Cost-effectiveness of neurostimulation in Parkinson's disease with early motor complications

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Cost-Effectiveness of Neurostimulation in Parkinson’s Disease With Early Motor Complications

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ABSTRACT: Background: Recent research efforts have focused on the effects of deep brain stimulation of the subthalamic nucleus (STN DBS) for selected patients with mild-to-moderate PD experiencing motor complications. Objectives: We assessed the cost utility of subthalamic DBS compared with the best medical treatment for German patients below the age of 61 with early motor complications of PD. Methods: We applied a previously published Markov model that integrated health utilities based on EuroQoL and direct costs over patients’ lifetime adjusted to the German health care payer perspective (year of costing: 2013). Effectiveness was evaluated using the Parkinson’s Disease Questionnaire 39 summary index. We performed sensitivity analyses to assess uncertainty.

Results: In the base-case analysis, the incremental cost-utility ratio for STN DBS compared to best medical treatment was 22,700 Euros per quality-adjusted life year gained. The time to, and costs for, battery exchange had a major effect on the incremental cost-utility ratios, but never exceeded a threshold of 50,000 Euros per quality-adjusted life year.

Conclusions: Our decision analysis supports the fact that STN DBS at earlier stages of the disease is cost-effective in patients below the age of 61 when compared with the best medical treatment in the German health care system. This finding was supported by detailed sensitivity analyses reporting robust results. Whereas the EARLYSTIM study has shown STN DBS to be superior to medical therapy with respect to quality...
of life for patients with early motor complications, this further analysis has shown its cost-effectiveness. © 2016 International Parkinson and Movement Disorder Society

Levodopa remains the mainstay of treatment for patients with Parkinson’s disease (PD). However, long-term treatment with L-dopa is accompanied with the occurrence of motor complications, which may considerably affect a patient’s daily activities and quality of life. During the past decades, surgical options have reemerged, and nonablative approaches such as deep brain stimulation of the subthalamic nucleus (STN DBS) have become additional treatment options in advanced stages of the disease. STN DBS is recommended for patients with advanced PD.1,2 Recently, clinical research has focused on younger patients (below the age of 61) with motor complications in earlier stages of the disease (H & Y I–III), and new results from a clinical phase III trial have shown favorable outcomes.3,4 STN DBS improved motor parkinsonian signs (measured by UPDRS III in OFF states), motor fluctuations and dyskinesia (measured by the UPDRS IV), and the ability to master activities of daily living (measured by the UPDRS II OFF); it also considerably improved the patients’ quality of life and reduced costs of medical treatment.4-7

New treatment options, however, may have new side effects, complications, and impediments and may also result in higher costs and resource use in the respective health care system. Therefore, systematic economic evaluations are indispensable to evaluate the effect of STN DBS on patients and assess the consequences for the health care system.

In the present study, the relationship between costs and improvements in quality of life were assessed using a cost-utility analysis and a cost-effectiveness analysis to justify additional costs associated with STN DBS for the German health care system. Compared to former cost-utility analyses that addressed patients with advanced PD,8-13 this study is the first to consider the cost utility of STN DBS in younger patients, often still participating in the workforce, at an earlier stage of the disease with just less than 3 years of motor complications by using data from a recent clinical trial.

Patients and Methods

We adapted a recently published Markov state-transition model for the application of STN DBS at an early stage of PD.8 Patients were either treated with best medical treatment (BMT) or additionally to BMT with STN DBS. The adapted model was based on data from a randomized, controlled trial with a 24-month follow-up (EARLYSTIM, 2006–2009) that included PD patients with an age between 18 and 60 years, disease duration of 4 years or more and with a disease severity rating below H & Y III on medication.5 All patients had suffered from motor complications for up to maximally 3 years. Detailed descriptions of the clinical trial have been published.3,4

Base-Case Analysis

We followed international guidelines for modeling.14,15 In the base-case analysis, we performed a cohort simulation using the most likely parameter values. A cycle length of 1 year and a lifelong analytic time horizon were chosen. To consider the German health care payer perspective, direct costs were obtained from a cost of illness study.16 Adaptations to the costs of STN DBS were calculated using data from the EARLYSTIM study.4 Furthermore, all costs were adapted to the year 2013 and presented in euros (EUR). Utilities were measured by the EuroQoL (EQ-5D) index with German tariffs and used to calculate quality-adjusted life years (QALYs). Effectiveness was measured using the Parkinson’s Disease Questionnaire 39 (PDQ-39) summary index.

To compare lifetime costs for STN DBS and BMT to gained QALYs, we calculated the incremental cost-utility ratio (ICUR) as (costs STN DBS – costs BMT) / (utilities STN DBS – utilities BMT). Additionally, we considered the incremental cost-effectiveness ratio (ICER) by calculating the costs per PDQ-39 summary index point gained.

To date, no official criteria exist to presume an intervention to be cost-effective in Germany. We considered a therapy to be cost-effective below a value of 50,000 EUR/QALY.17

Markov Model

The Markov model consists of six Markov states: H & Y OFF states I to V and a death state.8 In addition to these different OFF states, improvement under treatment was denoted by H & Y ON states. This model structure permitted a distinction between the natural progression of the disease and treatment effects. Transition probabilities describing the natural progression with H & Y OFF were based on a publication by Martilla and Rinne.18 Current costs and
utilities (EQ-5D index) and effectiveness (PDQ-39 summary index) were adapted to the H & Y ON stages, and data on the occurrence of motor complications were calculated by regression analyses using data from a German health care study. Both costs and health effects were half-cycle corrected and discounted with 3% p.a. to adjust for future values. Direct costs of the German health care payer perspective were used and adapted for the year 2013.

Mortality rates were obtained from the German statistical office for the year 2011 and adjusted by a PD-specific factor from Wermuth and colleagues. In addition, an STN DBS-specific mortality was considered.

Population

The population characteristics were derived from data of the EARLYSTIM study. The patients had received surgery, on average, at 52 years of age (standard deviation: ± 6.6), had experienced motor complications, on average, for 1.7 years, and were in the following states: H & Y OFF I (5%); H & Y OFF II (65%); H & Y OFF III (20%); and H & Y OFF IV (10%). In total, 52.6% of the patients were male.

STN DBS–Specific Costs

STN DBS–specific costs included costs for surgery and battery exchange, a reduction in drug costs and costs because of adverse events. The costs for bilateral electrode implantation, implantation of the neurostimulator (Activa devices), and hospital stay in the German health care system were 31,000 EUR. Battery exchange was assumed conservatively every 5 years. The costs for battery exchange were obtained from the diagnosis-related groups (DRG) system; thus, 15,000 EUR was considered. Changes in drug doses were derived from the EARLYSTIM study for the 24-month follow-up period, resulting in reductions of 57% in the first year and 39% afterward. Furthermore, the model considered inpatient and outpatient treatment based on the occurrence of adverse events. Data on adverse events related to STN DBS were extracted from the EARLYSTIM study and multiplied with DRG-specific costs for the treatment of adverse events. Thus, an increase in costs of 840 EUR for the first year and 250 EUR for the second year for adverse events of STN DBS–treated patients was calculated.

STN DBS–Specific Clinical Effects

Health-Related Quality of Life, Symptomatic Effects, and Motor Complications

Utilities were integrated by applying the EQ-5D index with German specific tariffs. Furthermore, clinical effectiveness was measured using the PDQ-39 summary index. Because no EQ-5D data for patients with early STN DBS were available, we estimated base-case parameters using the results of the regression analysis by Young and colleagues. Data of the EARLYSTIM study included the PDQ-39 summary index as the primary health-related quality of life (HRQoL) outcome. This was used to estimate the items of the EQ-5D and convert them by country-specific tariffs to the German EQ-5D index.

For patients treated with STN DBS, a reduction in quality of life attributed to side effects of surgery for 3 months directly after surgery was considered as a reduction of 80% for the first month and 50% for the second and third months after surgery. Therefore, a decrement of 0.074 QALYs in STN DBS-treated patients was calculated. Hereafter, quality of life improved in STN DBS patients compared with BMT by 0.09 QALYs for the first year and by 0.06 QALYs for the second year and afterward.

Utilities and effectiveness were adjusted according to the occurrence and severity of motor complications, which were improved following the treatment with STN DBS. Forty-one percent of the patients suffering from motor complications before surgery were free of them 1 year after surgery; 32% for these remained free after 2 years.

Sensitivity Analyses

Deterministic sensitivity analyses enable the examination of uncertainties in parameter choices on the one hand and the exploration of noncollected clinical data on the other hand. We therefore varied the following parameters in one-way sensitivity analyses (Table 1): discount rate, age, time until battery exchange, utility improvement, costs of adverse events, costs of battery exchange and surgery, mortality, and reduction rates for motor complications and utilities during the perioperative phase.

Drug costs, costs for surgery and battery exchange, and mortality rates varied by ±50%. The ranges for time to battery exchange were obtained from the literature. The parameters were varied by 2 years compared with the base-case scenario of changes every 5 years. The base-case parameter choices represented values of the implanted battery system from the EARLYSTIM study. Furthermore, parameter ranges for battery exchanges with the newly available rechargeable battery system had a time to exchange of 9 years. As suggested by the German Institute for Quality and Efficiency in Health Care (IQWiG), discount rates were varied between 0% and 10%. The patient’s age was controlled for values ±5 years and severity of disease by one H & Y stage up and down. In addition to the algorithm published by Young and colleagues, we used an algorithm to consider uncertainties in quality-of-life parameters by estimating the
EQ-5D using the UPDRS. Additionally, observational 12-month follow-up data from Valldeoriola and colleagues of 29 Spanish patients with advanced PD were integrated using an improvement in HrQoL of 0.221 QALYs.

**Statistical Analysis**

The parameter estimations and transformations for the Markov model were performed in Excel (Microsoft Corp, Redmond, WA), SAS (version 9.4; SAS Institute Inc., Cary, NC), and R software (version 2.15.1; R Foundation for Statistical Computing, Vienna, Austria). The Markov model was programmed in TreeAgePro 2014 (TreeAge, MA, USA).

**Results**

**Base-Case Analysis**

For a life-long time horizon, the mean discounted direct costs for patients with early PD were calculated to be 115,400 EUR/patient for patients treated with BMT and 151,800 EUR/patient for patients treated with STN DBS. For patients treated with BMT, the discounted quality-adjusted life expectancy were 12.25 QALYs for a life-long time horizon, whereas patients treated with STN DBS at the age of 52 years achieved 13.84 QALYs. Thus, an ICUR of 22,710 EUR/QALY for STN DBS compared with BMT was calculated.

Using the PDQ-39 summary index as an effectiveness measurement, a cumulative effectiveness of 1,670 points was obtained for patients treated with BMT and 1,270 points for patients treated with STN DBS. This resulted in an ICER of 89 EUR per PDQ-39 summary index point gained for patients treated with STN DBS compared with BMT. For detailed results of the cost-utility analysis, we refer to Table 2.

**Sensitivity Analyses**

The one-way sensitivity analyses resulted in ICURs ranging from 7,500 EUR/QALY to 45,700 EUR/QALY considering a life-long time horizon. The duration to battery exchange had a major effect on the ICUR, but never exceeded the threshold of 50,000 EUR/QALY. Furthermore, costs for battery exchange

**TABLE 1. Base-case and sensitivity analyses parameter values**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Base Case</th>
<th>Minimum</th>
<th>Maximum</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>52</td>
<td>47</td>
<td>57</td>
<td>4</td>
</tr>
<tr>
<td>Discount rate for cost and utility (%)</td>
<td>3</td>
<td>0</td>
<td>10</td>
<td>30</td>
</tr>
<tr>
<td>Time to battery exchange (years)</td>
<td>5</td>
<td>3</td>
<td>9</td>
<td>26.27</td>
</tr>
<tr>
<td>Changes in drug cost (EUR; average prediction: %)</td>
<td>First year: 57</td>
<td>±50%</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Afterward: 39</td>
<td>±50%</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Costs for adverse events (EUR)</td>
<td>First year: 840</td>
<td>±50%</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Afterward: 250</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Costs for battery exchange (EUR)</td>
<td>15,000</td>
<td>7,500</td>
<td>22,500</td>
<td>25</td>
</tr>
<tr>
<td>Costs for surgery (EUR)</td>
<td>31,000</td>
<td>15,500</td>
<td>46,500</td>
<td>25</td>
</tr>
<tr>
<td>STN DBS-specific mortality (%)</td>
<td>Male: 0.03</td>
<td>Male: 0.024</td>
<td>Male: 0.036</td>
<td>21-23</td>
</tr>
<tr>
<td></td>
<td>Female: 0.037</td>
<td>Female: 0.03</td>
<td>Female: 0.044</td>
<td></td>
</tr>
<tr>
<td>Initial population (H &amp; Y off) (%)</td>
<td>H &amp; Y I: 5</td>
<td>H &amp; Y I: 0</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>H &amp; Y II: 65</td>
<td>H &amp; Y II: 0</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>H &amp; Y III: 20</td>
<td>H &amp; Y III: 0</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>H &amp; Y IV: 10</td>
<td>H &amp; Y IV: 0</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Improvement of motor complications (% of patients got free of motor complications after surgery)</td>
<td>First year: 41</td>
<td>±50%</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Afterward: 32</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Utility improvement attributed to STN DBS (QALYs)</td>
<td>Young et al.</td>
<td>Valdeoriola et al., 0.221</td>
<td>4,13,29,31</td>
<td></td>
</tr>
<tr>
<td></td>
<td>First year: 0.09</td>
<td>Dams et al.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Afterward: 0.06</td>
<td>-estimation by PDQ-8: first year: 0.07, afterward: 0.04</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perioperative utility reduction measured by the EQ-5D index (QALYs)</td>
<td>0.074 for 3 months postsurgery</td>
<td>0.06</td>
<td>0.09</td>
<td>Expert opinion</td>
</tr>
</tbody>
</table>
and surgery, drug costs, and variations in improvement in motor complications resulted in changes between 15,000 and 30,000 EUR/QALY. Small influences with changes less than 8,000 EUR/QALY were observed for costs of adverse events, improvement in HrQoL, severity of disease, age, and mortality. The results of the one-way sensitivity analyses are shown in a Tornado diagram (Fig. 1).

A detailed report and discussion on uncertainties of the model structures and general assumptions were previously published.8 No changes were observed for uncertainties in transition probabilities. Furthermore, assumptions about the model structure resulted in small changes.

**Discussion**

We performed a decision analysis by adapting a previously published Markov model for PD.8 In the base-case analysis, we determined an incremental cost utility ratio of 22,700 EUR per QALY gained by using STN DBS instead of BMT in patients with PD suffering from early motor complications.

In sensitivity analyses, we examined the robustness of our lifetime model. We found that none of the parameter variations in these sensitivity analyses yielded an ICUR exceeding a threshold of 50,000 EUR/QALY (Fig. 1), and that parameter variations of the “time to battery exchange” had the greatest influence on the ICUR.

What do our findings mean? Our study adds information to the question whether DBS can be efficiently applied at an earlier time point than usually recommended in guidelines. Cost studies and other cost-effectiveness investigations suggest that an earlier use of DBS is more costly than drug treatment alone in PD patients. Such expenses can only be justified by gaining health advantages for the concerned patients. Our findings are important because we illustrated, for the first time, that the beneficial effects of DBS can be applied in early stages of PD for a generally accepted surplus price of 22,700 EUR per QALY gained.

**Internal Validation of Utility Estimates**

A current drawback in the evaluation of STN DBS is insufficient data for patients in early stages of PD undergoing surgery to calculate patient-level utility scores. Currently, six multiattribute instruments have been developed for the use in health-economic analyses (EuroQol EQ-5D Dimensions [EQ-5D], Health Utilities Index [HUI], Short-Form-6 Dimensions [SF6D], Assessment of Quality of Life [AQoL], 15 Dimensions [15D], and Quality of Well-Being [QWB]), all based on different descriptive systems and using different valuation methods.

The EQ-5D instrument is the most commonly used questionnaire to calculate QALYs, but only one study applied it to patients with advanced PD treated with STN DBS.13 No data on EQ-5D or other utility indices for PD patients treated with STN DBS in early PD stages are currently available. To overcome this obstacle, Young and colleagues developed an algorithm to map EQ-5D data from PDQ-39 data of 96 advanced PD patients receiving STN DBS.29 The PDQ-39 instrument is commonly used to assess HrQoL in patients with PD.

In our study, we used the algorithm by Young and colleagues29 for our base-case scenario to estimate the EQ-5D index and calculated QALY gains of 0.09 QALYs for the first year and 0.06 QALYs for the second year and afterward. To account for uncertainties, we considered all currently available evidence

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**TABLE 2. Base-case results and sensitivity analyses for the time horizon**

<table>
<thead>
<tr>
<th>Time Horizon (Years)</th>
<th>Strategy</th>
<th>Costs (EUR)</th>
<th>Utility (QALYs)</th>
<th>Incremental Costs (EUR)</th>
<th>Incremental Utility (QALYs)</th>
<th>ICUR (EUR/QALY)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lifetime (EQ-5D; base case)</td>
<td>BMT</td>
<td>115,400</td>
<td>12.25</td>
<td>36,400</td>
<td>1.60</td>
<td>22,700</td>
</tr>
<tr>
<td>1</td>
<td>BMT</td>
<td>2,400</td>
<td>0.37</td>
<td>30,300</td>
<td>0.01</td>
<td>3,135,600</td>
</tr>
<tr>
<td>5</td>
<td>BMT</td>
<td>22,500</td>
<td>4.05</td>
<td>35,000</td>
<td>0.35</td>
<td>101,900</td>
</tr>
<tr>
<td>10</td>
<td>BMT</td>
<td>47,700</td>
<td>5.77</td>
<td>37,500</td>
<td>0.73</td>
<td>51,400</td>
</tr>
</tbody>
</table>

Results of the cost-utility analysis for costs, incremental costs, incremental quality adjusted life years (QALYs) and incremental cost-utility ratios (ICUR). The base case consists of a lifetime horizon; a patient cohort aged 52 years in HY stages: HYoff I (5%), HYoff II (65%), HYoff III (20%) and HYoff IV (10%). Utility data using the EuroQol (EQ-5D) were estimated by the algorithm of Young et al.29 Effectiveness was measured by the Parkinson’s Disease Questionnaire 39 (PDQ-39) summary index. BMT: best medical treatment, STN DBS: deep brain stimulation of the subthalamic nucleus.

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**COST-UTILITY ANALYSIS FOR STN DBS IN EARLY PD**

Movement Disorders, Vol. 31, No. 8, 2016 1187
and evaluated the following scenarios in the respective sensitivity analyses:

1. Instead of the algorithm by Young and colleagues, we used an algorithm to derive the EQ-5D index based on the UPDRS by Dams and colleagues.\textsuperscript{31} Improvements of 0.07 QALYs for the first year and 0.04 thereafter were calculated. These were similar to the base-case parameters.

2. We used the UK EQ-5D index to take into account that Young and colleagues had established the algorithm using UK tariffs.\textsuperscript{29} Even though the predicted baseline values varied around 0.2 QALYs (0.8 for adjustments with German tariffs vs. 0.59 for adjustments with UK tariffs), differences between patients treated with STN DBS and BMT were similar. Differences in the predicted baseline values correspond to patients with H & Y ON 1.5 and 2.5, respectively.\textsuperscript{32} Both predictions seemed to be realistic; however, comparison with country-specific observational data is needed.

3. Finally, we used the EQ-5D data of the only available STN DBS study for patients with advanced PD. Valldeoriola and colleagues examined 29 patients and reported a difference of 0.221 QALYs between patients treated with STN DBS and BMT over a 12-month follow-up.\textsuperscript{13} Differences to our calculations might be explained by country-specific adaptations of the EQ-5D index or different effects of STN DBS in patients with early and advanced PD. In addition, the data of Valldeoriola and colleagues\textsuperscript{13} may not be reliable because of the limited sample size.

In conclusion of the extensive sensitivity analyses performed, the different scenarios never yielded an ICUR above the threshold of 50,000 EUR/QALY.

**External Validation**

To our best knowledge, no cost-utility analyses exist for STN DBS in patients in earlier stages of PD with motor complications. Published models evaluated STN DBS only for patients with advanced PD.\textsuperscript{9,33}

For Germany, two cost-utility analyses are available addressing treatment with STN DBS for patients with advanced PD.\textsuperscript{8,9}

Dams and colleagues evaluated the cost utility by comparing STN DBS to BMT.\textsuperscript{8} They concluded that STN DBS was cost-effective with an ICUR of 6,700 EUR/QALY for a life-long time horizon, where the costs were mainly driven by costs for surgery and battery exchange. Compared to our results for STN DBS at an earlier stage of the disease, the ICUR was very low. However, results are not directly comparable. First, cost adaptations were made to the years 2010 and 2013. Second, a recently introduced DRG for battery exchange was used, whereas in our former analyses, the DRG for a cardiac pacemaker exchange resulting in costs of 3,050 EUR was used.\textsuperscript{8}

Another recently published cost-utility analysis\textsuperscript{9} compared STN DBS for patients with advanced PD with continuous subcutaneous apomorphine and l-dopa/carbidopa intestinal gel (CSAI). The researchers concluded CSAI dominated STN DBS and therefore could be considered as an alternative treatment for...
patients with advanced PD, even though costs and utilities were nearly the same for both treatment options.9 Because CSAI is only licensed for patients with advanced PD, a comparison to STN DBS for patients with early PD would be merely academic.

In addition to these German studies, five international cost-effectiveness analyses were published for the health care system of the UK, Spain, and the United States (for a detailed overview of the results of former cost-effectiveness analyses, see Table 3).8-13

Eggington and colleagues and the National Institute for Health and Care Excellence compared treatment options of STN DBS and BMT over a time horizon of 5 years for the British health care system.11 Total costs of GB-£42,100 to GB-£68,970 for the treatment with STN DBS and GB-£28,100 to GB-£48,243 for the treatment with BMT were observed. Furthermore, utilities were reported to be 3.15 for the treatment with STN DBS and 2.20 for the treatment with BMT. Both costs and utilities were low compared to our results (EUR 151,800 and 13.85 QALYs for STN DBS and EUR 27,614 for BMT). Utilities were 0.7611 and 0.5401, respectively. Again, differences were based on a shorter time horizon, country-specific costs/utilities, and a different stage of the disease.

Valleoriola and colleagues evaluated the cost-effectiveness for the Spanish health care system.13 They chose a time horizon of 1 year and reported total costs of EUR 27,614 for the treatment with STN DBS and EUR 20,013 with BMT. Utilities were 0.7611 and 0.5401, respectively. Again, differences were based on a shorter time horizon, country-specific costs/utilities, and a different stage of the disease.

Tomaszewski and colleagues published a cost-utility analysis for the United States considering a lifetime horizon.12 They determined total costs of US-$452,000 for STN DBS and US-$417,000 for BMT. Utilities were 7.80 and 7.08, respectively. Compared to our results, costs and utilities were high even though incremental costs were similar and incremental utilities were lower. We integrated the parameter values used by Tomaszewski and colleagues into our model and received an ICUR of EUR 36,103 per QALY. This result was close to the result of Tomaszewski and colleagues with US-$49,194/QALY (around EUR 36,000 per QALY).

In conclusion, previous publications reported ICURs between EUR 6,677/QALY and a dominance of pharmacotherapy. As discussed in a previous article, differences in the ICURs of published cost-utility analyses were more likely a result of country-specific costs and utilities and variations in the severity of disease than of the model structure and transition probabilities.8

### Limitations

First, no long-term data for patients treated with STN DBS at a relatively early stage of disease exist. Therefore, the course of motor complications and quality of life (measured by the PDQ-39 summary index) were suggested to be linear, based on extrapolation of EARLYSTIM data and observational data from a published randomized, controlled trial examining STN DBS for patients with advanced PD.8 In addition, we fixed the effect of STN DBS on the improvement of quality of life to 4 years based on expert opinion. This resulted in utilities of 0.67 and an ICUR of 36,400 EUR/QALY for a life-long time horizon for patients treated with STN DBS.

Second, costs and utilities depended on the occurrence of motor complications and the severity of the disease rated by the H & Y scale. Given that drug

### Table 3. Base-case results reported in the literature

<table>
<thead>
<tr>
<th>Reference (Year of Costing, perspective)</th>
<th>Time Horizon (Years)</th>
<th>Country</th>
<th>Strategy</th>
<th>Costs</th>
<th>Utility (QALYs)</th>
<th>Incremental Costs</th>
<th>Incremental Utility (QALYs)</th>
<th>ICUR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Base-case analysis (this study)</td>
<td>Lifetime</td>
<td>Germany</td>
<td>BMT</td>
<td>EUR 115,400</td>
<td>12.25</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dams et al. (2010, health care provider perspective)</td>
<td>Lifetime</td>
<td>Germany</td>
<td>STN DBS</td>
<td>EUR 151,800</td>
<td>13.85</td>
<td>EUR 36,400</td>
<td>1.60</td>
<td>EUR 22,700/QALY</td>
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<td>Eggington et al. (2011, UK payer perspective)</td>
<td>5</td>
<td>UK</td>
<td>BMT</td>
<td>GB-£48,243</td>
<td>2.21</td>
<td>GB-£20,727</td>
<td>1.02</td>
<td>GB-£20,678/QALY</td>
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<tr>
<td>National Institute for Health and Care Excellence (1998, perspective of the NHS)</td>
<td>Lifetime</td>
<td>UK</td>
<td>STN DBS</td>
<td>GB-£68,970</td>
<td>2.21</td>
<td>GB-£20,727</td>
<td>1.02</td>
<td>GB-£20,678/QALY</td>
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<td>Valldeoriola and colleagues</td>
<td>Lifetime</td>
<td>Spain</td>
<td>BMT</td>
<td>EUR 133,174</td>
<td>11.62</td>
<td>EUR 6994</td>
<td>1.05</td>
<td>EUR 6677/QALY</td>
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<tr>
<td>Walter et al. (2014, payers perspective)</td>
<td>5</td>
<td>UK</td>
<td>BMT</td>
<td>GB-£28,100</td>
<td>3.14</td>
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<td>Tomaszewski et al. (2000, societal perspective)</td>
<td>Lifetime</td>
<td>US</td>
<td>BMT</td>
<td>US-$417,000</td>
<td>7.08</td>
<td></td>
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<tr>
<td>Valdeoriola (not reported)</td>
<td>1</td>
<td>Spain</td>
<td>BMT</td>
<td>EUR 20,013</td>
<td>0.5401</td>
<td></td>
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<tr>
<td>Walter et al. (2014, payers perspective)</td>
<td>Lifetime</td>
<td>Germany</td>
<td>CSAI</td>
<td>EUR 104,500.08</td>
<td>2.92</td>
<td>EU-£14,079</td>
<td>0.944</td>
<td>GB-£14,900/QALY</td>
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<tr>
<td>Dams et al. (2010, health care provider perspective)</td>
<td>Lifetime</td>
<td>Germany</td>
<td>STN DBS</td>
<td>EUR 105,737.08</td>
<td>2.85</td>
<td>EUR 1237.00</td>
<td>0.08</td>
<td>CSAI dominates DBS</td>
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<tr>
<td>Base-case results reported in the literature</td>
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</table>

Results of the cost-utility analysis for costs, incremental costs, incremental QALYs and ICUR: incremental cost-utility ratio; CSAI: continuous subcutaneous apomorphine and L-dopa/carbidopa intestinal gel.
costs might be influenced by motor complications, too, integrated improvement of motor complications and drug costs might lead to double-counting.

Third, differences in drug costs were integrated only for PD-specific medication. No data for adaptations of non-PD medications (e.g., antidepressants) were available for consideration in our model. Because of the non-neurological side effects of STN DBS, this might lead to an overestimation of direct costs for patients treated with STN DBS.

Fourth, a battery exchange every 5 years was assumed as the base-case scenario. Recently, a new rechargeable device has been introduced, which requests a battery exchange approximately only every 9 years. Considering additional costs for treatment with a rechargeable battery system, this may lead to surgery costs of 49,500 EUR and costs for battery exchange of 34,200 EUR. Adjustments attributed to these additional costs and considering a time horizon of 9 years resulted in an ICUR of 37,700 EUR/QALY. Furthermore, potential decreases in HrQoL attributed to the rechargeable battery system, (e.g., the time-consuming daily electric charging, the personal discomfort of recharging, etc.) were not taken into account and may lead to an overestimation of the effects of the rechargeable system. However, patients of the EARLYSTIM study were treated with a non-rechargeable battery system, and therefore 5 years to battery change with a nonrechargeable system was assumed as the base case scenario.

Finally, our cohort was not comparable to many other cohorts with respect to age: The average age at implantation was 52 years, which is at least 10 years earlier than in most of the German implantation centres. All patients still lived an active social life with a limited burden of disease; some of the patients were still working. Health costs in general have to be assumed to be lower in younger patients and, with a good motor effect, especially in this cohort, one might speculate whether this leads to more-pronounced changes than in elderly patients, who often have a multicausal need for health support.

Conclusions

Based on our decision-analytic cost-utility analysis, STN DBS should be considered to be cost-effective in younger patients with earlier stages of PD (H & Y I–III). An ICUR of 22,700 EUR/QALY was assessed for a life-long time horizon comparing STN DBS with BMT. The sensitivity analyses showed a major effect of time to battery exchange. Including values for the recently introduced rechargeable device system resulted in an ICUR of 37,600 EUR/QALY. Nevertheless, this system has not yet been used for PD patients with early motor complications treated with STN DBS. Therefore, data concerning the effects of the rechargeable device system are required. In addition, reliable data for the calculation of QALYs using different multiattribute instruments are urgently needed to provide trustworthy information on the denominator for an appropriate health economic evaluation of DBS in the future.

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References


