

ORIGINAL ARTICLE

Analysis of direct, indirect, and intangible costs of epilepsy

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QOLIE-10

Abstract

Introduction: A financial estimate has been made of the costs of epilepsy in adults.

Methods: A prospective, observational study, over a period of 6 months, on epileptic patients over 14 years old. Patients with concomitant diseases that could influence the outcome of the epilepsy were excluded. The direct costs included: treatment received, number of visits to neurology, primary care, and emergencies, number of days admitted to hospital, number and type of diagnostic tests, use of transport to and from hospital, and psychopedagogic and social support due to the epilepsy. The indirect costs were analysed according to, loss of work productivity of the patients, taking into account families where the patient needed supervision due to epilepsy. The total costs were derived from the sum of the direct and indirect costs. The intangible costs were calculated according to QOLIE-10 questionnaire.

Results: The mean direct cost per patient was € 1,055.20. The mean indirect financial costs came to € 1,528.80 per patient. The total cost associated to epilepsy was a mean of € 2,584 for each patient, mainly arising from loss of work days ($p < .05$). For intangible costs according to the QOLIE-10 scale a mean of 77.8 was obtained.

Conclusions: The greatest percentage of costs associated to epilepsy is due to the work productivity loss by the patients. The costs of psychological and social suffering in epilepsy lead to a deterioration in the quality of life.

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PALABRAS CLAVE

Coste;
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Indirectos;
Intangibles;
Farmacoeconomía;
Calidad de vida;
QOLIE-10

Análisis de costes directos, indirectos e intangibles de la epilepsia**Resumen**

Introducción: Se ha realizado una estimación económica de los costes de epilepsia en adultos.

Métodos: Estudio observacional prospectivo realizado durante 6 meses, en pacientes epilépticos mayores de 14 años. Se excluyeron los pacientes con enfermedades concomitantes que pudieran influir en la evolución de la epilepsia. Los costes directos incluyeron: tratamiento administrado, número de consultas en Neurología, Atención Primaria, y Urgencias, número de días de ingreso hospitalario, número y tipo de pruebas diagnósticas, uso de los medios de transporte al hospital y desde el hospital, y los apoyos psicopedagógicos y sociales por epilepsia. Los costes indirectos se analizaron en función de la pérdida de productividad laboral de los pacientes, con consideración de los familiares cuando los pacientes necesitaban supervisión a causa de la epilepsia. Los costes totales se derivaron de la suma de los costes directos e indirectos. Los costes intangibles se evaluaron según el cuestionario QOLIE-10.

Resultados: La media de los costes directos por paciente fue de 1.055,2 €. El gasto económico medio en los costes indirectos ascendió a 1.528,8 € por paciente. El total de los costes asociados a la epilepsia supuso una media de 2.584 € por cada paciente, derivados sobre todo de la pérdida de productividad laboral ($p < 0,05$). En los costes intangibles, según la escala QOLIE-10, la media obtenida fue de 77,8.

Conclusiones: El mayor porcentaje de los costes asociados a la epilepsia corresponde a la pérdida de productividad laboral de los pacientes. Los costes del sufrimiento psicológico y social en epilepsia provocan deterioro de la calidad de vida.

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Introduction

The economic cost of illnesses increases the repercussion these have on patients and their families.¹ In addition, chronic diseases are the main consumers of a country's health budgets.² For these reasons, in a context of growing health-care expenditure, economic studies applied to health take on particular importance. Therefore, understanding the costs of epilepsy, one of the most frequent neurological illnesses, increases awareness of how it affects individuals and society. This paper is aimed at carrying out an economic estimate of the direct, indirect and intangible costs of epilepsy in adults.

Patients and methods

It is a prospective observational study from the perspective of society with 6 months' follow-up conducted at the Neurology Department of the POVISA hospital in Vigo. The patients included were adults (>14 years) with a definite diagnosis of epilepsy according to the 1989 ILAE criteria.³ So that the costs analyzed could be attributed to epilepsy as such, patients with concomitant illnesses (tumours, degenerative diseases and metabolic pathologies) were excluded if these could influence the progress of epilepsy, the therapeutic protocols or on the repercussion of the treatments applied, although consideration was given to the cause of their epilepsy.

In order to achieve an economic estimate of epilepsy, after informed consent was obtained in writing, a

questionnaire developed for the purpose was applied to the patients to assess the direct, indirect and intangible costs. In the questionnaire, they indicated the number of days when their epilepsy had prevented them from going to work, their employment situation, the use of psychopaedagogical and social resources, and the QOLIE-10 questionnaire. To analyze the use of the various health-care services, our hospital's database was consulted as it shows all the activities provided for each patient. The direct costs included: the treatment administered (drugs, dosage and presentation), the number of visits to the Neurology specialist, the number of visits to the Primary Health-Care physician, and the number of times they attended an Emergency Room because incidents related with their epilepsy or its treatment, the number of days of hospital admission, the number and type of diagnostic tests performed (basic analysis, analysis of the levels of anti-epileptic drugs, imaging (cranial CAT scan, cranial magnetic resonance, cerebral SPECT, cerebral PET), electrocardiogram, electroencephalogram, sleep-deprived electroencephalogram, electroencephalogram with Holter, electroencephalogram with video and electrocardiogram with Holter), and the use of transportation in ambulance to and from hospital, and psychopaedagogical and social support. The indirect costs were analyzed in the light of their employment situation and the days they had not been able to go to work because of their illness, considering also the main family carer, when the former needed continuous care and supervision because of the epilepsy. In addition, an assessment was made of the costs derived from the loss of labour productivity in patients while they attended

clinics or while they were admitted; we also considered that of relatives accompanying the patients requiring supervision. The total costs were derived from the sum of the direct and indirect costs. The intangible costs included those related to patients' pain and suffering and were assessed using the QOLIE-10 questionnaire (on health status and the specific quality of life with epilepsy providing information on the patient's demands and concerns).⁴ The data obtained were converted into monetary units expressed in euros, as per the price tariff for the hospital costs applied by the Galician Health Service in 2005. Drug prices were taken from the 2005 Catalogue for Pharmaceutical Products. The loss of productivity was calculated using the human capital method on the basis of the minimum inter-professional wage for 2005.⁵ In order to estimate the cost over a year, the values obtained were multiplied by 2, as the study was conducted over 6 months.

Data analysis

The data regarding qualitative variables are expressed as absolute frequencies and percentages, and those referring to cost variables are expressed as means and standard deviation. In order to verify whether the differences in costs reached statistically significant differences, Wilcoxon's non-parametric test for matched data. Values were considered significant when p was less than 0.05. The SPSS 15.0 statistical programme for Windows was used for data analysis.

Results

The study analyzed 171 patients, of whom 90 were male (52.6%) and 81 females (47.4%). The mean age of the patients included was 41.6 years, with a standard deviation of 17.0 years, ranging between 14 and 89 years of age. It is noteworthy that 8 patients were under 18 (4.7%) and 15 patients were over 65, representing 8.8% of the total sample. The patients had been suffering for an average of 15.3 years, with a standard deviation of 15.2 years, although 35 patients (20.5%) were diagnosed in the six months prior to the inclusion in the study, and one patient had been suffering the illness for 70 years.

As for the type of crisis, 127 patients (74.3%) were diagnosed as having partial crises, and 44 (25.7%) generalized crises. By type of epilepsy, 54 patients (31.6%) had cryptogenic epilepsy, 39 (22.8%) idiopathic epilepsy, and 78 (45.6%) of the patients included suffered symptomatic epilepsy.

As for the degree of control of their illness, 68 patients (39.8%) did not suffer any crisis during the study or in the six months prior to inclusion and 103 (60.2%) continued to present epileptic crises, although 65 of these patients (38.0%) had only suffered fewer than 2 crises in that year, while 39 patients (22.8%) had suffered more than 2 crises in the year, of whom 12 (7%) had also attended consultations for epileptic surgery.

By the anti-epileptic treatment received by the patients, 9 (5.3%) remained treatment-free, 78 (45.6%) were on maintenance monotherapy, and 84 (49.1%) received more

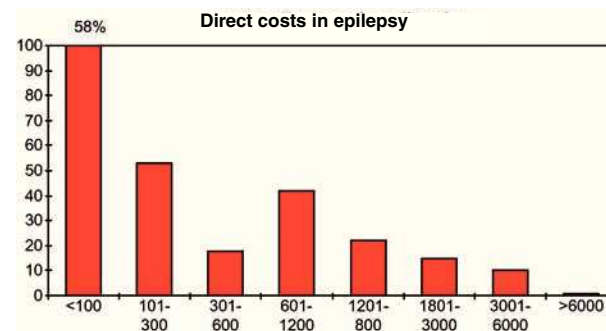


Figure 1 Distribution of the direct costs with values expressed in euros. The Y-axis shows the frequency of each cost tranche.

than one anti-epileptic drug to control their crises. Of the anti-epileptic drugs used, 61 patients (37.7%) received a drug considered classical and 19 (11.7%) were under treatment with a new drug, 19 patients (11.7%) received classical medication as polytherapy, 57 (35.2%) were taking both classical and new drugs, and 6 (3.7%) were being treated with polytherapy using new drugs.

Direct costs

In terms of the calculation of the direct economic costs, including the cost of drugs, the costs of medical visits and admissions, the costs of complementary tests and the costs of transportation and psychological and social resources, it has been seen that each individual included in the study spends an average of € 1,055.2, with a standard deviation of € 1,695.7. The lowest cost was € 15.5 and the highest was € 18,487.5. It is necessary to point out that 100 patients (58.4%) needed to spend less than € 100 and that, among the 12 patients (7%) attending consultations for epileptic surgery, the mean cost amounted to € 2,193.2 (\pm € 1,193.2). As for the cost per patient and year, the mean was € 2,110.4 (fig. 1).

Indirect costs

After assessing the indirect costs, the mean cost for each patient was € 1,528.8, with a standard deviation of € 1,625.8; the patient with the highest expenditure needed to spend € 6,141.9. In addition, it should be mentioned that 78 patients (45.6%) did not spend a single euro under this heading,

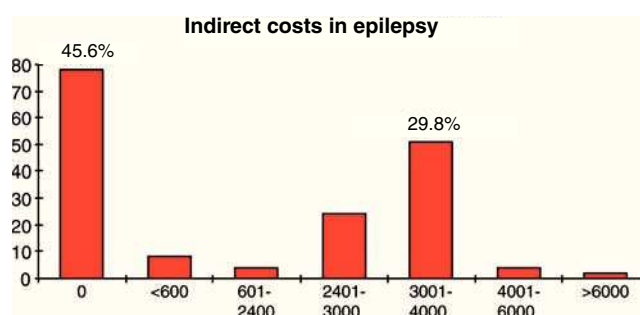


Figure 2 Distribution by indirect costs with values expressed in euros. The Y-axis shows the frequency of each cost tranche.

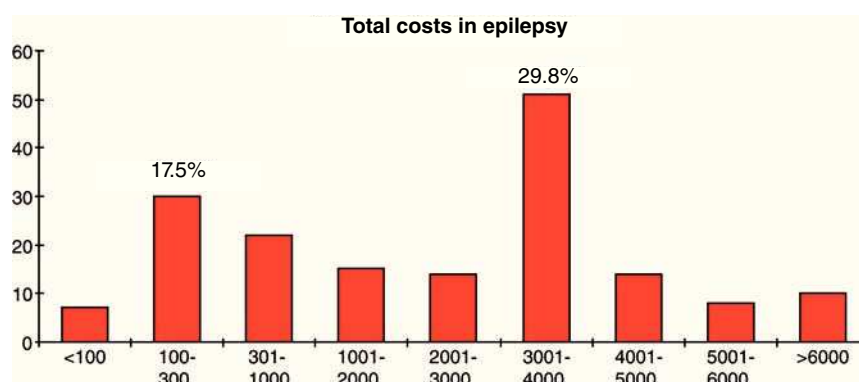


Figure 3 Distribution by total costs of epilepsy with values expressed in euros. The Y-axis shows the frequency of each cost tranche.

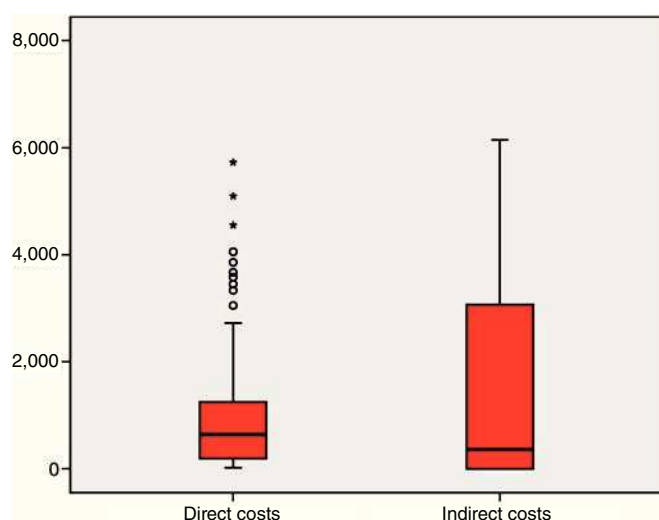


Figure 4 Box diagram showing the direct and indirect costs with values expressed in euros.

whereas 51 patients (29.8%) spent between 3,001 and 4,000 euros. The mean annual cost derived from the loss of productivity represents € 3,057.6 per patient (fig. 2).

Total costs of epilepsy

Adding together the direct and indirect costs found in the study, we obtain a mean of € 2,584 used by each patient

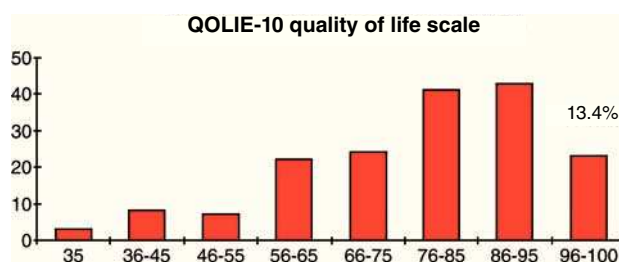


Figure 5 Distribution by QOLIE-10 quality of life scale. The Y-axis shows the frequency of each score range

included over the 6 months the study lasted, with a standard deviation of € 2,392.2; the maximum amount was € 20,539.5 and the minimum € 15.5. In addition, 30 patients (17.5%) spent between € 100 and € 300, whereas 51 patients (29.8%) used between € 3,001 and € 4,000. The estimated cost per patient was € 5,168 a year. It should be highlighted that, out of all the costs associated with epilepsy, the indirect costs have the greatest impact on the total ($p < 0.05$) (figs. 3 and 4).

Intangible costs

As for intangible costs, the use of the QOLIE-10 quality of life scale revealed that the mean score obtained by the patients included was 77.8 points, with a standard deviation of 16.8; the minimum score was 35 points, obtained by 3

Table 1 Descriptive statistics: mean cost, standard deviation, minimum and maximum value, percentage of patients with minimum and maximum value. Intangible costs by scores obtained on the QOLIE-10 questionnaire

Cost	Mean	Standard Deviation	Minimum	N. ° of patients (%)	Maximum	N. ° of patients (%)
Direct	1,055.2 €	1,695.7 €	15.5 €	1	1,8487.5 €	1
Indirect	1,528.8 €	1,625.8 €	0 €	78 (45.6%)	6,141.9 €	1
Total	2,528.4 €	2,392.2 €	15.5 €	1	20,539.5 €	1
Intangible	77.8	16.8	35	3	100	23 (13.4%)

patients, and the maximum was 100 points, the result obtained by 23 patients (13.4%) (fig. 5, table 1).

Discussion

The cost of epilepsy is a universal problem. For this reason, the European White Paper on Epilepsy proposes as the target for the 21st century the achievement of the availability of effective epilepsy care for all those needing it, independently of borders and economic constraints.⁶ In this sense, a six-month cost study of the illness has been carried out to estimate the costs associated with epilepsy from the social perspective in an attempt to determine which factors are associated with greater significance. The study has collated the data on 171 patients. The mean age of those included was 41.6 years and the distribution between men and women offers figures similar to the population mean in Spain in 2006.⁷ By type of crisis and type of epilepsy, a predominance of partial crises and symptomatic epilepsy has been found, analogously to the descriptions of community-based population studies,^{8,9} although logically the greater or lesser frequency of epilepsies with known aetiology is going to depend on the number and quality of diagnostic methods used.

As for the number of years that patients have been suffering from the illness, the mean was 15.3 years, although approximately 20.5% of them had been diagnosed in the six months prior to their inclusion in the study, and one patient had been suffering from the illness for 70 years. In other words, the study included both patients with recently diagnosed epilepsy (incidental cases) and patients with long-standing epilepsy (prevalent cases).

When analyzing the degree of control over the illness, our study has found that only 40% of the patients were crisis-free, a figure below the overall prognosis indicated in the literature for the control of epileptic crises, which comes to as much as 80% of patients achieving remission of their condition,¹⁰ albeit identical to those published in other observational, prospective and transversal studies carried out at epilepsy clinics.^{11,12} The difference between the degree of control over epilepsy between the studies carried out in neurology clinics versus the overall prognosis for the illness is related to the fact that well-controlled patients do not need to continue with follow-up visits with neurology specialists, as these responsibilities can be taken on by their primary-care physician. In fact, it is not possible to rule out a greater recruitment of patients with hard-to-control epilepsy, who are the ones with the highest likelihood of attending the clinics.

As for the type of treatment for the patients included, 45% remained with monotherapy and almost 50% received polytherapy for their epilepsy. Although the basic criterion for treatment of epilepsy is the use of a single anti-epileptic drug in order to reduce the risk of adverse effects, facilitate compliance and reduce the risk of interactions with other medications or idiosyncratic reactions, monotherapy is capable of controlling crises satisfactorily in approximately 75% of patients.^{6,13} Therefore, when adequate control of the crises is not achieved with a single drug, after attempting monotherapy again with a different drug, treatment should

be attempted with polytherapy using medicines presenting complementary mechanisms of action on the basis of the principle of rational polypharmacy.¹⁴ In this way, a study conducted in Spain pointed out that, prior to a diagnosis of drug-resistant epilepsy, the most common treatment was monotherapy but, after this diagnosis was reached, its treatment was polytherapy with a mean of 2.2 drugs used.¹⁵ The fact that 5% of the patients remain without treatment may be due to their recent diagnosis and that they have not yet started treatment or have abandoned it for various reasons (side effects, intolerance or tiredness at having to remain with a long-term treatment).

In the analysis of the types of drugs used in our patients, it should be noted that most of the patients in monotherapy receive a conventional drug while in polytherapy the most common option is to use a combination of classical and new drugs, similar to what has been published in other studies.¹⁶⁻¹⁸

In terms of the analysis of the direct costs, it has been found that the estimated annual cost doubles the mean per capita expenditure for the health system in Spain in 2003.¹⁹ This shows that suffering from epilepsy implies a very high cost for the health service, derived from the greater need for the use of services included in direct costs. However, it is necessary to indicate that 58% of the patients spent less than € 100 during the 6 months the study lasted, whereas the 7% who went to epilepsy surgery clinics had a mean cost of € 2,193.20, thus increasing the mean value of the direct costs derived from the additional specialist consultations, and due to the performance of special tests to identify the epileptogenic focus, even though none of them was operated on during the study. In comparison with other international studies, the results obtained imply that the direct costs incurred for each patient in Spain are almost 50 times higher than the expenditure in rural areas of Burundi, but approximately one half of that incurred at a third-level epilepsy centre in Germany.²⁰ In this sense, the costs generated by patients have been shown to vary significantly depending on where they are seen; the cost is highest at clinical hospitals with more advanced equipment, intermediate in general hospitals where patients are examined by a neurologist with specific qualifications in epilepsy without access to the latest technology and lowest in hospitals where they are seen by a general neurologist.²¹

With regard to the indirect costs, the mean value for each patient in our study was € 1,528.80 with 46% of patients not spending a single euro on this heading; this highlights that, although almost half of the people with epilepsy can access the employment market without any difficulty, the mean annual cost derived from the loss of productivity of patients implies approximately € 3,000 per annum. In fact, various studies have found that the unemployment rate among epileptic patients is at least twice as high as in the general population and, when epileptic patients find a job, they are usually in low-qualification positions. In addition, they also have difficulties in holding onto their jobs, leading to higher rates of precarious employment.²²⁻²⁹ Thus, most patients reported that their employment situation had been affected in some way by their illness, so they preferred not to inform the companies they worked for of their diagnosis.³⁰ Associated factors identified include the population's

ignorance of the illness, the frequency and severity of the crises, and such psycho-social variables as the patients' low self-esteem.³¹ Nonetheless, we must not overlook certain objective restrictions on finding employment in connection with the ability to drive vehicles or with jobs that may be life-threatening through the use of certain machinery or working at heights. Some of these issues could be minimized through the strict observance of risk prevention and occupational health and safety measures. On the other hand, the negative impact of epilepsy on employment sometimes affects other family members, as 20% of patients with recalcitrant epilepsy require constant care and supervision, which is why some of their relatives have to change their working conditions to adapt to these circumstances.³²

Adding together the total of direct and indirect costs in the study, the cost calculated during a year amounted to € 5,168, a figure similar to that estimated in a study conducted in Europe into the cost of brain diseases and approximately € 1,500 more than the mean per capita cost for social protection in Spain in 2003.¹⁹ This is derived, above all, from the loss of patients' workplace productivity, as the prevalence is greater among middle-aged individuals.³³⁻³⁵ In this sense, it should be mentioned that an assessment has been made of early retirement implications and the number of workdays caused by both crises and the need to attend clinics, considering both patients themselves and their relatives or those accompanying them, in the case of patients needing constant care and supervision due to their epilepsy. However, no account has been taken of the precariousness of their employment nor of the excess mortality caused by epilepsy. In order to calculate the loss of work-related productivity, the minimum interprofessional wage in Spain has been considered, rather than the real earnings of patients, so the indirect costs might possibly be even greater. Nonetheless, none of the patients included deceased during the execution of our study.

The importance of indirect costs for the total amount of the costs associated with epilepsy in adults has been related above all with the huge significance of early retirement due to epilepsy.^{33,36} In those under 14 years of age, direct costs are more important because, despite considering the loss of work-related productivity of the relatives accompanying the minor to clinics and hospital admissions, it must be remembered that the individuals at this age do not form part of the labour market.^{1,37}

Intangible costs are related to the pain and suffering endured by patients, thus causing a decline in their quality of life, social isolation and impairment of their personal satisfaction. Unfortunately, the psychological cost of an illness cannot be assessed from a monetary perspective. For this reason, in order to estimate the burden of the illness on patients' emotional wellbeing, we have taken quality of life measures using the QOLIE-10 scale. In this way, the mean score obtained by the patients included was 77.8 points, a figure similar to that obtained in the Spanish validation study for this scale.³⁸ The highest score, equivalent to a totally satisfactory life, was the result obtained by only 13.4% of patients, implying that the illness affects the quality of life of a majority of patients. In fact, the diagnosis of epilepsy has been associated since ancient times with a stigma of

marginalization that has caused loss of social status and the ability to maintain relationships with others. This stigma has been associated with feelings of anxiety, depression and disability due to the fact that the crises are unpredictable and uncontrollable, particularly in patients who do not respond adequately to treatment or who present side effects.^{27,39-41} Thus, several studies suggest that this feeling of social marginalization and mental distress has a major impact on their ability to find a job and on quality of life, leading many patients to wish not to inform their acquaintances that they suffer from epilepsy.⁴²⁻⁴⁴ However, the impact of the diagnosis of epilepsy is influenced in each individual patient by other factors such as their personality, the family and social support available to them, their intellectual level, their gender or the country in which they live⁴⁵.

Conflicts of interest

The authors declare they have no conflict of interest.

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