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Economic evidence in anxiety disorders: a review

Introduction

This review is part of the set of literature reviews being produced in the project Cost of Disorders of the Brain in Europe sponsored by the European Brain Council (EBC). The objective of this review is to provide an overview of the available economic evidence in the literature on affective disorders in Europe.

Objective

The objective of this research is to review the published literature of cost and cost-

of-illness assessments for the anxiety disorders in Europe. More specifically, the following disease areas are reviewed:

- Panic disorders (with and without agoraphobia)
- Agoraphobia without panic disorder
- Generalised anxiety disorder (GAD)
- Obsessive compulsive disorder
- Social phobia
- Any specific phobia (animal, natural environment, blood-injection injury, situational etc.)
- Anxiety disorders [not otherwise specified (NOS)]

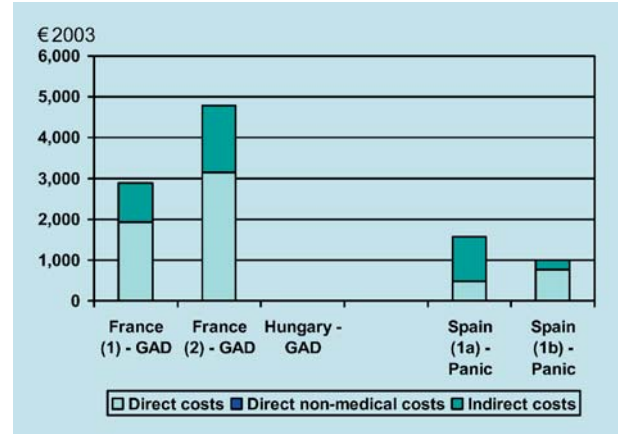


Fig. 1 ► Total cost per patient (€ 2003), GAD and panic disorder

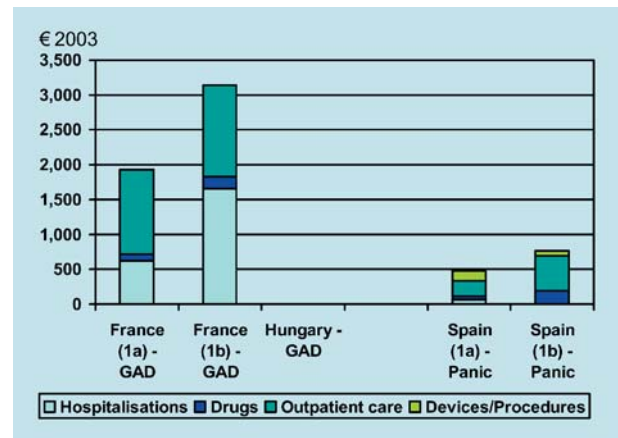


Fig. 2 ► Direct cost per patient (€ 2003), GAD and panic disorder

Methods

A systematic literature search and review was conducted. The literature was searched using the electronic databases PubMed/MEDLINE. The identified references were screened using a two-step approach prior to inclusion of reference in final review:

- Title, keywords and abstracts for all identified references in the literature search were screened for eligibility and inclusion in the review.
- Full articles that in the first screening step were identified as potentially eli-

gible were retrieved and reviewed for final assessment of eligibility for inclusion in the review.

Once identified as eligible for inclusion in the review, data were extracted for inclusion in the final literature review. Additionally, the reference lists of the identified potentially eligible studies were hand-searched for identification of additional references. Only literature in English was reviewed.

Literature search strategy

The literature searches were based on combined searches using disease-specific,

economic-specific and country-specific search terms. The specific terms used in the search strategy are specified in the following sections.

Disorder search terms

The following disorder-specific search terms were used in the literature searches:

- Panic disorder OR
- Agoraphobia OR
- Generalized anxiety disorder OR GAD OR
- Obsessive compulsive disorder OR OCD OR
- Social phobia OR
- Anxiety disorders NOS OR Anxiety disorders not otherwise specified

Economic search terms

The following economic search terms were used in the literature searches:

- Health economics OR
- Economics OR
- Costs OR Cost analysis OR
- Cost of illness OR
- Burden of illness OR

Table 1

Literature search and screening results overview		
	GAD	Panic disorder
No. of identified studies in initial literature search	83	3
No. of studies eligible for inclusion in final review	2	1
No. of studies by country		
France	1	
Hungary	1	
Spain		1

Table 2

Study characteristics						
Country	Reference	Approach/design	Follow-up/ time frame	Sample/prevalence	Currency	Year
France	[1]	Cross-sectional retrospective assessment of resource use and costs for patients with DSM-III-R GAD, without and with comorbidities. Study France (1a) gives results with/without and France (1b) with comorbidities.	3 months	n=604 with comorbidity n=395 w/o comorbidity	USD	n/a (1994 publication)
Hungary	[2]	Retrospective/prospective case-control 2-year pre-post design (with treatment vs. „usual care“ comparison). Diagnosis not clearly specified as GAD - rather „current anxiety“ and/or mood disorder at inclusion	1 year pre- and 1 year post-treatment	n=51 treatment group, n= 75 control group.	HUF	n/a (2002 submission)

Table 3

Study characteristics (panic disorder studies)						
Country	Reference	Approach/design	Follow-up/ time frame	Sample/prevalence	Currency	Year
Spain	[3]	Retrospective/prospective 2-year pre-post design. 1-year retrospective assessments pre-diagnosis and treatment and 1-year prospective assessments after diagnosis/treatment. Study Spain (1a) gives results 1-year pre-diagnosis/treatment, and Spain (1b) 1-year after diagnosis/treatment.	1 year pre- and 1 year post-treatment	n=61	USD	1992

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Table 4

Total cost per patient (original currency/year), GAD

Country	Reference	Total costs	Direct medical costs	Indirect costs	Currency	Year
France (1a) – with/without comorbidities	[1]	2936	1964	972	USD	n/a
France (1b) – with comorbidities	[1]	4868	3204	1664	USD	n/a
Hungary ^a	[2]					

Table 5

Total cost per patient (original currency/year), panic disorder

Country	Reference	Total costs	Direct medical costs	Indirect costs	Currency	Year
Spain (1a) – pre diag/treat	[3]	1552	476	1076	USD	1992
Spain (1b) – post diag/treat	[3]	985	758	228	USD	1992

Table 6

Direct cost per patient (original currency/year), GAD

Country	Reference	Total direct costs	Inpatient care	Drugs	Out-patient care	Currency	Year
France (1a) – with/without comorbidities	[1]	1 964	632	100	1232	USD	n/a
France (1b) – with comorbidities	[1]	3 204	1692	172	1340	USD	n/a
Hungary	[2]	17 697 ^a	2 ^b	17 697		HUF	n/a

^a Represents drug costs component only. ^b Average number of hospital days.

Table 7

Direct cost per patient (original currency/year), panic disorder

Country	Reference	Total direct costs	Inpatient care	Drugs	Out-patient care	Devices/procedures	Currency	Year
Spain (1a) – pre-diag/treat	[3]	476	62	51	217	147	USD	1992
Spain (1b) – post-diag/treat	[3]	758	0	191	494	73	USD	1992

- Economic evaluation OR
- Cost effectiveness OR
- Cost utility OR
- Cost benefit OR
- Cost minimization OR Cost minimisation

Countries

The literature search included a search of all current 25 EU membership countries, as well as Norway, Switzerland and Iceland.

EU member states. Belgium, Denmark, Germany, Greece, Spain, France, Ireland, Italy, Luxembourg, The Netherlands, Austria, Portugal, Finland, Sweden, United Kingdom, Czech Republic, Estonia, Cyprus, Latvia, Lithuania, Hungary, Malta, Poland, Slovenia and Slovakia

Other European countries. Norway, Switzerland, Iceland

Results

Literature search results

■ **Tables 1-3** summarize the findings from the initial literature search using the above specified search strategy and the number of studies identified as eligible for inclusion in the review after screening.

As no eligible studies were found for the other anxiety disorders, they have not been included in ■ **Table 1** above. The number of initially identified references for the other disorders was:

- Agoraphobia: 2
- OCD: 3
- Social phobia: 5
- Anxiety disorders NOS: 0

After screening, none of these was found to be eligible for inclusion in the review.

The following section summarizes the main findings from the detailed review of the identified GAD and panic disorder studies.

Literature review

In the following, the main findings from the reviewed anxiety studies are discussed and the detailed data extracted from the reviewed studies are presented in a set of tables. ■ **Tables 2 and 3** present the study

Table 8

Indirect cost per patient (original currency/year), GAD

Country	Reference	Total indirect costs	Short-term absence	Currency	Year
France (1a) – with/without comorbidities	[1]	972	972	USD	n/a
France (1b) – with comorbidities	[1]	1664	1664	USD	n/a
Hungary	[2]		15 ^a		

^aAverage number of days absent/on sick-leave

Table 9

Indirect cost per patient (original currency/year), Panic disorder

Country	Reference	Total indirect costs	Short-term absence	Currency	Year
Spain (1a) – pre diag/treat	[3]	1076	1076	USD	1992
Spain (1b) – post diag/treat	[3]	228	228	USD	1992

Table 10

Total cost per patient (€, 2003), GAD

Country	Reference	Total costs	Total direct medical costs	Total indirect costs
France (1a) – with/without comorbidities	[1]	2882	1928	954
France (1b) – with comorbidities	[1]	4778	3145	1633
Hungary	[2]	n/a	35 ^a	15 ^b

^aRepresents drug cost component only. ^bAverage number of days absent/on sick-leave

Table 11

Total cost per patient (€, 2003), panic disorder

Country	Reference	Total costs	Total direct medical costs	Total indirect costs
Spain (1a) – pre-diag/treat	[3]	1568	481	1087
Spain (1b) – post- diag/treat	[3]	996	766	230

characteristics, **Table 4-9** present costs as presented in the studies in original currency/year. **Tables 4 and 5** present the findings for total cost and its main cost components, direct medical and non-medical cost as well as indirect costs. **Tables 6 and 7** present the findings for total direct medical cost and its main components, inpatient care, drugs, outpatient care and devices/procedures. **Tables 8 and 9** present total indirect cost and its main components, short-term absence, early retirement and mortality, respectively.

To allow a comparison of the available data between different studies within a given country as well as between studies across countries, the following **Tables 10 – 15** and **Figs 1 and 2** present costs inflated and converted to cost levels ex-

pressed in € in the cost base level of year 2003. **Tables 10 and 11** present the findings for total cost and its main cost components. **Tables 12 and 13** present the findings for total direct medical costs and its main components and **Tables 14 and 15** present the findings for total indirect cost and its main components.

The French GAD study by Souetre et al. [1] is a cross-sectional 3months' retrospective assessment of the resource use and costs for patients with GAD, n=604 with and n=395 without comorbidities.

The Hungarian GAD study by Zambori et al. [2] is a case-control combined retrospective/prospective pre-post study of treatment vs. usual care after diagnosis. The diagnosis not clearly specified as GAD - rather "current anxiety" and/

or mood disorder at inclusion. This study, however, only reports cost data for the drug costs. For inpatient care and indirect costs only average number of hospital stay days, and average number of days absent from work on sick leave are reported. No costing has been done in this review for the Hungarian study data.

The only identified and reviewed panic study is a Spanish study with a 2-year combined retrospective/prospective design of n=61 patients in Spain.

The only GAD study useful for cost estimates is the French study by Souetre et al. [1]. This study provides estimates of the total costs for GAD ranging from € 2882 to € 4778 per patient per year for GAD, with and without comorbidities, respectively. The existence of comorbidities

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Table 12

Direct cost per patient (€, 2003), GAD

Country	Reference	Total direct costs	Inpatient care	Drugs	Outpatient care
France (1a) – with/without comorbidities	[1]	1928	620	98	1209
France (1b) – with comorbidities	[1]	3145	1661	169	1315
Hungary ^a	[2]	35	2 ^a	35	

^aAverage number of hospital days

Table 13

Direct cost per patient (€, 2003), panic disorder

Country	Reference	Total direct costs	Inpatient care	Drugs	Outpatient care	Devices/procedures
Spain (1a) – pre-diag/treat	[3]	481	62	51	219	148
Spain (1b) – post-diag/treat	[3]	766	0	193	499	74

Table 14

Indirect cost per patient (€, 2003), GAD

Country	Reference	Total indirect costs	Short-term absence
France (1a) – with/without comorbidities	[1]	954	954
France (1b) – with comorbidities	[1]	1633	1633
Hungary	[2]	15 ^a	15 ^a

^aAverage number of days absent/on sick-leave

Table 15

Indirect cost per patient (€, 2003), panic disorder

Country	Reference	Total indirect costs	Short-term absence
Spain (1a) – pre-diag/treat	[3]	1087	1087
Spain (1b) – post-diag/treat	[3]	230	230

thus increases the costs by approximately 65% for GAD (in France). The increase in costs for GAD with vs. without comorbidities is about the same also for the cost components direct medical costs and indirect costs (short-term absence from work). The total direct medical costs are € 1928 vs. € 3145 without and with comorbidities, respectively, and the indirect costs are € 954 vs. € 1633.

For the Spanish panic disorder study by Salvador-Carulla et al. [3], the results indicate that the total costs for panic disorder was € 1568 1 year prior to diagnosis and treatment and € 996 the year after diagnosis and treatment. The diagnosis and treatment thus reduced the total costs for panic disorder for the patient sample in Spain. As expected, the di-

rect medical costs increase after diagnosis/treatment whereas the indirect costs decrease. The average total direct cost was € 481 during the year prior to diagnosis and treatment and € 766 the year after, whereas the average indirect cost due to short-term absence from work was € 1087 vs. € 230. This study hence provides support for the offset of the total costs in diagnosing and treating patients with panic disorder.

A comparison between the GAD and panic disorder indicates a difference in the resource use/cost structure between the disorders in that the use of tests and procedures is quite pronounced in panic disorder, whereas the tests and procedures account for around 30% of the total direct medical costs during the year prior to

diagnosis and around 10% in the year after diagnosis and treatment. For GAD this cost component is not even measured. As the French GAD study is a retrospective study, it should have included any relevant resource use/costs occurring in the sample of charts reviewed.

Summary and conclusions

Based on this literature review, one obvious conclusion is that there are currently big gaps in the available literature regarding the costs of anxiety disorders in Europe. Very few studies reporting cost estimates were found. Only two studies in total were found for GAD, one from France and one from Hungary. Only one Spanish study was found for panic disorder.

No studies were found for the other anxiety disorders.

The reviewed studies reveal some cost patterns in France (for GAD) for patients with and without comorbidities and for Spain for panic disorder patients; but from a European-wide perspective, based on these scarce findings, the lack of available data makes it difficult, if not impossible, to use the identified data to extrapolate the costs in countries where no studies/data were found.

The only conclusion that can be made regarding this is the clear need for more research in this area, both in the Western European countries as well as in the Central and Eastern European countries.

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Economic evidence in brain tumour: a review

Introduction

The most striking feature of the literature on the cost of illness of brain tumours in Europe is the almost complete lack of comprehensive studies. There is, in fact, only one comprehensive study on the cost of brain tumours – a Swedish study published in the year 2000 [1]. The reasons for this are unclear. On the one hand, brain tumours are, thankfully, relatively rare. In comparison with prostate and breast tumours, the incidence is low. On the other hand, brain tumours often hit younger people and even small children, with the possible loss of many life years as the unfortunate consequence. After an overview of the epidemiology, classification and treatment of brain tumours, we will take a closer look at the Swedish study on the cost of brain tumours in Sweden in 1996, and briefly review some other studies with a more limited scope. For obvious reasons, the review section of this paper will be rather short. We will then go on to discuss the reasons for the lack of published studies and finally present some possible directions for further research in this area.

Brain tumours

Incidence and classification

Brain tumours represent about 2% of all newly diagnosed tumours. There were 1009 new cases in Sweden in the year 2000, which meant that the incidence was 11.3 per 100 000 inhabitants (Cancer Incidence in Sweden 2002). In Europe as a whole, there seems to be some variation in the incidence rates. In 1995, the incidence ranged from about 4 to about 11 per 100 000 inhabitants. Sweden is thus in

the upper range among European countries. For Europe as a whole, the incidence was 7.9/100 000 for men and 5.4/100 000 for women. There were fewer than 50 000 cases of cancer of the brain and central nervous system in Europe in 1995. The age-standardized mortality rates were 5.9/100 000 for men and 3.9/100 000 for women [2].

Brain tumours, or intracranial neoplasms, are a diverse set of tumours that are primarily classified by site and malignancy [3]. Astrocytomas are the most common; they represent about 45% of all brain tumours. Second most common are benign meningiomas, which represent about 15-20% of all cases. Astrocytomas belong to the larger category of gliomas, which also includes oligodendroglioma. Roughly speaking, gliomas represent 70% of the cases, and meningiomas make up the remaining 30%.

Brain tumours are classified in primary and secondary. Primary brain tumours originate in the brain itself, while secondary brain tumours are metastases originating in another part of the body. Secondary tumours are always malignant, while primary tumours occur in both benign and malignant forms. Although primary brain tumours are not as common as breast or lung carcinoma, brain tumours affect children and young people to a significant degree and cause a high portion of cancer mortality in these age groups. Primary brain tumours occur in all age groups, but are significantly more frequent in children and adolescents under 15 years old and in the elderly. For every person diagnosed with a brain tumour, an average of 22 years of life expectancy is lost according to Turini and Redaelli [4], which is high compared to most other tu-