CHILDREN'S headache training

CHaT 1

Pre-course handbook

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British Paediatric Neurology Association

Thank you for booking on a place at the CHaT1 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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1. CHaT1 Course Programme

2. Howells R. Headache in Childhood and Adolescence. *ACNR*. 2010; 10(5): 27-29
   A recent review article condensing core material from this course

3. Carville S et al. Diagnosis and management of headache in young people and adults: summary of NICE guidance. *BMJ*. 2012; 345: e5765

4. Viswanathan V et al. Childhood headaches: discrete entities or continuum? *Developmental Medicine & Child Neurology.* 1998; 40: 544-550

   Read this in conjunction with Lipton's paper in preparation for the afternoon debate

5. Lipton RB, Cady MD, Stewart WF, Wilks K, Hall C. Diagnostic lessons from the spectrum study. *Neurology.* 2002; 58 (Suppl 6): S27-S31

   Read this in conjunction with Viswanathan's paper in preparation for the afternoon debate

6. HEADSMART be brain tumour aware (from www.headsmart.org.uk)
   Summary of indicators for brain tumour in childhood

CHaT1 Timetable

Timing	*Title*	*Format*
8.45 – 9.15	*Registration with tea & coffee*	
9.15 – 9.30	Introduction	Lecture
9.30 – 9.50	Epidemiology & Classification	Lecture
9.50 - 10.20	History & Examination	Lecture
10.20 – 11.15	Important Secondary Headaches & Red Flags	Workshop
11.15 – 11.35	*Tea & coffee break*	
11.35 – 12.15	Migraine – pathophysiology, classification, variants	Lecture
12.15 – 13.00	Treatment of migraine	Workshop
13.00 – 13.45	*Lunch*	
13.45 – 14.15	Other primary headaches: tension-type, chronic daily headache including medication overuse, a bit on TACs	Lecture
14.15– 15.00	Other primary headaches – management (especially TTH, MOH)	Workshop
15.00 – 15.30	*Tea & coffee break*	
15.30 – 16.15	Migraine and tension-type headache: same or different?	Debate
16.15 – 16.45	Service delivery	Lecture
16.45 – 17.00	Summing up / Close	Lecture

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CHaT 1

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.[1]

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.[2]

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[3]. 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 >18cmH2O (age<8y with papilloedema) and >25cmH2O (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).[4]
- 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.[5]
- 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.[6,7]
- 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.[8]
- Recurrent short-lived limb pain in childhood (usually lower limb pain sufficient to prevent usual activities, lasting <72h and not attributable to another cause).[9]

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.[10] 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.[11]

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.[12,13] 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.[14] 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.[15] 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[16] (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,[17,18] association with other somatic symptoms and difficulties with family relationships.[19] 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.[20]
- Amitriptylline – 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.[21] Children and adolescents with medication-overuse frequently respond to medication withdrawal within a month.[22]

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.[23,24] 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.[25]

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.[1 2] 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.[3]

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*]

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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*][4]

- 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*][4]

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.

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[*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,[5] 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.

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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). 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). 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) 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.[7]

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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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.[6]

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Childhood headaches: discrete entities or continuum?

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The aims of this study were to investigate the signs and symptoms of recurrent headaches in children and to identify if there are any discrete groups of children whose headaches corresponded to the World Federation of Neurology (1969) definition of migraine. One-hundred and fifty children recruited from the neurology clinics at Royal Manchester, Booth Hall, and Birmingham Children's Hospitals were interviewed to complete a standardized questionnaire. The data were examined using cluster analysis followed by comparative analysis of the headache signs and symptoms in the different groups identified. No stable groups were identified (i.e., no group was reliably identified by different methods of cluster analysis) which corresponded to the World Federation of Neurology definition of migraine. This would suggest that this definition is not appropriate for the sample investigated. Three groups of children evolved after cluster analysis. None of these groups was in agreement with the International Headache Society classification of headaches. The groups were neither 'stable' clusters nor 'useful' in predicting prognosis. This outcome supports the continuum theory of headache syndromes.

Headaches in otherwise healthy children are common (Table I). Migraine is commonly considered as having three cardinal components: (1) a unilateral site; (2) associated gastrointestinal symptoms; (3) prodromal symptoms (aura). The relative importance of each of the components and the way in which they relate to each other has yet to be elucidated and a number of definitions of migraine has been proposed over the years.

Passchier et al. (1985) and Mindell et al. (1987) found an overlap of characteristics between the various traditional headache categories in children and were of the opinion that the two major forms of headache – migraine and tension headache – cannot be separated. Hockaday (1982, 1988) suggested that recurrent paroxysmal headaches in children should be accepted as migraine provided there is return to normal health, both mental and physical, between attacks and that other causes of headache have been excluded. She recognized that the distinction between migraine and tension headache is unclear and that both might coexist. Waters (1973), an epidemiologist, said '..it is important not to readily accept as a definite clinical entity, something that we cannot readily define'. In view of these findings the continuum theory was described.

The continuum theory suggests that tension- and migraine-type headaches are at extreme ends of a symptom spectrum rather than being individual discrete entities. Waters (1973) suggested that there is an increment in reported migraine symptoms with increasing headache severity. This would explain how migraine and tension headaches can coexist, why there are so many intermediate cases, and how the clinical and epidemiological data recently reviewed by Leston (1996) fail to identify tension-type headache and migraine as discrete entities. This has provided a new generation of definitions that lead to a much broader picture of migraine.

Whether or not migraine is a discrete clinical entity has implications for the following: (1) Information given to parents with regard to treatment and headache prevention. (2) Research – for example, in the past tension-headache patients have been used as controls for migraine patients. If both actually belong to the same symptom spectrum, this would invalidate any results obtained by such studies. (3) Treatment regimes for both types of headaches may be altered. (4) Aetiology – if migraine were a distinct clinical entity it would imply that it is due to a specific cause.

In 1988 the International Headache Society (IHS) (Olesen 1988) defined a classification and diagnostic criterion for headache disorders. The classification is based on a hierarchical system, rather as in the International Classification of Disease whereby coding up to four digits makes it possible to use the classification at different levels of sophistication. The result was seven migraine types which could be split further into a total of 10 syndromes. Similarly, tension headache was divided into three major groups which were split into a total of four subsets. Having so many varieties of tension- and migraine-type headaches could indicate that the continuum theory is probably more appropriate, each definition representing a single point on the headache continuum.

In an evaluation of the validity of the IHS classification of migraine by Merikangas et al. (1994), the symptoms that provided the best discrimination between migraine and other headache subtypes were photophobia, phonophobia,

and osmophobia, in combination with gastrointestinal symptoms. Two symptoms – osmophobia and difficulty in thinking during the attacks – had greater values for specificity and sensitivity than some of the current IHS criteria, such as pulsating quality and mild intensity. Seshia et al. (1994) and Seshia and Wolstein (1995) have suggested other modifications to the IHS criteria to be able to apply them to the paediatric population on a whole notably by using the term 'clinically probable' in the frequent cases where not all diagnostic criteria are met. They also suggest that a combination category of coexisting migraine- and tension-type headache be recognized.

The aims of this study were to: (1) Investigate if there are any discrete groups of symptoms within a single sample of children with recurrent headaches. These groups of symptoms will be examined to see if any correspond to either the IHS or World Federation of Neurology (1969) definition of migraine. (2) Examine the symptoms experienced by these subjects to contribute to the current knowledge about the childhood-headache syndromes. (3) Analyse the signs and symptoms experienced by the subjects between the groups and also within the groups.

Method

We recruited 150 children to the study from the neurology clinics at Royal Manchester, Booth Hall, and Birmingham Children's Hospitals. These children were consecutive first-time presenters with recurrent headaches of no known physical cause. All the children in the study had yet to undergo any form of treatment other than simple analgesia.

All the children were interviewed by one of the authors and a standardized questionnaire developed by the authors (see Appendix) during a pilot study was completed. If a question could not be answered by the child, one of their parents was consulted. Although the variables were marked on the questionnaire as never, sometimes, often, or always present according to the child's report during the interview, they were interpreted as either present or absent for ease in the primary analysis.

The frequency of distribution of the variables in the whole group was analysed. The symptoms were then subjected to cluster analysis. Cluster analysis is a technique that sorts the cases under consideration into groups so that the degree of association is high between members of the same group and low between members of different groups. A hierarchical agglomerative method is used where there is successive fusion of the cases into groups and those groups into larger groups. The process culminates when all the individuals are in a single group. At any particular stage, the groups that are fused are those which are closest or most similar in terms of symptom combination. The resulting solution is represented by a dendrogram which is a two-dimensional diagram illustrating the fusions which have been made at each successive stage of the analysis. The cluster analysis was carried out using three different methods – Ward's, single linkage, and average linkage.

During the interview with the children we were very precise about the use of language. For example, we were careful to indicate that a description such as 'throbbing' was being used in the sense of a pulsating or rhythmical banging rather than in the sense of very bad headaches. When a child was unsure of what to say they were not coaxed into a prejudged model or category defined by the doctor.

The questionnaire also defined a headache-severity score. Children were asked to define whether they 'Never', 'Sometimes', 'Often', or 'Always' had to: 'Go to bed', 'Stop what they were doing', 'Do much less than usual', or 'Could carry on what they were doing'. A severity score with a maximum of 12 was derived from their responses. Additionally a yes/no response was recorded against whether a child never had to stop what they were doing due to a headache.

Results

Of the 150 children enrolled in our study, 85 were male. The age range of the sample was 4 to 18 years; the mean age was 12.1 (SD 3.9) years.

Bilateral headaches were seen in 72.7% of children. Although the majority of the children complained of experiencing only one type of headache, 25.3% of them had two or three types of headache. Fifty-nine children (39.3%) described their headaches as pulsating or throbbing in character and 33 (22%) as pressing. Headaches were described as both throbbing and pressing by 14 (9.3%) children, whereas 55 (36.7%) subjects described various other characteristics, e.g. dull and 'like poking needles into my head'. Some were unable to describe their headaches clearly. Aura was experienced by 51 (34%) of the children. There was a positive family history of recurrent headaches in 59.4% of the children. Table II summarizes the frequencies of signs and symptoms.

CLUSTER ANALYSIS

Full data sets were available on 147 of the study children who were the subjects of the study analysis. Three children were excluded due to inadequate data sets. Dendrograms were produced to illustrate the progression of the agglomerative procedure. At the agglomerative stage before the three-group stage there were 10 groups identified by Ward's method. At this stage the clustering of cases varied greatly between the solutions identified by the average-linkage and single-linkage methods. The next agglomerative step led to three groups using Ward's method, greater concordance with average linkage but little with single linkage. The single-linkage analysis revealed no stable clusters. The average-linkage analysis gave five clusters, essentially by subdividing

Table I: Headache prevalence studies

Author	*Age (y)*	*Sex*	*Non-migraine (%)*	*Migraine (%)*	*Headaches in previous year (%)*
Valquist (1955)	10–12	M, F	13.3	4.5	
Bille (1962)	7–10	M	4.2	2.9	51
	11–15	M	7.6	3.7	66
	7–10	F	4.2	2.6	50
	11–15	F	11.2	6.2	69
Waters (1974)	10–16	M		9.0	85
	11–15	F		10.5	93
	10–16	F		12.0	93
Sparks (1978)	10–18	M		3.4	
	10–18	F		2.5	

group 1 (Ward's method) into those with predominantly visual as opposed to other associated symptoms which were neurological; and defining a very small group of children with a wide diversity of symptoms which did not readily fit into the other groups.

As the next step linked all the groups in the study, further analysis is based on the three groups identified using Ward's analysis at the fifth cluster-combination stage. The characteristics of these three clusters are shown in Table II.

Group 1

Most children in this group of 35 children (22 males, 13 females) experienced unilateral (80%) and pulsating (68.6%) headaches. Most experienced nausea (97.1%) and vomiting (65.7%). Phonophobia and photophobia were common. A positive family history of headaches was found in 62.9% of children.

Group 2

There were 27 children in this group (13 males, 14 females). They all had bilateral headaches described as being dull, stabbing, or more elaborate descriptions were given such as, 'like an eel swimming in my head'. Most complained of associated nausea (85.2%) and vomiting (44.4%). Visual symptoms like blurring of vision (63%), double vision (77.8%), and flashing lights (85.2%) were common. Associated features such as pallor or a runny nose were common in this group. A family history of a first-degree relative with headaches was found in 74.1% of children.

Group 3

This was the largest group with 85 children (48 males, 37 females). Bilateral headaches were seen in 87.1% of children. The character of the headaches was described as pulsating, pressing, or other in almost equal distribution. Most experienced nausea (63.5%) and some had vomiting (41.2%). The incidence of other associated symptoms was low. Pallor was described in 52.9% of the children. Family history of headaches was positive in 55.3% of children.

PRODROMAL SYMPTOMS

Aura was experienced by 34% of children. The prevalence of aura did not vary significantly among the three clusters. They were described variously as 'a funny feeling in my head', feeling hot, seeing flashes of light, 'an unusual feeling in my head', 'slight pain between my eyes', with several other variations.

TYPES OF HEADACHE

Only one type of headache was seen in 109 (74%) of the children. Two types of headache were reported by 32 (21.3%) of the children and six children (4%) had three types. One child (group 3) had a dull headache which persisted all the time with periods of unilateral headaches of pulsating character associated with nausea, vomiting, spinning sensations, and blurring of vision. The same child also complained of sharp headaches in the frontal region not associated with any other associated symptoms. This is typical of the children who complained of three types of headaches.

Table II: Cluster groups by variables

	Variables	*Group 1* N=35 (%)	*Group 2* N=27 (%)	*Group 3* N=85 (%)	*Entire sample* N=147 (%)
Character	Pulsating	68.6	18.5	32.9	39.3
	Pressing	11.4	7.4	30.6	22.0
	Other	17.1	51.9	40.0	36.7
Distribution	Unilateral	80.0	11.1	12.9	27.3
	Bilateral	17.1	100.0	87.1	72.7
Gastrointestinal	Nausea	97.1	85.2	63.5	75.3
	Vomiting	65.7	44.4	41.2	48.0
Aura		28.6	25.9	40.0	34.0
Neuro dysfunction	Spinning	45.7	77.8	32.9	44.0
	Paraesthesia	34.3	29.6	12.9	20.7
	Paresis	2.9	3.7	5.9	4.7
Auditory dysfunction	Loss of hearing	2.9	7.4	12.9	9.3
	Phonophobia	57.1	40.7	17.6	32.0
Visual disturbance	Blurred vision	31.4	63.0	30.6	36.7
	Double vision	5.7	77.8	9.4	21.3
	Loss of vision	0	18.5	1.2	4.0
	Photophobia	51.4	44.4	18.8	31.3
	Flashing lights	11.4	85.2	12.9	25.3
Other symptoms	Pallor	85.7	77.8	52.9	65.3
	Runny nose	25.7	51.9	17.6	26.2
	Puffy eyes	28.6	18.5	19.0	21.5
	Red eyes	25.7	25.9	21.4	22.8
Family history		62.9	74.1	55.3	59.4
Headache types	One				74.0
	Two				21.3
	Three				4.0

NEUROLOGICAL DYSFUNCTION

Spinning sensation was the commonest neurological dysfunction described in 44% of the children. Children in group 2 experienced the most neurological dysfunction. Paraesthesia and paresis were much less common.

GASTROINTESTINAL SYMPTOMS

Nausea was the commonest associated symptom experienced with the headaches (75.3%). Almost all the children in group 1 had nausea with the headaches. Vomiting was present in 48% of children in the whole sample.

AUDITORY AND VISUAL SYMPTOMS

Phonophobia was present in 32% of children but actual loss of hearing was very rare. Children in group 2 experienced the most visual symptoms – blurring (63%), double vision (77.8%), flashing lights (85.2%). The incidence of micropsia and loss of vision was very small. Photophobia was seen in 46 (31.3%) of the whole sample.

DURATION OF HEADACHES

The median duration of headaches was around 7 hours (range 0.2 to 96.0 hours) with wide variations. One child reported sharp headaches lasting around 2 minutes intermittently. There was no significant difference in the duration of headaches between group 1 (median 4.0 hours, range 0.2 to 96.0 hours), group 2 (median 8.0 hours, range 1.0 to 30.0 hours) and group 3 (median 4.0 hours, range 0.2 to 96.0 hours).

FREQUENCY OF HEADACHES

The median frequency of headaches in the whole sample was 7.0 headaches per month. There was no significant difference in headache frequency between the three groups: group 1 (median 7.3, range 1.0 to 30.0), group 2 (median 7.5, range 1.0 to 30.0), and group 3 (median 5.15, range 0.5 to 30.0). Headaches occurring every day of the month before a clinic visit were reported by 14.7% of the children in the study.

ASSOCIATED SIGNS AND SYMPTOMS

Pallor associated with headaches was reported as a prominent sign by 65.3% of the parents of children in our study. Red eyes, droopy eyelids, puffy eyelids, and a runny nose were some of the other associated signs reported by the children and their parents.

TRIGGER FACTORS

Trigger factors were identified by the child or parents for 39 children (26%). Parents of 14 of the children felt that foods like cheese, chocolate, cold drinks, or ice cream triggered the headaches. Exercise was reported as a trigger for 10 children. Other factors attributed were lack of sleep, reading, excitement, upsets at home or school, etc. One child reported 'pony-tail hair dressing' as a clear trigger for her headaches.

No significant differences were found (Mann–Whitney *U* test) when the three groups were compared for differences between recorded headache-severity scores: group 1, median 8.06 (range 4 to12); group 2, median 8.6 (range 3 to 12); and group 3, median 9.2 (range 3 to 12). In group 1, six children (17.1%) never had to stop activity with a headache; in group 2 this was true of one child (3.7%) and in group 3, of 17 children (20%). The observed differences between groups 1 and 3 in this respect were not significant but the differences between groups 2 and 3 were (P=0.033, Fisher exact test).

Discussion

The children in this study were a selected population in that they are hospital attenders, and therefore likely to be those children who have the most severe headaches. It could therefore be argued that they were more likely to have migraine- rather than tension-type headache. However, a previous audit of headache symptomatology in children attending our clinics indicated this not to be the case. This audit established that 36% had symptoms of tension-type headache, 36% had symptoms of migraine, and 28% had both, when the doctors they usually saw 'pigeon-holed' them into traditionally acknowledged groups. It can also be argued that the more severe headaches seen in hospital attenders are more likely to fit into readily defined groups.

Rasmussen (1996) suggested that a clinical interview would be much superior to a questionnaire-based study as the respondents cannot remain clear on the different types of headache when answering many questions. The experience from our present study would concur with that because although our consultation and interaction with the children and their families were questionnaire-based, the data were refined by personal interview.

The method of cluster analysis was chosen to help classify the subjects because it is not based on an already defined hypothesis. This prevents the possibility of observer bias trying to push subjects into groups in the context of a huge number of discrete variables. Latent class (factor analysis) would have been an alternative. This is better used, however, when many different measures (in this case observations) taken on a sample of people are explored to establish whether the measures are actually reflections of a smaller number of underlying factors: that is whether the symptoms can be grouped together in a specific way. In cluster analysis the focus is on whether the subjects can be grouped on the basis of their similarities. Cluster analysis has been used as a tool to help classification of headaches in the past by various authors (Diehr et al. 1982, Rossi et al. 1992). The present study showed three groups as revealed by Ward's method of cluster analysis (Everitt 1974).

We did not include headache frequency and duration in the cluster analysis because previous experience indicated these measures were unlikely to help us define the phenomenology. This opinion was born out when analysis identified no differences for these parameters between the study groups.

The majority of children in the study had bilateral headaches which would be in keeping with many of the previous studies of children (Congdon and Forsythe 1979, Barlow 1984, Gladstein et al. 1993, Seshia et al. 1994). Rossi et al. (1992) reported that 50% of the study population complained of the throbbing quality of their headaches. In the group of children we analysed, 39.3% of children described throbbing/pulsating headache. Nausea was the commonest associated feature occurring in 75.3% of the children. Children in group 1 mainly experienced hemicranial headaches of pulsating character associated

with gastrointestinal symptoms. Pallor and phonophobia were prominent symptoms in this group. Only 28.6% of these children had an aura. Under the IHS classification of headaches this group of children would fit into the category of having migraine headaches. On closer examination of the group, one realizes that in 31.4% of the children their headaches did not have a pulsating character, indeed 11.4% experienced a 'pressing' headache more characteristic of tension-type headache. Seventeen percent had bilateral headaches, very few had any associated visual symptoms other than minor blurring, and none of them had any of the typical aura types described (Dalessio 1994). So of the 35 children in group 1, over one-third of them do not fit into a clear group as laid out by the IHS criteria.

In the present study all the children in group 2 had bilateral headaches. Nausea, spinning sensation, and visual symptoms such as blurring of vision, double vision, and flashing lights were predominant in this group. Most of the children in this group experienced headaches of characters other than pulsating or pressing. This group of children would not fit into any of the typical groups described in the IHS criteria. Although these children experience a high proportion of associated symptoms fitting a definition of common migraine a number of other features such as the character of the headaches and the bilateral nature of the headaches are not typical.

The children in group 3 experienced mainly bilateral headaches associated with nausea but very few other symptoms. There was an equal distribution of children with pulsating or pressing headaches, or with headaches with other characteristics in this group. Eighty-five of 147 children were in this group. Again, there was difficulty in attempting to fit these children into a unifying diagnosis. It was also noted that 25.3% of the children in the whole group experienced more than one type of headache.

The findings of the present study would suggest that the emphasis of a definition should be on the signs and symptoms associated with the headache rather than the headache itself. The most useful classification clinically would be one that predicted specific factors such as the course of the headache, response to various treatments, and prognosis. This would allow a firm diagnosis and management plan to take place. The groupings that were obtained in this study were: (1) not stable, that is not reproduced by other methods of clustering; (2) not clinically 'useful'; (3) not in concordance with any of the typical groups described by the IHS criteria. A number of children also experience varying character, duration, and types of headaches at different times. These factors, together with the fact that an individual child can experience nausea, vomiting, or neurological symptoms with headache described as 'pressing' (traditionally tension-type), are all in keeping with the continuum theory of headaches (Bakal et al. 1979, Featherstone 1985, Marcus 1992). This has migraine-like features at one end of the spectrum and tension headaches at the other.

Conclusions

Cluster analysis failed to identify any stable groups of symptoms in our clinic-attenders that correspond to the World Federation of Neurology definition of migraine. This would suggest that this definition is not appropriate for this sample of children. Furthermore, the clusters that were identified did not correspond to any of the typical groups as laid down by the IHS. The IHS classification of headaches may not be appropriate for paediatric headache disorders. The lack of formation of stable clusters and the fact that none of the groups that was formed corresponded to the detailed IHS classification of headache disorders, would support the continuum theory of headache disorders. Finally we conclude that it seems not to be the severity of the headache which determines polarity within the symptom spectrum.

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Appendix

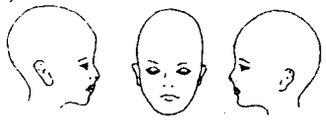
Questionnaire

NAME: DATE OF BIRTH:
HOSPITAL: HOSPITAL NO:

How many different sorts of headache do you experience?
No:

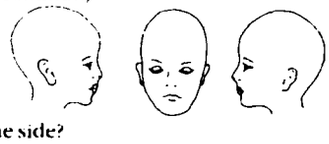
Can you describe them please?

SITE
TYPE A (most common)



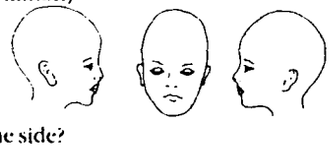
SHADE IN AREA
Is it always on the same side?

TYPE B (second most common)



Is it always on the same side?

TYPE C (third most common)



Is it always on the same side?

FREQUENCY
In the last 8 weeks – How many headaches of each type have you had?

	A	B	C

COMMENTS:
e.g. Headaches every day.

Do any of the following happen with your headaches?
(enter headache type A, B, or C)

	Never	Sometimes	Often	Always
Feeling sick				
Being sick				
Feel worse with bright lights				
Feel worse with noises				
Spinning round feeling				
Noise in ears				
Loss of hearing				
Funny vision				
Double vision				
Flashing lights				
Black/white				
Coloured balls				
Unsteadiness				
Difficulty with movement (state distribution)				
Difficulty with feeling unusual sensations anywhere (state distribution)				
Feel the need to sleep				
Relieved by sleep				
A warning of any sort				

AURA
If there is a warning what form does it take?
Details of symptoms:
State whether bilateral/unilateral
How long does it usually last?
Shortest:
Longest:

Is there a gap between warning and headache?
If yes, how long – usually:
shortest:
longest:
Persistent symptoms, which continue after headache has ceased
Detail: Unilateral/Bilateral
How long does it usually last?
Shortest:
Longest:
Frequency in last – 8 weeks
6 months
12 months

FAMILY HISTORY
Does your mother, father, brother or sister have troublesome headaches?
Which is your best hand?

QUALITY
How would you describe the pain? – Use child's own words
TYPE A
TYPE B
TYPE C
If helpful response – Ask:
In a typical bout is there head pain? (Y/N)

	TYPE A	TYPE B	TYPE C
Pulsating, throbbing or banging?			
Pressing or tightening?			
More sharp & localised?			

DURATION (mins)	TYPE A	TYPE B	TYPE C
How long does the headache usually last?			
What is the shortest duration?			
What is the longest duration?			

TRIGGERS
Do any of your headaches have a triggering factor?
(enter headache type)

	Never	Sometimes	Often	Always
Enter factor				

SEVERITY
What effect do your headaches have on you?
(enter headache type)

	Never	Sometimes	Often	Always
Have to stop what you are doing?				
Go to bed?				
Do much less than usual?				
You can carry on what you are doing?				

VISIBLE AUTONOMIC DISTURBANCE:
(enter headache type)

	Never	Sometimes	Often	Always
Goes pale				
Eye goes red				
Eye cries or waters				
Nose feels stuffy on that side				
Nose runs on that side				
Face of forehead feels sweaty				
Pupil alters size				
Eyelid droops				
Eyelid is swollen or puffy				

WHICH SIDE? Lt
Rt

Do any of your warning/after – or visible autonomic features ever happen on their own?

	Never	Sometimes	Often	Always

DETAIL:
(try to enter frequency)

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Diagnostic lessons from the Spectrum Study

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Article abstract—Migraine is a heterogeneous condition that causes symptoms that vary both among individuals and within individuals from attack to attack. We examined and reviewed several important lessons on the diagnosis of migraine learned from the distribution of headache types and patterns of treatment response in the Spectrum Study, including recruitment and diagnostic issues. The accuracy of an initial diagnosis, assigned by a clinician in the context of a clinical trial, was compared with the results of a final diagnosis, assigned by a neurologist, reviewing the initial evaluation as well as headache diaries for up to 10 attacks. Several lessons can be learned from the Spectrum Study. Recruitment difficulties teach us that disabling tension-type headache is difficult to find, suggesting that it is rare. Examination of the final diagnosis given after diary evaluations suggests that a diagnosis of migraine can usually be confirmed for patients with disabling headache. After reclassification of the final sample of 432 subjects, 24/75 (32%) patients initially clinically classified as having disabling episodic tension-type headache proved to have migraine or migrainous headache after a diary review. Among study participants, 90% of subjects with disabling headache (HIMQ score >250) had a migraine-related disorder. Treatment response suggests that, in migraineurs, tension-type headaches may have a pathophysiology similar to that of migraine. The diary data show that mild headaches in patients with disabling migraine often evolve into full-blown migraine. The Spectrum Study supports the view that, for patients with disabling episodic headache, migraine is often the correct diagnosis. In clinical practice, the suspicion of migraine should be high for patients experiencing episodic disabling headache. Assessment of headache-related disability may assist practitioners in making a diagnosis of migraine.

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Migraine is a common neurobiological disorder that affects 11 to 13% of the United States adult population.[1,2] According to the American Migraine Studies, the proportion of migraine sufferers who report a physician diagnosis of migraine in the United States has increased from 38% in 1989 to 48% in 1999.[3,4] This modest improvement in diagnosis is disappointing because more than half of the migraine sufferers meeting International Headache Society (IHS) criteria reported that they had never received a diagnosis of migraine.[3,4] In addition, despite the development of effective treatment strategies and guidelines, many migraine sufferers do not receive appropriate therapy.[3-5] Only 29% of migraine sufferers in the United States are currently very satisfied with their usual acute treatment.[5]

Migraine itself is a heterogeneous condition that causes symptoms that vary both among individuals and within individuals from attack to attack. Migraineurs may experience headache attacks of several types, including full-blown migraine with or without aura, migrainous headache, and episodic tension-type headaches (ETTH).[6,7] As part of the Spectrum Study,[7,8] issues concerning the diagnosis and treatment of migraine were evaluated. The accuracy of an initial diagnosis assigned by a clinician in the context of a clinical trial was compared with the results of a final diagnosis assigned by a neurologist who reviewed diary data but was blinded to the initial diagnosis. The methods of the Spectrum Study are reviewed here in brief but are published in full elsewhere.[7]

The Spectrum Study enrolled patients in one of three diagnostic groups (migraine, migrainous, and episodic tension-type headache) as defined by the IHS criteria.[7] Only patients who had substantial headache-related disability, as defined by a Headache Impact Questionnaire (HImQ) score of greater than 250 at screening, were eligible for study participation.[9,10] The HImQ is the forerunner of the Migraine Disability Assessment (MIDAS) questionnaire.[11-13] It measures headache severity by examining a composite of pain intensity and lost-time in various roles including work, household work, family, social and leisure activities. HImQ scores reflect headache frequency, pain intensity, and activity limitations over a 3-month period. Scores are highly correlated with both MIDAS and the Headache Impact Test (HIT).[14,15]

The enrollment requirement of an HImQ score greater than 250 was selected because it identifies the most disabled half of migraine sufferers in the general population. The investigators presumed that

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Table *Predicted types of attacks by initial IHS diagnosis*

IHS Diagnosis	Predicted attack type		
	Migraine	Migrainous	Tension-type headaches
Migraine	+	+	+
Migrainous	−	+	+
Tension-type headaches	−	−	+

therapy would be indicated for individuals whose primary headaches were that severe. We sought to determine whether the headache diagnosis of the patient, the characteristics of the individual headache attacks, or both would be most predictive of treatment response.[7,8]

At the screening visit, eligible patients were assigned to one of three mutually exclusive diagnostic groups by a clinical headache expert after a careful assessment. Diagnoses were assigned hierarchically. For example, patients who meet criteria for both migraine and tension-type headache were assigned to the migraine group.

We predicted that patients with migraine would have three types of attacks, that patients with migrainous headache would have two types of attacks, and that patients with tension-type headache would have only one type of attack (table). On review of the treatment diaries, we were surprised to find that some patients in the ETTH group had migrainous attacks as well as attacks of full-blown migraine. Similarly, some patients in the migrainous group unexpectedly had migraine attacks.

We decided to review all patients whose headache experience, as recorded in the study diaries, was incompatible with the initial diagnosis. An independent neurologist–headache specialist (KW), who did not have access to treatment results, conducted the review. The neurologist applied IHS criteria to the information available from the initial diagnostic interview and from the baseline headache features recorded in the headache diary. Here we examine some of the recruitment issues we experienced in this study. Then we examine the lessons learned regarding headache diagnosis by examining headache characteristics as well as treatment response.

Lesson 1: Disabling tension-type headache is difficult to find, suggesting that it is rare. We planned to enroll 200 migraine sufferers, 150 individuals with migrainous headache and 100 subjects with episodic tension-type headache. Two of three study sites recruited using telephone screening of the general population and by advertising. The third site recruited from a headache subspecialty center and by advertising. We were not able to meet our recruitment goals for disabling ETTH. Despite the fact that tension-type headache is four times more common than migraine,[16,17] we easily filled the migraine stratum of the study and had great difficulty filling the tension-type headache study. We had previously recruited large numbers of patients for tension-type headache studies when there was no requirement for disability.

The difficulty in recruiting arose because episodic tension-type headache sufferers with HImQ scores of greater than 250 were extraordinarily difficult to find. About half of migraine sufferers have this level of disability, yet only a small proportion of tension-type headache sufferers reach it. Because the recruitment denominator is not known we cannot provide precise statistics, but it is clear that disabling ETTH is much less common than disabling migraine.

Lesson 2: A diagnosis of migraine can usually be confirmed on the basis of diary data in patients with disabling headache. Based on the initial diagnosis, the treatment groups included migraine (58%), migrainous (25%), and ETTH (17%) (figure 1). In our classification algorithm for patients, migraine trumps migrainous, which trumps tension. The classification algorithm for individual attacks differs in that tension trumps migrainous. Using headache diaries, we found that, in the migraine group, subjects who treated attacks almost always had at least one attack of full-blown IHS migraine. Hence, an initial diagnosis of migraine in patients with disabling headache, in the context of this study, can almost always be confirmed.

Lesson 3: When patients with a diagnosis of disabling IHS migraine have headaches that meet criteria for migrainous or tension-type headache, these headaches often have a mechanism related to migraine. Of patients with an initial diagnosis of disabling migraine headaches, the distribution of headache attack types was as follows: migraine (70.5%), migrainous (6.5%), and tension-type headache (23%). Thus, the Spectrum Study supports the continuum model of headache for persons with migraine, in which ETTH, migrainous, and migraine headaches occur along a spectrum of headache presentations in migraineurs. Such attacks appear to be pathophysiologically related in migraineurs. This result supports the view of John Graham, who argued that migraine sufferers had mechanistically related big headaches (phenotypic migraine) and small headaches (phenotypic tension-type headache).[18] However, ETTH in individuals without IHS migraine may have a biologically distinct mechanism. It is also possible that disabling ETTH in individuals without IHS migraine is biologically similar to migraine and that such persons have headaches that run their course more quickly with or without treatment. We fully discuss the pathophysiologic and diagnostic implications of these findings elsewhere.[7]

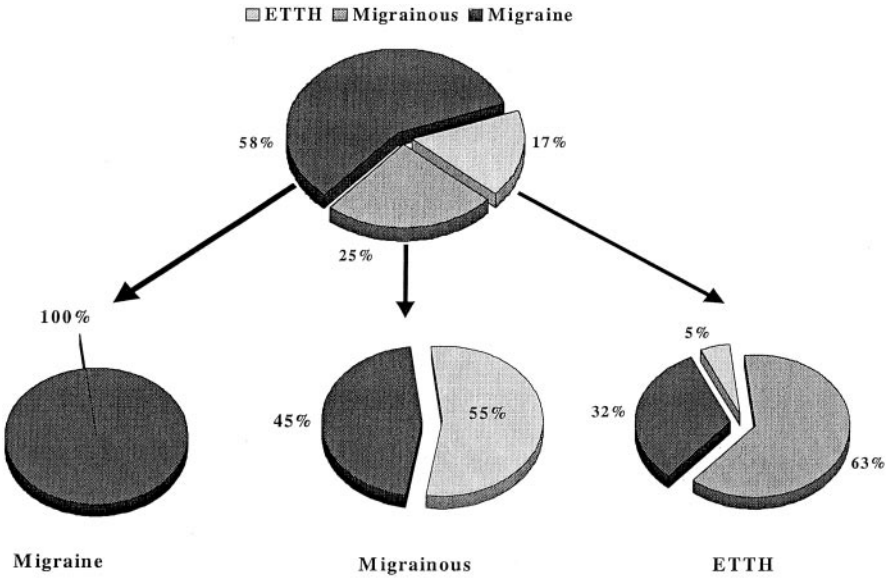

Figure 1. Initial clinical diagnosis compared with final headache diagnosis based on diary review.

Lesson 4: When a diagnosis of disabling ETTH is assigned even by a headache expert, patients often prove to have migraine based on diary review. Of the 75 subjects with an initial diagnosis of disabling ETTH, after diary review 24 (32%) were assigned a diagnosis of IHS migraine, four (5%) had migrainous headaches, and 47 (63%) remained in the ETTH group. What accounts for these unexpected discrepancies between the initial clinical and diary-based diagnoses? The initial diagnostic assessments were rigorous and were based on a careful interview, examination, and application of IHS criteria. The study clinicians were all headache specialists with years of diagnostic experience. Furthermore, each study site and each study clinician had patients re-classified based on the diary review. It therefore appears most unlikely that the need for diagnostic re-classification reflects carelessness or incompetence on the part of the study clinicians. It is much more likely that headache features reported at the time of the initial visit and the features recorded in the headache diaries were different.

Why would the reported headache features change? Perhaps the completion of headache diaries induced false-positive symptom reporting. Patients completing the diaries may have noticed and reported very mild features (i.e., throbbing, nausea, photophobia), features they did not recall when their histories were taken and features that led to "overdiagnosis" of migraine. The results, based on treatment, suggest that this is not the case. Sumatriptan is more effective than placebo as an acute treatment for migraine attacks in persons with IHS migraine. In persons initially diagnosed with tension-type headache but re-classified as migraine, sumatriptan was similarly effective. This finding suggests that re-classified patients truly had migraine. If the diaries had generated false-positive migraine diagnoses, we would have expected sumatriptan to be ineffective in these patients.

Another possible reason for the discrepancy may have resulted from our requirement of patients to withhold intervention until their headaches were moderate to severe. Before entering the study, many may have initiated treatment earlier in the headache process with over-the counter medications. These interventions may have modified the natural evolution of their headache. By structuring treatment and asking patients to wait until the headache was at least moderate, we may have "uncovered" migraine symptoms.

Lesson 5: In patients with disabling migraine, mild headaches often evolve into full-blown migraine. In the Spectrum Study, 26 migraine sufferers violated the protocol and treated at least one attack while the pain was mild. These 26 patients treated a total of 212 headaches, 46 headaches while pain was mild and 166 headaches while pain was moderate or severe. Fifty percent of the headaches (3/6) treated with placebo during mild pain worsened to moderate pain intensity within 1 hour of treatment.[8]

The likelihood for the progression from mild pain to moderate–severe pain observed in the Spectrum Study was confirmed in retrospective analyses of two other clinical trials and in a meta-analysis of the entire sumatriptan database.[19,20] These analyses showed that almost two-thirds of placebo-treated migraine attacks progressed to moderate or severe pain. Recent studies indicate that, over the course of a migraine attack, central and peripheral sensitization develops in many patients.[21,22] If pain can be stopped before sensitization occurs, the pain cascade common to acute migraine may be controlled, providing a possible biological substrate for the benefits of early treatment while pain is mild. Because this strategy is cost-effective on a treated-attack basis,[23] migraineurs with a high probability of progression from mild pain to moderate–severe pain should be

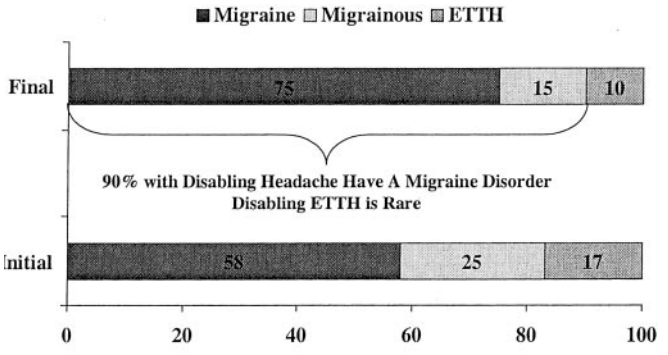

Figure 2. Implications on migraine diagnosis for patients with disabling headache.

instructed to treat their attacks early before this escalation occurs. Caution is required to avoid medication overuse.

Lesson 6: In clinical practice, the suspicion of migraine should be high for patients experiencing disabling episodic headaches. These results have important implications for the diagnosis and treatment of migraine in clinical practice. Disabling ETTH is hard to find, even in specialty practices. In the Spectrum Study, after evaluation by diary, 90% of subjects with disabling headache enrolled in the study had a form of migraine (migraine with aura, migraine without aura, or migrainous headache; figure 2). Although this result is derived from a selected sample, we devoted considerably greater effort to recruiting patients with disabling ETTH than to the other groups. These results support that the view, first promulgated by Jim Lance, that disabling episodic primary headache is probably migraine.[24] Assessment of headache-related disability could assist health-care practitioners in establishing a diagnosis of migraine. Other evidence from the literature supports the notion that headache disability is strongly linked to a migraine diagnosis. HImQ scores greater than 250 identify the upper half of migraine sufferers. Easier-to-use disability instruments, such as the Migraine Disability Assessment (MIDAS) and Headache Impact Test (HIT), are available for use. MIDAS scores greater than 12 and HIT scores greater than 50 have been shown to have high predictive value for migraine.[10,24] The high probability of the progression of mild pain to moderate–severe pain in patients with disabling migraine suggests that patients should be instructed to treat their attacks before this escalation occurs.

Discussion. The relationship of migraine to tension-type headache has long been one of the principal issues in the classification of primary headaches.[25-28] The IHS criteria assert that migraine and ETTH are distinct disorders.[29] Others have argued that migraine and tension-type headache differ in degree and not kind.[25-27] The Spectrum Study suggests that each of these views is partially correct.

Progress in headache classification requires that we distinguish between clinical symptomatic and etiologic approaches to classification. Clinical symptomatic classification systems are based on surface features, such as the pattern of pain and associated symptoms, referred to here as the headache phenotype. Etiologic classifications are based on the underlying biology of the disorders in question, referred to here as the headache biotype. With the exception of a few genetic forms of migraine, the biotypes for primary headaches are not known.

At the level of headache phenotype, the Spectrum Study demonstrates that, in patients with disabling episodic headache, a clinical diagnosis of migraine is usually correct. A clinical diagnosis of ETTH in patients with disabling headache proves to be incorrect in one-third of patients when the assessment uses a headache diary. We suggest that this reflects underreporting of migraine-defining features, at the time of the initial interview, in persons initially misdiagnosed with ETTH. It may also reflect the fact that patients attempt treatment before seeing a physician and that although those interventions may not prove clinically effective, they may limit or minimize certain clinical features that make symptom-based diagnosis difficult.

These results also suggest that, in persons with disabling migraine, phenotypic attacks of tension-type headache are of a migraine biotype. In contrast, pure ETTH is probably of a different biotype. Therefore, the same phenotype (ETTH) may reflect two different biotypes; in persons with migraine the biotype is related to migraine. In other words, migraine sufferers experience a spectrum of mechanistically related headaches including migraine, migrainous, and ETTH phenotypes. On the other hand, migraine and pure ETTH may be biologically distinct.

These results have several limitations. The clinical trial sample we evaluated was a sample of convenience. Systematic assessment of disability and diagnosis in representative primary care samples would be useful. In addition, inferring biotype from treatment response may be hazardous. It would be useful to have other methods (genetic, neuroimaging, and biochemical) for characterizing the biotypes of individuals and their attacks. Finally, migraine itself is likely to be biologically heterogeneous, and the headaches experienced by a given migraine sufferer may vary in biotype from attack to attack.

Despite these limitations, these results have implications for the primary care management of headache. Episodic, disabling primary headaches are usually migraine. Clinicians should maintain a high index of suspicion for migraine in headache patients with substantial headache-related disability. In a patient thought to have disabling tension-type headache, we strongly recommend using a headache diary to assess diagnosis. The present results suggest that

in about one-third of cases the patient will prove to have migraine.

Because mild attacks in patients with disabling migraine are likely to progress if untreated, patients should be treated early. The caveat is that all acute medications can cause medication-rebound headaches, so acute medications should be monitored to prevent the development of rebound headache.[30]

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

Fortunately brain tumours in children and young people are rare, but they happen.

- A quarter of childhood cancers occur in the brain
- Early detection of brain tumours can improve the outcome
- If you are worried you / your child has a brain tumour SAY this to your doctor
- The website www.headsmart.org.uk can provide further information, support and reassurance

If you are worried make an appointment with your doctor. Please remember any young person needing urgent medical help should be taken to the nearest emergency department or dial 999.

HEADSMART
be brain tumour aware

Any child with symptoms that are unusual for him or her, or are persistent or unexplained, should be seen by a GP. Please remember that any child needing urgent medical help should be taken to the nearest emergency department.
In an emergency dial 999.

The HeadSmart Campaign is run by a partnership between the Children's Brain Tumour Research Centre (CBTRC) at the University of Nottingham, the Royal College of Paediatrics and Child Health (RCPCH) and Samantha Dickson Brain Tumour Trust (SDBTT), and has been funded by The Health Foundation and SDBTT.

If you would like to talk to someone about brain tumours, or have been affected by the brain tumour symptoms campaign, please contact the support line at SDBTT on
0845 130 9733 or
e:mail: info@headsmart.org.uk

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HEADSMART
be brain tumour aware

HEADSMART
be brain tumour aware

This card will give you all the information you need to be brain tumour aware.

www.headsmart.org.uk

Under 5 Preschool

Brain tumours happen...
Symptoms include:

- Persistent / recurrent vomiting
- Balance / co-ordination / walking problems
- Abnormal eye movements
- Behaviour change, particularly lethargy
- Fits or seizures (not with a fever)
- 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"

5 - 11 Children

Brain tumours happen...
Symptoms include:

- Persistent / recurrent headache
- Persistent / recurrent vomiting
- Balance / co-ordination / walking problems
- Abnormal eye movements
- Blurred or double 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"

12 - 18 Young People

Brain tumours happen...
Symptoms include:

- Persistent / recurrent headache
- Persistent / recurrent vomiting
- Balance / co-ordination / walking problems
- Abnormal eye movements
- Blurred or double vision
- Behaviour change
- Fits or seizures
- Delayed or arrested puberty, slow growth

If your child has one of these, see your doctor
If two or more, ask for an "urgent referral"
Especially if growth or puberty is slow