PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (**http://bmjopen.bmj.com/site/about/resources/checklist.pdf**) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Acupuncture for acute migraine attacks in adults: a systematic review protocol
AUTHORS	Ruosang Du, Yang Wang, Xiaoxu Liu, Zhishun Liu

VERSION 1 - REVIEW

REVIEWER	Klaus Linde Institut of General Practice, Technsiche Universität München
REVIEW RETURNED	08-Dec-2014

GENERAL COMMENTS	The manuscript reports the protocol of a systematic review of randomized trials on the efficacy of acupuncture in the treatment of acute migraine attacks. Overall, the manuscript is clearly written and the methods are broadly adequate. Yet, I have a number of mostly minor concerns and suggestions for improvement: Major comments: 1) I am somewhat concerned about the of the quality of the referencing! When supporting the statement that acupuncture is widely used to treat headache the authors cite two RCTs. This does not make much sense. I cannot find citiations of references 14 to 16 (RCTs of migraine prophylaxis!?) in the text. Reference 26 (a clinical trial) does not fit to the mechanisms of action discussed before. 2) In my view the introduction should discuss more clearly why acupuncture is/should be relevant for treating acute migraine attacks. At least in Western countries patients typically treat attacks with medication. Acupuncture treatment implies that patients have to seek an acupuncturist during an attack. This has feasibility and cost implications. Do the authors expect acupuncture to be more effective than drugs like triptans, or will they benefit different patients/patients who do not benefit from more easily accessible options? Minor comments - Objectives: the description of the objectives reads rather vague. You might consider to use the PICOS format. - Type of studies: why do you include cross-over trials? For the treatment of a single attack that makes little sense. Do you consider trials investigating mulitple attacks in patients? - Types of interventions: you should shortly explain fire needling, warm needling and elongated needling. 'Conventional intervention' also is a very vague term. What exactly is included here? - Primary outcomes: it might make sense to explicitly cite (and discuss whether your outcomes fit to) the guidelines of the International Headache Society on RCTs of drugs for acute migraine. - Language restriction: it seems somewhat unfortunate to restrict the review a priori to trials published in Chinese and English. Can't that

	be avoided somehow? If you exclude trials already at the search level (?your search terms do not include language - which is good) one cannot even learn whether trials in other languages exist at all. I would recommed to not restrict languages at that stage. If you see that several potentially relevant trials are identified by your searches you could consider translation/inclusion of a reviewer speaking these languages. - Searches: will 'searches' truly be carried out by two reviewers independently? - Assessing risk of bias: Do you already have clear instructions how to rate the items? (e.g. will blinding be rated low risk in single-blind trials?) - Analyses: given your relatively wide intervention inclusion criteria I would strongly recommend to pre-define to some extent what comparisons you plan to do (e.g. separate for comparisons vs. no treatment, sham, drugs, other interventions). - Dealing with missing data: I would recommend to write "we will try to obtain the information...". Furthermore, there is some evidence suggesting that many older Chinese trials described as randomized are actually not properly randomized. Do you plan to obtain information here when descriptions on sequence generation and concealment in the paper are unclear? - Data Synthesis: RevMan 5.3 is now available. What means "excessive heterogeneity"? You only define "considerable" heterogeneity before. (Some statisticians believe Tau square is a better indicator of heterogeneity than I square)

REVIEWER	Shefton Parker RMIT University, School of Health Sciences, Melbourne, Australia
REVIEW RETURNED	10-Dec-2014

GENERAL COMMENTS	Whilst there appears good scope for a review in the target area and may provide of benefit to researchers and clinicians, the submission is lacking considerable information regarding the intervention and the disease. More detail is required in most sections and the quality of the writing requires great improvement to be considered publishable in a peer reviewed journal. I would suggest the authors seek further assistance in the language and formatting of the manuscript and consider registration with PROSPERO before submitting the protocol for publication and stating this in the manuscript that it has been registered. Please see some brief suggestions in the attached PDF of their submission. Also read other protocols for systematic reviews including those in the Cochrane database. I recommend using the cochrane method for systematic reviews and referring to this method as the chose method for the manuscript.

VERSION 1 – AUTHOR RESPONSE

Answer to Reviewer 1:

Major Comment 1: I am somewhat concerned about the quality of the referencing! When supporting the statement that acupuncture is widely used to treat headache the authors cite two RCTs. This does not make much sense. I cannot find citiations of references 14 to 16 (RCTs of migraine prophylaxis!?) in the text. Reference 26 (a clinical trial) does not fit to the mechanisms of action discussed before.
Response: We thank you very much for pointing out our mistake. References 14 to 16 should be

labeled together with references 11 to 13, which means the references of the sentence “Acupuncture has been widely used to treat headache, including migraine” should be references 11 to 16.But we have miswritten 16 as 13. Reference 26 is an unrelated reference in the original location, but we think this high-quality article could also be a reference of the sentence “Acupuncture has been widely used to treat headache, including migraine”. So we changed the order of the reference list and made this article as references 17.This all has been modified in the revised version. We do apologize for our carelessness.

Major Comment 2: In my view the introduction should discuss more clearly why acupuncture is/should be relevant for treating acute migraine attacks. At least in Western countries patients typically treat attacks with medication. Acupuncture treatment implies that patients have to seek an acupuncturist during an attack. This has feasibility and cost implications. Do the authors expect acupuncture to be more effective than drugs like triptans, or will they benefit different patients/patients who do not benefit from more easily accessible options?
Response: We thank you very much for your constructive comments. As you have mentioned, patients typically treat attacks with medication, including traditional analgesics, nonsteroidal anti-inflammatory drugs, and triptans. [1] Triptans accounted for almost 80% of antimigraine analgesics. [2] However, over one-third of the patients did not respond well to triptans and over half of them were willing to try other treatments than the one they were currently taking.[1]Some researchers thought there were unmet needs in acute migraine treatment.[3]In China, acupuncture has been used to treat migraine for thousands of years, and has been suggested by China Association for the Study Pain(CASP) as a complementary and alternative for migraine.[4]So there is a need to assess the effect of acupuncture and maybe acupuncture benefits different patients/patients who do not benefit from more easily accessible options.

REFERENCES
1. Rapoport AM. The therapeutic future in headache. Neurol Sci. 2012;33(suppl 1):S119–S125.
2. Todd AS, Rebecca B, Huma S, et al. The prevalence, impact, and treatment of migraine and severe headaches in the United States: a review of statistics from national surveillance studies. Headache 2013;53:427-36
3. Tfelt-Hansen P, Olesen J. Taking the negative view of current migraine t reatments: the unmet needs. CNS Drugs 2012;26:375–82.
4. China Association for the Study Pain (CASP).China diagnosis and management of migraine. Chinese Journal of Pain Medicine 2011,17:83.

Minor Comment 1: Objectives: the description of the objectives reads rather vague. You might consider to use the PICOS format.
Response: Thank you for your comments and suggestion. Cochrane Handbook for Systematic Reviews of Interventions [1] also gives suggestion on content of objectives:” This should begin with a precise statement of the primary objective of the review, ideally in a single sentence. Where possible the style should be of the form “To assess the effects of [intervention or comparison] for [health problem] for/in [types of people, disease or problem and setting if specified]”. This might be followed by a series of specific objectives relating to different participant groups, different comparisons of interventions or different outcome measures. It is not necessary to state specific hypotheses.”
We have modified the relevant content in the section of “Objectives” in the revised version as below:
”This systematic review aims to assess the efficacy and safety of acupuncture in treating acute migraine attacks in adults, compared to sham acupuncture, placebo, no treatment or other interventions.”

REFERENCES
1. Higgins JPT, Green S. Cochrane handbook for systematic review of intervention version 5.1.0

[updated March 2011].The Cochrane Collaboration 2011. http://www.cochrane-handbook.org (accessed 16 Dec 2014).

Minor Comment 2: Type of studies: why do you include cross-over trials? For the treatment of a single attack that makes little sense. Do you consider trials investigating mulitple attacks in patients?
Response: Thank you for your insightful suggestion. But data from the first period of a cross-over trial represent a parallel group trial, so we think the first period in randomized cross-over trials can be included. We will not consider trials investigating multiple attacks in patients.

Minor Comment 3: Types of interventions: you should shortly explain fire needling, warm needling and elongated needling. 'Conventional intervention' also is a very vague term. What exactly is included here?
Response: Warm needling: a needle with a firing moxa cylinder (a penetrating heat therapy which involves the burning of mugwort) attached to it, which can dispel coldness.
Fire needling: a needle is heated on a firing spirit lamp until the needle is red and hot, and then skin is pricked with the needle rapidly
Elongated needling: uses a needle that is usually longer than 5 cun. (125 mm) [1]
Several systematic review protocols[2-5]published in BMJ-Open also contain these types of interventions without explanation, so we are not sure if there is need to give an explanation in the article.
We have deleted the word “conventional” in the article. Because “conventional acupuncture” is a vague and unspecific medical term, which we meant describing acupuncture therapies in common use. Its typical methods have been listed in the section “Types of intervention” of our article, such as manual acupuncture, electroacupuncture (EA), scalp acupuncture, auricular acupuncture, eye acupuncture, fire needling, warm needling, elongated needling.

REFERENCES
1. Gao X-Y. Acupuncture Dictionary of China. Zhengzhou: Henan Science and Technology Press, 2002.
2. Zhou J, Peng W,Li W, et al. Acupuncture for patients with Alzheimer’s disease: a systematic review protocol. BMJ Open 2014; 4:e005896.
3. Wang W, Zhang T, Peng W, et al. Acupuncture for discomfort in patients during gastroscopy: a systematic review protocol. BMJ Open 2014; 4:e005735
4. Zhang T, Liu H,Liu Z, et al. Acupuncture for neurogenic bladder due to spinal cord injury: a systematic review protocol. BMJ Open 2014; 4:e006249
5. Li W, Peng W,Zhou J, et al. Acupuncture for postherpetic neuralgia: a systematic review protocol. BMJ Open 2014; 4:e005725

Minor Comment 4: Primary outcomes: it might make sense to explicitly cite (and discuss whether your outcomes fit to) the guidelines of the International Headache Society on RCTs of drugs for acute migraine.
Response:
In selecting the main outcome measures for this review, we have considered the guidelines for controlled trials of drugs in migraine issued by the IHS (the International Headache Society). [1]And four outcomes have been rated the most important outcomes by patients with acute migraine headaches: complete pain relief, no headache recurrence, rapid onset of pain relief, and no side effects.[2] we considered the guidelines of IHS, availability of data, patient preferences and some relevant researches[3-5]and made amendments about outcome measures in the revised version as follows:
Primary outcomes
Pain-free at 2 hours after the treatment, without the use of rescue medication.

Secondary outcomes
1. Headache relief (a decrease in headache from severe or moderate to none or mild within 2 h, before any rescue medication)
2. Sustained pain freedom (pain-free at 2 h with no use of rescue medication or relapse within the subsequent 46 h).
3. Incidence of relapse (recurrence).
4. Adverse events.
5. Migraine-associated symptoms (such as nausea, photophobia, phonophobia, etc.)

REFERENCES
1. International Headache Society Clinical Trials Subcommittee. Guidelines for controlled trials of drugs in migraine: third edition. a guide for investigators. Cephalalgia 2012; 32(1) 6–38.
2. Lipton RB, Stewart WF. Acute migraine therapy: do doctors understand what patients with migraine want from therapy? Headache1999;39(Suppl 2):S20–S26.
3. Bird S, Derry S, Moore RA. Zolmitriptan for acute migraine attacks in adults. Cochrane Database of Systematic Reviews 2014, Issue 5. Art. No.: CD008616.
4. Kirthi V, Derry S, Moore RA. Aspirin with or without an antiemetic for acute migraine headaches in adults. Cochrane Database of Systematic Reviews 2013, Issue 4. Art. No.: CD008041.
5. Peer TH. What efficacy measures are clinically relevant and should be used in Cochrane Reviews of acute migraine trials? A comment. Cephalalgia 2014; 0:1–3.

Minor Comment 5: Language restriction: it seems somewhat unfortunate to restrict the review a priori to trials published in Chinese and English. Can't that be avoided somehow? If you exclude trials already at the search level (?your search terms do not include language - which is good) one cannot even learn whether trials in other languages exist at all. I would recommed to not restrict languages at that stage. If you see that several potentially relevant trials are identified by your searches you could consider translation/inclusion of a reviewer speaking these languages.
Response: Compared to other languages, the number of acupuncture researches published in Chinese and English is the maximum. To be honest, for the limitations of our language ability and financial resources, we can only read and understand articles in Chinese and English.

Minor Comment 6: Searches: will 'searches' truly be carried out by two reviewers independently?
Response: Searches will be carried out by two reviewers independently, as we have written in the article. The data screening and selection process will also be carried out by two reviewers (RD and XL) independently.

Minor Comment 7: Assessing risk of bias: Do you already have clear instructions how to rate the items? (e.g. will blinding be rated low risk in single-blind trials?)
Response: We will use the Cochrane Collaboration's 'Risk of bias' tool to assess risk of bias. In Cochrane Handbook for Systematic Reviews of Interventions [1], detailed criteria is provided for making judgements about risk of bias. Because of the particularity of acupuncture manipulation, it is difficult to blind the acupuncturists. But the blinding of the participants and assessors is possible and should be considered to be the ideal. [2]So the blinding of the participants and assessors be rated low risk.

REFERENCES
1. Higgins JPT, Green S. Cochrane handbook for systematic review of intervention version 5.1.0 [updated March 2011].The Cochrane Collaboration 2011. http://www.cochrane-handbook.org (accessed 16 Dec 2014).
2. White AR, Filshie J, Cummings TM. Clinical trials of acupuncture: consensus recommendations for optimal treatment, sham controls and blinding. Complementary Therapies in Medicine 2001;9:237–45.

Minor Comment 8: Analyses: given your relatively wide intervention inclusion criteria I would strongly recommend to pre-define to some extent what comparisons you plan to do (e.g. separate for comparisons vs. no treatment, sham, drugs, other interventions).
Response: According to your comment on objectives (the first of the minor comments), we have pre-defined what comparisons we plan to do in the section of “Objectives” in the revised version. The review will compare acupuncture against sham acupuncture, placebo, no treatment, or any other treatment.

Minor Comment 9: Dealing with missing data: I would recommend to write "we will try to obtain the information...". Furthermore, there is some evidence suggesting that many older Chinese trials described as randomized are actually not properly randomized. Do you plan to obtain information here when descriptions on sequence generation and concealment in the paper are unclear?
Response: We accept your valuable suggestion on the writing of dealing with missing data. We will try to obtain information when descriptions on sequence generation and concealment in the paper are unclear, for some authors might randomize correctly and strictly but do not present clearly. So we will try our best to contact he first or corresponding authors to get more details. According to Cochrane Handbook for Systematic Reviews of Interventions [1], this may lead to overly positive answers. The handbook then suggests the reviewers using open-ended questions. Based on this suggestion, when descriptions on sequence generation and concealment in the paper are unclear, we can ask the author: “How did you decide which treatment the next patient should get?” or any other focused questions.

REFERENCES
1. Higgins JPT, Green S. Cochrane handbook for systematic review of intervention version 5.1.0 [updated March 2011].The Cochrane Collaboration 2011. http://www.cochrane-handbook.org (accessed 16 Dec 2014).

Minor Comment 10: Data Synthesis: RevMan 5.3 is now available. What means "excessive heterogeneity"? You only define "considerable" heterogeneity before. (Some statisticians believe Tau square is a better indicator of heterogeneity than I square)
Response: Thank you for your careful suggestion on the new version of RevMan and we have modified it in the revised version.
According to Cochrane Handbook for Systematic Reviews of Interventions [1], a number of options are available if (statistical) heterogeneity is identified among a group of studies that would otherwise be considered suitable for a meta-analysis. One option is if there is considerable variation in results, and particularly if there is inconsistency in the direction of effect, it maybe misleading to quote an average value for the intervention effect. In this situation, meta-analysis will not be suggested.
τ^2 [2]is an alternative quantification of heterogeneity in a meta-analysis is the among-study variance, calculated as part of a random effects meta-analysis. This is more useful for comparisons of heterogeneity among subgroups, but values depend on the treatment effect scale. I2 is thought to be preferable to the test of heterogeneity when assessing inconsistency across studies.

REFERENCES

1. Higgins JPT, Green S. Cochrane handbook for systematic review of intervention version 5.1.0 [updated March 2011].The Cochrane Collaboration 2011. http://www.cochrane-handbook.org (accessed 16 Dec 2014).
2. Higgins JPT, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. BMJ 2003; 327: 557-60.

Answer to Reviewer 2: Whilst there appears good scope for a review in the target area and may provide of benefit to researchers and clinicians, the submission is lacking considerable information regarding the intervention and the disease. More detail is required in most sections and the quality of the writing requires great improvement to be considered publishable in a peer reviewed journal.
I would suggest the authors seek further assistance in the language and formatting of the manuscript and consider registration with PROSPERO before submitting the protocol for publication and stating this in the manuscript that it has been registered.
Please see some brief suggestions in the attached PDF of their submission. Also read other protocols for systematic reviews including those in the Cochrane database. I recommend using the cochrane method for systematic reviews and referring to this method as the chose method for the manuscript.

Response: We thank you very much for your constructive and useful comments. We have made amendments according to your suggestions. For example, we discussed more clearly why acupuncture should be relevant for treating acute migraine attacks in the introduction. Other sections such as types of studies, types of intervention, types of outcome measures, dealing with missing data, data synthesis, subgroup analysis have also been revised.The revised manuscript was edited and proofread by a native
English-speaker. We have registered in PROSPERO and the number is CRD42014013352, as we have written in the abstract. We also have read some similar systematic review protocols published in the Cochrane database and BMJ-Open. This manuscript was written under the guideline of Cochrane handbook for systematic review of intervention (version 5.1.0).

VERSION 2 – REVIEW

REVIEWER	Shefton Parker RMIT University Australia
REVIEW RETURNED	19-Jan-2015

GENERAL COMMENTS	The review protocol has improved somewhat although there are still a number of areas that require further clarification and/or more detail. The intervention requires more detail as to its description as does the condition and its various classification types.The outcomes for the review have not been clearly defined which is a significant deficiency in the potential review. More research is needed into outcome measures for migraine. Treatment guidelines should be referenced as well as significant societies that have published recommendations for instruments or outcomes that evaluate migraine treatment. Further justification for the primary and secondary outcomes should be included. The writing quality has improved somewhat but still requires further refinement to sentence structure and language. Please see the attached comments and changes to the draft aimed to enhance the quality of the manuscript. The reviewer also provided a marked copy with detailed comments. Please contact the publisher for full information about it.

VERSION 2 – AUTHOR RESPONSE

Answer to Reviewer 2:

Comment 1: “migraine attacks” what do you mean by this? Symptoms of migraine attack ie. Analgesic pain relief, antiemetic? Prevention of migraine attack? Needs to be more specific.
Response: Thank you for your comment and suggestion. “migraine attacks” means the onset of migraine. This concept has been used by the International Headache Society (IHS). [1] Symptoms of migraine have been written at the beginning of the section” Description of the condition” in the article. Cochrane Handbook for Systematic Reviews of Interventions [2] also gives suggestion on content of objectives:” This should begin with a precise statement of the primary objective of the review, ideally in a single sentence. Where possible the style should be of the form “To assess the effects of [intervention or comparison] for [health problem] for/in [types of people, disease or problem and setting if specified]”. This might be followed by a series of specific objectives relating to different participant groups, different comparisons of interventions or different outcome measures. It is not necessary to state specific hypotheses.”
We have modified the relevant content in this part and the section of “Objectives” the revised version as below: ” This systematic review aims to determine whether acupuncture is effective and safe in relieving headache, preventing relapse and reducing migraine-associated symptoms in adults with acute migraine attacks.”

REFERENCES
1. International Headache Society Clinical Trials Subcommittee. Guidelines for controlled trials of drugs in migraine: third edition. A guide for investigators. Cephalalgia 2012; 32(1):6-38.
2. Higgins JPT, Green S. Cochrane handbook for systematic review of intervention version 5.1.0 [updated March 2011].The Cochrane Collaboration 2011. http://www.cochrane-handbook.org (accessed 16 Dec 2014).

Comment 2: Remove” Other weaknesses include highly variable outcome measurements, insufficient reporting of results, publication bias, or poor trial quality.”This is reported after the review is complete. You don’t know this until completed.
Response: Thank you so much for your professional suggestion. Accordingly, we have deleted this sentence in the revised article.

Comment 3: What is the biological mechanisima of migraine. Ie. It causes pain how? Vision problems how? Nausea how? Neurological symptoms how? etc. more detail needed.
Response: The mechanism of migraine is still widely debated. Relevant theories include the vascular and neurogenic theories, the trigeminovascular system and cortical spreading depression. [1-3] The prevailing view about the origin of pain and other migrainous symptoms is a brain state of altered excitability resulting in the activation and sensitization of trigeminal nociceptors which innervate the large blood vessels in the meninges. Then second-and third-order central trigeminovascular neurons are activated, which in turn activate different areas of the brain stem and forebrain. [3-5]

REFERENCES
1. Claudia F, Heidi G, Lyn R. Studies on the pathophysiology and genetic basis of migraine. Current Genomics 2013;14:300-15.
2. Noseda R, Burstein R. Migraine pathophysiology: anatomy of the trigeminovascular pathway and associated neurological symptoms, CSD, sensitization and modulation of pain. Pain 2013;12,154 Suppl 1:1-21.

3. Pietrobon D, Moskowitz MA. Pathophysiology of migraine. Annu Rev Physiol 2013;75:365-91.
4. Olesen J, Burstein R, Ashina M, et al.Origin of pain in migraine: evidence for peripheral sensitisation. Lancet Neurol 2009;8:679-90.
5. Levy D. Migraine pain and nociceptor activation—where do we stand? Headache 2010;50:909-16.

Comment 4: With aura and without aura define briefly what these are.
Response: The former is characterized by visual, sensory or central nervous system symptoms before the onset of headache and associated migraine symptoms, while the latter one does not have the premonitory symptomatology. [1]

REFERENCES
1. Headache Classification Committee of the International Headache Society (IHS).The international classification of headache disorders, 3rd edition (beta version).Cephalalgia 2013;33(9):644-6.

Comment 5: 1 reference for this whole section? Doesn't look as though the authors have explored the mechanism of migraine or its diagnosis in a lot of depth.
Response: This reference is about the international classification of headache disorders, which is published by the International Headache Society. It is the latest version and we think it has provided exhaustive descriptions on the diagnosis and symptoms of migraine.

Comment 6: "enormous" be careful not to overstate. Unless you are directly quoting then you should use quotations. – So how much is it? Show the monetary figure and just state the facts.
Response: A research based on the American Migraine Prevalence and Prevention (AMPP) Study showed that the average annual direct cost per person of episodic migraine was $1757 in the USA. [1]A cross-sectional survey in eight European Union (EU) countries representing 55% of the adult population has estimated a mean annual cost of migraine per person of €1222 and a total annual cost of €111 billion for adults aged 18 to 65 years. [2]

REFERENCES
1. Munakata J, Hazard E, Serrano D, et al. Economic burden of transformed migraine: results from the American Migraine Prevalence and Prevention (AMPP) Study. Headache 2009;49(4):498-508.
2. Linde M, Gustavsson A, Stovner LJ, Steiner TJ, Barré J, Katsarava Z, et al.The cost of headache disorders in Europe: the Eurolight project. European Journal of Neurology 2012;19(5):703-11.

Comment 7: Yet you only reference one study?
Response: The cited reference provides epidemiologic evidence on the association between migraine and cardiovascular and cerebrovascular diseases based on numerous studies.

Comment 8: What is acupuncture? Definition?
Response: Acupuncture plays an important role in Traditional Chinese Medicine (TCM) and it has a history of thousands of years. It cures disease by inserting needles into certain points in the body.

Comment 9: How do hemodynamic effects relate to analgesic effects? Please detail
Response: Thank you very much for your insightful suggestion. Studies [1-2] have demonstrated acupuncture might positively influence the abnormal cerebrovascular response in migraineurs during the interictal period, accompanied by a significant decrease of days with migraine headache. Nevertheless, the mode of action remains unknown. So we have deleted content about hemodynamics in the revised article.

REFERENCES

1. Bäcker M, Hammes M, Sander D, et al. Changes of cerebrovascular response to visual stimulation in migraineurs after repetitive sessions of somatosensory stimulation (acupuncture): a pilot study. Headache 2004;44:95-101.
2. Wallasch TM, Weinschuetz T, Mueller B, et al. Cerebrovascular response in migraineurs during prophylactic treatment with acupuncture: a randomized controlled trial. J Altern Complement Med 2012;18:777-83.

Comment 10: More detail needed. Why not well and what do you mean by 'not well' ie no efficacy, side effect etc.
Response: Thank you very much for the valuable suggestion. However, about one-third of migraine patients using triptans did not get headache relief at 2 hours after taking medication, [1-2], and over half were willing to try other treatments.[3]

REFERENCES

1. Rapoport AM, Tepper SJ, Bigal ME, et al. The triptan formulations: how to match patients and products. CNS Drugs 2003;17:431-47.
2. Rapoport AM, Tepper SJ. Triptans are all different. Arch Neurol2001;58:1479-80.
3. Rapoport AM. The therapeutic future in headache. Neurol Sci 2012;33 Suppl 1:S119-25.

Comment 11: Do you mean the symptoms of migraine attacks? Ie. Pain or nausea or preventing their onset? Your outcomes as a result are unclear you need to define this early in the review protocol.
Response: Thank you very much for your suggestion. We have modified this sentence as below:" However, no systematic review on acupuncture in relieving headache, preventing relapse and reducing migraine-associated symptoms in adults with acute migraine attacks has been conducted, so there is a lack of adequate evidence to assess its effectiveness and safety. "

Comment 12: See comment 11
Response: Thank you very much for your suggestion. Please see the response of Comment 1 and Comment 11. And we have made an amendment in the revised version.

Comment 13: Define these also (pharmaceutical drug? TMS? Etc).
Response:" other interventions" include specific medications (triptans, ergot alkaloids and derivatives, etc) and nonspecific medications (antiemetics, NSAIDs, butalbital-containing analgesics, opiate analgesics, etc) .[1-2]

REFERENCES

1. Silberstein SD. Practice parameter-evidence-based guidelines for migraine headache(an evidence-based review): report of the quality standards subcommittee of the American Academy of Neurology for the United States Headache Consortium. Neurology 2000;55:754-62.
2. Marmura MJ, Silberstein SD, Schwedt TJ. The acute treatment of migraine in adults: the American Headache Society evidence assessment of migraine pharmacotherapies. Headache 2015;55:3-20.

Comment 14: What are these migraine types (eg.)
Response: Migraine types (e.g. migraine without aura, migraine with aura or chronic migraine.)

Comment 15: explain the"course"
Response: We meant to say there is no time restriction on the history of migraine. But we have made a mistake using an inaccurate word. We are sorry for the wrong description and we have amended it as "duration of migraine" in the article.

Comment 16: frequency (of attack?)

Response: Thanks a lot for pointing out this issue, it should be frequency of attack.

Comment 17: do you mean ‘pain intensity’?
Response: Yes, we accepted your professional suggestion,” pain intensity” is more appropriate.

Comment 18: do you mean duration of symptoms prior to intervention of post intervention?
Response: Thank you for your review. ”duration” means ”duration of symptoms prior to the intervention when an attack happens”. We had changed this word to “timing for administering the acute therapy”.

Comment 19: As mentioned previously you need to explain firstly what acupuncture is then define what forms of acupuncture the review will include.
Response: We accept your valuable suggestion. We have made modifications accordingly, please see the response of Comment 8.

Comment 20: Please define” non-specific treatment”
Response: Drug therapies of acute migraine include specific medications (triptans, ergot alkaloids and derivatives, etc) and nonspecific medications (antiemetics, NSAIDs, butalbital-containing analgesics, opiate analgesics, etc). [1-2] So we rewritten this sentence as below:” Comparison interventions include sham acupuncture, placebo, no treatment, specific medications (triptans, ergot alkaloids and derivatives, etc), nonspecific medications (antiemetics, NSAIDs, butalbital-containing analgesics, opiate analgesics,etc). [1-2]”

REFERENCES
1. Silberstein SD. Practice parameter-evidence-based guidelines for migraine headache(an evidence-based review): report of the quality standards subcommittee of the American Academy of Neurology for the United States Headache Consortium. Neurology 2000;55:754-62.
2. Marmura MJ, Silberstein SD, Schwedt TJ. The acute treatment of migraine in adults: the American Headache Society evidence assessment of migraine pharmacotherapies. Headache 2015;55:3-20.

Comment 21: Why? You need to put this in the discussion section. Justify why you exclude studies and include others.
Response: Thank you for the constructive comment. Trials comparing acupuncture plus another treatment compared to the additional treatment can prove that acupuncture is effective, so we will include this kind of trial. This review aims to assess the effects and safety of acupuncture for acute migraine attacks, so those trials comparing different forms of acupuncture and those evaluating prophylaxis effect will be excluded.
Several systematic review protocols[1-4]published in BMJ-Open also state which kind of studies will be include or exclude, without any explanation, so we are not sure if there is need to give an explanation in the article.

REFERENCES
1. Zhou J, Peng W,Li W, et al. Acupuncture for patients with Alzheimer’s disease: a systematic review protocol. BMJ Open 2014; 4:e005896.
2. Wang W, Zhang T, Peng W, et al. Acupuncture for discomfort in patients during gastroscopy: a systematic review protocol. BMJ Open 2014; 4:e005735
3. Zhang T, Liu H,Liu Z, et al. Acupuncture for neurogenic bladder due to spinal cord injury: a systematic review protocol. BMJ Open 2014; 4:e006249
4. Li W, Peng W,Zhou J, et al. Acupuncture for postherpetic neuralgia: a systematic review protocol. BMJ Open 2014; 4:e005725

Comment 22: What scale is this measured on? Ie. VAS? Reference your outcome measure.
Response: Pain-free at 2 hours after the treatment means pain score is zero at 2 h. Scales measuring pain intensity are accepted for efficacy outcomes, such as the Visual Analogue Scale (VAS), Numerical Rating Scale (NRS), Verbal Rating Scale (VRS).

Comment 23: In this section you should outline clinical guideline recommendations for evaluating migraines clinically and/or for clinical trial. What are the standard outcome measurements? Then you need to justify why or why not utilizing them as your outcomes in your review. Ideally outcomes should explore validated and recognized outcome measures such that your findings are applicable to researchers and clinicians.
Response: In selecting the main outcome measures for this review, we have followed the guidelines for controlled trials of drugs in migraine issued by the IHS (the International Headache Society). [1]And four outcomes have been rated the most important outcomes by patients with acute migraine headaches: complete pain relief, no headache recurrence, rapid onset of pain relief, and no side effects. [2] When selecting the outcome measures, we have considered the guidelines of IHS, availability of data, patient preferences and some relevant researches. [3-5]

REFERENCES
1. International Headache Society Clinical Trials Subcommittee. Guidelines for controlled trials of drugs in migraine: third edition. A guide for investigators. Cephalalgia 2012; 32:6-38.
3. Lipton RB, Stewart WF. Acute migraine therapy: do doctors understand what patients with migraine want from therapy? Headache1999;39 Suppl 2:S20-6.
4. Bird S, Derry S, Moore RA. Zolmitriptan for acute migraine attacks in adults. Cochrane Database of Systematic Reviews 2014, Issue 5. Art. No.: CD008616.
5. Kirthi V, Derry S, Moore RA. Aspirin with or without an antiemetic for acute migraine headaches in adults. Cochrane Database of Systematic Reviews 2013, Issue 4. Art. No.: CD008041.
6. Peer TH. What efficacy measures are clinically relevant and should be used in Cochrane Reviews of acute migraine trials? A comment. Cephalalgia 2014; 0:1-3.

Comment 24: Electronic database? Ie. Excel?
Response:" Using a form" is refined to "Using a data extraction form (Excel)".

Comment 25: Ref?
Response: Thank you very much for your kind The reference is Cochrane handbook for systematic review of intervention. [1]

REFERENCES
1. Higgins JPT, Green S. Cochrane handbook for systematic review of intervention version 5.1.0 [updated March 2011].The Cochrane Collaboration 2011. http://www.cochrane-handbook.org (accessed 16 Dec 2014).

Comment 26: You need to discuss the range of outcome measures as mentioned previously.
Response: Thank you very much for your suggestion. Please see the response of Comment 23.

Comment 27: Remove this as you don't know these are in fact issues yet until the review is completed.
Response: Thank you so much for your professional suggestion. Accordingly, we have deleted this sentence in the article.

VERSION 3 – REVIEW

REVIEWER	Shefton Parker RMIT University Australia
REVIEW RETURNED	12-Feb-2015

GENERAL COMMENTS	The quality and content of the manuscript is improved considerably. Some minor formatting and editing of sentence structure has been suggested. A couple of minor queries remain which have been provided in the manuscript. Once the author has addressed these the manuscript should be forwarded for publishing provided there are no other concerns from reviewers.

VERSION 3 – AUTHOR RESPONSE

Answer to Reviewer 2:
Comment 1: update the “word count”
Response: Thank you very much for your reminding. We have updated the “word count” as 2237 in the revised article.

Comment 2: What about Linde 2009 you mention in the last paragraph? how will your review differ? Or state the existing review is older than 5 years so may also justify a new review.
Response: The systematic review made by Klaus Linde focused on the effect of acupuncture for migraine prophylaxis. Its objective was to investigate whether
acupuncture is effective in reducing headache frequency in patients with migraine, not the pain free or pain relief after the treatment. It excluded studies on acute migraine or headache. [1-2]

REFERENCES
1. Melchart D, Thormaehlen J, Hager S, et al. Acupuncture versus placebo versus sumatriptan for early treatment of migraine attacks: a randomized controlled trial. Journal of Internal Medicine 2003;253:181-8.
2. Pikoff, H. The effects of acupressure on headache pain: a placebo-controlled group outcome study [dissertation]. Buffalo, NY: State University of New York at Buffalo;1989.

Comment 3: references for these scales?
Response: Thank you for your valuable suggestion. The references for these scales are listed below:
1. International Headache Society Clinical Trials Subcommittee. Guidelines for controlled trials of drugs in migraine: third edition. A guide for investigators. Cephalalgia 2012; 32:6-38.
2. Loder E, Burch R. Measuring pain intensity in headache trials: which scale to use? Cephalalgia 2012; 32:179-82.

Comment 4: moved so relapse is explained prior to mention of relapse in
'sustained pain freedom' feel free to switch back to 2 but you need to explain relapse definition in its first instance of use regardless
Response: Thank you very much for your professional suggestion. We have modified in the revised

article as below:
Secondary outcomes
1. Headache relief (a decrease in headache from severe or moderate to none or mild within 2 h, before any rescue medication)
2. Sustained pain freedom (pain-free at 2 h with no use of rescue medication or relapse within the subsequent 46 h).
After 2-h pain freedom, any headache pain from 2 to 48 h after study drug administration, regardless of its severity, is considered a relapse or recurrence.
3. Incidence of relapse (recurrence).
4. Adverse events.
5. Migraine-associated symptoms (such as nausea, photophobia, phonophobia, etc.)

Comment 5: please update your results to Feb 2015
Response: Thank you very much for your reminding. We have made an amendment accordingly in the revised article.