APPENDICES

Key concepts used

Active development	The active substance is still in development (i.e. not terminated) in any of pre-clinical, Phase I, Phase II, Phase III or submission.
Charity	For the purpose of the survey, research funded by charities (organizations for public benefit that rely on donations for financial support) was combined with that of private not-for-profit organizations (those whose securities are not offered to the public)
Cost-benefit analysis	Type of economic evaluation that measures costs and benefits in monetary units and computes a net pecuniary gain/loss
Cost-effectiveness analysis	Type of economic evaluation that measures therapeutic effects in physical or natural units and computes a cost/effectiveness ratio for comparison purposes
DALYs	Used to express how a healthy life is affected by disease; it combines the years lost because of premature death and disability
Direct medical costs	Fixed and variable costs directly associated with a health care intervention
Direct non-medical costs	Non-medical costs associated with the provision of medical services
Drugs for brain diseases/brain drugs	Indicates all drugs specifically used for treating brain disorders
Effectiveness	Therapeutic consequence of a treatment in a real world condition
Efficacy	Benefit of a treatment under ideal and controlled clinical conditions (e.g. in a clinical trial)
EuroQol	Also known as EQ-5D; is a short self-report questionnaire to measure generic health-related quality of life in five dimensions: mobility, self-care, usual activity, pain/discomfort, and anxiety/depression. Each dimension is measured with one item and scored between 0 and 1 (0 equals death and 1 perfect health). It also includes a 0-100 graphic rating scale to measure overall health status called Visual Analog Scale (EQ-5D VAS).
Health-related quality of life (HRQoL)	Defined as the impact on an individual's well-being of their health, often encompassing physical, mental and psychological elements
ICER	Additional cost of producing an extra unit of outcome by one therapy compared to another
Indirect costs	Value of the output that is lost because people are impaired or too ill to work, e.g. short-term absence from work, early retirement pensions caused by disability and premature mortality
Intangible costs	Costs of pain and suffering as a result of illness or treatment
Phase I	Comprised of active substances between the "first human dose" and the "first patient dose"
Phase II	Comprised of active substances between the "first patient dose" and the "first pivotal dose"
Phase III	Comprised of active substances between the "first pivotal dose" and the "first submission"
Pre-clinical phase	Comprised of active substances between the "first toxicity dose" and the "first human dose"
QALYs	Outcome of a treatment measured as the number of years of life saved, adjusted for their utility (QoL)
Societal perspective	Implies that all costs, whether incurred by individuals, employers or government, should be taken into account
Regulatory review	Comprised of active substances between the "first submission" and the "first approval"

Clarification of disease areas

Brain disorders	Definition
Addiction disorders*	Addiction disorders are defined as substance abuse such as tobacco, alcohol and illicit drug use [85].
Affective disorders*	Affective disorders are defined as depression, bipolar disease and dysthymia [86].
Anxiety disorders*	Anxiety disorders are defined as any panic disorder, including agoraphobia, generalised anxiety disorder (GAD), obsessive compulsory disorder (OCD), social phobia and any other specific phobia (animal, natural, environment, blood-injection injury, situational, etc) [87].
Brain tumour*	Brain tumours, or intracranial neoplasms, are a diverse set of tumours that are primarily classified by site and malignancy; they include astrocytomas (gliomas) and benign meningiomas [88].
Dementia, including Alzheimer's disease (AD)*	Dementia is a syndrome characterized by a progressive loss of memory and other cognitive functions, leading to impairment of physical functions and ultimately to complete dependency [89].
Epilepsy*	Epilepsy is a symptom of a brain disease or a disease itself; it is characterized by a tendency to recurrent seizures and is defined by two or more epileptic seizures, unprovoked by any immediate identifiable cause [90].
Migraine and other headaches*	Headaches encompass a range of disorders. The present study only deals with migraine which is characterised by recurrent severe attacks of headache and other symptoms [91].
Multiple Sclerosis (MS)*	Autoimmune and chronic progressive disease of the central nervous system (CNS) that is characterized by inflammation and destruction of the myelin coating of nerve fibres [57].
Parkinson's disease*	Parkinson's disease is a neurodegenerative disease, causing symptoms such as rigidity, instability and, most typical, tremor [92].
Stroke*	Stroke is a clinical syndrome with several different pathologies; WHO has defined it as "a focal (or at times global) neurological impairment of sudden onset, and lasting more than 24 hours (or leading to death) of presumed vascular origin" [93].
Trauma or traumatic brain injury (TBI)*	TBI is defined as an insult to the brain caused by an external physical force, which leads to a temporary or permanent impairment of cognitive abilities and physical functioning [94].
Schizophrenia*	Schizophrenia is a psychotic disorder causing symptoms such as delusions, hallucinations, disorganized speech and grossly disorganized or catatonic behaviour; schizophrenia is accompanied by a marked impairment in social or occupational functioning [95].

* All references are taken from the *European Journal of Health Economics*: A review of European studies on the economic burden of brain diseases

Public funding survey

Set-up

The funding survey can be divided into the following four, partly overlapping, steps:

STEP 1 Date: September 2005	Making the questionnaire
STEP 2 Date: September 2005 – March 2006	Identifying funding actors, sending out questionnaire. Follow up contacts (e-mails and multiple phone calls). Verification of the list of funding agencies
STEP 3 Date: October 2005 – April 2006	Receiving the data, categorization, review and cross-checking. Contacting funding actors for more in-depth information where needed.
STEP 4 Date: January – April 2006	Results

STEP 1: Questionnaire

The questionnaire was designed to be easy to complete and give as precise and coherent data as possible from the different informants. The questionnaire was, for clarity, divided into two parts, one excel-sheet that contained specific questions and fields for filling in the data and one document with clarifying instructions and definitions for the questionnaire.

In the questionnaire, the agencies were asked to provide:

I) Verification of funding organization classification, either "government agency" or "charity".[1]
II) List of executive/board members.
III) Specification of funding source.
IV) Specification of annual direct spending: amounts and type of funding. Data for 2004 were asked for in particular and trends or specific data of previous years if available. [2]
V) Suggestion on literature references.
VI) Any general or specific comments.

The questionnaire proved to be too detailed and thereby deterrent for many funding actors. A prioritization of the information needed was therefore made, specified as their *annual funding of brain research in 2004* and *organization classification.*

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[1] The term "charity" includes both charities (organizations for public benefit that rely on donations for financial support) and private not-for-profit organizations (those whose securities are not offered to the public).
[2] Annual direct spending is defined as salaries of researchers, laboratory equipment used and any consumables and/or other costs of the research during a specific year.

Sweden served as a pilot case for the study, first by testing the selection of funding agencies and second by testing the format of the questionnaire. The first draft of the questionnaire and the instructions were revised after receiving the answers from the Swedish funding agencies. The questionnaire needed some clarifications in the instructions to reduce confusion and a need for two more general categories for brain research were raised and therefore added, namely "other brain disorders" and "basic research not related to specific disorders". The Swedish answers were also complemented with the new categories.

STEP 2: Selection

The major public funding agencies on a national basis in Europe were identified, including the European Commission. No trans-European charities were found to have any major role in funding brain research and thus, no such charaties were included. In the pilot study, the Swedish selection of funding agencies was wide, including small charities as well as universities. The funding agencies in Sweden were mainly found by surfing the internet and the Swedish registry of charities[3]. However, the wide selection showed that many of the small funding agencies did not even have the capacity to answer the questionnaire. Therefore, only major funding agencies are included in the rest of the European countries.

Swedish universities were asked to provide data on their contribution to brain research from the base grant (governmental contribution) and their internal foundations (classified as charities) and not external financiers since they are accounted for elsewhere. However, the pilot study showed that it was hard to acquire information on to which research area their different funds went. Since external grants (e.g. from the Swedish Research Council) constitute a large part of universities' research budget, universities were excluded to avoid double counting. Moreover, internal foundations were small and numerous and hard to comprehend.

To identify the major funding actors in the rest of Europe, national medical societies/ associations were contacted for assistance. These societies were not directly involved in research funding, but they represented professional groups in the brain research field[4]. Representatives of national societies were contacted and requested to submit information on the *major* public funding sources in their respective country. A couple of societies were contacted from each country to get as comprehensive a listing as possible. In addition to this method, the internet was searched for funding agencies. The list of funding agencies participating in the ECRM report was also reviewed and revised.

The identified public funding agencies either had a general (e.g. Wellcome Trust) or a disorder-specific purpose (e.g. Epilepsy Research Foundation). The selection was wide and some of the agencies turned out not to be funding research. The reason for contacting so many uncertain organizations was to avoid missing any large ones due to lack of language skills. In the end, 226 funding agencies were relevant to our study and therefore included in the funding survey. The identified funding agencies got the questionnaire by email. The funding actors without a known email address were sent a copy of the questionnaire by regular mail.

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[3] Swedish County Administration – Länsstyrelsen, www.stiftelser.lst.se

[4] The societies chosen were members/associates of International Union of Pharmacology (IUPHAR), International Brain Organization (IBRO), Federation of European Neuroscience Societies (FENS), European Federation of Neurological Societies (EFNS) and European College of Neuropsychopharmacology (ECNP). Not all members/associates were chosen. The selection was based on the number of societies already included from each country, to get an even amount of representatives across Europe.

Reminder letters were sent out and multiple phone calls were made to those who did not meet the deadline.

Representatives of National Neurological Societies were asked to verify the list of the funding agencies included in our study. The list was thereafter revised and additional funding agencies contacted for financial information.

STEP 3: Data

If agencies failed to complete the questionnaire or give data by email or telephone, their homepages were thoroughly searched for financial information. At the end, the funding survey had identified and obtained data for 161 funding actors, of which 113 were charities and 48 governmental agencies, giving a total response rate of 71.2%. The data were given in local currencies and were transformed into Euros using average annual data from Eurostat for 2004. If the latest available data were for an earlier year, they were then inflated by using rates from Eurostat. All data were converted into 2005 values.

Total spending on neuroscience research was sometimes reported as the total amount granted in 2004 for research programs (even though they lasted for many years) or the actual spending on the research program in 2004. If both types were available, the latter was chosen.

The data received from the funding agencies came in diverse detail, ranging from only total spending on research, to spending on brain research, to spending by disorder. Some agencies provided listings of projects funded instead of making the categorization themselves. These lists and the information obtained from homepages were hence categorized by the research team.

The categorization followed the same guidelines for the purpose of coherence. The guidelines impose overestimation in some cases and underestimation in others. The disorder-specific data were also categorized into neurological, neurosurgical or mental disorders. The categorization followed the following guidelines:

- Example of project title: “dementia and other disorders in the elderly” – total amount listed as “dementia”
- Example of project title: “dementia, Parkinson and other disorders in the elderly” – 50% each of the amount on “dementia” and “Parkinson”
- Where no specific disorder could be determined – it was put into the category “basic research not related to specific disorder”

Caveats

The data from the funding survey are subject to the following caveats.

- Missing organizations. The sample of funding agencies might be skewed and there can be missing organizations due to lack of language skills (foremost eastern states) and differences in accuracy by the national contact points in identifying public funding agencies. To correct for this, the funding actors were asked to comment if they noticed that any important funding actor had been omitted. Still, this is no guarantee for a perfect sample.
- Missing data. Stroke and brain tumour are listed under oncology and cardiovascular diseases, respectively, by the WHO. Research into these general fields might have had an impact on brain tumour and stroke, even though it is hard to account for how much.

These disorders' contribution of "basic research not related to disorder" to brain research can hence not be included in the total estimate. However, this should not alter the comparison between different disorders since "basic research not related to disorder" is not divided between the other brain disorders either.

- Inaccurate classification. The data submitted by the funding actors have not been controlled for correctness and thus, data might be inaccurately classified. Even though thorough instructions followed the questionnaire, some misunderstandings and differences in classifications are possible. Where to draw the line for brain research might also have caused differences in data inclusion.
- Different depths of information. For some projects, a great deal of information was submitted, whereby it was easier to connect the data submitted to a specific disorder. If the data could not be attributed to a specific disorder, they were classified as basic research. As a result, the data-sets, which contain little information on the projects, have a higher probability of getting more projects classified as basic research. If no project information was submitted, the data were not at all specified at a disorder specific level.
- Over- and underestimation. In the classification process, a project might be classified as specific to a disorder, even though the disorder might not be the primary focus of the project and/or have any impact on other disorders. On the other hand, some research grants might not be accurately included as related to a specific disorder, due to inaccurate information about the project or unforeseen consequences of a research project (e.g. a drug which turns out to be very useful for another disorder than intended).
- Careful interpretation of data. Many organizations have given rough estimations of their spending and many give research grants by application whereby the spending on disorders and different fields of science can differ between each year. Therefore, one should be careful in drawing any general conclusions from these estimates. It should also be noted that due to different financial years, the timeframe of annual spending was not exactly the same. Still, the data received gave annual spending over almost the same period.

STEP 4: Results

The national funding estimates from the different countries were corrected for purchasing power by using the comparative price levels (CPL) index from Eurostat, to enable a comparison across European countries. Nevertheless, data received were scarce for some countries, due to a poor response rate from major funding agencies. To correct for this and assess a probably more realistic estimate for the whole Europe, imputations were made based on the countries with the most comprehensive response from major funding actors. Those were: Austria, Belgium, Denmark, Estonia, Finland, Germany, Hungary, Iceland, Ireland, Luxembourg, Netherlands, Norway, Sweden, Switzerland and the U.K.

In the base case, an average of these reference countries' expenditure per capita was used as the base for imputing values to the rest of the countries. The imputation index used was based on the reference countries' R&D expenditure per capita. Sensitivity analyses were also made, using different indices for price adjustment and imputations. These include indices based on health expenditure per capita, R&D expenditure per capita and CPL, based on all countries included in the study and/or the reference countries only.

All results presented over different organization types and disorders were based on the data received from funding agencies. These data were then extrapolated to the total estimate from the imputed values.

Participants in funding survey

Country	Organization	Funding type	Reported Spending
Austria	Bundesministerium für Bildung, Wissenschaft und Kultur	Government Agency	yes
	Fonds zur Förderung der wissenschaftlichen Forschung (FWF)	Government Agency	yes
	Forschungsförderungsgesellschaft (FFG)	Government Agency	decline
	Jubiläumsfonds der Oesterreichischen Nationalbank	Government Agency	yes
	Ludwig-Boltzmann-Gesellschaft	Charity	no answer
	Parkinson Selbsthilfe Osterreich	Charity	no answer
	Wiener Wissenschafts-, Forschungs- und Technologiefonds	Charity	yes
	Government of Styria	Government Agency	yes
	Österreichische Gesellschaft für Neurologie	Charity	yes
	Österreichische Krebshilfe Dachverband	Charity	decline
	Österreichischen Schizophreniegesellschaft	Charity	no answer
Belgium	Association Parkinson ASBL	Charity	no answer
	Belgian Federation against Cancer	Charity	yes
	F.W.O.-Vlaanderen (Fund for Scientific Research - Flanders)	Charity	yes
	Flemish League against Cancer	Charity	yes
	I.W.T	Government Agency	yes
	Ligue Alzheimer	Charity	no answer
	Ligue Belge de la Sclerose en Plaques	Charity	yes
Cyprus	Cyprus Heart Foundation	Charity	no answer
	Cyprus MS Association	Charity	no answer
	Cyprus Parkinson's Disease Association	Charity	no answer
	Cyprus Rehabilitation Counselling Association (CRCA)	Charity	yes
	Mental Health Commission	Government Agency	yes
	The Cyprus Research Promotion Foundation	Charity	no answer
Czech Republic	Fokus	Charity	no answer
	Grant Agency of the Czech Republic (GACR) (Czech Science Foundation)	Government Agency	yes
	Internal Grant Agency of the Ministry of Health of the Czech Republic	Government Agency	no answer
	The Ministry of Education, Youth and Sports of the Czech Republic	Government Agency	decline
Denmark	Alzheimerforeningen	Charity	yes
	Danish Cancer Society	Charity	yes
	Danish Headache Society	Charity	no answer
	Danish Medical Research Council Forskningsstyrelsen	Government Agency	yes
	Dansk Epilepsi Selskab	Charity	yes
	Dansk Epilepsiforening	Charity	yes
	Dansk Kræftforskning Fond (Danish Cancer Research Foundation)	Charity	yes
	Dansk Parkinsonforening	Charity	yes
	Lundbeckfonden	Charity	yes
	The Danish Mental Health Fund	Charity	yes
	The Danish MS Society	Charity	yes

Country	Organization	Funding type	Reported Spending
Estonia	Enterprise Estonia	Government Agency	yes
	Estonian Heart Association	Charity	no answer
	Estonian Ministry of Education and Research	Government Agency	yes
	Estonian Science Foundation	Government Agency	yes
Finland	Finnish Cultural Foundation	Charity	yes
	Neurologistiftelsen	Charity	no answer
	Sigrid Juselius Foundation	Charity	yes
	Parkinson foundation	Charity	yes
	The Academy of Finland	Government Agency	yes
	The Finnish MS Society	Charity	zero spending
	The National Technological Agency - TEKES	Government Agency	yes
France	AFTOC	Charity	yes
	Association francaise contre les myopathies	Charity	yes
	Association pour la Recherche contre le Cancer	Charity	no answer
	Fondation de France	Government Agency	yes
	Fondation pour la Recherche Medicale	Government Agency	no answer
	France Alzheimer et Maladies Apparentées	Charity	yes
	FRC	Charity	yes
	INSERM	Government Agency	yes
	Institut National de la Recherche Agronomique (INRA)	Government Agency	no answer
	Le Centre national de la recherche scientifique (CNRS)	Government Agency	no answer
	Ligue Française contre la Sclérose en Plaques	Charity	decline
	Ministry of Health	Government Agency	no answer
Germany	Bundesministerium für Bildung und Forschung (BMBF)	Government Agency	yes
	Deutsche Alzheimer Gesellschaft	Charity	yes
	Deutsche Forschungsgemeinschaft	Government Agency	yes
	Deutsche Gesellschaft für bipolare Störungen e.V. (DGBS)	Charity	yes
	Deutsche Krebshilfe	Charity	yes
	Deutsche Migräne- und Kopfschmerzgesellschaft (DMKG)	Charity	yes
	Deutsche Multiple Sklerose Gesellschaft Bundesverband e.V. (DMSG)	Charity	decline
	Deutsche Parkinson Vereinigung	Charity	no answer
	Max-Planck Gesellschaft	Charity	decline
	Stiftung Deutsche Schlaganfall-Hilfe	Charity	yes
	The Hertie Foundation	Charity	yes
	Wilhelm-Sander-Stiftung	Charity	decline
	Volkswagen Stiftung	Charity	yes
Greece	Greek Association of AD and related disorders	Charity	no answer
	Greek Multiple Sclerosis Society	Charity	yes
	Ministry of Health and Welfare	Government Agency	decline
Hungary	Hungarian Scientific Research Fund	Government Agency	yes
	National Office of Research and Technology	Government Agency	yes
	Ministry of Health	Government Agency	yes

Country	Organization	Funding type	Reported Spending
Iceland	Icelandic Heart Association	Charity	no answer
	The Icelandic Science Fund, RANNIS	Government Agency	yes
	The University of Iceland Research Fund	Government Agency	yes
	University Hospital	Government Agency	yes
Ireland	Aware	Charity	yes
	Health Research Board	Government Agency	yes
	Higher Education Authority	Government Agency	yes
	IICN (Irish Institute of Clinical Neuroscience)	Charity	yes
	Irish Cancer Society	Charity	zero spending
	Mental Health Ireland	Charity	yes
	MS Society of Ireland Ltd	Charity	yes
	Science Foundation Ireland	Government Agency	yes
	The Irish Heart Foundation	Charity	yes
	The Migraine Association of Ireland	Charity	zero spending
Italy	Associazione Italiana per la Ricerca sul Cancro (AIRC)	Charity	no answer
	Associazione Italiana Sclerosi Multipla	Charity	no answer
	Associazione per la Ricerca sull'Epilessia e Sindromi Correlate - FOREP	Charity	no answer
	Consiglio Nazionale delle Ricerche	Government Agency	no answer
	Federazione Alzheimer Italia	Charity	no answer
	Fondazione IDEA, Istituto per Ricerca e la Prevenzione della Depressione ed dell'Ansia	Charity	no answer
	Fondazione Umberto Veronesi	Charity	yes
	Istituto Superiore di Sanità	Government Agency	no answer
	Ministero della Salute	Government Agency	yes
	Ministero dell'Istruzione dell' Università e della Ricerca	Government Agency	no answer
	Parkinson Italia	Charity	no answer
	Telethon	Charity	yes
Latvia	Latvian Council of Science	Government Agency	yes
Lithuania	Lithuanian State science and studies foundation	Government Agency	yes
	Ministry of Education and Science	Government Agency	no answer
Luxembourg	Association Parkinson Luxembourg	Charity	yes
	CRP-Santé (Centre de Recherche Publique)	Government Agency	yes
	Fondation luxembourgoise contre le Cancer	Charity	zero spending
	Fonds National de la Recherche	Government Agency	yes
Netherlands	Alzheimer Nederland	Charity	yes
	Dutch Cancer Society	Charity	yes
	Hersenstichting Nederland (Dutch Brain Foundation)	Charity	yes
	Internationale Stichting Alzheimer Onderzoek	Charity	yes
	Nationaal Epilepsie Fonds	Charity	yes
	Nationaal Fonds Geestelijke Volksgezondheid	Charity	yes
	Nederlandse Organisatie voor Wetenschappelijk Onderzoek (NWO-ALW)	Government Agency	yes
	Netherlands Heart Foundation	Charity	yes

Country	Organization	Funding type	Reported Spending
Netherlands	Netherlands Institute for Brain Research & Netherlands Ophthalmic Research Institute IOI/NIH	Government Agency	yes
	Parkinson Patienten Vereniging	Charity	yes
	Prinses Beatrix Fonds	Charity	yes
	STICHTING GGZ GRONINGEN	Charity	decline
	Stichting Internationaal Parkinson Fonds	Charity	yes
	Stichting MS Research	Charity	yes
	ZonMw (The Netherlands Organisation for Health Research and Development)	Government Agency	yes
Norway	Dr Einar Martens Foundation	Charity	yes
	Landsforeningen For Slagrammede (Norwegian Stroke Association)	Charity	decline
	Melzerfondet	Charity	yes
	Nasjonalforeningen Demensforbundet (& cardiovascular)	Charity	yes
	Norges Parkinsonforbund	Charity	yes
	Norsk Epilepsiforbund	Charity	yes
	Norwegian Cancer Society	Charity	yes
	Norwegian Council for Mental Health	Charity	yes
	The Research Council of Norway	Government Agency	yes
Poland	Ministry of Health	Government Agency	no answer
	Polish Anti-Cancer Committee	Charity	no answer
Portugal	Calouste Gulbenkian Foundation	Charity	no answer
	Fundação para a Ciência e a Tecnologia	Government Agency	yes
	Liga Portuguesa Contra a Epilepsia	Charity	yes
	Liga Portuguesa Contra o Cancro	Charity	no answer
Slovakia	Research and Development Agency	Government Agency	yes
	Slovak Academy of Sciences	Government Agency	no answer
	Slovenský Zväz Sclerosis Multiplex (SZSM)	Charity	no answer
	The League against Cancer of SR	Charity	zero spending
Slovenia	Ministry of Higher Education, Science and Technology	Government Agency	no answer
	Slovenian Heart Foundation	Charity	no answer
	Slovenian Research Agency	Government Agency	no answer
	Zdruz˘enje bolnikov s cerebrovaskularno boleznijo (Slovenian Stroke Association)	Charity	no answer
Spain	Asociación Española contra el Cáncer	Charity	yes
	Comunidad Autonoma de Madrid Alcalá	Government Agency	no answer
	FEDEM	Charity	no answer
	Federación Española de Parkinson	Charity	no answer
	Fundación La Caixa	Charity	yes
	Gerente Fundación Mutua Madrileña	Charity	yes
	Instituto de Salud Carlos III - FIS (Ministerio de Sanidad y Consumo)	Government Agency	yes
	Ministerio de Educación y Ciencia (Ministry of Education and Science)	Government Agency	yes
Sweden	Alzheimerfonden	Charity	yes

Country	Organization	Funding type	Reported Spending
Sweden	Barncancerfonden	Charity	yes
	Cancer- och allergifonden	Charity	yes
	Cancer och Trafik-skadefonden (CTRF)	Charity	yes
	Cancerfonden (The Swedish Cancer Society)	Charity	yes
	Demensförbudet	Charity	yes
	Epilesifonden (Svenska Epilepsiföreningen)	Charity	decline
	Gunnar Nilssons Cancerstiftelse	Charity	decline
	Hjärnfonden	Charity	yes
	Hjärt-Lungfonden	Charity	yes
	Knut och Alice Wallenbergs Stiftelse	Charity	decline
	NHR-fonden (Neurologiskt Handikappades Riksförbund)	Charity	yes
	Parkinsonfonden	Charity	yes
	Radiumhemmets forskningsfonder	Charity	yes
	Riksbankens Jubileumsfond	Charity	yes
	Rådet för Medicinsk tobaksforskning	Charity	decline
	SADF (Insamlingsstiftelsen för Alzheimer- och Demensforskning)	Charity	yes
	Stiftelsen för Strategisk Forskning (SSF)	Charity	yes
	Stiftelsen Solstickan	Charity	yes
	Stroke-Riksförbundet	Charity	yes
	Svenska sällskapet för medicinsk forskning (SSMF)	Charity	decline
	Systembolagets Råd för Alkoholforskning (SRA)	Charity	yes
	Vetenskapsrådet	Government Agency	yes
	VINNOVA	Government Agency	yes
	Vårdalstiftelsen	Charity	yes
	Åke Wibergs Stiftelse	Charity	decline
Switzerland	Association Alzheimer Suisse	Charity	yes
	Center for Technology and innovation	Government Agency	yes
	Schweizerische Multiple Sklerose Gesellschaft	Charity	yes
	Schweizerische Parkinsonvereinigung	Charity	yes
	Swiss Heart Foundation	Charity	yes
	Swiss National Science Foundation	Government Agency	yes
UK	Action Medical Research	Charity	yes
	Action on Addiction	Charity	yes
	Alzheimer Scotland – Action on Dementia	Charity	yes
	Alzheimer's Society	Charity	yes
	Alzhemer Research Trust	Charity	yes
	Association for International Cancer Research (AICR)	Charity	zero spending
	Biotechnology and Biological Sciences Research Council (BBSRC)	Government Agency	yes
	Brain Injury Rehabilitation Trust (BIRT)	Charity	yes
	Brain Research Trust	Charity	yes
	British Heart Foundation	Charity	yes
	BUPA foundation	Charity	yes

Country	Organization	Funding type	Reported Spending
UK	Cancer Research UK	Charity	yes
	Cerebra (The Foundation for the Brain Injured Child)	Charity	yes
	Department of Health	Government Agency	yes
	Economic and Social Research Council (ESRC)	Government Agency	yes
	Engineering and Physical Sciences Research Council (EPSRC)	Government Agency	yes
	Epilepsy Action (Brittish epilepsy Association)	Charity	yes
	Epilepsy Research Foundation	Charity	yes
	Marie Curie Cancer Care	Charity	decline
	Medical Research Council	Government Agency	yes
	Mental Health Foundation	Charity	yes
	Migraine Action Association	Charity	no answer
	MS Research and Relief Fund	Charity	yes
	MS Society of Great Britain and Northern Ireland	Charity	yes
	MS Trust	Charity	yes
	National Society for Epilepsy	Charity	yes
	Northern Ireland HPSS R&D	Government Agency	yes
	Parkinson's Disease Society	Charity	yes
	Schizophrenia Research Fund	Charity	yes
	Scottish Executive Health Department	Government Agency	yes
	The Fund for Epilepsy	Charity	yes
	The Migraine Trust	Charity	yes
	The Psychiatry Research Trust	Charity	no answer
	The Stroke Association	Charity	yes
	The Wellcome Trust	Charity	yes
	Wales office of R&D	Government Agency	yes
	Yorkshire Cancer Research	Charity	decline

Note: yes= data are received either directly from the organization or from their web page
no answer = failed to obtain
decline = could not answer the request for various reasons
zero spending = did not give any research funding in 2004

Result tables and calculations

Result tables from imputations

The following results were imputed using an Index which was based on the reference countries' R&D/capita. The indices used for price adjustment were different variations in the Comparative Price Level Index (CPL). All figures are in 2005 years value.

Comparative Price Level Index (CPL)	CPL based on reference countries**	CPL based on reference countries except UK	CPL based on all 28 countries	CPL based on EU-25
Austria*	2 973 044	2 983 168	2 537 043	2 681 155
Belgium*	7 523 377	7 548 998	6 420 065	6 784 745
Cyprus	*163 144*	*163 700*	*139 219*	*147 127*
Czech Rep	*6 650 572*	*6 673 220*	*5 675 257*	*5 997 630*
Denmark*	6 607 808	6 630 310	5 638 764	5 959 064
Estonia*	1 299 350	1 303 775	1 108 799	1 171 782
Finland*	5 636 369	5 655 564	4 809 789	5 083 000
France	*107 400 370*	*107 766 117*	*91 649 973*	*96 855 982*
Germany*	78 769 805	79 038 052	67 218 116	71 036 318
Greece	*3 895 027*	*3 908 292*	*3 323 817*	*3 512 620*
Hungary*	29 733 769	29 835 026	25 373 275	26 814 557
Iceland*	110 370	110 746	94 184	99 534
Ireland*	27 095 819	27 188 093	23 122 184	24 435 597
Italy	*50 476 775*	*50 648 672*	*43 074 294*	*45 521 050*
Latvia	*318 110*	*319 193*	*271 459*	*286 878*
Lithuania	*912 677*	*915 785*	*778 832*	*823 072*
Luxembourg*	398 472	399 829	340 035	359 351
Malta	*59 897*	*60 101*	*51 113*	*54 016*
Netherlands*	35 542 195	35 663 232	30 329 888	32 052 722
Norway*	9 976 602	10 010 577	8 513 521	8 997 116
Poland	*7 528 205*	*7 553 842*	*6 424 184*	*6 789 098*
Portugal	*4 552 919*	*4 568 424*	*3 885 228*	*4 105 921*
Slovakia	*1 086 532*	*1 090 233*	*927 191*	*979 859*
Slovenia	*1 843 898*	*1 850 178*	*1 573 488*	*1 662 868*
Spain	*32 949 506*	*33 061 714*	*28 117 421*	*29 714 579*
Sweden*	17 309 497	17 368 443	14 771 038	15 610 079
Switzerland*	8 632 573	8 661 971	7 366 596	7 785 042
UK*	311 777 033	312 838 774	266 054 545	281 167 287
EC	93 986 367	93 986 367	93 986 367	93 986 367
Total	855 210 084	857 802 393	743 575 685	780 474 418

Note: *reference country, **this result table is used in the analysis, figures in italics are imputed values
CPL has been used for adjusting the national estimates to comparative price levels and the Imputation index was used for the imputing values for the countries.
The indices are based on different groupings of countries. The mean value of the selected countries has been set to the value of 1. All countries have thereafter received their relative index value, based on the relationship of their original value to the mean.

The following results used an Index based on the Comparative Price Level of the reference countries, for price adjustment of reference countries' estimates; instead the Imputation Index differed for the following calculations. All figures are in 2005 years value.

Imputation Index	CPL Index based on reference countries	Index based on Health expenditure /capita for reference countries	Index based on Health expenditure /capita for all countries	Based on All countries R&D/capita
Austria*	2 973 044	2 973 044	2 973 044	2 973 044
Belgium*	7 523 377	7 523 377	7 523 377	7 523 377
Cyprus	*1 183 687*	*465 185*	*604 312*	*245 477*
Czech Rep	*9 717 183*	*11 305 752*	*14 687 072*	*10 006 864*
Denmark*	6 607 808	6 607 808	6 607 808	6 607 808
Estonia*	1 299 350	1 299 350	1 299 350	1 299 350
Finland*	5 636 369	5 636 369	5 636 369	5 636 369
France	*112 259 800*	*119 668 925*	*155 459 462*	*161 601 282*
Germany*	78 769 805	78 769 805	78 769 805	78 769 805
Greece	*16 560 623*	*11 070 291*	*14 381 189*	*5 860 701*
Hungary*	29 733 769	29 733 769	29 733 769	29 733 769
Iceland*	110 370	110 370	110 370	110 370
Ireland*	27 095 819	27 095 819	27 095 819	27 095 819
Italy	*103 467 942*	*94 886 977*	*123 265 738*	*75 950 498*
Latvia	*2 381 165*	*799 069*	*1 038 055*	*478 648*
Lithuania	*3 290 487*	*1 346 136*	*1 748 738*	*1 373 271*
Luxembourg*	398 472	398 472	398 472	398 472
Malta	*522 819*	*442 613*	*574 990*	*90 124*
Netherlands*	35 542 195	35 542 195	35 542 195	35 542 195
Norway*	9 976 602	9 976 602	9 976 602	9 976 602
Poland	*34 828 365*	*18 400 871*	*23 904 197*	*11 327 405*
Portugal	*15 607 832*	*12 508 787*	*16 249 910*	*6 850 606*
Slovakia	*5 170 711*	*1 554 537*	*2 019 468*	*1 634 864*
Slovenia	*2 641 405*	*2 492 077*	*3 237 407*	*2 774 444*
Spain	*65 167 583*	*52 792 835*	*68 582 095*	*49 577 878*
Sweden*	17 309 497	17 309 497	17 309 497	17 309 497
Switzerland*	8 632 573	8 632 573	8 632 573	8 632 573
UK*	311 777 033	311 777 033	311 777 033	311 777 033
EC	93 986 367	93 986 367	93 986 367	93 986 367
Total	1 010 172 053	965 106 507	1 063 125 083	965 144 512

Note: * = reference country, figures in italics are imputed values. CPL has been used for adjusting the national estimates to comparative price levels and the Imputation index was used for the imputing values for the countries. The indices are based on different groupings of countries. The mean value of the selected countries has been set to the value of 1. All countries have then received their relative index value, based on their original value's relationship to the mean.

Spending by organization type and reference country (2005)

Country	Charities	Government agencies	Total
Austria	124 581	2 848 463	2 973 044
Belgium	83 689	7 439 689	7 523 377
Denmark	4 265 816	2 341 992	6 607 808
Estonia	0	1 299 350	1 299 350
Finland	1 112 826	4 523 543	5 636 369
Germany	14 650 256	64 119 549	78 769 805
Hungary	0	29 733 769	29 733 769
Iceland	0	110 370	110 370
Ireland	239 639	26 856 180	27 095 819
Luxembourg	10 848	387 624	398 472
Netherlands	7 989 921	27 552 275	35 542 195
Norway	922 299	9 054 303	9 976 602
Sweden	7 329 341	9 980 156	17 309 497
Switzerland	704 782	7 927 791	8 632 573
UK	106 647 583	205 129 449	311 777 033
European Commission	0	93 986 367	93 986 367
Total	144 081 580	493 290 869	637 372 450

Total number of NCEs, CNS drugs and their share on the European market (1985 - 2004)

Approval years	All NCEs	CNS classification	Share
1985	21	1	4.76%
1986	20	1	5.00%
1987	26	0	0.00%
1988	21	3	14.29%
1989	27	4	14.81%
1990	42	4	9.52%
1991	31	5	16.13%
1992	30	1	3.33%
1993	51	0	0.00%
1994	34	5	14.71%
1995	56	6	10.71%
1996	59	6	10.17%
1997	50	7	14.00%
1998	58	11	18.97%
1999	58	3	5.17%
2000	47	4	8.51%
2001	48	6	12.50%
2002	34	2	5.88%
2003	23	1	4.35%
2004	40	4	10.00%
Total	776	**74**	**9.54%**

Total number of CNS NCEs by disease area

By disease areas	# NCEs	Share
Addiction disorders	3	4.05%
Affective disorders	13	17.57%
Anxiety disorders	2	2.70%
Brain tumour	1	1.35%
Dementia (incl. Alzheimer)	5	6.76%
Epilepsy	9	12.16%
Migraine and other headaches	7	9.46%
MS	4	5.41%
Parkinson	9	12.16%
Stroke	8	10.81%
TBI	0	0.00%
Schizophrenia	7	9.46%
Other brain disorders	6	8.11%
Total	**74**	

Number of CNS NCEs by disease area and spending over time (1995-2004)

	1995-1999			2000-2004		
By disease areas	**# NCEs**	**Share**	**Funding**	**# NCEs**	**Share**	**Funding**
Addiction disorders	1	3.03%	82,941,389.5	2	11.76%	359,258,365.9
Affective disorders	5	15.15%	414,706,947.7	3	17.65%	538,887,548.8
Anxiety disorders	0	0.00%	0.0	0	0.00%	0.0
Brain tumour	1	3.03%	82,941,389.5	0	0.00%	0.0
Dementia (incl. Alzheimer)	3	9.09%	248,824,168.6	2	11.76%	359,258,365.9
Epilepsy	4	12.12%	331,765,558.2	2	11.76%	359,258,365.9
Migraine and other headaches	3	9.09%	248,824,168.6	3	17.65%	538,887,548.8
MS	3	9.09%	248,824,168.6	1	5.88%	179,629,182.9
Parkinson	6	18.18%	497,648,337.3	1	5.88%	179,629,182.9
Stroke	4	12.12%	331,765,558.2	0	0.00%	0.0
TBI	0	0.00%	0.0	0	0.00%	0.0
Schizophrenia	2	6.06%	165,882,779.1	2	11.76%	359,258,365.9
Other brain disorders	1	3.03%	82,941,389.5	1	5.88%	179,629,182.9
Total	**33**		**2,737,065,855.0**	**17**		**3,053,696,110.0**

Calculation of NCEs: Cost per NCE and total spending of brain drug(s) by year (1985-2004)

Years	Number of NCEs	Cost per NCE in € million	Total spending in € million
1985	1	129,500,000.00	129,500,000.00
1986	1	165,000,000.00	165,000,000.00
1987	0	200,500,000.00	0.00
1988	3	218,250,000.00	654,750,000.00
1989	4	236,000,000.00	944,000,000.00
1990	4	253,750,000.00	1,015,000,000.00
1991	5	271,500,000.00	1,357,500,000.00
1992	1	289,250,000.00	289,250,000.00
1993	0	**307,000,000.00**	**0.00**
1994	5	324,750,000.00	1,623,750,000.00
1995	6	342,500,000.00	2,055,000,000.00
1996	6	360,250,000.00	2,161,500,000.00
1997	7	**378,000,000.00**	**2,646,000,000.00**
1998	11	507,250,000.00	5,579,750,000.00
1999	3	636,500,000.00	1,909,500,000.00
2000	4	765,750,000.00	3,063,000,000.00
2001	6	**895,000,000.00**	**5,370,000,000.00**
2002	2	1,024,250,000.00	2,048,500,000.00
2003	1	1,153,500,000.00	1,153,500,000.00
2004	4	1,282,750,000.00	5,131,000,000.00
Total	74	9,741,250,000.00	37,296,500,000.00
Average per year			1,962,973,684.21

Calculation of NCEs: Average annual spending of brain drugs by five-year periods (1985-2004)

Years	Number of NCEs	Cost per NCE	Total spending in €	Per year
1985-1989	9	NA	NA	NA
1990-1994	15	307,000,000	4,605,000,000	1,151,250,000
1995-1999	33	378,000,000	12,474,000,000	3,118,500,000
2000-2004	17	895,000,000	15,215,000,000	3,803,750,000

Calculations of R&D expenditure: R&D expenditure for neuroscience in Europe by year (1985-2004)

Years	R&D expenditures in € million	R&D expenditures in neuroscience
1985	4,642,000,000.00	450,970,300.00
1986	5,273,600,000.00	512,330,240.00
1987	5,905,200,000.00	573,690,180.00
1988	6,536,800,000.00	635,050,120.00
1989	7,168,400,000.00	696,410,060.00
1990	**7,800,000,000.00**	851,955,000.00
1991	8,431,600,000.00	920,941,510.00
1992	9,063,200,000.00	989,928,020.00
1993	9,694,800,000.00	1,058,914,530.00
1994	10,326,400,000.00	1,127,901,040.00
1995	**10,958,000,000.00**	1,616,852,900.00
1996	12,265,400,000.00	1,809,759,770.00
1997	13,572,800,000.00	2,002,666,640.00
1998	14,880,200,000.00	2,195,573,510.00
1999	16,187,600,000.00	2,388,480,380.00
2000	**17,495,000,000.00**	1,803,734,500.00
2001	*18,800,000,000.00*	1,938,280,000.00
2002	*20,164,000,000.00*	2,078,908,400.00
2003	**21,100,000,000.00**	2,175,410,000.00
2004	22,301,670,000.00	2,299,302,177.00
Total	242,566,670,000.00	28,127,059,277.00
Average per year		1,480,371,540.89

Calculations of R&D expenditure: Average annual spending of R&D expenditure for neuroscience by five-year periods (1985-2004)

Years	Total R&D expenditures	R&D expenditures in neuroscience	Per year
1985-1989	29,526,000,000.00	2,868,450,900.00	717,112,725.00
1990-1994	45,316,000,000.00	4,949,640,100.00	1,237,410,025.00
1995-1999	67,864,000,000.00	10,013,333,200.00	2,503,333,300.00
2000-2004	99,860,670,000.00	10,295,635,077.00	2,573,908,769.25

List of brain NCEs (1985-2004)

The list of all neurological drugs between 1985 and 2005 can be obtained from the authors upon request.

NCEs by disease areas	Approval years	Substance	ATC codes
Addiction disorders: alcohol and illicit substance disorders			
Camprals	*1996*	acamprosate	N07BB03
Revia®	*2000*	naltrexone hydrochloride	N07BB04
Zyban®	*2000*	bupropion hydrochloride	N07BA02
Affective disorders: depression, bipolar			
Aurorix	*1989*	moclobemide	N06AG02
Fevarin®	*1990*	fluvoxamine maleate	N06AB08
Tolvon®	*1990*	mianserin hydrochloride	N06AX03
Seroxat®	*1991*	paroxetine hydrochloride hemihydrate	N06AB05
Cipramil	*1992*	citalopram hydrobromide	N06AB04
Efexor	*1995*	venlafaxine, venlafaxine hydrochlorid	N06AX16
Fontex® Basal	*1995*	fluoxetine hydrochloride	N06AB03
Zoloft	*1995*	sertraline hydrochloride	N06AB06
Remeron®	*1996*	mirtazapine	N06AX11
Edronax	*1997*	reboxetine mesylate	N06AX18
Cipralex	*2001*	escitalopram, escitalopram oxalate	N06AX21
Xeristar	*2004*	duloxetine hydrochloride	N06AX21
Yentreve®	*2004*	duloxetine hydrochloride	N06AX21
Anxiety disorders: obsessive compulsive disorder, phobic disorder, panic disorder, and generalized anxiety			
Xanor®	*1985*	alprazolam	N05BA12
Buspar®	*1991*	buspirone hydrochloride	N05BE01
Brain tumour (cancer)			
Temodal	*1999*	temozolomide	L01AX03
Dementia (including Alzheimer's disease)			
Aricept	*1997*	donepezil hydrochloride	N06DA02
Exelon®	*1998*	rivastigmine hydrogentartrate	N06DA03
Prometax	*1998*	rivastigmine hydrogentartrate	N06DA03
Reminyl®	*2000*	galantamine hydrobromide	N06DA04
Ebixa	*2002*	memantine hydrochloride	N06DX01
Epilepsy			
Sabrilex®	*1990*	vigabatrin	N03AG04
Lamictal®	*1994*	lamotrigine	N03AX09
Neurontin	*1994*	gabapentin	N03AX12
Taloxa®	*1995*	felbamate	N03AX10
Topimax®	*1996*	topiramate	N03AX11
Pro-Epanutin	*1998*	fosphenytoin sodium	N03AB05
Trilleptal®	*1999*	oxcarbazepine	N03AF02
Keppra	*2000*	levetiracetam	N03AX14
LYRICA	*2004*	pregabalin	N03AX16

Migraine and other headaches			
Imigran®	*1991*	sumatriptan succinate	N02CC01
Naramig®	*1997*	naratriptan hydrochloride	N02CC02
Zomig®	*1997*	zolmitriptan	N02CC03
Maxalt®	*1998*	rizatriptan benzoate	N02CC04
Almogran	*2001*	almotriptan malate	N02CC05
Relpax	*2001*	eletriptan hydrobromide	N02CC06
Migard	*2002*	frovatriptan succinate monohydrate	N02CC07

Multiple Sclerosis			
Betaferon (Betaseron)	*1995*	interferon bet-1b	L03AB08
Avonex	*1997*	interferon bet-1a	L03AB07
Rebif	*1998*	interferon bet-1a	L03AB07
Copaxone	*2001*	glatiramer acelate	L03AX13

Parkinson's disease			
Madopark®	*1988*	benserazide hydrochloride, levodopa	N04BA02
Eldepryl®	*1989*	selegiline hydrochloride	N04BD01
Requip®	*1996*	ropinirole hydrochloride	N04BC04
Daquiran	*1997*	pramipexole, pramipexole dihydrochloride monohydrate	N04BC05
Sifrol®	*1997*	pramipexole, pramipexole dihydrochloride monohydrate	N04BC05
Comtan	*1998*	entacapone	N04BX02
Comtess®	*1998*	entacapone	N04BX02
Mirapexin	*1998*	pramipexole, pramipexole dihydrochloride monohydrate	N04BC05
Apo-go Pen	*2001*	apomorphine hydrochloride	N04BC07

Stroke			
Zocord®	*1988*	simvastatin	C10AA01
Nimotop®	*1989*	nimodipine	C08CA06
Actilyse®	*1990*	alteplase	B01AD02
Cozaar®	*1994*	losartan potassium	C09CA01
Actilyse®	*1995*	alteplase	B01AD02
Crixivan®	*1996*	indinavir sulphate	J05AE02
Iscover	*1998*	clopidogrel hydrogensulfate	B01AC04
Plavix	*1998*	clopidogrel hydrogensulfate	B01AC04

TBI			

Schizophrenia			
Leponex®	*1989*	clozapine	N05AH02
Roxiam	*1991*	remoxipride hydrochloride monohyddrate	N05AL04
Risperdal®	*1993*	risperidone	N05AX08
Zyprexa®	*1996*	olanzapine	N05AH03
Zeldox	*1998*	ziprasidone hydrochloride	N05AE04
Seroquel®	*2003*	quetiapine fumarate	N05AH04
Abilify	*2004*	aripiprazole	N05AX12

Other brain disorders: neuromuscular disorders (myasthenia gravis – muscles disease, amyotrophic lateral sclerosis - ALS, and neuropathy), development disorders such as ADHD, sleeping disorders, and conduct disorders			
Halcion®	*1986*	triazolam	N05CD05
Lanexat	*1988*	bensodiazepinantagonist	V03AB25
Imovane®	*1991*	zopiclone	N05CF01
Stilnoct	*1994*	zolpidem tartrate	N05CF02
Sonata®	*1999*	zaleplon	N05CF03
Modiodal®	*2001*	modafinil	L01AX03