



## Topic Exploration Report

Topic explorations are designed to provide a high-level briefing on new topics submitted for consideration by Health Technology Wales. The main objectives of this report are to:

1. Inform discussions on new topics received by HTW.
2. Determine the quantity and type of evidence available on a topic.
3. Assess the topic against HTW selection criteria.

Topic:	Occipital nerve stimulation for medically refractory chronic cluster headache
Topic exploration report number:	TER062
Referrer:	Andrew Champion, WHSSC
Topic exploration undertaken by:	Health Technology Wales

### Aim of Search

Health Technology Wales researchers searched for evidence on the use of occipital nerve stimulation (ONS) for the treatment of medically refractory chronic cluster headaches.

### Summary of Findings

#### *Secondary research*

NHS England published their Clinical Commissioning Policy (CCP) 'Occipital Nerve Stimulation (ONS) for adults with intractable chronic migraines and medically refractory chronic cluster headaches' (D08/P/c) in 2015. In it ONS was commissioned for adults with a confirmed diagnosis of refractory chronic cluster headaches. Reference is made within the CCP to the 2013 NICE Interventional Procedures Guidance (IPG) on ONS for intractable chronic migraine (IPG452). To date NICE have published two further IPGs on cluster headaches, but neither addresses ONS. The first addressed sphenopalatine ganglion stimulation (IPG527) and the second transcutaneous stimulation (IPG552), published in 2015 and 2016 respectively.

The NICE clinical guideline 'Headaches in over 12s: diagnosis and management' (CG150, published 2012, updated 2015) does not discuss peripheral nerve stimulation for any headache type.

NICE published a Medtech innovation briefing 'gammaCore for cluster headache' (MIB162) in October 2018, however this is stimulation of the vagus not occipital nerve.

One additional systematic review was published in 2018 (Cadalso et al). This evaluated the efficacy of electrical stimulation of the occipital nerve in intractable primary headache disorders and concluded that ONS may be effective when compared to sham therapy. However,

the meta-analysis undertaken was only for chronic migraine sufferers. The full-text needs to be consulted to determine what conclusion, if any, is drawn for cluster headaches.

#### *Primary research*

Ten primary studies on ONS and chronic cluster headaches were identified (published since 2015). In those reporting results in the abstract (n=5), ONS appears to be effective. One study reported on the long term effects of ONS.

Sixteen primary studies evaluate other nerve stimulation treatments (vagus, deep brain, sphenopalatine ganglion) for chronic cluster headaches.

#### *Economic studies*

The only cost-effectiveness study located was for gammaCore (non-invasive vagus nerve stimulation).

#### *Ongoing Trials*

Four ongoing trials to evaluate ONS to treat chronic headaches, one of which is a systematic review were identified. Two others assessing acute relief for chronic cluster headaches were identified.

## Conclusions

ONS is commissioned by NHS England for medically refractory chronic cluster headaches, but there is no published guidance.

One systematic review and a number of primary studies on ONS for chronic cluster headaches have been published since NHS England published the clinical commissioning policy.

It is unclear at this stage whether any relevant evidence is available with which to assess the cost-effectiveness of occipital nerve stimulation for medically refractory chronic cluster headaches.

## Areas of Uncertainty

There is a body of evidence on stimulation of peripheral nerves in the head other than the occipital nerve. It is unclear whether the scope should be widened to include stimulation of these other nerves (in particular vagus & sphenopalatine ganglion).

## Feasibility of Technology Assessment

If ONS is effective, the quality of life of patients will be improved, but it is unclear whether there is sufficient evidence upon which to base a technology assessment, or what the impact on NHS Wales would be were ONS to be recommended.

There is potential for quality improvement by undertaking an assessment of ONS as treatment is commissioned in NHS England but there is no published guidance.

HTW's Assessment Group concluded to progress this topic to Evidence Appraisal. This will be/was published as EAR0.13.

## Brief literature search results

Resource	Results
HTA organisations	
<a href="#">Healthcare Improvement Scotland:</a>	No relevant results for cluster headaches
<a href="#">Health Technology Assessment Group</a>	No relevant results for cluster headaches
<a href="#">Health Information and Quality Authority</a>	No relevant results for cluster headaches
UK guidelines and guidance	
<a href="#">SIGN</a>	No relevant results for cluster headaches
<a href="#">NICE</a>	<ul style="list-style-type: none"> <li>• NICE. (2015). Implantation of a sphenopalatine ganglion stimulation device for chronic cluster headache. Interventional procedures guidance IPG527. National Institute for Health and Care Excellence. Available at: <a href="https://www.nice.org.uk/guidance/ipg527">https://www.nice.org.uk/guidance/ipg527</a> [Accessed 28 May 2019].</li> <li>• NICE. (2015). Headaches in over 12s: diagnosis and management. Clinical guideline CG150. National Institute for Health and Care Excellence. Available at: <a href="https://www.nice.org.uk/guidance/cg150">https://www.nice.org.uk/guidance/cg150</a> [Accessed 28 May 2019].</li> <li>• NICE. (2016). Transcutaneous stimulation of the cervical branch of the vagus nerve for cluster headache and migraine. Interventional procedures guidance IPG552. National Institute for Health and Care Excellence. Available at: <a href="https://www.nice.org.uk/guidance/ipg552">https://www.nice.org.uk/guidance/ipg552</a> [Accessed 28 May 2019].</li> <li>• NICE. (2018). gammaCore for cluster headache. Medtech innovation briefing MIB162. National Institute for Health and Care Excellence. Available at: <a href="https://www.nice.org.uk/advice/mib162">https://www.nice.org.uk/advice/mib162</a> [Accessed 28 May 2019].</li> </ul>
Secondary literature and economic evaluations	
<a href="#">EUnethTA</a>	No relevant results for cluster headaches
<a href="#">ECRI</a>	No relevant results for cluster headaches
<a href="#">Cochrane library</a>	No relevant results for cluster headaches
Medline	<p>ONS results:</p> <ul style="list-style-type: none"> <li>• Cadalso RT, Jr., Daugherty J, Holmes C, et al. (2018). Efficacy of Electrical Stimulation of the Occipital Nerve in Intractable Primary Headache Disorders: A Systematic Review with Meta-Analyses. <i>Journal of Oral &amp; Facial Pain and Headache</i>. 32(1): 40-52. doi: <a href="https://dx.doi.org/10.11607/ofph.1784">https://dx.doi.org/10.11607/ofph.1784</a></li> </ul>
Primary studies	
Medline	<p>ONS results:</p> <ul style="list-style-type: none"> <li>• Fontaine D, Blond S, Lucas C, et al. (2017). Occipital nerve stimulation improves the quality of life in medically-intractable chronic cluster headache: Results of an observational prospective study. <i>Cephalalgia</i>. 37(12): 1173-9. doi: <a href="https://dx.doi.org/10.1177/0333102416673206">https://dx.doi.org/10.1177/0333102416673206</a></li> <li>• Gaul C, Roguski J, Dresler T, et al. (2017). Efficacy and safety of a single occipital nerve blockade in episodic and chronic cluster headache: A prospective observational study. <i>Cephalalgia</i>. 37(9): 873-80. doi: <a href="https://dx.doi.org/10.1177/0333102416654886">https://dx.doi.org/10.1177/0333102416654886</a></li> </ul>

- Lainez MJ, Guillaumon E. (2017). Cluster headache and other TACs: Pathophysiology and neurostimulation options. *Headache*. 57(2): 327-35. doi: <https://dx.doi.org/10.1111/head.12874>
- Leone M, Proietti Cecchini A, Messina G, et al. (2017). Long-term occipital nerve stimulation for drug-resistant chronic cluster headache. *Cephalalgia*. 37(8): 756-63. doi: <https://dx.doi.org/10.1177/0333102416652623>
- Magis D, Gerard P, Schoenen J. (2016). Invasive occipital nerve stimulation for refractory chronic cluster headache: what evolution at long-term? Strengths and weaknesses of the method. *Journal of Headache & Pain*. 17: 8. doi: <https://dx.doi.org/10.1186/s10194-016-0598-9>
- Miller S, Lagrata S, Matharu M. (2019). Multiple cranial nerve blocks for the transitional treatment of chronic headaches. *Cephalalgia*. 333102419848121. doi: <https://dx.doi.org/10.1177/0333102419848121>
- Miller S, Watkins L, Matharu M. (2017). Treatment of intractable chronic cluster headache by occipital nerve stimulation: a cohort of 51 patients. *European Journal of Neurology*. 24(2): 381-90. doi: <https://dx.doi.org/10.1111/ene.13215>
- Miller S, Watkins L, Matharu M. (2018). Predictors of response to occipital nerve stimulation in refractory chronic headache. *Cephalalgia*. 38(7): 1267-75. doi: <https://dx.doi.org/10.1177/0333102417728747>
- Nguyen JP, Nizard J, Kuhn E, et al. (2016). A good preoperative response to transcutaneous electrical nerve stimulation predicts a better therapeutic effect of implanted occipital nerve stimulation in pharmacologically intractable headaches. *Neurophysiologie Clinique*. 46(1): 69-75. doi: <https://dx.doi.org/10.1016/j.neucli.2015.12.002>
- Rozen TD. (2019). High-Volume Anesthetic Suboccipital Nerve Blocks for Treatment Refractory Chronic Cluster Headache With Long-Term Efficacy Data: An Observational Case Series Study. *Headache*. 59(1): 56-62. doi: <https://dx.doi.org/10.1111/head.13394>
- Santos Lasaosa S, Gago Veiga A, Guerrero Peral AL, et al. (2018). Patterns of anaesthetic pericranial nerve block in headache patients. *Neurologia*. 33(3): 160-4. doi: <https://dx.doi.org/10.1016/j.nrl.2016.05.016>

Non ONS results:

- Akram H, Miller S, Lagrata S, et al. (2016). Ventral tegmental area deep brain stimulation for refractory chronic cluster headache. *Neurology*. 86(18): 1676-82. doi: <https://dx.doi.org/10.1212/WNL.0000000000002632>
- Chabardes S, Carron R, Seigneuret E, et al. (2016). Endoventricular Deep Brain Stimulation of the Third Ventricle: Proof of Concept and Application to Cluster Headache. *Neurosurgery*. 79(6): 806-15.
- Holle-Lee D, Gaul C. (2016). Noninvasive vagus nerve stimulation in the management of cluster headache: clinical evidence and practical experience. *Therapeutic Advances in Neurological Disorders*. 9(3): 230-4. doi: <https://dx.doi.org/10.1177/1756285616636024>
- Magis D, D'Ostilio K, Thibaut A, et al. (2017). Cerebral metabolism before and after external trigeminal nerve stimulation in episodic migraine. *Cephalalgia*. 37(9): 881-91. doi: <https://dx.doi.org/10.1177/0333102416656118>

	<ul style="list-style-type: none"> <li>• Magis D, D'Ostilio K, Lisicki M, et al. (2018). Anodal frontal tDCS for chronic cluster headache treatment: a proof-of-concept trial targeting the anterior cingulate cortex and searching for nociceptive correlates. <i>Journal of Headache &amp; Pain</i>. 19(1): 72. doi: <a href="https://dx.doi.org/10.1186/s10194-018-0904-9">https://dx.doi.org/10.1186/s10194-018-0904-9</a></li> <li>• Miller S, Matharu M. (2017). Non-invasive Neuromodulation in Primary Headaches. <i>Current Pain &amp; Headache Reports</i>. 21(3): 14. doi: <a href="https://dx.doi.org/10.1007/s11916-017-0608-x">https://dx.doi.org/10.1007/s11916-017-0608-x</a></li> <li>• Mwamburi M, Liebler EJ, Tenaglia AT. (2017). Cost-effectiveness of gammaCore (non-invasive vagus nerve stimulation) for acute treatment of episodic cluster headache. <i>American journal of managed care</i>. 23(16 Suppl): S300-S6</li> </ul>
<p><a href="#">Cochrane library</a></p>	<p>ONS results:</p> <ul style="list-style-type: none"> <li>• (2019). Proceedings #7: trigeminal and Occipital Neuromodulation for Rapid Pain Reduction in Occipital Migraines. <i>Brain stimulation</i>. 12(2): e65-e6. doi: <a href="https://dx.doi.org/10.1016/j.brs.2018.12.176">https://dx.doi.org/10.1016/j.brs.2018.12.176</a></li> </ul> <p>Non ONS results:</p> <ul style="list-style-type: none"> <li>• Barloese M, Petersen AS, Guo S, et al. (2018). Sphenopalatine ganglion stimulation induces changes in cardiac autonomic regulation in cluster headache. <i>Clinical physiology and functional imaging</i>. 38(5): 808-15. doi: <a href="https://dx.doi.org/10.1111/cpf.12484">https://dx.doi.org/10.1111/cpf.12484</a></li> <li>• Barloese MC, Jürgens TP, May A, et al. (2016). Cluster headache attack remission with sphenopalatine ganglion stimulation: experiences in chronic cluster headache patients through 24 months. <i>Journal of headache and pain</i>. 17(1): 67. doi: <a href="https://dx.doi.org/10.1186/s10194-016-0658-1">https://dx.doi.org/10.1186/s10194-016-0658-1</a></li> <li>• Gaul C, Diener HC, Silver N, et al. (2016). Non-invasive vagus nerve stimulation for PREvention and Acute treatment of chronic cluster headache (PREVA): a randomised controlled study. <i>Cephalalgia</i>. 36(6): 534-46. doi: <a href="https://dx.doi.org/10.1177/0333102415607070">https://dx.doi.org/10.1177/0333102415607070</a></li> <li>• Gaul C, Magis D, Liebler E, et al. (2017). Effects of non-invasive vagus nerve stimulation on attack frequency over time and expanded response rates in patients with chronic cluster headache: a post hoc analysis of the randomised, controlled PREVA study. <i>Journal of headache and pain</i>. 18(1): 22. doi: <a href="https://dx.doi.org/10.1186/s10194-017-0731-4">https://dx.doi.org/10.1186/s10194-017-0731-4</a></li> <li>• Goadsby PJ, de Coo IF, Silver N, et al. (2018). Non-invasive vagus nerve stimulation for the acute treatment of episodic and chronic cluster headache: a randomized, double-blind, sham-controlled ACT2 study. <i>Cephalalgia</i>. 38(5): 959-69. doi: <a href="https://dx.doi.org/10.1177/0333102417744362">https://dx.doi.org/10.1177/0333102417744362</a></li> <li>• Guo S, Petersen AS, Schytz HW, et al. (2018). Cranial parasympathetic activation induces autonomic symptoms but no cluster headache attacks. <i>Cephalalgia</i>. 38(8): 1418-28. doi: <a href="https://dx.doi.org/10.1177/0333102417738250">https://dx.doi.org/10.1177/0333102417738250</a></li> <li>• Sava SL, Cosseddu A, D'Ostilio K, et al. (2015). Anodal transcranial direct stimulation (tDCS) targeting the anterior cingulate gyrus for the preventive treatment of chronic cluster headache: a proof-of-concept trial. <i>Cephalalgia</i>. 35(6 SUPPL. 1): 91. doi: <a href="https://dx.doi.org/10.1177/0333102415581304">https://dx.doi.org/10.1177/0333102415581304</a></li> <li>• Schoenen J, Jensen RH, Lantéri-Minet M, et al. (2013). Stimulation of the sphenopalatine ganglion (SPG) for cluster headache treatment. Pathway CH-1: a randomized, sham-controlled study. <i>Cephalalgia</i>. 33(10): 816-30. doi: <a href="https://dx.doi.org/10.1177/0333102412473667">https://dx.doi.org/10.1177/0333102412473667</a></li> </ul>

	<ul style="list-style-type: none"> <li>• Silberstein SD, Mechtler LL, Kudrow DB, et al. (2016). Non-Invasive Vagus Nerve Stimulation for the ACute Treatment of Cluster Headache: findings From the Randomized, Double-Blind, Sham-Controlled ACT1 Study. Headache. 56(8): 1317-32. doi: <a href="https://dx.doi.org/10.1111/head.12896">https://dx.doi.org/10.1111/head.12896</a></li> </ul>
Ongoing secondary research	<p><a href="#">PROSPERO database</a></p> <p>ONS results:</p> <ul style="list-style-type: none"> <li>• Cottin SC, Cantin L, Prudhomme M, et al. (2019). Occipital nerve stimulation (ONS) for non-migrainous chronic headaches : a systematic review protocol. PROSPERO CRD42019121623 Available at: <a href="http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42019121623">http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42019121623</a> [Accessed 3 June 2019].</li> <li>• Medrea I, Osman N, Christie S, et al. (2019). Protocol for a comparison of therapies for cluster headache; systematic review, updated meta-analysis, and network meta-analysis of medication effect by class (acute and preventative) and by headache subtype (episodic and chronic). PROSPERO CRD42019127986 Available at: <a href="http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42019127986">http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42019127986</a> [Accessed 3 June 2019].</li> </ul> <p>Non ONS results:</p> <ul style="list-style-type: none"> <li>• Neto NNM. (2017). Posterior hypothalamic stimulation in chronic cluster headache: a systematic review. PROSPERO CRD42017055704. Available at: <a href="http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42017055704">http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42017055704</a> [Accessed 3 June 2019].</li> </ul>
Ongoing primary research	<p><a href="#">Clinicaltrials.gov</a></p> <p>ONS results:</p> <ul style="list-style-type: none"> <li>• NCT00205894. (2006). Occipital Nerve Stimulation to Treat Chronic Headaches. Clinical Trials. Available at: <a href="https://ClinicalTrials.gov/show/NCT00205894">https://ClinicalTrials.gov/show/NCT00205894</a> [Accessed 3 June 2019].</li> <li>• NCT01151631. (2018). Occipital Nerve Stimulation in Medically Intractable Chronic Cluster Headache. Clinical Trials. Available at: <a href="https://ClinicalTrials.gov/show/NCT01151631">https://ClinicalTrials.gov/show/NCT01151631</a> [Accessed 3 June 2019].</li> <li>• NCT02081482. (2015). Cerebral Metabolism in Patients With Refractory Chronic Cluster Headache Treated by Occipital Nerve Stimulation. Clinical Trials. Available at: <a href="https://ClinicalTrials.gov/show/NCT02081482">https://ClinicalTrials.gov/show/NCT02081482</a> [Accessed 3 June 2019].</li> <li>• Cottin SC, Cantin L, Prudhomme M, et al. (2019). Occipital nerve stimulation (ONS) for non-migrainous chronic headaches : a systematic review protocol. PROSPERO CRD42019121623 Available at: <a href="http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42019121623">http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42019121623</a> [Accessed 3 June 2019].</li> </ul> <p>Possible mention of ONS:</p> <ul style="list-style-type: none"> <li>• NCT01701245. (2014). Prevention and Acute Treatment of Chronic Cluster Headache Compared to Standard of Care. Clinical Trials. Available at: <a href="https://ClinicalTrials.gov/show/NCT01701245">https://ClinicalTrials.gov/show/NCT01701245</a> [Accessed 3 June 2019].</li> <li>• NCT01958125. (2014). A Randomized Multicentre Study for the Acute Relief of Episodic and Chronic Cluster Headache. Clinical Trials. Available at: <a href="https://ClinicalTrials.gov/show/NCT01958125">https://ClinicalTrials.gov/show/NCT01958125</a> [Accessed 3 June 2019].</li> </ul> <p>Non ONS results:</p>

	<ul style="list-style-type: none"> <li>• NCT01792817. (2014). Non-invasive Neurostimulation of the Vagus Nerve for the Treatment of Cluster Headache. Clinical Trials. Available at: <a href="https://ClinicalTrials.gov/show/NCT01792817">https://ClinicalTrials.gov/show/NCT01792817</a> [Accessed 3 June 2019].</li> <li>• NCT02462395. (2016). Anodal Transcranial Direct Stimulation (tDCS) for the Treatment of Chronic Cluster Headache. Clinical Trials. Available at: <a href="https://ClinicalTrials.gov/show/NCT02462395">https://ClinicalTrials.gov/show/NCT02462395</a> [Accessed 3 June 2019].</li> <li>• NCT00662935. (2008). Evaluation of Efficacy and Safety of Deep Brain Stimulation (DBS) in Chronic and Treatment-Resistant Cluster Headache(CH). Clinical Trials. Available at: <a href="https://ClinicalTrials.gov/show/NCT00662935">https://ClinicalTrials.gov/show/NCT00662935</a> [Accessed 3 June 2019].</li> <li>• NCT01255813. (2013). Sphenopalatine Ganglion Stimulation for the Acute Treatment of Cluster Headache. Clinical Trials. Available at: <a href="https://ClinicalTrials.gov/show/NCT01255813">https://ClinicalTrials.gov/show/NCT01255813</a> [Accessed 3 June 2019].</li> <li>• NCT01677026. (2018). Data Collection on the ATI Neurostimulation System: SPG Stimulation for Cluster Headache. Clinical Trials. Available at: <a href="https://ClinicalTrials.gov/show/NCT01677026">https://ClinicalTrials.gov/show/NCT01677026</a> [Accessed 3 June 2019].</li> <li>• NCT02168764. (2019). Sphenopalatine Ganglion Stimulation for the Treatment of Chronic Cluster Headache. Clinical Trials. Available at: <a href="https://ClinicalTrials.gov/show/NCT02168764">https://ClinicalTrials.gov/show/NCT02168764</a> [Accessed 3 June 2019].</li> <li>• NCT03567590. (2021). The Efficacy and Safety of Sphenopalatine Ganglion Pulsed Radiofrequency Treatment for Cluster Headache. Clinical Trials. Available at: <a href="https://ClinicalTrials.gov/show/NCT03567590">https://ClinicalTrials.gov/show/NCT03567590</a> [Accessed 3 June 2019].</li> </ul>
Other	
Evidence identified by topic proposer	<ul style="list-style-type: none"> <li>• NHS England. (2015). Clinical commissioning policy: occipital nerve stimulation for adults with intractable chronic migraines and medically refractory chronic cluster headaches. NHS England D08/P/c. Available at: <a href="https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2015/07/d08-p-c.pdf">https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2015/07/d08-p-c.pdf</a> [Accessed 23 May 2019].</li> <li>• NICE. (2013). Occipital nerve stimulation for intractable chronic migraine. Interventional procedures guidance IPG452. National Institute for Health and Care Excellence. Available at: <a href="https://www.nice.org.uk/guidance/ipg452">https://www.nice.org.uk/guidance/ipg452</a> [Accessed 23 May 2019].</li> </ul>
NHS Website	<ul style="list-style-type: none"> <li>• NHS. (2017). Cluster headaches. National Health Service. Available at: <a href="https://www.nhs.uk/conditions/cluster-headaches/">https://www.nhs.uk/conditions/cluster-headaches/</a> [Accessed 28 May 2019].</li> </ul>

Date of search:	23 <sup>rd</sup> May & 3 <sup>rd</sup> June 2019
Concepts used:	occipital nerve stimulation, peripheral nerve stimulation, cluster headache(s); restricted to 2016-date.