Scottish Intercollegiate Guidelines Network

NHS Quality Improvement Scotland

Diagnosis and management of headache in adults

A national clinical guideline

National meeting draft
August 2007

KEY TO EVIDENCE STATEMENTS AND GRADES OF RECOMMENDATIONS

LEVELS OF EVIDENCE

1^{++}	High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias
1^{+}	Well conducted meta-analyses, systematic reviews of RCTs, or RCTs with a low risk of bias
1^{-}	Meta-analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2^{++}	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^{+}	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^{-}	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 supporting evidence on which the evidence 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^{++}, and directly applicable to the target population*; or*

A body of evidence consisting principally of studies rated as 1^{+}, directly applicable to the target population, and demonstrating overall consistency of results

B A body of evidence including studies rated as 2^{++}, directly applicable to the target population, and demonstrating overall consistency of results*; or*

Extrapolated evidence from studies rated as 1^{++} or 1^{+}

C A body of evidence including studies rated as 2^{+}, directly applicable to the target population and demonstrating overall consistency of results*; or*

Extrapolated evidence from studies rated as 2^{++}

D Evidence level 3 or 4*; or*

Extrapolated evidence from studies rated as 2^{+}

GOOD PRACTICE POINTS

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

1 Introduction

1.1 THE NEED FOR A GUIDELINE

Headache is common, affecting over 90% of the general population in the United Kingdom (UK).[1] It accounts for 4.4% of consultations in primary care[2] and 30% of neurology outpatient consultations.[3, 4] Migraine is the most common severe form of primary headache affecting about six million people in the UK and can cause significant disability.[5] The World Health Organisation ranks migraine in its top 20 disabling conditions for females aged 15 to 44.[6] It is estimated that migraine costs the UK almost £2 billion a year in direct and indirect costs,[7] with over 100,000 people absent from work or school because of migraine every working day.[8] Chronic headache, defined as headache on more than 15 days a month, affects four per cent of the UK population.[9] Healthcare professionals and patients worry about serious rare causes of headaches such as brain tumours.[9] General practitioners (GPs) are often uncertain about when to refer patients to secondary care.[2]

Healthcare professionals often find the diagnosis of headache difficult. Relatively little time is spent teaching headache at undergraduate and postgraduate levels with an emphasis on the rarer secondary headaches rather than the more common primary headaches. General Practitioners refer 2-3% of patients consulting for headaches[2] to neurological clinics which provide a service for excluding secondary headache but may not provide a headache management service. Most primary headache can be managed in primary care and investigations are rarely needed.[10]

There are effective therapies for many of the primary headaches[9, 11] but treatments can cause headache themselves.[9] 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.[12, 13]

There are already other headache guidelines available in the UK,[9, 11] but they are not strictly evidenced based. There is a need for specific guidelines for Scotland that reflect the needs of the Scottish population and the health resources that are available.

1.2 REMIT OF THE GUIDELINE

This guideline provides recommendations based on current evidence for best practice in the diagnosis and management of headache in adults (age greater than 18). The International Classification of Headache Disorders 2nd edition runs to 14 sections and lists over 200 headache types.[14] A comprehensive review of all headache is beyond the scope of these guidelines. With respect to primary headache this guideline focuses on the more common disorders such as migraine and tension-type headache, and reviews some of the rarer primary headaches because they have recognisable features with specific treatments. The main secondary headache reviewed is medication overuse headache as the overuse of headache medication can make the management of primary headache difficult. "Red flags" for secondary headache (ie headache caused by another condition) are highlighted and a guide to the main investigations used in headache is provided.

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

1.3 DEFINITIONS

The guideline uses the definitions of headache types classified in the International Headache Society International Classification of Headache Disorders, 2nd edition.[14] Definitions are listed in Annex 1.

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 PATIENT VERSION

A patient version of this guideline is under consideration.

Not available with this draft.

1.4.2 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 the section on implementation.

1.5 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**.

2 Symptoms and signs of headache

2.1 INTRODUCTION

Most patients with headache who present in primary care have primary headache.[15] Presentation with secondary headache is rare. In primary headache findings on neurological examination are usually normal and investigations are not helpful for diagnosis.[10, 16] It has been estimated that in patients presenting with stable episodic headache and a normal neurological examination the chance of finding a relevant abnormality on neuro-imaging is as low as 0.2%.[10] 2+ 4

The history is of prime importance in the evaluation of a patient with headache.[9, 16] The aim of the history is to classify the headache type and screen for secondary headache using 'red flag' symptoms (*see section 2.2*). An inadequate history is the probable cause of most misdiagnosis of headache type.[9] 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 3*). Diaries and tools to aid diagnosis are discussed in section 3. 4

2.1.1 MIGRAINE

Migraine is a recurrent headache disorder resulting in attacks lasting four to 72 hours, occurring as infrequently as one per year or as often as daily. The median frequency is 1-2 per month.[17] Chronic migraine is classified as migraine occurring on more than 15 days per month for more than three months.[14] 4

The headache is typically unilateral, builds up over minutes to hours and is pulsating. It is moderate to severe in intensity and is associated with nausea and/or photophobia or phonophobia. It is disabling and aggravated by routine physical activity.[14] 4

Migraine is classified as either migraine with aura or migraine without aura depending on the presence or absence of aura.[14] Aura may occur without headache. 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). There is a characteristic evolution/spread of symptoms over ≥5 minutes and resolution within 60 minutes.[14] Different aura symptoms may occur in succession, for example visual to sensory to speech. An alternative diagnosis, such as a transient ischaemic attack should be considered if the aura has an abrupt onset or is very short.[18, 19] Prolonged aura of more than an hour should also raise the possibility of a vascular event[18, 19] or another secondary cause (*see section 2.2*). 4 3

Clinicians miss the diagnosis of migraine in as many as 50% of patients.[15, 20-22] Often the wrong diagnosis of episodic tension-type headache is given. In the Landmark study 98% of physician diagnoses of migraine were confirmed with prospective diaries.[15] When prospective diaries were reviewed for headaches diagnosed as episodic tension-type headache 82% of the physician diagnoses were changed to migraine or probable migraine. 2+

As many as 75% of patients with migraine describe neck pain associated with migraine attacks and patients may present with more than one headache type. Any single International Headache Society (IHS) 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%.[18] 4

Because of the difficulty in differentiating between migraine without aura and infrequent episodic tension-type headache the IHS 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.[14] In patients with more than one type of headache the IHS suggests a hierarchical diagnosis strategy with the diagnosis based on the most severe headache. 4

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

- episodic severe headache that causes disability [11, 23, 24]
- nausea[16, 23]
- sensitivity to light during migraine headache[16, 23]
- sensitivity to light between migraine attacks[25]
- aura (in 15 – 33%)[16, 18]
- exacerbation by physical activity[16]
- sensitivity to noise[16]
- positive family history of migraine (50% in first degree relatives).[16]

2+ 4 3

The features which give the greatest sensitivity and specificity are nausea and sensitivity to light (*see section 3.4*).[23] 3

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

2.1.2 TENSION-TYPE HEADACHE

Tension-type headache (TTH) is the most common primary headache disorder. Its lifetime prevalence in the general population ranges from 30 – 78% in different studies.[14]

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.[14] The pain is typically bilateral, characteristically pressing or tightening in quality and mild to moderate in intensity. Nausea is not present and it is not aggravated by physical activity. There may be associated pericranial tenderness, sensitivity to light or sensitivity to noise. 4

Disabling ETTH is rare. Most patients with ETTH do not consult a primary care clinician.[15, 22] Migraine is often mistaken for ETTH in the initial diagnosis (*see section 2.1.1*).[15] 2+

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

2.1.3 TRIGEMINAL AUTONOMIC CEPHALALGIAS

The trigeminal autonomic cephalalgias (TACs) are rare disorders, characterised by attacks of severe unilateral pain in a trigeminal distribution.[14, 26] They are associated with prominent ipsilateral cranial autonomic features. Cluster headache (CH) is the most common of the trigeminal autonomic cephalalgias, although paroxysmal hemicrania (PH) is probably under-recognised. Short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT) is 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 IHS classification requires ipsilateral autonomic features to occur with an attack (*see annex 1*). 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. 4

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.[14] 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).[14]

Before a diagnosis of cluster headache can be made, secondary "mimics" need to be excluded.[26] Symptomatic cluster headache has been described after infections and with vascular and neoplastic lesions. 4

Paroxysmal hemicrania has similar characteristics to cluster headache, although attacks are shorter, more frequent and it is more common in women. The IHS criteria require a complete response to indomethacin for the diagnosis and ipsilateral autonomic features to occur with an attack (*see annex 1*).[14, 26] 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. 4

SUNCT has similar characteristics to cluster headache and paroxysmal hemicrania. Attacks are shorter 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. Relapses and remissions are erratic.[14, 26, 27] 3 4

Secondary "mimics" are common and need to be excluded before a diagnosis of paroxysmal hemicrania or SUNCT can be made.[26] 3 4

The following features differentiate trigeminal autonomic cephalalgias from migraine:[16, 26] 3 4

- Onset: rapid in TAC, gradual in migraine
- Duration: TACs < 3 hours, migraine 4 - 72 hours
- Frequency: multiple attacks may occur daily in TACs
- Restlessness during an attack: 100% in cluster headache, 50% in paroxysmal hemicrania
- Prominent ipsilateral autonomic features in TACs.

Features which differentiate trigeminal autonomic cephalalgias from each other are listed in Annex 2.

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

☑ Patients with a suspected trigeminal autonomic cephalalgia should be referred for specialist assessment and neuro-imaging.

2.1.4 HEMICRANIA CONTINUA

Hemicrania continua is a continuous strictly unilateral headache that waxes and wanes in intensity without disappearing completely.[14, 26] Brief stabbing pain may be superimposed on the continuous headache and may be accompanied by ipsilateral autonomic features. While it is very rare, it is an important diagnosis to consider as there is an absolute response to indomethacin.[26] 4

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

☑ Patients with suspected hemicrania continua should be referred for specialist assessment and neuro-imaging.

2.1.5 NEW DAILY PERSISTENT HEADACHE

Headache that is daily and unremitting from onset is classified as new daily persistent headache.[14] 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. This is a headache syndrome which can have any phenotype. Secondary headaches to consider are subarachnoid haemorrhage, meningitis, raised intracranial pressure, low cerebrospinal fluid (CSF) pressure and post-traumatic headache. 4

☑ Patients with new daily persistent headache require further investigation for causes of secondary headache.

2.2 SYMPTOMS AND SIGNS OF SECONDARY HEADACHE

In patients with a pattern of headache, neurological examination is normal other than occasional ptosis during and persisting after an attack of cluster headache.[10, 16] The presence of focal symptoms and/or abnormal neurological signs significantly increases the chance of finding an abnormality.[10, 16, 28, 29] Neurological examination including fundoscopy is therefore essential when patients first present. 3

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

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:

- New onset headache in patients who are aged over 50[29-31] 4
- abrupt onset (thunderclap)[28-30, 32, 33]
- focal symptoms including atypical aura greater than one hour[32, 34, 35]
- abnormal neurological examination[28, 29, 35, 36]
- altered mental status[28, 30, 34]
- altered characteristics or associated features of headache[31]
- headache that changes with posture[37] 3
- headache worse in the morning and during physical activity, and the valsalva manoeuvre[38]
- patients with risk factors for thrombosis[34, 39, 40]
- new onset headache in a patient with a history of HIV infection[41]
- jaw claudication[16]
- neck stiffness[30]
- fever[42]
- new onset headache in a patient with a history of cancer.[9]

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

2.2.1 THUNDERCLAP HEADACHE

Thunderclap headache is defined by the IHS as a high-intensity headache of abrupt onset mimicking that of a ruptured aneurysm. Maximum intensity is reached in less than a minute. Sudden severe headache may also occur during sexual activity or exercise.[14] 4

A significant minority of thunderclap headache is secondary. When a patient presents for the first time with a sudden severe headache they should be referred urgently (same day) for consideration of a secondary cause, particularly subarachnoid haemorrhage (SAH).[28-30] Other causes of sudden severe headache include: intracerebral haemorrhage, cerebral venous thrombosis, arterial dissection and pituitary apoplexy.[14] 3 4

There are no reliable features in the history to differentiate between primary and secondary thunderclap headache and SAH can present with milder sudden onset headache.[30] In a retrospective study of patients with sudden severe headache and negative CT head scans, 15% of lumbar punctures performed were positive for xanthochromia.[43] It is therefore essential to refer patients who present for the first time with sudden severe headache for further investigation. 3

D **Patients with a first presentation of sudden severe headache, exertional headache or headache which starts during sexual activity should be referred on the same day for specialist assessment.**

2.2.2 RAISED INTRACRANIAL PRESSURE

Headache associated with raised intracranial pressure is usually worse lying down and may awaken the patient from sleep. It may also be precipitated by valsalva manoeuvres (eg coughing, straining and stooping), sexual intercourse, or physical exertion.[10, 28] Visual obscurations, transient changes in vision with change in posture or valsalva, suggest raised CSF pressure.[38] Any of these symptoms should prompt referral for neuro-imaging. 4

Intracranial tumours rarely produce headache until quite large, particularly in neurologically 'silent' areas such as the frontal lobes.[9] Pituitary and posterior fosse 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 focal signs (eg personality change, homonymous hemianopia, hemiparesis). Heightened suspicion is appropriate if there is a history of cancer elsewhere.[9] 4

In an audit of 324 patients with an imaging diagnosis of an intracranial tumour, headache was the first symptom in 23% but by the time of presentation was the only symptom in 0.2%. All other patients had focal symptoms or signs. Seizure was the most common focal symptom (21%).[44] 3

Idiopathic intracranial hypertension presents with symptoms and signs consistent with raised intracranial pressure, normal neuro-imaging (including cerebral venous 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.[38] 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 thrombosis, various medications and CSF inflammation, infection or malignancy. 4

If a patient presents with headache and a combination of all or some of the following; fever, neck stiffness, focal signs or seizures, infection of the central nervous system (CNS) should be considered.[30, 42] This may be diffuse (meningitis or encephalitis) or localized (brain abscess). Heightened suspicion is appropriate if there is a history of HIV or immunosupression.[41] 3

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

D **Patients with headache, fever, neck stiffness, seizures and/or abnormal neurological examination should be referred for same day specialist assessment.**

2.2.3 INTRACRANIAL HYPOTENSION

In patients with reduced CSF pressure there is a clear postural component to their headache. Once the headache becomes chronic it often loses its postural component. The headache develops or worsens soon after assuming an upright posture and lessens or resolves shortly after lying down.[37] Low pressure headache is caused by CSF leakage. The commonest cause is a diagnostic lumbar puncture, however, spontaneous dural leakage can occur and is often not recognised. 4

D **Spontaneous intracranial hypotension should be considered in all patients with headache developing or worsening after standing or sitting.**

2.2.4 GIANT CELL (TEMPORAL) ARTERITIS

Giant cell arteritis (GCA) should be suspected 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 is often 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. Prominent, beaded, or enlarged temporal arteries are the most predictive physical sign. An erythrocyte sedimentation rate (ESR) of less than 50 makes the diagnosis unlikely, but does not exclude the diagnosis.[45] 4

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

2.2.5 ANGLE CLOSURE GLAUCOMA

Angle closure glaucoma is rare before middle age. Family history, female sex and hypermetropa 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.[31, 46] Intermittent angle closure glaucoma may precede acute angle closure and the eye may not be red. The diagnosis should be considered in a patient with headache associated with a red eye, halos or unilateral visual aura. 4

D **Glaucoma should be considered in a patient with headache associated with a red eye, halos or unilateral visual aura.**

2.2.6 CARBON MONOXIDE POISONING

Symptoms of sub-acute carbon monoxide poisoning include headaches, nausea, vomiting, dizziness, muscular weakness and blurred vision.[9] 4

2.2.7 MEDICATION OVERUSE HEADACHE

Overuse of all acute headache treatments including simple and combination analgesics can cause medication overuse headache.[14] Further information is available in section 8. 4

3 Assessment tools

3.1 INTRODUCTION

A number of tools have been developed to aid headache diagnosis, assess headache impact and related disability and assess response to treatment. Most of these tools are migraine specific but some can be helpful for patients with other headaches. In clinical practice physicians usually ask questions about headache symptoms. Whilst this is important, asking questions about impact can change a clinician's perception of how severe a patient's migraine is.[47] This information influences treatment choice and the need for follow up.

Patients, primary care clinicians and headache specialists commonly get the diagnosis wrong.[15, 22] This may be because of limited consultation time or poor patient recall. Keeping a prospective diary over a few weeks can improve diagnosis.[9, 15, 22] 2+ 4

3.2 HIT AND HIT-6

The Health Impact Test (HIT) and HIT-6 are retrospective questionnaires based on the patient's experience of headache over the previous four weeks.

HIT is a series of questions that the patient answers via the internet. The answer to one question determines the next question. This is known as dynamic health assessment using computerised adaptive testing (CAT). In practice only five questions have to be answered in order to grade the headache of the majority of patients. Standardised statistical methods have shown that CAT is a valid way of asking the appropriate questions.[48, 49] It is a valid tool for assessing headache impact by measuring health status.[50] It performs well for determining diagnostic label, but is less sensitive for measuring severity of pain.[51] Patients with chronic headache typically score 57-63, migraine in the range of 54-59, and tension-type headache 34-45.[22, 50-52] 3

HIT-6 is a paper version using six of the internet based questions across the following domains; pain, social role limitations, cognitive functioning, psychological distress and vitality. A score is produced at the end of the test. It has been shown to be a valid assessment tool.[53] Patients with a high HIT-6 score are more likely to be diagnosed and treated for migraine by their GP.[52] It is a useful tool for evaluating headache impact on health related quality of life in patients attending a hospital based headache clinic and in general practice.[54, 55] 3

HIT and HIT-6 scores correlate well with self reported change in headache and can be used for monitoring treatment response.[53, 56] 3

3.3 MIDAS

The Migraine Disability Assessment Questionnaire (MIDAS) is a paper based retrospective questionnaire consisting of five questions looking at lost time in three activity domains; work or school, household work and family, social or leisure activities based on the previous three months.[57] The score is based on the number of days lost when migraine has caused at least 50% loss in productivity in the employment and household work domains. The total score can be higher than the actual number of days lost as any one day can be counted in each of the three domains.

MIDAS has been shown to meet physicians' concepts of important clinical criteria, to exhibit high internal consistency, test-retest reliability, accuracy, ease of use and score.[17, 57-59] It can help doctor-patient communication.[60] MIDAS scores have been shown to correlate with diagnosis based on physicians' estimates of pain and disability based on patients' medical histories.[61] MIDAS has limitations:

- disability is measured during but not between headaches
- if headache covers work and non-work portions of the same day this is counted as two days
- the lowest score for MIDAS shows that disability is minimal or infrequent, but does not reflect that the patient could have severe headache. More patients in higher grades report severe headache, but 8.4% of patients with the lowest grade had more than six headaches of severe intensity per year.[60]
- it does not assess the full spectrum of headache, covering only 35% of the range between moderate and severe intensity. Patients with frequent headache all score the highest grade.[58]

3
4

There is good correlation between a headache diary and MIDAS score to measure migraine disability.[62] Headache diaries may still be required as MIDAS may underestimate headache intensity and overestimate headache frequency.

3

Age, headache frequency, average pain intensity and frequency of exacerbating pain were significantly and independently associated with MIDAS score.[63] Patients with chronic migraine had higher scores for all categories except average pain intensity which was higher for patients with episodic migraine (34.9 vs 19.3, $p<0.001$).[64] This highlights the main limitation of MIDAS, where it estimates the overall disability in the previous three months, rather than the disability associated with each individual attack. It is therefore more likely to score infrequent severe migraine as 'minimal or no disability'.

3

There is a moderately strong correlation between MIDAS and standard tools for measuring generic health status, short form -36 (SF-36) ($r=0.707$ and 0.572).[65] Decreasing quality of life scores on the physical and mental subscales of SF-12 are associated with increasing MIDAS grade.[60] MIDAS can be used as a disability scale, but it only covers physical and social domains, and not the emotional domains.

3

Small scale studies have shown that MIDAS is sensitive to change and can be used as an outcome measure for monitoring patients during treatment.[58]

4

3.4 ID MIGRAINE

A single cohort study of the ID Migraine assessment showed that three screening questions could be used to diagnose migraine.[23] The test was considered positive if two or more answers were positive. The questions asked were:

- Did you feel nauseated or sick to your stomach?
- Does light bother you (a lot more than when you don't have headaches)?
- Do you have functional impairment due to headache in the last three months? (scored positively if disability was reported on any one day in the past three months.

3

The three questions gave a sensitivity 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 89.9 to 95.8), false positive rate of 19%.

3.5 HEADACHE DIAGNOSTIC SCREENING QUESTIONNAIRE

The Headache Diagnostic Screening Questionnaire (DSQ) is a self administered eight item questionnaire and scoring system which has been shown to be useful when completed by a pharmacist, rather than a patient alone or GP diagnosis. It was most sensitive for migraine with aura (patient completed 81.8%, pharmacist completed, 90.9%) and least sensitive for chronic headache without medication use (11.8% in both groups).[66] 3

3.6 MIGSEV SCALE

The MIGSEV scale is a seven item questionnaire used to assess the severity of an individual migraine attack. It has been validated for use in clinical practice, but the scoring system is complicated and not intuitive.[67, 68] 3

3.7 MIGRAINE-ACT QUESTIONNAIRE

The Migraine Assessment of Current Therapy (Migraine-ACT) questionnaire uses four questions to identify patients who require a change in their current acute migraine treatment. Studies have shown it to be reliable and valid.[69, 70] 3

3.8 RECOMMENDATIONS

D

Headache tools are not essential in clinical practice but can be used as an aid to diagnosis and management, using the following :

- **diagnosis of headache can be assisted by using diaries**
- **HIT-6 and the ID migraine screener can assist headache diagnosis in primary and secondary care**
- **diagnosis of patients with headache can be assisted in the pharmacy by the use of DSQ**
- **headache disability including migraine can be assessed using CAT HIT, HIT-6 and MIDAS**
- **Migraine ACT assesses acute treatment of patients with migraine and can help determine whether a change in therapy is required**
- **MIDAS and HIT can be used as an outcome measure when following up patients with headache.**

4 Investigations

Further investigation is required when headache is accompanied by any of the features of secondary headaches described in section 2.2.

The vast majority of primary headaches do not require investigation. In keeping with the remit of these guidelines (*see section 1.2*) this section focuses on primary headaches. There are also infrequent but important situations when secondary causes can mimic primary headaches.

4.1 COMPUTERISED TOMOGRAPHY SCAN

Neuro-imaging including computerised tomography (CT) of the brain is not indicated in the investigation of patients with migraine with no red flag symptoms and a normal neurological examination.[10, 36, 41] | 4

The US Headache Consortium guidelines showed that in patients diagnosed with migraine, a rate of 0.2%(upper CI 0.6%) of intracranial abnormality was found.[36] In a prospective study where patients with headache of greater than four weeks duration received neuro-imaging (CT brain scan, magnetic resonance imaging, or both) the yield for significant intracranial abnormalities was 0.4% in patients with migraine, 0.8% in patients with tension-type headache, and 5% (one out of 20 patients) with cluster headache. In a subgroup of 188 patients with headache which did not fit clearly into a defined headache type, significant intracranial abnormality was found in 3.7%(CI 1.5, 7.5%).[71] | 4
2+

Other studies support the use of neuro-imaging in patients with headache who have unexplained abnormal neurological signs.[28, 32, 36] | 4

Patients presenting with new type headache who are HIV positive warrant urgent CT scanning.[28] | 4

Unenhanced CT should be performed on patients with thunderclap headache as soon as possible after onset. If negative results are obtained from both brain CT and lumbar puncture with cerebrospinal fluid analysis (*see section 4.3*) within two weeks of onset of thunderclap headache, then subarachnoid haemorrhage can be excluded from diagnosis.[28, 30, 72] In a case series of 116 patients with suspected subarachnoid haemorrhage presenting at accident and emergency with sudden onset headache, CT brain scan revealed subarachnoid haemorrhage in 97.5% within the first 24 hours with a reduction in sensitivity thereafter.[43] This suggests that CT brain scan is most sensitive when carried out as soon as possible after onset of thunderclap headache. | 4

Sudden severe headaches precipitated by sexual activity can be diagnosed as primary if they cannot be attributed to another disorder.[14] On first onset of this headache it is essential to exclude subarachnoid haemorrhage and arterial dissection (*see annex 1*). Based upon expert opinion, evaluation for vascular abnormality or subarachnoid haemorrhage with neuro-imaging and lumbar puncture is prudent in the investigation of these headaches.[73] This paper suggests that patients presenting within hours of onset of sex induced headaches should have a CT brain scan followed by lumbar puncture. | 4

D **It is unnecessary to perform neuro-imaging in patients with migraine who have no atypical features and who have a normal neurological examination.**

D **CT of the brain should be performed in patients with headache who have unexplained abnormal neurological signs, unless MRI is indicated.**

D **Unenhanced CT should be performed as soon as possible and preferably within six to 12 hours after onset of thunderclap headache.**

4.2 MAGNETIC RESONANCE IMAGING

The US Headache Consortium concludes that there is insufficient evidence to show whether CT is preferable to magnetic resonance imaging (MRI) for patients who have no abnormal neurological signs.[36] It suggests that MRI is more sensitive in identifying white matter lesions and developmental venous anomalies. MRI is more sensitive than CT for identifying clinically insignificant neurological abnormalities.[36]	4
In a retrospective review of 402 records of patients who had chronic headache without other neurological symptoms or findings, major abnormality on MRI of the brain was found in only one (0.6%) of the subgroup of 161 patients with migraine.[74] This suggests that patients with migraine who have no abnormal neurological symptoms or signs do not require neuro-imaging.	3
Another retrospective review of 306 neurology patient records all of whom had MRI brain evaluation for chronic or recurrent headache in the presence of a normal neurological examination, showed a low yield of clinically important intracranial abnormality of 0.7%.[75] MRI brain scan is therefore not indicated in patients with headache who have no abnormal symptoms or signs.	3
Expert opinion suggests that brain MRI should be performed on all patients with cluster headache, paroxysmal hemicrania and SUNCT in order to exclude the wide variety of secondary causes.[25, 26] Patients presenting with cluster headache should have brain MRI performed in order to exclude cluster headache 'mimics'.[26]	4
Primary cough headache (valsalva manoeuvre headache) which is precipitated rather than aggravated by cough or straining may be diagnosed only after structural lesions such as posterior fossa tumour are excluded by neuro-imaging (see annex 1).[14] Expert opinion suggests that every patient with cough headache should have an MRI brain scan to rule out posterior fossa lesion.[73]	4
Benign exertional headache which is precipitated rather than aggravated by exertion can be diagnosed as primary if they are not associated with any other disorder (*see annex 1*).[14] On first occurrence of this headache type subarachnoid haemorrhage or arterial dissection needs to be excluded.[14] Based on expert opinion, the evaluation of headaches precipitated by exertion should include MRI and magnetic resonance angiography to exclude structural cause or vascular abnormality.[73]	4
A small case control study of spinal MRI in patients with post lumbar puncture headache or spontaneous intracranial hypotension concluded that venous plexus volume at C2 was significantly higher in patients with post lumbar puncture headache and spontaneous intracranial hypotension 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 not present in the controls. [76] There is insufficient evidence on which to base a recommendation for spinal MRI.	2-
Several small case series show an association between spontaneous intracranial hypotension or postural headache and the demonstration of diffuse pachymeningeal gadolinium enhancement on brain MRI.[77-79] This suggests there may be a role for MRI with gadolinium looking for pachymeningeal enhancement in patients with postural headaches, but there is insufficient evidence on which to base a recommendation.	3
A randomised controlled trial of 150 patients with chronic daily headache seen 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, however, 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 did not receive a scan.[80]	1+

D **Brain MRI should be carried out in all patients presenting with cluster headache, paroxysmal hemicrania or SUNCT to exclude symptomatic cases or 'mimics' of these conditions.**

☑ Brain MRI should be carried out in patients presenting with headache precipitated by cough or exertion.

4.3 LUMBAR PUNCTURE

Lumbar puncture (LP) with CSF analysis is an appropriate investigation in patients with thunderclap headache who have normal neuro-imaging in order to exclude a diagnosis of subarachnoid haemorrhage.[30, 43, 81 72] — 4 3 2+

Lumbar puncture and CSF analysis should be performed after six hours (or preferably 12 hours) from the onset of thunderclap headache.[43, 72, 82] There should be no delay if meningitis is suspected.[72] In patients presenting late, LP can be carried out up to two weeks from the onset of the thunderclap headache.[43, 72, 82] Lumbar puncture was positive in 15% of those with negative brain scans.[43] A retrospective review concluded that in patients with suspected subarachnoid haemorrhage and normal cranial imaging, lumbar puncture should be carried out from 12 hours of onset and could be useful up to two weeks from onset of the headache.[82] — 3 4

Expert opinion suggests that lumbar puncture should be carried out following CT brain scan in patients presenting within hours of onset of sex induced headache.[73] — 4

☑ Neuro-imaging should be performed first in patients with headache who require lumbar puncture.

☑ In patients who require a lumbar puncture for thunderclap headache, oxyhaemoglobin and bilirubin should be included as part of CSF analysis.

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

4.4 ERYTHROCYTE SEDIMENTATION RATE

A systematic review concluded that increased erythrocyte sedimentation rate (ESR) is useful in predicting likely presence or absence of giant cell arteritis in patients with suggestive symptoms. The mean ESR in patients with GCA was 88 mm/hr compared with a mean ESR of 10mm/hr in patients without GCA. Low ESR was more important in ruling out a diagnosis of ESR than an elevated ESR was in confirming one.[45] — 2-

A retrospective case series found that both ESR and C-reactive protein (CRP) had a high sensitivity for detection of GCA. CRP had a higher sensitivity (100% vs 92% ESR). Combining ESR and CRP gave the highest specificity.[83] C-reactive protein levels in the patients with giant cell arteritis varied between 0.5 and 34.5 mg/dl (median 4.35 mg/dl). The odds of a positive biopsy were two times greater with an ESR of 47 to 107mm/hour ($p = 0.454$) and 3.2 times greater with CRP above 2.45 mg/dl ($p = 0.208$).[83] — 3

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

D **ESR greater than 47 mm/hour and CRP greater than 2.45 mg/dl (24.5mg/l) are useful indicators in the diagnosis of patients with suspected giant cell arteritis.**

4.5 OTHER INVESTIGATIONS

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

5 Migraine (with and without aura)

5.1 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 recommended commencing with an analgesic and anti-emetic, if required, and escalating to 5HT1 receptor agonist (triptan) if this approach fails.[9] | 4

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

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.[84]

Three well conducted randomised controlled trials (RCTs) showed that 48-52% of patients with acute migraine experienced pain relief at two hours after medication with aspirin 900-1,000 mg.[85-87] A combination of paracetamol 1,000 mg, aspirin 1,000 mg and caffeine 260 mg may be more effective (84% relief at two hours) than aspirin 500 mg or sumatriptan 50 mg alone for patients with mild to moderate migraine.[88] | 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.[89] Ibuprofen 400 mg is as effective as aspirin 1,000 mg or sumatriptan 50 mg for pain relief at two hours.[85] Ketoprofen 75-150 mg also provided relief to 62% of patients with migraine at two hours.[90] | 1++

The NSAID tolfenamic acid rapid tablets 200 mg is licensed specifically for the treatment of acute attack 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.[91]

A **Aspirin 900 mg is recommended for acute treatment in patients with all severities of migraine.**

A **Ibuprofen 400 mg or ketoprofen 100 mg are 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 attack.

Few studies on the efficacy of oral paracetamol alone in the treatment of patients with acute migraine were identified. Combination therapies with tramadol or aspirin appear to be more effective (56-84%).[88, 92] Intravenous (IV) paracetamol had only a modest relief effect at two hours (37%).[93] | 1+

5.1.2 TRIPTANS

Triptans provide significant pain relief to patients with acute migraine within two hours of administration and improve patients' quality of life.[94-98]	1++ 1+
Rizaptriptan 10 mg (number needed to treat, NNT, 3.1) is more effective than sumatriptan 50 mg (NNT 4), sumatriptan 100 mg (NNT 4.3) and naratriptan 2.5 mg (NNT 9.2).[94] Eletriptan 80 mg is also more effective at pain relief within two hours than sumatriptan 100 mg.[96] Almotriptan 12.5 mg, eletriptan 80 mg and rizatriptan 10 mg resulted in a higher percentage of patients pain free at two hours than sumatriptan.[96] Almotriptan 12.5 mg achieved the highest efficacy and adverse event profile than the other triptans.[96] It also performed better when compared to cafergot, a combination of ergotamine 1mg and caffeine 100 mg.[95]	1++
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 in the study. 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.[97] [88] It was statistically equipotent with aspirin and ibuprofen in relief of migraine headache at two hours, but significantly better than aspirin for pain free outcome at two hours (37.1% of patients pain free versus 27.1%).[85] Patients who do not gain good headache relief from sumatriptan 50 mg may have a better response to almotriptan.[99] Triptans should not be used in patients with a history of ischaemic heart disease or angina, and use with ergotamine should be avoided.[84]	1++ 1+ 1++
Patients who do not gain good headache relief from sumatriptan 50 mg may have a better response to almotriptan 12.5 mg.[99]	1+
Oral triptans should not be taken too early and are best taken during the established headache phase of an attack.[9]	4
The evidence for triptan nasal sprays and subcutaneous injection in acute migraine is limited. Sumatriptan nasal spray is not useful if vomiting precludes oral therapy since its bioavailability depends largely on ingestion. Zolmitriptan nasal spray may be useful if vomiting is already occurring since 30% may be absorbed through the oral mucosa. If a rapid response is important 6 mg sumatriptan subcutaneously is an option.[9]	4

Triptans are contraindicated in patients with ischaemic heart disease, previous myocardial infarction, coronary vasospasm or uncontrolled or severe hypertension.[84]

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

A **Almotriptan 12.5 mg is recommended as a first line triptan in acute migraine.**

A **Patients with severe migraine attacks should be treated with rizatriptan 10 mg or eletriptan 80 mg if other therapies have been ineffective.**

A **If a patient does not respond to one triptan another triptan should be offered as it may give the desired response.**

D **Triptans should be taken after the onset of a migraine attack.**

5.1.3 ANTI-EMETICS

Anti-emetics may be used for symptoms of nausea and vomiting associated with migraine such as prochloperazine 3-6 mg buccal table or domperidone 10 mg oral or rectal. Anti-emetics are also of use as a prokinetic to promote gastric emptying, such as metoclopramide 10 mg or domperidone 20 mg.[9] | 4

A meta-analysis of results from RCTs showed that intravenous metoclopramide is effective in reducing headache pain from acute migraine (OR 2.84, 95% CI 1.05 to 7.68). IV metoclopramide was equally or more effective than comparative treatments for pain, nausea and relapse outcomes reported in all studies.[100] | 1++

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 ($P < 0.0001$). There is a high level of adverse events associated with haloperidol, such as sedation and restlessness which limits its use for the management of patients with migraine.[101] | 1+

D **Oral and rectal anti-emetics can be used for nausea and vomiting and to promote gastric emptying associated with acute migraine attacks.**

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

5.1.4 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.[97] A combination of ergotamine and caffeine (Cafergot) also performed less well than eletriptan for better headache response and pain free rates.[95] | 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.[84]

A **Ergotamines are less effective than other treatments for patients with acute migraine and should only be considered as a last resort.**

5.1.5 CAFFEINE

Evidence on caffeine was limited to the inclusion of caffeine with combinations of other therapies (*see sections 5.1.1 and 5.1.4*).

5.1.6 OTHER THERAPIES

No evidence was identified for the efficacy of COX-2 inhibitors, corticosteroids, indomethacin or opiates. COX-2 inhibitors are not available in the UK. The British Association for the Study of Headache recommends avoiding the use of opiates for acute treatment due to side effects such as nausea, systemic shutdown and potential addiction.[9] | 4

☑ Opiate analgesics should not be used for the treatment of patients with acute migraine attacks.

5.2 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 a prolonged migraine). 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.[36] 4

General principles when using preventive treatment for migraine include:

- most preventive drugs should be titrated slowly to an effective or maximum dose in order to avoid side effects[9]
- preventive medication should be given a trial at least six to eight weeks following dose titration[9]
- the choice of preventive medication should be guided by their side effect profile. A suggested guide is outlined below.[84]

4

Preventive drug	Do not use in patients with:	Preferred in patients with:
Beta blockers	Asthma Chronic obstructive pulmonary disease Diabetes Bradycardia Peripheral vascular disease	Comorbid anxiety
Tricyclics	Angle closure glaucoma	Comorbid depression Comorbid tension-type Headache
Topiramate	Renal stones Angle closure glaucoma Pregnancy	Comorbid obesity
Valproate	Obesity Liver disease Pregnancy	Comorbid depression

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

5.2.1 BETA BLOCKERS

Propranolol 40-240 mg per day is effective in reducing the frequency of migraine.[36] A Cochrane review found that the overall relative risk of response for propanolol was 1.94 (95% CI, 1.61 to 2.35) indicating a significant effect of propanolol over placebo.[102] — 4, 1++

The US Headache Consortium found a high degree of certainty that propanolol provides moderate reduction in headache frequency and index.[36] Timolol, atenolol and nadolol are likely to be beneficial based upon comparison with placebo or propanolol.[36] Direct comparison of metoprolol and propanolol suggests that metoprolol is as effective a propranolol in the prevention of migraine.[36] — 4

Beta blockers with intrinsic sympathomimetic action appear to be ineffective in the prevention of migraine.[36] — 4

A **Propranolol 40-240 mg per day can be used as prophylaxis in patients with migraine.**

D **Timolol, atenolol and metoprolol can be used in the prophylaxis of migraine.**

5.2.2 ANTI-EPILEPTICS

A Cochrane review has shown that, as a class, anticonvulsants 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 anticonvulsants than with placebo. The NNTs for each are[103]:

- all anticonvulsants: 3.8 (CI 3.2 to 4.6)
- valproate: 3.3 (CI 1.9 to 8.9)
- gabapentin: 3.3 (CI 2.1 to 8.4)
- topiramate: 3.5 (CI 2.8 to 4.9).

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 propanolol and when sodium valproate was compared to flunarizine.[103] — 1++

Gabapentin is more effective than placebo for patients with episodic migraine, with the median four week migraine rate being 2.7 for patients treated with gabapentin compared to 3.5 for patients treated with placebo ($p = 0.006$).[104] The study had a high drop-out rate among the gabapentin treated patient group in this study and therefore the result interpretation should be cautious. — 1-

Topiramate significantly reduces the number of acute migraine episodes from 5.26 to 2.6 per 28 days ($p < 0.001$)[105] as well as causing a greater mean reduction in migraine frequency than placebo (1.55 vs 0.47, $p = 0.001$).[106, 107] The mean monthly frequency decreased significantly for patients receiving 100 mg per day of topiramate (from 5.4 to 3.3, $p < 0.001$) and for patients receiving 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.[108] — 1++, 1+

Topiramate 100 mg per day is similar to propanolol with respect to reductions in migraine frequency, responder rates and daily rescue medication usage.[109] — 1+

It has been reported to significantly improve health related quality of life measures in patients with migraine when compared to placebo.[110] — 1+

Patients with chronic migraine and medication overuse headache who are treated with topiramate show a significantly lower 28 day headache frequency when compared to placebo (8.1 vs 20.6, $p < 0.0007$).[111]	1+
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.[112]	1-
In a study of patients with episodic migraine treated with sodium valproate the mean monthly frequency of attacks reduced from 5.4 to 4.0 and the headache intensity from 7.7 to 5.8 ($p < 0.001$).[113] In patients treated with topiramate the mean monthly headache frequency 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.	1+

A **Patients with episodic migraine and chronic migraine can be treated with topiramate to reduce headache frequency and severity.**

A **Patients with episodic migraine can be treated with sodium valproate to reduce headache frequency and severity.**

A **Patients with episodic and chronic migraine can be treated with gabapentin to reduce headache frequency.**

5.2.3 ANTIDEPRESSANTS

Antidepressants are associated with an overall improvement ratio of 2.1 (95% CI 1.6-.6) in patients with migraine. The level of improvement varies with the class of treatment drug with improvement ratio varying from 1.7 (95% CI 1.3-2.2) for tricyclic antidepressants to 4.9 (95% CI 1.9-13) for SSRIs.[114]	1+
A Cochrane review showed no significant difference between the use of selective serotonin reuptake inhibitors (SSRIs) and placebo in the reduction of migraine frequency or severity.[115] The headache index was not statistically significant when comparing SSRI to placebo at 8 or 12 weeks. The combined SMD when using a random-effects model was -0.14 at 8 weeks and -0.32 at 12 weeks. Fluoxetine was the most commonly studied SSRI.	2++
Amitriptyline is effective in the prophylaxis of migraine at a dose of 25-150 mg per day.[36] This guideline found there was consistent good evidence that amitriptyline is significantly better than placebo in reducing headache index and frequency.	4
An RCT of patients who had migraine without aura found that venlafaxine 150 mg is superior to placebo and to venlafaxine 75 mg in the prophylaxis of patients with migraine.[116] 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.[117]	1+
The prophylactic effect of venlafaxine has been compared to amitryptyline 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 ($p > 0.05$).[117]	1+

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

B **SSRIs should not be prescribed to patients requiring prophylaxis of migraine.**

B **Venlafaxine is an effective alternative to tricyclic antidepressants for prophylaxis of migraine.**

5.2.4 OTHER THERAPIES

Flunarizine in doses of 5 mg and 10 mg a day has been compared to propanolol 160 mg for the prophylactic treatment of patients with migraine. Both flunarizine groups were at least as effective as propanolol ($p < 0.001$). No significant differences between the three treatments were found with regard to safety.[118] Flunarizine is not licensed for use in the UK.	1+
Candesartan performed well against placebo with a relative reduction of 22% in the number of days patients who took candesartan experienced migraine.[119]	1+
Aspirin may be associated with a small treatment effect in the prophylaxis of migraine among middle aged women, but this showed no statistically significant effect (59.6% vs 56.4% for placebo, OR 1.13).[120]	1+
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 ($p = 0.304$). This drug is therefore no more effective than placebo for the prophylactic treatment of migraine.[121]	1+
Acetazolamide is poorly tolerated in patients with migraine and does not offer any beneficial prophylactic effect when compared to placebo.[122]	1-
Hyperbaric oxygen has no role in the preventive treatment of migraine.[123]	1-
Lanepitant (a 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 $p = 0.065$).[124] Lanepitant is not licensed for use in the UK.	1+
A trial of patients with headache treated with buspirone showed a 43.3% reduction in headache frequency compared to those on placebo ($p = 0.0025$). This effect was thought not to be secondary to its anxiolytic effect.[125]	1-
The efficacy of botulinum toxin A for prophylaxis of episodic migraine has been studied in a multicentre RCT. The primary efficacy end point was the mean reduction from baseline in the frequency of migraine days at day 180 in the placebo non-responder stratum. 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.[126]	1+

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

6 Tension-type headache

6.1 ACUTE TREATMENT

A large randomised controlled trial showed that aspirin 500 -1,000 mg had a high response rate in relieving pain at two hours in patients with episodic tension-type headache (75%; p = 0.009 and 70% 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%).[127] 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.**

6.2 PHARMACOLOGICAL PROPHYLAXIS

6.2.1 ANTIHYPERTENSIVES

While studies have shown that high blood pressure does not usually cause headache, blood pressure lowering treatments can reduce the prevalence of headache.[128] 2++

A meta-analysis indicated that angiotensin II receptor antagonists reduce the frequency of headache.[129] An RCT showed that lisinopril has a significant effect on the reduction of hours and days with headache and migraine.[130] Neither of these studies specified headache type or identified patients with hypertension within the trial. 1-, 1+

6.2.2 ANTI-EPILEPTICS

One RCT was identified which showed a 9.1% difference in headache free rates for patients with chronic daily headache who were treated with gabapentin versus those on placebo (p = 0.0005).[131] 1+

6.2.3 ANTIDEPRESSANTS

A Cochrane review has shown no significant difference between treatment with placebo and fluoxetine for reduction in headache frequency and severity.[115] 2++

Tricyclic antidepressants are more effective in reducing chronic headache than SSRIs.[114, 115] 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 were also noted to reduce headache duration significantly by 1.26 hours per day and headache index scores in a marginally significant way. Amitryptyline in doses of 25- 75 mg was the most commonly studied tricyclic antidepressant.[114] 1+

One RCT showed that mirtazapine could be used as an alternative to tricyclic antidepressants in the treatment of patients with chronic tension-type headache. It showed a significant reduction in headache frequency (p = 0.005), duration (p = 0.03) and intensity (p = 0.03) compared to placebo.[132] There was no wider body of evidence on which to base a recommendation. 1+

Sertraline did not show a significant improvement on severity and frequency of chronic tension-type headache when compared to placebo.[133] 1+

An RCT on the efficacy of venlafaxine extended release tablets in the prophylactic treatment of patients with tension-type headache showed that the median number of days with headache 1+

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.

A **Tricyclic antidepressants, particularly amitryptyline, are recommended for use as prophylactic treatment for patients with chronic tension-type headache.**

A **Venlafaxine may be an effective alternative to tricyclic antidepressants for prophylaxis of tension-type headache.**

6.2.4 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.[134] 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.[135] 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 the headache index in patients with a chronic daily headache (migraine and tension-type), ($p = 0.0025$).[136] 1+

7 Trigeminal autonomic cephalalgias

7.1 ACUTE TREATMENT

Few well conducted trials have been carried out on patients with cluster headache, possibly due to the spontaneous course of the condition.[137]

7.1.1 TRIPTANS

Subcutaneous injection of 6 mg sumatriptan relieves pain in 73-96% of patients with acute cluster headache within 15 minutes.[138-141] Sumaptriptan 20 mg taken nasally relieves only 48% of patients at 15 minutes, and 57% at 30 minutes.[142, 143]

1 + +
2-
1 +

Nasal zolmitriptan provides pain relief at 30 minutes for 40% of patients given 5 mg and 62% of those given 10 mg.[144] The same doses of oral zolmitriptan provided relief at 30 minutes for 57-60% of patients with episodic cluster headache.[145]

1 + +

A **Subcutaneous injection of 6 mg sumatriptan is recommended for the treatment of patients with acute cluster headache.**

7.1.2 OXYGEN

The acute use of 100% oxygen inhalation at normal pressure (7 L/min for 15 min) is widely suggested but there is only evidence from one small RCT.[137, 146] A tight-fitting, non-rebreathing mask should be used.

1 +

Trials have been conducted on the use of hyperbaric oxygen but no consistent prophylactic effect has been demonstrated.[123, 147, 148]

1 + +
1 +
1-

7.1.3 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 ($p < 0.001$).

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.

7.1.4 STEROIDS

Evidence in support of oral steroids is very limited.[137] A small trial showed that a single oral dose of prednisone can rapidly benefit patients with cluster headache.[149]

1 +

Injection of steroids into the suboccipital region may stop cluster headache attacks for four weeks in up to 80% of patients, but is technically more difficult to achieve.[150]

1-

7.2 PHARMACOLOGICAL PROPHYLAXIS

7.2.1 CALCIUM CHANNEL BLOCKERS

Verapamil for the preventive management of cluster headaches has been studied in a number of open label studies with each demonstrating a significant reduction in the frequency and severity of headaches.[26] In a small double blind study and when compared to placebo 86% of patients receiving verapamil showed an improvement of >50% reduction in headache frequency while the placebo group showed no response.[151] | 4 1-

D **Verapamil can be used for the preventive treatment of cluster headaches.**

7.2.2 LITHIUM

Lithium was studied in a small double blind placebo controlled trial which was stopped early because superiority over placebo could not be established.[152] Both lithium and verapamil have been shown to be superior to placebo in one small trial.[26] | 1- 4

7.2.3 ERGOTAMINE

Methysergide, dihydroergotamine, ergotamine and methylergometrine as well as pizotifen and steroids have all been shown to be effective in small open label studies conducted many decades ago.

7.2.4 ANTICONVULSANTS

Valproate has been studied in a double bind placebo controlled trial which did not show any significant difference between the group receiving valproate compared to the group receiving placebo for cluster headaches.[153] | 1-

In open label studies topiramate and gabapentin have been found to be effective for patients with cluster headaches.[26] | 4

7.2.5 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 ($p = = 0.0026$). When compared to placebo (physiological saline).[150] | 1+

7.2.6 NON-STEROIDAL ANTI-NFLAMMATORY DRUGS

Indomethacin is effective for the management of paroxysmal hemicrania and hemicrania continua.[26] | 4

8 Medication overuse headache

8.1 RISK FACTORS

Medication overuse headache (MOH) is defined as headache which is present for 15 days or more, has developed or worsened while taking medication, and resolves within two months after discontinuation of the overused medication (*see annex 1*).[14]	4
Medication overuse headache is reported in migraine, tension-type headache, hemicrania continua, new daily persistent headache and cluster headache and SUNCT.[27, 154-157] Patients with cluster headache and SUNCT who develop MOH tend to have a personal or family history of migraine.[156]	3 4
Medication overuse headache may occur with ten doses per month for triptans, ergots, opiates or combination analgesics and 15 doses per month for simple analgesics.[14]	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.[154]	3
Patients who overuse medications are more likely to develop chronic daily headache.[158, 159] 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).[158]	3
In an audit of nine GP practices <16.2% of patients met IHS criteria for triptan overuse.[160]	3
Patients with frequent headache are at increased risk of developing chronic daily headache.[158] 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.[161]	2+
In patients with chronic daily headache the DSM-IV criteria for dependence behaviour was significantly more common in those who met IHS criteria for medication overuse headache.	2+

D **Medication overuse headache should be considered in all patients with chronic daily headache (headache ≥15 days / month for >3 months).**

D **If discontinuation of the overused medication does not resolve headache or result in a return to the original headache pattern within two months the diagnosis should be reconsidered.**

D **When assessing patients for headache 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 psychiatric comorbidity or dependence behaviour should have these conditions treated independently and referral to a psychiatrist considered.**

8.2 TREATMENT

Abrupt withdrawal of precipitating agent is considered to be the treatment of choice in the majority of patients with medication overuse headache.[157, 162-166] | 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.[162] The number of patients achieving headache freedom at 14 days was 85% for the triptan group, 57% ergot and 23% analgesic. Withdrawal symptoms were also shorter in the triptan group. Zeeberg et al confirm the findings on medication type, and also found that migraine was more likely to improve than tension-type headache.[166] | 3

On long term follow up at one year and four years a relapse rate of 45% after successful withdrawal was found.[167] 94% relapsed in the first year. Relapse rate varied with headache type (22% 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. | 3

Duration of withdrawal headache depends on the medication overused.[162, 166] Duration is shorter and withdrawal more likely to be successful in patients taking triptans and ergots than in patients taking opiates, simple or combination analgesics. Withdrawal symptoms are also shorter for triptans. One of the studies did not find differences between primary headache type, but another reported that withdrawal was more successful in migraine than in TTH or mixed headache. | 3

No studies were identified comparing abrupt versus gradual withdrawal, although patients overusing opioids (and benzodiazepines and barbiturates) benefit from gradual withdrawal.[157, 165] | 3, 4

Structured advice is as good as inpatient and outpatient detoxification programmes, in patients not overusing opiods.[164] There is similar reduction in headache frequency with abrupt withdrawal with education alone when compared with patients also given prednisolone or naratriptan.[163] | 2+

A number of inpatient strategies have been used. There is limited information based on small case series of selected patients available for dihiydroergotamine, sodium valproate and lidocaine.[157] 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

C **Patients with medication overuse headache 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 opioid dependence should be considered for gradual withdrawal.**

Abrupt withdrawal from medication initially results in worsening of headache.[162, 165, 166] Patients given prednisolone or naratriptan had fewer withdrawal symptoms, used fewer symptomatic medications and required to use symptomatic medications for a shorter time.[163] No significant difference was found between prednisolone and naratriptan. | 2+, 3

The use of amitryptyline, topiramate and sodium valproate for medication overuse headache has been studied in small randomized controlled and uncontrolled trials.[105, 165, 168] Naproxen has been used in an unblinded randomised trial in ergotamine induced headache and was shown to ameliorate withdrawal symptoms.[165] | 1-, 2-, 3

Prophylactic treatments are not effective when patients are overusing medications.[165, 169] After withdrawal of the overused agent, the efficacy of prophylactic agents returned. | 3

9 Pregnancy, contraception and other hormonal factors

9.1 PREGNANCY

Where possible, the use of medication in pregnancy should be avoided, particularly in the first trimester. Paracetamol has been used routinely during all stages of pregnancy for pain relief and overall there seems to be no clear evidence of harmful effects on the fetus.[170-173] 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-moderate pain during pregnancy.[171, 173] As with any medication used during pregnancy, paracetamol should be taken at the lowest effective dose for the shortest time necessary.

If short term analgesia with an NSAID is required in the first or second trimester, then ibuprofen would be the preferred agent.[171] Aspirin is contraindicated during pregnancy.[84] 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.[171]

Three systematic reviews agreed that there is no robust evidence of an increased risk of fetal abnormalities in babies born to mothers who took sumatriptan during pregnancy.[174-176] There is a non-significant trend to an increased risk of preterm births (before 37 weeks) and miscarriages following the use of sumatriptan during pregnancy.[174, 175] There is insufficient evidence to advocate the use of triptans during pregnancy. 2+ 2-

☑ Paracetamol 1,000 mg should be used to treat patients with acute migraine during pregnancy.

9.2 ORAL CONTRACEPTION

Evidence from meta-analyses and systematic reviews suggests a significant increased risk of ischaemic stroke among women with migraine, with a relative risk of between 1.85 to 2.16.[177-179] This risk is greater in women who use the combined oral contraceptive pill (COCP), with an increased risk of ischaemic stroke of two to four times that of the non-users without migraine.[177] Patients suffering migraine with aura using the COCP have a relative risk of 8.72 for developing stroke.[178] The World Health Organisation 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.[177] 2++

B **Women suffering from migraine with aura should not use combined oral contraceptives.**

B **Patients with migraine without aura who are over the age of 35 should not use combined oral contraceptives.**

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.

9.3 MENSTRUAL MIGRAINE

Many women with migraine report an increased frequency and severity of migraine attacks around the time of menstruation. Evidence suggests that this is related to low blood oestrogen levels.[180-184] Perimenstrual supplementation with phyto-oestrogens or oestradiol can reduce the risk of menstrual migraine (RR, 0.78)[183] but a rebound increase in migraine tends to occur after the treatment phase, so it is not recommended. 2+ 1+ 2-

9.3.1 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 (p0.05).[185] 1++

A single RCT showed that mefenamic acid gave 79% of patients effective relief at two hours, compared to 16% on placebo (p<0.03).[186] 1++

Neither study showed any evidence to suggest patients with menstrual migraine are more difficult to treat in terms of acute therapy than patients with other headache types. No evidence was identified on the possible prophylactic effect of NSAIDs for treating patients with menstrual migraine, although this is a widely used strategy.

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

9.3.2 TRIPTANS

Zolmitriptan, sumatriptan, naratriptan and rizatriptan have been shown to be effective in relieving symptoms in patients with acute attacks of menstrual migraine.[187-190] 1++ 2-

Frovatriptan 2.5 mg per day or naratriptan 1mg twice per day taken as prophylaxis 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.[191, 192] 1++

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

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 can be used for the prophylaxis of menstrual migraine.**

9.4 MENOPAUSE

The perimenopause is the time of peak prevalence of migraine without aura in women.[183, 193-196] 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.[196, 197] Women who had a surgical menopause had a higher prevalence of migraine.

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).[193] The two questions to consider are:

- Does HRT increase the risk of ischaemic stroke in women with migraine?
- What influence does HRT have on migraine (without aura) severity and frequency?

HRT has been shown to increase the risk of stroke in all women. The women's health initiative randomised controlled trial showed a hazard ratio of 1.41 for HRT and stroke (CI 1.07-1.85).[198] | 2++

No studies have assessed the relationship between migraine, HRT and stroke. Kittner concluded that there is no compelling evidence that HRT increases or decreases the risk of ischaemic stroke in women with migraine.[199] Tzourio has shown that migraine is not a risk factor for stoke in women older than 45.[200] MacGregor and Silberstein conclude that migraine is not a contraindication for HRT.[201, 202] There is no current evidence to suggest HRT should not be prescribed to women with migraine. | 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).[195, 203] One small study has shown that the transdermal route for oestrogen administration is less likely than the oral route to make migraine worse.[203] This is supported by expert opinion.[202] | 3 2-4

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

D **If a patient taking HRT experiences worsening migraine it should be considered that the HRT may be the cause.**

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

10 Lifestyle factors

10.1 DIET

Little good quality evidence was identified on whether diet modification is effective in reducing the frequency and severity of headaches. A narrative review suggests there is no evidence for foods triggering migraine.[204] 1-

No significant benefit was shown from Omega-3 fatty acids in reducing the incidence of migraine.[205] 1+

10.2 TRIGGER AVOIDANCE

Evidence identified on trigger factors for headache was very limited and of low quality.

A survey of patients with headache suggested that a reduction in caffeine intake and addressing sleep problems may reduce disability associated with headache.[206] 3

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

10.3 EXERCISE

Evidence on exercise was mostly 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.[207] This effect may relate to patients' belief in the therapy or therapist.[208] 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 ($p = 0.000$).[209] 1+

A **Exercise could be considered as part of a combined therapies programme to help patients reduce the frequency and severity of migraine and cervicogenic headaches.**

10.4 SLEEP

No good quality evidence was found relating to sleep and headache. There is a possible link between obstructive sleep apnoea and chronic headache, although the studies did not include headache as a primary symptom.[210, 211] 2-

10.5 STRESS MANAGEMENT

For patients with chronic TTH stress management was more effective when combined with antidepressant medication, although stress management alone was still more successful than placebo. This study had a high drop-out rate.[212] 1-

Multidisciplinary intervention, including stress management was effective in patients with migraine.[209] Results from a survey of patients with migraine suggest that reduction in stress can relieve headache symptoms.[213] 1+ 3

11 Complementary therapies

11.1 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.[214] | 1+

11.2 REFLEXOLOGY

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

11.3 MINERALS, VITAMINS AND HERBS

Collective data review has not shown 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.[215] A CO2-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 ($p = 0.0456$).[216] | 1++ / 1-

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 ($p = 0.0012$).[217] | 1-

In a small study of questionable methodology 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).[218] | 1-

Niacin (oral or intravenous) may have beneficial effects for patients with migraine and tension-type headaches.[219] | 4

Intravenous magnesium has an analgesic effect similar to metoclorpropamide and to placebo when administered for the treatment of patients with an acute migraine attack.[220] 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.[221] | 1+

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.[222] | 1-

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.[223] | 1-

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

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

12 Psychological therapies

For patients with migraine, a single RCT suggests multidisciplinary intervention, including exercise, stress management, relaxation, diet and massage are effective but it is unclear which specific intervention has the greatest benefit.[209] Stress management is discussed in section 10.5. 1+

No good quality evidence was identified addressing the use of cognitive behavioural therapy or hypnotherapy in the treatment of patients with headache.

13 Physical therapies

Due to the nature of physical therapies, it is difficult to conduct blinded trials. Studies are therefore subject to attention and placebo effects which may introduce bias in the results, leading to a downgrading in their methodological assessment.

13.1 CERVICAL MANUAL THERAPY

In a systematic review there was no conclusive evidence that spinal manipulation benefits patients with headache.[224] This is based on studies which were considered to be poor quality. It may be of benefit to patients with migraine.[225] Evidence for patients with tension-type headache was inconclusive.[226] 1++

13.2 MASSAGE

For patients with TTH the benefit of massage as part of soft tissue manipulation is inconclusive.[226] 1++

Massage as part of a multidisciplinary intervention for patients with migraine appears effective and sustained.[209] 1+

Physical therapy which includes massage is beneficial in reducing headache frequency and severity in patients with cervical headache.[227]

13.3 TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION

A Cochrane review, which identified two small trials, and an RCT provide weak evidence that transcutaneous electrical nerve stimulation (TENS) can be of benefit to patients with migraine or TTH.[225, 228] 1++ 1+

13.4 POSTURAL/EXERCISE ADVICE

See section 10.3

13.5 ACUPUNCTURE

A Cochrane review reported that due to heterogeneity, low quality studies and contradictory results there is no conclusive evidence for the use of acupuncture in patients with migraine or TTH, although trends were towards benefit.[229] Since this was published a large well conducted RCT has reported benefits and cost effectiveness of acupuncture, especially for the prevention of migraine.[230] 1++

One small RCT showed benefit in the use of electroacupuncture in patients with TTH, although this may not be widely available in the NHS in Scotland.[231]

A **Acupuncture should be considered for preventive management of patients with migraine.**

13.6 ORAL REHABILITATION

A Cochrane review found no evidence from RCTs that occlusal adjustment treats or prevents headache in patients with temporomandibular disorders (TMD).[232] 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.[233] 1+

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

B **As occlusal adjustment is an invasive and irreversible treatment with no evidence of effectiveness for the treatment of patients with headache associated with TMD, it is not recommended.**

14 Information for discussion with patients and carers

14.1 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 14.2.

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 it really migraine or is it a brain tumour?

It is very unusual for headache or migraine to be the first sign of a brain tumour. Most common headaches are not caused by anything abnormal with the brain. For some types of headache your GP might refer you for a CT scan to help with diagnosis.

Is it going to go away?

People have different experiences of how often headaches and migraines occur, and how long they last. It is not a condition that can be cured but 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 lifestyle which may trigger the headaches, such as stress.

Why me?

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. Keeping a headache diary can help to show if there is anything in your lifestyle which may be causing the headaches to occur, such as stress.

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?

For mild to moderate headaches there are a lot of over the counter medicines 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 other drugs, such as triptans 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 risks with taking this treatment?

Unfortunately taking the medication frequently can cause headaches known as medication overuse headache. If this happens stopping taking the medication will stop the extra headaches. You should consult your GP if you are worried that your medication is causing more headaches.

Women who are pregnant are not advised to take prescribed headache medications as there may be a risk of harm to your child.

There are several different types of medication that can help relieve headaches and migraine, so if you are unhappy with the treatment you have been prescribed talk to your GP about trying an alternative.

Are there any complementary therapies to treat headache?

Studies on complementary therapies, such as homeopathy, have shown that they are not helpful in reducing headaches. There are no complementary therapies which are currently recommended for alleviating headaches or reducing their frequency.

14.2 SOURCES OF FURTHER INFORMATION

The British Association for the Study of Headache
Website: www.bash.org.uk/
BASH is the United Kingdom national society member of the International Headache Society and the European Headache Federation (EHF). It is open to all healthcare professionals with an interest in headache.

The Migraine Action Association
Unit 6 Oakley Hay Lodge Business Park
Great Folds Road
Great Oakley
Northamptonshire
NN18 9AS
Tel: 01536 461333
Enquiries: 0870 050 5898
Fax: 01536 461444
Email: info@migraine.org.uk
Website: 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
Website: www.mipca.org.uk/
MIPCA is the premier society in the UK 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
Website: 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
Website: http:// www.ouchuk.org
Provides support, information and advice for coping with cluster headaches.

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
Website: www.chronicpaininfo.org
Runs local support groups for people with chronic pain.

Pain Concern
PO Box 13256
Haddington
EH41 4YD
United Kingdom
Tel: 01620 822572, Mon-Fri 9-5pm, Fri evening 6.30-7.30pm
Fax: 01620 829138
Email: info@painconcern.org.uk
Website: www.painconcern.org.uk
Provides information and support for pain sufferers and their carers, factsheets and leaflets to help manage pain and a listening-ear helpline which offers the opportunity to talk to another pain sufferer.

15 Implementation and audit

15.1 LOCAL IMPLEMENTATION

Implementation of national clinical guidelines is the responsibility of each NHS Board and is an essential part of clinical governance. It is acknowledged that every Board cannot implement every guideline immediately on publication, but mechanisms should be in place to ensure that the care provided is reviewed against the guideline recommendations and the reasons for any differences assessed and, where appropriate, addressed. These discussions should involve both clinical staff and management. Local arrangements may then be made to implement the national guideline in individual hospitals, units and practices, and to monitor compliance. This may be done by a variety of means including patient-specific reminders, continuing education and training, and clinical audit.

15.2 RESOURCE IMPLICATIONS

- Identifying patients with psychiatric comorbidity and dependence behaviour and treating them appropriately, may improve their care and reduce the impact of medication overuse headache. It may however lead to increased referrals to the psychiatric services.

15.3 KEY POINTS FOR AUDIT

Not available in this draft.

15.4 RECOMMENDATIONS FOR RESEARCH

Not available in this draft.

16 Development of the guideline

16.1 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. 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**

16.2 THE GUIDELINE DEVELOPMENT GROUP

Dr David P B Watson *(Chair)*	*General Practitioner, Hamilton Medical Group, Aberdeen*
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Ms Helen Duncan	*Lay representative, Haddington*
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Mrs Suzie Harrold	*Senior Physiotherapist, Glasgow Royal Infirmary*
Ms Michele Hilton Boon	*Information Officer, SIGN*
Dr Gillian Smith	*Oral Medicine Consultant, Glasgow Dental Hospital*
Ms Ailsa Stein	*Programme Manager, SIGN*
Dr Alok Tyagi	*Consultant Neurologist, Southern General Hospital, Glasgow*
Ms Heather Wallace	*Chairman, Pain Concern, Haddington*

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.

16.3 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 (GIN). 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 (http://www.sign.ac.uk/guidelines/published/support/). The main searches were supplemented by material identified by individual members of the guideline development group.

16.4 CONSULTATION AND PEER REVIEW

16.4.1 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 xx 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.

16.4.2 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. SIGN is very grateful to all of these experts for their contribution to the guideline.

Title and full name	*Job title, Work place, City*
Title and full name	*Job title, Work place, City*
Title and full name	*Job title, Work place, City*
Title and full name	*Job title, Work place, City*
Title and full name	*Job title, Work place, City*

16.4.3 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:

Professor Gordon Lowe	*Chair of SIGN; Co-Editor*
Dr Safia Qureshi	*SIGN Programme Director; Co-Editor*
Dr Sara Twaddle	*Director of SIGN; Co-Editor*

Abbreviations

CAT Computerised adaptive testing

CH Cluster headache

CNS Central nervous system

COCP Combined oral contraceptive pill

CPH Chronic paroxysmal hemicrania

CRP C-reactive protein

CSF Cerebrospinal fluid

CT Computerised tomography

CTTH Chronic tension-type headache

DSM-IV Diagnostic and Statistical Manual, 4th edition

DSQ Headache Diagnostic Screening Questionnaire

ESR Erythrocyte sedimentation rate

ETTH Episodic tension-type headache

GCA Giant cell arteritis

GP General practitioner

HIT Health Impact Test

HRT Hormone replacement therapy

IHS International Headache Society

IIH Idiopathic intracranial hypertension

IV Intravenous

LP Lumbar puncture

MIDAS Migraine Disability Assessment Questionnaire

MOH Medication overuse headache

MRI Magnetic resonance imaging

NNT Number needed to treat

NSAIDS Non-steroidal anti-inflammatory drugs

OR Odds ratio

PH Paroxysmal hemicrania

RCT Randomised controlled trial

RR Relative risk

SAH Subarachnoid haemorrhage

SIGN Scottish Intercollegiate Guidelines Network

SSRI Selective serotonin reuptake inhibitor

SUNCT Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing

TA Temporal arteritis

TAC Trigeminal autonomic cephalalgia

TENS Transcutaneous electrical nerve stimulation

TMD Temporomandibular disorders

TTH Tension-type headache

UK United Kingdom

Annex 1

International Headache Society Classification

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

Previously used terms:

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

1.2.1 Typical aura with migraine headache

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 symptoms1 and/or unilateral sensory symptoms
2. at least one aura symptom develops gradually over ≥5 minutes and/or different aura symptoms occur in succession over ≥5 minutes
3. each symptom lasts ≥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

Description: Migraine headache occurring on 15 or more days per month for more than 3 months in the absence of medication overuse.

Diagnostic criteria:

A. Headache fulfilling criteria C and D for 1.1 *Migraine without aura* on ≥15 days/month for >3 months

B. Not attributed to another 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

As for 2.1 Infrequent episodic tension-type headache except:

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

2.3 Chronic tension-type headache

As for 2.1 Infrequent episodic tension-type headache except:

A. Headache occurring on ≥15 days per month on average for >3 months (≥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 ≥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 indomethacin.

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 indomethacin

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 disorder1

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

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

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 ≥ 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 indomethacin.

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 indomethacin

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

Medication overuse headache is defined as:[14]

A Headache present on ≥ 15 days / month fulfilling criteria C and D

B Regular overuse for > 3 months of one or more drugs that can be taken for acute and / or symptomatic treatment of headache (bunching of treatment days with long periods without medication intake is much less likely to cause medication overuse headache)

ergotamine overuse headache: intake on ≥ 10 days / month

triptan overuse headache: intake on ≥10 days / month

analgesic* overuse headache: intake on ≥15 days / month

opiod overuse headache: intake on ≥10 days / month

combination analgesic† overuse headache: intake on ≥10 days / month

C Headache has developed or markedly worsened during medication overuse

D Headache resolves or reverts to its previous pattern within two months after discontinuation of overused medication.

*Analgesics: aspirin, NSAID's, paracetamol

†Combination analgesics: combination of any of the above with codeine (or other opioid) or caffeine

Annex 2

Differentiation between trigeminal cephalalgias

The following differentiate trigeminal autonomic cephalalgias from each other:[26, 27, 234]

- 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, 0% SUNCT
- Episodic form predominates in CH, Chronic form predominates in PH
- Response to indomethacin is absolute in paroxysmal hemicrania, but indomethacin is ineffective in CH or SUNCT
- Alcohol frequently triggers CH, occasionally triggers PH and does not trigger SUNCT.

3 4

Differentiation between trigeminal neuralgia

The following differentiate trigeminal autonomic cephalalgias from trigeminal neuralgia:[16, 26, 27]

- Trigeminal neuralgia may coexist with cluster headache and paroxysmal hemicrania (cluster-tic, and paroxysmal hemicrania-tic syndromes)
- Location: Orbital, supra-orbital, temporal in TAC's; Trigeminal neuralgia is more common in the maxillary and mandibular divisions than ophthalmic division of the trigeminal nerve
- Duration: In trigeminal neuralgia pain duration is brief (few seconds) easily distinguishing it from CH and PH
- There are no autonomic symptoms in trigeminal neuralgia, distinguishing it from SUNCT.

3 4

Annex 3

Headache history[9]

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

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