Topic proposal

I understand that this proposal will be retained by the SIGN Programme Lead and be made available on the SIGN website for time period that the proposal is being considered. **Only proposals with a completed Declaration of Interests for the principal proposer will be considered**	
1.	**What is the problem/need for a guideline/clinical scenario?**
	Clinicians treating patients with episodic and chronic migraine need clear guidance on choice of preventer therapies. The original guideline (SIGN 107 Diagnosis and management of Headache in Adults) gave recommendations on treatment but not in a hierarchal structure. Since the publication of this guideline there is more published evidence on which therapies are likely to be more effective in particular patient groups. There is also new evidence for botox therapy and there are now medical devices that have some evidence for treating migraine headache.
2.	**Burden of the condition**
	Mortality nil
	Incidence ➢ 50% of all patients with migraine have 12 or more attacks a year
	Prevalence 14.3% of the UK population have migraine 2% of the UK population have chronic migraine (headache on 15 or more days a month) references 1.Headache Disorders -*not respected, not resourced,* A Report of the All-Party Parliamentary Group on Primary Headache Disorders (APPGPHD) House of Commons, March 2010 2. The global burden of migraine: measuring disability in headache disorders with WHO's Classification of Functioning, Disability and Health (ICF) J Headache Pain (2005) 6:429–440 DOI 10.1007/s10194-005-0252-4
3.	**Variations**
	In practice in Scotland Primary care: many GPs not aware of headache guidelines, headache teaching variable Secondary Care: some patients have no access to second line medications including flunarazine and botox.
	In health outcomes in Scotland Difficult to quantify
4.	**Areas of uncertainty to be covered**
	Key question 1 What is the hierarchal choice for migraine preventer medications? What should be used first line, second line and third line?
	Key question 2 What is the role of Botox in treatment of chronic migraine?
	Key question 3 What is the role of medical devices in the management of migraine?

5.	**Areas that will not be covered**
	Acute therapy for migraine, excluding secondary causes of headache
6.	**Aspects of the proposed clinical topic that are key areas of concern for patients, carers and/or the organisations that represent them**
	Patients having access to appropriate medications that have an evidence base. That the appropriate medicine is given in an effective dose with due consideration to co-morbid medical conditions.
7.	**Population**
	Included Patients with a diagnosis of migraine whether episodic or chronic.
	Not included Patients with any other headache diagnosis
8.	**Healthcare setting**
	Included Primary and secondary care
	Not included N/A
9.	**Potential**
	Potential to improve current practice Giving clear hierarchal advice on migraine preventers should help clinicians make the correct choice of therapies for their patients
	Potential impact on important health outcomes (name measureable indicators) MIDAS (migraine disability assessment) questionnaire scores should reduce which means migraine has less impact on day to day functioning.
	Potential impact on resources (name measureable indicators) Less patients with migraine should be referred to secondary care if treatment regimes improve though there may be more referrals for chronic migraine if patient eligible for botox
10.	**What evidence based guidance is currently available?**
	Out-of-date (list) SIGN 107 Diagnosis and management of Headache in Adults
	Current (list) 1. International Classification of Headache Disorders http://cep.sagepub.com/content/33/9/629.long 2. NICE headache guidelines 2012 https://www.nice.org.uk/guidance/cg150 3. British Association for the Study of Headache Guidelines 2014 http://www.bash.org.uk/guidelines/
11.	**Relevance to current Scottish Government policies**
	The **Scottish National Neurological standards** were published in 2009 and their implementation approved by each health board. There is a headache subsection. The standards are based on clinical evidence including SIGN. **The National Neurological Advisory Group (NNAG)** was set up in 2012 with funding from Scottish government, to oversee and support NHS Boards as they implement improvements through their 3 Year Plans. The NNAG has work streams to support NHS Boards to meet the

	criteria contained within the Clinical Standards for Neurological Health Services . The NNAG aims to create and develop an infrastructure to support NHS Boards and other partners to: 1. Improve patient's outcomes for those with neurological conditions or symptoms. 2. Empower all staff to deliver safe and effective person centred healthcare services. The NNAG has a headache subgroup that will review the National Neurological Standards and their implementation. http://www.healthcareimprovementscotland.org/programmes/long_term_conditions/neurological_health_services/neurological_standards.aspx
12.	**Who is this guidance for?**
	All clinicians managing patients with migraine
13.	**Implementation**
	Links with existing audit programmes NNAG work stream on audit of headache referrals
	Existing educational initiatives BASH education meetings Health Board 3 year plans include local headache education meetings
	Strategies for monitoring implementation Use of second line therapies in secondary care Use of first line therapies before referral to secondary care
14.	**Primary contact for topic proposal**
	David Watson (david.watson@nhs.net), Hamilton Medical Group, 4 Queens Road, Aberdeen, AB15 4ZT
15.	**Group(s) or institution(s) supporting the proposal**
	Scottish Headache Interest Group NNAG headache subgroup Migraine Trust

Declaration of Interests

Please complete all sections and if you have nothing to declare please put 'N/A

Having read the SIGN Policy on Declaration of Competing Interests I declare the following competing interests for the previous year, and the following year. I understand that this declaration will be retained by the SIGN Programme Lead and be made available on the SIGN website for time period that the proposal is being considered.

Signature:	
Name:	David Watson
Relationship to SIGN:	Topic proposal primary contact
Date:	25.3.15
Date received at SIGN:	25.3.15

Personal Interests

Remuneration from employment

	Name of Employer and Post held	Nature of Business	Self or partner/ relative	Specific?
Details of employment held which may be significant to, or relevant to, or bear upon the work of SIGN	NHS Grampian, GPwSI headache	GPwSI	self	

Remuneration from self employment

	Name of Business	Nature of Business	Self or partner/ relative	Specific?
Details of self employment held which may be significant to, or relevant to, or bear upon the work of SIGN	GP Partner Hamilton Medical Group, Aberdeen	GP	self	

Remuneration as holder of paid office

	Nature of Office held	Organisation	Self or partner/ relative	Specific?
Details of office held which may be significant to, or relevant to, or bear upon the work of SIGN	N/A			

Remuneration as a director of an undertaking

	Name of Undertaking	Nature of Business	Self or partner/ relative	Specific?
Details of directorship held which may be significant to, or relevant to, or bear upon the work of SIGN	N/A			

Remuneration as a partner in a firm

	Name of Partnership	Nature of Business	Self or partner/ relative	Specific?
Details of Partnership held which may be significant to, or relevant to, or bear upon the work of SIGN	N/A			

Shares and securities

	Description of organisation	Description of nature of holding (value need not be disclosed)	Self or partner/ relative	Specific?
Details of interests in shares and securities in commercial healthcare companies, organisations and undertakings	N/A			

Remuneration from consultancy or other fee paid work commissioned by, or gifts from, commercial healthcare companies, organisations and undertakings

	Nature of work	For whom undertaken and frequency	Self or partner/ relative	Specific?
Details of consultancy or other fee paid work which may be significant of to, or relevant to, or bear upon the work of SIGN	N/A			

Details of gifts which may be significant to, or relevant to, or bear upon the work of SIGN	N/A			

Non-financial interests

	Description of interest	Self or partner/ relative	Specific?
Details of non-financial interests which may be significant to, or relevant to, or bear upon the work of SIGN	Attended Chronic Migraine meeting in 2014 sponsored by Allergan		

Non-personal interests

	Name of company, organisation or undertaking	Nature of interest
Details of non-personal support from commercial healthcare companies, organisations or undertakings	N/A	

*Signature*_____ *Date: 25.3.15*_____

Thank you for completing this form.

Please return to
Roberta James
SIGN Programme Lead
SIGN Executive, Healthcare Improvement Scotland,
Gyle Square | 1 South Gyle Crescent | Edinburgh | EH12 9EB

t: **0131 623 4735**
e:**roberta.james@nhs.net**

Data Protection

Your details will be stored on a database for the purposes of managing this guideline topic proposal. We may retain your details so that we can contact you about future Healthcare Improvement Scotland activities. We will not pass these details on to any third parties. Please indicate if you do not want your details to be stored after the proposal is published.

Initial screen

Purpose: initial screening by SIGN Senior Management Team to exclude proposals that are neither clinical, nor multi-professional, nor appropriate for the SIGN process.

1.	**Is this an appropriate clinical topic for a SIGN guideline?** Is it a clinical topic, what is the breadth of the topic and is there a need for the guideline as identified in the proposal?	
	Yes, it is an update to an established SIGN guideline.	
2.	**Is there a suitable alternative product which would address this topic?** Would another Healthcare Improvement Scotland product better address the topic?	
	No	
3.	**Has this topic been considered before and rejected?** What were the reasons for rejection and are they still applicable	
	SIGN 107 has already been published. This provides an update to reflect new evidence in migraine.	
4.	**Outcome**	
	Go forward to the next stage of topic selection.	**Yes**
	Reject	

Suitability screen

Purpose: screening by the Guideline Programme Advisory Board to select applications suitable for inclusion in the SIGN topic selection process.

1.	**Is there an owner for the project?** (preferably an individual)
	Yes
2.	**Is this a clinical priority area for NHSScotland?**
	This is a priority area for primary care. Migraine is a large contributor to time off work. There is an issue with people not getting the correct treatment.
3.	**Is there a gap between current and optimal practice? OR Is there wide variation in current practice?** (is this an area of clinical uncertainty)
	There is wide variation in practice between GPs. There is also the problem of self prescription and overuse of codeine.
4.	**Is there a suitable guideline already available that could be adapted?** (not necessarily by SIGN)
	This is an update to a specific section of SIGN 107: Diagnosis and management of headache in adults and will be a stand alone guideline. There are some guidelines from NICE that could be used in the evidence base.
5.	**Is there adequate literature to make an evidence-based decision about appropriate practice?** (is effective treatment proven and would it reduce mortality or morbidity)
	Yes
6.	**Would the proposed practice change result in sufficient change in outcomes** (health status, provider and consumer satisfaction and cost) **to justify the effort?**
	Yes, individuals' day to day functioning should improve (fewer work days lost) and ther be fewer inappropriate referrals (impact on secondary care).
	How big is the gap?
	There is a gap but cannot quantify on available information.
	How much effort will it take to close the gap?
	The proposed guideline would not be difficult to implement through NHS boards and professional bodies.
7.	**Is there a perceived need for the guideline, as indicated by a network of relevant stakeholders?**
	Yes, there are sufficient engaged stakeholders.
8.	**Is there a reasonable likelihood that NHSScotland could implement the change?**
	Yes, see section 6.

9.	**Does the proposer have any conflicts of interest? If so how will these be managed?**	
	There are no conflicts of interest.	
10.	**Outcome**	
	Go forward to the next stage of topic selection	**YES**
	Reject	
11.	**Decision**	
	Ratified by SIGN Council for inclusion on the SIGN guideline development programme	**Date**
	Comment	**10/02/16**

Scope of recent evidence

Resources searched:

GIN + National Guidelines Clearinghouse 11

NICE 6

Cochrane Library 22

CRD databases (includes DARE (49), HTA (8), NHS EED (21), CENTRAL (1056 RCTS)

INAHTA (0)

Medline (to update DARE only) – 25 SRs

Dates searched: 2005- August 2015

Guidelines

AHRQ - Agency for Healthcare Research + Quality. EFNS guideline on the drug treatment of migraine – revised report of an EFNS task force. European Federation of Neurological Societies. NGC:008157. 2009. url: http://www.guideline.gov/content.aspx?id=24517

BACKGROUND:

Migraine is one of the most frequent disabling neurological conditions with a major impact on the patients' quality of life.

OBJECTIVES:

To give evidence-based or expert recommendations for the different drug treatment procedures in the particular migraine syndromes based on a literature search and the consensus of an expert panel.

METHODS:

All available medical reference systems were screened for the range of clinical studies on migraine with and without aura and on migraine-like syndromes. The findings in these studies were evaluated according to the recommendations of the European Federation of Neurological Societies (EFNS) resulting in level A, B, or C recommendations and good practice points.

RECOMMENDATIONS:

For the acute treatment of migraine attacks, oral non-steroidal antiinflammatory drug (NSAID) and triptans are recommended. The administration should follow the concept of stratified treatment. Before intake of NSAID and triptans, oral metoclopramide or domperidone is recommended. In very severe attacks, intravenous acetylsalicylic acid or subcutaneous sumatriptan are drugs of first choice. Status migrainosus can be treated by cortoicosteroids, although this is not universally held to be helpful, or dihydroergotamine. For the prophylaxis of migraine, betablockers (propranolol and metoprolol) flunarizine, valproic acid, and topiramate are drugs of first choice. Drugs of second choice for migraine prophylaxis include amitriptyline, naproxen, petasites, and bisoprolol.

AHRQ - Agency for Healthcare Research + Quality. Canadian Headache Society guideline for migraine prophylaxis. Canadian Headache Society. NGC:009344. 2012. url: http://www.guideline.gov/content.aspx?id=38455

OBJECTIVES:

The primary objective of this guideline is to assist the practitioner in choosing an appropriate prophylactic medication for an individual with migraine, based on current evidence in the medical literature and expert consensus. This guideline is focused on patients with episodic migraine (headache on ≤ 14 days a month).

METHODS:

Through a comprehensive search strategy, randomized, double blind, controlled trials of drug treatments for migraine prophylaxis and relevant Cochrane reviews were identified. Studies were graded according to criteria developed by the US Preventive Services Task Force. Recommendations were graded according to the principles of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group. In addition, a general literature review and expert consensus were used for aspects of prophylactic therapy for which randomized controlled trials are not available.

RESULTS:

Prophylactic drug choice should be based on evidence for efficacy, side-effect profile, migraine clinical features, and co-existing disorders. Based on our review, 11 prophylactic drugs received a strong recommendation for use (topiramate, propranolol, nadolol, metoprolol, amitriptyline, gabapentin, candesartan, butterbur, riboflavin, coenzyme Q10, and magnesium citrate) and 6 received a weak recommendation (divalproex sodium, flunarizine, pizotifen, venlafaxine, verapamil, and lisinopril). Quality of evidence for different medications varied from high to low. Prophylactic treatment strategies were developed to assist the practitioner in selecting a prophylactic drug for specific clinical situations. These strategies included: first time strategies for patients who have not had prophylaxis before (a beta-blocker and a tricyclic strategy), low side effect strategies (including both drug and herbal/vitamin/mineral strategies), a strategy for patients with high body mass index, strategies for patients with co-existent hypertension or with co-existent depression and /or anxiety, and additional monotherapy drug strategies for patients who have failed previous prophylactic trials. Further strategies included a refractory migraine strategy and strategies for prophylaxis during pregnancy and lactation.

CONCLUSIONS:

There is good evidence from randomized controlled trials for use of a number of different prophylactic medications in patients with migraine. Medication choice for an individual patient requires careful consideration of patient clinical features.

Bryans R, Descarreaux M, Duranleau M, Marcoux H, Potter B, Ruegg R, et al. **Evidence-based guidelines for the chiropractic treatment of adults with headache**. 2011. url: http://www.guideline.gov/content.aspx?id=35109

Treatment of Migraine

•Spinal manipulation is recommended for the management of patients with episodic or chronic migraine with or without aura. This recommendation is based on studies that used a treatment frequency 1 to 2 times per week for 8 weeks (evidence level, moderate).

•Weekly massage therapy is recommended for reducing episodic migraine frequency and for improving affective symptoms potentially linked to headache pain (evidence level, moderate).

•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).

•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).

Burgunder JM, Finsterer J, Szolnoki Z, Fontaine B, Baets J, Van Broeckhoven C, et al. **EFNS guidelines on the molecular diagnosis of channelopathies, epilepsies, migraine, stroke, and dementias**. 2010. url: http://www.guideline.gov/content.aspx?id=25709

OBJECTIVES: These EFNS guidelines on the molecular diagnosis of channelopathies, including epilepsy and migraine, as well as stroke, and dementia are designed to summarize the possibilities and limitations of molecular genetic techniques and to provide diagnostic criteria for deciding when a molecular diagnostic work-up is indicated. SEARCH STRATEGY: To collect data about planning, conditions, and performance of molecular diagnosis of these disorders, a literature search in various electronic databases was carried out and original papers, meta-analyses, review papers, and guideline recommendations were reviewed. RESULTS: The best level of evidence for genetic testing recommendation (B) can be found for a small number of syndromes, cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy, severe myoclonic epilepsy of infancy, familial recurrent hemorrhages, familial Alzheimer's disease, and frontotemporal lobar degeneration. Good practice points can be formulated for a number of other disorders. CONCLUSION: These guidelines are provisional, and the future availability of molecular genetic epidemiological data about the neurogenetic disorders under discussion in our article will allow improved recommendation with an increased level of evidence.

Economics Ioh. **Guideline for Primary Care Management of Headache in Adults**. 2012. url: http://www.topalbertadoctors.org/file/guideline-for-primary-care-management-of-headache-in-adults.pdf

Objectives

•To help Alberta clinicians make evidence-informed decisions about the care of adult patients (aged 18 years or older) with headache

•To increase the use of evidence-informed approaches to the prevention, assessment, diagnosis, and treatment of headache for patients in primary care

•To promote appropriate specialist referrals and use of diagnostic tests in patients with headache

•To encourage patients to engage in appropriate self-care

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.** 2012. url: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3335449/

OBJECTIVE: To provide updated evidence-based recommendations for the preventive treatment of migraine headache. The clinical question addressed was: Are nonsteroidal anti-inflammatory drugs (NSAIDs) or other complementary treatments effective for migraine prevention? METHODS: The authors analyzed published studies from June 1999 to May 2009 using a structured review process to classify the evidence relative to the efficacy of various medications for migraine prevention. RESULTS: The author panel reviewed 284 abstracts, which ultimately yielded 49 Class I or Class II articles on migraine prevention; of these 49, 15 were classified as involving nontraditional therapies, NSAIDs, and other complementary therapies that are reviewed herein. RECOMMENDATIONS: Petasites (butterbur) is effective for migraine prevention and should be offered to patients with migraine to reduce the frequency

and severity of migraine attacks (Level A). Fenoprofen, ibuprofen, ketoprofen, naproxen, naproxen sodium, MIG-99 (feverfew), magnesium, riboflavin, and subcutaneous histamine are probably effective for migraine prevention (Level B). Treatments considered possibly effective are cyproheptadine, Co-Q10, estrogen, mefenamic acid, and flurbiprofen (Level C). Data are conflicting or inadequate to support or refute use of aspirin, indomethacin, omega-3, or hyperbaric oxygen for migraine prevention. Montelukast is established as probably ineffective for migraine prevention (Level B).

Improvement IfCS. **Diagnosis and Treatment of Headache**. 2013. url: https://www.icsi.org/_asset/qwrznq/Headache.pdf

Objectives

•To increase the accurate diagnosis of primary headaches in patients age 12 years and older

•To increase the percentage of patients with primary headache diagnosis who receive educational materials about headache

•To increase the percentage of patients with primary headache syndrome who receive prophylactic treatment

•To increase the percentage of patients with migraine headache who have improvement in their functional status

•To increase the percentage of patients with migraine headache who have a treatment plan or report adherence to a treatment plan

•To decrease the percentage of patients with migraine headache who are prescribed opiates and barbiturates for the treatment of migraines to less than 5%

•To increase the percentage of patients with migraine headache who have appropriate acute treatment

NICE. **Percutaneous closure of patent foramen ovale for recurrent migraine**. 2010. url: http://www.nice.org.uk/guidance/ipg370

The foramen ovale is a hole in the wall that divides the two upper chambers of the heart. The hole is present in the heart of a developing fetus, but normally closes up soon after the baby is born. If it fails to close it is known as a patent foramen ovale (PFO). In most people, this doesn't cause any problems but some studies have suggested that there could be a link between having a PFO and recurrent migraines. This procedure involves passing a device through a large vessel in the groin up into the heart and closing/blocking the hole in the wall of the heart.

NICE. **Botulinum toxin type A for the prevention of headaches in adults with chronic migraine**. 2012. url: http://www.nice.org.uk/guidance/ta260

NICE recommends botulinum toxin type A as a possible treatment for preventing headaches in some adults with chronic migraine (see below).

Who can have botulinum toxin type A?

You should be able to have botulinum toxin type A if you have chronic migraine (that is, you have headaches on at least 15 days each month, with migraine on at least 8 of these days) and:

•you have already tried at least three different drug treatments to prevent your chronic migraine headaches, but these have not worked and

•you are not taking too many painkillers or using them too often.

Botulinum toxin type A treatment should be stopped if:

•the number of days you have a chronic migraine headache each month hasn't reduced by at least 30% after two courses of botulinum toxin type A treatment or

•your chronic migraine changes to episodic migraine (that is, you have fewer than 15 days with headaches each month) for 3 months in a row.

Why has NICE said this?

NICE looks at how well treatments work, and also at how well they work in relation to how much they cost the NHS. In clinical trials, botulinum toxin type A treatment was shown to reduce the severity of chronic migraine headaches and how often they occur. The cost of botulinum toxin type A treatment is justified by the benefits it provides.

NICE. **Headaches: Diagnosis and management of headaches in young people and adults**. 2012. url: http://www.nice.org.uk/guidance/cg150

This guideline offers evidence-based advice on the diagnosis and management of tension-type headache, migraine (including migraine with aura and menstrual-related migraine), cluster headache and medication overuse headache in young people (aged 12 years and older) and adults

NICE. **Occipital nerve stimulation for intractable chronic migraine**. 2013. url: http://www.nice.org.uk/guidance/ipg452

A migraine is a severe headache usually felt as a throbbing pain at the front or on one side of the head. Some people also have other symptoms, such as nausea and sensitivity to light. Occipital nerve stimulation involves implanting electrodes, an impulse generator and connecting insulated wires under the skin. The electrodes are implanted near the occipital nerve located just beneath the skin at the back of the head and the impulse generator is usually implanted at a site in the torso. The patient uses a remote control to deliver electrical impulses to the occipital nerve with the aim of masking the pain.

NICE. **Migraine prophylaxis: flunarizine** [ESUOM33]. 2014. url: http://www.nice.org.uk/advice/esuom33/chapter/Key-points-from-the-evidence

Flunarizine is a calcium channel blocker that reduces smooth muscle spasm. Overall, the studies included in this evidence summary suggest that flunarizine is as effective as propranolol or topiramate at reducing the frequency of migraines in adults. In children, flunarizine was more effective than placebo at reducing migraine frequency, and as effective as nimodipine, aspirin, propranolol or dihydroergotamine. However, all of the studies in children were small and of poor quality. The most common adverse effect of flunarizine is weight gain.

Regulatory status: unlicensed. This topic was prioritised because of the potential clinical impact of long-term prescribing in primary care

NICE. **Transcranial magnetic stimulation for treating and preventing migraine**. 2014. url: http://www.nice.org.uk/guidance/ipg477

Migraine is a common condition characterised by recurrent, pulsatile, unilateral or bilateral headaches that can last for hours to days and are often accompanied by nausea, and sensitivity to light and sound. Migraine headache may be preceded by an aura, which can include visual or olfactory disturbances, or difficulties with speech (dysphasia). The second edition of International Classification of Headache Disorders (International Headache Society 2004) provides a classification of migraine types.

Current treatment for migraine aims to prevent or stop episodes and manage symptoms with drugs such as triptans, analgesics and anti-emetics (as recommended in Headaches: diagnosis and management of headaches in young people and adults [NICE clinical guideline 150]). Other treatments include nerve blocks, botulinum toxin type A injections (as recommended in Botulinum toxin type A for the prevention of headaches in adults with chronic migraine [NICE technology appraisal guidance 260]) or acupuncture.

Radiology ACo. **ACR Appropriateness Criteria® headache — child**. 2012. url: https://acsearch.acr.org/docs/69439/Narrative/

•Primary headache

•No imaging is indicated for typical migraine.

•In ophthalmologic migraine with focal neurologic symptoms of unilateral ptosis or complete third-nerve palsy, MRI is recommended.

•MRI is also recommended for patients with miscellaneous findings such as vertigo, basilar artery migraine syndrome, persistent confusion migraine syndrome, progressive chronic headache, or hemiplegic migraine.

•MRI should be performed for patients with seizures and postictal headaches.

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**. 2012. url:

http://www.neurology.org/content/78/17/1337.full.pdf+html

OBJECTIVE: To provide updated evidence-based recommendations for the preventive treatment of migraine headache. The clinical question addressed was: What pharmacologic therapies are proven effective for migraine prevention? METHODS: The authors analyzed published studies from June 1999 to May 2009 using a structured review process to classify the evidence relative to the efficacy of various medications available in the United States for migraine prevention. RESULTS AND RECOMMENDATIONS: The author panel reviewed 284 abstracts, which ultimately yielded 29 Class I or Class II articles that are reviewed herein. Divalproex sodium, sodium valproate, topiramate, metoprolol, propranolol, and timolol are effective for migraine prevention and should be offered to patients with migraine to reduce migraine attack frequency and severity (Level A). Frovatriptan is effective for prevention of menstrual migraine (Level A). Lamotrigine is ineffective for migraine prevention (Level A).

Health Technology Assessments

Are homeopathic remedies clinically and cost effective in the treatment of migraine and osteoarthritis? (Structured abstract). Health Technology Assessment Database. 2014; 3. [cited: url: http://www.healthcareimprovementscotland.org/our_work/technologies_and_medicines/shtg_-_evidence_notes/evidence_note_53.aspx

Published systematic reviews of homeopathy for migraine and osteoarthritis provide limited evidence on clinical effectiveness compared with standard care.

Homeopathy for migraine has not been compared with active treatment in randomised controlled trials (RCTs), and only one of four RCTs found homeopathy to be superior to placebo.

In three RCTs, drug treatments for osteoarthritis had similar or better effects on pain than homeopathic remedies, and in one RCT homeopathy had a similar effect to hyaluronic acid injection.

Published systematic reviews of homeopathy for migraine and osteoarthritis contain insufficient information to inform conclusions about safety.

No evidence on the cost effectiveness of homeopathy for migraine was identified; and the evidence from a single cost-minimisation analysis of one homeopathic preparation for osteoarthritis is not generalisable to the United Kingdom (UK).

There is a need for higher quality research to reliably inform decisions on the provision of homeopathy services

Cadth. **Triptans for migraine headaches: a review of clinical evidence on safety** (Structured abstract). Health Technology Assessment Database. 2012; 3. [cited: url: https://www.cadth.ca/media/pdf/htis/mar-2012/RC0333%20Triptans%20Final.pdf

RESEARCH QUESTION

What is the clinical evidence on the safety and harms of triptans for migraine headaches?

KEY MESSAGE

While no consistent differences were found between triptans in the rates of overall AEs, a small number of studies suggest oral, intranasal and subcutaneous sumatriptan are associated with chest pain and tachycardia. The most common AEs include dizziness, drowsiness, paresthesia, nausea and fatigue. One study suggests that providing a clinical limit of 27 rizatriptan ODT 10 mg/month did not reduce the number of migraine days compared with providing a formulary limit of 9 tablets per month. Regardless of quantity, rizatriptan ODT 10 mg was well tolerated as AEs were similar between groups.

Cadth. **Maxillary artery ligation for the treatment of cluster or migraine headaches: clinical effectiveness and guidelines** (Structured abstract). Health Technology Assessment Database. 2014; 3. [cited: url: https://www.cadth.ca/media/pdf/htis/jan-2014/RB0638%20MAL%20for%20Cluster%20Headaches%20Final.pdf

RESEARCH QUESTIONS

1. What is the clinical effectiveness of maxillary artery ligation for the treatment of cluster or migraine headaches?

2. What are the evidence-based guidelines regarding the use of maxillary artery ligation for the treatment of cluster or migraine headaches?

KEY MESSAGE

One relevant non-randomized study regarding the use of maxillary artery ligation for the treatment of cluster headaches was identified. No relevant health technology assessment reports, systematic reviews, meta-analyses, randomized controlled trials, or evidence-based guidelines were identified.

OVERALL SUMMARY OF FINDINGS

The identified non-randomized study examined the use of an intraoral technique for maxillary artery cauterization and cauterization of the terminal branches of the external carotid artery in five patients with cluster headaches.1 Limited detail is provided in the abstract beyond the statement that four of the five patients experienced cessation of cluster headache attacks following the surgery.

Cadth. **OnabotulinumtoxinA (Botox - Allergan Inc.) indication: chronic migraine** (Structured abstract). Health Technology Assessment Database. 2014; 3. [cited: url: https://www.cadth.ca/media/cdr/complete/SR0345_complete_Botox-May-30-14.pdf

Recommendation:

The Canadian Drug Expert Committee (CDEC) recommends that onabotulinumtoxinA (OA) not be listed for the management of chronic migraine.

Reason for the Recommendation:

1. Two randomized controlled trials (RCTs) (PREEMPT-1 and PREEMPT-2) demonstrated that OA was statistically superior to placebo for improving health-related quality of life and reducing the number of headache days and migraine/probable migraine days in patients with chronic migraine; however, the absolute difference between the OA and placebo groups was relatively small for this chronic condition (range of –1.4 to –2.3 headache days per 28-day period and –1.6 to –2.3 migraine/probable migraine per 28-day period).

2. There were significant limitations with the design of the PREEMPT-1 and PREEMPT-2 trials, such as the potential inclusion of patients with medication overuse headache, which precludes an accurate assessment of the clinical benefits of OA in the management of chronic migraine.

Jefferson T, Migliore A, Abraha I,Montedori A**. Implantable devices for the closure of patent foramen ovale (PFO) in adults: rapid HTA report** (Structured abstract). Health Technology Assessment Database. 2013; 3. [cited: url: http://www.agenas.it/images/agenas/hta/report_hta/Rapid_HTA_Report_PFO_.pdf

Percutaneous closure of patent foreman ovale (PFO) is one of the treatment options for patients with PFO suffering from transient ischemic attacks (TIA), cryptogenic stroke or persistent migraine. At time of writing, none of the several CE marked PFO closure devices have been approved by the US Food and Drug Administration (FDA). Currently there are 12 different PFO closure devices available on the Italian market and it has been estimated, that in 2012, 2,541 PFO procedures were performed. The price for a single PFO closure device ranged from € 5,535 to € 6,868 (excluding VAT), resulting in an estimated impact on the Servizio Sanitario Nazionale (SSN) budget of € 15 millions in 2012. We performed a systematic review and a meta-analysis of clinical studies in which patients with PFO suffering from TIAs, cryptogenic stroke or persistent migraine underwent insertion of percutaneous devices for the closure of PFO were compared to patients treated by usual care. We included 6 primary studies: 5 controlled clinical trials (CCT), and 1 randomised controlled trial (RCT). In the 5 CCTs we found that percutaneous closure of PFO was better than medical treatment in reducing stroke, TIA or the combination of both even if in the presence of significant heterogeneity. Poor methodological study quality and heterogeneity undermines our confidence in the results of this review. We attempted to stratify by device type the overall pooling of study data but it resulted in loss of power and further fragmentation of the evidence base. The safety profile of the technology appears to be of concern, in that 4.7% of device- or procedure-related serious adverse events were observed in the only RCT included. We recommend that large multicentre, sufficiently powered, and properly randomised trials be carried out in Europe with particular attention to patient selection and risk/benefit ratio.

Shamliyan TA, Kane RL, Ramakrishnan R,Taylor FR. **Migraine in children: preventive pharmacologic treatments** (Structured abstract). Health Technology Assessment Database. 2013; 3. [cited: url: http://www.effectivehealthcare.ahrq.gov/ehc/products/313/1515/migraine-children-report-130524.pdf

Objectives. To assess the comparative effectiveness and safety of preventive pharmacologic treatments for community-dwelling children with episodic or chronic migraine.

Data sources. We searched major electronic bibliographic databases, including Medline® and Cochrane Central Register of Controlled Trials, and trial registries up to May 20, 2012.

Review methods. We performed a systematic review of original studies published in English that examined episodic or chronic migraine and rates of complete cessation or reduction of monthly migraine frequency by ≥50 percent, reduction in migraine-related disability, and improvement in quality of life with off-label drugs. (No preventive drugs were approved in children.) Also eligible were studies that compared drugs with nonpharmacologic intervention or drug management programs. We calculated absolute risk differences, pooled them with random-effects models, and calculated numbers of outcome events attributable to treatment effects per 1,000 treated.

Results. Prevention of episodic migraine in children was examined in 24 publications of randomized controlled trials (RCTs) that enrolled 1,578 children and in 16 nonrandomized studies. Evidence was low strength due to risk of bias and imprecision. Propranolol was estimated to result in complete cessation of migraine attacks in 713 per 1,000 children treated (95-percent confidence interval [CI], 452 to 974) (one RCT). Trazodone (one RCT) and nimodipine (one RCT) decreased migraine days more effectively than placebo. Topiramate (two RCTs), divalproex (one RCT), and clonidine (one RCT) were no more effective than placebo in preventing migraine. Sodium valproate demonstrated no significant differences for migraine prevention or migraine-related disability compared with propranolol (two RCTs) or topiramate (one RCT). Metoprolol

tended to be less effective than stress management in preventing migraine or reducing migraine severity (one RCT). Propranolol had less effect than self-hypnosis on absolute number of migraine attacks (one RCT). Multidisciplinary drug management was more effective than usual care in preventing migraine in children and adolescents (one RCT), but the effect was not sustained at 6 months. Divalproex sodium (one RCT) resulted in treatment discontinuation due to adverse effects more often than placebo. Treatment discontinuation due to adverse effects did not differ between topiramate (two RCTs), trazodone (one RCT), propranolol (one RCT), or clonidine (one RCT) and placebo. Topiramate increased risk of paresthesia, upper respiratory tract infection, and weight loss. No RCTs examined prevention of chronic migraine in children.

Conclusions. Limited low-strength evidence suggests that propranolol was more effective than placebo for preventing episodic migraine in children, with no bothersome adverse effects that could lead to treatment discontinuation. Long-term preventive benefits are unknown both for drugs and nonpharmacologic interventions. No studies examined quality of life or provided evidence for individualized treatment decisions. Future randomized trials of drugs with favorable benefits-to-harms ratio in adults are needed to identify effective and safe treatments to prevent episodic and chronic migraine in children

Shamliyan TA, Kane RL,Taylor FR. **Migraine in adults: preventive pharmacologic treatments** (Structured abstract). Health Technology Assessment Database. 2013; 3. [cited: url: http://www.effectivehealthcare.ahrq.gov/ehc/products/313/1453/migraine-report-130408.pdf

Objectives. To assess comparative effectiveness and safety of preventive pharmacologic treatments for community-dwelling adults with episodic or chronic migraine.

Data sources. We searched major electronic bibliographic databases and trial registries up to May 20, 2012.

Review methods. We performed a systematic review of published, English-language original studies of pharmacologic treatments for prevention of episodic or chronic migraine. Studies that compared drugs with inactive controls, nonpharmacologic interventions, or other drugs were eligible. Outcomes evaluated included rates of complete migraine cessation, ≥50 percent reduction in monthly migraine frequency, reduction in migraine-related disability, and improvement in quality of life. We calculated absolute risk differences, pooled them with random-effects models and with Bayesian network meta-analysis, and calculated numbers of outcome events attributable to treatments per 1,000 participants treated.

Results. Of 5,244 retrieved references, 245 publications of randomized controlled clinical trials (RCTs) and 76 publications of nonrandomized therapeutic studies met eligibility criteria. Most enrollees were middle-aged Caucasian women, with an average of five monthly migraine attacks. Few trials reported the proportion of obese subjects, but many subjects were overweight. More than half of the RCTs defined migraine according to the International Headache Society criteria. Studies excluded adults with severe medical or psychiatric illnesses or contraindications to examined drugs. Strength of evidence was mostly low due to risk of bias and imprecision in individual RCTs and pooled estimates.

For chronic migraine, botulinum toxin formulations were examined in 20 RCTs of 4,237 adults. Onabotulinumtoxin A was more effective than placebo in reducing monthly chronic migraine attacks by ≥50 percent (low-strength evidence from 3 RCTs of 459 adults) with inconsistent improvement in quality of life. Pooled analyses demonstrated that per 1,000 treated adults, 170 (95% confidence interval [CI], 82 to 258) would experience ≥50 percent reduction in migraine frequency, 155 (95% CI, 90 to 220) would experience adverse effects, and 26 (95% CI, 10 to 43) would discontinue treatments due to bothersome adverse effects. Topiramate reduced disability in patients with chronic migraine but failed to decrease monthly migraine frequency by ≥50 percent (low-strength evidence from one RCT of 328 adults). Individual RCTs examined the comparative effectiveness of onabotulinumtoxin A with topiramate or divalproex and found no differences in chronic migraine prevention. Propranolol combined with topiramate treatment demonstrated no benefits in nonresponders to topiramate monotherapy (low-strength evidence from one RCT of 191 adults).

For episodic migraine, RCTs examined 59 drugs from 14 drug classes. All approved drugs (topiramate, divalproex, timolol, and propranolol), some off-label beta blockers, ACE inhibitors, and the angiotensin II receptor antagonist candesartan were better than placebo in reducing episodic monthly migraine frequency by ≥50 percent. Drugs would result in clinical improvement in 200 to 400 patients per 1,000 treated. Adverse effects leading to treatment discontinuation were examined in 68 RCTs. Topiramate, off-label antiepileptics, and antidepressants resulted in bothersome adverse effects leading to treatment discontinuation more often than placebo.

Limited direct evidence of comparative effectiveness from head-to-head RCTs demonstrated no consistent significant differences in outcomes with examined drugs in patients with episodic migraine. Exploratory indirect adjusted frequentist analysis offered low-strength evidence that the angiotensin II receptor blocker candesartan was more effective than approved drugs including topiramate, propranolol, timolol, and divalproex. Exploratory network Bayesian metaanalysis offered low-strength evidence that angiotensin inhibiting drugs (captopril, lisinopril, candesartan) were the most effective and tolerable for episodic migraine prevention in adults who have no contraindications to examined drugs.

Individual RCTs of drug-management interventions for episodic migraine offered low-strength evidence that compared with usual care, multidisciplinary team care improved quality of life and reduced migraine-related disability; a headache management program resulted in complete cessation of migraine; a minimal-contact cognitive-behavioral program improved patient satisfaction with treatments; headache school decreased overuse of drugs for acute headache attacks and reduced migraine disability; pharmaceutical care improved self-efficacy; and an intensive pharmaceutical care campaign had no statistically significant impact on use of acute drugs.

Conclusions. For chronic migraine, onabotulinumtoxin A reduced migraine attacks but increased the risk of adverse effects and treatment discontinuation due to adverse effects. For episodic migraine, approved drugs are effective but increase risk of adverse effects and treatment discontinuation due to adverse effects. Some off-label beta blockers and angiotensin inhibiting drugs are effective without bothersome harms and therefore offer the best benefits-to-harms ratio. We could not determine the long-term (i.e., trials of more than 3 months' duration), preventive benefits and adherence with drugs. Evidence on improving quality of life was inconsistent across individual drugs. Evidence for individualized treatment decisions is very limited. Future research should examine the role of patient characteristics on drug benefits and safety.

Sumamo Schellenberg E, Dryden DM, Pasichnyk D, Ha C, Vandermeer B, Friedman BW, et al. **Acute migraine treatment in emergency settings** (Structured abstract). Health Technology Assessment Database. 2012; 3. [cited: url: http://effectivehealthcare.ahrq.gov/ehc/products/289/1323/CER84_Migraine_FinalReport_20121119.pdf

Objectives. To compare the effectiveness and safety of parenteral pharmacological interventionsto treat migraine headaches in adults presenting to the emergency department (ED).

Data sources. In consultation with a librarian, we searched 10 electronic databases, conferenceproceedings, clinical trials registers, and reference lists.

Methods. Two reviewers independently selected studies, assessed risk of bias, extracted data,and graded the strength of evidence (SOE). Data were pooled using a random-effects model. Amixed-treatment analysis was performed for pain relief and akathisia.

Results. Nine classes of drugs were investigated in 71 controlled trials. Risk of bias was low for28 percent of the trials, unclear for 61 percent, and high for 11 percent. Overall, activeinterventions were more effective than placebo for pain relief and headache recurrence. Mosthead-to-head comparisons for pain reduction were based on single trials resulting in insufficientSOE. The mixed-treatment analysis showed that the most effective treatments were combinationtherapy (i.e., dihydroergotamine [DHE] added to either neuroleptics or metoclopramide) orneuroleptic monotherapy (low SOE), with a pain reduction of approximately 40 mm on a visualanalog scale (VAS). Metoclopramide monotherapy, opioids, and nonsteroidal antiinflammatories

(NSAIDs) were the next most effective treatments, with a pain reduction of approximately 24 mm (low SOE). Other agents (e.g., DHE, triptans, orphan agents) were less effective, with a pain reduction of approximately 12-16 mm. Short-term side effects were infrequent, and considered minor and self-limiting. No two studies reported the same side effects for the same pair of interventions; therefore, the SOE is insufficient to conclude which treatment results in more or fewer adverse effects. Based on the mixed-treatment analysis, the odds of experiencing akathisia symptoms following administration of metoclopramide or neuroleptic agents were 9.4 and 10.7 times greater than with placebo, respectively. The risk of sedation following administration of metoclopramide or neuroleptic agents was 17 percent. The most common short-term side effects for triptans were skin reactions, local reactions, and sedation. For patients receiving DHE, the most common side effects were skin and local reactions, sedation, digestive issues, nausea or vomiting, and chest symptoms. Few side effects were reported for NSAIDS or opioids. In patients receiving magnesium sulfate, high rates of skin flushing and local reactions were reported.

The available evidence failed to identify variable responsiveness based on subgroups. Migraine relapse can be prevented with intravenous systemic corticosteroids provided in the ED, particularly in patients with prolonged headaches (>72 hours).

Conclusion. Many agents are effective in the treatment of acute migraine headache when compared with placebo. Several treatments provide insufficient evidence for continued use. Neuroleptic monotherapy and DHE in combination with either metoclopramide or neuroleptics appear to be the most effective options for pain relief (VAS). Systemic corticosteroids effectively prevent headache relapse, especially in patients with prolonged headaches. More research is required to identify the most effective parenteral treatments for adults with acute migraine

Cochrane reviews

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. [cited: url: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002919.pub3/abstract

Background: This is an updated version of the original Cochrane review published in 2005 on selective serotonin reuptake inhibitors (SSRIs) for preventing migraine and tension-type headache. The original review has been split in two parts and this review now only regards migraine prevention. Another updated review is under development to cover tension-type headache.Migraine is a common disorder. The chronic forms are associated with disability and have a high economic impact. In view of discoveries about the role of serotonin and other neurotransmitters in pain mechanisms, selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) have been evaluated for the prevention of migraine.Objectives: To determine the efficacy and tolerability of SSRIs and SNRIs compared to placebo and other active interventions in the prevention of episodic and chronic migraine in adults.Search methods: For the original review, we searched MEDLINE (1966 to January 2004), EMBASE (1994 to May 2003), the Cochrane Central Register of Controlled Trials (CENTRAL 2003, Issue 4), and Headache Quarterly (1990 to 2003). For this update, we applied a revised search strategy to reflect the broader type of intervention (SSRIs and SNRIs). We searched CENTRAL (2014, Issue 10), MEDLINE (1946 to November 2014), EMBASE (1980 to November 2014), and PsycINFO (1987 to November 2014). We also checked the reference lists of retrieved articles and searched trial registries for ongoing trials.Selection criteria: We included randomised controlled trials comparing SSRIs or SNRIs with any type of control intervention in participants 18 years and older of either sex with migraine.Data collection and analysis: Two authors independently extracted data (migraine frequency, index, intensity, and duration; use of symptomatic/analgesic medication; days off work; quality of life; mood improvement; cost-effectiveness; and adverse events) and assessed the risk of bias of trials. The primary outcome of this updated review is

migraine frequency.Main results: The original review included eight studies on migraine. Overall, we now include 11 studies on five SSRIs and one SNRI with a total of 585 participants. Six studies were placebo-controlled, four compared a SSRI or SNRI to amitriptyline, and one was a head-to-head comparison (escitalopram versus venlafaxine). Most studies had methodological or reporting shortcomings (or both): all studies were at unclear risk of selection and reporting bias. Follow-up rarely extended beyond three months. The lack of adequate power of most of the studies is also a major concern.Few studies explored the effect of SSRIs or SNRIs on migraine frequency, the primary endpoint. Two studies with unclear reporting compared SSRIs and SNRIs to placebo, suggesting a lack of evidence for a difference. Two studies compared SSRIs or SNRIs versus amitriptyline and found no evidence for a difference in terms of migraine frequency (standardised mean difference (SMD) 0.04, 95% confidence interval (CI) -0.72 to 0.80; I2 = 72%), or other secondary outcomes such as migraine intensity and duration.SSRIs or SNRIs were generally more tolerable than tricyclics. However, the two groups did not differ in terms of the number of participants who withdrew due to adverse advents or for other reasons (one study, odds ratio (OR) 0.39, 95% CI 0.10 to 1.50 and OR 0.42, 95% CI 0.13 to 1.34).We did not find studies comparing SSRIs or SNRIs with pharmacological treatments other than antidepressants (e.g. antiepileptics and anti-hypertensives).Authors' conclusions: Since the last version of this review, the new included studies have not added high quality evidence to support the use of SSRIs or venlafaxine as preventive drugs for migraine. There is no evidence to consider SSRIs or venlafaxine as more effective than placebo or amitriptyline in reducing migraine frequency, intensity, and duration over two to three months of treatment. No reliable information is available at longer-term follow-up. Our conclusion is that the use of SSRIs and SN Is for migraine prophylaxis is not supported by evidence.

Bennett Michael H, French C, Schnabel A, Wasiak J,Kranke P. Normobaric and hyperbaric oxygen therapy for migraine and cluster headache. Cochrane Database of Systematic Reviews. 2008; 3. [cited: url: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD005219.pub2/abstract

Background: Migraine and cluster headaches are severe and disabling. Migraine affects up to 18% of women, while cluster headaches are much less common (0.2% of the population). A number of acute and prophylactic therapies are available. Hyperbaric oxygen therapy (HBOT) is the therapeutic administration of 100% oxygen at environmental pressures greater than one atmosphere, while normobaric oxygen therapy (NBOT) is oxygen administered at one atmosphere.Objectives: To assess the safety and effectiveness of HBOT and NBOT for treating and preventing migraine and cluster headaches.Search methods: We searched the following in May 2008: CENTRAL, MEDLINE, EMBASE, CINAHL, DORCTIHM and reference lists from relevant articles. Relevant journals were hand searched and researchers contacted.Selection criteria: Randomised trials comparing HBOT or NBOT with one another, other active therapies, placebo (sham) interventions or no treatment in patients with migraine or cluster headache.Data collection and analysis: Three reviewers independently evaluated study quality and extracted data.Main results: Nine small trials involving 201 participants were included. Five trials compared HBOT versus sham therapy for acute migraine, two compared HBOT to sham therapy for cluster headache and two evaluated NBOT for cluster headache.Pooling of data from three trials suggested that HBOT was effective in relieving migraine headaches compared to sham therapy (relative risk (RR) 5.97, 95% confidence interval (CI) 1.46 to 24.38, P = 0.01). There was no evidence that HBOT could prevent migraine episodes, reduce the incidence of nausea and vomiting or reduce the requirement for rescue medication. There was a trend to better outcome in a single trial evaluating HBOT for the termination of cluster headache (RR 11.38, 95% CI 0.77 to 167.85, P = 0.08), but this trial had low power.NBOT was effective in terminating cluster headache compared to sham in a single small study (RR 7.88, 95% CI 1.13 to 54.66, P = 0.04), but not superior to ergotamine administration in another small trial (RR 1.17, 95% CI 0.94 to 1.46, P = 0.16). Seventy-six per cent of patients responded to NBOT in these two trials.No serious adverse effects of HBOT or NBOT were reported.Authors' conclusions: There was some evidence that HBOT was effective for the termination of acute migraine in an unselected population, and weak evidence that NBOT was similarly effective in cluster headache. Given the cost and poor availability of HBOT, more research should be done on patients unresponsive to standard therapy. NBOT is cheap, safe and easy to apply, so will probably continue to be

used despite the limited evidence in this review.

Bird S, Derry S,Moore RA. Zolmitriptan for acute migraine attacks in adults. Cochrane Database of Systematic Reviews. 2014; 5. [cited: url: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008616.pub2/abstract

Background: Migraine is a common, disabling condition and a burden for the individual, health services, and society. Zolmitriptan is an abortive medication for migraine attacks, belonging to the triptan family. These medicines work in a different way to analgesics such as paracetamol and ibuprofen.Objectives: To determine the efficacy and tolerability of zolmitriptan compared to placebo and other active interventions in the treatment of acute migraine attacks in adults.Search methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library, MEDLINE, EMBASE, and the Oxford Pain Relief Database, together with three online databases (www.astrazenecaclinicaltrials.com, www.clinicaltrials.gov, and apps.who.int/trialsearch) for studies to 12 March 2014. We also searched the reference lists of included studies and relevant reviews.Selection criteria: We included randomised, double-blind, placebo- or active-controlled studies, with at least 10 participants per treatment arm, using zolmitriptan to treat a migraine headache episode.Data collection and analysis: Two review authors independently assessed trial quality and extracted data. We used numbers of participants achieving each outcome to calculate risk ratios and numbers needed to treat for an additional beneficial effect (NNT) or harmful effect (NNH) compared with placebo or a different active treatment.Main results: Twenty-five studies (20,162 participants) compared zolmitriptan with placebo or an active comparator. The evidence from placebo-controlled studies was of high quality for all outcomes except 24 hour outcomes and serious adverse events where only limited data were available. The majority of included studies were at a low risk of performance, detection and attrition biases, but did not adequately describe methods of randomisation and concealment.Most of the data were for the 2.5 mg and 5 mg doses compared with placebo, for treatment of moderate to severe pain. For all efficacy outcomes, zolmitriptan surpassed placebo. For oral zolmitriptan 2.5 mg versus placebo, the NNTs were 5.0, 3.2, 7.7, and 4.1 for pain-free at two hours, headache relief at two hours, sustained pain-free during the 24 hours postdose, and sustained headache relief during the 24 hours postdose, respectively. Results for the oral 5 mg dose were similar to the 2.5 mg dose, while zolmitriptan 10 mg was significantly more effective than 5 mg for pain-free and headache relief at two hours. For headache relief at one and two hours and sustained headache relief during the 24 hours postdose, but not pain-free at two hours, zolmitriptan 5 mg nasal spray was significantly more effective than the 5 mg oral tablet.For the most part, adverse events were transient and mild and were more common with zolmitriptan than placebo, with a clear dose response relationship (1 mg to 10 mg).High quality evidence from two studies showed that oral zolmitriptan 2.5 mg and 5 mg provided headache relief at two hours to the same proportion of people as oral sumatriptan 50 mg (66%, 67%, and 68% respectively), although not necessarily the same individuals. There was no significant difference in numbers experiencing adverse events. Single studies reported on other active treatment comparisons but are not described further because of the small amount of data.Authors' conclusions: Zolmitriptan is effective as an abortive treatment for migraine attacks for some people, but is associated with increased adverse events compared to placebo. Zolmitriptan 2.5 mg and 5 mg benefited the same proportion of people as sumatriptan 50 mg, although not necessarily the same individuals, for headache relief at two hours.

Chronicle Edward P,Mulleners Wim M. Anticonvulsant drugs for migraine prophylaxis. Cochrane Database of Systematic Reviews. 2004; 3. [cited: url: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003226.pub2/abstract

Background: This review has been split and updated in a series of four new reviews, all with the author byline Linde M, Mulleners WM, Chronicle EP, McCrory DC. The new titles are:1. Topiramate for the

prophylaxis of episodic migraine in adults. Cochrane Database of Systematic Reviews 2013, Issue 6. Art. No.: CD010610. DOI: 10.1002/14651858.CD010610.2. Valproate (valproic acid or sodium valproate or a combination of the two) for the prophylaxis of episodic migraine in adults. Cochrane Database of Systematic Reviews 2013, Issue 6. Art. No.: CD010611. DOI: 10.1002/14651858.CD010611.3. Gabapentin or pregabalin for the prophylaxis of episodic migraine in adults. Cochrane Database of Systematic Reviews 2013, Issue 6. Art. No.: CD010609. DOI: 10.1002/14651858.CD010609.4. Antiepileptics other than gabapentin, pregabalin, topiramate, and valproate for the prophylaxis of episodic migraine in adults. Cochrane Database of Systematic Reviews 2013, Issue 6. Art. No.: CD010608. DOI: 10.1002/14651858.CD010608.Readers are referred to those reviews for updated results.Anticonvulsant drugs seem to be useful in clinical practice for the prophylaxis of migraine. This might be explained by a variety of actions of these drugs in the central nervous system.Objectives: To describe and assess the evidence from controlled trials on the efficacy and tolerability of anticonvulsants for preventing migraine attacks in adult patients with migraine.Search methods: We searched PubMed (1966-December 2005), EMBASE (1974-December 2005) and the Cochrane Central Register of Controlled Trials (CENTRAL, Issue 3, 2005), and handsearched Headache and Cephalalgia through April 2006.Selection criteria: Studies were required to be prospective, controlled trials of anticonvulsant drugs taken regularly to prevent the occurrence of migraine attacks and/or to reduce the intensity of those attacks.Data collection and analysis: Studies were selected and data extracted by two independent reviewers. For migraine frequency data, standardized mean differences (SMDs) were calculated for individual studies and pooled across studies. For dichotomous data on significant reduction in migraine frequency, odds ratios (ORs) and numbers-needed-to-treat (NNTs) were similarly calculated. Adverse events were analyzed by calculating numbers-needed-to-harm (NNHs) for studies using similar agents.Main results: Twenty-three papers met the inclusion criteria. In total, data from 2927 patients were considered. Analysis of data from 10 trials (n = 902) demonstrates that anticonvulsants, considered as a class, reduce migraine frequency by about 1.3 attacks per 28 days as compared to placebo (WMD -1.31; 95% confidence interval [CI] -1.99 to -0.63). Data from 13 trials (n = 1773) show that anticonvulsants, considered as a class, also more than double the number of patients for whom migraine frequency is reduced by 50% or more relative to placebo (RR 2.25; 95% CI 1.79 to 2.84; NNT 3.9; 95% CI 3.4 to 4.7). For six trials of sodium valproate and divalproex sodium, NNHs for five clinically important adverse events ranged from 7.0 to 18.8. For six trials of topiramate, NNHs for seven adverse events (100 mg dose) ranged from 2.4 to 31.2.Authors' conclusions: Anticonvulsants appear to be both effective in reducing migraine frequency and reasonably well tolerated. There is noticeable variation among individual agents, but there are insufficient data to know whether this is due to chance or variation in true efficacy. Acetazolamide, clonazepam, lamotrigine and vigabatrin were not superior to placebo (one trial each). Relatively few robust trials are available for agents other than sodium valproate/divalproex sodium and topiramate; gabapentin in particular needs further evaluation. Trials designed with sufficient power to compare different drugs are also necessary.

Derry Christopher J, Derry S,Moore RA. Sumatriptan (intranasal route of administration) for acute migraine attacks in adults. Cochrane Database of Systematic Reviews. 2012; 2. [cited: url: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009663/abstract

Background: Migraine is a highly disabling condition for the individual and also has wide-reaching implications for society, healthcare services, and the economy. Sumatriptan is an abortive medication for migraine attacks, belonging to the triptan family. Intranasal administration may be preferable to oral for individuals experiencing nausea and/or vomiting, although it is primarily absorbed in the gut, not the nasal mucosa.Objectives: To determine the efficacy and tolerability of intranasal sumatriptan compared to placebo and other active interventions in the treatment of acute migraine attacks in adults.Search methods: We searched Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, online databases, and reference lists for studies through 13 October 2011.Selection criteria: We included randomised, double-blind, placebo- and/or active-controlled studies using intranasal sumatriptan to treat a migraine headache episode, with at least 10 participants per treatment arm.Data collection and analysis: Two review authors independently assessed trial quality and extracted data. We used numbers of

participants achieving each outcome to calculate relative risk (or 'risk ratio') and numbers needed to treat to benefit (NNT) or harm (NNH) compared to placebo or a different active treatment.Main results: Twelve studies (4755 participants) compared intranasal sumatriptan with placebo or an active comparator. Most of the data were for the 10 mg and 20 mg doses. Sumatriptan surpassed placebo for all efficacy outcomes. For sumatriptan 10 mg versus placebo the NNTs were 7.3, 7.4, and 5.5 for pain-free at two hours, and headache relief at one and two hours, respectively. For sumatriptan 20 mg versus placebo the NNTs were 4.7, 4.9, and 3.5, respectively, for the same outcomes. The 20 mg dose was significantly better than the 10 mg dose for each of these three primary efficacy outcomes.Relief of headache-associated symptoms, including nausea, photophobia, and phonophobia, was greater with sumatriptan than with placebo, and use of rescue medication was lower with sumatriptan than placebo. For the most part, adverse events were transient and mild and were more common with sumatriptan than placebo.Direct comparison of sumatriptan with active treatments was limited to two studies, one comparing sumatriptan 20 mg and dihydroergotamine (DHE) 1 mg, and one comparing sumatriptan 20 mg with rizatriptan 10 mg.Authors' conclusions: Intranasal sumatriptan is effective as an abortive treatment for acute migraine attacks, relieving pain, nausea, photophobia, phonophobia, and functional disability, but is associated with increased adverse events compared with placebo.

Derry Christopher J, Derry S,Moore RA. Sumatriptan (oral route of administration) for acute migraine attacks in adults. Cochrane Database of Systematic Reviews. 2012; 2. [cited: url: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008615.pub2/abstract

Background: Migraine is a highly disabling condition for the individual and also has wide-reaching implications for society, healthcare services, and the economy. Sumatriptan is an abortive medication for migraine attacks, belonging to the triptan family.Objectives: To determine the efficacy and tolerability of oral sumatriptan compared to placebo and other active interventions in the treatment of acute migraine attacks in adults.Search methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, online databases, and reference lists for studies through 13 October 2011.Selection criteria: We included randomised, double-blind, placebo- and/or active-controlled studies using oral sumatriptan to treat a migraine headache episode, with at least 10 participants per treatment arm.Data collection and analysis: Two review authors independently assessed trial quality and extracted data. We used numbers of participants achieving each outcome to calculate relative risk (or 'risk ratio') and numbers needed to treat to benefit (NNT) or harm (NNH) compared to placebo or a different active treatment.Main results: Sixty-one studies (37,250 participants) compared oral sumatriptan with placebo or an active comparator. Most of the data were for the 50 mg and 100 mg doses. Sumatriptan surpassed placebo for all efficacy outcomes. For sumatriptan 50 mg versus placebo the NNTs were 6.1, 7.5, and 4.0 for pain-free at two hours and headache relief at one and two hours, respectively. NNTs for sustained pain-free and sustained headache relief during the 24 hours postdose were 9.5 and 6.0, respectively. For sumatriptan 100 mg versus placebo the NNTs were 4.7, 6.8, 3.5, 6.5, and 5.2, respectively, for the same outcomes. Results for the 25 mg dose were similar to the 50 mg dose, while sumatriptan 100 mg was significantly better than 50 mg for pain-free and headache relief at two hours, and for sustained pain-free during 24 hours. Treating early, during the mild pain phase, gave significantly better NNTs for pain-free at two hours and sustained pain-free during 24 hours than did treating established attacks with moderate or severe pain intensity.Relief of associated symptoms, including nausea, photophobia, and phonophobia, was greater with sumatriptan than with placebo, and use of rescue medication was lower with sumatriptan than with placebo. For the most part, adverse events were transient and mild and were more common with the sumatriptan than with placebo, with a clear dose response relationship (25 mg to 100 mg).Sumatriptan was compared directly with a number of active treatments, including other triptans, paracetamol (acetaminophen), acetylsalicylic acid, non-steroidal anti-inflammatory drugs (NSAIDs), and ergotamine combinations.Authors' conclusions: Oral sumatriptan is effective as an abortive treatment for migraine attacks, relieving pain, nausea, photophobia, phonophobia, and functional disability, but is associated with increased adverse events.

Derry Christopher J, Derry S,Moore RA. Sumatriptan (rectal route of administration) for acute migraine attacks in adults. Cochrane Database of Systematic Reviews. 2012; 2. [cited: url: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009664/abstract

Background: Migraine is a highly disabling condition for the individual and also has wide-reaching implications for society, healthcare services, and the economy. Sumatriptan is an abortive medication for migraine attacks, belonging to the triptan family. Rectal administration may be preferable to oral for individuals experiencing nausea and/or vomiting.Objectives: To determine the efficacy and tolerability of rectal sumatriptan compared to placebo and other active interventions in the treatment of acute migraine attacks in adults.Search methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, online databases, and reference lists for studies through 13 October 2011.Selection criteria: We included randomised, double-blind, placebo- and/or active-controlled studies using rectally administered sumatriptan to treat a migraine headache episode, with at least 10 participants per treatment arm.Data collection and analysis: Two review authors independently assessed trial quality and extracted data. We used numbers of participants achieving each outcome to calculate relative risk (or 'risk ratio') and numbers needed to treat to benefit (NNT) or harm (NNH) compared to placebo or a different active treatment.Main results: Three studies (866 participants) compared rectally administered sumatriptan with placebo or an active comparator. Most of the data were for the 12.5 mg and 25 mg doses. For the majority of efficacy outcomes, sumatriptan surpassed placebo. For sumatriptan 12.5 mg versus placebo the NNTs were 5.2 and 3.2 for headache relief at one and two hours, respectively. Results for the 25 mg dose were similar to the 12.5 mg dose, and there were no significant differences between the two doses for any of the outcomes analysed. The NNTs for sumatriptan 25 mg versus placebo were 4.2, 3.2, and 2.4 for pain-free at two hours, headache relief at one hour, and headache relief at two hours, respectively.Relief of functional disability was greater with sumatriptan than with placebo, with NNTs of 8.0 and 4.0 for the 12.5 mg and 25 mg doses, respectively. For the most part, adverse events were transient and mild and were more common with sumatriptan than with placebo, but there were insufficient data to perform any analyses.Direct comparison of sumatriptan with active treatments was limited to one study comparing sumatriptan 25 mg with ergotamine tartrate 2 mg + caffeine 100 mg.Authors' conclusions: Based on limited amounts of data, sumatriptan 25 mg, administered rectally, is an effective treatment for acute migraine attacks, with participants in these studies experiencing a significant reduction in headache pain and functional disability within two hours of treatment. The lack of data on relief of headache-associated symptoms or incidence of adverse events limits any conclusions that can be drawn.

Derry Christopher J, Derry S,Moore RA. Sumatriptan (subcutaneous route of administration) for acute migraine attacks in adults. Cochrane Database of Systematic Reviews. 2012; 2. [cited: url: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009665/abstract

Background: Migraine is a highly disabling condition for the individual and also has wide-reaching implications for society, healthcare services, and the economy. Sumatriptan is an abortive medication for migraine attacks, belonging to the triptan family. Subcutaneous administration may be preferable to oral for individuals experiencing nausea and/or vomitingObjectives: To determine the efficacy and tolerability of subcutaneous sumatriptan compared to placebo and other active interventions in the treatment of acute migraine attacks in adults.Search methods: We searched Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, online databases, and reference lists for studies through 13 October 2011.Selection criteria: We included randomised, double-blind, placebo- and/or active-controlled studies using subcutaneous sumatriptan to treat a migraine headache episode, with at least 10 participants per treatment arm.Data collection and analysis: Two review authors independently assessed trial quality and extracted data. We used numbers of participants achieving each outcome to calculate relative risk (or 'risk ratio') and numbers needed to treat to benefit (NNT) or harm (NNH) compared to placebo or a different active treatment.Main results: Thirty-five studies (9365 participants) compared subcutaneous sumatriptan with placebo or an active comparator. Most of the data were for the 6 mg dose. Sumatriptan surpassed

placebo for all efficacy outcomes. For sumatriptan 6 mg versus placebo the NNTs were 2.9, 2.3, 2.2, and 2.1 for pain-free at one and two hours, and headache relief at one and two hours, respectively, and 6.1 for sustained pain-free at 24 hours. Results for the 4 mg and 8 mg doses were similar to the 6 mg dose, with 6 mg significantly better than 4 mg only for pain-free at one hour, and 8 mg significantly better than 6 mg only for headache relief at one hour. There was no evidence of increased migraine relief if a second dose of sumatriptan 6 mg was given after an inadequate response to the first.Relief of headache-associated symptoms, including nausea, photophobia, and phonophobia, was greater with sumatriptan than with placebo, and use of rescue medication was lower with sumatriptan than placebo. For the most part, adverse events were transient and mild and were more common with sumatriptan than placebo.Sumatriptan was compared directly with a number of active treatments, including other triptans, acetylsalicylic acid plus metoclopramide, and dihydroergotamine, but there were insufficient data for any pooled analyses.Authors' conclusions: Subcutaneous sumatriptan is effective as an abortive treatment for acute migraine attacks, quickly relieving pain, nausea, photophobia, phonophobia, and functional disability, but is associated with increased adverse events.

Derry Christopher J, Derry S,Moore RA. Sumatriptan (all routes of administration) for acute migraine attacks in adults - overview of Cochrane reviews. Cochrane Database of Systematic Reviews. 2014; 5. [cited: url: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009108.pub2/abstract

Background: Migraine is a highly disabling condition for the individual and also has wide-reaching implications for society, healthcare services, and the economy. Sumatriptan is an abortive medication for migraine attacks, belonging to the triptan family. It is available for administration by four different routes: oral, subcutaneous, intranasal, and rectal.Objectives: To summarise evidence from four Cochrane intervention reviews on the efficacy and tolerability of sumatriptan in the treatment of acute migraine attacks in adults by four routes of administration (oral, subcutaneous, intranasal, and rectal) compared with both placebo and active comparators.Methods: The included reviews were written by the authors of this overview; no additional searching was carried out. All included reviews were conducted according to a standard protocol and reported a standard set of outcomes. From each individual review we extracted results for pain relief at different levels, and adverse events. No additional statistical comparison was undertaken as part of the overview. We focused on the most important findings for doses and routes licensed in North America or Europe (oral 25 mg, 50 mg, 100 mg; subcutaneous 4 mg, 6 mg; intranasal 5 mg, 10 mg, 20 mg; rectal 25 mg).Main results: Included reviews provided data for 18 different dose and route of administration combinations in 52,236 participants. Data for the primary outcomes sought were generally well reported, and involved adequate numbers of participants to give confidence in the results, except for the rectal route of administration, where numbers were low.Subcutaneous administration was the most effective, with pain reduced from moderate or severe to none by two hours in almost 6 in 10 people (59%) taking 6 mg sumatriptan, compared with approximately 1 in 7 (15%) taking placebo; the number needed to treat (NNT) was 2.3 (95% confidence interval 2.1 to 2.4) with 2522 participants in the analysis. The most commonly used doses of oral, rectal, and intranasal sumatriptan also provided clinically useful pain relief, with the oral 50 mg dose providing complete relief of pain in almost 3 in 10 people (28%) compared with about 1 in 10 (11%) after placebo (NNT 6.1 (5.5 to 6.9) in 6447 participants). Subcutaneous administration provided more rapid pain relief than the other routes. Taking medication early, when pain was mild, was more effective than waiting until the pain was moderate or severe.The most effective dose of sumatriptan for each route of administration for the outcome of headache relief (pain reduced from moderate or severe to none or mild) at two hours was oral 100 mg (NNT 3.5 (3.2 to 3.7) in 7811 participants), subcutaneous 6 mg (NNT 2.1 (2.0 to 2.2) in 2738 participants), intranasal 20 mg (NNT 3.5 (3.1 to 4.1) in 2020 participants), and rectal 25 mg (NNT 2.4 (1.9 to 3.4) in 240 participants).Adverse events were generally of mild or moderate severity, of short duration, and more common with subcutaneously administered sumatriptan and higher doses of oral and intranasal sumatriptan than with other dose and route combinations.Authors' conclusions: Sumatriptan is an effective abortive treatment for acute migraine attacks, but is associated with increased adverse events relative to placebo. The route of administration influences efficacy, particularly within the first hour after administration. Subcutaneous

sumatriptan shows the greatest efficacy in terms of pain relief, but at the expense of relatively high levels of adverse events, and with a high financial cost compared with other routes. Information about the relative efficacy of the different routes of administration for different outcomes should help to inform decisions about the suitability of sumatriptan as a migraine treatment, as well as about the most appropriate way to administer the treatment for individual patients.

Derry S,Moore RA. Paracetamol (acetaminophen) with or without an antiemetic for acute migraine headaches in adults. Cochrane Database of Systematic Reviews. 2013; 4. [cited: url: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008040.pub3/abstract

Background: This is an updated version of the original Cochrane review published in Issue 11, 2010 (Derry 2010). Migraine is a common, disabling condition and a burden for the individual, health services and society. Many sufferers choose not to, or are unable to, seek professional help and rely on over-the-counter analgesics. Co-therapy with an antiemetic should help to reduce nausea and vomiting, which are commonly associated with migraine.Objectives: To determine the efficacy and tolerability of paracetamol (acetaminophen), alone or in combination with an antiemetic, compared with placebo and other active interventions in the treatment of acute migraine in adults.Search methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE and the Oxford Pain Relief Database for studies through 4 October 2010 for the original review, and to 13 February 2013 for the update. Two clinical trials registers (ClinicalTrials.gov and gsk-clinicalstudyregister.com) were also searched on both occasions.Selection criteria: We included randomised, double-blind, placebo- or active-controlled studies using self-administered paracetamol to treat a migraine headache episode, with at least 10 participants per treatment arm.Data collection and analysis: Two review authors independently assessed trial quality and extracted data. Numbers of participants achieving each outcome were used to calculate relative risk and numbers needed to treat (NNT) or harm (NNH) compared with placebo or other active treatment.Main results: Searches for the update identified one additional study for inclusion. Eleven studies (2942 participants, 5109 attacks) compared paracetamol 1000 mg, alone or in combination with an antiemetic, with placebo or other active comparators, mainly sumatriptan 100 mg. For all efficacy outcomes paracetamol was superior to placebo, with NNTs of 12 (19% response with paracetamol, 10% with placebo), 5.0 (56% response with paracetamol, 36% with placebo) and 5.2 (39% response with paracetamol, 20% with placebo) for 2-hour pain-free and 2- and 1-hour headache relief, respectively, when medication was taken for moderate to severe pain.Paracetamol 1000 mg plus metoclopramide 10 mg was not significantly different from oral sumatriptan 100 mg for 2-hour headache relief; there were no 2-hour pain-free data.Adverse event rates were similar between paracetamol and placebo, and between paracetamol plus metoclopramide and sumatriptan. No serious adverse events occurred with paracetamol alone, but more serious and/or severe adverse events occurred with sumatriptan than with the combination therapy (NNH 32).Authors' conclusions: Paracetamol 1000 mg alone is statistically superior to placebo in the treatment of acute migraine, but the NNT of 12 for pain-free response at two hours is inferior to at of other commonly used analgesics. Given the low cost and wide availability of paracetamol, it may be a useful first choice drug for acute migraine in those with contraindications to, or who cannot tolerate, non-steroidal anti-inflammatory drugs (NSAIDs) or aspirin. The addition of 10 mg metoclopramide gives short-term efficacy equivalent to oral sumatriptan 100 mg. Adverse events with paracetamol did not differ from placebo; serious and/or severe adverse events were slightly more common with sumatriptan than with paracetamol plus metoclopramide.

Derry S, Rabbie R,Moore RA. Diclofenac with or without an antiemetic for acute migraine headaches in adults. Cochrane Database of Systematic Reviews. 2013; 4. [cited: url: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008783.pub3/abstract

Background: This review is an update of a previously published review in Issue 2, 2012 (Derry 2012a). Migraine is a common, disabling condition and a burden for the individual, health services and society. Many sufferers choose not to, or are unable to, seek professional help and rely on over-the-counter (OTC) analgesics. Diclofenac is an established analgesic, and new formulations using the potassium or epolamine salts, which can be dissolved in water, have been developed for rapid absorption, which may be beneficial in acute migraine. Co-therapy with an antiemetic should help to reduce the nausea and vomiting commonly associated with migraine.Objectives: To determine the efficacy and tolerability of diclofenac, alone or in combination with an antiemetic, compared to placebo and other active interventions in the treatment of acute migraine headaches in adults.Search methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, the Oxford Pain Relief Database, ClinicalTrials.gov, and reference lists for studies through 27 September 2011 for the original review and 15 February 2013 for the update.Selection criteria: We included randomised, double-blind, placebo-controlled or active-controlled studies, or both, using self administered diclofenac to treat a migraine headache episode, with at least 10 participants per treatment arm.Data collection and analysis: Two review authors independently assessed trial quality and extracted data. We used numbers of participants achieving each outcome to calculate relative risk (or 'risk ratio') and numbers needed to treat to benefit (NNT) or harm (NNH) compared to placebo or a different active treatment.Main results: Five studies (1356 participants, 2711 attacks) compared oral diclofenac with placebo, and one also compared it with sumatriptan; none combined diclofenac with a self administered antiemetic. Four studies treated attacks with single doses of medication, and two allowed an optional second dose for inadequate response. Only two studies, with three active treatment arms, provided data for pooled analysis of primary outcomes. For single doses of diclofenac potassium 50 mg versus placebo (two studies), the NNTs were 6.2, 8.9, and 9.5 for pain-free at two hours, headache relief at two hours, and pain-free responses at 24 hours, respectively.Similar numbers of participants experienced adverse events, which were mostly mild and transient, with diclofenac and placebo.There were insufficient data to evaluate other doses of oral diclofenac, or to compare different formulations or different dosing regimens; only one study compared oral diclofenac with an active comparator (oral sumatriptan 100 mg).Authors' conclusions: Oral diclofenac potassium 50 mg is an effective treatment for acute migraine, providing relief from pain and associated symptoms, although only a minority of patients experience pain-free responses. Adverse events are mostly mild and transient and occur at the same rate as with placebo.

Kirthi V, Derry S,Moore RA. Aspirin with or without an antiemetic for acute migraine headaches in adults. Cochrane Database of Systematic Reviews. 2013; 4. [cited: url: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008041.pub3/abstract

Background: This is an updated version of the original Cochrane review published in Issue 4, 2010 (Kirthi 2010). Migraine is a common, disabling condition and a burden for the individual, health services and society. Many sufferers choose not to, or are unable to, seek professional help and rely on over-the-counter analgesics. Co-therapy with an antiemetic should help to reduce nausea and vomiting commonly associated with migraine headaches.Objectives: To determine the efficacy and tolerability of aspirin, alone or in combination with an antiemetic, compared to placebo and other active interventions in the treatment of acute migraine headaches in adults.Search methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, the Oxford Pain Relief Database, ClinicalTrials.gov, and reference lists for studies through 10 March 2010 for the original review and to 31 January 2013 for the update.Selection criteria: We included randomised, double-blind, placebo-controlled or active-controlled studies, or both, using aspirin to treat a migraine headache episode, with at least 10 participants per treatment arm.Data collection and analysis: Two review authors independently assessed trial quality and extracted data. Numbers of participants achieving each outcome were used to calculate relative risk and numbers needed to treat (NNT) or harm (NNH) compared to placebo or other active treatment.Main results: No new studies were found for this update. Thirteen studies (4222 participants) compared aspirin 900 mg or 1000 mg, alone or in combination with metoclopramide 10 mg, with placebo or other active comparators, mainly sumatriptan 50 mg or 100 mg. For all efficacy outcomes, all active treatments were

superior to placebo, with NNTs of 8.1, 4.9 and 6.6 for 2-hour pain-free, 2-hour headache relief, and 24-hour headache relief with aspirin alone versus placebo, and 8.8, 3.3 and 6.2 with aspirin plus metoclopramide versus placebo. Sumatriptan 50 mg did not differ from aspirin alone for 2-hour pain-free and headache relief, while sumatriptan 100 mg was better than the combination of aspirin plus metoclopramide for 2-hour pain-free, but not headache relief; there were no data for 24-hour headache relief.Adverse events were mostly mild and transient, occurring slightly more often with aspirin than placebo.Additional metoclopramide significantly reduced nausea ($P < 0.00006$) and vomiting ($P = 0.002$) compared with aspirin alone.Authors' conclusions: We found no new studies since the last version of this review. Aspirin 1000 mg is an effective treatment for acute migraine headaches, similar to sumatriptan 50 mg or 100 mg. Addition of metoclopramide 10 mg improves relief of nausea and vomiting. Adverse events were mainly mild and transient, and were slightly more common with aspirin than placebo, but less common than with sumatriptan 100 mg.

Law S, Derry S,Moore RA. Naproxen with or without an antiemetic for acute migraine headaches in adults. Cochrane Database of Systematic Reviews. 2013; 10. [cited: url: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD009455.pub2/abstract

Background: Migraine is a common, disabling condition and a burden for the individual, health services, and society. Many sufferers choose not to, or are unable to, seek professional help and rely on over-the-counter analgesics. Naproxen is a non-steroidal anti-inflammatory drug (NSAID); its efficacy in acute migraine has not been established by systematic reviews. Co-therapy with an antiemetic should help to reduce the nausea and vomiting commonly associated with migraine headaches.Objectives: To determine the efficacy and tolerability of naproxen, alone or in combination with an antiemetic, compared with placebo and other active interventions in the treatment of acute migraine headaches in adults.Search methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL) on The Cochrane Library, MEDLINE, EMBASE, and the Oxford Pain Relief Database, together with two online databases (www.gsk-clinicalstudyregister.com and www.clinicaltrials.gov) and reference lists, for studies to 22 May 2013.Selection criteria: We included randomised, double-blind, placebo- or active-controlled studies, with at least 10 participants per treatment arm, using naproxen alone or with an antiemetic to treat a migraine headache episode.Data collection and analysis: Two review authors independently assessed trial quality and extracted data. We used numbers of participants achieving each outcome to calculate risk ratios and numbers needed to treat (NNT) or harm (NNH) compared with placebo or a different active treatment.Main results: We included six studies using naproxen 275 mg, 500 mg, or 825 mg to treat attacks of moderate or severe pain intensity. Overall, 1241 participants took naproxen (275 mg to 825 mg), 229 took sumatriptan 50 mg, 173 took naratriptan 2.5 mg, and 1092 took placebo. No studies combined naproxen with an antiemetic. Studies using naproxen 275 mg provided no useable data for analysis.Naproxen (500 mg and 825 mg) was better than placebo for pain-free response and headache relief. At two hours, the NNT for pain-free response was 11 (95% CI 8.7 to 17) (17% response with naproxen, 8% with placebo; risk ratio 2.0 (1.6 to 2.6), moderate quality) and for headache relief was 6.0 (4.8 to 7.9) (45% response with naproxen, 29% with placebo; risk ratio 1.6 (1.4 to 1.8), moderate quality). The NNT for sustained pain-free response during the 24 hours post dose was 19 (13 to 34) (12% response with naproxen, 6.7% with placebo), and for sustained headache relief during the 24 hours post dose was 8.3 (6.4 to 12) (30% response with naproxen, 18% with placebo). Analysing only the lower dose of 500 mg of naproxen did not significantly change the results. Adverse events, which were mostly mild or moderate in severity and rarely led to withdrawal, were more common with naproxen than with placebo when the 500 mg and 825 mg doses were considered together, but not when the 500 mg dose was analysed alone.There were insufficient data for analysis of naproxen compared with sumatriptan, and no data suitable for analysis of naproxen compared with naratriptan.Authors' conclusions: Naproxen is statistically superior to placebo in the treatment of acute migraine, but the NNT of 11 for pain-free response at two hours suggests that it is not a clinically useful treatment. Cochrane reviews examining other commonly used analgesics for acute migraine have reported better (lower) NNT results for the same outcome. Naproxen is not clinically useful as a stand-alone analgesic in acute migraine, as it is effective in fewer than 2 people in 10.

Law S, Derry S,Moore RA. Sumatriptan plus naproxen for acute migraine attacks in adults. Cochrane Database of Systematic Reviews. 2013; 10. [cited: url: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008541.pub2/abstract

Background: Migraine is a common disabling condition and a burden for the individual, health services, and society. Effective abortive treatments include the triptan and non-steroidal anti-inflammatory classes of drugs. These drugs have different mechanisms of action and combining them may provide better relief. Sumatriptan plus naproxen is now available in combination form for the acute treatment of migraine.Objectives: To determine the efficacy and tolerability of sumatriptan plus naproxen (administered together as separate tablets or taken as a fixed-dose combination tablet) compared with placebo and other active interventions for the acute treatment of migraine headaches in adults.Search methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL) on The Cochrane Library, MEDLINE, and EMBASE, together with two online databases (www.gsk-clinicalstudyregister.com and www.clinicaltrials.gov) for studies to 2 August 2013. We also searched the reference list of included studies and relevant reviews.Selection criteria: We included randomised, double-blind, placebo- or active-controlled studies, with at least 10 participants per treatment arm, using sumatriptan plus naproxen to treat a migraine headache episode.Data collection and analysis: Two review authors independently assessed trial quality and extracted data. We used numbers of participants achieving each outcome to calculate risk ratio and numbers needed to treat to benefit (NNT) or harm (NNH) compared with placebo or a different active treatment.Main results: We included 12 studies using sumatriptan 85 mg or 50 mg plus naproxen 500 mg to treat attacks of mild, moderate, or severe pain intensity: 3663 participants received combination treatment, 3682 placebo, 964 sumatriptan, and 982 naproxen. No studies were considered to be at high risk of bias for any of the criteria evaluated.Overall, the combination was better than placebo for pain-free and headache relief responses. At two hours, the NNT for pain-free response was 3.1 (95% CI 2.9 to 3.5) when the baseline pain was mild (50% response with sumatriptan plus naproxen compared with 18% with placebo), and 4.9 (4.3 to 5.7) when baseline pain was moderate or severe (28% with sumatriptan plus naproxen compared with 8% with placebo; risk ratio 3.65 (3.0 to 4.5); high quality evidence). Using 50 mg of sumatriptan, rather than 85 mg, in the combination did not significantly change the result. Treating early, when pain was still mild, was significantly better than treating once pain was moderate or severe for pain-free responses at two hours and during the 24 hours post dose. Adverse events were mostly mild or moderate in severity and rarely led to withdrawal; they were more common with the combination than with placebo.Where the data allowed direct comparison, combination treatment was superior to either monotherapy, but adverse events were less frequent with naproxen than sumatriptan.Authors' conclusions: Combination treatment was effective in the acute treatment of migraine headaches. The effect was greater than for the same dose of either sumatriptan or naproxen alone, but additional benefits over sumatriptan alone are not large. More participants achieved good relief when medication was taken early in the attack, when pain was still mild. Adverse events were more common with the combination and sumatriptan alone than with placebo or naproxen alone.

Linde K, Allais G, Brinkhaus B, Manheimer E, Vickers A,White Adrian R. Acupuncture for migraine prophylaxis. Cochrane Database of Systematic Reviews. 2009; 1. [cited: url: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD001218.pub2/abstract

Background: Acupuncture is often used for migraine prophylaxis but its effectiveness is still controversial. This review (along with a companion review on 'Acupuncture for tension-type headache') represents an updated version of a Cochrane review originally published in Issue 1, 2001, of The Cochrane Library.Objectives: 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 migraine.Search methods: The

Cochrane Pain, Palliative & Supportive Care Trials Register, CENTRAL, MEDLINE, EMBASE and the Cochrane Complementary Medicine Field Trials Register were searched to January 2008.Selection criteria: We included randomized trials with a post-randomization observation period of at least 8 weeks that compared the clinical effects of an acupuncture intervention with a control (no prophylactic treatment or routine care only), a sham acupuncture intervention or another intervention in patients with migraine.Data collection and analysis: Two reviewers checked eligibility; extracted information on patients, interventions, methods and results; and assessed risk of bias and quality of the acupuncture intervention. Outcomes extracted included response (outcome of primary interest), migraine attacks, migraine days, headache days and analgesic use. Pooled effect size estimates were calculated using a random-effects model.Main results: Twenty-two trials with 4419 participants (mean 201, median 42, range 27 to 1715) met the inclusion criteria. Six trials (including two large trials with 401 and 1715 patients) compared acupuncture to no prophylactic treatment or routine care only. After 3 to 4 months patients receiving acupuncture had higher response rates and fewer headaches. The only study with long-term follow up saw no evidence that effects dissipated up to 9 months after cessation of treatment. Fourteen trials compared a 'true' acupuncture intervention with a variety of sham interventions. Pooled analyses did not show a statistically significant superiority for true acupuncture for any outcome in any of the time windows, but the results of single trials varied considerably. Four trials compared acupuncture to proven prophylactic drug treatment. Overall in these trials acupuncture was associated with slightly better outcomes and fewer adverse effects than prophylactic drug treatment. Two small low-quality trials comparing acupuncture with relaxation (alone or in combination with massage) could not be interpreted reliably.Authors' conclusions: In the previous version of this review, evidence in support of acupuncture for migraine prophylaxis was considered promising but insufficient. Now, with 12 additional trials, there is consistent evidence that acupuncture provides additional benefit to treatment of acute migraine attacks only or to routine care. There is no evidence for an effect of 'true' acupuncture over sham interventions, though this is difficult to interpret, as exact point location could be of limited importance. Available studies suggest that acupuncture is at least as effective as, or possibly more effective than, prophylactic drug treatment, and has fewer adverse effects. Acupuncture should be considered a treatment option for patients willing to undergo this treatment.

Linde K,Rossnagel K. Propranolol for migraine prophylaxis. Cochrane Database of Systematic Reviews. 2004; 2. [cited: url: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD003225.pub2/abstract

Background: Propranolol is one of the most commonly prescribed drugs for migraine prophylaxis.Objectives: We aimed to determine whether there is evidence that propranolol is more effective than placebo and as effective as other drugs for the interval (prophylactic) treatment of patients with migraine.Search methods: Potentially eligible studies were identified by searching MEDLINE/PubMed (1966 to May 2003) and the Cochrane Central Register of Controlled Trials (Issue 2, 2003), and by screening bibliographies of reviews and identified articles.Selection criteria: We included randomised and quasi-randomised clinical trials of at least 4 weeks duration comparing clinical effects of propranolol with placebo or another drug in adult migraine sufferers.Data collection and analysis: Two reviewers extracted information on patients, methods, interventions, outcomes measured, and results using a pre-tested form. Study quality was assessed using two checklists (Jadad scale and Delphi list). Due to the heterogeneity of outcome measures and insufficient reporting of the data, only selective quantitative meta-analyses were performed. As far as possible, effect size estimates were calculated for single trials. In addition, results were summarised descriptively and by a vote count among the reviewers.Main results: A total of 58 trials with 5072 participants met the inclusion criteria. The 58 selected trials included 26 comparisons with placebo and 47 comparisons with other drugs. The methodological quality of the majority of trials was unsatisfactory. The principal shortcomings were high dropout rates and insufficient reporting and handling of this problem in the analysis. Overall, the 26 placebo-controlled trials showed clear short-term effects of propranolol over placebo. Due to the lack of studies with long-term follow up, it is unclear whether these effects are stable after stopping propranolol. The 47 comparisons with calcium antagonists, other beta-blockers, and a variety of other drugs did not yield any clear-cut differences. Sample size was, however, insufficient in most trials to establish equivalence.Authors' conclusions: Although many trials have relevant

methodological shortcomings, there is clear evidence that propranolol is more effective than placebo in the short-term interval treatment of migraine. Evidence on long-term effects is lacking. Propranolol seems to be as effective and safe as a variety of other drugs used for migraine prophylaxis.

Linde M, Mulleners Wim M, Chronicle Edward P,McCrory Douglas C. Antiepileptics other than gabapentin, pregabalin, topiramate, and valproate for the prophylaxis of episodic migraine in adults. Cochrane Database of Systematic Reviews. 2013; 6. [cited: url: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010608/abstract

Background: Some antiepileptic drugs but not others are useful in clinical practice for the prophylaxis of migraine. This might be explained by the variety of actions of these drugs in the central nervous system. The present review is part of an update of a Cochrane review first published in 2004, and previously updated (conclusions not changed) in 2007.Objectives: To describe and assess the evidence from controlled trials on the efficacy and tolerability of antiepileptic drugs other than gabapentin, pregabalin, topiramate, and valproate (which are the subjects of separate Cochrane reviews) for preventing migraine attacks in adult patients with episodic migraine.Search methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL; The Cochrane Library 2012, Issue 12), PubMed/MEDLINE (1966 to 15 January 2013), MEDLINE In-Process (current week, 15 January 2013), and EMBASE (1974 to 15 January 2013) and handsearched Headache and Cephalalgia through January 2013.Selection criteria: Studies were required to be prospective, controlled trials of antiepileptic drugs other than gabapentin, pregabalin, topiramate, and valproate taken regularly to prevent the occurrence of migraine attacks, to improve migraine-related quality of life, or both.Data collection and analysis: Two review authors independently selected studies and extracted data. For headache frequency data, we calculated mean differences (MDs) between antiepileptic drugs and comparators (placebo, active control, or same drug in a different dose) for individual studies and pooled these across studies. For dichotomous data on responders (patients with ? 50% reduction in headache frequency), we calculated odds ratios (ORs) and numbers needed to treat (NNTs). We also summarised data on adverse events from placebo-controlled trials and calculated risk differences (RDs) and numbers needed to harm (NNHs).Main results: Eleven papers describing 10 unique trials met the inclusion criteria. The 10 trials reported results for nine antiepileptic drugs other than gabapentin, pregabalin, topiramate, and valproate. Six of the eight drugs investigated in placebo-controlled trials were not better than placebo in reducing headache frequency per 28-day period during treatment (clonazepam, lamotrigine, oxcarbazepine, and vigabatrin) and/or in the proportion of responders (acetazolamide, carisbamate, lamotrigine, oxcarbazepine). One prospective, randomised, double-blind, single cross-over trial of 48 patients demonstrated a significant superiority of carbamazepine over placebo in the proportion of responders (OR 11.77; 95% confidence interval (CI) 3.92 to 35.32). The NNT was 2 (95% CI 2 to 3). In a small prospective, randomised, double-blind, parallel-group trial, levetiracetam 1000 mg was significantly superior to placebo in reducing headache frequency per 28-day period during treatment (MD -2.40; 95% CI -4.52 to -0.28; 26 patients), as well as in the proportion of responders (OR 26.07; 95% CI 1.30 to 521.91; 26 patients). The NNT was 2 (95% CI 1 to 4). The same trial examined levetiracetam 1000 mg versus topiramate 100 mg and found a small but significant difference favouring topiramate in headache frequency per 28-day period during treatment (MD 1.40; 95% CI 0.14 to 2.66; 28 patients). There was no significant difference between levetiracetam and topiramate in the proportion of responders (OR 0.71; 95% CI 0.16 to 3.23; 28 patients). Finally, one trial with 75 participants examined zonisamide versus topiramate (200 and 100 mg, respectively) and found no significant difference between them in reduction of headache frequency from baseline during the third month of treatment. Adverse events for active treatment versus placebo were available for all investigated drugs except levetiracetam, vigabatrin, and zonisamide. A high prevalence of adverse events was noted for carbamazepine, with a NNH of only 2 (95% CI 2 to 4).Authors' conclusions: Available evidence does not allow robust conclusions regarding the efficacy of antiepileptic drugs other than gabapentin, pregabalin, opiramate, and valproate in the prophylaxis of episodic migraine among adults. Acetazolamide, carisbamate, clonazepam, lamotrigine, oxcarbazepine, and vigabatrin were not more effective than placebo in reducing headache frequency. In one trial each, carbamazepine and levetiracetam were significantly superior to placebo in reducing headache frequency, and there was no significant difference in

proportion of responders between zonisamide and active comparator. These three positive studies suffer from considerable methodological limitations.

Linde M, Mulleners Wim M, Chronicle Edward P,McCrory Douglas C. Gabapentin or pregabalin for the prophylaxis of episodic migraine in adults. Cochrane Database of Systematic Reviews. 2013; 6. [cited: url: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010609/abstract

Background: Some antiepileptic drugs but not others are useful in clinical practice for the prophylaxis of migraine. This might be explained by the variety of actions of these drugs in the central nervous system. The present review is part of an update of a Cochrane review first published in 2004, and previously updated (conclusions not changed) in 2007.Objectives: To describe and assess the evidence from controlled trials on the efficacy and tolerability of gabapentin/gabapentin enacarbil or pregabalin for preventing migraine attacks in adult patients with episodic migraine.Search methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL; The Cochrane Library 2012, Issue 12), PubMed/MEDLINE (1966 to 15 January 2013), MEDLINE In-Process (current week, 15 January 2013), and EMBASE (1974 to 15 January 2013) and handsearched Headache and Cephalalgia through January 2013.Selection criteria: Studies were required to be prospective, controlled trials of gabapentin/gabapentin enacarbil or pregabalin taken regularly to prevent the occurrence of migraine attacks, to improve migraine-related quality of life, or both.Data collection and analysis: Two review authors independently selected studies and extracted data. For headache frequency data, we calculated mean differences (MDs) between gabapentin and comparator (placebo, active control, or gabapentin in a different dose) for individual studies and pooled these across studies. For dichotomous data on responders (patients with ? 50% reduction in headache frequency), we calculated odds ratios (ORs) and numbers needed to treat (NNTs). We also summarised data on adverse events from all single dosage studies and calculated risk differences (RDs) and numbers needed to harm (NNHs).Main results: Five trials on gabapentin and one trial on its prodrug gabapentin enacarbil met the inclusion criteria; no reports on pregabalin were identified. In total, data from 1009 patients were considered. One trial each of gabapentin 900 mg (53 patients), and gabapentin titrated to 1200 mg (63 patients) and 1800 mg (122 patients) failed to show a statistically significant reduction in headache frequency in the active treatment group as compared to the placebo group, whereas one trial of gabapentin titrated to 1800 to 2400 mg (113 patients) demonstrated a small but statistically significant superiority of active treatment for this outcome (MD -0.80; 95% confidence interval (CI) -1.55 to -0.05). The pooled results of these four studies (MD -0.44; 95% CI -1.43 to 0.56; 351 patients) do not demonstrate a significant difference between gabapentin and placebo. One trial of gabapentin titrated to 1800 mg (122 patients) failed to demonstrate a significant difference between active treatment and placebo in the proportion of responders (OR 0.97; 95% CI 0.45 to 2.11), whereas one trial of gabapentin titrated to 1800 to 2400 mg (113 patients) demonstrated a small but statistically significant superiority of active treatment for this outcome (OR 2.79; 95% CI 1.09 to 7.17). The pooled results of these two studies (OR 1.59; 95% CI 0.57 to 4.46; 235 patients) do not demonstrate a significant difference between gabapentin and placebo. Comparisons from one study (135 patients) suggest that gabapentin 2000 mg is no more effective than gabapentin 1200 mg. One trial of gabapentin enacarbil (523 participants) failed to demonstrate a significant difference versus placebo or between doses for gabapentin enacarbil titrated to between 1200 mg and 3000 mg with regard to proportion of responders; there was also no evidence of a dose-response trend. Adverse events, most notably dizziness and somnolence, were common with gabapentin.Authors' conclusions: The pooled evidence derived from trials of gabapentin suggests that it is not efficacious for the prophylaxis of episodic migraine in adults. Since adverse events were common among the gabapentin-treated patients, it is advocated that gabapentin should not be used in routine clinical practice. Gabapentin enacarbil is not efficacious for the prophylaxis of epi odic migraine in adults. There is no published evidence from controlled trials of pregabalin for the prophylaxis of episodic migraine in adults.

Linde M, Mulleners Wim M, Chronicle Edward P,McCrory Douglas C. Topiramate for the prophylaxis of episodic migraine in adults. Cochrane Database of Systematic Reviews. 2013; 6. [cited: url:

http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010610/abstract

Background: Some antiepileptic drugs but not others are useful in clinical practice for the prophylaxis of migraine. This might be explained by the variety of actions of these drugs in the central nervous system. The present review is part of an update of a Cochrane review first published in 2004, and previously updated (conclusions not changed) in 2007.Objectives: To describe and assess the evidence from controlled trials on the efficacy and tolerability of topiramate for preventing migraine attacks in adult patients with episodic migraine.Search methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL; The Cochrane Library 2012, Issue 12), PubMed/MEDLINE (1966 to 15 January 2013), MEDLINE In-Process (current week, 15 January 2013), and EMBASE (1974 to 15 January 2013) and handsearched Headache and Cephalalgia through January 2013.Selection criteria: Studies were required to be prospective, controlled trials of topiramate taken regularly to prevent the occurrence of migraine attacks, to improve migraine-related quality of life, or both.Data collection and analysis: Two review authors independently selected studies and extracted data. For headache frequency data, we calculated mean differences (MDs) between topiramate and comparator (placebo, active control, or topiramate in a different dose) for individual studies and pooled these across studies. For dichotomous data on responders (patients with ? 50% reduction in headache frequency), we calculated odds ratios (ORs) and, in select cases, risk ratios (RRs); we also calculated numbers needed to treat (NNTs). We calculated MDs for selected quality of life instruments. Finally, we summarised data on adverse events from placebo-controlled trials and calculated risk differences (RDs) and numbers needed to harm (NNHs).Main results: Twenty papers describing 17 unique trials met the inclusion criteria. Analysis of data from nine trials (1737 participants) showed that topiramate reduced headache frequency by about 1.2 attacks per 28 days as compared to placebo (MD -1.20; 95% confidence interval (CI) -1.59 to -0.80). Data from nine trials (1190 participants) show that topiramate approximately doubled the proportion of responders relative to placebo (RR 2.02; 95% CI 1.57 to 2.60; NNT 4; 95% CI 3 to 6). Separate analysis of different topiramate doses produced similar MDs versus placebo at 50 mg (-0.95; 95% CI -1.95 to 0.04; three studies; 520 participants), 100 mg (-1.15; 95% CI -1.58 to -0.71; six studies; 1620 participants), and 200 mg (-0.94; 95% CI -1.53 to -0.36; five studies; 804 participants). All three doses significantly increased the proportion of responders relative to placebo; ORs were as follows: for 50 mg, 2.35 (95% CI 1.60 to 3.44; three studies; 519 participants); for 100 mg, 3.49 (95% CI 2.23 to 5.45; five studies; 852 participants); and for 200 mg, 2.49 (95% CI 1.61 to 3.87; six studies; 1025 participants). All three doses also significantly improved three or more domains of quality of life as compared to placebo. Meta-analysis of the three studies that included more than one dose of topiramate suggests that 200 mg is no more effective than 100 mg. With regard to mean headache frequency and/or responder rate, seven trials using active comparators found (a) no significant difference between topiramate and amitriptyline (one study, 330 participants); (b) no significant difference between topiramate and flunarizine (one study, 83 participants); (c) no significant difference between topiramate and propranolol (two studies, 342 participants); (d) no significant difference between topiramate and relaxation (one study, 61 participants); but (e) a slight significant advantage of topiramate over valproate (two studies, 120 participants). Relaxation improved migraine-specific quality of life significantly more than topiramate. In trials of topiramate against placebo, seven adverse events (AEs) were reported by at least three studies. These were usually mild and of a non-serious nature. Except for taste disturbance and weight loss, there were no si nificant differences in the frequency of AEs in general, or of the seven specific AEs, between placebo and topiramate 50 mg. AEs in general and all of the specific AEs except nausea were significantly more common on topiramate 100 mg than on placebo, with NNHs varying from 3 to 25, and the RDs versus placebo were even higher for topiramate 200 mg, with NNHs varying from 2 to 17.Authors' conclusions: Meta-analysis demonstrates that topiramate in a 100 mg/day dosage is effective in reducing headache frequency and reasonably well-tolerated in adult patients with episodic migraine. This provides good evidence to support its use in routine clinical management. More studies designed specifically to compare the efficacy or safety of topiramate versus other interventions with proven efficacy in the prophylaxis of migraine are needed.

Linde M, Mulleners Wim M, Chronicle Edward P,McCrory Douglas C. Valproate (valproic acid or sodium valproate

or a combination of the two) for the prophylaxis of episodic migraine in adults. Cochrane Database of Systematic Reviews. 2013; 6. [cited: url: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD010611/abstract

Background: Some antiepileptic drugs but not others are useful in clinical practice for the prophylaxis of migraine. This might be explained by the variety of actions of these drugs in the central nervous system. The present review is part of an update of a Cochrane review first published in 2004, and previously updated (conclusions not changed) in 2007.Objectives: To describe and assess the evidence from controlled trials on the efficacy and tolerability of valproate (valproic acid or sodium valproate or a combination of the two) for preventing migraine attacks in adult patients with episodic migraine.Search methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL; The Cochrane Library 2012, Issue 12), PubMed/MEDLINE (1966 to 15 January 2013), MEDLINE In-Process (current week, 15 January 2013), and EMBASE (1974 to 15 January 2013) and handsearched Headache and Cephalalgia through January 2013.Selection criteria: Studies were required to be prospective, controlled trials of valproate taken regularly to prevent the occurrence of migraine attacks, to improve migraine-related quality of life, or both.Data collection and analysis: Two review authors independently selected studies and extracted data. For headache frequency data, we calculated mean differences (MDs) between valproate and comparator (placebo, active control, or valproate in a different dose) for individual studies and pooled these across studies. For dichotomous data on responders (patients with ? 50% reduction in headache frequency), we calculated odds ratios (ORs) and, in select cases, risk ratios (RRs); we also calculated numbers needed to treat (NNTs). We calculated MDs for Migraine Disability Assessment (MIDAS) scores. We also summarised data on adverse events from placebo-controlled trials and calculated risk differences (RDs) and numbers needed to harm (NNHs).Main results: Ten papers describing 10 unique trials met the inclusion criteria. Analysis of data from two trials (63 participants) showed that sodium valproate reduced headache frequency by approximately four headaches per 28 days as compared to placebo (MD -4.31; 95% confidence interval (CI) -8.32 to -0.30). Data from four trials (542 participants) showed that divalproex sodium (a stable combination of sodium valproate and valproic acid in a 1:1 molar ratio) more than doubled the proportion of responders relative to placebo (RR 2.18; 95% CI 1.28 to 3.72; NNT 4; 95% CI 2 to 11). One study of sodium valproate (34 participants) versus placebo supported the latter findings (RR for responders 2.83; 95% CI 1.27 to 6.31; NNT 3; 95% CI 2 to 9). There was no significant difference in the proportion of responders between sodium valproate versus flunarizine (one trial, 41 participants) or between divalproex sodium versus propranolol (one trial, 32 participants). Pooled analysis of post-treatment mean headache frequencies in two trials (88 participants) demonstrates a slight but significant advantage for topiramate 50 mg over valproate 400 mg (MD -0.90; 95% CI -1.58 to -0.22). For placebo-controlled trials of sodium valproate and divalproex sodium, NNHs for clinically important adverse events ranged from 7 to 14.Authors' conclusions: Valproate is effective in reducing headache frequency and is reasonably well tolerated in adult patients with episodic migraine.

Rabbie R, Derry S,Moore RA. Ibuprofen with or without an antiemetic for acute migraine headaches in adults. Cochrane Database of Systematic Reviews. 2013; 4. [cited: url: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD008039.pub3/abstract

Background: This is an updated version of the original review published in Issue 10, 2010 (Rabbie 2010). Migraine is a common, disabling condition and a burden for the individual, health services and society. Many sufferers do not seek professional help, relying instead on over-the-counter analgesics. Co-therapy with an antiemetic should help to reduce symptoms commonly associated with migraine headaches.Objectives: To determine efficacy and tolerability of ibuprofen, alone or in combination with an antiemetic, compared to placebo and other active interventions in the treatment of acute migraine headaches in adults.Search methods: We searched the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE, the Oxford Pain Relief Database, ClinicalTrials.gov, and reference lists for studies through 22 April 2010 for the original review and to 14 February 2013 for the update.Selection criteria: We included randomised, double-blind, placebo- or active-controlled studies using self-

administered ibuprofen to treat a migraine headache episode, with at least 10 participants per treatment arm.Data collection and analysis: Two review authors independently assessed trial quality and extracted data. Numbers of participants achieving each outcome were used to calculate relative risk and number needed to treat (NNT) or harm (NNH) compared to placebo or other active treatment.Main results: No new studies were found for this update. Nine included studies (4373 participants, 5223 attacks) compared ibuprofen with placebo or other active comparators; none combined ibuprofen with a self-administered antiemetic. All studies treated attacks with single doses of medication. For ibuprofen 400 mg versus placebo, NNTs for 2-hour pain-free (26% versus 12% with placebo), 2-hour headache relief (57% versus 25%) and 24-hour sustained headache relief (45% versus 19%) were 7.2, 3.2 and 4.0, respectively. For ibuprofen 200 mg versus placebo, NNTs for 2-hour pain-free (20% versus 10%) and 2-hour headache relief (52% versus 37%) were 9.7 and 6.3, respectively. The higher dose was significantly better than the lower dose for 2-hour headache relief. Soluble formulations of ibuprofen 400 mg were better than standard tablets for 1-hour, but not 2-hour headache relief.Similar numbers of participants experienced adverse events, which were mostly mild and transient, with ibuprofen and placebo.Ibuprofen 400 mg did not differ from rofecoxib 25 mg for 2-hour headache relief or 24-hour headache relief.Authors' conclusions: We found no new studies since the last version of this review. Ibuprofen is an effective treatment for acute migraine headaches, providing pain relief in about half of sufferers, but complete relief from pain and associated symptoms for only a minority. NNTs for all efficacy outcomes were better with 400 mg than 200 mg in comparisons with placebo, and soluble formulations provided more rapid relief. Adverse events were mostly mild and transient, occurring at the same rate as with placebo.

Wider B, Pittler Max H,Ernst E. Feverfew for preventing migraine. Cochrane Database of Systematic Reviews. 2015; 4. [cited: url: http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002286.pub3/abstract

Background: This review is an update of a previously published review in the Cochrane Database of Systematic Reviews on 'Feverfew for preventing migraine' (2004, Issue 1). Feverfew (Tanacetum parthenium L.) extract is a herbal remedy, which has been used for preventing attacks of migraine.Objectives: To systematically review the evidence from double-blind randomised controlled trials (RCTs) assessing the clinical efficacy and safety of feverfew monopreparations versus placebo for preventing migraine.Search methods: For this updated version of the review we searched CENTRAL, MEDLINE, EMBASE and AMED to January 2015. We contacted manufacturers of feverfew and checked the bibliographies of identified articles for further trials.Selection criteria: We included randomised, placebo-controlled, double-blind trials assessing the efficacy of feverfew monopreparations for preventing migraine in patients of any age. We included trials using clinical outcome measures, while we excluded trials focusing exclusively on physiological parameters. There were no restrictions regarding the language of publication.Data collection and analysis: We systematically extracted data on patients, interventions, methods, outcome measures, results and adverse events. We assessed risk of bias using the Cochrane 'Risk of bias' tool and evaluated methodological quality using the Oxford Quality Scale developed by Jadad and colleagues. Two review authors (BW and MHP for this update, MHP and EE for the original version) independently selected studies, assessed methodological quality and extracted data. We resolved disagreements concerning evaluation of individual trials through discussion.Main results: We identified one new study for this update, resulting in six trials (561 patients) meeting the inclusion criteria. Five of the six trials reported on the main outcome, migraine frequency. Although five of the trials were generally of good methodological quality, all studies were either of unclear or high risk of bias with regards to sample size. Pooled analysis of the results was not possible due to the lack of common outcome measures and heterogeneity between studies in terms of participants, interventions and designs.The most recent trial added to this version of the review is rigorous and larger (n = 218), using a stable feverfew extract at a dose determined by a previous dose-finding trial. It reports that feverfew reduced migraine frequency by 1.9 attacks from 4.8 to 2.9 and placebo by 1.3 from to 4.8 to 3.5 per month, resulting in a difference in effect between feverfew and placebo of 0.6 attacks per month. For the secondary outcome measures intensity and duration of migraine attacks, incidence and severity of nausea and vomiting, and global assessment no statistically significant differences were reported. Results of previous trials are not

convincing: three trials reporting positive effects of feverfew are all of small sample size (17 to 60 participants), while two rigorous trials (n = 50, 147) did not find significant differences between feverfew and placebo. Only mild and transient adverse events, most commonly gastrointestinal complaints and mouth ulcers, were reported in the included trials.Authors' conclusions: Since the last version of this review, one larger rigorous study has been included, reporting a difference in effect between feverfew and placebo of 0.6 attacks per month. This adds some positive evidence to the mixed and inconclusive findings of the previous review. However, this constitutes low quality evidence, which needs to be confirmed in larger rigorous trials with stable feverfew extracts and clearly defined migraine populations before firm conclusions can be drawn. It appears from the data reviewed that feverfew is not associated with any major safety concerns.

Other Systematic reviews

Amoozegar F,Pringsheim T. Rizatriptan for the acute treatment of migraine: consistency, preference, satisfaction, and quality of life (Provisional abstract). Patient Preference and Adherence. 2009; 2. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12012052364/frame.html

Rizatriptan is a 5HT (IB/ID) agonist with proven efficacy in the acute treatment of migraine headache. We performed a systematic review of the literature for clinical trials of rizatriptan incorporating important patient outcomes including consistency of response, preference, satisfaction, and quality of life. We found evidence that rizatriptan provides consistent relief of migraine attacks and that patients prefer rizatriptan over other treatments because of its speed of relief. Patient satisfaction with rizatriptan is significantly higher than placebo, but appears equivalent to most other triptans. Migraine-specific quality of life at 24 hours is significantly better in patients treated with rizatriptan compared to placebo, while overall long-term quality of life is less affected. The published clinical trials included in this systematic review are subject to bias due to the open-label nature of preference trials and the doses chosen for comparison in head-to-head trials.

Asseburg C, Peura P, Oksanen T, Turunen J, Purmonen T,Martikainen J. Cost-effectiveness of oral triptans for acute migraine: mixed treatment comparison (Structured abstract). International Journal of Technology Assessment in Health Care. 2012; 4. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cleed/articles/NHSEED-22012040635/frame.html

BACKGROUND:

The cost-effectiveness of triptans in the treatment of migraine has not been assessed since generic sumatriptan entered the Finnish market in 2008.

METHODS:

Using systematic review and mixed treatment comparison, the effectiveness of triptans was estimated with regard to 2-hour response, 2-hour pain-free, recurrence, and any adverse event, using published clinical data. Direct and indirect costs (2010 EUR, societal perspective) and quality-adjusted life-years (QALYs) were evaluated over one acute migraine attack using a decision-tree model.

RESULTS:

The meta-analysis combined data from fifty-six publications. The highest probability of achieving the primary outcome, "sustained pain-free, no adverse event" (SNAE), was estimated for eletriptan 40 mg (20.9 percent). Sumatriptan 100 mg was the treatment with lowest estimated costs (€20.86), and the incremental cost-effectiveness ratio of eletriptan 40 mg compared with sumatriptan 100 mg was €43.65 per SNAE gained (€19,659 per QALY gained).

CONCLUSION:

Depending on the decision-maker's willingness-to-pay threshold, either sumatriptan 100 mg or eletriptan 40 mg is likely to be cost-effective

Bailey B,McManus BC. Treatment of children with migraine in the emergency department: a qualitative systematic review (Structured abstract). Pediatric Emergency Care. 2008; 5. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12008104491/frame.html

OBJECTIVE:

To evaluate which treatment could be effective in the emergency department (ED) for children with migraine and status migrainosus, we carried out a qualitative systematic review of randomized controlled trials (RCTs) that evaluated treatment that could be used for those conditions.

METHODS:

Databases (Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, Cochrane Controlled Trials Register, MedLine, and EMBASE) were searched for RCTs that evaluated treatment of migraine in children (<18 years of age). Guidelines published on the subject were checked for missed references. Characteristics of the identified studies as well as primary outcome (headache relief), other recognized primary outcomes, and adverse events were abstracted. Quality of the RCTs was evaluated using the Jadad score.

RESULTS:

Of the 14 trials included in the review, only 1 was performed in an ED after other treatments have failed. In that situation, prochlorperazine was more effective than ketorolac in relieving pain at 1 hour. Other treatments were evaluated by neurologists on their outpatients who started the studied drugs early at the beginning of the migraine without previous treatment. In that situation, ibuprofen (n = 3) and acetaminophen (n = 1) were better than placebo for pain relief. The efficacy of intranasal sumatriptan (n = 4), oral rizatriptan (n = 3), and oral zolmitriptan (n = 2) for pain relief was unclear. Oral sumatriptan (n = 1) and oral dihydroergotamine (n = 1) were not effective.

CONCLUSIONS:

There is a lack of studies addressing the question of treatment in the ED for children experiencing migraine. Although other treatments were found effective in children with migraine, none was evaluated in the ED except prochlorperazine and ketorolac.

Bakola E, Skapinakis P, Tzoufi M, Damigos D,Mavreas V. Anticonvulsant drugs for pediatric migraine prevention: an evidence-based review (Structured abstract). European Journal of Pain. 2009; 9. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12009109669/frame.html

BACKGROUND:

The use of anticonvulsant drugs for the prevention of migraine in children and adolescents has been supported in the past.

AIMS:

To evaluate the available evidence for the efficacy and safety of anticonvulsants drugs in the prevention of migraine attacks in children and adolescents.

METHODS:

Studies were selected through a comprehensive literature search. We included all types of study designs (controlled and uncontrolled) due to the limited evidence. Monthly migraine frequency was used as the primary outcome measure in most of the studies. Studies were classified into levels of evidence according to their design.

RESULTS:

Fourteen studies were included with a total of 939 patients. Topiramate (4 randomized controlled trials [RCT], two uncontrolled trials), sodium valproate/divalproex sodium (two RCTs, one uncontrolled trial, two retrospective chart reviews) levetiracetam and zonisamide (both only uncontrolled studies) are the anticonvulsants that have been reported in the literature. The findings show that valproate is not different from placebo and topiramate may not be different but further randomized trials are needed. All drugs were well tolerated in this age group with no serious events reported.

CONCLUSIONS:

The use of anticonvulsants in the prevention of migraine in children and adolescents is not adequately supported by methodologically sound RCTs. More research is needed in the future to establish the efficacy and safety of specific agents.

Barnes NP. Migraine headache in children. Clinical Evidence 2015;

INTRODUCTION: Diagnosis of migraine headache in children can be difficult as it depends on subjective symptoms; diagnostic criteria are broader than in adults. Migraine occurs in 3% to 10% of children and increases with age up to puberty. Migraine spontaneously remits after puberty in half of children, but if it begins during adolescence it may be more likely to persist throughout adulthood.

METHODS AND OUTCOMES: We conducted a systematic review and aimed to answer the following clinical questions: What are the effects of treatments for acute attacks of migraine headache in children? What are the effects of pharmacological prophylaxis for migraine headache in children? We searched: Medline, Embase, The Cochrane Library, and other important databases up to June 2014 (Clinical Evidence reviews are updated periodically; please check our website for the most up-to-date version of this review). We included harms alerts from relevant organisations such as the US Food and Drug Administration (FDA) and the UK Medicines and Healthcare products Regulatory Agency (MHRA).

RESULTS: Twenty-three studies were included. We performed a GRADE evaluation of the quality of evidence for interventions.

CONCLUSIONS: In this systematic review we present information relating to the effectiveness and safety of the following interventions. For acute symptom relief: 5HT1 agonists [such as triptans], non-steroidal anti-inflammatory drugs [NSAIDs], and paracetamol. And, for prophylaxis: beta-blockers, flunarizine, pizotifen, and topiramate.

Batty AJ, Hansen RN, Bloudek LM, Varon SF, Hayward EJ, Pennington BW, et al. The cost effectiveness of onabotulinumtoxinA for the prophylaxis of headache in adults with chronic migraine in the UK (Structured abstract). Journal of Medical Economics. 2013; 7. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cleed/articles/NHSEED-22013019520/frame.html

BACKGROUND:

Although chronic migraine is associated with substantial disability and costs, few treatments have been shown to be effective. OnabotulinumtoxinA (Botox, Allergan Inc., Irvine, CA) is the first treatment to be licensed in the UK for the prophylaxis of headaches in adults with chronic migraine. This study aims to evaluate the cost-effectiveness of onabotulinumtoxinA in this indication in the UK.

METHODS:

A state-transition (Markov) model was developed comparing onabotulinumtoxinA to placebo. Efficacy data and utility values were taken from the pooled Phase III REsearch Evaluating Migraine Prophylaxis Therapy (PREEMPT) clinical trials program (n = 1384). Estimates of resource utilisation were taken from the International Burden of Migraine Study (IBMS), and stopping rules were informed by published medical guidelines and clinical data. This study estimated 2-year discounted costs and quality-adjusted life years (QALYs) from the UK National Health Service perspective.

RESULTS:

At 2 years, treatment with onabotulinumtoxinA was associated with an increase in costs of £1367 and an increase in QALYs of 0.1 compared to placebo, resulting in an incremental cost-effectiveness ratio (ICER) of £15,028. Treatment with onabotulinumtoxinA reduced headache days by an estimated 38 days per year at a cost of £18 per headache day avoided. Sensitivity analysis showed that utility values had the greatest influence on model results. The ICER remained cost-effective at a willingness to pay threshold of £20,000-£30,000/QALY in the majority of scenario analyses as well as in probabilistic sensitivity analysis, where onabotulinumtoxinA was cost-effective on 96% of occasions at a threshold of £20,000/QALY and 98% of occasions at £30,000/QALY.

CONCLUSION:

OnabotulinumtoxinA has been shown to reduce the frequency of headaches in patients with chronic migraine and can be considered a cost-effective use of resources in the UK National Health Service. The uncertainties in the model relate to the extrapolation of clinical data beyond the 56-week trial.

Brigo F, Storti M, Nardone R, Fiaschi A, Bongiovanni LG, Tezzon F, et al. Transcranial magnetic stimulation of visual cortex in migraine patients: a systematic review with meta-analysis (Provisional abstract). Database of Abstracts of Reviews of Effects. 2012; 1. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12012042094/frame.html

We systematically reviewed the literature to evaluate the prevalence of phosphenes and the phosphene threshold (PT) values obtained during single-pulse transcranial magnetic stimulation (TMS) in adults with migraine. Controlled studies measuring PT by single-pulse TMS in adults with migraine with or without aura (MA, MwA) were systematically searched. Prevalence of phosphenes and PT values were assessed calculating mean difference (MD) and odds ratio (OR) with 95 % confidence intervals (CI). Ten trials (277 migraine patients and 193 controls) were included. Patients with MA had statistically significant lower PT compared with controls when a circular coil was used (MD -28.33; 95 % CI -36.09 to -20.58); a similar result was found in MwA patients (MD -17.12; 95 % CI -23.81 to -10.43); using a figure-of-eight coil the difference was not statistically significant. There was a significantly higher phosphene prevalence in MA patients compared with control subjects (OR 4.21; 95 % CI 1.18-15.01). No significant differences were found either in phosphene reporting between patients with MwA and controls, or in PT values obtained with a figure-of-eight coil in MA and MwA patients versus controls. Overall considered, these results support the hypothesis of a primary visual cortex hyper-excitability in MA, providing not enough evidence for MwA. A significant statistical heterogeneity reflects clinical and methodological differences across studies, and higher temporal variabilities among PT measurements over time, related to unstable excitability levels. Patients should therefore be evaluated in the true interictal period with an adequate headache-free interval. Furthermore, skull thickness and ovarian cycle should be assessed as possible confounding variables, and sham stimulation should be performed to reduce the rate of false positives. Phosphene prevalence alone cannot be considered a measure of cortical excitability, but should be integrated with PT evaluation.

Brown JS, Papadopoulos G, Neumann PJ, Price M, Friedman M,Menzin J. Cost-effectiveness of migraine prevention: the case of topiramate in the UK (Structured abstract). Cephalalgia. 2006; 12. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cleed/articles/NHSEED-22006002434/frame.html

The aim of this study was to assess the cost-effectiveness of topiramate vs. no preventive treatment in the UK. Model inputs included baseline migraine frequency, treatment discontinuation and response, preventive and acute medical cost per attack [2005 GBP (pound)] and gain in health utility. Outcomes included monthly migraines averted, acute and preventive treatment costs and cost per quality-adjusted life year (QALY). Topiramate was associated with 1.8 fewer monthly migraines and a QALY gain of 0.0384. The incremental cost of topiramate vs. no preventive treatment was about 10 UK pounds per migraine averted and 5700 UK pounds per QALY. Results are sensitive to baseline monthly migraine frequency, triptan use rate and the gain in utility. Incorporating savings from reduced work loss (about 36 UK pounds per month) suggests that topiramate would be cost saving compared with no preventive treatment. This analysis suggests that topiramate is a cost-effective treatment for migraine prevention compared with no preventive treatment.

Brown JS, Rupnow MF, Neumann P, Friedman M,Menzin J. Cost effectiveness of topiramate in the prevention of migraines in the United States: an update (Structured abstract). Managed Care Interface. 2006; 12. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cleed/articles/NHSEED-22007000385/frame.html

A previously published decision-analytic model assessing the clinical and economic consequences of topiramate versus no preventive treatment in migraineurs was updated with new published literature and unpublished clinical trial data. The model captured baseline migraine days, treatment discontinuation, treatment response (i.e., > or = 75%, 50%-74%, and < 50% reduction in migraine frequency), hours of disability, cost of preventive therapy, cost of acute treatment (pharmacy and medical service), and wages. Topiramate was associated with 29 fewer migraine-days and 78 fewer hours of disability per year, compared with no preventive treatment. The incremental cost per migraine-day averted for topiramate versus no preventive treatment was dollar 29 when only direct medical costs were considered and dollar 2 when total costs were included. Model results were sensitive to baseline migraine-days, response probability, and probability of an attack being treated with a triptan. Topiramate may be a cost-effective treatment for the prevention of migraine.

Busch V,Gaul C. Exercise in migraine therapy. Is there any evidence for efficacy: a critical review (Structured abstract). Headache. 2008; 6. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12008105496/frame.html

BACKGROUND:

Some migraine patients find that regular exercise helps in reducing the frequency of headache attacks. In addition, exercise in migraine is recommended from many headache experts. However, most of these recommendations refer to some anecdotal reports or observational studies in literature stating that regular exercise can reduce the frequency and severity of migraine.

OBJECTIVE:

The purpose of this review is to investigate whether recommendations for exercise in migraine are based on sufficient data to cope with requirements of an evidence-based modern migraine therapy. The review summarizes and discusses all available trials on this topic.

RESULTS:

Eight studies und 4 case reports investigated the therapeutic role of aerobic exercise on migraine headache. Some results are controversial regarding the efficacy of sports intervention in migraine. The majority of studies did not find a significant reduction of headache attacks or headache duration and only indicate a reduction of pain intensities in migraine patients due to regular exercise. The grade of recommendation of exercise in migraine based on evidence based medicine (EBM)-criteria is presently B-C. But due to methodological limitations, the available data are insufficient for a final statement on this topic.

CONCLUSIONS:

To further recommend exercise in migraine based on EBM-criteria, more studies are imperative. Future studies should adhere to the rules for randomized clinical trials in pharmacological migraines prophylaxis. Implications for further studies are given

Butera G, Biondi-Zoccai GG, Carminati M, Caputi L, Usai S, Bussone G, et al. Systematic review and meta-analysis of currently available clinical evidence on migraine and patent foramen ovale percutaneous closure: much ado about nothing? (Provisional abstract). Catheterization and Cardiovascular Interventions. 2010; 4. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12010003614/frame.html

OBJECTIVES:

To investigate the role of transcatheter closure of patent foramen ovale on the occurrence of migraine.

BACKGROUND:

In recent years, a potential relationship between, migraine, stroke, and patent foramen ovale (PFO) has emerged.

METHODS:

BioMedCentral, Google Scholar, and PubMed from January 2000 to December 2008 were systematically searched for pertinent clinical studies. Secondary sources were also used. Secondary prevention studies of transcatheter closure for patent foramen ovale were required to include at least more than 10 patients followed for more than 6 months. The primary end-point was the rate of cured or significantly improved migraine after percutaneous PFO closure.

RESULTS:

After excluding 637 citations, we finally included a total of 11 studies for a total of 1,306 patients. Forty percent of the subjects included suffered from migraine, while most had a previous history of transient ischemic attack/stroke and were investigated retrospectively. Quantitative synthesis showed that complete cure of migraine in 46% (95% C.I.25-67%), while resolution or significant improvement of migraine occurred in 83% (95% C.I. 78-88%) of cases.

CONCLUSIONS:

Notwithstanding the limitations inherent in the primary studies, this systematic review suggests that a significant group of subjects with migraine, in particular if treated after a neurological event, may benefit from percutaneous closure of their patent foramen ovale. However, many questions remain unsolved.

Butt JH, Franzmann U,Kruuse C. Endothelial function in migraine with aura - a systematic review. Headache 2015;55(1):35-54

BACKGROUND: An increased risk of ischemic stroke is repeatedly reported in young subjects with migraine with aura (MA). Such may be caused by changes in endothelial function. The present review evaluates current evidence on endothelial function in MA patients.

METHODS: A systematic search of electronic databases (Medline, Embase, Cochrane library) was performed, and a search in associated reference lists of identified studies was done.

RESULTS: In total, 27 studies met inclusion criteria for this review. Six studies assessed endothelial function by flow-mediated dilation; four reported no differences compared with healthy subjects, one study reported an increase and one study a decrease in migraineurs. Peripheral arterial tonometry was applied in one study where no changes were detected between groups. Likewise, applying venous occlusion plethysmography elicited comparable responses. Arterial function was investigated in six studies; increased augmentation

index and decreased arterial distensibility were reported in migraineurs, whereas findings regarding pulse wave velocity were dissimilar. However, when investigating levels of endothelial progenitor cells, two studies reported reduced levels in migraineurs, and several studies on endothelial markers in the areas of inflammation, oxidative stress, and coagulation found increased endothelial activation in migraineurs, particularly in MA. One study, assessing cerebral endothelial function using transcranial Doppler sonography, reported lower cerebrovascular reactivity to L-arginine in the posterior cerebral arteries in migraineurs.

CONCLUSION: Endothelial dysfunction appears not to be of importance in MA patients. However, the studies were few with a wide variety of techniques applied in small groups of patients. Endothelial biomarkers were increased in patients indicating a possible subtle change in the endothelium. Further investigations on larger groups of patients combining testing of endothelial dysfunction as well as biomarkers are warranted to identify whether or not endothelial changes may play a role in the increased risk of stroke in young MA patients.

Cameron C, Kelly S, Hsieh S-C, Murphy M, Chen L, Kotb A, et al. Triptans in the Acute Treatment of Migraine: A Systematic Review and Network Meta-Analysis. Headache 2015;55 Suppl 4(221-35

BACKGROUND: Although triptans are widely used in the acute management of migraine, there is uncertainty around the comparative efficacy of triptans among each other and vs non-triptan migraine treatments. We conducted systematic reviews and network meta-analyses to compare the relative efficacy of triptans (alone or in combination with other drugs) for acute treatment of migraines compared with other triptan agents, non-steroidal anti-inflammatory drugs (NSAIDs), acetylsalicylic acid (ASA), acetaminophen, ergots, opioids, or anti-emetics.

METHODS: The Cochrane Library, MEDLINE, and EMBASE were searched for randomized controlled trials that compared triptans (alone or in combination with other drugs) with placebo-controlled or active migraine treatments. Study selection, data extraction, and quality assessment were completed independently by multiple reviewers. Outcome data were combined and analyzed using a Bayesian network meta-analysis. For each outcome, odds ratios, relative risks, and absolute probability of response were calculated.

RESULTS: A total of 133 randomized controlled trials met the inclusion criteria. Standard dose triptans relieved headaches within 2 hours in 42 to 76% of patients, and 2-hour sustained freedom from pain was achieved for 18 to 50% of patients. Standard dose triptans provided sustained headache relief at 24 hours in 29 to 50% of patients, and sustained freedom from pain in 18 to 33% of patients. Use of rescue medications ranged from 20 to 34%. For 2-hour headache relief, standard dose triptan achieved better outcomes (42 to 76% response) than ergots (38%); equal or better outcomes than NSAIDs, ASA, and acetaminophen (46 to 52%); and equal or slightly worse outcomes than combination therapy (62 to 80%). Among individual triptans, sumatriptan subcutaneous injection, rizatriptan ODT, zolmitriptan ODT, and eletriptan tablets were associated with the most favorable outcomes.

INTERPRETATION/CONCLUSIONS: Triptans are effective for migraine relief. Standard dose triptans are associated with better outcomes than ergots, and most triptans are associated with equal or better outcomes compared with NSAIDs, ASA, and acetaminophen. Use of triptans in combination with ASA or acetaminophen, or using alternative modes of administration such as injectables, may be associated with slightly better outcomes than standard dose triptan tablets.

Cao Y,Zheng OJ. Tonabersat for migraine prophylaxis: a systematic review (Provisional abstract). Pain Physician. 2014; 1. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12014007858/frame.html

BACKGROUND:

Randomized clinical trials assessing the efficacy and tolerability of tonabersat compared with placebo as prophylaxis for migraine were systematically reviewed in this study. By analyzing all available data, we

aimed to establish an overall estimate of any association in order to more accurately inform clinicians and care-givers about how to prevent migraines.

OBJECTIVE:

To evaluate the efficacy and tolerability of tonabersat when it is used for migraine prevention.

STUDY DESIGN:

Systematic review of tonabersat for migraine prophylaxis.

METHODS:

Computerized database search of The Cochrane Pain, Palliative & Supportive Care Trials Register, The Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library), Pubmed, and EMBASE for randomized, double-blind, placebo-controlled trials on tonabersat for migraine until January, 2013. We also searched the ongoing trials. We did not impose any language restrictions.The quality assessment and clinical relevance criteria utilized were the Cochrane Pain, Palliative & Supportive Care review group criteria as utilized for randomized trials.

OUTCOME MEASURES:

The primary outcome measure was the change in mean number of migraine headache days. The secondary outcome measures were change in attacks, responder rates, the reduction of the consumption of rescue medication, and adverse events.

RESULTS:

For this systematic review, 133 studies were identified. Of these, 131 studies were excluded, and a total of 2 studies (after removal of duplicate publications) met inclusion criteria for methodological quality assessment with the randomized trial study. The evidence for tonabersat for migration prophylaxis failed to demonstrate a reduction when compared to placebo because of a lack of evidence. But the good tolerability supports further exploration of tonabersat in the prevention of migraine attacks.

LIMITATIONS:

The limitation of this systematic review was a lack of available evidence.

CONCLUSION:

There is fair evidence for migraine prophylaxis, but a lack of available evidence for tonabersat for migraine prophylaxis. Although tonabersat failed to demonstrate a significantly greater reduction of migraine headache days than placebo, it was well tolerated. Future work should further investigate the utility of tonabersat in the preventive management of migraine.

Chen LC,Ashcroft DM. Meta-analysis examining the efficacy and safety of almotriptan in the acute treatment of migraine (Provisional abstract). Headache. 2007; 8. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12007003402/frame.html

OBJECTIVE:

To evaluate the comparative efficacy and safety of oral almotriptan in treating acute migraine attacks.

BACKGROUND:

Almotriptan is an oral selective sertonin(1B/1D) receptor agonist (triptan) with a high bioavailability and short half-life, developed for the treatment of migraine. In recent years, a number of randomized controlled trials have been published examining the efficacy and safety of almotriptan in the acute treatment of migraine.

METHODS:

Systematic review and meta-analysis of randomized controlled trials (RCTs) using a random-effects model to estimate the pooled rate ratios (RRs) and 95% confidence intervals (95%CI) for the proportions of patients achieving headache relief and pain-free responses at 1 or 2 hours post-dose, sustained pain-free response at 2-24 hours post-dose, and safety outcomes (proportions of patients experiencing any adverse events, dizziness, somnolence, asthenia, and chest tightness) comparing almotriptan against placebo, other triptans, and different dosages of almotriptan. Absolute rate differences (ARDs) for 2-hour headache relief, pain free, and sustained pain free responses between almotriptan and placebo were also calculated.

RESULTS:

Eight RCTs involving 4995 patients were included in the analysis. Almotriptan 12.5 mg was significantly more effective than placebo for all efficacy outcomes (RRs ranged from 1.47 to 2.15; ARDs ranged from 0.01 to 0.28) and there were no significant differences in any of the safety outcomes. There were also no significant differences in efficacy outcomes comparing almotriptan 12.5 mg against sumatriptan 100 mg and zolmitriptan 2.5 mg, but almotriptan 12.5 mg was associated with significantly fewer adverse events than sumatriptan 100 mg (RR: 0.39, 95%CI: 0.23, 0.67). However, there was no significant difference between almotriptan and sumatriptan in terms of clinically important adverse effects, such as dizziness, somnolence, asthenia, and chest tightness. Almotriptan 12.5 mg was significantly less effective than almotriptan 25 mg for 1-hour pain-free response (RR: 0.45, 95%CI: 0.21, 0.95), but associated with significantly fewer patients experiencing adverse events (RR: 0.61, 95%CI: 0.41, 0.91) than almotriptan 25 mg.

CONCLUSIONS:

Almotriptan 12.5 mg is an effective treatment for acute attacks of migraine, in particular, it has been found to be as effective as sumatriptan 100 mg and zolmitriptan 2.5 mg. The risk of adverse events associated with almotriptan 12.5 mg was similar to placebo and significantly lower than sumatriptan 100 mg. Further research is required to assess the comparative efficacy of almotriptan against other triptans.

Chen LC,Ashcroft DM. Meta-analysis of the efficacy and safety of zolmitriptan in the acute treatment of migraine (Structured abstract). Headache. 2008; 2. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12008104038/frame.html

OBJECTIVE:

To assess the relative efficacy and safety of zolmitriptan in the treatment of acute migraine attacks.

BACKGROUND:

Zolmitriptan is a second-generation triptan developed for the treatment of migraine. Numerous randomized controlled trials (RCTs) have been carried out to compare different dosages and formulations of zolmitriptan against other treatments for acute migraine.

METHODS:

Random effects meta-analysis of 24 RCTs, including 15,408 patients suffering from acute migraine attacks. Subgroup analyses compared differences in response between different dosages and formulations of zolmitriptan, and other triptan comparators.

RESULTS:

Zolmitriptan 2.5 mg tablet was found to be as effective as almotriptan 12.5 mg, eletriptan 40 mg, sumatriptan 50 mg and 100 mg and more effective than naratriptan 2.5 mg in terms of 2-hour pain-free rates. Likewise, zolmitriptan 5 mg tablet was as effective as sumatriptan 50 mg and 100 mg in 2-hour pain-free rates. Compared against zolmitriptan 2.5 mg tablet, eletriptan 80 mg was more effective in achieving headache

relief, pain-free and sustained pain-free responses, and rizatriptan 10 mg was more effective in terms of sustained pain-free rates. Zolmitriptan 2.5 mg tablet was associated with a lower risk of adverse events than eletriptan 80 mg but higher risk than naratriptan 2.5 mg and rizatriptan 10 mg. Zolmitriptan 5 mg tablet was superior to zolmitriptan 2.5 mg tablet in achieving 1- and 2-hour pain-free response. There were no significant differences in 1- and 2-hour headache relief and adverse event rates between the different formulations of zolmitriptan 2.5 mg.

CONCLUSIONS:

Zolmitriptan 2.5 mg tablet is an effective treatment for acute attacks of migraine showing similar efficacy to almotriptan 12.5 mg, eletriptan 40 mg, and sumatriptan 50 mg, and being more effective than naratriptan 2.5 mg in terms of pain-free response at 2 hours post dose. Zolmitriptan 2.5 mg tablet was also as effective as rizatriptan 10 mg in terms of headache relief and pain-free response but less effective in terms of sustained pain-free response.

Chen Y-F, Bramley G, Unwin G, Hanu-Cernat D, Dretzke J, Moore D, et al. Occipital nerve stimulation for chronic migraine--a systematic review and meta-analysis. PLoS ONE [Electronic Resource] 2015;10(3):e0116786

BACKGROUND: Chronic migraine is a debilitating headache disorder that has significant impact on quality of life. Stimulation of peripheral nerves is increasingly being used to treat chronic refractory pain including headache disorders. This systematic review examines the effectiveness and adverse effects of occipital nerve stimulation (ONS) for chronic migraine.

METHODS: Databases, including the Cochrane Library, MEDLINE, EMBASE, CINAHL and clinical trial registers were searched to September 2014. Randomized controlled trials (RCTs), other controlled and uncontrolled observational studies and case series (n> 10) were eligible. RCTs were assessed using the Cochrane risk of bias tool. Meta-analysis was carried out using a random-effects model. Findings are presented in summary tables and forest plots.

RESULTS: Five RCTs (total n=402) and seven case series (total n=115) met the inclusion criteria. Pooled results from three multicenter RCTs show that ONS was associated with a mean reduction of 2.59 days (95% CI 0.91 to 4.27, I2=0%) of prolonged, moderate to severe headache per month at 3 months compared with a sham control. Results for other outcomes generally favour ONS over sham controls but quantitative analysis was hampered by incomplete publication and reporting of trial data. Lead migration and infections are common and often require revision surgery. Open-label follow-up of RCTs and case series suggest long-term effectiveness can be maintained in some patients but evidence is limited.

CONCLUSIONS: While the effectiveness of ONS compared to sham control has been shown in multiple RCTs, the average effect size is modest and may be exaggerated by bias as achieving effective blinding remains a methodological challenge. Further measures to reduce the risk of adverse events and revision surgery are needed.

SYSTEMATIC REVIEW REGISTRATION: this systematic review is an update and expanded work of part of a broader review registered with PROSPERO. Registration No. CRD42012002633.

Choi H,Parmar N. The use of intravenous magnesium sulphate for acute migraine: meta-analysis of randomized controlled trials (Provisional abstract). European Journal of Emergency Medicine. 2014; 1. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12013046400/frame.html

OBJECTIVE:

The objective of this study was to assess the efficacy and tolerability of intravenous magnesium for the treatment of acute migraine in adults.

SELECTION CRITERIA:

Double-blind, randomized controlled trials of intravenous magnesium for acute migraine in adults.

DATA SOURCES:

Cochrane Central Register of Controlled Trials, Medline, EMBASE, CINAHL, National Research Register Archive, ACP Journal Club, the US Government's Clinical Trial Database, Conference Proceedings, and other sources.

RESULTS:

Overall, 1203 abstracts were reviewed and five randomized controlled trials totalling 295 patients were eligible for the meta-analyses. The percentage of patients who experienced relief from headache 30 min following treatment was 7% lower in the magnesium groups compared with the controls [pooled risk difference=-0.07, 95% confidence interval (CI)=-0.23 to 0.09]. The percentage of patients who experienced side-effects or adverse events was greater in the magnesium groups compared with controls by 37% (pooled risk difference=0.370, 95% CI=0.06-0.68). The percentage of patients who needed rescue analgesic medications was slightly lower in the control groups, but this was not significant (pooled risk difference=-0.021, 95% CI=-0.16 to 0.12).

CONCLUSION:

The meta-analyses have failed to demonstrate a beneficial effect of intravenous magnesium in terms of reduction in pain relief in acute migraine in adults, showed no benefit in terms of the need for rescue medication and in fact have shown that patients treated with magnesium were significantly more likely to report side-effects/adverse events.

Colman I, Friedman BW, Brown MD, Innes GD, Grafstein E, Roberts TE, et al. Parenteral dexamethasone for acute severe migraine headache: meta-analysis of randomised controlled trials for preventing recurrence (Structured abstract). Bmj. 2008; 2. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12008103316/frame.html

OBJECTIVE:

To examine the effectiveness of parenteral corticosteroids for the relief of acute severe migraine headache and prevention of recurrent headaches.

DESIGN:

Meta-analysis.

DATA SOURCES:

Electronic databases (Cochrane Central Register of Controlled Trials, Medline, Embase, LILACS, and CINAHL), conference proceedings, clinical practice guidelines, contacts with industry, and correspondence with authors.

SELECTION CRITERIA:

Randomised controlled trials in which corticosteroids (alone or combined with standard abortive therapy) were compared with placebo or any other standard treatment for acute migraine in adults.

REVIEW METHODS:

Two reviewers independently assessed relevance, inclusion, and study quality. Weighted mean differences and relative risks were calculated and are reported with 95% confidence intervals.

RESULTS:

From 666 potentially relevant abstracts, seven studies met the inclusion criteria. All included trials used standard abortive therapy and subsequently compared single dose parenteral dexamethasone with placebo, examining pain relief and recurrence of headache within 72 hours. Dexamethasone and placebo provided similar acute pain reduction (weighted mean difference 0.37, 95% confidence interval -0.20 to 0.94). Dexamethasone was, however, more effective than placebo in reducing recurrence rates (relative risk 0.74, 95% confidence interval 0.60 to 0.90). Side effect profiles between dexamethasone and placebo groups were similar.

CONCLUSION:

When added to standard abortive therapy for migraine headache, single dose parenteral dexamethasone is associated with a 26% relative reduction in headache recurrence (number needed to treat=9) within 72 hours.

Cousins G, Hijazze S, Laar FA,Fahey T. Diagnostic accuracy of the ID migraine: a systematic review and meta-analysis (Structured abstract). Headache. 2011; 7. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12011004926/frame.html

OBJECTIVE:

The purpose of this systematic review with meta-analysis is to determine the diagnostic accuracy of the identification of migraine (ID Migraine) as a decision rule for identifying patients with migraine.

BACKGROUND:

The ID Migraine screening tool is designed to identify patients with migraine in primary care settings. Several studies have validated the ID Migraine across various clinical settings, including primary care, neurology departments, headache clinics, dental clinics, ear, nose, and throat (ENT) and ophthalmology.

METHODS:

A systematic literature search was conducted to identify all studies validating the ID Migraine, with the International Headache Criteria as the reference standard. The methodological quality of selected studies was assessed using the Quality of Diagnostic Accuracy Studies tool. All selected studies were combined using a bivariate random effects model. A sensitivity analysis was also conducted, pooling only those studies using representative patient groups (primary care, neurology departments, and headache clinics) to determine the potential influence of spectrum bias on the results.

RESULTS:

Thirteen studies incorporating 5866 patients are included. The weighted prior probability of migraine across the 13 studies is 59%. The ID Migraine is shown to be useful for ruling out rather than ruling in migraine, with a greater pooled sensitivity estimate (0.84, 95% confidence interval 0.75-0.90) than specificity (0.76, 95% confidence interval 0.69-0.83). A negative ID Migraine score reduces the probability of migraine from 59% to 23%. The sensitivity analysis reveals similar results.

CONCLUSIONS:

This systematic review quantifies the diagnostic accuracy of the ID Migraine as a brief, practical, and easy to use diagnostic tool for Migraine. Application of the ID Migraine as a diagnostic tool is likely to improve appropriate diagnosis and management of migraine sufferers.

Cui X-p, Ye J-x, Lin H, Mu J-s,Lin M. Efficacy, safety, and tolerability of telcagepant in the treatment of acute migraine: a meta-analysis. Pain Practice 2015;15(2):124-31

Although triptans are widely used for treating acute migraine, they are contraindicated or not effective in a large proportion of patients. Hence, alternative treatments are needed. Calcitonin gene-related peptide receptor antagonists, such as telcagepant, have been under investigation as a treatment for acute migraine. A meta-analysis of the efficacy of telcagepant vs. placebo and triptans (zolmitriptan or rizatriptan) was performed. Randomized controlled trials were indentified from databases using the following search terms: migraine; calcitonin gene-related peptide; calcitonin gene-related peptide receptor antagonists; efficacy; safety, and telcagepant. The primary outcome measure was pain freedom 2 hours after first treatment. The secondary outcome measure was pain relief 2 hours after first treatment. Eight trials were included in the meta-analysis (telcagepant = 4011 participants). The difference in pain freedom at 2 hours significantly favored telcagepant over placebo (odds ratio = 2.70, 95% confidence interval = 2.27-3.21, P < 0.001) and triptans over telcagepant (odds ratio = 0.68, 95% confidence interval = 0.56-0.83, P < 0.001). The difference in pain relief at 2 hours significantly favored telcagepant over placebo (odds ratio = 2.48, 95% confidence interval = 2.18-2.81, P < 0.001). The difference in pain relief at 2 hours did not significantly favor telcagepant over triptans or vice versa (odds ratio = 0.76, 95% confidence interval = 0.57-1.01, P = 0.061). These findings indicate that telcagepant can be effective for treating acute migraine. Calcitonin gene-related peptide receptor antagonists represent a potentially important alternative means of treating acute migraine.

Dai Z, Zhong J, Xiao P, Zhu Y, Chen F, Pan P, et al. Gray matter correlates of migraine and gender effect: A meta-analysis of voxel-based morphometry studies. Neuroscience 2015;299(88-96

BACKGROUND: An increasing number of neuroimaging studies have revealed gray matter (GM) anomalies of several brain regions by voxel-based morphometry (VBM) studies in migraineurs. However, not all the studies reported entirely consistent findings. Our aim is to investigate concurrence across VBM studies to help clarify the structural anomalies underpinning this condition.

METHODS: A systematic search of VBM studies of patients with migraine and healthy controls (HC) published in PubMed and Embase databases from January 2000 to March 2014 was conducted. A quantitative meta-analysis of whole-brain VBM studies in patients with migraine compared with HC was performed by means of anisotropic effect size version of signed differential mapping (AES-SDM) software package.

RESULTS: Nine studies comprising 222 patients with migraine and 230 HC subjects were included in the present study. Compared to HC subjects, the patients group showed consistent decreased GM in the posterior insular-opercular regions, the prefrontal cortex, and the anterior cingulate cortex. Results remained largely unchanged in the following jackknife sensitivity analyses. Meta-regression analysis showed that a higher percentage of females in the patient sample was associated with decreased GM in the right dorsolateral prefrontal cortex.

CONCLUSIONS: This is the first quantitative whole-brain VBM meta-analysis in migraine showing strong evidence of brain GM anomalies within the pain-processing neural network. Further longitudinal investigations are needed to determine whether these structural anomalies are reversible with effective treatment on migraine.

Deng ZQ, Zheng H, Zhao L, Zhou SY, Li Y,Liang FR. Health economic evaluation of acupuncture along meridians for treating migraine in China: results from a randomized controlled trial (Provisional abstract). BMC Complementary and Alternative Medicine. 2012; 2. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cleed/articles/NHSEED-22012040213/frame.html

BACKGROUND:

To evaluate different types of acupuncture treatment for migraine in China from the perspective of health economics, particularly the comparison between treatment of specific acupoints in Shaoyang meridians and penetrating sham acupoints treatment.

METHODS:

Data were obtained from a multicenter, randomized controlled trial of acupuncture treatment in patients with migraine. Four-hundred eighty migraineurs were randomly assigned to 3 arms of treatment with genuine acupoints and 1 arm of penetrating sham acupoints. The primary outcome measurement was the cost-effectiveness ratio (C/E), expressed as cost per 1 day reduction of headache days from baseline to week 16. Cost-comparison analyses, differences in the migraine-specific quality of life questionnaire (MSQ), and the incremental cost-effectiveness ratio were taken as secondary outcome measurements. In addition, a sensitivity analysis was conducted.

RESULTS:

The total cost per patient was ¥1273.2 (95% CI 1171.3-1375.1) in the Shaoyang specific group, ¥1427.7 (95% CI 1311.8-1543.6) in the Shaoyang non-specific group, ¥1490.8 (95% CI 1327.1-1654.6) in the Yangming specific group, and ¥1470.1 (95% CI 1358.8-1581.3) in the sham acupuncture group. The reduced days with migraine were 3.972 ± 2.7, 3.555 ± 2.8, 3.793 ± 3.6, and 2.155 ± 3.7 in these 4 groups ($P < 0.05$ for each genuine acupoints group vs the sham group), respectively, at week 16. The C/Es of the 4 groups were 320.5, 401.6, 393.1, and 682.2, respectively. Results of the sensitivity analysis were consistent with that of the cost-effectiveness analysis. The Shaoyang specific group significantly improved in all 3 MSQ domains compared with the sham acupuncture group.

CONCLUSIONS:

Treatment of specific acupoints in Shaoyang meridians is more cost-effective than that of non-acupoints, representing a dramatic improvement in the quality of life of people with migraine and a significant reduction in cost. Compared with the other 3 groups, Shaoyang-specific acupuncture is a relatively cost-effective treatment for migraine prophylaxis in China

Derry S, Wiffen PJ, Moore RA,Bendtsen L. Ibuprofen for acute treatment of episodic tension-type headache in adults. Cochrane Database of Systematic Reviews 2015;7(CD011474

BACKGROUND: Tension-type headache (TTH) affects about one person in five worldwide. It is divided into infrequent episodic TTH (fewer than one headache per month), frequent episodic TTH (1 to 14 headaches per month), and chronic TTH (15 headaches a month or more). Ibuprofen is one of a number of analgesics suggested for acute treatment of headaches in frequent episodic TTH.

OBJECTIVES: To assess the efficacy and safety of oral ibuprofen for treatment of acute episodic TTH in adults.

SEARCH METHODS: We searched CENTRAL (The Cochrane Library), MEDLINE, EMBASE, and our own in-house database to January 2015. We sought unpublished studies by asking personal contacts and searching on-line clinical trial registers and manufacturers' websites.

SELECTION CRITERIA: We included randomised, placebo-controlled studies (parallel-group or cross-over) using oral ibuprofen for symptomatic relief of an acute episode of TTH. Studies had to be prospective and include at least 10 participants per treatment arm.

DATA COLLECTION AND ANALYSIS: Two review authors independently assessed studies for inclusion, and extracted data. Numbers of participants achieving each outcome were used to calculate risk ratio (RR) and number needed to treat for an additional beneficial outcome (NNT) or number needed to treat for an additional harmful outcome (NNH) of oral ibuprofen compared to placebo for a range of outcomes, predominantly those recommended by the International Headache Society (IHS).

MAIN RESULTS: We included 12 studies, all of which enrolled adult participants with frequent episodic TTH. Nine used the IHS diagnostic criteria, but two used the older classification of the Ad Hoc Committee, and one did not describe diagnostic criteria but excluded participants with migraines. While 3094 people with TTH participated in these studies, the numbers available for any form of analysis were lower than this; placebo was taken by 733, standard ibuprofen 200 mg by 127, standard ibuprofen 400 mg by 892, and fast-acting

ibuprofen 400 mg by 230. Participants had moderate or severe pain at the start of treatment. Other participants were either in studies not reporting outcomes we could analyse, or were given one of several active comparators in single studies.For the IHS-preferred outcome of being pain free at 2 hours the NNT for ibuprofen 400 mg (all formulations) compared with placebo was 14 (95% confidence interval (CI), 8.4 to 47) in four studies, with no significant difference from placebo at 1 hour (moderate quality evidence). The NNT was 5.9 (4.2 to 9.5) for the global evaluation of 'very good' or 'excellent' in three studies (moderate quality evidence). No study reported the number of participants experiencing no worse than mild pain at 1 or 2 hours. The use of rescue medication was lower with ibuprofen 400 mg than with placebo, with the number needed to treat to prevent one event (NNTp) of 8.9 (5.6 to 21) in two studies (low quality evidence).Adverse events were not different between ibuprofen 400 mg and placebo; RR 1.1 (0.64 to 1.7) (high-quality evidence). No serious adverse events were reported.

AUTHORS' CONCLUSIONS: Ibuprofen 400 mg provides an important benefit in terms of being pain free at 2 hours for a small number of people with frequent episodic tension-type headache who have an acute headache with moderate or severe initial pain. There is no information about the lesser benefit of no worse than mild pain at 2 hours.

Evers S. The efficacy of triptans in childhood and adolescence migraine (Provisional abstract). Current Pain and Headache Reports. 2013; 7. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12013046963/frame.html

Studies on the acute treatment of migraine in children and adolescents are rare and difficult to design. In particular, the high placebo response in some trials makes it difficult to prove efficacy of a verum drug. All available placebo-controlled trials on the acute migraine treatment in children and adolescents with a triptan were analyzed with respect to different end points (rate of pain free and pain relief at 2 hours; rate of adverse events). We identified 6 crossover and 11 parallel group trials. Although the trials were heterogenous with respect to the triptans and the dosage, pooled data were calculated. The pooled responder rate of triptans for 2 hours pain free was 36.0 % in crossover trials (significant difference to placebo with 17.7 %) and 32.5 % in parallel group trials (significant difference to placebo with 26.3 %). Triptans also showed a significantly higher pain relief rate at 2 hours than placebo both in crossover and parallel group trials. The rate of adverse events was significantly higher after triptans than after placebo. However, triptans were well tolerated in all trials. At least 1 trial with significant efficacy was found for sumatriptan (10-20 mg nasal spray), zolmitriptan (2.5-5 mg tablet), rizatriptan (5-10 mg tablet), and almotriptan (12.5-25 mg tablet). Placebo rates for efficacy were considerably lower in crossover trials than in parallel group trials. This analysis suggests that parallel group trials on the acute treatment of migraine in children and adolescents with a triptan show a very low therapeutic gain because of a high placebo rate. The verum response rates, however, are very similar to those seen in adulthood trials. However, there is sufficient evidence that at least some triptans are efficacious even in childhood and adolescence.

Evers S, Savi L, Omboni S, Lisotto C, Zanchin G,Pinessi L. Efficacy of frovatriptan as compared to other triptans in migraine with aura. Journal of Headache & Pain 2015;16(514

BACKGROUND: The treatment of migraine attacks with aura by triptans is difficult since triptans most probably are not efficacious when taken during the aura phase. Moreover, there are insufficient data from randomised studies whether triptans are efficacious in migraine attacks with aura when taken during the headache phase. In this metaanalysis, we aimed to compare the efficacy of frovatriptan versus rizatriptan, zolmitriptan, and almotriptan.

METHODS: Five double-blind, randomized, controlled crossover trials were pooled. All trials had an identical design. Patients were asked to treat three consecutive migraine attacks with frovatriptan 2.5 mg and three consecutive migraine attacks with a comparative triptan (rizatriptan 10 mg; zomitriptan 2.5 mg; almotriptan 12.5 mg).

RESULTS: In this analysis, 117 migraine attacks with aura could be included (intention-to-treat population). The

mean headache intensity after 2 hours was 1.2 +/- 1.0 for frovatriptan and 1.6 +/- 1.0 for the other triptans ($p<0.05$); all triptans showed significant improvement of headache. Frovatriptan resulted in significantly lower relapse rates at 24 hours and 48 hours when taken in migraine attacks with aura.

CONCLUSIONS: Our data suggest that frovatriptan is efficacious and even superior in some endpoints also when taken during the headache phase in migraine attacks with aura. This is of particular importance for those many patients who have migraine attacks both without and with aura.

Faber C, Garcia RM, Davis J,Guyuron B. A socioeconomic analysis of surgical treatment of migraine headaches (Provisional abstract). Plastic and Reconstructive Surgery. 2012; 4. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cleed/articles/NHSEED-22012023405/frame.html

BACKGROUND:

This study is meant to compare the direct and indirect cost of migraine headache care before and after migraine surgery and to evaluate any postoperative changes in patient participation in daily activities.

METHODS:

Eighty-nine patients enrolled in a migraine surgery clinical trial completed the Migraine-Specific Quality-of-Life Questionnaire, the Migraine Disability Assessment questionnaire, and a financial cost report preoperatively and 5 years postoperatively.

RESULTS:

Mean follow-up was 63.0 months (range, 56.9 to 72.6 months). Migraine medication expenses were reduced by a median of $1997.26 annually. Median cost reduction for alternative treatment expenses was $450 annually. Patients had a median of three fewer annual primary care visits for the migraine headache treatment, resulting in a median cost reduction of $320 annually. Patients missed a median of 8.5 fewer days of work or childcare annually postoperatively, with a median regained income of $1525. The median total cost spent on migraine headache treatment was $5820 per year preoperatively, declining to $900 per year postoperatively. Total median cost reduction was $3949.70 per year postoperatively. The mean surgical cost was $8378. Significant improvements were demonstrated in all aspects of the Migraine-Specific Quality-of-Life Questionnaire and the Migraine Disability Assessment questionnaire.

CONCLUSIONS:

Surgical deactivation of migraine trigger sites has proven to be effective for the treatment of severe migraine headache. This study illustrates that the surgical treatment is a cost-effective modality, reducing direct and indirect costs. Patients may also expect improvements in the performance of and increased participation in activities of daily living.

Friedman BW, Kapoor A, Friedman MS, Hochberg ML,Rowe BH. The relative efficacy of meperidine for the treatment of acute migraine: a meta-analysis of randomized controlled trials (Structured abstract). Annals of Emergency Medicine. 2008; 6. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12009101877/frame.html

STUDY OBJECTIVE:

Despite guidelines recommending against opioids as first-line treatment for acute migraine, meperidine is the agent used most commonly in North American emergency departments. Clinical trials performed to date have been small and have not arrived at consistent conclusions about the efficacy of meperidine. We performed a systematic review and meta-analysis to determine the relative efficacy and adverse effect profile of opioids compared with nonopioid active comparators for the treatment of acute migraine.

METHODS:

We searched multiple sources (Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, CINAHL, and LILACS, emergency and headache medicine conference proceedings) for randomized controlled trials comparing parenteral opioid and nonopioid active comparators for the treatment of acute migraine headache. Our primary outcome was relief of headache. If this was unavailable, we accepted rescue medication use or we transformed visual analog scale change scores by using an established procedure. We grouped studies by comparator: a regimen containing dihydroergotamine, antiemetic alone, or ketorolac. For each study, we calculated an odds ratio (OR) of headache relief and then assessed clinical and statistical heterogeneity for the group of studies. We then pooled the ORs of headache relief with a random-effects model.

RESULTS:

From 899 citations, 19 clinical trials were identified, of which 11 were appropriate and had available data. Four trials involving 254 patients compared meperidine to dihydroergotamine, 4 trials involving 248 patients compared meperidine to an antiemetic, and 3 trials involving 123 patients compared meperidine to ketorolac. Meperidine was less effective than dihydroergotamine at providing headache relief (OR=0.30; 95% confidence interval [CI] 0.09 to 0.97) and trended toward less efficacy than the antiemetics (OR=0.46; 95% CI 0.19 to 1.11); however, the efficacy of meperidine was similar to that of ketorolac (OR=1.75; 95% CI 0.84 to 3.61). Compared to dihydroergotamine, meperidine caused more sedation (OR=3.52; 95% CI 0.87 to 14.19) and dizziness (OR=8.67; 95% CI 2.66 to 28.23). Compared to the antiemetics, meperidine caused less akathisia (OR=0.10; 95% CI 0.02 to 0.57). Meperidine and ketorolac use resulted in similar rates of gastrointestinal adverse effects (OR=1.27; 95% CI 0.31 to 5.15) and sedation (OR=1.70; 95% CI 0.23 to 12.72).

CONCLUSION:

Clinicians should consider alternatives to meperidine when treating acute migraine with injectable agents.

Gelfand AA, Goadsby PJ,Allen IE. The relationship between migraine and infant colic: a systematic review and meta-analysis. Cephalalgia 2015;35(1):63-72

CONTEXT: Infant colic is a common and distressing disorder of early infancy. Its etiology is unknown, making treatment challenging. Several articles have suggested a link to migraine.

OBJECTIVE: The objective of this article was to perform a systematic review and, if appropriate, a meta-analysis of the studies on the relationship between infant colic and migraine.

DATA SOURCES: Studies were identified by searching PubMed and ScienceDirect and by hand-searching references and conference proceedings.

STUDY SELECTION: For the primary analysis, studies specifically designed to measure the association between colic and migraine were included. For the secondary analysis, studies that collected data on colic and migraine but were designed for another primary research question were also included.

DATA EXTRACTION: Data were abstracted from the original studies, through communication with study authors, or both. Two authors independently abstracted data.

MAIN OUTCOMES AND MEASURES: The main outcome measure was the association between infant colic and migraine using both a fixed-effects model and a more conservative random-effects model.

RESULTS: Three studies were included in the primary analysis; the odds ratio for the association between migraine and infant colic was 6.5 (4.6-8.9, $p < 0.001$) for the fixed-effects model and 5.6 (3.3-9.5, $p = 0.004$) for the random-effects model. In a sensitivity analysis wherein the study with the largest effect size was removed, the odds ratio was 3.6 (95% CI 1.7-7.6, $p = 0.001$) for both the fixed-effects model and random-effects model.

CONCLUSIONS: In this meta-analysis, infant colic was associated with increased odds of migraine. If infant colic is a migrainous disorder, this would have important implications for treatment. The main limitation of this meta-analysis was the relatively small number of studies included.Copyright © International Headache Society 2014 Reprints and permissions: sagepub.co.uk/journalsPermissions.nav.

Gil-Gouveia R, Oliveira AG,Martins IP. Assessment of cognitive dysfunction during migraine attacks: a systematic review. Journal of Neurology 2015;262(3):654-65

Patients consistently report cognitive impairment during migraine attacks, yet the documentation of such dysfunction by neuropsychological evaluation has lacked similar consistency. This incongruence may be due to discrepant study designs, assessment tools and small samples sizes. To search for evidence of decline in cognitive functions during a migraine attack, compared to headache-free performance. The secondary objective was to determine if the eventual decline had a consistent neuropsychological pattern. Systematic review of the medical literature using PubMed and Cochrane library databases without limitations or restrictions from inception to March 2014, using the search terms "migraine", "cognition", "neuropsychological". We included studies in episodic migraine that had a neuropsychological evaluation performed during an attack. From 1,023 titles screened, a total of 10 articles met criteria for inclusion and were fully reviewed. Only five of these studies, comprising a total of 163 individuals, had enough data to allow an appraisal of the study question. All five studies were positive in documenting some type of reversible cognitive impairment during the migraine attack. The pattern of cognitive impairment most often documented was of executive dysfunction, but the presence of bias induced by the choice of tests and of small samples prevents this finding from being conclusive. This review supports the existence of reversible cognitive dysfunction during the migraine attack, corroborating patients' subjective descriptions. Further work is needed to establish the pattern of cognitive dysfunction, their underling pathophysiological mechanisms and the impact of these symptoms in migraine-associated disability.

Guyuron B, Kriegler JS, Davis J,Amini SB. Comprehensive surgical treatment of migraine headaches (Structured abstract). Plastic and Reconstructive Surgery. 2005; 1. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cleed/articles/NHSEED-22005000256/frame.html

The purpose of this study was to investigate the efficacy of surgical deactivation of migraine headache trigger sites. Of 125 patients diagnosed with migraine headaches, 100 were randomly assigned to the treatment group and 25 served as controls, with 4:1 allocation. Patients in the treatment group were injected with botulinum toxin A for identification of trigger sites. Eighty-nine patients who noted improvement in their migraine headaches for 4 weeks underwent surgery. Eighty-two of the 89 patients (92 percent) in the treatment group who completed the study demonstrated at least 50 percent reduction in migraine headache frequency, duration, or intensity compared with the baseline data; 31 (35 percent) reported elimination and 51 (57 percent) experienced improvement over a mean follow-up period of 396 days. In comparison, three of 19 control patients (15.8 percent) recorded reduction in migraine headaches during the 1-year follow-up ($p < 0.001$), and no patients observed elimination. All variables for the treatment group improved significantly when compared with the baseline data and the control group, including the Migraine-Specific Questionnaire, the Migraine Disability Assessment score, and the Short Form-36 Health Survey. The mean annualized cost of migraine care for the treatment group (925 dollars) was reduced significantly compared with the baseline expense (7612 dollars) and the control group (5530 dollars) ($p < 0.001$). The mean monthly number of days lost from work for the treatment group (1.2) was reduced significantly compared with the baseline data (4.41) and the control group (4.4) ($p = 0.003$). The common adverse effects related to injection of botulinum toxin A included discomfort at the injection site in 27 patients after 227 injections (12 percent), temple hollowing in 19 of 82 patients (23 percent), neck weakness in 15 of 55 patients (27 percent), and eyelid ptosis in nine patients (10 percent). The common complications of surgical treatment were temporary dryness of the nose in 12 of 62 patients who underwent septum and turbinate surgery (19.4 percent), rhinorrhea in 11 (17.7 percent), intense scalp itching in seven of 80 patients who underwent forehead surgery (8.8 percent), and minor hair loss in five (6.3 percent). Surgical deactivation of migraine trigger sites can eliminate or significantly reduce migraine

symptoms. Additional studies are necessary to clarify the mechanism of action and to determine the long-term results.

Henry BM, Roy J, Ramakrishnan PK, Vikse J, Tomaszewski KA,Walocha JA. Association of migraine headaches with anatomical variations of the Circle of Willis: Evidence from a meta-analysis. Neurologia i Neurochirurgia Polska 2015;49(4):272-7

BACKGROUND: Several studies have attempted to investigate whether variations in the Circle of Willis (COW) are more common in migraine patients and whether the subsequent changes in perfusion may contribute to the pathomechanism of migraine. However, studies are not in agreement as to whether or not there is an increased prevalence of COW variations in migraineurs.

OBJECTIVE: To determine if migraine headaches are associated with variations in morphology of the COW.

METHODS: A systemic search of the major electronic databases was performed for articles studying the association of variations in the COW and migraine. Data on the prevalence of variations in patients with migraine were extracted and pooled into the meta-analysis.

RESULTS: A total of four articles (n=807 patients) were deemed eligible for the meta-analysis. Migraine, regardless of subtype, was found to be associated with variations in the COW (OR=2.27, 95%CI 1.53-3.38, p<0.0001). An incomplete posterior circle (OR=2.60, 95%CI 1.79-3.76, p<0.00001) was found to be more strongly associated with migraine than an incomplete anterior circle (OR=2.01, 95%CI 1.15-3.53, p=0.01). In sub-group analysis, migraine with aura was found to be associated with both an incomplete posterior (OR=3.55, 95%CI 2.25-5.59, p<0.00001) and an incomplete anterior circle (OR=2.35, 95%CI 1.20-4.62, p=0.01). Migraine without aura was found only to be associated with an incomplete posterior circle (OR=2.10, 95%CI 1.39-3.17, p=0.0004).

CONCLUSIONS: Migraine is associated with anatomical variations in both the anterior and posterior portions of the COW. However, larger prospective trials are needed to determine the true prevalence of variations and their pathological significance.

Hens M, Villaverde-Hueso A, Alonso V, Abaitua I,Posada de la Paz M. Comparative cost-effectiveness analysis of oral triptan therapy for migraine in four European countries (Structured abstract). European Journal of Health Economics. 2013; 2. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cleed/articles/NHSEED-22013027427/frame.html

AIM:

To assess the differences in the cost-effectiveness of oral triptan therapy for migraines among European countries.

METHODS:

A cost-effectiveness analysis of triptan therapy for migraine was conducted from a health-care payer perspective in four European countries (France, Italy, Spain and the UK). The study included those orally administered triptans available in all of these countries (almotriptan, brand-name sumatriptan, generic sumatriptan, zolmitriptan), and it was performed using a decision-tree model that incorporated costs of the drugs and probabilities associated with the possible events and outcomes. Average cost-effectiveness ratios were calculated in two different scenarios.

RESULTS:

The average cost-effectiveness ratio showed wide variations across the different countries, these differences being up to 131 % (almotriptan), 77 % (brand-name sumatriptan), 153 % (generic sumatriptan) and 77 % (zolmitriptan). Generic sumatriptan was the most cost-effective drug analysed in the studied countries.

CONCLUSIONS:

Caution must be taken when trying to transfer conclusions of pharmacoeconomics studies on migraines even in neighbouring countries. This cross-country variability is a concern for decision-makers and also for the elaboration of international recommendations and clinical practice guidelines.

Hepp Z, Bloudek LM,Varon SF. Systematic review of migraine prophylaxis adherence and persistence (Provisional abstract). Journal of Managed Care Pharmacy. 2014; 1. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12014001182/frame.html

BACKGROUND:

Migraine is a common neurological disease affecting 12% of Americans and millions worldwide. Medication adherence has been studied extensively in many chronic conditions, with poor adherence adversely affecting treatment outcomes. However, little is known about adherence to oral prophylaxis for migraine.

OBJECTIVE:

To examine the literature on assessing oral prophylaxis medication adherence and persistence among migraine patients.

METHODS:

A systematic search of the PubMed (1966 to present) and EMBASE (1974 to present) databases was conducted to locate prospective and retrospective observational studies and randomized controlled trials (RCTs) of propranolol, amitriptyline, and topiramate. RCTs were pooled, weighted by sample size, and stratified by drug and length of study. Average persistence rates and reasons for discontinuation cited in RCTs were examined for each medication.

RESULTS:

A total of 788 unique articles were identified using the search criteria, 33 of which were included in the final review. Observational studies (n = 14) showed adherence ranges of 41% to 95% at 2 months, 21% to 80% at 6 months, and 35% to 56% at 12 months and persistence ranges of 41% to 88% at 2 months, 19% to 79% at 6 months, and 7% to 55% at 12 months. Pooled persistence from RCTs on propranolol, amitriptyline, and topiramate (n = 19) showed rates of 77%, 55%, and 57%, respectively, at 16-26 weeks. Adverse events were the most common reason for discontinuation cited (24% for topiramate and 17% for amitriptyline).

CONCLUSION:

Observational studies and pooled data from RCTs demonstrate poor adherence and persistence to oral migraine prophylaxis.

Huang Y, Cai X, Song X, Tang H, Huang Y, Xie S, et al. Steroids for preventing recurrence of acute severe migraine headaches: a meta-analysis (Structured abstract). European Journal of Neurology. 2013; 8. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12013020778/frame.html

BACKGROUND AND PURPOSE:

Recurrence of migraine headaches after treatment is common. The evidence regarding steroids for preventing migraine headache recurrence is controversial. This meta-analysis examined the effectiveness of steroids for prevention of recurrent headaches.

METHODS:

Databases (PubMed, Embase and the Cochrane Library) and conference proceedings were searched for

randomized controlled trials comparing steroids and placebo in the treatment of migraine headaches. Two independent reviewers assessed studies and extracted data. Relative risks (RRs) of headache recurrence and adverse events were calculated and reported with 95% confidence intervals (95% CIs).

RESULTS:

Eight studies with 905 patients were included. Pooled analysis showed that when steroids were added to standard abortive therapy they reduced the rate of moderate or severe headache recurrence after 24-72 h of follow-up evaluation (RR = 0.71; 95% CI = 0.59-0.86). There was no significant benefit of steroids compared with placebo in the proportion of totally resolved migraines (RR = 1.11; 95% CI = 0.94-1.32). The side effects of steroids are mild and not significant except for dizziness. Subgroup meta-analysis showed that parenteral dexamethasone tends to be more effective in reducing moderate or severe recurrent headaches (RR = 0.68; 95% CI = 0.55-0.84). However, no significant differences were found between oral administration and parenteral administration of steroids (P = 0.37).

CONCLUSION:

When steroids are added to standard abortive therapy for migraine headaches, they are effective and safe for preventing moderate or severe headache recurrence.

Jackson JL, Cogbill E, Santana-Davila R, Eldredge C, Collier W, Gradall A, et al. A Comparative Effectiveness Meta-Analysis of Drugs for the Prophylaxis of Migraine Headache. PLoS ONE [Electronic Resource] 2015;10(7):e0130733

OBJECTIVE: To compare the effectiveness and side effects of migraine prophylactic medications.

DESIGN: We performed a network meta-analysis. Data were extracted independently in duplicate and quality was assessed using both the JADAD and Cochrane Risk of Bias instruments. Data were pooled and network meta-analysis performed using random effects models.

DATA SOURCES: PUBMED, EMBASE, Cochrane Trial Registry, bibliography of retrieved articles through 18 May 2014.

ELIGIBILITY CRITERIA FOR SELECTING STUDIES: We included randomized controlled trials of adults with migraine headaches of at least 4 weeks in duration.

RESULTS: Placebo controlled trials included alpha blockers (n = 9), angiotensin converting enzyme inhibitors (n = 3), angiotensin receptor blockers (n = 3), anticonvulsants (n = 32), beta-blockers (n = 39), calcium channel blockers (n = 12), flunarizine (n = 7), serotonin reuptake inhibitors (n = 6), serotonin norepinephrine reuptake inhibitors (n = 1) serotonin agonists (n = 9) and tricyclic antidepressants (n = 11). In addition there were 53 trials comparing different drugs. Drugs with at least 3 trials that were more effective than placebo for episodic migraines included amitriptyline (SMD: -1.2, 95% CI: -1.7 to -0.82), -flunarizine (-1.1 headaches/month (ha/month), 95% CI: -1.6 to -0.67), fluoxetine (SMD: -0.57, 95% CI: -0.97 to -0.17), metoprolol (-0.94 ha/month, 95% CI: -1.4 to -0.46), pizotifen (-0.43 ha/month, 95% CI: -0.6 to -0.21), propranolol (-1.3 ha/month, 95% CI: -2.0 to -0.62), topiramate (-1.1 ha/month, 95% CI: -1.9 to -0.73) and valproate (-1.5 ha/month, 95% CI: -2.1 to -0.8). Several effective drugs with less than 3 trials included: 3 ace inhibitors (enalapril, lisinopril, captopril), two angiotensin receptor blockers (candesartan, telmisartan), two anticonvulsants (lamotrigine, levetiracetam), and several beta-blockers (atenolol, bisoprolol, timolol). Network meta-analysis found amitriptyline to be better than several other medications including candesartan, fluoxetine, propranolol, topiramate and valproate and no different than atenolol, flunarizine, clomipramine or metoprolol.

CONCLUSION: Several drugs good evidence supporting efficacy. There is weak evidence supporting amitriptyline's superiority over some drugs. Selection of prophylactic medication should be tailored according to patient preferences, characteristics and side effect profiles.

Jackson JL, Kuriyama A,Hayashino Y. Botulinum toxin A for prophylactic treatment of migraine and tension headaches in adults: a meta-analysis (Structured abstract). Jama. 2012; 2. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12012019639/frame.html

CONTEXT:

Botulinum toxin A is US Food and Drug Administration approved for prophylactic treatment for chronic migraines.

OBJECTIVE:

To assess botulinum toxin A for the prophylactic treatment of headaches in adults.

DATA SOURCES:

A search of MEDLINE, EMBASE, bibliographies of published systematic reviews, and the Cochrane trial registries between 1966 and March 15, 2012. Inclusion and exclusion criteria of each study were reviewed. Headaches were categorized as episodic (<15 headaches per month) or chronic (≥15 headaches per month) migraine and episodic or chronic daily or tension headaches.

STUDY SELECTION:

Randomized controlled trials comparing botulinum toxin A with placebo or other interventions for headaches among adults.

DATA EXTRACTION:

Data were abstracted and quality assessed independently by 2 reviewers. Outcomes were pooled using a random-effects model.

DATA SYNTHESIS:

Pooled analyses suggested that botulinum toxin A was associated with fewer headaches per month among patients with chronic daily headaches (1115 patients, -2.06 headaches per month; 95% CI, -3.56 to -0.56; 3 studies) and among patients with chronic migraine headaches (n = 1508, -2.30 headaches per month; 95% CI, -3.66 to -0.94; 5 studies). There was no significant association between use of botulinum toxin A and reduction in the number of episodic migraine (n = 1838, 0.05 headaches per month; 95% CI, -0.26 to 0.36; 9 studies) or chronic tension-type headaches (n = 675, -1.43 headaches per month; 95% CI, -3.13 to 0.27; 7 studies). In single trials, botulinum toxin A was not associated with fewer migraine headaches per month vs valproate (standardized mean difference [SMD], -0.20; 95% CI, -0.91 to 0.31), topiramate (SMD, 0.20; 95% CI, -0.36 to 0.76), or amitriptyline (SMD, 0.29; 95% CI, -0.17 to 0.76). Botulinum toxin A was associated with fewer chronic tension-type headaches per month vs methylprednisolone injections (SMD, -2.5; 95% CI, -3.5 to -1.5). Compared with placebo, botulinum toxin A was associated with a greater frequency of blepharoptosis, skin tightness, paresthesias, neck stiffness, muscle weakness, and neck pain.

CONCLUSION:

Botulinum toxin A compared with placebo was associated with a small to modest benefit for chronic daily headaches and chronic migraines but was not associated with fewer episodic migraine or chronic tension-type headaches per month.

Keezer MR, Bauer PR, Ferrari MD,Sander JW. The comorbid relationship between migraine and epilepsy: a systematic review and meta-analysis. European Journal of Neurology 2015;22(7):1038-47

A number of studies have suggested a pathophysiologic link between migraine and epilepsy. Our aim was to examine the relative lifetime prevalence of migraine in people with epilepsy (PWE) as well that of epilepsy in migraineurs. We carried out a systematic review, searching five electronic databases, specified bibliographies and conference abstracts in order to identify population-based studies that measured the

lifetime co-prevalence of migraine and epilepsy. Two reviewers independently screened all titles and abstracts, carried out a risk of bias assessment and extracted the data. Meta-analyses were carried out using random effects models. Of the 3640 abstracts and titles screened, we identified 10 eligible studies encompassing a total of 1,548,967 subjects. Few of the studies used validated case ascertainment tools and there were inconsistent attempts to control for confounding. There was an overall 52% increase in the prevalence of migraine among PWE versus those without epilepsy [PR: 1.52 (95% CI: 1.29, 1.79)]. There was an overall 79% increase in the prevalence of epilepsy among migraineurs versus those without migraine [PR: 1.79 (95% CI: 1.43, 2.25)]. Subgroup analyses revealed that the method of ascertaining the epilepsy or migraine status of subjects was an important source of inter-study heterogeneity. Additional high quality primary studies are required, ones that use validated and accurate methods of case ascertainment as well as control for potential confounders.

Kelly AM, Walcynski T,Gunn B. The relative efficacy of phenothiazines for the treatment of acute migraine: a meta-analysis (Structured abstract). Headache. 2009; 9. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12009109942/frame.html

OBJECTIVE AND BACKGROUND:

Ranges of agents are used in the emergency departments to treat migraine headache. Some experts suggest that phenothiazines are among the most effective; clinical trials have been small with varied results. We performed a systematic review and meta-analysis to determine the relative effectiveness of phenothiazines compared with placebo and other active agents for the treatment of acute migraine.

METHODS:

We searched MEDLINE, EMBASE, CINAHL, Cochrane database, and international clinical trial registers for randomized controlled trials comparing parenteral phenothiazines with placebo or another active parenteral agent for treatment of acute migraine in adults. The primary outcome was relief of headache, and secondary outcome was clinical success. Analysis was for phenothiazines vs placebo, pooled other active agents, and metoclopramide for each outcome. Odds ratios (ORs) were calculated and pooled by using a random effects model (RevMan v5).

RESULTS:

Thirteen trials were appropriate and had available data. Phenothiazines were compared with placebo in 5 trials and to another active agent in 10 (metoclopramide 4). Phenothiazine was more effective than placebo for headache relief (OR 15.02, 95% confidence interval [CI] 7.57-29.82) and clinical success (OR 8.92, 95% CI 4.08-19.51). Phenothiazines were more effective than other agents combined (OR 2.04, 95% CI 1.25-3.31) and the metoclopramide subgroup (OR 2.25, 95% CI 1.29-3.92) for clinical success, but no differences were found for headache relief. The clinical success rate of phenothiazines was 78% (95% CI 74-82).

CONCLUSION:

Phenothiazines are more effective than placebo for the treatment of migraine headache and have higher rates of clinical success than other agents against which they have been compared.

Kindelan-Calvo P, Gil-Martinez A, Paris-Alemany A, Pardo-Montero J, Munoz-Garcia D, Angulo-Diaz-Parreno S, et al. Effectiveness of therapeutic patient education for adults with migraine. A systematic review and meta-analysis of randomized controlled trials (Provisional abstract). Database of Abstracts of Reviews of Effects. 2014; 2. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12014052221/frame.html

OBJECTIVE:

Our aim was to systematically review and meta-analyze the effectiveness of therapeutic patient education for

migraine.

METHODS:

A literature search of multiple electronic databases (MEDLINE, EMBASE, PEDro, CINAHL, and PsychINFO) was conducted to identify randomized control trials (RCTs) published in the English and Spanish languages up to and including May 2013. Two reviewers independently selected the studies, conducted the quality assessment (Delphi list), and extracted the results. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses method was used throughout the systematic review and meta-analysis. Standardized mean difference (SMD) and 95% confidence intervals (CIs) were calculated for relevant outcome measures (headache frequency, headache disability, self-efficacy, depressive symptoms, and quality of life) and pooled in a meta-analysis using the random effects model.

RESULTS:

Fourteen RCTs were included in the systematic review. Only nine studies were included in the meta-analysis. The median quality score was 6.14 ± 1.29 (range: 5-9). There was strong-moderate evidence for intermediate-term effectiveness of therapeutic patient education on headache frequency (five studies: N = 940, SMD = -0.24, 95% CI of -0.48 to -0.01, P = 0.03), headache disability (four studies: N = 799, SMD = -1.02, 95% CI of -1.95 to -0.08, P = 0.03), and quality of life (three studies: N = 674, SMD = 0.36, 95% CI of 0.05-0.67, P = 0.02). There was no evidence for either short-term or intermediate-term effectiveness of therapeutic patient education on self-efficacy or depressive symptoms.

CONCLUSION:

This systematic review revealed strong-moderate evidence for intermediate-term effectiveness of therapeutic patient education for migraine. Further high-quality RCTs are required for conclusive determination of its effectiveness.

Lisotto C, Guidotti M, Zava D,Savi L. Frovatriptan and rizatriptan economic evaluation: the FREEVA study (Provisional abstract). Journal of Headache and Pain. 2013; 1. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cleed/articles/NHSEED-22013054069/frame.html

BACKGROUND:

The present pharmacoeconomic study compared the direct and indirect costs of using frovatriptan versus rizatriptan in the acute treatment of migraine.

METHODS:

Data on the cost-efficacy of the two triptans were derived from a recently published Italian, multicenter, randomized, double-blind, cross-over patient preference study, comparing frovatriptan versus rizatriptan. The direct costs were obtained by calculating the drug consumption, both of triptans and rescue medications. Prices of currently marketed drugs were obtained from Italian Drug Agency price list. The indirect costs were those related to absenteeism from the workplace due to migraine.

RESULTS:

129 of the 148 patients with a current history of migraine randomized to the two study drugs and completing the study were analyzed. The number of attacks treated with only 1 dose of study drug was higher with frovatriptan (157 vs. 147), whereas the number of attacks treated with ≥2 doses of study medication was higher with rizatriptan (122 vs. 110 and 74 vs. 67, respectively). However, more patients treated with frovatriptan took a rescue medication (71 vs. 59). The total direct cost per attack (including study drug rescue medication) was 9.12 € for frovatriptan and 13.54 € for rizatriptan ($p < 0.05$ between-treatments). As for indirect costs, in the group of patients treated with frovatriptan the mean number of lost working hours was significantly ($p < 0.05$) lower (1.5 h) compared to the subjects who used rizatriptan (2.8 h). Based on the earned income per unit of work, indirect costs per attack resulted to be 24.55 € for frovatriptan and

45.84 € for rizatriptan. Overall, the total costs, including direct and indirect costs, were evaluated to be 33.67 € for frovatriptan and 59.38 € for rizatriptan, respectively.

CONCLUSIONS:

Within the limitations of this model analysis, frovatriptan was found to be significantly more cost-effective than rizatriptan. This outcome can be explained by the lower acquisition cost of frovatriptan, the need for fewer doses, and the loss of fewer working hours. This finding could drive selection of the most appropriate oral treatment for acute migraine attacks based on both individual patient's needs and the cost-effectiveness of the available drugs.

Liu R, Geng P, Ma M, Yu S, Yang M, He M, et al. MTHFR C677T polymorphism and migraine risk: a meta-analysis (Provisional abstract). Journal of the Neurological Sciences. 2014; 1-2. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12013064782/frame.html

Many molecular epidemiological studies were carried out in recent years to assess the association between the MTHFR C677T polymorphismand migraine risk in diverse populations.However, the results remain controversial rather than conclusive. The objective of this study was to investigate the role of C677T MTHFR polymorphism in migraine pathogenesis. We performed a meta-analysis of published case–control studies concerning the association of the C677T MTHFR polymorphism and migraine. Pooled ORs were established using both random and fixed effects models. This meta-analysis on 17 studies with 8903 cases and 27,637 controls showed that the allele 677T was associated with a significantly increased risk of total migraine in Asians (TT vs. CT + CC: OR = 1.62, 95% CI: 1.13–2.32, PH= 0.573, I2 = 0.0%; T vs. C: OR = 1.18, 95% CI: 1.00–1.40, PH= 0.147, I2 = 44.1%). Similar results were also presented in Asian populations with MA (TT vs. CC: OR=1.62, 95% CI: 1.11– 3.75; TT vs. CT+CC: OR=2.00, 95% CI: 1.01–3.95; T vs. C: OR=1.31, 95% CI: 1.02–1.69) without significant heterogeneity. We conclude that the C677T MTHFR polymorphism, responsible for a reduction of the MTHFR activity in folate metabolism, may act as a genetic susceptibility factor for migraine, MA in particular among the subjects of Asian descent.

Lo MY, Lin JG, Ong MW,Sun WZ. Cerebral hemodynamic responses to acupuncture in migraine patients: a systematic review (Provisional abstract). Database of Abstracts of Reviews of Effects. 2013; 2. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12014024832/frame.html

We review the literature conjoining acupuncture, migraine, and cerebral hemodynamics. To do so, we searched PubMed in March 2013 for studies investigating cerebral hemodynamics with functional magnetic resonance imaging (fMRI), near-infrared spectroscopy (NIRS), transcranial Doppler (TCD) ultrasound, and other tools in migraineurs, acupuncture recipients, and migraineurs receiving acupuncture. Our search identified 1321 distinct articles – acupuncture (n = 463), migraine (n = 866), and both (n = 8). Only three (n = 3) satisfied our inclusion criteria. Based on these three, we found the following: (1) Acupuncture may positively influence not just dynamic, but also static cerebral autoregulation during the interictal phase, depending on the intervals between sessions of acupuncture as dose units. (2) TCD can detect pretreatment differences between responders and non-responders to acupuncture, which may be predictive of clinical response. (3) “Point-through-point” needling (at angles connecting acupoints) may be clinically superior to standard acupuncture, thus needling angles may affect treatment effectiveness. None of the reviewed articles investigated patient responses during migraine attack. Although the 2009 Cochrane review affirmed acupuncture as effective prophylaxis for migraine, few studies investigated the cerebrovascular aspects – only analyzing arterial blood flow, but not microcirculation. Future research is warranted in monitoring brain tissue oxygenation to investigate acupuncture as both a preventive and abortive treatment for migraine, varying the type and dose interval and analyzing variations in clinical response.

Luykx J, Mason M, Ferrari MD,Carpay J. Are migraineurs at increased risk of adverse drug responses: a meta-

analytic comparison of topiramate-related adverse drug reactions in epilepsy and migraine (Structured abstract). Clinical Pharmacology and Therapeutics. 2009; 3. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12009103084/frame.html

To compare adverse drug reactions (ADRs) to topiramate in patients with migraine and patients with epilepsy, we systematically reviewed all published randomized controlled trials (RCTs) that compare topiramate monotherapy in epilepsy and migraine. We included four epilepsy RCTs (N = 1,179 patients; vs. active comparators) and six migraine RCTs (N = 1,723 patients; vs. placebo). Behavioral ADRs and headache were found only in the case of epilepsy, whereas cognitive complaints and alteration of taste were found only in the case of migraine. The risk ratios (RRs) for paresthesia in migraine vs. epilepsy trials were 2.5 (99% confidence interval (CI): 1.66-3.77) for 50 mg, 2.7 (99% CI: 1.80-3.97) for 100 mg, and 3.0 (99% CI: 1.95-4.56) for 200 mg. For ADR-related dropouts, the RR was 2.5 (95% CI: 2.03-2.98) for 50 mg but no different for the other doses. We conclude that when treated with the same doses of topiramate, migraineurs show different ADRs than patients with epilepsy and are more likely to drop out because of ADRs.

Malik R, Freilinger T, Winsvold BS, Anttila V, Vander Heiden J, Traylor M, et al. Shared genetic basis for migraine and ischemic stroke: A genome-wide analysis of common variants. Neurology 2015;84(21):2132-45

OBJECTIVE: To quantify genetic overlap between migraine and ischemic stroke (IS) with respect to common genetic variation.

METHODS: We applied 4 different approaches to large-scale meta-analyses of genome-wide data on migraine (23,285 cases and 95,425 controls) and IS (12,389 cases and 62,004 controls). First, we queried known genome-wide significant loci for both disorders, looking for potential overlap of signals. We then analyzed the overall shared genetic load using polygenic scores and estimated the genetic correlation between disease subtypes using data derived from these models. We further interrogated genomic regions of shared risk using analysis of covariance patterns between the 2 phenotypes using cross-phenotype spatial mapping.

RESULTS: We found substantial genetic overlap between migraine and IS using all 4 approaches. Migraine without aura (MO) showed much stronger overlap with IS and its subtypes than migraine with aura (MA). The strongest overlap existed between MO and large artery stroke (LAS; p = 6.4 x 10(-28) for the LAS polygenic score in MO) and between MO and cardioembolic stroke (CE; p = 2.7 x 10(-20) for the CE score in MO).

CONCLUSIONS: Our findings indicate shared genetic susceptibility to migraine and IS, with a particularly strong overlap between MO and both LAS and CE pointing towards shared mechanisms. Our observations on MA are consistent with a limited role of common genetic variants in this subtype.

Marchenko A, Etwel F, Olutunfese O, Nickel C, Koren G,Nulman I. Pregnancy outcome following prenatal exposure to triptan medications: a meta-analysis. Headache 2015;55(4):490-501

BACKGROUND: Migraine is a common disorder among women of childbearing age. Triptan medications are effective and commonly used to treat migraines in pregnancy. However, the reproductive safety of this group of drugs has not yet been confirmed. The aim of this study was to determine the reproductive safety of triptan medications by performing a literature review and a meta-analysis.

METHODS: Available publications regarding pregnancy outcomes following prenatal exposure to triptans from 1991 to 2013 were identified and reviewed according to the inclusion criteria. A random-effects meta-analysis model was implemented to combine the available pregnancy outcome data for the exposed and comparison groups.

RESULTS: One case-control study and 5 cohort studies met the inclusion criteria. The included studies provided information on duration of gestation, major congenital malformations, and spontaneous abortions of infants following prenatal triptan exposure. The 6 studies included 4208 infants of women who used sumatriptan or other triptan medications, and 1,466,994 children of women who did not use triptans during pregnancy. No significant increases in rates for major congenital malformations (MCMs), prematurity, or spontaneous abortions were found when comparing the triptan-exposed group to the migraine - no triptans control group (odds ratio [OR]=0.84 [0.61-1.16]; OR=0.90 [0.35-2.30]; OR=1.27 [0.58-2.79], respectively). There were no increased rate of MCMs (OR=1.18 [0.97-1.44]) or prematurity (OR=1.16 (0.67-1.99) when the triptan-exposed group was compared with the healthy controls; however, there was a significant increase in the rates of spontaneous abortions (OR=3.54 [2.24-5.59]). When the migraine no-triptan group was compared with healthy controls, a significant increase in the rates of MCMs was found (OR=1.41 [1.11-1.80]).

CONCLUSION: The use of triptans during pregnancy does not appear to increase the rates for MCMs or prematurity. The increased rates of spontaneous abortions in the triptan-exposed group and the increased rates of MCM in the migraine no-triptan group require further research.

Mett A,Tfelt-Hansen P. Acute migraine therapy: recent evidence from randomized comparative trials (Structured abstract). Current Opinion in Neurology. 2008; 3. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12008106849/frame.html

(1) A wide array of data regarding acute migraine treatment are available, but few trials strictly adhere to International Headache Society guidelines for patient inclusion criteria.(2) Triptans appear to have similar efficacy profiles, but among newer triptans, almotriptan offers improved tolerability over sumatriptan.(3) Combination indomethacin/caffeine/prochlorperazine most likely has similar therapeutic efficacy to triptan therapy, with further research needed to complete understanding of any potential differences between these treatments.(4) Multi-targeted combination therapy with a triptan plus a non-steroidal anti-inflammatory (NSAID), such as sumatriptan/naproxen sodium, is more effective in acute migraine treatment than monotherapy with either agent alone.(5) It is unclear whether triptans offer clinically relevant benefits over aspirin or NSAIDs in migraine patients. Thus NSAIDs, particularly effervescent aspirin, should be considered the first-line treatment of migraine attacks.

Morey V, Rothrock,J F. Examining the utility of in-clinic "rescue" therapy for acute migraine (Provisional abstract). Headache. 2008; 6. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cleed/articles/NHSEED-22008101245/frame.html

BACKGROUND:

Management options currently are limited for patients with acute migraine whose symptoms prove refractory to self-administered therapy.

OBJECTIVE:

To evaluate the clinical utility and cost-effectiveness of a management program offering in-clinic "rescue" treatment for patients with acute migraine.

METHODS:

Two hundred consecutive migraine patients presenting to a university-based headache clinic were randomized to receive either optimal self-administered medical therapy for acute migraine ("standard therapy") or similar therapy plus the option of in-clinic parenteral drug administration should self-administered therapy prove ineffective ("rescue therapy"). Patients randomized to the latter group were restricted to a maximum of 2 "rescue visits" per month, and all patients were followed for one year. Patients "rescued" in clinic were contacted by telephone 24 hours following treatment to evaluate their treatment response. The primary

analysis involved a comparison of the number of emergency department (ED) visits for headache recorded within each group over the one-year period of study. For all ED visits in the rescue group and for a randomly selected and equal number of ED visits within the standard group, the direct costs associated with those visits were assessed, and the direct costs of all in-clinic rescue visits also were recorded and analyzed.

RESULTS:

The 2 groups studied were similar in terms of age, gender ratio, migraine subtype, migraine-related disability status at baseline and type/extent of medical insurance coverage. Over the one-year study period, the rescue group recorded 423 in-clinic rescue visits and reported 27 ED visits for headache treatment. The standard therapy group reported 73 ED visits (27 vs 73 visits; P < .01). The total direct costs associated with ED visits were $45,330 for the rescue group (mean $1690 per ED visit) and (by extrapolation from the sample selected) $147,971 for the standard therapy group (mean $2027 per ED visit). The total direct cost of the 423 "rescue visits" was $33,647 (mean $80 per visit). In 79% of the 423 rescue encounters, the patients involved reported no residual functional disability 24 hours following treatment. Of those in the rescue group who sought in-clinic rescue, 89% reported themselves "very satisfied" with such management.

CONCLUSION:

Providing the alternative of in-clinic "rescue" for acute migraine refractory to self-administered therapy offers an attractive alternative for patients and appears to substantially lower use of an ED for headache treatment and the cost associated with that use.

Mulleners WM,Chronicle EP. Anticonvulsants in migraine prophylaxis: a Cochrane review (Structured abstract). Cephalalgia. 2008; 6. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12008103925/frame.html

Several trials have asserted that some anticonvulsant drugs seem to be useful for the prophylaxis of migraine, but systematic reviews are sparse. We independently searched PubMed, EMBASE and the Cochrane Central Register of Controlled Trials until 2005, as well as Headache and Cephalalgia through April 2006, for prospective, controlled trials of anticonvulsant drugs. Data were calculated and pooled across studies and expressed as standardized mean differences, odds ratios and numbers-needed-to-treat. Anticonvulsants, considered as a class, reduce migraine frequency by about 1.3 attacks per 28 days compared with placebo, and more than double the number of patients for whom migraine frequency is reduced by > or = 50% relative to placebo. Sodium valproate/divalproex sodium and topiramate were better than placebo, whereas acetazolamide, clonazepam, lamotrigine and vigabatrin were not; gabapentin, in particular, needs further evaluation. Trials designed with sufficient power to compare different drugs are also necessary

Mulleners WM, McCrory DC,Linde M. Antiepileptics in migraine prophylaxis: an updated Cochrane review. Cephalalgia 2015;35(1):51-62

INTRODUCTION: The efficacy of several antiepileptics in the preventive treatment of episodic migraine in adults has been systematically reviewed. Because many trial reports have been published since then, an updated systematic review was warranted.

METHODS: We searched the Cochrane Central Register of Controlled Trials, PubMed/MEDLINE (1966 to January 15, 2013), MEDLINE In-Process (current week, January 15, 2013), and EMBASE (1974 to January 15, 2013) and hand-searched Headache and Cephalalgia through January 2013. Prospective, controlled trials of antiepileptics taken regularly to prevent the occurrence of migraine attacks, to improve migraine-related quality of life, or both, were selected.

RESULTS: Mean headache frequency on topiramate and sodium valproate is significantly lower than placebo.

Likewise, topiramate and divalproex demonstrated favorable results for the proportion of subjects with > 50% reduction of migraine attacks. For topiramate, 100 mg and 200 mg outperformed 50 mg, but this was paralleled by a higher adverse event rate. For valproate/divalproex, a dose-effect correlation could not be established. There was no unequivocal evidence of efficacy for any of the other antiepileptics.

CONCLUSION: Topiramate, sodium valproate and divalproex are effective prophylactic treatments for episodic migraine in adults. In contrast to previous reports, there is insufficient evidence to further support the use of gabapentin.

Mullins CD, Weis KA, Perfetto EM, Subedi PR,Healey PJ. Triptans for migraine therapy: a comparison based on number needed to treat and doses needed to treat (Structured abstract). Journal of Managed Care Pharmacy. 2005; 5. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cleed/articles/NHSEED-22006006363/frame.html

OBJECTIVE:

Managed care and other decision makers need sound comparative information to support the formulary selection process and reimbursement decisions for the treatment of migraine. The objective of this study was to compare currently marketed triptan therapies using number-needed-to-treat (NNT) and doses-needed-to-treat (DNT) measures. DNT was further used to derive triptan treatment cost to achieve 100 successfully treated patients such that the cost-effectiveness of each treatment regime could be compared from the payer perspective.

METHODS:

Using published meta-analysis data to categorize patients as treatment success or failure, an NNT and a DNT were derived for each triptan. Treatment success was defined as achieving a 2-hour pain response, sustained through 24 hours postdose. Costs were derived by multiplying DNT by the average wholesale price (AWP) minus 15% for each triptan.

RESULTS:

Eletriptan 40 mg had the lowest NNT, with 361 patients needing to be treated in order to have 100 patients achieve clinical benefit; rizatriptan 5 mg had the highest NNT (597 patients). Eletriptan 40 mg required 388 doses to successfully treat 100 patients.the lowest number of doses of the triptans considered; rizatriptan 5 mg required the highest number (662 doses). Eletriptan 40 mg had the lowest total triptan cost of USD 5,630 to successfully treat 100 patients. The highest total triptan cost of treatment was USD 11,136 for naratriptan 2.5 mg.

CONCLUSIONS:

Eletriptan 40 mg provides the best value in terms of the lowest DNT, assuming an approximately equal AWP discount for each triptan. Eletriptan 40 mg also was found to have the lowest total triptan cost to successfully treat 100 patients. Future research should further explore the utility of DNT in managed care decision making.

Nestoriuc Y,Martin A. Efficacy of biofeedback for migraine: a meta-analysis (Structured abstract). Pain. 2007; 1-2. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12007000923/frame.html

In this article, we meta-analytically examined the efficacy of biofeedback (BFB) in treating migraine. A computerized literature search of the databases Medline, PsycInfo, Psyndex and the Cochrane library, enhanced by a hand search, identified 86 outcome studies. A total of 55 studies, including randomized controlled trials as well as pre-post trials, met our inclusion criteria and were integrated. A medium effect size (d =0.58, 95% CI=0.52, 0.64) resulted for all BFB interventions and proved stable over an average follow-up phase of 17 months. Also, BFB was more effective than control conditions. Frequency of

migraine attacks and perceived self-efficacy demonstrated the strongest improvements. Blood-volume-pulse feedback yielded higher effect sizes than peripheral skin temperature feedback and electromyography feedback. Moderator analyses revealed BFB in combination with home training to be more effective than therapies without home training. The influence of the meta-analytical methods on the effect sizes was systematically explored and the results proved to be robust across different methods of effect size calculation. Furthermore, there was no substantial relation between the validity of the integrated studies and the direct treatment effects. Finally, an intention-to-treat analysis showed that the treatment effects remained stable, even when drop-outs were considered as nonresponders.

Nestoriuc Y, Martin A, Rief W,Andrasik F. Biofeedback treatment for headache disorders: a comprehensive efficacy review (Structured abstract). Applied Psychophysiology and Biofeedback. 2008; 3. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12009102838/frame.html

The aim of the present review was to critically evaluate the documented evidence regarding the efficacy of biofeedback for the two most prevalent headache conditions--migraine and tension-type headache. Drawing upon two recently published meta-analyses, data from 150 outcome studies, including randomized controlled trials as well as uncontrolled quasi-experimental designs, were screened. Of these, 94 studies were selected for inclusion according to predefined criteria. Meta-analytic integrations were carried out separately for the two conditions of interest. The main results were medium-to-large mean effect sizes for biofeedback in adult migraine and tension-type headache patients. Treatment effects remained stable over an average follow-up period of 14 months, both in completer and intention-to-treat analyses. Headache frequency was the primary outcome variable and showed the largest improvements. Further significant effects were shown for perceived self-efficacy, symptoms of anxiety and depression, and medication consumption. Reduced muscle tension in pain related areas was observed in electromyographic feedback for tension-type headache. Biofeedback was more effective than waiting list and headache monitoring conditions in all cases, while electromyographic feedback for tension-type headache showed additional significant effects over placebo and relaxation therapies. Levels of efficacy (migraine: efficacious, level 4; tension-type headache: efficacious and specific, level 5) and recommendations for future research are provided.

Ornello R, Ripa P, Pistoia F, Degan D, Tiseo C, Carolei A, et al. Migraine and body mass index categories: a systematic review and meta-analysis of observational studies. Journal of Headache & Pain 2015;16(27

BACKGROUND: Several studies have assessed the associations between migraine and underweight, pre-obesity or obesity, with conflicting results. To assess the consistency of the data on the topic, we performed a systematic review and meta-analysis of the available observational studies.

METHODS: Multiple electronic databases were systematically searched up to October 2014 for studies assessing the association between migraine and body mass index categories (underweight, pre-obesity, or obesity).

RESULTS: Out of 2,022 records, we included 15 studies. When considering the 11 studies following the World Health Organization BMI cutoffs, we found an increased risk of having migraine in underweight subjects (pooled adjusted effect estimate [PAEE] 1.21; 95% CI, 1.07-1.37; P=0.002) and in obese women (PAEE 1.44; 95% CI, 1.05-1.97; P=0.023) as compared with normal weight subjects; additionally, pre-obese subjects had an increased risk of having chronic migraine (PAEE 1.39; 95% CI, 1.13-1.71; P=0.002). When considering all the 15 studies, we additionally found an increased risk of having migraine in obese as compared with normal weight subjects (PAEE 1.14; 95% CI, 1.02-1.27; P=0.017); additionally, obese subjects had an increased risk of having chronic migraine (PAEE 1.75; 95% CI, 1.33-2.29; P<0.001). The pooled analysis did not indicate an increased risk of having migraine in pre-obese subjects.

CONCLUSIONS: The meta-analysis of the available observational studies suggested an association between migraine and obesity likely mediated by gender and migraine frequency. Further studies taking into account gender, migraine type, frequency, activity, and duration could provide more robust evidence.

Orr SL, Aube M, Becker WJ, Davenport WJ, Dilli E, Dodick D, et al. Canadian Headache Society systematic review and recommendations on the treatment of migraine pain in emergency settings. Cephalalgia 2015;35(3):271-84

BACKGROUND: There is a considerable amount of practice variation in managing migraines in emergency settings, and evidence-based therapies are often not used first line.

METHODS: A peer-reviewed search of databases (MEDLINE, Embase, CENTRAL) was carried out to identify randomized and quasi-randomized controlled trials of interventions for acute pain relief in adults presenting with migraine to emergency settings. Where possible, data were pooled into meta-analyses.

RESULTS: Two independent reviewers screened 831 titles and abstracts for eligibility. Three independent reviewers subsequently evaluated 120 full text articles for inclusion, of which 44 were included. Individual studies were then assigned a US Preventive Services Task Force quality rating. The GRADE scheme was used to assign a level of evidence and recommendation strength for each intervention.

INTERPRETATION: We strongly recommend the use of prochlorperazine based on a high level of evidence, lysine acetylsalicylic acid, metoclopramide and sumatriptan, based on a moderate level of evidence, and ketorolac, based on a low level of evidence. We weakly recommend the use of chlorpromazine based on a moderate level of evidence, and ergotamine, dihydroergotamine, lidocaine intranasal and meperidine, based on a low level of evidence. We found evidence to recommend strongly against the use of dexamethasone, based on a moderate level of evidence, and granisetron, haloperidol and trimethobenzamide based on a low level of evidence. Based on moderate-quality evidence, we recommend weakly against the use of acetaminophen and magnesium sulfate. Based on low-quality evidence, we recommend weakly against the use of diclofenac, droperidol, lidocaine intravenous, lysine clonixinate, morphine, propofol, sodium valproate and tramadol.

Pascual J, Mateos V, Roig C, Sanchez-del-Rio M,Jimenez D. Marketed oral triptans in the acute treatment of migraine: a systematic review on efficacy and tolerability (Provisional abstract). Headache. 2007; 8. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12007003403/frame.html

BACKGROUND:

In the current literature, there is neither a reported systematic review comparing the efficacy of triptans at 30 minutes and 1 hour after the migraine treatment, nor data related to efficacy of new marketed triptans.

OBJECTIVE:

The main objective of this analysis was to compare the efficacy and tolerability of currently marketed oral, non-reencapsulated triptan formulations vs placebo in the treatment of moderate-to-severe migraine attacks.

METHODS:

A systematic review of double-blind, randomized clinical trials reporting data after a single migraine attack was conducted. Efficacy results are shown using relative risk ratios with 95% confidence intervals. A sensitivity analysis was also conducted.

RESULTS:

After reviewing 221 publications, 38 studies were included. All marketed triptans provided significant relief and/or absence of pain at 2 hours, and relief at 1 hour when compared with placebo. After 30 minutes, fast-dissolving sumatriptan 50 and 100 mg, sumatriptan 50 mg, and rizatriptan 10 mg showed significant relief when compared to placebo, whereas the fast-dissolving formulation of sumatriptan 100 mg was the only oral triptan that was superior to placebo in meeting the pain-free endpoint. On the other hand, fast-dissolving sumatriptan 50 and 100 mg and eletriptan 40 mg showed a lower rate of recurrence than

placebo, whereas rizatriptan 10 mg was the only triptan with a recurrence rate greater than that of placebo. Adverse events associated with treatment with tablet formulations of sumatriptan and zolmitriptan were significantly more frequent than those of the placebo group. The inclusion of trials with reencapsulated triptans in the analysis introduced minor specific changes in these results.

CONCLUSION:

This analysis updates the comparative data available for the 7 currently marketed oral triptans and clearly demonstrates their efficacy when compared to placebo, even with stricter endpoints, such as efficacy at 30 minutes. No triptan exhibited better tolerability than placebo. Results are diverse, depending on the triptan, which probably is a reflection of heterogeneous pharmacokinetics

Patel ZM, Kennedy DW, Setzen M, Poetker DM,Delgaudio JM. "Sinus headache": rhinogenic headache or migraine? An evidence-based guide to diagnosis and treatment (Provisional abstract). International Forum of Allergy and Rhinology. 2013; 3. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12013018469/frame.html

BACKGROUND:

Patients present to physicians across multiple disciplines with the complaint of sinus headache. This lay term is widely accepted in the media, yet has been repeatedly questioned in the medical literature, and experts in the fields of otolaryngology, neurology, and allergy have agreed that it is an overused and often incorrect diagnosis in the majority of patients. There have been review articles and consensus panels established regarding this issue, but thus far no guidelines based purely on a review of the level of evidence provided by the literature.

METHODS:

A systematic review of the literature was performed and the Clinical Practice Guideline Manual, Conference on Guideline Standardization (COGS), and the Appraisal of Guidelines and Research Evaluation (AGREE) instrument recommendations were followed. Study inclusion criteria were: adult population >18 years old, self-diagnosed or physician-diagnosed "sinus headache," clearly defined diagnostic criteria in diagnostic studies, and clearly defined primary clinical end-point in therapeutic studies.

RESULTS:

We identified and evaluated the literature on diagnosing and treating patients with a primary complaint of sinus headache. The literature was reviewed for both quality of research design as well as benefit and harm of the proposed interventions.

CONCLUSION:

If a thorough neurologic and otolaryngologic evaluation is performed, the majority of patients presenting with sinus headache in the absence of significant acute inflammatory findings will be diagnosed with migraine. In this situation, the appropriate treatment for the majority of patients presenting with sinus headache is migraine directed therapy. In a highly select group of patients, directed nasal surgery addressing endonasal contact points may be an option.

Posadzki P,Ernst E. Spinal manipulations for the treatment of migraine: a systematic review of randomized clinical trials (Provisional abstract). Cephalalgia. 2011; 8. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12011004124/frame.html

AIMS:

The objective of this systematic review was to assess the effectiveness of spinal manipulations as a treatment for

migraine headaches.

METHOD:

Seven databases were searched from inception to November 2010. All randomized clinical trials (RCTs) investigating spinal manipulations performed by any type of healthcare professional for treating migraine headaches in human subjects were considered. The selection of studies, data extraction and validation were performed independently by two reviewers.

RESULTS:

Three RCTs met the inclusion criteria. Their methodological quality was mostly poor and ranged between 1 and 3 on the Jadad scale. Two RCTs suggested no effect of spinal manipulations in terms of Headache Index or migraine duration and disability compared with drug therapy, spinal manipulation plus drug therapy, or mobilization. One RCT showed significant improvements in migraine frequency, intensity, duration and disability associated with migraine compared with detuned interferential therapy. The most rigorous RCT demonstrated no effect of chiropractic spinal manipulation compared with mobilization or spinal manipulation by medical practitioner or physiotherapist on migraine duration or disability.

CONCLUSIONS:

Current evidence does not support the use of spinal manipulations for the treatment for migraine headaches

Pringsheim T, Davenport WJ,Dodick D. Acute treatment and prevention of menstrually related migraine headache: evidence-based review (Structured abstract). Neurology. 2008; 17. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12008103366/frame.html

Menstrually related migraine (MRM) headache is common in women and associated with substantial disability. Compared to nonmenstrual migraine, MRM attacks are more severe, longer in duration, and have a poorer response to analgesics. The purpose of this guideline is to provide a systematic review and meta-analysis of the existing therapy trials for MRM and evidence-based recommendations for acute and short-term preventive treatment of MRM headache. Prospective, double-blind, randomized controlled trials of any pharmacologic agent for the symptomatic relief or prevention of MRM headache were included in the guideline. The main outcomes considered were the pain response and pain-free response at 2 hours for acute treatment trials, and the incidence of MRM or the number of days on which MRM attacks occurred for short-term prevention trials. Nineteen trials were included in the analysis. The US Preventive Services Task Force quality criteria were used to assess trial quality and to grade recommendations. Based on the evidence, grade B recommendations can be made for the use of sumatriptan 50 and 100 mg, mefenamic acid 500 mg, and rizatriptan 10 mg for the acute treatment of MRM. For the preventive treatment of MRM, there are grade B recommendations for the perimenstrual use of transcutaneous estrogen 1.5 mg, frovatriptan 2.5 mg twice daily, and naratriptan 1 mg twice daily. Choosing among treatment strategies must be based on clinical considerations.

Pringsheim T, Davenport WJ, Mackie G, Worthington I, Aube M, Christie SN, et al. Systematic review: medications for migraine prophylaxis ? section II (Provisional abstract). Canadian Journal of Neurological Sciences. 2012; Supplement 2. [cited: url: http://journals.cambridge.org/download.php?file=%2FCJN%2FCJN39_S2%2FS0317167100015109a.pdf&code=86af158778ed8bc59ea5e022a6df2e32

Objective: To assess the evidence base for drugs used for prophylaxis of episodic migraine (headache on ≤ 14 days a

month) in Canada. Methods: A detailed search strategy was employed to find relevant published clinical trials. All abstracts were reviewed for eligibility by two reviewers. Only double-blind randomized clinical trials with placebo or active drug controls were included in the analysis. Studies were graded with respect to

methodological quality according to the US Preventative Services Task Force. Recommendations were graded according to the principles of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) Working Group, using a consensus group. Results: Nineteen medications were evaluated. Seventeen were recommended for use in migraine prophylaxis. Four received a strong recommendation – high quality evidence (topiramate, propranolol, metoprolol, and amitriptyline), four received a strong recommendation – moderate quality evidence (nadolol, gabapentin, candesartan, butterbur), and three received a strong recommendation – low quality evidence (riboflavin, co-enzyme Q10, and magnesium citrate). Three medications received a weak recommendation – high quality evidence (divalproex sodium, flunarizine, and pizotifen), and three received a weak recommendation – low quality evidence (venlafaxine, verapamil, and lisinopril). A strong recommendation was made

not to use two medications in patients with episodic migraine: botulinum toxin type A (high quality evidence), and feverfew (moderate quality evidence). Conclusion: Our systematic review formulated recommendations for the available medications for migraine prophylaxis according to the GRADE method. This should be helpful for practitioners who prescribe medications for migraine prophylaxis.

Ramsberg J,Henriksson M. The cost-effectiveness of oral triptan therapy in Sweden (Structured abstract). Cephalalgia. 2007; 1. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cleed/articles/NHSEED-22007000174/frame.html

The literature suggests that triptans are cost effective compared with older types of migraine treatment. However, which of the triptans that is most cost effective has not been established. We compared the costs and effects of triptan treatment from a Swedish societal perspective, using evidence from the literature. A probabilistic cost-effectiveness model was constructed to investigate the costs and effects of treating a single attack in a typical migraine patient. The end-point used in the base-case analysis was sustained pain free without any adverse events (SNAE). We searched the scientific literature for meta-analyses reporting the efficacy of oral triptans. All treatments except rizatriptan 10 mg and eletriptan 40 mg were dominated. The incremental cost per SNAE of rizatriptan 10 mg compared with eletriptan 40 mg was approximately 100 euro. There was substantial uncertainty concerning the results, but probabilistic analysis showed that rizatriptan 10 mg and eletriptan 40 mg had the highest probability of being cost-effective.

Roberto G, Raschi E, Piccinni C, Conti V, Vignatelli L, D'Alessandro R, et al. Adverse cardiovascular events associated with triptans and ergotamines for treatment of migraine: systematic review of observational studies. Cephalalgia 2015;35(2):118-31

BACKGROUND: Apart from the underlying cardiovascular (CV) risk associated with migraine, both triptans and ergotamines can induce vasoconstriction and potentially increase the risk of serious ischemic events. Because of the low frequency of such events in eligible patients, randomized controlled trials are not exhaustive to assess the drug-related CV risk. Observational studies are, therefore, an essential source of information to clarify this matter of concern.

AIM: The aim of this study was to systematically review the available published observational studies investigating the risk of serious CV events in triptan or ergotamine users, as compared to unexposed migraineur controls.

METHODS: We systematically searched MEDLINE and EMBASE electronic databases for cohort or case-control studies up to December 1, 2013. Studies retrieved from CDSR, DARE and HTA databases of the Cochrane Library were used for snowballing. Studies investigating the risk of any CV outcome in patients with a migraine diagnosis and exposed to triptans or ergotamines were considered for inclusion. Selection of studies, data extraction, and risk of bias assessment were conducted independently by two reviewers. Pooled odds ratios (ORs) with 95% confidence interval (95% CI) were computed using a random-effects model for studies and outcomes judged eligible for quantitative data synthesis.

RESULTS: From a total of 3370 citations retrieved, after duplicate removal and screening, only four studies met the

inclusion criteria (three nested case-control analyses and one retrospective cohort study). These studies investigated the risk of different CV outcomes associated with either the recency or the intensity of exposure to the studied drugs. As for the intensity of use, the pooled OR of serious ischemic events was 2.28 (95% CI 1.18-4.41; I (2)=0%) for ergotamine use (two studies), whereas for triptans (three studies) it was 0.86 (95% CI 0.52-1.43; I (2)=24.5%). Recent use of ergotamines was not significantly associated with any CV outcome (only one available study). Two studies investigated the risk of stroke related to recent triptan use: the first study reported an OR of 0.90 (0.64-1.26), and the second one suggested an increased risk of 2.51 (1.10-5.71). In this case, because of the high degree of heterogeneity, results were not pooled.

CONCLUSIONS: To date, few comparative observational studies have investigated the CV safety of migraine-specific drugs in clinical practice. Evidence gathered here suggests that intense consumption of ergotamines may be associated with an increased risk of serious ischemic complications. As for triptans, available studies do not suggest strong CV safety issues, although no firm conclusions can be drawn. In particular, evidence on stroke risk is conflicting. However, if an increase of the absolute stroke risk in recently exposed patients does actually exist, it must be small. Overall, residual uncontrolled confounding factors reduce the confidence in the risk estimates collected from the included studies. Further investigations are needed to better define the risk for rare but serious CV events related to triptan and ergotamine use for treatment of migraine.

Ruggeri M. The cost effectiveness of Botox in Italian patients with chronic migraine (Provisional abstract). Neurological Sciences. 2014; Supplement 1. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cleed/articles/NHSEED-22014023149/frame.html

Migraine is a primary headache which World Health Organization ranks in 19th place in the list of disabling diseases. In Europe, in 2004, the total costs for migraine were quantified by Stovner and Berg, Eur J Neurol, 12(s1) (2005) at <euro>27 billion. The objective of this study is to provide an estimate of the incremental cost-effectiveness ratio (ICER) of the treatment of chronic migraine with Botox compared to treatment with placebo in the perspective of the Italian National Health Service and society. To do this we studied the disease progression in a cohort of 688 individuals (patients enrolled in the study PREEMPT) via the application of a Markov model. Over a period of 2 years, the total costs of the experimental arm of the model amounted to <euro>3,274 compared with a gain of 1.34 QALYs. In contrast, the costs of the control arm amounted to <euro>2,395 with a gain of 1.24 QALYs. It follows that the incremental costs amounted to <euro>889 compared to an incremental gain of 0.09 QALYs in favor of the experimental arm. The relationship between costs and incremental QALYs generated an ICER of <euro>9,407/QALY. The incremental cost-effectiveness ratio, therefore, is favorable compared to the value usually considered by NICE as a threshold limit for reimbursement which ranges between <euro>20,000 and <euro>40,000/QALY.

Sacco S, Ornello R, Ripa P, Tiseo C, Degan D, Pistoia F, et al. Migraine and risk of ischaemic heart disease: a systematic review and meta-analysis of observational studies. European Journal of Neurology 2015;22(6):1001-11

BACKGROUND AND PURPOSE: Several studies have assessed the risk of ischaemic heart diseases in migraineurs, drawing different conclusions. To define and update the issue, a systematic review and meta-analysis of the available observational studies was performed.

METHODS: PubMed and EMBASE were systematically searched up to April 2014 for observational studies dealing with the risk of any form of ischaemic heart disease in migraineurs. Studies assessing migraine as exposure and several types of ischaemic heart disease as outcomes were included in the analysis. A random effects model was used to pool the effect sizes.

RESULTS: Out of 3348 records, 15 studies (one case-control, one cross-sectional and 13 cohort studies) were identified and were included in the meta-analysis. The pooled analysis indicated an increased risk of myocardial infarction (pooled adjusted effect estimate 1.33, 95% confidence interval 1.08-1.64; P = 0.007)

and of angina (pooled adjusted effect estimate 1.29, 95% confidence interval 1.17-1.43; P < 0.0001) in migraineurs compared to non-migraineurs.

CONCLUSIONS: Based on our data indicating an association of migraine with myocardial infarction and angina and on previous data showing an association of migraine, and particularly migraine with aura, with an increased risk for stroke, migraine can be appropriately considered an overall risk factor for cardiovascular diseases.

Saha S,Koley M. Homeopathic treatment of headaches & migraine: a meta-analysis of the randomized controlled trials (Provisional abstract). Asian Journal of Pharmaceutical and Clinical Research. 2013; Supplement 3. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12013059274/frame.html

Background: Homeopathy seems scientifically implausible and is the most controversial forms of CAM therapies. This review aims to summarize treatment effects of individualized homeopathy in headaches and migraine.

Methods: Relevant studies were identified by a comprehensive literature search in electronic databases, reference list of relevant papers, and contacts with experts. Randomized controlled trials comparing individualized homeopathic treatment strategy with placebo were eligible. Information on patients, methods, interventions, outcomes, and results was extracted in a standardized manner and quality was assessed using a checklist and scoring system. Trials providing sufficient data were pooled in a quantitative meta-analysis. Risk ratio above 1 indicated benefit. Bias effects were examined in funnel plot model.

Results: A total of four randomized placebo-controlled trials involving 390 patients were considered for the analysis. Methodological quality of the trials was variable. The combined risk ratio for the four studies entered into the meta-analysis was 1.58 (95% CI 0.8 to 3.1) [when corrected for publication bias it becomes 0.98 (0.5, 1.9), i.e. negative], showing positive trend, but no statistically significant difference in favor of homeopathy.

Conclusion: The results of our meta-analysis are not compatible with the notion that homeopathy has significant effect beyond placebo. However, the evidences are not convincing because of methodological inconsistencies and are too insufficient to arrive at a definite conclusion. Further replications are warranted provided the trials are rigorous and systematic.

Schabert E,Crow WT. Impact of osteopathic manipulative treatment on cost of care for patients with migraine headache: a retrospective review of patient records (Provisional abstract). Journal of the American Osteopathic Association. 2009; 8. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cleed/articles/NHSEED-22010001548/frame.html

CONTEXT:

Migraine headache is highly prevalent in the United States, resulting in large healthcare expenditures.

OBJECTIVE:

To determine whether the use of osteopathic manipulative treatment (OMT) at an osteopathic family practice residency clinic affected the cost of treating patients with migraine headache, compared with non-OMT care at the osteopathic clinic and care at an allopathic family practice residency clinic.

METHODS:

A retrospective review of electronic medical records from patients treated for migraine at two residency clinics within the Florida Hospital organization from July 1, 2002, to June 30, 2007. One of the clinics was osteopathic and offered OMT services, and the other clinic was allopathic and did not offer OMT. All costs compiled during the office visits and costs of prescribed medications were tabulated for each patient. Patients' pain-severity ratings, as reported in office visits in 2006 and 2007, were also tabulated.

RESULTS:

Electronic medical records from 631 patients, representing 1427 migraine-related office visits, were analyzed. Average cost per patient visit was approximately 50% less at the osteopathic clinic than at the allopathic clinic ($195.63 vs $363.84, respectively; P<.001). This observed difference was entirely attributable to the difference in the average number of medications prescribed per visit at the two clinics, with 0.696 prescriptions at the osteopathic clinic and 1.285 prescriptions at the allopathic clinic (P<.001). This difference in prescription number resulted in a lower average medication cost per visit at the osteopathic clinic than at the allopathic clinic ($106.94 vs $284.93, respectively; P<.001). Patients at the osteopathic clinic were 5 years younger on average than at the allopathic clinic (P<.001). No statistically significant difference was observed between the two practices in patients' ratings of pain severity.

CONCLUSION:

The inclusion of OMT in a treatment regimen for patients with migraine headache may lower the cost of the treatment regimen. However, further study is needed to confirm these results.

Shamliyan TA, Choi JY, Ramakrishnan R, Biggs Miller J, Wang SY, Taylor FR, et al. Preventive pharmacologic treatments for episodic migraine in adults (Provisional abstract). Journal of General Internal Medicine. 2013; 9. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12013022096/frame.html

OBJECTIVES:

Systematic review of preventive pharmacologic treatments for community-dwelling adults with episodic migraine.

DATA SOURCES:

Electronic databases through May 20, 2012.

ELIGIBILITY CRITERIA:

English-language randomized controlled trials (RCTs) of preventive drugs compared to placebo or active treatments examining rates of ≥50 % reduction in monthly migraine frequency or improvement in quality of life.

STUDY APPRAISAL AND SYNTHESIS METHODS:

We assessed risk of bias and strength of evidence and conducted random effects meta-analyses of absolute risk differences and Bayesian network meta-analysis.

RESULTS:

Of 5,244 retrieved references, 215 publications of RCTs provided mostly low-strength evidence because of the risk of bias and imprecision. RCTs examined 59 drugs from 14 drug classes. All approved drugs, including topiramate (9 RCTs), divalproex (3 RCTs), timolol (3 RCTs), and propranolol (4 RCTs); off-label beta blockers metoprolol (4 RCTs), atenolol (1 RCT), nadolol (1 RCT), and acebutolol (1 RCT); angiotensin-converting enzyme inhibitors captopril (1 RCT) and lisinopril (1 RCT); and angiotensin II receptor blocker candesartan (1 RCT), outperformed placebo in reducing monthly migraine frequency by ≥50 % in 200-400 patients per 1,000 treated. Adverse effects leading to treatment discontinuation (68 RCTs) were greater with topiramate, off-label antiepileptics, and antidepressants than with placebo. Limited direct evidence as well as frequentist and exploratory network Bayesian meta-analysis showed no statistically significant differences in benefits between approved drugs. Off-label angiotensin-inhibiting drugs and beta-blockers were most effective and tolerable for episodic migraine prevention.

LIMITATIONS:

We did not quantify reporting bias or contact principal investigators regarding unpublished trials.

CONCLUSIONS:

Approved drugs prevented episodic migraine frequency by ≥50 % with no statistically significant difference between them. Exploratory network meta-analysis suggested that off-label angiotensin-inhibiting drugs and beta-blockers had favorable benefit-to-harm ratios. Evidence is lacking for long-term effects of drug treatments (i.e., trials of more than 3 months duration), especially for quality of life.

Shamliyan TA, Kane RL, Ramakrishnan R,Taylor FR. Episodic migraines in children: limited evidence on preventive pharmacological treatments (Provisional abstract). Journal of Child Neurology. 2013; 10. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12013033324/frame.html

The authors conducted a systematic literature review of preventive pharmacological treatments for episodic childhood migraines searching several databases through May 20, 2012. Episodic migraine prevention was examined in 24 publications of randomized controlled trials that enrolled 1578 children in 16 nonrandomized studies. Single randomized controlled trials provided low-strength evidence that propranolol would result in complete cessation of migraine attacks in 713 per 1000 children treated (95% confidence interval, 452-974); trazodone and nimodipine decreased migraine days, while topiramate, divalproex, and clonidine were no more effective than placebo in preventing migraines. Migraine prevention with multidisciplinary drug management was not sustained at 6 months. Divalproex resulted in treatment discontinuation due to adverse effects, and topiramate increased the risk of paresthesia, upper respiratory tract infection, and weight loss. Long-term preventive benefits and improvement in disability and quality of life are unknown. No studies examined quality of life or provided evidence for individualized treatment decisions.

Shuhendler AJ, Lee S, Siu M, Ondovcik S, Lam K, Alabdullatif A, et al. Efficacy of botulinum toxin type A for the prophylaxis of episodic migraine headaches: a meta-analysis of randomized, double-blind, placebo-controlled trials (Structured abstract). Pharmacotherapy. 2009; 7. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12009107906/frame.html

STUDY OBJECTIVE:

To assess the efficacy of botulinum toxin type A in lowering the frequency of migraine headaches in patients with episodic migraines.

DESIGN:

Meta-analysis of eight randomized, double-blind, placebo-controlled trials.

PATIENTS:

A total of 1601 patients with a history of episodic migraine headaches classified as those experiencing headaches fewer than 15 times/month over a 3-month period.

MEASUREMENTS AND MAIN RESULTS:

PubMed, Google Scholar, and the Cochrane Library were searched from inception to October 2007 in order to locate randomized, double-blind, placebo-controlled trials that compared the efficacy of pericranial botulinum toxin A injections with placebo in the prevention of migraines in patients with a history of episodic migraine headaches. The primary outcome of interest was change from baseline to end point in migraine frequency (number of migraines/month). A random effects model was used to combine study results, and the standardized mean difference (Cohen's d) in migraine frequency between the placebo and botulinum toxin A groups was reported. Effect sizes (d) less than 0.2 were considered small. Quality assessment was performed by using the Downs and Black scale. Eight randomized, double-blind, placebo-controlled clinical trials (1601 patients) presented a quantitative assessment of the efficacy of botulinum toxin A versus placebo. The overall treatment effect size of botulinum toxin A over placebo for 30, 60, and 90 days after

injection was d -0.06 (95% confidence interval [CI] - 0.14-0.03, z=1.33, p=0.18), d -0.05 (95% CI -0.14-0.03, z=1.22, p=0.22), and d -0.05 (95% CI -0.13-0.04, z=1.07, p=0.28), respectively. Even after controlling for a high placebo effect, and after dose stratification, no significant effect of botulinum toxin A in reducing migraine frequency/month was seen over placebo.

CONCLUSION:

Botulinum toxin A for the prophylactic treatment of episodic migraine headaches was not significantly different from placebo, both from a clinical and statistical perspective.

Singh A, Alter HJ,Zaia B. Does the addition of dexamethasone to standard therapy for acute migraine headache decrease the incidence of recurrent headache for patients treated in the emergency department: a meta-analysis and systematic review of the literature (Structured abstract). Academic Emergency Medicine. 2008; 12. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12009101970/frame.html

OBJECTIVES:

Neurogenic inflammation is thought to play a role in the development and perpetuation of migraine headache. The emergency department (ED) administration of dexamethasone in addition to standard antimigraine therapy has been used to decrease the incidence of recurrent headaches at 24 to 72 hours following evaluation. This systematic review details the completed trials that have evaluated the use of dexamethasone in this role.

METHODS:

The authors searched MEDLINE, EMBASE, CINAHL, LILACS, recent emergency medicine scientific abstracts, and several prepublication trial registries for potential investigations related to the research question. The authors included studies that incorporated randomized, double-blind, placebo-controlled methodology and that were performed in the ED. A fixed-effects and random-effects model was used to obtain summary risk ratios (RRs) and 95% confidence intervals (CIs) for the self-reported outcome of moderate or severe headache on follow-up evaluation.

RESULTS:

A pooled analysis of seven trials involving 742 patients suggests a modest but significant benefit when dexamethasone is added to standard antimigraine therapy to reduce the rate of patients with moderate or severe headache on 24- to 72-hour follow-up evaluation (RR = 0.87, 95% CI = 0.80 to 0.95; absolute risk reduction = 9.7%). The treatment of 1,000 patients with acute migraine headache using dexamethasone in addition to standard antimigraine therapy would be expected to prevent 97 patients from experiencing the outcome of moderate or severe headache at 24 to 72 hours after ED evaluation. The sensitivity analysis yielded similar results with sequential trial elimination, indicating that no single trial was responsible for the overall result. Adverse effects related to the administration of a single dose of dexamethasone were infrequent, mild, and transient.

CONCLUSIONS:

These results suggest that dexamethasone is efficacious in preventing headache recurrence and safe when added to standard treatment for the management of acute migraine headache in the ED.

Slof J. Cost-effectiveness analysis of early versus non-early intervention in acute migraine based on evidence from the 'Act when Mild' study (Structured abstract). Applied Health Economics and Health Policy. 2012; 3. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cleed/articles/NHSEED-22012018297/frame.html

BACKGROUND:

In spite of the important progress made in the abortive treatment of acute migraine episodes since the introduction of triptans, reduction of pain and associated symptoms is in many cases still not as effective nor as fast as would be desirable. Recent research pays more attention to the timing of the treatment, and taking triptans early in the course of an attack when pain is still mild has been found more efficacious than the usual strategy of waiting for the attack to develop to a higher pain intensity level.

OBJECTIVE:

To investigate the cost effectiveness of early versus non-early intervention with almotriptan in acute migraine.

METHODS:

An economic evaluation was conducted from the perspectives of French society and the French public health system based on patient-level data collected in the AwM (Act when Mild) study, a placebo-controlled trial that compared the response to early and non-early treatment of acute migraine with almotriptan. Incremental cost-effectiveness ratios (ICERs) were determined in terms of QALYs, migraine hours and productive time lost. Costs were expressed in Euros (year 2010 values). Bootstrapping was used to derive cost-effectiveness acceptability curves.

RESULTS:

Early treatment has shown to lead to shorter attack duration, less productive time lost, better quality of life, and is, with 92% probability, overall cost saving from a societal point of view. In terms of drug costs only, however, non-early treatment is less expensive. From the public health system perspective, the (bootstrap) mean ICER of early treatment amounts to €0.38 per migraine hour avoided, €1.29 per hour of productive time lost avoided, and €14,296 per QALY gained. Considering willingness-to-pay values of approximately €1 to avoid an hour of migraine, €10 to avoid the loss of a productive hour, or €30,000 to gain one QALY, the approximate probability that early treatment is cost effective is 90%, 90% and 70%, respectively. These results remain robust in different scenarios for the major elements of the economic evaluation.

CONCLUSIONS:

Compared with non-early treatment, a strategy of early treatment of acute migraine with almotriptan when pain is still mild is, with high probability, cost saving from the French societal perspective and can be considered cost effective from the public health system point of view.

Slof J, Badia X, Magaz S, Lainez MJ, Galvan J,Heras J. Cost-efficacy of oral triptans in the treatment of acute migraine (Structured abstract). Journal of Medical Economics. 2005; 2. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cleed/articles/NHSEED-22005008113/frame.html

The objective of this study was to compare the efficiency of oral triptans currently used in the treatment of acute migraine in Spain. Using a decision analytic model, a cost-efficacy analysis was performed from the payer's perspective. Efficacy was assessed in terms of sustained pain-free patients, with data extracted from a recent meta-analysis of clinical trials. Chest-related and central nervous system-related adverse events were also considered. For the economic analysis, the cost of drug treatment and the management of adverse events were determined.

A group of three triptans (naratriptan 2.5 mg, sumatriptan 50 mg and almotriptan 12.5 mg) was found to dominate all other triptans in the sense that the other triptans were more expensive but did not show higher efficacy. Naratriptan 2.5 mg offered the lowest cost of the three, while almotriptan 12.5 mg showed the highest level of efficacy. The incremental cost-efficacy ratio for sumatriptan 50 mg versus naratriptan 2.5 mg was €23.09 per sustained pain-free patient. The incremental cost-efficacy ratio for almotriptan 12.5 mg versus sumatriptan 50 mg was €10.45 per sustained pain-free patient.

However, 95% confidence intervals for efficacy and costs of almotriptan 12.5 mg overlapped with those of rizatriptan 10 mg, while 95% confidence intervals of sumatriptan 50 mg overlapped with those of naratriptan 2.5 mg, zolmitriptan 2.5 mg and eletriptan 40 mg. A third cluster of triptans with overlapping confidence intervals, showing higher costs but not higher efficacy than almotriptan 12.5 mg and rizatriptan 10 mg, included sumatriptan 100 mg, zolmitriptan 5 mg and eletriptan 80 mg.

It is concluded that, combining clinical and economic considerations, rizatriptan 10 mg and, particularly, almotriptan 12.5 mg are the most appealing triptans in Spain

Read More: http://informahealthcare.com/doi/abs/10.3111/200508027043

Smelt AFH, Blom JW, Dekker F, Akker ME, Knuistingh Neven A, Zitman FG, et al. A proactive approach to migraine in primary care: a pragmatic randomized controlled trial (Provisional abstract). CMAJ: Canadian Medical Association Journal. 2012; 4. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cleed/articles/NHSEED-22012014696/frame.html

BACKGROUND:

Migraine is a common, disabling headache disorder that leads to lost quality of life and productivity. We investigated whether a proactive approach to patients with migraine, including an educational intervention for general practitioners, led to a decrease in headache and associated costs.

METHODS:

We conducted a pragmatic randomized controlled trial. Participants were randomized to one of two groups: practices receiving the intervention and control practices. Participants were prescribed two or more doses of triptan per month. General practitioners in the intervention group received training on treating migraine and invited participating patients for a consultation and evaluation of the therapy they were receiving. Physicians in the control group continued with usual care. Our primary outcome was patients' scores on the Headache Impact Test (HIT-6) at six months. We considered a reduction in score of 2.3 points to be clinically relevant. We used the Kessler Psychological Distress Scale (K10) questionnaire to determine if such distress was a possible effect modifier. We also examined the interventions' cost-effectiveness.

RESULTS:

We enrolled 490 patients in the trial (233 to the intervention group and 257 to the control group). Of the 233 patients in the intervention group, 192 (82.4%) attended the consultation to evaluate the treatment of their migraines. Of these patients, 43 (22.3%) started prophylaxis. The difference in change in score on the HIT-6 between the intervention and control groups was 0.81 ($p = 0.07$, calculated from modelling using generalized estimating equations). For patients with low levels of psychological distress (baseline score on the K10 ≤ 20) this change was -1.51 ($p = 0.008$), compared with a change of 0.16 ($p = 0.494$) for patients with greater psychological distress. For patients who were not using prophylaxis at baseline and had two or more migraines per month, the mean HIT-6 score improved by 1.37 points compared with controls ($p = 0.04$). We did not find the intervention to be cost-effective.

INTERPRETATION:

An educational intervention for general practitioners and a proactive approach to patients with migraine did not result in a clinically relevant improvement of symptoms. Psychological distress was an important confounder of success

Suthisisang C, Poolsup N, Kittikulsuth W, Pudchakan P,Wiwatpanich P. Efficacy of low-dose ibuprofen in acute migraine treatment: systematic review and meta-analysis (Provisional abstract). Annals of Pharmacotherapy. 2007;

11. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12007003863/frame.html

BACKGROUND:

Nonsteroidal antiinflammatory drugs such as aspirin and ibuprofen have been shown to be effective in treating migraine.

OBJECTIVE:

To evaluate the efficacy of low-dose ibuprofen for treatment of acute migraine attack.

METHODS:

Clinical trials were identified through electronic searches (MEDLINE, EMBASE, EBM review, and the Cochrane Library) up to November 2006 and historical searches of relevant articles. Studies were included if they (1) were double-blind, randomized, placebo-controlled trials that evaluated ibuprofen tablets in moderate or severe migraine attacks in patients greater than 16 years of age, (2) evaluated at least one migraine attack, and (3) reported headache relief, pain-free, sustained pain-free, or relief of other migraine-associated symptoms at 2 hours. The MeSH search terms used were migraine disorders, headache, vascular headache, ibuprofen, adult, and clinical trial. This was followed by a key word search using migraine, cephalalgia, and cephalgia as key words. The reference lists of relevant articles were also scanned to identify possible published trials. There was no language restriction. Two authors extracted data independently. Disagreements were resolved through discussion.

RESULTS:

Ibuprofen 200 and 400 mg were more effective than placebo in reducing pain intensity and eliminating pain (pain-free) within 2 hours in adults with moderate or severe migraine attacks. For the 200 mg dose, the number needed to treat was 8 (95% CI 5 to 20) for headache relief and 13 (95% CI 8 to 50) for pain-free. The risk ratios for headache relief and pain-free were 1.89 (95% CI 1.45 to 2.46; $p < 0.0001$) and 2.15 (95% CI 1.24 to 3.73; $p = 0.0063$), respectively, for ibuprofen 400 mg. The 24-hour sustained pain-free outcome with ibuprofen was no better than with placebo. Ibuprofen 400 mg increased the chance of relief in photophobia and phonophobia by 30% (95% CI 8 to 57; $p < 0.01$) and 49% (95% CI 23 to 81; $p < 0.0001$), respectively.

CONCLUSIONS:

The available evidence suggests that ibuprofen 200 and 400 mg are effective in reducing headache intensity and rendering patients pain-free at 2 hours. Photophobia and phonophobia improved with 400 mg dosing. Due to the limited data and the shortcomings of the available evidence, further studies are needed.

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 (Structured abstract). Headache. 2010; 5. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12010004169/frame.html

OBJECTIVE:

To assess the efficacy and safety of naproxen sodium in the treatment of acute migraine attacks.

BACKGROUND:

Non-steroidal anti-inflammatory drugs including naproxen sodium have been used in treating migraine attack. A number of clinical trials of naproxen sodium in migraine have been reported. However, it remains to be established whether naproxen sodium unequivocally offers clinical benefits taken into account the desired outcomes in acute migraine therapy as recommended by the International Headache Society.

METHODS:

Clinical trials were identified through electronic searches (MEDLINE, EMBASE, EBM review, and the Cochrane

Library) up to June 2009 and historical searches of relevant articles. Studies were included in the meta-analysis if they were (1) double-blind, randomized, placebo-controlled trials that evaluated naproxen sodium tablet in moderate or severe migraine attacks in adult patients, and (2) reporting the efficacy in terms of headache relief, pain-free, relief of migraine-associated symptoms, sustained headache relief, sustained pain-free, or headache recurrence. Data extraction and study quality assessment were performed independently by 2 investigators. Disagreements were resolved by a third investigator. Treatment effects and adverse effects were expressed as risk ratio. A random effects model was used when significant heterogeneity existed, otherwise the fixed effects model was performed.

RESULTS:

We identified 16 published randomized controlled trials of naproxen in the treatment of migraine. Four trials met the inclusion criteria and were included in the meta-analysis. Naproxen sodium was more effective than placebo in reducing pain intensity and providing pain-free within 2 hours in adults with moderate or severe migraine attacks. The pooled risk ratios were 1.58 (95% confidence interval [CI] 1.41-1.77, P < .00001), and 2.22 (95% CI 1.46-3.37, P = .0002), respectively, for headache relief at 2 hours and pain-free at 2 hours. It was also effective in achieving headache relief at 4 hours, relief of migraine-associated symptoms, sustained headache relief, and sustained pain-free responses. There was no significant difference in headache recurrence rate between naproxen sodium and placebo. The risk of any adverse event was greater with naproxen sodium than with placebo (pooled risk ratio 1.29, 95% CI 1.04-1.60, P = .02). The adverse events commonly associated with naproxen sodium were nausea, dizziness, dyspepsia, and abdominal pain.

CONCLUSIONS:

The available evidence suggests that naproxen sodium is more effective but may cause more adverse events than placebo in the acute treatment of moderate to severe migraine. It is effective in reducing headache intensity, rendering pain-free at 2 hours and improving migraine-associated symptoms. However, its effectiveness relative to other active comparators needs to be better defined by appropriate head-to-head clinical trials.

Suthisisang CC, Poolsup N, Suksomboon N, Lertpipopmetha V,Tepwitukgid B. Efficacy and safety of sumatriptan plus naproxen sodium in the acute treatment of migraine: systematic review and meta-analysis of randomized controlled trials (Provisional abstract). Headache 2011;50(5):808-18

Objective.—To assess the efficacy and safety of naproxen sodium in the treatment of acute migraine attacks.

Background.—Non-steroidal anti-inflammatory drugs including naproxen sodium have been used in treating migraine attack. A number of clinical trials of naproxen sodium in migraine have been reported. However, it remains to be established whether naproxen sodium unequivocally offers clinical benefits taken into account the desired outcomes in acute migraine therapy as recommended by the International Headache Society.

Methods.—Clinical trials were identified through electronic searches (MEDLINE, EMBASE, EBM review, and the Cochrane Library) up to June 2009 and historical searches of relevant articles. Studies were included in the meta-analysis if they were (1) double-blind, randomized, placebo-controlled trials that evaluated naproxen sodium tablet in moderate or severe migraine attacks in adult patients, and (2) reporting the efficacy in terms of headache relief, pain-free, relief of migraine-associated symptoms, sustained headache relief, sustained pain-free, or headache recurrence. Data extraction and study quality assessment were performed independently by 2 investigators. Disagreements were resolved by a third investigator. Treatment effects and adverse effects were expressed as risk ratio. A random effects model was used when significant heterogeneity existed, otherwise the fixed effects model was performed.

Results.—We identified 16 published randomized controlled trials of naproxen in the treatment of migraine. Four trials met the inclusion criteria and were included in the meta-analysis. Naproxen sodium was more

effective than placebo in reducing pain intensity and providing pain-free within 2 hours in adults with moderate or severe migraine attacks. The pooled risk ratios were 1.58 (95% confidence interval [CI] 1.41–1.77, P < .00001), and 2.22 (95% CI 1.46–3.37, P = .0002), respectively, for headache relief at 2 hours and pain-free at 2 hours. It was also effective in achieving headache relief at 4 hours, relief of migraine-associated symptoms, sustained headache relief, and sustained pain-free responses. There was no significant difference in headache recurrence rate between naproxen sodium and placebo. The risk of any adverse event was greater with naproxen sodium than with placebo (pooled risk ratio 1.29, 95% CI 1.04–1.60, P = .02). The adverse events commonly associated with naproxen sodium were nausea, dizziness, dyspepsia, and abdominal pain.

Conclusions.—The available evidence suggests that naproxen sodium is more effective but may cause more adverse events than placebo in the acute treatment of moderate to severe migraine. It is effective in reducing headache intensity, rendering pain-free at 2 hours and improving migraine-associated symptoms. However, its effectiveness relative to other active comparators needs to be better defined by appropriate head-to-head clinical trials.

Taggart E, Doran S, Kokotillo A, Campbell S, Villa-Roel C,Rowe BH. Ketorolac in the treatment of acute migraine: a systematic review (Provisional abstract). Headache. 2013; 2. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12013017378/frame.html

This systematic review examined the effectiveness of parenteral ketorolac (KET) in acute migraine. Acute migraine headaches are common emergency department presentations, and despite evidence for various treatments, there is conflicting evidence regarding the use of KET. Searches of MEDLINE, EMBASE, Cochrane, CINAHL, and gray literature sources were conducted. Included studies were randomized controlled trials in which KET alone or in combination with abortive therapy was compared with placebo or other standard therapy in adult patients with acute migraine. Two reviewers assessed relevance, inclusion, and study quality independently, and agreement was measured using kappa (k). Weighted mean differences (WMD) and relative risks are reported with 95% confidence intervals (CIs). Overall, the computerized search identified 418 citations and 1414 gray literature citations. From a list of 34 potentially relevant studies (k = 0.915), 8 trials were included, involving over 321 (141 KET) patients. The median quality scores were 3 (interquartile range: 2-4), and two used concealed allocation. There were no baseline differences in 10-point pain scores (WMD = 0.07; 95% CI: -0.39, 0.54). KET and meperidine resulted in similar pain scores at 60 minutes (WMD = 0.31; -0.68, 1.29); however, KET was more effective than intranasal sumatriptan (WMD = -4.07; 95% CI: -6.02 to -2.12). While there was no difference in pain relief at 60 minutes between KET and phenothiazine agents (WMD = 0.82; 95% CI: -1.33 to 2.98), heterogeneity was high (I(2) = 70%). Side effect profiles were similar between KET and comparison groups. Overall, KET is an effective alternative agent for the relief of acute migraine headache in the emergency department. KET results in similar pain relief, and is less potentially addictive than meperidine and more effective than sumatriptan; however, it may not be as effective as metoclopramide/phenothiazine agents.

Taylor FR. Tobacco, Nicotine, and Headache. Headache 2015;55(7):1028-44

BACKGROUND: Migraineurs variably attribute the cause of their headache to tobacco exposure, whereas tobacco is often stated to cause headache-related disability worldwide. Given tobacco's physiological and emotional addictiveness and migraine's substantial economic impact, improved functionality can be difficult for those with migraine exposed to tobacco products. Environmental tobacco exposure in indoor spaces and workplaces is associated with exacerbation of headache. Avoidance of headache triggers is included in most comprehensive migraine treatment programs, yet tobacco awareness, avoidance, or coping is rarely emphasized as part of that regimen.

OBJECTIVE: The aims of this study were to examine the various types of tobacco products to which headache sufferers are exposed and the known basic mechanisms by which tobacco (nicotine) exposure promotes headache pain, and to review the extensive literature on tobacco related to headache with a detailed

descriptive narrative providing the basis for conclusions regarding association of noncluster headache-related tobacco exposure. Tobacco-related recommendations are offered.

METHODS: MEDLINE, EMBASE, and Google Scholar databases were searched without yearly restriction through the date of submission (May 2015), using the MeSH terms "tobacco," "tobacco products," "smoking," "tobacco use," "headache," and "headache disorders." The selection of articles was not limited to English studies or to humans. Articles were excluded when "headache" and "tobacco" were not both mentioned with data provided. Case series were included. Bibliographies of all articles were screened for additional relevant articles.

RESULTS: Although migraineurs worldwide report tobacco smoke among triggers, it is rarely among the highest in frequency, and biases abound with predominantly noncontrolled retrospective data. Prospective population-based diary data are extremely limited, and no controlled trials exist to confirm a cause and effect for headache of any type. Although some studies are nonsupportive and even conflicting, headache, pain, and tobacco exposure currently remain associated.

CONCLUSION: Conflicting data support the validity of patient-reported environmental tobacco exposure as a headache trigger. Prospective controlled studies are needed, but unlikely to be performed, to determine the extent that tobacco influences the headache process, in addition to other under-recognizedfactors. Meanwhile, because of numerous other negative health effects, decreased tobacco exposure should be recommended to headache patients of all ages in hopes of decreasing disability and improving functionality.

Thomas MC, Musselman ME,Shewmaker J. Droperidol for the treatment of acute migraine headaches. Annals of Pharmacotherapy 2015;49(2):233-40

OBJECTIVE: To evaluate the safety and efficacy of droperidol for the relief of acute migraine headaches.

DATA SOURCES: A MEDLINE search (1946 to August 2014) was performed using the following keywords and associated medical subject headings: droperidol, inapsine, headache, migraine, and migraine disorder.

STUDY SELECTION AND DATA EXTRACTION: The search was conducted to identify randomized controlled trials comparing droperidol with placebo or an active control in adult patients with acute migraine headaches that were published in English. Primary end points included acute headache improvement after the intervention. Safety end points included the frequency of extrapyramidal symptoms, somnolence, and cardiac adverse effects.

DATA SYNTHESIS: In all, 5 manuscripts are included in this review. Patients presenting to the emergency department with acute headache desire rapid pain relief, which was the primary objective in each of the evaluated studies. Droperidol was better than placebo and at least as effective as comparator drugs such as prochlorperazine, meperidine, or olanzapine using droperidol doses of 2.5 to 5 mg, given either intramuscularly (IM) or intravenously (IV). The most commonly reported adverse effects were extrapyramidal symptoms and sedation. Cardiac adverse effects were not reported in any of the studies; however, only 2 articles described using cardiac monitoring.

CONCLUSIONS: Parenteral droperidol is an effective option for the treatment of acute migraine. The minimum effective dose is 2.5 mg given IM or IV. Clinicians must be aware of the risk for adverse events, select appropriate patients, perform EKG monitoring for patients at risk of QTc prolongation, and institute treatment if necessary.

Thompson M, Gawel M, Desjardins B, Ferko N,Grima D. An economic evaluation of rizatriptan in the treatment of migraine (Structured abstract). Pharmacoeconomics. 2005; 8. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cleed/articles/NHSEED-22005008326/frame.html

BACKGROUND:

Migraine is a common, chronic, neurovascular disorder, generally characterised by attacks of severe headache and autonomic nervous system dysfunction. Triptans are selective serotonin 5-HT(1B/1D) receptor agonists that represent effective therapeutic options for moderate-to-severe migraine attacks but with higher acquisition costs relative to usual care therapies.

OBJECTIVE:

The objective of this study was to examine the cost effectiveness of rizatriptan treatment compared with 'Usual Care' or other triptans available in Canada for patients with moderate-to-severe migraine for whom other therapies (e.g. NSAIDs, simple analgesics) are insufficient or contraindicated.

METHODS:

A decision-analysis model was created to estimate migraine treatment costs over a 24-hour period in patients with a diagnosis of moderate-to-severe migraine as defined by the International Headache Society criteria. Costs and clinical outcomes were observed over a 24-hour period from therapy initiation. Efficacy measures consisted of 'pain-free response at 2 hours' and 'sustained pain free for 2-24 hours'. Oral rizatriptan 10 mg was compared with other oral triptans (i.e. sumatriptan 50 or 100 mg), naratriptan 2.5 mg and zolmitriptan 2.5 mg, based on a meta-analysis and compared with 'Usual Care' based on a naturalistic study of people who experience migraine and who were similar to the target population. 'Usual Care' was defined as an aggregate of medications prescribed for the Canadian population for the indication of migraine, weighted by the relative frequency of use of prescriptions over a 1-year period. Analyses were conducted from the Ontario (Canada) Ministry of Health and Long-Term Care (MOH<C) perspective and the broader societal perspective. Results are presented as the cost per migraine attack aborted (i.e. pain free at 2 hours), as well as the cost per QALY. Several one-way sensitivity analyses were conducted to test the robustness of the model. All costs are expressed in 2002 $Can.

RESULTS:

Cost estimates are similar to previously published Canadian studies. Rizatriptan compared with 'Usual Care' produced an incremental cost per attack aborted of $Can49.82 and a cost per QALY gained of $Can31 845 from the MOH<C perspective. When a societal perspective was considered (which included time loss from paid and unpaid work activities), rizatriptan dominates 'Usual Care': that is, it is cost saving and more effective. All other triptans are also dominated by rizatriptan as they offer higher costs and lower efficacy.

CONCLUSIONS:

This study shows that rizatriptan treatment for patients who experience moderate-to-severe migraines may represent a cost-effective strategy for improving care of migraine patients in Canada.

Wabnitz A,Bushnell C. Migraine, cardiovascular disease, and stroke during pregnancy: systematic review of the literature. Cephalalgia 2015;35(2):132-9

OBJECTIVE: The objective of this article is to review the literature relating migraine, cardiovascular disease, and stroke during pregnancy in order to better define the relationship between migraines and vascular disease.

METHODS: We conducted a systematic review of the literature using Medline and Cochrane Review with the following search terms: migraine AND pregnancy and vascular disease OR myocardial infarction OR heart disease OR stroke OR cerebrovascular disease OR hypertension in pregnancy. We also reviewed the bibliographies of papers identified in this search to obtain additional relevant studies.

RESULTS: Of the 219 papers obtained with the primary search, we found 17 that were topically relevant. Altogether, there is an increased risk both of gestational hypertension (OR range from 1.23 to 1.68) and preeclampsia (OR range 1.08 to 3.5) in migraineurs compared to nonmigraineurs. In addition, there is an association between an increased risk of ischemic stroke in pregnancy (OR range 7.9 to 30.7), particularly with active migraine. There is also an association between migraine and increased risk of acute myocardial

infarction and heart disease (OR 4.9; 95% CI 1.7, 14.2), and thromboembolic events during pregnancy (deep venous thrombosis OR 2.4; 95% CI 1.3, 4.2 and pulmonary embolus OR 3.1; 95% CI 1.7, 5.6).

CONCLUSION: In this review, we summarized the association between migraine and risk of vascular disease during pregnancy, based on the available literature. Given the limited amount of data, more research on these associations is needed to determine which women with migraine may be at risk while pregnant.

Witt CM, Reinhold T, Jena S, Brinkhaus B,Willich SN. Cost-effectiveness of acupuncture treatment in patients with headache (Structured abstract). Cephalalgia. 2008; 2. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cleed/articles/NHSEED-22008000737/frame.html

The aim was to assess costs and cost-effectiveness of additional acupuncture treatment in patients with headache compared with patients receiving routine care alone. A randomized, controlled trial was conducted, including patients (> or =18 years old) with primary headache (more than 12 months, at least two headaches/month). Outcome parameters were quality of life (Short Form 36), direct and indirect costs differences during the 3-month study period and the incremental cost-effectiveness ratio (ICER) of acupuncture treatment. A total of 3182 patients (1613 acupuncture; 1569 controls) with headache were included (77.4% women, mean age and standard deviation 42.6 +/- 12.3; 22.6% men, 47.2 +/- 13.4). Over 3 months costs were higher in the acupuncture group compared with the control [euro857.47; 95% confidence interval 790.86, 924.07, vs. euro527.34 (459.81, 594.88), P < 0.001, mean difference: euro330.12 (235.27, 424.98)]. This cost increase was primarily due to costs of acupuncture [euro365.64 (362.19, 369.10)]. The ICER was euro11 657 per QALY gained. According to international cost-effectiveness threshold values, acupuncture is a cost-effective treatment in patients with primary headache.

Xia W, Zhu M, Zhang Z, Kong D, Xiao W, Jia L, et al. Effect of Tianshu capsule in treatment of migraine: a meta-analysis of randomized control trials (Provisional abstract). Journal of Traditional Chinese Medicine. 2013; 1. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12013022342/frame.html

OBJECTIVE:

To review the efficacy of Tianshu capsule in the treatment of migraine.

METHODS:

Retrieving papers from Pubmed, cochrane central register of controlled trials (CENTRAL), Weipu database (VIP), China biology medicine (CBM), China national knowledge infrastructure (CNKI), and Wanfang Data. Two reviewers retrieved and extracted the information independently. Retrieval time scale is up to August 2012. Software Review Manager 5.1 was used for analysis.

RESULTS:

A total of 10 studies including 937 migraine patients. The merged data shows Tianshu capsule had a higher effective rate in treating migraine, and there is no significant heterogeneity between Tianshu capsule group and control group (Chi2 = 6.33, df = 9, P = 0.71, I2 = 0%), OR = 4.18 [95% CI (2.93,5.95)]. Tianshu capsule alone compared to conventional therapy also showed advantages, and there was low heterogeneity (chi2 = 4.53, df = 3, P = 0.21, I2 = 34%), OR = 3.95 [95% CI (2.32, 6.72)]. Meta-analysis results show that clinical efficacy of Tianshu capsule was better than that of the control group in the treatment of migraine and there was a significant difference (P < 0.000 01).

CONCLUSION:

Tianshu capsule had better efficacy in the treatment of migraine with fewer adverse effects.

Xiao Y, Yuan L, Liu Y, Sun X, Cheng J, Wang T, et al. Traditional Chinese patent medicine for prophylactic treatment of migraine: a meta-analysis of randomized, double-blind, placebo-controlled trials. European Journal of Neurology 2015;22(2):361-8

BACKGROUND AND PURPOSE: A large number of traditional Chinese patent medicines (TCPMs) are widely used to treat migraine in China. However, it is uncertain whether there is robust evidence on the effects of TCPMs for migraine. A meta-analysis of randomized, double-blind, placebo-controlled trials was performed to evaluate the efficacy and safety of TCPMs in patients with migraine.

METHODS: Comprehensive searches were conducted on the Medline database, Cochrane Library, the China National Knowledge Infrastructure database, the Chinese Biomedical Literature database and the Wanfang database up to December 2013. Summary estimates, including 95% confidence intervals (CIs), were calculated for frequency of migraine attacks, response rate and headache intensity.

RESULTS: A total of seven trials including 582 participants with migraine met the selection criteria. TCPM was significantly more likely to reduce the frequency of migraine attacks compared with placebo (standardized mean difference -0.54; 95% CI -0.72, -0.36; P < 0.001). TCPM was associated with an improvement of response rate compared with placebo (summary relative risk 4.63, 95% CI 2.74, 7.80, P < 0.001; therapeutic gain 24.1%; number needed to treat 4.1). Headache intensity was attenuated by TCPM compared with placebo (standardized mean difference -1.33; 95% CI -1.79, -0.87; P < 0.001). The adverse events of TCPM were no different from those of placebo.

CONCLUSION: TCPMs are effective and well tolerated in the prophylactic treatment of migraine.

Yao G, Yu TM, Han XM, Mao XJ,Li B. Therapeutic effects and safety of olcegepant and telcagepant for migraine: a meta-analysis (Provisional abstract). Neural Regeneration Research. 2013; 10. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12014011347/frame.html

OBJECTIVE: To evaluate the therapeutic effects and adverse reactions of olcegepant and telcagepant for the treatment of migraine.

DATA RETRIEVAL: We identified studies using Medline (1966-01/2012-06), PubMed (1966-01/2012-06), Scopus (1980-01/2012-06), Cochrane Central Register of Controlled Trials (1980-01/2012-06) and China National Knowledge Infrastructure (1980-01/2012-06).

SELECTION CRITERIA: The included studies were double-blind, randomized and placebo-controlled trials of olcegepant or telcagepant for the treatment of single acute migraine in patients with or without aura. Adverse reaction data were also included. Two independent investigators performed quality evaluation and data extraction using Jadad scoring. Meta-analyses were undertaken using RevMan 5.0.25 software.

MAIN OUTCOME MEASURES: Pain relief rate, pain-free rate, and incidence of adverse reactions were measured in patients 2 and 24 hours after injection of olcegepant and oral telcagepant.

RESULTS: Six randomized, controlled trials were included. Meta-analysis demonstrated that compared with placebo, the pain relief rate (odds ratio, OR = 5.21, 95% confidence interval, CI: 1.91-14.2, P < 0.01) and pain-free rate (OR = 31.11, 95% CI: 3.80-254.98, P < 0.01) significantly increased 2 hours after 2.5 mg/d olcegepant treatment. Pain relief rate and pain-free rate 2 and 24 hours after treatment with telcagepant 150 mg/d and 300 mg/d were superior to placebo (P < 0.01). Moreover, the remission rate of unrelenting headache was higher after 24 hours of 300 mg/d telcagepant treatment compared with 150 mg/d (OR = 0.78, 95% CI: 0.62-0.97, P < 0.05). The incidence of adverse reactions with olcegepant was not significantly greater than placebo (P = 0.28), but within 48 hours of administration of telcagepant 300 mg/d, the incidence of adverse reactions was higher than placebo (OR = 1.21, 95% CI: 1.04-1.42, P < 0.01). Few studies have compared the therapeutic effects of olcegepant and telcagepant.

CONCLUSION: The calcitonin-gene-related peptide receptor antagonists olcegepant and telcagepant have shown good therapeutic effects in the treatment of migraine. Moreover, the incidence of adverse reactions compares favorably with placebo, although liver transaminases may become elevated after long-term use.

Yu J, Smith KJ,Brixner DI. Cost effectiveness of pharmacotherapy for the prevention of migraine: a Markov model application (Provisional abstract). CNS Drugs. 2010; 8. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cleed/articles/NHSEED-22010001469/frame.html

BACKGROUND:

There are few data about the cost effectiveness of prophylactic medications for migraine. Clinical trials have shown several preventive agents to be useful in reducing the frequency of migraine attack while having tolerable side effects.

OBJECTIVE:

To compare the cost effectiveness of adding preventive treatment to abortive therapy for acute migraine with abortive therapy for acute migraine alone in the primary care setting.

METHODS:

A Markov decision analytic model with a cycle length of 1 day, a time horizon of 365 days and three health states was used to perform an analysis comparing the cost effectiveness and utility of five treatments for migraine prophylaxis (amitriptyline 75 mg/day, topiramate 100 and 200 mg/day, timolol 20 mg/day, divalproex sodium 1000 mg/day or propranolol 160 mg/day) with treatment of acute migraine alone for the management of migraine in the primary care setting. One-way and probabilistic sensitivity analyses were performed to test the robustness of the results.

RESULTS:

The expected total annual cost for the use of preventive agents ranged from $US2932 to $US3887, compared with $US3960 for the use of abortive medications only. In the baseline analysis, use of each of the five preventive agents generated more quality-adjusted life-years (QALYs) and incurred lower costs compared with abortive medications only. Monte Carlo Simulation suggested that amitriptyline 75 mg/day was most likely to be considered a cost-effective option versus the other five therapies, followed by timolol 20 mg/day, topiramate 200 mg/day, topiramate 100 mg/day, divalproex sodium 1000 mg/day and propranolol 160 mg/day when the willingness-to-pay (WTP) for society is <$US18 000 per QALY gained.

CONCLUSIONS:

Preventive medications appear to be a cost-effective approach to the management of migraine in the primary care setting compared with the approach of abortive treatment only. Among those preventive agents, probabilistic sensitivity analysis suggests that, when the societal WTP is <$US18 000 per QALY gained, amitriptyline 75 mg/day is most likely to be considered a cost-effective option.

Zhang L,Hay JW. Cost-effectiveness analysis of rizatriptan and sumatriptan versus Cafergot in the acute treatment of migraine (Structured abstract). CNS Drugs. 2005; 7. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cleed/articles/NHSEED-22005006493/frame.html

BACKGROUND:

Both ergotamine and selective serotonin 5-HT(1B/1D) receptor agonists ('triptans') are currently used in the treatment of moderate to severe migraine. Ergotamine is a traditional therapy with a lower drug acquisition cost compared with triptans. It has been shown that triptans are more efficacious than ergotamine, but the higher acquisition costs and shorter duration of action are disadvantages of triptans compared with

ergotamine.

OBJECTIVE:

The purpose of this study was to provide a comparison of the cost-effectiveness of rizatriptan 10 mg and sumatriptan 50 mg tablets with that of a fixed-dose combination of ergotamine tartrate plus caffeine (Cafergot) in the treatment of an acute migraine attack. The cost-effectiveness of rizatriptan in comparison with sumatriptan was also assessed

METHODS:

Three separate decision tree models were developed (model 1: rizatriptan vs Cafergot; model 2: sumatriptan vs Cafergot; model 3: rizatriptan vs sumatriptan). The time horizon was 1 year. Cost-effectiveness analysis was conducted from the societal perspective using cost and effectiveness estimates from the literature. All costs were converted to US dollars (2003). The cost-effectiveness ratio was expressed as incremental cost per quality-adjusted life-year (QALY) gained.

RESULTS:

Base case evaluation showed that both rizatriptan and sumatriptan dominated Cafergot. The net annual saving associated with use of rizatriptan was US dollars 622.98 per patient, with an incremental QALY of 0.001. Use of sumatriptan resulted in a saving of US dollars 620.90 and an increase in QALY. The cost-effective ratios were not sensitive to changes in key variables such as efficacy, utility, drug costs, hospitalisation cost and patient preference over alternative therapies. The study further showed that rizatriptan is more cost effective than sumatriptan, as evidenced by its lower cost and greater effectiveness. Sensitivity analysis showed that the cost-effectiveness ratios were sensitive to moderate changes in drug efficacy.

CONCLUSION:

Rizatriptan and sumatriptan were less costly and more effective than Cafergot in the treatment of an acute migraine attack. Rizatriptan was somewhat less costly and more effective than sumatriptan. Additional quality-of-life studies are needed to confirm the benefits of using triptans in the management of migraine.

Zhou L, Chen P, Liu L, Zhang Y, Liu X, Wu Y, et al. Systematic review and meta-analysis of traditional Chinese medicine in the treatment of migraines (Provisional abstract). American Journal of Chinese Medicine. 2013; 5. [cited: url: http://onlinelibrary.wiley.com/o/cochrane/cldare/articles/DARE-12013061216/frame.html

Migraine is a chronic disorder characterized by recurrent moderate to severe headaches often in association with a number of autonomic nervous system symptoms. It is a common disease and incidence has increased yearly. Chinese medical treatments are popularly used in Asian countries, although they vary in effectiveness. In this study, we applied a systematic review method and combined meta-regression with meta-subgroup analysis to explore heterogeneity of clinical therapeutic efficacy upon meta-analysis of randomized controlled Chinese medical treatments for migraine. We also aimed to provide a more effective Chinese prescription and to advance the knowledge in evaluating validity of preventing or alleviating migraine symptoms with Chinese medical treatments. Twenty randomized migraine control trails, including 2246 patients, were collected from online databases: PubMed, MEDLINE, EMBASE, CENTRAL of Cochrane Library, CBM, integrated version of CMCI/CMCC, TCM online, CDFD, and CMFD from January 2000 to December 2011. The results showed that the major factors influencing therapeutic efficacy were either the specific medicine form of or its prescription type ($p < 0.05$). The use of TCM decoctions, especially those that condition the viscera, treat from the perspective of "wind", and target the Shaoyang gateway, could be the best migraine treatment in clinical TCM practice (RR > 1.30).

CENTRAL search for RCTs

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