Health Information and Quality Authority

An tÚdarás Um Fhaisnéis agus Cáilíocht Sláinte

Health technology assessment of a national deep brain stimulation service in Ireland

Technical Report

11 October 2012

Safer Better Care

About the Health Information and Quality Authority

The Health Information and Quality Authority (HIQA) is the independent Authority established to drive continuous improvement in Ireland's health and personal social care services, monitor the safety and quality of these services and promote person-centred care for the benefit of the public.

The Authority's mandate to date extends across the quality and safety of the public, private (within its social care function) and voluntary sectors. Reporting to the Minister for Health and the Minister for Children and Youth Affairs, the Health Information and Quality Authority has statutory responsibility for:

- **Setting Standards for Health and Social Services** – Developing person-centred standards, based on evidence and best international practice, for those health and social care services in Ireland that by law are required to be regulated by the Authority.

- **Social Services Inspectorate** – Registering and inspecting residential centres for dependent people and inspecting children detention schools, foster care services and child protection services.

- **Monitoring Healthcare Quality and Safety** – Monitoring the quality and safety of health and personal social care services and investigating as necessary serious concerns about the health and welfare of people who use these services.

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- **Health Information** – Advising on the efficient and secure collection and sharing of health information, evaluating information resources and publishing information about the delivery and performance of Ireland's health and social care services.

Foreword

Deep brain stimulation (DBS) is a surgical procedure for the management of motor function symptoms in patients with movement disorders – including Parkinson's disease, essential tremor and dystonia – that are no longer adequately controlled by drug therapy. In the absence of a DBS service in Ireland, patients are currently referred to DBS centres abroad for assessment, surgery and follow-up care. Funding for eligible patients is provided through the Treatment Abroad Scheme.

In September 2011, the Health Information and Quality Authority (the Authority) agreed to undertake a health technology assessment (HTA) on the provision of DBS services in response to a request from the National Director of Quality and Patient Safety in the Health Service Executive (HSE). The purpose of this HTA was to examine the implications of a national DBS service in Ireland for current and future patients and the resource requirements and costs of such a service compared to the current service provided through the Treatment Abroad Scheme.

Work on the HTA was undertaken by an Evaluation Team from the HTA Directorate of the Authority. A multidisciplinary Expert Advisory Group (EAG) was convened to advise the Authority during the conduct of this assessment.

The Authority would like to thank its Evaluation Team, the members of the EAG and all who contributed to the preparation of this report.

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Dystonia Ireland

Parkinson's Disease Association of Ireland

Medtronic

St. Jude Medical

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* Martin Flattery left the Authority in February 2012

Conflicts of Interest

None reported.

Abbreviations

AANN	American Association of Neuroscience Nurses
BFMRS	Burke-Fahn-Marsden dystonia rating scale
BIA	Budget impact analysis
CE	Conformité Européenne
CI	Confidence interval
CMA	Cost-minimisation analysis
CT	Computed tomography
DBS	Deep brain stimulation
DRS-2	Dementia rating scale-2
EAG	Expert Advisory Group
EEA	European Economic Area
EQ-5D	EuroQol 5 dimension health survey
ET	Essential tremor
EU	European Union
FTM	Fahn-Tolosa-Martin tremor rating scale
GPi	Globus pallidus interna
HES	Hospital episode statistics (UK)
HIU	Health Intelligence Unit
HSE	Health Service Executive
HTA	Health technology assessment
ICER	Incremental cost-effectiveness ratio
IPG	Implantable pulse generator
MDT	Multidisciplinary team
MRI	Magnetic resonance imaging
NHS	National Health Service (UK)
NICE	National Institute for Health and Clinical Excellence
PD	Parkinson's disease
PDQ-39	39-item Parkinson's disease questionnaire
PET	Positron emission tomography
QALY	Quality-adjusted life year
RCT	Randomised controlled trial
SCG	Specialised Commissioning Group
SD	Standard deviation
SF-36	36 item Short-form health survey
STN	Subthalamic nucleus
TAS	Treatment Abroad Scheme
TWSTRS	Toronto Spasmodic Torticollis Rating Scale
UPDRS	Unified Parkinson's Disease Rating Scale
VIM	Ventralis intermedium

1 Introduction to Technical Report

1.1 Introduction

On 21 September 2011, Dr Philip Crowley, the National Director of Quality and Patient Safety in the Health Service Executive (HSE), requested that the Health Information and Quality Authority (the Authority) undertake a health technology assessment (HTA) in relation to the provision of a national deep brain stimulation (DBS) service for the treatment of selected movement disorders in adults.

The request for a formal HTA was based on the increasing number of patients being referred abroad for DBS. Patients deemed clinically suitable for DBS have been referred to centres outside Ireland, predominantly in the UK, since 1997. Funding for treatment is provided through the Treatment Abroad Scheme (TAS) operated by the HSE which provides for the cost of approved treatment in another EU/EEA member state or Switzerland through the issue of form E112. The need for a national DBS service has been questioned based on the increasing volume and cost of referrals through the TAS.

DBS is a surgical procedure for the relief of motor function symptoms in patients with movement disorders that are no longer adequately controlled by drug therapy. These movement disorders include conditions such as Parkinson's disease, essential tremor and dystonia. In contrast to other surgical techniques that involve the permanent ablation or destruction of brain tissue, DBS is a reversible procedure that enables activity in parts of the brain to be disrupted through the use of an adjustable electronic current.

Since 1997, it is estimated that over 130 patients have received DBS through the TAS. While enabling eligible patients to have prompt access to beneficial treatment in recognised DBS specialist centres, the scheme is not without its disadvantages. Patients must be able to travel overseas for initial assessment, surgery and ongoing follow up, with the patient thereby incurring travel costs and potentially travel costs for a companion for those patients unable to travel without assistance. The need to travel may also exclude otherwise eligible patients who are unable to make this journey. There are also logistical issues and difficulties for patients experiencing adverse effects or complications subsequent to their surgery that necessitate a return journey to the DBS centre.

1.2 Terms of Reference

Based on the available evidence, the HSE will consider if there should be a national DBS service for patients with movement disorders compared to the current situation, where funding is provided for eligible patients to access surgery in another EU/EEA member state through the Treatment Abroad Scheme. In consultation with the HSE, a number of key questions were developed in relation to the standards and guidelines to which a high quality and safe DBS service should adhere, the resources and organisational structures required to provide such a service and the costs and budget impact of a national service compared to the current standard whereby care is provided through the Treatment Abroad Scheme. Answers to these questions, which underpinned the Terms of Reference of this HTA will inform the decision of the HSE.

The Terms of Reference were:

- Describe the epidemiology and evidence of clinical effectiveness and safety of deep brain stimulation for relevant conditions (selected movement disorders in adults – Parkinson's disease, dystonia and essential tremor).
- Estimate the demand for a national deep brain stimulation service for relevant conditions.
- Describe the organisational issues associated with the setting up of a high quality national DBS service within the health system in terms of the resources and organisational structures required.
- Perform an economic analysis of the provision of a national DBS service compared to the current practice of providing this therapy through the Treatment Abroad Scheme and estimate the budget impact of provision of such a service.
- Consider any ethical, legal or social issues relating to a national deep brain stimulation service.

The specific remit of this HTA was to assess the provision of DBS services for selected movement disorders in adults (Parkinson's disease, dystonia and essential tremor) for which treatment is currently routinely funded by the HSE. The use of DBS for other indications was beyond the scope of this HTA.

1.3 Overall approach

Following an initial scoping of the technology, the Terms of Reference of this assessment were agreed between the Authority and the Health Service Executive (HSE). The Authority convened an expert advisory group (EAG) comprising representation from relevant stakeholders including the HSE, clinicians with specialist expertise and representatives of patients' organisations. The role of the EAG was to

inform and guide the process, provide expert advice and information and to provide access to data, where appropriate. A full list of the membership of the EAG is available in the acknowledgements section on page 6 of this report. The Terms of Reference of the EAG were to:

- Contribute to the provision of high quality and considered advice by the Authority to the Health Service Executive.
- Contribute fully to the work, debate and decision-making processes of the group by providing expert guidance, as appropriate.
- Be prepared to provide expert advice on relevant issues outside of group meetings, as requested.
- Provide advice to the Authority regarding the scope of the analysis.
- Support the Evaluation Team led by the Authority during the assessment process by providing expert opinion and access to pertinent data, as appropriate.
- Review the project plan outline and advise on priorities, as required.
- Review the draft report from the Evaluation Team and recommend amendments, as appropriate.
- Contribute to the Authority's development of its approach to HTA by participating in an evaluation of the process on the conclusion of the assessment.

The Authority appointed an Evaluation Team comprised of internal staff from its HTA Directorate to carry out the assessment. The Terms of Reference of the HTA were agreed by the EAG at the initial meeting of the group along with service specifications for a patient-centered, high quality and safe service. Detailed service maps based on these specifications were discussed and feedback obtained from each of the members of the EAG. A final draft report was reviewed by the EAG and subsequently presented to the Board of the Authority for approval prior to submission to the HSE and the Minister for Health.

2 Background

Deep Brain Stimulation (DBS) is a neurosurgical intervention for the management of movement disorders such as Parkinson's disease, dystonia and essential tremor. This chapter describes the technology. It provides an overview of the epidemiology of Parkinson's disease, dystonia and essential tremor and reviews the efficacy of DBS in their management. It also estimates the potential demand for a DBS service if provided in Ireland.

2.1 Description of the technology

DBS is an established technology that uses a surgically implanted pulse generator device called a *neurostimulator*, similar to a cardiac pacemaker, to deliver controlled electrical stimulation to precisely targeted areas in the brain. Stimulation aims to interrupt faulty communication between the brain and the muscles that result in involuntary muscle movements. However, the exact mechanism of action of DBS is uncertain. The technology may enable patients suffering from various movement disorders to have greater control over their symptoms resulting in an improved quality of life. However, DBS does not cure the underlying condition and, unlike ablative surgery, its effects are reversible. The three primary targets for DBS are the ventralis intermedium (VIM) in the thalamus, the subthalamic nucleus (STN) and the globus pallidus interna (GPi) of the brain (Table 2.1).

Table 2.1 Primary targets for DBS

Primary targets for DBS	Indication
Ventralis intermedium (VIM) in the thalamus	Used in patients with predominantly severe and disabling tremor. It is now rarely used in Parkinson's disease (PD) as it has been shown that other symptoms continue to progress, causing significant disability not controlled by this treatment.
Subthalamic nucleus (STN)	Indicated for tremor, dyskinesia, rigidity, bradykinesia*, akinesia**, and speech difficulties. It is the most common target of DBS for PD.[1]
Globus pallidus interna (GPi)	Used for dyskinesias, tremor rigidity, bradykinesia and akinesia.

** Slow movement.*

*** Inability to initiate movement due to difficulty selecting and, or activating motor programmes in the central nervous system.*

A DBS system consists of the following:[2;3]

- **Implantable pulse generator (IPG)** – a surgically implanted, battery-operated device which generates mild electrical pulses. It consists of a primary cell or rechargeable battery and a programmable computer chip. The IPG (also known as a neurostimulator) is implanted in the lower chest or upper abdomen.
- **One or more leads and extensions** – surgically implanted thin wires that deliver the mild electrical pulses from the IPG to the target area in the brain via electrodes. The electrodes are attached to the tip of the lead which is implanted in the brain.
- **Programmer** (non-implanted external component) – a device that allows a clinician to fine-tune the way the electrical stimulation is delivered to the brain.
- **Patient controller** (non-implanted external component) – a remote control device that allows patients to check the battery in their device, to turn their device on and off, or adjust preferences for the patient programmer.
- **Recharger** – for rechargeable devices only.

The implantable pulse generators are available as either single channel or dual channel devices for unilateral (one side) and bilateral (two sided) stimulation, respectively. The devices may be either rechargeable or non-rechargeable. Depending on usage, the battery life of a non-rechargeable device is approximately two to five years while that of a rechargeable device is 9 to 10 years. Recent developments in DBS technology include the availability of new hardware and software that allow DBS lead integrity to be checked at the time of lead placement potentially averting patient morbidity and additional surgery due to faulty leads. It may also be useful for the isolation of a new short or open circuit in an existing implanted and otherwise intact DBS system, thus having the potential to reduce additional surgeries due to a faulty lead.[4]

At the time of this report, CE-marked DBS implantable pulse generators were commercially available from two companies, Medtronic Inc. and St. Jude Medical. A third competitor, Boston Scientific, was in early clinical trials of its own DBS platform for Parkinson's disease.[5] Details of the European approval history are included in Table 2.2. Currently, it is stated that Medtronic is the market leader in the supply of DBS technology and it is estimated that approximately 85,000 patients worldwide have obtained DBS interventions as of January 2011.[6] The leads are approved for all indications and may be used interchangeably with any of the licensed IPG devices.

Table 2.2 Regulatory approval history of DBS devices in Europe

Indication	Medtronic	St Jude Medical
	Approval year	Approval year
Essential tremor	1993	-
Dystonia	2003	-
Advanced Parkinson's disease	1998	2009
Obsessive compulsive disorder	2009	-
Epilepsy	2010	-

Implantation of the DBS pulse generator requires a multidisciplinary team and involves several steps, see Chapter 3 for details. In summary, DBS uses stereotactic surgery to implant electrodes in specific target areas in the brain. Firstly, the brain is mapped using magnetic resonance imaging (MRI) or a computed tomography (CT) scan to locate the target area. The testing leads are then inserted into one (unilateral) or both (bilateral) sides of the basal ganglia of the brain through small holes made in the skull under local or general anaesthesia. The electrodes are manipulated based on clinical responses and interpretation of the microelectrode recording data to determine the optimal nuclei to be stimulated. The testing electrodes are removed and replaced with permanent leads. Finally, the leads are connected via an extension wire that runs under the skin of the head, neck and shoulder to the implantable pulse generator which is most commonly implanted in the anterior chest wall just below the collarbone.

The logistics of DBS surgery may vary according to the DBS treatment site (e.g. thalamic or subthalamic) and the treatment facility, with the components of the DBS apparatus implanted over one or two procedures. The DBS apparatus can be activated immediately after surgery or a number of weeks later depending on the patient's diagnosis. The stimulation parameters are programmed by the neurologist using an external programming unit. The goal of programming is to obtain maximal symptom suppression and improvement in function while minimising adverse events. The stimulation parameters may be adjusted in subsequent sessions according to the patient's needs and to achieve optimum results. Patient programmers are also available which enable patients to adjust their stimulation parameters within defined ranges, allowing different settings to be used for different activities. A detailed description of the pre-operative, intra-operative and post-operative management of the patient is included as part of Chapter 3.

Following DBS surgery, diathermy must be avoided as it can interfere with DBS and cause life-threatening complications. The use of MRI is possible, but must be restricted to the specialist setting using protocols that have been evaluated for safety. There may be restrictions in the implantation of other devices, including cardiac devices, with careful monitoring required for potential interactions.

2.2 Parkinson's disease

Parkinson's disease is the most common neurodegenerative movement disorder. It is an adult-onset, chronic, disabling, progressive disease, the primary risk factor for which is increasing age. Parkinson's disease is caused by degeneration of dopamine-producing neurons in the substantia nigra leading to progressive dopaminergic deficiency. It is characterised by four cardinal motor symptoms: resting tremor, rigidity, bradykinesia and postural instability. Onset is usually asymmetric, gradually spreading to the contra-lateral side with disease progression. Non motor symptoms, unrelated to dopamine deficiency, are common particularly as the disease advances.[7;8]

The diagnosis of Parkinson's disease is based on neurological history, symptoms and clinical examination. The most common presenting symptom is asymmetric resting tremor, although bradykinesia may be more common among older patients. Clinical presentation varies between patients with symptoms often going unrecognised or unreported for years. There are no definitive diagnostic tests, although neuro-imaging may be used to exclude other causes of parkinsonian symptoms.[7]

2.2.1 Epidemiology and disease burden

Parkinson's disease is common. Incidence and prevalence increase with increasing age, with peak incidence rates at approximately 75 years. Based on data from the US, prevalence in the general population has been estimated at 0.3%, increasing to 0.5% of the population aged 54 to 74 years and 1 to 2% of the population aged 75 years and older.[7] The average age of onset is approximately 60 years with onset uncommon in individuals less than 40 years of age.[7] It is about 1.5 times more common in men than in women. Mortality in Parkinson's disease is high compared to the general population; life expectancy and age at time of death are reduced for all ages of onset, but with the greatest reductions in life expectancy seen in individuals with young onset disease.[9]

Prevalence of Parkinson's disease in Ireland is unknown. Currently there are no reliable methods for estimating the disease burden of neurological conditions in Ireland. In a 2010 report by the Neurological Association of Ireland, it was estimated that there are 6,000 to 7,000 individuals with Parkinson's disease in Ireland, 1,000 of whom are over 80 years of age.[10] Prevalence of Parkinson's disease has been

assessed in a number of UK studies, with an estimated age-adjusted prevalence rate of 168/100,000 reported.[11]

2.2.2 Management

Currently, there is no cure for Parkinson's disease nor has any existing therapy been shown to reverse or slow progression of the disease. The goal of treatment is to maintain functional independence and quality of life for as long as possible by providing symptomatic relief and by minimising undue adverse events. For all stages of Parkinson's disease, drug therapy is the medical treatment of choice. Motor symptoms in early stage disease may be effectively managed with levodopa and other adjunctive agents that correct the dopaminergic activity and restore function. These medications usually provide good control of motor symptoms for four to six years. However, complications arise with longer use and higher doses; an estimated 10% of patients become refractory with each year of use.[12] After this, disability often progresses despite best medical management and many patients develop troublesome long-term motor complications, including motor fluctuations, dyskinesias and dystonia.

Surgery may be considered in individuals who have responded poorly to drugs and, or have severe medication-related adverse events and, or have severe fluctuations in response to drug therapy. Alternative surgical techniques for medication-refractory Parkinson's disease include pallidotomy, thalamotomy and subthalamotomy. These are ablative procedures that involve permanent, destructive lesioning of abnormally hyperactive deep brain nuclei in the globus pallidus, thalamic nucleus and subthalamic nucleus, respectively. Although effective for refractory symptoms, lesional surgery and in particular bilateral surgery, is associated with a risk of permanent severe complications including cognitive impairment, hemiparesis and dysarthria. Ablative surgery has therefore largely been outmoded by the availability of the reversible, non-destructive surgical option, deep brain stimulation.[13;14]

2.2.2.1 Efficacy and safety of DBS in Parkinson's disease

As noted, treatments for Parkinson's disease aim to improve quality of life by improving movement function while minimising treatment-related complications. Quality of life is frequently measured by recording the patient's self-evaluation of their functional status by use of the validated 39-item Parkinson's Disease Questionnaire (PDQ-39). Efficacy of treatment is most commonly measured using the Unified Parkinson's Disease Rating Scale (UPDRS) – a combined tool of four subscales including mental state, behaviour and mood (I); activities of daily living (II); motor examination (III); and complications of therapy in the last week (IV).

The efficacy and safety of DBS in the management of patients with Parkinson's disease that have failed medical management has been extensively reported in the

literature. DBS has been compared to best medical therapy and to other surgical techniques such as pallidotomy. The comparative efficacy and safety of DBS at different neurological sites (subthalamic, pallidal and thalamic) has also been assessed.

Impact of DBS on quality of life has been assessed in a number of randomised controlled trials (RCTs) using the standardised Parkinson's Disease Questionnaire 39 (PDQ-39). Compared to best medical care, significant improvements in 7 of the 8 subscales were noted at 6-month follow up for patients (n=121) receiving DBS compared to best medical therapy.[15] In the PD-SURG trial (n=366), significant improvements were noted in three of the eight domains (mobility: -9.9 [95%CI-13.8 to -0.4]; activities of daily living: -12.4 [-17.3 to -7.5]; and bodily discomfort: -7.5 [-12.6 to -2.4]) at 12-month follow-up compared to best medical therapy. The differences in the summary index (-4.7) was lower than that seen in two trials that reported results after six months follow-up (mean: -8.7) and was consistent with results of a trial with 24 month follow-up[16] and may indicate that initial improvements in quality of life may not be sustained in the long term.[17]

The benefits in quality of life have been mirrored by clinically meaningful improvements in the UPDRS scale against which efficacy is measured. Significant improvements in the ability of patients to perform activities of daily living (as measured by UPDRS II) of 24% to 26% at 6 and 12 months post surgery, respectively are reported compared to no improvement in those on medical therapy only.[1;15;17] Significant improvements in motor function (UPDRS III) measured off medication at 6 and 12 months follow-up for DBS compared to best medical therapy are also reported with reductions of 28% and 30% noted at six months[15] and 12 months follow-up[17], respectively. Minimal change or worsening of scores was noted for patients on medication during the same interval.[15;17] RCT level data also support a reduction in levodopa-induced dyskinesia (UPDRS IV) of 83% at six months and 50-70.5% at 12-months post surgery compared to patients receiving medical therapy.[1;17;18] This is likely due to the average reduction in levodopa dose at 6 months post DBS surgery of 50 to 71%, with sustained reductions of 33-73% maintained at 12 months post surgery. This data contrasts with minimal changes in levodopa dose in patients treated with medical therapy only over the 6 to 12-month follow-up period.[15;17]

Findings from observational studies are largely consistent with the RCT data. In a meta-analysis of 34 published studies of subthalamic DBS, improvements in average quality of life (34.5% ±15.3% in PDQ-39), activities of daily living (UPDRS II: -50%), motor scores (UPDRS III -52%) and dyskinesia (UPDRS IV:- 69.1%) were noted compared to the pre-operative baseline along with a 55.9% reduction (95% CI: 50%-61.8%) in levodopa dose following surgery.[19]

In contrast to the cardinal symptoms of Parkinson's disease (tremor, rigidity and bradykinesia), the effect of DBS on postural instability and gait disability is less certain. It has been noted that despite improvements in posture and gait function post-surgery, patients tend to fall more. A meta-analysis of 11 studies reporting the long term efficacy of DBS (minimum three year post surgery follow-up; mean 4.5 years) noted that improvements in cardinal symptoms were maintained over five years in both the 'on' and 'off' medication state, whereas benefits in gait and posture function declined progressively over time. Differences in the duration of response depending on the site of stimulation were noted, with limited evidence to suggest that GPi may be superior to STN for sustaining gait and posture function.[20]

RCT data indicate that the risk of serious adverse events was 3.8 and 4.3 times higher in DBS patients followed up for six months compared to best medical therapy, with 40% of patients in the DBS arm experiencing a serious adverse event.[15;17] Infection was the most common surgery-related serious adverse event, occurring in 10-20% of patients. Deaths related to cerebral haemorrhage were reported in both trials. Common adverse events related to worsening or uncontrolled Parkinson's disease symptoms.[15;17] Findings from observational studies are largely consistent with these RCT data. Reports of hardware infection relating to DBS surgery vary from 0 to 15.2% in the published literature with a mean infection rate of 4.7% (range 0.9-22%) reported in a recent meta-analysis of 3,550 patients.[21] Infections may occur months or even years following surgery and may relate to systemic infections (sepsis), cellulitis or skin erosion.[22] Common sites of infections are between the electrodes and extension arms, and in the implantable pulse generator (IPG) pocket. Infections are commonly managed by local (partial) or total hardware removal with re-implantation at another site after the infection has resolved. Consistent with other surgical procedures involving the implantation of hardware, antibiotic prophylaxis is also routinely used in DBS surgery to reduce the risk of post-operative infection.[21]

The risk of hardware complications causing sudden loss of stimulation efficacy following previous symptom control is reported to occur in between 2.7% to 50% of patients. The wide variation has been attributed to differences in duration of follow-up, patient selection, surgical technique, neurosurgeon experience and changes in the availability of hardware over time. Sudden failure of stimulation may be caused by electromagnetic interference, implanted pulse generator (IPG) malfunction or battery exhaustion, internal IPG wire breakage, wire or lead fracture, disconnections and lead dislocation. The management of the complication depends on its cause and includes patient training and education to avoid electromagnetic interference, hardware replacement and repositioning of the electrodes.[22]

Commonly reported post-operative issues for patients with Parkinson's disease include weight gain, dyskinesias, axial symptoms, speech dysfunction, tonic muscle contraction, paraesthesia, eyelid and ocular disturbances and behavioural and cognitive issues.[22]

On the basis of published evidence, DBS has been recommended as a symptomatic adjunct to levodopa and for the treatment of motor symptoms in patients with advanced Parkinson's disease in a number of international clinical guidelines.[18;23;24] The need for careful identification of patients has been highlighted, with reports that 30% of DBS failures can be ascribed to inappropriate indication(s) for surgery.[14] Usual indications for surgery include a diagnosis of advanced Parkinson's disease for at least five years, with motor complications that are refractory to best medical treatment in patients who are levodopa responsive, biologically fit with no clinically significant active co-morbidity including mental health problems, for example, depression or dementia.[12;13;25]

2.2.2.2 Cost-effectiveness of DBS surgery for Parkinson's disease

The cost-effectiveness of DBS surgery for Parkinson's disease has been estimated in a number of HTA's. A 2005 Ontario Ministry of Health report estimated the total cost per DBS surgery including one year follow-up to range from $24,430 to $28,420 ($ CAD). Based on these cost estimates and an estimated average decrease in UPDRS motor function score of 22 points (20%) in the first year after surgery, the estimated cost-effectiveness of DBS was $11,650 per 10-point decrease in UPDRS motor subscale.[12] The authors did not report whether or not they considered this to be cost-effective.

A 2006 assessment by the Medical Services Advisory Committee in Australia estimated the discounted cost of a DBS surgery over five years to be $67,475 to $73,204 ($ AUD). Quality of life as an economic variable could not be calculated, however it was estimated that the cost of a 23.7 point improvement in the UPDRS III (motor function) score is A$20,232 - A$25,961.[13] The authors of this report concluded that "robust information on cost-effectiveness is unlikely to emerge but the total cost is acceptable for patients in whom other therapies are insufficient."

Cost-effectiveness has also been assessed in a number of other studies with estimates ranging from €34,839 /QALY (2007, Spain) to US$49,000 / QALY (2001, USA). However, estimates of costs have been limited to those incurred in the first year post-surgery, excluding ongoing potential costs due to monitoring, battery changes and complications.[26;27]

2.3 Tremor

Tremor is an involuntary rhythmic, repetitive movement, most frequently affecting the upper limbs. It can occur at rest or be brought on (or aggravated) by posture or intentional movement. Due to its impact on fine movement control, severe tremor can be disabling. It is associated with a number of different neurological diseases including essential tremor and multiple sclerosis.[28]

Essential tremor is the most common form of tremor encountered in movement disorder clinics. Tremor severity and handicap vary substantially with many patients not seeking medical care possibly due to limited functional impairment. Essential tremor is progressive and disability is reported in 90% of patients seeking medical care. Severely affected end-stage patients are unable to feed or dress themselves.[29] Head and voice tremor are common in patients with essential tremor; however, hand tremor is usually the predominant symptom.[30]

Tremor is also associated with multiple sclerosis, occurring in an estimated 25 to 60% of patients. It may involve the head, neck, vocal cords, trunk and limbs. Postural tremor and intention tremor are the most prevalent tremor forms while true rest tremor is unusual.[31;32]

2.3.1 Epidemiology and disease burden

Essential tremor is one of the most common neurological disorders. Prevalence in the general population is estimated to be 0.3%, although estimates vary due to issues of diagnostic threshold, overlooked diagnosis or unclear diagnostic criteria. Prevalence increases with age, with estimates increasing from 4.0% of those aged 40 years and older to 21.7% of those aged 95 years and older.[29]

2.3.2 Management

To date, no curative treatment exists for essential tremor. Management of the disorder is focussed on symptom control with pharmacotherapy as the primary treatment. However, it is estimated that between 25 and 55% of patients with essential tremor are medication-refractory.[29] Drug treatment is frequently ineffective, rarely reduces tremor to asymptomatic levels, and is frequently complicated by troublesome adverse effects that limit persistence with therapy.[29;33]

Surgery is usually reserved for patients with severe disabling tremor and functional disability that interferes with daily living and for tremor refractory to the highest tolerated doses of medications. Thalamotomy (gamma knife or stereotactic radiofrequency) is reported to be effective in 73% to 93% of patients with medication-refractory essential tremor, but is accompanied by permanent

complications in 9% to 23% of patients with tremor recurring in approximately 20% of patients.[34]

Pharmacological therapy has been reported to provide some effect for tremor associated with multiple sclerosis, but published evidence of effectiveness is very limited. Lesional surgery is an alternative in those with severe tremor with reports of initial tremor reduction of 93.8% with thalamotomy that persisted in 63.5% of patients at 12 months or more. Functional improvement was reported in only 47.8% of patients and adverse events were common.[32] Published evidence is limited: most studies are small, observational, retrospective case series with data on length of follow-up, adverse events and effect on functional status poorly reported. Current data suggest that thalamotomy and DBS are comparable procedures for disabling tremor in multiple sclerosis.[32]

2.3.2.1 Efficacy and safety of DBS in essential tremor

There are currently no high quality long term studies regarding the safety and efficacy of DBS in patients with essential tremor. Recent evidence-based clinical guideline updates from the Quality Standards Sub-Committee of the American Academy of Neurology note that 'there is limited evidence to support the safety and efficacy of DBS in patients with essential tremor'. Recommendations were limited to Level C advice, that is, DBS is 'possibly effective'.[33]

A systematic review of the safety and efficacy of DBS for essential tremor was published by Flora et al. in 2010.[34] Seventeen studies published between 1990 and 2007 were included. The quality of the evidence was noted to be very limited. In the absence of controlled trials, evidence was limited to case series of patients which in some cases were further compromised by the failure to identify appropriate effectiveness scales a priori; failure to record that all patients were treatment refractory before DBS surgery; outcome assessors that were either not blinded or not reported as such; short duration of follow-up; failure to report the resolution, consequences or long-term outcomes related to adverse events; absence of a pre-operative baseline or high loss to follow up.

No study reported on quality of life outcomes for patients.

A total of 430 patients (study range 7 to 62 patients) who had received DBS for essential tremor were identified. Where reported, the mean age at surgery ranged from 60 to 73.8 years. The duration of follow-up ranged from three months to six years. Losses to follow-up of 96 patients were reported. Studies were categorised as before / after DBS or DBS stimulation on / off to allow the effect of the stimulation to be analysed separately to that of the surgery. Twelve studies reported outcomes for patients when DBS was switched on compared to off, of which 10 used the Fahn-Tolosa-Martin (FTM) tremor rating scale to assess effectiveness. Length of follow-up

ranged from three months to a mean of six years post-operatively. Regardless of the FTM sub-scores used, a significant improvement was reported when DBS was switched on compared to off (10 studies) and compared to baseline (seven studies). This improvement was noted to persist in the three studies that followed-up patients for three or more years. A possible benefit of bilateral compared to unilateral stimulation was noted in two studies. Effectiveness data pre-and post-DBS-surgery could be assessed for three studies. Study size ranged from 8 to 27 patients, with mean length of follow-up ranging from 12.5 to 27 months. A significant improvement in the FTM scale was reported in all three studies with the improvement in mean tremor score ranging from 47.4% to 75.8%. Most adverse events were mild, related to thalamic stimulation, and could potentially be treated by changing the stimulation settings. Serious outcomes were rare. The studies poorly reported the resolution or consequences of the mild or serious outcomes. However the authors concluded that DBS is a relatively safe treatment for essential tremor.[34]

In a systematic review of the literature published by Deuschl et al.[30] the efficacy of DBS in the management of hand, head and voice tremor was assessed. Studies with at least five patients assessed for more than one year and published between 2005 and 2010 were included. No controlled trials were identified. Nine studies reporting the effect of thalamic DBS on upper limb tremor were identified. All were uncontrolled case series. Study size ranged from 19 to 37 patients with a mean duration of follow-up ranging from 1 to 7.2 years. Tremor amplitude improved approximately 90% from baseline in all studies, although loss of tremor control over time, which could often be corrected by increasing the stimulation voltages or frequency, was noted in some studies possibly due to tolerance to stimulation or disease progression. Nine studies that assessed the efficacy of unilateral (five studies) or bilateral (four studies) DBS of the Vim nucleus were identified. All were uncontrolled case series; study size ranged from 4 to 24 patients. The improvement in tremor amplitude ranged from 33% to 82%; with bilateral DBS appearing more effective than unilateral stimulation. Six studies reported the effect of DBS on voice tremor. Voice tremor improved from baseline in all studies, with bilateral DBS appearing more effective than unilateral stimulation, although it was also noted to be more likely to produce dysphagia and dysarthria. Common side effects of thalamic stimulation included dysarthria (3-18%), paraesthesias (6-36%), dystonia (2-9%), balance disturbance (3-8%), ataxia 6% and limb weakness (4-8%). Although these adverse events can usually be reduced or eliminated by adjusting the stimulus parameters, they could be treatment limiting with patients discontinuing use of their stimulator because of intolerable side effects.[30]

A systematic review of the literature reported initial tremor suppression in 96% of patients who underwent DBS for disabling tremor associated with multiple sclerosis (n=97) with post-operative improvement in function reported in 85.2% of those who

had a functional disability assessment (n=46). Serious adverse events including intracerebral haemorrhage (n=3) were common with disease relapse or progression reported during follow-up. The published evidence was limited to small, observational, retrospective case series with poor reporting on length of follow-up, adverse events and effect on functional status. In this systematic review, DBS was viewed to be comparable to thalamotomy, but potentially less useful due to the need for chronic management post-surgery and the ongoing risk of hardware complications and infection.[32] Long-term functional benefit with DBS is thought unlikely due to the progressive nature of multiple sclerosis and the ongoing symptoms of dysmetria and ataxia associated with tremulous multiple sclerosis.[31;32]

2.3.2.2 Cost-effectiveness

Cost-effectiveness of DBS for essential tremor was assessed in the 2008 HTA published by the Medical Services Advisory Committee (Australia).[35] Using a 10-year time horizon and assuming a battery life of five years, the cost per patient was estimated to be $91,250 ($ AUD). Data on quality of life were limited, so cost-effectiveness could not be assessed. The potential for reduction in caregiver burden and improvement in productivity due to patients returning to work were noted for those patients that respond to therapy. The report concluded that DBS was sufficiently effective, relatively safe and had an acceptable total cost for the management of essential tremor in patients experiencing severe disability (including inability to feed or toilet independently) and for whom other therapies were insufficient.[35]

2.4 Dystonia

Dystonia is a movement disorder characterised by sustained muscle spasms and contractions that often results in painful, repetitive, twisting movements or abnormal postures. Dystonia is usually a lifelong condition with persistent pain and disability. It is classified according to aetiology (primary or secondary), age of onset (early or late) and distribution of affected body regions (focal or generalised). In contrast to primary dystonia which is not attributable to an exogenous cause or degenerative disorder, secondary dystonia is caused by either an exogenous source such as stroke or trauma or due to other degenerative or inherited disorders. Presentation of the disorder before or after the age of 20 has been used to classify the disorder as 'early' or 'late onset'. Dystonia may be limited to a particular group of muscles (focal dystonia) or may affect most of the body (generalised dystonia). Most people with dystonia have a normal life expectancy. However, dystonia may lead to significant functional and social impairment and often results in a substantial reduction in quality of life; extreme cases of generalised dystonia can lead to total disability.[36]

2.4.1 Epidemiology and disease burden

Dystonia is a rare condition. Prevalence estimates vary widely, most likely due to the absence of validated clinical criteria and tests for diagnosing dystonia. It occurs more frequently in women. In the US, prevalence of focal dystonia is estimated to be 30/100,000 people while estimates for generalised dystonia range from 0.2 to 6.7 /100,000. Prevalence of primary dystonia is estimated at 15.2 /100,000.[36]

2.4.2 Management

Currently, there is no cure for dystonia; management focuses on symptom control with a view to improving quality of life. Pharmacotherapy is first-line treatment and primarily includes the use of repeated injections of botulinum toxin for the management of focal dystonia. There is limited evidence to support the use of other medications; high doses of anticholinergics are possibly effective. For both generalised and focal dystonia, surgical therapy is considered second line in those that are medication refractory and have significant impairment in quality of life. Destructive or ablative procedures (e.g. myectomy, thalamotomy, pallidotomy) are now rarely used due to their apparent ineffectiveness and significant risk of morbidity and mortality.[35;36]

2.4.2.1 Efficacy and safety of DBS

A systematic review and meta-analysis of the safety and effectiveness of DBS for dystonia was included in a 2008 HTA published by the Medical Services Advisory Committee (Australia).[35] One randomised control trial (RCT) and 28 studies of level IV evidence (case series and case reports) were identified. The quality of the evidence was limited by the small number of individuals analysed, the paucity of high level evidence and the variability of the reporting of efficacy and adverse events. Efficacy was best for primary generalised dystonia and primary focal dystonia.

DBS was found to be effective for medically refractory patients with primary generalised dystonia in a meta-analysis of 17 case series including outcomes for 187 patients (mean age at surgery: 30.6 years). A 60% weighted mean improvement in the Burke-Fahn-Marsden Dystonia Rating Scale (BFMRS) clinical score was documented at the maximal follow-up of 12.6 months post-DBS-surgery ($p<0.0001$). DBS surgery also appears to benefit patients with primary focal dystonia. A meta-analysis of seven studies revealed a significant improvement ($p<0.00001$) in the mean total Toronto Spasmodic Torticollis Rating Scale (TWSTRS) after DBS with a reduction of 30 points in the 85 point scale (median follow up: 15 months). There was also a significant improvement in all individual TWSTRS sub-scores (severity, disability and pain) after DBS ($p<0.00001$). The effectiveness of DBS for secondary dystonia was found to vary according to the type of dystonia; evidence was limited

by the small patient numbers and the inclusion of a number of case reports of single patient outcomes. Although improvements in clinical dystonia scales were noted for many patients, the effectiveness of DBS in several types of secondary dystonia was found to be inconclusive.

Based on the systematic review, DBS appears to be relatively safe for dystonia. Although there was substantial variability in the reporting of adverse events, the majority of adverse events were mild and were resolved by changing the stimulation parameters. Severe adverse events were relatively rare, however, overall long-term outcomes related to these events were poorly reported.[35]

The use of DBS for dystonia has also been evaluated by the National Institute for Health and Clinical Effectiveness in the UK[37]. Efficacy data to inform the guidance was based on a limited case series of 22 patients with significant improvements on the Burke-Fahn-Marsden dystonia rating scale and global disability score from baseline noted at 12 month follow up [46.3 to 21.0 ($p<0.001$) and 11.6 to 6.5 ($p<0.001$), respectively]. The guidance noted that the current evidence on the safety and efficacy of DBS appeared adequate to support its use, provided that appropriate arrangements were in place for consent, audit and clinical governance.[28] This is supported by a subsequent meta-analysis conducted in 2010[38] that identified 157 papers reporting individual data for 466 patients, which found that patients with primary forms of dystonia, myoclonus dystonia, subtypes of heredodegenerative dystonia and tardive dystonia have a greater than 50% mean improvement in dystonia severity following DBS. Results of DBS treatment in other forms of heredodegenerative dystonia and secondary dystonia were less consistent.

2.4.2.2 Cost-effectiveness

Yianni et al[39] conducted a prospective study of 26 patients undergoing DBS for the treatment of dystonia in the UK. A cost-utility analysis was performed using pre- and post-procedure Euroquol (EQ-5D) questionnaire data. Costs were calculated retrospectively. Overall cost per patient based on bilateral procedure to the GPi was £31,866 (2003), achieving a gain of 0.94 quality-adjusted life years. The cost-effectiveness of £33,980 per QALY was judged to compare favourably to therapies for other conditions.

Cost-effectiveness of DBS for dystonia was also assessed in the 2008 HTA published by the Medical Services Advisory Committee[35] (Australia). Using a 10-year time horizon and assuming a battery life of two years, the cost per patient was estimated to be $136,278 ($ AUD) with an estimated ICER of $229,000 per QALY. It was noted that there was significant uncertainty with this estimate particularly regarding long-term changes in quality of life for those not undergoing surgery. The cost-effectiveness did not consider the potential substantial productivity gains associated

with return to work for patients and caregivers. The report concluded that the DBS was sufficiently effective, relatively safe and had an acceptable total cost for the management of end-stage primary and secondary dystonia in patients experiencing severe disability (including inability to feed or toilet independently) and for whom other therapies were insufficient.

2.5 Other indications

Considerable research and technology development is still underway with applications in the management of conditions such as Tourette's syndrome, depression, obsessive compulsive disorder, epilepsy and chronic neuropathic pain being assessed.[40] DBS for these indications is not routinely funded in Ireland or in other health systems, such as the NHS, due to the limited clinical effectiveness data currently available.

2.6 Estimated demand for a national deep brain stimulation service

At present Parkinson's disease accounts for approximately 74% of all referrals for DBS for movement disorders in Ireland, with dystonia and tremor accounting for 11% and 15%, respectively[41]. Absolute figures for the number of patients diagnosed with Parkinson's, essential tremor or dystonia in Ireland are currently unavailable. UK age-adjusted prevalence rates are reported to be 168/100,000 for Parkinson's disease[11], 20/100,000 for essential tremor[42] and 16/100,000 for dystonia.[42] Approximately 5% of patients with each of these diagnoses may be suitable for DBS.[42] Applying these figures to Ireland results in an estimate of 7,560 people with Parkinson's disease, 378 of whom are candidates for DBS; 900 people with essential tremor, 45 of whom would be eligible for treatment and 720 patients with dystonia, of whom 36 may benefit from DBS. Overall this would indicate a cohort of approximately 460 patients in Ireland who could potentially be offered DBS treatment. Since approximately 130 patients have already received treatment via the TAS, this would indicate that the upper estimate of the number of remaining Irish patients is 330.

While this method of estimation has been used in previously published reports,[12] there are limitations with its use. It is based on population prevalence and therefore includes the relatively higher numbers of patients with Parkinson's disease aged in their 70's and 80's, many of whom are less likely to meet the eligibility criteria for surgery due to disease progression, co-morbidity, etc.. An alternative method of estimating demand for a national service is to examine the level of demand experienced for DBS within the NHS service in the UK. There, funding for DBS is authorised at a local level by primacy care trusts (PCTs) based on commissioning policies devised by regional specialised commissioning groups. DBS is currently

approved by the majority of these commissioning groups for Parkinson's disease, essential tremor and dystonia, although some only routinely fund DBS for Parkinson's disease, citing insufficient evidence to support its use in dystonia and essential tremor.[43;44] NHS hospital episode statistics (HES) data for England show that DBS services for a population of 53,012,500 treat approximately 221 new patients each year. This indicates that a mature service providing DBS for movement disorders will have an annual uptake rate of approximately 4.2 per million of population. If it is assumed that the prevalence of Parkinson's disease, dystonia and essential tremor are similar in Ireland to the UK, then a comparable national DBS service in Ireland would treat approximately 19 new patients each year. Of note, there are a number of criteria used to select patients with Parkinson's disease for treatment in various PCT's, including:

- having an established diagnosis of idiopathic Parkinson's disease
- having dopamine responsive disease
- not having psychiatric morbidity; depression, risk of suicide or significant cognitive impairment
- being in good general health and being considered to have a reasonable life expectancy
- having received and failed to respond adequately to, or being unable to tolerate appropriate medical therapy
- having symptoms severe enough to significantly compromise quality of life and activities of daily living.

Any differences between the current UK service and a prospective national service will affect the reliability of the estimate of demand. This may also be affected by changing trends in DBS usage, such as the proposed use of DBS in early stage Parkinson's disease.[45]

Differences between the current demand for DBS treatment (approximately 13 new patients per year) via the TAS and the population-adjusted demand based on English data could be due to a number of factors. These include artificial reductions in demand due to difficulties for patients in travelling abroad, constraints in receiving an appointment with a consultant neurologist or a decreased level of referrals from a neurology service lacking in experience in assessing and referring patients for DBS treatment.

2.7 Key messages

- Deep brain stimulation is used to treat the symptoms of neurological movement disorders. It does not cure or halt the progression of the underlying disease. Unlike ablative surgery, DBS is reversible and stimulation parameters can be adjusted to meet the needs of the patient.
- DBS is an established treatment option that has been funded by the HSE since 1997. There is good quality evidence to show that DBS is more effective than best medical therapy in the treatment of dopamine responsive Parkinson's disease with severe motor symptoms that cannot be adequately controlled with medication. There is also evidence to show that DBS is effective in medication-refractory dystonia and essential tremor, however, the evidence base for these indications is of a lower methodological quality.
- Risks associated with the procedure include infection, device malfunction, cerebral haemorrhage, dyskinesias, axial symptoms, speech dysfunction, tonic muscle contraction, paraesthesia, eyelid and ocular disturbances and behavioural and cognitive issues.
- It is estimated that at present there are approximately 330 patients who may be eligible for DBS treatment for movement disorders in Ireland who are not currently in receipt of DBS services. However, not all of these patients may choose to avail of treatment.
- At present there are an estimated 13 new patients undergoing DBS surgery for movement disorders each year via the Treatment Abroad Scheme. Based on data from comparable services in the UK and assuming similar prevalence and uptake rates, uptake of a national DBS service in Ireland would increase to approximately 19 new patients undergoing DBS surgery for movement disorders per annum.

3 Deep brain stimulation service specification

3.1 Introduction

This chapter examines the published literature describing service standards and resource requirements for the provision of a deep brain stimulation (DBS) service. It maps out the current procedures in place for patients who receive this treatment through the Treatment Abroad Scheme (TAS). Finally, the resource requirements of a prospective national service are estimated using relevant literature and through consultation with the Expert Advisory Group (EAG), in order to identify the equipment, personnel and other resources needed to deliver a comparable service in Ireland.

3.2 Review of DBS service standards

A search was carried out to identify international literature on the provision of high quality DBS services. Searches were conducted in the Cochrane Library, MEDLINE, and the websites of national health services that provide DBS services, as well as those of relevant neurological and movement disorder associations. The purpose of the review was to provide a description of the standards currently in place in countries that provide this treatment in terms of the resources, expertise and support services required for each stage of the procedure.

3.2.1 Results

Table 3.1 shows a summary of the identified literature.

Table 3.1 Deep brain stimulation service literature

Name	Date	Type	Source	Country of Origin
Deep Brain Stimulation for Parkinson's Disease - An Expert Consensus and Review of Key Issues[14]	2011	Journal article	Panel of international experts	International
Deep Brain Stimulation for Movement Disorders Commissioning Policy[44]	2011	Policy document	East Midlands Clinical Priorities Advisory Group (NHS)	UK
National Toolkit for the Designation of Providers of Deep Brain Stimulation[46]	2011	Service standard	NHS	UK
Care of the Movement Disorder Patient with Deep Brain Stimulation - AANN Clinical Practice Guidelines[47]	2009	Clinical guideline	American Association of Neuroscience Nurses	USA
Policy on the use of deep brain	2008	Policy	NORCOM (NHS)	UK

stimulation to treat adults with movement disorders[48]		document		
Deep brain stimulation for tremor and dystonia (excluding Parkinson's disease)[28]	2006	Clinical guidance	NICE	UK
Deep brain stimulation for Parkinson's disease[25]	2003	Clinical guidance	NICE	UK

3.2.2 Descriptive summary

A number of different types of publication containing information about the delivery of high quality DBS services and the standards governing these were identified in the literature review. The UK's National Institute for Health and Clinical Excellence (NICE) has published two guidance documents: *DBS for Parkinson's disease*;[25] and *DBS for tremor and dystonia (excluding Parkinson's disease)*.[28;44] Both conclude that clinical evidence "support[s] the use of the procedure, provided that normal arrangements are in place for consent, audit and clinical governance." A number of NHS commissioning reports are also available[44;48;49] that describe the procedure and outline the eligibility criteria patients must meet to access the service. These also provide some information on the referral pathways that have been developed, as well as a limited description of the resources needed to provide the service.

A clinical guideline published by the American Association of Neuroscience Nurses[47] provides a description of the DBS procedure for the treatment of movement disorders, as well as the pre and post-operative care that is required. This document also provides a comprehensive account of the procedure for programming of the device. The typical settings required for essential tremor and dystonia are discussed, along with the potential side-effects of stimulation and how these can be managed. An expert consensus document on DBS in Parkinson's disease by Bronstein et al[14] includes information on programming DBS devices for patients with Parkinson's disease, along with discussion on a range of technical aspects of the procedure and complications that can arise due to hardware issues.

The UK's National Health Services' (NHS) National Toolkit for the Designation of Providers of Deep Brain Stimulation[46] provides information about service standards and resource requirements in relation to UK DBS centres. These NHS standards are particularly relevant since the majority of Irish patients referred through the Treatment Abroad Scheme have received their treatment in the UK. Any new DBS service should adhere to a comparable set of criteria to ensure that patients receive a level of care that is at least equivalent to that currently being offered.

The standards are divided under seven headings, each with a list of requirements that are rated according to when they need to be in place (prior to or post-

designation) and their importance (essential or ideal, but not essential). The UK standards include specifications for paediatric DBS services. Paediatric services are not included in the terms of reference for this project, the remit of which is limited to the use of DBS for movement disorders in adults. The seven different areas for which standards have been developed are:

1. The network approach – ensuring that DBS is integrated into wider neurology services (including the patient's local neurology services) and that measures are in place to ensure effective communication.
2. Making choices – providing the necessary information and support to allow patients to make an informed decision regarding treatment.
3. The patient experience – providing the facilities and support to allow patients to have the best possible experience with the hospital in which treatment is being provided.
4. Access to services – making sure that services are planned around the needs of the patient and that services are delivered in a timely and efficient manner.
5. Age appropriate care – ensuring services deliver care that is age-appropriate and facilitate the transition to other services where appropriate.
6. Excellent care – detailing the requirements of a DBS service in terms of resources, expertise and volume of patients required to maintain a high quality service.
7. Team delivered – making sure that patient care is delivered in a coordinated way by a range of skilled professionals and that adequate records and outcome monitoring are in place.

The individual service specifications are reproduced below followed by a discussion of possible implications for a prospective national DBS service where relevant. Since paediatric DBS services are not within the scope of this analysis, standards relating to the treatment of children and the progression from paediatric to adult services are not discussed in detail.

Standard 1 – The Network Approach[46]		
1a	DBS Centres should provide comprehensive care which is linked to the patient's local neurology centre and enable as much of the care to take place as close to the patient's home as possible.	A
1b	DBS Centres will collaborate with each other reflecting that collectively they provide a national service and to develop and embed best practice. Further, they will collaborate at a clinical, audit research and administrative level and will take part in formal inter-unit peer review.	Y
1c	There will be agreed written guidelines at each of the neurosurgical centres providing DBS and referring neurology centres covering communication between clinicians and between clinicians and parents and carers. The guidelines will be agreed with local referring neuroscience centres and patient groups.	A
1d	There will be specific guidelines within each area covered by a DBS neurosurgical centre for the treatment of children. These will be agreed between the surgical centre, referring	R

	paediatric neurology centres and commissioners.	
1e	A registry should be established on a national basis and provide multi-centred audit.	AV
1f	A set of outcome measurement criteria will be agreed between neurosurgical units and commissioners and outcomes set against such criteria will be reported annually.	Y

Key: R - Must be in place for designation and remain in place.
A - Robust plans must be in place to achieve the standard within an agreed timescale of less than 12 months from designation.
Y - Highly desirable, but would not prevent designation; agreed plans should be in place to achieve this standard over the next few years.
AV - Ideally in place but not essential.

This standard specifies the need for adequate and documented systems of communication to be developed between DBS centres and referring neurology clinics, as well as between clinicians, patients and carers. It also highlights the desirability of setting up information management systems and agreed outcomes reporting in order to facilitate clinical audit and ongoing evaluation of the service. In contrast to the UK, which has multiple DBS centres, it is possible that a single DBS centre could meet the annual demand for DBS in Ireland. There is also the question of whether a national service would maintain the practice of providing long term patient care jointly between a DBS centre and the patient's local neurology services, or whether the overall care of patients selected for DBS treatment would be transferred to neurologists with DBS experience. Both these factors will influence how a national service would be structured and the systems it will need to develop to meet the requirements of the network approach.

Standard 2 – Making Choices[46]		
2a	DBS Centres should encourage patients and carers to actively participate at every stage of their care and be able to demonstrate how such encouragement is provided.	R
2b	Patients and carers should be helped to understand their condition and the effects of DBS treatment (the potential risks as well as the benefits); the likely results of the treatment and the possible consequences of their decisions so that they are able to give informed consent. They also need to understand the risks, morbidity and side effects of continuing medical management.	R
2c	Information should be available to patients and carers in a wide range of formats and on more than one occasion. The information should be clear, understandable and culturally sensitive and evidence based. When given verbally, information given should be precisely documented.	R
2e	Patients, carers and GPs should be given details of who they can contact within the clinical team should they have questions and concerns.	R
2f	Patients and carers whose first language is not English must be provided with appropriate interpreting and translation services.	R
2g	Patients and carers should be given details of available recognised support groups.	R
2h	Patients and carers (and where appropriate a child) should be given an agreed, written care plan. For older children this may be determined by local provider policy.	R

Key: R - Must be in place for designation and remain in place.

Standard 3 – The Patient Experience[46]		
3a	There must be facilities in place to ensure easy and convenient access for patients and carers. Facilities should include appropriate and convenient accommodation at	R

	reasonable cost close to the hospital.	
3b	Patients and carers should be provided with accessible information about the service and the hospital including information about amenities in the local area, travelling, parking and public transport.	R
3c	Staff in the multi-disciplinary team should have training and be supported in communication skills.	R
3d	Patients and carers should be encouraged to provide feedback on the quality of care and their experience of the service. Centres must demonstrate how they take such feedback into account when planning and delivering their services.	R
3e	There must be access to culturally appropriate support services including faith support, social workers and interpreters.	R
3f	Patients, carers and support groups must be regularly updated with appropriate information on clinical issues of clinical governance and the results of local and national audits.	R
3g	Patient satisfaction surveys and equality and diversity monitoring data should be collected on a regular basis (at least annually) and shared within the centre and disclosed to commissioners.	R

Key: R - Must be in place for designation and remain in place.

Involving and supporting patients, as well as the implementation of measures designed to ensure that a DBS centre consistently works towards improving the patient experience are other key areas identified in the UK standards. Resources will be required to accomplish this, however they are not necessarily confined to the DBS service and guidelines governing these issues will equally apply to the wider organisations within which DBS may be provided.

Standard 4 – Access To Services[46]		
4a	Each DBS Centre should have pathways of care for treatment of each indication which have been written down and agreed with commissioners.	R
4b	There should be clear criteria for access to the service agreed with SCG [Specialised Commissioning Group] commissioners for each centre.	R
4c	Once approved for surgery, patients should receive their surgery as soon as possible. Each SCG should agree how they will monitor referral to treatment times.	R
4d	Patients should not require additional prior approval from commissioners for replacement implanted pulse generators (IPGs) unless the cost has risen beyond guidelines agreed with SCG commissioners. Centres must keep SCG commissioners up to date with expected patient referrals for replacement IPGs.	R
4e	Each SCG will agree a cost card with the designated provider as part of the designation process to clearly identify what costs will be picked up by the SCG for these services including follow up costs.	R

Key: R - Must be in place for designation and remain in place.

The criteria governing access to services are designed around the organisational structures and commissioning pathways in place in the UK. Developing processes that will allow a prospective national DBS service to meet similar criteria will need to be developed as part of the service planning stage. This will include agreement in regard to the referral process, patient selection criteria, treatment schedule and funding mechanisms.

Standard 5 – Age-Appropriate Care[46]		
5a	The patient's management plan should be reviewed at each consultation to make sure that it continues to be relevant to their age and stage of development.	R
5b	Children treated within the DBS services should be made aware of their treatment options and contribute to the treatment decisions from an appropriate age and in line with other services and standards.	R

Key: R - Must be in place for designation and remain in place.

Standard 6 – Excellent Care[46]		
6a	Deep Brain Stimulation will be undertaken within a neurosciences centre that provides both surgical and medical neurology services. Each centre will undertake at least 10 - 15 new patient DBS procedures (total all types) a year. New DBS centres will agree the pace at which they reach the recommended minimum numbers of assessments and procedures with commissioners.	R
6b	Designated centres should be assessing at least 15 -20 patients a year for deep brain stimulation procedures. The effect of the minimum threshold should not be to bar new entrants from providing a service where this is directly commissioned and where appropriate mentoring and audit arrangements are put in place to minimise the extent of any learning curve on patient outcomes. New entrants seeking to provide a service should not do so without commissioner approval.	R
6c	DBS Centres will agree pathways of care with their host SCG.	R
6d	Established designated centres should be performing at least 10 - 15 deep brain stimulation procedures a year (this may include children if the centre is recognised to undertake DBS on children).	R
6e	Newly established centres should agree a transition/mobilisation plan with their SCG lead commissioner to develop their service safely while they build up the number of patients treated.	R
6f	Centres which undertake DBS on children should be part of a programme undertaking at least 10 - 15 cases year (6a).	R
6g	Centres will have onsite access to: • Experienced surgeons (preferably two) with appropriate evidence of Continuing Professional Development to cover the rota • Experienced neurologists with appropriate evidence of CPD to cover the rota • Neurophysiologist if DBS for epilepsy • Neuroradiologist • Theatre nursing staff • Nurse Practitioner or similar specialist nurse • Key liaison worker to work with primary care agencies post discharge • Physiotherapists • Senior management support • Audit and MDT coordinator • Clerical and administration staff	R
6h	Staff must have access to suitable IT facilities to perform their roles effectively.	A
6i	There must be a suitable induction programme for all new staff members with access to competency based assessment at all levels.	A
6j	Centres will have access to: • Neurosurgical facilities suitable for all acute work, including implant surgery, and sub-speciality multidisciplinary facilities as necessary • Theatres suitably equipped for implant work • Critical care beds • Inpatient surgical beds on an appropriate ward • Appropriate outpatient facilities • Appropriate day-case facilities • Magnetic resonance imaging (MRI) scanner	R

	• Computerised tomography (CT) scanner • Access to DaTSCAN scanning • Access to Positron Emission Tomography (PET) scanning	
6k	Staff and facilities specifically for the care of children if surgery is performed on children at the centre.	R
6l	Outcomes measure tools should be agreed with SCG commissioners, used consistently and reported on annually to commissioners and other DBS Centres (see 7.1f).	R
6m	Centres will have procedures for identifying, analysing and reporting infection, complication and revision rates to local commissioners and across designated centres.	R

Key: R - Must be in place for designation and remain in place.
A - Robust plans must be in place to achieve the standard within an agreed timescale of less than 12 months from designation.

The 'excellent care' standard contains a number of criteria that relate directly to the resources required to deliver a high quality service. The standard specifies a minimum of 10 new surgical procedures per annum and a minimum of 15 new assessments for DBS to be performed annually. Designated centres also need to have a range of appropriately qualified clinical and support staff, including a specialist nurse, physiotherapist and a liaison officer to link with primary care. DBS centres also need to have access to a range of facilities, including a neurosurgical theatre, critical care beds and appropriate inpatient and outpatient services. There are specific criteria for imaging equipment, including specifications for onsite MRI and CT imaging and access to DaTSCAN and PET scanning facilities. Systems to ensure accurate recording and reporting of complication and revision rates are also specified.

Standard 7 – Team Delivered[46]		
7a	The management of each patient should be discussed and planned at a joint neurosurgical / neurology Multi-Disciplinary Team (MDT) (jointly with paediatric neurology if a child).	**R**
7b	Patients will be cared for by MDTs containing adequate numbers of specifically trained staff.	**R**
7c	The attendance and activities of the MDT should be maintained in a register.	**R**
7d	All clinicians, nursing and allied health professional staff will take part in a programme of continuing professional development which can be evidenced.	**R**
7e	All clinical teams will operate within a robust and documented clinical governance framework that includes undertaking clinical audit.	**R**
7f	Each centre will have an internal database and outcomes monitoring tool with standardised coding.	**R**
7g	It is desirable that each centre should have an up-to-date research strategy and programme which documents current and planned research activity.	**A**
7h	Long term follow-up audits should be in place.	**R**

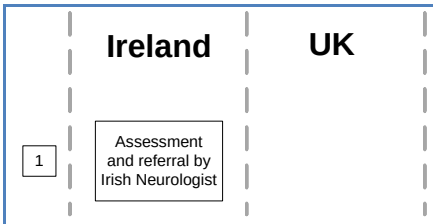
Key: R - Must be in place for designation and remain in place.
A - Robust plans must be in place to achieve the standard within an agreed timescale of less than 12 months from designation.

3.3 Process mapping

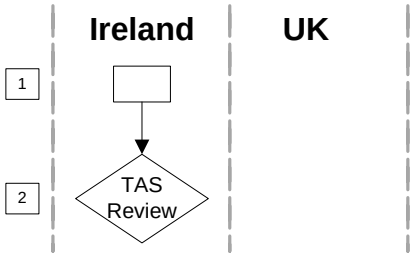
The majority of Irish patients that have undergone DBS have been treated in the UK, with the highest number of referrals being made to Frenchay Hospital, Bristol, and the John Radcliffe Hospital, Oxford. Between 2008 and 2010, these two hospitals accounted for approximately 85% of all DBS referrals made through the TAS. A limited number of DBS cases have also been carried out in Ireland both in the public and private healthcare system since 2008. A map of the individual stages involved in the referral and treatment process, along with the equipment, personnel and other resources required for each step, was drawn up in consultation with these two centres. The Expert Advisory Group (EAG) provided additional input in relation to the UK process map, using their experience of how the scheme has operated thus far. The EAG also provided input into a process map for a prospective national service, including details of how this might differ from the current model. The process map is intended to represent a summary of the main stages involved in the DBS process and the key resource requirements for each of these stages. The aim of the process map is to outline a comparable package of care to that currently provided to Irish patients in the UK; it is not intended to describe all possible configurations of the service or to define individual roles and the scope for involvement of other health professionals at various stages.

Currently, the treatment path differs slightly depending on the centre where the patient undergoes DBS surgery, due to differences in the surgical technique used and the scheduled follow up. An in-depth exploration of the relative differences in terms of clinical outcomes between different techniques is beyond the scope of this project; rather a description of the impact of these differences on the delivery of a service is provided. Under the terms of the TAS, care of the patient reverts to the referring consultant following treatment abroad. The referring consultant would typically continue to see the patient at regular intervals in parallel with the DBS follow-up provided through the TAS. These have also been included in the flowchart to reflect the overall process of care over the course of the treatment period. Given that the majority of Irish patients have received treatment in the UK, the process map is based on the UK service. However under the terms of the TAS the treatment could potentially be provided through the public system in any of the 29 countries of the European Union (EU), European Economic Area (EEA) or Switzerland.

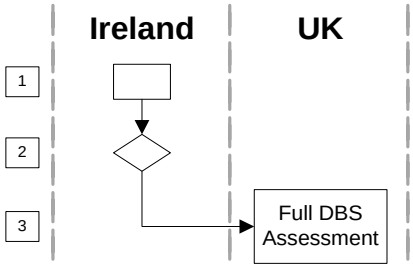
3.3.1 Process map of existing DBS service delivery model



1: Referral by a medical consultant	
Description: For patients to be eligible to receive treatment abroad, a referral must be made on their behalf by a consultant. In the case of DBS, patients will generally have been attending their neurologist for a number of years prior to being referred, and will have exhausted their options in regard to pharmacological treatment. During this time patients may have undergone some of the tests required to assess their suitability for DBS and may also have had an MRI performed to rule out structural abnormalities or demyelinating plaques in the brain. In some cases a specific appointment is needed before a referral is made, to carry out a number of initial assessments and/or to perform MRI. At present, some patients are referred by other neurologists to the Dublin Neurological Institute so that their suitability for DBS can be assessed locally by a neurologist experienced in DBS prior to a referral overseas being made through the TAS. Prior to making a referral, the option of DBS treatment is discussed with the patient, along with the potential risks. If they decide to proceed, an application is made to the TAS, followed by referral to a UK centre if this is approved.	
Duration	1.5 hours
Personnel	Consultant neurologist, Specialist nurse
Equipment	MRI scan
Other	N/A



2: Application reviewed per TAS criteria	
Description: The HSE process the referral according to the criteria laid down in the Treatment Abroad Scheme (TAS). In the case of complex or unclear cases the referral is passed onto the Health Intelligence Unit (HIU) within the HSE for review and a recommendation. Since care of the patients reverts back to the referring consultant after each episode of treatment abroad, a separate TAS application is required for each additional overseas treatment episode. The timeframe for decision making is generally 5 working days, however for applications that require review by the HIU a decision is usually made within 20 working days. The main reason for applications being rejected is that DBS is not a proven treatment for the patient's condition. Decisions can be delayed for a number of reasons. Patient representative groups report that the overall process can take between three and six months.	
Duration	0.5 hrs (+0.5 hrs for HIU review)
Personnel	TAS staff, HIU staff
Equipment	N/A
Other	N/A



3: DBS assessment tests

Description: In order to assess patient suitability for DBS treatment, a comprehensive assessment is performed in the UK. This includes an overnight inpatient stay for patients with Parkinson's disease as tests must be conducted in both the 'on-meds' and 'off-meds' states. A number of psychological tests are also conducted, with a full neuropsychology assessment being performed if necessary. For patients with tremor or dystonia this comprehensive assessment is conducted on an outpatient basis. An MRI scan for patients with mid-brain tremor is performed either at this assessment or later as part of the surgical admission. MRI may be performed under general anaesthetic if required. It is reported that between 20 to 30 percent of patients who undergo full assessment do not proceed to surgery.

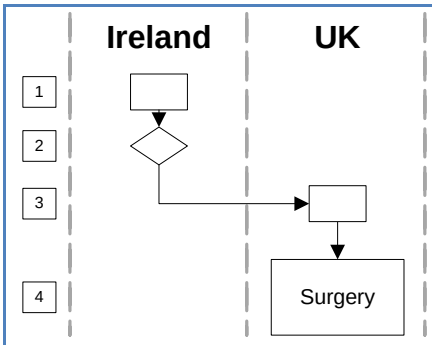
The assessment for patients with Parkinson's disease includes the following:

- UPDRS I-IV, CAPSIT, Tinetti Balance and Gait, Purdue Pegboard, Dyskinesia Rating Scale
- DRS-2, Non-motor symptoms interview, Beck Depression Scale, Beck Anxiety Inventory, option of full neuropsychology assessment
- patient motor fluctuation diary, fall and freezing records, PDQ 39, SF 36, non-motor symptoms questionnaire, video assessment

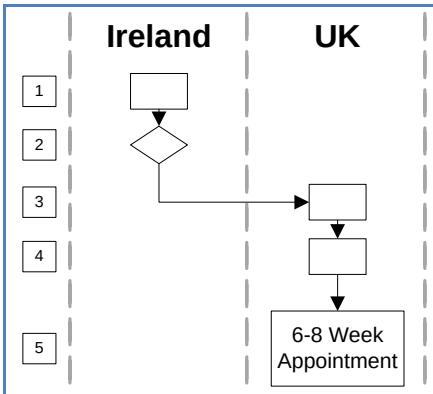
For patients with tremor and dystonia, the assessment includes:

- Purdue Peg Board (Tremor), Burke Fahn-Marsden Scale (Dystonia), TWSTRS (Dystonia), Clinical Tremor Rating Scale (Both)
- DRS-2, non-motor symptoms interview, Beck depression and anxiety tests, option of full neuropsychology assessment
- SF36

Duration	2 days (PD), 1 day (Tremor and Dystonia)
Personnel	Neurologist, specialist nurse, neuropsychologist
Equipment	Assessment equipment, video, MRI (if applicable)
Other	The time needed to perform these test varies between patients, and can be related to how tired the patient becomes over the course of the day. In addition, some patients who have travelled from Ireland may need to remain in the UK longer than their hospital admission, staying in hotels or other accommodation until they are fit enough to make the journey home.



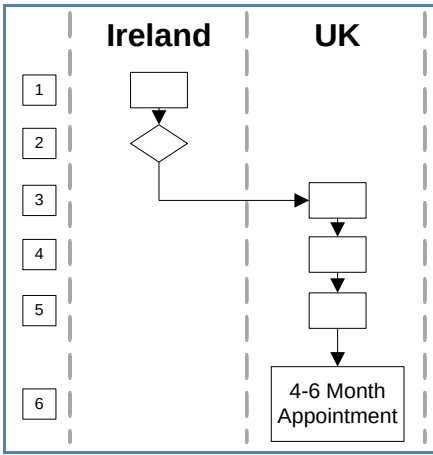
4: Surgery	
Description: Different surgical techniques exist for implantation of the electrodes at the target site. Analysis of the relative benefits and risks of each of these is beyond the scope of this project. The choice of approach has implications for the equipment required and for the length of stay associated with the operation. A frame-based approach involves the application of a stereotactic frame (e.g. Leksell/CRW frame) to the patient's head under general anaesthesia. An MRI of the head with the frame attached is loaded on to navigation software in order to plan the positioning of the electrodes. Alternatively, a frameless approach is also available, where an MRI taken after fiducials have been attached to the skull is used in conjunction with a stereotactic guidance system (e.g. Nexframe) to facilitate accurate positioning. Implantation of the electrodes can be carried out with the patients awake or under general anaesthesia. A CT scan is taken prior to implantation and again afterwards to check the position of the electrodes. If the patient is awake, test stimulation can be applied during the surgery to ensure that that the electrodes are positioned correctly. The duration of surgery can vary between three and six hours. Operative time depends on a number of factors, including whether bilateral or unilateral implantation is required. Implantation of the electrodes and implantable pulse generator (IPG) can be carried out in the same operation or on two separate days over the course of the surgical admission. Average hospital stay can vary from 4 to 10 days. A proportion of patients will require high dependency beds and longer stays in the event of complications or adverse events. For patients with essential tremor and dystonia, stimulation is usually started before the patient is discharged. Patients with Parkinson's disease do not have the stimulator turned on until their first follow up appointment, six to eight weeks after surgery.	
Duration	Electrodes and IPG implanted together, hospital stay: typically 4-5 days Electrodes and IPG implanted separately, hospital stay: typically 5-10 days
Personnel	Neurosurgeon, radiologist, anaesthetist, surgical registrar, specialist nurse, theatre nurses (3), neurologist
Equipment	MRI, CT, stereotactic guidance system, navigation software, DBS electrodes and IPG, DBS programmer
Other	General surgical theatre equipment and support services are also required. If patients are unable to travel following their discharge they may need to stay in hotels or other accommodation until they are fit enough to make the journey home. Additional costs may also arise due to the fact that certain airlines restrict travel for up to 10 days post-surgery unless the patient has written confirmation that they are fit to travel from their clinician



5: First follow-up appointment

Description: Patients are seen six to eight weeks after surgery for an outpatient appointment with their neurologist and specialist nurse. For patients with dystonia and tremor whose devices were activated directly after surgery, the appointment is used to adjust their settings and medication. Patients with dystonia can take up to three months to see the effects of stimulation so it may not always be possible to observe the effect of stimulation at this appointment. For patients with Parkinson's disease, the appointment is used to begin stimulation and programme the device. This could take up to a day to complete given the need to adjust settings and teach the patient how to use the device. The majority of this work is performed by the specialist nurse. The surgeon may also review the patient to assess post-surgical wound healing and how the patient is tolerating the device. However, it may not always be necessary for the surgeon to be present at this appointment.

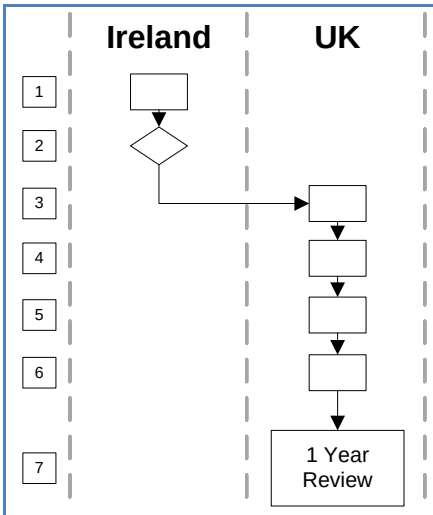
Duration	1 day outpatient appointment
Personnel	Neurologist, Specialist Nurse
Equipment	Device programmer
Other	N/A



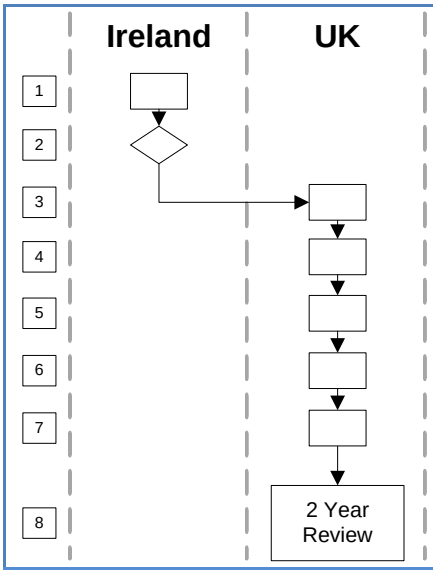
6: Second follow-up appointment

Description: The second follow-up appointment is scheduled approximately six months after surgery. The patient is seen by the specialist nurse and neurologist, in order to review the effect of stimulation and adjust stimulation parameters and/or medication, as appropriate. Patients with Parkinson's disease tend to need longer appointments given the need to take account of the on-meds and off-meds states when adjusting the stimulation settings.

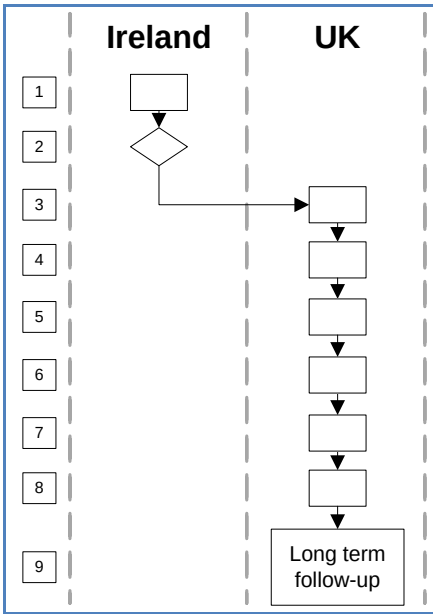
Duration	1 day outpatient appointment
Personnel	Neurologist, specialist nurse
Equipment	Device programmer
Other	N/A



7: One year review	
Description: At the one year review appointment, the complete set of tests conducted as part of the initial DBS assessment are repeated, in order to compare the effect of the treatment with baseline data. The assessment is conducted in off-meds/off-stimulation, on-meds/off-stimulation and on-meds/on-stimulation (for PD) or on-stimulation/off-stimulation (for tremor and dystonia) states. The patient is reviewed by their neurologist and their medication or stimulation parameters are adjusted as necessary. Similarly to the initial assessment, PD patients are required to stay in hospital overnight, while the assessment of patients with tremor or dystonia is done on an outpatient basis. A psychological assessment can also be performed at this review, if required.	
Duration	2 days – PD, 1 day – tremor and dystonia
Personnel	Neurologist, specialist nurse, neuropsychologist (if needed)
Equipment	Assessment tests, video equipment
Other	N/A



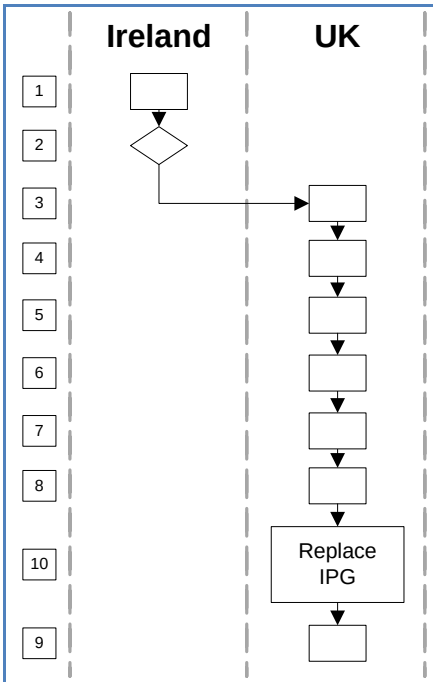
8: Two-year review	
Description: The two-year appointment is used to review the patient and make any additional changes to medication or stimulation parameters. A number of tests and questionnaires are repeated (e.g. Beck depression and anxiety, SF36, DRS2).	
Duration	1 day outpatient appointment
Personnel	Specialist nurse, neurologist (if needed)
Equipment	N/A
Other	N/A



9: Long term follow-up

Description: The long term follow up schedule differs between centres in the UK. In some centres both PD, dystonia and tremor patients are followed up at one, two and five years, whereas in other centres patients with dystonia or tremor are followed up annually, with PD follow-up at one, three and five years. At these appointments, patients undergo the same series of tests performed at the one-year review, with similar equipment and personnel requirements.

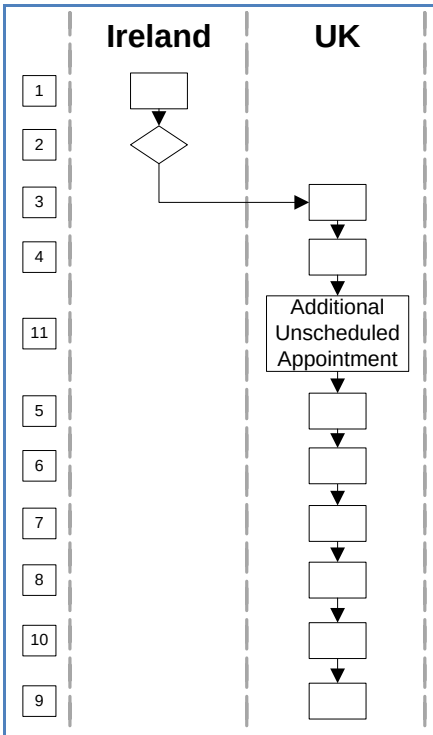
Duration	2 days inpatient – PD; 1 day outpatient – tremor and dystonia
Personnel	Neurologist, specialist nurse, neuropsychologist (if needed)
Equipment	Assessment tests, video equipment
Other	N/A



10: Battery replacement

Description: The DBS device emits a warning six to eight weeks before its battery becomes entirely depleted. The frequency with which replacement batteries are needed is determined by the type of IPG (rechargeable or non-rechargeable), the stimulation parameters used and whether bilateral or unilateral electrode implantation was performed. Rechargeable IPG's have a much longer battery life, but need to be recharged regularly by the patient. The settings required by dystonia patients are generally higher, resulting in a shorter battery life. It is reported that, on average, a patient with Parkinson's disease with a non-rechargeable IPG and bilateral stimulation will require a replacement device every three to five years. For patients with dystonia this can be as often as every 12 to 18 months. Rechargeable IPG's can have up to nine years battery life but since they have not been available until recently – the first rechargeable device was approved for use in Europe in August 2008 – their long-term performance is still being examined. The operation to replace the IPG is carried out under general anaesthetic, lasts approximately 45 minutes and does not require any imaging. The depleted IPG is removed, and a new device inserted and connected up to the existing electrodes. The settings from the old device are then programmed into the new one. There is currently a recommendation within the TAS that all IPG's are replaced with rechargeable models where appropriate, to minimise the number of repeat visits required.

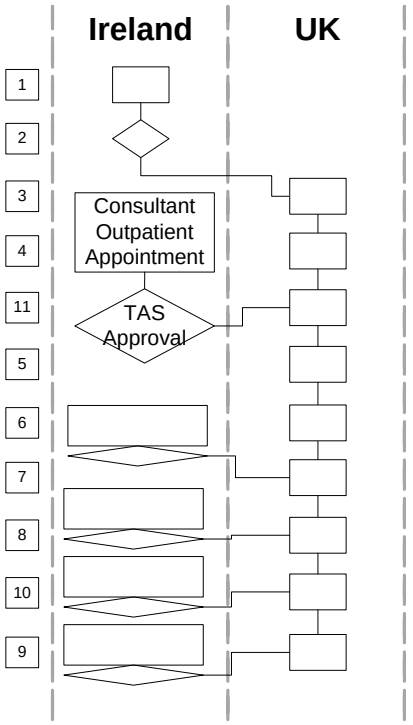
Duration	1-2 night hospital stay
Personnel	Neurosurgeon, neurologist, specialist nurse, theatre staff (nurses, anaesthetist, etc.)
Equipment	IPG, DBS programmer
Other	General surgical theatre equipment and support services are required.



11: Additional unscheduled appointment

Decision: The treatment pathway shown up to now is an idealised representation of the major stages of a DBS service. In practice, a proportion of Irish patients will require additional unscheduled visits to UK DBS clinics following complications, adverse events associated with stimulation and for additional programming of the device. Given the wide range of issues that patients could potentially face, incorporating such events is difficult. UK centres operate a telephone service that allows Irish patients to contact a specialist nurse when they have concerns or experience problems. While this can help resolve many issues, there will be times when the patient will have to travel to the UK. It was reported that this usually occurs in the first year after implantation. Following discussion with the EAG it was felt that the inclusion of one unscheduled visit in the first year would more accurately reflect the overall experience of Irish patients to date. Since this would be an unscheduled visit, another application to the TAS would need to be made, potentially at very short notice.

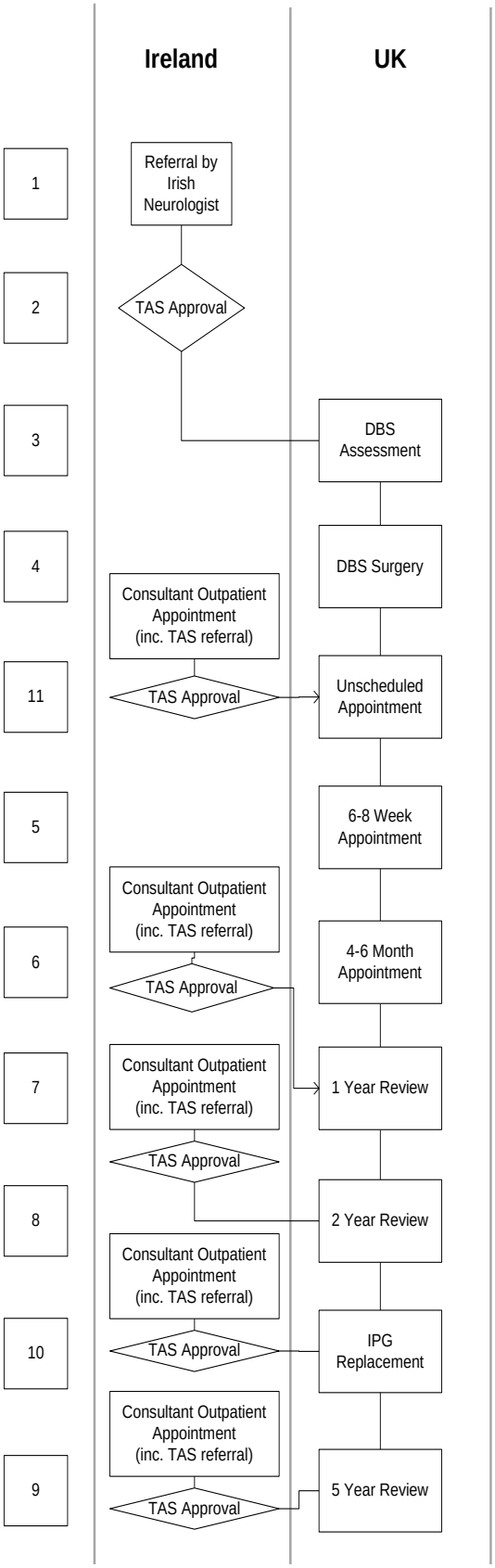
Duration	1 day outpatient appointment
Personnel	Neurologist, specialist nurse
Equipment	Device programmer
Other	Duration, personnel and equipment may vary depending on the reason for the visit.



12: Ongoing review appointments in Ireland

Description	Patients receiving DBS treatment through the TAS must remain under the ongoing clinical management of an Irish-based neurologist. Regular outpatient appointments are scheduled to monitor medication and disease progression, as well as any other problems that may arise. In addition, specialist nurses in Ireland act as a point of contact for patients throughout this period and both they and the referring consultant work with UK staff to provide continuity of care and support for the patient. With the exception of multiple planned episodes within the same year for which a single E112 form can be generated, a request to the TAS for a new E112 form must be generated for each new episode of care. Therefore, each episode of care in the UK must be preceded by a review appointment by an Irish-based neurologist. To reflect this it is necessary to include ongoing appointments in Ireland over the course of the DBS treatment in the process map.
Duration	1-3 hours
Personnel	Neurologist, specialist nurse
Equipment	N/A
Other	N/A

Overall DBS process map



This process map outlines the major stages involved in the current DBS service provided through the TAS. There are a range of other professionals involved in providing acute and long term care to DBS patients. A review[14] of DBS for Parkinson's disease recommends that "DBS surgery is best performed by an experienced surgeon with specific expertise in stereotactic and functional neurosurgery who should be working as part of an inter-professional team that includes a movement disorder neurologist, neuropsychologist, psychiatrist, and neurophysiologist". In addition the support of allied health professionals is important given the symptoms of the diseases and the fact that complications can include speech and gait difficulties. Therefore patients who avail of this service need to be able to access speech and language therapy and physiotherapy services if required. In addition to the availability of neurosurgeons and neurologists, the UK standards for the designation of DBS centres[46] also specifies the following:

- neurophysiologist if DBS for epilepsy
- neuro-radiologist
- theatre nursing staff
- nurse practitioner or specialist nurse
- key liaison worker
- physiotherapists
- senior management support
- audit and MDT coordinator
- clerical and administrative staff

Feedback from patient representative groups has indicated that the time from being referred to approval of a DBS application can vary between three and six months. UK centres schedule appointments once approval has been granted and the wait times between approval being granted and the full DBS assessment being completed are between 8 and 18 weeks. Once patients have undergone the full assessment the waiting time for surgery is approximately three months. While these figures are estimates based on the experiences of UK DBS centres and Irish patient groups, they indicate a waiting time of between 8 to 13 months from referral to surgery.

3.3.2 Discussion

The purpose of this HTA is to compare alternative ways of providing DBS treatment for Irish patients. An important step towards this is defining how the current system operates and gaining an overall picture of the total amount of care provided over the course of the treatment. Section 3.2 outlines the current sequence of events and the activity associated with each stage of the process for patients accessing DBS surgery through the TAS. The impact of this service configuration on patients is examined in more detail in Chapter 5.

There are a number of areas of uncertainty within the process map. These include issues relating to the different surgical approaches that exist and the difficulty describing a generic treatment path for patients who may differ considerably in the type and severity of symptoms they experience. Where these issues arose, assumptions were made based on consultations with UK service providers and the members of the Expert Advisory Group.

Variability related to the technical aspects of the treatment includes the use of rechargeable and non-rechargeable devices – this influences the frequency of IPG (implantable pulse generator) replacement operations. The other major source of variation is whether the surgery is completed in one or two stages, which impacts on the length of hospital stay required.

The greatest amount of uncertainty relates to modelling the need for additional appointments due to complications associated with the treatment, or for other reasons. Some of the issues experienced by Irish patients in the aftermath of surgery can be handled without having to make another trip abroad. However for other problems, particularly those that are related to the hardware itself (e.g. lead breakages, etc.), there is no option but to travel abroad to the specialist DBS centre. Overall, it was felt that an average of four visits in year one would reflect the experience to date, taking into account that many will not need to make unscheduled trips, but others may require multiple repeat visits. When modelling a similar service in Ireland, these assumptions about the need for additional care will

also be incorporated to avoid skewing any comparison of different methods of service configuration.

In addition to the resources required to provide the DBS service, another important metric is the time taken to access the service. There are two distinct types of access that need to be considered. The first is access to the full DBS assessment and elective surgery for new candidates. The second is access for patients with DBS implants who require ongoing appointments for adjustment of the stimulation settings, clinical review or for unexpected complications such as infection or device breakage. Some of these appointments can be planned in advance but others may need to be scheduled at short notice. Measures to ensure that a prospective national DBS service would be able to provide access in a timely manner will also need to be considered when comparing options for DBS service provision. This could pose a challenge within the context of existing neurosurgery capacity within the Irish healthcare service, which as of May 2012 had 532 patients awaiting neurosurgical procedures.[50]

3.4 Resource requirements for a national DBS service

An exploration of the potential resource requirements of a national DBS service was carried out based on the analysis of the service that is currently being provided through the TAS, and with reference to published literature on service standards. Members of the Expert Advisory Group provided their input either through completion of a questionnaire or during interviews. The expected configuration of the service, as well as the anticipated resource requirements at each stage is shown below.

3.4.1 National DBS service resource requirements

The resource requirements of a prospective national service are described below, along with the duration of each activity and the equipment and personnel required.

1. Initial assessment and referral

As with the current situation, it is likely that patients will have been receiving care for an extended period of time prior to being referred for an assessment for DBS. Some initial assessments may have been performed and some imaging may have been carried out as part of earlier investigations. This will not differ greatly from the existing situation with the exception that since a DBS service is available in Ireland, specialist DBS staff (e.g. movement disorder nurse) may not be involved prior to the full assessment, as is generally the case in the UK.

Activity	Duration	Equipment	Staff
Assessment	1.5-2 hours	N/A	Neurologist

2. Full DBS assessment

Once a referral has been accepted by the DBS service a full assessment is scheduled. This involves a range of physical, psychological and quality of life assessments that are used as a baseline measurement of the patient's symptoms, as well as to investigate their suitability for DBS treatment.

The type of tests conducted and the length of time needed to conduct them is dependent on the indication for which DBS is being considered. There can also be a degree of variability within individual patient groups. For example, some patients will need to complete a full neuropsychological assessment in addition to the brief psychological assessment that all patients undergo. Patient fatigue can also play a role in determining how long it takes to complete tasks and whether all tests can be completed in one day or if an overnight stay is required. The requirement for Parkinson's disease patients to be assessed in both on-meds and off-meds states means that these assessments take significantly longer than assessments of patients with tremor and dystonia. However in contrast to the existing system, a prospective national service may not require all PD patients to be admitted on an inpatient basis, since it may be possible to perform all the required tests in one full day, assuming that the patients felt well enough to continue for the period of time involved. If a full neuropsychological test is needed this could be scheduled for an alternative date. An MRI may also be required before a decision is made about proceeding to surgery, if one is not already available. A summary of the expected resource requirements of this assessment is given below.

	Activity	**Duration**	**Equipment**	**Staff**
PD	UPDRS 1-4	2 – 4 hours (to be carried out in on-meds and off-meds states)	Individual assessments and any associated equipment	Neurologist Specialist nurse
	CAPSIT Timed Tests			
	Tinetti Balance and Gait Assessment			
	Dyskinesia Rating Scale			
	Purdue Pegboard			
	Dementia Rating Scale 2 (DRS-2)	1-1.5 hours		
	Non motor symptom interview			
	Beck Depression Scale			
	Beck Anxiety Inventory			
	Patient recorded data	0.5 hours		
	PDQ-39			
	SF-36			
	Video Assessment	0.5 hours	Video recording equipment	
	Optional full neuropsychological assessment	1.5 - 2 hours	Individual assessments	Neuropsychologist/ Neuropsychiatrist
Tremor	Clinical Tremor Rating Scale (Part A-C)	0.5-1 hour	Individual assessments and any associated equipment	Neurologist Specialist nurse
	Purdue Pegboard			
	DRS-2	1-1.5 hours		
	Non motor symptom interview			
	Becks Depression Scale			
	Becks Anxiety Inventory			
	SF-36			
	Video assessment	0.5 hours	Video recording equipment	
	Optional full neuropsychological assessment	1.5 – 2 hours	Individual assessments	Neuropsychologist/ Neuropsychiatrist
Dystonia	Burke-Fahn-Marsden	0.5 – 1 hour	Individual	Neurologist

	(BFM) Scale		assessments and any associated equipment	Specialist nurse
	Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) (Only for cervical or neck involvement)			
	Clinical Tremor Rating Scale (Part A – C) (if dystonic tremor)			
	DRS-2	1 – 1.5 hours		
	Non motor symptom interview			
	Becks Depression Scale			
	Becks Anxiety Inventory			
	SF-36			
	Video Assessment	0.5 hours	Video recording equipment	
	Optional full neuropsychological assessment	1.5 – 2 hours	Individual assessments	Neuropsychologist/ Neuropsychiatrist

3. Surgery

There are a number of different surgical techniques that can be adopted, and these have different implications for the resource requirements. In consultation with the EAG, it was decided that the surgical approach that has been used in the limited number of procedures conducted to date in Ireland would most accurately reflect the design of a prospective national DBS service. This approach is most closely aligned with that currently used in the Walton Centre in Liverpool, and uses a 'frameless' technique, where the electrodes are implanted while the patient is awake. The resource requirements analysis also assumes that the electrodes and IPG will be implanted during the same operation, with implications for the average lengths of stay associated with the procedure. In regard to the imaging services needed for the procedure, it is assumed that an Irish service will involve an MRI and CT scan being carried out after the patient has had fiducial markers applied under general anaesthetic. These images are used in conjunction with navigation software to plan where the electrodes will be placed. During the main surgery the electrodes are inserted using a stereotactic guidance system. Another CT scan is performed following implantation to check the position of the electrodes.

Activity	**Duration**	**Equipment**	**Staff**
Overall length of stay for the procedure	4 to 5 days	N/A	N/A
Attach stereotactic system and perform imaging	2 - 2.5 hours	General Anaesthesia Neurosurgical theatre equipment MRI CT Fiducial markers	Anaesthetist Radiologist Neurosurgeon Theatre nurse
Pre-implantation planning	1 – 1.5 hours	Imaging and positioning software	Neurosurgeon
Implantation of DBS system	5 – 6 hours	Anaesthesia Neurosurgical theatre equipment CT	Anaesthetist Neurosurgeon (x2) Surgical registrar Neurologist

		DBS device (IPG and electrodes)	Theatre nurse (x3)
Programming and patient training (for those having stimulation started immediately)	1-2 hours	DBS programmer	Neurologist Specialist Nurse

4. First follow-up appointment

For patients who have had the DBS device activated immediately after surgery, the first follow-up appointment at six to eight weeks after surgery is used to review the patient's progress and to adjust stimulation as required. For patients with Parkinson's disease, stimulation will be first activated at this stage. Stimulation is adjusted for on-meds and off-meds states. In an Irish service where the overall care of the patient is transferred to the DBS neurologist, this appointment would also include an overall review of medication and other relevant issues. As such it is likely that some of these appointments could take a considerable amount of time, depending on the needs of the patient. The figures given below are estimates that are assumed to reflect the majority of cases.

Activity	Duration	Equipment	Staff
Clinical review Device programming	2 – 3 hours	DBS programmer	Neurologist Specialist nurse

5. Second follow-up appointment

The second follow-up appointment takes place 4-6 months after surgery. The purpose of this is to review the patient and adjust stimulation settings as needed. The length of time needed for this appointment will depend on how well the patient is tolerating the device and the amount of readjustment of stimulation parameters that is required.

Activity	Duration	Equipment	Staff
Clinical review Device programming	2 – 3 hours	DBS programmer	Neurologist Specialist nurse

6. One year review

At the one year review the complete set of tests conducted prior to surgery are repeated in order to compare the results with the pre-DBS data. The assessment regime will depend on the patient's diagnosis, with patients with Parkinson's disease taking longer due to the need to perform the tests in both the on-meds and off-meds states. In the current system, appointments for patients with Parkinson's disease are on an inpatient basis, while patients with dystonia or tremor are seen as outpatients. In a prospective Irish service it may be possible to see patients with Parkinson's disease as outpatients and complete all tests in the same day. However, the appointment time required will still be approximately twice that for dystonia and tremor, and some patients will require an overnight stay. No imaging procedures are performed at this stage.

For a description of the resource requirement for this stage see section 1. Full DBS Assessment

7. Ongoing reviews

Ongoing review appointments are needed to follow-up with the patients and make any changes to medication and/or stimulation in response to the changing needs of the patient. The length of time needed for this appointment will depend on how well the patient is tolerating the device and the amount of readjustment needed.

Activity	Duration	Equipment	Staff
Clinical review Device programming	2 – 3 hours	DBS programmer	Neurologist Specialist nurse

8. Long term follow-up
To assess the long term results of DBS treatment in light of any disease progression that may have occurred since implantation, patients are again assessed using the same tests performed at the one-year review. The timing of this review differs between centres, with tests being repeated at three years or five years. No imaging procedures are performed at this stage.
For a description of the resource requirement for this stage see section 1. Full DBS Assessment

9. IPG replacement			
The activity associated with this appointment is per the existing process (see step 10 of the process map for the existing service, pg 52). During the operation the leads are disconnected from the existing IPG, which is taken out and replaced. The leads are then reconnected and the setting from the old device programmed into the new one. No imaging procedures are performed as part of this operation. There is a recommendation within the TAS that all IPG's are replaced with rechargeable models in order to minimise the amount of repeat visits needed. However the use of rechargeable IPG's may by contraindicated in some cases.			
Activity	**Duration**	**Equipment**	**Staff**
Overall length of stay for the procedure	1-2 night stay	N/A	N/A
Surgical replacement of implantable pulse generator	1 – 2 hours	Anaesthesia Surgical theatre equipment DBS device (IPG only)	Surgeon Surgical registrar Theatre nurse (x2)
Device programming	0.5 hours	DBS programmer	Specialist nurse

10. Additional unscheduled reviews			
Unscheduled reviews will be required by some patients in response to complications associated with the treatment, or to address other unforeseen issues as they arise. To account for this, an additional appointment is included in year one. While some patients may require more than one additional appointment and others may require none at all, after consultation with the EAG it was assumed that an average of four appointments in year one represented the best estimate of the required care if DBS were made available in Ireland.			
Activity	**Duration**	**Equipment**	**Staff**
Clinical review	2 – 3 hours	DBS programmer	Neurologist Specialist nurse
Device programming			

3.5 Discussion

An estimate of the resources required to provide a national DBS service in Ireland for eligible adults with movement disorders is calculated based on the service that is currently provided through the TAS and taking account of relevant service standards.

In order for this to represent a valid comparison between two approaches to delivering the service, it is assumed that both approaches result in equivalent clinical outcomes for people who would be in a position to access either. At present, there are patients who cannot access DBS treatment via the TAS because they are unable or unwilling to travel abroad, but who could access DBS if it were available in Ireland. For these patients, the relative differences are unimportant as they can only avail of one option and not the other. This is a broader issue that is dealt with in

chapter 5. The assumption of equivalent clinical outcomes for patients who could access either system is based on having an Irish multidisciplinary team with appropriate qualifications and expertise delivering a service that adheres to comparable service standards and best international practice in all areas of DBS. However, there is inevitably going to be a period at the beginning of the service where the level of experience and efficiency lags behind that of well-established services that benefit from the accumulated experience of many years of providing care for patients with movement disorders. During the time it would take to develop this experience and ramp up the capacity of the service to meet the level of demand, it may be necessary to source care for a proportion of DBS patients through the TAS.

Another point to consider in relation to a national DBS service in Ireland is whether the overall care of patients receiving DBS treatment would be transferred to a DBS neurologist with appropriate training and experience who would be responsible for managing the patient's medication and stimulation parameters on an ongoing basis. The alternative is for the patient to continue to see their original neurologist throughout their DBS treatment, which would necessitate separate neurology outpatient review appointments in parallel with DBS follow up. Given the interaction between the effects of medication and stimulation, there are benefits to having the same clinician managing both. This also reduces the number of appointments that patients need to attend and improves efficiency; though it may mean that some patients have to travel further to see their consultant. Obviously this case does not arise in the subset of patients whose original neurologist is also involved in the delivery of a DBS service.

The potential effect of the establishment of a national service compared to the existing system includes:

- Reduced administrative burden for new referrals and for patients who need to receive additional unscheduled care at short notice
- Greater continuity of care if management of all aspects of their care is performed within the same service
- A proportion of patients who would have needed inpatient stays in order to undergo all tests can be assessed on an outpatient basis
- A national service would be more convenient for existing DBS patients who would not have to travel as far for their follow-up care.
- Patients who are not in a position to travel overseas to access the treatment may be able to avail of it in Ireland.

The process flow diagram for the current DBS service delivery model shows how the delivery of care for patients with movement disorders is divided between local neurology services and a DBS centre abroad. Any new Irish service would need to

consider how it would deal with existing DBS patients currently receiving their ongoing care through the TAS. The terms of the TAS stipulate that funding is provided only if:

- *The treatment is among the benefits provided for by Irish legislation* ***and***
- *The treatment is not available within the competent state* ***or***
- *The treatment cannot be provided within the time normally necessary for obtaining it in the competent state, taking account of the patient's current state of health and the probable course of illness.*[51]

However, no definition has been provided for timely care and current practice is that patients cannot be funded through the TAS if the treatment is available within the country. Permission has been granted for treatment abroad only on a case-by-case basis where there is an exceptional clinical need, with specific approval required for each episode of care. If a national DBS service were established, all existing DBS patients would have to receive all ongoing follow-up care in Ireland. This would add a significant resource requirement to the new service which would need to be planned for in relation to the set-up and implementation of such a service

The idea of modelling a hybrid service where some of the assessment and follow-up is provided in Ireland, with the surgical implantation of the electrodes and IPG continuing to be provided through the TAS, was discussed within the EAG. While such a service configuration could potentially reduce the number of trips abroad that patients have to make, it would pose significant challenges in regard to continuity of care and would not increase access for those unable to travel. Therefore an analysis of a hybrid DBS service was not performed for the purposes of this project.

3.6 Summary

A review of relevant literature identified a number of sources of information on the resources required to provide DBS services for movement disorders as well as service standards governing their implementation. The NHS standards for the designation of DBS centres are particularly relevant given that the majority of Irish patients that have received DBS to date have been treated in the UK.

Information derived from the literature was combined with the results of consultation with two UK DBS centres and the Authority's Expert Advisory Group in order to map out the current DBS process in Ireland and provide a description of the resources required to establish a comparable service within the Irish healthcare system.

A prospective national DBS service is expected to differ from the current service in a number of respects, including the amount of administration required and the degree

of inconvenience experienced by patients in travelling to appointments. The impact of a national DBS service on waiting times to access treatment is an important factor that is not represented in the process map. This issue is considered in greater detail in chapter 5. A newly established national service would also need time to develop the level of experience and service capacity that is currently available from UK DBS centres.

This analysis examines the resources needed to provide a DBS service for adults with Parkinson's disease, dystonia and tremor, based on comparable services in the UK. It does not consider wider issues involved in the field of DBS treatment, such as the growing number of indications being considered for this treatment,[52] including depression, epilepsy and obsessive compulsive disorder, and DBS treatment for children.[53]

3.7 Key messages

- A number of international organisations including the UK NHS have developed standards and service specifications for the provision of a high quality DBS service.
- As the majority of Irish patients accessing DBS through the TAS have been treated in the UK, the NHS specifications have been used as a basis for a comparable national DBS service capable of providing an equivalent standard of care.
- The potential benefits of a national DBS service include: greater access to the service for patients for whom overseas travel is difficult; potential for some inpatient appointments to be performed on an outpatient basis; and elimination of the administrative burden associated with the TAS.
- Challenges associated with the establishment of a national DBS service include: growing the capacity of the service to meet the demand for DBS for movement disorders in Ireland; developing a cohesive core team of professionals with the experience and expertise to provide an efficient DBS service that is comparable to the existing service provided via the TAS; ensuring that adequate access to services is maintained for new referrals as well as those requiring follow up and support following the implantation of the device.
- There are a number of areas of potential uncertainty encountered when mapping the current DBS process. These include complication rates and the need for unscheduled additional appointments, technical considerations such as different surgical approaches and the proportion of patients who will have rechargeable and non-rechargeable devices implanted.

4 Economic evaluation

The purpose of this HTA is to evaluate the cost of providing a national DBS service in Ireland for the treatment of selected movement disorders. The purpose of this section is to:

- develop an economic model for the provision of a DBS service in Ireland
- compare the costs of a national DBS service to the existing system of referring patients for treatment abroad
- determine the budget impact of establishing a DBS service in Ireland.

4.1 Description of the economic model

Economic modelling facilitates the combination of data on costs and benefits from different sources and allows these to be extrapolated into the future.[54] This analysis presumes that benefits (i.e. health outcomes) will be equivalent whether the DBS service is provided in Ireland or abroad. As benefits are equivalent, only differences in cost are considered – this type of approach is called a cost-minimisation analysis. The budget impact analysis (BIA) provides a means to predict the potential financial impact of introducing a new technology into a healthcare system. BIA addresses the affordability of the technology (e.g. the net annual financial cost of adopting the technology for a finite number of years).

4.1.1 Study question

What is the difference in cost between the provision of a DBS service in Ireland and continuing to refer patients for treatment abroad through the E112 Treatment Abroad Scheme (TAS)?

4.1.2 Type of evaluation

It is assumed that the proposed national DBS service will operate to similar quality standards to those DBS services currently used abroad, and hence patients will experience equivalent safety and clinical outcomes. As there is no meaningful difference in terms of important patient outcomes between the technologies being compared, this evaluation is a cost-minimisation analysis (CMA).

4.1.3 Study perspective

Costs are assessed from the perspective of the publicly-funded health and social care system in Ireland, with a view to providing advice that maximises health gain for the population and represents the most efficient use of the finite resources available to the Health Service Executive (HSE). Only direct medical costs (i.e. fixed and variable

medical costs associated with the provision of a technology) are included. Indirect costs, such as those accrued by individual patients, are not considered in this analysis.

4.1.4 Technology

The technology being assessed is the provision of a DBS service in Ireland.

4.1.5 Choice of comparators

The comparator is the existing system of funding patients to receive DBS treatment in another EU/EEA member state through the E112 Treatment Abroad Scheme (TAS). To date, the majority of patients receiving DBS through the TAS scheme have received their treatment in the UK. For the purposes of this evaluation, the existing DBS service in terms of costs is defined as the UK service.

4.1.6 Target population

The target population is adults with selected movement disorders (specifically Parkinson's disease, dystonia and essential tremor) that are eligible for DBS surgery.

4.1.7 Time horizon

For the cost-minimisation analysis, costs are accrued over a 10 year time horizon. Costs are calculated for procedures that arise during the time horizon, including: initial assessment, implantation of the DBS device, battery replacement, device programming, device removal after complications, review appointments, and flights from Ireland to the UK.

4.1.8 Outline of the model structure

The model is structured as a cost-minimisation comparing the proposed national service to the existing DBS services that patients avail of in the UK. A probabilistic model is used which explicitly takes into account the uncertainty of the model parameters. The main parameters are therefore defined by statistical distributions rather than point estimates. The model is run for 10,000 simulations, selecting new parameter values from the defined distributions in each simulation.

In each simulation, for each year of the time horizon, a cohort of patients is generated. In the first year all patients have an initial assessment, DBS surgery and an interim review. In the second year they have an interim and a major review. There is an interim review in the third year and a major review in the sixth year. Dystonia patients receive a new (rechargeable) battery after 18 months and all other patients receive one after four years. Each year some patients develop complications requiring a full or partial device replacement. Costs are then computed for providing

the service in the UK and in Ireland, based on the simulated demand for each procedure type.

For the cost-minimisation, costs are accrued based on a single cohort of patients over the time horizon. For the budget impact analysis, costs are accrued by all cohorts receiving treatment in a given year.

4.1.9 Sensitivity analysis

A probabilistic model is used which explicitly takes into account the uncertainty of the model parameters. As part of the model evaluation, all of the key parameters are varied within plausible ranges that have been derived from published evidence and advice from the Expert Advisory Group. As the structure of the economic model presented here is inherently stochastic, the outputs are equivalent to a multivariate probabilistic sensitivity analysis.

A univariate sensitivity analysis shows how influential each parameter is and how sensitive the results are to fluctuations in each parameter. Given the uncertainty around the parameters themselves, it is important to understand how this translates into uncertainty about the results. Each parameter in turn is fixed at its upper and lower bounds while all the other parameters are varied as per the fully probabilistic model. The variance in results due to each parameter can be displayed as a tornado plot.

4.2 Model parameters

The economic model requires a range of input parameters including: duration and staffing requirements of procedures; cost of devices and imaging; device failure rate; rate of unscheduled appointments; and demand for services. These parameters are not known with certainty, and hence generally have a base-case or median value, and an associated range or distribution of values. The purpose of this section is to detail the values used for the key parameters.

4.2.1 Discount rate

Discounting is a technique that allows comparison between costs and benefits that occur at different times. It reflects a societal preference for benefits to be realised in the present and costs to be experienced in the future. Costs and benefits were discounted at the rate of 4% as prescribed in Irish guidelines.[54] The discount rate was not varied in the main analysis.

4.2.2 Duration of procedures and staff requirements

Nine distinct procedures were identified that encompassed the treatment pathways experienced by DBS patients and that are currently provided through the UK services. The procedures are: initial assessment; device implant; device removal; battery replacement; device programming; interim review; and major review. The initial assessment and major review are distinct for patients with Parkinson's disease, and are structured as an inpatient rather than outpatient visit. Each of the nine procedures requires input from a number of different staff as outlined in Table 4.1 below.

Table 4.1 Staff time (in hours) by procedure

Staff grade	Initial assessment (PD)	Initial assessment (ET and dystonia)	Implantation	Device removal	Battery replacement	Device programming	Interim review	Major review (PD)	Major review (ET & dystonia)
Consultant neurosurgeon	0	0	10.5	0.75	1.5	0.5	2.5	0	0
Consultant neurologist	5.25	2.5	5.5	0.75	0	0	0	7	4.25
Specialist nurse	5.25	2.5	1.5	0.75	0	0.5	2.5	7	4.25
Neurophysicist	0	0	0	0	0	0	0	0	0
Radiologist	0	0	2.25	0.75	0	0	0	0	0
Anaesthetist	0	0	7.75	0.75	1.5	0	0	0	0
Surgical registrar	0	0	10.5	0.75	1.5	0	0	0	0
Anaesthetic registrar	0	0	7.75	0.75	1.5	0	0	0	0
Neuropsychologist	1.75	1.75	0	0	0	0	0	0	0
Theatre nurse	0	0	7.75	0.75	1.5	0	0	0	0
Scrub nurse	0	0	5.5	0.75	1.5	0	0	0	0
Circulating nurse	0	0	5.5	0.75	0	0	0	0	0
Operating department assistant	0	0	5.5	0.75	1.5	0	0	0	0

In the model, staff time was varied by ±10% to account for uncertainty in procedure times. It was assumed that the attendance rate at interim assessments after the five-year major review would be of the order of 90% (95% CI: 85-94%).

It was assumed that under the current service provision, prior to each procedure in the UK a patient must first be referred by their neurologist in Ireland. This necessitates a referral appointment typically lasting one hour each with a neurologist and specialist nurse. The specialist nurse must spend an additional 30 minutes preparing the forms required for TAS approval. In practice, all scheduled appointments falling within a 12-month period may be entered on a single form. For the model, it was assumed that all scheduled appointments for a patient in any given calendar year will require a single referral appointment. All unscheduled visits, such as device removal or programming, will require a referral appointment for each visit. As the time spent processing applications by TAS staff was deemed to be minimal and not impacting directly on the delivery of frontline services, it was not included in the model.

4.2.3 Length of stay

The length of stay information is derived from the Hospital Episode Statistics for England published by the NHS. It was assumed that a national service set up in Ireland would achieve similar length of stay statistics to the UK service. It was assumed that interim and major reviews, and device programming could all be achieved on an outpatient basis in a national DBS service.

Table 4.2 Length of stay by procedure

Procedure	Length of stay (days), mean (SD)
Initial assessment (PD)	1.0 (0.0)
Initial assessment (ET and dystonia)	0
Implantation	7.7 (1.0)
Device removal	8.1 (1.0)
Battery replacement	3.3 (0.5)
Unscheduled appointment	5.3 (0.5)
Device programming	0
Interim review	0
Major review (PD)	1.0 (0.0)
Major review (ET and dystonia)	0

4.2.4 Target population and mortality

The model was restricted to an adult population of patients with movement disorders, specifically Parkinson's disease, dystonia, or essential tremor. As both battery life and the nature of the pre-operative and major assessments are dependent on the condition, the proportion of patients with each condition was estimated from TAS data and incorporated into the model (Table 4.3).

Table 4.3 Proportion of patients with each condition

Condition	Proportion of patients (95% CI)
Parkinson's disease	0.74 (0.62 – 0.83)
Dystonia	0.11 (0.05 – 0.20)
Essential tremor	0.15 (0.08 – 0.25)

Given the age profile of typical DBS patients, some degree of mortality could be anticipated. Evidence suggests that life expectancy among patients with Parkinson's disease is approximately 10 years shorter than that of the general population.[9] Based on the age distribution of the DBS patient population, the annual mortality rate for DBS patients was estimated to be 2.3% (95% CI: 1.8-2.9%).

For the cost-minimisation model, a cohort of 10 patients (95% CI: 8-13) were followed for a 10 year period. For the BIA, costs included those generated by patients repatriated from services abroad in addition to new patients. It was assumed that the volume of patients treated with DBS increased from five in 1998 to 10 from 2000 onwards. Based on the modelling assumptions, there are approximately 146 patients alive currently receiving ongoing DBS treatment in the UK who will be repatriated if a service is established in Ireland.

It is assumed that not all patients referred for assessment each year proceed to surgery. Approximately 66% (95% CI: 57 to 75%) of referrals result in surgery. In the model the assessments that do not result in surgery are counted in the budget impact assessment. For the cost-minimisation model, only patients that have a DBS procedure are included in the analysis.

4.2.5 Complications

Once implanted, a DBS device may lead to a variety of complications, most typically device failure or infection. Device failure can arise for a variety of reasons, most typically lead breakage. For each patient cohort, the percentage of patients experiencing complications requiring surgical intervention was assumed to be 3.7% (95% CI: 1.1-8.6%) in the first year, and 0.9% (95% CI: 0.1-4.2%) each year thereafter. It was assumed that 70% (95% CI: 61-79%) of patients with complications would require battery replacement and the remainder would require a new implant.[55] For the purposes of the model, it was presumed that batteries could not be reused, even if they are functional at the time of removal.

It was presumed that the percentage of patients developing complications would remain constant over the time horizon. Complications that do not require device removal were not included in the model on the grounds that they are potentially treated in Ireland under the current system.

4.2.6 Device programming

Under the current DBS service provision, implanted devices occasionally require reprogramming in a UK centre. Based on TAS data, the percentage patients requiring reprogramming in each cohort is approximately 3.8% (95% CI: 0.6-12.1%) in the first year, and 0.8% (95% CI: 0.03-4.2%) each year thereafter. Reprogramming is carried out in an outpatient setting.

4.2.6 Battery life

Evidence suggests that battery life varies both by patient and by condition. For patients with Parkinson's disease and essential tremor, it was assumed that the battery from the initial implant of the device would last four years. For patients with dystonia, it was assumed that the battery would last 18 months. It was also assumed that all patients requiring a replacement battery would receive a rechargeable battery with a nine-year lifespan. It was assumed therefore that rechargeable batteries would be replaced after nine years.

4.2.7 Private health insurance

A proportion of DBS patients have private health insurance. Based on the age distribution of patients, the model used a median proportion of 0.32 (95% CI: 0.24-0.41) patients having private health insurance.[56] It was assumed that all such patients would avail of their health insurance to cover the costs of DBS treatment in the existing service. Of patients without health insurance, it was assumed that 24% (95% CI: 14-36%) would not have a medical card.

DBS is covered as a treatment benefit for eligible patients by the main health insurers in Ireland up to a total of €65,000 per annum. However, often patients must pay these costs upfront and are subsequently reimbursed by the health insurers. To reduce the burden this may place on patients, the TAS will fund these upfront costs on behalf of the patient (in addition to their travel costs which are not reimbursed by health insurance) and is subsequently reimbursed by the health insurers. In the Irish system, the amount recovered by the HSE from private insurers for a bed reflects a per diem accommodation charge that is linked to the type of bed the patient occupies. The per diems as of June 2012 for a semi-private and a private bed in a Tier I public hospital are €933 and €1046, respectively. In addition, there is a statutory per diem charge of €75 (capped at a maximum of €750 for a given patient in any 12 month period) for all non-medical card holders that applies regardless of the bed designation. This statutory per diem may be covered by private health insurance for patients with such cover. In the model it was assumed that private health insurance only covers for inpatient procedures in the UK and that all outpatient episodes are paid for by the TAS. It was assumed that the current

arrangements for reimbursement from private health insurance will continue to apply for the duration of the time horizon. The model was run on the basis of patients with private health insurance being accommodated in a public bed, with the alternatives tested in a sensitivity analysis. It was assumed that the statutory charge of €75 per day, up to maximum of €750 in a year, is recouped from all patients without a medical card.

4.2.8 Costs

Only direct costs relevant to the publicly-funded health and social care system are included in the evaluation. For all models this includes: theatre staff costs, theatre equipment costs, anaesthetic costs, and hospital stay costs. It was assumed that DBS surgery would only be undertaken in a specialist neurosurgical referral centre. Therefore, no capital costs were included in the model as it was assumed that the relevant equipment that could incur capital costs (e.g. MRI, O-arm CT, navigation software) is already in place. Prices are current with staff costs taken from the mid-point of published Department of Health 2010 pay-scales,[57] adjusted for pay-related costs in accordance with national guidelines.[54] Transfer payments (VAT) are excluded in the cost-minimisation model. It was assumed that for an Irish service, an MRI would be required for initial assessment. For implantation and device removal, it was assumed that one MRI and two CT scans would be required. For the current service provision, it was assumed that all patients undergo an MRI in Ireland prior to referral for initial assessment in the UK.

Two device manufacturers, Medtronic and St. Jude Medical, made submissions detailing costs for the DBS device and replacement batteries. As there were differences in the quoted prices, both were used in the model. In each simulation the model would randomly pick one or other manufacturer with equal probability. It was assumed that a non-rechargeable battery will be used in the initial DBS implant, and that a rechargeable battery will be used when replacement becomes necessary, in line with current TAS policy.

Table 4.4 Costs used in the economic model

Cost item	Source	Cost (€)
Flights	TAS	271.00
Staff (per hour)		
Consultant neurosurgeon	DOH	200.09
Consultant neurologist	DOH	200.09
Specialist nurse	DOH	48.76
Neurophysicist	DOH	200.09
Consultant radiologist	DOH	200.09
Consultant anaesthetist	DOH	200.09
Surgical registrar	DOH	65.27
Anaesthetic registrar	DOH	65.27
Neuropsychologist	DOH	87.87

Theatre nurse	DOH	38.65
Scrub nurse	DOH	38.65
Circulating nurse	DOH	38.65
Operating department assistant	DOH	31.29
MRI scan	PP	446.60
CT scan	PP	329.00
Chest X-ray	PP	94.25
Device (per item, including battery)	Medtronic	19,325.00
	St. Jude Medical	GBP 14,220.00
Battery – rechargeable (per item)	Medtronic	20,500.00
	St. Jude Medical	GBP 11,725.00
Battery – recharger (per item)	Medtronic	2,016.00
	St. Jude Medical	GBP 1,840.00
Consumables (per operation)	Medtronic	4,492.00
Inpatient (per diem) (DRG B02A/B/C)	DRG	696.34
Anaesthetic (per hour)	UTH	120.00
UK service provision		
Initial assessment (PD)	UK	GBP 2,226.00
Initial assessment (ET and dystonia)	UK	GBP 227.00
Implantation	UK	GBP 22,611.00
Device removal	TAS	GBP 28,306.02
Battery (rechargeable)	TAS	GBP 21,998.87
Device programming	TAS	GBP 560.23
Interim review	UK	GBP 227.00
Major review (PD)	UK	GBP 961.00
Major review (ET and dystonia)	UK	GBP 227.00
Exchange rate (GBP:Euro)		0.81 (SD 0.065)

Abbreviations: PD – Parkinson's disease; ET – essential tremor; TAS – Treatment Abroad Scheme; DOH – Department of Health; PP – private provider; UTH - university teaching hospital; DRG - diagnosis related group; UK – UK service provider; GBP – British Sterling.

Costs were varied in the model to reflect uncertainty in prices. For the proposed Irish service, costs were varied separately for: the DBS device (which included the battery, leads, charger, controller and consumables from the operation); the per diem charge; imaging (varied simultaneously for CT, MRI and X-ray); and anaesthesia. As disaggregated costs were not available for the UK service, the cost of all procedures in the UK was varied ±20% in each simulation. The average cost of return flights to the UK was varied based on the TAS data with a median of €271 (95% CI: €66-€1,125). The exchange rate was current (June 2012) with the standard deviation computed based on the observed variation over 12 months from July 2011 to June 2012. The prices quoted for St. Jude Medical devices were given in Sterling and converted using the exchange rate applied in that simulation.

4.2.9 Budget impact analysis (BIA)

The BIA is conducted from the perspective of the publicly-funded health and social care system and reports the costs for each year in which they occur, in this case for a timeframe of five years. The data for the BIA are the same as those used in the economic analysis with the difference being that prices are inclusive of VAT, and no discounting is applied.[58] The cost of all items of surgical consumables and the non-implantable parts of the DBS device are subject to VAT at 23%. As with the cost-minimisation model, no capital costs were included in the model. The results are reported as the annual and five year cost of providing a DBS programme in Ireland.

4.3 Results of the cost-minimisation analysis

The model was run based on patients with private health insurance being accommodated in public beds within a publicly funded hospital. The average discounted cost per patient over 10 years was calculated for an Irish service and the existing UK service. The average difference in cost (i.e. cost per patient for the Irish service minus the cost of the UK service) is also presented.

4.3.1 Cost-minimisation

The estimated cost per patient over 10 years in the proposed Irish service is €65,726 (95% CI: €52,853-€86,959). The cost of the equivalent UK service is an estimated €44,664 (95% CI: €32,892-€65,308) per patient over 10 years. The additional cost per patient over 10 years for an Irish service is €20,898 (95%CI: €5,447-€36,540).

Table 4.5 Discounted cost per patient

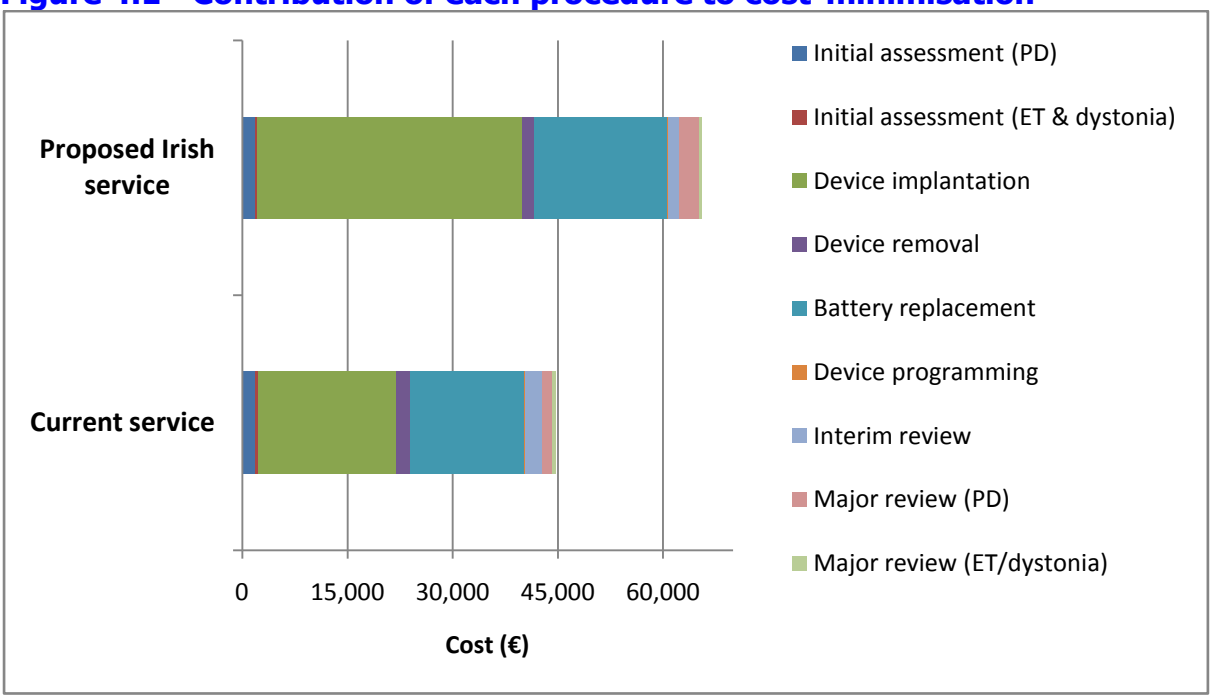
Scenario	Discounted cost per patient (€) over ten years	
	Median	(95% CI)
Irish service	65,726	(52,853-86,959)
Current service	44,664	(32,892-65,308)
Difference	20,898	(5,447-36,540)

Note: Difference is calculated as the median across all simulations rather than the difference between the median calculated for each service

The Irish service was estimated to be less expensive per patient in only 0.54% of simulations. It should be noted that there is substantial uncertainty around the estimates of the difference in cost, as indicated by the confidence bounds. Nine procedures were identified that are part of the typical DBS patient pathways. Of the nine procedures, the cost difference between the Irish and existing service was comparable in most cases when private health insurance was not taken into account. The main exceptions were the typical cost of device implantation was on average an additional €8,912 more, and the cost of battery replacement which was on average €3,888 less in an Irish service. When the impact of private health insurance was

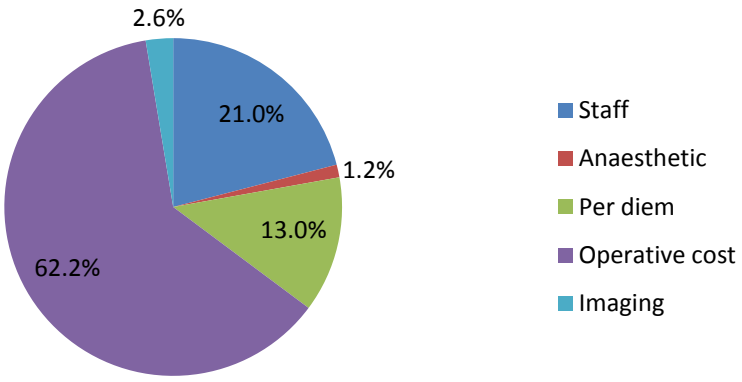
added, device implantation was on average €17,967 more in an Irish service and battery replacement became €2,770 more expensive in the Irish service. Clearly, the difference in cost of device implantation is the main driver of the overall difference over 10 years (Figure 4.1).

Figure 4.1 Contribution of each procedure to cost-minimisation



The cost of the proposed Irish service could also be disaggregated into a number of elements: staff; anaesthetic; hospital per diem; device and operative consumables; and imaging (MRI and CT). The majority of the cost (62%) is generated by the device, battery and consumables used during implantation of the device. Staff time contributes 21% to the cost-minimisation.

Figure 4.2 Contribution of cost elements to cost per patient in the proposed Irish service



4.3.2 Budget impact analysis (BIA)

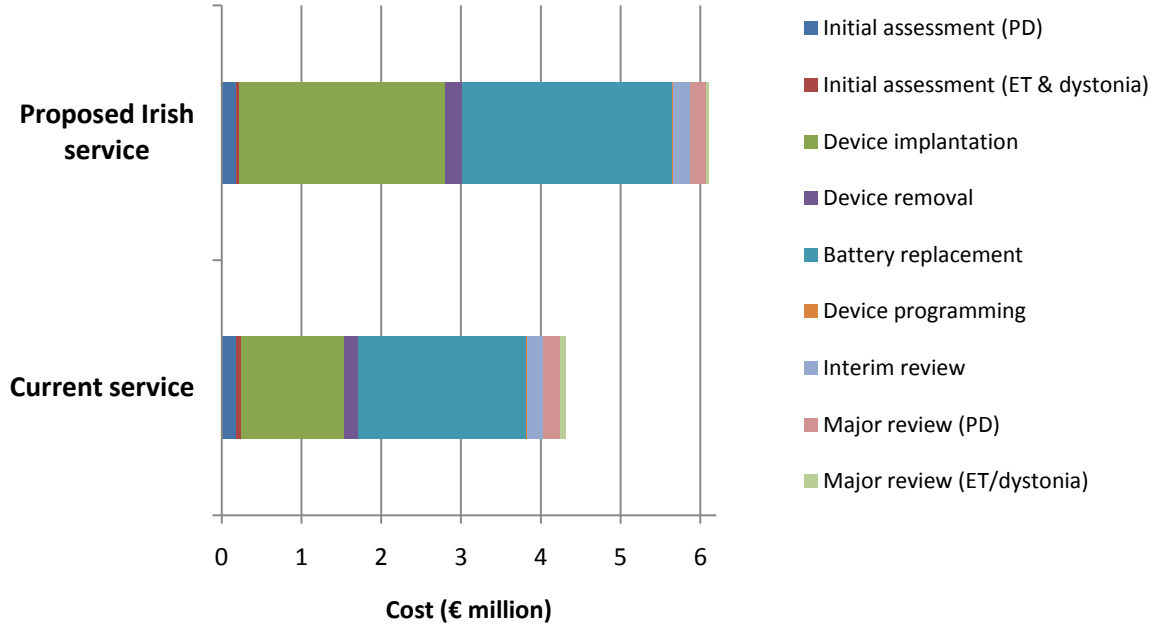
The results of the BIA are shown in Table 4.6 below. The BIA is based on a volume of 13 new patients undergoing DBS surgery per annum (95% CI: 11-15) in addition to continuing care for all existing DBS patients treated through the TAS. An Irish-based service would incur an additional budget impact of over €370,000 per annum, with a cumulative additional budget impact of €1.84 million over five years (95% CI: €0.32 million to €3.55 million). The five-year budget impact of an Irish service is less than the current service in 1% of simulations.

Table 4.6 Budget impact (€ million) by year

Year	Irish service	Current service	Difference	Cumulative difference
1	1.21 (0.93-1.67)	0.85 (0.62-1.20)	0.37 (0.07-0.71)	0.37 (0.07-0.71)
2	1.22 (0.93-1.68)	0.85 (0.62-1.21)	0.37 (0.07-0.72)	0.73 (0.13-1.41)
3	1.23 (0.93-1.70)	0.86 (0.63-1.23)	0.37 (0.07-0.72)	1.10 (0.20-2.13)
4	1.23 (0.93-1.72)	0.86 (0.62-1.24)	0.37 (0.06-0.72)	1.47 (0.26-2.85)
5	1.24 (0.93-1.74)	0.87 (0.62-1.25)	0.37 (0.06-0.73)	1.84 (0.32-3.55)

VAT has a relatively minor impact in the budget impact analysis as it is only applied to certain elements of the DBS device. As with the cost-minimisation, the procedure causing the additional budget impact of the proposed Irish service is the device implantation (Figure 4.3).

Figure 4.3 Contribution of each procedure to the budget impact



The projected average number of procedures per annum is given by procedure type in Table 4.7 below. With the exception of interim reviews, the volume of other procedure types was projected to be stable over the five- year time horizon.

Table 4.7 Average volume of procedures per annum by procedure type and year

Procedure	Year				
	1	2	3	4	5
Initial assessment (PD)	9.5	9.5	9.6	9.5	9.6
Initial assessment (ET/dystonia)	3.5	3.5	3.4	3.4	3.5
Device implant	13.5	13.5	13.5	13.6	13.6
Device removal	1.7	1.8	1.8	1.9	1.9
Battery replacement	22.7	22.7	22.8	22.8	22.9
Device reprogramming	1.6	1.6	1.7	1.7	1.8
Interim review	62.4	66.3	69.2	70.5	74.1
Major review (PD)	17.8	17.8	17.8	17.8	17.8
Major review (ET/dystonia)	6.4	6.5	6.5	6.4	6.4

The provision of a national DBS service will generate an increased requirement for a variety of resources. Table 4.8 outlines the key additional resources that would be incurred by a national DBS service treating the same number of patients that are currently treated annually through the TAS.

Table 4.8 Increased resource requirements by year for selected resources

Resource	Year				
	1	2	3	4	5
Consultant neurosurgeon (hrs)	334	344	352	355	365
Consultant neurologist (hrs)	218	214	211	210	206
Specialist nurse (hrs)	270	274	277	278	281
Theatre time (hrs)	111	112	112	113	113
Surgical bed days	225	226	227	228	228
Outpatient appointments	74	78	81	82	86
CT scans	30	31	31	31	31
MRI scans	35	35	35	35	35

4.3.3 Univariate sensitivity analysis

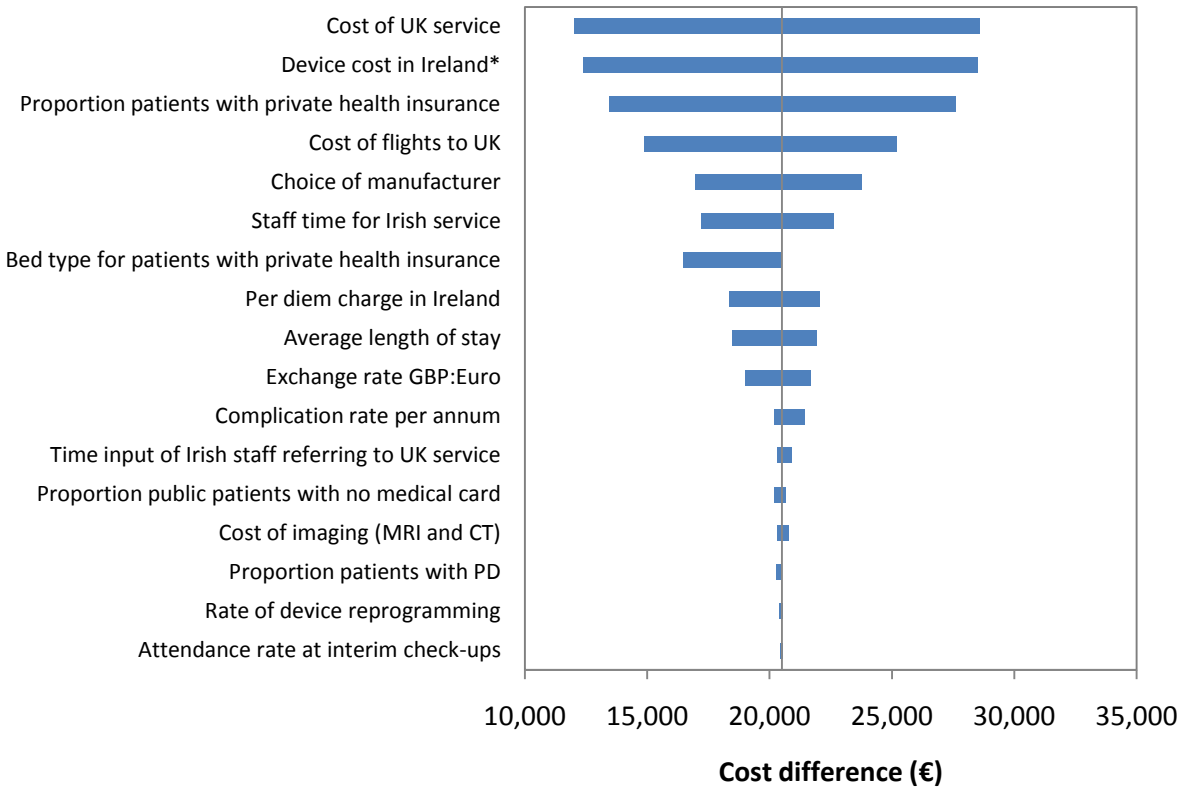
In accordance with the national guidelines, univariate sensitivity analyses are presented to show how influential each parameter is and how sensitive the results are to fluctuations in each parameter.

The most influential parameters were the cost of the UK service and the device cost in Ireland. Varying each of these parameters had a similar impact, producing a fluctuation of almost €8,000 in the cost difference (Figure 4.4). It should be borne in mind that the UK cost was varied en bloc as no disaggregated costs were available.

In reality, it is unlikely that all costs would fluctuate by the same extent at the same time. The next most influential parameter was the proportion of patients with private health insurance. Setting this parameter at its upper and lower confidence bounds produced a fluctuation of €7,000 in the cost difference. The cost of flights to the UK and choice of manufacturer also have a large impact on cost difference. The upper bound for UK flights was quite high, and may reflect the fact that often flights will be booked close to the date of admission.

Other parameters with significant influence on the results are complication rates and average length of stay.

Figure 4.4 Tornado plot of univariate sensitivity analysis

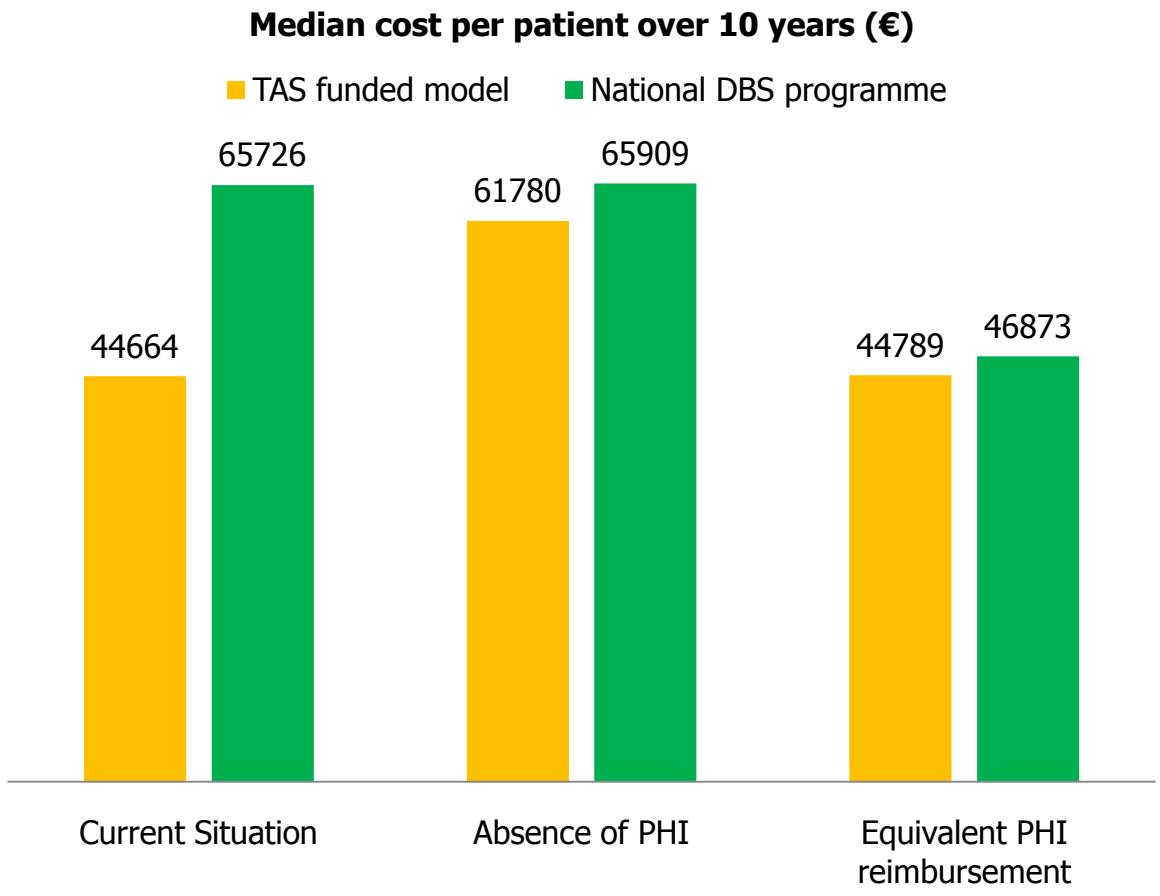


* Device cost includes device, controller, battery, leads and consumables used in surgery

Given the influence of private health insurance, the model was run with a scenario where no patients had private health insurance. In a scenario analogous to a single payer system, where the total cost of DBS care for an individual patient is entirely borne by one provider, the cost difference is €4,147 per patient (95% CI: -€12,698 to €21,440) over 10 years, with the cost of the Irish service less than the current UK service in 30% of simulations. In the corresponding budget impact assessment, assuming the total cost of DBS care is borne by a single payer, the incremental budget impact of an Irish DBS service compared to a service through TAS would decrease to €81,300 (95% CI: -€1.61 million to €1.85 million), with the estimated

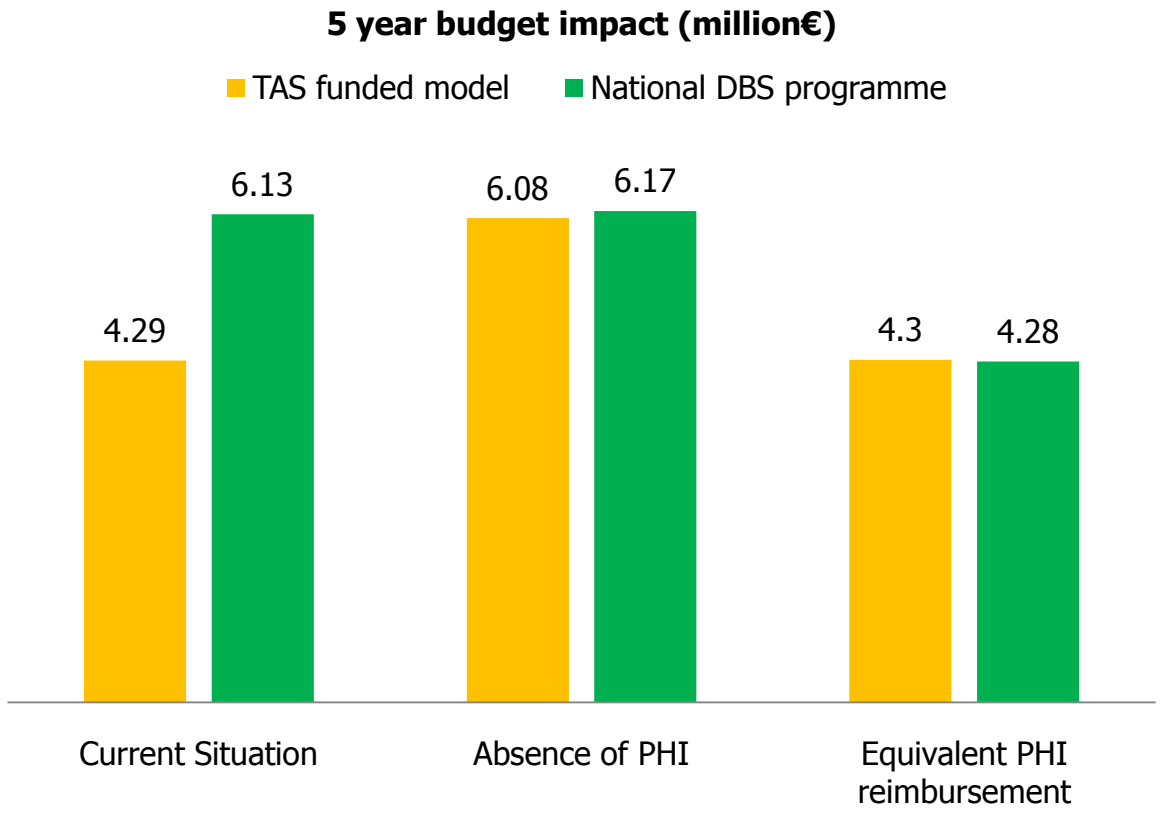
average costs of the two service models being €6.17 and €6.08 million, respectively. Alternatively, if the system of private health cover was changed such that private health insurance would reimburse the full cost of inpatient episodes in Ireland for insured patients, the cost difference would reduce to €1,911 per patient (95% CI: -€11,044 to €14,453) over 10 years. In this scenario the cost of the Irish service is less than the current UK service in 38% of simulations. The budget impact is negative so that over five years an Irish service would cost €22,500 less than the current service (95% CI: -€1.25 million to €1.22 million). See figures 4.5 and 4.6 below for a comparison of the cost per patient and budget impact for each of these scenarios compared to the base case analysis.

Figure 4.5 Median discounted cost per patient over 10 years in the base case analysis compared to two scenarios in regard to private health insurance



Key: PHI – Private Health Insurance

Figure 4.6 Estimated median 5 year budget impact for the base case analysis compared to two scenarios in regard to private health insurance



Key: PHI – Private Health Insurance

As can be seen above, it is possible to have a positive cost-minimisation and negative budget impact. The BIA takes into account all patients repatriated rather than a single cohort, therefore the contribution of each procedure to the total cost differs from the cost-minimisation. For example, in the proposed Irish service, device implantation generates 58% of the costs in the cost-minimisation but only 42% in the BIA. Battery replacement generates 29% and 43% of the costs in the cost-minimisation and BIA, respectively. Compared to the cost-minimisation analysis, the BIA includes a higher frequency of procedures that are lower cost in a proposed Irish service. Hence, the higher cost per patient in the cost-minimisation analysis, but the negative incremental budget impact compared to the existing service.

The costs for MRI and CT scans were obtained from private providers. It is possible that these were relatively high compared to those possible in a high volume hospital. The model was run with the cost of an MRI and CT scan both set to €200 to determine the sensitivity of the result to the cost of imaging. With a lower cost of

imaging, there is a modest impact on the cost difference, which reduces to €20,042 per patient (95% CI: €5,227 to €36,130) from €20,898 (95%CI: €5,447 to €36,540).

4.4 Discussion

The introduction of a DBS service to Ireland will lead to increased costs of €20,898 (95%CI: €5,447 to €36,540) per patient over 10 years. The five-year budget impact of an Irish service is €1.84 million more than the estimated €4.29 million for the existing model of care assuming no change in the number of new patients undergoing treatment. With the establishment of an Irish DBS service, the terms of TAS require that all patients currently receiving treatment abroad would have to be repatriated. Partly due to the repatriation of DBS patients, if an Irish DBS service is established there will be substantial resource implications in terms of staff, theatre time and bed days that must also be taken into consideration.

The parameter values used in the model are subject to uncertainty. To account for this uncertainty, a probabilistic model is used. From the sensitivity analysis, it is apparent that the increased cost is significantly impacted by current arrangements for patients with private health insurance. The existing system is likely to change given the proposed introduction of universal health insurance (UHI), which will impact significantly on how treatment is funded. Irrespective of UHI, there is also the possibility of a DRG-based payments system being introduced for patients with private health insurance that may result in publicly-funded hospitals recouping the full cost of treatment for patients with appropriate private cover. However, these developments are speculative at present and the main results of this evaluation are based on existing arrangements regarding private health insurance. It should be noted that a number of other factors, such as the cost of the UK service and the projected device cost in Ireland, also have a significant influence on the cost-difference. The importance of the device cost points to the potential for reducing the cost of an Irish service through price negotiation. The staff costs used in this analysis are taken from the mid-point of published Department of Health 2010 pay-scales. Any future reductions in rates of pay for some or all of the professional groups included in the economic model will impact on the results.

Under the assumption that no capital costs will be generated in establishing an Irish service, the cost per patient is unaffected by volume whereas the budget impact is directly proportional to the number of patients. In the main analysis, it was presumed that current demand is static at approximately 13 new cases per annum. This volume broadly reflects the experience to date. However, it is possible that demand will increase with the availability of a local service. Applying the experience of a mature system, such as that available in the UK, it is possible that an Irish service could have to accommodate 19 new DBS cases for movement disorders per

annum. As it was assumed that no capital costs would be incurred by a national DBS service, any increase in the number of DBS patients undergoing surgery will likely result in a proportional increase in the budget impact of the service. However, the initial growth of a new national DBS service is likely to be constrained by the need to build local capacity and expertise, and to develop a service safely while building up the number of patients treated. It was assumed that in the short to medium term, capacity in a national service would meet but not exceed current demand.

The BIA model incorporates estimates of the ongoing demand for services generated by DBS patients who underwent surgery in the UK. The number of procedures is possibly an overestimate, which may reflect a reducing uptake of reviews over time by patients.

The economic models used in this study are restricted to the HSE perspective and exclude indirect costs such as those accrued by patients and their families. Although reasonable transport costs for patients and potentially a carer are reimbursed through the TAS National Travel Policy[59], accommodation and subsistence costs for travel companions are not reimbursed and may represent a significant out-of-pocket expenditure for those patients unable to travel alone.

The economic analysis and BIA examine the cost of treating comparable numbers of patients through either an Irish or a UK-based service; that is, they explore the incremental cost to the HSE for patients that can avail of either model of care and excludes those patients who cannot access care in the UK due to the requirement to travel. Little is documented on the healthcare utilisation and cost to the HSE of the cohort currently unable to avail of DBS. There is a potential that the cost to the HSE of providing DBS surgery for these patients could be offset by a reduction in their use of other healthcare resources (e.g. medications, hospital admissions, home help) subsequent to successful surgery reducing the potential budget impact of an expanded national DBS service.

4.5 Key messages

- Economic evaluation in HTA involves the comparative analysis of alternative courses of action. In this HTA, the cost of an Irish DBS service was compared to the existing Treatment Abroad Scheme approach to accessing services.
- Probabilistic models were used to carry out the economic analysis. Values for key parameters for the economic model were mainly informed through primary data collection and literature review and were endorsed by the Expert Advisory Group.
- The economic models used in this study are restricted to the perspective of the publicly-funded health and social care system and only

incorporate direct costs.

- It is assumed that the proposed Irish DBS service will operate to similar quality standards to those DBS services currently used abroad; hence patients will experience equivalent safety and clinical outcomes. With equivalent patient outcomes, a cost-minimisation analysis (CMA) was used.
- It was estimated that an Irish DBS service would incur a discounted cost of €65,726 (95% CI: €52,853 to €86,959) per patient over 10 years. This compares to €44,664 (95% CI: €32,892 to €65,308) per patient for the existing service. An Irish service will cost an additional €20,898 (95%CI: €5,447 to €36,540) per patient over 10 years.
- The incremental budget impact of an Irish DBS service is €0.37 million (95% CI: €0.07 million to €0.71 million) in the first year. Over five years, the incremental budget impact of an Irish DBS service is €1.84 million (95% CI: €0.32 million to €3.55 million) more than the €4.29 million required to fund the same number of patients through the TAS. Provision of an Irish DBS service will have resource implications for staff, imaging services, theatre time and bed days.
- In a scenario analogous to a single payer system, where the total cost of DBS care for an individual patient is entirely borne by one provider, the cost difference between the service delivery models is reduced to €4,147 per patient over 10 years. In sensitivity analyses, changes to the relative contribution by private health insurance companies to the cost of DBS care for patients with private health insurance substantially influenced the estimated five-year budget impact of the different service delivery models and could potentially render a national programme more affordable than in the base case analysis.
- Any changes in the cost of the DBS device to the HSE as a result of price negotiation are also likely to impact significantly on the affordability of a national service.

5 Patient-related, organisational and ethical considerations

5.1 Introduction

This chapter reviews the implications for patients as well as organisational and ethical considerations concerning the provision of a national deep brain stimulation (DBS) service compared to the current process whereby access to treatment is provided outside of Ireland via the E112 Treatment Abroad Scheme (TAS). The TAS scheme is briefly described along with the use of the scheme to fund DBS procedures to date. The patient-related, organisational and ethical issues associated with these two possible models of care are then discussed.

5.2 Treatment Abroad Scheme

The Treatment Abroad Scheme (TAS) is operated by the Health Service Executive (HSE) for individuals entitled to treatment in another EU/EEA member state under EU Regulation 1408/71. The scheme, operated in accordance with procedures set out in EU Regulation 574/72 under the direction of guidelines from the Department of Health, provides financial assistance toward the cost of treatment in public health facilities in another member state. This assistance is provided in the form of an EU/EEA model form E112 for appropriately referred individuals meeting the relevant eligibility criteria.

Patients require prior authorisation from the HSE before travelling abroad for treatment. An application for treatment along with a referral letter must be submitted by an Irish-based public consultant detailing: the patient's condition, the proposed treatment that is being applied for and the planned treatment facility. The consultant must certify that the proposed treatment is:

- a proven form of medical treatment
- medically necessary and will meet the patient's need
- among the benefits provided for by Irish legislation
- either not available within the State or cannot be provided within the normal required time, taking account of the patient's current state of health and the probable course of illness.

The proposed treatment facility (located in an EU/EEA state) must accept the EU/EEA form E112 (IE) and be a recognised hospital or other location under the control of a registered medical practitioner. Since 2010, applications for the TAS have been centralised within the HSE. The HSE notes that they will endeavour to

give a decision on applications within 20 working days of receipt of the fully completed application forms and supporting documents. However, applications requiring the advice of a medical expert may take longer to process. Separate E112 forms are issued in respect of each specific episode of care. Approval may be granted for multiple visits when these are recommended by the referring consultant, however, the local TAS office must be contacted confirming each appointment and providing proof of each appointment date, so that an E112 may be issued in advance. Patients may be liable for the cost of care if authorisation is not obtained prior to travel; post-dated forms are only considered in the case of extreme emergencies. The cost of travel for the patient and, if necessary, a caregiver is covered by the TAS National Travel Policy; the cost of accommodation and subsistence are not.[51]

The most common treatment types that patients have accessed under the TAS are DBS, cardiac transplantation, nasal ciliary brushings, sap scans and liver transplantation. Cumulative spending on the TAS scheme between 2008 and April 2012 is estimated at in excess of €42 million.[60] DBS is funded for eligible Irish patients with selected movement disorders such as Parkinson's disease, essential tremor and dystonia. DBS is not routinely funded for other conditions; approval may be granted on an exceptional basis following independent case review by a medical expert within the HSE.[61]

Approximately 130 patients have been referred overseas for DBS since 1997. Between 1997 and 2011 the estimated total expenditure on DBS treatment is approximately €8 million, including travel costs for patients and carers.[41;62] DBS is a chronic treatment: subsequent to an initial assessment and surgery, patients continue to require follow-up care for as long as they have an implanted DBS system to include battery changes, management of potential complications and adjustment of stimulator settings to optimise benefit. This care may continue for decades with the interval between treatment visits extending to years for patients with stable conditions who are not experiencing difficulties.

Until recently, approval for the TAS was provided at a regional level in Ireland, with invoices submitted retrospectively. This combined with inconsistencies in the categorisation of treatments means that based on the information available to this HTA, it is not readily apparent exactly how many patients have undergone DBS surgery and how many are still actively receiving care. Between 2008 and April 2012, it is estimated that 118 patients travelled abroad to attend a DBS service. This cohort of 118 includes patients who have newly undergone DBS surgery as well patients who may have received their DBS surgery up to several years previously. Possibly excluded from this cohort are patients who had their initial DBS surgery prior to 2008, but who have not had a follow-up visit (or for whom invoices have yet to be

received) during the 2008 to 2012 interval. Based on the available data, it is estimated that on average 13 new patients undergo DBS surgery each year. With the exception of two patients treated in France, all patients referred for DBS through the TAS between 2008 and 2012 have received care in the UK (most commonly in the Frenchay Hospital in Bristol and the Radcliffe Hospital in Oxford). Approximately 60% of patients had Parkinson's disease as their referring diagnosis, with a further 25% being referred for essential tremor and dystonia.[41]

At present, patients who meet the criteria for funding and are able to travel abroad have good access to DBS services through the TAS. Currently, targets for the period of time between referral, assessment and surgery are provided by UK centres at the outset of treatment and the experience to date has been that these targets are consistently met. During discussions with the two main UK centres providing this treatment to Irish patients, no capacity limitation that might adversely affect continued access was reported. Irish referrals are treated the same as referrals from within the NHS for the purposes of scheduling treatment.

5.3 Patient-related issues

A number of patient-related issues have been highlighted by patients, patient representative organisations and healthcare providers in relation to the provision of care through the TAS. While acknowledging that the scheme enables Irish patients to access beneficial treatment in specialised centres, the requirement to travel abroad for care can place a significant burden on the patient and their families and may limit some patients from availing of care.

With the exception of the billing from the DBS centre for care provided, responsibility for all logistical, financial and social arrangements relating to the treatments funded through the TAS lie with the patient and their family. These may include obtaining passports, travel booking and payment, transport and accommodation arrangements for the patient and a caregiver. Patients may need to fund up-front costs of up to €2,300, including flight costs for the patient and a caregiver, in the first year that DBS surgery is carried out. Reasonable airfare costs may be subsidised for the patient, and potentially for a caregiver for those unable to travel without assistance through the TAS National Travel Policy. Patients must submit evidence of their expenditure and are reimbursed retrospectively for approved trips. Transport by air ambulance is limited to patients requiring emergency transfer or where the referring consultant specifies the use of air ambulance transport.[61] Subsistence and accommodation costs are not reimbursed. These may include costs of remaining in the UK after being discharged from hospital if the patient does not feel well enough to travel at that point. Community welfare assistance may be available to support families, however such support in the form of exceptional needs payment would

usually only be available to those already in receipt of an income support payment from the Department of Social Protection. It has previously been documented that there may be a lack of equity and consistency in the financial support available and a lack of clarity in relation to entitlements, especially for those who were not covered by the General Medical Services (medical card) Scheme.[63] These processes, together with the TAS application processes, should be clear to ensure transparency and fairness. Travelling abroad for family members may result in additional costs and logistical challenges associated with time off work or care of other dependents. This may prevent some patients from being able to access care. Of note, certain airlines restrict travel for up to 10 days post-surgery unless the patient has written confirmation that they are fit to travel from their clinician. If so restricted, patients may have delays and associated accommodation and subsistence costs between their discharge from hospital and being able to return home.[64]

Patients have identified stress associated with travelling and planning for their DBS care. To be initially eligible for DBS, patients must be refractory to other treatments and, for patients with dystonia and essential tremor must have significant functional impairment associated with their condition. Lengthy door-to-door journey times on public and commercial carriers may therefore be very challenging. This situation may be exacerbated for patients with Parkinson's disease as the IPG device is not activated until their first follow-up visit post surgery; these patients must travel home with the additional burden of having undergone a lengthy neurosurgical procedure while having obtained no improvement in their underlying functional status. Also, as discussed in Chapter 2, DBS is a chronic treatment that does not cure or delay the ongoing degenerative process in Parkinson's disease. Patients who may have been fit for travel at the time of DBS surgery will inevitably become more disabled over time and may thus experience increasing difficulties in accessing their necessary ongoing DBS care overseas.

Recent standardisation of the TAS administration process requires patients to submit a new E112 application in advance of each appointment (except where multiple planned appointments are needed in the same year). This change has been identified by patients and providers as a significant logistical burden, giving rise to concerns that the form will not be issued in sufficient time for the patient to make the necessary travel arrangements to get to their appointment. For unscheduled visits not initially approved as part of the treatment course (e.g. due to treatment-related complications), patients must first submit signed application forms from their referring consultant, again potentially adding to the patient burden and stress.

Continuity of care for patients receiving treatment and follow-up across two different health systems may be an issue for the current DBS service. Patients have identified the need for clarity regarding who to contact if they have questions or concerns in relation to their DBS care, particularly in the event of complications and

emergencies. The majority of care provided to DBS patients through the TAS is elective and can be coordinated in a timely and effective manner within and between the clinicians and service providers. However, patients requiring urgent or unscheduled care must first obtain approval through the TAS, often at short notice. This necessitates a review by their Irish-based neurologist, submission and approval of the relevant paperwork, organisation of transport arrangements (and potentially accommodation for a carer) all at short notice. Patients may be cared for by a multi-disciplinary team of providers both in Ireland and at the DBS specialist service. This fragmentation of care may have implications for the quality of patient care. To ensure the provision of a safe and integrated service it is critical that there are clear governance arrangements for the coordination of care and clarity of accountability for each element of care.[63] Patients, nurse specialists, carers and GPs should be given details of who they can contact within the clinical team(s) if they have questions or concerns.

The need for a patient-centred approach to care by the HSE in respect of patients funded to receive treatment abroad has been recommended previously.[63] This should take account of the broader welfare, psychosocial and financial needs of the patient and their caregiver travelling abroad for treatment. It should ensure clear arrangements and structures are in place to provide the necessary support and that this is clearly communicated to those accessing this service.[63]

5.4 Organisational issues

In Ireland, there are two specialist centres for neurosurgery located in Beaumont Hospital in Dublin and Cork University Hospital (CUH). Beaumont Hospital is the *de facto* national tertiary referral centre for certain complex procedures. Severe deficiencies in the provision of neurosurgical services that negatively impact on the capacity of the services to meet demand in Ireland have been identified[65], including lengthy waiting lists at all entry points to the neurosurgical services (emergency and elective inpatient, day patient and outpatient); inadequate staffing, dedicated neurosurgical beds, theatre access and availability of specialised equipment; limited development in subspecialty areas of neurosurgery; a disproportionate level of emergency surgery to elective surgery; limited numbers of rehabilitation and long term services nationally causing delayed discharges from the acute services; difficulty in planning elective admissions; and inefficiencies in theatre utilisation.[65]

Although investments in neurosurgical services have taken place to address some of these issues, there are ongoing issues with neurosurgical capacity as evidenced by lengthy waiting lists for elective neurosurgical procedures. In 2010, there were a total of 65 adult neurosurgery beds in Beaumont Hospital, while 1,915 patients underwent neurosurgery. The National Treatment Purchase Fund maintains public

hospital waiting lists and waiting times nationally on the Patient Treatment Register.[66] Data from this register in May 2012 indicate that 532 adult patients were on hospital waiting lists for elective neurosurgery in Beaumont and CUH combined, 88% of whom were on the waiting list for Beaumont Hospital (see Table 5.1 for waiting times). Almost 40% of patients were on the waiting list for over six months.[67]

Table 5.1 Hospital waiting times for adult neurosurgical procedures

Hospital	Waiting time (months) as of 17 May 2012					Total patients*
	<3	<6	<9	<12	>12	
Beaumont	158	116	104	71	20	469
Cork	29	22	12	0	0	63
Total	187	138	116	71	20	532

*Waiting lists do not take account of patients awaiting DBS surgery in neurosurgical centres outside Ireland.

DBS surgery is a lengthy and complicated procedure. It is estimated that each DBS surgery would displace two existing neurosurgical procedures.[68] A service providing ten new DBS surgeries a year would therefore displace 20 existing procedures. Without investment in additional resources, this would add to existing waiting lists for other patients and may mean delays also for patients scheduled for DBS surgery in a new national DBS service. In addition, patients may have lengthy waits before being first seen by a neurosurgeon in Ireland. Although currently not collated in the Patient Treatment Register, reports suggest that the waiting time from referral by a general practitioner (GP) to see neurology specialists can be up to 13 months (depending on the consultant) with patients waiting up to 16 months for some consultants on the neurosurgery list.[69] As noted, deficiencies in service provision are multifactorial and may not be simply addressed by the recruitment of additional staff. Currently, Irish patients have an average waiting time of approximately 8 to 13 months from the time they are first referred by their consultant to undergoing DBS surgery. This includes the time from submission of completed paperwork to the TAS, assessment in the DBS specialist centre and subsequent surgery.

Service specifications for a high quality DBS service were outlined in Chapter 3. These include recommendations regarding the minimum number of patients that must be assessed and treated each year, that there is onsite access to preferably two experienced neurosurgeons and an appropriately constituted multidisciplinary team, and that the site has access to a full range of resources including a neurosurgical theatre, range of imaging equipment, critical care beds and appropriate inpatient and outpatient services. It is recommended that DBS is

undertaken within a neurosciences centre that provides both surgical and medical neurology services. Also recommended is that as much of the care as possible should ideally take place close to the patients home to ensure easy and convenient access.[70] Published literature also notes that "DBS surgery is best performed by an experienced surgeon with specific expertise in stereotactic and functional neurosurgery working as part of an inter-professional team (movement disorder neurologist, neuropsychologist, psychiatrist, and neurophysiologist)"[14] and that lower complication rates can be achieved (approximately 4%) if DBS is carried out in a specialised centre.[12] Consideration of these standards and the necessary learning curve required for a DBS team to work proficiently to deliver the best possible outcomes for patients would need to be considered in the potential establishment of any new service. In Ireland it is envisioned that, in line with sub-speciality training requirements in other surgical disciplines, responsibility for developing training programmes and guidelines for the practice of DBS will fall to the appropriate surgical training bodies.

The wider benefits of creating a national DBS service in Ireland should also be considered. For example, the creation of a national DBS service may prepare the Irish healthcare service for the potential growth in the numbers of indications for which DBS will be indicated and routinely used as standard of care in the future. Use for indications such as Tourette's syndrome, depression, obsessive compulsive disorder, epilepsy and chronic neuropathic pain is currently the subject of considerable international research. However, the use of DBS for these indications is not routinely funded in Ireland or in other health systems, such as the NHS, due to the limited clinical effectiveness data currently available. Through the current TAS process, the HSE has a mechanism to restrict the availability of DBS to those indications for which reimbursement has been agreed. In a prospective national service, the range of indications for which DBS is used may change as decisions regarding the type of patients to be treated are usually made at a local level and at the discretion of the treating clinicians. Without additional resources, any expansion in the range of conditions treated may result in reduced access to DBS for patients with Parkinson's disease, dystonia or essential tremor.

5.5 Ethical considerations

A challenge with healthcare distribution is obtaining a balance between the expectations of different patients and a fair distribution of resources to allow for the best medical outcomes for the most people. The EUnetHTA* core HTA model is used in this assessment to identify the relevant ethical issues.[71] Two relevant themes

* European collaboration that consists of government-appointed organisations, regional agencies and non-for-profit organisations that produce or contribute to HTA.

were identified: the ethical issues associated with the use of DBS as a technology; and the ethical issues arising from a decision to continue with the current arrangement of providing access to DBS through the TAS or to commence a new national DBS service.

The published literature on the ethical issues surrounding DBS treatment primarily focuses on informed consent.[6;40;72] Informed consent is important to ensure that the potential adverse events associated with surgery, psycho-social adjustment post-surgery, potential changes in personal identity due to DBS, and patient and family expectations for surgical improvement, are discussed and understood.[72] In addition, the close links between industry and academia with respect to DBS technology are discussed in the literature, and the need for declared conflicts of interest highlighted to ensure transparency.[72]

Potential ethical issues have been identified in relation to the absence of a national DBS service and the need for patients to travel outside the country in order to access care. As outlined in section 5.3, due to the travel requirement (which is particularly onerous for those with significant disease-related functional impairment) and the fact that the responsibility for the financial, social and logistical arrangements for accessing care reside with the patient and their family, patients that are judged to be unable or perceive themselves to be unable to undertake these commitments are denied access to potentially beneficial surgery. The current system may therefore be perceived as inequitable for these patients.

Conversely, ethical issues may also arise in relation to the opportunity costs associated with the establishment of a national DBS service. Without a substantial investment in resources, the additional service requirements associated with DBS surgery may result in reduced overall hospital bed and theatre availability for other neurosurgical patients, thereby increasing their waiting time for elective surgery. In Chapter 4, it was identified that, particularly given the current financing arrangements for patients with private health insurance, a national DBS service is likely to cost the HSE more than the comparable service currently provided through the TAS. Reallocation of resources could affect the existing health care system as it may divert resources from other effective treatments for the same conditions or from the overall healthcare fund. If an investment were to be made in DBS in Ireland, questions of equity of access and justice would still persist.

Finally, restricting patients' choice of where they can access treatment could be considered an infringement on their right to personal autonomy. However, it should be noted that this right, particularly in the healthcare setting, is not absolute. Healthcare budgets are finite and an individual's right to choose certain treatments, services or location of these services may conflict with other values or priorities, such as equity or the need to benefit the wider community.

5.6 Key messages

- The TAS enables timely access for eligible Irish patients to specialised DBS neurosurgical services in other European countries. However, the requirement to travel adds financial and logistical difficulties for patients and may limit access to treatment for otherwise eligible patients who are unable to travel.
- Challenges for the current model of DBS care include the need for streamlined access to urgent DBS care and the need to ensure continuity of care for patients receiving long term treatment and follow-up across two different healthcare systems. Clear governance arrangements for the coordination of care and clarity and accountability for each element of care is essential to ensure the provision of a safe and integrated service that achieves optimal patient outcomes.
- The rights of patients applying to the TAS, the welfare benefits available to them and the approval and appeal processes, should be clear and consistent to ensure fairness, equity of access and to reduce stress associated with the application process.
- Deficiencies in the existing Irish neurosurgical services have been identified and are evidenced by the lengthy waiting list for elective neurosurgery. These deficiencies are multi-factorial and may not be easily resolved. Significant investment in resources may be required to ensure that any new national DBS service could meet service specifications for a high quality service, provide timely access to care and not impinge on the current access to neurosurgical services for non-DBS patients.
- The main ethical issue with respect to DBS in the published literature relates to informed consent.
- There are issues regarding equity of access with the existing system of referring patients abroad for DBS treatment as there is a sub-group of patients that are unable to avail of care due to the requirement to travel. However, establishment of a new national service may impact on existing neurosurgical patients, delaying further their access to necessary care and generating new ethical issues regarding equity of access to care. Furthermore, without an increase in resources, expansion in the range of conditions treated by a national DBS service may result in reduced access to DBS for patients with Parkinson's disease, dystonia or essential tremor.
- A decision to implement a new national DBS service may have implications for resource allocation of existing technologies and services. This decision should be guided by ethical principles that take into account the application of these

principles to the individual, but also the costs and benefits to the broader community.

6 Summary and conclusions

The purpose of this HTA was to examine the implications of establishing a national deep brain stimulation (DBS) service in Ireland compared to the existing approach of delivering this service through the Treatment Abroad Scheme (TAS). A prospective national service was modelled based on the existing service provided in the UK and with reference to the UK service standards that govern its provision. It was assumed that the prospective national service would result in equivalent clinical outcomes for patients. Therefore, the two service delivery options were compared on the basis of the cost to the HSE, the implications for patients and with consideration of how a national DBS service would integrate into existing neurological services in Ireland.

6.1 Summary of clinical effectiveness

DBS for selected movement disorders has been provided through the Irish healthcare system since 1997. As an established treatment option for the symptoms of medically-refractive Parkinson's disease, dystonia and essential tremor, the clinical effectiveness of the treatment itself was not the focus of this analysis. However a brief summary of the evidence in each of these indications is provided in chapter 2.

There is good quality randomised controlled trial (RCT) evidence that DBS is more effective than best medical treatment for dopamine-responsive Parkinson's disease with severe motor symptoms that cannot be adequately controlled with medication, for outcomes such as mobility, performance of the activities of daily living and reduced bodily discomfort.[15] Increased quality of life scores in these areas are supported by improvements in motor symptoms and functional ability as measured by the Unified Parkinson's Disease Rating Scale (UPDRS).[15] Risks associated with the treatment include infection, device malfunction, cerebral haemorrhage, dyskinesias, axial symptoms, speech dysfunction, tonic muscle contraction, paraesthesia, eyelid and ocular disturbances and behavioural and cognitive issues.[22]

The quality of the evidence of effectiveness of DBS in dystonia and essential tremor is more limited than for Parkinson's disease, consisting mainly of observational study designs. Pooled results of case series[35] involving patients with primary generalised dystonia and primary focal dystonia show statistically significant improvements in symptoms as measured by the Burke-Fahn-Marsden Dystonia Rating Scale (BFMRS) and Toronto Spasmodic Torticollis Rating Scale (TWSTRS). Although improvements in clinical dystonia scales were noted for many patients, the effectiveness of DBS in several types of secondary dystonia was found to be inconclusive. For essential tremor there is pooled evidence from 17 studies[34] that shows a statistically significant decrease in tremor, as measured by the Fahn-Tolosa-Martin (FTM) tremor

rating scale. However, the methodological quality of the evidence for this indication is poor.

6.2 Epidemiology and estimated demand for DBS services

At present Parkinson's disease accounts for approximately 74% of all referrals for DBS for movement disorders in Ireland, with dystonia and tremor accounting for 11% and 15%, respectively.[41] Absolute figures for the number of patients diagnosed with Parkinson's, essential tremor or dystonia in Ireland are currently unavailable. Using UK prevalence rates combined with DBS eligibility rates derived from the experience of mature UK DBS centres, it is estimated that there are a total of 460 Irish patients who would be suitable candidates for DBS treatment. Since approximately 120 Irish patients have already been treated, this leaves an estimated pool of 330 potential DBS patients in Ireland (see section 2.5). However this does not take into account patients who would choose not to undergo DBS treatment.

An alternative method of estimating the likely demand for a national service is to examine the level of demand experienced within the English NHS service where DBS is routinely funded by most commissioning bodies for patients with Parkinson's disease, essential tremor and dystonia that meet eligibility requirements. Assuming comparable population prevalence rates and treatment patterns to England for Parkinson's disease, dystonia and essential tremor, an Irish DBS service would treat approximately 19 new patients each year. Demand may be influenced by future trends in DBS usage; a possible example of this may be a trend towards surgical treatment of early stage Parkinson's disease, which has been the focus of recent research.[45]

Differences between the current demand for DBS treatment (approximately 13 new referrals per year) via the TAS and the population-adjusted demand based on English hospital episode statistics (HES) data could be caused by a combination of factors. These include artificial reductions in demand due to difficulties for patients in travelling abroad, constraints in receiving an appointment with a consultant neurologist or a decreased level of referrals from a neurology service lacking in experience in assessing and referring patients for DBS treatment.

Research on the use of DBS in a range of indications beyond those included in this HTA, including chronic pain, epilepsy, depression and obsessive-compulsive disorder, is ongoing. At present, DBS is not routinely funded for these indications due to limited evidence of clinical effectiveness. However, further research may result in an increased demand for DBS services for indications other than movement disorders.

6.3 DBS service specification

An exploration of the potential resource requirements of a national DBS service was carried out based on input from the EAG, the TAS and with reference to published literature on service standards. DBS is a long term treatment for a chronic condition; long term follow-up and support are required and demand for the service is cumulative. International service standards for a high quality service include specifications for integration of care; informed consent; the patient experience; access to services; age-appropriate care; the resources, expertise and volume of care required to maintain a high quality service; and the use of a team-delivered approach that audits outcomes. These factors must all be considered in the design of a national service.

Challenges that exist in relation to the setting up of a national DBS service include the development of a multi-disciplinary team of appropriately trained professionals with the support services required to provide the volume of care expected, in accordance with appropriate quality standards. In addition to initial set-up, a DBS team must have and be able to maintain the competencies needed to offer the most appropriate care according to the individual patient needs. International standards for excellent care specify an annual minimum of 15 new DBS assessments and 10 new DBS surgeries per specialist centre, with transition plans recommended for new centres so they may develop their services safely while building the number of patients treated. There has been a small number of DBS procedures carried out in Ireland since 2008. These have been performed on a case by case basis and have involved health professionals from a range of institutions in Ireland and Northern Ireland. As a result there is an existing level of neurological and neurosurgical experience within the Irish healthcare service in this area. However, it may be anticipated that it may take a number of years for a new national service to scale up to meet the anticipated demand for DBS surgery.

Potential efficiencies that could be realised with a national DBS service compared to the existing services through the TAS include a reduction in the administrative burden associated with the TAS, a potential for some inpatient appointments to be carried out on an outpatient basis and streamlining of neurological reviews due to a proportion of patients only needing to attend one neurologist rather than an Irish-based neurologist and a UK-DBS specialist. The latter may not be possible for all patients, some of whom would continue to see their local (non-DBS trained) neurologist for regular reviews with additional appointments being scheduled with a national DBS centre.

6.4 Economic analysis and budget impact

The results of the cost-minimisation analysis show that the per-patient cost of providing DBS services in Ireland will increase the cost to the HSE by €20,898 per patient over 10 years; the median current cost per patient for the existing TAS funded service is €44,664. The difference is largely as a result of the fact that patients with private health insurance can have a greater proportion of their treatment costs covered if it is provided through the TAS than through a national service. Based on the assumption that approximately 32% of DBS patients will have private health insurance, an Irish service will result in a 47% (€20,898) increase on current TAS costs per patient over 10 years. In a scenario analogous to a single payer system, where the entire cost of DBS care for an individual patient is entirely borne by one provider, the cost difference is reduced to €4,147 per patient over 10 years. There is a degree of uncertainty associated with many of the cost estimates. In order to accommodate this uncertainly, estimates have been varied within plausible ranges and a sensitivity analysis was performed to investigate the major factors affecting the results.

The budget impact analysis was conducted using the status-quo in regard to private health insurance coverage of DBS and assumed that 32% of DBS patients will have private health insurance. Based on the estimates of demand and costs outlined in chapter 5, it shows that over the first five years a national DBS service will cost over €1.84 million more than the €4.29 million required to treat the same number of patients through the TAS. In sensitivity analyses, changes to the relative contribution by private health insurance companies to the cost of DBS care for patients with private health insurance substantially influenced the estimated five-year budget impact of the different service delivery models and could potentially render a national programme more affordable than in the base case analysis.

The economic analysis carried out in this HTA only examined the comparative costs from the perspective of the publicly funded health and social care system. It did not include costs to the patient associated with accessing the treatment.

The likely demand for an Irish DBS service is based on the experience of the TAS to date as well as the epidemiology of Parkinson's disease, essential tremor and dystonia. However, limitations associated with these data and changing trends in the management of these patients may affect the accuracy of the estimates used in this analysis.

6.5 Patient-related, organisational and ethical considerations

From a patient's perspective, the most obvious implication of a national service is that they would no longer have to travel abroad to receive treatment. Since overseas travel and accommodation represent a significant logistical and economic burden for the patient, its removal would have benefits both for existing patients receiving on-going follow up as well as patients who have been either unable or unwilling to travel abroad. This may allow more Irish patients to receive DBS treatment. It may also improve the overall patient experience. A national service has the potential to improve the continuity of care for DBS patients and facilitate increased integration between DBS ongoing treatment and other services which patients may be accessing within Ireland. It may also result in better access to urgent DBS care, since the need for TAS approval and overseas travel at short notice will be eliminated.

Challenges for the current model of DBS care include the need for streamlined access to urgent DBS care and the need to ensure continuity of care for patients receiving long term treatment and follow-up across two different healthcare systems. Clear governance arrangements for the coordination of care and clarity and accountability for each element of care is essential to ensure the provision of a safe and integrated service that achieves optimal patient outcomes. The rights of patients applying to the TAS, the welfare benefits available to them and the approval and appeal processes, should be clear and consistent to ensure fairness, equity of access and to reduce stress associated with the application process.

Challenges that exist in relation to the establishment of a national DBS service include the development of a multi-disciplinary team of appropriately trained professionals with the support services required to provide the volume of care expected, in accordance with appropriate quality standards. A DBS team must have and be able to maintain the competencies needed to offer the most appropriate care according to the individual patient's needs. In Ireland it is envisioned that, in line with sub-speciality training requirements in other surgical disciplines, responsibility for developing training programmes and guidelines for the practice of DBS will fall to the appropriate surgical training bodies.

DBS is a long-term treatment for a chronic condition – appropriate infrastructure will be required for ongoing surveillance and support and must take account of the fact that demand will be cumulative. This demand already exists in relation to the cohort of patients who have received the treatment through the TAS. Therefore in addition to meeting the needs of new referrals, a prospective national service would also have to provide follow-up care, including clinical reviews and IPG replacement operations, to an existing group of approximately 130 patients. Balancing the need to steadily ramp up the capacity of a new service with the numbers of existing

patients requiring treatment will be a considerable challenge particularly in the context of the significant capacity constraints in the existing Irish neurosurgical services. As a new national DBS service would place an extra demand on existing resources (e.g. theatre-time, bed days, consultant appointments, etc), it would be important that appropriate service planning is carried out prior to its introduction to ensure that existing neurological services are not affected or that patient's access to DBS services are not curtailed by the establishment of a national DBS service.

The use of DBS is being investigated for a wide range of additional indications; however, due to the limited clinical effectiveness data currently available, funding for these indications is not routinely provided in Ireland or in other healthcare systems such as the NHS. Through the current TAS process, the HSE has a mechanism to restrict the availability of DBS to those indications for which reimbursement has been agreed. In a prospective national service, the range of indications for which DBS is used may change as decisions regarding the type of patients to be treated are usually made at a local level and at the discretion of the treating clinicians. Without additional resources, any expansion in the range of conditions treated may result in reduced access to DBS for patients with Parkinson's disease, dystonia or essential tremor.

The main ethical issue with respect to DBS surgery in the published literature relates to informed consent. A new national DBS service may address the existing equity issues that exist in relation to the sub-group of otherwise eligible patients unable to travel for DBS care. However, without additional resources to support its introduction it may give rise to new ethical issues in relation to justice and equity for existing patients due to the diversion of resources from other effective treatments or from the overall healthcare fund.

6.6 Conclusions

There is evidence to indicate that DBS is an effective treatment for certain patients with treatment-refractory Parkinson's disease. Evidence for essential tremor and dystonia is weaker, but experts have concluded that DBS is an appropriate second-line therapy for patients with significant functional impairment that have failed to have an adequate response from conventional therapy. The HSE has funded DBS treatment for these indications since 1997, and so far over 130 patients have been treated. Approximately 13 new patients a year with Parkinson's disease, essential tremor and dystonia are referred for DBS treatment through the TAS. Given the epidemiology of the diseases and the experience of DBS services in the UK, this represents an under-supply of services in this area. If a national DBS service was established in Ireland, it is anticipated that the demand for DBS surgery for the specified movement disorders would increase from 13 to 19 patients per year.

Results of an economic analysis comparing the current TAS service delivery model to a prospective national DBS service show that an Irish service will cost more per patient. Given the existing arrangements with regard to private health insurance, where a greater proportion of costs can be met by insurers under the TAS scheme, an Irish service would result in a 47% increase in per-patient costs. A budget impact analysis (BIA) was conducted using the current status-quo with regard to reimbursement by insurers and assuming that 32% of DBS patients hold private health insurance. This shows that an Irish service would cost an additional €1.84 million over the first five years of the service compared to the €4.29 million required to treat the same number of patients through the TAS. In a scenario analogous to a single payer system, where the entire cost of DBS care for an individual patient is entirely borne by one provider, the cost difference is reduced to approximately €4,000 per patient over 10 years. In sensitivity analyses, changes to the relative contribution by private health insurance companies to the cost of DBS care for patients with private health insurance substantially influenced the estimated five-year budget impact of the different service delivery models and could potentially render a national programme more affordable than in the base case analysis.

A prospective national service that replaces the current TAS service delivery model would have implications for patients, the organisation of services and resource requirements. DBS is a long-term treatment for a chronic condition; demand for services is cumulative, with patients treated in preceding years requiring ongoing care in addition to the care required for new referrals. Adequate planning and resources would be required to ensure continuity or care is maintained, sufficient service capacity is available for existing patients, levels of access to DBS treatment are maintained for new referrals and that the development of a national DBS service does not negatively impact access of other patients to existing neurosurgical services. A new service would also need to meet appropriate quality standards to ensure that a consistently high quality of care is provided, as well as developing the skills, experience and capacity to meet the demand for DBS.

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Glossary of terms

Term	Meaning
Ablative surgery	A procedure in which a tissue or body part is removed or destroyed by surgery
Adverse event	Any undesirable experience associated with the use of a medical product in a patient
Akinesia	Inability to initiate movement due to difficulty selecting and/or activating motor programs in the central nervous system.
Autonomy	In ethics analysis, the patient's right of self-determination concerning medical care. It may be used in various senses including freedom of action, effective deliberation and authenticity. It supports such moral and legal principles as respect for persons and informed consent. Making decisions for oneself, in light of a personal system of values and beliefs.
Basal ganglia	Part of the brain that controls movement. It is a collection of associated cell groups that include the substantial nigra, which produces dopamine, striatum where dopamine is released, caudate nucleus, putamen, globus pallidus and subthalamic nucleus.
Bilateral stimulation	The neurostimulator devices are available as either single (unilateral stimulation) channel or dual (bilateral stimulation) channel devices. For bilateral stimulation the testing leads are inserted into both sides of the basal ganglia of the brain.
Bradykinesia	Slow movement. It is often associated with an impaired ability to adjust the body's position.
Budget impact analysis	The financial impact of the introduction of a technology or service on the capital and operating budgets of a government or agency.
Capital costs	The non-recurring cost of investment in items that remain useful beyond the period when costs are incurred.
Clinical outcome	An outcome of major clinical importance that is defined on the basis of the disease being studied (e.g. fracture in osteoporosis, peptic ulcer healing and relapse rates).
Comparator	The technology to which an intervention is compared.
Complication	A secondary disease or condition that develops in the course of a primary disease or condition and arises either as a result of it or from independent causes.
Computed tomography (CT)	An image produced by a CT scanner. X-rays are taken from different angles and are put together by a computer to generate a series of cross-sections of the part of the body being scanned. This can build up a very detailed picture of the inside of the body, and provide accurate information on the size and position of a tumour.
Confidence interval (CI)	Depicts the range of uncertainty about an estimate of a treatment effect.
Conformité Européenne (CE) Mark	EU directives outline requirements under which a medical device (as well as other commercial goods) can be marketed across all EU member states after earning a CE mark in any one member country. These directives categorize devices into four classes (I, IIa, IIb, and III) on the basis of increasing risks associated with their intended use.
Contraindication	A clinical symptom or circumstance indicating that the use of an otherwise advisable intervention would be inappropriate.
Cost-minimisation analysis (CMA)	A determination of the least costly among alternative interventions that are assumed to produce equivalent outcomes.
Diathermy	The use of high-frequency electrical currents as a form of physical therapy and in surgical procedures
Discount rate	The interest rate used to discount or calculate future costs and benefits so as to arrive at their present values, e.g. 3% or 5%. This is also known as the opportunity cost of capital investment.

Discounting	The process used in cost analyses to mathematically reduce future costs and/or benefits/outcomes to their present value.
DRG	The diagnosis related group (DRG) is a code that classifies a hospital episode according to three components: the major diagnosis category; surgical, medical or 'other' episode type; and severity of episode. DRGs are used as the basis for costing hospital episodes. In Ireland the Australian refined (AR) version of DRGs is used.
Dysarthria	Speech that is characteristically slurred, slow, and difficult to understand.
Dyskinesias	The presence of involuntary movements, such as the choreiform movements seen in some cases of rheumatic fever or the characteristic movements of tardive dyskinesia. Some forms of dyskinesia are side effects of certain medications, particularly L-dopa and, in the case of tardive dyskinesia, antipsychotic drugs.
Dysmetria	An inability or impaired ability to accurately control the range of movement in muscular acts.
Dystonia	A movement disorder characterised by involuntary and uncontrollable muscle spasms which can force affected parts of the body into abnormal, sometimes painful, movements or postures. It can be of primary or secondary origin and can also be associated with Parkinson's disease.
Economic evaluation	Application of analytical methods to identify, measure, value, and compare costs and consequences of alternatives being considered; addresses issue of efficiency to aid decision making for resource allocation.
Economic model	Economic models provide a means of bringing together different types of data from a range of sources and provide a framework for decision making under conditions of uncertainty. Modelling may be used to combine different data sets changing the information collected from a clinical trial into a form that can be used, to extrapolate short-term clinical data to longer term, to link intermediate with final endpoints, to generalise from clinical trial settings to routine practice and to estimate the relative effectiveness of technologies where these have not been directly compared in clinical trials.
Effectiveness	The benefit (e.g. to health outcomes) of using a technology for a particular problem under general or routine conditions.
Efficacy	The benefit of using a technology for a particular problem under ideal conditions, for example, in a laboratory setting or within the protocol of a carefully managed randomized controlled trial.
Efficiency	The extent to which the maximum possible benefit is achieved out of available resources.
Epidemiology	The study of the distribution and determinants of health-related states or events in specified populations.
Equity	In ethical analysis, equity assumes fairness in the allocation of resources or treatments among different individuals or groups.
Essential tremor (ET)	Uncontrollable shaking (tremor) of the hands and head and sometimes other parts of the body. It is the most common of all movement disorders and is estimated to affect 3 to 4 million people in the US. In more than half of cases, essential tremor is inherited in an autosomal dominant manner. The mainstays of treatment are drugs such as propranolol and primidone.
Ethics	A general term for what is often described as the science of morality. In philosophy, ethical behaviour is that which is good. The goal of a theory of ethics is to determine what is good, both for the individual and for society as a whole.
Globus Pallidus interna (GPi) DBS	The primary target in the brain for DBS used for dyskinesias and tremor rigidity.
Health economics	The application of the principles and rules of economics in the area of health and healthcare, including the evaluation of health policy and the health system from an economic perspective; health system planning; the demand for and supply of healthcare; economic evaluation of medical technologies and procedures; the determinants of health and its valuation, and analysis of the performance of

	healthcare systems in terms of equity and allocative efficiency.
Health outcomes	The results or impact on health of any type of intervention (or lack of) (e.g. a clinical procedure, health policy or programme, etc.).
Health technology	Any intervention that may be used to promote health, to prevent, diagnose or treat disease or for rehabilitation or long-term care. This includes the pharmaceuticals, devices, procedures and organisational systems used in healthcare.
Health technology assessment (HTA)	The systematic evaluation of properties, effects, and/or impacts of health care technology. It may address the direct, intended consequences of technologies as well as their indirect, unintended consequences. Its main purpose is to inform technology-related policymaking in healthcare. HTA is conducted by interdisciplinary groups using explicit analytical frameworks drawing from a variety of methods.
Health-related quality of life	A multi-dimensional measure comprising the physical and mental health perceptions of a patient in terms of health status, health risks, functional status, social support, and socioeconomic status.
HTA	Health technology assessment.
Implantable Pulse Generator (IPG)	A small unit used in deep brain stimulation. It is implanted (under general anaesthetic) under the skin in the chest, rather like a pacemaker. The IPG contains the battery and the electrical signals for the stimulation. The IPG is programmed by the clinician using a computer, but on a day-to-day basis the stimulation can be switched 'on' and 'off' by the person with Parkinson's using a hand-hand programmer or a magnet.
Incidence	The rate of occurrence of new cases of a disease or condition in a population at risk during a given period of time, usually one year.
Incremental cost	The additional costs that one intervention imposes over another.
Incremental cost effectiveness ratio (ICER)	The additional cost of the more expensive intervention as compared with the less expensive intervention divided by the difference in effect or patient outcome between the interventions, e.g. additional cost per QALY.
Indication	A clinical symptom, risk factor, or circumstance for which the use of a particular intervention would be appropriate as determined or specified.
Informed consent	The legal and ethical requirement that no significant medical procedure can be performed until the competent patient has been informed of the nature of the procedure, risks and alternatives, as well as the prognosis if the procedure is not done. The patient must freely and voluntarily agree to have the procedure done.
Investigational Device Exemption (IDE)	A regulatory category and process in which the US Food and Drug Administration (FDA) allows specified use of an unapproved health device in controlled settings for purposes of collecting data on safety and efficacy/effectiveness; this information may be used subsequently in a pre-marketing approval application.
Justice	In ethical analysis, justice is the distribution of benefits, burdens and costs fairly.
Levodopa	A drug that is used in the clinical treatment of Parkinson's disease and dopamine-responsive dystonia.
Literature review	A summary and interpretation of research findings reported in the literature. May include unstructured qualitative reviews by single authors as well as various systematic and quantitative procedures such as meta-analysis. (Also known as overview.)
Magnetic resonance imaging (MRI)	A method of analysing brain structure and function that involves placing a person in a strong magnetic field and directing radio waves at them. The magnetic field causes the nuclei of hydrogen atoms in the body tissue to align themselves in a certain direction, in a certain energy state. The radio waves deflect them, and when these waves are switched off and the nuclei swivel back, they remit electromagnetic signals, which can be processed into a series of layered images.
Neurologist	A neurologist deals with the diagnosis and treatment of all categories of disease involving the central, peripheral, and autonomic nervous systems, including their

	coverings, blood vessels, and all effector tissue, such as muscle.
Neurons	A nerve cell that receives and sends electrical signals over long distances within the body. A neuron receives electrical input signals from sensory cells (called sensory neurons) and from other neurons. The neuron sends electrical output signals to muscle neurons (called motoneurons or motor neurons) and to other neurons. A neuron that simply signals another neuron is called an interneuron.
Neuropathic pain	Chronic pain resulting from injury to the nervous system. The injury can be to the central nervous system (brain and spinal cord) or the peripheral nervous system (nerves outside the brain and spinal cord).
Neurostimulator	Consists of a battery and a programmable computer chip and is most commonly implanted in the anterior chest wall just below the collarbone. The leads are connected via an extension wire that runs under the skin of the head, neck and shoulder to the neurostimulator.
Neurosurgeon	A neurosurgeon deals with various surgical operations to do with the nervous system, which encompasses the spinal cord, brain, skull and peripheral nerves. They will play a part in both the operative and non-operative treatment of patients, ensuring that excellent patient care is offered.
Neurosurgery	Surgery treating the central nervous system, peripheral nervous systems and spinal column diseases amenable to surgical intervention. Neurosurgical conditions include primarily brain, spinal cord, vertebral column and peripheral nervous system disorders.
Non-maleficence	The minimisation of harm to others.
Observational study	A study in which the investigators do not manipulate the use of, or deliver, an intervention (e.g. do not assign patients to treatment and control groups), but only observe patients who are (and sometimes patients who are not as a basis of comparison) exposed to the intervention, and interpret the outcomes.
Opportunity cost	The amount that could be spent on alternative healthcare strategies if the health technology in question was not used.
Outcomes	Components of patients' clinical and functional status after an intervention has been applied.
Outlier	An observation differing so widely from the rest of the data as to lead one to suspect that a gross error may have been committed.
p value	In hypothesis testing, the probability that an observed difference between the intervention and control groups is due to chance alone if the null hypothesis is true.
Pallidotomy	A surgical operation / ablative procedure performed on the abnormally hyperactive deep brain nuclei in the globus pallidus to destroy it. The purpose of this operation is to relieve involuntary movements or muscular rigidity, as, for example, in Parkinson's disease.
Paralysis	Loss of voluntary movement (motor function). Paralysis that affects only one muscle or limb is partial paralysis, also known as palsy; paralysis of all muscles is total paralysis, as may occur in cases of botulism.
Parkinson's disease	Parkinson's disease is the most common neurodegenerative movement disorder. It is an adult-onset, chronic, disabling, progressive disease, the primary risk factor for which is increasing age. Parkinson's disease is caused by degeneration of dopamine-producing neurons in the substantia nigra leading to progressive dopaminergic deficiency. It is characterised by four cardinal motor symptoms: resting tremor, rigidity, bradykinesia and postural instability. Onset is usually asymmetric, gradually spreading to the contra-lateral side with disease progression. Non motor symptoms, unrelated to dopamine deficiency, are common particularly as disease advances.
Pathology	The anatomic and physiological deviations from the normal that constitute disease or characterize a particular disease.
Patient selection bias	A bias that occurs when patients assigned to the treatment group differ from patients assigned to the control group in ways that can affect outcomes, e.g. age

	or disease severity.
Peer review	The process by which manuscripts submitted to health, biomedical, and other scientifically oriented journals and other publications are evaluated by experts in appropriate fields (usually anonymous to the authors) to determine if the manuscripts are of adequate quality for publication.
Perioperative	Relating to, occurring in, or being the period around the time of a surgical operation.
Postoperative	Relating to, occurring in, or being the period following a surgical operation.
Preference	Preference is a generic term and a concept that refers to the desirability of a health outcome. Both utility and value are special cases of the general term/concept of preference.
Prevalence	The number of people in a population with a specific disease or condition at a given time, usually expressed as a proportion of the number of affected people to the total population.
Probabilistic sensitivity analysis (PSA)	A type of sensitivity analysis where probability distributions are applied to a plausible range of values for key parameters to capture uncertainty in the results. A Monte Carlo simulation is performed and a probability distribution of expected outcomes and costs is generated.
Quality of life (QOL)	See **Health-related quality of life**.
Quality-adjusted life year (QALY)	A unit of healthcare outcomes that adjusts gains (or losses) in years of life subsequent to a healthcare intervention by the quality of life during those years.
Refractory	Not yielding, or not yielding readily, to treatment.
Refractory symptoms	A refractory symptom is one that cannot be adequately controlled despite aggressive efforts to identify a tolerable therapy that does not compromise consciousness.
Relative risk (RR) (risk ratio)	The ratio of (statistical) risk in the intervention group to the risk in the control group. A relative risk of one indicates no difference between comparison groups. For undesirable outcomes a RR that is less than one indicates that the intervention was effective in reducing the risk of that outcome.
Reliability	The extent to which an observation that is repeated in the same, stable population yields the same result (i.e. test-retest reliability).
Risk assessment	The qualitative or quantitative estimation of the likelihood of adverse effects that may result from exposure to specified health hazards or from the absence of beneficial influences.
SD	See **Standard Deviation**.
Selection bias	Error due to systematic differences in characteristics between those who are selected for study and those who are not.
Sensitivity analysis	A means to determine the robustness of a mathematical model or analysis (such as a cost-effectiveness analysis or decision analysis) that tests a plausible range of estimates of key independent variables (e.g. costs, outcomes, probabilities of events) to determine if such variations make meaningful changes the results of the analysis.
Standard deviation (SD)	A measure of the dispersion of a set of data from its mean.
Statistical significance	Statistical significance: a conclusion that an intervention has a true effect, based upon observed differences in outcomes between the treatment and control groups that are sufficiently large so that these differences are unlikely to have occurred due to chance, as determined by a statistical test.
Stereotactically	A method in neurosurgery and neurological research for locating points within the brain using an external, three dimensional frame of reference to enable the precise localisation of a tissue.
Subthalamic nucleus (STN) DBS	The primary target for DBS indicated for tremor, dyskinesia, rigidity, bradykinesia, akinesia, speech difficulties and freezing in the 'off' state. It is the most common

	target of DBS for Parkinson's disease.
Subthalamotomy	Ablative procedure that involves permanent, destructive lesioning of abnormally hyperactive deep brain nuclei in the subthalmic nucleus.
Systematic review (systematic overview)	A form of structure literature review that addresses a question that is formulated to be answered by analysis of evidence, and involves objective means of searching the literature, applying predetermined inclusion and exclusion criteria to this literature, critically appraising the relevant literature, and extraction and synthesis of data from the evidence base to formulate findings.
Technology assessment	See **Health Technology Assessment**.
Thalamotomy	Ablative procedure that involves permanent, destructive lesioning of abnormally hyperactive deep brain nuclei in the thalamic nucleus.
Time horizon	The time span used in the assessment that captures the period over which meaningful differences between costs and outcomes between competing technologies would be expected to accrue.
Tornado plot	Diagrammatic display of the results of one-way sensitivity analysis. Each bar represents the range of change in model results when the parameter is varied from its minimum to maximum values.
Treatment Abroad Scheme (TAS)	The TAS (E112 application form) is operated by the Health Service Executive (HSE) and enables patients to receive treatment in another member state if they cannot be given this medical care in Ireland or within the time normally necessary for obtaining that treatment.
Unilateral stimulation	The neurostimulator devices are available as either single (unilateral stimulation) channel or dual (bilateral stimulation) channel devices. For unilateral stimulation the testing leads are inserted into one side of the basal ganglia of the brain.
Univariate sensitivity analysis	Vary one critical component of the calculation at a time by a meaningful amount.
Utility	In economic and decision analysis, the desirability of a specific level of health status or health outcome, usually expressed as being between zero and one (e.g. death typically has a utility value of zero and a full healthy life has a value of one).
Value	A cardinal measure of the preference for, or desirability of, a specific level of health status or a specific health outcome, measured under certainty.
Variable	Any quantity that varies. A factor that can have different values.
Variance	A measure of the variation shown by a set of observations, defined by the sum of the squares of deviations from the mean, divided by the number of degrees of freedom in the set of observations.
Ventralis intermedium (VIM) in the thalamus	The primary target for DBS used in patients with predominantly severe and disabling tremor. It is now rarely used in Parkinson's disease as it has been shown that other symptoms continue to progress, causing significant disability not controlled by this treatment.

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