Interpreting Health Economics Data in Parkinson's Disease

Richard Dodel

Professor, Department of Neurology, Philipps-University Marburg

Abstract

Demands from both healthcare authorities and hospital managers, make the estimation of the cost of Parkinson's disease (PD) and cost-effectiveness of treatments increasingly important. In 2005, the direct cost of PD in Europe was estimated as €10.7 billion per year, but this may only consist of approximately 60 % of the total costs associated with this condition. These values are being updated in 2010, but in 2005 the future costs were also estimated and were predicted to double by 2030 in developed countries globally. Recent data also show that important national differences affect the total cost of illness and the individual factors that make up the total. There are limited data available on the cost-effectiveness of treatment options for advanced PD, such as continuous dopaminergic stimulation (CDS) therapies or deep brain stimulation (DBS). Therefore, comparisons are difficult. DBS has been assessed in a small number of cost-effectiveness analyses, and these suggest that in the long term (i.e., when analyses assess costs over five years or more) DBS may be cost-effective. Incremental cost-effectiveness ratios for DBS range from approximately €10,000 per quality-adjusted life-year (QALY) to €50,000 per QALY, which would make DBS cost-effective according to World Health Organization definitions. Future work on the cost-effectiveness of CDS therapies for advanced PD will help to determine their role in future treatment algorithms.

Keywords

Parkinson's disease, cost-effectiveness, continuous dopaminergic stimulation therapies

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Correspondence: Richard Dodel, Department of Neurology, Philipps-University Marburg, Rudolf-Bultmannstr 8, 35039 Marburg, Germany. E: dodel@med.uni-marburg.de

There is a greater demand for cost-effectiveness data on pharmacological agents for many reasons – one major reason being the increasing number of countries with health technology assessment agencies that use cost-effectiveness data to aid their decision-making (such as the National Institute for Health and Clinical Excellence [NICE] in the UK and the Institute for Quality and Efficiency in Health Care [IQWIG] in Germany). There is therefore a greater need for healthcare professionals to become aware of the 'language' of economics.

Measurement of costs associated with healthcare are split into direct costs (drugs, inpatient care, other therapies, diagnostics and care, among others), indirect costs (unemployment, early retirement, etc., as a result of the disease) and intangible costs (dependency, psychological effects, pain, etc.). By their nature, intangible costs are difficult to measure and are mostly excluded from health economic evaluations.[1]

Health economic evaluations can be non-comparative cost of illness studies, which, for example, measure the cost of an illness to the whole of society. Alternatively, non-comparing cost-analyses may look at a specific aspect of management, such as the cost of magnetic resonance imaging (MRI) scans for patients with neurological conditions.

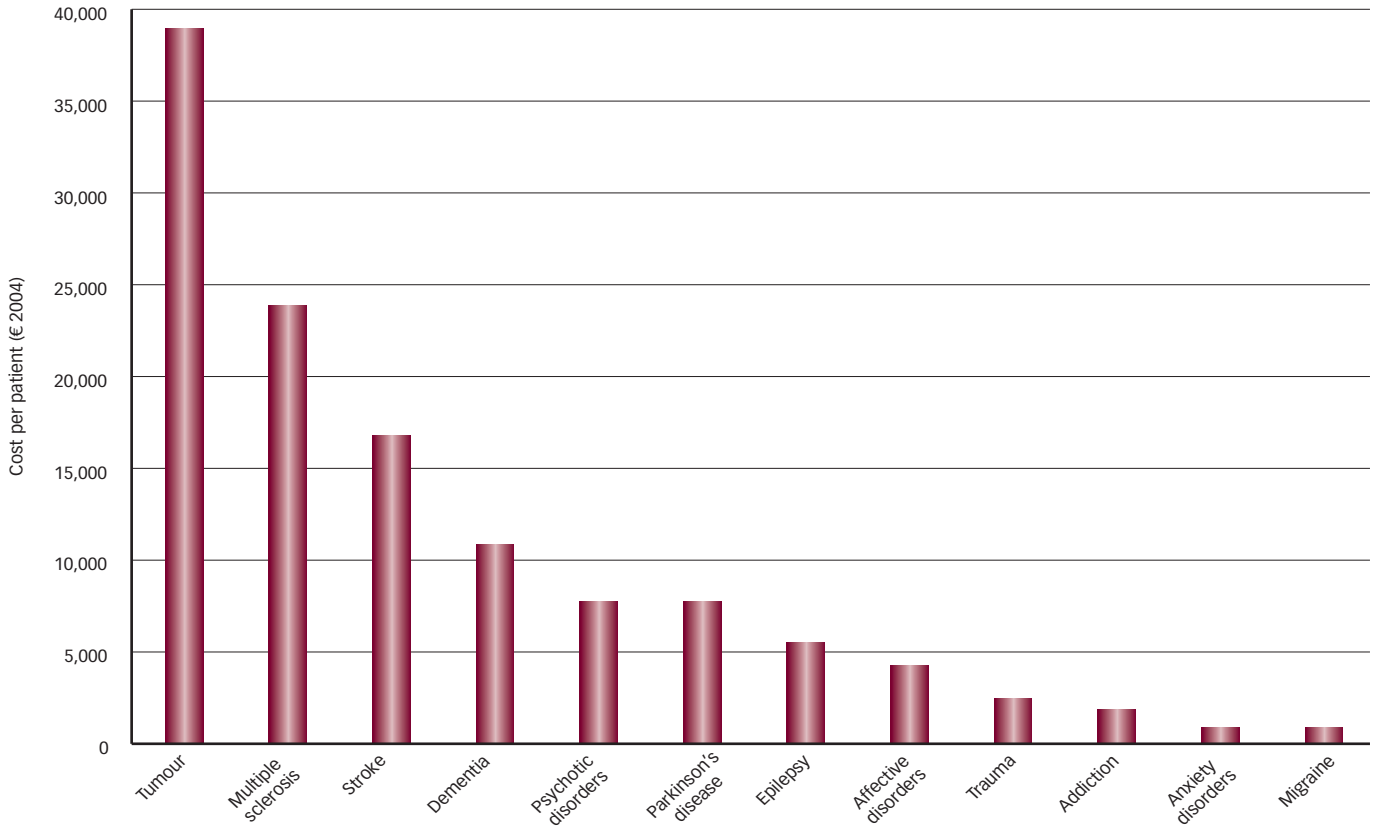
Comparative health economic analyses compare the cost of two or more alternatives. Such comparative analyses can be cost–cost analyses, cost–benefit analyses, cost–effect analyses or cost–utility analyses. Most health economic evaluations use cost–effect analysis, which calculates the cost-per-unit of effect (such as change in Unified Parkinson's Disease Rating Scale [UPDRS] score), or cost–utility analysis, which measures cost-per-utility unit (usually quality-adjusted life-years [QALYs]).

In this article, the cost of illness for Parkinson's disease (PD) is discussed, and the health economic data on treatment options for advanced PD, including continuous dopaminergic stimulation (CDS) treatment, are presented.

Cost of Illness of Parkinson's Disease

Of the 466 million people in Europe, 104 million have brain disorders (excluding brain disorders as a co-morbidity of other conditions), 51.2 million have a neurological disease and approximately 1.1 million (0.24 %) have PD (according to 2005 data).[2–4] An estimated associated total cost for PD across Europe was €10.7 billion per year.[3] This consisted of over €4.5 billion in healthcare costs and over €6.1 billion in direct non-medical costs, but this may be an under-estimation as it did not include indirect costs – these indirect costs could account for approximately 40 % of total costs. Compared to other brain disorders, PD is relatively expensive per patient (see *Figure 1*).[3] The number of cases of PD is set to increase by up to 25 % in many countries and by over 100 % in some of the world's most heavily

Figure 1: Cost Per Case of Different Brain Disorders in Europe[3]



Source: Reproduced with permission from John Wiley & Sons.[3]

Table 1: Socioeconomic Consequences of Dementia in Parkinson's Disease, as Measured in the European Cost of Illness Study (Data From Germany)

Characteristic	Dementia (MMSE ≤25)	No Dementia (MMSE >25)
Inpatient stay	17.5 %	10 %
Inpatient rehabilitation	18 %	5 %
Physician visits	9	8
Drug costs (€)	4,015	3,120
Quality of life (measured by EQ-5D)	56 %	63 %
Carer working	12 %	26 %
Carer with morbidity	46 %	26 %
Carer quality of life (measured by EQ-5D)	74 %	82 %

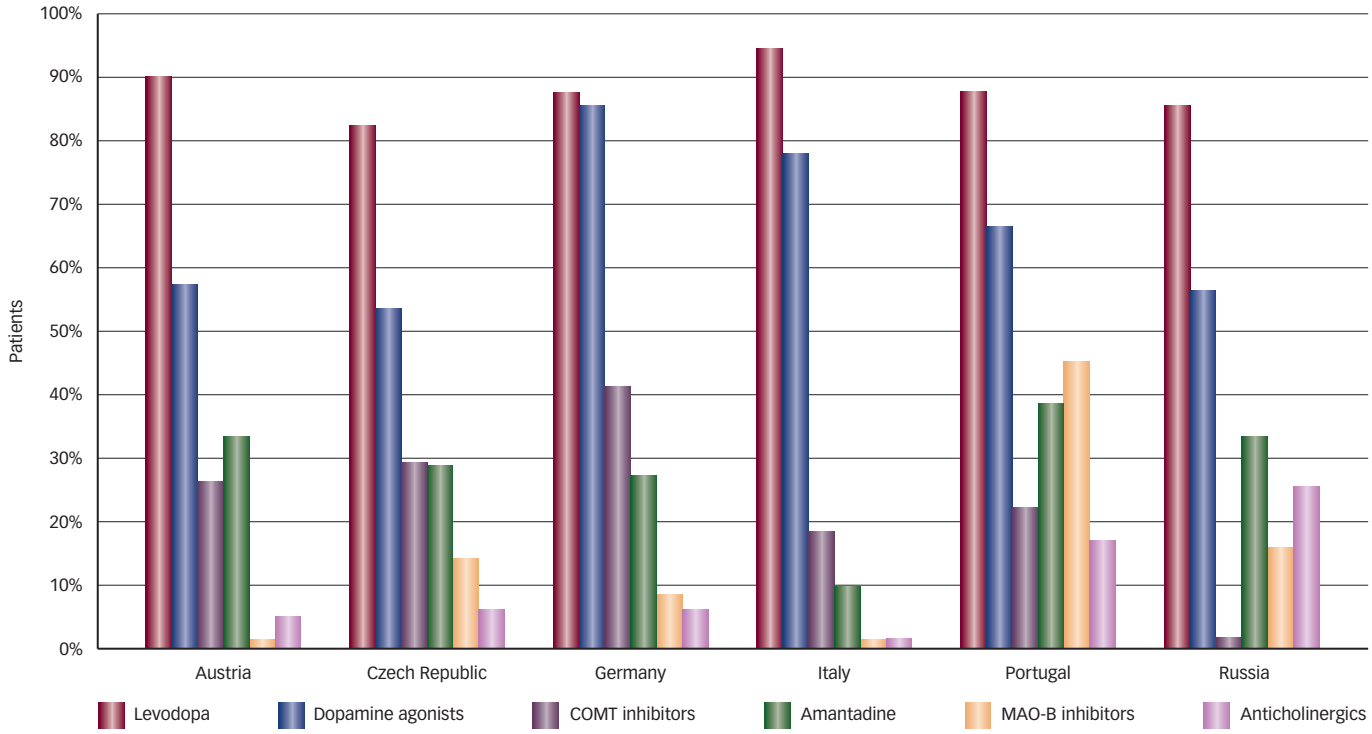
EQ-5D = European quality of life-5 dimensions; MMSE = mini mental state examination.

populated countries such as India and China by 2030[5] – this will result in an even greater financial impact in the near future.

A more recent European study has assessed the cost of PD in a survey of movement disorder units in Austria, the Czech Republic, Germany, Italy and Portugal (plus two non-EU countries, Russia and the US).[6–9] Costs per patient per year ranged from €2,620 in Russia to €9,810 in Austria, but in all countries there was a clear correlation between increasing cost and higher Hoehn and Yahr stage. The components of cost varied between countries – for example, inpatient costs constituted a greater proportion of costs in Germany and Portugal than in other countries, medication costs made up the largest proportion of costs in Germany but not in other countries and the costs of care accounted for a greater proportion of costs in the Czech Republic and Italy than in other countries – but indirect costs were consistent. Dopamine agonists are expensive drugs to use (compared with levodopa) and variations in PD medication used in different countries explain why medication costs make up different proportions of the total costs (see *Figure 2*). In Germany, dopamine agonists are used more frequently than in other countries (see *Figure 2*). However, these data reflect practices in the major specialist centres and in smaller centres (such as in rural areas) management practices may vary – for example, in Germany the use of dopamine agonists is considerably less frequent in the smaller centres than *Figure 2* would suggest.

When assessing the impact of complications on the costs of PD, data from the German participants in the European cost of illness study showed that dyskinesias doubled the cost per patient per year from €5,040 (for those with no dyskinesia) to €10,760, and motor fluctuations increased cost per patient per year from €6,040 to €11,040. Psychiatric diseases are known to increase the odds ratio (OR) of a patient with PD going into a nursing home (OR 2–2.5 with dementia; OR 17 with psychosis).[10,11] Nursing home care and other institutionalised care is expensive, and this again highlights the need to consider such patients, who may not always be included in cost analyses. In the European cost of illness study (German part), the costs associated with PD patients with dementia (mini mental state examination [MMSE] scores ≤25) were higher at all age groups than those associated with patients with MMSE scores >25. Factors that may have influenced this increased cost in patients with dementia are listed in *Table 1*. Interestingly, the presence of dementia had a minor impact (or in some cases no impact) on some direct costs, such as the number of visits to the physician and direct drug costs, whereas the wider impact on inpatient care and on the carers is greater. Many other motor and non-motor complications, such

Figure 2A: Parkinson's Disease Medication Use in Different Countries, in the European Cost of Illness Study[9]



as autonomic dysfunction, are likely to affect the cost of illness in PD but there is a lack of information on these effects. Assessment of the impact that individual domain scores (in the various symptom scales for PD) have on costs may be a useful exercise in future when assessing the cost of illness.

Cost-effectiveness Evaluation of Treatments

Focusing on the costs associated with treating advanced PD, and in particular on the cost-effectiveness of CDS treatments, more data are needed to draw firm conclusions.

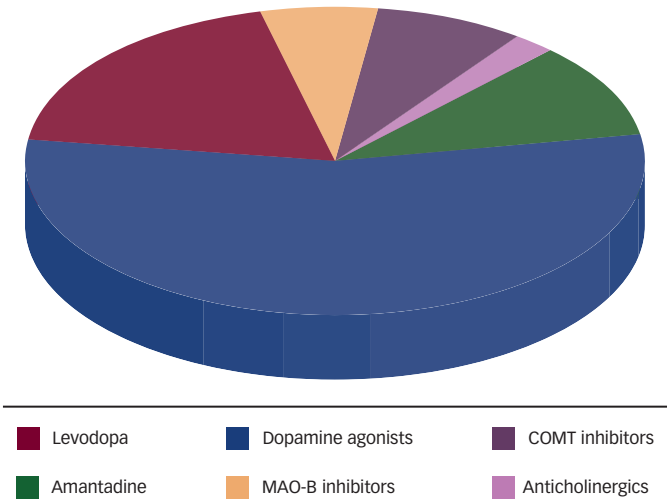
Duodopa®

Few data are available that investigated the cost of carbidopa/levodopa intraduodenal gel infusion (Duodopa®) treatment for advanced PD. Nyholm and co-workers evaluated the cost and outcome of Duodopa in a decision-analytic model with data from a crossover study with 24 PD patients.[12] Mean utility scores (measured using the 15D) were higher in the treatment group (0.77 versus 0.72) and expected two-year costs were Swedish Krona (SEK)562,000 (approximately €61,000). The cost per QALY varied between SEK456,000 and SEK6.1 million. Another study based on three patients suggested that compared with an annual treatment cost of €2,594 per patient with good control on oral medication, the first year of Duodopa treatment had a cost of €40,112 per patient with advanced disease, decreasing to €35,511 in subsequent years when the patient had stabilised on Duodopa treatment.[13] However, clearly more data are needed before an accurate assessment of the cost-effectiveness of Duodopa can be made.

Subcutaneous Apomorphine Infusion

Similarly, there are very few cost-effectiveness data with subcutaneous apomorphine infusion (APO). There is only one study that used appropriate analysis, and this compared the cost of APO and deep brain stimulation (DBS) in three patients with PD.[14] The estimated daily cost for APO was €200 and for DBS was €112 in these three patients (approximately €73,000 and €40,880 per year, respectively). The lower costs with DBS were evident even in the first year after surgery. However, no reasonable conclusions can be drawn from such a small number of patients, and as with Duodopa, more cost-effectiveness data are needed for APO treatment.

Figure 2B: The Relative Cost of Different Drugs[9]



COMT = catechol-O-methyl transferase; MAO-B = monoamine oxidase-B. Source: Reprinted with permission from Elsevier.[9]

Deep Brain Stimulation

There are better data from well-designed cost-effectiveness studies of DBS than the other CDS treatments, but these are still limited in their scope and it is difficult to draw firm conclusions. In a US-based analysis, DBS was compared with best medical treatment, but only direct (lifetime) costs were calculated.[15] Under base-case assumptions,

DBS provided an additional 0.72 QALY over best medical treatment at an additional cost of US$35,000 (US$417,000 for best medical treatment and US$452,000 for DBS). This gave an incremental cost-effectiveness ratio of US$49,194 per QALY. The base case assumed a 30 % improvement in quality of life (QoL) with DBS and any improvement at this level or higher would make DBS a cost-effective option. If QoL improvements with DBS were <18 % versus best medical therapy, DBS would not be considered cost-effective (>US$100,000 per QALY) and improvements of 18–30 % would result in questionable cost-effectiveness.[15] Cost-effectiveness of DBS would be achieved, based on this analysis, if QoL is improved by >30 %, there are no significant complications and if the battery in the DBS unit lasts for >5 years. However, there were drawbacks to this analysis – most importantly, at the time of the study there was no adequate evaluation of QoL and the estimates of QoL were based on UPDRS scores; there was no distinction between DBS of the subthalamic nucleus (DBS-STN) and DBS of the globus pallidus pars interna (DBS-GPi); and clinical data were also insufficient in 2001, so a Delphi method was used to estimate efficacy.[15]

A subsequent comparison of DBS and best medical treatment estimated that DBS produced an approximately 23 % improvement in QoL in the first year after surgery.[16] The cost of DBS (€18,456) was partially offset by reduced drug costs (€3,799 in patients receiving DBS and €13,208 with best medical treatment) and other medical costs (€1,280 in patients receiving DBS and €4,017 with best medical treatment). A resulting cost-effectiveness ratio was calculated as €34,389 per QALY.[16] The conclusion of the authors was that this incremental cost-effectiveness ratio was "within appropriate limits to consider subthalamic stimulation as an efficient therapy".[16]

In our group, we have conducted a cost-effectiveness comparison of DBS versus best medical treatment using a similar but more detailed model than previous studies (unpublished data). Our data indicate that DBS is not cost-effective in the first two years after surgery (incremental cost-effectiveness ratio of €408,607 per QALY and €68,499 per QALY in year one and two, respectively), but after five years or more, DBS is a cost-effective approach compared with best medical treatment (€25,205 per QALY after five years, €17,519 per QALY after 10 years and €12,039 per QALY after 20 years). However, it should be noted that there are limited data on the effects of DBS after 10 years and these long-term cost-effectiveness calculations used extrapolation from shorter-term data.

These data on DBS, although limited, do suggest that DBS is cost-effective, if using the World Health Organization definition, which is a cost-effectiveness ratio of €21,742–65,227 per QALY. In the UK, the NICE definition is somewhat stricter (€22,222–33,333 per QALY), but the most recent cost-effectiveness analyses of DBS also fall within this range. Unfortunately, there are no economic data to compare DBS with the other CDS therapies, and it is impossible to conclude on the cost-effectiveness of these other therapies.

Physiotherapy

It is important to acknowledge the role of non-pharmacological management of PD and, therefore, it is also important to consider the cost-effectiveness of such approaches. The recent ParkinsonNet trial of community-based physiotherapy included a cost-analysis.[17] Although outcomes were not changed with physiotherapy and QoL was not significantly improved, costs were reduced by approximately 20 % (cost calculations included the cost of physiotherapy, medication, consultation, day-hospital rehabilitation, hospital admissions, home care, informal care and the productivity loss of the patient's partner). If the cost-effectiveness ratio is calculated, physiotherapy cost is €39,600 per QALY. This would suggest that the cost-effectiveness of physiotherapy is marginal, but this trial ran for 24 weeks and it is possible that longer-term studies could provide more favourable outcomes and a more favourable cost per QALY.

Conclusions

Cost data on PD in Europe are not as comprehensive as might be expected, but the burden of care is great and set to increase in the next 20 years. Effective treatment for PD is expensive and direct costs are high. These increase as the disease progresses, but cost data on therapies for advanced PD are sparse. Indeed, it is currently impossible to make rational decisions on the cost-effectiveness of the CDS therapies, Duodopa, APO and DBS. There are few studies of these three CDS therapies and no comparisons of the cost of each therapy. As the data set on efficacy and QoL of CDS treatments increases, it may become possible to do more detailed cost-effectiveness comparisons, and initial data do suggest that, in the long-term, DBS is cost-effective. ■

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