Cost-Effectiveness Analysis of Deep Brain Stimulation in Patients with Parkinson's Disease in Japan

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OBJECTIVE: **Deep brain stimulation (DBS) is an effective surgical option for treating Parkinson's disease (PD). DBS is invasive, with a high initial cost. In Japan, questions have been raised about its cost-effectiveness and the resulting improvements in outcome. The aim of this study was to evaluate the cost-effectiveness of DBS for PD in Japan, particularly whether early or late DBS is more cost-effective.**

METHODS: **We used a Markov cohort simulation to follow the clinical course of DBS for PD. We conducted a survey to capture QOL scores among healthy Japanese volunteers. Transition probabilities were estimated from randomized clinical trials. We determined direct medical costs from the perspective of the Japanese health care system. Outcomes were assessed as quality-adjusted life years. We conducted univariate and probabilistic sensitivity analyses.**

RESULTS: **DBS costs an additional 10.3 million Japanese yen (US$85,100; exchange rate on October 28, 2015 was 121 yen to $1) for a gain of 3.2 quality-adjusted life years. The incremental cost-effectiveness ratio was 3.1 million yen ($25,600). The incremental cost-effectiveness ratio was 8.5 million yen ($70,200) for early DBS, 3.1 million yen ($25,600) for intermediate DBS, and 3.3 million yen ($27,200) for late-stage DBS.**

CONCLUSIONS: **Our model suggests that DBS is cost-effective in the Japanese health care system. DBS is more cost-effective if performed in the intermediate rather than early or late stages of PD.**

INTRODUCTION

Parkinson's disease (PD) affects more than 4 million people in the world, and 9 million people are expected to suffer from it by 2030.[1] After Alzheimer disease, PD is globally the second most common neurodegenerative disorder.[2] In Japan, the number of patients diagnosed with PD was estimated to be approximately 139,000 in 2008.[3] PD is a progressive disease, characterized by tremor, rigidity, bradykinesia, and postural disturbances. These motor symptoms can initially be controlled with levodopa and other dopaminergic drugs. However, over the longer term, medical treatments lose their efficacy and patients develop such complications as motor fluctuations.[4] Because of increased disability, motor complications, and the risk of falls, PD significantly influences quality of life (QOL) as the disease progresses.[5-8]

With technologic advances, surgical treatments have been developed to deal with these long-term motor complications. Deep-brain stimulation (DBS), which requires implanting electrodes to stimulate specific areas of the brain, is an effective surgical option for improving mobility and reducing involuntary movement.[9-16] DBS has been approved by Japan's Ministry of Health, Labour and Welfare for use in PD patients where medical treatment provides insufficient symptom control. The United Kingdom National Institute for Health and Clinical Excellence

Key words
- Cost-effectiveness
- Deep brain stimulation
- Parkinson's disease
- QOL scores
- Markov model
- Quality-adjusted life-year

Abbreviations and Acronyms
DBS: Deep brain stimulation
H&Y: Hoehn and Yahr
ICER: Incremental cost-effective ratio
PD: Parkinson's disease
QALY: Quality-adjusted life-year
QOL: Quality of life

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(NICE) has also recommended the use of DBS for patients with motor complications that cannot controlled by medical treatment.[17] In a recent study of patients with severe symptoms, DBS gave better results when performed at a relatively early stage of PD than later.[18,19] DBS has a high initial cost; the cost of bilateral implantations is approximately 3.6 million yen (US$29,700; the exchange rate on October 28, 2015 was 121 yen to $1). DBS is invasive, and it may therefore have a negative long-term impact on QOL for PD patients, as well as creating an economic burden on the health care system. As yet, however, no economic evaluation of DBS has been reported for Japan. The aim of the present study was to evaluate the cost-effectiveness of DBS for PD in Japan and determine whether early or late DBS is more cost-effective.

METHODS

Model Structure

From the perspective of the Japanese health care insurance system, we developed a Markov model using TreeAge Pro 2014 software (TreeAge Software, Inc., Williamstown, Massachusetts, USA) to assess the cost-effectiveness of DBS compared with medical treatment alone. That model is widely used in economic evaluations when assessing decision problems, and it is also the predominant methodology used to determine cost-effectiveness for PD.[20] The stochastic model structure appears in Figure 1. Markov models assume that a patient is always in one of a finite number of discrete health states—called Markov states. All events are represented as transitions from one state to another. We used the Hoehn and Yahr (H&Y) scale[21] to indicate the symptoms of PD progress in the model. That scale involves a simple staging assessment, which evaluates the severity of motor symptoms, progressing from H&Y stage 1 to H&Y stage 5. Our model included medical therapy being able to provide sufficient symptom control, which was measured by the percentage of symptom control during a waking day: symptoms 0%–25% of the time (ON, controlled) or 26%–100% (OFF, uncontrolled). The model also included adverse events and death.

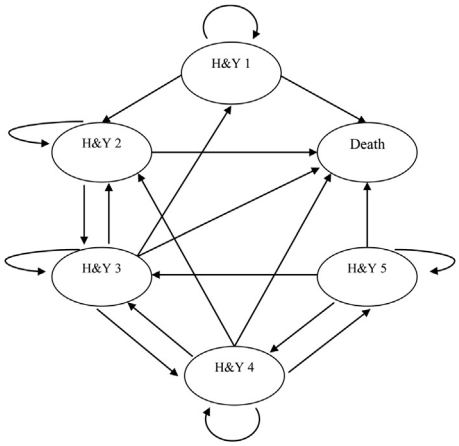

Figure 1. Structure of Markov model. The treatment benefits of deep-brain stimulation are reflected in improved disability level as evident in a reduction in the H&Y stage from 3–5 to 1–3. The model includes medical therapy being able to provide sufficient symptom control, as measured by the percentage of symptom control during a waking day: symptoms 0%–25% of the time (ON, controlled) or 26%–100% (OFF, uncontrolled) and adverse events.

The time horizon of the analysis was 10 years, which we considered sufficiently long to observe a therapeutic effect. Our model patient was a 60-year-old Japanese male. The cycle length was 6 months. The Markov model assumes that PD patients undergoing medical treatment at the various H&Y stages enter the model at treatment initiation. The treatment benefits of DBS, as evident in improved disability level, were reflected in the H&Y stage decreasing from 3–5 to 1–3. Our model also included improvement in symptom control as a result of DBS, which was reflected in a change from the uncontrolled (OFF) to controlled (ON) state. In the first cycle of the DBS arm of the study, the above changes indicated improved disability level and symptom control. In the first cycle of the medical treatment arm and in subsequent cycles of both arms, patients could remain in the same stage or transit to the next H&Y stage with worse symptom control.

To evaluate the cost-effectiveness of DBS in early or later stages of PD, the initial distribution was established in 3 scenario analyses: 1) early stage, defined as patients in H&Y stage 3 with uncontrolled symptoms; 2) intermediate stage, defined as patients in H&Y stage 4 with uncontrolled symptoms, which was the base case; and 3) late stage, defined as patients in H&Y stage 5 with uncontrolled symptoms.

Transition Probabilities

The probability of transition from one health state to another was estimated using clinical trial data. We employed beta uncertainty distributions. We assumed no prior information about any of the transition probabilities and selected a uniform base value. We calculated the probabilities using the following equation, based on Bayes' theorem:

Transition probability (θ) is distributed as Beta (a, b) = Beta (n + 1, n − x + 1)

a, b: parameters of Beta distribution

n: number of patients transiting from health state A to B

x: number of patients starting at health state A

Posterior mean θ = a/a + b

Posterior distribution = $ab/(a + b)^{-2}$ (a + b + 1)

The transition probability (θ) was calculated for each 6-month period using the following equation, where the parameters of the Beta distribution were obtained from clinical data for the 6-month period:

Annual transition probability = − Beta (a, b) / the applicable time period

P (transition probability per 6-month period) = 1 − e ^ (− P (annual transition probability) × 6/12)

Using the H&Y scale, Tanei et al.[22] reported an improvement in disability level after DBS treatment for Japanese PD patients. We