Title:	Vagus nerve stimulation for epilepsy
Agency:	Medical Services Advisory Committee (MSAC) MDP 106 Commonwealth Department of Health and Ageing GPO Box 9849 Canberra ACT 2601 http://www.msac.gov.au
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Aim:
To assess the safety, effectiveness and cost-effectiveness of vagus nerve stimulation (VNS) in addition to anti-epileptic drug (AED) therapy relative to AED therapy alone in all patients, and with or without the ketogenic diet in children. This assessment considered VNS therapy only in patients with medically refractory epilepsy, who had previously failed or were unsuitable for intracranial surgery.

Results and Conclusions:
Safety:
Two deaths were reported (one adult and one child) with use of VNS therapy, however, in neither case was VNS clearly implicated in the deaths.
The most commonly reported adverse events were hoarseness (12–100%) and coughing (1–46%), of which the majority of cases were mild, transient or responsive to a reduction of stimulation parameters. Other reported complications included pain, infection, dysphagia, paraesthesia, dyspnoea and device removal. Intra-operative arrhythmia was reported in two fair quality studies (Level IV intervention evidence) at rates of 1% and 11%. These incidents did not result in device removal nor were any adverse sequelae reported.
The majority of complications associated with VNS or the implantation of the device are likely to be considered acceptable by people with epilepsy. Nevertheless, VNS therapy is provided as an adjunct to AED therapy and, as such, the adverse events resulting from VNS therapy occur in addition to those of AED therapy.

Effectiveness:
Forty nine studies reported on the effectiveness of VNS plus AED therapy of which one good quality study provided level II intervention evidence, and three fair quality studies provided level III-2 intervention evidence.
No evidence regarding the effect of VNS plus AED therapy relative to AED therapy alone on epilepsy-related mortality was identified. However, as such deaths are often closely associated with a seizure, it is likely that epilepsy-related deaths may decrease if seizure frequency is also reduced.
The assessment of the effectiveness of VNS plus AED therapy in improving patient quality of life was complicated by the likely insensitivity of the tools used to measure this outcome. Expert opinion suggests that quality of life improvements are seen in patients following VNS therapy, and that the best indicator of such changes is a decrease in seizure frequency. Statistically significant reductions in seizure frequency relative to AED therapy alone (6–8%) were seen in patients following VNS plus AED therapy (41–50%) (level II and III-2 intervention evidence). However, these studies were limited by selection bias and uncertainty regarding the generalisability of the data. Clinically relevant reductions in seizure frequency of 50% or more were seen in up to 40% of patients. Level IV intervention evidence indicates that VNS plus AED therapy has a clinically significant effect in reducing seizure frequency in children with Lennox-Gastaut syndrome.

The limited evidence (level IV intervention evidence) regarding the effect of VNS plus AED therapy on drop attacks, a very debilitating seizure type, is suggestive of a greater reduction in children than adults.

Cost Effectiveness:

The high risk of selection bias and concerns regarding the generalisability of the comparative data resulted in uncertainty surrounding the net benefit of VNS plus AED therapy. As a consequence, a formal cost-effectiveness analysis was not performed.

The financial implications associated with providing VNS plus AED therapy indicate that the total healthcare costs would be an additional cost of $652,000 annually. This is based on the assumption that 30 patients would receive a VNS implant each year. Potential leakage could see this estimate significantly increase to $1,630,000 per year.

The greatest cost associated with VNS therapy is the cost of the device itself.

It should be noted that this financial analysis does not consider the likely substantive downstream costs associated with battery depletion which would require the implantation of a new pulse generator. These costs cannot be accurately estimated on the basis of the data available.

Recommendation:

The MSAC has considered the safety, effectiveness and cost-effectiveness for vagus nerve stimulation in addition to anti-epileptic medication for patients with medically refractory epilepsy. It was compared with continued or modified anti-epileptic drug therapy for all patients, and for children it was also compared with or without a ketogenic diet.

MSAC finds the procedure is reasonably safe in the context of the condition being treated.

MSAC finds there is insufficient evidence of effectiveness and net benefit of vagal nerve stimulation therapy for patients with medically refractory epilepsy.

Formal economic analysis was not conducted in view of the uncertainty of net clinical benefit.

MSAC recommends that public funding arrangements for vagus nerve stimulation for epilepsy remain unchanged.

The Minister for Health and Ageing noted this advice on 28 August, 2008.

Methods:

Medline, Embase, The Cochrane Library, and several other biomedical databases, HTA and other internet sites were searched (1990 - October 2007). Specific journals were handsearched and reference lists pearled. Studies were included in the review using pre-determined PICO selection criteria and reasons for exclusion were documented. Study quality was appraised, data extracted in a standardised manner, and findings synthesised qualitatively.

Prepared by Adelaide Health Technology Assessment (AHTA) on behalf of the MSAC