Non-Invasive Vagus Nerve Stimulation As A Treatment For Headache Patients With MultiMorbidty: Real World Experience In English Primary Care

Strickland I1, Davis S2, Ward J3, Amato F1, Errico JP1

1electroCore LLC, Basking Ridge, NJ, USA, 2Interface Clinical Services, Leeds, United Kingdom, 3Oaklands Health Centre, Holmfirth, United Kingdom

Introduction

Multimorbidity
- Guidelines published by The National Institute for Health and Care Excellence (NICE) describe the need to optimise the care received by patients with multimorbidity.
- The aim of these guidelines is to improve patient quality-of-life and reduce unnecessary clinical appointments and unplanned care.

Healthcare resource utilisation
- Data from 233 patients who attended the first two clinics has been used to calculate the impact of gC on healthcare resource utilisation.
- There was a significant 10% reduction in the mean number of GP appointments attended by patients after gC initiation, compared to a matched period prior to the first clinic (Figure 4).
- There was a significant 21% reduction in the mean number of referrals made by GPs after gC initiation, compared to a matched period prior to the first clinic (Figure 5).
- In real terms the gammaCore multimorbidity clinical trial realised 184 and 42 “avoided” primary and secondary care appointments respectively (Figures 4 and 5).

Methods

Patient identification
- A clinical pharmacist interrogated GP practice computer systems in 7 primary care practices in the UK to identify 18-70 year old patients diagnosed with 2 or more functional diagnoses of the following conditions: primary headache, psychiatric/psychological disorders, anxiety & depression, chronic pain, rheumatological symptoms, epilepsy or insomnia.

Clinic design
- Patients who voluntarily attended the first clinic were asked to complete a health-related quality of life questionnaire (EQ-5D-5L and EQ-VAS).
- Patients willing to use gammaCore (gC) as an adjunct to their current treatment regimen were trained to use the device, given a device to take home, and asked to administer 3 bilateral nVNS doses per day (Figure 1, 12 minutes total therapy time per day).
- Two further face-to-face clinics were conducted to check stimulation technique, adherence to therapy and to address any questions that patients may have.

Statistical analyses
- Descriptive statistics were used to compare patient reported health outcomes before and after gC initiation. Differences in the average number of GP consultations attended and referrals made were calculated using a paired parametric t Test.

Results

Patient reported health outcomes
- Results on the impact of gC on patient reported health outcomes have been generated from all available data sets. At weeks 8 and 40 there were 145 and 61 patients respectively who provided EQ-5D-5L data.
- At week 8, gC patients had significantly improved depression and anxiety levels compared to the pre-gC group (P<0.001).
- Improvements in EQ-5D-5L dimensions were observed in patients’ levels of Fatigue, Ance, in ability to perform usual activities, and levels of Anxiety/depression (Table 1).
- Mean EQ-VAS scores reported at week 8 and week 40 were significantly higher than those reported prior to gC initiation (P<0.05 for both time points).

Table 1. Patient demographics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Clinic attendees</th>
<th>Week 8 patients</th>
<th>Week 40 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female, No. (%)</td>
<td>166 (72.5)</td>
<td>97 (65.9)</td>
<td>51 (65.7)</td>
</tr>
<tr>
<td>Mean age (y), mean ± SD</td>
<td>52 ± 12</td>
<td>52 ± 13</td>
<td>52 ± 13</td>
</tr>
</tbody>
</table>

Table 2. Numbers and proportions reporting levels within EQ-5D-5L dimensions: Prior to starting gC and then at 8 weeks post-gC initiation (n=233)

<table>
<thead>
<tr>
<th>Dimension</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-gC (n=233)</td>
<td>9.2%</td>
<td>17.9%</td>
<td>11.9%</td>
<td>8.6%</td>
<td>13.7%</td>
<td>62.1%</td>
</tr>
<tr>
<td>Post-gC (n=233)</td>
<td>4.3%</td>
<td>8.6%</td>
<td>14.7%</td>
<td>9%</td>
<td>9.4%</td>
<td>46.4%</td>
</tr>
</tbody>
</table>

Figure 1. 10 X 10 dot plot representing patient reported outcome change, according to the Pareto classification of health change. EQ-5D-5L values provided before and then at 8 and 40 weeks after starting gC therapy.
A preliminary cost-utility analysis of non-invasive vagus nerve stimulation therapy in patients suffering with headache and functional disorder multi-morbidity

Michelle Jenks1, Steve Davis2, Frank Amato3, J.P. Errico3, Iain Strickland3
1 York Health Economics Consortium, Enterprise House, Innovation Way, University of York, Heslington, York, YO10 5NG
2 Interface Clinical Services, Leeds, United Kingdom
3 electroCore LLC, Basking Ridge, NJ, USA

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BACKGROUND AND OBJECTIVES
Non-invasive vagus nerve stimulation (nVNS), delivered via the therapeutic medical device gammaCore® (electroCore LLC, New Jersey, United States of America), has been shown to be efficacious in the treatment of primary headache disorders [1]. Previous analyses have demonstrated that nVNS delivered by gammaCore® (gC) is a cost-effective treatment in patients with cluster headaches [2].

nVNS improves the quality of life for patients suffering with multiple, medically unexplained, functional disorders such as headache, gastrointestinal disorders, depression and anxiety [3]. Multi-morbidity typically describes individuals with two or more chronic medical conditions. These individuals may experience reduced quality of life, functional decline and increased use of healthcare resources [4]. Within the United Kingdom (UK), it is estimated that one in six patients are multi-morbid and that around one third of all general practice consultations are for multi-morbid patients [4].

The objective of this study was to estimate the cost-utility of nVNS therapy plus standard care in patients suffering with headache and functional disorder multi-morbidity versus standard care alone. The analysis was conducted from a UK National Health Service (NHS) perspective.

### Table 1: Key model input parameters

<table>
<thead>
<tr>
<th>Resource usage input parameters (per person per month)</th>
<th>nVNS + standard care</th>
<th>Standard care</th>
<th>Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP consultations</td>
<td>0.43</td>
<td>0.54</td>
<td>NHS cohort study [4]</td>
</tr>
<tr>
<td>Prescriptions</td>
<td>3.81</td>
<td>3.65</td>
<td>NHS cohort study</td>
</tr>
<tr>
<td>Secondary care visit</td>
<td>0.08</td>
<td>0.10</td>
<td>NHS cohort study</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Unit costs Input parameter Source</th>
</tr>
</thead>
<tbody>
<tr>
<td>GP consultation</td>
</tr>
<tr>
<td>Prescription cost</td>
</tr>
<tr>
<td>nVNS cost</td>
</tr>
</tbody>
</table>

### METHODS

A decision analytic model was developed in Microsoft Excel to estimate the cost-utility of nVNS over both a one-year and two-year time horizon. The model utilised EQ-5D-5L and healthcare resource data collected from a cohort study set in nVNS primary care clinics within the NHS designed to treat multi-morbid patients (n=233) [3]. Included patients had two or more diagnoses codes under the following disorders: headache, anxiety or depression, gastrointestinal disorders, pain, sinus/nasal symptoms, tinnitus or epilepsy. Resource use data were combined with unit cost data to determine the cost implications of multi-morbid patients either with or without the use of nVNS. Costs included within the model comprised primary care visits; prescription costs; secondary care visits and device related costs. Device costs were applied for the duration during which patients remained on treatment. Participants were instructed to use the device bilaterally, three times a day.

Utility scores were elicited using the EQ-5D-5L scores collected at baseline and every four weeks during the clinical study and applying Kaplan-Meier methods to account for censoring. Utility at baseline was used in the standard care arm of the model. The key input parameters are shown in Table 1.

The primary outcome of the model was an estimated incremental cost per QALY compared nVNS + standard care, to standard care alone over a 12 month period. Deterministic sensitivity analyses (DSA) were conducted to assess the impact of bias on the results of the model. Exploratory analysis were also conducted by extrapolating the data over a two-year time horizon.

### RESULTS

Over a one-year time horizon comparing nVNS + standard care with standard care alone, an ICER of £13,368 per QALY is estimated (Table 2). nVNS would, therefore, be considered cost-effective at a £20,000 per QALY threshold. Cost savings are generated from a reduction in GP consultation costs and a reduction in referrals to secondary care, whilst device related and additional prescription costs are incurred. A 0.1 QALY gain per patient is estimated. Based upon a £20,000 per QALY threshold, a net monetary benefit of £631 per patient and net health benefit of 0.03 per patient are derived.

DSA demonstrated the utility values in both arms of the model to be key drivers of the analysis (Figure 1). nVNS remains cost-effective at a £20,000 per QALY threshold where the difference in QALYs per patient is 0.065 or greater. An exploratory analysis conducted over a 2-year time horizon estimated ICERs of between £11,194 and £15,067 per QALY depending upon the extrapolation method used.

### Table 2: Estimated results at one-year

<table>
<thead>
<tr>
<th>nVNS + standard care</th>
<th>Standard care</th>
<th>Incremental</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costs per person</td>
<td>£2,015</td>
<td>£743</td>
</tr>
<tr>
<td>QALYs per person</td>
<td>0.68</td>
<td>0.58</td>
</tr>
<tr>
<td>ICER</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Figure 1: Tornado diagram

#### CONCLUSIONS

Based on preliminary data, from a UK NHS perspective, nVNS + standard care is estimated to be cost-effective at a £20,000 per QALY threshold compared to standard care alone in patients with functional multi-morbidities. The use of comparative clinical data within the model would strengthen these conclusions.

### REFERENCES


### CONTACT US

michelle.jenks@york.ac.uk
Telephone: +44 1904 324870
Website: www.yhec.co.uk
http://www.minerva-network.com/
http://www.yhec-linkedin.com