Selected reviews of Economic Evaluations relating to Neuorology

Economic and human costs of restless legs syndrome
Reinhold T, Muller-Riemenschneider F, Willich S N, Bruggenjergen B; Pharmacoeconomics 2009; 27(4);267-279

Study Question: Restless legs syndrome (RLS) is a common and often underestimated neurological disorder, with a prevalence ranging from approximately 2.5% to 10% in Western industrialised countries. The aim of this study was to summarise the research findings on the human and economic costs associated with RLS in populations without any co-morbidities or potentially confounding health conditions. A further objective was to identify studies on the cost-effectiveness of RLS treatments. In order to do this, a systematic literature review was performed based primarily on MEDLINE, EMBASE, and Cochrane Library Data. Studies published before August 2008 were included if they assessed quality of life in patients suffering from RLS, determined total or patient-related costs attributable to RLS, and/or evaluated the cost-effectiveness of treatment options for RLS. Fifteen publications met all of the selection criteria and were included in the present review. Seven abstracts that focused on the economic burden of RLS and/or the cost-effectiveness of different treatment strategies in RLS patients were also included.

Patient Group: People with restless legs syndrome (RLS) and without any co-morbidities or potentially confounding health conditions. Patient data were taken from a systematic review of the literature (primarily from MEDLINE, EMBASE, and Cochrane Library Data). Studies were excluded if they concentrated on specific patient subgroups, investigated secondary RLS, or were published as narrative reviews.

Key Results: RLS was associated, in the included studies, with reductions in quality of life similar to those seen in patients with other chronic conditions. The cost-of-illness studies were heterogeneous but indicated that RLS was associated with a substantial economic burden, resulting in high direct and indirect costs to society. Based on these findings, the authors conclude that, although effective and cost-effective treatments appear to be available (e.g. pramipexole), further research is warranted, especially regarding the economic burden of RLS and the cost-effectiveness of available treatment options.

Teleradiology in neurosurgery: experience in 1024 cases

Study Question: The computer technology used in teleradiology has developed rapidly in the last decade. However, more sophisticated systems have cost more. Telephone consultation and teleradiology has already been shown to significantly improve outcomes by allowing early implementation of therapy in head injury patients. In addition, teleradiology probably has more impact in neurosurgery than in other medical disciplines, because neurosurgical services are mostly
concentrated in regional centres with long distances to peripheral hospitals. The aim of this study was to analyse the authors’ five-year experience in 1,024 emergency cases to evaluate the technical stability, reliability and cost of a simple analogue teleradiology system in neurosurgery.

**Patient Group:** 945 patients (1,024 neurosurgical procedures in seven referring hospitals in Germany) (median age 67 yrs; range 7-95 yrs) undergoing teleradiology between June 1995 and June 2000. The diagnoses on presentation were intracerebral haematoma (50%), trauma (27%), subarachnoid haemorrhage (4%), stroke (5%) and others (14%).

**Key Results:** Retrospective analysis showed that in 67% of cases admission and therefore ground-based transportation of the patients to the authors’ neurosurgical centre was not necessary for different reasons (moribund status, no surgical intervention required or no neurosurgical problem at all). If each patient had been transferred, then the potential savings for ground transportation were 340 € per case (with accompanying physician of the affiliated hospital) or 374 € per case (with accompanying experienced ICU physician), respectively. The total cost of the image transfer system for all eight hospitals was 96,000 €; this was amortised after 282 teleconsultations, which occurred after 15 months of usage. Based on these findings, the authors conclude that a simple teleradiology system in neurosurgery enables rapid and reliable telephone consultations, mainly on patients with trauma, stroke and intracerebral haematoma at low cost.

**The quality of life and economic burden of neuropathy in diabetic patients in Germany in 2002 - results from the diabetic microvascular complications (DIMICO) study**


**Study Question:** To analyse health-related quality of life (HRQOL) in patients with diabetic neuropathy (DN), and to describe resource utilization and annual costs associated with DN to evaluate its economic impact in Germany. The study uses national, multicentre, retrospective data and considers both the societal perspective and the perspective of the statutory health insurance (SHI). Patients were categorised into 5 severity groups: Group 1 - sensory-motor neuropathy without symptoms (N no S); Group 2 - sensory-motor neuropathy with symptoms (insensitivity, pain) (N with S); Group 3 - neuropathic foot, foot ulcer, foot deformities (FU); Group 4 - lower extremity amputation in the year 2002 (Amp 02); and Group 5 - lower extremity amputation before the year 2002 (Amp <02).

**Patient Group:** 185 Men and women aged 18 years or older, with type 1 or type 2 diabetes mellitus and DN diagnosed on or before 02 January 2002, and treated for DN in the year 2002, who were willing to give written informed consent (n=35 in group 1; n=47 in group 2; n=32 in group 3; n=24 in group 4; and n=47 in group 5). Patients who were pregnant in the year 2002 or participated in a clinical trial during that time were not allowed to enter the study.

**Key Results:** The majority of DN patients were severely impaired with regard to general physical HRQOL, while disease specific HRQOL decreased continuously with increasing DN severity. From the societal perspective, the average annual costs of DN per patient ranged from €431 in group 1 to €21,476 in group 5. The German statutory health insurance covered more than two thirds of the total costs of DN.
Trigeminal neuralgia treated with pregabalin in family medicine settings: its effect on pain alleviation and cost reduction

Study Question: The aim of the study was to assess the effect of pregabalin (PGB) on pain alleviation in patients with trigeminal neuralgia, and summarise the use of both health care and non-health care resources, and associated costs. The study was a secondary analysis of a prospective observational study of treatment of refractory NeP. Two patterns of PGB treatment were compared (add on and monotherapy), and compared in terms of pain (Short Form McGill Pain Questionnaire (SF-MFQ)), use of health care resources and productivity.

Patient Group: 65 pregabalin (PGB)-naive patients with neuropathic pain receiving PGB as monotherapy (n = 36) or combined with other drugs (n = 29) who were refractory to previous analgesia with chronic pain. The mean age of the patients was 56 years (standard deviation 14 years) and 60% were female.

Key Results: Treatment with pregabalin (PGB) was associated with a significant reduction in pain, total Short Form McGill Pain Questionnaire (SF-MFQ) reduction in PGB treated patients (-11.1, standard deviation 7.5, p<0.001) compared to baseline. PGB monotherapy was associated with a greater reduction in pain (SF-MFQ) -13.1 (standard deviation 8.1) compared with -8.8 (standard deviation 7.1) in PGB add-on (p=0.038). PGB treatment was associated with an additional cost of €174 in drugs, but these costs were offset by cost savings in non-pharmalogical therapies (-Euros259), medical visits and hospitalisations (-€324), ancillary tests (-€211), health care costs (-€621) and indirect costs (-€1210). The total cost saving in costs was -€1831, and there were no differences in total cost savings between PGB add-on and monotherapy. The authors concluded that PGB was effective as a treatment for trigeminal neuralgia and resulted in cost savings.

Cost-effectiveness analysis for trigeminal neuralgia: Cyberknife vs microvascular decompression

Study Question: To assess the cost-effectiveness of cyberknife radiosurgery (CKR) versus microvascular decompression (MVD) for patients with medically unresponsive trigeminal neuralgia. This was done through an observational, incidence-based, study undertaken at two hospitals in Italy. The study was undertaken from the hospital perspective.

Patient Group: Patients with medically unresponsive trigeminal neuralgia (TN) treated with MVD surgery and TN patients treated by CKR. Excluded were patients with typical pain, multiple sclerosis, <18 years of age, or follow-up <6 months.

Key Results: A total of 40 patients were enrolled in the study with 20 patients for both arms. The CKR group had a mean age of 74.2 years (12.8), range 40-88 years, 60% female. The MVD group had
a mean age of 61.9 years (9.7), range 41-75 years, 55% female. The age difference was significant (p=0.002). Fewer MVD patients had prior TN treatment (30% vs 40%). All patients ranked highly at baseline for BNI, but it was highest in the CKR group (85% in the V class; p=0.001). The cost of MVD was €6,641 per patient vs €4,389 in the CKR group. The difference of €2,253 is mostly explained by an average of 3.5 hours in the operating theatre for MVD compared with 70 min radiation for CKR and the cost of hospital stay for MVD patients. The two procedures appeared to be equally effective at 6 month follow-up, with a difference in resource consumption: CKR reducing hospital costs by an average of 34% per patient. The robustness of these results was confirmed in appropriate sensitivity analyses. The authors conclude that CKR was considered to be a cost-saving alternative compared with the surgical intervention.

**A cost-utility analysis of pregabalin in the management of peripheral neuropathic pain**


**Study Question:** Studies have shown the superior effectiveness of pregabalin compared with placebo (usual care) in the treatment of peripheral neuropathic pain. In the current health care environment, budgets are limited and so the development of new treatments is not based on efficacy and safety alone. Therefore, the aim of this study was to assess the cost per QALY of pregabalin in the management of peripheral neuropathic pain. In order to do this, pregabalin on top of "usual care" was compared with "usual care" alone, where usual care was defined as a mix of drug therapies, excluding anti-epileptic drugs (AEDs). A Markov model was developed to simulate the evolution of a patient cohort over one year, and applied cycles of four weeks. During each cycle, patients remained in one out of four possible states: severe, moderate or mild pain, and therapy withdrawal. The analysis was conducted from the perspective of the health care payer.

**Patient Group:** Patients with an existing diagnosis of peripheral neuropathic pain who are treated with either pregabalin on top of "usual care", or "usual care" one (usual care was defined as a mix of drug therapies, excluding anti-epileptic drugs [AEDs]). During each cycle of four weeks, patients remained in 1 out of 4 possible states: severe, moderate or mild pain, and therapy withdrawal. Patient data were obtained from a trial comparing usual care plus placebo to usual care plus pregabalin, at either 150, 300, or 300/600 mg/day (the latter depending on clearance of creatinin).

**Key Results:** Usual care resulted in a yearly cost of €6,200 compared to €5,984 for an all dose pregabalin-mix, meaning a cost saving of €216 per patient. Utility increase was 0.01 for the pregabalin-mix (QALY 0.510 usual care; 0.520 pregabalin-mix). Monte Carlo analysis showed cost savings were not significant. However, the utility gain, albeit small, was statistically significant. Based on these findings, the authors conclude that in the considered patient population, at the specialist level, pregabalin is at least cost neutral to current usual care (without AEDs) and offers a slight but significant increase in quality of life.
Study Question: The PROCESS (prospective, randomized, controlled, multicenter study of patients with failed back surgery syndrome) trial demonstrated that the addition of spinal cord stimulation (SCS) to conventional medical management (CMM) provides improved pain relief, health-related quality of life (HRQoL) and functional capacity of failed back surgery syndrome (FBSS) patients with chronic neuropathic back and leg pain. The authors aimed to summarise the generic health-related quality of life and costs at 6-months follow up using the PROCESS trial. Patients were assessed at baseline and at 3- and 6-months after starting treatment. Healthcare resource consumption data was collected prospectively for each patient and included screening and implant costs, medications, non-drug therapy and complications, and were costed at 2005 - 2006 prices using UK and Canadian figures. HRQoL was assessed in the trial using the patient completed the EuroQol-5D (EQ-5D). The arms of the trial were compared on an intention to treat (ITT) basis. Cost and EQ-5D data were analysed using ordinary least squares regression (OLS), and analysis of covariance used to estimate the difference in change in EQ-5D between the SCS and CMM groups from baseline to 3-months and from baseline to 6-months.

Patient Group: 100 patients, mean age 51 years approximately 50% male, recruited from in the UK, Canada, Italy, Spain, Australia, Israel, Belgium, Switzerland between April 2003 and June 2005. Patients were eligible if aged 18 years or older with leg pain of radicular origin with or without associated less severe back pain. Patients were randomised to either conventional medical management (CMM) (n=52) receive spinal cord stimulation (SCS) alongside CMM (n=48).

Key Results: The total average patient cost over 6 months of follow-up was £15,081 (CAN$19,486; €12,653) in the spinal cord stimulation (SCS) arm and £3573 (CAN$3994; €2594) in the conventional medical management (CMM) arm. The difference in mean cost, adjusted for differences in patient characteristics, between treatments was £11,373 (95%, confidence interval £9513, £13,234) or CAN$15,395 (95% confidence interval CAN$12,990, CAN$17,799) or €9997 (95% confidence interval €8435, €11,557), and statistically significant (p<0.001). The main cost drivers were hospitalisations, surgery, leads and hardware, although there were considerable cost savings in non-drug pain treatment. The baseline EQ-5D score for the CMM group was 0.18 (standard deviation 0.31) and 0.13 (standard deviation 0.30) in the SCS group. The EQ-5D scores improved in both arms, but the improvement in the SCS treated arm, adjusted for baseline values and patient characteristics, was significantly greater at 3 months (difference in change 0.25, 95% confidence interval 0.12, 0.37) and 6 months (difference in change 0.21, 95% confidence interval 0.09, 0.33). The authors concluded that compared to CMM alone, SCS increases health-related quality of life in patients with chronic back and leg pain with a neuropathic component following one or more surgeries at an increased cost to the health system over 6 months of follow up.