Cost-Effectiveness Analysis of Vagal Nerve Blocking for Morbid Obesity

Jeffrey C. Yu, AB; Bruce Wolfe, MD; Robert I. Griffiths, ScD, MS; Raul Rosenthal, MD; Daniel Cohen, MA; and Iris Lin, PhD

ABSTRACT

OBJECTIVES: To assess the lifetime cost-effectiveness of intermittent, reversible vagal nerve blocking (via the implantable weight loss device vBloc) therapy versus conventional therapy as treatment for patients who are class 2 obese with diabetes and for those who are class 3 obese with or without diabetes, who have found pharmacotherapy and behavioral therapies ineffective, but are not prepared or willing to undergo current bariatric surgical options.

STUDY DESIGN: A cost-effectiveness model was designed to simulate weight loss, diabetes remission, and costs in patients with obesity undergoing vagal nerve blocking therapy versus conventional therapy.

METHODS: The model compared 2 treatment arms, vagal nerve blocking therapy and conventional therapy, and for each treatment arm included 4 health states based on body mass index (BMI) class. Using Monte Carlo simulation, patients entered the model one at a time and could transition between health states by experiencing BMI change. The model focused on change in BMI and diabetes remission as predictors of healthcare costs, health-related quality of life, and survival. Inputs for vagal nerve blocking effectiveness were obtained from the ReCharge trial; however, remaining inputs were estimated from published literature. Incremental cost-effectiveness ratios (ICERs) were evaluated in terms of cost per quality-adjusted life-year (QALY) gained.

RESULTS: ICERs for vagal nerve blocking versus conventional therapy in patients who were class 2 and class 3 obese were estimated to be $17,274 and $21,713 per QALY gained, respectively. Sensitivity analyses showed results to be robust to reasonable variation in model inputs, with the upper limit of ICERs remaining below $30,000 for all sensitivity analysis scenarios assessed.

CONCLUSIONS: Vagal nerve blocking therapy provides a cost-effective alternative to conventional therapy in patients who are class 2 obese with diabetes and in those who are class 3 with or without diabetes.

Am J Manag Care. 2017;23(8):e245-e252

It is estimated that more than one-third (34.9%) of adults in the United States are obese, with 8.8% considered class 2 obese (body mass index [BMI] = 35.0-39.9) and 6.0% considered class 3 obese (BMI ≥40.0).[1] Lifestyle modifications, in the form of changes in food intake and activity level, and pharmaceutical therapy provide modest weight loss and have been demonstrated to be effective for some patients.[2,3] At present, bariatric surgery has proven to be the most effective treatment option for significant weight loss and improvement in health.[4]

Although bariatric surgery has demonstrated clinical efficacy in treatment of morbid obesity, recent evidence suggests that only a small percentage of patients who qualify for and would benefit from bariatric surgery ever undertake this mode of therapy.[5] According to the results of one study published in 2015 using the 2007 to 2012 National Health and Nutrition Examination Survey (NHANES) database, it was estimated that as many as 15% of US adults (32 million) may be eligible for bariatric surgery based on the 2013 Guideline for the Management of Overweight and Obesity in Adults.[6] However, according to the American Society for Metabolic and Bariatric Surgery (ASMBS), in 2013, only 179,000 bariatric surgical procedures were performed—a figure that is significantly below the number of potentially eligible candidates.[6,7]

Another consideration for bariatric surgery is the associated mortality over time, with 1-year mortality at 2.4% and 5-year mortality at 6.4% for US adults. Adjusted analyses found no significant association between bariatric surgery and all-cause mortality in the first year of follow-up and significantly lower mortality at 5 and 10 years of follow-up.[8] The gap in adoption of surgical treatments presents an opportunity to evaluate other low-risk, well-tolerated, and minimally invasive weight loss treatments.

The unmet need in current weight loss options is also associated with significant economic cost burden. Between 1998 and 2006, the annual medical cost burden of obesity increased from 6.5% to 9.1% of annual medical spending in the United States.[9] In 2008 US dollars, the economic burden of obesity in the United States was estimated to be $147 billion per year.[9] The current treatment gap

TAKEAWAY POINTS

Vagal nerve blocking therapy is a minimally invasive alternative to conventional therapy for the treatment of obesity and is positioned for patients who have found pharmacotherapy and behavioral therapies ineffective, but are not prepared or willing to undergo current bariatric surgical options.

- A lifetime cost-effectiveness analysis of vagal nerve blocking versus conventional therapy in patients with class 2 and class 3 obesity was conducted.
- Patients experienced incremental cost-effectiveness ratios less than $30,000 in base and sensitivity analyses, demonstrating vagal nerve blocking therapy to be cost-effective relative to conventional therapy.
- Model design incorporated both body mass index class stratification and diabetes remission, and simulated cost and quality-adjusted life-year outcomes.

in obesity, as well as the growing economic burden, has created meaningful value in the development and economic assessment of low-risk, well-tolerated, and minimally invasive treatment options.

One such option is vagal blocking using electrodes implanted through laparoscopic surgery. The Safety and Efficacy of vBloc Therapy Delivered by the Maestro Rechargeable System for the Treatment of Obesity (ReCharge) trial, a multicenter, randomized trial, evaluated vagal nerve blocking (via the implantable weight loss device vBloc) therapy through a sham-control design. This type of therapy uses a unique intermittent, vagal nerve blocking method to affect the perception of hunger and fullness and is delivered by a pacemaker-like device.[10] The device is implanted through minimally invasive laparoscopic surgery and uses electrodes to block neural signal transmission to the vagus nerve,[10] which is known to play a key role in satiety, metabolism, and autonomic control in upper gastrointestinal tract function.[11] Vagal nerve blocking therapy is a reversible procedure and one that is neither anatomy altering nor restricting.[10] According to the ASMBS position statement, it has demonstrated statistically significant excess weight loss in the short term and a low incidence of severe adverse events (AEs) and revision.[12]

Compared with more invasive bariatric alternatives, vagal nerve blocking therapy provides a durable and less invasive weight loss therapy option, with a strong safety profile.[10] Other available minimally invasive weight loss procedures include gastric balloon and gastric banding. Relative to gastric balloon therapy, in which the device is removed at or within 6 months of placement,[13,14] vagal nerve blocking presents a durable and longer-term treatment option. In addition, the safety and efficacy of balloon therapy beyond 6 months have not been established. Further, the intent of the gastric balloon therapy is to offer a replacement balloon following the required removal at 6 months, for a potentially indefinite length of time. Even though gastric banding presents a similar perioperative safety profile as a vagal nerve blocking device, it is associated with high rates of reoperation[15] and late complications, such as band slippage and pouch dilation,[16] and in recent years, rates of use have declined. Among bariatric surgeries, the proportion of gastric banding surgeries decreased from 35.4% in 2011 to 14.0% in 2013.[17]

The objective of this study was to assess the cost-effectiveness of vagal nerve blocking versus conventional therapy. The population of interest was defined as individuals who had not been successful with behavioral therapy or pharmacotherapy and who sought an alternative that was cost-effective, minimally invasive, and demonstrated favorable comparative safety. Findings presented in this paper add to the current literature by providing insight into the cost-effectiveness of a newer mode of obesity treatment (vagal nerve blocking therapy) versus conventional therapy.

METHODS

Model Overview

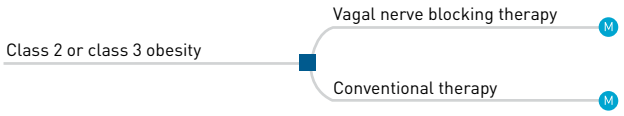
This cost-effectiveness model was developed in TreeAge Pro 2014 (TreeAge Software, Inc; Williamstown, MA), and it was designed to compare the vagal nerve blocking device with conventional therapy in patients who are class 2 obese with diabetes and those who are class 3 with or without diabetes. The model contained 4 BMI health states: not obese (<30 kg/m^2), class 1 obesity (30.0-34.9 kg/m^2), class 2 obesity (35.0-39.9 kg/m^2), and class 3 obesity (≥40 kg/m^2). Through Monte Carlo simulation methods, patients were modeled one at a time[18] and transitioned between health states by experiencing BMI change based on the treatment arm. Patients were tracked throughout the model and accumulated costs and utilities associated with their BMI levels. At the end of the model, incremental cost-effectiveness ratios (ICERs) were presented as cost per quality-adjusted life-years (QALYs) gained.

Model Structure

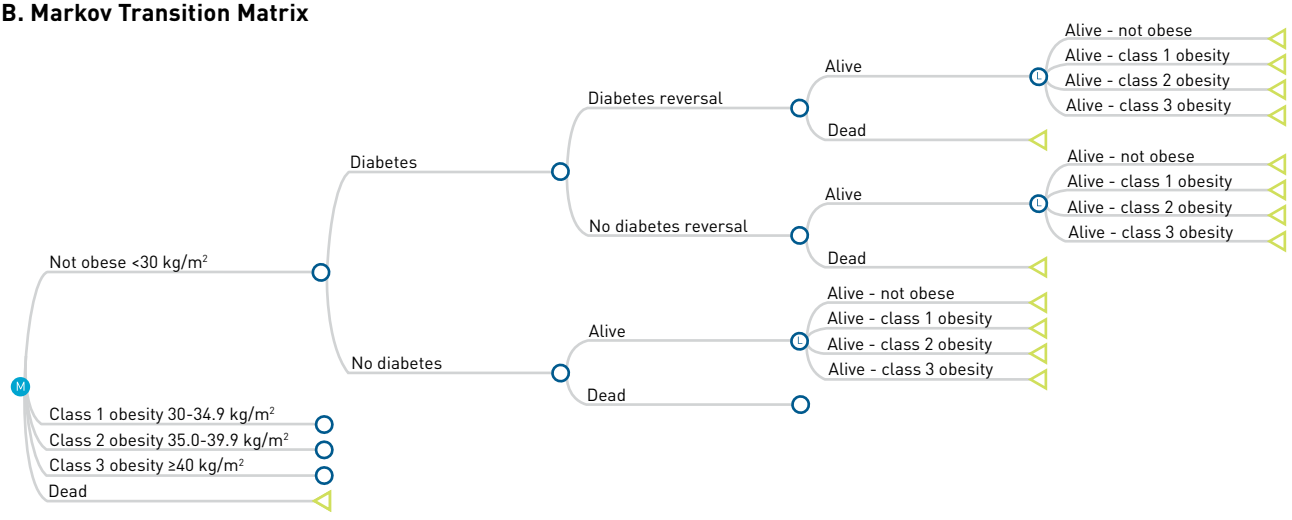
The model compared 2 treatment arms—vagal nerve blocking and conventional therapy—over a lifetime horizon. As described previously, vagal nerve blocking therapy is a minimally invasive bariatric surgical option. Conventional therapy, in the form of lifestyle counseling, was selected as the comparator for vagal nerve blocking therapy, as candidates for this type of therapy were patients who had not been successful in losing weight under medical management (eg, pharmacotherapy) and were not willing or ready to undergo other bariatric surgical options. Other minimally invasive weight loss procedures include gastric balloon and gastric banding. However, balloon therapy was not included in the model as its safety and efficacy beyond 6 months had not been established. Gastric banding was excluded as a comparator because its use has decreased substantially in recent years.

FIGURE 1. Model Schematics

A. Population and Comparator Arms



B. Markov Transition Matrix



The model was built on change in BMI and diabetes status as predictors of cost and health-related quality of life. Over the course of the model, patients could experience BMI change, diabetes remission, and mortality. Costs and utilities were associated with BMI, and over the course of the model, patients accumulated costs and utilities by remaining in, or transitioning from, various BMI levels.

Each treatment arm was associated with the 4 BMI health states previously mentioned. At model entry, patients undergoing vagal nerve blocking and conventional therapy were placed in initial BMI health states according to their baseline BMI, which was determined by mean class 2 and class 3 BMIs in the ReCharge trial. Experiencing change in BMI allowed patients to transition between BMI health states. Diabetes and diabetes remission were also incorporated in the model structure. At baseline, patients were assigned an initial diabetes status according to their initial BMI health state, based on the indication explored in the ReCharge trial. In subsequent model cycles, patients were assigned a probability of diabetes remission, which was a function of the BMI trajectory associated with the treatment arm. The vagal nerve blocking device model also incorporated device replacement, as well as revision surgeries associated with both initial and device replacement implantations.

The final health state was death, for which a probability derived from the literature was applied at the end of each cycle. Patients remained in the model until death or age 100, whichever occurred first. A schematic of the model health states and transitions are provided in **Figure 1**.

Model Process

At model entry, patients were assigned ages from a sampled distribution (mean = 47; standard deviation [SD] = 10) and sent through the model one at a time to receive vagal nerve blocking and conventional therapy in separate but parallel simulations. The age distribution was selected to align with the ReCharge trial population.[10] Patients entering the model in class 2 and class 3 were assigned baseline BMIs of 37.5 and 42.5, respectively, according to the ReCharge trial, and placed in corresponding class 2 obesity and class 3 obesity initial health states. All class 2 patients were then assigned the variable of diabetes in the first cycle, and those in class 3 were assigned a probability of having diabetes, as per the indication evaluated in the ReCharge trial. Also, a probability of device revision surgery was assigned to patients in the nerve blocking arm.

As patients cycled through the model, they could experience change in BMI (specific to class 2 or 3) as per the BMI trajectory

TABLE 1. Model Parameters

Model Parameters	Estimates			
	Class 2		Class 3	
	Conventional Therapy	vBloc[a] Therapy	Conventional Therapy	vBloc[a] Therapy
Baseline age, years[10]	47 (10)		47 (10)	
Baseline BMI (kg/m^2)	37.5		42.5	
BMI trajectory[b]				
Cumulative change in BMI: month 12	0.00%	−11.20%	0.00%	−9.18%
Cumulative change in BMI: month 24	0.00%	−9.33%	0.00%	−7.29%
Cumulative change in BMI: month 30	0.00%	−9.60%	0.00%	−8.00%
Change in BMI: month 31 onward	0.00%	0.00%	0.00%	0.00%
Baseline probability of diabetes	100%		50%	
Diabetes remission probability (per cycle)[21]	0.00%	0.27%	0.00%	0.18%
Initial device and procedure cost (US$)	N/A	$20,000	N/A	$20,000
Replacement device and procedure cost (US$)	N/A	$17,000	N/A	$17,000
Probability of device revision surgery (per cycle)[10]				
First year post device implantation	0.00%	0.10%	0.00%	0.10%
Second year post device implantation	0.00%	0.05%	0.00%	0.05%
Cost of device revision surgery (US$)[10]	N/A	$10,732	N/A	$10,732
Medical cost (per cycle) (US$)[20]	$0.0964 \times (BMI)^2 - 3.7591 \times (BMI) + 116.29$		$0.0964 \times (BMI)^2 - 3.7591 \times (BMI) + 116.29$	
EQ-5D utility (per cycle)[19]				
Diabetes	$-0.0108 (BMI) + 0.8654$		$-0.0108 (BMI) + 0.8654$	
No diabetes	$-0.0128 (BMI) + 1.0254$		$-0.0128 (BMI) + 1.0254$	
Relative risk of mortality (per cycle)[23]	$0.007275 \times (BMI)^2 - 0.3754 \times (BMI) + 5.6933$		$0.007275 \times (BMI)^2 - 0.3754 \times (BMI) + 5.6933$	
Discount rate (per cycle)	0.07%		0.07%	

BMI indicates body mass index; EQ-5D, EuroQol 5 Dimension questionnaire; N/A, not applicable.
[a]vBloc neurometabolic therapy (an implantable weight loss device) is a registered product of EnteroMedics Inc (St. Paul, MN).
[b]In applying BMI trajectory in the model, weekly mean percent BMI change was interpolated from monthly and weekly data from the ReCharge trial. Only data at months 12, 24, and 30 are displayed here and show change in BMI relative to initial system implant.

from the ReCharge trial and were able to transition between health states. As the ReCharge trial provided BMI change data for up to 30 months, it was conservatively assumed that BMI change beyond 30 months was flat. Conventional therapy patients did not experience BMI change, an assumption previously implemented in bariatric surgery cost-effectiveness analyses by Ackroyd et al.[19]

Additionally, patients were given the probability of experiencing diabetes remission during each cycle, which was BMI-driven, and as such, diabetes remission could not occur in the vagal nerve blocking therapy arm. It was assumed that patients who had experienced diabetes remission remained diabetes-free for the remainder of the model. At the end of each cycle, patients were assigned a probability of death. Those who survived in a given cycle continued to the next cycle. At the end of 9 years, the patients receiving vagal nerve blocking therapy who remained in the model were given a device replacement, and a probability of device revision surgery was applied to those who received a replacement. Patients were tracked throughout the model and were assigned literature-based costs and utilities associated with their BMI level and diabetes status for each cycle. Costs and utilities were then aggregated at the end of each patient's journey through the model.

Model Inputs

Model inputs included in the analysis are presented in **Table 1** and were derived from the scientific literature, ReCharge trial, and publicly available databases.

BMI trajectory. Data for baseline BMI and BMI change for patients in the class 2 and class 3 analyses came from the ReCharge trial. Mean percent change in BMI was calculated for class 2 patients and class 3 patients on a weekly basis.

Health-related quality of life. In order to assess health-related quality of life, we used utility equations from Ackroyd et al that were dependent on both BMI and diabetes status.[19] These utility equations expressed quality of life in terms of The EuroQOL 5

Dimensions questionnaire (EQ-5D) scoring and were used to assign utilities to patients at the start of each cycle. Quality of life scores were then calculated using these EQ-5D utility values as adjustors.

Costs. Estimates for healthcare costs were derived from Arterburn et al, who reported adult per capita total healthcare expenditure by BMI category.[20] First, we plotted adult per capita total healthcare expenditures against BMI and then we performed a univariate regression analysis in which we estimated the coefficient describing the association between BMI and adult per capita total healthcare expenditure. As Arterburn et al assessed total healthcare expenditures, it was assumed that costs associated with obesity sequelae were folded into the total expenditures.[20] Total healthcare expenditures were inflated from 2000 to 2015 levels using the medical component of the Consumer Price Index.

The cost of vagal nerve blocking therapy was incorporated as an initial device and installation cost of $20,000 in the base-case, and as the model allowed for assumptions around device replacement, a $17,000 vagal nerve blocking device replacement cost was also incorporated at the end of year 9 for all patients receiving vagal nerve blocking therapy. These values were obtained through communication with the product manufacturer. In sensitivity analyses, this cost parameter was varied up and down by 25%. Patients were assigned only 1 vBloc device replacement in their lifetime. The likelihood of a second device replacement was variable and dependent on several factors, including age. Given the mean baseline age of 47 years, on average, patients would be 65 at the time the second device would require replacement, and it is not expected that patients would receive another device implant at that age. For simplicity in the model, we made the assumption of 1 replacement. However, we also considered that potential changes in the device's battery life expectancy and adoption of vagal nerve blocking therapy among younger patients may ultimately result in more than 1 replacement. Device revision surgery costs for initial device implantation and replacement were also incorporated in the model.

Diabetes remission. Probabilities for diabetes remission were estimated from rates observed in Gregg et al, which provided annual probabilities of diabetes remission for patients on an intensive lifestyle intervention (ILI), starting in various BMI categories.[21] Diabetes remission rates from the Gregg et al ILI cohort were deemed appropriate for the vagal nerve blocking arm, as weight loss observed in the ILI cohort was comparable to weight loss observed for vagal nerve blocking therapy in the ReCharge trial. As Gregg et al only provided data up to 12 months, the rate of diabetes remission at the end of 12 months was carried forward for months 13 to 30. After month 30, the rate of remission was set to 0 to parallel the lack of BMI change after month 30 for vagal nerve blocking therapy patients, as the assumption was that change in BMI drove diabetes remission in the model. These estimates from Gregg et al were utilized because the ReCharge trial limited the participation of those with type 2 diabetes and there were not enough patients in the trial to assess diabetes remission.[10]

Device revision surgery. Patients were assigned probabilities for device revision surgery and associated costs in the first and second years after initial device implantation, based on available data from the ReCharge trial and the product manufacturer. These probabilities and costs were also applied in the first and second year after device replacement.

Mortality. Probability of death was a function of both age and BMI and was applied at the end of each cycle. We employed the methodology previously used by Campbell et al,[22] in which mortality rates adjusted for BMI and age were estimated by applying BMI-specific relative risk ratios[23] to age-specific all-cause mortality rates from the 2010 US life tables.[24] Therefore, at any given age, patients with higher BMI had higher mortality risk. In order to obtain BMI-specific RRs, we first plotted the RR of death described by Flegal et al[23] against BMI, and then performed a univariate regression analysis in which we estimated the coefficient describing the association between BMI and RR of death.

Discounting. A 3.50% annual discount rate was assumed.[25] This was converted to a weekly rate and applied to utilities and costs for each weekly cycle.

Obtaining weekly rates. To accommodate the weekly cycles used in the model, the data for BMI change, total healthcare expenditures, diabetes remission rates, mortality rates, and discount rates were adjusted to weekly rates using the Declining Exponential Approximation of Life Expectancy method outlined by Beck et al.[26]

Model Outcomes

Model outcomes were evaluated over a lifetime horizon for the class 2 and class 3 analyses. For each comparator, cumulative total healthcare costs were collected in addition to QALYs, which are a measure of both the quality and quantity of life, and were calculated by adjusting the life-years for each patient by their quality of life, as captured by literature-based EQ-5D scoring. To compare the vagal nerve blocking and conventional therapy arms, an ICER expressed as dollars per QALY gained was calculated. The ICER was estimated by dividing the difference in costs between vagal nerve blocking and conventional therapy by the difference in QALYs between the treatment arms.

RESULTS

Base-Case Results

Base-case results were generated for both the class 2 and class 3 analyses under a lifetime horizon and are presented in **Table 2**. Mean discounted lifetime total healthcare costs were $123,607 for vagal nerve blocking and $96,141 for conventional therapy in class 2 patients and $129,183 for vagal nerve blocking and $102,259 for conventional therapy in class 3 patients. Mean discounted QALYs

TABLE 2. Cost-Effectiveness Ratios (Relative to Conventional Therapy) for Base-Case Analyses

	Class 2		Class 3	
	vBloc[a] Therapy	Conventional Therapy	vBloc[a] Therapy	Conventional Therapy
Total direct medical costs[b]	$123,607	$96,141	$129,183	$102,259
QALYs[b]	9.27	7.68	7.92	6.68
ICER	$17,274/QALY	N/A	$21,713/QALY	N/A

ICER indicates incremental cost-effectiveness ratio; N/A, not applicable; QALY, quality-adjusted life-year.
[a]vBloc neurometabolic therapy (an implantable weight loss device) is a registered product of Entero-Medics Inc (St. Paul, MN).
[b]Costs and QALYs were discounted at a 3.5% annual rate.

were 9.27 for vagal nerve blocking therapy and 7.68 for conventional therapy in class 2 patients and 7.92 for vagal nerve blocking and 6.68 for conventional therapy in class 3 patients. The ICER for vagal nerve blocking therapy versus conventional therapy in class 2 patients was $17,274 per QALY gained and $21,713 per QALY gained in class 3 patients.

Sensitivity Analyses

To test the robustness of the base case results, multiple 1-way sensitivity analyses were conducted. Model parameters tested included costs, utility, change in BMI, proportion of class 3 patients with diabetes, diabetes remission, and mortality rates. For most parameters, the sensitivity analysis tested inputs at 75% and 125% of the base-case value. The proportion of class 3 patients with diabetes was tested using 25 percentage points below and above the base-case value. Sensitivity analysis parameters are shown in **Table 3**.

A series of 1-way sensitivity analyses were performed for patients with both class 2 and class 3 obesity and results are presented in tornado diagrams in **Figure 2**. Among both the class 2 and class 3 populations, the top 3 drivers of variation in the ICER were the EQ-5D utility values applied for patients without diabetes, BMI trajectory, and the procedural costs associated with initial vBloc device implantation. These sensitivity analyses showed the class 2 and class 3 ICERs to be robust to reasonable variation in model inputs. We performed an additional analysis, incorporating a transient utility decrement of 25% for 2 weeks after both initial device implantation and replacement for the vagal nerve blocking arm. This transient disutility was extracted from a cost-effective analysis by Comay et al of the endoscopic Stretta procedure,[27] which

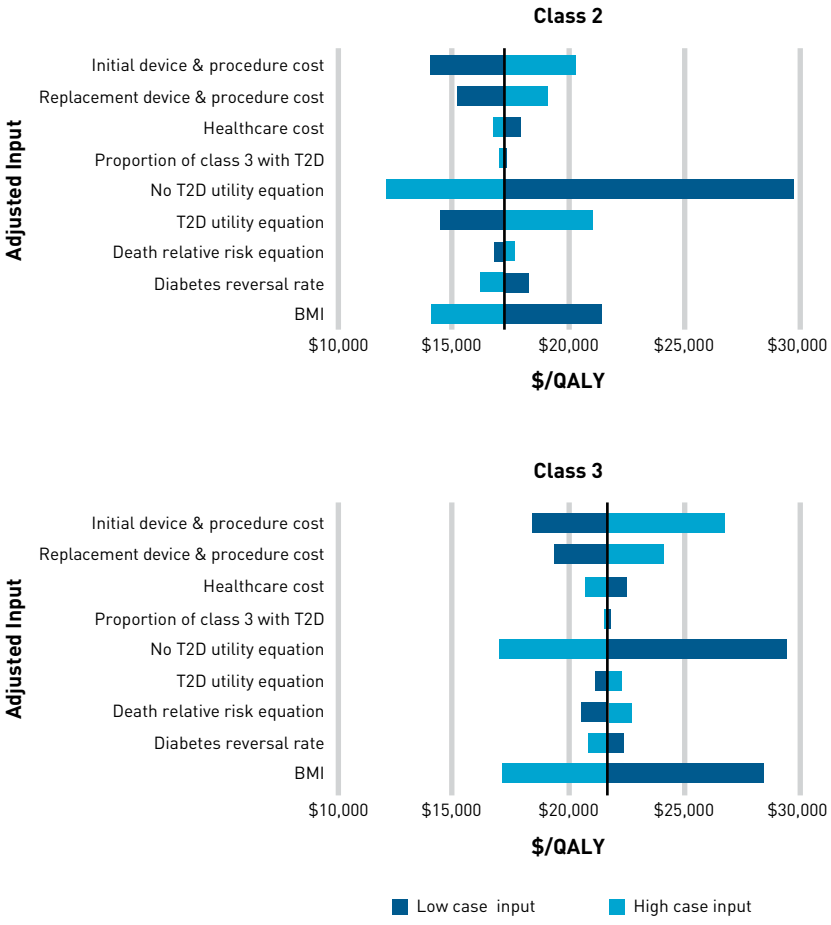
TABLE 3. Sensitivity Analysis Inputs

	Estimates							
	Class 2				Class 3			
	Conventional Therapy		vBloc[a] Therapy		Conventional Therapy		vBloc[a] Therapy	
Sensitivity Analysis Parameters	Low	High	Low	High	Low	High	Low	High
BMI trajectory								
Cumulative change in BMI: month 12	0.00%	0.00%	−8.40%	−14.00%	0.00%	0.00%	−6.89%	−11.48%
Cumulative change in BMI: month 24	0.00%	0.00%	−7.00%	−11.66%	0.00%	0.00%	−5.47%	−9.11%
Cumulative change in BMI: month 30	0.00%	0.00%	−7.20%	−12.00%	0.00%	0.00%	−6.00%	−10.00%
Change in BMI: month 31 onward	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
Baseline probability of diabetes	100%	100%	100%	100%	25%	75%	25%	75%
Diabetes remission probability (per cycle)	0.00%	0.00%	0.20%	0.34%	0.00%	0.00%	0.13%	0.22%
Initial device and procedure cost (US$)	N/A	N/A	$15,000	$25,000	N/A	N/A	$15,000	$25,000
Replacement device & procedure cost (US$)	N/A	N/A	$12,750	$21,250	N/A	N/A	$12,750	$21,250
	Low				High			
Medical cost (per cycle)	$0.75 \times [0.0964 \times (BMI)^2 - 3.7591 \times (BMI) + 116.29]$				$1.25 \times [0.0964 \times (BMI)^2 - 3.7591 \times (BMI) + 116.29]$			
EQ-5D utility (per cycle)								
Diabetes	$0.75 \times [-0.0108 (BMI) + 0.8654]$				$1.25 \times [-0.0108 (BMI) + 0.8654]$			
No diabetes	$0.75 \times [-0.0128 (BMI) + 1.0254]$				$1.25 \times [-0.0128 (BMI) + 1.0254]$			
Relative risk of mortality (per cycle)	$0.75 \times [0.007275 \times (BMI)^2 - 0.3754 \times (BMI) + 5.6933]$				$1.25 \times [0.007275 \times (BMI)^2 - 0.3754 \times (BMI) + 5.6933]$			

BMI indicates body mass index; EQ-5D, EuroQol 5 Dimensions questionnaire; N/A, not applicable.
[a]vBloc neurometabolic therapy (an implantable weight loss device) is a registered product of EnteroMedics Inc (St. Paul, MN).

is a minimally invasive endoscopic procedure used in gastroesophageal reflux disease. In this additional analysis, ICERs were $17,507 and $21,820 per QALY gained in class 2 and class 3, respectively. For all sensitivity scenarios, the upper limits of the ICER estimates remained below the conventionally accepted $50,000 cost-effectiveness threshold in the United States.[28] Probabilistic sensitivity analysis was also performed and results were consistent with reported findings.

FIGURE 2. One-way Sensitivity Analyses for Incremental Cost-Effectiveness Ratios in Patients With Class 2 and Class 3 Obesity[a]



BMI indicates body mass index; QALY, quality-adjusted life-year; $/QALY, dollars per quality-adjusted life-year; T2D, type 2 diabetes.

[a]Selected inputs were varied below (low-case input) or above (high-case input) their base value. Resulting cost-effectiveness ratios (cost per quality-adjusted life-year [QALY] gained) are graphed for each adjusted input, relative to base case cost-effectiveness ratios.

DISCUSSION

In this analysis, Monte Carlo modeling techniques were used to evaluate the cost-effectiveness of vagal nerve blocking therapy versus conventional therapy over a lifetime horizon of class 2 patients with diabetes and class 3 patients with or without diabetes. Assuming a $20,000 initial cost for the vBloc device and installation, the estimated ICER for vagal nerve blocking versus conventional therapy was $16,907 per QALY gained among class 2 patients and $21,424 per QALY gained among class 3 patients. Sensitivity analyses showed the cost-effectiveness results to be robust to reasonable variations in model assumptions.

Our model design was based on previous bariatric surgery cost-effectiveness models published in the peer-reviewed literature. Prior analyses have stratified outcomes by BMI, such as in Campbell et al, which compared laparoscopic gastric banding (LAGB) and laparoscopic Roux-en-Y gastric bypass (LRYGB) to no treatment.[22] Other analyses have also incorporated diabetes and diabetes remission, such as in the analysis by Hoerger et al, which also compared LAGB and LRYGB to no treatment.[29] In our model design, we stratified outcomes by class 2 and class 3 obesity and incorporated diabetes and diabetes remission in the model structure.

Campbell et al observed ICERs for LAGB and LYRGB (vs no treatment) to be $5400 and $5600 per QALY gained, respectively[22]; and Hoerger at al observed ICERs for LAGB and LRYGB (vs no surgery) to be $11,000 to $13,000 per QALY gained and $7000 to $12,000 per QALY gained, respectively.[29] Although the results of our study show that vagal nerve blocking therapy is cost-effective, the ICERs estimated from our model are higher than ICERs published for LAGB and LYRGB.

Limitations

Because of the lack of BMI data from the ReCharge trial past 30 months, BMI in the vagal nerve blocking therapy arm was assumed to remain constant beyond 30 months in order to conservatively model out a lifetime horizon. By applying this assumption in the model, additional cost savings or losses from weight loss past 30 months may not have been fully captured. More long-term data may further elucidate the value of vagal nerve blocking, and the ASMBS has encouraged participation in clinical studies and a prospective collection of outcomes for this therapy.[12]

We did not include AEs associated with the vagal nerve blocking procedure in the base case analysis as commonly observed AEs from the trial were not high-cost events (eg, pain in the

neuroregulator site, heartburn/dyspepsia, and other types of pain). Although utility values used in the model were dependent on diabetes status, healthcare expenditures applied in the model were not explicitly dependent on diabetes status, but on BMI-specific average overall healthcare expenditures in the general obese population. Even though this allows for a conservative approach, it is possible that additional cost savings or losses experienced by patients with diabetes remission undergoing vagal nerve blocking therapy may not be fully captured in the model.

CONCLUSIONS

This analysis provides a cost-effectiveness evaluation of a new weight loss therapy that may present an affordable and minimally invasive option for patients seeking alternatives to currently available weight loss treatments. Recent cost-effectiveness analyses in bariatric surgery have compared bariatric surgical options such as LAGB and LRYGB versus no treatment.[22,29] The designs of these previous models have informed this model's design for capturing the impact of BMI class and diabetes remission on costs, clinical outcomes, and cost-effectiveness.

Our findings suggest that vagal nerve blocking therapy is likely to be a cost-effective alternative to conventional therapy among class 2 patients with diabetes and class 3 patients with or without diabetes. ICERs from base-case and sensitivity analyses fell below $30,000 per QALY gained, suggesting that vagal nerve blocking therapy represents good value for money from a US payer perspective. ■

Author Affiliations: Boston Health Economics, Inc (JCY, RIG, IL), Waltham, MA; Oregon Health & Science University (BW), Portland, OR; Cleveland Clinic Florida (RR), Weston, FL; EnteroMedics, Inc (DC), St. Paul, MN.

Source of Funding: This study was funded by EnteroMedics, Inc.

Author Disclosures: Mr Yu and Dr Lin are employees of, and Dr Griffiths is a consultant to, Boston Health Economics, Inc, which consulted for EnteroMedics, Inc. Mr Cohen is employed by, and owns stock in, EnteroMedics. Dr Wolf received a contract from EnteroMedics to conduct the ReCharge study. The remaining authors report no relationship or financial interest with any entity that would pose a conflict of interest with the subject matter of this article.

Authorship Information: Concept and design (JCY, RIG, DC, IL); acquisition of data (JCY); analysis and interpretation of data (JCY, RIG, DC, IL); drafting of the manuscript (JCY, BW, RIG, RR, DC, IL); critical revision of the manuscript for important intellectual content (JCY, BW, RIG, RR, DC, IL); statistical analysis (JCY, RIG, IL); provision of patients or study materials (DC); obtaining funding (DC); administrative, technical, or logistic support (JCY); and supervision (JCY, BW, RIG, RR, IL).

Address Correspondence to: Iris Lin, PhD, Boston Health Economics, 20 Fox Rd, Waltham, MA 02451. E-mail: iris.lin@bhei.com.

REFERENCES

1. Shields M, Carroll MD, Ogden CL. Adult obesity prevalence in Canada and the United States. *NCHS Data Brief.* 2011;(56):1-8.
2. Wing RR, Bolin P, Brancati FL, et al; The Look AHEAD Research Group. Cardiovascular effects of intensive lifestyle intervention in type 2 diabetes. *N Engl J Med*. 2013;369(2):145-154. doi: 10.1056/NEJMoa1212914.
3. Bray GA. Medications for weight reduction. *Med Clin North Am.* 2011;95(5):989-1008. doi: 10.1016/j.mcna.2011.06.009.
4. Picot J, Jones J, Colquitt JL, et al. The clinical effectiveness and cost-effectiveness of bariatric (weight loss) surgery for obesity: a systematic review and economic evaluation. *Health Technol Assess.* 2009;13(41):1-190, 215-357, iii-iv. doi: 10.3310/hta13410.
5. Behary J, Kumbhari V. Advances in the endoscopic management of obesity. *Gastroenterol Res Pract.* 2015;2015:757821. doi: 10.1155/2015/757821.
6. Stevens J, Oakkar EE, Cui Z, Cai J, Truesdale KP. US adults recommended for weight reduction by 1998 and 2013 obesity guidelines, NHANES 2007-2012. *Obesity.* 2015:23(3):527-531. doi: 10.1002/oby.20985.
7. Kumbhari V, Oberbach A, Nimgaonkar A. Primary endoscopic therapies for obesity and metabolic diseases. *Curr Opin Gastroenterol.* 2015;31(5):351-358. doi: 10.1097/MOG.0000000000000203.
8. Arterburn DE, Olsen MK, Smith VA, et al. Association between bariatric surgery and long-term survival. *JAMA.* 2015;313(1):62-70. doi: 10.1001/jama.2014.16968.
9. Finkelstein EA, Trogdon JG, Cohen JW, Dietz W. Annual medical spending attributable to obesity: payer- and service-specific estimates. *Health Aff*. 2009;28(5):w822-w831. doi: 10.1377/hlthaff.28.5.w822.
10. Ikramuddin S, Blackstone RP, Brancatisano A, et al. Effect of reversible intermittent intra-abdominal vagal nerve blockade on morbid obesity: the ReCharge randomized clinical trial [erratum in JAMA. 2015;313(1):95]. *JAMA.* 2014;312(9):915-922. doi: 10.1001/jama.2014.10540.
11. Berthoud H. Vagal and hormonal gut-brain communication: from satiation to satisfaction. *Neurogastroenterol Motil.* 2008;20(supp1):64-72. doi: 10.1111/j.1365-2982.2008.01104.x.
12. Papasavas P, El Chaar M, Kothari SN; America Society for Metabolic and Bariatric Surgery Clinical Issues Committee. American Society for Metabolic and Bariatric Surgery position statement on vagal blocking therapy for obesity. *Surg Obes Relat Dis.* 2016;12(3):460-461. doi: 10.1016/j.soard.2015.12.004.
13. ORBERA nonsurgical weight loss balloon system. Orbera website. https://www.orbera.com. Accessed June 10, 2016.
14. ReShape Weight Loss Balloon System. ReShape Medical website. https://reshapeready.com. Accessed July 5, 2017.
15. Cobourn C, Degboe A, Super PA, et al. Safety and effectiveness of LAP-BAND AP System: results of Helping Evaluate Reduction in Obesity (HERO) prospective registry study at 1 year. *J Am Coll Surg.* 2013;217(5):907-918. doi: 10.1016/j.jamcollsurg.2013.06.010.
16. Hamdan K, Somers S, Chand M. Management of late postoperative complications of bariatric surgery. *Br J Surg.* 2011;98(10):1345-1355. doi: 10.1002/bjs.7568.
17. New procedure estimates for bariatric surgery: what the numbers reveal. American Society for Metabolic and Bariatric Surgery website. http://connect.asmbs.org/may-2014-bariatric-surgery-growth.html. Accessed June 10, 2016.
18. O'Hagan A, Stevenson M, Madan J. Monte Carlo probabilistic sensitivity analysis for patient level simulation models; efficient estimation of mean and variance using ANOVA. *Health Econ.* 2007;16(10):1009-1023.
19. Ackroyd R, Mouiel J, Chevallier JM, Daoud F. Cost-effectiveness and budget impact of obesity surgery in patients with type-2 diabetes in three European countries. *Obes Surg.* 2006;16(11):148-1503.
20. Arterburn DE, Maciejewski ML, Tsevat J. Impact of morbid obesity on medical expenditures in adults. *Int J Obes.* 2005;29(3):334-339.
21. Gregg EW, Chen H, Wagenknecht LE, et al; Look AHEAD Research Group. Association of an intensive lifestyle intervention with remission of type 2 diabetes. *JAMA.* 2012;308(23):2489-2496. doi: 10.1001/jama.2012.67929.
22. Campbell J, McGarry LJ, Shikora SA, Hale BC, Lee JT, Weinstein MC. Cost-effectiveness of laparoscopic gastric banding and bypass for morbid obesity. *Am J Manag Care.* 2010;16(7):e174-e187.
23. Flegal KM, Graubard BI, Williamson DF, Gail MH. Excess deaths associated with underweight, overweight, and obesity. *JAMA.* 2005;293(15):1861-1867.
24. Arias E. National Vital Statistics Reports: United States life tables, 2010. CDC website. http://www.cdc.gov/nchs/data/nvsr/nvsr63/nvsr63_07.pdf. Published November 6, 2014. Accessed May 1, 2015.
25. Gray AM, Clarke PM, Wolstenholme JL, Wordsworth S. *Applied Methods of Cost-Effectiveness Analysis in Healthcare.* 1st ed. New York, NY: Oxford University Press; 2010.
26. Beck JR, Pauker SG, Gottlieb JE, Klein K, Kassirer JP. A convenient approximation of life expectancy (the "DEALE"): II. Use in medical decision-making. *Am J Med.* 1982;73(6):889-897.
27. Comay D, Adam V, da Silveira EB, Kennedy W, Mayrand S, Barkun AN. The Stretta procedure versus proton pump inhibitors and laparoscopic Nissen fundoplication in the management of gastroesophageal reflux disease: a cost-effectiveness analysis. *Can J Gastroenterol*. 2008;22(6):552-558.
28. Simoens S. How to assess the value of medicines? *Front Pharmacol.* 2010;1(115). doi: 10.3389/fphar.2010.00115.
29. Hoerger TJ, Zhang P, Segel JE, Kahn HS, Barker LE, Couper S. Cost-effectiveness of bariatric surgery for severely obese adults with diabetes. *Diabetes Care.* 2010;33(9):1933-1939. doi: 10.2337/dc10-0554.

Full text and PDF at **www.ajmc.com**