

Cost of Brain Disorders in Italy – A Review

Maura Pugliatti,^{1,2} Paola Cossu,¹ Patrik Sobocki³ and Ettore Beghi⁴

1. Department of Neuroscience, University of Sassari; 2. Department of Public Health and Primary Health Care, University of Bergen;
3. Department of Learning, Informatics, Management and Ethics, Karolinska Institute; 4. 'Mario Negri' Institute, Milan

Abstract

Brain disorders represent 35% of the total disease burden in Europe and 37% of the total disease burden in European regions with very low child mortality and low adult mortality; the latter group includes Italy. The negative socioeconomic impact of this burden is reflected in two fundamental issues: consumption of resources and state of health. In recent years, the European Brain Council (EBC), a co-ordinating council formed by European organisations and patient associations in neurological disorders, has encouraged and supported projects aimed at analysing the socioeconomic burden of brain disorders in Europe. Within the EBC, the pan-European study on Cost of Disorders of the Brain in Europe (CDBE) aimed at reporting the best possible estimates of the societal cost of 12 brain disorders (addiction, affective disorders, anxiety disorders, tumours, dementia, epilepsy, migraine and other headaches, multiple sclerosis, Parkinson's disease, psychotic disorders, stroke and trauma) based on the existing literature, using an *ad hoc* cost model. The aggregated results for Italy from the CDBE study are reviewed in this paper.

Keywords

Brain disorders, cost, societal perspective, health economics, Italy

Disclosure: The authors have no conflicts of interest to declare.

Acknowledgements: The authors gratefully acknowledge support from the European Brain Council on behalf of the Cost of Disorders of the Brain in Europe Study Group.

Received: 9 January 2009 **Accepted:** 23 July 2009 *DOI:* 10.17925/ENR.2009.04.02.120

Correspondence: Maura Pugliatti, Clinica Neurologica, University of Sassari, Viale San Pietro 10, 07100 Sassari, Italy. E: maurap@uniss.it

Brain disorders represent 35% of the total disease burden in Europe and 37% of the total disease burden in European regions with very low child mortality and low adult mortality; the latter group includes Italy.¹ The negative socioeconomic impact of this burden is reflected in two fundamental issues: consumption of resources and state of health.²

In recent years, the European Brain Council (EBC), a co-ordinating council formed by European organisations in psychiatry, neurology, neurosurgery, basic neuroscience and European patient associations, has encouraged and supported projects aimed at analysing the socioeconomic burden of brain disorders in Europe. These initiatives were ultimately intended to provide recommendations on research, teaching and awareness in public health.

Within the EBC, the pan-European study on Cost of Disorders of the Brain in Europe (CDBE) aimed at reporting the best possible estimates of the cost of 12 brain disorders (addiction, affective disorders, anxiety disorders, tumours, dementia, epilepsy, migraine and other headaches, multiple sclerosis, Parkinson's disease, psychotic disorders, stroke and trauma) based on the existing literature, using an *ad hoc* cost model.³ Other disorders of the brain, such as amyotrophic lateral sclerosis and neuromuscular and developmental disorders, were not included in the CDBE because of heterogeneity or lack of epidemiological and/or cost data.

In the CDBE, costs were assessed under a societal perspective. Included were healthcare costs regardless of who pays (the

individual, a private insurer or the public through taxes and social insurance), as well as costs outside the medical sector.

The aggregated results for Italy from the CDBE study have been published elsewhere⁴ and are reviewed in this article.

Materials and Methods

The methodological bases with regard to the epidemiological analyses and cost studies for this review have been described in detail elsewhere.¹ In brief, data from European cost-of-illness studies were collected. Direct medical and non-medical costs and indirect costs were included in the analysis. Intangible costs (i.e. the economic value of disease-related pain, suffering and loss of quality of life) could not be considered. All economic data were transformed to euros and were referred to 2004. The cost data were expressed in an international measure, the purchasing power parity (€PPP) exchange rate, which allows comparisons of economic data between countries by equalising the purchasing power of different currencies for a given basket of goods.

Cost Model

Three major sources of data were combined to predict the cost of these brain disorders: economic data, epidemiological data and international statistics. Disease-specific prevalence data and the annual cost of a case with the defined disease were collected separately. Bottom-up cost studies conducted at patient level were included to estimate the disease costs for 2004. The total cost of a

Table 1: Prevalence of 'Brain Disorders' in Italy

Brain Disorder	Men	Women	Total	Age Group (years)	References
Alcohol dependence (per 100)	1.1	0.7	–	15–65	16
Alcohol dependence (per 100)	0.3	0.2	–	14–90	16
Alcohol dependence (per 100)	–	–	0.1	18+	17, 18
Drug addiction (per 1000)	–	–	7–8	15–64	19
Depressive episodes (per 100)	–	–	6.5	18+	20
Bipolar type I disorder (mania) (per 100) ^a	0.7	1.9	1.3	15+	21
Bipolar type I disorder (mania) (per 100)	–	–	0.4	15+	21
Bipolar type II disorder (hypomania) (per 100) ^a	0.0	0.4	0.2	15+	21
Bipolar type II disorder (hypomania) (per 100)	0.0	0.2	0.1	15+	21
Cyclothymic disorders (per 100) ^a	0.2	1.6	0.4	15+	21
Cyclothymic disorders (per 100)	0.22	0.56	0.4	15+	21
Panic disorder (per 100)	–	–	1.4	15+	21
Generalised anxiety (per 100)	–	–	4–7	14+	21, 22
Social phobia (per 100)	–	–	3.7	14+	21, 22
Dementia (per 100) ^b	–	–	1.2	65–74	15
Dementia (per 100) ^b	–	–	4.5	75–84	15
Dementia (per 100) ^b	–	–	32.2	85+	15
Epilepsy (per 1000) ^c	3.5–7.1	3.2–5.2	3.3–6.2	All ages	23
Epilepsy (per 1000) ^c	–	–	4.5	5–14	23
Headache (per 100) ^a	35.5	46.2	46	7+	24
Headache (per 100) ^a	16.5–36.6	26.3–62.1	21.8–51	65+	24
Headache (per 100) ^a	19.9	28.1	23.9	11–14	24
Migraine (per 100) ^a	2.3–7.4	6.4–13.8	4.6–11	65+	24
Migraine (per 100) ^a	2.7	3.3	3.0	11–14	24
Tension-type headache (per 100) ^a	13.2	18.4	16–44.5	65+	24
Chronic headaches (per 100) ^a	2.5	6.0	4.4	65 +	24
Multiple sclerosis (per 100,000)	68–111	37–50	53–81	All ages	25
Multiple sclerosis (per 100,000) ^d	205–208	83–95	144–152	All ages	25, 26
Parkinson's disease (per 100,000)	–	–	168–315	All ages	27
Parkinson's disease (per 100,000)	–	–	165	35+	27
Parkinson's disease (per 100,000)	–	–	1,500	60+	27
Stroke (per 100,000)	79–150	42–80	–	25–44	28
Stroke (per 100,000)	868–4,864	548–1,114	–	45–64	28
Stroke (per 100,000)	5,095–9,172	3,416–7,038	–	65–84	28
Stroke (per 100,000)	12,237	10,178	–	85+	28

a. One-year prevalence; b. Alzheimer's disease: 50%; vascular dementia: 45%; other types: 5%; c. Active epilepsy (i.e. seizures and/or treatment in the preceding five years); d. Sardinia, insular Italy.

single disorder was thus the product of the prevalence and the cost per case. When Italian epidemiological and cost data were not available for an individual brain disorder, the values were predicted by the model by extrapolating data from other European countries. Prevalence data were stratified according to age, gender and disorder severity, if applicable. The validated model and prediction methods, as well as the sensitivity analysis to test the cost model, have been described in detail elsewhere.^{3,4,5} The key parameters employed in the costing model were tested in a sensitivity analysis.

Results

Prevalence

The CDBE study was based on the prevalence of the 12 brain disorders as estimated for 2004.¹ Estimates for Italy are reported in *Table 1*. No country-specific prevalence data were available at that time for illicit drug dependence and psychotic disorders, including schizophrenia and schizoaffective and delusional disorders.

For brain tumours and trauma, incidence data were also available. The overall age-standardised incidence rate of malignant brain tumour for Italy was estimated at 6.2 per 100,000 in men and 4.2 per 100,000 in

women.⁶ As for brain trauma, incidence rates were reported for the calendar year 1998 at between 250 and 314 per 100,000 in Romagna and Trentino, with peaks at one to four, 20–30 and ≥70 years of age.⁷

Based on these rates, in Italy the estimated total number of individuals with any of the 12 brain disorders considered was 12.4 million in 2004, i.e. more than 20% of the Italian population. The distribution of estimated cases with brain disorders in Italy by clinical condition is presented in *Figure 1*.

Cost per Patient

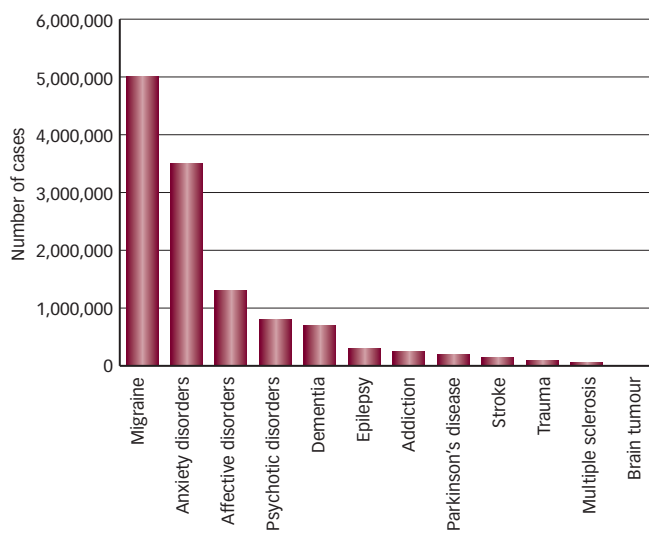
The cost per patient for each of the 12 brain disorders is shown in *Figure 2*. The highest cost was found for brain tumours and multiple sclerosis, whereas the lowest was for anxiety disorders and migraine.

Total Cost of Brain Disorders.

The direct, indirect and total costs of the 12 brain disorders in Italy, calculated in €PPP million, was estimated at €40.8 billion (see *Table 2*). The sensitivity tests gave an estimated cost range of €30.9–51.0 billion.

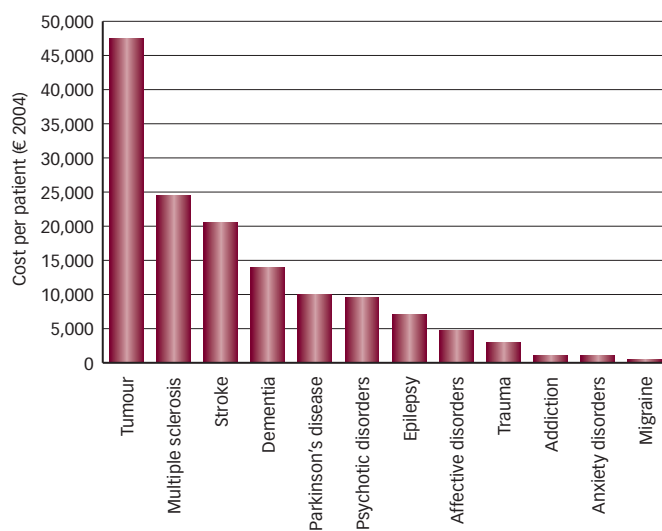
The most relevant sources of expenditure were psychotic/affective disorders and addiction (€18.7 billion), followed by neurological

Figure 1: Estimated Number of Cases of Brain Disorders in Italy, 2004^a



The number of cases of stroke and trauma is based on incidence data. Results on addiction omit nicotine dependence. With permission from Springer-Verlag.

Figure 2: Cost per Patient of Specific Brain Disorders in Italy, 2004^a



With permission from Springer-Verlag.

(€12.4 billion) and neurosurgical disorders (€1.0 billion). Dementia was the most expensive brain disorder (€8.6 billion). Among the neurological disorders, migraine was most costly (€3.5 billion), followed by stroke (€3.4 billion) and epilepsy (€2.3 billion). Direct medical costs were the leading cost item for psychiatric and neurosurgical disorders, direct non-medical costs for dementia and indirect costs for neurological disorders.

Cost of Brain Disorders by Resource Items

These data are presented in detail in *Table 3*. Direct medical and non-medical costs amounted to €17.1 billion and €11.1 billion, respectively, or 42 and 27% of total costs, respectively. Brain disorders represented 14% of the total direct healthcare costs in Italy, with 7% of the total drug sales attributed to the treatment of brain disorders.

Indirect costs were €12.6 billion (31%), mostly due to production loss for sick leave. The total cost of brain disorders (direct and indirect) represented 3% of the country's gross national product.

Cost of Brain Disorders per Inhabitant

The overall cost of brain disorders per Italian citizen has been estimated at €706 per year. A more detailed breakdown is provided in *Table 4*.

Discussion

In this review, the estimated cost of 12 brain disorders in Italy in 2004 highlights a relevant economic burden for the country, as it accounts for up to 3% of gross national product and costs each citizen €706 per year.

Psychiatric disorders account for more than half of the total costs, especially psychotic and affective disorders. Schizophrenia in particular is one of the most costly psychiatric illnesses.⁸ Anxiety and migraine are fairly inexpensive per single patient but, due to their high prevalence, they are very expensive at a societal level.

While affective disorders are the most costly brain disorders in Europe,³ dementia is the most costly brain disorder in Italy. This difference can be explained by an underestimation of the number of affective disorders in Italy due to scarce epidemiological reports in relation to cultural attitudes. Italians are less prone than other Europeans to consider depression a medical problem and thus worthy of medical care. A survey has shown that medical advice in view of the depressive symptoms was never sought by 62% of the subjects classified as suffering from major depression.⁹ However, having three or more physician visits and drug therapies was twice as common and having four or more instrumental examinations was three times as common in patients with major depression compared with non-depressed individuals. Significant loss of productivity at work or as part of global activities was four times more common in patients with major depression than in non-depressed individuals.

Alcohol consumption is widespread in Italian communities, and a large proportion of the population drinks above the World Health Organization (WHO)-established cut-off, i.e. 40g/day for males and 20g/day for females.¹⁰ 'Heavy drinking' is significantly higher in females compared with males, with regional differences that are important to consider from a socioeconomic perspective. In the past 20 years, Italian lifestyles have changed radically, and alcohol habits have changed, with increased consumption especially in the young adult female population; this can be attributed to women's emancipation and a social levelling-off between the genders.¹¹ From a health economic perspective, the burden of high alcohol consumption must be viewed not only as a 'brain' disorder (dependence) but also as a cause of increased morbidity (hepatic cirrhosis, gastrointestinal disorders, cardiomyopathy, poly-neuropathy, haemorrhagic stroke and mortality); its burden accounts for up to 5% of the gross national product of industrialised European countries.¹²

Gerzeli and co-workers¹³ have estimated that the societal costs in the first six months following stroke were €11,600 per patient, 53% of which was direct medical costs, 39% direct non-medical costs

Table 2: Cost of Brain Disorders in Italy by Area of Interest⁴

	Direct Medical Costs	Direct Non-medical Costs	Indirect Costs	Total Cost
Neurosurgical Disorders	594	36	373	1,002
Brain tumour	158	36	373	567
Trauma	436			436
Neurological Disorders	3,473	3,372	5,579	12,424
Epilepsy	495	618	1,196	2,308
Migraine	233		3,297	3,530
Multiple sclerosis	176	688	295	1,159
Parkinson's disease	935	1,105		2,040
Stroke	1,633	961	792	3,386
Neurological/Psychiatric Disorders	2,297	6,351		8,648
Dementia	2,297	6,351		8,648
Psychiatric Disorders	10,765	1,339	6,608	18,713
Addiction	671	385	400	1,456
Affective disorders	1,874		4,618	6,492
Anxiety disorders	1,941		1,590	3,531
Psychotic disorders	6,279	954		7,234
All Brain Disorders	17,129	11,097	12,560	40,787

All costs in €million (purchasing power parity). Numbers are rounded. With permission from Springer-Verlag.

and 8% indirect costs. Age, disability level and type of hospital ward were the most significant predictors of such costs.

The drug costs for brain disorders account for only 7% of the total Italian drug market. In Italy direct medical costs compared with non-medical costs were proportionally higher for neurosurgical and psychiatric disorders and for migraine and stroke. The direct non-medical costs especially dominated multiple sclerosis and dementia, the difference being due to the clinical features of the diseases and/or their differential management.

The overall economic burden of brain disorders in Italy, as well as in other European settings, is very likely underestimated due to lack of reliable prevalence and economic data for some disorders. Moreover, as for stroke, brain tumour and trauma, the costs are grossly underestimated as they are based on incidence. The costs of brain trauma were between €5,622 and €8,951, as predicted from other European countries. However, based on the Diagnosis Related Group (DRG) system, the estimated cost of severe brain trauma with tracheostomy due to prolonged coma was €53,922 in Emilia Romagna, and €10,134 if based on the DRG for craniotomy due to trauma, even in patients with a mild to moderate injury. Based on DRG, mildly injured patients admitted to the hospital with head concussion cost between €2,286 and €4,078. Furthermore, the cost of admission to an Italian hospital is €940 per day in neurosurgical wards and close to €2,000 per day in intensive care units.¹⁴

Methodological Considerations

Study design, population sampling method and accuracy of assessment and diagnosis vary among studies. Crude rates reflect different population age structures, and comparisons between age- and sex-standardised rates to a common referral population are almost always unavailable. Prevalence is not univocally expressed, and estimates can be found as point-prevalence, one-year prevalence or lifetime prevalence.

Most of the cost-of-illness studies considered for implementing the cost model were prevalence-based and bottom-up, a design that is

Table 3: Distribution of Total Cost of Brain Disorders in Italy by Resource Use Components⁴

	Cost	%
Direct Healthcare Costs	17,129	42
Hospitalisation	9,385	23
Drugs	2,109	5
Outpatient care	5,440	13
Medical devices	196	0.5
Direct Non-medical Costs	11,097	27
Social services	7,776	19
Informal care	2,164	5
Adaptations	945	2
Transportation	212	1
Total Indirect Costs	12,560	31
Sick leave	10,527	26
Early retirement	1,156	3
Premature death	876	2
Total Costs	40,787	100

Costs in €million. Numbers are rounded. With permission from Springer-Verlag.

Table 4: Cost per Inhabitant of Specific Brain Disorders in Italy, 2004⁴

Brain Disorder	Direct Medical Costs	Direct Non-medical Costs	Indirect Costs	Total Cost
All disorders	298	194	218	706
Epilepsy	40	110	0	150
Stroke	109	17	0	125
Affective disorders	32	0	80	112
Anxiety disorders	34	0	28	61
Multiple sclerosis	4	0	57	61
Trauma	28	17	14	59
Migraine	9	11	21	40
Psychotic disorders	16	19	0	35
Addiction	12	7	7	25
Parkinson's disease	3	12	5	20
Dementia	3	1	6	10
Tumour	8	0	0	8

Costs in €million (purchasing power parity). With permission from Springer-Verlag.

limited to small samples of patients and might preclude inferences to the general target population. Most of the reported health economic studies do not include indirect nor intangible costs. Also, due to co-morbidity, allocating patients to different groups of disorders can be problematic, and double-counting of costs may be underestimated. If cost studies are incidence-based, they cover only the first year with disease, which is generally the most expensive.

For age-related conditions such as dementia and stroke, recruitment of elderly populations is complex and potentially affected by selection bias, as individuals are more easily enrolled from institutions.¹⁵ On the other hand, severe cognitive disorders and old age may lead to higher refusal rates, interfering with the health economic assessment. Epidemiological and cost data on child-related disorders are especially scarce.

Conclusions

Due to the ageing of the Italian population, the socioeconomic burden of brain diseases is expected to increase remarkably. Qualified research is needed in this field using prospective designs and standardised screening instruments in order to obtain comparable epidemiological and cost data at a national and international level. ■



Maura Pugliatti is a Neurologist and Assistant Professor of Neurology in the Department of Neurosciences at the University of Sassari in Italy. Her scientific work is characterised by high-quality international research in the field of multiple sclerosis (MS). Within the European Brain Council she has provided specific expertise for the Panel of Epidemiology of MS, ultimately aimed at estimating the socioeconomic burden of the disease in Europe.



Paola Cossu is a Neurologist and Research Fellow in the Department of Neurosciences at the University of Sassari in Italy. She collaborates with Dr Pugliatti and international teams of highly qualified researchers in the field of neuroepidemiology and public health with regard to multiple sclerosis and epilepsy.



Ettore Beghi is Head of the Laboratory of Neurological Disorders at the 'Mario Negri' Institute in Milan. He is an active member of many scientific associations, for which he has also held leadership roles. He is an Associate Editor of *Epilepsia*, sits on the Editorial Board of *Neuroepidemiology, Clinical Neurology & Neurosurgery, Inpharma* and *Clinical Drug Investigation* and is a reviewer for many other journals. Dr Beghi is the author of more than 300 scientific publications.

- Olesen J, Leonardi M, The burden of brain diseases in Europe, *Eur J Neurol*, 2003;10:471–7.
- Drummond M, *Principles of economic appraisal in health care*, Oxford University Press, 1980.
- Andlin-Sobocki P, Jönsson B, Wittchen HU, Olesen J, Cost of disorders of the brain in Europe, *Eur J Neurol*, 2005;12(Suppl. 1):1–27.
- Pugliatti M, Sobocki P, Beghi E, et al., Cost of Disorders of the Brain in Europe Study Group. Cost of disorders of the brain in Italy, *Neurol Sci*, 2008;29:99–107.
- Sobocki P, Jönsson B, Angst J, Rehnberg C, Cost of depression in Europe, *J Ment Health Policy Econ*, 2006;9:87–98.
- Ekman M, Westphal M, Cost of brain tumour in Europe, *Eur J Neurol*, 2005;12(Suppl. 1):45–9.
- Wittchen HU, Jacobi F, Size and burden of mental disorders in Europe – a critical review and appraisal of 27 studies, *Eur Neuropsychopharmacol*, 2005;15:357–76.
- Garattini L, Barbui C, Clemente R, et al., On behalf of the Study Group SCORE. Direct Costs of Schizophrenia and Related Disorders in Italian Community Mental Health Services: A Multicenter, Prospective 1-Year Follow-up Study, *Schizophrenia Bulletin*, 2004;30:295–302.
- Battaglia A, Dubini A, Mannheimer R, Pancheri P, Depression in the Italian community: epidemiology and socio-economic implications, *Int Clin Psychopharmacol*, 2004;19:135–42.
- Guerrini I, Gentili C, Guazzelli M, Alcohol consumption and heavy drinking: a survey in three Italian villages, *Alcohol Alcohol*, 2006; 41(3):336–40.
- Scafato E, Epidemiologia dell'alcol e del mondo femminile, *Ann Ist Super Sanità*, 2004;40(1):25–33.
- World Health Organization (WHO), Alcohol policies in Europe, In: *Alcohol in the European Region consumption, harm and policies*, Nina Rehn and the National Counterparts of European Alcohol Action Plan, 2001:43–76.
- Gerzeli S, Tarricone R, Zolo P, et al, The economic burden of stroke in Italy. The Eclipse Study: Economic Longitudinal Incidence-based Project for Stroke Evaluation, *Neurol Sci*, 2005;26:72–80.
- Gioia V, Traumi gravi, ecco i costi delle cure hub&spoke I, *Il Sole 24 Ore*, 20-26 set, 2005:22–3.
- Berr C, Wancata J, Ritchie K, Prevalence of dementia in the elderly in Europe, *Eur Neuropsychopharmacol*, 2005;15:463–71.
- Rehm J, Room R, van den Brink W, Jacobi F, Alcohol use disorders in EU countries and Norway: An overview of the epidemiology, *Eur Neuropsychopharmacol*, 2005;15:377–88.
- Alonso J, Ferrer M, Romera B et al., The European Study of the Epidemiology of Mental Disorders (ESEMEd/MHEDEA 2000) project. Rationale and methods, *Int J Meth Psychiatr Res*, 2002;11:55–67.
- Alonso J, Angermeyer MC, Bernert S, et al., Prevalence of mental disorders in Europe: Results from the European Study of the Epidemiology of Mental Disorders (ESEMEd) project, *Acta Psychiatr Scand*, 2004;(Suppl.):21–7.
- Rehm J, Room R, van den Brink W, Kraus L, Problematic drug use and drug use disorders in EU countries and Norway: an overview of the epidemiology, *Eur Neuropsychopharmacol*, 2005;15:389–97.
- Paykel ES, Brugha T, Fryers T, Size and burden of depressive disorders in Europe, *Eur Neuropsychopharmacol*, 2005;15:411–23.
- Pini S, de Queiroz V, Pagnin D, et al., Prevalence and burden of bipolar disorders in European countries, *Eur Neuropsychopharmacol*, 2005;15:425–34.
- Lieb R, Becker E, Altamura C, The epidemiology of generalized anxiety disorder in Europe, *Eur Neuropsychopharmacol*, 2005;15:445–52.
- Forsgren L, Beghi E, Öun A, Sillanpää M, The epidemiology of epilepsy in Europe – a systematic review, *Eur J Neurol*, 2005;12:245–53.
- Stovner LJ, Zwart J-A, Hagen K, et al., Epidemiology of headache in Europe, *Eur J Neurol*, 2006;13:333–45.
- Pugliatti M, Rosati G, Carton H, et al., The epidemiology of multiple sclerosis in Europe, *Eur J Neurol*, 2006;13:700–22.
- Granieri E, Casetta I, Govoni V, et al., The increasing incidence and prevalence of MS in a Sardinian province, *Neurology*, 2000;55:842–7.
- von Campenhausen S, Bornschein B, Wick R, et al., Prevalence and incidence of Parkinson's disease in Europe, *Eur Neuropsychopharmacol*, 2005;15:473–90.
- Truelsen T, Piechowski-Jozwiak B, Bonita R, et al., Stroke incidence and prevalence in Europe: a review of available data, *Eur J Neurol*, 2006;13:581–98.