

# BACKGROUNDS

Fact sheets on each disorder

Executive summary

## MENTAL, NEUROLOGICAL AND NEUROSURGICAL DISEASES

### Cost of brain disorders distributed by medical speciality and specific brain disorder

The total cost of brain disorders is an aggregated result of the twelve most prevalent disorders. It has already been observed that both the cost per case of specific brain disorders and the total number of cases with the different brain disorders differ substantially. Consequently, it is also expected that the aggregated cost result differs from one brain disorder to another.

**Mental disorders** amounted to €240 billion and hence constitute 62 % of the total cost (excluding dementia), followed by

**Neurological diseases** (excluding dementia) totalling €84 billion (22 %).

**Neurosurgical diseases** made up a smaller fraction of the total cost of brain disorders in Europe, reaching a cost of €8 billion. Dementia, which is considered both a mental disorder and a neurological disease, amounted to €55 billion.

### **Cost of brain disorders in Europe by disease area (€PPP million)**

€ million	Healthcare costs	Direct non-medical costs	Indirect costs	Total cost
<i>Neurosurgical diseases</i>	<i>4 099</i>	<i>269</i>	<i>3 155</i>	<i>7 523</i>
Brain tumour	1 162	269	3 155	4 586
Trauma	2 937			2 937
<i>Neurological diseases</i>	<i>21 294</i>	<i>20 092</i>	<i>42 381</i>	<i>83 934</i>
Epilepsy	2 752	4 240	8 554	15 546
Migraine and other headaches	1 495		25 507	27 002
Multiple sclerosis	2 194	3 977	2 598	8 769
Parkinson's disease	4 582	6 140		10 722
Stroke	10 263	5 901	5 730	21 895
<i>Neurological/mental disorder</i>	<i>12 840</i>	<i>42 337</i>		<i>55 176</i>
Dementia	12 840	42 337		55 176
<i>Mental disorders</i>	<i>97 221</i>	<i>9 336</i>	<i>132 985</i>	<i>239 542</i>
Addiction	16 655	3 962	36 657	57 274
Affective disorders	28 639		77 027	105 666
Anxiety disorders	22 072		19 301	41 372
Psychotic disorders	29 855	5 374		35 229
<b>All brain disorders</b>	<b>100 305</b>	<b>29 530</b>	<b>177 876</b>	<b>386 175</b>

Note. Purchasing power parity (PPP) is an international measure enabling researchers to compare economic data between countries by adjusting for the relative purchasing power in the respective countries. Gross domestic product is a measure of the total national income in a country.

# ADDICTION

## (Illicit drug dependence, Alcohol dependence)

### **Background:**

A cluster or pattern of symptoms, including compulsion or strong desire to use, impaired capacity to control, tolerance, withdrawal, preoccupation with the substance, where a great deal of time is spent on obtaining, using and trying to stop taking the substance; and continuation of use despite evidence of harmful consequences.

Substance use disorders (SUD), i.e. alcohol, drug or nicotine (nicotine is not included in the cost estimate) dependence and abuse or harmful use of these substances have been linked to a considerable burden of disease in Europe according to recent estimations by the World Health Organization. The exact amount is hard to quantify, because quite often consequences of SUD in a risk factor framework are not distinguished from consequences of substance use *per se*. For instance, lung cancer usually is related to tobacco smoking, and not to nicotine dependence. However, it can be estimated that at least 10 % of the overall burden of disease in this region is attributable to SUD.

### **Prevalence, age, gender & geography:**

Prevalence of addiction in Europe is high and affects more than 10 % of the population, with nicotine dependence being most prevalent, and illicit drug dependences the least prevalent SUDs. However, data on alcohol and drug dependence are scarce in several European nations, especially in the new admission countries. Since illicit drug use is an illegal activity it is hard to estimate the precise prevalence.

### **CDBE estimate:**

Total prevalence of addiction in Europe: 9,194,244 people (only alcohol and illicit drug addiction – not nicotine).

Total annual cost of addiction in Europe: €57,274,000,000.

# AFFECTIVE DISORDERS

## (Depression, Bipolar)

### **Background:**

Affective or mood disorders comprise a group of disorders that are characterized by clinically significant mood disturbances. Modern classificatory definitions, such as in the ICD-10 (WHO 1992) or in DSM-IV (APA 1994), define these disorders by the presence of a specific number of symptoms and by specifying duration, severity thresholds, distress, disability and diagnostic exclusions. Fairly convergent, both classification systems define three major groups of disorders with various subtypes; Major depression, Bipolar disorder, and cyclothymic and dysthymic disorders.

This CDBE study focuses on major depression and bipolar, because data on dysthymia and cyclothymia were largely lacking. It should also be noted that major depression with its criteria replaces by and large the older and unreliable terminology of so-called endogenous, neurotic and reactive depression, whereas bipolar disorder replaces in a more reliable way the past concept of manic-depression.

Major depression is the most frequent and most frequently studied of the affective disorders, it is defined during a period of at least 2 weeks in which the person suffers from at least five of a total of nine core depressive symptoms. In addition numerous other criteria must be met such as impairment, suffering, it must be excluded that other medical or substance related factors are responsible for these symptoms as well as other mental disorders that mimic such mood states.

Bipolar disorder describes a usually episodic and clinically sometimes extremely severe and dramatic presentation, in the past labelled "manic depression". Bipolar disorder encompasses several phenotypes; cross-sectional bipolar, patients may present as either by depressive, or manic, or hypomanic episodes; additionally a wide spectrum of other psychopathological features may be present.

### **Prevalence, age, gender & geography:**

Major depression: Every year 7-9 % of the adult population suffers from a depressive episode; the lifetime risk of major depression has been estimated to be even higher (12-16 %). Epidemiological data on these rates need some caution: Some studies do only report major depressive episodes without properly excluding the history of hypomanic or manic episodes in the previous history. Other studies only rely on cross-sectional self report by the patient without clinical ratings of depression history information. Thus these estimates carry the danger of overestimating depression rates.

Females reveal rates that are twice as high as those for males. Age of first onset of major depression can be any time, although some more recent studies suggest that the first onset of major depression has shifted into earlier ages.

Bipolar: The prevalence estimates in European studies vary between less than 1 % and over 5 %.

### **CDBE estimate:**

Total prevalence of affective disorders in Europe: 20,857,669 people.

Total annual cost of affective disorders in Europe: €105,666,000,000.

# ANXIETY DISORDERS

(Panic disorders, GAD, Specific phobia, OCD, Agoraphobia, Social phobia)

## **Background:**

Anxiety disorders as defined by modern diagnostic classification systems typically comprise of a wide range of quite different conditions. The spectrum of anxiety disorders ranges from panic disorder and Generalized Anxiety Disorders (GAD) to various types of phobic disorders (social phobia, agoraphobia, specific phobia subtypes etc) and even includes conditions like Obsessive-Compulsive Disorder (OCD) and Post-traumatic Stress Disorder (not considered in the CDBE-study)

Despite the seemingly striking differences in symptoms and impairment, natural course and severity as well as treatment, anxiety disorders all share the same core diagnostic features: namely the core role of anxiety reactions and avoidance behaviour in the development and/or the expression of the illness.

Panic disorder: The core feature of panic disorder is the occurrence of spontaneous panic attacks, associated by a subsequent enduring anxious predisposition and the fearful expectation of subsequent attacks. As a result of the panic attacks, most panic patients also develop agoraphobia.

Agoraphobia denotes a complex behavioural syndrome of persistent and enduring excessive fear reactions and avoidance in relation to all outside home situations (leaving the house alone, using public transportation, shops and open places). Both panic disorder and agoraphobia carry an additional high risk of secondary complications, in particular of developing major depression and substance use dependence (sedating drugs and alcohol).

GAD: The core features of generalized anxiety disorder are chronic (persisting for 6 months or more) anxious worrying associated with a syndrome consisting of symptoms of hypervigilance, hyperarousal and tension. Similar to panic, GAD has also been described as a high-utilizer group of all types of resources, including inpatient care.

Social phobia and specific phobias: Irrespective of many etiological and clinical differences the core features of phobic disorders are intensive fear reactions that consistently occur in anticipation or at confrontation with the respective fear stimuli.

## **Prevalence, age and gender:**

According to most recent epidemiological studies, anxiety disorders overall are almost always confirmed to be among the most prevalent mental disorders, with a lifetime cumulative incidence risk of 11 to over 20 %, depending on the range of disorders covered, with females revealing approximately twice the prevalence of males.

With the exception of panic disorder and GAD, anxiety disorders share an early onset – mostly before age of 16 – and a considerable degree of persistence over a lifetime.

Family genetic studies demonstrate that anxiety disorders “run in families”, although the mechanisms of this familiar aggregation remain poorly understood.

Panic disorder: The lifetime prevalence of panic disorder is estimated to be 3-5 %, the 12-month prevalence 2 %. Onset is typically in the 20s, although the disorder may also start in early adolescence.

Agoraphobia has a prevalence of approximately 4 % or 2 % in the past 12 months.

GAD is a severe, disabling and chronic disorder in adulthood affecting overall 2-3 % (12-month), respectively 5 % (lifetime) of the adult population. Unlike all other anxiety disorders, GAD incidence is highest in the 30s and 40s, severe and stable GAD in adolescence is rare. Prevalence rates are highest in females over age of 45 (8-10 %). Further, there are indications that GAD is the most frequent anxiety disorder in old age (>65).

Specific phobias are by far the most frequent and the earliest onset conditions of all anxiety disorders before the age of 20.

**CDBE estimate:**

Total prevalence of anxiety disorders in Europe: 41,407,747 people.

Total annual cost of in Europe: € 41,372,000,000

# BRAIN TUMOUR

**Background:**

Brain tumours are classified into primary and secondary, where the former originate in the brain itself, and the latter are metastases originating in another part of the body. Secondary brain tumours are always malignant, while primary brain tumours occur both in benign and malignant forms. Brain tumours represent about 1-2 % of all newly diagnosed tumours, and account for about 2 % of all cancer-related deaths.

**Prevalence, age and gender:**

In Europe, the incidence of malignant primary brain tumours was 7.9/100,000 for men and 5.4/100,000 for women in 1995. The average age-standardized mortality rates were 5.9/100,000 for men and 3.9/100,000 for women.

**CDBE estimate:**

Total prevalence of brain tumour in Europe: 135,251 people.

Total annual cost of brain tumour in Europe: €4,586,000,000.

# DEMENTIA

## Background:

According to the Diagnostic and Statistical Manual of Mental Disorders, 3rd ed. revised (DSM-III-R), the criteria for dementia include demonstrable evidence of impairment in memory and either a) impairment in one other intellectual function (abstract thinking, judgment or impairment of higher cortical functions) or b) a personality change. These disturbances must be sufficient to interfere with work, usual social activities or relationships with others.

Another popular definition proposes that “dementia is the decline of memory and other cognitive functions in comparison with the patient’s previous level of function as determined by a history of decline in performance and by abnormalities noted from clinical examination and neuropsychological tests”.

## Prevalence, age, gender & geography:

The table presents the prevalence per 100 in countries with available data

**Table 2. Prevalence (per 100, with 95% confidence interval) in selected European Studies, by age**

Country	65-74	75-84	≥ 85
Belgium [14] *	4.4 [3.2-5.9]	11.1 [9.1-13]	11.5 [9.1-14]
Denmark [15]**	4.7[3.8-5.6]	11.4 [9.7-13]	-
Finland [16]	-	18.3[15-22]	39.4 [31-48]
France [17] *	2.9 [2.1-3.8]	7.1 [5.6-8.5]	21.6 [18-25]
Germany [18] **	-	9.4 [7.7-11]	34.8 [30-40]
Italy [19] *	1.2 [0.6-2.5]	4.5[2.7-7.3]	32.2 [24-41]
Netherlands [20] *	1.4 [1-1.9]	10.9 [9.4-12]	34.8 [31-38]
Spain [21] *	3.2 [1.8-4.7]	8.3 [5.9-11]	20 [12-28]
Spain [22]	-	13.9 [11-17]	27.1 [23-32]
Sweden [23] **	-	13.5 [11-16]	33.4 [30-37]
UK [24] *	1.4 [1.0-2.0]	6.4 [5.4-7.6]	19.9 [18-22]
European average	2.1	6.9	24.1

\* Data used in the model

\*\* Studies based on sub-populations, not used on the model

## CDBE estimate:

Total prevalence of dementia in Europe: 4,886,252 people.

Total annual cost of dementia in Europe: € 55,176,000,000.

# EPILEPSY

## **Background:**

Epilepsy is a symptom-complex characterized by repeated unprovoked seizures. An unprovoked seizure is a seizure occurring in the absence of precipitating factors. Unprovoked seizures include events occurring in the absence of a recognized etiological or risk factor (idiopathic and cryptogenic seizures) and events occurring in patients with antecedent stable (non-progressing) CNS insults (remote symptomatic seizures).

The disease severity varies considerably from patient to patient, but the societal costs for epilepsy are high, mainly due to severe epilepsy in a substantial part of the epilepsy population. This makes it important to assess the costs for patients with epilepsy, not least since several new anti-epileptic drugs have been introduced in recent years.

Epilepsy is a treatable clinical condition. About 50 % of cases achieve seizure remission soon after onset of treatment; seizures can be controlled after one or more treatment changes in about 25-35 % of cases, leaving 15-25 % of patients with drug-resistant epilepsy. Seizure control may be obtained in a variable proportion of these cases by surgical resection of the epileptogenic lesion.

## **Prevalence, age & gender:**

The worldwide annual incidence epilepsy ranges from 24 to 53 per 100,000 and the incidence of single seizures is 33-44 per 100,000.

Epilepsy is a fairly common clinical condition affecting all ages and with a fairly similar distribution across Europe. The prevalence of the disease is slightly higher in males than in females, although most studies show shifting rates between sexes in different age groups. As with prevalence, the incidence of epilepsy is slightly higher in males than in females, although similar rates between genders or a female predominance have occasionally been found.

The prevalence of epilepsy is slightly different in children and adolescents (4.5-5 per 1,000), adults (6 per 1,000), and in the elderly (7 per 1,000). By contrast, the mean annual incidence of the disease tends to vary significantly according to age, being about 70 per 100,000 in children and adolescents, 30 per 100,000 in adults, and 100 per 100,000 in the elderly.

Modest differences can be found in the etiology of epilepsy between Europe and developing countries, which may reflect a different distribution of environmental factors and different genetic backgrounds.

## **CDBE estimate:**

Total prevalence of epilepsy in Europe: 2,690,608 people.

Total annual cost of epilepsy in Europe: €15,546,000,000.

# MIGRAINE

## **Background:**

Migraine is a relatively severe form of headache occurring in attacks usually lasting between four hours and three days, and with disabling accompanying phenomena such as nausea or vomiting, severe intolerance to light, sound odours and body movement.

In a WHO report from 2000 grading the severity of different disorders, a patient with a severe migraine attack was considered to be as disabled as one with active psychosis, dementia or tetraplegia.

Irrespective of the diagnosis, the consequence for most headache sufferers is that normal function is interrupted by headache episodes at irregular and unpredictable intervals, and this may impose severe limitations on their daily lives, both at school, work and during leisure time. This, and the fact that these disorders seem to be extremely prevalent all over the world make them important from an economic perspective.

Relatively recent and population-based studies indicate that 14-15 % of the adult population were absent from work due to headaches in Denmark and England, and the number of days missed from work ranged from around 1100 to 1300 days per 1000 employed persons per year in these studies. The number of days with reduced efficacy at work was estimated to be four times higher and thus result in an even greater loss of work time than the days missed.

## **Prevalence, age & gender:**

Considering the epidemiologic data, large variations in the prevalence of both headache and migraine were found among different European countries (Table 1). Both headache and migraine were most prevalent in the age groups from 20 to 50 years in both sexes, and there was a clear female preponderance in all age groups except among children. By selecting articles that covered age groups from at least 25 to 60 years the average one-year prevalence of headache was found to be 51 % (61 % women and 44 % men), of migraine 14 % (17 % in women and 8 % in men), and of "chronic headache" 4 % (6 % in women and 2 % in men).

## **CDBE estimate:**

Total prevalence of migraine in Europe: 40,777,009 people.

Total annual cost of migraine in Europe: €27,002,000,000.

# MULTIPLE SCLEROSIS

## **Background:**

Multiple sclerosis (MS) is a chronic progressive highly disabling disorder with a considerable social impact and economic consequences despite its relatively limited prevalence. It is an acquired inflammatory and neurodegenerative immuno-mediated disorder of the central nervous system, characterised by inflammation, demyelination and primary or secondary axonal degeneration. It is clinically manifested by multiple neurological dysfunctions (e.g. visual and sensory disturbances, limb weakness, gait problems and bladder and bowel symptoms) often increasingly disabling over time due to irreversible functional disability.

Economic consequences are predominantly the early loss of work capacity due to the development of physical disability and the impact of fatigue in a population of young adults, the requirement for hospitalisation during severe disease exacerbations and the need for assistance in activities of daily living.

The efficacy of immunoprophylactic therapies on disease course is overall modest and the disease shows heterogeneity with respect to its pathogenesis, clinical manifestations and prognosis. Etiology is unknown. MS is a complex multifactorial disorder, in which environmental factors are hypothesised to interact with genetically susceptible individuals.

## **Prevalence, age & gender:**

European mean total MS prevalence rate is currently estimated at 79 cases per 100,000 pop. According to prevalence rates, European countries can be grouped as follows: Malta (0-34 per 100,000); Cyprus, Estonia, France, Greece, Hungary, Ireland, Latvia, Lithuania, Poland, Portugal and Spain (35-69 per 100,000); Austria, Belgium, Czech Rep., Germany, Italy, Norway, Slovenia, The Netherlands, (70-104 per 100,000); Denmark, Iceland, Switzerland, United Kingdom (105-139 per 100,000) and Finland and Sweden (140 per 100,000 and over).

Mean prevalence rates for men are 57 cases per 100,000 and 110 for women. The highest prevalence estimates have been found for age group 35-64 for both women and men.

MS is more common in northern countries than in tropical and subtropical areas. Also it is more common in Caucasians.

## **CDBE estimate:**

Total prevalence of MS in Europe: 379,599 people.

Total annual cost of MS in Europe: €8,769,000,000.

# PARKINSON'S DISEASE

## **Background:**

Parkinson's Disease (PD) is one of the most common chronic neurodegenerative diseases. Main symptoms of PD are bradykinesia, rigidity, rest tremor, and postural instability. In addition to the motor symptoms mental disorders like depression or psychosis, autonomic and gastrointestinal dysfunction may occur, which considerably impair the quality of life of PD patients. Although the cerebral structures undergoing neurodegeneration in PD are well characterised, the causing mechanisms of the disease are still unknown.

No cure has been found to stop the progressive course of the disease and severe disability may occur in its later stages.

## **Prevalence, age and gender:**

The prevalence and incidence rates for PD are approximately 108 to 257/100,000 and 11 to 19/100,000 per year, respectively. When only older age groups (>60 years) are included, rates of prevalence and incidence are much higher: 1,280 to 1,500/100,000 and 346/100,000, respectively.

No evident difference in the prevalence of PD between the two sexes can be registered.

## **CDBE estimate:**

Total prevalence of Parkinson's Disease in Europe: 1,158,990 people.

Total annual cost of Parkinson's Disease in Europe: € 10,722,000,000.

# PSYCHOTIC DISORDERS (Schizophrenia)

## **Background:**

Schizophrenia is the most chronic and disabling of the severe mental illnesses. It is a devastating disease of the brain. People with schizophrenia often suffer symptoms such as hearing internal voices not heard by others, or believing that other people are reading their minds, controlling their thoughts, or plotting to harm them. These symptoms may leave them terrified and introverted. Even if it is not a very frequent disease, it is among the most burdensome and costly illnesses worldwide. The impacts of schizophrenia are long lasting and sometimes profound.

Current treatment methods are based on reducing the symptoms of schizophrenia and lessening the risks that symptoms will return. Available treatments can relieve many symptoms, but most people with schizophrenia continue to suffer some symptoms throughout their lives. However, when treated in its earliest stage, it might allow the patients to reintegrate the society and live a life as normal as possible.

## **Prevalence, age and gender:**

The risk of developing schizophrenia is approximately 1 % for a total population. No evident difference in the prevalence of schizophrenia between the two sexes can be registered. Schizophrenia typically takes its off-set at age 15-30.

## **CDBE estimate:**

Total prevalence of psychotic disorders in Europe: 3,687,173 people.

Total annual cost of psychotic disorders in Europe: €35,229,000,000.

# STROKE

## **Background:**

Stroke is a vascular disorder, characterised by the sudden death of brain cells due to a reduced or ruined supply of blood. The costs for stroke treatment and rehabilitation are already considerable and the increasing number of subjects with stroke is likely to increasingly burden health systems in the future.

## **Prevalence, age and gender:**

In the European Union (EU), Iceland, Norway, and Switzerland an estimated 1.1 million new stroke events occur each year and currently 6 million subjects live in these countries having survived a stroke. According to population projections from the United Nations the number of new stroke events will increase to 1.5 million per year in 2025 in these countries if stroke incidence rates remain stable solely due to demographic changes.

Stroke prevalence increases with age. While stroke prevalence rates are higher in men in younger age groups several studies report that women have the highest stroke prevalence rates in older age groups. Rates increase from approximately 5,000 per 100,000 in subjects aged less than 75 years to 10,000 or more per 100,000 in those aged 80+.

## **CDBE estimate:**

Total prevalence of stroke in Europe: 1,128,986 people.

Total annual cost of stroke in Europe: €21,895,000,000.

# TRAUMA

## **Background:**

Traumatic brain injury (TBI) is defined as an insult to the brain that leads to temporary or permanent impairments of cognitive abilities and physical functioning. Head injury results from an interaction between an individual and an external agent such as a mechanical force, and contributes significantly to the outcome in one half of all deaths resulting from trauma. This mechanical force may be related to road traffic accidents, falls (with or without alcohol consumption) and work/sport accidents. Trauma injures neural tissue by primary (direct brain tissue injury) or secondary mechanisms (increased intracranial pressure, ischemia related to general hypoxia and hypotension).

Costs of hospitalization vary by injury type, averaging according to US studies at \$20,084 for gunshot wounds, \$20,522 for motor vehicle crashes, \$15,860 for falls, and \$19,949 for blows to the head.

Those patients with moderate or severe TBI who survive are often unable to return to full employment and require some degree of rehabilitation. This means that TBI is related to significant direct medical and non-medical costs in terms of hospitalisation, outpatient care and rehabilitation, indirect costs due to lost productivity, and intangible costs due to reduced quality of life.

## **Prevalence, age and gender:**

Approximately 1,600,000 head injured patients are admitted to hospital care in Europe producing a brain injury rate of 235 per 100,000 and causing as many as 66,000 deaths per year.

## **CDBE estimate:**

Total prevalence of trauma in Europe: 708,954 people.

Total annual cost of trauma in Europe: €2,937,000,000.

# Executive summary of CDBE

**Background:** Brain disorders (psychiatric, neurological and neurosurgical diseases together) figure among the leading causes of disease and disability. Yet, knowledge of the epidemiological and economic impact of brain disorders has been relatively under-researched in Europe. WHO data suggest that brain disorders cause 35 % of the burden of all diseases in Europe.

**Objectives:** This study estimates the economic cost of disorders of the brain in Europe based on the published epidemiological and economic evidence. A secondary objective was to identify gaps in both epidemiological and economic evidence on brain disorders thus providing focus for future research efforts.

**Methods:** A model was developed to combine epidemiological and economic data on brain disorders in Europe and thus estimate their total cost. More specifically, this consisted of the following steps: (1) transform and convert available economic data to a defined time period as well as currency (€2004) (2) adjust country specific economic data for purchasing power and relative size of economy (3) impute data for countries where no data is available (4) combine epidemiology and economic data to estimate the total cost of a defined disease (5) add the cost of all selected disorders to arrive at the total cost for Europe. The model drew on data collected from extensive literature reviews in the epidemiology and economic burden of brain disorders in Europe, conducted by twelve groups of European epidemiologists and health economists. The cost data was calculated as cost per patient, and epidemiologic data were primarily reported as 12-month prevalence estimates. National and international statistics for the model were retrieved from the OECD and Eurostat databases. The aggregated annual cost estimates were presented in Euro for 2004.

**Results:** The total number of estimated cases of brain disorders in Europe is 127 million. The total annual cost of brain disorders in Europe was estimated at €386 billion in 2004. Direct medical expenditures alone totalled €135 billion, comprising inpatient stays (€78 billion), outpatient visits (€45 billion) and drug costs (€13 billion). Attributable indirect costs resulting from lost work days and productivity loss due to permanent disability due to brain disorders and mortality were €179 billion, of which the mental disorders were the most prevalent. Direct non-medical costs (social services, informal care and other direct costs) totalled €72 billion.

Mental disorders amounted to €240 billion and hence constituted 62 % of the total cost (excluding dementia), followed by neurological diseases (excluding dementia) totalling €84 billion (22 %). Neurosurgical diseases made up a smaller fraction of the total cost of brain disorders in Europe, reaching a cost of €8 billion. Dementia, which is considered as both a mental disorder and a neurological disease, amounted to €55 billion. The average cost of brain disorders in Europe was €829 per inhabitant (based on a total number of inhabitants in Europe of 466 million). However, the cost per inhabitant is different between European countries, and in general cost of brain disorders per inhabitant is higher in Western European countries compared with the EU admission countries. 70 % of the total cost of brain disorders is attributable to the five major countries in Europe (Germany, UK, France, Spain and Italy). These countries together hold 64 % of the total population in Europe.

Due to scarcity of data, the total cost results only partially include direct non-medical cost (e.g. community care and informal care) and indirect costs, and completely omit intangible costs. An example shows the cost of dementia increases by 25 % when including informal care and the cost of multiple sclerosis increases by at least 50 % when including intangible costs.

**Discussion:** The scarcity of both epidemiologic and health economic data in several countries and for specific brain disorders have led to conservative inclusions of cost items and population age groups. Bearing this in mind, along with the fact that the scope of the present study was restricted to the most prevalent brain disorders, this leads to the conclusion that the true economic cost of disorders of the brain is substantially higher, perhaps in the range €500-700 billion. Brain disorders are, thus, substantially more costly than other important fields of medicine such as heart disease, cancer and diabetes. However, the burden of brain disorders is seldom viewed as a holistic field in this way. Instead, individual disorders are seen in isolation. If training efforts, research funding and health care resources were allocated according to this new knowledge, a very considerable increase in funding of brain related activities should take place. The cost estimations are the best possible based on the economic and epidemiological data available in Europe today. However, the study has identified major shortcomings both in the epidemiological and economic evidence on brain disorders in Europe, in particular in the EU admission countries. More research of a systematic, prospective, collaborative nature is needed in order to accurately estimate the cost of disorders of the brain in Europe.

**Conclusion:** Based on extensive literature reviews, the present study provides best possible estimates of the cost of disorders of the brain in Europe in 2004. In 28 countries with a population of 466 million, more than 100 million were affected by at least one brain disorder. The total cost was €386 billion (€386.000.000.000). Brain research funding, health care resource allocation and teaching at medical schools are proportionately much smaller. The huge cost and burden of brain disorders calls for increased efforts in research, health care and teaching.

**Recommendations:** Based on this extensive study the following is recommended:

- An increase in health care efforts to help sufferers of brain disorders and those people with disabilities that arise from a previous brain disorder.
- Immediately, or as soon as possible, an increase in efforts in brain research at EU level to €500 million per year or 0.1 % of the annual cost of brain disorders as the only possibility for curbing the rising cost of these disorders.
- A similar increase in national efforts should follow as soon as possible.
- To increase teaching in brain related subjects at medical schools and other life science educations.