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Impact of vagus nerve stimulation on secondary care burden in children and adults with epilepsy: Review of routinely collected hospital data in England

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ABSTRACT

Purpose: We evaluated the long-term medical and economic benefits of vagus nerve stimulation (VNS) therapy for 704 adults and children with epilepsy. A pre–post analysis was conducted using Hospital Episode Statistics (HES) data (April 2008–July 2014). Seven hundred and four patients with epilepsy diagnoses (ICD-10 G40.x or G41.x), one or more procedures for vagus nerve stimulator implantation, and six or more months of available HES data pre- and post-VNS were selected. The pre-VNS period averaged 39.1 months. The post-VNS period extended from implantation to device removal, death, or study end (up to six years), with a mean duration of 36.4 months. Incidence rate ratios (IRRs) and cost differences (£2014) were estimated. Mean age was 28.3 years.
Results: Inpatient admissions decreased post-VNS compared with pre-VNS (adjusted IRR = 0.81, $P < 0.001$). Overall, outpatient consultations increased post-VNS compared with pre-VNS (adjusted IRR = 1.34, $P < 0.001$). However, outpatient consultations exhibited a decreasing trend in the post-VNS period (adjusted IRR = 0.96, $P < 0.001$), suggesting that much of the increased outpatient activity in the post-VNS period relates to follow-up management of the VNS device in the immediate period following implantation, with comparable outpatient resource burden at 36 months post-VNS. No significant changes in clinical events were observed; however, average epilepsy-related medical costs were lower post-VNS than pre-VNS (adjusted cost difference −£110 quarterly, $P = 0.001$).
Conclusions: Vagus nerve stimulation is associated with increased outpatient resource utilization and decreased inpatient admissions, with a reduction in long-term epilepsy-related medical costs post-implantation.

1. Introduction

Epilepsy is a common neurological condition characterized by recurrent unprovoked seizures and affects approximately 1% of people in the United Kingdom [1]. The majority of individuals diagnosed with epilepsy maintain good seizure control when treated with pharmacological therapies. However, for up to 30% of patients, pharmacological therapies are either unable to provide sufficient seizure control or lead to severe side effects that render such therapies unsuitable – so-called 'drug-resistant' epilepsy [2]. Individuals with drug-resistant epilepsy represent a significant financial burden on health-care resources, requiring combinations of medication (often with newer, more expensive antiepileptic drugs), as well as more outpatient time and hospitalization [3]. The direct and indirect costs of managing individuals with established epilepsies in the UK have been estimated at two billion pounds a year [4].

Vagus nerve stimulation (VNS Therapy® — Cyberonics, Inc.) is one of several surgical options for adults and children with drug-resistant epilepsy and is recommended as an adjunctive therapy for drug-resistant epilepsy in children by the UK's National Institute of Health and Social Care Excellence [5]. Vagus nerve stimulation therapy is commissioned by NHS England, the UK's central commissioning body, for adults and children with drug-resistant focal-onset or generalized seizures who are unsuitable for resective surgery, have tried a number of pharmacological therapies, and suffer frequent seizures. The decision to recommend VNS therapy for a patient must involve a multidisciplinary clinical team involving neurosurgery and epilepsy specialist nursing capabilities, and the procedure itself must be conducted in a neurosurgical specialist center [6].

The VNS therapy implantation is a straightforward surgical procedure. A battery-powered pulse generator device is implanted under

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the skin of the upper left chest, and a lead tunneled under the skin is connected to the left vagus nerve in the neck. Stimulation parameters (current intensity, pulse width, signal frequency, and on/off cycles) are programmed into the pulse generator via an external programming wand. Patients or carers may manually activate the stimulator in the event of an oncoming seizure; they may also temporarily inhibit stimulation by holding a magnet over the generator [7]. Battery longevity varies by generator model and programmed settings, but the majority of devices will last at least seven years [8], and the battery can be replaced under local anesthetic. A typical treatment regimen might comprise intermittent stimulation for 30 s every 5 min throughout the day and night [9].

The effectiveness of VNS in reducing seizure frequency and duration has been shown in a number of clinical trials [10–12]. Further, the 'real-world' effectiveness of VNS in drug-resistant epilepsy has been studied among pediatric and adult patients in a number of European countries, with many suggesting that VNS can substantially reduce seizure burden, improve behavior and cognition [13], and improve health-related quality of life (HRQoL) [14,15]. A recent Cochrane systematic evaluation of VNS for drug-resistant partial epilepsy showed favorable efficacy and tolerability profiles, with low withdrawal rates and relatively minor adverse effects [16]. However, the authors also pointed to a substantial paucity of data in this field, suggesting that 'further high-quality research' was needed to sufficiently support their conclusions.

A number of US-based studies show that VNS can decrease the secondary care burden of such patients through reduced seizure events and epilepsy-related injuries [17–19]; however, few studies have explored the effectiveness of VNS and resulting resource use in UK patients with epilepsy. To the authors' knowledge, none yet have utilized national-level secondary care databases for this purpose. A 2003 study by Forbes et al. (updated in 2008) utilized meta-analytic methods to estimate the cost–utility of VNS with data from randomized clinical trials; the results suggest that VNS is a cost-effective therapy for patients with drug-resistant epilepsy, with a cost-per-QALY (quality-adjusted life-year) estimate of £4423 [20,21]. However, further evidence from 'real-world' data – i.e., outside of a trial setting – showing that downstream savings could offset some of the initial financial outlay would reinforce the cost-effectiveness of VNS. Further, it would suggest that wider use could alleviate some of the burden on the UK health system, at a time of financial constraints and significant pressure on secondary care providers. The aim of the study therefore was to explore the demands on secondary care pre- and post-VNS and estimate the financial impact of the intervention.

2. Material and methods

2.1. Data source

We used routinely available national data obtained from Hospital Episode Statistics (HES) from April 2008 to July 2014. The HES database contains information on inpatient admissions, outpatient appointments, and Accident & Emergency (A&E) attendances at NHS and private hospitals in England, with more than 12 million new records added each year. All NHS hospitals in England are required to contribute to this database. The HES database is managed by the NHS Health and Social Care Information Centre and is available for research without ethics approval. For inpatient admissions, the data available consist of a number of coded records for each admission, which are called "episodes". Each episode represents the time period of an inpatient admission during which a patient was under the clinical care of a particular consultant team. Each episode contains diagnoses coded in the *International Statistical Classification of Diseases and Related Health Problems, 10th Revision* (ICD-10) related to the reason for hospital admission. Each episode also contains procedures coded in the *Office of Population Censuses and Surveys Classification of Interventions and Procedures version 4.7* (OPCS-4.7).

2.2. Study design and sample

A retrospective longitudinal open-cohort design was employed (Fig. 1). The study population was selected based on the following inclusion criteria: (1) one or more HES records containing diagnosis (ICD-10) codes G40 'Epilepsy' and/or G41 'Status epilepticus'; and (2) one or more HES records containing (OPCS-4.7) 'procedure' code A33.1 ('Introduction of neurostimulator into cranial nerve') and 'site of intervention' code Z04.4 ('Vagus nerve (x)'); and (3) at least six months of data for either side of the vagus nerve stimulator implantation episode (i.e., patients receiving implantation between October 2008 and January 2014). The start date of the vagus nerve stimulator implantation episode was termed the "index date".

Each patient's observation period extended from the index date until removal of the device, death (in-hospital deaths only), or end of the study period (maximum 6 years of follow-up), whichever occurred first. This period was referred to as the "post-VNS period". The period extending up to 6 years before the index date was used to assess baseline covariates, including demographics and psychiatric and epilepsy-related comorbidities. As patient characteristics may vary over time, each patient's observation period was divided into distinct and uninterrupted quarters (90-day episodes).

2.2.1. Outcomes

All outcomes were compared between the pre- and post-VNS periods (both consisting of up to 23 quarters), normalized on a per-patient per-quarter basis.

2.2.2. Rates of resource utilization and epilepsy-related clinical events

The incidence rates of health-care services and epilepsy-related events were calculated as the number of services/events (i.e., unique visit days) divided by patient-quarters of observation. The following resource utilization services were examined: overall inpatient admissions, epilepsy-related inpatient admissions, overall A&E attendances, overall outpatient visits, and epilepsy-related and neurologist outpatient visits. Epilepsy-related clinical events measured included fractures, head

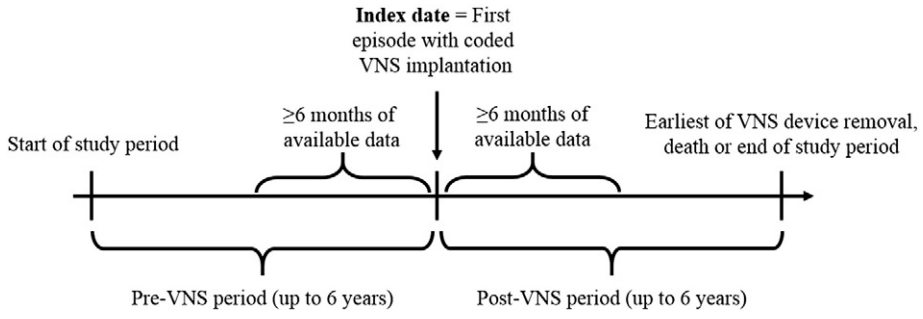

Fig. 1. Study design.