

# Estimating the Savings of a Migraine-Free Life: Results from the Spanish Atlas

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## ABSTRACT

**Background:** Migraine is a common and costly neurological disorder. The aim of this study was to quantify the costs of chronic (CM) and episodic migraine (EM) in Spain, evaluating the impact of psychiatric comorbidities and disability, and estimate the economic savings of reducing the number of migraine days by 50%.

**Methods:** This was a cross-sectional analysis of data from patients with migraine who participated in the Spanish Migraine Atlas. The participants were invited to complete a structured questionnaire including the following scales: Headache Needs Assessment (HANA), Hospital Anxiety and Depression Scale (HADS), and Migraine Disability Assessment Scale (MIDAS)

**Results:** 475 patients were included, 187 with CM (39.4%). Total costs per patient/year were: €16,578.2 ±€34,568.1 for CM and €6,227.8 ±€6,515.7 for EM. Moreover, a higher degree of disability according to MIDAS scale significantly increases the total cost of migraine, while the presence of psychiatric comorbidity increase costs for EM patients only. The reduction of one migraine day per month decreases average total costs by €744.14 per patient/year for EM and €663.20 per patient/year for CM, while reducing by 50% the number of migraine days, the economic savings would be €2,232.44 per patient/year ( $R^2=0.927$ ) for EM and €6,631.99 per patient/year ( $R^2=0.886$ ) for CM.

**Conclusions:** The costs associated with migraine are driven by migraine frequency and the degree of disability, while psychiatric comorbidity only influences the cost of EM patients. These results

highlight the need to optimise migraine management to reduce the economic migraine burden. Future studies are warranted to confirm our results.

**Short running title:** Estimating the Savings of a Migraine Free Life

**Keywords:** migraine, chronic migraine, costs, burden, quality of life, disability, psychiatric comorbidity.

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## INTRODUCTION

Migraine is a common, disabling headache disorder, affecting 12% of the Spanish population (1) and represents the first cause of disability in people under 50 years of age (2). According to the ICHD-3 (3), migraine is categorised as episodic (<15 days/month) and chronic ( $\geq$ 15 days/month).

Several studies conducted in the US and different countries across Europe, have shown that migraine, but chronic migraine (CM) in particular, causes considerable direct and indirect economic costs (4–11). Direct costs represent the expenditure associated with medical resource utilisation, while indirect costs are defined as expenses incurred from productivity loss resulting from migraine. The economic burden of migraine varies greatly between countries (7), but indirect costs (IC) accounted for the majority of the total cost in most studies (8,12,13). Moreover, migraine is associated with higher rates of comorbid psychiatric conditions that may influence total cost (14).

However, studies analysing the economic burden of migraine in Spain, including IC are scarce (8), and no studies have been carried out that assess the influence of comorbid anxiety and depression on costs. Additionally, data from previous studies were conducted more than 10 years ago (7,8), and these results do not include the direct non-health care costs (DNHC). Therefore, it is necessary to update the direct and indirect cost of EM and CM and assess the impact of migraine frequency, headache-related disability, quality of life, and psychiatric comorbidity (anxiety and depression) on the economic burden of migraine.

The aim of the present study was i) to comparatively quantify the costs of CM and EM; ii) assess the impact of quality of life, psychiatric comorbidities, and disability over the economic burden of migraine and; iii) to estimate the economic savings when reducing the number of migraine days per patient per year by 50%.

## METHODS

### *Study design*

The Spanish Migraine Atlas 2018 was an initiative of the Spanish Patient's Association of Migraine and Headache (AEMICE), carried out by the Health & Territory Research Group (HTR) of the University of Seville, in collaboration with the Headache Study Group of the Spanish Neurological Society (GECSN) and with the financial support of Novartis Spain.

### *Data Source (Survey)*

The questionnaire was prepared by the HTR research group, taking into account the opinion of a panel comprised of headache experts, psychologists and migraine sufferers and after a scientific literature review (15). In addition, the impact of migraine on quality of life, probability of psychiatric comorbidity, and disability levels were evaluated using different scales (16-18): Headache Needs Assessment (HANA), Hospital Anxiety and Depression Scale (HADS), and Migraine Disability Assessment Scale (MIDAS). The HANA is a migraine-specific quality of life instrument measuring two dimensions of the chronic impact of migraine: frequency and bothersomeness (16). This scale contains the following seven domains: i) anxiety/worry; ii) depression/discouragement; iii) self-control; iv) energy; v) function/work; vi) family/social activities; and vii) overall impact of migraine.

HADS is an instrument designed for screening potential anxiety and depression rather than grading the severity of anxiety and depression in the general population (17). The HADS

questionnaire included 14 items, seven of which evaluate anxiety (HADS-A) and a further seven that evaluate depression (HADS-D). Each item is scored on a scale of 0–3, resulting in an overall score of 0–21 for both HADS-A and HADS-D to detect possible cases of depression and anxiety. According to the score obtained in the HADS scale it is possible to distinguish between no case: 0-7; borderline case: 8-10 and case: 11-21 for both anxiety and depression (17).

Additionally, disability was measured using the MIDAS scale, with a 5-item questionnaire designed to evaluate disability within the past three months (18). A score from 0–270 is used to indicate the overall level of disability due to migraine based on the following grading system: grade I, little or no disability (score of 0–5) ; grade II, mild disability (score of 6–10) ; grade III, moderate disability (score of 11–20); and grade IV, severe disability (score of  $\geq 21$ )(19). The highest category is subdivided into grade IV-A, severe disability (scores of 21–40) and grade IV-B, describing a very severe (scores of 41–270).

In order to validate the whole questionnaire, one pilot test was carried out by 20 personal interviews of migraine patients, which contributed to the improvement of understanding and completing the survey. After this process, the final questionnaire consisted of 124 items. The complete questionnaire is available and can be consulted online as an annex to the Spanish Migraine Atlas report (15).

Between June and September 2017, an online cross-sectional survey was performed within the framework of the Spanish Migraine Atlas, using a non-probability sampling methodology. The questionnaire was disseminated through the AEMICE patient association and patients filled it out voluntarily and anonymously. This survey was performed in full accordance with the Spanish law on data protection. As this was not an interventional study, no ethics committee approval was required. However, all patients agreed to their participation through informed consent, and provided consent for aggregated reporting of research findings, before completing the survey. Of a total of 2,653 patients with migraine who began the questionnaire, after the validation, screening and cleaning process, the valid sample was made up of 1,283 patients. However, as one of the objectives of the present study was to assess the impact of quality of life, psychiatric comorbidities and disability, we estimated only the costs produced by the patients who answered all questions including MIDAS, HADs, and HANA scales: total Migraine=475; EM=288; and CM=187 (Figure 1). All patients included had been seen by a doctor within the last year and had received a medical diagnosis of migraine. The classification between CM and EM was established using the number of headache days reported by patients.

[Insert Figure 1]

### ***Variables***

The questionnaire included variables related to healthcare service utilisation (diagnostic tests, medical visits, emergency visits, and hospital admissions), private service utilisation incurred by the patients (visits to private specialists and other complementary treatments for migraine), data related to the patient's labour productivity losses in the past year and the scores of HANA, HADS, and MIDAS.

### ***Costs analysis***

To assess the burden of migraine in Spain, the following were calculated: Direct Healthcare Costs (DHC), assumed by the national public health system; DNHC borne by the patient; and IC (20–24). In the present study, the IC were derived only from the patient's labour productivity losses due to medical visits, sick leave, and hospital admission days related to migraine in the economically

active population, since this was the information included in the survey. Costs were calculated independently for patients with CM and EM. All costs were expressed in Euros referring to the year 2017, with the exception of the unit price per normal working hour in Spain, which was last updated in 2015 (25). The pharmacological costs were acquired from the economic study carried out in Spain in 2012 by Bloudek et al (7). The annual increase in the consumer price index of pharmaceutical products (26), was applied to the operating costs for 2010 used by Bloudek et al (7).

The costs related to medical visits, tests, and emergency room visits was obtained from the prices published in the Official Bulletins of the 17 Spanish Autonomous Communities. Average rates for 2017 were used due to the variability of prices between the different Autonomous Communities.

The DNHC were self-reported by patients, including costs for visits to private specialists, other complementary treatments for migraine including physical aerobic exercise; psychological treatment; acupuncture; and specific diet.

We estimated the financial savings from the 50% reduction in migraine days indirectly, using the average number of migraine days per month reported by patients who participated in this study and differentiating by migraine type.

### ***Statistical analysis***

Descriptive statistics (number of valid cases, mean, and SD) were calculated for all continuous variables and frequencies and percentages were calculated for categorical variables for the overall migraine, distinguishing between CM and EM.

For the annual cost, mean and SD were calculated distinguishing between CM and EM. The percentages of each of the costs were calculated using the cost of each category and the total cost per patient per year.

In addition, the cost comparison between CM and EM was carried out using the distribution established according to the HANA, HADS and MIDAS scales. The non-parametric Mann-Whitney analysis was used due to the absence of a normal distribution. Statistical significance was established at  $p < 0.05$ .

In order to verify the relationship between costs and impact of migraine on quality of life (HANA) Pearson correlations were made for each of the costs for CM and EM ( $r = 0.337$   $p < 0.001$ ).

A dot plot representing the values along a numeric line has been used to show possible accumulations, trends, variability, dispersion, and how the average total cost of migraine was distributed by number of days per month with a headache. Using Pearson's correlation coefficient, we measured the degree of association between the number of days with migraine per month and average total costs ( $r = 0.763$ ,  $p < 0.001$ ). The average total costs relative to the number of migraine days per month have been estimated using simple linear regression.

## **RESULTS**

The preliminary analyses were performed on a sample of 1,283 patients, obtaining an average total cost of €7,766.84 (CM: €12,970.08; EM: €5,041.38), of which €1,955.17 belonged to direct health care cost (CM: €3,847.29; €964.19), €1,146.30 belonged to direct non-health care costs (CM: €1,657.96; EM: €878.04) and €4,665.38 belonged to indirect costs (CM: €7,464.83; EM: €3,199.15) (Table 1).

[Insert Table 1]

In order to evaluate the impact of anxiety/depression, quality of life and disability on the costs derived from migraine, cases in which values were missing for any of the three validated scales (HADS, HANA and MIDAS) were discarded, obtaining a final sample of 475 patients, of whom 187 had CM (39.4%). The mean age was 36.83 ( $\pm$  10.75) years, with 89.9% being women. Overall EM and CM groups were comparable with respect to age and gender. CM patients had a lower proportion of university degrees ( $p=0.003$ ), higher unemployment ( $p=0.036$ ), and were more likely to be members of a Spanish migraine patient association ( $p=0.002$ ). CM patients are also more likely than EM patients to have depression (32.1% vs 10.8%,  $p < 0.001$ ) or anxiety (56.15% vs 36.1%,  $p < 0.001$ ). According to MIDAS, those with CM are more likely to suffer severe disability than EM patients ( $p < 0.001$ ) (Table 2).

[Insert Table 2]

The average total cost for patients with migraine was €10,302.6 $\pm$  22,808.7) per year, 55% corresponding to IC, 30% to DHC, and 15% to DNHC (Table 3). IC for patients with CM and EM are respectively: CM=€8,233.9 per year; EM=€3,891.6 per year ( $p < 0.001$ ).

[Insert Table 3]

Positive correlations were found between anxiety level and costs for EM. Thus, as the anxiety level increases (HADS-A), so does IC ( $p=0.011$  and  $r=0.150$ ) and total costs ( $p=0.003$  and  $r=0.173$ ). The same applied to depression level (HADS-D) and costs for EM patients, since as the depression value increases, so does DHC ( $p=0.005$  and  $r=0.164$ ), IC ( $p < 0.001$  and  $r=0.302$ ), and total costs ( $p < 0.001$  and  $r=0.306$ ). We found no statistical correlation between anxiety or depression and costs for CM. Positive correlation between all types of cost and the HANA and MIDAS scales were observed in CM and EM (Table 4).

[Insert Table 4]

We have calculated averages for anxiety and depression (chart 1) according to the number migraine days per month. In the case of MC, HADS values fluctuate with greater dispersion, while in EM HADS values, follow a linear trend with respect to migraine days.

[Insert Chart 1]

Table 5 shows how the total costs, DHC, DNHC, and IC of migraine increase as the MIDAS score increases, meaning that this relationship is statistically significant ( $p < 0.001$  Kruskal Wallis test). Total costs are twice as high for the Grade IVB according to MIDAS for patients with CM.

[Insert Table 5]

The results of the Pearson correlation ( $R=0.763$   $p < 0.001$ ) explain how increasing the number of days with migraine leads to an increase in average total costs (chart 2). According to the regression analysis, the annual average economic savings from the reduction of one day of migraine per month was estimated at €744.14 for EM and €663.20 for CM while the 50% reduction of days without migraine (corresponding to 6 days per month for EM and 20 days per month for CM) would lead to an average economic saving of €2,232.44 per year for EM and €6,631.99 per year for CM.

[Insert Chart 2]

## DISCUSSION

The present study shows that migraine, but particularly CM, is associated with increased direct and IC. The annual cost for patients with CM is more than two and a half times as high as in those with EM, and the largest proportion of expenditure is due to IC. More importantly, we found that reducing one migraine day per month may save annually €744.14 per EM patient and €663.20 per CM patient, while the 50% reduction in days with migraine per month would lead to an average economic saving of €2,232.44 per year for EM and €6,631.99 per year for CM.

Our findings are in line with previous studies where the cost of CM was found to be approximately three times higher than EM (7,10,13). People with CM are more likely than those with EM to visit their primary care physician, neurologist, the emergency department, and be admitted to a hospital. Furthermore, patients with CM are less likely to be employed and the disability related to migraine is associated with a reduction in productivity at work. As estimated in other studies (8,13,27), IC represents the largest proportion of expenditure in our study, although there exist studies that do not corroborate the same results (10). These apparent contradictory results might be explained by the variability of costs in different national healthcare systems with different management strategies for migraine, but also due to the different methodologies used to recruit patients. Also, socio-demographic differences, particularly educational level and employment status may influence IC. In this study, most patients had university studies and were working, in contrast with the study of Messali et al. (10). In the present sample, the average cost savings per day without migraine was slightly higher in EM in comparison with CM patients. Our results may be explained because the proportion of unemployed individuals was higher in CM and this may influence the economic burden, as production loss at work represented the main part of the costs.

We observed that the burden of migraine and associated-costs are largely driven by migraine frequency but also by degree of disability, measured by the MIDAS scale as previously reported(28–30). The cost of migraine was much higher in subjects with CM and in those with moderate or severe disability compared to little disability. Our data are consistent with previous studies in which frequency and severity of migraine increase DHC (6,7,29,31), but also IC (8,13,27). Similarly, there is a statistically significant relationship between the costs of migraine and quality of life, with higher costs associated with those who experience more limitations in their daily life (27).

In the present study the annual DHC was €5,910 for CM and €1,185 for EM patients, and the IC ranges from €3,891 (EM) to €8,233 (CM). In comparison with prior studies in Spain (7), DHC for CM has more than doubled, mainly due to the increase in emergency room visits and hospital admissions in patients analysed in the present study - while IC for EM remains similar. IC is also much higher than reported in another European study (8) that included patients from Spain. All these changes in cost, particularly in CM patients, may be explained by including patients with a more severe type of migraine, but also due to changes in chronic migraine management.

Comorbid psychiatric conditions are more frequent in patients with CM and, previous evidence suggests that it may contribute to the increase in costs (11,14). In our sample, anxiety and depression occur at high rates in CM compared with EM as previously reported (4,28). However, anxiety and depression were both associated with an increase in total cost, but only in patients with EM. In our sample, most CM patients focus on the extreme values of the HADS scale for both

depression and anxiety. Therefore, there is no linear trend in the increase of depression and anxiety with respect to costs. In other words, since depression and anxiety values are mostly high, there is not the necessary change to make the increase in costs statistically significant. It can be argued that patients with CM have been probably suffering anxiety or depression for a longer period of time than EM patients, and have developed different strategies to better cope with psychiatric comorbidity, reducing the influence on disability and cost. Furthermore, the diagnosis of anxiety and depression was based in HADS scores and not confirmed with a structured clinical interview. Therefore, we cannot exclude that some CM patients have been misclassified and this may influence our results. In accordance with our findings, previous studies reported that the presence of psychiatric comorbidity was not associated with an increase in the costs of migraine in Spain or France as it occurs in other European countries (7). In patients with EM, interictal anxiety is associated with lost productive time (32) probably because the concern about suffering a new migraine attack may generate an increase in healthcare utilisation, a reduction in the patient's labour productivity, and as a consequence could increase healthcare costs. Future studies should examine whether medical costs in patients with migraine and psychiatric comorbidity could be decreased by improving the diagnosis and treatment of depression and anxiety.

Migraine is underdiagnosed and undertreated worldwide (33,34). Currently, the proportion of migraine patients who receive triptans is very low and more than one in five candidates for preventive therapy do not receive it (34). Furthermore, it has been observed that inadequate acute migraine treatment is associated with an increased risk of chronic migraine (35) and following management guidelines could reduce migraine days and disability in most patients (36). In the present study, we show that the reduction of only one migraine day per month may save €744.14 per patient per year for EM and €663.20 for CM. Therefore, adequate migraine management may not only reduce the number of migraine days, but could also have an enormous impact on the overall cost of migraine.

One of the strengths of the present study lies in the fact that to our knowledge it is the first exhaustive study analysing the health-economic consequences of migraine in Spain, including a considerable number of patients with CM. The present study includes information beyond that related to DHC by estimating the DNHC assumed by patients and the IC derived from labour productivity losses, in addition to including validated scales for disability (MIDAS) and quality of life (HANA). The diagnoses of anxiety and depression (HADS) were based on clinical scales and not self-reported, reducing diagnostic bias.

This study is subject to a number of limitations and therefore, the results of this research must be interpreted with caution. First of all, migraine diagnosis was based self-reported. Although all patients had previously been diagnosed by a physician, migraine diagnosis could not be confirmed. Another bias of the survey is that in order to be completed on an online platform, patients had to have Internet access in addition to having the necessary skills to deal with technology. In addition, a high proportion of patients accessed the survey through the AEMICE patient association so it is possible that patients with severe forms of migraine are overrepresented. Moreover, the cost was analysed using cross-sectional data, thus the annual costs have been estimated on the basis of the monthly costs declared by the patients at the time of the survey, without it being possible to collect information throughout the year. Therefore, it may be necessary to perform prospective studies with a higher number of patients to accurately estimate the annual savings of reducing the number of migraine days. In addition, the survey was long, and this explains the high non-response rates observed in the present study that may affect



sample representativeness negatively. **Finally**, it should be noted that this survey did not include questions about the type of medication used. Therefore, this data was estimated based on previous studies that included Spanish patients (7) in which the unit price of medicines used refer to 2010. For the calculation of the final cost per medication, the annual increase of treatments in Spain from 2010 to 2017 was taken into account (26).

## CONCLUSIONS

In Spain, in comparison with EM, CM is associated with greater migraine related to disability, higher cost, and lower quality of life. The cost of migraine is mainly driven by migraine frequency, while psychiatric comorbidity influences cost only in EM patients. Our findings show the significant annual saving of reducing one migraine day per month (€744.14 for EM and €663.20 for CM), even further if this reduction is 50% of days without migraine would lead to an average economic savings of €2,232.44 for EM and €6,631.99 for CM, and highlights the potential impact of an adequate acute and preventive treatment on the overall economic burden of migraine. Future studies are warranted to confirm our results.

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**Table 1.** Annual average costs per patient (euros 2017)

<b>Cost typology</b>	<b>M (n=1283) Mean(± SD)</b>	<b>CM (n=441) Mean(± SD)</b>	<b>EM (n=842) Mean(± SD)</b>	<b>p-value</b>
<b>Direct Health Care Cost</b>	<b>1.955,17(± 12.487,57)</b>	<b>3.847,29(± 21.017,51)</b>	<b>964,19(± 1933,47)</b>	<b>&lt;0.001</b>
Medical visits (HCP) <sup>1</sup>	263,74 (± 549,74)	424,94(± 688,30)	179,30(± 438,25)	<b>&lt;0.001</b>
Medical tests <sup>2</sup>	97,21 (± 227,69)	152,81 (± 305,24)	68,09 (± 166,78)	<b>&lt;0.001</b>
Visits to the emergency room <sup>3</sup>	459,49( ± 1.238,52)	771,38 (± 1.789,05)	296,17 (± 765,52)	<b>&lt;0.001</b>
Hospital admissions	807,22 (± 11535,62)	1.873,88 (±19.543,39)	248,55 (± 1.453,39)	<b>&lt;0.001</b>
Medication (total)	327,51 <sup>a</sup>	624,28 <sup>a</sup>	172,08 <sup>a</sup>	<b>&lt;0.001</b>
<b>Direct Non-Health Care Cost</b>	<b>1.146,30 (± 1864,07)</b>	<b>1.657,96 (± 2551,33)</b>	<b>878,04 (± 1296,84)</b>	<b>&lt;0.001</b>
Medical visits	110,91(± 418,51)	192,28(± 546,01)	68,28(± 325,17)	<b>&lt;0.001</b>
Complementary treatments	229,38(± 649,29)	364,32(± 857,70)	158,52(± 493,07)	<b>&lt;0.001</b>
Preventive Treatments	362,67)( ± 519,75)	515,64(± 730,26)	282,48(± 337,78)	<b>&lt;0.001</b>
Physical activity	170,23(± 402,26)	174,12(± 338,29)	168,12(± 338,29)	0.063
Diet	157,60(± 557,42)	234,72(± 641,37)	117,24(± 503,66)	<b>&lt;0.001</b>
Emotional Care	115,51(± 487,54)	176,88(± 698,12)	83,37(± 323,01)	0.073
<b>Indirect Costs</b>	<b>4.665,38 (± 7.154,28)</b>	<b>7.464,83 (± 9.579,24)</b>	<b>3199,15 (± 4.873,67)</b>	<b>&lt;0.001</b>
<b>TOTAL COST patient/year</b>	<b>7.766,84 (± 15.382,02)</b>	<b>12.970,08 (± 24.160,90)</b>	<b>5.041,38 (± 5.799,38)</b>	<b>&lt;0.001</b>

Abbreviations: SD = Standard Deviation; CM = Chronic Migraine; EM= Episodic Migraine; M= Migraine

<sup>1</sup>Medical visits (HCP): general Practitioner, neurologist, paediatrician and otolaryngologist

<sup>2</sup>Medical tests: scanner/computed tomography (TC), MRI and spinal tap, or lumbar puncture

<sup>3</sup>Visits to the emergency room: emergency (visits), emergency (tests), scanner/computed tomography (TC), magnetic resonance, spinal tap, or lumbar puncture

<sup>a</sup> Pharmacological costs were updated, using the year over year growth of IPC for pharmaceutical products (INE,2017), starting from the costs (year 2010) extracted from the Bloudek's study (2012).