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## ORIGINAL ARTICLE

### Depressive symptoms associated with changes in circadian rhythms. Concordance in perception between doctor and patient, clinical impact and its response to current antidepressant drugs

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#### KEYWORDS

Depression;  
Circadian rhythms

**Abstract** This is a descriptive, transversal and multicenter study using self-administered surveys concurrently to collect the opinions of two groups (psychiatrists and patients) and discuss their disagreements.

The scope of study are hospital services, outpatient centres, individual professional consultation and other assistance system, public or private, which provides psychiatric care in Spain. Participated in this study 319 psychiatrists and 957 patients with the diagnosis of depression, stratified by autonomous communities. The populations they are intended to infer the results of this study were all patients diagnosed with depression and antidepressant treatment, and the group of specialists in psychiatry responsible for clinical monitoring at the national level.

In the study sample, depressive symptoms related to circadian rhythms are very common: they are experienced by more than 65% of patients surveyed, except the "early morning awakening insomnia" (54%) and "fatigue, anergy and unresponsiveness" (37%). In general, and endorsing the study hypothesis, the prevalence of almost all analysed depressive symptoms is significantly underestimated by psychiatrists about the perception of the patients themselves. Only the presence of "fatigue, anergy and unresponsiveness" is more often observed by professionals than by patients, perhaps by nature be of particular somatic symptoms that may suggest to the clinician to rule out underlying organic pathology.

In light of the results presented it is concluded that disturbances in circadian rhythms are core aspects of depression and frequent cause of key symptoms and residual symptoms of patients in treatment. These disorders appear to be underestimated by professionals and only partially solved with existing antidepressant drugs.

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**PALABRAS CLAVE**

Depresión;  
Ritmos circadianos

# **Síntomas depresivos relacionados con la alteración de los ritmos circadianos. Concordancia entre la percepción de médicos y pacientes sobre prevalencia, impacto clínico y su respuesta a los fármacos antidepresivos actuales**

**Resumen** Se trata de un estudio descriptivo, transversal y multicéntrico realizado mediante encuestas autoadministradas para recoger de forma concurrente las opiniones de dos grupos de estudio (psiquiatras y pacientes) y analizar sus discordancias.

El ámbito de estudio lo constituyen servicios hospitalarios, centros ambulatorios, consultas profesionales individuales y cualquier otro dispositivo asistencial, público o privado, donde se presta atención psiquiátrica en España. En el presente estudio participaron 319 psiquiatras y 957 pacientes diagnosticados de depresión, de procedencia estratificada por comunidades autónomas. Las poblaciones a las que se pretenden inferir los resultados de este estudio son el conjunto de pacientes diagnosticados de depresión y en tratamiento antidepresivo, y el colectivo de especialistas en psiquiatría responsables de su seguimiento clínico, a nivel estatal.

En la muestra de estudio, los síntomas depresivos relacionados con los ritmos circadianos resultan muy comunes: son percibidos por más del 65% de los pacientes encuestados, excepto el "insomnio de despertar precoz" (54%) y la "fatiga, anergia y apatía" (37%). En general, y refrendando la hipótesis de estudio, la prevalencia de la práctica totalidad de los síntomas depresivos analizados es significativamente infravalorada por los psiquiatras, respecto a la percepción de los propios pacientes. Sólo la presencia de "fatiga, anergia y apatía" es más frecuentemente considerada por los profesionales que por los pacientes, quizá por resultar síntomas de especial carácter somático que pueden indicar al clínico la necesidad de descartar la presencia de una afección orgánica subyacente.

A la luz de los resultados presentados, cabe concluir que los trastornos de los ritmos circadianos son aspectos nucleares de la depresión y causa frecuente de síntomas clave y síntomas residuales de los pacientes en tratamiento. Estos trastornos parecen insuficientemente considerados por los profesionales y sólo parcialmente resueltos con los fármacos antidepresivos actuales.

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## **Introduction**

Today, depressive disorders are considered chronic diseases with a tendency toward frequent relapses which, for many patients, means remaining on active antidepressant therapy over long periods of time.<sup>1</sup> This had made the risk-benefit analysis of antidepressant drugs a fundamental line of research in psychopharmacology, for these drugs must combine effectiveness; absence of adverse effects that may impair the patient's ability to function; and low risk for drug interactions, iatrogenesis in concomitant conditions, and discontinuation syndrome in the event of treatment abandonment or withdrawal.

In terms of many of these aspects, the antidepressants currently available represent an improvement over traditional antidepressant agents (tricyclics and tetracyclics). Even so, many patients do not achieve full remission of their clinical picture and manifest residual and subclinical depressive symptoms over a long period of time—a factor associated with the likelihood of having a relapse of the depressive disorder.<sup>2</sup>

Among the core manifestations of the depressive symptom complex are those related to circadian rhythm disturbances,

such as marked variations in mood and energy over the course of the day, which result in a noticeable impairment for everyday activities, primarily in the morning hours. These symptoms are usually accompanied by sleep disturbances.<sup>3</sup> Other typical alterations in biological rhythms are changes in appetite (with the resulting weight changes) and changes in sexual desire.

Many of these symptoms stemming from circadian rhythm disturbances are not entirely controlled with the usual antidepressant therapy and remain as residual symptoms of the depressive picture over a long period of time. Sometimes the very use of certain antidepressants turns out to be a determining factor in the aggravation of some of these symptoms, such as sleep disturbances or sexual problems—common residual symptoms in these patients.<sup>4,5</sup>

The underlying hypothesis for this study is that depressed patients experience symptoms related to circadian rhythm disturbances more often than the psychiatrists suspect this under routine practice conditions. It is possible that, for various reasons, psychiatrists assess the presence and impact of these symptoms on the patient's everyday life in a different way, as well as their potential to influence satisfaction and treatment compliance.<sup>6-13</sup>

In this context, it is particularly fitting that studies be conducted focusing on the need to explore how the depressed patient experiences his/her disease and views the therapeutic decisions that may impact him/her—above all considering that depression is one of the chronic disease paradigms that gives rise to disability, deterioration in the quality of life, dependence, and iatrogenic risk. With this intention, there is a growing initiative known as *patient centred medicine*, widely supported in the English-speaking medical world,<sup>14–20</sup> that aims to reorient the practice of medicine toward actively taking the needs patients feel into consideration when making clinical decisions.

For all these reasons, the primary objective of this study is to identify possible differences in subjective perception that may exist between patients who are on antidepressant therapy under naturalistic conditions and the psychiatrists who follow them clinically—differences in the perception of depressive symptoms related to circadian rhythm disturbances and their impact on everyday living, as well as differences between the two groups surveyed in terms of the level of satisfaction with the current antidepressant therapy when used under routine clinical practice conditions.

## Materials and methods

This is a multi-centre, transversal, descriptive study conducted through self-administered surveys for gathering, simultaneously, the opinions of the two groups of informants (psychiatrists and patients) on the same items, the main study variables, and analysing possible disagreements between them.

The scope of the study consists of hospital services, outpatient centres, individual professional practices, and any other public or private healthcare entity in Spain where psychiatric care is rendered. The populations to whom the results of this study are meant to apply are the gamut of patients, nationwide, diagnosed with depression and on antidepressant therapy and the psychiatrists, nationwide, who are responsible for following them clinically.

For this purpose, a sample of 320 psychiatrists, stratified by Autonomous Communities in proportion to their population, were invited to participate voluntarily through participation application forms distributed to a group of psychiatrists systematically selected from a chronological listing of those visited by the Sponsor's sales network during the study period. Although the group of psychiatrists resulting from this process was not immune to a possible self-selection bias, owing to its size and geographical distribution, this sample of psychiatrists in Spain is believed to be adequately representative.

In turn, from among those patients seen on a routine basis in their practice, each investigator enrolled in the study the first three eligible patients who agreed to collaborate starting on a randomly determined date (7 September 2008). The eligibility criteria established were: male or female at least 18 years of age, with diagnosis of major depressive disorder, under active treatment with any antidepressant drug within at least the previous 6 weeks, able to understand and fill out the study survey. Patients

with depressive episodes in the context of bipolar disorder and those already enrolled in a clinical trial at the time of the consultation were excluded. Patients were allowed to receive, per their doctor's judgment, other concomitant treatments, related or unrelated to the study disease, that were maintained under routine use conditions prior to their enrolment in the study.

For the study, information and anonymous opinions were meticulously collected through a written survey completed by psychiatrists and patients who voluntarily agreed to participate after the required informed consent had been obtained. Personally identifiable information was not collected, nor were the patients subjected to any other intervention or the psychiatrists to any changes in their routine clinical practice.

Information was collected via corresponding structured surveys completed on one single occasion by each participating psychiatrist and patient. The psychiatrists completed their professional survey prior to selecting patients so that their professional judgment would be kept free of any possible influence from knowing what the patients expressed on their own surveys. After this, selection of the three patients for the study was begun; these patients filled out their survey during the same consultation in which they were enrolled as a study case, and there was no follow-up or subsequent intervention of any kind.

Valid surveys from 319 psychiatrists and 957 patients with depression were collected and analysed—a sample enabling results to be evaluated with a high degree of precision (with a random error of  $\pm 5.5\%$  for the psychiatrist surveys and  $\pm 3.2\%$  for the patient surveys, for a 95% confidence interval (CI), assuming a random selection of surveyees and the least favourable mathematical outcome, where  $p=q=0.5$ ).

Both surveys included an initial description of the basic characteristics of the groups whose opinions were compared. The psychiatrist survey began with an initial description of the participant's professional profile, aspects of their practice, and their clinical experience with depression as well as age and sex; type of medical centre; healthcare setting; years of practice; patient load; and the surveyee's opinions about his/her personal experience in treating depressed patients. The patient survey began with a description of the individual's demographic and clinical-therapeutic profile variables such as age and sex; marital status; offspring; educational level; natural history of the disorder (first episode / previous episodes); time since onset of the current depressive episode and time on antidepressant therapy; and current antidepressant medication (tricyclic, tetracyclic, selective serotonin reuptake inhibitor [SSRI], selective serotonin-norepinephrine reuptake inhibitor [SNRI], atypicals, and others) as well as other concomitant therapies (benzodiazepines, gamma-aminobutyric acid [GABA]-selective agonists, and others).

Then, as independent study variables, the two surveys evaluated each group's opinion as to the incidence of depressive symptoms related to circadian rhythm disturbances (in the patient's case, a logical variable—yes/no—as to the experience of each individual symptom, and in the psychiatrist's case, an estimated

percentage for his/her clinical impression of the overall incidence). Each of the following symptoms was specifically assessed: diurnal variation in mood; disturbances in sleep-wake rhythm (difficulty falling asleep, difficulty staying asleep, waking early); changes in appetite; disruption in social rhythms (family, job, etc.); and constitutional symptoms experienced (fatigue, anergy, and apathy).

To examine the impact depressive symptoms related to circadian rhythm disturbances have on everyday life, the patients and the psychiatrists used the same 7-point ordinal intensity scale with anchoring linguistic quantifiers at either end (1=none, 7=very high)—a tool proven to be consistent and good for use with parametric techniques.<sup>21</sup>

In addition, the patients judged the response of these symptoms to the antidepressant therapy prescribed under routine practice conditions, and the psychiatrists assessed the need to order additional treatments to relieve them.

Finally, each survey included an assessment of the psychiatrist's satisfaction with the antidepressants available on the date of the study and with the results obtained in using them under routine practice conditions, as well as a personal assessment of the patient's overall satisfaction (taking into account the perceived risk/benefit) with his/her current antidepressant therapy. In both cases, the same 7-point ordinal scale described above was used.

Preliminary versions of the two study surveys were evaluated in corresponding pilot tests (cognitive pretest) conducted with 20 patients and 10 psychiatrists. After this use experience, the survey was evaluated expressly for suitability of the type of questions vis-à-vis the study objectives; the comprehensibility of the wording and length of the statements; whether the response categories were correct; the logic of their internal order; and how long it took to administer the survey. Following this process, changes were introduced to improve the survey's applicability. The scale for the impact depressive symptoms have on the patient's everyday living and on patient satisfaction with current therapy was subjected to test-retest by repeating the application of the scale with both groups at an interval of at least 15 days, and this demonstrated a high level of repeatability of results (intraclass correlation coefficients were greater than 0.85 for each group and for both variables).

Version 13.0 of the SPSS-W integrated package was used for the statistical analysis. Qualitative variables were described through calculation of the relative frequency distribution (percentage). Quantitative variables were described in terms of centralization and dispersion measurements of their use. For each descriptive statistical estimator, its 95% CI was constructed. The difference between the incidence estimated by the psychiatrist and the incidence in the patient's experience (of symptoms related to circadian rhythm disturbances) was evaluated for significance by comparing the 95% CI range for the corresponding percentages (the overlap of these intervals being considered indicative of no significance in the difference appreciated).

The significance of the difference between the psychiatrists' opinions and the patients' opinions about

the impact of symptoms related to circadian rhythm disturbances on everyday living was determined using a Mann-Whitney U test (in which the null hypothesis is that the opinions of the two groups, collected using the survey's 7-point ordinal scale, are of equal distribution).

## Results

The participants for this study included 319 psychiatrists and 957 patients diagnosed with depression who, in terms of referral source, were stratified by Autonomous Communities.

### Professional and practice profile of psychiatrists surveyed

the mean age of the psychiatrists surveyed was 47 years (95% CI, 46.1-47.9), with a median age of 48 years and including a wide range from 30 to 73 years. The majority of the group were men (in a proportion of about 3:1, men to women) whose professional work was primarily in the public sector (59.7%, although 34.9% of individuals were combining this with work in the private sector, and the remaining 5.3% stated that they had an exclusively private practice. The most common healthcare setting for the surveyees was the outpatient mental health centre (57.5%, followed by hospital psychiatric services (27%) and then private practice (15.4%).

The surveyees' professional experience varied between 1 and 42 years, with a mean of 17.4 years (95% CI, 16.5-18.4) and a median of 17 years. On average, the subsample of men was significantly more experienced, with 18.9 years compared to 14.3 years for the women (Mann-Whitney U test,  $P < .001$ ). Table 1 shows the surveyees' estimates for some indicators of activity in the healthcare field, as described.

### Demographic and clinical-therapeutic profile of patients surveyed

the mean age of the patients surveyed was 47.9 years (95% CI, 47.1-48.7), with a median age of 47 years and including a wide range from 19 to 82 years. In terms of gender, the sample was made up of a higher proportion of men (68.1%). The majority of the surveyees were married (61.8% compared to 18.5% single, 12.7% divorced/separated, and 7% widowed), and their self-declared level of education was as shown in figure 1.

Of the patients surveyed, 66.6% were being followed due to the recurrence of a previous depressive disorder. The number of previous episodes was 3.6, on average (95% CI, 3.3-3.8), with a median of 3 episodes and a range from 1 to 20 episodes. The average time from onset of the current depressive episode was 8.1 months (95% CI, 7.5-8.7), with a median of 6 months. The average duration of the current antidepressant therapy was 7.5 months (95% CI, 6.8-8.2), with a median of 4 months.

The antidepressant drug the patients were receiving at the time of the study was the initial treatment for that episode in 49.5% of cases; a change in treatment from the

**Table 1** Description of the clinical experience of the psychiatrists who participated, with their depressed patients, and aspects of their practice

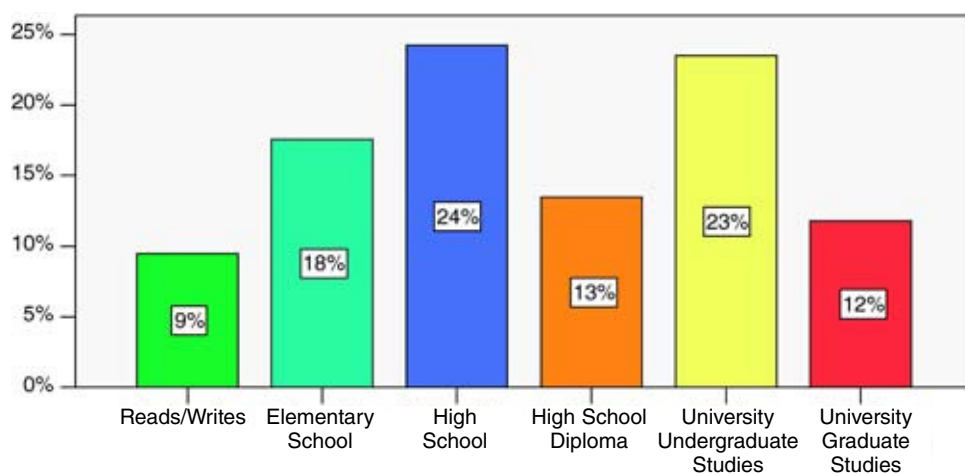
Indicators	Mean	95%CI	Median
Total patients seen per day	16.2	15.3-17.1	15
Percentage of patients seen who have depression	47.7	45.7-49.7	50
Antidepressant treatments prescribed per week	35.6	32.8-38.4	30
Mean target duration of an antidepressant therapy (months) <sup>a</sup>	13.1	12.2-14.0	12
Patients' actual duration on antidepressant therapy	8.4	7.5-9.3	6
Percentage of depressed patients treated with drugs	92.3	91-93.5	95
Percentage of depressed patients treated with psychotherapy	34.2	31.4-37.0	30
Percentage of depressed patients treated with other alternatives	6.8	5.6-8.0	1
Discontinuations of antidepressant therapy prior to the time desired (%) <sup>b</sup>	28.4	26.9-30	30
Percentage of depressed patients who have sexual dysfunction	57.8	54.7-60.9	60
Percentage of depressed patients who have weight gain	37.2	34.1-40.3	30
Percentage of depressed patients who have insomnia	50.6	47.4-57.3	60

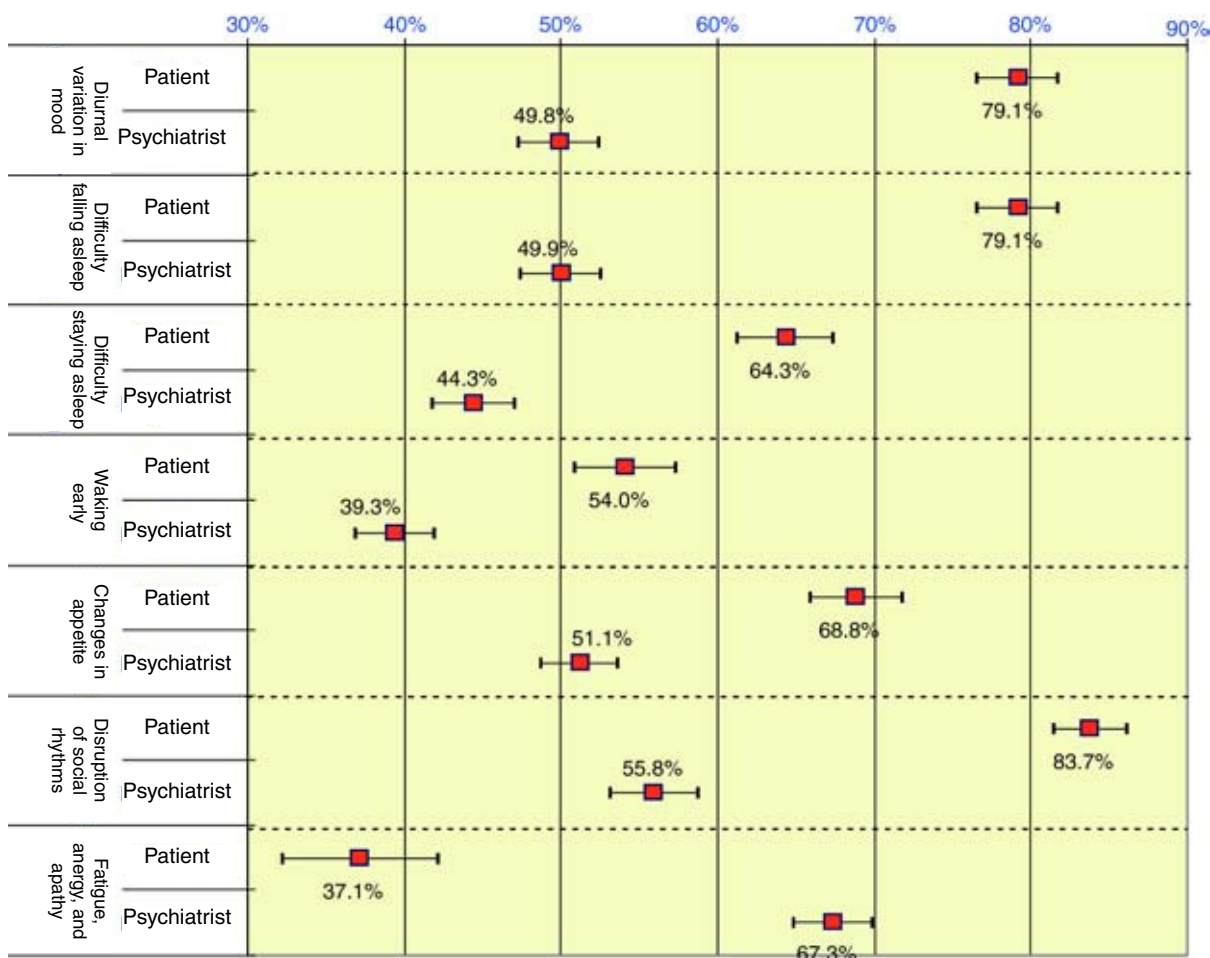
CI: confidence interval.

<sup>a</sup> Mean target duration is understood to mean the intended duration at the start of the treatment process.<sup>b</sup> The psychiatrists identified the following as reasons for discontinuing treatment, in decreasing order of frequency (according to their average scores on the Likert 7-point scale, where 1=very infrequent; 7=very frequent): insufficient improvement, side effects, relapse or recurrence, and poor compliance.**Table 2** Evaluation of the differences between the psychiatrist's professional opinion and the patient's experience in terms of the incidence of depressive symptoms related to circadian rhythm disturbances

Incidence of the symptom	Psychiatrists		Patients	
	Mean percentage	95%CI	Percentage	95%CI
Diurnal variation in mood	49.8	47.2-52.4	79.1	76.5-81.7
Difficulty falling asleep	49.9	47.3-52.5	79.1	76.4-81.7
Difficulty staying asleep	44.3	41.7-47.0	64.3	61.2-67.3
Waking early	39.3	36.9-41.8	54.0	50.8-57.2
Changes in appetite	51.1	48.6-53.6	68.8	65.8-71.7
Disruption of social rhythms	55.8	53.0-58.7	83.7	81.3-86.1
Fatigue, anergy, and apathy	67.3	64.8-69.8	37.1	32.2-42.0

CI: confidence interval.

**Figure 1** Educational level of patients surveyed.



Explanatory Note: For each symptom, the mean incidence estimated by psychiatrists and the actual percentage of patients experiencing the symptom are indicated, with their corresponding 95% CI.

**Figure 2** Comparison of the psychiatrist's professional opinion and the patient's experience in terms of the incidence of depressive symptoms related to circadian rhythm disturbances.

previous drug in 40% of cases; and further treatment with a new antidepressant drug (due to insufficient response to the first one) in the remaining 10.5% of cases. The therapeutic groups most prescribed for the study patients were the SSRI (44.6%) and the SNRI (36%), followed by the tricyclic antidepressants (6.6%), mirtazapine (5.2%), tetracyclics (4.8%), reboxetine (0.7%), and others.

Of the patients surveyed, 92% were also receiving concomitant therapies, the benzodiazepines being the most common pharmacological group (in 73% of cases).

### Comparison of psychiatrist and patient opinions about depressive symptoms related to circadian rhythm disturbances

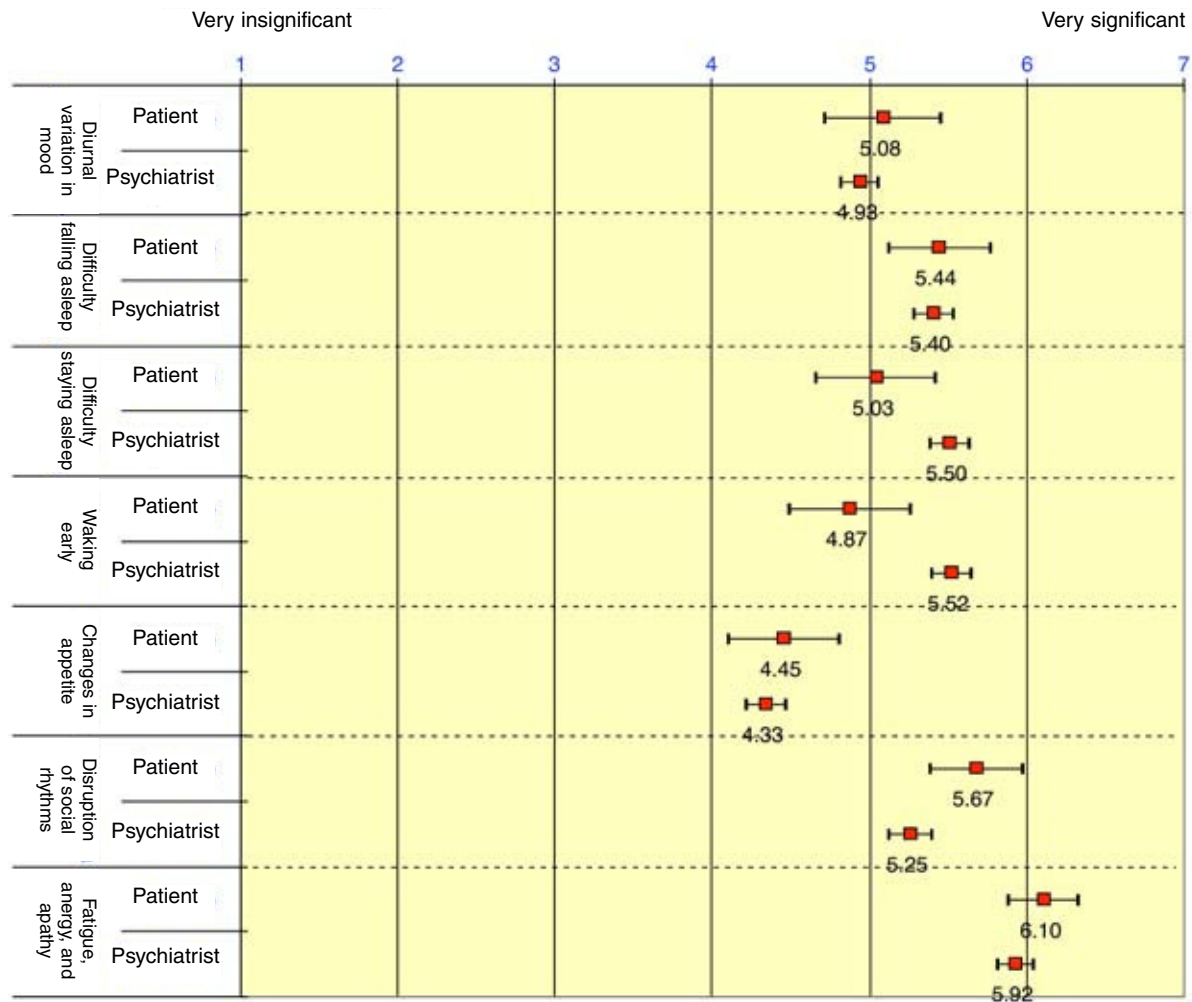
Figure 2 shows the comparison between 1) the estimate given in advance by the psychiatrists surveyed (based on their clinical experience) of the percentage of their depressed patients who have each of the symptoms related to circadian rhythm disturbances and 2) the actual

percentage of patients who stated on the survey that they had experienced those symptoms. The symptoms analysed in this comparison are: diurnal variation in mood; difficulty falling asleep; difficulty staying asleep; difficulty with waking early; changes in appetite; social disruption (family, job, etc.) related to the imbalance in biological rhythms; and constitutional symptoms (fatigue, anergy, and apathy).

Table 2 compares differences between the psychiatrist's professional opinion and the patient's experience in terms of the incidence of depressive symptoms related to circadian rhythm disturbances.

Figure 3 shows the comparison between 1) the psychiatrist's estimate of the degree of impairment in depressed patients' everyday functioning (activities of daily living) occasioned by each of those symptoms due to circadian rhythm disturbances and 2) the actual experience of the study patients themselves, with both evaluators using the same Likert-type, 7-point, ordinal rating scale from 1 (none) to 7 (a lot).





Explanatory Note: For each symptom, the average of the scores given by the psychiatrists and the patients on the ordinal rating scale of 1 (none) to 7 (a lot) is indicated, with their corresponding 95% CI for the mean.

**Figure 3** Comparison of the psychiatrist's professional opinion and the patient's experience in terms of the impact depressive symptoms related to circadian rhythm disturbances have on the patient's everyday functioning.

**Table 3** Evaluation of the differences between the psychiatrist's professional opinion and the patient's experience in terms of the impact depressive symptoms have on the patient's everyday functioning (activities of daily living)

Impact of symptoms on patient's everyday activity	Psychiatrists		Patients		P <sup>b</sup>
	Mean <sup>a</sup>	Median <sup>a</sup>	Mean <sup>a</sup>	Median <sup>a</sup>	
Diurnal variation in mood	5.08	5	4.98	5	.057
Difficulty falling asleep	5.44	6	5.40	6	.232
Difficulty staying asleep	5.03	6	5.50	6	.125
Waking early	4.87	6	5.52	5	.010
Changes in appetite	4.33	4	4.45	4	.248
Disruption of social rhythms	5.25	5	5.67	6	<.001
Fatigue, anergy, and apathy	5.92	6	6.10	6	.061

<sup>a</sup>Mean and median calculated from the scores of the two groups surveyed (psychiatrists and patients) on a Likert-type, 7-point, ordinal rating scale from 0 (none) to 7 (a lot).

<sup>b</sup>Statistical significance of the possible differences in distribution of the two groups' responses via a Mann-Whitney U test for data from ordinal scales.  $P < .05$  was considered significant.

**Table 4** Percentage of psychiatrists who believe that depressive symptoms related to circadian rhythm disturbances usually require treatment in addition to the conventional antidepressant

Symptom	Percentage of psychiatrists	95%CI
Difficulty falling asleep	99	97.9-100
Difficulty staying asleep	93	90.2-95.8
Difficulty with waking early	51	45.5-56.5
Fatigue, anergy, and apathy	43.6	38.2-49.0
Diurnal variation in mood	43	37.6-48.4
Disruption of social rhythms	28.3	23.4-33.2
Changes in appetite	25.6	20.8-30.4

CI: confidence interval.

Table 3 identifies the symptoms for which these differences are statistically significant ( $P < .05$ ), using a hypothesis test appropriate for contrasting the distributions of an ordinal variable in two comparison groups (Mann-Whitney U test).

Table 4 summarizes the professional opinion of the psychiatrists surveyed regarding the need for additional treatments to control the residual depressive symptoms related to circadian rhythms that persist despite effective antidepressant therapy.

Finally, both groups surveyed were asked for their opinion on the degree of overall satisfaction with the current antidepressant therapy (integrating the therapeutic results achieved, the presence of any residual symptoms, and the presence of any adverse effects), through a Likert-type, 7-point ordinal scale from 1 (completely dissatisfied) to 7 (completely satisfied), on which the group score for the psychiatrists was higher (mean 5.1, median 5) than the score for the patients (mean 4.6, median 4),  $P = .01$  (Mann-Whitney U test).

## Discussion

In this nationwide study, the opinions of two large, parallel, multi-centre samples were analysed and compared: a group of patients with a long-standing personal depressive disorder (average of 3 previous depression episodes per subject), and a group of psychiatrists with a lengthy professional career (17 years on average) who were responsible for the patients' treatment. Owing to these factors, with freedom from the intentional nature of the study participant selection process, it was felt that the two groups would ensure opinions on depression and its treatment that were sufficiently knowledgeable as to properly represent their respective populations of origin and enable the objectives proposed for the study to be analysed.

Desynchronization of social rhythms, insomnia, variations in mood, sexual problems, changes in appetite, and anergy and apathy are some of the common symptoms of depression generally associated with the circadian rhythm disturbances typical of this disease, although sometimes they are also related to the antidepressant drug used itself. In many patients, these problems persist as residual symptoms in spite of them receiving adequate therapy. The study compared 1) the psychiatrists' professional impression

(based on their clinical experience) of the significance of these depressive symptoms related to circadian rhythm disturbances and 2) the information obtained from the patients themselves when they were questioned about this, specifically, under the hypothesis that there are significant differences in perception between these two parties to the therapeutic relationship. Identifying the possible differences of opinion between the two may help clinicians to be more attuned to the real needs of depressed patients and to reorient psychiatric practice in healthcare so that patients' opinions are taken into consideration.

In the study sample, depressive symptoms related to circadian rhythms were quite common: more than 65% of the patients surveyed experienced them, except in the case of "difficulty with waking early" (54%) and "fatigue, anergy, and apathy" (37%). Generally speaking—and lending support to the study hypothesis—the incidence of practically all the depressive symptoms analysed is seriously underestimated by the psychiatrists in comparison with how the patients themselves experience them. Only the presence of "fatigue, anergy, and apathy" is contemplated more often by the psychiatrists than by the patients, perhaps because these symptoms, being markedly somatic in nature, may suggest to the clinician the need to rule out the presence of an underlying comorbidity.

Except in the case of sleep disorders (both "difficulty staying asleep" and "difficulty with waking early"), the psychiatrists also tended to underestimate the negative impact circadian depressive symptoms have on patients' ability to function and on their everyday activity, in comparison to how their patients experience them. However, not all the differences of opinion appreciated on this point were significant: strictly speaking, only "difficulty with waking early" (overestimated by the psychiatrists) and "disruption of social rhythms" (underestimated by the psychiatrists) reached the conventional significance level on a contrast test where the null hypothesis assumes the non-existence of differences in opinion between the two groups (assessed via the distribution of each group's scores on the same 1-7 ordinal scale). These results may be considered a corollary to a well-described clinical attitude in the majority of specialties: clinicians tend to focus their attention and interventions preferentially on those patient complaints for which they have effective therapeutic options available (such as the hypnotics, in the case mentioned).



Logically, in keeping with their professional judgment, almost all the study patients (92%) were being treated with antidepressant drugs. In general, personal satisfaction with the results obtained from their particular treatment, as reported by the study patients, was moderately inferior to the overall satisfaction the psychiatrists reported with the therapeutic resources at their disposal and the results they obtained with them in their clinical practice. In any case, about 40% of the pharmacotherapy treatments prescribed were discontinued prematurely due to insufficient improvement in the symptoms or the appearance of side effects. Therefore, the persistence of residual symptoms in patients who had an inadequate response to a partially effective drug was a common clinical scenario in the routine practice of the psychiatrists surveyed.

The psychiatrists' and patients' satisfaction with the results of the antidepressant therapies presented in this study must be understood as applicable to the drugs that were available or routinely used in Spain as of the date the surveys were taken (2008)—basically the SSRI (particularly escitalopram) and the SNRI (particularly venlafaxine).

In light of the results presented, it seems reasonable to suppose that the circadian rhythm disturbances may be an important aspect of depression, as well as the cause of a significant portion of the residual symptoms in patients under treatment. It appears that these disorders are not properly taken into consideration by the psychiatrists and are only partially resolved with current antidepressant drugs. In this regard, it would be beneficial to make active and ongoing assessment of the presence of these symptoms a part of routine psychiatric practice in follow-up visits and antidepressant therapy checkups and, when necessary, to contemplate with the patient the option to round out treatment with specific drugs to improve these symptoms. Practically all the psychiatrists surveyed recognized that the presence of residual symptoms in their depressed patients—sleep-related symptoms, in particular—usually requires specific treatment in addition to the antidepressant.

A psychiatric practice centred on the patient's needs as he/she perceives them could point to the need to reorient the treatment of many depressed patients in an effort to achieve the most complete and rapid remission of symptoms possible—aiming, in particular, for control of the symptoms most resistant to conventional drugs. New, recently introduced pharmacological agents which, in their action, are specific for the circadian rhythm disturbances described (such as agomelatine) may play a clear and prominent role in the optimization of therapy required in depressive disorders. The clinical effectiveness shown to date under naturalistic practice conditions appears to confirm the high expectations generated for this new agent in the antidepressant therapeutic arsenal.

## Conflict of interest

Servier Laboratories provided logistical and financial support for conducting this study and participated in the distribution and collection of field materials.

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