



## Precourse Workbook

2018 Edition





Thank you for registering at the CHaT course. We've designed this course in response to what doctors like you have told us you want to learn about, using interactive sessions focused around cases and the best available evidence.

This pre-course material is designed to orient you to the subject matter we will cover on the day of the course. Please read it thoroughly.

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3. HEADSMART be brain tumour aware (from [www.headsmart.org.uk](http://www.headsmart.org.uk))  
*Summary of indicators for brain tumour in childhood*

# Headache in Childhood and Adolescence



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The aim of this review article is to equip you with a paediatric perspective of headache: the commonalities and differences between that seen in childhood and adulthood in terms of presentation, diagnosis and management.

Headache is extremely common in childhood and adolescence. By the age of seven, half of all children will have experienced a headache of one sort or another. Almost all young people will have by the age of 15. The burden of paediatric headache is huge. A recent study showed that 020% of young adolescents suffered from headache which reduced their ability to function for more than 12 days in a three month period and which was associated with reduction in quality of life greater than that of teenagers with diabetes or asthma. Despite this, most young chronic headache sufferers never get to see a headache specialist.<sup>1</sup>

### History (Figure 1)

Most children and adolescents will attend a consultation with their parents. Involve even the very young patient in the information-gathering part of the visit; a child as young as five can give you a history of pulsating headache aggravated by movement. Parents can provide a perspective on their child's personality, ambitions and worries, all of which can influence the prevalence and experience of headache.<sup>2</sup>

### Examination

In the first article in this series on paediatric neurology Anna Maw discussed the approach to paediatric neurology examination. A detailed neurological assessment by confrontation can be successfully performed in most school-age children, can avoid the need for brain imaging when normal and offer reassurance for patients and parents<sup>3</sup>. Include:

- Assessment of growth (plot on UK standard growth chart, to include head circumference in a child <4 years).
- Evaluation for meningism, irritability and conscious level.
- Blood pressure measurement.
- Auscultation of scalp and eyes for bruits
- Inspection of mouth for bruxism.
- Bimanual palpation of jaw whilst patient opens and closes mouth.
- Inspection of skin for neurocutaneous syndromes.

Even in the presence of normal neurology however, the presence of 'red flags' should alert you to consider brain imaging or other investigations. Red flags include acute onset of severe headache, headache at night or on waking from sleep with vomiting, or progressive headache with behaviour change and / or academic failure.

### Figure 1: Elements of headache history in childhood / adolescence

#### Headache

- Attack duration, quality, severity, site
- Relationship to posture, coughing etc
- Aggravating and relieving factors: lights, noise, movement, smells, sleep
- Triggers: sleep change, worry, excitement, missed meals, sunshine, caffeine, periods
- Pattern of headache progression

**Analgesia + attack treatments:** remember medication overuse headache

#### Related symptoms

- Vagal symptoms including pallor, dark rings, syncope
- Fever, confusion, behaviour change
- Aura: visual aura more frequent but dysarthria + vertigo are common in childhood migraine

#### Past medical history

- Neonatal / early childhood, eg prematurity related intraventricular bleeding, VP shunt
- History of childhood periodic syndromes
- Obesity (idiopathic intracranial hypertension, obstructive sleep apnoea)
- Blocked nose + facial pain
- Jaw locking / pain on eating, teeth grinding
- Head / neck trauma
- Licit + illicit drug use
- Other systemic disease

#### Family and social history

- Carefully evaluate family history of 'migraine'
- Family structure and events: factors which provoke or protect against anxiety and depression
- School, academic performance, friends, exercise, ambition, tendency to worry

### Secondary headache in childhood and adolescence

The vast majority of secondary headache in childhood and adolescence is associated with other symptoms or examination findings of neurological deficit. Figure 2 highlights some pointers to secondary headaches encountered more commonly in early life.

**Figure 2: Important considerations when screening for secondary headaches in childhood / adolescence**

**Acute severe headache**

- *Infection* eg meningitis - the younger the patient the less specific signs of meningism are for meningitis.
- *Venous thrombosis* - headache quality is variable in quality and site with no relationship between site of headache and location of the thrombus save in sigmoid sinus thrombosis. Consider in childhood especially where otitis media / mastoiditis / dehydration are present, or in the presence of hypercoagulable states such as inflammatory bowel disease and nephrotic syndrome. Cranial neuropathies including hemianopia, deafness, oculomotor and abducens palsies are common, with acute raised intracranial pressure signs in lateral sinus thrombosis.
- *Intracranial haemorrhage* - more likely due to bleed into tumour or venous infarct, or from AVM rather than from a berry aneurysm

**Acute recurrent headache**

- *Idiopathic or symptomatic occipital epilepsy* – post-ictal headache (2/3 of patients) may be indistinguishable from migraine. Unlike migraine, seizures may occur several times a day. A careful history of visual phenomena accompanying headache will be discriminating. With or without blindness, visual hallucinations of occipital seizures usually last 1-3 minutes, are non-progressive, multi-coloured and circular vs the linear, zigzag and dichromatic features of migraine aura. May involve other non-occipital ictal phenomena eg those arising from involvement of temporal lobe.
- *Chiari malformation-related headache* – symptoms attributable to brain protrusion through the foramen magnum include headache, ataxia, vertigo, hearing loss, neck pain and dysarthria aggravated by coughing and Valsalva manoeuvre. Surgical decompression is required for truly symptomatic cases.

**Chronic progressive headache**

- *Brain tumour* (98% accompanied by other neurology eg eye movement disorder, ataxia).
- *VP shunt blockage / failure* – acute or chronic headache, drowsiness and vomiting all overlap with other common paediatric diagnoses, but a combination of all three in a child with a shunt makes blockage highly likely. An unchanged CT scan does not rule out shunt blockage.
- *Idiopathic intracranial hypertension* – post-pubertal IIH is similar to ‘adult’ IIH with female sex and obesity predominating. In prepubertal children obesity is uncommon; strabismus and a stiff neck may accompany or occur without headache. Opening CSF pressure of >18cmH<sub>2</sub>O (age<8y with papilloedema) and >25cmH<sub>2</sub>O (age>8 or less than 8 without papilloedema) should suggest IIH in prepubertal children.

**Primary headache in childhood and adolescence**

**Migraine**

The most prevalent primary headache in childhood and adolescence, prior to puberty migraine shows early male predominance with 3-11% prevalence. Migraine is more common after puberty (up to a quarter of adolescents) and girls catch up with boys in terms of prevalence. Migraine has been reported in toddlers, behaviour change and vomiting being the predominant symptoms at this age. Spontaneous remission does occur in a large minority of adolescents, with a much reduced chance if migraine is still occurring after 18 years of age. Catamenial migraine is rare in the paediatric population.

IHS criteria for paediatric migraine are different to adult migraine (Figure 3) but the 2-72 hour duration limit is thought to be restrictive as some childhood migraine attacks are very short indeed. Childhood migraine is more likely to be bilateral (bitemporal / bifrontal) compared to adult migraine. Aura occurs in 15%, most commonly visual. Vagal phenomena are often prominent.

Acute confusional migraine is uncommon, with confusion and dysarthria dominating attacks encountered after minor head injury or exercise. This migraine variant, associated with focal slowing on EEG and hypoperfusion on SPECT imaging, can cause considerable diagnostic difficulty at first presentation.

**Figure 3: IHS criteria for childhood migraine without aura**

*Five or more headaches lasting 1-72 hours with at least two of the following characteristics*

- Unilateral or bilateral pain
- Throbbing pain
- Moderate or severe pain
- Pain aggravated by routine physical activity

*and at least one of the following*

- Nausea / vomiting
- Photophobia / phonophobia

The paediatric migraineur may have a history of one or more ‘childhood periodic syndromes’ thought to be migraine variants although there is no clear predictive relationship between many of these and later migraine headache:

- Benign paroxysmal torticollis of infancy (regular attacks of acute agitation, vomiting, pallor and torticollis lasting a few minutes in a toddler).<sup>4</sup>
- Benign paroxysmal vertigo (acute vertigo, nystagmus lasting a few minutes, usually in a pre-adolescent child) – the commonest cause of recurrent childhood vertigo other than recurrent otitis media. The latter is easy to spot by identifying conductive hearing loss and visualising the inflamed eardrum.<sup>5</sup>
- Cyclical vomiting syndrome (incapacitating recurrent vomiting lasting several days sometimes needing hospital admission for fluid support) – strong association with migraine headache and often precipitated by travel, not to be confused with metabolic conditions or Panayiotopoulos seizures.<sup>6,7</sup>
- Abdominal migraine (periodic headache, pallor and abdominal pain which may be associated with other GI symptoms and fever) – the relationship between this and recurrent abdominal pain of childhood is unclear although they can be delineated by application of the Rome III criteria.<sup>8</sup>
- Recurrent short-lived limb pain in childhood (usually lower limb pain sufficient to prevent usual activities, lasting <72h and not attributable to another cause).<sup>9</sup>

Familial (FHM) and sporadic (SHM) hemiplegic migraine variants have both been linked to channelopathies encoded by mutations in CACNA1A, ATP1A2 or SCN1A genes. FHM mutations have been found in family members with non-hemiplegic migraine.<sup>10</sup> Alternating hemiplegia of childhood is an entirely different condition to FHM / SHM, being an early onset (<18 months) progressive disorder where episodes of alternating and worsening hemiplegia are associated with choreoathetosis and dystonic posturing, progressive developmental delay and episodic ophthalmoplegia (unlike FHM or SHM). Episodes last minutes to hours, are usually precipitated by excitement or tiredness and relieved by sleep.<sup>11</sup>

**Prevention and treatment of paediatric migraine**

Composite data from a small number of randomised, placebo-controlled trials show that ibuprofen, nasal sumatriptan / zolmitriptan and oral rizatriptan are effective migraine attack treatments.<sup>12,13</sup> Preventative therapy has a very poor evidence base in childhood migraine and high quality intervention studies are badly needed. Propranolol and flunarizine have been shown to be effective prophylactic agents, but in only one study each.<sup>14</sup> Pizotifen, amitriptylline, clonidine, nimodipine, anticonvulsants and anti-emetics have not been shown to work although most studies examining these drugs concern small numbers of patients.

Use of complementary therapies for paediatric headache is widespread, and most parents want their clinicians to be able to advise on such therapies even when they do not prescribe them.<sup>15</sup> Despite this, there are no randomised controlled trials for herb-based remedies showing any benefit in childhood migraine. There is no convincing evidence of a link between biogenic amines and migraine but an oligoantigenic diet may benefit severely affected paediatric migraineurs resistant to other treatments. The importance of good sleep hygiene should be emphasised and may be enough for some children's migraines to be prevented without recourse to medication, especially in pre-adolescents. Obesity, like migraine prevalent within the paediatric population, is thought to be a risk factor for chronic migraine but there are no studies as yet which determine the impact of weight loss on migraine frequency in the paediatric population.

### Tension type headache

This is a poorly researched primary headache in childhood and adolescence but is probably more common than and at least as debilitating as migraine<sup>16</sup> (Figure 4). Epidemiological evidence from large populations of adolescents with tension-type headache suggest behavioural phenotypes different to migraineurs: a high incidence of anxiety and depression, a tendency to derive stress from academic achievements,<sup>17,18</sup> association with other somatic symptoms and difficulties with family relationships.<sup>19</sup> Opinion is divided as to whether migraine and tension type headaches represent distinct entities.

#### Figure 4: IHS criteria for tension-type headache

At least 10 headaches lasting 30 minutes to 7 days with at least two of the following:

- Pressing / tightening quality
- Bilateral location
- Mild or moderate pain (may inhibit but does not prevent daily activity)
- Pain not aggravated by routine physical activity

and both of the following

- No nausea or vomiting
- No photophobia / phonophobia, or one but not the other is present

### Prevention and treatment of paediatric tension-type headache

There is no evidence for pharmacological treatment or prophylaxis for childhood tension-type headache although the following may help:

- Limiting analgesic only to the most incapacitating headaches, to avoid medication overuse.
- Cognitive behavioural therapies, for which there is a large evidence base, especially for

biofeedback methods. Group therapies may work.

- Maintain healthy physical exercise and sleep routines.
- Offering to write to a patient's school to encourage a staff response to mild-moderate headache whereby the patient takes prompt analgesia and remains in lessons rather than being sent home. This stops children and adolescents from falling behind socially and academically.
- Manual therapies eg stretching, trigger point release, TENS machine use.
- Topical peppermint / menthol derivatives (4Head, TigerBalm) – no evidence in childhood but a blinded study of adult patients suggests benefit over placebo and similar level of efficacy when compared with paracetamol.<sup>20</sup>
- Amitriptyline – no evidence for use specifically in this headache type but commonly used where pharmacotherapy sought.

### Medication overuse headache

This commonly encountered headache in children and adolescents should always be considered as a potential cause of chronic daily headache. It can occur with almost any headache attack treatment including tryptans, the latter tending to cause medication overuse more quickly than analgesics.<sup>21</sup> Children and adolescents with medication-overuse frequently respond to medication withdrawal within a month.<sup>22</sup>

### Short duration headaches

Recurrent headache, lasting seconds to minutes are rare in childhood, and can be difficult to classify according to IHS criteria as features are variable. There is no robust evidence base for management of short duration headache in childhood. Idiopathic stabbing headache is the most widely reported, and in childhood is less likely to be associated with other primary headaches than in adulthood.<sup>23,24</sup> Like episodic and chronic paroxysmal hemicrania, idiopathic stabbing headache should respond to indomethacin. Cluster headache is rarer still, but as in adulthood appears to be responsive to a range of treatments including oxygen, tryptans, verapamil and dihydroergotamine.<sup>25</sup>

### Summary

This synopsis of paediatric headache shows how much is common to both childhood and adult headaches, but how they differ in presentation, differential diagnosis and treatment. Paediatric headache is the Cinderella of paediatric neurology specialties, but it is worthy of more attention and research, being so common and yet so disruptive to young people's lives. Not before time, the National Institute for Clinical Excellence is now consulting on guidance for new onset headache in adults and adolescents, with guidance for headache in younger children following on in the next few years.

Follow progress at

<http://guidance.nice.org.uk/CG/Wave23/2>. ♦

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## PRACTICE

## GUIDELINES

## Diagnosis and management of headaches in young people and adults: summary of NICE guidance

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This is one of a series of *BMJ* summaries of new guidelines based on the best available evidence; they highlight important recommendations for clinical practice, especially where uncertainty or controversy exists.

Headaches are a common problem that many clinicians in primary and secondary care find difficult to treat.<sup>1,2</sup> Once the serious causes of headache have been excluded (such as infection, tumour, bleeding, and arteritis), the major health and social burden of headaches can be attributed to primary headache disorders (cluster headache, migraine, and tension-type headache) and headache caused by the overuse of medications. Straightforward advice is needed for anyone working in the NHS on the diagnosis and treatment of these common disorders and the prevention of medication overuse headache.

This article summarises the most recent recommendations from the National Institute for Health and Clinical Excellence (NICE) on the diagnosis and management of headaches in young people and adults.<sup>3</sup>

### Recommendations

NICE recommendations are based on systematic reviews of the best available evidence and explicit consideration of cost effectiveness. When minimal evidence is available, recommendations are based on the Guideline Development Group's experience and opinion of what constitutes good practice. Evidence levels for the recommendations are given in *italic* in square brackets.

### Assessment: indications for considering additional investigation

- Evaluate people who present with headache and any of the following features, and consider the need for further investigations or referral (or both):
  - Worsening headache with fever

- Sudden onset headache that reaches maximum intensity within five minutes
- New onset neurological deficit
- New onset cognitive dysfunction
- Change in personality
- Impaired level of consciousness
- Recent (typically within the past three months) head trauma
- Headache triggered by cough, valsalva (trying to breathe out with nose and mouth blocked), or sneeze
- Headache triggered by exercise
- Orthostatic headache (headache that changes with posture)
- Symptoms suggestive of giant cell arteritis
- Symptoms and signs of acute narrow angle glaucoma
- A substantial change in the characteristics of their headache.

[All based on the experience and opinion of the Guideline Development Group (GDG)]

- Consider further investigations or referral (or both) for people who present with new onset headache and any of the following:
  - Compromised immunity, caused, for example, by HIV or immunosuppressive drugs
  - Age under 20 years and a history of malignancy
  - A history of malignancy known to metastasise to the brain
  - Vomiting without other obvious cause.

[Based on very low quality evidence from two cohort studies, one of which was in an indirect population, and the experience and opinion of the GDG]

## Diagnosis

- Diagnose primary headaches such as tension-type headache, migraine, or cluster headache according to the features in the table.

[Based on the experience and opinion of the GDG, informed by the International Headache Society ICHD-II (International Classification of Headache Disorders II) criteria]<sup>4</sup>

- Be alert to the possibility of medication overuse headache in people whose headache developed or worsened while they were taking the following drugs for three months or more:
  - Triptans, opioids, ergots, or combination analgesic drugs on 10 days a month or more, or
  - Paracetamol, aspirin, or a non-steroidal anti-inflammatory drug (NSAID), either alone or in any combination, on 15 days a month or more.

[Based on the experience and opinion of the GDG, informed by the International Headache Society ICHD-II criteria]<sup>4</sup>

## Management

### All headaches

- Do not refer people diagnosed as having tension-type headache, migraine, cluster headache, or medication overuse headache for neuroimaging solely for reassurance.

[Based very low quality to moderate quality evidence from one randomised controlled trial]

- Include the following in discussions with the person with a headache disorder:
  - A positive diagnosis, including an explanation of the diagnosis and reassurance that other pathology has been excluded, and
  - The options for management, and
  - Recognition that headache is a valid medical disorder that can have a serious impact on the person and his or her family or carers.

[Based on observational studies ranging from poorly reported to well reported]

- Explain the risk of medication overuse headache to people who are using acute treatments for their headache disorder.

[Based on the experience and opinion of the GDG]

### Tension-type headache

- Consider aspirin, paracetamol, or an NSAID for acute treatment, taking into account the person's preferences, comorbidities, and risks of adverse events.

[Based on low quality evidence from randomised controlled trials]

Because of an association with Reye's syndrome, do not offer preparations containing aspirin to people aged under 16 years.

- Do not offer opioids for acute treatment.

[Based on the absence of evidence for effectiveness and the experience and opinion of the GDG]

- Consider a course of up to 10 sessions of acupuncture over five to eight weeks for the prophylactic treatment of chronic tension-type headache.

[Based on low and very low quality evidence from single blind randomised controlled trials]

### Migraine with or without aura

- Offer combination therapy with an oral triptan and an NSAID, or an oral triptan and paracetamol, for acute treatment, taking into account the person's preferences, comorbidities, and risk of adverse events. For people aged 12-17 years consider a nasal triptan in preference to an oral triptan.

[Based on very low to low quality evidence from direct comparisons in randomised controlled trials, which fed into mixed treatment comparisons in a network meta-analysis, and corresponding cost effectiveness analysis]

- For people in whom oral preparations (or nasal preparations in people aged 12-17 years) for acute treatment are ineffective or not tolerated:
  - Offer a non-oral preparation of metoclopramide or prochlorperazine, and
  - Consider adding a non-oral NSAID or triptan if these have not been tried.

[The first point is based on very low to low quality evidence from randomised controlled trials. The second point is based on the experience and opinion of the GDG and indirect evidence of very low to low quality evidence from randomised controlled trials]

- Offer topiramate or propranolol for prophylactic treatment according to the person's preference, comorbidities, and risk of adverse events. Advise women and girls of childbearing potential that topiramate is associated with a risk of fetal malformations and can impair the effectiveness of hormonal contraceptives. Ensure they are offered suitable contraception.

[Based on low to high quality evidence from direct comparisons in randomised controlled trials, which fed into mixed treatment comparisons in a network meta-analysis, and corresponding cost effectiveness analysis]

- If both topiramate and propranolol are unsuitable or ineffective, consider a course of up to 10 sessions of acupuncture over five to eight weeks or gabapentin (up to 1200 mg/day) according to the person's preference, comorbidities, and risk of adverse events.

[Based on low to high quality evidence from direct comparisons in randomised controlled trials, which fed into mixed treatment comparisons in a network meta-analysis, and corresponding cost effectiveness analysis]

- Advise people with migraine that riboflavin (400 mg once a day) can reduce the frequency and intensity of migraine in some people.

[Based on moderate quality evidence from randomised controlled trials]

### Combined hormonal contraceptive use by women and girls with migraine

- For those who have migraine with aura, do not routinely offer combined hormonal contraceptives for contraception.

[Based on the experience and opinion of the GDG]

### Menstrual migraine

- For women and girls with predictable menstrual related migraine that does not respond adequately to standard acute treatment, consider treatment with frovatriptan (2.5 mg twice a day) or zolmitriptan (2.5 mg twice or three times a day) on the days that migraine is expected.



[Based on low quality evidence from two randomised controlled trials and the experience and opinion of the GDG]

### Cluster headache

- Offer oxygen and a subcutaneous or nasal triptan for acute treatment.

[Based on moderate quality evidence from randomised controlled trials]

- When using oxygen for acute treatment:
  - Use 100% oxygen at a flow rate of at least 12 L per minute with a non-rebreathing mask and a reservoir bag, and
  - Arrange provision of home and ambulatory oxygen.

[The first point is based on moderate quality evidence from randomised controlled trials and the experience and opinion of the GDG. The second point is based on the experience and opinion of the GDG]

- When using a subcutaneous or nasal triptan, ensure the person is offered an adequate supply of triptans. This should be calculated according to the person's history of cluster bouts, taking into account the manufacturer's maximum daily dose.

[Based on the experience and opinion of the GDG]

- Consider verapamil for prophylactic treatment during a bout of cluster headache. If unfamiliar with its use for cluster headache, seek specialist advice before starting verapamil, including advice on electrocardiographic monitoring.

[Based on very low and low quality evidence from one randomised controlled trial]

### Primary headaches during pregnancy

- Offer pregnant women paracetamol for the acute treatment of migraine. Consider the use of a triptan or an NSAID after discussing the woman's need for treatment and the risks associated with the use of each drug during pregnancy.

[Based on very low quality evidence from three prospective cohort studies and the experience and opinion of the GDG]

- Seek specialist advice if prophylactic treatment for migraine is needed during pregnancy.

[Based on the experience and opinion of the GDG]

- Seek specialist advice if treatment for cluster headache is needed during pregnancy.

[Based on low and very low quality evidence from one cohort study with an indirect population and the experience and opinion of the GDG]

### Medication overuse headache

- Explain to people with medication overuse headache that it is treated by withdrawing the drugs that are overused.

[Based on very low quality evidence from one open label randomised controlled trial and the experience and opinion of the GDG]

- Advise people to stop taking all overused acute headache drugs for at least one month and to stop abruptly rather than gradually.

[Based on the experience and opinion of the GDG]

- Advise people that headache symptoms will probably get worse in the short term before they improve and that there may be associated withdrawal symptoms. Provide them with close follow-up and support according to their needs.

[Based on the experience and opinion of the GDG]

- Consider prophylactic treatment for the underlying primary headache disorder in addition to withdrawal of overused drugs.

[Based on the experience and opinion of the GDG]

### Overcoming barriers

The use of combination therapy as the first choice treatment for migraine is innovative and should improve acute treatment. Compliance may, however, be better when people take one drug only, and the guideline provides this alternative. Alongside other considerations, patient preference should inform choice of acute migraine treatments. At the time of publication (September 2012), not all the recommended drugs had marketing authorisation in the United Kingdom for the indication specified or for young people. Prescribers should follow relevant professional guidance and take full responsibility for the decision when prescribing drugs that do not have marketing authorisation. Because topiramate is recommended as first line agent for migraine prophylaxis, prescribers and patients will need to be aware of its safe use in women and girls of childbearing potential. Its enzyme inducing potential means that many hormonal contraceptives may be unreliable. Prescribers should consult authoritative guidance, such as the *British National Formulary (BNF)* or guidance from the Royal College of Obstetricians and Gynaecologists Faculty of Sexual and Reproductive Healthcare,<sup>5</sup> when advising on contraceptive use. In treating those with cluster headaches, general practitioners and oxygen supply companies should ensure that an urgent supply of oxygen is readily available. Challenges around medication overuse headaches include the need to recognise the risk factors, plus early preventive advice. Advice to stop taking drugs abruptly may not be welcome, especially as a definite diagnosis can be made only after the headaches resolve, which occurs in only half of those who succeed in stopping. No recommendation has been made for other therapist delivered interventions, such as manual therapy, exercise, cognitive behavioural therapy, or self management programmes because of the absence of evidence. The guideline makes research recommendations in some of these areas.

The members of the Guideline Development Group were Ria Bhola, Sam Chong, Brendan Davies, Mark Dunne-Willows, Carole Gavin, Kay Kennis, David Kernick, Manjit Matharu, Peter May, Wendy Thomas, Martin Underwood (chair), and William Whitehouse. The technical team at the National Clinical Guideline Centre comprised Sara Buckner, Serena Carville, Elisabetta Fenu, Zahra Naqvi, Norma O'Flynn, Smita Padhi, Tim Reason, and Carlos Sharpin.

Contributors: SC wrote first draft. All authors reviewed the draft, were involved in writing further drafts, and reviewed and approved the final version for publication. MU is guarantor.

Competing interests: All authors have completed the ICMJE uniform disclosure form at [www.icmje.org/coi\\_disclosure.pdf](http://www.icmje.org/coi_disclosure.pdf) (available on request from the corresponding author) and declare: all authors were funded by NICE for the submitted work; after completion of the guideline and before its publication a member of MU's division obtained substantial funding from Bayer for an investigator led study in an unrelated clinical area; no other relationships or activities that could appear to have influenced the submitted work.

Provenance and peer review: Commissioned; not externally peer reviewed.

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## Further information on the guidance

### Methods

The guideline was developed using current NICE guideline methodology ([www.nice.org.uk/aboutnice/howwework/developingniceclinicalguidelines/developing\\_nice\\_clinical\\_guidelines.jsp](http://www.nice.org.uk/aboutnice/howwework/developingniceclinicalguidelines/developing_nice_clinical_guidelines.jsp)). The Guideline Development Group (GDG) comprised three general practitioners (including the chair, and two with a special interest in headache), two neurologists, one paediatric neurologist, one pain specialist, three lay members, an emergency medicine physician, a pharmacist, and a specialist headache nurse.

The group developed clinical questions, collected and appraised clinical evidence, and evaluated the cost effectiveness of proposed interventions through literature review and original economic modelling. The draft guideline went through a rigorous reviewing process, in which stakeholder organisations were invited to comment; the group took all comments into consideration when producing the final version of the guideline. Quality ratings of the evidence were based on GRADE (Grading of Recommendations Assessment, Development and Evaluation) methodology ([www.gradeworkinggroup.org](http://www.gradeworkinggroup.org)). These relate to the quality of the available evidence for assessed outcomes rather than the quality of the clinical study. Quality assessment of diagnostic studies was based on QUADAS-II methodology ([www.bris.ac.uk/quadas/quadas-2](http://www.bris.ac.uk/quadas/quadas-2)) and presented in customised GRADE tables. When standard methodology could not be applied, a customised quality assessment was undertaken. These assessments were presented as a narrative summary of the evidence or in customised GRADE tables (for example, for qualitative and prognostic reviews).

### Network meta-analysis for the acute and prophylactic treatment of migraine

Two network meta-analyses were conducted as part of the clinical review. The advantage of network meta-analysis over conventional meta-analysis is that it enables treatment effects to be calculated for all interventions simultaneously, so that they can be ranked on the basis of efficacy using all available direct and indirect evidence from randomised controlled trials, while preserving randomisation. Results of the network meta-analysis were used to facilitate recommendations through treatment rankings and parameterisation of effect sizes for the economic models. In the network meta-analysis for acute treatment of migraine, triptan plus NSAID combination therapy was found to be the most effective. In the network meta-analysis for prophylactic treatment of migraine topiramate was found to be the most effective.<sup>7</sup>

### Cost effectiveness analysis for acute treatment of migraine

An economic model was developed from an NHS and Personal Social Services perspective to compare the cost effectiveness of six interventions for acute treatment of migraine. Triptan plus NSAID combination therapy was the most cost effective treatment at a willingness to pay threshold of £20 000 (€25 290; \$31 790) per quality adjusted life year in the base case and all sensitivity analyses.

### Cost effectiveness analysis for prophylactic treatment of migraine

An economic model was developed from an NHS and Personal Social Services perspective to compare the cost effectiveness of five interventions for prophylactic treatment of migraine. Topiramate was the most cost effective treatment, at a willingness to pay threshold of £20 000 per quality adjusted life year.

### Points to consider

At the time of publication (September 2012), the following drugs did not have UK marketing authorisation for the indications they have been recommended for:

- Prochlorperazine (except for the relief of nausea and vomiting) and gabapentin for migraine
- Frovatriptan and zolmitriptan for menstrual migraine
- Nasal triptan for cluster headache.

The following drugs did not have a UK marketing authorisation for people aged under 18 years at the time of publication for the indication recommended:

- Triptan (except for nasal triptan) and topiramate for migraine
- Subcutaneous triptan or verapamil for cluster headache.

Riboflavin (400 mg) does not have marketing authorisation for migraine but is available as a food supplement.

The prescriber should follow relevant professional guidance and take full responsibility for the decision. The patient (or his or her parent or carer) should provide informed consent, which should be documented.

### Future research

The GDG identified some important questions that need to be answered:

- Is amitriptyline a clinically and cost effective prophylactic treatment for recurrent migraine?
- Is pizotifen a clinically and cost effective prophylactic treatment for recurrent migraine?
- Is topiramate a clinically and cost effective prophylactic treatment for recurrent cluster headache?
- Can a psychological intervention such as cognitive behavioural therapy improve headache outcomes and quality of life for people with chronic headache disorders?
- Can a course of steroid treatment or drugs used for headache prophylaxis help people with medication overuse headaches withdraw from medication?

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Cite this as: *BMJ* 2012;345:e5765

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## Table

**Table 1 | Diagnosis of tension-type headache, migraine, and cluster headache**

Headache feature	Tension-type headache		Migraine (with or without aura)		Cluster headache	
Pain location*	Bilateral		Unilateral or bilateral		Unilateral (around the eye, above the eye, and along the side of the head or face)	
Pain quality	Pressing or tightening (non-pulsating)		Pulsating (throbbing or banging in young people aged 12–17 years)		Variable (can be sharp, boring, burning, throbbing, or tightening)	
Pain intensity	Mild or moderate		Moderate or severe		Severe or very severe	
Effect on activities	Not aggravated by routine activities of daily living		Aggravated by, or causes avoidance of, routine activities of daily living		Restlessness or agitation	
Other symptoms	None		Unusual sensitivity to light or sound (or both), or nausea or vomiting (or both). †Aura symptoms can occur with or without headache; they are fully reversible, develop over at least 5 minutes, and last for 5-60 minutes. Typical aura symptoms include visual symptoms such as flickering lights, spots or lines, or partial loss of vision (or a combination thereof); sensory symptoms such as numbness or pins and needles (or both); and speech disturbance		On the same side as the headache: red or watery eye (or both); nasal congestion or runny nose (or both); swollen eyelid; forehead and facial sweating; constricted pupil or drooping eyelid (or both)	
Duration of headache	30 minutes to continuous		4-72 hours in adults; 1-72 hours in people aged 12-17 years		15-180 minutes	
Frequency	<15 days a month	≥15 days a month for more than 3 months	<15 days a month	≥15 days a month for more than 3 months	1 every other day to 8 per day, ‡ with continuous remission§ >1 month	1 every other day to 8 per day, ‡ with continuous remission§ <1 month in a 12 month period
Diagnosis	Episodic tension-type headache	Chronic tension type headache¶	Episodic migraine (with or without aura)	Chronic migraine with or without aura**	Episodic cluster headache	Chronic cluster headache

\*Headache pain can be felt in the head, face, or neck.

†See full guideline for further information on the diagnosis of migraine with aura.

‡The frequency of recurrent headaches during a cluster headache bout.

§The pain-free period between cluster headache bouts.

¶Chronic migraine and chronic tension-type headache commonly overlap; if the patient has any features of migraine, diagnose chronic migraine.

\*\*The National Institute for Health and Clinical Excellence has developed technology appraisal guidance on botulinum toxin type A for the prevention of headaches in adults with chronic migraine.<sup>6</sup>

Any child or teenager with symptoms that are unusual for him or her, or are persistent or unexplained, should be seen by a GP. If you are worried, make an appointment with your doctor.

➤ Please remember any child or teenager needing urgent medical help should be taken to the nearest emergency department or dial 999.

**10 children and teenagers are diagnosed with a brain tumour every week in the UK. That's more than one a day.**

**Early diagnosis of brain tumours can save lives.**

HeadSmart is funded and promoted by The Brain Tumour Charity and run in partnership with the Children's Brain Tumour Research Centre (CBTRC) and the Royal College of Paediatrics and Child Health (RCPCH).

If you would like to talk to someone about brain tumours, please contact the Support & Info Line at The Brain Tumour Charity on:

Freephone

**0800 800 0004**

or email

**[support@thebraintumourcharity.org](mailto:support@thebraintumourcharity.org)**

**[headsmart.org.uk](http://headsmart.org.uk)**

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# HEAD SMART

## EARLY DIAGNOSIS OF BRAIN TUMOURS

**symptoms card**

This card is designed to help you know and spot the signs and symptoms of brain tumours in children and teenagers.

## BABIES

UNDER 5 YEARS



Persistent/recurrent vomiting



Balance/co-ordination/  
walking problems



Abnormal eye movements  
or suspected loss of vision



Behaviour change,  
particularly lethargy



Fits or seizures (not with a fever)



Abnormal head position such  
as wry neck, head tilt or stiff neck



Increasing head circumference  
(crossing centiles)

If your child has one of these, see your doctor,  
if two or more, ask for an 'urgent referral'



## CHILDREN

5 - 11 YEARS



Persistent/recurrent headache



Persistent/recurrent vomiting



Balance/co-ordination/  
walking problems



Abnormal eye movements



Blurred or double vision/  
loss of vision



Behaviour change



Fits or seizures



Abnormal head position such  
as wry neck, head tilt or stiff neck

If your child has one of these, see your doctor,  
if two or more, ask for an 'urgent referral'



## TEENS

12 - 18 YEARS



Persistent/recurrent headache



Persistent/recurrent vomiting



Balance/co-ordination/  
walking problems



Abnormal eye movements



Blurred or double vision/  
loss of vision



Behaviour change



Fits or seizures



Delayed or  
arrested puberty

If you or your child has one of these, see your  
doctor, if two or more, ask for an 'urgent referral'

