Expected Budget Impact of Expanded Use of VNS Therapy®

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BACKGROUND

Approximately 30% of patients with epilepsy have drug-resistant epilepsy (DRE).[1] Treatment options for patients with DRE are limited and include removal of the damaged section of the brain that is causing the epileptic seizures, severing the corpus callosum that connects the two hemispheres of the brain, deep brain stimulation, and Vagus Nerve Stimulation Therapy (VNS Therapy).[2]

Despite the long-term proven effectiveness of VNS Therapy[3], the time to initial implant occurs approximately 20 years after initial diagnosis[4,5] and after an average of 7 antiepileptic drugs (AEDs) have been tried.[6]

VNS Therapy has been shown to reduce resource use[7] and costs[7,8] compared to AEDs alone.

OBJECTIVE

The objective of this research was to estimate, from the perspective of a United States (US) health care payer, the budget impact and population health outcomes that may be expected with expanded use of VNS Therapy among patients ≥ 12 years of age with DRE with partial onset seizures.

METHODS

An Excel model was developed to compare the costs of continued AED treatment with the costs of VNS Therapy in addition to AED therapy.

Patient Population

The estimated eligible patient population is calculated to be 1,536 based on an assumed 1-million-member plan, with 84% of the plan population ≥ 12 years of age.[9] Of those, 0.94% have epilepsy[10], 57% of which have partial-onset seizures[11] and 36% of which have DRE[1].

In addition, the model assumes that 95% of patients ≥ 12 years with partial-onset seizures who have DRE currently do not have VNS Therapy. Although DRE has been defined by the International League Against Epilepsy as "a failure of two tolerated and appropriately chosen and used AED schedules, whether as monotherapy or in combination, to achieve sustained seizure freedom"[12], the duration of epilepsy for patients who undergo VNS Therapy placement has been reported to be approximately 20 years[4,5], suggesting that the percentage of patients with DRE without VNS Therapy is high.

Model Cost Inputs

Model inputs included the cost associated with the VNS Therapy device, adverse event costs, and drug costs (Table 1). (All costs are presented in 2016 US dollars.)

Table 1: Model Inputs (Cost Per Person)

Cost Component	Without VNS	With VNS	Sources/Assumptions
VNS Device Costs			
VNS system device (generator, lead, tunneler)	Not applicable	$36,329	LivaNova Price List[13]. Assumes each patient receives 1 implant.
Procedure for full system placement	Not applicable	$2,661	Cost estimate based on 1.5 hours of surgical time.[14]
Neurologist visits for programming	Not applicable	$319	Based on national average cost for neurologist visit for programming[15], assuming 3 neurologist visits.[16]
Battery (Generator) replacement (per person per year)	Not applicable	$2,178	Includes battery cost[13], procedure cost (30 minutes of surgical time)[14], and cost of neurologist visit for reprogramming.[15] Assumes 50% of patients will have a battery replacement at 7 years.[16]
Adverse Event Costs*			
Neurologist visit for cough (one-time cost)	$0.00	$40	Incidence of 37.5% × unit cost of $106
Neurologist visit for voice alteration (one-time cost)	$0.00	$42	Incidence of 39.7% × unit cost of $106
Surgical site infection, which results in device removal (one-time cost)	Not applicable	$95	Incidence of 2.8% × unit cost of $3,397
Drug Costs			
AEDs (cost per year)	$6,502	$6,502	Average cost calculated as the average daily cost of lacosamide, lamotrigine, topiramate, oxcarbazepine, levetiracetam, carbamazepine, tiagabine[17], assuming that 2 AEDs are used per day.

*Cough and voice alteration incidence rates for VNS Therapy are calculated as the weighted average of rates reported in clinical trials E03 (Cyberonics, 1997, Volume 18, Table 21) and E05 (Cyberonics, 1997, Volume 1, Table 32.2).[17] The incidence of surgical site infection and subsequent device removal is the percentage of VNS Therapy placements that subsequently required removal due to surgical site infection based on the manufacturer's safety database.[18] No adverse events are included for patients not receiving VNS Therapy. Cost of neurologist visit from Cyberonics VNS Therapy Hospital Codes (2016).[19] Patients with surgical site infection incur the cost of the VNS Therapy implantation and VNS Therapy removal (at a default cost of $3,397) and do not receive the benefit from VNS Therapy. The default cost of VNS Therapy removal is the US national average for device removal.[14]

Seizure-Related Costs

Seizure-related costs for hospitalizations, emergency department (ED) visits, and neurologist visits are calculated by estimating expected levels of seizure frequency for patients without VNS Therapy and for patients with VNS Therapy.

All patients begin in the "≥ 10 seizures per month" health state. Every 3 months, VNS Therapy patients transition to a health state according to patient allocations among these categories based on post hoc analysis of data from VNS Therapy clinical trials E03 and E05[16]. Response and seizure freedom rates have been shown to increase over time with VNS Therapy, with approximately 8% of patients achieving seizure freedom at 2 years.[3]

The model includes seizure-related resource utilization estimates for hospitalizations, ED visits, and neurologist visits by seizure frequency, which are multiplied by the corresponding unit costs to calculate the annual resource costs by seizure frequency (Table 2).

Table 2: Annual Resource Utilization and Costs, by Resource and Seizure Frequency

	Annual Resource Utilization (Cost)			
Resource (Unit Cost*)	**Number of Seizures Per Month**			
	0 (Seizure Free)	**< 1**	**> 1 to < 10**	**≥ 10**
Hospitalization[a] ($12,360)	0.00 $0	0.48 $5,933	0.96 $11,866	4.80 $59,330
ED visit ($1,079)	0.00 $0	0.42 $453	0.85 $917	3.57 $3,852
Neurologist visit ($106.44)	16.62 $1,769	17.37 $1,849	18.12 $1,929	22.54 $2,399

*Hospitalization costs[a], inflated to 2016 USD[b], ED visit costs[c,d], inflated to 2016 USD[b], neurologist visit cost.[e]
[a]The default input assumption of no hospitalizations for the seizure-free category is based on a study by Kristian et al.[f] [b]The default annual number of hospitalizations for the < 1 seizure/month category is estimated as the midpoint between the annual hospitalizations for the seizure-free category and the > 1 to < 10 seizures/month category. The default annual number of hospitalizations for the > 1 to < 10 seizures/month category is based on a study by Bernstein et al.[g] [c]The default annual number of hospitalizations for the ≥ 10 seizures/month category is calculated as the ratio of the mean number of hospitalizations for patients responding and not responding to an AED, where response was measured in clinical trials where the baseline seizure frequency was 26.3/month and where responders had an average seizure frequency of 6.31/month.[h] The resulting number of hospitalizations for nonresponders was 5 times higher than for responders. For the default annual number of hospitalizations for the ≥ 10 seizures/month category, the model assumes it is 5 times that of the > 1 to < 10 seizures/month category.[h]

The resulting seizure-related costs without and with VNS Therapy are shown in Table 3.

Table 3: Seizure-Related Costs Without and With VNS Therapy

	1st Year		2nd Year		3rd Year	
	Without VNS Therapy	With VNS Therapy	Without VNS Therapy	With VNS Therapy	Without VNS Therapy	With VNS Therapy
Hospitalization	$59,330	$38,737	$59,330	$34,954	$59,330	$33,536
ED visits	$3,852	$2,571	$3,852	$2,329	$3,852	$2,238
Neurologist visits	$2,399	$2,193	$2,399	$2,154	$2,399	$2,139
Total	**$65,581**	**$43,501**	**$65,581**	**$39,437**	**$65,581**	**$37,913**

RESULTS

- VNS Therapy resulted in a net cost savings due to the expected reduction in seizure frequency (Figure 2).
- On average, VNS Therapy resulted in a net cost savings of $77,480 per patient over 5 years.
- The initial cost of the VNS Therapy device, placement, and programming ($39,309) was offset in 1.7 years after VNS Therapy device placement (Figure 3).
- Reductions in hospitalizations are the main contributor to the cost savings with VNS Therapy (Figure 4).

Figure1: Percent of Patients by Number of Seizures Per Month

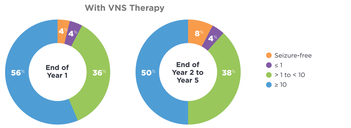


Figure 2: Cumulative Costs for Patients Without and With VNS Therapy With Break-even Analysis

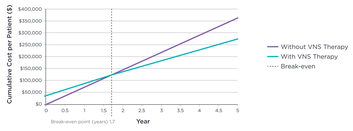
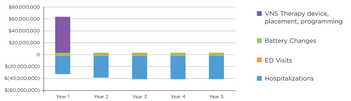


Figure 3: Total Plan Budget Impact by Cost Category



DISCUSSION

Helmers et al. analyzed Medicaid data from 1,635 patients and estimated total costs (inpatient, outpatient, ED, and drug [AED and non-AED]) for 6 months pre-VNS Therapy and up to 3 years post-VNS Therapy initiation.[22] The study found that the cost of VNS Therapy (device, placement, and outpatient visits) was outweighed by the cost savings at about 1.5 years; similar to the finding from the current modeled analysis.

Helmers et al. also reported the incidence for seizure-related hospitalizations pre-VNS Therapy and for the 3 years post-VNS Therapy initiation.[22] The incidence for seizure-related hospitalizations was reduced by approximately 50% by the end of the second year post-VNS Therapy and remained at this level for year 3. Bernstein et al. analyzed Kaiser Permanente administrative data pre- and post-VNS Therapy initiation and found that at 4 years post-VNS Therapy initiation, hospitalization admissions were reduced by 70%, ED visits were reduced by 99%, and outpatient visits were reduced by 91% compared to the year before implantation.[7]

In comparison, the current VNS Therapy modeled analysis estimated, by year 5, a reduction in hospitalizations by 40%, ED visits by 39%, and neurologist visits by 10% with VNS Therapy compared to without VNS Therapy. The current model may be more conservative because it does not include the potential reductions in resource use that patients with ≥ 10 seizures per month may have with VNS Therapy. For example, a study by Boon et al., which included 15 patients pre- and post-VNS Therapy initiation, reported that even among patients who continued to have ≥ 10 seizures per month after VNS Therapy initiation, there was a decrease in hospital admissions and direct medical costs.[23]

The results of the current analysis, which use literature-based estimates, are consistent and perhaps conservative compared with other published studies of the cost and resource use reductions that may be expected with VNS Therapy.

The US Food and Drug Administration recently approved an age expansion to include patients as young as 4 years old in the indication for VNS Therapy as an adjunctive therapy in reducing the frequency of seizures in patients 4 years of age and older with partial onset seizures that are refractory to antiepileptic medications.[24] VNS Therapy in younger patients has been shown to be at least as effective, if not more effective, than in the currently modeled patient population (≥ 12 years old)[9,25]; therefore, it would be expected that expanding the population to include patients ≥ 4 would result in additional cost savings. Additional research is needed to determine the budget impact of expanding the population.

CONCLUSIONS

VNS Therapy is a proven intervention that offers a long-term solution for patients with DRE by reducing seizure frequency, which leads to lower resource utilization and lower costs.

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ACKNOWLEGEMENTS

The model structure was adapted from a model used in the LivaNova submission to MSAC (Application 1358.1) for vagus nerve stimulation for patients with refractory epilepsy (June 2016), which was developed by Dominic Tilden and Koji Makino of THEMA Consulting Pty Ltd. Study was conducted by RTI Health Solutions and was funded by LivaNova PLC.

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Presented at:
American Epilepsy Society,
December 1-5, 2017,
Washington, D.C., United States

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