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**107**

## **Diagnosis and management of headache in adults**

*A national clinical guideline*



***November 2008***

# KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS

## LEVELS OF EVIDENCE

- 1<sup>++</sup> High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
- 1<sup>+</sup> Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias
- 1<sup>-</sup> Meta-analyses, systematic reviews, or RCTs with a high risk of bias
- 2<sup>++</sup> High quality systematic reviews of case control or cohort studies  
High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal
- 2<sup>+</sup> Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal
- 2<sup>-</sup> Case control or cohort studies with a high risk of confounding or bias and a significant risk that the relationship is not causal
- 3 Non-analytic studies, eg case reports, case series
- 4 Expert opinion

## GRADES OF RECOMMENDATION

*Note: The grade of recommendation relates to the strength of the evidence on which the recommendation is based. It does not reflect the clinical importance of the recommendation.*

- A** At least one meta-analysis, systematic review, or RCT rated as 1<sup>++</sup>, and directly applicable to the target population; or  
A body of evidence consisting principally of studies rated as 1<sup>+</sup>, directly applicable to the target population, and demonstrating overall consistency of results
- B** A body of evidence including studies rated as 2<sup>++</sup>, directly applicable to the target population, and demonstrating overall consistency of results; or  
Extrapolated evidence from studies rated as 1<sup>++</sup> or 1<sup>+</sup>
- C** A body of evidence including studies rated as 2<sup>+</sup>, directly applicable to the target population and demonstrating overall consistency of results; or  
Extrapolated evidence from studies rated as 2<sup>++</sup>
- D** Evidence level 3 or 4; or  
Extrapolated evidence from studies rated as 2<sup>+</sup>

## GOOD PRACTICE POINTS

- Recommended best practice based on the clinical experience of the guideline development group.

NHS Quality Improvement Scotland (NHS QIS) is committed to equality and diversity. This guideline has been assessed for its likely impact on the six equality groups defined by age, disability, gender, race, religion/belief, and sexual orientation.

For the full equality and diversity impact assessment report please see the “published guidelines” section of the SIGN website at [www.sign.ac.uk/guidelines/published/numlist.html](http://www.sign.ac.uk/guidelines/published/numlist.html). The full report in paper form and/or alternative format is available on request from the NHS QIS Equality and Diversity Officer.

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Scottish Intercollegiate Guidelines Network

**Diagnosis and management of  
headache in adults**

A national clinical guideline



November 2008

**ISBN 978 1 905813 39 1**

**Published November 2008**

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purpose of implementation in NHSScotland

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# 1 Introduction

## 1.1 THE NEED FOR A GUIDELINE

Headache is common, with a lifetime prevalence of over 90% of the general population in the United Kingdom (UK).<sup>1</sup> It accounts for 4.4% of consultations in primary care<sup>2</sup> and 30% of neurology outpatient consultations.<sup>3,4</sup>

Headache disorders are generally classified as either primary or secondary, and these classifications are further divided into specific headache types. Primary headache disorders are not associated with an underlying pathology and include migraine, tension-type, and cluster headache. Secondary headache disorders are attributed to an underlying pathological condition and include any head pain of infectious, neoplastic, vascular, or drug-induced origin.<sup>5</sup>

Migraine is the most common severe form of primary headache affecting about six million people in the UK in the age range 16-65, and can cause significant disability.<sup>6</sup> The World Health Organisation (WHO) ranks migraine in its top 20 disabling conditions for women aged 15 to 44.<sup>7</sup> It is estimated that migraine costs the UK almost £2 billion a year in direct and indirect costs,<sup>8</sup> with over 100,000 people absent from work or school because of migraine every working day.<sup>9</sup> Tension-type headache affects over 40% of the population at any one time. Although less of a burden to the individual sufferer than migraine, its higher prevalence results in a greater societal burden, with as many lost days from work as with migraine.<sup>10</sup> Chronic headache, defined as headache on 15 or more days per month, affects three per cent of people worldwide.<sup>10</sup>

Healthcare professionals often find the diagnosis of headache difficult and both healthcare professionals and patients worry about serious rare causes of headaches such as brain tumours.<sup>2,11</sup> General practitioners (GPs) are often uncertain about when to refer patients to secondary care.<sup>2</sup> GPs refer 2-3% of patients consulting for headaches to neurological clinics.<sup>2</sup> This may allow the exclusion of secondary headache but often does not provide a headache management service. Most primary headache can be managed in primary care and investigations are rarely needed.<sup>12</sup>

There are effective therapies for many of the primary headaches<sup>11,13</sup> but treatments can cause headache themselves.<sup>11</sup> Despite this many patients are inappropriately prescribed analgesics and many patients with headache never consult their doctor because of poor expectations of what doctors can offer.<sup>14,15</sup>

## 1.2 REMIT OF THE GUIDELINE

This guideline provides recommendations based on evidence for best practice in the diagnosis and management of headache in adults. The International Classification of Headache Disorders lists over 200 headache types and a comprehensive review of all headaches is beyond the scope of these guidelines.<sup>16</sup> This guideline focuses on the more common primary headaches such as migraine and tension-type headache, and addresses some of the rarer primary headaches which have recognisable features with specific treatments. Secondary headache due to medication overuse is addressed, as the overuse of headache medication can compromise the management of primary headache. "Red flags" for secondary headache are highlighted. A guide to the main investigations used in headache is provided.

Disorders that primarily cause facial pain, such as trigeminal neuralgia, are outwith the remit of this guideline, as is treatment of meningitis.

This guideline will be of interest to healthcare professionals in primary and secondary care, including general practitioners, community pharmacists, opticians and dental practitioners, and patients with headache.

### 1.3 DEFINITIONS

The guideline uses the definitions given in the International Headache Society International Classification of Headache Disorders, 2<sup>nd</sup> edition (see *Annex 2*).<sup>16</sup>

### 1.4 STATEMENT OF INTENT

This guideline is not intended to be construed or to serve as a standard of care. Standards of care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge and technology advance and patterns of care evolve. Adherence to guideline recommendations will not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care aimed at the same results. The ultimate judgement must be made by the appropriate healthcare professional(s) responsible for clinical decisions regarding a particular clinical procedure or treatment plan. This judgement should only be arrived at following discussion of the options with the patient, covering the diagnostic and treatment choices available. It is advised, however, that significant departures from the national guideline or any local guidelines derived from it should be fully documented in the patient's case notes at the time the relevant decision is taken.

#### 1.4.1 ADDITIONAL ADVICE TO NHSSCOTLAND FROM NHS QUALITY IMPROVEMENT SCOTLAND AND THE SCOTTISH MEDICINES CONSORTIUM

NHS QIS processes multiple technology appraisals (MTAs) for NHSScotland that have been produced by the National Institute for Health and Clinical Excellence (NICE) in England and Wales.

The Scottish Medicines Consortium (SMC) provides advice to NHS Boards and their Area Drug and Therapeutics Committees about the status of all newly licensed medicines and any major new indications for established products.

SMC advice and NHS QIS validated NICE MTAs relevant to this guideline are summarised in section 16.3.

#### 1.4.2 DRUG LICENSING STATUS

The majority of headache treatments commonly used do not have a specific licence for this indication in the UK. In this guideline, recommendations which include the use of licensed drugs outwith the terms of their licence reflect the evidence base reviewed. More details on licensing status are given in Annex 6.

## 2 Key recommendations

The following recommendations were highlighted by the guideline development group as being clinically very important. They are the key clinical recommendations that should be prioritised for implementation. The clinical importance of these recommendations is not dependent on the strength of the supporting evidence.

### 2.1 SYMPTOMS AND SIGNS

**C** Patients who present with a pattern of recurrent episodes of severe disabling headache associated with nausea and sensitivity to light, and who have a normal neurological examination, should be considered to have migraine.

Migraine has specific treatment options. It is often underdiagnosed with up to 50% of patients misdiagnosed with another headache type.<sup>17-20</sup> Better recognition allows more effective treatment.

**D** Patients who present with headache and red flag features for potential secondary headache should be referred to a specialist appropriate to their symptoms for further assessment.

Most patients have primary headache and do not require further investigation.<sup>12,20</sup> Red flag warning features highlight which patients require further investigation for potential secondary headache.

**D** Patients with a first presentation of thunderclap headache should be referred immediately to hospital for same day specialist assessment.

Thunderclap headache is a medical emergency as it may be caused by subarachnoid haemorrhage.

**D** Giant cell arteritis should be considered in any patient over the age of 50 presenting with a new headache or change in headache.

Giant cell arteritis is a medical emergency because of the possibility of neurological and visual complications and availability of effective treatment.

### 2.2 ASSESSMENT TOOLS

**D** Practitioners should consider using headache diaries and appropriate assessment questionnaires to support the diagnosis and management of headache.

The use of diaries and questionnaires can aid diagnosis and prompt discussion of symptoms and the impact of the headaches on quality of life. This can help guide treatment and ensure appropriate follow up.

### 2.3 INVESTIGATIONS

**D Neuroimaging is not indicated in patients with a clear history of migraine, without red flag features for potential secondary headache, and a normal neurological examination.**

Magnetic resonance imaging (MRI) and computerised tomography (CT) can identify neurological abnormalities incidental to the patient's presenting complaint, which may result in heightened patient anxiety and clinician uncertainty.<sup>21,22</sup> Further investigation and treatment of incidental abnormalities can cause both morbidity and mortality and investigation should generally be reserved for patients with "red flag features".

**D In patients with thunderclap headache, unenhanced CT of the brain should be performed as soon as possible and preferably within 12 hours of onset.**

**C Patients with thunderclap headache and a normal CT should have a lumbar puncture.**

Subarachnoid blood degrades rapidly. Performing CT brain imaging as soon as possible maximises the chance of accurate diagnosis. Even timely CT brain imaging may not pick up subarachnoid blood, so lumbar puncture is also required. Lumbar puncture should be delayed till 12 hours after headache onset.

### 2.4 MIGRAINE

**A Oral triptans are recommended for acute treatment in patients with all severities of migraine if previous attacks have not been controlled using simple analgesics.**

Migraine is associated with significant disability and is often under-treated. A stepped approach for acute treatment of migraine is recommended, starting with aspirin or an NSAID. If this is not effective a triptan should be used.

**D Opioid analgesics should not be routinely used for the treatment of patients with acute migraine due to the potential for development of medication overuse headache.**

Opioids and opioid-containing analgesics are associated with medication overuse headache and their use can result in dependence. They have no role in the treatment of migraine.

**B Women with migraine with aura should not use a combined oral contraceptive pill.**

Migraine with aura and the combined oral contraceptive pill are both independent risk factors for ischaemic stroke. Although the absolute increased risk of stroke is small, this increased risk is unacceptable when equally effective alternative methods of contraception are available.

### 2.5 TRIGEMINAL AUTONOMIC CEPHALALGIAS

**A Subcutaneous injection of 6 mg sumatriptan is recommended as the first choice treatment for the relief of acute attacks of cluster headache.**

Individual attacks of cluster headache are very severe and build up rapidly. The onset of action of oral triptans is too long and subcutaneous or nasal triptans are required.

## 2.6 MEDICATION OVERUSE HEADACHE

**D** Medication overuse headache must be excluded in all patients with chronic daily headache (*headache  $\geq 15$  days / month for  $> 3$  months*).

**D** Clinicians should be aware that patients using any acute or symptomatic headache treatment are at risk of medication overuse headache. Patients with migraine, frequent headache and those using opioid-containing medications or overusing triptans are at most risk.

Medication overuse results in the development of chronic daily headache. Stopping the overused medication usually results in improvement in headache frequency and severity. The risks of medication overuse headache should be discussed with all patients when initiating acute treatment for migraine.

## 3 Symptoms and signs

### 3.1 INTRODUCTION

Most patients with headache who present in primary care have primary headache.<sup>20</sup> Patients may have more than one type of primary headache (eg migraine without aura and tension-type headache) and each headache type should be dealt with separately.<sup>16</sup> Presentation with secondary headache is rare. In primary headache, findings on neurological examination are usually normal and investigations are not helpful for diagnosis.<sup>12,23</sup>

2+

4

The individual patient's history is of prime importance in the evaluation of headache.<sup>11,23</sup> The aim of the history is to classify the headache type(s) and screen for secondary headache using "red flag" features (see section 3.3). An inadequate history is the probable cause of most misdiagnosis of the headache type.<sup>11</sup> The British Association for the Study of Headache has produced a list of questions to help with taking a patient's headache history (see Annex 4). Diaries and tools to aid diagnosis are discussed in section 4.

4

The evidence base regarding signs and symptoms is limited to observational studies and the recommendations are based mainly on case series and expert opinion.

### 3.2 PRIMARY HEADACHE

#### 3.2.1 MIGRAINE

Migraine is the most common severe primary headache disorder.<sup>6,10</sup> The global lifetime prevalence is 10% in men and 22% in women.<sup>10</sup>

A migraine headache is characteristically:

- unilateral
- pulsating
- builds up over minutes to hours
- moderate to severe in intensity
- associated with nausea and/or vomiting and/or sensitivity to light and/or sensitivity to sound
- disabling
- aggravated by routine physical activity.<sup>16</sup>

4

Migraine is classified by the presence or absence of aura.<sup>16</sup> A typical aura comprises fully reversible visual and/or sensory and/or dysphasic speech symptoms. Symptoms may be positive (eg flickering lights, spots, zig zag lines, tingling) and negative (eg visual loss, numbness). Symptoms characteristically evolve over  $\geq 5$  minutes and resolve within 60 minutes.<sup>16</sup> Different aura symptoms may occur in succession. A transient ischaemic attack should be considered if the aura has a very rapid onset, there is simultaneous rather than sequential occurrence of different aura symptoms, the aura is purely negative or is very short.<sup>24,25</sup> Prolonged aura should raise the possibility of a secondary cause (see section 3.3).<sup>24,25</sup> Aura may occur without headache.

4

3

Recurrent attacks lasting four to 72 hours, occur as infrequently as one per year or as often as daily. The median frequency is one to two per month.<sup>26</sup> Chronic migraine is classified as migraine occurring on 15 or more days per month for more than three months.<sup>16,27</sup> In chronic migraine the headache may have features more typical of tension-type headache (see Annex 2).

4

Fifty per cent of patients with migraine are misdiagnosed with another headache type.<sup>17-20</sup> Often the wrong diagnosis of episodic tension-type headache is given. When prospective diaries were reviewed for headaches diagnosed as episodic tension-type headache, in the Landmark study, 82% of the physician diagnoses were changed to migraine or probable migraine.<sup>20</sup>

2+

As many as 75% of patients with migraine describe neck pain associated with migraine attacks. Patients may present with more than one headache type. Any single International Classification of Headache Disorders (ICHD-II) criterion will be missing in up to 40% of patients; 40% of patients report bilateral pain, 50% describe the pain as non-pulsating, and vomiting occurs in less than 33%.<sup>24</sup>

4

Given the difficulty in differentiating between migraine without aura and infrequent episodic tension-type headache the ICHD-II criteria require five attacks before a diagnosis of migraine without aura can be made. Two attacks are required for the diagnosis of migraine with aura.<sup>16</sup> In patients with more than one type of headache the International Headache Society (IHS) suggests a hierarchical diagnostic strategy with the diagnosis based on the most severe headache.

4

Cohort studies and case studies have highlighted the features of a history that help to differentiate migraine from other headache. Not all have to be present to make the diagnosis:

- episodic severe headache that causes disability<sup>13,28,29</sup>
- nausea<sup>23,28</sup>
- sensitivity to light during headache<sup>23,28</sup>
- sensitivity to light between attacks<sup>30</sup>
- sensitivity to noise<sup>23</sup>
- typical aura (in 15–33% of patients with migraine)<sup>23,24</sup>
- exacerbation by physical activity<sup>23</sup>
- positive family history of migraine.<sup>23,31</sup>

2+

4

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When combined with assessment of functional impairment, the features which give the greatest sensitivity and specificity for the diagnosis of migraine are nausea and sensitivity to light.<sup>28</sup>

3

**C Patients who present with a pattern of recurrent episodes of severe disabling headache associated with nausea and sensitivity to light, and who have a normal neurological examination, should be considered to have migraine.**

### 3.2.2 TENSION-TYPE HEADACHE

Tension-type headache (TTH) is the most common primary headache disorder.<sup>10</sup> It has a global lifetime prevalence of 42% in men and 49% in women. The pain is generally not as severe as in migraine.<sup>10</sup>

The pain is typically bilateral, characteristically pressing or tightening in quality and mild to moderate in intensity. Nausea is not present and the headache is not aggravated by physical activity. There may be associated pericranial tenderness, sensitivity to light or sensitivity to noise. Episodic tension-type headache (ETTH) occurs in episodes of variable duration and frequency. Chronic tension-type headache (CTTH) occurs on more than 15 days per month for more than three months.<sup>16</sup>

4

Disabling ETTH is rare. Most patients with ETTH do not consult a primary care clinician.<sup>19,20</sup> Migraine is often mistaken for ETTH in the initial diagnosis (see section 3.2.1).<sup>20</sup>

2+

**C A diagnosis of tension-type headache should be considered in a patient presenting with bilateral headache that is non-disabling where there is a normal neurological examination.**

### 3.2.3 TRIGEMINAL AUTONOMIC CEPHALALGIAS

Trigeminal autonomic cephalalgias (TACs) are rare and are characterised by attacks of severe unilateral pain in a trigeminal distribution.<sup>16,32</sup> They are associated with prominent ipsilateral cranial autonomic features. Cluster headache (CH) is the most common TAC (estimated prevalence 1 in 1,000). Paroxysmal hemicrania (PH) is probably under-recognised (estimated prevalence 1 in 50,000).<sup>32</sup> Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) and short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms (SUNA) are very rare.

4

3

Cluster headache attacks cause severe, strictly unilateral pain. The pain is located in one or a combination of orbital, supraorbital, or temporal regions. The ICHD-II classification requires ipsilateral autonomic features to occur with an attack (see Annex 2). Each attack starts and ceases abruptly, lasting 15 minutes to three hours and the patient is restless during an attack. The frequency of attacks varies from one every other day to eight per day. There may be a continuous background headache between attacks and migrainous features may be present (see section 3.2.1). There is often a striking circadian rhythm; attacks often occur at the same time each day and clusters occur at the same time each year.<sup>32</sup> Eighty to 90% of patients have episodic cluster headache where attacks “cluster” into periods lasting weeks to months, separated by periods of headache freedom. The remaining 10-20% have chronic cluster headache (no remission within one year or remissions last less than one month).<sup>16</sup>

4

Paroxysmal hemicrania has similar characteristics to cluster headache, but attacks are shorter (2-45 minutes), more frequent (up to 40 per day) and it is more common in women. The majority of patients have the chronic rather than episodic form. Most attacks are spontaneous but 10% can be precipitated mechanically by bending or rotating the head. Diagnosis using ICHD-II criteria consists of the presence of a complete response to indometacin and ipsilateral autonomic features during an attack (see Annex 2).<sup>16,32</sup>

4

SUNCT has similar characteristics to cluster headache and paroxysmal hemicrania. Attacks are shorter (2-250 seconds) and more frequent (up to 30 per hour). They occur as single stabs, groups of stabs or in an overlapping fashion (“sawtooth”). Bouts may last one to three hours at a time. Conjunctival injection and/or tearing are a requirement for the diagnosis. Attacks may be spontaneous or triggered by trigeminal (eg touching face) or extra-trigeminal (eg exercise) manoeuvres. Relapses and remissions are erratic.<sup>16,32,33</sup> SUNA is a proposed classification for patients with the headache characteristics of SUNCT, but with other cranial autonomic features.

3  
4

Secondary mimics are common and need to be excluded before a diagnosis of cluster headache, PH, SUNCT or SUNA can be made. For example, symptomatic cluster headache has been described after infections and with vascular and neoplastic lesions. In the case of PH a good response to indometacin does not exclude a secondary cause.<sup>32</sup>

3  
4

Features differentiating TACs from migraine are listed in Table 1. Features which differentiate trigeminal autonomic cephalalgias from each other and from trigeminal neuralgia, are listed in Annex 3.

Table 1: Features distinguishing TACs from migraine. <sup>23,32,33</sup>

	Headache type			
	SUNCT	PH	CH	Migraine
Duration	2-250 secs	2-45 mins	15 mins–3 hrs	4-72 hrs
Onset	rapid	rapid	rapid	gradual
Frequency	1/day-30/hr	1-40/day	1 every other day-8 /day	< 1/year-1/day (median 1-2/ month)
Restlessness during an attack	50%	50%	100%	0%
Ipsilateral autonomic features	prominent	prominent	prominent	occasional

3  
4

**D** When a patient presents with frequent, brief, unilateral headaches with autonomic features a trigeminal autonomic cephalgia should be considered.

**D** Patients with a new suspected trigeminal autonomic cephalgia should be referred for specialist assessment.

## 3.2.4 HEMICRANIA CONTINUA

Hemicrania continua is a continuous strictly unilateral headache that waxes and wanes in intensity without disappearing completely.<sup>16,32</sup> Brief stabbing pain may be superimposed on the continuous headache and may be accompanied by ipsilateral autonomic features. While it is rare, it is an important diagnosis to consider as there is an absolute response to indometacin.<sup>32</sup>

4

Secondary mimics are common and need to be excluded before a diagnosis of primary hemicrania continua can be made. A good response to indometacin does not exclude a secondary cause.<sup>32</sup>

4

**D** When a patient presents with chronic daily headache which is strictly unilateral, hemicrania continua should be considered.

**D** Patients with a new suspected hemicrania continua should be referred for specialist assessment.

## 3.2.5 NEW DAILY PERSISTENT HEADACHE

Headache that is daily and unremitting from onset is classified as new daily persistent headache.<sup>16</sup> It is essential to consider secondary headache and allow three months to elapse before a diagnosis of primary new daily persistent headache can be made. New daily persistent headache can have any phenotype. Secondary headaches to consider are subarachnoid haemorrhage (SAH), meningitis, raised intracranial pressure, low cerebrospinal fluid (CSF) pressure, giant cell arteritis and post-traumatic headache.<sup>34</sup>

4

In patients with new daily persistent headache, referral for specialist assessment should be considered.

## 3.3 SECONDARY HEADACHE

Secondary headache (ie headache caused by another condition) should be considered in patients presenting with new onset headache or headache that differs from their usual headache. Observational studies have highlighted the following warning signs or red flags for potential secondary headache which requires further investigation:

**Red flag features:**

- new onset or change in headache in patients who are aged over 50<sup>12,35-37</sup>
- thunderclap: rapid time to peak headache intensity (seconds to 5 mins)<sup>35,36,38-41</sup>
- focal neurological symptoms (eg limb weakness, aura <5 min or >1 hr)<sup>24,25,37,39,42,43</sup>
- non-focal neurological symptoms (eg cognitive disturbance)<sup>38,42</sup>
- change in headache frequency, characteristics or associated symptoms<sup>12,24,37,38</sup>
- abnormal neurological examination<sup>12,36,38,43</sup>
- headache that changes with posture<sup>44,45</sup>
- headache wakening the patient up (NB migraine is the most frequent cause of morning headache)<sup>12,45</sup>
- headache precipitated by physical exertion or valsalva manoeuvre (eg coughing, laughing, straining)<sup>12,45</sup>
- patients with risk factors for cerebral venous sinus thrombosis<sup>42,46,47</sup>
- jaw claudication or visual disturbance<sup>23,48</sup>
- neck stiffness<sup>35,49</sup>
- fever<sup>49</sup>
- new onset headache in a patient with a history of human immunodeficiency virus (HIV) infection<sup>38</sup>
- new onset headache in a patient with a history of cancer.<sup>11</sup>

4  
3

**D Patients who present with headache and red flag features of potential secondary headache should be referred to an appropriate specialist for further assessment.**

In patients with a stable pattern of headache, neurological examination is normal other than occasional ptosis during and persisting after an attack of cluster headache.<sup>12,23</sup> The presence of focal or non-focal symptoms and/or abnormal neurological signs significantly increases the chance of there being an abnormality.<sup>12,23,36,38</sup> An appropriate clinical examination, a neurological examination including fundoscopy, and blood pressure measurement are essential when patients first present.<sup>11</sup>

3

**D Patients presenting with headache for the first time or with headache that differs from their usual headache should have a clinical examination, a neurological examination including fundoscopy, and blood pressure measurement.**

- Neurological examination in patients first presenting with headache should include:
  - fundoscopy
  - cranial nerve assessment, especially pupils, visual fields, eye movements, facial power and sensation and bulbar function (soft palate, tongue movement)
  - assessment of tone, power, reflexes and coordination in all four limbs
  - plantar responses
  - assessment of gait, including heel-toe walking.

There should be more detailed assessment if prompted by the history. The examination should be tailored to include any focal neurological symptoms.

3.3.1 THUNDERCLAP HEADACHE

Thunderclap headache may be primary or secondary. It is defined by the ICHD-II as a high-intensity headache of rapid onset mimicking an SAH from a ruptured aneurysm with maximum intensity being reached in less than a minute.<sup>16</sup> In most patients thunderclap headache peaks instantaneously. In a small case series 19% of patients with SAH had headache that reached maximum severity more gradually (up to 5 minutes).<sup>41</sup> Sudden severe headache may also occur during sexual activity or exercise.<sup>16</sup>

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Other causes of sudden severe headache include: intracerebral haemorrhage, cerebral venous sinus thrombosis, arterial dissection and pituitary apoplexy.<sup>16</sup>

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There are no reliable features to differentiate between primary and secondary thunderclap headache and SAH can present with milder sudden onset headache.<sup>35</sup> A significant minority of thunderclap headache is secondary. In one case series 11% of patients with thunderclap headache had SAH.<sup>35</sup> When a patient presents for the first time with a sudden severe headache they should be referred immediately for consideration of a secondary cause, particularly SAH (this includes delayed presentation).<sup>35,36,38</sup>

3

If negative results are obtained from both brain computerised tomography and lumbar puncture with cerebrospinal fluid analysis (see section 5.2) within two weeks of onset of thunderclap headache, subarachnoid haemorrhage can be excluded from diagnosis.<sup>35,38,50</sup>

4

**D Patients with a first presentation of thunderclap headache should be referred immediately to hospital for same day specialist assessment.**

3.3.2 MEDICATION OVERUSE HEADACHE

Overuse of all acute headache treatments including simple and combination analgesics can cause medication overuse headache (see section 9).<sup>16</sup>

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## 3.3.3 CERVICOGENIC HEADACHE

The contribution of cervical spine disorders to migraine and tension-type headache is poorly understood. Fourteen to 18% of chronic headaches are cervicogenic in origin, ie result from a musculoskeletal dysfunction in the cervical spine.<sup>51</sup>

Cervicogenic headache consists of a unilateral or bilateral pain localised to the neck and occipital region which may project to regions on the head and/or face (see Annex 2).<sup>16</sup> Pain may be precipitated or aggravated by particular neck movements or sustained neck postures and is associated with altered neck posture, movement, muscle tone contour and/or muscle tenderness.<sup>11,52</sup> Manual examination identifying articular mobility, muscle extensibility and range of motion, in the form of flexion and extension may assist diagnosis.<sup>51</sup> A headache may also be cervicogenic in origin if there is clinical, laboratory and/or imaging evidence of a disorder or lesion within the cervical spine (ICHD-II).<sup>16</sup>

- D Neck examination should be carried out in all patients presenting with headache including assessment of:**
- neck posture
  - range of movement
  - muscle tone
  - muscle tenderness.

## 3.3.4 RAISED INTRACRANIAL PRESSURE

Headache associated with raised intracranial pressure is usually worse when the patient is lying down and may awaken them from sleep. It may also be precipitated by valsalva manoeuvres (eg coughing, laughing, straining), sexual intercourse, or physical exertion.<sup>12,38</sup> Visual obscurations, transient changes in vision with change in posture or valsalva, suggest raised CSF pressure.<sup>45</sup> Any of these symptoms should prompt referral for urgent specialist assessment.

Intracranial tumours rarely produce headache until quite large, particularly in neurologically 'silent' areas such as the frontal lobes.<sup>11</sup> Pituitary and posterior fossa tumours are the exception to this. Haemorrhage into a tumour may cause sudden severe headache, but it is more common for these patients to present with seizures or neurological symptoms (eg cognitive change) or signs (eg homonymous hemianopia, hemiparesis). Heightened suspicion is appropriate if there is a history of cancer elsewhere in the body.<sup>11</sup>

In an audit of 324 patients with an imaging diagnosis of an intracranial tumour, headache was the first symptom in 23% but at the time of presentation was the sole symptom in only 0.2%. All other patients had focal symptoms or signs. Seizure was the most common focal symptom (21%).<sup>53</sup> In a large primary care case controlled study of 3,505 patients with primary brain tumour and 17,173 matched controls the positive predictive value (PPV) of isolated headache as the only symptom was 0.09% (95% CI 0.08 to 0.10). The PPV of new onset seizure was 1.2% (95% CI 1.0 to 1.4).<sup>54</sup>

Idiopathic intracranial hypertension (incidence 1-3/100,000 all; 21/100,000 in women aged 15-45) presents with symptoms and signs consistent with raised intracranial pressure, typically normal neuroimaging (including computerised tomography or magnetic resonance venography to exclude cerebral venous sinus thrombosis) and a raised CSF pressure. The headache is initially episodic then usually progresses over weeks to daily headache with features typical of raised intracranial pressure.<sup>45</sup> Other symptoms and signs commonly present include: transient visual obscurations, pulsatile tinnitus, sixth nerve palsy, enlarged blind spots and papilloedema. It is most frequently seen in obese women of childbearing age. The aetiology is unclear in the majority of cases, but secondary causes to consider include cerebral venous sinus thrombosis, various medications (eg tetracyclines and retinoids) and CSF inflammation, infection or malignancy.

If a patient presents with headache and a combination of all or some of fever, neck stiffness, focal signs or seizures, then infection of the central nervous system (CNS) should be considered.<sup>35,49</sup> This may be diffuse (meningitis or encephalitis) or localised (brain abscess). Heightened suspicion is appropriate if there is a history of HIV or immunosuppression.<sup>38</sup>

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**D** Patients with headache and features suggestive of raised intracranial pressure should be referred urgently for specialist assessment.

**D** Patients with headache and features suggestive of CNS infection should be referred immediately for same day specialist assessment.

### 3.3.5 INTRACRANIAL HYPOTENSION (SPONTANEOUS OR IATROGENIC)

In patients with reduced CSF pressure there is a clear postural component to the headache. The headache develops or worsens soon after assuming an upright posture and lessens or resolves shortly after lying down.<sup>44</sup>

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Once the headache becomes chronic it often loses its postural component. Low pressure headache is caused by CSF leakage. The commonest cause is a diagnostic lumbar puncture but spontaneous dural leakage can occur and is often not recognised.

**D** Intracranial hypotension should be considered in all patients with headache developing or worsening after assuming an upright posture.

### 3.3.6 GIANT CELL (TEMPORAL) ARTERITIS

Giant cell arteritis (GCA) should be considered in any patient over the age of 50 presenting with headache. Headache is usually diffuse rather than localised to the temple. It is generally persistent and may be severe. The patient may be systemically unwell. Scalp tenderness is common but has a low predictive value of a positive temporal artery biopsy. Jaw claudication is the most reliable predictor, but is not always present. Any patient with jaw claudication and headache should be considered to have GCA until proven otherwise. Visual disturbance is the next most reliable predictor. Prominent, beaded, or enlarged temporal arteries are the most predictive physical sign. A normal erythrocyte sedimentation rate (ESR) makes the diagnosis unlikely, but does not exclude it.<sup>48</sup>

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**D** Giant cell arteritis should be considered in any patient over the age of 50 presenting with a new headache or change in headache.

Patients with symptoms suggestive of giant cell arteritis should be referred urgently for specialist assessment.

### 3.3.7 ANGLE CLOSURE GLAUCOMA

Angle closure glaucoma is rare before middle age. Family history, female sex and hypermetropia are recognised risk factors. Presentation is variable. The patient may have a mid-dilated pupil and red eye with impaired vision, indicating acutely raised intraocular pressure. Alternatively angle closure glaucoma may present as non-specific headache, eye pain, halos around lights or headache mimicking migraine with aura.<sup>37,55</sup> Intermittent angle closure glaucoma may precede acute angle closure and the eye may not be red.<sup>37</sup> The diagnosis should be considered in a patient with headache associated with a red eye, halos or unilateral visual symptoms.

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**D** Angle closure glaucoma should be considered in a patient with headache associated with a red eye, halos or unilateral visual symptoms.

Acute angle closure glaucoma is an ophthalmological emergency.

### 3.3.8 CARBON MONOXIDE POISONING

Symptoms of sub-acute carbon monoxide poisoning include headaches, nausea, vomiting, dizziness, muscular weakness and blurred vision.<sup>11</sup>

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## 4 Assessment tools

A number of tools have been developed to aid headache diagnosis, assess headache impact and related disability and measure response to treatment. Table 2 summarises a number of tools which are readily available via the internet. In clinical practice physicians usually ask questions about headache symptoms. Whilst considering symptoms is important, asking questions about impact can change a clinician's perception of how severe a patient's headache or migraine is.<sup>56</sup> This information influences treatment choice and the need for follow up.

Patients, primary care clinicians and headache specialists commonly get the diagnosis wrong.<sup>19,20</sup> This may be because of limited consultation time or poor patient recall. Clinician review and analysis of a prospective diary that records headache symptoms over a few weeks can improve diagnosis.<sup>11,19,20</sup>

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**D** Practitioners should consider using headache diaries and appropriate assessment questionnaires to support the diagnosis and management of headache.

A sample weekly headache diary is displayed in Annex 5.

Table 2 Tools for headache diagnosis and assessment of impact.

Tool	Applications/Benefits	Format	Basis	Limitations
<p>Headache Impact Test (HIT /HIT 6)</p> <p>www.headachetest.com/</p>	<ul style="list-style-type: none"> <li>▪ assess headache impact</li> <li>▪ determine diagnostic label</li> <li>▪ monitor treatment response <sup>57,58</sup></li> </ul> <p>Patients with a high HIT-6 score are more likely to be correctly diagnosed and treated for migraine by their GP.</p> <p>Typical scores are chronic headache 57-63 migraine 54-59 TTH 34-45. <sup>19,59-61</sup></p>	<p>Internet or paper based questionnaire</p> <p>5/6 questions</p> <p>Computerised adaptive testing. <sup>62,63</sup></p>	<p>Retrospective tool based on patient's experience of headache over the previous 4 weeks. It assesses:</p> <ul style="list-style-type: none"> <li>▪ pain</li> <li>▪ social role limitations</li> <li>▪ cognitive functioning</li> <li>▪ psychological distress</li> <li>▪ vitality</li> </ul>	<p>Limited sensitivity for measuring severity of pain<sup>61</sup></p>
<p>Migraine Disability Assessment (MIDAS)</p> <p>www.midas-migraine.net/edu/question/Default.asp</p>	<ul style="list-style-type: none"> <li>▪ assess headache impact</li> <li>▪ monitor treatment response</li> </ul> <p>Scores correlate with diagnosis based on physicians' estimates of pain and disability based on patients' medical histories.<sup>64</sup></p> <p>High internal consistency, test-retest reliability, accuracy and ease of use.<sup>26, 65-67</sup></p>	<p>5 item paper based questionnaire</p>	<p>Retrospective tool based on time lost in 3 activity domains over previous 3 months.<sup>66</sup></p> <ul style="list-style-type: none"> <li>▪ work or school</li> <li>▪ household, work and family</li> <li>▪ social or leisure activities</li> </ul>	<p>Gives all patients with frequent headache a high score. One headache may count multiple times because of the scoring domains.<sup>65, 68-70</sup></p> <p>Domains exclude emotional impact.</p>
<p>ID Migraine</p> <p>www.migraineclinic.org.uk/</p>	<ul style="list-style-type: none"> <li>▪ determine diagnostic label<sup>28</sup></li> </ul> <p>Sensitivity for migraine of 0.81 (95% CI, 0.77 to 0.85), specificity of 0.75 (95% CI 0.64 to 0.84) and a positive predictive value of 0.93 (95% CI 0.90 to 0.96).</p>	<p>3 item paper based screening questionnaire</p>	<p>Retrospective based on experience of:</p> <ul style="list-style-type: none"> <li>▪ gastric symptoms</li> <li>▪ light sensitivity</li> <li>▪ functional impairment</li> </ul>	<p>False positive rate of 19%.</p>

## 5 Investigations

### 5.1 NEUROIMAGING

#### ***When is neuroimaging required?***

Investigation should be avoided in principle if it does not lead to a change in management or it is unlikely to reveal a relevant abnormality. Occasionally, neuroimaging may be required on an individual basis if a patient is disabled by fear of serious pathology.<sup>71</sup>

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The vast majority of primary headaches do not require neuroimaging. In a prospective study where patients with headache for more than four weeks underwent neuroimaging (CT, MRI or both), significant intracranial abnormalities were found in 0.4% of patients with migraine, 0.8% of patients with tension-type headache, and in 5% (one out of 20 patients) of those with cluster headache. In a subgroup of 188 patients without clearly defined headache type, significant intracranial abnormality was found in 3.7%.<sup>72</sup>

2+

A meta-analysis of neuroimaging studies estimated a 0.2% prevalence of significant intracranial abnormalities in patients with migraine and a normal neurological examination.<sup>12</sup> In a retrospective review of 402 patients with chronic headache without neurological symptoms or signs, relevant abnormalities on MRI were found in 0.6% of patients with migraine, 1.4% of patients with tension-type headache and 14.1% of patients with “atypical headache”.<sup>73</sup> In another retrospective review MRI revealed relevant intracranial abnormalities in 0.7% of patients with chronic or recurrent headache and a normal neurological examination.<sup>74</sup>

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Neuroimaging in patients with headache and an abnormal neurological examination is significantly more likely to reveal an underlying cause.<sup>12,39,40</sup> Further investigation is required to exclude secondary aetiology when headache is accompanied by red flags (see section 3.3).

4

#### ***Incidental abnormalities***

Both MRI and CT can identify neurological abnormalities incidental to the patient’s presenting complaint and which may result in heightened patient anxiety and clinician uncertainty.<sup>21,22</sup> Cranial MRI in 2,536 healthy young males revealed incidental abnormalities in 6.55%.<sup>22</sup> A prospective cohort study of 2,000 volunteers (mean age, 63.3 years; age range 45-96 years) who received brain MRI revealed incidental abnormalities in 13.5%.<sup>21</sup>

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#### ***Patient reassurance***

A randomised controlled trial of 150 patients with chronic daily headache in a specialist clinic found that patients who received MRI had a decrease in anxiety levels at three months, but that the reduction in anxiety was not maintained at one year. Patients with high scores on the hospital anxiety and depression scale who did not receive a scan had significantly higher health service costs overall due to a greater use of healthcare resources such as psychiatric and psychology services than comparable patients who received a scan.<sup>75</sup>

1+

#### ***CT versus MRI***

In ruling out secondary causes of headache MRI is more sensitive than CT in identifying white matter lesions and developmental venous anomalies.<sup>12</sup> The European Federation of Neurological Societies guidelines suggest that MRI is the imaging modality of choice because of this greater sensitivity.<sup>76</sup> The US headache consortium concluded that MRI may be more sensitive than CT in identifying clinically insignificant abnormalities, but not more sensitive in identifying clinically significant pathology relevant to the cause of the headache.<sup>71</sup>

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- D** Neuroimaging is not indicated in patients with a clear history of migraine, without red flag features for potential secondary headache, and a normal neurological examination.
- D** Clinicians requesting neuroimaging should be aware that both MRI and CT can identify incidental neurological abnormalities which may result in patient anxiety as well as practical and ethical dilemmas with regard to management.
- D** Brain CT should be performed in patients with headache who have unexplained abnormal neurological signs, unless the clinical history suggests MRI is indicated.

5.1.1 COMPUTERISED TOMOGRAPHY AND THUNDERCLAP HEADACHE

ICHD-II classification states that normal brain imaging and CSF are required before a diagnosis of primary thunderclap headache can be made.<sup>16</sup> 4

When SAH is suspected, CT brain scan should be carried out as soon as possible to maximise sensitivity. Sensitivity of CT for subarachnoid haemorrhage is 98% at 12 hours dropping to 93% by 24 hours.<sup>50</sup> 4

A normal CT brain scan is insufficient to rule out SAH and a lumbar puncture is required in patients with normal CT scans (see section 5.3).

If negative results are obtained from both brain CT and lumbar puncture with cerebrospinal fluid analysis within two weeks of onset of thunderclap headache, then SAH can be excluded from diagnosis.<sup>35,38,50</sup> 4

Sudden severe headaches precipitated by sexual activity can be diagnosed as primary if they cannot be attributed to another disorder.<sup>16</sup> On first onset of this headache it is essential to exclude SAH and arterial dissection.<sup>77</sup> 4

- D** In patients with thunderclap headache, unenhanced CT of the brain should be performed as soon as possible and preferably within 12 hours of onset.

5.1.2 MAGNETIC RESONANCE IMAGING

Expert opinion suggests that MRI should be considered in patients with cluster headache, paroxysmal hemicrania or SUNCT, in order to exclude the wide variety of secondary causes.<sup>32</sup> 4

In a review of 31 cases in which a TAC or TAC like syndrome was associated with a structural lesion and the treatment of the lesion resulted in significant clinical improvement, 11 out of 31 had a pituitary adenoma. Only 10 out of the 31 cases had atypical presenting features.<sup>78</sup> In a prospective study of 43 patients with SUNCT and nine patients with SUNA, cranial imaging was carried out in 36 with SUNCT and eight with SUNA. Twelve patients (11 with SUNCT, 1 with SUNA) of the 44 who received cranial imaging had significant intracranial abnormalities.<sup>33</sup> 3  
2+

- D** Brain MRI should be considered in patients with cluster headache, paroxysmal hemicrania or SUNCT.

In a retrospective study in patients with cough-induced headaches (n = 30), exertional headaches (n = 28) and sexual headaches (n = 14); 17 out of 30 patients with cough-induced headache had chiari type 1 malformation; 10 out of 28 patients with headache induced by exertion had SAH, 1 had sinusitis and 1 had brain metastases; and 1 out of 13 patients with explosive orgasmic headache had SAH.<sup>79</sup> 3

Primary cough headache (Valsalva manoeuvre headache) which is precipitated rather than aggravated by coughing, laughing or straining may be diagnosed only after structural lesions are excluded by neuroimaging.<sup>16</sup> Patients with cough headache should have an MRI brain scan to rule out posterior fossa lesion.<sup>77</sup> 4

- D** Brain MRI should be carried out in patients presenting with headache which is precipitated, rather than aggravated, by cough.

Benign exertional headache which is precipitated rather than aggravated by exertion can be diagnosed as primary if it is not associated with any other disorder (see Annex 2).<sup>16</sup> ICHD-II classification states that on first occurrence subarachnoid haemorrhage or arterial dissection need to be excluded.<sup>16</sup> Similar percentages of patients with benign thunderclap headache and confirmed SAH were provoked by exertion in two prospective case series so exertion alone does not predict SAH.<sup>35,41</sup> Expert opinion suggests that neuroimaging should be carried out to exclude a structural cause or vascular abnormality in patients with exertional headache. If headaches are prolonged beyond a few hours, are accompanied by focal neurological symptoms or vomiting, or appear de novo after the age of 40 the chance of finding a relevant abnormality is increased.<sup>77</sup>

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- Further investigation should be considered in patients with headaches which are precipitated, rather than aggravated, by exercise.

A small case control study of spinal MRI in patients with post lumbar puncture headache and spontaneous intracranial hypotension concluded that venous plexus volume at C2 was significantly higher in patients than in the controls. Spinal hygromas were present in 67% of patients with spontaneous intracranial hypotension and 73% of patients with post lumbar puncture headache, but were not present in controls.<sup>80</sup>

3

Several small case series show an association between spontaneous intracranial hypotension and diffuse pachymeningeal gadolinium enhancement on brain MRI.<sup>81-83</sup>

3

- All patients with suspected low pressure headache should be referred to a specialist for consideration of the most appropriate investigation.

## 5.2 LUMBAR PUNCTURE IN SUBARACHNOID HAEMORRHAGE

Lumbar puncture (LP) with CSF analysis is appropriate for patients with thunderclap headache and normal neuroimaging to exclude a diagnosis of subarachnoid haemorrhage.<sup>35,50,84,85</sup> One prospective study found that lumbar puncture was positive for subarachnoid haemorrhage in 21% of patients with thunderclap headache (5 out of 23 patients) who had a normal CT brain scan.<sup>35</sup>

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In a case series, lumbar puncture was performed in 40 out of 81 patients presenting with thunderclap headache and a normal CT brain scan. 15% of these had a lumbar puncture positive for SAH.<sup>85</sup>

3

Since xanthochromia (bilirubin and oxyhaemoglobin) can only be detected in CSF after 12 hours, lumbar puncture and CSF analysis should be delayed 12 hours from the onset of thunderclap headache.<sup>50,86,87</sup> In patients presenting late, LP can be informative up to two weeks from the onset of the thunderclap headache.<sup>50,86</sup>

3

Spectrophotometry is the recommended method of CSF analysis and should be performed on the final sample of CSF collected. Following lumbar puncture, the presence of CSF bilirubin is the key result suggestive of SAH, and is usually accompanied by oxyhaemoglobin.<sup>87</sup>

4

Opening pressure should be measured routinely in all lumbar punctures.<sup>87</sup>

4

**C** Patients with thunderclap headache and a normal CT should have a lumbar puncture.

**D** In patients who require a lumbar puncture for thunderclap headache, oxyhaemoglobin and bilirubin should be included in cerebrospinal fluid analysis.

Opening pressure should be measured when lumbar puncture is indicated in patients with headache.

In patients with suspected subarachnoid haemorrhage, neuroimaging should be performed prior to lumbar puncture.

Lumbar puncture in CT negative patients with suspected subarachnoid haemorrhage should be carried out as soon as possible after 12 hours has elapsed from the onset of symptoms.

In delayed presentations, lumbar puncture can be performed up to two weeks from onset of symptoms.

### 5.3 ERYTHROCYTE SEDIMENTATION RATE, C-REACTIVE PROTEIN AND PLASMA VISCOSITY IN GIANT CELL ARTERITIS

Increased erythrocyte sedimentation rate (ESR) may be useful in predicting the presence or absence of GCA in patients with suggestive symptoms. Mean ESR in patients with GCA was 88 mm/hr compared with a mean ESR of 10 mm/hr in patients without GCA. The difference was not statistically significant.<sup>48</sup> Four per cent of patients with positive temporal artery biopsy results had a normal value ESR.<sup>48</sup>

A retrospective case series of 363 patients who underwent temporal artery biopsy for suspected GCA found that both ESR and C-reactive protein (CRP) had a high sensitivity for detection of GCA. C-reactive protein had a higher sensitivity than ESR (100% vs 92%). Combining ESR and CRP gave the highest specificity (97%) than CRP alone (83% in men and 79% in women).<sup>88</sup> In patients with suspected GCA, the odds of a positive biopsy were 3.2 times greater with CRP above 24.5 mg/l ( $p=0.0208$ ); two times greater with an ESR between 47 and 107 mm/hr compared to an ESR less than 47 mm/hr ( $p=0.0454$ ); the odds of a positive biopsy was 2.7 times greater than 107 mm/hr relative to an ESR less than 47 mm/hr ( $p=0.0106$ ).<sup>88</sup>

**D** ESR and/or CRP (but preferably a combination of these diagnostic tests to maximise sensitivity and specificity) should be measured in patients with suspected giant cell arteritis.

Plasma viscosity is used in the diagnosis of GCA, but no studies on its effectiveness were identified.

### 5.4 OTHER INVESTIGATIONS

No evidence was identified on the benefits of routine full blood count assessment or the use of X-ray of the cervical spine in the diagnosis of patients with headache.

## 6 Migraine

### 6.1 ACUTE TREATMENT

The treatment of acute migraine attacks should be selected for each patient according to severity and frequency of attacks, other symptoms, patient preference and history of treatment. A stepped approach can be used, commencing with an analgesic and anti-emetic, if required, and escalating to 5HT1 receptor agonist (triptan) as required. A non-steroidal anti-inflammatory drug (oral/rectal or intramuscular) can be given following, or added to, a triptan for resistant attacks.<sup>11</sup>

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- Practitioners should recognise that a patient's standard therapy may not give a consistent response across all attacks. A strategy for managing resistant attacks should be planned with patients.
- When initiating acute treatment for migraine the risks of medication overuse headache should be discussed with the patient.

The proportion of patients who become pain free two hours post-dose has become the preferred and clinically most relevant primary end point. However, the ideal efficacy end point is sustained pain free: the proportion of patients who were pain free by two hours post-dose and who do not have a recurrence of moderate or severe headache and who do not use any rescue headache medication 2-24 hours post-dose.<sup>89</sup>

1+

#### 6.1.1 NON-STEROIDAL ANTI-INFLAMMATORY DRUGS (INCLUDING ASPIRIN) AND PARACETAMOL

Aspirin, ibuprofen and paracetamol are inexpensive and widely available over-the-counter therapies, making them a good option for first line treatment. Aspirin and ibuprofen should be avoided in patients with asthma or peptic ulceration.<sup>90</sup>

Three well conducted RCTs showed that 48-52% of patients with acute migraine experienced pain relief at two hours after taking aspirin 900-1,000 mg.<sup>91-93</sup> A combination of paracetamol 1,000 mg, aspirin 1,000 mg and caffeine 260 mg may be more effective (84% pain relief at two hours) than aspirin 500 mg or sumatriptan 50 mg alone for patients with mild to moderate migraine.<sup>94</sup>

1++  
1+

In an RCT ibuprofen 200-400 mg relieved pain in 41% of patients with migraine within two hours, although severe initial headache was only relieved by the 400 mg dose.<sup>95</sup> Ibuprofen 400 mg is as effective as aspirin 1,000 mg or sumatriptan 50 mg for pain relief at two hours.<sup>91</sup> Ketoprofen 75-150 mg also provided relief to 62% of patients with migraine at two hours.<sup>96</sup>

1++

The NSAID tolfenamic acid rapid tablets 200 mg is licensed specifically for the treatment of acute attacks of migraine. Diclofenac, flurbiprofen, ibuprofen and naproxen are also licensed for use in migraine. For patients with nausea and vomiting, diclofenac suppositories 100 mg can be used for pain.<sup>97</sup>

In a placebo-controlled RCT, paracetamol 1,000 mg relieved 57.8% of moderate (but not severe) attacks of migraine within two hours.<sup>98</sup>

1++

- A** Aspirin 900 mg is recommended for acute treatment in patients with all severities of migraine.
- A** Ibuprofen 400 mg is recommended for acute treatment in patients with migraine.
- Other NSAIDs (tolfenamic acid, diclofenac, naproxen and flurbiprofen) can be used in the treatment of acute migraine attacks.
- B** Paracetamol 1,000 mg is recommended as acute treatment for mild to moderate migraine.

6.1.2 TRIPTANS

Triptans provide significant pain relief to patients with acute migraine within two hours of administration and improve patients' quality of life.<sup>99-103</sup> | 1++  
1+

**Triptans vs pharmacy and over-the-counter medicines**

Sumatriptan 100 mg achieved significantly less headache relief compared with aspirin 900 mg and metoclopramide 10 mg in patients presenting after their first migraine attack.<sup>102</sup> Sumatriptan 50 mg also achieved significantly less headache relief at two hours compared with a combination of aspirin 1,000 mg, paracetamol 1,000 mg and caffeine 260 mg for patients with mild to moderate headache.<sup>94, 102</sup> It was statistically equipotent with aspirin (1,000 mg) and ibuprofen (400 mg) in reducing headache severity at two hours, but significantly better than aspirin for pain-free outcome at two hours (37.1% of patients pain free versus 27.1%).<sup>91</sup> | 1+  
1++

**Triptans vs ergots**

Eletriptan 40 mg and 80 mg had significantly better headache response rate and pain-free rate at two hours than cafergot<sup>®</sup>, a combination of ergotamine 1 mg and caffeine 100 mg.<sup>100</sup> | 1+

**Triptan vs triptan**

The following comparison of various triptans is based largely on three systematic reviews. In a large review and meta-analysis, the activities of all oral triptans (except frovatriptan) were compared with sumatriptan 100 mg.<sup>104</sup> Another systematic review compared efficacy and tolerability of triptans with placebo.<sup>105</sup> A systematic review of RCTs examined efficacy and tolerability of frovatriptan compared with placebo.<sup>106</sup> | 1++  
1+

Sumatriptan 50 mg is available from the community pharmacist without prescription to treat previously diagnosed migraine.

Table 3: Comparison of the main efficacy and tolerability measures for the oral triptans versus 100 mg sumatriptan.\*

	Initial 2h relief	Sustained pain free	Consistency	Tolerability
Sumatriptan 25 mg	-	=/-	-	+
Sumatriptan 50 mg	=	=	=/-	=
Zolmitriptan 2.5 mg	=	=	=	=
Zolmitriptan 5 mg	=	=	=	=
Naratriptan 2.5 mg	-	-	-	++
Rizatriptan 5 mg	=	=	=	=
Rizatriptan 10 mg	+	+	+(+)	=
Eletriptan 20 mg	-	-	-	=
Eletriptan 40 mg	=/+	=/+	=	=
Eletriptan 80 mg	+(+)	+	=	-
Almotriptan 12.5 mg	=	+	+	++

= indicates no difference when compared with sumatriptan 100 mg  
 + indicates better when compared with sumatriptan 100 mg  
 - indicates inferior when compared with sumatriptan 100 mg

\* Table cited from Ferrari MD, Roon KI, Lipton RB, Goadsby PJ. Oral triptans (serotonin 5-HT<sub>1B/1D</sub> agonists) in acute migraine treatment: a meta-analysis of 53 trials Lancet, 2001; 358(9294): 1674.

**Response at two hours**

Compared with 100 mg sumatriptan, 10 mg of rizatriptan and 80 mg of eletriptan showed higher initial two hour relief.<sup>104</sup> | 1++

**Sustained pain-free at two hours**

Compared with sumatriptan 100 mg, 80 mg eletriptan, 12.5 mg almotriptan, and 10 mg rizatriptan showed higher sustained pain-free rates at two hours post-dose.<sup>104</sup> | 1++

Rizatriptan 10 mg (number needed to treat (NNT)=3.1) showed higher pain-free rates at two hours than sumatriptan 50 mg (NNT=4.0), sumatriptan 100 mg (NNT=4.3) and naratriptan 2.5 mg (NNT=9.2).<sup>99</sup> | 1+

Frovatriptan 2.5 mg was more effective than placebo for pain-free rate at two hours (relative risk (RR) 3.70, 95% CI 2.59-5.29,  $p < 0.0001$ ) and at four hours post-dose (RR 2.67, 95% CI 2.21-3.22,  $p < 0.0001$ ).<sup>106</sup> | 1+

**Recurrence rates 2-24 hours**

Comparison of headache recurrence rates for different triptans is problematic. Less potent, slower acting triptans which only relieve milder headaches tend to show lower recurrence rates because mild headaches may be less likely to recur. Compared with sumatriptan 100 mg (30%, 95% CI 27-33), recurrence rates were lower for 40-80 mg eletriptan and higher for 5 and 10 mg rizatriptan.<sup>104</sup> The risk of headache recurrence within 24 hours was reduced by frovatriptan, (RR 0.74, 95% CI 0.59-0.93,  $p = 0.009$ ) but this apparent benefit needs to be assessed in the light of confounding by headache severity.<sup>106</sup> | 1++  
| 1+

**Sustained pain-free rates**

Compared with sumatriptan 100 mg (rate =20%, 95% CI 18-21), sustained pain-free rates were higher for 10 mg rizatriptan, 80 mg eletriptan and 12.5 mg almotriptan and lower for 20 mg eletriptan.<sup>104</sup> | 1++

**Consistency**

Triptans produced a response to headache at two hours in at least one of three treated attacks in 79-89% of patients, compared with around 50% in placebo, two of three treated attacks in 47-72% of patients, compared with 17-33% in placebo and three of three treated attacks in 16-47% of patients compared with up to 9% in placebo.<sup>104</sup> | 1++

Triptan use led to freedom from pain at two hours in 51-59% of patients, compared with 18% in placebo. Sustained pain-free response in two of three treated attacks was achieved in 14-42% of patients compared with 3-13% with placebo and three of three treated attacks in 1-17% of patients compared with <2% with placebo.<sup>104</sup> | 1++

Compared with placebo, the highest consistency rates were for 100 mg sumatriptan and 12.5 mg almotriptan.<sup>104</sup>

**Adverse event rates**

100 mg sumatriptan had a mean placebo subtracted rate of any adverse events of 13% (95% CI 8-18). Rates for other triptans overlap, except for lower values for 2.5 mg naratriptan and 12.5 mg almotriptan; these rates also do not differ from placebo.<sup>104</sup> | 1++

**Recommendations on triptan use**

Triptans are contraindicated in patients with ischaemic heart disease, previous myocardial infarction, coronary vasospasm or uncontrolled or severe hypertension. Triptans should be used with caution in hemiplegic migraine.<sup>90</sup>

**A** Oral triptans are recommended for acute treatment in patients with all severities of migraine if previous attacks have not been controlled using simple analgesics.

**A** Almotriptan 12.5 mg, eletriptan 40-80 mg or rizatriptan 10 mg, are the preferred oral triptans for acute migraine.

The response to individual triptans is idiosyncratic. Patients who do not respond to one triptan may have a good response to a different triptan.<sup>107</sup> | 1++

**B** If a patient does not respond to one triptan an alternative triptan should be offered.

Triptans should not be taken during the aura and should be taken at or soon after the onset of the headache phase of a migraine attack.<sup>11</sup> | 4

**D** Triptans should be taken at, or soon after, the onset of the headache phase of a migraine attack.

***Triptan nasal sprays/subcutaneous injections***

Sumatriptan nasal spray is not useful if vomiting precludes oral therapy as its bioavailability depends on ingestion. Zolmitriptan nasal spray may be useful if vomiting is already occurring as 30% is absorbed through the nasal mucosa. In patients with severe attacks of migraine which are resistant to oral or nasal triptans, subcutaneous injection of sumatriptan 6 mg remains an option.<sup>11</sup> This offers the fastest and highest level of pain relief, but carries an increased risk of adverse events which may limit its use for some patients. | 4

Nasal zolmitriptan or subcutaneous sumatriptan should be considered in severe migraine or where vomiting precludes oral route or where oral triptans have been ineffective.

***Triptan and NSAID combinations***

Two replicate double blind RCTs have compared the efficacy and safety of a fixed dose combination of 85 mg sumatriptan and 500 mg naproxen sodium with placebo and with monotherapy with sumatriptan succinate or naproxen sodium in the acute treatment of migraine.<sup>108</sup> The incidence of headache relief two hours after dosing (the reduction of pain from moderate/severe intensity to mild/no pain without use of rescue medication) were 65%, 55%, 44% and 28% with sumatriptan-naproxen sodium, sumatriptan monotherapy, naproxen sodium monotherapy and placebo, respectively in study 1 (p<0.001 for sumatriptan-naproxen sodium, sumatriptan and naproxen sodium versus placebo; p=0.009 for sumatriptan naproxen sodium versus sumatriptan). The corresponding percentages in study 2 were 57%, 50%, 43% and 29% (p=0.03 for sumatriptan-naproxen sodium versus sumatriptan). Sumatriptan-naproxen sodium was significantly more effective than monotherapy with sumatriptan or naproxen sodium for the incidence of 24 hour sustained pain-free response in both studies. In study 1, the incidence of sustained pain-free response was 25% with sumatriptan-naproxen sodium compared with 16% with sumatriptan monotherapy (p<0.01), 10% with naproxen sodium monotherapy (p<0.001) and 8% with placebo (p<0.001). The corresponding incidences in study 2 were 23% with sumatriptan-naproxen sodium compared with 14% with sumatriptan monotherapy (p<0.001), 10% with naproxen monotherapy (p<0.001) and 7% with placebo (p<0.001). | 1+

**C** A combination of sumatriptan 50-100 mg and naproxen sodium 500 mg may be helpful in acute migraine particularly in prolonged attacks which are associated with recurrence.

## 6.1.3 ANTI-EMETICS

Anti-emetics such as prochlorperazine 3-6 mg buccal tablets or domperidone 10 mg oral or 30 mg rectal, may be used for symptoms of nausea and vomiting associated with migraine. Anti-emetics such as metoclopramide 10 mg or domperidone 20 mg are also useful as a prokinetic to promote gastric emptying.<sup>11</sup>

4

**D Oral and rectal anti-emetics can be used in patients with acute migraine attacks to reduce symptoms of nausea and vomiting and to promote gastric emptying.**

A systematic review identified six double blind RCTs evaluating the combination of aspirin and metoclopramide for the treatment of acute migraine attacks.<sup>109</sup> The dose of metoclopramide (10 mg) was constant in all trials, but the dose of aspirin varied from 650–900 mg. Four compared the combination with placebo, two with oral sumatriptan (100 mg) one with oral dihydroergotamine mesilate (5 mg) and one with aspirin (650 mg) alone. The combination was significantly better than placebo for pain relief at two hours in all four RCTs. Sumatriptan was better in one RCT and equivalent in the other for pain relief at two hours. Improvement in nausea was not significantly different. The combination was significantly better than oral dihydroergotamine for pain relief at two hours. In the only RCT to compare the combination with aspirin alone, there was no difference in pain relief at two hours. The number of patients in this RCT was small.

1+

**B A combination of aspirin and metoclopramide can be used for the treatment of patients with acute migraine attacks.**

A double blind crossover RCT compared the fixed combination droperamol<sup>®</sup> (paracetamol 500 mg and domperidone 10 mg) with 50 mg sumatriptan. There was no significant difference in headache relief at two (36.4% vs 33.3%) and four (49.2% vs 41.9%) hours between the two treatments. Improvement in nausea was the same with both treatments. Fewer side effects were reported with droperamol<sup>®</sup>.<sup>110</sup> Headache improvement using the fixed combination paramax<sup>®</sup> (paracetamol 500 mg and metoclopramide 5 mg) was not significantly different to placebo.<sup>102</sup> Two double blind RCTs have compared the fixed combination migramax<sup>®</sup> (lysine acetylsalicylate 1620 mg and metoclopramide 10 mg) with placebo. In both headache relief was superior with migramax<sup>®</sup> compared to placebo (56% vs 28%, 57% vs 24%). The second study also compared migramax<sup>®</sup> with sumatriptan 100 mg. There was no significant difference. Fewer side effects were reported in the migramax<sup>®</sup> group.<sup>102</sup>

1+

**B Fixed analgesic/anti-emetic combinations can be used for the treatment of patients with acute migraine attacks.**

Intravenous anti-emetic can be used in a hospital setting for migraine which is not responsive to standard treatment.

A well conducted meta-analysis of RCTs of variable quality showed that intravenous metoclopramide is more effective than placebo in reducing headache pain from acute migraine (odds ratio (OR) 2.84, 95% CI 1.05 to 7.68).<sup>111</sup>

1++

Metoclopramide is not licensed for treatment of pain in migraine.

An RCT demonstrated that haloperidol IV 5 mg significantly relieves migraine headache in 80% of patients compared to 15% of patients treated with sodium chloride ( $p < 0.0001$ ). Haloperidol is associated with a high level of adverse events such as sedation and restlessness which limits its use in patients with migraine.<sup>112</sup>

1+

**B IV metoclopramide can be used in the acute management of patients with migraine.**

6.1.4 ERGOTAMINE

Ergotamine is superior in efficacy to placebo but is less effective in relieving acute migraine symptoms than triptans, NSAIDs, isometheptene or opioid comparators. It is not well tolerated.<sup>102</sup> A combination of ergotamine and caffeine (Cafergot<sup>®</sup>) also performed less well than eletriptan for better headache response and pain-free rates.<sup>100</sup>

1++

Ergotamine can cause side effects such as nausea, vomiting, abdominal pain and muscular cramps. It should not be used in patients who have cerebrovascular or cardiovascular disease.<sup>90</sup>

**A Ergotamine is not recommended for patients with acute migraine.**

6.1.5 CAFFEINE

Evidence on the use of caffeine as a treatment for headaches was limited to the inclusion of caffeine with combinations of other therapies (see sections 6.1.1 and 6.1.4).

6.1.6 OTHER THERAPIES

No evidence was identified for the efficacy of COX-2 inhibitors, corticosteroids, indometacin or opioids.

There is a risk of medication overuse with all acute treatments for migraine (see section 9.1). This risk is greatest for opioid-containing analgesics eg Migraleve<sup>®</sup>, Syndol<sup>®</sup> and Solpadeine<sup>®</sup>.<sup>113</sup>

2+

**D Opioid analgesics should not be routinely used for the treatment of patients with acute migraine due to the potential for development of medication overuse headache.**

6.2 PHARMACOLOGICAL PROPHYLAXIS

Preventive pharmacological treatment for migraine should be considered in patients with recurring migraines that significantly interfere with their daily routine, in the presence of contraindication to, failure of, or overuse of acute therapies and in uncommon forms of migraine (hemiplegic migraine, basilar artery migraine or migraine with prolonged aura). The goal of preventive therapy is to reduce the attack frequency, severity and duration, improve responsiveness to treatment of acute attacks and reduce migraine associated disability.

4

General principles for preventive treatment for migraine:

- most preventive drugs should be titrated slowly to an effective or maximum dose in order to minimise side effects<sup>11</sup>
- preventive medication should be given a trial of at least six to eight weeks following dose titration<sup>11</sup>
- the choice of preventive medication should be guided by their side effect profile and the patient's comorbid conditions
- after six to 12 months of effective prophylaxis, gradual withdrawal should be considered.<sup>114</sup>

4

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Alongside preventive migraine treatment patients should also have access to appropriate medications for treatment of acute attacks of migraine.

A suggested guide to the use of prophylaxis is outlined in Table 4.<sup>11,90</sup>

Table 4 Prophylactic therapies for patients with migraine

Preventive drug	Use with caution in patients with: (not an exhaustive list)	May be preferred in patients with:
Beta blockers	Asthma	Comorbid anxiety
	Diabetes	
	Bradycardia	
	Peripheral vascular disease	
	Comorbid depression	
Tricyclics	Angle closure glaucoma	Comorbid depression
		Comorbid tension-type headache
		Sleep disturbance
Topiramate	Renal stones	Comorbid obesity
	Angle closure glaucoma	
	Pregnancy	
Valproate	Obesity	Comorbid depression
	Liver disease	
	Pregnancy	

- When considering antiepileptic medication for prophylaxis of migraine in women of reproductive age, advice and counselling regarding the potential teratogenic side effects of these drugs should be given.

### 6.2.1 BETA BLOCKERS

Propranolol 80-240 mg per day is effective in reducing the frequency of migraine.<sup>115</sup> A Cochrane review found that the overall relative risk of response to treatment for propranolol was 1.94 (95% CI, 1.61 to 2.35) indicating that propranolol is approximately twice as effective as placebo in reducing headache frequency.<sup>116</sup> Data on headache intensity were reported inconsistently. The US Headache Consortium considers potential placebo response to be at least 20%.<sup>115</sup>

4  
1++

The US Headache Consortium found a high degree of certainty that propranolol provides moderate reduction in headache frequency, intensity and/or duration. Timolol, atenolol and nadolol are likely to be beneficial based upon comparison with placebo or propranolol. Direct comparison of metoprolol and propranolol suggests that metoprolol is as effective as propranolol in the prevention of migraine.<sup>115</sup>

4

Atenolol is not licensed for use in migraine.

When propranolol is prescribed to a patient using rizatriptan, the patient should be advised to halve the dose of rizatriptan and in addition not to take rizatriptan within two hours of taking propranolol.<sup>90</sup>

4

**A** Propranolol 80-240 mg per day is recommended as first line therapy for prophylaxis in patients with migraine.

**D** Timolol, atenolol, nadolol and metoprolol can be used as alternatives to propranolol as prophylaxis in patients with migraine.

6.2.2 ANTIEPILEPTICS

A Cochrane review has shown that, as a class, antiepileptics can reduce the frequency of migraine by 1.4 attacks per 28 days. Patients are 2.4 times more likely to experience a 50% or greater reduction in migraine frequency when using antiepileptics compared with placebo. The NNT to achieve a 50% or greater reduction in migraine frequency for each are:<sup>117</sup>

1++

- all antiepileptics: 3.9 (95% CI 3.4 to 4.7)
- topiramate: 3.9 (95% CI 3.4 to 5.1)
- sodium valproate: 3.1 (95% CI 1.9 to 8.9)
- gabapentin: 3.3 (95% CI 2.1 to 8.4).

Topiramate significantly reduces the number of acute migraine episodes from 5.26 to 2.60 per 28 days ( $p < 0.001$ )<sup>118</sup> as well as causing a greater mean reduction in migraine frequency than placebo (1.55 vs 0.47,  $p = 0.001$ ).<sup>119,120</sup> The mean monthly frequency decreased significantly for patients receiving 100 mg per day of topiramate (from 5.4 to 3.3,  $p < 0.001$ ) or 200 mg per day of topiramate (from 5.6 to 2.6,  $p < 0.001$ ) as compared to placebo. There was a trend towards higher adverse incidents in patients who received 200 mg per day of topiramate.<sup>121</sup>

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1+

Topiramate 100 mg per day is similar to propranolol 160 mg with respect to reductions in migraine frequency, responder rates and daily use of rescue medication.<sup>122</sup>

1+

In another study comparing topiramate therapy with placebo in patients with chronic migraine, treatment with topiramate resulted in a statistically significant mean reduction of days with migraine when compared with placebo (topiramate 6.4 versus placebo 4.1,  $p = 0.032$ ).<sup>123</sup>

1+

Three well conducted RCTs assessing the role of topiramate in migraine prevention were pooled. The data were analysed with regard to the number of headache days during the final four weeks of the treatment. The number of headache days per month in the topiramate versus placebo treated groups was  $7.3 \pm 3.0$  versus  $7.3 \pm 3.1$  during baseline and  $4.1 \pm 4.2$  versus  $5.6 \pm 4.9$  during the final four weeks ( $p < 0.001$ ). At the end of the study eight versus 16 patients fulfilled ICHD-II criteria for chronic headache ( $p = 0.082$ ). A significantly lower number of patients receiving topiramate reported an increase in headache days per month by the end of the study when compared with placebo (66 versus 88 patients, respectively,  $p < 0.05$ ).<sup>124</sup>

1+

Topiramate improves health related quality of life measures in patients with migraine taking part in RCTs when compared with placebo.<sup>125</sup>

1+

Topiramate is licensed for use in the preventive treatment of migraine but its initiation is restricted to those offering specialist care with treatment managed under specialist supervision or shared care arrangements.

In a small study with a short follow-up period there was no significant difference in beneficial effects between topiramate and valproate in terms of number of days with migraine or MIDAS scores, when given to patients with chronic migraine.<sup>126</sup>

1-

No significant difference in the number of patients reporting a 50% reduction in migraine frequency was observed when divalproex sodium (valproic acid) was compared with propranolol and when sodium valproate was compared with flunarizine (see section 6.2.4).<sup>117</sup>

1++

In a study comparing the effect of 400 mg of sodium valproate with 50 mg of topiramate in patients with episodic migraine, treatment with sodium valproate reduced the mean monthly frequency of attacks from 5.4 to 4.0 and the headache intensity from 7.7 to 5.8 ( $p < 0.001$ ).<sup>127</sup> In patients treated with topiramate the mean monthly headache frequency was reduced from 5.4 to 3.2 and headache intensity from 6.9 to 3.7 ( $p < 0.001$  in each case). There was no significant difference in these outcome measures between the two drugs.<sup>127</sup>

1+

Gabapentin is more effective than placebo for patients with episodic migraine, with a median four week migraine rate of 2.7 for patients treated with gabapentin compared to 3.5 for patients treated with placebo ( $p=0.006$ ).<sup>128</sup> The study had a high drop-out rate in the treatment group.

1<sup>+</sup>

**A** In patients with episodic migraine and chronic migraine topiramate 50-200 mg per day is recommended to reduce headache frequency and severity.

**A** In patients with episodic migraine sodium valproate 800-1,500 mg per day is recommended to reduce headache frequency and severity.

**C** Patients with episodic and chronic migraine can be treated with gabapentin 1,200 -2,400 mg per day to reduce headache frequency.

### 6.2.3 ANTIDEPRESSANTS

In a meta-analysis of 38 trials of antidepressants in patients with chronic headache only amitriptyline was studied in sufficient numbers of patients to demonstrate statistically significant effect. It reduced headache index (measure of headache burden calculated from frequency and severity) in both migraine and tension-type headache. The six studies of selective serotonin reuptake inhibitors (SSRIs) that measured effects on headache burden found no significant benefits.<sup>129</sup>

1<sup>+</sup>

A Cochrane review showed no significant difference between the use of SSRIs and placebo in the reduction of migraine frequency or severity.<sup>130</sup> Fluoxetine was the most commonly studied SSRI.

1<sup>++</sup>

There is consistent good evidence that amitriptyline is significantly better than placebo in reducing headache index and frequency and it is effective in the prophylaxis of migraine at a dose of 25-150 mg per day.<sup>115</sup>

4

An RCT found that venlafaxine 150 mg is superior to placebo and to venlafaxine 75 mg in the prophylaxis of patients with migraine without aura.<sup>131</sup> There was a significant reduction in the number of days patients on venlafaxine 150 mg had headaches, compared to placebo ( $p=0.006$ ). They consumed considerably fewer analgesics and there was greater patient satisfaction with venlafaxine 150 mg or 75 mg compared to placebo. When the global efficacy was considered 80% of patients in the venlafaxine 75 mg group and 88.2% of patients in the 150 mg group evaluated treatment benefits as either good or very good.<sup>132</sup>

1<sup>+</sup>

The prophylactic effect of venlafaxine has been compared to amitriptyline in patients with migraine. In this crossover RCT the pain parameters were significantly improved in both groups compared to the washout period ( $p<0.05$ ) but there was no significant difference between the groups ( $p>0.05$ ).<sup>132</sup>

1<sup>+</sup>

**B** SSRIs are not recommended in the prophylaxis of migraine.

**B** Amitriptyline 25-150 mg per day is recommended for patients requiring prophylaxis of migraine.

**B** Venlafaxine 75-150 mg per day is an effective alternative to tricyclic antidepressants for prophylaxis of migraine.

## 6.2.4 OTHER THERAPIES

**Pizotifen**

Pizotifen is a long established prophylactic agent and is commonly used in the UK. Most of the studies on pizotifen were conducted in the 1970s. Between 30 and 50% of patients have reported that using pizotifen reduces the number of attacks.<sup>133</sup>

Two multicentre studies, one a double blind placebo-controlled (study 1) and the other an open study (study 2) were conducted to assess if pizotifen prophylaxis (in doses of 1.5 mg per day) improved migraine. The median of the monthly attack rate was lower in patients receiving pizotifen and sumatriptan than in those receiving placebo and sumatriptan (study 1; 3.5 versus 3.9,  $p=0.008$ ), or sumatriptan alone (study 2; 2.9 versus 3.2,  $p=0.23$ ). They also conclude that pizotifen may be better reserved for those patients who have four or more attacks per month.<sup>133</sup>

1+

Pizotifen is of limited value in prophylaxis of migraine.

**Methysergide**

Methysergide was one of the first drugs to be used for the prevention of migraine but its use is limited by the potential for causing retroperitoneal and retropleural fibrosis with prolonged use.<sup>90</sup> In four placebo-controlled trials methysergide was significantly better than placebo at reducing migraine frequency.<sup>115</sup>

1+

Methysergide should only be used under specialist supervision.

**Flunarizine**

Flunarizine in doses of 5 mg and 10 mg a day has been compared to propranolol 160 mg for the prophylactic treatment of patients with migraine. Both flunarizine groups were at least as effective as propranolol in reducing attack frequency ( $p<0.001$ ). No significant differences between the three treatments were found with regard to safety.<sup>134</sup>

1+

**Botulinum toxin A**

The efficacy of botulinum toxin A for prophylaxis of episodic migraine was studied in a multicentre RCT. The primary efficacy end point was the mean reduction in the frequency of migraine days at day 180. All groups improved with no significant differences ( $p=0.817$ ). At day 180 the frequency of migraine episodes was reduced from baseline means by 1.6, 1.7, 1.5 and 1.4 for Botulinum toxin A 225U, 150U and 75U and placebo respectively.<sup>135</sup>

1+

**A** Botulinum toxin A is not recommended for the prophylactic treatment of migraine.

**Candesartan**

In one small study candesartan performed well against placebo with a relative reduction of 22% in the number of days patients experienced migraine.<sup>136</sup>

1+

**Aspirin**

One study showed that aspirin may be associated with a small prophylactic effect in migraine among middle aged women, but this was not statistically significant (self reported improvement in frequency at 36 months, 59.6% vs 56.4% for placebo, OR 1.13).<sup>137</sup>

1+

**Montelukast**

Montelukast given over three months to patients with migraine resulted in 15.4% patients reporting at least a 50% reduction in migraine attack frequency, as compared to 10.3% for placebo ( $p=0.304$ ).<sup>138</sup>

1+

**Acetazolamide**

Acetazolamide is poorly tolerated in patients with migraine and does not offer any beneficial prophylactic effect when compared to placebo.<sup>139</sup> | 1-

**Hyperbaric oxygen**

Hyperbaric oxygen has no role in the preventive treatment of migraine.<sup>140</sup> | 1-

**Lanepitant**

Lanepitant (a neurokinin NK1 antagonist) is no better than placebo for the preventive treatment of migraine. The number of patients with a 50% reduction in days with headache was 41% for lanepitant compared to 22% for placebo ( $p=0.065$ ).<sup>141</sup> Lanepitant is not licensed for use in the UK. | 1+

**Buspirone**

Patients with migraine and anxiety disorder treated with buspirone showed a 43.3% reduction in headache frequency compared to 10.3% with placebo ( $p=0.0025$ ). There was no association of the headache response with the anxiolytic effect.<sup>142</sup> | 1-

## 7 Tension-type headache

### 7.1 ACUTE TREATMENT

A large RCT (n = 638) showed that aspirin had a high response rate for relief of pain at two hours in patients with episodic tension-type headache (75% for 1,000 mg; p = 0.0009 and 70% for 500 mg p = 0.011). Paracetamol 1,000 mg had a similar rate (71% p = 0.007) and both performed well compared with response to placebo (54.5%).<sup>143</sup>

1++

No studies were identified on any other therapies for the acute treatment of patients with tension-type headache.

**A Aspirin and paracetamol are recommended for acute treatment in patients with tension-type headache.**

### 7.2 PHARMACOLOGICAL PROPHYLAXIS

#### 7.2.1 ANTIHYPERTENSIVES

High blood pressure does not usually cause headache, although blood pressure lowering treatments can reduce the prevalence of headache.<sup>144</sup>

2++

A meta-analysis indicated that angiotensin II receptor antagonists reduce the frequency of headache.<sup>145</sup> An RCT showed that lisinopril has a significant effect on the reduction of hours and days with headache and migraine.<sup>146</sup> Neither of these studies specified headache type or identified patients with hypertension within the trial.

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1+

#### 7.2.2 ANTIEPILEPTICS

One RCT was identified which showed a 9.1% difference in headache free rates benefiting patients with chronic daily headache who were treated with gabapentin versus those on placebo (p = 0.0005).<sup>147</sup>

1+

#### 7.2.3 ANTIDEPRESSANTS

A Cochrane review has shown no significant difference between treatment with placebo and fluoxetine for reduction in headache frequency and severity.<sup>130</sup>

2++

Tricyclic antidepressants are more effective in reducing chronic headache than SSRIs.<sup>129,130</sup> A significantly higher intake of analgesic medication was seen in patients treated with SSRIs than in patients treated with tricyclic antidepressants, equivalent to five or more doses per month (95% CI 1 to 9). Tricyclic antidepressants also reduced headache duration by 1.26 hours per day and headache index scores based on frequency and severity. Amitriptyline in doses of 25-75 mg was the most commonly studied tricyclic antidepressant.<sup>129</sup>

1+

**A Tricyclic antidepressants, particularly amitriptyline, 25-150 mg per day, are recommended as the agents of choice where prophylactic treatment is being considered in a patient with chronic tension-type headache.**

A small RCT (n = 24) of mirtazapine in patients with chronic tension-type headache showed a significant reduction in headache frequency (p = 0.005), duration (p = 0.03) and intensity (p = 0.03) compared to placebo.<sup>148</sup>

1-

Sertraline did not show a significant improvement on severity and frequency of chronic tension-type headache when compared to placebo.<sup>149</sup>

1+

A small RCT (n = 60) on the efficacy of venlafaxine extended release tablets (150 mg per day) in the prophylactic treatment of patients with tension-type headache showed that the median number of days with headache decreased from baseline in the venlafaxine group in two out of the three periods studied, but not in the placebo group (p = 0.05 and 0.033). The number needed to treat for responders (> 50% reduction in days with headache) was 3.48.<sup>150</sup>

1+

## 7.2.4 OTHER THERAPIES

A multicentre RCT assessing the efficacy of botulinum toxin A in the prophylactic treatment of chronic tension-type headaches showed no statistically significant difference between placebo and the four botulinum toxin A groups in the number of TTH free days per month.<sup>151</sup> A statistically significant difference favouring placebo versus botulinum toxin A 150U was observed (4.5 versus 2.8 tension headache free days per month,  $p = 0.007$ ).

1+

Botulinum toxin A has been shown to be effective for the treatment of patients with headache associated with neck dystonias.<sup>152</sup>

1+

**B Botulinum toxin A is not recommended for the preventive treatment of chronic tension-type headache.**

Tizanidine has been shown to be superior to placebo in reducing headache (as measured by combination of frequency, duration and intensity) in patients with a chronic daily headache (migraine and tension-type,  $p = 0.0025$ ).<sup>153</sup>

1+

## 8 Trigeminal autonomic cephalalgias

### 8.1 ACUTE TREATMENT OF CLUSTER HEADACHE

Few well conducted trials have been carried out on patients with cluster headache, possibly due to the spontaneous course of the condition.<sup>154</sup>

#### 8.1.1 TRIPTANS

Subcutaneous injection of 6 mg sumatriptan relieves pain in 73-96% of patients with acute cluster headache within 15 minutes.<sup>155-158</sup> Nasal administration of 20 mg sumatriptan acts more slowly, relieving pain in 57% of patients at 30 minutes.<sup>159</sup>

2-  
1++

Nasal zolmitriptan 5 mg and 10 mg provide acute attack relief at 30 minutes in 50% and 63% of cluster headache patients respectively.<sup>160</sup> Oral zolmitriptan 10 mg relieves acute attack pain in 47% patients with episodic cluster headache at 30 minutes.<sup>161</sup>

1++

**A** Subcutaneous injection of 6 mg sumatriptan is recommended as the first choice treatment for the relief of acute attacks of cluster headache.

**A** Nasal sumatriptan or zolmitriptan is recommended for treatment of acute attacks of cluster headache in patients who cannot tolerate subcutaneous sumatriptan.

#### 8.1.2 OXYGEN

In a small double blind crossover study conducted over 20 years ago, 19 men with cluster headache were treated with 100% oxygen versus air inhalation at 6 l/minute via a non-rebreathable mask over 15 minutes. The average relief score for all oxygen treated patients was  $1.93 \pm 0.22$  (out of a possible score of 3.0). For air the treatment relief score was  $0.77 \pm 0.23$ .<sup>162</sup> In a previous study it was reported that 75% of 52 randomly selected patients with cluster headaches, reported significant pain relief when treated with 100% oxygen at a rate of 7 l/min for 15 minutes.<sup>163</sup>

1+

A tight fitting, non-rebreathing mask should be used. Information on availability of suitable masks and loan of appropriate regulator equipment is available from [www.ouchuk.org/html/](http://www.ouchuk.org/html/)

100% oxygen (7-12 litres per minute) should be considered for the treatment of acute attacks in all patients with cluster headache.

Trials have been conducted on the use of hyperbaric oxygen but no consistent prophylactic effect has been demonstrated.<sup>140,164,165</sup>

1++  
1+  
1-

#### 8.1.3 LIDOCAINE

An RCT demonstrated that 10% nasal drops of lidocaine brought pain relief within 37 minutes in patients with acute cluster headache, compared to 59 minutes for those on a saline placebo ( $p < 0.001$ ).<sup>166</sup>

1+

For patients whose attacks of cluster headache are not well relieved by subcutaneous or nasal triptan and inhaled 100% oxygen, 10% intranasal lidocaine drops can be considered to help speed relief for acute attacks.

## 8.2 PHARMACOLOGICAL PROPHYLAXIS

### 8.2.1 CALCIUM CHANNEL BLOCKERS

Open label studies show that verapamil reduces the frequency and severity of cluster headaches.<sup>32</sup> | 4

In a small double blind study 86% of patients receiving verapamil (360 mg per day) showed an improvement of > 50% reduction in headache frequency while the placebo group showed no response.<sup>167</sup> | 1+

Higher doses of verapamil (up to 960 mg per day) have been used and are recommended for the preventive treatment of cluster headaches. Regular electrocardiogram monitoring is required.<sup>168</sup> | 4

**B Verapamil 240-960 mg is recommended for the prophylaxis of cluster headache.**

### 8.2.2 LITHIUM

A small double blind placebo-controlled trial using lithium (800 mg per day) in patients with cluster headache was stopped early because superiority over placebo could not be established.<sup>169</sup> Both lithium and verapamil have been shown to be superior to placebo in one small trial.<sup>32</sup> | 1-  
4

### 8.2.3 ERGOTS

Ergotamine has previously been used for the preventive treatment of cluster headaches but no trial evidence for this is available.<sup>32</sup> | 4

### 8.2.4 5-HT ANTAGONISTS

There are no contemporary placebo-controlled trials on the use of methysergide in cluster headaches. A small trial found pizotifen to be effective for cluster headaches but a further review has concluded that the effect is minimal.<sup>168</sup> | 4

### 8.2.5 MELATONIN

In a small double blind study (20 patients with cluster headache) melatonin significantly reduced headache frequency compared with placebo ( $p < 0.03$ ).<sup>170</sup> | 1-

### 8.2.6 ANTIEPILEPTICS

A double blind placebo-controlled trial of valproate for treatment of cluster headaches found no beneficial effect. The study had an unusually high placebo response rate.<sup>171</sup> | 1-

In open label studies topiramate and gabapentin have been found to be effective for patients with cluster headaches.<sup>32</sup> | 4

### 8.2.7 STEROIDS

A double blind placebo-controlled trial compared suboccipital injection of a mixture of long and rapid acting betamethasone with the injection of physiological saline in patients with episodic and chronic cluster headache. Eighty five per cent of patients injected with steroid became headache free in the first week after injection compared to none in the placebo group ( $p = 0.0001$ ). At four weeks eight of 11 responders remained attack free ( $p = 0.0026$ ).<sup>172</sup> | 1+

Expert opinion suggests that oral steroids can be used for the short term preventive treatment of cluster headaches although no contemporary trial evidence is available.<sup>168</sup> | 4

### 8.3 TREATMENT OF PAROXYSMAL HEMICRANIA, HEMICRANIA CONTINUA AND SUNCT

Responsiveness to indometacin is integral to the diagnosis of paroxysmal hemicrania and hemicrania continua. Indometacin is effective in doses of up to 225 mg per day.<sup>32</sup> | 4

Lamotrigine may be effective for the treatment of the SUNCT syndrome.<sup>32,168</sup> | 4

**D** Indomethacin up to 225mg is recommended for the prophylaxis of paroxysmal hemicrania and hemicrania continua.

## 9 Medication overuse headache

### 9.1 DEFINITIONS AND ASSESSMENT

Medication overuse headache (MOH) is defined as headache which is present for 15 days or more per month and which has developed or worsened while taking regular symptomatic medication (see Annex 2).<sup>16,27,173</sup> 4

Medication overuse headache is reported in migraine, tension-type headache, hemicrania continua, new daily persistent headache, cluster headache and SUNCT.<sup>33,174-177</sup> Patients with cluster headache and SUNCT who develop MOH usually have a personal or family history of migraine.<sup>33,176</sup> 3  
4

ICHD-II criteria suggest medication overuse headache should be considered with use on ten days per month for triptans, ergots, opioids or combination analgesics and on 15 days per month for simple analgesics.<sup>173</sup> 4

Patients with a history of migraine headache who frequently use pain medications for non-headache pain are at increased risk of developing chronic daily headache.<sup>174</sup> 3

Patients who overuse medications are more likely to develop chronic daily headache.<sup>113,178</sup> The risk depends on which medication is being overused (opioid OR 4.4; triptan OR 3.7; ergot OR 2.9; analgesics OR 2.7).<sup>113</sup> 3

In an audit of nine GP practices fewer than 16.2% of patients who were using triptans for headache met ICHD-II criteria for triptan overuse.<sup>179</sup> 3

Patients with frequent headache are at increased risk of developing chronic daily headache.<sup>113</sup> The more frequent the headache the greater the risk (5-9 headaches per month = OR 7.6; 10-15 headaches per month = OR 25.4). 3

Patients with chronic daily headache meeting the criteria for medication overuse headache evolving from episodic tension-type headache were found to be more likely to have a mood disorder than those with chronic tension-type headache without medication overuse. Patients with chronic daily headache meeting the criteria for medication overuse headache evolving from migraine were found to be more likely to have a mood disorder, depression, anxiety disorder or obsessive compulsive disorder than chronic tension-type headache without medication overuse.<sup>180</sup> 2+

In patients with chronic daily headache the DSM-IV criteria for dependence behaviour were significantly more common in those who met ICHD-II criteria for medication overuse headache.<sup>180</sup> 2+

**D** Medication overuse headache must be excluded in all patients with chronic daily headache (*headache  $\geq$  15 days / month for  $>$  3 months*).

**D** Clinicians should be aware that patients using any acute or symptomatic headache treatment are at risk of medication overuse headache. Patients with migraine, frequent headache and those using opioid-containing medications or overusing triptans are at most risk.

**C** When diagnosing medication overuse headache, psychiatric comorbidity and dependence behaviour should be considered.

**C** Patients with medication overuse headache who have psychiatric comorbidity or dependence behaviour should have these conditions treated independently. Referral to a psychiatrist or a clinical psychologist should be considered.

9.2 TREATMENT

Abrupt withdrawal of the precipitating agent is the treatment of choice in the majority of patients with medication overuse headache.<sup>177,181-185</sup> 3  
2+

In a case series of 98 patients who underwent withdrawal from medication all but three patients experienced an improvement in headache frequency at 14 days. 85% of patients taking triptan, 57% of patients taking ergot and 23% of patients taking analgesic achieved headache freedom at 14 days. Duration of withdrawal symptoms was shortest in the triptan group.<sup>181</sup> These findings were confirmed in a second study which also found that migraine was more likely to improve than tension-type headache.<sup>186</sup> 3

Follow up of patients with successful withdrawal showed a relapse rate of 45% at one and four years. Of those who relapsed 94% did so in the first year. Relapse rate varied with headache type (22% for migraine, 73% for TTH and 77% for mixed headache). Analgesics had the highest relapse rate (52%). Only 22% of ergot and 17% of triptan overusers relapsed.<sup>187</sup> A group looking at disability following medication withdrawal found a sustained improvement in MIDAS disability scores during three year follow up.<sup>188</sup> 3

Duration of withdrawal headache depends on the medication overused.<sup>181,186</sup> Duration is shorter and withdrawal more likely to be successful in patients taking triptans and ergots than in patients taking opioids, simple or combination analgesics. Withdrawal symptoms are also shorter for triptans. 3

Abrupt withdrawal from medication initially results in worsening of headache.<sup>181,184,186</sup> 2+

No studies were identified comparing abrupt versus gradual withdrawal. Expert opinion emphasises the need to withdraw opioids (and benzodiazepines and barbiturates) gradually.<sup>177,184</sup> 4

Structured advice about medication overuse, benefits of medication withdrawal and withdrawal symptoms is as good as inpatient and outpatient detoxification programmes, in patients not overusing opioids.<sup>183</sup> There is similar reduction in headache frequency with abrupt withdrawal with education alone when compared with patients also given prednisolone or naratriptan.<sup>182</sup> 2+

A number of intravenous inpatient treatments are used in specialist centres. There is limited information based on small case series of selected patients available for dihydroergotamine, sodium valproate and lidocaine.<sup>177</sup> No recommendation can be made on the basis of these, but referral to a specialist service should be considered if outpatient withdrawal is not successful. 4

Medication withdrawal should be attempted in all patients with medication overuse headache.

**C Patients with medication overuse headache caused by simple analgesics or triptans should be advised to abruptly withdraw the overused medication. In the majority of patients this can be as an outpatient with structured advice.**

**D Patients with medication overuse headache caused by opioids and opioid-containing analgesics should be considered for gradual withdrawal of the overused medications.**

A well conducted RCT in patients admitted to hospital for abrupt medication withdrawal, showed that there was no difference in the frequency or severity of withdrawal headache in patients given prednisolone (60 mg), followed by a six day taper compared with placebo. Symptomatic medication use, to alleviate withdrawal symptoms, was the same in both groups (no analgesics were allowed).<sup>189</sup> It has been argued that this dose of prednisolone was not sufficient.<sup>190</sup> A smaller RCT showed that a larger dose of prednisolone (100 mg for five days) significantly reduced withdrawal headache compared with placebo. There was also a trend to less use of symptomatic medication, but this was not significant.<sup>190</sup> A quasi-randomised cohort study in patients abruptly withdrawing symptomatic medication as outpatients, showed that patients given prednisolone or naratriptan had fewer withdrawal symptoms, used fewer symptomatic medications and used symptomatic medications for a shorter time than patients given structured advice alone.<sup>182</sup> No significant difference was found between prednisolone and naratriptan. 1+

Three small RCTs (two well conducted) have shown that topiramate is useful in medication overuse headache.<sup>118,191,192</sup> Topiramate reduced the mean number of monthly migraine days by  $3.5 \pm 7.1$  despite ongoing medication overuse.<sup>191</sup> A similar response to topiramate was seen in a second study in which patients were instructed to significantly restrict medication use during the study period. Those treated with topiramate showed a significantly lower 28 day headache frequency when compared to placebo (8.1 vs 20.6,  $p < 0.0007$ ).<sup>192</sup>

1+  
1-

Topiramate is not licensed in the UK for use in medication overuse headache.

Amitriptyline and sodium valproate reduce headache during abrupt withdrawal in patients with medication overuse headache, in small randomised controlled and uncontrolled trials.<sup>118,184,193</sup> Naproxen has been shown to ameliorate withdrawal symptoms in ergotamine-induced headache.<sup>184</sup>

1-  
2-  
3

A prospective cohort study in patients who had no response to various prophylactic treatments when overusing symptomatic medications found that the efficacy of prophylactic treatment returned after successful medication withdrawal.<sup>185</sup>

3

**D** If frequent headache persists after symptomatic medications have been withdrawn, prophylactic agents may be effective and should be considered.

**C** In patients with medication overuse headache, topiramate may be considered in order to reduce the total number of headache days.

## 10 Pregnancy, contraception, menstruation and the menopause

### 10.1 PREGNANCY

Where possible, the use of medication in pregnancy should be avoided, particularly in the first trimester. Paracetamol, however, has been used routinely during all stages of pregnancy for relief of headache and overall there seems to be no clear evidence of harmful effects on the fetus.<sup>194-197</sup> If drug treatment is considered essential then paracetamol, at the recommended therapeutic doses, is the analgesic of choice for the short term relief of mild to moderate pain during pregnancy.<sup>195,197</sup> As with any medication used during pregnancy, paracetamol should be taken at the lowest effective dose for the shortest time necessary.

4

If short term analgesia with an NSAID is required in the first or second trimester, ibuprofen or aspirin can be used.<sup>195</sup> Aspirin is contraindicated during the third trimester of pregnancy.<sup>90</sup> Whilst limited, the available evidence does not indicate that exposure to ibuprofen before 20 weeks of pregnancy is associated with an increased risk of birth defects or spontaneous abortions. Long term exposure or exposure to high doses in late pregnancy is associated with an increased risk of fetal complications.<sup>195</sup>

4

Three systematic reviews found no robust evidence of an increased risk of fetal abnormalities in babies born to mothers who took sumatriptan during pregnancy.<sup>198-200</sup> There is a non-significant trend to an increased risk of pre-term births (before 37 weeks) and miscarriages following the use of sumatriptan during pregnancy.<sup>198,199</sup> There is insufficient evidence to advocate the use of triptans during pregnancy.

2+  
2-

Some anti-emetics can be used with caution in pregnancy. There is no evidence for teratogenicity for buclizine and cyclizine.<sup>90</sup> Prochlorperazine is safe in the first two trimesters.<sup>90</sup>

4

- Paracetamol 1,000 mg is the treatment of choice in pregnancy for all patients with migraine and tension-type headache when the pain is sufficient to require analgesia.
- If paracetamol provides insufficient analgesia aspirin 300 mg or ibuprofen 400 mg can be used in the first and second trimester of pregnancy.

### 10.2 ORAL CONTRACEPTION

Migraine and the use of the combined oral contraceptive pill (COCP) are both independent risk factors for stroke. It is important to discuss stroke risk with women with migraine who require oral contraception.

The risk of stroke in women aged 25 to 44 is very low. The annual incidence of all types of cerebral infarction has been estimated as four per 100,000 in women aged 25-34 and 11 per 100,000 in women aged 35-44.<sup>201</sup> The annual incidence of ischaemic stroke in women aged 25-44 has been estimated as 4.4 per 100,000.<sup>202</sup>

4  
2++

A WHO collaborative showed that for women with migraine the overall odds ratio for all stroke was 1.78 (95% CI 1.14 to 2.77), 3.54 (95% CI 1.30 to 9.61) for ischaemic stroke and 1.10 (95% CI 0.63 to 1.94) for haemorrhagic stroke. The odds ratio for stroke in women with migraine with aura was 3.81 (95% CI 1.26 to 11.5) and for migraine without aura 2.97 (95% CI 0.66 to 13.5).<sup>203</sup> Evidence from other meta-analyses and systematic reviews also suggests a significant increased risk of ischaemic stroke among women with migraine, with a relative risk of between 1.85 (95% CI 1.44 to 2.36) to 2.16 (95% CI 1.89-2.48).<sup>204,205</sup>

2++

The increased risk of ischaemic stroke with a COCP is related to dose. Studies show an odds ratio varying between 2.08 (95% CI 1.55-2.80) to 2.74 (95% CI 2.24-3.35).<sup>206</sup> | 2++

Women with migraine with aura using a COCP have a relative risk of 8.72 (95% CI 5.05 -15.05) for developing stroke.<sup>204</sup> | 2++

**B Women with migraine with aura should not use a combined oral contraceptive pill.**

The WHO advises that women over the age of 35 suffering from migraine without aura also have an increased risk of ischaemic stroke if they take COCP.<sup>206,207</sup> | 4

**D Patients with migraine without aura who are over the age of 35 should not use a combined oral contraceptive pill.**

No evidence was identified on the safety or the efficacy of reducing the frequency and severity of menstrual migraine in patients using progesterone or long-acting implantable contraceptives.

### 10.3 MENSTRUATION

More than 50% of women with migraine report an increased frequency and severity of migraine attacks around the time of menstruation. Evidence suggests that this is related to the withdrawal of oestrogen in the late luteal phase of the menstrual cycle.<sup>208-213</sup> Standard acute migraine drugs work for the majority of women. Fewer than 10% of women report migraine "exclusively" with menstruation and at no other time of the month. | 2+  
1+  
2-

#### 10.3.1 SIMPLE ANALGESICS

A meta-analysis of three RCTs looking at the use of a fixed formulation of aspirin, paracetamol and caffeine in the acute treatment of patients with menstrual migraine attacks showed that the treatment relieved 61% of headaches at two hours, compared with 29% of patients given placebo ( $p=0.05$ ).<sup>214</sup> | 1++

A single RCT showed that mefenamic acid gave 79% of patients effective relief at two hours, compared to 16% with placebo ( $p<0.03$ ).<sup>215</sup> | 1++

**A Patients with acute menstrual migraine can be treated with mefenamic acid or a combination of aspirin, paracetamol and caffeine.**

#### 10.3.2 TRIPTANS

Zolmitriptan, sumatriptan, naratriptan and rizatriptan have been shown to be effective in relieving symptoms in patients with acute attacks of menstrual migraine.<sup>216-219</sup> | 1++  
2-

**A Sumatriptan, zolmitriptan, naratriptan and rizatriptan are recommended for the acute treatment of patients with menstrual migraine.**

#### 10.3.3 PROPHYLAXIS FOR MENSTRUAL MIGRAINE

Specific menstrual migraine prophylaxis should only be considered in women with regular and predictable menstrual cycles.

**Hormone manipulation**

A systematic review of four small case studies, three for the prevention of menstrually related migraine and one for the prevention of pure menstrual migraine, concluded that perimenstrual supplementation with oestradiol can reduce the risk of menstrual migraine (RR 0.78, 95% CI 0.62 to 0.99) but can cause a rebound increase in migraine after the treatment phase.<sup>211,220</sup> The risk of rebound headache was 68% for oestradiol 1.5 mg gel and five per cent for oestradiol 1.5 mg patches. Due to significant clinical heterogeneity, meta-analyses of these trials was not possible. The studies alone are too small to make a recommendation on using oestradiol for the prevention of menstrual migraine. | 4

There is insufficient evidence to make any recommendations on the use of phyto-oestrogens.

**Triptans**

Frovatriptan 2.5 mg per day or naratriptan 1 mg twice per day significantly reduces the risk of menstrual migraine if taken for two days before the onset of menses and then for a further four days, or five days respectively.<sup>221,222</sup> 1++

Two studies of naratriptan showed that the number of days with menstrually associated migraine in women given treatment versus placebo were five days versus 6.5 days (p=0.005) and 5.3 days versus six days (p=0.018). Eleven per cent of patients experienced no migraine versus three per cent on placebo (p<0.05). In both studies patients experienced rebound headache after stopping the naratriptan.<sup>275</sup> 1++

**A Frovatriptan 2.5 mg/day or naratriptan 1 mg twice daily taken two days before day one of the menstrual cycle then for a further four or five days respectively is recommended for the prophylaxis of menstrual migraine.**

**NSAIDs**

No evidence was identified on the possible prophylactic effect of NSAIDs for treating patients with menstrual migraine, although this is a widely used strategy. There is limited evidence that mefenamic acid and naproxen can be effective for headache associated with dysmenorrhoea.<sup>213</sup>

**10.4 MENOPAUSE**

The perimenopause is the time of peak prevalence of migraine without aura in women.<sup>211, 223-226</sup> This is thought to be due to oestrogen fluctuations associated with disrupted menstrual cycles. Migraine declines after spontaneous menopause in women who are vulnerable to hormone change such as those with premenstrual syndrome.<sup>226,227</sup> Women who had a surgical menopause had a higher prevalence of migraine.<sup>226</sup>

The perimenopause often results in climacteric symptoms (eg vasomotor symptoms such as night sweats, hot flushes, and insomnia, as well as memory loss/forgetfulness and mood swings) that might get better with hormone replacement therapy (HRT).<sup>223</sup>

HRT has been shown to increase the risk of stroke in all women. The women’s health initiative RCT showed a hazard ratio of 1.41 for HRT and stroke (95% CI 1.07-1.85).<sup>228</sup> 2++

No studies have assessed the relationship between migraine, HRT and stroke. An editorial review concluded that there is no compelling evidence that HRT increases or decreases the risk of ischaemic stroke in women with migraine.<sup>229</sup> Migraine is not a risk factor for stroke in women older than 45 and is not a contraindication for HRT.<sup>230-232</sup> 4  
2-  
4

HRT can make migraine worse. Current users of HRT had an odds ratio for migraine without aura of 1.42 (95% CI 1.41-1.76).<sup>225, 233</sup> One small study has shown that the transdermal route for oestrogen administration is less likely than the oral route to make migraine worse.<sup>233</sup> This is supported by expert opinion.<sup>232</sup> 3  
2-  
4

**D HRT can be prescribed to menopausal and perimenopausal women with migraine.**

**D If a patient taking HRT experiences worsening migraine, HRT should be considered as a possible cause.**

If the patient is using oral HRT and experiences worsening migraine, transdermal HRT should be considered.

# 11 Lifestyle factors

The studies reviewed for this section involve combinations of interventions, making assessment of their individual contribution to headaches difficult.

## 11.1 DIET

Although many patients report that various foods trigger their migraine, an editorial review found no good quality published evidence to support this.<sup>234</sup> No evidence was identified to support the prophylactic effect of general avoidance of cheese or chocolate, or for any other dietary manipulation in patients with migraine.<sup>11,235,236</sup> | 1-  
4  
3

Dietary supplementation with omega-3 fatty acids does not reduce the incidence of migraine.<sup>237</sup> | 1+

Expert opinion suggests that omission or altered timing of meals may be associated with migraine in some patients, eg missing breakfast may trigger a late morning attack, and so patients should be encouraged to eat regularly.<sup>11</sup> | 4

Patients with migraine should be encouraged not to miss meals.

## 11.2 TRIGGER AVOIDANCE

Limited and low quality evidence was identified in relation to possible trigger factors for headache.

A survey of patients with headache suggested that a reduction in caffeine intake and addressing sleep problems may reduce disability associated with headache.<sup>238</sup> | 3

No good quality evidence was identified on whether mobile phone signals relate to headache symptoms.

## 11.3 EXERCISE

The evidence on exercise was mainly limited to exercise included in combined therapies programmes.

For patients with cervicogenic headache, low load cervical exercise and manipulation were effective in reducing frequency and intensity of headache, but there was no additional statistically significant benefit when therapies were combined.<sup>239</sup> This effect may relate to patients' belief in the therapy or therapist.<sup>240</sup> | 1+

For patients with migraine, multidisciplinary intervention including group supervised exercise therapy sessions (along with stress management and relaxation therapy lectures, dietary advice and massage therapy) provided improvements in frequency, intensity and duration of headache and quality of life.<sup>241</sup> | 1+

## 11.4 SLEEP

No good quality evidence was found relating to sleep and headache. There may be an association between obstructive sleep apnoea and chronic headache, although studies did not include headache as a primary symptom.<sup>242,243</sup> Changes in sleep pattern, eg sleeping longer at weekends or sleep disturbance due to stress, may be associated with migraine, although there may be confounding factors related to the altered sleep.<sup>11,235,236</sup> | 2-  
4

**11.5 STRESS MANAGEMENT**

In a prospective analysis of the factors related to headache in migraineurs, tension and stress were associated with increased risk of migraine, whereas holidays, relaxation after stress and after divorce decreased the hazard.<sup>236</sup> 3

Multidisciplinary intervention, including stress management was effective in patients with migraine.<sup>241</sup> Results from a survey of patients with migraine suggest that reduction in stress can relieve headache symptoms.<sup>244</sup> 1+  
3

**B Stress management should be considered as part of a combined therapies programme to help patients reduce the frequency and severity of migraine headaches.**

For patients with chronic TTH, stress management was more effective when combined with antidepressant medication, although stress management alone was still more effective than placebo. This study had a high drop-out rate.<sup>245</sup> 1-

## 12 Psychological therapies

Various methodological problems have been encountered with the research identified in this area. These include:<sup>246,247</sup>

- difficulties in blinding trials in this area of research
- lack of standardisation and description of patient groups, interventions and their delivery and outcome measures
- use of inappropriate self selected patient groups
- ethical issues around pharmacological versus psychological interventions.

For patients with migraine, a single RCT suggests multidisciplinary intervention, including exercise, stress management, relaxation, diet and massage are effective in reducing pain frequency duration and intensity and improving quality of life, but it is unclear which specific intervention has the greatest benefit.<sup>241</sup> Stress management is discussed in section 11.5.

1+

No good quality contemporary evidence was identified for cognitive behavioural therapy or any specific relaxation therapy or biofeedback technique. The US Headache Consortium guidelines for migraine headache included evidence from 1966-1996 and recommended that relaxation training, thermal biofeedback combined with relaxation training, electromyographic biofeedback and cognitive behavioural therapy may be considered as treatment options for prevention of migraine.<sup>248</sup>

4

No good quality evidence was identified for hypnotherapy.

## 13 Physical therapies

It is not possible to conduct blinded trials of physical therapies. Studies are subject to attention and placebo effects which may introduce bias. A number of studies examine the effects of combinations of treatments making the effectiveness of the individual therapies difficult to ascertain. The role of exercise is discussed in section 11.3.

### 13.1 MANUAL THERAPY

Manual therapy covers a number of interventions including spinal manipulation therapy (SMT) and spinal mobilisation.

#### *Cervicogenic headache*

In a Cochrane systematic review five studies of spinal manipulation therapy for cervicogenic headache were described. SMT was compared with placebo, mobilisation, NSAIDs, exercise and massage plus placebo laser.<sup>249</sup> Although the studies were too dissimilar for results to be pooled, there was moderate evidence that SMT is superior to no treatment in reducing headache pain and frequency one week and 12 months following six weeks of treatment and superior to placebo SMT for pain, disability and number of headache sites three weeks after treatment. A comparison with massage plus placebo laser found SMT produced a significantly greater decrease in pain intensity (effect size 0.6; 95% CI 0.1-1.1).

1++

**B** Spinal manipulation therapy should be considered in patients with cervicogenic headache.

#### *Migraine*

A Cochrane systematic review identified three studies of effectiveness of spinal manipulation in migraine compared with amitriptyline, spinal mobilisation and placebo electrotherapy.<sup>249</sup> The studies were too dissimilar for results to be pooled and the evidence of effectiveness is too limited to lead to recommendation.

1++

#### *Tension-type headache*

Two studies of SMT in patients with chronic tension-type headache were included in a Cochrane systematic review.<sup>249</sup> In one study SMT was inferior to amitriptyline for effect on pain intensity during six weeks of treatment, although this was reversed at four weeks post-treatment. The second study examined the immediate effects of a single treatment and found more pain reduction in the SMT group than in a no-treatment control group.

1++

A systematic review of a range of manual therapies for pain reduction in tension-type headache found no rigorous positive effect of manual therapies.<sup>250</sup>

1+

A small single blind RCT (n = 26) found that three osteopathic treatments, one each week for three weeks, plus relaxation exercises, increased the number of headache free days per week in patients with TTH compared with relaxation exercises alone (0.21 days to 1.79 days, p = 0.016).<sup>251</sup>

1+

An RCT in a mixed group of patients with episodic and chronic TTH compared a craniocervical training programme combined with physiotherapy with physiotherapy alone. There was a positive and clinically relevant effect on headache frequency at six months following a six week programme. 85% of patients in the treatment group (n = 39) experienced a reduction of ≥ 50% in their headache frequency at six months compared to 35% in the control group.<sup>252</sup>

1+

## 13.2 MASSAGE

For patients with episodic TTH the benefit of massage as part of soft tissue manipulation is inconclusive.<sup>250</sup> | 1++

As part of a multidisciplinary intervention for patients with migraine massage appears effective with statistically significant reductions in frequency, intensity and duration of pain, and improved quality of life compared to controls which is maintained three months post-intervention.<sup>241</sup> The separate effect of massage is not clear. | 1+

There is insufficient evidence to make a recommendation on the use of massage in the treatment of patients with headache.

## 13.3 TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION

A Cochrane review identified two trials where transcutaneous electrical nerve stimulation (TENS) was used as part of a combined physical therapies intervention.<sup>249</sup> In a single RCT in patients with transformed migraine (MOH), TENS resulted in a statistically significant reduction in number of headache days per month, 21 days at baseline versus 11 days one month after TENS, ( $p < 0.05$ ) but this benefit was not evident at four months.<sup>253</sup> | 1++  
| 1+

There is insufficient evidence to make a recommendation on the use of TENS in the treatment of patients with headache.

## 13.4 ACUPUNCTURE

Interpretation of the evidence base for acupuncture is complicated by the lack of standardisation of interventions, the choice of control and comparison groups and the range of outcome measures employed. In addition to difficulties in blinding and concealment, trials very often have high drop-out rates (> 10%). A review examining the methodology of 13 studies noted that the majority of studies of acupuncture in patients with migraine are of poor quality, with conflicting results.<sup>254</sup> | 1+

A Cochrane systematic review of 26 studies found that the majority of trials had methodological and/or reporting shortcomings and suggested there was no conclusive evidence for the use of acupuncture in patients with migraine or TTH, although trends were towards benefit.<sup>255</sup> | 1++

In a large ( $n = 401$ ), well conducted RCT in patients with chronic headache disorder, predominantly migraine, headache scores at 12 months were significantly reduced in patients having acupuncture compared to usual care.<sup>256</sup> | 1+

A number of RCTs in patients with a range of chronic headache types found that sham acupuncture (eg needling superficially at points distant from the segments of true treatment points) was as effective as real acupuncture. This may be mediated through generation of non-specific physiological effects.<sup>257-260</sup> | 1+  
| 1-

**B** Acupuncture should be considered for preventive management in patients with migraine.

### 13.5 ORAL REHABILITATION

No good quality evidence was found to determine whether the use of acrylic splints is effective for patients with migraine.

Temporomandibular disorders (TMD) include symptoms such as joint clicking, facial pain and limitation of mandibular movement. Headache is included as one of the diagnostic criteria for TMD (but is not diagnostic alone). There is inconsistency in criteria between studies and headache type may not be defined.<sup>261,262</sup> A Cochrane review found no evidence from RCTs that occlusal adjustment treats or prevents headache in patients with temporomandibular disorders.<sup>262</sup>

1++

One study showed that occlusal splint therapy may be effective for headache as part of TMD but there are concerns about cases of aspiration of small splints and changes in tooth positions.<sup>263</sup>

1+

**B** Occlusal adjustment is not recommended for treatment of patients with headache associated with temporomandibular disorders.

## 14 Complementary therapies

### 14.1 HOMEOPATHY

A systematic review of four randomised placebo-controlled double blind trials concluded that homeopathy is not effective in the prophylaxis of migraine beyond a placebo effect.<sup>264</sup>

1<sup>+</sup>

### 14.2 REFLEXOLOGY

No evidence was identified for the effectiveness of reflexology in reducing the frequency and severity of headaches.

### 14.3 MINERALS, VITAMINS AND HERBS

A Cochrane review concluded that there is insufficient evidence that feverfew is efficacious beyond placebo for preventing migraine. In four trials of acceptable size two showed that the frequency of migraine reduced with feverfew while two trials did not.<sup>265</sup> A CO<sub>2</sub> extract of feverfew was shown to reduce the migraine frequency by 1.9 attacks per month as compared to 1.3 attacks in the placebo group ( $p=0.0456$ ).<sup>266</sup>

1<sup>++</sup>  
1<sup>-</sup>

#### **A** Feverfew is not recommended for preventive treatment of patients with migraine.

Petasites hybridus root (butterbur) in a dose of 75 mg per day has been shown to reduce migraine attack frequency by 48% over four months as compared to a 28% reduction with placebo ( $p=0.0012$ ).<sup>267</sup>

1<sup>-</sup>

In a small study coenzyme Q10 was shown to be superior to placebo for attack frequency, headache days, and days with nausea. The responder rate for attack frequency was 14.4% for placebo and 47.6% for CoQ10 (NNT = 3).<sup>268</sup>

1<sup>-</sup>

Niacin (oral or intravenous) may have beneficial effects for patients with migraine and tension-type headaches.<sup>269</sup>

4

Intravenous magnesium has an analgesic effect similar to IV metoclopramide and to placebo when administered for the treatment of patients with an acute migraine attack.<sup>270</sup> A double blind RCT found no significant difference between the group receiving placebo or magnesium. The patients receiving magnesium had significantly more ( $p=0.03$ ) side effects as compared to placebo.<sup>271</sup>

1<sup>+</sup>

#### **B** Intravenous magnesium is not recommended as treatment in patients with acute migraine attack.

Riboflavin in a dose of 200 mg per day has been compared to placebo and found to have a responder rate of 56% versus 9% for attack frequency and 59% versus 15% for the number of migraine days.<sup>272</sup>

1<sup>-</sup>

A combination of riboflavin 400 mg, magnesium 300 mg and feverfew 100 mg was not found to be more effective than placebo containing riboflavin 25 mg.<sup>273</sup>

1<sup>-</sup>

# 15 Information provision

## 15.1 FREQUENTLY ASKED QUESTIONS

These frequently asked questions and suggested answers are intended as a prompt for discussion between healthcare professionals and patients with headache concerns. They are not designed for direct distribution to patients, but might be incorporated into locally developed patient information materials. General patient information leaflets and further patient information is available from the organisations listed in section 15.2.

### **What is the difference between headache and migraine?**

There are many different types of headache. The most common is tension-type headache which causes mild to moderate pain on both sides of the head.

Migraine usually causes moderate to severe pain on one side of the head and many people also feel or are sick. They may feel uncomfortable with bright light or noise. Sometimes people with migraine experience 'aura' which can cause changes to their sight, such as flashing lights or spots, and numbness or 'pins and needles' in their hands and face.

### **Is a brain tumour causing my headache?**

Most common headaches are not caused by tumours. It is very unusual for headache to be the sole symptom of a brain tumour.

### **Is it going to go away?**

People have different experiences of how often headaches and migraines occur, and how long they last. There are treatments which can help to prevent headaches occurring as frequently and which can help reduce the severity of the pain. Keeping a headache diary may help as it can show whether there are any patterns in your headaches.

### **Why me?**

A tendency to troublesome headaches often runs in families. Many headache disorders are genetically linked. Headaches affect over 90% of the population in the UK at some time in their life, although some people experience much worse or more frequent headaches than others.

### **When should I consult my GP?**

If you experience new severe headache, sudden headache, prolonged headache or a change in your usual headache pattern you should see your doctor.

If you have been prescribed medication and your headaches continue you should go back to your GP to discuss trying different treatment, and to make sure that the medicine itself is not causing more headaches (known as medication overuse headache).

### **What treatments are available?**

There are many medicines available without prescription which can relieve headache and migraine, such as aspirin, paracetamol and ibuprofen.

If your headaches are more severe or occur frequently your GP can prescribe drugs to reduce the pain or prevent headaches occurring so often. If your treatment is not helping, go back to your GP as there may be another treatment which will work better for you.

Other therapies, such as acupuncture, or a combined programme of relaxation and exercise, may also help to reduce the frequency of your headaches.

### **Are there any problems with taking medicines for headache?**

Taking medication too frequently can cause headaches known as medication overuse headache. Medicines for immediate pain relief should not generally be taken on more than 10 days per month. You should consult your GP if you are worried that your medication is causing more headaches or any side effects.

Women who are pregnant are advised to discuss headache medication with their pharmacist or GP.

## 15.2 SOURCES OF FURTHER INFORMATION

### **The British Association for the Study of Headache**

[www.bash.org.uk/](http://www.bash.org.uk/)

BASH is the United Kingdom national society member of the International Headache Society and the European Headache Federation. It is open to all healthcare professionals with an interest in headache.

### **The British Pain Society**

Third Floor, Churchill House  
35 Red Lion Square  
London, WC1R 4SG  
Tel: 020 7269 7840 • Fax: 020 7831 0859

Email: [info@britishpainsociety.org](mailto:info@britishpainsociety.org)

The British Pain Society has published a number of booklets aimed specifically for patients. Each publication is available to download free of charge, in PDF format.

### **The Migraine Action Association**

27 East Street  
Leicester, LE1 6NB  
Tel: 0116 275 8317 • Fax: 0116 254 2023  
Email: [info@migraine.org.uk](mailto:info@migraine.org.uk) • Website: [www.migraine.org.uk/](http://www.migraine.org.uk/)

The Migraine Action Association provides information for healthcare professionals and patients on the causes, diagnosis and treatment of migraine.

### **Migraine in Primary Care Advisers**

[www.mipca.org.uk/](http://www.mipca.org.uk/)

MIPCA is a UK society dedicated to the management of headache in primary care, and has strong links with the Migraine Action Association (the UK patient support group), academic societies and governmental groups. It runs three special interest groups, on research, education and how to set up a headache clinic.

### **The Migraine Trust**

55-56 Russell Square  
London, WC1B 4HP  
Tel: 020 7436 1336 • Helpline: 020 7462 6601, Monday to Friday 10am - 5pm  
Fax: 020 7436 2880  
Email: [info@migrainetrust.org](mailto:info@migrainetrust.org) • [www.migrainetrust.org/](http://www.migrainetrust.org/)

The Migraine Trust is a medical research and patient support charity for the condition. It supports sufferers and their families by funding and promoting research, providing information and raising awareness of migraine as a significant public health problem.

### **Organisation for the Understanding of Cluster Headache**

OUCH (UK), Pyramid House  
956 High Road  
London, N12 9RX  
Helpline: 01646 651 979  
[www.ouchuk.org](http://www.ouchuk.org)

Provides support, information and advice on coping with cluster headaches. Can assist with supply of and contacts for appropriate equipment for oxygen treatment.

**Pain Association Scotland**

Cramond House

Cramond Glebe Road

Edinburgh, EH4 6NS

Tel (Enquiries only): 0800 783 6059 • Tel (Office): 0131 312 7955 • Fax: 0131 312 6007

[www.chronicpaininfo.org](http://www.chronicpaininfo.org)

Runs local support groups for people with chronic pain.

**Pain Concern**

PO Box 13256

Haddington, EH41 4YD

Tel: 01620 822572 • Fax: 01620 829138

Email: [info@painconcern.org.uk](mailto:info@painconcern.org.uk) • [www.painconcern.org.uk](http://www.painconcern.org.uk)

Provides information and support for pain sufferers and their carers, factsheets and leaflets to help manage pain and a helpline.

## 16 Implementing the guideline

This section provides advice on the resource implications associated with implementing the key clinical recommendations, and advice on audit as a tool to aid implementation.

Implementation of national clinical guidelines is the responsibility of each NHS Board and is an essential part of clinical governance. Mechanisms should be in place to review care provided against the guideline recommendations. The reasons for any differences should be assessed and addressed where appropriate. Local arrangements should then be made to implement the national guideline in individual hospitals, units and practices.

### 16.1 RESOURCE IMPLICATIONS

The guideline development group did not identify any significant resource implications associated with implementing the recommendations.

### 16.2 AUDITING CURRENT PRACTICE

A first step in implementing a clinical practice guideline is to gain an understanding of current clinical practice. Audit tools designed around guideline recommendations can assist in this process. Audit tools should be comprehensive but not time consuming to use. Successful implementation and audit of guideline recommendations requires good communication between staff and multidisciplinary team working.

The guideline development group has identified the following as key points to audit to assist with the implementation of this guideline:

#### 16.2.1 PRIMARY CARE

GPs should review all patients who are prescribed 12 or more triptans a month to consider the diagnosis of medication overuse headache. Reducing triptan use may help to reduce headache frequency.

Audit how often patient information leaflets are given to patients. Patient understanding of headache improves management of the headache.

#### 16.2.2 SECONDARY CARE

Review all patients with admission for thunderclap headache and audit how many have had an LP if the CT scan is negative.

The number of patients in the health board area with cluster headache that are known to the specialist headache services.

### 16.3 ADVICE TO NHSSCOTLAND FROM THE SCOTTISH MEDICINES CONSORTIUM

The SMC has approved certain formulations of sumatriptan.

Frovatriptan has been accepted for the treatment of patients during the headache phase of migraine attacks with or without aura.

Topiramate is accepted for restricted use within NHSScotland for the prophylaxis of migraine headache in adults.

Further information is available from the SMC website, [www.scottishmedicines.org.uk/](http://www.scottishmedicines.org.uk/)

There are no MTAs relevant to this guideline.

## 17 The evidence base

### 17.1 SYSTEMATIC LITERATURE REVIEW

The evidence base for this guideline was synthesised in accordance with SIGN methodology. A systematic review of the literature was carried out using search strategies devised by a SIGN information specialist. Databases searched include Medline, Embase, CINAHL, PsycINFO, and the Cochrane Library. For most searches, the year range covered was 2001-2007. Internet searches were carried out on various websites including the US National Guideline Clearinghouse, NLH Guidelines Finder, and Guidelines International Network (G-I-N). The Medline version of the database search strategies for each key question can be found on the SIGN website in the section covering supplementary guideline material ([www.sign.ac.uk/guidelines/published/support/](http://www.sign.ac.uk/guidelines/published/support/)). The main searches were supplemented by material identified by individual members of the guideline development group.

### 17.2 RECOMMENDATIONS FOR RESEARCH

The guideline development group was not able to identify sufficient evidence to answer all of the key questions asked in this guideline. The following areas for further research have been identified:

- Comparison of acute versus gradual withdrawal of overused medications in medication overuse headache. Which is the best strategy for use in primary care?
- Does education on headache diagnosis and management change GPs' pattern of referral to secondary care neurological and headache services? What is appropriate headache education?
- Does open access to CT brain scanning change GPs' pattern of referral to secondary care neurological and headache services?
- Does the use of headache diaries by GPs in routine clinical practice improve diagnostic accuracy of headache type?

### 17.3 REVIEW AND UPDATING

This guideline was issued in 2008 and will be considered for review in three years. Any updates to the guideline in the interim period will be noted on the SIGN website: [www.sign.ac.uk](http://www.sign.ac.uk)

## 18 Development of the guideline

### 18.1 INTRODUCTION

SIGN is a collaborative network of clinicians, other healthcare professionals and patient organisations and is part of NHS Quality Improvement Scotland. SIGN guidelines are developed by multidisciplinary groups of practising clinicians using a standard methodology based on a systematic review of the evidence. The views and interests of NHS Quality Improvement Scotland as the funding body have not influenced any aspect of guideline development, including the final recommendations. Further details about SIGN and the guideline development methodology are contained in "SIGN 50: A Guideline Developer's Handbook", available at [www.sign.ac.uk](http://www.sign.ac.uk)

### 18.2 THE GUIDELINE DEVELOPMENT GROUP

Dr David P B Watson (Chair)	<i>General Practitioner, Hamilton Medical Group, Aberdeen</i>
Dr Callum Duncan (Secretary)	<i>Consultant Neurologist, Aberdeen Royal Infirmary</i>
Dr Anne Coker	<i>General Practitioner, Dundee</i>
Ms Arlene Coulson	<i>Principal Clinical Pharmacist, Ninewells Hospital, Dundee</i>
Dr Roger Cull	<i>Honorary Consultant Neurologist, Western General Hospital, Edinburgh</i>
Ms Helen Duncan	<i>Lay representative, Haddington</i>
Dr Murray Fleming	<i>General Practitioner, Clydebank Health Centre</i>
Ms Penelope Fraser	<i>Lead Clinician/Consultant Clinical Psychologist, Ninewells Hospital, Dundee</i>
Mrs Suzie Harrold	<i>Senior Physiotherapist, Glasgow Royal Infirmary</i>
Ms Michele Hilton Boon	<i>Information Officer, SIGN</i>
Dr Gillian Smith	<i>Oral Medicine Consultant, Glasgow Dental Hospital</i>
Ms Ailsa Stein	<i>Programme Manager, SIGN</i>
Dr Lorna Thompson	<i>Programme Manager, SIGN</i>
Dr Alok Tyagi	<i>Consultant Neurologist, Southern General Hospital, Glasgow</i>
Ms Heather Wallace	<i>Chairman, Pain Concern, Haddington</i>

The membership of the guideline development group was confirmed following consultation with the member organisations of SIGN. All members of the guideline development group made declarations of interest and further details of these are available on request from the SIGN Executive. Guideline development and literature review expertise, support and facilitation were provided by the SIGN Executive.

### 18.3 CONSULTATION AND PEER REVIEW

#### 18.3.1 NATIONAL OPEN MEETING

A national open meeting is the main consultative phase of SIGN guideline development, at which the guideline development group presents its draft recommendations for the first time. The national open meeting for this guideline was held on 5 September 2007 and was attended by 123 representatives of all the key specialties relevant to the guideline. The draft guideline was also available on the SIGN website for a limited period at this stage to allow those unable to attend the meeting to contribute to the development of the guideline.

## 18.3.2 SPECIALIST REVIEW

This guideline was also reviewed in draft form by the following independent expert referees, who were asked to comment primarily on the comprehensiveness and accuracy of interpretation of the evidence base supporting the recommendations in the guideline. The guideline group addresses every comment made by an external reviewer, and must justify any disagreement with the reviewers' comments.

Dr Anish Bahra	<i>Consultant Neurologist, National Hospital for Neurology and Neurosurgery, London</i>
Mr Richard Bowen	<i>Patient representative, Lanarkshire</i>
Dr Rodney Burnham	<i>Registrar, Royal College of Physicians, London</i>
Dr Richard Coleman	<i>Consultant Neurologist, Aberdeen Royal Infirmary</i>
Dr Richard J Davenport	<i>Consultant Neurologist, Western General Hospital, Edinburgh</i>
Dr Paul Davies	<i>Consultant Neurologist, Northampton General Hospital</i>
Mrs Ruth M Edwards	<i>Lecturer in Pharmacy Practice, The Robert Gordon University, Aberdeen</i>
Dr John Gibson	<i>Consultant in Oral Medicine, Dundee Dental Hospital and School</i>
Mr David Gill	<i>Head of Pharmacy, Angus Community Health Partnership</i>
Professor Donald M Hadley	<i>Consultant Neuroradiologist and Professor in Radiology, Southern General Hospital, Glasgow</i>
Dr Chris Isles	<i>Consultant Physician, Dumfries and Galloway Royal Infirmary</i>
Dr Avinash Kanodia	<i>Consultant Radiologist, Perth Royal Infirmary</i>
Dr E Anne MacGregor	<i>Honorary Research Director, The City of London Migraine Clinic</i>
Dr Alan Merry	<i>General Practitioner, Ardrossan</i>
Ms Lesley Murray	<i>Senior Clinical Pharmacist, Southern General Hospital, Glasgow</i>
Dr Christian Neumann	<i>Consultant Neurologist, Falkirk and District Royal Infirmary</i>
Dr John Olson	<i>Consultant in Medical Ophthalmology, Aberdeen Royal Infirmary</i>
Mr David Paul	<i>Patient representative, Bearsden</i>
Dr Richard C Peatfield	<i>Consultant Neurologist, Charing Cross Hospital, London</i>
Dr Philip Rutledge	<i>Consultant in Medicines Management, Lothian NHS Board</i>
Dr Rani Sinnak	<i>Consultant Clinical (Neuro and Health) Psychologist, Ayrshire Central Hospital</i>
Ms Cathy Stillman-Lowe	<i>Independent Oral Health Promotion Adviser, Reading</i>
Dr Tom Whitmarsh	<i>Consultant Physician, Glasgow Homeopathic Hospital</i>
Professor Joanna M Zakrzewska	<i>Consultant in Oral Medicine, Eastman Dental Hospital, London</i>

## 18.3.3 SIGN EDITORIAL GROUP

As a final quality control check, the guideline is reviewed by an editorial group comprising the relevant specialty representatives on SIGN Council to ensure that the specialist reviewers' comments have been addressed adequately and that any risk of bias in the guideline development process as a whole has been minimised. The editorial group for this guideline was as follows:

Dr Keith Brown	<i>Chair of SIGN; Co-Editor</i>
Dr John Gillies	<i>Royal College of General Practitioners</i>
Ms Fiona McMillan	<i>Royal Pharmaceutical Society of Great Britain</i>
Dr Safia Qureshi	<i>SIGN Programme Director; Co-Editor</i>
Dr Graeme Simpson	<i>Royal College of Physicians of Edinburgh</i>

## Abbreviations

<b>CAT</b>	Computerised adaptive testing
<b>CH</b>	Cluster headache
<b>CI</b>	Confidence interval
<b>CNS</b>	Central nervous system
<b>COCP</b>	Combined oral contraceptive pill
<b>CPH</b>	Chronic paroxysmal hemicrania
<b>CRP</b>	C-reactive protein
<b>CSF</b>	Cerebrospinal fluid
<b>CT</b>	Computerised tomography
<b>CTTH</b>	Chronic tension-type headache
<b>DSM-IV</b>	Diagnostic and Statistical Manual, 4 <sup>th</sup> edition
<b>ESR</b>	Erythrocyte sedimentation rate
<b>ETTH</b>	Episodic tension-type headache
<b>GCA</b>	Giant cell arteritis
<b>GP</b>	General practitioner
<b>HIT</b>	Headache impact test
<b>HIV</b>	Human immunodeficiency virus
<b>HRT</b>	Hormone replacement therapy
<b>ICHD</b>	International Classification of Headache Disorders
<b>IHS</b>	International Headache Society
<b>LP</b>	Lumbar puncture
<b>MIDAS</b>	Migraine Disability Assessment Questionnaire
<b>MOH</b>	Medication overuse headache
<b>MRI</b>	Magnetic resonance imaging
<b>MTA</b>	Multiple technology appraisal
<b>NDPH</b>	New daily-persistent headache
<b>NHS QIS</b>	NHS Quality Improvement Scotland
<b>NICE</b>	National Institute for Health and Clinical Excellence
<b>NNT</b>	Number needed to treat
<b>NSAIDS</b>	Non-steroidal anti-inflammatory drugs
<b>OR</b>	Odds ratio
<b>PH</b>	Paroxysmal hemicrania
<b>PPV</b>	Positive predictive value
<b>RCT</b>	Randomised controlled trial
<b>RR</b>	Relative risk
<b>SAH</b>	Subarachnoid haemorrhage

<b>SIGN</b>	Scottish Intercollegiate Guidelines Network
<b>SMC</b>	Scottish Medicines Consortium
<b>SMT</b>	Spinal manipulation therapy
<b>SSRI</b>	Selective serotonin reuptake inhibitor
<b>SUNA</b>	Short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms
<b>SUNCT</b>	Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing
<b>TA</b>	Temporal arteritis
<b>TAC</b>	Trigeminal autonomic cephalgia
<b>TENS</b>	Transcutaneous electrical nerve stimulation
<b>TMD</b>	Temporomandibular disorder
<b>TTH</b>	Tension-type headache
<b>UK</b>	United Kingdom
<b>WHO</b>	World Health Organisation

# Annex 1

## Key questions used to develop the guideline

DIAGNOSIS AND INVESTIGATION	
Key question	See guideline section
1. In patients > 18 yrs presenting with primary or secondary headache what are the critical signs and symptoms that help determine headache diagnosis and which patients should be referred?	3, 9.1
2. In patients with migraine or chronic headache, what tools are most effective in assessing headache severity, frequency and social and economic impact? Include: MIDAS (migraine disability and assessment score) HIT (headache impact test) SF36	4
3. In patients presenting with headache what is the evidence that the following investigations are effective in confirming diagnosis? a) CT scan b) MRI c) X-ray of the cervical spine d) full blood count e) ESR/CRP/plasma viscosity f) lumbar puncture	5
MANAGEMENT	
4. In patients with the following types of headache: Migraine with or without aura Tension headache Cluster headache and its variants (trigeminal autonomic cephalalgia, paroxysmal hemicrania, hemicrania continua) Jolts and jabs (primary stabbing headache) Medication overuse Cervicogenic – secondary headache Low pressure headache Oromandibular Benign intracranial hypertension / idiopathic intracranial hypertension  what lifestyle factors have been shown to be effective in reducing frequency and severity of acute and chronic headache? a) diet b) exercise c) sleep d) stress management e) trigger avoidance	11

<p>5. In patients with the following types of headache:</p> <ul style="list-style-type: none"> <li>Migraine with or without aura</li> <li>Tension headache</li> <li>Cluster headache and its variants (trigeminal autonomic cephalalgia, paroxysmal hemicrania, hemicrania continua)</li> <li>Jolts and jabs (primary stabbing headache)</li> <li>Medication overuse</li> <li>Cervicogenic – secondary headache</li> <li>Low pressure headache</li> <li>Oromandibular</li> <li>Benign intracranial hypertension/idiopathic intracranial hypertension</li> </ul> <p>which pharmacological therapies for acute attack are the most effective for immediate pain freedom or pain freedom at 24 hours?</p> <ul style="list-style-type: none"> <li>a) aspirin</li> <li>b) paracetamol</li> <li>c) NSAIDs</li> <li>d) COX-2 inhibitors</li> <li>e) anti-emetics</li> <li>f) corticosteroids</li> <li>g) triptans</li> <li>h) oxygen</li> <li>i) intranasal lidocaine</li> <li>j) indomethacin</li> <li>k) ergotamine</li> <li>l) opiates</li> <li>m) caffeine</li> </ul> <p>Outcomes: Scale used is 0 1 2 3 where 0 = no headache 1 = mild headache 2 = moderate headache 3 = severe headache</p> <p>pain free is score down to 0 pain relief is 2 or 3 headache to 1</p> <p>[consider comorbidities]</p>	<p>6.1, 7.1, 8.1, 8.3, 9.2</p>
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<p>6. In patients with the following types of headache:  Migraine with or without aura  Tension headache  Cluster headache and its variants (trigeminal autonomic cephalalgia, paroxysmal hemicrania, hemicrania continua  Jolts and jabs (primary stabbing headache)  Medication overuse  Cervicogenic – secondary headache  Low pressure headache  Oromandibular  Benign intracranial hypertension/idiopathic intracranial hypertension</p> <p>which prophylactic pharmacological therapies are most effective in reducing frequency and severity of headaches?</p> <ol style="list-style-type: none"> <li>beta blockers</li> <li>antiepileptics</li> <li>serotonin antagonists (pizotifen, methysergide, cyproheptadine)</li> <li>antidepressants</li> <li>ACE inhibitors</li> <li>angiotensin-II receptor antagonists</li> <li>low-dose aspirin</li> <li>lithium</li> <li>verapamil and other calcium channel blockers</li> <li>indomethacin and other NSAIDs</li> <li>corticosteroids</li> <li>ergotamine</li> </ol> <p>Outcomes:  Scale used is 0 1 2 3 where  0 = no headache  1 = mild headache  2 = moderate headache  3 = severe headache</p> <p>pain free is score down to 0  pain relief is 2 or 3 headache to 1</p> <p>[consider comorbidities]</p>	<p>6.2, 7.2, 8.2, 9.2</p>
<p>7. In patients with chronic headache are psychological therapies effective in reducing frequency and severity of headaches? Consider:</p> <ol style="list-style-type: none"> <li>cognitive behavioural therapy (CBT)</li> <li>biofeedback and relaxation</li> <li>stress management</li> <li>hypnotherapy</li> </ol>	<p>12</p>

<p>8. In patients with chronic headache are physical therapies effective in reducing frequency and severity of headaches? Consider:</p> <ul style="list-style-type: none"> <li>a) cervical manual therapy (manipulation or mobilisation)</li> <li>b) osteopathy</li> <li>c) chiropracty</li> <li>d) physiotherapy</li> <li>e) massage</li> <li>f) transcutaneous electrical nerve stimulation (TENS)</li> <li>g) postural or exercise advice</li> <li>h) acupuncture</li> <li>i) occlusal splint therapy/oral rehabilitation</li> </ul>	13
<p>9. In patients with chronic headache are complementary therapies effective in reducing frequency and severity of headaches? Consider:</p> <ul style="list-style-type: none"> <li>a) homeopathy</li> <li>b) reflexology</li> <li>c) minerals, vitamins and herbs</li> <li>d) magnesium</li> <li>e) riboflavin</li> <li>f) butterbur</li> <li>g) feverfew</li> <li>h) coenzyme Q</li> </ul>	14
<p>10. In patients with medication overuse headache what management strategies are effective?</p>	9
<p>HORMONAL HEADACHE AND HEADACHE IN PREGNANCY</p>	
<p>11. In women experiencing predominantly menstrual migraine what drugs are safe and effective in reducing the frequency and severity of headaches?</p> <ul style="list-style-type: none"> <li>a) combined oral contraceptives</li> <li>b) progesterone</li> <li>c) oestrogen supplementation</li> <li>d) long-acting implantable contraceptives</li> <li>e) triptans</li> <li>f) mefenamic acid and other NSAIDs</li> </ul>	10.3
<p>12. In women who are menopausal and experiencing migraine is hormone replacement therapy (HRT) safe and effective in reducing the frequency and severity of headaches?</p>	10.4

<p>13. In pregnant women with headache what is the safety of the following treatments:</p> <ul style="list-style-type: none"> <li>a) aspirin</li> <li>b) paracetamol</li> <li>c) NSAIDs</li> <li>d) COX-2 inhibitors</li> <li>e) anti-emetics</li> <li>f) corticosteroids</li> <li>g) triptans</li> <li>h) oxygen</li> <li>i) intranasal lidocaine</li> <li>j) indomethacin</li> <li>k) ergotamine</li> <li>l) opiates</li> <li>m) caffeine</li> <li>n) beta blockers</li> <li>o) antiepileptics</li> <li>p) serotonin antagonists (pizotifen, methysergide, cyproheptadine)</li> <li>q) tricyclic antidepressants</li> <li>r) SSRIS</li> <li>s) ace inhibitors</li> <li>t) angiotensin-II receptor antagonists</li> <li>u) low-dose aspirin</li> <li>v) lithium</li> <li>w) verapamil and other calcium channel blockers</li> </ul>	<p>10.1</p>
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## Annex 2

### Selected Diagnostic Criteria from International Headache Society Classification (ICHD-II)<sup>\*16,27</sup>

#### 1 Migraine

##### 1.1 Migraine without aura

Description: Recurrent headache disorder manifesting in attacks lasting 4–72 hours. Typical characteristics of the headache are unilateral location, pulsating quality, moderate or severe intensity, aggravation by routine physical activity and association with nausea and/or photophobia and phonophobia.

Diagnostic criteria:

- A. At least 5 attacks, 1 fulfilling criteria B–D
- B. Headache attacks lasting 4–72 hours (untreated or unsuccessfully treated)
- C. Headache has at least two of the following characteristics:
  - 1. unilateral location
  - 2. pulsating quality
  - 3. moderate or severe pain intensity
  - 4. aggravation by or causing avoidance of routine physical activity (eg walking or climbing stairs)
- D. During headache at least one of the following:
  - 1. nausea and/or vomiting
  - 2. photophobia and phonophobia
- E. Not attributed to another disorder

##### 1.2 Migraine with aura

Description: Recurrent disorder manifesting in attacks of reversible focal neurological symptoms that usually develop gradually over 5–20 minutes and last for less than 60 minutes. Headache with the features of migraine without aura usually follows the aura symptoms. Less commonly, headache lacks migrainous features or is completely absent.

Diagnostic criteria:

- A. At least 2 attacks fulfilling criterion B
- B. Migraine aura fulfilling criteria B and C for one of the subforms 1.2.1–1.2.6
- C. Not attributed to another disorder

\*Cited from International Headache Society. The International classification of headache disorders, 2nd edition. Cephalgia 2004;24 (Supp 1): 8-160.

1.2.1 *Typical aura with migraine headache*

Diagnostic criteria:

- A. At least 2 attacks fulfilling criteria B–D
- B. Aura consisting of at least one of the following, but no motor weakness:
  - 1. fully reversible visual symptoms including positive features (eg flickering lights, spots or lines) and/or negative features (ie loss of vision)
  - 2. fully reversible sensory symptoms including positive features (ie pins and needles) and/or negative features (ie numbness)
  - 3. fully reversible dysphasic speech disturbance
- C. At least two of the following:
  - 1. homonymous visual symptoms<sup>1</sup> and/or unilateral sensory symptoms
  - 2. at least one aura symptom develops gradually over  $\geq 5$  minutes and/or different aura symptoms occur in succession over  $\geq 5$  minutes
  - 3. each symptom lasts  $\geq 5$  and  $< 60$  minutes
- D. Headache fulfilling criteria B–D for 1.1 *Migraine without aura* begins during the aura or follows aura within 60 minutes
- E. Not attributed to another disorder

1.5.1 *Chronic migraine*

- A. Headache (tension-type and/or migraine) on  $\geq 15$  days per month for at least 3 months\*
- B. Occurring in a patient who has had at least five attacks fulfilling criteria for 1.1 Migraine without aura
- C. On  $\geq 8$  days per month for at least 3 months headache has fulfilled C1 and/or C2 below, that is, has fulfilled criteria for pain and associated symptoms of migraine without aura
  - 1. Has at least two of a–d
    - (a) unilateral location
    - (b) pulsating quality
    - (c) moderate or severe pain intensity
    - (d) aggravation by or causing avoidance of routine physical activity (eg walking or climbing stairs)
  - and at least one of a or b
    - (a) nausea and/or vomiting
    - (b) photophobia and phonophobia
  - 2. Treated and relieved by triptan(s) or ergot before the expected development of C1 above
- D. No medication overuse and not attributed to another causative disorder

## 2 Tension-type headache

### 2.1 Infrequent episodic tension-type headache

Description: Infrequent episodes of headache lasting minutes to days. The pain is typically bilateral, pressing or tightening in quality and of mild to moderate intensity, and it does not worsen with routine physical activity. There is no nausea but photophobia or phonophobia may be present.

Diagnostic criteria:

- A. At least 10 episodes occurring on <1 day per month on average (<12 days per year) and fulfilling criteria B–D
  - B. Headache lasting from 30 minutes to 7 days
  - C. Headache has at least two of the following characteristics:
    1. bilateral location
    2. pressing/tightening (non-pulsating) quality
    3. mild or moderate intensity
    4. not aggravated by routine physical activity such as walking or climbing stairs
  - D. Both of the following:
    1. no nausea or vomiting (anorexia may occur)
    2. no more than one of photophobia or phonophobia
  - E. Not attributed to another disorder
- ± Increased pericranial tenderness on manual palpation

### 2.2 Frequent episodic tension-type headache

Diagnostic criteria:

As for 2.1 Infrequent episodic tension-type headache except:

- A. At least 10 episodes occurring on  $\geq 1$  but <15 days per month for at least 3 months ( $\geq 12$  and <180 days per year) and fulfilling criteria B–D (2.1)

### 2.3 Chronic tension-type headache

Diagnostic criteria:

As for 2.1 Infrequent episodic tension-type headache except:

- A. Headache occurring on  $\geq 15$  days per month on average for >3 months ( $\geq 180$  days per year) and fulfilling criteria B–D (2.1)

### 3 Cluster headache and other trigeminal autonomic cephalalgias

#### 3.1 Cluster headache

Description: Attacks of severe, strictly unilateral pain which is orbital, supraorbital, temporal or in any combination of these sites, lasting 15–180 minutes and occurring from once every other day to 8 times a day. The attacks are associated with one or more of the following, all of which are ipsilateral: conjunctival injection, lacrimation, nasal congestion, rhinorrhoea, forehead and facial sweating, miosis, ptosis, eyelid oedema. Most patients are restless or agitated during an attack.

Diagnostic criteria:

- A. At least 5 attacks fulfilling criteria B–D
- B. Severe or very severe unilateral orbital, supraorbital and/or temporal pain lasting 15–180 minutes if untreated
- C. Headache is accompanied by at least one of the following:
  1. ipsilateral conjunctival injection and/or lacrimation
  2. ipsilateral nasal congestion and/or rhinorrhoea
  3. ipsilateral eyelid oedema
  4. ipsilateral forehead and facial sweating
  5. ipsilateral miosis and/or ptosis
  6. a sense of restlessness or agitation
- D. Attacks have a frequency from one every other day to 8 per day
- E. Not attributed to another disorder

##### 3.1.1 Episodic cluster headache

At least two cluster periods lasting 7–365 days and separated by pain-free remission periods of  $\geq 1$  month

##### 3.1.2 Chronic cluster headache

Attacks recur over  $> 1$  year without remission periods or with remission periods lasting  $< 1$  month

#### 3.2 Paroxysmal hemicrania

Description: Attacks with similar characteristics of pain and associated symptoms and signs to those of cluster headache, but they are shorter-lasting, more frequent, occur more commonly in females and respond absolutely to indometacin.

Diagnostic criteria:

- A. At least 20 attacks fulfilling criteria B–D
- B. Attacks of severe unilateral orbital, supraorbital or temporal pain lasting 2–30 minutes
- C. Headache is accompanied by at least one of the following:
  1. ipsilateral conjunctival injection and/or lacrimation
  2. ipsilateral nasal congestion and/or rhinorrhoea
  3. ipsilateral eyelid oedema
  4. ipsilateral forehead and facial sweating
  5. ipsilateral miosis and/or ptosis

- D. Attacks have a frequency above 5 per day for more than half of the time, although periods with lower frequency may occur
- E. Attacks are prevented completely by therapeutic doses of indometacin
- F. Not attributed to another disorder

### 3.2.1 Episodic paroxysmal hemicrania

At least two attack periods lasting 7–365 days and separated by pain-free remission periods of  $\geq 1$  month

### 3.2.2 *Chronic paroxysmal hemicrania (CPH)*

Attacks recur over  $> 1$  year without remission periods or with remission periods lasting  $< 1$  month

### 3.3 Short-lasting Unilateral Neuralgiform headache attacks with Conjunctival injection and Tearing (SUNCT)

Description: This syndrome is characterised by short-lasting attacks of unilateral pain that are much briefer than those seen in any other TAC and very often accompanied by prominent lacrimation and redness of the ipsilateral eye.

Diagnostic criteria:

- A. At least 20 attacks fulfilling criteria B–D
- B. Attacks of unilateral orbital, supraorbital or temporal stabbing or pulsating pain lasting 5–240 seconds
- C. Pain is accompanied by ipsilateral conjunctival injection and lacrimation
- D. Attacks occur with a frequency from 3 to 200 per day
- E. Not attributed to another disorder

Short-lasting Unilateral Neuralgiform headache attacks with cranial Autonomic symptoms (SUNA)

Description: This syndrome is characterised by short-lasting attacks of unilateral pain that are much briefer than those seen in any other TAC and very often accompanied by prominent cranial autonomic features.

Diagnostic criteria:

- A. At least 20 attacks fulfilling criteria B–D
- B. Attacks of unilateral orbital, supraorbital or temporal stabbing or pulsating pain lasting from 2 seconds to 10 minutes
- C. Pain is accompanied by one of:
  1. conjunctival injection and/or lacrimation
  2. nasal congestion and/or rhinorrhoea
  3. eyelid oedema
- D. Attacks occur with a frequency of  $> 1$  per day for more than half the time
- E. No refractory period follows attacks triggered from trigger areas
- F. Not attributed to another disorder

**4 Other primary headaches**

**4.1 Primary stabbing headache**

Description: Transient and localised stabs of pain in the head that occur spontaneously in the absence of organic disease of underlying structures or of the cranial nerves.

Diagnostic criteria:

- A. Head pain occurring as a single stab or a series of stabs and fulfilling criteria B–D
- B. Exclusively or predominantly felt in the distribution of the first division of the trigeminal nerve (orbit, temple and parietal area)
- C. Stabs last for up to a few seconds and recur with irregular frequency ranging from one to many per day
- D. No accompanying symptoms
- E. Not attributed to another disorder

**4.2 Primary cough headache**

Description: Headache precipitated by coughing or straining in the absence of any intracranial disorder.

Diagnostic criteria:

- A. Headache fulfilling B and C
- B. Sudden onset, lasting from one second to 30 minutes
- C. Brought on by and occurring only in association with coughing, straining and/or valsalva manoeuvre
- D. Not attributable to another disorder

**4.3 Primary exertional headache**

Description: Headache precipitated by any form of exercise.

Diagnostic criteria:

- A. Pulsating headache fulfilling criteria B and C
- B. Lasting from five minutes to 48 hours
- C. Brought on by and occurring only during or after physical exertion
- D. Not attributed to another disorder

**4.4 Primary headache associated with sexual activity**

Description: Headache precipitated by sexual activity, usually starting as a dull bilateral ache as sexual excitement increases and suddenly becoming intense at orgasm, in the absence of any intracranial disorder.

**4.4.1 Preorgasmic headache**

Diagnostic criteria:

- A. Dull ache in the head and neck associated with awareness of neck and/or jaw muscle contraction and fulfilling criterion B
- B. Occurs during sexual activity and increases with sexual excitement
- C. Not attributed to another disorder

#### 4.4.2 Orgasmic headache

Diagnostic criteria:

- A. Sudden severe headache fulfilling criterion B
- B. Occurs at orgasm
- C. Not attributed to another disorder

#### 4.5 Hypnic headache

Description: Attacks of dull headache that always awaken the patient from asleep.

Diagnostic criteria:

- A. Dull headache fulfilling criteria B–D
- B. Develops only during sleep, and awakens patient
- C. At least two of the following characteristics:
  - 1. occurs > 15 times per month
  - 2. lasts  $\geq$  15 minutes after waking
  - 3. first occurs after age of 50 years
- D. No autonomic symptoms and no more than one of nausea, photophobia or phonophobia
- E. Not attributed to another disorder

#### 4.6 Primary thunderclap headache

Description: High-intensity headache of abrupt onset mimicking that of ruptured cerebral aneurysm.

Diagnostic criteria:

- A. Severe head pain fulfilling criteria B and C
- B. Both of the following characteristics:
  - 1. sudden onset, reaching maximum intensity in < 1 minute
  - 2. lasting from 1 hour to 10 days
- C. Does not recur regularly over subsequent weeks or months
- D. Not attributed to another disorder

#### 4.7 Hemicrania continua

Description: Persistent strictly unilateral headache responsive to indometacin.

Diagnostic criteria:

- A. Headache for > 3 months fulfilling criteria B–D
- B. All of the following characteristics:
  - 1. unilateral pain without side-shift
  - 2. daily and continuous, without pain-free periods
  - 3. moderate intensity, but with exacerbations of severe pain

- C. At least one of the following autonomic features occurs during exacerbations and ipsilateral to the side of pain:
  1. conjunctival injection and/or lacrimation
  2. nasal congestion and/or rhinorrhoea
  3. ptosis and/or miosis
- D. Complete response to therapeutic doses of indometacin
- E. Not attributed to another disorder

4.8 New daily-persistent headache (NDPH)

Description: Headache that is daily and unremitting from very soon after onset (within 3 days at most). The pain is typically bilateral, pressing or tightening in quality and of mild to moderate intensity. There may be photophobia, phonophobia or mild nausea.

Diagnostic criteria:

- A. Headache for > 3 months fulfilling criteria B–D
- B. Headache is daily and unremitting from onset or from < 3 days from onset
- C. At least two of the following pain characteristics:
  1. bilateral location
  2. pressing/tightening (non-pulsating) quality
  3. mild or moderate intensity
  4. not aggravated by routine physical activity such as walking or climbing stairs
- D. Both of the following:
  1. no more than one of photophobia, phonophobia or mild nausea
  2. neither moderate or severe nausea nor vomiting
- E. Not attributed to another disorder

**Secondary Headaches**

8.2 Medication overuse headache

Diagnostic criteria:

- A. Headache present on  $\geq 15$  days/month
- B. Regular overuse for > 3 months of one or more acute/symptomatic treatment drugs as defined under sub forms of 8.2.
  1. Ergotamine, triptans, opioids, or combination analgesic medications on  $\geq 10$  days/month on a regular basis for > 3 months
  2. Simple analgesics or any combination of ergotamine, triptans, analgesics opioids on  $\geq 15$  days/month on a regular basis for > 3 months without overuse of any single class alone
- C. Headache has developed or markedly worsened during medication overuse

### 11.2.1 Cervicogenic Headache

#### Diagnostic Criteria:

- A. Pain referred from a source in the neck and perceived in one or more regions of the head and/or face, fulfilling criteria C & D
- B. Clinical, laboratory &/or imaging evidence of a disorder or lesion within the cervical spine or soft tissues of the neck known to be, or generally accepted as, a valid cause of headache
- C. Evidence that the pain can be attributed to the neck disorder or lesion based on at least one of the following
  - 1. Demonstration of clinical signs that implicate a source of pain in the neck
  - 2. Abolition of headache following diagnostic blockade of a cervical structure or its nerve supply using placebo or other adequate control
- D. Pain resolves in 3 months after successful treatment of the causative disorder or lesion.

### 11.7 Headache or facial pain attributed to temporomandibular joint (TMJ) disorder

#### Diagnostic Criteria:

- A. Recurrent pain in one or more regions of the head and/or face fulfilling criteria C and D
- B. X-ray, MRI and/or bone scintigraphy demonstrate TMJ disorder
- C. Evidence that pain can be attributed to the TMJ disorder, based on at least one of the following:
  - 1. pain is precipitated by jaw movements and/or chewing of hard or tough food
  - 2. reduced range of or irregular jaw opening
  - 3. noise from one or both TMJs during jaw movements
  - 4. tenderness of the joint capsule(s) of one or both TMJs
- D. Headache resolves within 3 months, and does not recur, after successful treatment of the TMJ disorder

## Annex 3

### Differentiation between trigeminal autonomic cephalalgias

The following differentiate trigeminal autonomic cephalalgias from each other:<sup>32, 33, 274</sup>

- Gender: CH is more common in men (M:F 3.5-7:1); PH is more common in women (M:F 1:2.13-2.36); SUNCT is more common in men (M:F 2:1)
- Duration: CH 15min-3hr; PH 2-45min; SUNCT 2-250s
- Frequency: CH 1 every other day – 8/day; PH 1-40/day; SUNCT 1/day – 30/hour
- Restlessness during an attack: 100% in cluster headache, 50% in paroxysmal hemicrania, 50% in SUNCT
- Episodic form predominates in CH, Chronic form predominates in PH
- Response to indometacin is absolute in paroxysmal hemicrania, but indometacin is ineffective in CH or SUNCT
- Alcohol frequently triggers CH, occasionally triggers PH and does not trigger SUNCT.

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### Differentiation from trigeminal neuralgia

The following differentiate trigeminal autonomic cephalalgias from trigeminal neuralgia:<sup>23,32,33</sup>

- Trigeminal neuralgia may coexist with cluster headache and paroxysmal hemicrania (cluster-tic, and paroxysmal hemicrania-tic syndromes)
- Location: Orbital, supra-orbital, temporal in TACs; in trigeminal neuralgia the pain occurs in the maxillary and mandibular divisions of the trigeminal nerve in 90%, when present in the ophthalmic division it has usually been in the other two divisions for many years
- Duration: In trigeminal neuralgia pain duration is brief (few seconds) easily distinguishing it from CH and PH
- Autonomic symptoms are not prominent in trigeminal neuralgia and when present the disorder has usually been established for many years, distinguishing it from SUNCT where autonomic features are very prominent.

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## Annex 4

### Headache history<sup>11</sup>

#### **1. How many different headache types does the patient experience?**

Separate histories are necessary for each. It is reasonable to concentrate on the most bothersome to the patient but others should always attract some enquiry in case they are clinically important.

#### **2. Time questions**

- a) Why consulting now?
- b) How recent in onset?
- c) How frequent, and what temporal pattern (especially distinguishing between episodic and daily or unremitting)?
- d) How long lasting?

#### **3. Character questions**

- a) Intensity of pain
- b) Nature and quality of pain
- c) Site and spread of pain
- d) Associated symptoms

#### **4. Cause questions**

- a) Predisposing and/or trigger factors
- b) Aggravating and/or relieving factors
- c) Family history of similar headache

#### **5. Response questions**

- a) What does the patient do during the headache?
- b) How much is activity (function) limited or prevented?
- c) What medication has been and is used, and in what manner?

#### **6. State of health between attacks**

- a) Completely well, or residual or persisting symptoms?
- b) Concerns, anxieties, fears about recurrent attacks, and/or their cause

# Annex 5

## Weekly Headache Diary

WEEK 1	Please score the pain of your headache out of 10 and indicate if you have any other symptoms as listed.						
	Sun	Mon	Tue	Wed	Thur	Fri	Sat
Headache (0 = none 10 = worse)							
Feeling sick (Yes/No)							
Vomiting (Yes/No)							
Other symptoms (Yes/No)							
Duration of attack (hours)							
Had to lie down (Yes/No)							
Time away from normal activities (hours)							
Number of tablets of medicine taken:							
Prescribed							
Over the counter							
Menstruation (Yes/No)							

## Annex 6

### Drug licensing status

All the drugs recommended in this guideline are licensed for the indication in the recommendation with the following exceptions:

Section	Drug
6.1.2	Sumatriptan/naproxen sodium fixed combination is not licensed for the treatment of acute migraine.
6.2.1	Atenolol is not licensed for the prophylaxis of patients with migraine.
6.2.2	Gabapentin and sodium valproate are not licensed for the treatment of migraine.
6.2.3	Amitriptyline and venlafaxine are not licensed for the prophylaxis of migraine.
7.2.3	Tricyclic antidepressants are not licensed for the prophylaxis of tension-type headache.
8.1.3	Lidocaine is not licensed for the treatment of headache.
8.2.1	Verapamil is not licensed for the prophylaxis of cluster headache.

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**ISBN 978 1 905813 39 1**

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