Cost-Effectiveness of Deep Brain Stimulation for Parkinson’s Disease

Lindsay Bockstedt, Medtronic, Inc.
Agenda

• Overview of Economic Burden of Parkinson’s Disease
• Deep Brain Stimulation
• Clinical Evidence
• Cost-Effectiveness Evidence
• Cost-Effectiveness for DBS in United States
• Where is CEA for DBS today?
• Lessons Learned
Costs Burden of Parkinson’s Disease (PD)

- Cost of PD escalates as the disease progresses, placing an economic burden on the healthcare system, society and patients themselves
- Cost estimates of PD vary country to country
  - The main drivers of the total direct cost of PD are hospitalisation and drug costs
  - The main drivers of total indirect cost are nursing care and productivity loss
  - In study of U.S. Medicare beneficiaries, PD patients had significantly higher adjusted annual health care expenses than beneficiaries without PD ($18,528 vs. $10,818 dollars)

Quality of Life for Patients with Parkinson’s Disease

- Burden of Parkinson’s disease is high – significant impact on quality of life
  - Impacts on activities of daily living (ADLs), self esteem, mental health
  - Levodopa treatment
- 19th of the leading 20 causes of disability adjusted life years (DALY)
- Diminished working capacity

Hirayama MS, Gobbi S, Gobbi LT, et al. Quality of life (QoL) in relation to disease severity in Brazilian Parkinson’s patients as measured using the WHOQOL-BREF. Arch Gerontol Geriatr. 2008;46(2):147-60
SF-36 Results of PD Patients Compared to General Population

RQL was significantly reduced for PD patients on all 8 dimensions of the SF-36 (physical functioning [PF], role limitations (physical problems) [RP], bodily pain [BP], general health [GH], vitality [VT], social functioning [SF], role limitations (emotional problems) [RE], and mental health [MH]).

Deep Brain Stimulation

• Since 1997, Deep Brain Stimulation (DBS) has been approved to treat the symptoms of essential and Parkinson's tremor
• DBS is an adjustable, reversible therapy using an implanted neurostimulator and lead(s) that electrically stimulates targeted areas of the brain
• DBS enables better control of primary symptoms of PD (tremor, rigidity, slowness) and dyskinesia
  – Improve quality of life
  – Offset costs as intended for patients with progressive PD
Clinical Evidence

• Motor function and activities of daily living significantly improves for DBS patients in short term and long term (5 yr) follow-up (Unified Parkinson’s Disease Rating Scale (UPRDS) II and UPDRS III)\(^1^\)-\(^7\)

• HRQOL significantly improved in DBS patients in short-term and long-term follow-up (PDQ-39, SF-36, EQ5D)

• Antiparkinsonian medications decrease in STN-DBS 30-80% after surgery\(^8^\)-\(^19\)

• Correlations between motor function improvement and medication reduction with quality of life improvements
Results of a Meta-Analysis

Meta analysis of literature from 1993-2004

- UPDRS III score: 52%
- Levodopa equivalent daily dose: 56%
- Dyskinesia: 69%
- Off time (duration): 68%
- Quality of life (PDQ-39): 34%

Cost and Resource Utilization of DBS

• Need to understand the cost/resource utilization components of DBS therapy and best medical therapy (BMT)
  – Changes within groups
  – Changes between groups

• DBS specific costs
  – Upfront implantation cost related to the hospitalization(s)
  – Programming frequency
  – Follow-up visits
  – Replacement frequency

• DBS and BMT costs
  – Antiparkinsonian medication
  – Standard of care/disease management
Cost and Resource Utilization Evidence

• Multiple comparisons of costs before and after DBS show that DBS significantly reduces the cost of PD care \(^{20-22}\).

• In a French cost study, the 6 month costs of PD decreased from €10,087 before surgery to €1,673 after surgery (\(p<0.0001\)) \(^{20-21}\).
  – The cost of the procedure including physicians’ visits, hospitalizations and device implant during 6 months was €47,330.

• In a German cost study, costs before DBS (€15,991±2,636) versus costs 2 years after DBS (€7,223±717) were significantly different (\(P<0.0001\)) \(^{21}\).
  – While treatments costs increase the first year, mainly due to surgery costs, treatments costs are reduced the second year (-54% versus pre-operative values).
Cost and Resource Utilization Reductions Seen with DBS Therapy Primarily Driven by Reduction in Medication

- The 6 month signification cost reduction seen in the French cost study primarily driven by changes in medication

- In German cost study, the average annual cost of antiparkinsonian medications significantly decreases post DBS compared with pre surgery (the first year after DBS): from €11,242 to €3,760

- Patients experienced a 32% reduction in antiparkinsonian medications the first year and a 39% reduction the second year

- When considering all treatments costs, STN-DBS pays off from the second year as motor symptoms improve significantly and antiparkinsonian medications are reduced
DBS Cost Utility Evidence

- Studies to date have estimated that DBS compared with oral medical therapy costs an additional £19,500 to £27,000 per QALY.\(^{28}\)

- Cost/QALY is lower than the £20,000 to £30,000/QALY threshold suggesting that DBS is a cost-effective treatment option in PD.
Evidence Reviews

• Health Technology Assessments
  – For patients with advanced PD, in the short-term, there is level 1b evidence, and level 3a in the long-term (5 years) for the use of bilateral STN-DBS
  – NICE, UK HTA concludes that “Current evidence of the safety and efficacy of deep brain stimulation for Parkinson’s disease appears adequate to support the use of the procedure”
  – The ICER value [of DBS compared with BMT] falls within an accepted range of cost effectiveness

• Meta Analyses
  – Consistent short-term and long-term improvements in PD symptoms and HRQOL are reported in clinical studies
  – Synthesis of the available literature indicates that STN DBS improves motor activity and activities of daily living in patients with advanced PD

• Literature reviews
  – The intervention obtaining the maximal improvement in global HRQoL, measured by means of generic and specific instruments, is bilateral STN DBS
  – The excellent response of subthalamic DBS on the PDQ-39 summary index is also confirmed by Kleiner-Fisman
U.S. DBS Cost Effectiveness Evidence

- Limited CEA evidence for DBS Therapy in the U.S.
- One CUA from 2001 estimates the incremental cost-effectiveness ratio (ICER) to be approximately $49,000/QALY\textsuperscript{24}
  - At time of analysis no utility weighted QoL or surgical costs of DBS were published
  - Modeled a 49% reduction in medication
  - Results driven by changes in QoL and medication reduction
- Why isn’t there a larger body of CEA evidence from a U.S. perspective?
  - Need/Environment?
  - Labeling?
FDA Labeling

- Bilateral stimulation of the internal globus pallidus (GP) or the subthalamic nucleus (STN) … is indicated for adjunctive therapy in reducing some of the symptoms of advanced, levodopa-responsive Parkinson's disease that are not adequately controlled with medication.

- Unilateral thalamic stimulation … is indicated for the suppression of tremor in the upper extremity. The system is intended for using patients who are diagnosed with Essential Tremor or Parkinsonian tremor not adequately controlled by medications and where the tremor constitutes a significant functional disability.
Stimulation Targets

- Subthalamic nucleus (STN) and globus pallidus interna (GPI) are stimulation targets for Parkinsonian tremor.
- STN stimulation is the target of choice (high efficacy and low energy consumption) in PD for the reduction of motor fluctuations and dyskinesias; the decrease in levodopa use enhancing its efficacy on dyskinesias.
- The GPI can be used as a target for Parkinson’s disease but evidence does not demonstrate antiparkinsonian medication reduction.
DBS Feasibility and Global Pivotal

• When feasibility study phase of initial PD clinical study began, we were not aware of medication reduction seen with STN-DBS
• Feasibility study quickly expanded into a global pivotal
• Medications were collected, but not rigorously enough to support a medication reduction claim since unaware of the medication reductions
• Subsequent studies (post-approval) will need to be submitted to support this claim
How Does the Labeling Impact the CEA of DBS in the U.S.?

• Pivotal study did not support a medication reduction claim for STN-DBS
• Medication reduction is the area where the largest health care resource utilization reduction occurs
• Similarly, reductions in medications correlated with improvements in QoL since substantially reduce dyskensia side effects of antiparkinsonian medications
• Labeling does not support claims regarding changes in medication reduction or quality of life improvement
  – ICER = ΔCosts/ΔQoL
• Prohibited from using CEA models that model changes in costs and QoL driven by medication reduction
  – Ability to demonstrate cost-effectiveness is hindered
Lessons Learned

• Strategic alignment with clinical and reimbursement/health economic teams
  – Proactively determine the areas of health resource utilization that will be affected by the therapies being studied
  – Collection of meaningful data from a payer perspective
• Budget for more pragmatic post-approval studies
  – Capture realistic changes in health care utilization
References

References

21. Impact of Deep Brain Stimulation (DBS) of the sub-thalamic nucleus (STN) on health-related quality of life (HRQOL) and healthcare resource use in advanced parkinsonian patients. 2003