not Know" recommendation for manual traction.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. Accepted by GUC as "Do Not Know". **SR (G9)**

Intervention*	Parking lot item(s) and other miscellaneous requests by the GUC; SC actions	Subcommittee meetings		Final decision by Subcommittee and GUC; Evidence source
		Review/discussion/ deliberation†‡	Expertise of participants	
Hypnotherapy **(Do Not Know – *Alberta CPG* 1st Edition)** EO (GDG)	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on hypnotherapy for TTH.	14 October 2015. Subcommittee meeting. No SR found. Status quo.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. Accepted by GUC as status quo. **EO (GUC)**
Massage **(Do Not Know – Alberta CPG 1st Edition)** SR (G4) (also nominated by stakeholders)	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on massage for TTH.	14 October 2015. Subcommittee meeting. Two SRs reviewed.[31,32] Status quo. Change insufficient to inconclusive for consistency with recommendation wording protocol.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. Accepted by GUC as status quo. **SR (G4, G10)**
Transcutaneous electrical nerve stimulation (TENS) **(Do Not Know – *Alberta CPG* 1st Edition)** SR (G4)	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on TENS.	14 October 2015. Subcommittee meeting. No SR found. Status quo. Change insufficient to inconclusive for consistency with recommendation wording protocol.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. Accepted by GUC as status quo. **SR (G4)**
Trigger point injections/dry needling **New recommendation**	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on trigger point injections/dry needling for TTH.	14 October 2015. Subcommittee meeting. Two SRs reviewed.[33,34] Add as a "Do Not Know" recommendation for TTH.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. GUC. Accepted by GUC as "Do Not Know" for TTH, **SR (IHE Database)**
Clomipramine **New recommendation**	11 December 2015. Subcommittee meeting. Review two RCTs[35,36] on clomipramine for TTH cited by G10. Discuss via email communication.	18 January 2016 to 22 February 2016. Email correspondence of Subcommittee. Only one RCT[35] focuses on clomipramine. Given the shortcomings in the analysis and reporting, it was suggested to omit clomipramine from the *Alberta CPG*.	Office-Based Pharmacy Subcommittee (see details in *Table K.6*)	*7 March 2016*. GUC. Do not add to *Alberta CPG*.

Intervention*	Parking lot item(s) and other miscellaneous requests by the GUC; SC actions	Subcommittee meetings		Final decision by Subcommittee and GUC; Evidence source
		Review/discussion/ deliberation†‡	Expertise of participants	
Ketoprofen **New recommendation**	11 December 2015. Subcommittee meeting. Ketoprofen is available in Canada but is not widely used by patients with TTH. 20 January 2016. Email correspondence of Subcommittee co-chair. Review two RCTs[37,38] cited by G10. Check availability of ketoprofen 25 mg immediate release tablets.	10 February 2016 to 25 February 2016. Email correspondence of Subcommittee co-chair. The 25 mg dose seems to be effective and could be added in the *Alberta CPG*. However, ketoprofen is only available in Canada in enteric-coated or slow-release forms, which make it unsuitable for the acute treatment of headache. Canada does not have the 25 mg immediate release tablet available; 50 mg tablet would increase side effects, and the guideline already recommends three other NSAIDs for TTH. Do not include in the *Alberta CPG*.	Neurology Pharmacy HTA research	*7 March 2016*. GUC. Do not add to *Alberta CPG*.
L-5-hydroxytryptophan **New recommendation**	11 December 2015. Subcommittee meeting. Review one RCT from G10 (Italy).	20 January 2016. Email correspondence of Subcommittee co-chair. The RCT[39] showed no significant change in headache days or headache intensity.	Neurology HTA research	*7 March 2016*. GUC. Do not add to *Alberta CPG*.
		11 February 2016 to 22 February 2016. Email correspondence of Subcommittee members: do not add to *Alberta CPG*.	Office-Based Pharmacy Subcommittee (see details in *Table K.6*)	
Tiger balm **New recommendation**	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on tiger balm for TTH. Review one RCT from G10 (Italy).	11 December 2015. Subcommittee meeting. No SR found. The RCT[40] published in 1996, was funded by Tiger Medicals Ltd. There are different formulations and types across countries, but no details were provided in the study. Do not add to *Alberta CPG*.	Office-Based Pharmacy Subcommittee (see details in *Table K.6*)	*7 March 2016*. GUC. Do not add to *Alberta CPG*.
Metoclopramide IV **New recommendation**	27 August 2015. Subcommittee meeting. Review one RCT[41] from G10 (Italy) to see if they are misdiagnosing the headache type.	6 to 22 September 2015. Email correspondence of Subcommittee. Evidence is not strong enough for a recommendation. Do not add to *Alberta CPG*.	Parenteral Therapies Subcommittee (see details in *Table K.6*)	*7 March 2016*. GUC. Do not add to *Alberta CPG*.

Intervention*	Parking lot item(s) and other miscellaneous requests by the GUC; SC actions	Subcommittee meetings		Final decision by Subcommittee and GUC; Evidence source
		Review/discussion/ deliberation[†‡]	Expertise of participants	
Chlorpromazine IV **New recommendation**	27 August 2015. Subcommittee meeting. Don't usually see TTH in the emergence department. Suggested not to include in *Alberta CPG*.	2 September 2015. Subcommittee meeting. Retrieve RCT cited by G10.[42] 7 September 2015. Email correspondence of Subcommittee. RCT not well reported and patient group probably not representative of the patients seen in Alberta emergency departments. Do not add to *Alberta CPG*.	Parenteral Therapies Subcommittee (see details in *Table K.6*)	*7 March 2016*. GUC. Do not add to *Alberta CPG*.

CPG: clinical practice guideline; EO: expert opinion; GDG: Guideline Development Group; GUC: Guideline Update Committee (see role and membership in *Appendix A* and *Appendix B*); HTA: health technology assessment; IV: intravenous; RCT: randomized controlled trial; SC: Steering Committee; SR: systematic review; TENS: transcutaneous electrical nerve stimulation; TTH: tension-type headache

Parking lot item – Any activity that involved review of individual studies referenced in the seed guideline(s), systematic reviews published between January 2008 and May 2015, or other requests that were required by the GUC before a final decision could be made.

*Interventions were sourced from the *Alberta CPG*, 1st Edition, new seed guideline(s), stakeholder requests, or systematic reviews (IHE Database). They are listed in the same order in which they are written in the *Alberta CPG*. Original recommendations from the seed guidelines are listed in *Appendix J*. References for the seed guidelines are available in *Appendix H*.

[†]Detailed information on the searches conducted and on data extraction from studies is available upon request.

[‡]The number of SRs may vary if there were multiple publications of the same study.

TABLE K.4: Management of cluster and cervicogenic headache

Intervention*	Parking lot item(s) and other miscellaneous requests by the GUC; SC actions	Subcommittee meetings		Final decision by Subcommittee and GUC; Evidence source
		Review/discussion/ deliberation[†‡]	Expertise of participants	
Transitional therapy for cluster headache				
Occipital nerve blockade **New recommendation**	7 October 2015. Subcommittee meeting. Supplementary search for SRs on occipital nerve blocks for prophylaxis of cluster headache.	7 October 2015. Subcommittee meeting. Need to emphasize that occipital nerve block is a bridging treatment, not a standalone treatment; include G11 recommendation as a "Do", remove mention of acute treatment. Email correspondence of Subcommittee co-chair: wordsmithing of recommendation.	Interventional Therapies Subcommittee (see details in *Table K.6*)	*21 March 2016*. Accepted by GUC as "Do". **RCT (G11) + EO (GUC)**
		19 December 2015. No SR was found; 33 reviews excluded.	Neurology HTA research	
		7 March 2016. GUC meeting. Asked for further wording refinements which were implemented by Subcommittee co-chair.	Neurology	
Cervicogenic headache				
Exercise **(Do – *Alberta CPG* 1st Edition)** EO (GDG) (also nominated by stakeholders)	25 May 2015. GUC face-to-face meeting. Review evidence cited by G9.	14 October 2015. Subcommittee meeting. Reviewed evidence cited by G9.[43,44] *Exercise*: Status quo. Change insufficient to inconclusive for consistency with recommendation wording protocol. *Deep neck flexor training*: Add as a "Do" recommendation for deep neck flexor training to avoid confusion with exercise recommendation; check RCT[44] for detail on treatment frequency.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. *Exercise*: Remove second sentence from recommendation. Accepted by GUC as status quo. **SR (IHE Database)** *Deep neck flexor training*: Accepted by GUC as "Do". **RCT (G9)**

Intervention*	Parking lot item(s) and other miscellaneous requests by the GUC; SC actions	Subcommittee meetings		Final decision by Subcommittee and GUC; Evidence source
		Review/discussion/ deliberation[†‡]	Expertise of participants	
Spinal manipulation and mobilization **(Do – *Alberta CPG* 1st Edition)** SR (G4, IHE Database) **Additional information** (also nominated by stakeholders)	25 May 2015. GUC face-to-face meeting. Review evidence cited by G9 for information about long-term use (frequency, intensity) and harms.	14 October 2015. Subcommittee meeting. Reviewed evidence cited by G9.[43] Status quo.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. Accepted by GUC as status quo. **SR (G4, G9, IHE Database)**

EO: expert opinion; GDG: Guideline Development Group; GUC: Guideline Update Committee (see role and membership in *Appendix A* and *Appendix B*); HTA: health technology assessment; RCT: randomized controlled trial; SC: Steering Committee; SR: systematic review

Parking lot item – Any activity that involved review of individual studies referenced in the seed guideline(s), systematic reviews published between January 2008 and May 2015, or other requests that were required by the GUC before a final decision could be made.

*Interventions were sourced from the *Alberta CPG*, 1st Edition, new seed guideline(s), stakeholder requests, or systematic reviews (IHE Database). They are listed in the same order in which they are written in the *Alberta CPG*. Original recommendations from the seed guidelines are listed in *Appendix J*. References for the seed guidelines are available in *Appendix H*.

†Detailed information on the searches conducted and on data extraction from studies is available upon request.

‡The number of SRs may vary if there were multiple publications of the same study.

TABLE K.5: Other parking lot items

Intervention*	Parking lot item(s) and other miscellaneous requests by the GUC; SC actions	Subcommittee meetings		Final decision by Subcommittee and GUC; Evidence source
		Review/discussion/ deliberation†‡	Expertise of participants	
Self-management **New recommendation**	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on components of what might constitute 'self-management'.	18 November 2015. Subcommittee meeting. Reviewed two SRs.[45,46] Add Kindelan-Calvo et al. (2014)[46] SR as an evidence source for last paragraph of Appendix E in *Alberta CPG*. Put in preamble that some apps are useful but may need to be cautious about their quality. This is an active area of interest but there is no information on whether they improve patient outcomes.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. GUC. Accepted background statement.
Lifestyle factors **New recommendation**	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on lifestyle factors that have an effect on headache severity.	18 November 2015. Subcommittee meeting. Reviewed one SR.[47] Add screening for sleep apnea to the Lifestyle and Migraine Trigger Management Background Statement on page 14 of the *Alberta CPG*. 24 February 2016. Email correspondence of Subcommittee co-chair: wordsmithing of statement.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. GUC. Accepted background statement with minor wording revision.
Massage **New recommendation**	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on massage for the following headache types: migraine, tension-type, cervicogenic, medication overuse, cluster headache, and hemicrania continua.	18 November 2015. Subcommittee meeting. Reviewed one SR.[48] Add as a "Do Not Know" recommendation for migraine, TTH, and cervicogenic headache.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. GUC. Accepted by GUC as "Do Not Know" for migraine, TTH, and cervicogenic headache. **SR (IHE Database)** (migraine) **EO (GUC)** (TTH and cervicogenic headaches)
Cranial-sacral therapy **New recommendation**	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on cranial-sacral therapy for the following headache types: cervicogenic, medication overuse, cluster headache, and hemicrania continua.	18 November 2015. Subcommittee meeting. Reviewed one SR.[32] Add as a "Do Not Know" recommendation for cervicogenic headache.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. GUC. Accepted by GUC as "Do Not Know" for cervicogenic headache. **EO (GUC)**

Intervention*	Parking lot item(s) and other miscellaneous requests by the GUC; SC actions	Subcommittee meetings		Final decision by Subcommittee and GUC; Evidence source
		Review/discussion/ deliberation†‡	Expertise of participants	
Low-level laser therapy **New recommendation**	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on laser therapy for the following headache types: migraine, tension-type, cervicogenic, medication overuse, cluster, hemicrania continua.	14 October 2015. Subcommittee meeting. No SR found. Add as a "Do Not Know" recommendation. 18 November 2015. Subcommittee meeting. Add migraine, TTH, and cervicogenic as indications.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. GUC. Accepted by GUC as "Do Not Know" for migraine, TTH, and cervicogenic headache. **EO (GUC)**
National Upper Cervical Chiropractic Association (NUCCA) procedure **New recommendation**	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on the NUCCA procedure for the following headache types: migraine, tension-type, cervicogenic, medication overuse, cluster, and hemicrania continua.	14 October 2015. Subcommittee meeting. No SR found. Add as a "Do Not Know" recommendation for migraine, TTH, and cervicogenic headache.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. GUC. Accepted by GUC as "Do Not Know" for migraine, TTH, and cervicogenic headache. **EO (GUC)**
Trigger point injections/dry needling **New recommendation**	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on trigger point injections/dry needling for the following headache types: migraine, cervicogenic, medication overuse, cluster, and hemicrania continua.	14 October 2015. Subcommittee meeting. No SR found. Add as a "Do Not Know" recommendation for cervicogenic headache.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. GUC. Accepted by GUC as "Do Not Know" for cervicogenic headache. **EO (GUC)**
Acceptance and commitment therapy **New recommendation**	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on acceptance and commitment therapy for the following headache types: migraine, tension-type, cervicogenic, medication overuse, cluster, and hemicrania continua.	18 November 2015. Subcommittee meeting. No SR found. Do not add to *Alberta CPG*.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. GUC. Do not add to *Alberta CPG* for these indications.
Acupuncture **New recommendation**	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on acupuncture for the following headache types: cervicogenic, medication overuse, cluster headache, and hemicrania continua.	18 November 2015. Subcommittee meeting. No SR found. Do not add to *Alberta CPG*.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. GUC. Do not add to *Alberta CPG* for these indications.
Manipulation **New recommendation**	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on manipulation for the following headache types: medication overuse, cluster, and hemicrania continua.	18 November 2015. Subcommittee meeting. No SR found. Do not add to *Alberta CPG*.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. GUC. Do not add to *Alberta CPG* for these indications.

Intervention*	Parking lot item(s) and other miscellaneous requests by the GUC; SC actions	Subcommittee meetings		Final decision by Subcommittee and GUC; Evidence source
		Review/discussion/ deliberation[†‡]	Expertise of participants	
Running, walking, cardio exercises **New recommendation**	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on aerobic exercise for the following headache types: migraine, tension-type, cervicogenic, medication overuse, cluster, and hemicrania continua.	18 November 2015. Subcommittee meeting. Reviewed one SR.[49] Do not add to *Alberta CPG*.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. GUC. Do not add to *Alberta CPG* for these indications.
Mobilization **New recommendation**	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on mobilization for the following headache types: migraine, medication overuse, cluster headache, and hemicrania continua.	18 November 2015. Subcommittee meeting. No SR found. Do not add to *Alberta CPG*.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. GUC. Do not add to *Alberta CPG* for these indications.
Reiki therapy **New recommendation**	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on mobilization for the following headache types: migraine, tension-type, cervicogenic, medication overuse, cluster, hemicrania continua.	18 November 2015. Subcommittee meeting. No SR found. Do not add to *Alberta CPG*.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. GUC. Do not add to *Alberta CPG*.
Relaxation techniques **New recommendation**	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on mobilization for the following headache types: cervicogenic, cluster, or hemicrania continua.	18 November 2015. Subcommittee meeting. No SR found. Do not add to *Alberta CPG*.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. GUC. Do not add to *Alberta CPG* for these indications.
Transcutaneous electrical nerve stimulation (TENS) **New recommendation**	25 May 2015. GUC face-to-face meeting. Supplementary search for SRs on TENS for the following headache types: cervicogenic, medication overuse, cluster, and hemicrania continua.	18 November 2015. Subcommittee meeting. No SR found. Do not add to *Alberta CPG*.	Rehabilitation Subcommittee (see details in *Table K.6*)	*21 March 2016*. GUC. Do not add to *Alberta CPG* for these indications.

CPG: clinical practice guideline; EO: expert opinion; GUC: Guideline Update Committee (see role and membership in *Appendix A* and *Appendix B*); NUCCA: National Upper Cervical Chiropractic Association; SC: Steering Committee; SR: systematic review; TENS: transcutaneous electrical nerve stimulation; TTH: tension-type headache

Parking lot item – Any activity that involved review of individual studies referenced in the seed guideline(s), systematic reviews published between January 2008 and May 2015, or other requests that were required by the GUC before a final decision could be made.

*Interventions were sourced from the *Alberta CPG*, 1st Edition, new seed guideline(s), stakeholder requests, or systematic reviews (IHE Database). They are listed in the same order in which they are written in the *Alberta CPG*. Original recommendations from the seed guidelines are listed in *Appendix J*. References for the seed guidelines are available in *Appendix H*.

[†]Detailed information on the searches conducted and on data extraction from studies is available upon request.

[‡]The number of SRs may vary if there were multiple publications of the same study.

TABLE K.6: Expertise of subcommittee participants

Rehabilitation Subcommittee (Group 1)	Interventional Therapies Subcommittee (Group 2)	Parenteral Therapies Subcommittee (Group 3)	Office-Based Pharmacy Subcommittee (Group 4)
• Family physician-chronic pain management (co-chair) • Pain management and psychology (co-chair) • Spine biomechanics, chiropractor • Physical therapy • Family physician • Occupational therapy • HTA research	• Radiology (co-chair) • Neurology (co-chair) • Family physician-chronic pain management • Family physician • HTA research	• Family physician (co-chair) • Neurology (co-chair) • Pharmacist • Family physician • HTA research	• Pharmacist (co-chair) • Neurology (co-chair) • Family physician-chronic pain management (n=3) • Family physician (n=2) • Registered nurse • HTA research

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APPENDIX L: List of New and Revised Recommendations

New or Revised Recommendation(s)	Nature of Revision	Final Category*
Headache Diagnosis and Investigation		
Diagnose chronic migraine with medication overuse	Revised wording	✓
Elderly patient with new headache	Revised wording	✓
Atypical headaches and changes in headache pattern	Updated evidence source[†]; revised wording	✓
Persistent headache attributed to head trauma	New recommendation	?
Management of Migraine Headache		
Lifestyle factors	Updated evidence source; revised wording	✓
Early treatment of migraine attacks	Updated evidence source	✓
Multimodal multidisciplinary care	New recommendation	✓
NSAIDs and acetaminophen	Updated evidence source; additional information	✓
Triptans	Updated evidence source; additional information	✓
Triptan and NSAID combinations	Updated evidence source	✓
Antiemetics	Updated evidence source	✓
Dihydroergotamine	Updated evidence source	✓
Opioids	Updated evidence source; additional information	x
Butalbital	Updated evidence source; additional information	x
Intranasal lidocaine	New recommendation	?
Migraine prophylaxis: Indications for migraine preventive medication	Updated evidence source; additional information	✓
Migraine prophylaxis: Prescribing a migraine preventive medication	Updated evidence source; additional information	✓
Migraine prophylaxis: Beta-blockers	Updated evidence source	✓
Migraine prophylaxis: Antidrepressants	Updated evidence source	✓
Migraine prophylaxis: Selective serotonin reuptake inhibitors	Reviewed evidence source[‡]	
Migraine prophylaxis: Antiepileptics	Updated evidence source	✓
Migraine prophylaxis (episodic): Gabapentin	Reviewed evidence source; category change from “Do” to “Do Not Do”	x
Migraine prophylaxis Riboflavin, magnesium citrate, co-enzyme Q10	Updated evidence source	✓
Migraine prophylaxis: Butterbur	Reviewed and updated evidence source; category change from “Do” to “Do Not Do”	x
Migraine prophylaxis: Candesartan	Updated evidence source; additional information	✓
Migraine prophylaxis: Lisinopril	New recommendation	✓
Migraine prophylaxis: Pizotifen	Updated evidence source	✓

New or Revised Recommendation(s)	Nature of Revision	Final Category*
Migraine prophylaxis: Flunarizine	Updated evidence source	✔
Migraine prophylaxis (episodic): OnabotulinumtoxinA	New recommendation	x
Migraine prophylaxis: NSAIDs	Revised wording	x
Migraine prophylaxis: Verapamil	Updated evidence source	?
Migraine prophylaxis: Melatonin	New recommendation	?
Migraine prophylaxis (chronic): OnabotulinumtoxinA	Updated evidence source	✔
Migraine prophylaxis (chronic): Topiramate	New section/recommendation	✔
Migraine prophylaxis (chronic): Amitriptyline	New section/recommendation	✔
Migraine prophylaxis (chronic): Gabapentin	New section/recommendation	?
Relaxation training, biofeedback, and cognitive behavioural therapy	Updated evidence source	✔
Acupuncture	Updated evidence source	✔
Hyperbaric oxygen	Reviewed and updated evidence source	✔
Normobaric oxygen	Reviewed evidence source	✔
Intra-oral acrylic splints	Reviewed evidence source	?
Spinal manipulation	Updated evidence source	?
Hypnotherapy; Transcutaneous electrical nerve stimulation	Reviewed evidence source	?
Single-pulse or repetitive transcranial magnetic stimulation; Transcutaneous supraorbital nerve stimulation; Cranial-sacral therapy; Low-level laser therapy; NUCCA procedure	New recommendations	?
Invasive therapies: Occipital nerve blocks for migraine	New section/recommendation	?
Menstrual migraine: Frovatriptan	Updated evidence source	✔
Menstrual migraine: Prophylactic treatment: continuous use of oral contraceptives	New recommendation	✔
Migraine treatment in pregnancy: Acute medications	Updated evidence source	✔/x
Migraine treatment in pregnancy: Sumatriptan§	Reviewed and updated evidence source; category change from “Do Not Know” to “Do”	✔
Migraine treatment in pregnancy: Metoclopramide	New recommendation	✔
Migraine treatment in pregnancy: Domperidone	New recommendation	x
Migraine treatment in pregnancy: Dimenhydrinate	New recommendation	?
Migraine treatment during lactation	New section/recommendations	✔/x
Parenteral treatment of refractory migraine: Hydration; Ketorolac IM, IV; Metoclopramide IV; Prochlorperazine IV; Chlorpromazine IV; Sumatriptan SC; Dihydroergotamine mesylate IV	New section/recommendations	✔
Parenteral treatment of refractory migraine: Steroids to prevent headache recurrence	New section/recommendation	✔
Parenteral treatment of refractory migraine: Steroids for acute treatment	New section/recommendation	x
Parenteral treatment of refractory migraine: Parenteral opioid analgesics	New section/recommendation	x

New or Revised Recommendation(s)	Nature of Revision	Final Category*
Management of Tension-Type Headache		
Acetaminophen; Combination analgesics	Updated evidence source	✓
Exercise	Reviewed evidence source	✓
Acupuncture	Updated evidence source	✓
Hypnotherapy; Transcutaneous electrical nerve stimulation	Reviewed evidence source	?
Massage	Reviewed and updated evidence source	?
Spinal manipulation; Manual traction; Trigger point injections or dry needling; Cranial-sacral therapy; Low-level laser therapy; NUCCA procedure	New recommendations	?
Tension-type headache treatment in pregnancy: acute medications	Updated evidence source	✓/x
Management of Cluster Headache		
Acute therapy	Updated evidence source	✓
Pharmacological prophylactic therapy: Verapamil; Lithium	Updated evidence source	✓
Transitional therapy: occipital nerve blockade	New section/recommendation	✓
Other Headache Disorders: Cervicogenic Headache		
Exercise	Revised wording	✓
Deep neck flexor training	New recommendation	✓
Cervical spinal manipulation	Updated evidence source	✓
Cervical spinal mobilization	Updated evidence source	✓
Massage, Cranial-sacral therapy; Low-level laser therapy; NUCCA procedure; Trigger point injections/dry needling	New recommendations	?

IM: intramuscular; IV: intravenous; NUCCA: National Upper Cervical Chiropractic Association; NSAID: non-steroidal anti-inflammatory drug; SC: subcutaneous

✓ "Do" category - indicates that the action should be undertaken

x "Do Not Do" category - indicates that the action should not be undertaken

? "Do Not Know" category - indicates that there was either insufficient evidence or a lack of conclusive evidence to make a definitive decision regarding the action

[†]Updated evidence source: recommendation supported by a new seed guideline or by an update of a previously cited seed guideline

[‡]Reviewed evidence source: the IHE Database was searched to identify recently published systematic reviews

[§]Sumatriptan is recommended for use in pregnancy only under specific circumstances.

APPENDIX M: Sample of the Additional Information Provided to the Guideline Update Committee and Subcommittees

AMBASSADOR PROGRAM – HEADACHE GUIDELINE 1ST UPDATE PARKING LOT ITEM

ACUPUNCTURE FOR TENSION-TYPE HEADACHE (TTH)

Rehabilitation Subcommittee (Group 1) October 14/15:

Question:
Consider adding a separate recommendation on acupuncture for TTH.

Actions:
Look for SRs on acupuncture for TTH.

Rehabilitation Subcommittee (Group 1):
Ted Findlay, Kate Gerry, Adrian Gretton, Greg Kawchuck, Alison McLean, Paul Taenzer

Section A

Information abstracted from the systematic reviews retrieved from a literature search conducted by the IHE librarians (Table A.1).

SECTION A

Systematic Reviews on Acupuncture for TTH Retrieved by the IHE Literature Search

Inclusion criteria

- *Intervention*: acupuncture.
- *Condition*: TTH (diagnostic criteria developed by the International Headache Society).
- *Target population*: patients who were 18 years of age or older. Reviews that refer to adult patients without providing a specific age range were also included.
- *Type of study*: systematic reviews. An article was deemed to be a systematic review if it met all of the following criteria as defined by Cook et al. (1997):[1]
    - focused clinical question;
    - explicit search strategy;
    - use of explicit, reproducible, and uniformly applied criteria for article selection;
    - critical appraisal of the included studies using a quality tool or checklist;
    - qualitative or quantitative data synthesis.
- *Publication limits*: reviews with a search end dates from January 2008 onwards (generally the median shelf life of a systematic review is 7 years).[2]
- *Language limits*: English.

Exclusion criteria

- Systematic reviews focused on children or adolescents, or patients with specific causes for headache such as head or neck trauma (except for cervicogenic headache), cranial or cervical vascular disorder, non-vascular intracranial disorder (e.g., neoplasm or idiopathic intracranial hypertension), use of a substance or its withdrawal (except for secondary medication overuse headache), temporomandibular joint disorder, infection, disorder of homeostasis, psychiatric disorder, or disorder or lesion of the cranium, neck, eyes, ears, nose, sinuses, teeth, mouth or other facial or cranial structures.
- Quasi-systematic reviews and narrative reviews. A review was considered to be quasi-systematic if it used a systematic search strategy to identify literature, but did not use a quality tool or checklist to critically appraise the included studies. Narrative reviews were evidence syntheses that reported neither a systematic search strategy nor a method of appraising the quality of the included studies.

Literature selection process

Articles were excluded that, on the basis of their abstract, clearly did not meet the inclusion criteria. Copies of the full text of potentially eligible studies were retrieved. In some cases, when the full text of the article was retrieved, closer examination revealed that it did not meet the inclusion criteria specified by the protocol. Consequently these papers were excluded (Appendix A.1).

When two or more systematic reviews had identical comparators and patient populations, only the most recently published review was included, unless it was less comprehensive than the earlier review.

For reference, when there were no systematic reviews available on the topic of interest, a summary of the conclusions from excluded quasi-systematic and narrative reviews was provided, when available.

Literature search strategy

The abstracts of English language articles of possible systematic reviews focused on TTH that were published from January 2008 (search end date of reviews) to May 2015 were reviewed. The search strategy is outlined in Appendix A.2 for your information.

References

1. Cook DJ, Mulrow CD, Haynes RB. Systematic reviews: Synthesis of best evidence for clinical decisions. *Annals of Internal Medicine* 1997;126:376-80.
2. Shojania KG, Sampson M, Ansari MT, Ji J, Doucette S, Moher D. How quickly do systematic reviews go out of date? A survival analysis. *Annals of Internal Medicine* 2007;147(4):224-33.

Table A.1: Summary of data from the systematic reviews on acupuncture for treatment of TTH

Review	Study Population	Comparison/Outcome/ Intervention Details	Relevant Results/Authors' Conclusions*
Linde et al. (2009)[1] Germany, Italy, United Kingdom, USA **Objective:** To investigate whether acupuncture is: a) more effective than no prophylactic treatment/routine care only; b) more effective than 'sham' (placebo) acupuncture; and c) as effective as other interventions in reducing headache frequency in patients with episodic or chronic TTH **Studies Reviewed:** 11 randomised controlled trials (RCTs) **Financial support:** The study received funding from: the National Institute of Arthritis and Musculoskeletal and Skin Diseases, USA; the National Center for Complementary and Alternative Medicine, USA; and the International Headache Society This review includes trials in which some of the reviewers were involved. These trials were reviewed by at least two other members of the review team. Two authors have received travel reimbursement and fees for speaking on research at meetings from acupuncture societies (British, German and Spanish Medical Acupuncture Societies; Society of Acupuncture Research). Two authors received an honorarium for preparing and delivering presentations on acupuncture research at the 2007 meeting of the Society for Acupuncture Research. One author is employed by the British Medical Acupuncture Society.	**Included Patients:** Total number: 2317 (median 62; range 10 to 1265) Condition: Chronic TTH (2 RCTs); episodic TTH (2 RCTs); both types of TTH or not stated (7 RCTs) (International Headache Society criteria [7 RCTs]) Age: Range mean 33 to 57 years (10 RCTs); median 38 years (1 RCT) Race: Not stated **Inclusion Criteria:** RCTs with a follow up of at least 8 weeks after randomization; adults with episodic and/or chronic tension-type headache; the treatments had to involve needle insertion at acupuncture points, pain points, or trigger points and had to be described as acupuncture **Exclusion Criteria:** Trials in which a clearly inappropriate method of randomization was used; studies including patients with headaches of various types unless separate results were presented for patients with tension-type; trials that only compared different forms of acupuncture; studies investigating other methods of stimulating acupuncture points without needle insertion (for example, laser stimulation or transcutaneous electrical stimulation); trials reporting only physiological or laboratory parameters or those with outcome measurement periods of less than 8 weeks (from randomization to final observation)	**Intervention:** Treatments involving needle insertion at acupuncture points, pain points, or trigger points that were described as acupuncture (range 4 to 15 sessions) **Comparisons:** Treatment of acute headaches only or routine care; sham acupuncture; other treatments **Outcomes Measured:** Proportion of responders, headache frequency, pain intensity, headache scores, analgesic use **Provider:** Acupuncturist (5 RCTs); physician (3 RCTs); physiotherapist (1 RCT); not stated (2 RCTs) **Setting:** Outpatient department (6 RCTs); primary care practice (4 RCTs); physiotherapy clinic (1 RCT)	Acupuncture versus routine care (2 RCTs with low risk of bias): Both found statistically significant and clinically relevant short-term (up to 3 months) benefits of acupuncture over control for: • Response: responder rate ratios were 11.36 (95% confidence interval [CI] 3.69 to 34.98; 45% responders in the acupuncture group and 4% in the control group) and 2.68 (95% CI 2.22 to 3.23; 47% versus 17%); • Number of headache days at 3 months was 6.4 and 3.4 days. Only one trial measured analgesic use and a headache score; there were significantly better results in the acupuncture group. Long-term effects (beyond 3 months) were not investigated. Acupuncture versus sham acupuncture (6 RCTs of good quality): Small but statistically significant benefits of acupuncture over sham (5 RCTs) were found for: • Pooled responder rate ratio 1.24 (95% CI 1.05 to 1.46; 50% responders in acupuncture groups and 41% in the sham groups) 3 to 4 months after randomization; • Weighted mean difference in headache days per 4 weeks was 1.92 days (95% CI 0.72 to 3.15). Regarding headache intensity, a significant difference was found only at 5 to 6 months after randomization Three trials reported data on frequency of analgesic use. There was a small, significant effect of acupuncture over sham controls (standardized mean differences [SMDs] 0.31 and 0.30, respectively) for frequency of analgesic use. Acupuncture versus physiotherapy, massage, or relaxation (4 RCTs): Three of the four had important methodological or reporting shortcomings. Their findings are difficult to interpret, but collectively suggest slightly better results for number of headache days in the control groups. **Safety:** Not reported. **Authors' Conclusion:** The authors concluded that acupuncture could be a valuable non-pharmacological tool in patients with frequent episodic or chronic tension-type headaches. However, point selection plays a less important role than acupuncturists have thought, and a relevant part of the clinical benefit might be due to powerful placebo effects or needling effects not dependent on the selection of traditional points.

Review	Study Population	Comparison/Outcome/ Intervention Details	Relevant Results/Authors' Conclusions*
Hao et al. (2013)[2] Australia **Objective:** To identify the factors that might contrite to the conflicting outcomes about the efficacy of acupuncture for TTH **Studies Reviewed:** 5 RCTs Note: 4 of the RCTs were included in Linde et al. (2009) but different subgroup analyses were performed **Financial support:** No competing financial interests exist	**Included Patients:** Total number: 838 (range 40 to 409) Condition: Tension-type headache (International Headache Society criteria or Ad Hoc committee's criteria) Age: Range mean 30 to 50 years Race: Not stated **Inclusion Criteria:** RCTs or quasi-RCTs of adults patients with TTH that employed invasive acupuncture needling and needled acupoints, Ashi point, and/or trigger/tender points **Exclusion Criteria:** Studies did not have a sham acupuncture control group; point injections were used; dry needling was employed; or results for patients with TTH were not reported separately from those with other types of headache	**Intervention:** Invasive acupuncture needling that needled acupoints, Ashi point, and/or trigger/tender points (range 8 to 15 sessions over 4 to 8 weeks) Manual acupuncture (4 RCTs); electroacupuncture (1 RCT) **Comparators:** Sham acupuncture **Outcomes Measured:** Headache days **Provider:** Acupuncturist (2 RCTs); physician (2 RCTs); not stated (1 RCT) **Setting:** Outpatient department (2 RCTs); university clinic (1 RCT); health centre (1 RCT); not stated (1 RCT)	All five RCTs were of high methodological quality. Acupuncture versus sham acupuncture (5 RCTs): No difference between groups with regard to headache days (SMD -0.31, 95% CI -0.72 to 0.09) after at least 3 months' follow-up. Electroacupuncture (1 RCT) versus manual acupuncture (4 RCTs): Electroacupuncture was more efficacious (SMD -1.60, 95% CI -2.33 to -0.88) than manual acupuncture (SMD -0.13, 95% CI –0.41 to 0.14) with respect to headache days. Needle retention: Needle retention with 30 minutes (4 RCTs; SMD -0.46, 95% CI -0.87 to -0.06) was better than no needle retention (1 RCT; SMD 0.45, 95% CI –0.11 to 1.01) with respect to headache days. Treatment frequency: Treatment twice/week (4 RCTs; SMD -0.46, 95% CI -0.87 to -0.06) was better than treatment once/week (1 RCT; SMD 0.45, 95% CI –0.11 to 1.01) with respect to headache days. **Safety:** Not reported. **Authors' Conclusion:** Results from meta-analysis showed no statistically significant difference between real and sham acupuncture on headache days. Stimulation mode, needle retention, and treatment frequency are important factors contributing to the outcome of acupuncture treatment for TTH. The ideal treatment protocol for TTH could be electroacupuncture with 30-miunte needle retention and twice-weekly treatment.

[1]Linde K, Allais G, Brinkhaus B, Manheimer E, Vickers A, White AR. Acupuncture for tension-type headache. *Cochrane Database of Systematic Reviews* 2009;CD007587.

[2]Hao X, Xue CC, Dong L, Zheng Z. Factors associated with conflicting findings on acupuncture for tension-type headache: Qualitative and quantitative analyses. *Journal of Alternative and Complementary Medicine* 2013;19(4):285-97.

APPENDIX A.1

Table A.1.1: Summary of excluded reviews on acupuncture for TTH (listed in alphabetical order of first author)

Study	Study Type	Reason for Exclusion
Acupuncture for tension-type headaches and migraine. *Drug and Therapeutics Bulletin* 2010;48(6):62-5.	Narrative review	Not a systematic review
Adams J, Barbery G, Lui C-W. Complementary and alternative medicine use for headache and migraine: A critical review of the literature. *Headache* 2013; 53(3):459-73.	Systematic review	No results related to acupuncture and TTH
Bendtsen L. Drug and nondrug treatment in tension-type headache. *Therapeutic Advances in Neurological Disorders* 2009;2:155-61.	Narrative review	Not a systematic review
Bronfort G, Haas M, Evans R, Leininger B, Triano J. Effectiveness of manual therapies: the UK evidence report. *Chiropractic & Osteopathy* 2010; 18:3.	Systematic review	No detailed results on acupuncture and TTH
Clar C, Tsertsvadze A, Court R, Hundt GL, Clarke A, Sutcliffe P. Clinical effectiveness of manual therapy for the management of musculoskeletal and non-musculoskeletal conditions: systematic review and update of UK evidence report. *Chiropractic & Manual Therapies* 2014; 22(1):12. Update of Bronfort et al. (2010) above	Systematic review	No results related to acupuncture and TTH
Feise R. Is acupuncture effective for headaches? *Journal of the American Chiropractic Association* 2010;47:22-3.	Review of Linde et al. (2009)	Not a systematic review
Fernández-de-las-Peñas C, Schoenen J. Chronic tension-type headache: what is new? *Current Opinion in Neurology* 2009; (22): 254-261.	Narrative review	Not a systematic review
Hart J. Tension headaches: emerging complementary therapies. *Alternative & Complementary Therapies* 2010; 16(4):213-16.	Narrative review	Not a systematic review
Hopton A, Macpherson H. Acupuncture for chronic pain: Is acupuncture more than an effective placebo? A systematic review of pooled data from meta-analyses. *Pain Practice* 2010;10(2):92-102.	Systematic review	Included one review on TTH and one on chronic headache, but the results for different headache types were pooled – the only data available for TTH was headache days per month Included review on TTH was superseded by Linde et al. (2009)
Saligari D. Acupuncture for headache. *Journal of the Acupuncture Association of Chartered Physiotherapists* 2010;35-9.	Narrative review	Not a systematic review
Sherman KJ, Coeytaux RR. Acupuncture for the treatment of common pain conditions: chronic back pain, osteoarthritis, and headache. *JCOM* 2009;16:224-30.	Narrative review	Not a systematic review
Sit RWS, Liu S, Chung VCH. Is acupuncture effective in reducing headache frequency amongst patients with episodic or chronic tension-type headache in primary care settings? *Advances in Integrative Medicine* 2014;1(2):99-100.	Synopsis of Linde et al. (2009)	Not a systematic review
Sun-Edelstein C, Mauskop A. Alternative headache treatments: Nutraceuticals, behavioral and physical treatments. *Headache* 2011; 51(3):469-83.	Quasi-systematic review	Not a systematic review The only results related to TTH and acupuncture are sourced from Linde et al. (2009)

Study	Study Type	Reason for Exclusion
Vickers AJ, Cronin AM, Maschino AC, Lewith G, MacPherson H, Foster NE, Sherman KJ, Witt CM, Linde K; Acupuncture Trialists' Collaboration. Acupuncture for chronic pain: individual patient data meta-analysis. *Archives of Internal Medicine* 2012;172(19):1444-53.	Systematic review	Pooled results for TTH and migraine
Yu S, Han X. Update of chronic tension-type headache. *Current Pain and Headache Reports* 2014;19:469.	Narrative review	Not a systematic review
Zhao L, Guo Y, Wang W, Yan LJ. Systematic review on randomized controlled clinical trials of acupuncture therapy for neurovascular headache. *Chinese Journal of Integrated Traditional and Western Medicine* 2011; 17(8): 580-6.	Systematic review	Results pooled for all neurovascular headaches

APPENDIX A.2

The original literature search was conducted by the IHE Research Librarian in December 2006 and the latest update search was conducted on May 20 to 22, 2015 (for literature databases) and June 8 to 11, 2015 (for health technology assessment agency websites and grey literature) (Table A.2.1). Publication types were limited to systematic reviews or health technology assessments.

Medical Subject Headings (MeSH) terms relevant to this topic are: *headache*; *headache disorders*; *migraine*; *migraine disorders*.

Table A.2.1: Databases and search terms used in the search strategy

Database	Search Date/ Edition	Search Terms†
The Cochrane Library *http://www.thecochranelibrary.com*	May 20, 2015	headache* OR migraine* OR hemicrania* OR cephalgia* OR cephalalgia* OR sunct in Record Title or Keywords, from 2010
PubMed *http://www.pubmed.gov*	May 20, 2015	1. Search "Headache Disorders"[MeSH] OR "Headache"[MeSH] Filters: Publication date from 2010/10/20 to 2015/12/31; English 2. ((headache OR headaches OR migraine OR migraines OR cephalgia* OR cephalalgia* OR hemicrania* OR SUNCT) AND (inprocess[sb] OR publisher[sb] OR pubmednotmedline[sb])) Filters: Publication date from 2010/10/20 to 2015/12/31; English 3. (headache[ti] OR headaches[ti] OR migraine[ti] OR migraines[ti] OR cephalgia*[ti] OR cephalalgia*[ti] OR hemicrania*[ti] OR SUNCT[ti] or head pain*[ti]) Filters: Publication date from 2010/10/20 to 2015/12/31; English 4. Search (search[tiab] OR meta-analysis[Publication Type] OR MEDLINE[tiab] OR (systematic[tiab] AND review[tiab])) 5. (#1 OR #2 OR #3) AND #4 6. #5 Limits: All Child: 0-18 years 7. #5 Limits: All Adult: 19+ years 8. #5 NOT (#6 NOT #7) 9. (child*[ti] or pediatric*[ti] or paediatric*[ti] or adolescen*[ti] or school*[ti] or teen*[ti] or juvenile*[ti]) not adult*[ti] 10. #8 NOT #9
CRD Databases (HTA, DARE, NHS EED) *http://www.york.ac.uk/inst/crd/crddatabases.htm*	May 20, 2015	1 MeSH DESCRIPTOR Headache EXPLODE ALL TREES 2 MeSH DESCRIPTOR Headache Disorders EXPLODE ALL TREES 3 (headache* OR migraine* OR cephalgia* OR cephalalgia* OR hemicrania* OR SUNCT):TI 4 #1 OR #2 OR #3 5 * FROM 2010 TO 2015 6 #4 AND #5
EMBASE Licensed Resource (OVID Interface)	May 20, 2015	1. (headache$ OR migraine$ OR hemicrania$ OR cephalgia$ OR cephalalgia$ OR sunct).ti. 2. *"headache and facial pain"/ OR *chronic paroxysmal hemicrania/ OR *cluster headache/ OR *drug induced headache/ OR *headache/ OR *hypnic headache/ OR *primary headache/ OR *postdural puncture headache/ OR *sinus headache/ OR *sunct syndrome/ OR *vascular headache/ OR exp *chronic daily headache/ OR exp *migraine/ OR exp *tension headache/ OR exp *trigeminal autonomic cephalalgia/ 3. meta-analys$.mp OR search$.tw. OR review.pt. 4. (1 OR 2) AND 3 5. ((child$ OR pediatric$ OR paediatric$ OR adolescent$ OR school$

Database	Search Date/ Edition	Search Terms†
		OR teen$ OR juvenile$) NOT adult$).jw,ti. 6. (4 NOT 5) 7. ("201042" OR "201043" OR "201044" OR "201045" OR "201046" OR "201047" OR "201048" OR "201049" OR 20105$ OR 2011$ OR 2012$ OR 2013$ OR 2014$ OR 2015$).em. 8. 6 AND 7 9. limit 8 to English language **Note:** The * before the subject headings in this search limits the search to records where the subject heading is considered by the indexer to be one of the foci of the article.
Web of Science Licensed Resource (ISI Interface)	May 21, 2015	#1: TI=((headache* OR migraine* OR cephalgia* OR cephalalgia* OR hemicrania* OR SUNCT) AND TS=("systematic review" OR metaanalys* OR "systematically reviewed" OR meta-analys*)) #2: TS=(child* OR pediatric* OR paediatric* OR juvenile* OR teen* OR adolescen* OR school*) NOT TS=adult* #3: #1 NOT #2 DocType=All document types; Language=English; Databases=SCI-EXPANDED, SSCI, A&HCI Timespan=2010-2015
CINAHL Licensed Resource (OVID Interface)	May 22, 2015	S1. (MH Headache+ AND (TI meta analy* OR AB meta analy* OR MH meta analysis OR TX metaanalys* OR MH systematic review OR PT review OR PT systematic review)) S2. (TI (migraine* OR headache* OR cephalgia* OR cephalalgia* OR hemicrania* OR SUNCT) AND TX (meta analy* OR metaanalys* OR systematic review)) S3. S1 OR S2 S4. Limit S3 to Age Groups: Fetus, Conception to Birth, Infant, Newborn 0-1 month, Infant, 1-23 months, Child, Preschool 2-5 years, Child, 6-12 years, Adolescence, 13-18 years S5. S4 NOT (S4 AND MW Adult) S6. (S3) NOT (S5) Limiters - Published Date: 20100101-20151231; Language: English
Library Catalogues		
Proquest Dissertations and Theses Full Text Licensed Resource (Proquest Interface)	June 5, 2015	Headache* OR migraine*
Government		
Alberta Health http://www.health.gov.ab.ca	June 5, 2015	headache OR migraine systematic-review OR meta-analysis
Health Canada (site searched with Google)	June 5, 2015	"systematic review" | "meta analysis" migraine OR headache site:hc-sc.gc.ca Date: past year
HTA Agencies/Coverage Agencies		
INESS *https://www.inesss.qc.ca/en/home.html*	June 8, 2015	Headache; headaches; migraine; migraines
CADTH *http://www.cadth.ca/index.php/en/hta/reports-publications/search*	June 8, 2015	Headache; headaches; migraine; migraines
ICES *http://www.ices.on.ca/*	June 8, 2015	Headache; headaches; migraine; migraines

Database	Search Date/ Edition	Search Terms†
HTA at McGill *http://www.mcgill.ca/tau/*	June 8, 2015	Browsed list
OHTAC *http://www.hqontario.ca/evidence/publications-and-ohtac-recommendations/ontario-health-technology-assessment-series*	June 8, 2015	Browsed list
NICE (UK) Evidence Search *https://www.evidence.nhs.uk/*	June 8, 2015	Headache; headaches; migraine; migraines
NIHR HTA *http://www.nets.nihr.ac.uk/programmes/hta*	June 8, 2015	Searched projects and HTA journal for "Headache; headaches; migraine; migraine"
BlueCrossBlue Shield Technology Assessments *http://www.bcbs.com/blueresources/tec/vols/*	June 10, 2015	Browsed list of TEC assessments
Aetna Clinical Policy Bulletins *http://www.aetna.com/about/cov_det_policies.html*	June 10, 2015	Headache; migraine
Agency for Healthcare Research and Quality (AHRQ): *http://www.ahrq.gov/research/findings/evidence-based-reports/index.html*	June 10, 2015	Headache; migraine
Grey Literature		
Google *http://www.google.ca*	June 10, 2015	headache OR migraine systematic-review OR meta-analysis -pubmed -bmj
TRIP Database *www.tripdatabase.com*	June 11, 2015	(title:headache or migraine) from:2010 to:2015

Notes:

†*Limits*: Publication type: systematic reviews and health technology assessments; publication date 2010 to 2015. These limits were applied in databases where such functions are available.

Truncation: The * and $ symbol are truncation character that retrieves possible suffix variations of the root word e.g., surg* retrieves surgery, surgical, surgeon, etc. In databases accessed via the OVID platform the truncation character is $.

Semicolons are used to indicate terms that were searched separately.

APPENDIX N: Sample of Documents Used to Track Committee Deliberations

TABLE N.1: Sample of working document for the Guideline Update Committee and subcommittees

Item	Alberta CPG Recommendations/Evidence source	Discussion/Decision	Recommendation: status quo or changes/ Evidence source
Migraine during pregnancy	**Alberta CPG** 1st edition (p. 27) × **Preventive drugs for migraine should be avoided during pregnancy where possible.** ✓ **Preventive drugs for migraine should be gradually discontinued prior to the commencement of a planned pregnancy or should be stopped as soon as possible during an unplanned pregnancy.** ✓ **When it is necessary to continue migraine prophylaxis during pregnancy, obtaining specialist advice should be considered.** **Evidence source:** EO (GDG)	**June 14/15**: Co-chair email communication: Research Team to search for SRs/review use of magnesium during pregnancy. **Oct 28/15: Subcommittee meeting**: Being able to deliver on having all preventative drugs in pregnancy as referrals through specialists (i.e., may not be able to see a specialist in time). *Parking lot*: Search IHE Database for SRs on magnesium during pregnancy. **Dec 4/15:** SR evidence reviewed by Research Team (no systematic review found to respond to inclusion criteria; 31 articles excluded).	**Status quo**
New statement/ recommendation & additional information on strategy	**G8 (Canada)** (p. Suppl. 2: 38) i. Migraine drug prophylaxis is best avoided during pregnancy if at all possible. Strategies involving trigger management, maintenance of good hydration, regular meals, regular sleep and attention to other lifestyle factors should be considered. ii. (new) Magnesium is considered the safest migraine prophylactic during pregnancy. iii. If migraine drug prophylaxis is necessary during pregnancy, the best choice is a beta-blocker (propranolol or metoprolol) or if these are contraindicated or ineffective, amitriptyline or nortriptyline. **Evidence source:** Expert consensus based on NR (7); NRCS (2); G (1); Other (1)	**Dec 11/15: Subcommittee meeting**: Originally said was safest, now more published on risks of high dose IV; US FDA issued warning and changed category in May 2015; no SRs found, many excluded NRs; only mentioned in general, not in pregnancy section of 1st edition of guideline → voted to include in background statement. ACTION ITEM Add in background statement. **Jan 2/16: Email correspondence co-chair:** I don't think we need to add anything, as we recommend specialist advice if prophylaxis is considered during pregnancy.	Do not add magnesium during pregnancy to *Alberta CPG*

CPG: clinical practice guideline; EO: expert opinion; G: guideline; G8: seed guideline (see references in *Appendix H*); GDG: Guideline Development Group; IHE: Institute of Health Economics; IV: intravenous; NR: narrative review; NRCS: non-randomized comparative study; SR: systematic review; US FDA: United States Food and Drug Administration

TABLE N.2: Sample of abridged working document summarizing subcommittee outcomes for the Guideline Update Committee

Item	Alberta CPG Recommendations/Evidence source	Action	Recommendation/Evidence source
Migraine during pregnancy No change	**Alberta CPG** 1st edition (p. 27) × **Preventive drugs for migraine should be avoided during pregnancy where possible.** ✓ **Preventive drugs for migraine should be gradually discontinued prior to the commencement of a planned pregnancy or should be stopped as soon as possible during an unplanned pregnancy.** ✓ **When it is necessary to continue migraine prophylaxis during pregnancy, obtaining specialist advice should be considered.** **Evidence source:** EO (GDG)	• Looked for SR evidence on use of magnesium during pregnancy: none found • Do not add magnesium in *Alberta CPG* • Keep current *Alberta CPG* as is	**Status quo**
Reason for review: *New recommendation from G8* *Additional information [strategy]*	**G8 (Canada)** (p. Suppl. 2: 38) i. Migraine drug prophylaxis is best avoided during pregnancy if at all possible. Strategies involving trigger management, maintenance of good hydration, regular meals, regular sleep and attention to other lifestyle factors should be considered. ii. (new) Magnesium is considered the safest migraine prophylactic during pregnancy. iii. If migraine drug prophylaxis is necessary during pregnancy, the best choice is a beta-blocker (propranolol or metoprolol) or if these are contraindicated or ineffective, amitriptyline or nortriptyline. **Evidence source:** Expert consensus based on NR (7); NRCS (2); G (1); Other (1)		Do not add magnesium during pregnancy in *Alberta CPG*.

CPG: clinical practice guideline; EO: expert opinion; G: guideline; G8: seed guideline (see references in *Appendix H*); GDG: Guideline Development Group; NR: narrative review; NRCS: non-randomized comparative study; SR: systematic review

APPENDIX O: List of Recommendations with Evidence Sourced from IHE Database Systematic Reviews

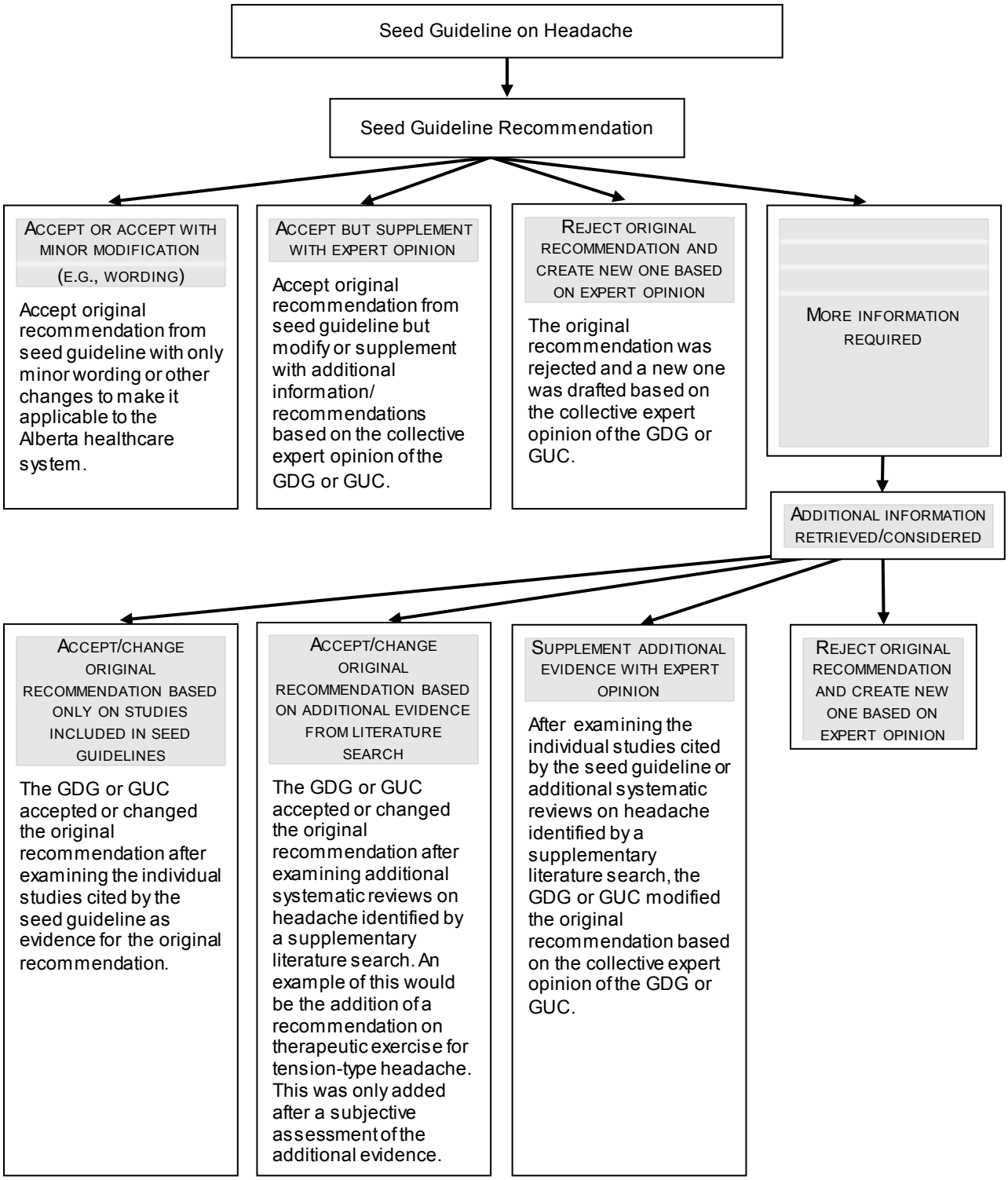
Recommendation/ Evidence Source	Systematic Reviews*
Headache diagnosis and investigation	
Neuroimaging in typical migraine Unexplained focal signs in the patient with headache Unusual headache precipitants Cluster headache and other uncommon primary headache syndromes CS (G4) + qSR (IHE Database)	Detsky ME, McDonald DR, Baerlocher MO, Tomlinson GA, McCrory DC, Booth CM. Does this patient with headache have a migraine or need neuroimaging? *JAMA* 2006;296(10):1274-83.
Management of migraine headache	
NSAIDs and acetaminophen SR (G1d, G7, IHE Database)	Rabbie R, Derry S, Moore RA, McQuary HJ. Ibuprofen with or without an antiemetic for acute migraine headaches in adults. *Cochrane Database of Systematic reviews* 2010;(10):CD008039. Suthisisang C, Poolsup N, Kittikulsuth W, Pudchakan P, Wiwatpanich P. Efficacy of low-dose ibuprofen in acute migraine treatment: Systematic review and meta-analysis. *Annals of Pharmacotherapy* 2007;41(11):1782-1791. Suthisisang CC, Poolsup N, Suksomboon N, Lertpipopmetha V, Tepwitukgid B. Meta-analysis of the efficacy and safety of naproxen sodium in the acute treatment of migraine. *Headache* 2010;50(5):808-18.
Selective serotonin reuptake inhibitors SR (G4, IHE Database)	Banzi R, Cusi C, Randazzo C, Sterzi R, Tedesco D, Moja L. Selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) for the prevention of migraine in adults. *Cochrane Database of Systematic Reviews* 2015;(4):CD002919.
Gabapentin SR (IHE Database)	Linde M, Mulleners WM, Chronicle EP, McCrory DC. Gabapentin or pregabalin for the prophylaxis of episodic migraine in adults. *Cochrane Database of Systematic Reviews* 2013;(6):CD010609.
Relaxation training, biofeedback, and cognitive behavioural therapy SR (G3, G10, IHE Database)	Nestoriuc Y, Martin A. Efficacy of biofeedback for migraine: A meta-analysis. *Pain* 2007;128(1-2):111-27. Nestoriuc Y, Martin A, Rief W, Andrasik F. Biofeedback treatment for headache disorders: A comprehensive efficacy review. *Applied Psychophysiology Biofeedback* 2008;33(3):125-40.
Acupuncture SR (G4, G11, IHE Database)	Linde K, Allais G, Brinkhaus B, Manheimer E, Vickers A, White AR. Acupuncture for migraine prophylaxis. 2009. *Cochrane Database of Systematic Reviews*, CD001218(1).
Hyperbaric oxygen for acute treatment RCT (G1b) + SR (IHE Database)	Bennett MH, French C, Schnabel A, Wasiak J, Kranke P. Normobaric and hyperbaric oxygen therapy for migraine and cluster headache. *Cochrane Database of Systematic Reviews* 2008, Issue 3 Art No: CD005219 2008.

Recommendation/ Evidence Source	Systematic Reviews*
Cranial-sacral therapy SR (IHE Database)	Wanderley D, Lemos A, De Andrade CL, De Oliveira DA. Manual therapies for pain relief in patients with headache: A systematic review. *Revista Neurociencias* 2014;23(1):89-96.
Spinal manipulation SR (G4, G10, G11, IHE Database)	Posadzki P, Ernst E. Spinal manipulations for the treatment of migraine: A systematic review of randomized clinical trials. *Cephalagia* 2011;31(8):964-70.
Menstrual migraine: acute medications RCT (G4) + SR (IHE Database)	Pringsheim T. Acute treatment and prevention of menstrually related migraine headache: Evidence-based review. *Neurology* 2008;70(17):1555-63.
Menstrual migraine: frovatriptan RCT (G1c, G4) + SR (IHE Database)	Pringsheim T. Acute treatment and prevention of menstrually related migraine headache: Evidence-based review. *Neurology* 2008;70(17):1555-63.
Ketorolac IM, IV RCT (G10) + SR (IHE Database) + EO (GUC)	Orr SL, Aube M, Becker WJ, Davenport WJ, Dilli E, Dodick D, Giammarco R, Gladstone J, Leroux E, Pim H, Dickinson G, Christie SN. Canadian Headache Society systematic review and recommendations on the treatment of migraine pain in emergency settings. *Cephalalgia* 2015; (35): 271-84. Taggart E, Doran S, Kokotillo A, Campbell S, Villa-Roel C, Rowe B H. Ketorolac in the treatment of acute migraine: a systematic review. *Headache* 2013;53:277-87.
Tension-type headache	
Exercise SR (IHE Database)	Fricton J, Velly A, Ouyang W, Look JO. Does exercise therapy improve headache? a systematic review with meta-analysis. *Current Pain Headache Report* 2009;13(6):413-9. Bronfort G, Nilsson N, Haas M, Evans R, Goldsmith CH, Assendelft WJ, et al. Non-invasive physical treatments for chronic/recurrent headache. *Cochrane Database of Systematic Reviews* 2004;(3):CD001878.
Trigger point injections or dry needling SR (IHE Database)	France S, Bown J, Nowosilskyj M, Mott M, Rand S, Walters J. Evidence for the use of dry needling and physiotherapy in the management of cervicogenic or tension-type headache: A systematic review. *Cephalalgia* 2014;34(12):994-1003. Kim TH, Lee CR, Choi TY, Lee MS. Intramuscular stimulation therapy for healthcare: a systematic review of randomised controlled trials. *Acupuncture in Medicine 2012;30:286-90.*
Cervicogenic headache	
Exercise SR (IHE Database)	Fricton J, Velly A, Ouyang W, Look JO. Does exercise therapy improve headache? a systematic review with meta-analysis. *Current Pain Headache Report* 2009;13(6):413-9. Bronfort G, Nilsson N, Haas M, Evans R, Goldsmith CH, Assendelft WJ, et al. Non-invasive physical treatments for chronic/recurrent headache. *Cochrane Database of Systematic Reviews* 2004;(3):CD001878.
Cervical spinal manipulation SR (G4, G9, IHE Database)	Bronfort G, Nilsson N, Haas M, Evans R, Goldsmith CH, Assendelft WJ, et al. Non-invasive physical treatments for chronic/recurrent headache. *Cochrane Database of Systematic Reviews* 2004;(3):CD001878. Gross A, Miller J, D'Sylva J, Burnie SJ, Goldsmith CH, Graham N, et al. Manipulation or mobilization for neck pain. *Cochrane Database of Systematic Reviews* 2010;(1): CD004249.

Recommendation/ Evidence Source	Systematic Reviews*
Cervical spinal mobilization SR (G4, G9, IHE Database)	Bronfort G, Nilsson N, Haas M, Evans R, Goldsmith CH, Assendelft WJ, et al. Non-invasive physical treatments for chronic/recurrent headache. *Cochrane Database of Systematic Reviews* 2004;(3):CD001878. Gross A, Miller J, D'Sylva J, Burnie SJ, Goldsmith CH, Graham N, et al. Manipulation or mobilization for neck pain. *Cochrane Database of Systematic Reviews* 2010;(1): CD004249.
Massage SR (IHE Database)	Wanderley D, Lemos A, De Andrade CL, De Oliveira DA. Manual therapies for pain relief in patients with headache: A systematic review. *Revista Neurociencias* 2014;23(1):89-96.

*Some systematic reviews may also have been cited by the recently published seed guidelines.

APPENDIX P: Process Used to Formulate Recommendations



GDG: Guideline Development Group (1st Edition); GUC: Guideline Update Committee (2nd Edition)

APPENDIX Q: Recommendation Categories

Definitions for *Do*, *Do Not Do*, *Do Not Know*

DO

Recommendations sourced from seed guidelines

When the Ambassador Program Guideline Development Group (GDG) or Guideline Update Committee (GUC) accepted the intent of the original recommendation in the seed guideline(s), the original wording was preserved where possible. Thus, recommendations were classified as "Do" when the original guideline recommended or provided a prescriptive direction to perform the action, or used the term "effective" to describe it.

The seed guidelines used different systems to grade or categorize the level of evidence supporting each recommendation and the strength or type of recommendation made. However, generally all of the guidelines recommended an action or described it as effective when this statement was supported by:

- results from at least one study of strong design for answering the question addressed,
- generally consistent results from multiple studies of strong design for answering the question addressed, or
- the clinical experience of the Guideline Development Group (GDG).

Recommendations not sourced from seed guidelines

New recommendations were classified as "Do" when a supplementary literature search found at least one relevant systematic review presenting consistent evidence to support the action from a minimum of two critically appraised primary studies of at least moderate quality (as assessed by the authors of the review) or five primary studies of undefined quality.*

Expert Opinion

When the Ambassador Program GDG or GUC supplemented a recommendation or created a new one based on expert opinion, it was classified "Do" when the collective professional opinion of the GDG or GUC supported the action.

DO NOT DO (Not Recommended)

Recommendations sourced from seed guidelines

When the GDG or GUC accepted the gist of the original recommendation in the seed guideline(s), the original wording was preserved where possible. Thus, recommendations were classified as "Do Not Do" when the original guideline recommended against or provided a prescriptive direction not to perform the action, used the term "ineffective" to describe it, or stated that the evidence did "not support" it.

The seed guidelines used different systems to grade or categorize the level of evidence supporting each recommendation and the strength or type of recommendation made. However, generally all of the guidelines recommended against performing an action or described it as ineffective when this statement was supported by:

- results from at least one study of strong design for answering the question addressed,

- generally consistent results from multiple studies of strong design for answering the question addressed, or
- the clinical experience of the GDG or GUC.

Recommendations not sourced from seed guidelines

New recommendations were classified as "Do Not Do" when a supplementary literature search found at least one relevant systematic review presenting consistent evidence that did not support the action from a minimum of two critically appraised primary studies of at least moderate quality (as assessed by the authors of the review) or five primary studies of undefined quality.*

Expert Opinion

When the Ambassador Program GDG or GUC supplemented a recommendation or created a new one based on expert opinion, it was classified "Do Not Do" when the collective professional opinion of the GDG or GUC did not support the action.

DO NOT KNOW

Recommendations sourced from seed guidelines

When the GDG or GUC accepted the intent of the original recommendation in the seed guideline(s), the original wording was preserved where possible. Thus, recommendations were classified as "Do Not Know" when the original guideline did not recommend for or against the action or stated that there was "no evidence", "insufficient or conflicting evidence", or "no good evidence" to support its use.

The seed guidelines used different systems to grade or categorize the level of evidence supporting each recommendation and the strength or type of recommendation made. However, generally all of the guidelines stated that evidence for a particular action was lacking or insufficient when:

- effectiveness was demonstrated in a general sense but not specifically for headache,
- the studies were of poor quality, inappropriately designed to answer the question addressed, or presented conflicting results, which precluded the determination of effectiveness or the balance of benefits and harms,
- only one study of any design was available, or
- no studies of any design were available.

Recommendations not sourced from seed guidelines

New recommendations were classified as "Do Not Know" and worded as follows.

- "There is insufficient evidence to recommend for or against" the action: when a supplementary literature search found no relevant systematic reviews.
- "There is inconclusive evidence to recommend for or against" the action: when a supplementary literature search found at least one relevant systematic review presenting evidence from primary studies that were of poor quality, exhibited significant heterogeneity in the populations studied or methods used, were inappropriately designed to answer the question addressed, or presented conflicting or equivocal results.

Recommendations unchanged by new seed guidelines

Recommendations listed as "Do Not Know" in the previous edition of the guideline:

- were changed to "Do" when a supplementary literature search found at least one relevant systematic review presenting consistent evidence to support the action from a minimum of two critically appraised primary studies of at least moderate quality (as assessed by the authors of the review) or five primary studies of undefined quality*;
- were changed to "Do Not Do" when a supplementary literature search found at least one relevant systematic review presenting consistent evidence that did not support the action from a minimum of two critically appraised primary studies of at least moderate quality (as assessed by the authors of the review) or five primary studies of undefined quality*;
- remained as "Do Not Know" when a supplementary literature search found either no relevant systematic reviews or at least one relevant systematic review presenting conflicting or equivocal results or stating that the evidence in relation to the action was "limited", "inconclusive", "inconsistent", or "insufficient".

Expert Opinion

When the Ambassador Program GDG or GUC supplemented a recommendation or created a new one based on expert opinion, it was classified "Do Not Know" when the collective professional opinion of the GDG or GUC was equivocal with respect to supporting the action.

*The number of studies is arbitrary and is not supported by literature.

APPENDIX R: Feedback on Guideline Documents

FIGURE R.1: Sample of the online survey sent to Guideline Update Committee and subcommittee members (August 2016)

IHE INSTITUTE OF HEALTH ECONOMICS ALBERTA CANADA

Alberta Ambassador Program - Headache Guideline 2016 Update

Section 1: New/Substantively changed recommendations

Headache Diagnosis and Investigation

Persistent Headache Attributed to Head Trauma - New recommendation

Draft recommendation	Evidence source*
Persistent Headache Attributed to Head Trauma **DO NOT KNOW** There is insufficient evidence to recommend for or against neuroimaging in patients with persistent headache attributed to head trauma who do not have new focal signs or other red flags to indicate the need for neuroimaging. If, on a case by case basis, it is felt that there may be a need for neuroimaging, specialist referral is recommended.	EO (GUC)

* EO: expert opinion; GUC: Guideline Update Committee

5. Is the above recommendation clear and, if not, where can it be improved?

◯ Yes

◯ No

If 'no', please explain:

6. In your practice setting, are there barriers to the implementation of this recommendation that we should be aware of?

◯ Yes

◯ No

If 'yes', please describe:

5

Note: The online survey was sent to all GUC and subcommittee members in August 2016 for feedback on the draft version of the *Alberta CPG* 2nd Edition.

TABLE R.1: Suggestions for improving the guideline from Guideline Update Committee and subcommittee members (n=6) (August 2016)

Question	Response/Feedback
What is your discipline?	• Family physician (n=4) • Pharmacist (n=1) • Registered nurse (n=1)
What AHS zone do you work in?	• Calgary (n=5) • South (n=1)
Have you ever printed off and/or directed a patient to any of the patient information sheets that accompany the first edition of the guideline?	• Yes (n=5) • No (n=1)
Would you print off and/or direct a patient to a comprehensive brochure that incorporates all of the information from the individual patient information sheets that accompany this guideline?	• Yes (n=6)
Is the above recommendation clear and, if not, where can it be improved?*	<u>Multimodal multidisciplinary care (management of migraine headache)</u> Yes: 5; No: 1 Consider deleting the comma between ...'relaxation, and stress'... for greater clarity. <u>NSAIDs and acetaminophen (management of migraine headache)</u> Yes: 6; No: 0 It's certainly clear. I'm not sure there are patients for whom faster onset of therapeutic effect is NOT desired, and I think that the magnitude of difference in reality is somewhat magnified by industry, but I feel very comfortable making that judgement for myself, and don't see a need to change the recommendation. <u>Opioids (management of migraine headache)</u> Yes: 4; No: 2 1. I am assuming that the examples are representative of the combination analgesics. Would tylenol#3 be a better example than codeine? 2. Butorphanol generally would not fit into the "Strong opioid" category due to its mixed agonist-antagonist activity and possible ceiling effect. It might be better to state "Strong opioids (e.g., morphine, oxycodone) and the mixed opioid agonist-antagonist butorphanol should be avoided and used only in exceptional circumstances... <u>Migraine treatment during lactation (management of migraine headache)</u> Yes:5; No: 1 I am not sure about the nadolol in breastfeeding recommendation - LexiComp rates it "limited human data - potential toxicity" and Lactmed states "Because of its relatively extensive excretion into breastmilk and its renal excretion, other beta-adrenergic blocking drugs are preferred to nadolol, especially while nursing a newborn or preterm infant."

Question	Response/Feedback
Please provide any comments you have about the medication table.*	(2 comments) 1. - naproxen sodium OTC Aleve(R) is 220 mg - I believe the evidence shows that histamine receptor antagonists are not recommended at all for NSAID GI prophylaxis (only PPIs and misoprostol) - ? include 50 mg powder for oral solution (sachet) (Cambia(R)) for diclofenac potassium? - recommendation for ibuprofen was a 400 mg dose (not 600 mg)? - new max dose of diclofenac is 100 mg/day as per Health Canada advisory re: increased risk of CV events 2. venlafaxine XR comes as capsules (not tablets)
If you have any further comments on any of the sections reviewed in this survey and/or anything from the emailed full guideline draft not reviewed in this survey (e.g., background statements, appendices), please provide them below.*	(1 comment) Objective 1: Is the objective "to increase the use of evidence-informed approaches..." or "to provide evidence-informed approaches..."?

Note: Feedback on the draft version of the *Alberta CPG* 2nd Edition received in August 2016 via an online survey (see Figure R.1 for sample page) sent to all GUC and subcommittee members.

*Only recommendations which generated comments are provided above.

TABLE R.2: Barriers to implementing the *Alberta CPG* recommendations – summary of responses from Guideline Update Committee and subcommittee members (n=6) (August 2016)

Question	Feedback
In your practice setting, are there barriers to the implementation of these recommendations that we should be aware of?	Persistent headache attributed to head trauma (headache diagnosis and investigation) Yes: 1; No: 5 There isn't always specialist opinion available and therefore could we say... 'specialist opinion should be considered.' Multimodal multidisciplinary care (management of migraine headache) Yes: 1; No: 5 Long wait list for the headache clinic. Need additional resources for refractory migraine especially when accompanied by yellow flags. Medications for migraine prophylaxis: chronic migraine (management of migraine headache) Yes:1; No: 5 Access to appropriately trained individuals to administer botox Non-pharmacological therapy: deep neck flexor training (cervicogenic headache) Yes: 0; No: 6 Familiarity of physicians with this technique
From your perspective, do you have any comments on potential resource implications associated with implementing any of the above reviewed recommendations?	(1 comment) Aside from a strong knowledge transfer program and enhanced multidisciplinary team clinics at the primary care level. No additional suggestions.

Note: Feedback on the draft version of the *Alberta CPG* 2nd Edition received in August 2016 via an online survey (see Figure R.1 for sample page) sent to all GUC and subcommittee members. Only recommendations which generated comments are provided above.

TABLE R.3: Suggestions for improving patient information sheets from IHE Lay Advisory Committee members (n=8) (April 2016)

Theme/ Information Sheet	Feedback*
General opinion	The committee felt this was excellent information and noted that many of the suggestions previously provided on the 1st Edition of the *Alberta CPG* had been incorporated into the current draft. They questioned whether the public is accessing this through the IHE website or whether doctors are handing the sheets out. The face of the IHE is very academic. There should be a user-friendly face for the public. It is terrific that the public can get evidence-based information instead of un-reviewed information on the web.† • The guidelines are divided into six documents. There are large sections that are repeated in each of the documents. • Patients with migraine headaches often find it difficult to read large volumes; "too much writing." Repetitive, long documents are difficult for people with limited reading skills. • It would be useful to have a separate information sheet for Pregnancy and Headaches. • Each of the documents refers to headache diaries. Headache diaries are extremely helpful and maybe this warrants a separate document. The committee thought an interactive diary would be very helpful. • The medication section should build on the Choosing Wisely Project, i.e., "more is not better." • The documents should caution people about using natural remedies, especially butterbur. • The committee questioned having a separate document for tension-type headaches. It is only one cause of headache and could be dealt with under self-management.

Note: Feedback on the draft patient materials of the *Alberta CPG* 2nd Edition received during a presentation to the IHE Lay Advisory Committee on April 22, 2016 in Edmonton.

*These comments were focused on encouraging patients to engage in appropriate self-care.

†This summary does not include the detailed suggestions made on recommendation wording.

TABLE R.4: Feedback on the patient brochure from Calgary Headache Assessment & Management Program patients (n=2) (January/February 2017)

Question	Feedback
Is there any wording that is difficult to understand?	1. No, I found it very reader friendly. 2. The only things I didn't understand were some of the items listed under "what doesn't work for headaches" on page 22 but I don't think that's important.
Are there things that you'd like us to add to the brochure?	1. Perhaps some visual pictures, emphasizing the various regions of pain. 2. Perhaps include a sample headache diary.
Are there parts that are not important and should be removed from the brochure?	1. Some parts were a little repetitive. 2. I think some of it is a bit repetitive and could be condensed (e.g., pg. 5-6 writing in the diary).
Are there other pages/sections where you would like a web-link to further information?	1. Perhaps the pages that listed the drug/methods of treatment. 2. Migraines – as a long-term sufferer, I know the more information you can get, the more helpful.
Is there anything else you can think of that would make the brochure more helpful to people with headaches?	1. No, overall I found it informative. 2. My only concern is that at 23 pages, people won't read it all. Otherwise, it is well written.
Other comments (written on brochure)	• *Re: symptoms of migraines (pg. 9):* I think there are other indicators e.g., pain on one side. I suffer from migraines but rarely feel nauseated and am not particularly light sensitive.

Note: Feedback on the final version of the patient brochure for *Alberta CPG* 2nd Edition was received via a mail-in survey between January and February 2017, after the guideline and companion materials had been published on the TOP and IHE websites. Any future editions of the materials will take this feedback into account.

APPENDIX S: Declaration of Competing Interest Form

IHE INSTITUTE OF HEALTH ECONOMICS ALBERTA CANADA

Declaration of Competing Interest

Project Name: **Headache Guidelines in Primary Care – 1st Update**

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1. I agree to have my name acknowledged as a contributor on the development of the guideline on headache.

   Yes ☐ No ☐

   If not, please be assured that we would respect your preference.

2. If yes, please list name, degrees, position, title and affiliation as you wish them to appear in the guideline.

   Name: _____

   Degrees: _____

   Position Title: _____

   Affiliation: _____

   Area of expertise: _____

All contributors are required to disclose circumstances which could be perceived to be a competing interest.

Competing interest is considered to be financial interest or non-financial interest, either direct or indirect that could affect the recommendations contained in this guideline.

Please note that declaring financial and/or non-financial competing interest helps us to fully inform our stakeholders about this aspect and does not mean that the person would not be in a position to act as an expert, or that his/her contributions would be incorrect or biased.

If you have any questions or concerns, please contact Christa Harstall, Director HTA, by e-mail at charstall@ihe.ca.

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Potential competing interest	NO	YES
Ownership of stock, stock options or other financial instruments of a product's manufacturer or manufacturers of competitive products (excluding mutual fund ownership).	☐	☐
Honoraria or other compensation from a manufacturer or a special interest group for writing a publication or participating in the development of the guideline.	☐	☐
Grant, honoraria or other compensation from a manufacturer or a special interest group for conducting research	☐	☐
Currently, or within the last 2 years: • Consultancy or employment with a manufacturer or a special interest group. • Speaker fees, educational grants and/or travel assistance provided by a manufacturer or a special interest group. • Any other direct or indirect relationship with a manufacturer or a special interest group which could be perceived to be a competing interest.	☐	☐

If yes to any of the above or if there is any other potential competing interest, please describe below:

_____

_____

_____

Signature _____ Date _____

Printed Name _____

Thank you for completing this form. Please return the form by mail or fax to:

Institute of Health Economics
Attention: HTA
1200, 10405 Jasper Avenue
Edmonton, Alberta, Canada T5J 3N4
Fax: (780) 448-0018

TABLE S.1: Competing interests declared by GUC members

Affiliation, Discipline, Area of Expertise	Declared Interest
Werner Becker MD, BSc, FRCP(C), Co-Chair Professor, Department of Clinical Neurosciences, University of Calgary Neurology	Received consulting fees for medical advisory boards from Allergan, Amgen, and Novartis. Received speaker's honoraria from Allergan, Amgen, and Serono. Received clinical trials research support from Allergan and Amgen.
MD, FRCPC (Neurology), CSCN Diplomate, BSc Clinical Assistant Professor, Division of Neurology, Department of Clinical Neurosciences, University of Calgary Neurology	Received speaker's honoraria from Allergen.