Ontario
Health Quality Ontario
Qualité des services
de santé Ontario

OHTAC Recommendation: Deep Brain Stimulation for Treatment-Resistant Depression

Ontario Health Technology Advisory Committee

August 2013

Background

A preliminary evidence review[a] was conducted by the Evidence Development and Standards branch (EDS) of Health Quality Ontario to answer the following question:

- What is the clinical effectiveness and safety of deep brain stimulation compared with no deep brain stimulation (i.e., usual care) for treatment-resistant depression?

An estimated 10% to 20% of patients with depression do not respond to adequate courses of conventional therapies such as antidepressant drugs, psychotherapy, and electroconvulsive therapy, and therefore are referred to as having treatment-resistant depression. Deep brain stimulation (DBS) for treatment-resistant depression is a nonpharmacological treatment that involves focal stimulation at a specific neuroanatomic target such as the subcallosal cingulate white matter, the ventral caudate/ventral striatum, and the nucleus accumbens. The procedure requires surgical implantation of unilateral or bilateral electrodes and a permanently implanted neurostimulator. Electrical stimulation is transmitted from the stimulator implanted in the subclavicular area to the leads that are connected to each other by an extension that runs under the scalp and skin of the neck. Advantages of deep brain stimulation are its reversibility and the ability to telemetrically and noninvasively adjust stimulation variables to maximize benefits and minimize side effects.

Conclusions

The conclusions for the outcomes of depression severity, overall response, complete response, and adverse events are as follows:

Depression Severity

- Based on very low quality of evidence, patients show an improvement in depression severity after deep brain stimulation therapy.

Overall Response (Response to Therapy)

- Based on very low quality of evidence, approximately 50% of patients respond to DBS therapy.

Complete Response (Remission)

- Based on very low quality of evidence, approximately one-third of patients enter remission after DBS therapy.

Adverse Events

- Based on very low quality of evidence, only 3 of 7 studies reported patient suicide (the most serious and nonreversible adverse event) after deep brain stimulation therapy.

[a] Preliminary evidence reviews are abbreviated evidence-based analyses for topics in which the body of literature is not well defined and/or the regulatory status is investigational.

Decision Determinants

A decision-making framework has been developed by OHTAC that consists of 7 guiding principles for decision making, and a decision-making tool, called the Decision Determinants (DD) tool. When making a decision, OHTAC considers 4 explicit main criteria: overall clinical benefit, value for money, feasibility of adoption into health system, and consistency with expected societal and ethical values. For more information on the Decision-Making Framework, please refer to the *Decision Determinants Guidance Document* (http://www.hqontario.ca/en/mas/tech/pdfs/2011/guide_decision.pdf) and http://www.hqontario.ca/en/mas/ohtac_decision_frame.html.

A summary of the Decision Determinants can be viewed in Appendix 1.

OHTAC Recommendations

Following the preliminary evidence review, OHTAC made the following recommendations:

- OHTAC is unable to recommend the use of deep brain stimulation for treatment-resistant depression at this time because:
  - The device is not licensed in Canada for treatment-resistant depression.
  - The evidence suggests a beneficial effect of deep brain stimulation in treatment-resistant depression; however, this conclusion is based on very low quality of evidence.
- If Health Canada licenses the product for treatment-resistant depression in Canada, OHTAC will consider reviewing the technology again, if requested to do so.
- In view of ongoing clinical trial activity in the area, EDS should update its review and report back to OHTAC in 12 months, if the product has been licensed at that time.

Appendix 1 - Decision Determinants

Table 1: Decision Determinants Criteria Considerations for Deep Brain Stimulation (DBS) for Treatment-Resistant Depression (TRD)

Decision Criteria	Sub-Criteria	Considerations and Questions for OHTAC to Consider
Overall Clinical Benefit	**Effectiveness**	**What is the effectiveness and safety of DBS compared with no DBS (i.e., usual care) for TRD?** **Patient Outcomes** • Depression severity: data were not suitable for a meta-analysis. Based on qualitative assessment, 4 of 7 studies showed a statistically significant decrease in HDRS. (VERY LOW QUALITY) (4 obs) (n = 49) • Overall response: data were not suitable for a meta-analysis. Based on qualitative assessment and simple statistics, approximately 50% of TRD patients exhibit an overall response to DBS. (VERY LOW QUALITY) (7 obs) (n = 104) • Complete response: data were not suitable for a meta-analysis. Based on qualitative assessment and simple statistics, approximately 35% of TRD patients exhibit a complete response to DBS. (VERY LOW QUALITY) (5 obs) (n = 73)
	Safety	• Adverse events: data were not suitable for a meta-analysis. Based on qualitative assessment, suicide was reported in 3 of 7 studies. • Cognitive functions were improved or stable in 6 of 7 studies. (VERY LOW QUALITY) (7 obs) (n = 94)
	Burden of Illness	TRD occurs in 10% to 20% of depressed patients. Over the lifetime, 12.2% of Canadians report symptoms that meet criteria for depression.
	Need	The need is high. Patients are resistant to standard therapies.
Consistency With Expected Societal/Ethical Values	**Expected Societal Values**	Unknown
	Expected Ethical Values	Unknown
Value for Money	**Economic Evaluation and Feasibility**	No costing was performed.
Feasibility of Adoption Into Health System	**Organizational Feasibility**	Unknown

Abbreviations: DBS, deep brain stimulation; HDRS, Hamilton Depression Rating Scale; obs, observational studies; OHTAC, Ontario Health Technology Advisory Committee; TRD, treatment-resistant depression.