4-year surveillance (2016)

Headaches in over 12s: diagnosis and management (2012) NICE guideline CG150

Appendix A: Summary of new evidence from surveillance

1.1 Assessment

150– 01	**For young people and adults with HIV presenting with new onset headache, how common are serious intracranial abnormalities?**
150– 02	**For young people and adults with a history of malignancy presenting with new onset headache, how common are serious intracranial abnormalities?**
150– 03	**For young people and adults presenting with early morning headache or new onset frequent headache that lasts for more than one month, how common are serious intracranial abnormalities?**

Recommendations derived from these questions

1.1.1 Evaluate people who present with headache and any of the following features, and consider the need for further investigations and/or referral*:

- worsening headache with fever
- sudden-onset headache reaching maximum intensity within 5 minutes
- new-onset neurological deficit
- new-onset cognitive dysfunction
- change in personality
- impaired level of consciousness
- recent (typically within the past 3 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. [2012]

1.3.2 Consider further investigations and/or referral if a person diagnosed with a headache disorder develops any of the features listed in recommendation 1.1.1.

1.1.2 Consider further investigations and/or referral 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. [2012]

* For information on referral for suspected tumours of the brain or central nervous system see the NICE guideline on suspected cancer.

Surveillance decision

No new information was identified at any surveillance review.

These questions should not be updated.

150– 04 What is the accuracy of case finding questionnaires for diagnosing primary headache disorders and medication overuse headache?

Recommendations derived from this question

The GDG decided not to make any recommendations for case finding questionnaires for the diagnosis of primary headache.

Surveillance decision

This review question should not be updated.

Evidence Update and 2-year surveillance summary
No relevant evidence was identified.

4-year surveillance summary
No relevant evidence was identified.

Topic expert feedback
A topic expert highlighted that there is new evidence related to a tool aimed to identify people with chronic migraine.

Impact statement
We did not identify new evidence relevant to this question.

New evidence is unlikely to impact on the guideline.

150– 05 What is the clinical effectiveness of using diaries for the diagnosis in people with suspected primary headaches and medication overuse headache?

Recommendations derived from this question

1.1.3 Consider using a headache diary to aid the diagnosis of primary headaches. [2012]

1.1.4 If a headache diary is used, ask the person to record the following for a minimum of 8 weeks:

- frequency, duration and severity of headaches
- any associated symptoms
- all prescribed and over the counter medications taken to relieve headaches
- possible precipitants
- relationship of headaches to menstruation. [2012]

Surveillance decision

No new information was identified at any surveillance review.

This review question should be not updated.

1.2 Diagnosis

150– 06 For young people and adults with headache, what are the key diagnostic features of the following headaches: migraine with or without aura; menstrual related migraine; chronic migraine; tension-type headache; cluster headache and medication overuse headache?

Recommendations derived from this question

Tension‑type headache, migraine (with or without aura) and cluster headache

1.2.1 Diagnose tension‑type headache, migraine or cluster headache according to the headache features in the table. [2012]

Headache feature	Tension-type headache	Migraine (with or without aura)	Cluster headache
Pain location[1]	Bilateral	Unilateral or bilateral	Unilateral (around the eye, above the eye and along the side of the head/face)
Pain quality	Pressing/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 and/or sound or nausea and/or vomiting **Aura** [2] Symptoms can occur with or without headache and: are fully reversible develop over at least 5 minutes last 5−60 minutes Typical aura symptoms include visual symptoms such as flickering lights, spots or lines and/or partial loss of vision; sensory symptoms such as numbness and/or pins and needles; and/or speech disturbance		On the same side as the headache: red and/or watery eye nasal congestion and/or runny nose swollen eyelid forehead and facial sweating constricted pupil and/or drooping eyelid	
Duration of headache	30 minutes–continuous		4–72 hours in adults 1–72 hours in young people aged 12–17 years		15–180 minutes	
Frequency of headache	< 15 days per month	≥ 15 days per month for more than 3 months	< 15 days per month	≥ 15 days per month for more than 3 months	1 every other day to 8 per day[3], with remission[4]> 1 month	1 every other day to 8 per day[3], with a continuous remission[4]<1 month in a 12-month period
Diagnosis	**Episodic tension-type headache**	**Chronic tension-type headache** [5]	**Episodic migraine (with or without aura)**	**Chronic migraine** [6]**(with or without aura)**	**Episodic cluster headache**	**Chronic cluster headache**

[1] Headache pain can be felt in the head, face or neck.

[2] See recommendations 1.2.2, 1.2.3 and 1.2.4 for further information on diagnosis of migraine with aura.

[3] The frequency of recurrent headaches during a cluster headache bout.

[4] The pain-free period between cluster headache bouts.

[5] Chronic migraine and chronic tension-type headache commonly overlap. If there are any features of migraine, diagnose chronic migraine.

[6] NICE has developed technology appraisal guidance on botulinum toxin type A for the prevention of headaches in adults with chronic migraine (headaches on at least 15 days per month of which at least 8 days are with migraine).

Migraine with aura

1.2.2 Suspect aura in people who present with or without headache and with neurological symptoms that:

- are fully reversible and
- develop gradually, either alone or in succession, over at least 5 minutes and
- last for 5–60 minutes. [2012]

1.2.3 Diagnose migraine with aura in people who present with or without headache and with one or more of the following typical aura symptoms that meet the criteria in recommendation 1.2.2:

- visual symptoms that may be positive (for example, flickering lights, spots or lines) and/or negative (for example, partial loss of vision)
- sensory symptoms that may be positive (for example, pins and needles) and/or negative (for example, numbness)
- speech disturbance. [2012]

1.2.4 Consider further investigations and/or referral for people who present with or without migraine headache and with any of the following atypical aura symptoms that meet the criteria in recommendation 1.2.2:

- motor weakness or
- double vision or
- visual symptoms affecting only one eye or
- poor balance or
- decreased level of consciousness. [2012]

Menstrual-related migraine

1.2.5 Suspect menstrual-related migraine in women and girls whose migraine occurs predominantly between 2 days before and 3 days after the start of menstruation in at least 2 out of 3 consecutive menstrual cycles. [2012]

1.2.6 Diagnose menstrual-related migraine using a headache diary (see recommendation 1.1.4) for at least 2 menstrual cycles. [2012]

Medication overuse headache

1.2.7 Be alert to the possibility of medication overuse headache in people whose headache developed or worsened while they were taking the following drugs for 3 months or more:

- triptans, opioids, ergots or combination analgesic medications on 10 days per month or more **or**
- paracetamol, aspirin or an NSAID, either alone or in any combination, on 15 days per month or more. [2012]

Surveillance decision

This review question should not be updated.

Evidence Update and 2-year surveillance summary

No relevant evidence was identified.

4-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

A topic expert highlighted an inequality in people with communication disabilities:

> 'people with severe and profound intellectual disability or communication disorder cannot give a clear history of or complain of headache.'

It was also highlighted that there are available new apps for smartphones to help patients to identify migraine triggers but no evidence was identified on the effectiveness of these smartphone apps.

Impact statement
We did not identify new evidence relevant to this question. Smartphone apps to help patients to identify seem to be available but no evidence was identified on the effectiveness of these interventions.

The NICE guideline CG150 development group reviewed the 2nd edition of The International Headache Classification (ICHD-2) to develop the recommendations related with this question. ICHD-2 is the current version of the classification, and recently an online version of this 2nd edition has been launched (http://ihs-classification.org/en/).

New evidence is unlikely to impact on the guideline recommendations.

1.3 Management

All headache disorders

150– 07 What is the clinical effectiveness, and patients' and practitioners' experience of using diaries for the management of people with suspected primary headaches and medication overuse headache?

Recommendations derived from this question

1.3.1 Consider using a headache diary:

- to record the frequency, duration and severity of headaches
- to monitor the effectiveness of headache interventions
- as a basis for discussion with the person about their headache disorder and its impact. [2012]

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

150– 08 Should young people and adults with suspected primary headaches undergo brain imaging to rule out serious pathology?

150– 09 For people with the following primary headaches (migraine with or without aura, menstrual related migraine, chronic migraine, tension type headache, cluster headache), what is the clinical evidence and cost-effectiveness of imaging as a management strategy?

Recommendations derived from these questions

1.3.3 Do not refer people diagnosed with tension-type headache, migraine, cluster headache or medication overuse headache for neuroimaging solely for reassurance. [2012]

1.3.28 Discuss the need for neuroimaging for people with a first bout of cluster headache with a GP with a special interest in headache or a neurologist.

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

Information and support for people with headache disorders

150– 10 What information and support do people with primary headaches say they want?

Recommendations derived from this question

1.3.4 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 significant impact on the person and their family or carers. [2012]

1.3.5 Give the person written and oral information about headache disorders, including information about support organisations. [2012]

1.3.6 Explain the risk of medication overuse headache to people who are using acute treatments for their headache disorder. [2012]

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

Tension-type headache

150– 11 In people with tension type headache, what is the clinical and cost-effectiveness of acute pharmacological treatment with aspirin, NSAIDs, opioids and, paracetamol?

Recommendations derived from this question

1.3.7 Consider aspirin*, paracetamol or an NSAID for the acute treatment of tension-type headache, taking into account the person's preference, comorbidities and risk of adverse events. [2012]

1.3.8 Do not offer opioids for the acute treatment of tension-type headache. [2012]

*Because of an association with Reye's syndrome, preparations containing aspirin should not be offered to people aged under 16 years.

Surveillance decision

This question should not be updated.

Evidence Update and 2-year surveillance summary

No relevant evidence was identified.

4-year surveillance summary

A Cochrane review assessed the efficacy of oral ibuprofen for acute treatment of tension type headache in adults [1]. Only randomised controlled trials (RCT) were included. Authors identified 12 studies that included 3094 people with moderate or severe pain. Ibuprofen (400mg) was associated with a reduction of the use of rescue medication, higher global evaluation 'good or excellent', and higher proportion of people being pain free at 2 hours after treatment administration compared with placebo. No differences were identified in adverse events between the interventions compared. The certainty in the evidence was assessed as high-moderate. Authors concluded that ibuprofen is an effective treatment for tension type headache.

Another Cochrane review assessed the use of paracetamol for acute treatment of episodic tension type headaches in adults [2]. Only RCTs including cross-over studies were selected. Authors included 23 studies in people with moderate-severe pain (n=8079). Paracetamol was associated with more people being pain free, and being pain-free or mild pain at two hours, and less use of rescue medication compared with placebo (quality of the evidence high-moderate). No differences were identified in the efficacy between paracetamol and ketoprofen (25 mg) or ibuprofen (400mg) or in adverse events between paracetamol and placebo. No differences were identified between paracetamol 500mg to 650 mg and placebo in the outcomes assessed. A systematic review (SR) assessed parental drugs as a second line therapy in tension type headache [3]. Authors included eight RCTs which compared different parenteral treatments (intravenous, intramuscular or subcutaneous administration) with another active comparator or placebo (n=486). Authors reported the results narratively given the heterogeneity in the methods and interventions compared in the studies included. The risk of bias of the included studies was assessed as low-high.

Metamizole[1], chlorpromazine, and metoclopramide were more effective than placebo in the reduction of pain one hour after the administration of the medication. The doses and administration routes were not specified in the abstract.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

New evidence identified related to the use of oral non-steroidal anti-inflammatory drugs and paracetamol is consistent with NICE guideline CG150 recommendations.

NICE guideline CG150 does not make recommendations on parenteral treatment as a second line therapy for tension type headaches. New evidence identified in this field is heterogeneous and limited; therefore it is considered that does not have an impact on current NICE guideline CG150 recommendations.

New evidence is unlikely to impact on the guideline.

[1] Metamizole is not available in the UK due to safety concerns.

150– 12 For people with primary headaches, what is the clinical evidence and cost-effectiveness of non-pharmacological management with acupuncture?

Recommendations derived from this question

1.3.9 Consider a course of up to 10 sessions of acupuncture over 5–8 weeks for the prophylactic treatment of chronic tension-type headache. [2012]

Surveillance decision

This review question should not be updated.

Evidence Update and 2-year surveillance summary
No relevant evidence was identified.

4-year surveillance summary
Tension type headache

A Cochrane review assessed the efficacy of acupuncture for prevention of tension type headache in adults [4]. A total of 12 RCTs were included (n=2349).

More people treated with acupuncture experienced a reduction in headache frequency of 50% or more compared with control. Similar results were reported when acupuncture was compared with sham acupuncture. No differences were identified in adverse effects between the groups compared. When comparing acupuncture with other therapies including physiotherapy, massage or exercise, authors highlighted that the results were not adequately reported. For these comparisons, authors reported that no differences were identified in most of the outcomes assessed between interventions but no more details were described in the abstract. The certainty in the evidence was considered moderate-low. Authors concluded that acupuncture is an effective option for the management of tension-type headaches.

Migraine

One SR assessed the efficacy of verum acupuncture for the treatment of migraine [5]. A total of ten RCTs at low risk of bias were included (n=997). Verum acupuncture was associated with a better total effective rate compared with sham acupuncture. Verum acupuncture was also associated with a reduction in the rate of recurrences but no differences were identified in terms of headache intensity, frequency or duration, and use of medication between the interventions compared.

Topic expert feedback
No topic expert feedback was relevant to this evidence.

Impact statement
New evidence identified suggests that acupuncture is an effective intervention for prevention of tension type headache in adults. It is consistent with current NICE guidance.

In migraine, evidence from one SR showed that verum acupuncture have some benefits in terms of total effective rate and reduction of recurrences however it is not better than placebo in most of the important outcomes assessed. It is considered that this new evidence identified does not have impact on current NICE guideline CG150 recommendations.

New evidence is unlikely to change guideline recommendations.

150– 13 **In people with tension type headache, what is the clinical evidence and cost-effectiveness for prophylactic pharmacological treatment with ACE inhibitors and angiotensin II receptor blockers (ARBs), antidepressants (SNRIs, SSRIs, tricyclics), beta blockers or antiepileptics?**

Recommendations derived from this question

The GDG decided that there was not enough evidence to make a recommendation for the pharmacological prophylactic treatment of tension type headaches.

Surveillance decision

This review question should not be updated.

Evidence Update and 2-year surveillance summary
No relevant evidence was identified.

4-year surveillance summary
A Cochrane review assessed the efficacy of selective serotonin re-uptake inhibitors (SSRIs) or serotonin-norepinephrine reuptake inhibitors (SNRIs) as prophylactic treatments of tension type headaches in adults [6]. Eight RCTs were included (n=412). SSRIs assessed were citalopram, sertraline, fluoxetine, paroxetine, fluvoxamine. Venlafaxine was the only SNRI evaluated.

No differences were identified between SSRIs or SNRIs and placebo in the frequency of tension type headaches. Similar results were reported when comparing SSRIs or SNRIs with amitriptyline. A reduction of the use of symptomatic/analgesic medication for acute attacks was associated with SSRIs compared with placebo but not with amitriptyline. Amitriptyline was associated with a reduction of the analgesic use compared with SSRIs. In terms of headache duration and intensity, no differences were identified between SSRIs and placebo or other antidepressants. Tricyclics were associated with less tolerability compared with SSRIs or SNRIs. Authors did not identify studies comparing SSRIs or SNRSs with other pharmacological or no pharmacological interventions and concluded that the evidence is scarce to recommend the use of SSRIs or SNRs as prophylactic treatment of tension type headaches.

Topic expert feedback
No topic expert feedback was relevant to this evidence.

Impact statement
At the time of the guideline, the GDG decided that there was not enough evidence to make recommendations about prophylactic pharmacological treatment for tension type headaches. New evidence found about the use of antidepressants (SSRIs, SNRIs or amitriptyline) was considered scarce and it showed no benefit compared with placebo or other antidepressants in most of the important outcomes assessed. It is considered that this new evidence identified does not have an impact on NICE guideline CG150.

New evidence is unlikely to impact on the guideline.

Migraine with or without aura

150– 14 **In people with migraine with or without aura, what is the clinical and cost-effectiveness of acute pharmacological treatment with:**

antiemetics; aspirin; NSAIDs; opioids; paracetamol; triptans; ergots and corticosteroids?

Recommendations derived from this question

1.3.10 Offer combination therapy with an oral triptan*and an NSAID, or an oral triptan* and paracetamol, for the acute treatment of migraine, taking into account the person's preference, comorbidities and risk of adverse events. For young people aged 12–17 years consider a nasal triptan in preference to an oral triptan*. [2012]

1.3.11 For people who prefer to take only one drug, consider monotherapy with an oral triptan*, NSAID, aspirin** (900 mg) or paracetamol for the acute treatment of migraine, taking into account the person's preference, comorbidities and risk of adverse events. [2012]

1.3.12 When prescribing a triptan* start with the one that has the lowest acquisition cost; if this is consistently ineffective, try one or more alternative triptans. [2012]

1.3.13 Consider an anti-emetic in addition to other acute treatment for migraine even in the absence of nausea and vomiting. [2012]

1.3.14 Do not offer ergots or opioids for the acute treatment of migraine. [2012]

1.3.15 For people in whom oral preparations (or nasal preparations in young people aged 12–17 years) for the acute treatment of migraine 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. [2012]

* At the time of publication (November 2015), triptans (except nasal sumatriptan) did not have a UK marketing authorisation for this indication in people aged under 18 years. Nasal sumatriptan did not have a UK marketing authorisation for this indication in people aged under 12 years. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. See the General Medical Council's Good practice in prescribing medicines – guidance for doctors and the prescribing advice provided by the Joint Standing Committee on Medicines (a joint committee of the Royal College of Paediatrics and Child Health and the Neonatal and Paediatric Pharmacists Group) for further information.

** Because of an association with Reye's syndrome, preparations containing aspirin should not be offered to people aged under 16 years.

† At the time of publication (November 2015), metoclopramide did not have a UK marketing authorisation for use in children and young people for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

†† At the time of publication (November 2015), prochlorperazine (except a buccal preparation) did not have a UK marketing authorisation for this indication but was licensed for the relief of nausea and vomiting. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. See the General Medical Council's Good practice in prescribing medicines – guidance for doctors and the prescribing advice provided by the Joint Standing Committee on Medicines (a joint committee of the Royal College of Paediatrics and Child Health and the Neonatal and Paediatric Pharmacists Group) for further information.

Surveillance decision

This review question should not be updated.

Oral, nasal and self-administrated subcutaneous treatments

Evidence Update and 2-year surveillance summary

Two studies were identified relevant to this area [7,8].

The first study was a RCT that investigated the efficacy and safety of oral rizatriptan[2] for acute

[2] At the time of publication of this Evidence Update, triptans (except nasal sumatriptan) did not have UK marketing authorisation for this

treatment of migraine in children and young people aged 6–17 years.

Young people aged 12–17 years who took rizatriptan were more likely to be free from pain 2 hours later than were those who took placebo. The incidence of adverse events was similar in the rizatriptan and the placebo groups. The most common adverse effects were somnolence, nausea, fatigue, dizziness, upper abdominal pain, and asthenia.

The main limitations of this study were that the rate of placebo response was relatively high, there was not include an active comparator and only children and young people who had not been successfully treated with NSAIDs or paracetamol were included, so the findings may not be generalisable to all children and young people with migraine.

The second RCT compared combined oral sumatriptan and naproxen sodium[3] with placebo in young people aged 12–17 years with moderate-to-sever migraine.

In the modified intention-to-treat population (n=490), participants who received sumatriptan/naproxen were more likely to be free from pain at 2 hours and 24 hours than were those on placebo. The incidence of adverse events was similar in the groups studied.

Limitations of the study included that combined oral sumatriptan/naproxen was not tested against either drug alone. The fixed dose sumatriptan and naproxen sodium combination does not have UK marketing authorisation and is not available in the UK. The exact dose regimen used is not easily replicated using products marketed in the UK.

It was considered that this new evidence was consisted with current NICE guideline CG150 recommendations.

4-year surveillance summary

A Cochrane review evaluated the combination of sumatriptan plus naproxen (separate tablets or fixed-dose combination) for the treatment of acute migraine attacks in adults [9]. A total of 12 RCTs were included in the analyses. The doses assessed were 85 mg sumatriptan, 50 mg sumatriptan, and 500mg naproxen. Sumatriptan combined with naproxen was associated with higher proportion of attacks pain-free and headache relief at two hours compared with placebo or the same dose of either drug given alone. The results were independent of the dose of sumatriptan used. Sumatriptan alone or in combination was associated with a higher incidence of adverse events compared with placebo or naproxen. The certainty in the evidence was considered high-moderate. Authors concluded that the combination of sumatriptan and naproxen is effective for the treatment of acute migraine attacks.

A Cochrane review evaluated the efficacy and safety of zolmitriptan for the treatment of acute migraine attacks in adults [10]. A total of 25 RCTs were included and the majority compared doses of 2.5 mg or 5 mg of zolmitriptan with placebo.

Zolmitriptan was associated with a higher proportion of attacks pain-free and headache relief at two hours, sustained pain-free and headache relief during the following day after treatment compared with placebo. It was also associated with a higher incidence of adverse events (transient and mild). The studies included were considered of high quality for almost all the outcomes assessed. Authors concluded that zolmitriptan is an effective option for the treatment of migraine attacks but it is also associated with adverse events compared with placebo.

A Cochrane overview of reviews assessed the efficacy and tolerability of sumatriptan for the treatment of acute migraine attacks in adults [11]. A total of four Cochrane reviews were included. Authors focused their description on doses and routes of administration licensed in North America and Europe. The doses and routes described were oral 25 mg, 50 mg, 100 mg; subcutaneous 4 mg, 6 mg; intranasal 5 mg, 10 mg, 20 mg; and rectal 25 mg. Subcutaneous administration of 6mg sumatriptan was associated with greater pain relief (moderate or severe to no pain) by two hours compared with placebo. Other doses and routes of administration were also effective in pain reduction. Subcutaneous administration was associated with a more rapid symptom relief compared with other routes. This administration route as well as higher doses of oral and

indication in children and young people aged under 18 years.

[3] At the time of publication of this Evidence Update, combined dose sumatriptan and naproxen sodium did not have UK marketing authorisation and was not available in the UK.

intranasal sumatriptan was associated with higher risk of adverse events. Authors described the more effective's doses for pain relief for each route of administration. These dose were oral 100 mg, subcutaneous 6 mg, intranasal 20 mg, and rectal 25 mg. Authors concluded that sumatriptan is an effective treatment for acute migraine in adults, but it is also associated with a higher incidence of adverse events compared to placebo. Subcutaneous administration is associated with a higher efficacy compared with other routes but with an increase of adverse events (and higher cost).

A Cochrane review assessed different drugs for the treatment of acute migraine attacks in children and adolescents [12]. Children are outside the remit of NICE guideline CG150; therefore only results in adolescents are described.

A total of 7630 adolescents were included in the studies identified. Fifty percent of the studies included assessed sumatriptan. Other drugs evaluated were almotriptan, eletriptan, naratriptan, rizatriptan, sumatriptan plus naproxen sodium, zolmitriptan, paracetamol, ibuprofen, and dihydroergotamine. Triptans were associated with higher proportion of attacks pain-free compared with placebo in adolescents. They were also associated with a higher incidence of adverse events (mostly mild adverse events). The combination of sumatriptan plus naproxen was also effective in the treatment of acute migraine attacks in adolescents. The certainty in the evidence was considered moderate.

One RCT compared 25 mg promethazine plus 50 mg sumatriptan with 50 mg sumatriptan plus placebo for the treatment of migraine (with or without aura) in adults [13]. A total of 216 patients were included in the analysis. Participants who received promethazine plus sumatriptan were more likely to be headache free at 2-hour and 4-hours compared with those on sumatriptan alone. The combination of promethazine plus sumatriptan was also associated with a lower incidence of headache recurrence within 24-48 hours after the treatment compared with sumatriptan alone but with an increase of the somnolence and extrapyramidal symptoms. Authors concluded that the combination of a triptan with antiemetics is an effective option for the treatment of migraine attacks.

Topic expert feedback
No topic expert feedback was relevant to this evidence.

Impact statement
New evidence identified supports current NICE guideline recommendations.

This evidence shows that the combination of triptans and NSAID is effective in the treatment of acute migraine. It also shows that triptans are effective in the treatment of acute migraine attacks but they lead to an increase of adverse events (mostly mild). The addition of antiemetics to triptans is also an effective option for the treatment of acute migraine.

New evidence is unlikely to change guideline recommendations.

Intravenous, intramuscular and subcutaneous administered treatments

Evidence Update and 2-year surveillance summary
No relevant evidence was identified.

4-year surveillance summary
A SR with meta-analysis assessed the efficacy of intravenous magnesium for acute migraine in adult population[4, 15]. A total of five studies were included (n=295). The doses of intravenous magnesium sulfate were not described in the abstract. Intravenous magnesium sulfate was not associated with a relief of headache 30 minutes after the treatment administration compared with control. It was associated with an increase of side-effects or adverse events compared with controls. No differences were identified in terms of use of rescue analgesic medications. Authors concluded that intravenous administration magnesium does not improve migraine beneficial outcomes and it is more likely to produce harms.

A RCT evaluated intravenous administration diphenhydramine as adjuvant therapy for acute migraine [16]. Intravenous diphenhydramine 50mg plus intravenous metoclopramide 10mg was compared with placebo plus intravenous metoclopramide 10mg in 208 people with an acute moderate or severe headache. An interim analysis showed no difference in terms

[4] Off-label use.

of reduction of pain one hour after medication administration, sustained relief at 48 hours, and in length of stay between the interventions compared. Authors concluded that intravenous administration diphenhydramine is not an effective option as adjuvant therapy for acute migraine.

We identified two RCTs that assessed the use of intravenous dexketoprofen as a treatment of acute migraine. One study compared intravenous dexketoprofen with placebo (n=224) [17], and the other study with 1000mg paracetamol (n=200) [18]. In both studies the dose of dexketoprofen was 50 mg. Intravenous dexketoprofen was associated with a reduction of pain at 45 mins after medication administration and with a reduction of the use of rescue drugs compared with placebo. No adverse events were reported. No differences were identified in terms of pain reduction between dexketoprofen and paracetamol. Dexketoprofen is licensed only for oral administration in UK.

A Cochrane overview of reviews previously summarised in the section 'oral, nasal and self-administrated subcutaneous treatments' assessed the efficacy of sumatriptan for the treatment of acute migraine attacks in adults [11]. Authors of this overview concluded that subcutaneous administration of sumatriptan was associated with a higher efficacy compared with other routes (oral, intranasal, rectal) but with an increase of adverse events (and higher cost).

Topic expert feedback
No topic expert feedback was relevant to this evidence.

Impact statement
New evidence identified shows that magnesium sulfate and diphenhydramine are not effective interventions for the treatment of acute migraine episodes. It is considered that this new evidence does not have an impact on current recommendations.

New evidence shows that non-oral NSAID or triptans are effective in the treatment of acute migraine. It is considered that this new evidence support current NICE guideline CG150 recommendations.

New evidence is unlikely to change guideline recommendations.

Normobaric oxygen therapy and hyperbaric oxygen therapy

Evidence Update and 2-year surveillance summary
No relevant evidence was identified.

4-year surveillance summary
A Cochrane review assessed the normobaric oxygen therapy (NBOT) and hyperbaric oxygen therapy (HBOT) as prophylaxis or treatment of migraine and cluster headache [19].

A total of 11 RCTs were included in the Cochrane review, five of them assessed HBOT for treatment of acute migraine (n=103) but only three were finally include in the meta-analysis of the results. HBOT was associated with a reduction of migraine headaches compared with sham therapy. There was no evidence that HBOT was associated lower incidence of nausea and vomiting, or with a reduction of the use of rescue medication. Authors concluded that more research is needed to determine the role of the HBOT use in acute migraine.

Topic expert feedback
No topic expert feedback was relevant to this evidence.

Impact statement
We identified a Cochrane review that assessed the use of HBOT in the treatment of migraine attacks. In general, the quality of the evidence identified was considered low. The studies included had small sample sizes and they were considered of poor quality. Therefore, it is considered that the new evidence identified have no impact on current NICE guideline CG150 recommendations.

New evidence is unlikely to change guideline recommendations.

150– 15 **In people with chronic or episodic migraine (with or without aura), what is the clinical evidence and cost-effectiveness of prophylactic pharmacological treatment with: antidepressants (SNRIs, SSRIS, tricyclics), centrally acting alpha adrenergic-receptor agonists, beta blockers, calcium channel blockers, antiepileptics, other serotonergic modulators, NMDA receptor antagonists?**

Recommendations derived from this question

1.3.16 Discuss the benefits and risks of prophylactic treatment for migraine with the person, taking into account the person's preference, comorbidities, risk of adverse events and the impact of the headache on their quality of life. [2012]

1.3.17 Offer topiramate or propranolol* for the prophylactic treatment of migraine 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 if needed. [2015]

1.3.18 Consider amitriptyline** for the prophylactic treatment of migraine according to the person's preference, comorbidities and risk of adverse events. [new 2015]

1.3.19 Do not offer gabapentin for the prophylactic treatment of migraine. [new 2015]

1.3.20 If both topiramate and propranolol[12] are unsuitable or ineffective, consider a course of up to 10 sessions of acupuncture over 5–8 weeks according to the person's preference, comorbidities and risk of adverse events. [2012, amended 2015]

1.3.21 For people who are already having treatment with another form of prophylaxis and whose migraine is well controlled, continue the current treatment as required. [2012, amended 2015]

1.3.22 Review the need for continuing migraine prophylaxis 6 months after the start of prophylactic treatment. [2012]

*At the time of publication (November 2015), topiramate did not have a UK marketing authorisation for use in children and young people for this indication. Propranolol did not have a UK marketing authorisation for use in children under 12 years for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

**At the time of publication (November 2015), amitriptyline did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

Surveillance decision

This review question should not be updated.

Evidence Update and 2-year surveillance summary

Pharmacological prophylaxis with topiramate

A Cochrane review analysed prospective, randomised or pseudo-randomised controlled trials of the effect of prophylactic topiramate on frequency of migraines (n=1737)[20]. Studies were sought of adults with episodic migraine who self-administered topiramate regularly during headache-free periods to prevent migraines.

Topiramate was more effective than placebo at reducing the number of migraines, resulting in around 1 less headache per month. Three different topiramate doses studied were studied (50 mg, 100 mg, 200 mg). All of them were similarly effective compared with placebo. The response rate for topiramate was twice as high as that with placebo. Adverse events were reported by a large proportion of study participants treated with topiramate but these were usually mild.

The results were heterogeneous and the authors reported that that several of the included studies were 'almost certainly underpowered' and that 9 trials had at least 1 area at high risk of bias (for example, allocation concealment, blinding, or selective reporting).

We identified one RCT comparing cinnarizine with topiramate as prophylactic treatments of migraine in children and adolescents [14]. However the information provided in the abstract related to the participants included was limited and we were unable to determinate if the study met the inclusion criteria of NICE guideline CG150.

It was considered that this new evidence identified was consisted with NICE guideline CG150 recommendations.

Pharmacological prophylaxis with gabapentin, gabapentin enacarbil or pregabalin

A Cochrane review assessed the prophylactic use of gabapentin, its prodrug gabapentin enacarbil, and pregabalin[5] (n=1009)[21].

No differences were identified in the number of responders between gabapentin and placebo and the overall risk of adverse events were similar between these two groups. However, people on gabapentin had a higher risk of dizziness, somnolence, and abnormal thinking.

No trials comparing gabapentin with active comparators were found, and no trials of pregabalin for migraine prophylaxis were identified. Diagnostic criteria, baseline headache frequency, washout periods for previous medication, rules for rescue medication, and the statistical analyses used varied among the studies included. The authors note that these findings contradict those of their previous SR of gabapentin and other published analyses of the drug because of the inclusion of previously confidential research reports that became available because of legal proceedings.

A RCT assessed the efficacy and safety of four different doses of gabapentin enacarbil or migraine prophylaxis (n=526) [22]. The doses assessed were 1200 mg, 1800 mg, 2400 mg or 3000 mg and were compared with placebo. None of the evaluated doses were better than placebo. No differences were identified in terms of adverse events between the groups compared.

The evidence suggests that gabapentin and gabapentin enacarbil are no better than placebo for prophylactic treatment of migraine in adults and are commonly associated with adverse events.

This evidence was assessed in the 2-year surveillance review and the final decision was NICE to update this clinical question. The question was updated in 2015.

Pharmacological prophylaxis with valproic acid, sodium valproate or valproate semisodium

A Cochrane review analysed effect of prophylactic valproic acid, sodium valproate, or a combination of these (valproate semisodium) on frequency of migraines in adults (n=542) [23]. Not enough data were available from these trials to calculate the effect of this combination on headache frequency. The response rate for valproate semisodium was twice as high as for placebo. Two trials found that sodium valproate produced a greater reduction in 28-day headache frequency than placebo. One further trial compared three different doses of sodium valproate and found that doses that produced lower serum concentrations of valproate were associated a slightly lower headache frequency than doses that produced higher serum concentrations. The remaining three trials compared sodium valproate or valproate semisodium with active comparators: flunarizine[6], propranolol and topiramate. None of these studies reported significant differences between sodium valproate or valproate semisodium and the active comparators. The proportion of patients receiving valproate semisodium or sodium valproate who withdrew from trials owing to adverse effects varied from 8% to 19%.

Given that few data on change in headache frequency was reported in the studies analysed in this review, it was considered that this evidence was unlikely to have an impact on NICE guideline CG150.

[5] At the time of publication of the Evidence Update, gabapentin enacarbil and pregabalin did not have UK marketing authorisation for this indication and were not considered for NICE CG150.

[6] At the time of the Evidence Update publication, flunarizine did not have UK marketing authorisation and was not available in the UK.

Pharmacological prophylaxis of migraine with other drugs in adults

A SR assessed the effects of several types of prophylactic pharmacological treatments on headache frequency in adults with episodic migraine [24]. The studies looked at 59 drugs, and most were in the USA and western countries. In pooled meta-analyses, the following drugs were more effective than placebo at reducing monthly migraine frequency by more than 50%[7]: 1) the antiepileptics topiramate, gabapentin, and valproate semisodium; 2) the beta-blockers propranolol, timolol, and metoprolol; and 3) the calcium channel blocker nimodipine. Small single randomised controlled trials found that the angiotensin-converting enzyme inhibitor lisinopril and the angiotensin II receptor blocker candesartan were also effective at reducing migraine frequency. In a network meta-analysis, angiotensin-inhibiting drugs were the most effective class of drug compared with placebo, followed by the antiadrenergic drug clonidine, beta-blockers and the antiepileptic drug valproate semisodium. All drugs except beta-blockers were more likely than placebo to cause adverse effects that led to treatment discontinuation. Clonidine is licenced for prevention of recurrent migraine in adults. However, the British National Formulary advises that clonidine is not recommended for prophylaxis of migraine because it can aggravate depression and cause insomnia.

The poor quality of the evidence identified almost all the drugs assessed (except topiramate).

A randomised cross-over study assessed the efficacy of the angiotensin II blocker candesartan compared with propranolol for prophylaxis- with or without aura (n=72) [25].

Candesartan and propranolol were associated with fewer days with migraine per four week compared with placebo. No differences were identified between candesartan and propranolol. Adverse events were higher with propranolol but not with candesartan compared with placebo.

Limitations of this study included that the effects of 1 study agent may have been carried over into the next study period, despite the wash-out period. The reduction in headaches was small and probably not clinically relevant (0.58 days with candesartan and 0.62 days with propranolol).

All this evidence suggested that angiotensin-inhibiting drugs and beta-blockers may be effective options for reducing migraine frequency. In the 2-year surveillance review it was considered that prescribing practice has changed since NICE guideline CG150 was published. As such, the network meta-analysis on which this section of the guideline was based should be updated to include the new evidence identified on angiotensin-inhibiting drugs and to include any new drugs used. The final decision was NICE to update this clinical question. This question was updated in 2015.

Pharmacological prophylaxis of migraine in children and young people

A SR assessed the effectiveness and safety of a range of prophylactic pharmacological treatments for migraine in children and young people [26].

Topiramate and trazodone hydrochloride were more effective than placebo at reducing the number of headaches per month in episodic migraine. The following drugs[8] were not significantly better than placebo: clonidine, flunarizine, piracetam, pizotifen, propranolol, sodium valproate, and fluoxetine. Topiramate and sodium valproate were associated with more adverse effects than placebo. Not enough comparative effectiveness data on prophylactic medication for migraine was available to allow a network meta-analysis. Ten studies with comparative effectiveness analyses showed that flunarizine was more effective than piracetam at reducing headache frequency but

[7] At the time of publication of the Evidence Update, valproate semisodium, nimodipine, lisinopril and candesartan did not have UK marketing authorisation for this indication and were not considered for NICE CG150.

[8] At the time of publication of the Evidence Update, trazodone hydrochloride, clonidine, piracetam, sodium valproate, fluoxetine and cinnarizine did not have UK marketing authorisation for this indication in children and young people aged under 18 years, and was not considered for NICE CG150. Clonidine is licenced for prevention of recurrent migraine in adults. However, the British National Formulary advises that clonidine is not recommended for prophylaxis of migraine because it can aggravate depression and cause insomnia.

no better than aspirin or dihydroergotamine[9]. Propranolol was as effective as behavioural therapy but no better than valproate, cinnarizine or flunarizine.

The results were heterogeneous, the studies included were generally small and short (mean duration = 12weeks), and few of them used intention-to-treat analyses.

Limited evidence suggests that prophylactic use of topiramate and trazodone hydrochloride reduces headache frequency in children and young people with episodic migraine, whereas other commonly used drugs, including propranolol, may not be effective. NICE guideline CG150 recommends offering topiramate or propranolol prophylaxis for young people aged 12 years and over with migraine with or without aura. However given the shortcomings of the studies included in the meta-analysis, this evidence was considered unlikely to have an impact on NICE guideline CG150.

4-year surveillance summary

One Cochrane review assessed the efficacy and safety of SSRIs and SNRIs in the prevention of migraine in adults [27]. A total of 11 RCTs were included (n=585). Overall SSRIs or SNRIs were not superior to placebo or amitriptyline as a prophylactic treatment of migraine in the main outcomes considered (migraine frequency, intensity, and duration).

A Cochrane review assessed the normobaric oxygen therapy (NBOT) and hyperbaric oxygen therapy (HBOT) as prophylaxis or treatment of migraine and cluster headache [19]. There was no evidence that HBOT could prevent migraine episodes. Results related to NBOT as a prophylactic treatment in migraine were not reported in the abstract.

A network meta-analysis assessed the effectiveness of different pharmacological interventions for the prophylaxis of migraine [28]. Authors included RCTs but total number of studies included was unclear in the abstract. The results showed that amitriptyline was better than candesartan, fluoxetine, propranolol, topiramate and valproate as a prophylactic treatment of migraine. No differences were identified between amitriptyline, atenolol, flunarizine, clomipramine or metoprolol. Authors concluded that there are different drugs that could be beneficial in the prophylaxis of migraine. Authors also highlighted that evidence was considered weak to support the use of amitriptyline over the others, and the choice of the treatment must take into account patients characteristics, preferences, and harms.

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

Taking into account the evidence identified in the Evidence Update published in 2014, the final decision of the 2-year surveillance review was to update this question. The update was published in 2015.

In this 4-year surveillance point, we identified new evidence assessing different interventions for the prevention of migraine in adults. A Cochrane review concluded that SSRIs and SNRIs were no superior to placebo or amitriptyline in the prevention of migraine attacks. SNRIs or SSRIs are not options considered in the prophylaxis of migraine in NICE guideline CG150. We identified another Cochrane review that assessed the use of NBOT and HBOT but it did not identified evidence of the efficacy of the HBOT for the prevention of migraine. The results related to NBOT were not reported in the abstract, so its efficacy is unclear in this context. Finally a network meta-analysis assessing different pharmacological interventions showed that different drugs are valid options in the prophylaxis of migraine. In their analysis amitriptyline seemed to be superior to other drugs (including topiramate and propranolol) but authors concluded that there was weak evidence to support the use of amitriptyline over the other options available.

It is considered that the new evidence identified does not have an impact on current NICE guideline CG150 recommendations.

New evidence is unlikely to change guideline recommendations.

[9] At the time of publication of this Evidence Update, flunarizine and dihydroergotamine did not have UK marketing authorisation and were not available in the UK.

Combined hormonal contraceptive use by women and girls with migraine

150– 16 What risks are associated with use of hormonal contraception in females aged 12 or over with migraine?

Recommendations derived from this question

1.3.24 Do not routinely offer combined hormonal contraceptives for contraception to women and girls who have migraine with aura. [2012]

Surveillance decision

This review question should not be updated.

Evidence Update and 2-year surveillance summary
No relevant evidence was identified.

4-year surveillance summary
No relevant evidence was identified.

Topic expert feedback
Topic experts highlighted discrepancies between the new UK Medical Eligibility Criteria for Contraceptive Use (UKMEC) guideline and NICE guideline CG150:

> 'The new UKMEC (2016) say use of CHC is MEC2 in migraine without aura , and MEC 3 if new or worsening migraine, whereas [NICE guideline] CG150 says choice of contraception unrestricted if no aura.'

Impact statement
No new evidence was identified related to the risk associated with use of hormonal contraception in women aged 12 or over with migraine. One topic expert highlighted a new version of the UKMEC. NICE guideline CG150 does not recommend the routine use of combined hormonal contraceptives for contraception in women and girls who have migraine with aura (recommendation 1.3.24). This is in line with current UKMEC recommendations in which the use of combined hormonal contraception in women with migraine with aura (at any age) is classified in the category 4 for initiation and continuation; that is to say 'a condition which represents an unacceptable health risk if the method [combined hormonal contraception] is used.' NICE guideline CG150 does not make recommendations in patients with migraine without aura.

New evidence is unlikely to change guideline recommendations

Menstrual-related migraine

150– 17 **In people with pure menstrual and menstrual related migraine, what is the clinical evidence and cost effectiveness for prophylactic pharmacological treatment with: ACE inhibitors and angiotensin II receptor antagonists (ARBs), antidepressants (SNRIs, SSRIs, tricyclics), beta blockers, calcium channel blockers, antiepileptics, triptans, other serotonergic modulators, NSAIDs, and hormonal therapy (contraceptives)?**

Recommendations derived from this question

1.3.25 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 migraine is expected. [2012]

* At the time of publication (November 2015), frovatriptan did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. See the General Medical Council's Good practice in prescribing medicines – guidance for doctors and the prescribing advice provided by the Joint Standing Committee on Medicines (a joint committee of the Royal College of Paediatrics and Child Health and the Neonatal and Paediatric Pharmacists Group) for further information.

** At the time of publication (November 2015), zolmitriptan did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. See the General Medical Council's Good practice in prescribing medicines – guidance for doctors and the prescribing advice provided by the Joint Standing Committee on Medicines (a joint committee of the Royal College of Paediatrics and Child Health and the Neonatal and Paediatric Pharmacists Group) for further information.

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

Treatment of migraine during pregnancy

150– 18 **What is the evidence for adverse fetal events in females with primary headaches during pregnancy using triptans, oxygen, or verapamil?**

Recommendations derived from this question

1.3.26 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 medication during pregnancy. [2012]

1.3.27 Seek specialist advice if prophylactic treatment for migraine is needed during pregnancy. [2012]

1.3.35 Seek specialist advice if treatment for cluster headache is needed during pregnancy. [2012]

*At the time of publication (November 2015), triptans (except nasal sumatriptan) did not have a UK marketing authorisation for this indication in people aged under 18 years. Nasal sumatriptan did not have a UK marketing authorisation for this indication in people aged under 12 years. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. See the General Medical Council's Good practice in prescribing medicines –

guidance for doctors and the prescribing advice provided by the Joint Standing Committee on Medicines (a joint committee of the Royal College of Paediatrics and Child Health and the Neonatal and Paediatric Pharmacists Group) for further information.

Surveillance decision

This review question should not be updated.

Evidence Update and 2-year surveillance summary

A population-based cohort study assessed the safety of triptans during pregnancy (n=1465) [29]. The most commonly triptans used were sumatriptan, rizatriptan, eletriptan and zolmitriptan. Women that redeemed prescriptions for triptans between seven months and 1 month before pregnancy only were compared with those that did not redeem triptans during the study period. After controlling for maternal age and previous stillbirth or miscarriage, women who redeemed prescriptions for triptans during pregnancy were at no higher risk of miscarriage or stillbirth than those who did not take triptans before or during pregnancy. No link was found between triptan redemption during pregnancy and congenital malformations. Women who redeemed triptans during the second trimester of pregnancy had a higher risk of low birth weight infants and postpartum haemorrhage. However, the risk of postpartum haemorrhage was also raised among women in the disease comparison group. Limitations of this study include that the prescription redemption data could not show whether the triptans were taken and at what point in pregnancy. In addition, the overall rate of congenital malformations in the study was low (5.1%), so the analyses may have been underpowered for this outcome.

It was considered that this new evidence support current NICE guideline CG150 recommendations.

4-year surveillance summary

No relevant evidence was identified.

Topic expert feedback

Topic experts highlighted that there is new evidence about the use of sumatriptan in pregnancy.

Impact statement

Evidence identified in the previous Evidence Update and 2-year surveillance review was considered to support current NICE guideline CG150 recommendations. Topic experts highlighted that there is new evidence about the use of sumatriptan in pregnancy; however no new evidence was identified in this 4-year surveillance review.

New evidence is unlikely to change guideline recommendations.

Cluster headache

150– 19 In people with cluster headache, what is the clinical evidence and cost-effectiveness for acute pharmacological treatment with: aspirin, paracetamol, oxygen, triptans, ergots, NSAIDs, and opioids?

Recommendations derived from this question

1.3.29 Offer oxygen and/or a subcutaneous*or nasal triptan** for the acute treatment of cluster headache. [2012]

1.3.30 When using oxygen for the acute treatment of cluster headache:

- use 100% oxygen at a flow rate of at least 12 litres per minute with a non‑rebreathing mask and a reservoir bag and
- arrange provision of home and ambulatory oxygen. [2012]

1.3.31 When using a subcutaneous* or nasal triptan**, ensure the person is offered an adequate supply of triptans calculated according to their history of cluster bouts, based on the manufacturer's maximum daily dose. [2012]

1.3.32 Do not offer paracetamol, NSAIDS, opioids, ergots or oral triptans for the acute treatment of cluster headache. [2012]

* At the time of publication (November 2015), subcutaneous triptans did not have a UK marketing authorisation for this indication in people aged under 18 years. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. See the General Medical Council's Good practice in prescribing medicines – guidance for doctors and the prescribing advice provided by the Joint Standing Committee on Medicines (a joint committee of the Royal College of Paediatrics and Child Health and the Neonatal and Paediatric Pharmacists Group) for further information.

** At the time of publication (November 2015), nasal triptans did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. See the General Medical Council's Good practice in prescribing medicines – guidance for doctors and the prescribing advice provided by the Joint Standing Committee on Medicines (a joint committee of the Royal College of Paediatrics and Child Health and the Neonatal and Paediatric Pharmacists Group) for further information.

Surveillance decision

This review question should not be updated.

Evidence Update and 2-year surveillance summary
No relevant evidence was identified.

4-year surveillance summary
A Cochrane review that assessed NBOT and HBOT as prophylaxis or treatment of migraine and cluster headache [19]. A total of 11 RCTs were included in this Cochrane review: three assessed NBOT (n=145) and two HBOT (n=29) for the treatment of cluster headache. The other studies included assessed these interventions for acute migraine (5 studies) or for a mixed group of headaches (1 study); therefore they are not described further.

In one study NBOT was identified as an effective treatment for cluster headache compared with sham therapy but in another small study NBOT was not superior to ergotamine in the treatment of cluster headaches. In a third trial the proportion of attacks that responded to the treatment was higher with NBOT than with placebo. HBOT was not associated with an effective termination of cluster headaches in one small trial.

Topic expert feedback
No topic expert feedback was relevant to this evidence.

Impact statement
New evidence of limited quality shows that NBOT is effective for the termination of cluster headache. It is considered it is consistent with current NICE guideline CG150 recommendations.

New evidence is unlikely to change guideline recommendations.

150– 20 In people with cluster headache, what is the clinical evidence and cost-effectiveness for prophylactic pharmacological treatment with: calcium channel blockers, corticosteroids, lithium, melatonin, antiepileptics and other serotonergic modulators.

Recommendations derived from this question

1.3.33 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 electrocardiogram monitoring. [2012]

1.3.34 Seek specialist advice for cluster headache that does not respond to verapamil*. [2012]

* At the time of publication (November 2015), verapamil did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or their parent or carer) should provide informed consent, which should be documented. See the General Medical Council's Good practice in prescribing medicines – guidance for doctors and the prescribing advice provided by the Joint Standing Committee on Medicines (a joint committee of the Royal College of Paediatrics and Child Health and the Neonatal and Paediatric Pharmacists Group) for further information.

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

Medication overuse headache

150– 21 What is the clinical evidence and cost-effectiveness of withdrawal strategies (of abortive treatments), psychological therapies, corticosteroids and NSAIDs for the treatment of probable medication overuse headache?

Recommendations derived from this question

1.3.36 Explain to people with medication overuse headache that it is treated by withdrawing overused medication. [2012]

1.3.37 Advise people to stop taking all overused acute headache medications for at least 1 month and to stop abruptly rather than gradually. [2012]

1.3.38 Advise people that headache symptoms are likely to get worse in the short term before they improve and that there may be associated withdrawal symptoms, and provide them with close follow-up and support according to their needs. [2012]

1.3.39 Consider prophylactic treatment for the underlying primary headache disorder in addition to withdrawal of overused medication for people with medication overuse headache. [2012]

1.3.40 Do not routinely offer inpatient withdrawal for medication overuse headache. [2012]

1.3.41 Consider specialist referral and/or inpatient withdrawal of overused medication for people who are using strong opioids, or have relevant comorbidities, or in whom previous repeated attempts at withdrawal of overused medication have been unsuccessful. [2012]

1.3.42 Review the diagnosis of medication overuse headache and further management 4–8 weeks after the start of withdrawal of overused medication. [2012]

Surveillance decision

This review question should not be updated.

Evidence Update and 2-year surveillance summary

Prophylactic treatment

A RCT assessed the efficacy of prednisone for the treatment of withdrawal headache in people with medication overuse headache [30]. A total of 96 participants with a diagnosis of migraine or episodic tension-type headache seeking treatment to medication overuse headache randomly assigned to prednisone (100 mg) or placebo (100 mg) once a day during the first five days of the withdrawal period. No differences were identified in the number of hours with headache at three days and five days following withdrawal or during the 14 days of following time between prednisone and placebo. Prednisone was associated with less

request of rescue medication during the first five days after withdrawal but not during the 14 days of observation.

Limitations of this study include the long recruitment period (2004 to 2009) and high drop-out rate (19%), and the majority of patients (71%) went through medication withdrawal on an inpatient basis, an approach that NICE guideline CG150 does not recommend should be used routinely in England.

A RCT found similar results that prednisolone did not affect the number of days with headache in people with medication overuse headache undergoing medication withdrawal [31].

NICE guideline CG150 suggests that prophylactic treatment may be considered in people with medication overuse headache undergoing withdrawal of the overused medication. However, the guidance does not make any recommendations specifically to use or not use corticosteroids. It was considered that this new evidence was unlikely to have an impact on NICE guideline CG150.

Inpatient withdrawal

A prospective randomised cohort study compared advice alone with structured inpatient and outpatient withdrawal programmes in patients with medication overuse headache (n=141) [32]. The interventions compered were: 1) education on medication overuse headache and advice to withdraw the overused medications; 2) an outpatient withdrawal programme comprising the same education and advice as the first group plus prednisone and individualised prophylaxis treatment; and 3) a 10-day inpatient withdrawal programme with education and advice, steroids, fluid replacement, antiemetics (metoclopramide hydrochloride) and individualised prophylaxis treatment.

Inpatient treatment was associated with a higher response rate compared with the other two groups evaluated. The response rate was defined as the participants who took NSAIDS less than 15 days/month or other symptomatic medications less than 20 days/month.

Inpatient treatment was also associated with a higher proportion of patients who experienced more than 50% reduction in headache frequency from baseline compared with the other two groups assessed.

Limitations of this study include that the sample size was relatively small and it assessed a highly complex group of patients. In addition, it was conducted at a single tertiary referral centre, and the education and advice component of each treatment may not be reproducible in non-specialised centres.

This evidence showed that inpatient treatment is more effective than outpatient treatment or education alone at achieving medication withdrawal in people with migraine and complicated medication overuse headache. NICE guideline CG150 states that inpatient withdrawal should be reserved for people who are using strong opioids, have relevant comorbidities, or have previously been unsuccessful at withdrawal of overused medication. This evidence was considered consistent with the current guidance and therefore unlikely to have an impact on NICE guideline CG150.

4-year surveillance summary

A cluster-RCT compared a brief intervention with usual care in patients with medication overuse headache (n=60) [33]. The brief intervention was delivered by general practitioners and consisted in individual feedback about the risk of medication overuse headache and recommendations about how to reduce overuse. Brief intervention was associated with a reduction in medication and the number of days with headaches per month compared with usual care. Follow-up six months after showed similar results [34].

Topic expert feedback

No topic expert feedback was relevant to this evidence.

Impact statement

New evidence is consistent with current recommendations.

New evidence is unlikely to change guideline recommendations.

Prophylactic non-pharmacological management of primary headaches with manual therapies

150– 22 For people with primary headaches, what is the clinical evidence and cost-effectiveness of non-pharmacological management with manual therapies?

Recommendations derived from this question

The GDG decided there was not enough evidence to make a recommendation for or against the use of manual therapies for the prophylactic treatment of tension type headache or migraine.

Surveillance decision

This review question should not be updated.

Tension headache

Evidence Update and 2-year surveillance summary
No relevant evidence was identified.

4-year surveillance summary
A SR with meta-analysis assessed the efficacy of multimodal manual therapy compared it with pharmacological treatment for tension type headache [35]. The type of manual therapies and drugs compared were not described in the abstract of the study. A total of five RCTs were included and the results showed that manual therapies are better than pharmacological treatment in the reduction of the frequency, intensity, and duration of the headaches straightaway after the treatment. No differences were identified in terms of headache intensity at longer follow-up. Authors reported that the results were heterogeneous and must be interpreted with caution.

Topic expert feedback
No topic expert feedback was relevant to this evidence.

Impact statement
New evidence identified was limited and considered unlikely to have an impact on NICE guideline CG150.

New evidence is unlikely to impact on the guideline.

Migraine with or without aura

Evidence Update and 2-year surveillance summary
No relevant evidence was identified.

4-year surveillance summary
A RCT assessed the effectiveness of osteopathic treatment in people with chronic migraine (n=105) [36]. Osteopathic treatment plus pharmacological therapy was compared with sham plus pharmacological therapy and with pharmacological therapy alone. The main outcome was the change from baseline in the headache impact test (HIT-6) score. Osteopathic therapy was associated with a reduction in the HIT-6 score, drug consumption, days of migraine, pain intensity, and functional disability compared with sham therapy plus pharmacological treatment or pharmacological treatment alone.

Topic expert feedback
No topic expert feedback was relevant to this evidence.

Impact statement
New evidence from one small RCT showed that osteopathic treatment could be an option in the treatment of migraine. It is considered that the new evidence identified is insufficient to have an impact on NICE guideline CG150.

New evidence is unlikely to impact on the guideline.

Prophylactic non-pharmacological management of primary headaches with psychological therapies

150– 23 For people with primary headaches, what is the clinical evidence and cost-effectiveness of non-pharmacological management with psychological therapies?

Recommendations derived from this question

The GDG agreed not to make a recommendation on the use of psychological therapies for the prophylactic treatment of primary headaches.

Surveillance decision

This review question should not be updated.

Tension headache

Evidence Update and 2-year surveillance summary
No relevant evidence was identified.

4-year surveillance summary
No relevant evidence was identified.

Topic expert feedback
Topic experts highlighted that:

> 'Mindfulness is being increasingly talked about as helpful- particularly for chronic migraine which is a difficult group to manage'.

Impact statement
Although topic experts highlighted that mindfulness is now being considered as an option for chronic migraine, no new evidence was identified in this area to suggest an update is required.

New evidence is unlikely to impact on the guideline.

Migraine with or without aura

Evidence Update and 2-year surveillance summary
Cognitive behavioural therapy

A RCT compared cognitive behavioural therapy (CBT) with headache education alongside medication (amitriptyline[10]) in young people with chronic migraine [37]. Young people aged 10–17 years with a diagnosis of chronic migraine and at least moderate migraine-related disability were included (n=135).

CBT was associated with fewer days with headache per month compared with education group.

Limitations of the study included the small sample size, the inclusion of a very specific group of patients that limits the transferability of the results and the no inclusion of an inactive comparator group to test solely the effect of the cognitive behavioural therapy.

NICE guideline CG150 does not make any recommendations on CBT for migraine owing to lack of evidence, but this research was considered to provide 'proof of concept' that CBT on top of medication may be effective in a subset of young people with chronic migraine. The nature of the population included in this study limits the generalisability of the findings, and the intervention may be difficult to replicate in the NHS. As such this evidence, alone, was considered unlikely to have an impact on NICE guideline CG150.

4-year surveillance summary
No relevant evidence was identified.

[10] Amitriptyline is not licenced for migraine prophylaxis in the UK.

Topic expert feedback
One stakeholder highlighted two studies in this area [38,39].

The first study was a pilot RCT assessing a brief guided self-help CBT plus relaxation for migraine (n=75) [38]. The intervention consisted in was compared with standard medical care. Authors reported a small number of drop-outs concluding that a trial in the UK context is feasible.

The second study was a SR that assessed the efficacy of psychological therapies for migraine in adults. Inclusion criteria were not described in the abstract [39]. A total of 24 studies were included a slightly majority of them with low risk of bias (17/24). Authors reported that psychological interventions produce an improvement of headache-related and psychological outcomes but these outcomes were not described in the abstract. Authors highlighted that most of the studies were conducted in USA and this fact could have impact on the generalisability of the results to other settings non-privately funded. They concluded that the evidence identified supports the use of psychological interventions but more research is needed in the UK context.

Impact statement
Two studies highlighted by one stakeholder emphasised the relevance of the research in this area, especially in the UK context.

One study was a pilot RCT that concluded that a bigger trial assessing a brief guided self-help CBT plus relaxation is feasible in UK. The second one was a SR that showed that psychological interventions might have a role in the treatment of the headaches but more research is needed in the NHS context.

Similar conclusions were made in the previous Evidence Update and 2-year surveillance Review where evidence with limited generalisability of its findings was identified and considered unlikely to have an impact on NICE guideline CG150.

New evidence is unlikely to impact on the guideline.

Prophylactic non-pharmacological management of primary headaches with dietary supplements and herbal remedies

150– 24 **For people with primary headaches, what is the clinical evidence and cost-effectiveness of non-pharmacological management with dietary supplements (e.g. magnesium, vitamin B12, coenzyme Q10 and riboflavin (B2)?**

150– 25 **For people with primary headaches, what is the clinical evidence and cost-effectiveness of non-pharmacological management with herbal remedies?**

Recommendations derived from these questions

1.3.23 Advise people with migraine that riboflavin (400 mg* once a day) may be effective in reducing migraine frequency and intensity for some people. [2012]

* At the time of publication (November 2015), riboflavin did not have a UK marketing authorisation for this indication but is available as a food supplement. When advising this option, the prescriber should take relevant professional guidance into account. See the General Medical Council's Good practice in prescribing medicines – guidance for doctors and the prescribing advice provided by the Joint Standing Committee on Medicines (a joint committee of the Royal College of Paediatrics and Child Health and the Neonatal and Paediatric Pharmacists Group) for further information.

Surveillance decision

This review question should not be updated.

Dietary supplements

Evidence Update and 2-year surveillance summary
No relevant evidence was identified.

4-year surveillance summary
No relevant evidence was identified.

Topic expert feedback
No topic expert feedback was relevant to this evidence.

Impact statement
No new information was identified at any surveillance review.

New evidence is unlikely to change guideline recommendations.

Herbal remedies

Evidence Update and 2-year surveillance summary
No relevant evidence was identified.

4-year surveillance summary
We identified a Cochrane review evaluating the efficacy and safety of feverfew in the prevention of migraine attacks [40]. A total of six RCTs were included but the results were presented narratively given the heterogeneity of the population, interventions and outcomes assessed. In general there is a lack of consistent evidence to support the use of feverfew as a prophylactic treatment of migraine attacks. One trial with a low risk of bias found that feverfew reduced the monthly frequency of migraines attacks by 0.6 compared with placebo, but no differences were identified in other outcomes assessed (intensity and duration of migraine attacks, nausea and vomiting and global assessment). Three other trials showed positive results whereas another two trials did not find significant differences between feverfew and placebo. No serious adverse events were reported.

Topic expert feedback
No topic expert feedback was relevant to this evidence.

Impact statement
New evidence identified related to the use of feverfew as a prophylactic treatment of migraine showed heterogeneous results. The Cochrane review assessing this intervention included six RCTs but given the differences in their methods it was not possible to pool the results. In general it was considered that here is a lack of consistent evidence to recommend the use of feverfew in this context. The new evidence identified was considered unlikely to have an impact on current NICE guideline CG150 recommendations.

New evidence is unlikely to change guideline recommendations.

Prophylactic non-pharmacological management of primary headaches with exercise

150– 26 For people with primary headaches, what is the clinical evidence and cost-effectiveness of non-pharmacological management with exercise programmes?

Recommendations derived from this question

The GDG decided that there was not enough evidence to form a recommendation for or against the use of exercise for migraine.

Surveillance decision

No new information was identified at any surveillance review.

This review question should not be updated.

Prophylactic non-pharmacological management of primary headaches with education and self-management

150– 27 For people with primary headaches, what is the clinical evidence and cost-effectiveness of non-pharmacological management with education and self-management programmes?

Recommendations derived from this question

The GDG decided that there was not enough evidence to form a recommendation for or against the use of exercise for migraine

Surveillance decision

This review question should not be updated.

Evidence Update and 2-year surveillance summary
No relevant evidence was identified.

4-year surveillance summary
A SR evaluated the efficacy of therapeutic patient education for migraine in adults [41].

A total of 14 studies were identified and nine were included in the meta-analysis of the results. Therapeutic patient education programmes were associated with a decrease in the number of headaches, headaches disability, and an improvement in the quality of life compared with control group in the intermediate-term. No differences were identified between the groups in terms of self-efficacy or depressive symptoms either in the short or intermediate term. No details about the interventions included in the therapeutic patient education group or in the control group were described in the abstract.

Topic expert feedback
No topic expert feedback was relevant to this evidence.

Impact statement
New evidence identified shows that therapeutic patient education interventions might have a role in the management of migraine. However, it is unclear what the characteristics of the patient education programmes assessed and population were included in the study. Although some benefits were identified in the intermediate-term it is unclear the benefit at long term. Therefore it is considered that evidence identified is limited in quantity and quality and unlikely to have an impact on NICE guideline CG150.

New evidence is unlikely to impact on the guideline.

NQ – 01 In people with chronic or episodic migraine (with or without aura), what is the clinical evidence and cost-effectiveness of occipital nerve block?

This question was not addressed by the guideline.

New evidence has subsequently been identified and considered for possible addition to the guideline as a new question.

Surveillance decision

This question should not be added.

Evidence Update and 2-year surveillance summary
No relevant evidence was identified.

4-year surveillance summary
A RCT compared the combination of corticosteroids plus anaesthetic with placebo plus anaesthetic in occipital nerve blockage as prophylactic treatment of migraine [42]. A total of 69 participants were randomly allocated to receive injections with 20 mg methylprednisolone plus 2.5ml 0.5% bupivacaine or placebo (2.75ml normal saline) plus 0.25ml 1% lidocaine without epinephrine. No differences were identified in the reduction of moderate or severe headaches between the groups compared.

Topic expert feedback
Topic experts highlighted that occipital nerve block is being used for migraine and cluster headaches.

Impact statement
New evidence identified is limited and considered insufficient to have an impact on NICE guideline CG150.

New evidence is unlikely to impact on the guideline.

NQ – 02 In people with chronic migraine (with or without aura) or cluster headache, what is the clinical evidence and cost-effectiveness of invasive or non-invasive nerve stimulators?

This question was not addressed by the guideline.

New evidence has subsequently been identified and considered for possible addition to the guideline as a new question.

Surveillance decision

This question should not be added.

Evidence Update and 2-year surveillance summary
No relevant evidence was identified.

4-year surveillance summary
One SR assessed the impact of occipital nerve stimulation for chronic migraine on different outcomes. RCTs and case-control studies were included (n=517) [43]. Pooled results from RCTs showed that occipital nerve stimulation is

associated with lower number of days with prolonged, moderate to severe headaches per month compared with sham control. Authors reported that data informing other outcomes were incomplete but seemed to favour occipital nerve stimulation. Adverse events were common with occipital nerve stimulation (infections, lead migration) and required revision with surgery. Authors concluded that the results identified favouring occipital nerve stimulation were modest and might be influenced by the quality of the included studies.

A randomised open-label trial assessed the effectiveness of non-invasive vagus nerve stimulation as an adjunctive prophylactic treatment of cluster headache (n=97) [44]. All the patients included received standard care. The group receiving standard care alone was the control group. Non-invasive vagus nerve stimulation was associated with a reduction of the number of attack per week and with a higher response rate compared with control group. Serious adverse events were not reported.

We identified four different NICE interventional procedures: NICE interventional procedure guidance IPG559 and NICE interventional procedure guidance IPC552 both published in 2016, NICE interventional procedure IPG477 published in 2014, and NICE interventional procedure IPG452 published in 2013.

NICE interventional guidance IPG559 offers guidance on transcutaneous electrical stimulation of supraorbital nerve for the prevention of migraine in adults. NICE interventional procedure guidance IPC522 gives guidance in transcutaneous stimulation of the cervical branch of the vagus nerve to cluster headache and migraine in adults. NICE interventional procedure IPC477 offers guidance in the use of transcranial magnetic stimulation during the aura before a migraine episode or at the start of a migraine episode. Finally, NICE interventional procedure IPC452 offers guidance on the use of occipital nerve stimulation for intractable chronic migraine.

The recommendation for all these procedures is the same: 'this procedure should only be used with special arrangements for clinical governance, consent and audit or research'.

Topic expert feedback

Topic expert feedback highlighted that there are various nerve stimulators now on the market. For example gamma core, cefaly and sTMS devices. Other devices mentioned were Single pulse Transcranial Magnetic stimulation (the ENeura device), External neurostimulation of the vagus nerve (The Gammacore device), and Supraorbaitla nerve stimulation devices (Cefaly).

> 'The current guidelines also do not consider the place and role of device therapies that are available and being recommended by some clinicians for migraine and cluster headache treatment'.

Impact statement

New evidence was identified related to the use of occipital nerve stimulation for chronic migraine and non-invasive vagus nerve stimulation as adjuvant treatment for cluster headaches. However, the quality and quantity of the evidence was considered limited and unlike to have an impact on current NICE guideline CG150.

Four NICE interventional procedures recently published were also identified. They assessed the use of different devices for the treatment of migraine and cluster headache. The evidence identified in the NICE interventional procedures was considered limited in quantity and quality. They concluded that use of these devices is only recommended with special arrangements for clinical governance, consent and audit or research. Given these recommendations and the limited new evidence identified in this surveillance review, it was considered that this question should not be added to NICE guideline CG150.

New evidence is unlikely to impact on the guideline.

Research recommendations

Priority

These research recommendations were deemed priority areas for research by the guideline committee. At this 4-year surveillance review time point a decision will be taken on whether to retain the research recommendations or stand them down.

1 Amitriptyline to prevent recurrent migraine

RR – 01 Is amitriptyline a clinically and cost effective prophylactic treatment for recurrent migraine?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

The research recommendation will be removed from the NICE version of guideline and the NICE research recommendations database because there is no evidence of research activity in this area.

2 Pizotifen to prevent recurrent migraine

RR – 02 Is pizotifen a clinically and cost effective prophylactic treatment for recurrent cluster headache?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

It was proposed to remove the research recommendation from the NICE version of the guideline and the NICE research recommendations database because there is no evidence of research activity in this area. We considered the views of stakeholders through consultation. It was decided to retain this research recommendation based on the feedback from stakeholder consultation.

3 Topiramate to prevent recurrent cluster headache

RR – 03 Is topiramate a clinically and cost effective prophylactic treatment for recurrent cluster headache?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

The research recommendation will be removed from the NICE version of guideline and the NICE research recommendations database because there is no evidence of research activity in this area.

4 Psychological interventions to manage chronic headache disorders

RR – 04 Does a psychological intervention such as cognitive behavioural therapy (CBT) improve headache outcomes and quality of life for people with chronic headache disorders?

New evidence relevant to the research recommendation was found and summarised in Q150-23 but an update of the related review question is not planned because the new evidence is insufficient to trigger an update.

The research recommendation will be retained because there is evidence of research activity in this area.

5 Pharmacological treatments for headache prophylaxis to aid withdrawal treatment in medication overuse headache

RR – 05 Does a course of steroid treatment or pharmacological treatments used for headache prophylaxis help people with medication overuse headaches withdraw from medication?

No new evidence relevant to the research recommendation was found and no ongoing studies were identified.

The research recommendation will be removed from the NICE version of guideline and the NICE research recommendations database because there is no evidence of research activity in this area.

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