

Noninvasive Vagus Nerve Stimulation for Cluster Headache and Migraine

Recommendation

MONTH 2024



**Ontario
Health**

Draft Recommendation

Ontario Health, based on guidance from the Ontario Health Technology Advisory Committee, recommends against publicly funding noninvasive vagus nerve stimulation for people with cluster headache or migraine.

Rationale for the Recommendation

The Ontario Health Technology Advisory Committee made the above recommendation after considering the clinical, economic, and patient preferences and values evidence reported in the health technology assessment.¹

For the acute treatment or prevention of cluster headaches, the committee concluded that there is uncertainty about the clinical benefits of using noninvasive vagus nerve stimulation (nVNS). As well, the cost of publicly funding nVNS for acute or preventive treatment was high, even when assuming a low adoption rate for the technology. The estimated total cost over 5 years of publicly funding nVNS for acute treatment was \$11.88 million and for prevention was \$9.92 million.

For the acute treatment of migraine, nVNS may provide benefits related to short-term pain relief (i.e., pain relief 2 hours after treatment), but there was uncertainty about its effect on the important health outcomes of sustained pain relief and pain freedom. The estimated total cost over 5 years of publicly funding nVNS for the acute treatment of migraine was very high, at \$1.12 billion. For the prevention of migraine, there was uncertainty about the benefits of nVNS for important clinical outcomes. The estimated total cost over 5 years of publicly funding nVNS for the prevention of migraine was very high, at \$278.77 million.

Ontario Health Technology Advisory Committee members took into account the lived experience of people with cluster headache and migraine, who described the negative impact of cluster headache and migraine on their daily lives, mental health, social and family relationships, and work. They also noted the difficulty they encountered in finding effective treatment options.

The committee acknowledges that the evidence is encouraging for nVNS as a potential noninvasive treatment for cluster headache or migraine. However, more evidence is needed to improve the certainty of its effectiveness for important clinical outcomes.

Decision Determinants for Noninvasive Vagus Nerve Stimulation for Cluster Headache and Migraine

Overall Clinical Benefit

Effectiveness

How effective is the health technology/intervention likely to be (taking into account any variability)?

Cluster Headache

For the acute treatment of cluster headache, the evidence from 2 randomized controlled trials (RCTs) was uncertain about the effect of nVNS on response to treatment (i.e., pain relief; Grading of Recommendations, Assessment, Development and Evaluations [GRADE]: Low to Very low), pain freedom (GRADE: Low to Very low), and the duration of an attack (GRADE: Low). There was no statistically significant reduction in acute medication use with nVNS (GRADE: Moderate).

For the prevention of cluster headache, the evidence from 1 RCT suggested that nVNS may be beneficial in reducing the frequency of cluster headache attacks (GRADE: Low), reducing acute medication use (GRADE: Low), and improving quality of life based on generic (GRADE: Low) and disease-specific measures (GRADE: Very low).

Migraine

For the acute treatment of migraine, the evidence from 1 RCT suggested that nVNS probably improves response to treatment at 2 hours (i.e., pain relief; GRADE: Moderate), but this response was not sustained to 24 hours (GRADE: Low). There was no statistically significant improvement in pain freedom at 2 hours after the first treated attack (GRADE: Moderate), and the evidence was very uncertain about the proportion of people who achieved pain freedom at 2 hours for 50% or more of migraine attacks (GRADE: Very low). The impact of nVNS on mean pain intensity was very uncertain (GRADE: Very low), and there was little to no difference in acute medication use (GRADE: Low).

For the prevention of migraine, the evidence from 4 RCTs was uncertain about the effect of nVNS on the number of headache and migraine days; no statistically significant improvements were observed (GRADE: Low). There was little to no difference in acute medication use (GRADE: Low), and the evidence was very uncertain about the impact of nVNS on quality of life and functional tests (GRADE: Very low).

Safety

How safe is the health technology/intervention likely to be?

Cluster Headache

For acute treatment and prevention, the evidence about adverse events was uncertain. Overall, there was no statistically significant difference in the proportion of people who experienced 1 or more adverse events when nVNS was used for the prevention of cluster headache, and no serious device-related adverse events were noted (GRADE: Low).

Migraine

For the acute treatment of migraine, the data were insufficient to determine the number of adverse events with nVNS compared with sham treatment, although no serious adverse events were reported (no GRADE assessment for this outcome). For the prevention of migraine, the evidence suggested that nVNS may make little to no difference in any adverse events (GRADE: Low); however, the evidence was very uncertain regarding the impact of nVNS on serious adverse events or device-related adverse events (GRADE: Very low), and no long-term outcomes were available.

Burden of Illness

What is the likely size of the burden of illness pertaining to this health technology/intervention?

Cluster Headache

Global population-based studies estimate that 0.1% of the population has cluster headache. The typical age of onset is approximately 30 years, and the condition primarily affects adults. An estimated 10% to 15% of people with cluster headache have the chronic subtype.

Migraine

In Ontario in 2010/11, 8.8% of the population were estimated to have a diagnosis of migraine. Women are more likely to report migraine than men (11.8% vs. 4.7%), with prevalence highest among those aged 30 to 49 years (12.1% overall).

Need

How large is the need for this health technology/intervention?

Cluster Headache

Cluster headaches are extremely debilitating, affecting people's quality of life and interfering with their ability to participate in daily activities, social activities, or work. Cluster headache is associated with a high prevalence of secondary psychiatric comorbidities, including depression, anxiety, and suicidal thoughts during an attack. Limited options are available for the acute and preventive treatment of cluster headache. People often experience incomplete effect, substantial side effects, contraindications, or suboptimal uptake.

Migraine

Migraine greatly affects people's quality of life; it is considered the second leading cause of disability around the world – first among women and girls aged 15 to 49 years. Although options are available for the acute and preventive treatment of migraine, treatment is complex, and an individualized process of trying different treatments is often required. People often have contraindications to treatment or experience incomplete effect, substantial side effects, or issues adhering to the treatment regimen.

Patient Preferences and Privacy

Patient Preferences and Values

Do patients have specific preferences, values, or needs related to the health condition, health technology/intervention, or life impact that are relevant to this assessment?

People with migraine and cluster headache reported that it had a substantial negative impact on their life. They viewed nVNS favourably overall and emphasized the importance of expanding access to noninvasive treatment options for cluster headache.

Autonomy, Privacy, Confidentiality, and/or Other Relevant Ethical Principles as Applicable

Are there concerns regarding accepted ethical or legal standards related to patient autonomy, privacy, confidentiality, or other ethical principles that are relevant to this assessment?

People with cluster headache and migraine felt that having access to noninvasive treatment options was integral to patient autonomy.

Equity and Patient Care

Equity of Access or Outcomes

Are there disadvantaged populations or populations in need whose access to care or health outcomes might be improved or worsened that are relevant to this assessment?

Access to nVNS treatment requires out-of-pocket payment or coverage through private insurance; this may represent an inequity in access. However, because the effectiveness of nVNS is uncertain, there is no appreciable inequity in terms of health outcomes for people who can access nVNS compared with those who cannot.

Patient Care

Are there challenges in the coordination of care for patients or other system-level aspects of patient care (e.g., timeliness of care, care setting) that might be improved or worsened that are relevant to this assessment?

No impact on patient care or coordination is expected with nVNS.

Cost-Effectiveness

Economic Evaluation

How efficient is the health technology/intervention likely to be?

Cluster Headache

For the acute treatment of cluster headache, we did not conduct a primary economic evaluation because of a lack of data for health state utilities (which measure health-related quality of life). Therefore, the cost-effectiveness of nVNS for the acute treatment of cluster headache is unknown.

For the prevention of cluster headache, nVNS in addition to standard care was more effective and more costly than standard care alone. It led to an additional 0.1945 quality-adjusted life years (QALYs) and an additional cost of \$5,317 per person, resulting in an incremental cost-effectiveness ratio (ICER) of \$27,338 per QALY gained. At the commonly used willingness-to-pay (WTP) values of \$50,000 and \$100,000 per QALY, the probabilities of nVNS in addition to standard care being cost-effective were 88.5% and 97%, respectively. However, these findings should be interpreted with caution because the clinical inputs used to inform our modelling were of low quality (GRADE: Low to Very low).

Migraine

For the acute treatment of migraine, we did not conduct a primary economic evaluation because of a lack of data for health state utilities and challenges in translating the available temporary clinical outcomes (e.g., treatment response at 2 hours) into QALYs. Therefore, the cost-effectiveness of nVNS for the acute treatment of migraine is unknown.

For the prevention of migraine, nVNS in addition to standard care was similarly effective and more costly compared with standard care alone. It led to an additional 0.0066 QALYs and an additional cost of \$6,324, resulting in an ICER of \$952,116 per QALY gained. nVNS was highly unlikely to be cost-effective at commonly used WTP values of \$50,000 and \$100,000 per QALY gained.

Feasibility of Adoption Into Health System

Economic Feasibility

How economically feasible is the health technology/intervention?

Cluster Headache

Publicly funding nVNS for the acute treatment of cluster headache would lead to additional costs of \$0.76 million in year 1 to \$4.04 million in year 5, for a total of \$11.88 million over 5 years.

Publicly funding nVNS for the prevention of cluster headache would lead to additional costs of \$0.63 million in year 1 to \$3.37 million in year 5, for a total of \$9.92 million over 5 years.

Migraine

Publicly funding nVNS for the acute treatment of migraine would lead to additional costs of \$71.56 million in year 1 to \$381.62 million in year 5, for a total of \$1.12 billion over 5 years.

Publicly funding nVNS for the prevention of migraine would lead to additional costs of \$17.76 million in year 1 to \$94.69 million in year 5, for a total of \$278.77 million over 5 years.

Organizational Feasibility

How organizationally feasible is it to implement the health technology/intervention?

If nVNS were publicly funded, the mechanism for funding the device is unclear.

Reference

1) TBD

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