NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Clinical Practice – Surveillance Programme

Clinical guideline
CG150: Headaches: diagnosis and management of headaches in young people and adults.

Publication date
September 2012

Surveillance report for GE
October 2014

Surveillance recommendation
GE is asked to consider the proposal to update the following clinical question in the guideline using the Standing Committee for Updates via the Clinical Guidelines Update Team:

- In people with migraine with or without aura, what is the clinical evidence and cost-effectiveness for prophylactic pharmacological treatment with: ACE inhibitors and ARBs; antidepressants; beta blockers; calcium channel blockers; antiepileptics; and other serotonergic modulators?

GE are asked to note that this 'yes to update' proposal will not be consulted on.

Key findings

			Potential impact on guidance	
			Yes	**No**
Evidence identified from Evidence Update			✓	
Anti-discrimination and equalities considerations				✓
Feedback from Triage Panel meeting			✓	
No update	**CGUT update**	Standard update	Transfer to static list	Change review cycle
	✓			

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Surveillance review of CG150: Headaches: diagnosis and management of headaches in young people and adults.

Background information

Guideline issue date: 2012
2 year review: 2014

NCC: National Clinical Guidelines Centre

Triage panel recommendation

1. Through the 2 year Evidence Update of CG150 new evidence which may potentially impact guideline recommendations was identified in the following two clinical areas concerned with prophylactic pharmacological treatment of migraine. These were considered by the Triage Panel:

2. *Pharmacological prophylaxis of migraine with antiepileptics in adults*

   A Cochrane review[1] and an RCT[2] examining the prophylactic treatment of migraine in adults with gabapentin and gabapentin enacarbil were identified in the Evidence Update. Overall, these two studies suggest that gabapentin and gabapentin enacarbil are no better than placebo for the prophylactic treatment of migraine. Furthermore, these drugs were found to commonly be associated with adverse events. The Triage Panel indicated that the recommendation to consider gabapentin as a second line drug should be reconsidered. This was because of the new evidence identified and due to concerns about the quality of the original trial evidence that have now come to light.

Decision: NICE to update this clinical question using Standing Committee for Updates via the Clinical Guidelines Update Team.

3. *Pharmacological prophylaxis of migraine with other drugs in adults*

A network meta-analysis[3] assessing the effects of several prophylactic pharmacological treatments for migraine in adults was identified in the Evidence Update. This showed that angiotensin-inhibiting drugs were the most effective compared to placebo followed by clonidine (an antiadrenergic drug), betablockers, and the antiepileptic drug valproate semisodium. Adverse effects were more likely to occur in all drugs, when compared to placebo, apart from betablockers. An RCT[4] examining the effectiveness of candesartan for the prophylactic treatment of migraine was also identified in the Evidence Update. Results showed that candesartan and propranolol led to significantly fewer days with migraine per four weeks compared to placebo. However, no difference in efficacy was seen between candesartan and propranolol. The rate of adverse events was found to be significantly higher with propranolol when compared with placebo. This was not the case for candesartan.The Triage Panel indicated that prescribing practice has changed since CG150 . As such, the Network Meta-analysis (NMA) on which this section of the guidline is based should be updated to include the new evidence identified on angiotensin-inhibiting drugs and to include any new drugs currently used.

Decision: NICE to update this clinical question using Standing Committee for Updates via the Clinical Guidelines Update Team.

2-year Evidence Update

4. The Evidence Update on CG150: Headaches was used as a source of evidence for this surveillance review and considered new evidence since the guideline was published. The search dates of the Evidence Update were 13 March 2012 to 26 March 2014.

5. New evidence that may impact on recommendations was identified relating to one section of the guideline as described above.

Ongoing research

6. None identified.

Anti-discrimination and equalities considerations

7. None identified.

Implications for other NICE programmes

8. This guideline relates to a published quality standard on headaches in young people and adults (QS42, published 2013)

9. An update of the clinical question on the prophylactic pharmacological treatment of migraine is unlikely to impact on any of the Quality Statements within the Quality Standard.

Conclusion

10. Through the Evidence Update of CG150 new evidence which may potentially impact guideline recommendations was identified in the following areas of the guideline and discussed at the Triage Panel meeting:
    a. Pharmacological prophylaxis of migraine with antiepileptics in adults
    b. Pharmacological prophylaxis of migraine with other drugs in adults

11. These areas considered by the Triage Panel were assessed as requiring an update at this time. This update could be achieved by updating the following question in the guideline:
    a. In people with migraine with or without aura, what is the clinical evidence and cost-effectiveness for prophylactic pharmacological treatment with: ACE inhibitors and ARBs; antidepressants; beta blockers; calcium channel blockers; antiepileptics; and other serotonergic modulators?

12. For all other areas of the guideline no evidence was identified which would impact on recommendations.

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Centre for Clinical Practice
October 2014

Appendix 1 - Decision matrix

Surveillance and identification of triggers for updating CG150. The table below provides summaries of the evidence/intelligence that were identified for the triage panel meeting on 22nd September 2014.

Main findings and conclusion of the 2-year Evidence Update (September 2014)	Is there any new evidence/intelligence identified during this 2-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Impact of findings of this 2-year Evidence Update on guideline recommendations
150-01 For young people and adults with HIV presenting with new onset headache, how common are serious intracranial abnormalities?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
150-02 For young people and adults with a history of malignancy presenting with new onset headache, how common are serious intracranial abnormalities?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
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?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
150-04 What is the accuracy of case finding questionnaires for diagnosing primary headache disorders and medication overuse headache?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
150-05 What is the clinical effectiveness of using diaries for the diagnosis in people with suspected primary headaches and medication overuse headache?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
150-06 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?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
150-07 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?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
150-08 Should young people and adults with suspected primary headaches undergo brain imaging to rule out serious pathology?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
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?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
150-10 What information and support do people with primary headaches say they want?			

Main findings and conclusion of the 2-year Evidence Update (September 2014)	Is there any new evidence/intelligence identified during this 2-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Impact of findings of this 2-year Evidence Update on guideline recommendations
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
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?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
150-12 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?			
Two studies assessing the efficacy and safety of oral Triptans, with or without NSAID, for migraine were identified. One study[5] was an RCT examining oral rizatriptan compared to placebo in young people (n=1382) who had a history of migraine whilst the second study[6] was an RCT comparing combined oral sumatriptan and naproxen sodium with placebo in young people (n=683) with a history of moderate to severe migraine. The Evidence Update concluded that in young people with migraine, oral Triptans, with or without NSAID, were more effective than placebo in eliminating migraine pain at two hours.	Not applicable	Not applicable	Overall, the new evidence suggests that oral Triptans are beneficial for the treatment of migraine in young people. This is consistent with recommendations in CG150 which recommend treating migraine with an oral or ideally a nasal triptan, alone or with an NSAID or Paracetamol, in young people aged 12 years and over.
150-13 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?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
150-14 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?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
150-15 In people with migraine with or without aura, what is the clinical evidence and cost-effectiveness for prophylactic pharmacological			

Main findings and conclusion of the 2-year Evidence Update (September 2014)	Is there any new evidence/intelligence identified during this 2-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Impact of findings of this 2-year Evidence Update on guideline recommendations
treatment with: ACE inhibitors and ARBs; antidepressants; beta blockers; calcium channel blockers; antiepileptics; and other serotonergic modulators?			
Topiramate A Cochrane review[7] was identified which examined prophylactic topiramate on the frequency of migraine. The included 17 trials compared topiramate with placebo, an active control or a different dose of topiramate. The Evidence Update concluded that regular prophylactic topiramate treatment is more efficacious that placebo in reducing headache frequency in those with episodic migraine. NICE recommends topiramate as a first-line prophylactic treatment for adults and young people. Therefore this evidence is consistent with CG150. **Gabapentin, gabapentin enacarbil or pregabalin** A Cochrane review[1] and and RCT[2] were identified which investigated the prophylactic use of gabapentin,gabapentin enacarbil and pregabalin compared to placebo in adults with migraine. The Evidence Update concluded that gabapentin and gabapentin enacarbil are no better than placebo for the prophylactic treatment of migraine. Furthermore, they are also more commonly associated with adverse events.	Not applicable	Not applicable	For topiramate, the new evidence of it's effectiveness is consistent with current guideline recommendations which recommend topiramate as a first-line prophylactic treatment for adults and young people. The evidence on gabapentin and gabapentin enacarbil suggests that they are no better than placebo and are commonly associated with adverse events. This is not in line with the current NICE recommendation which recommenda gabapentin for prophylactic treatment of migraine in adults and young people in whom topiramate and propranolol are unsuitable or ineffective.

Main findings and conclusion of the 2-year Evidence Update (September 2014)	Is there any new evidence/intelligence identified during this 2-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Impact of findings of this 2-year Evidence Update on guideline recommendations
The authors for the Cochrane review note that their findings contradict those found in a previous review[8]. This is because the current review included previously confidential research that became available. **Alporic acid, sodium valproate or valproate semisodium** A Cochrane review[9] was identified which examined valopric acid, sodium valoprate or a combination of these, compared to placebo, on the frequency of migraines in adults. Ten trials were included The Evidence Update concluded that sodium valproate and valproate semisodium were effective prophylactic treatments for reducing migraine frequency in adults with migraine. NICE does not currently make any recommendations on these treatments for the prevention of migraine because, the Evidence Update suggests, the evidence identified during the guideline production process was poor quality and, in most cases, did not report the preferred outcome. The Evidence Update states that this evidence is unlikely to impact on the guideline because of the lack of data on change in headache frequency that was reported in the studies analysed by the included Cochrane review. **Other drugs** A network meta-analysis[3] and RCT[4] were identified that assessed several types of prophylactic pharmacological			As such, this evidence may impact on the guideline. The evidence on soldium valproate and valproate semisodium is unlikely to impact on CG150. This is because few trials were included in the Cochrane review that reported the preferred outcome. For other drugs, the evidence suggests that angiotensin-inhibiting drugs are an effective prophylactic treatment for migraine. Currently CG150 does not make any recommendations on it's use. Therefore, the new evidence has a potential to impact on this guideline. The evidence for prophylactic pharmacological treamtents in children

Main findings and conclusion of the 2-year Evidence Update (September 2014)	Is there any new evidence/intelligence identified during this 2-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Impact of findings of this 2-year Evidence Update on guideline recommendations
treatments for migraine in adults. The network meta-analysis included 215 RCTs and 76 non-randomised studies looking at 59 drugs including antiepileptics, beta-blockers, angiotensin-inhibiting drugs, clonidine and Lisinopril. The RCTexamined candesartan. The Evidence Update concluded that angiotensin-inhibiting drugs and beta-blockers may be effective in reducing migraine frequency, Currently, NICE recommends the beta-blocker propranolol but does not make any recommendations on angiotensin-inhibiting drugs. As such, they suggest that the new evidence may have a potential impact on CG150. **Children and young people** A meta-analysis[10] was identified which investigated the effectiveness of a range of prophylactic pharmacological treatments for migraine in children and young people. Twenty one studies were included and the drugs examined included topiramate, trazodone hydrochloride, clonidine, flunarizine, piracetam, pizotifen, propranolol, sodium valproate and fluoxetine. The Evidence update concluded that there is limited evidence suggesting the prophylactic use of topiramate and trazodone hyrocholride for reducing headache frequency in children and young people. There was also limited evidence for other commonly used drugs being ineffective. It is suggested that given the short comings			and young people is unlikely to currently impact on CG150. This is because the evidence on the effectiveness or ineffectiveness of such treatments is currently limited.

Main findings and conclusion of the 2-year Evidence Update (September 2014)	Is there any new evidence/intelligence identified during this 2-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Impact of findings of this 2-year Evidence Update on guideline recommendations
of the studies included in the meta-anlaysis that the evidence is unlikely to impact on this guideline.			
150-16 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)?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
150-17 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?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
150-18 For people with primary headaches, what is the clinical evidence and cost-effectiveness of non-pharmacological management with acupuncture?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
150-19 For people with primary headaches, what is the clinical evidence and cost-effectiveness of non-pharmacological management with manual therapies?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
150-20 For people with primary headaches, what is the clinical evidence and cost-effectiveness of non-pharmacological management with psychological therapies?			
An RCT (n=135)[11] was found that investigated cognitinve behavioural therapy (CBT) and compared it to headache eduction alongside medication in young people with chronic migraine. The Evidence Update concluded that intensive CBT plus amitriptyline is more effective than headache education plus medication in reducing headache frequency in young people. However, CG150 does not currently make any recommendations on CBT for migraine because of a lack of evidence. It was suggested that the nature of the population included in the RCT limits the generalisability	Not applicable	Not applicable	The RCT identified suggests that CBT is beneficial for the prophylactic treatment of migraine in young people. However, the evidence is currently insufficient and so unlikely to impact on CG150. More trials investigating CBT for the prophylactic treatment of migraine are needed

Main findings and conclusion of the 2-year Evidence Update (September 2014)	Is there any new evidence/intelligence identified during this 2-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Impact of findings of this 2-year Evidence Update on guideline recommendations
of it's findings and that the intervention may be difficult to replicate in the NHS. Consequently, the above RCT, on it's own, is unlikely to impact on this guideline. Further large RCTs are needed to confirm or refute the effectivenss of CBT for the prophylactic treatment of migraine in young people.			before it can be considered for inclusion in the guideline. The new evidence does relate to a research recommendation which recommends a pragmatic RCT to test whether psychological intervention such as CBT improve headache outcomes and quality of life for people with chronic headache disorders.
150-21 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))?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
150-22 For people with primary headaches, what is the clinical evidence and cost-effectiveness of non-pharmacological management with herbal remedies?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
150-23 For people with primary headaches, what is the clinical evidence and cost-effectiveness of non-pharmacological management with exercise programmes?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
150-24 For people with primary headaches, what is the clinical evidence and cost-effectiveness of non-pharmacological management with education and self-management programmes?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable
150-25 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?			

Main findings and conclusion of the 2-year Evidence Update (September 2014)	Is there any new evidence/intelligence identified during this 2-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Impact of findings of this 2-year Evidence Update on guideline recommendations
Prophylactic treatment Two RCTs were identified that investigated the prophylactic treatment of medication overuse headache. One RCT[12] examined the effectiveness of prednisone for the treatment of withdrawal headache in adults with medication overuse headache. Ninety six patieints were randomised to 100mg prednisone or 100mg of placebo. The second RCT[13] examined prednisolone in adults with migraine or tension-type headache and probabale medication overuse headache (n=100). Patients were randomised to prednisolone or placebo for the first six days after withdrawal. From the above studies, the Evidence Update concluded that prophylaxis with these drugs during the first few days after headache medication withdrawal is not effective at reducing headache in those with medication overuse headache. However, this evidence is unlikely to impact on the guideline because CG150 does not currently make any recommendations specifically to use or not use corticosteroids. **Inpatient Withdrawal** A cohort study[14] was found which compared advice alone with structured inpatient and outpatient programmes in people with medication overuse headache. Patients (n=141) received either education on medication overuse headache and advice to withdraw the overuse medications, an outpatient withdrawal programme comprising the same education and advice	Not applicable	Not applicable	The new evidence suggests that prednisone and prednisolone are not effective for the prophylactic treatment of medication overuse headaches. This evidence is currently unlikely to impact on CG150 as this guideline does not make any recommendations to use or not use these drugs. For inpatient withdrawal, the evidence suggests that inpatieint programmes are more effective than outpatient programmes or education alone.This is consistent with the current recommendation in CG150 to reserve inpatient withdrawal for those who are using strong opioids, have relevant comorbidities or have previously been unsuccessful at

Main findings and conclusion of the 2-year Evidence Update (September 2014)	Is there any new evidence/intelligence identified during this 2-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Impact of findings of this 2-year Evidence Update on guideline recommendations
as the first group plus prednisone and individualised prophylactic treatment or a 10 day inpatient withdrawal programme with education, advice, steroids, fluid replacement, antiemetics and individualised prophylactic treatment. The Evidence Update concluded that inpatient treatment appears more effective that outpatient treatment or education alone for achieving medication withdrawal in those with migraine and complicated medication overuse headache. They state that this evidence is consistent with current NICE recommendations to reserved inpatient withdrawal for those who are using strong opioids, have relevant comorbidities or have previously been unsuccessful at withdrawal of overused medication.			withdrawal of overused medication.
150-26 What is the evidence for adverse fetal events in females with primary headaches during pregnancy using triptans, oxygen, or verapamil?			
A population-based cohort study[15] (n=181,125) was identified that assessed the use of Triptans during pregnancy. From this, the Evidence Update concluded that triptan use during pregnancy was not associated with miscarriage, stillbirth or congential malformations. This evidence was consistant with the current NICE recommendation to use Triptans during pregnancy.	Not applicable	Not applicable	The new evidence suggests that Triptan use during pregnancy does not result in miscarriage, stillbirth or congential malformations. As such, this evidence is consisitent with the current guideline recommendation to use Triptans during pregnancy.

Main findings and conclusion of the 2-year Evidence Update (September 2014)	Is there any new evidence/intelligence identified during this 2-year surveillance review (2014) that may change this conclusion?	Clinical feedback from the GDG	Impact of findings of this 2-year Evidence Update on guideline recommendations
150-27 What risks are associated with use of hormonal contraception in females aged 12 or over with migraine?			
No new key evidence was found for this section	Not applicable	Not applicable	Not applicable

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