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Correlation between diagnosis of depression and symptoms present in primary care patients

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Depression is a chronic disease with a high prevalence that normally is episodic and an average episodic duration of 16 weeks. No analyses that evaluate the correlation between the evolution of the episode and its appearance have been found. The aim of this study is to analyze the correlation between symptomatic progression (appearance, maintenance, remission of different symptoms) and the evolution of the diagnosis of depression (onset, maintenance, and remission) in a cohort of patients diagnosed with and without major depression.

A prospective cohort study was performed with a one year follow-up in which a random sample of 741 subjects attending primary care was interviewed. Diagnosis of depression was made according to DSM-IV criteria and symptoms presented were analyzed. These subjects were re-evaluated at 6 months and 12 months.

Depressed mood state, decreased interest or anhedonia and symptoms related to sleep (insomnia or hypersomnia), agitation, feeling of guilt, fatigue or energy loss, are consistent with the diagnosis. The rest of the symptoms display an evolution independent of the diagnostic trends.

In Primary Care, it is important to know which are the key symptoms in the evolution of the diagnosis in order to achieve full remission of depression and avoid maintenance of residual symptoms that can become prodromal.

Keywords: Depression, Symptoms, Evolution, Diagnosis

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Correlación entre el diagnóstico de depresión y la sintomatología presentada en pacientes de atención primaria

La depresión mayor es una enfermedad crónica con una alta prevalencia que cursa habitualmente de manera episódica, con una duración media del episodio de 16 semanas. No se han encontrado análisis que evalúen la concordancia entre la aparición de los mismos y la evolución del episodio. El objetivo de este estudio es analizar la concordancia entre la evolución sintomática (aparición, mantenimiento, remisión de los diversos síntomas) y la evolución del diagnóstico de depresión mayor (aparición, mantenimiento y remisión) en una cohorte de personas con y sin diagnóstico de depresión mayor.

Se realizó un estudio de cohortes prospectivo a un año de seguimiento en el que se entrevistó a una muestra aleatoria de 741 sujetos que acudían a consultas de atención primaria, se elaboró el diagnóstico de depresión según criterios del DSM-IV y se analizó la sintomatología que presentaba. Estos sujetos fueron re-evaluados a los 6 meses y 12 meses.

El estado de ánimo deprimido, la disminución del interés o anhedonia y los síntomas relacionados con el sueño (insomnio o hipersomnia), la agitación, el sentimiento de culpa y la fatiga o pérdida de energía son concordantes con el diagnóstico. El resto de los síntomas muestran una evolución independiente de la evolución del diagnóstico.

En Atención Primaria, es importante conocer qué síntomas son claves en la evolución del diagnóstico con la finalidad de conseguir la remisión total de la depresión y evitar mantenimiento de sintomatología residual que puede dar lugar a pródomos.

Palabras clave: Depresión, Sintomatología, Evolución, Diagnóstico

INTRODUCTION

Depression is one of the most frequent conditions seen in the health care medical visits, mainly in Primary Care.¹⁻³ In fact, more than one fourth of Primary Care patients have symptoms of depression.⁴

Although estimates on their incidence and prevalence vary in different countries and studies, it is accepted that 2-16% of individuals suffer a unipolar depression during their lifetime.^{5,6} Some follow-up studies also show that depressive disorder is often recurrent and can become acute in 25% of the patients.⁵

Mean duration of a depressive episode is 16 weeks.⁷ Studies following the natural course of the disease suggest that at one year following the diagnosis of depression, 40% of the subjects still have symptoms, these being sufficiently severe to fulfill the criteria of a major depressive episode. Approximately 20% continue to have some symptoms, although these do not fulfill criteria for the diagnosis of a major depressive episode (such as major depressive disorder, in partial remission).

Different studies have analyzed the relationship between residual symptoms (symptoms maintained when the disorder is in remission) and prodromic symptoms (initial symptoms that precede the disorder), the former having a strong prognostic value (reversion phenomenon). This residual symptom can progress to relapse prodromes. These results imply important consequences since the subjects may begin a relapse-remission circle. Thus, the patient must be closely monitored during the different phases of the disease regarding the symptoms that occur and the residual symptoms, if existing, in order to improve his/her quality of life.^{8,9}

Considering the importance of the symptoms (occurring during the depressive episode, residual or prodromic symptoms) in the diagnosis of depression, and their importance in regards to the disease prognosis, no correlative analysis has been found in the literature in this regards. The objective of this study is to analyze concordance between each symptom in an individual way (appearance, maintenance, remission of the different symptoms) and the evolution of the diagnosis of depression (appearance, maintenance, and remission) in a cohort of Primary Care Patients.

METHODS

A prospective cohort study at one year of follow-up within the Primary Care setting was performed.

The project is part of a multicenter study funded by the Fondo de Investigaciones Sanitarias (Fund for Healthcare

Research) (FIS 04/2450) and has been approved by the Ethics Committee of Aragon.

As this study is a substudy of the national project Predict, whose objective was to develop and validate an innovating inventory of multifactorial risk to be used by primary care physicians to predict the onset and duration of a major depression episode, the size of the sample was calculated on the basis of an anticipated predictive validity of the inventory of risk factors. Assuming a 15% rate of depression, 2193 measurements would be required in the total participating communities in order to determine the ROC in the curve with a 95% confidence and interval of $\pm 5\%$. This amount needs to be doubled in order to use an independent test that would give predictive validity to the risk score based on a random selection of 50% of the study sample. That is, 4386 persons would be needed in the national sample, this reaching 5625 subjects, to make it possible to easily achieve the necessary response rate, even including 22% losses at the end of follow-up. The sample size that would correspond to the capture of the Zaragoza group was 740 subjects.

In this study, a mean of five physicians participated in each one of these six Health Care Sites, four of them urban and rural, from the province of Zaragoza. The selection of the sample was performed by systematic random sampling from the list of patients who came to the family doctor for any reason during the years 2005-2007. The first patient and then one out of every five subjects were selected from the list. If the patient selected fulfilled the inclusion criteria, he/she was invited to participate. If said patient did not fulfill the inclusion criteria or did not want to participate in the study, the next patient on the list was selected. This was done until completing the sample size. Inclusion criteria were: age between 18-75 years, having severe cognitive deterioration evaluated by means of the Mini Mental test adapted to Spanish,¹⁰ or any other disorder and/or severe organic disease that endangers their life and being residents of the study location.

A total of 958 patients were randomly selected, 71 of whom were excluded because they finally did not fulfill some of the previously mentioned inclusion criteria and 146 who refused to participate, 741 patients remaining. This study cohort was made up of the latter.

Qualified personnel (psychologists) were selected to perform the fieldwork. They were given specific training to avoid data bias. The interviewers also had a telephone and mail contact to be used in case of any doubt that could arise during the project.

All the study participants signed the informed consent. Of the 741 subjects who completed the initial evaluation (cutoff or T0), 567 (76.5%) were re-evaluated at 6 months

(T6) and 492 (66.4%) at 12 months (T12) in regards to the baseline moment to know their evolution in the diagnosis and their depressive symptoms. This study cohort included subject with a diagnosis of depression, those with depressive symptoms who did not fulfill the diagnostic criteria of depression and persons without depressive symptoms.

Data were collected on age, gender and reason for refusal for those patients who refused to form a part of the study and no significant differences were observed for the variables between both groups, participants and non-participant.

The result endpoint was the positive diagnosis of major depressive episode according to the DSM-IV criteria,¹¹ evaluated by the Composite International Diagnostic Interview version 2, 1997 (CIDI), which was developed and validated by the WHO.¹² This scale makes it possible to analyze the symptoms presented by each patient individually. The symptoms forming a part of the diagnostic criteria of the DSM-IV were selected, as shown in table 1.

Sociodemographic variables as age in years, gender, civil status, who the subject lives with, academic level and work situation were also collected.

Civil status was recoded into: Single, Married and others (separated, divorced and widow(er). Academic level was

divided into "Without studies but can read and write, Primary, Secondary or Occupational Training and Others (Diploma, Degree and Doctorate). Finally, the work situation was recoded into: "With contract/self-employed, retired, Caregiver of the family and home and Others that includes unemployed, disabled, students, long-term patients, etc.

The concordance of the evolution of the symptoms and diagnosis according to the DSM-IV was categorized into: appearance (baseline absence but presence at 6 or 12 months, respectively), maintained presence (presence maintained in both evaluations), maintained absence (absence maintained in both evaluations) or remission (baseline presence but absence at 6 or 12 months, respectively).

Regarding the statistical analysis, a descriptive analysis was initially performed using frequencies and percentages since the variables analyzed were categorical.

To establish if there was a relation between the principal endpoint (depression yes/no) and age, given the amount of data analyzed, the Student's T parametric contrast was used. To establish this relationship with the rest of the variables considered, contingency tables with the Chi-square statistics were used, also performing an analysis using the *Standardized Residuals* of Haberman to know between which categories of the variables the association was established.

Table 1	Symptoms required for the diagnosis according to the DSM-IV
DSM-IV	
S1: Depressed mood most of the day, nearly every day, as indicated by the subject per se (e.g., feeling sad or empty) or observation made by others (e.g., appears tearful).	
S2: Markedly diminished interest or pleasure in all, or almost all, activities most of the day, nearly every day (as reported by the subject per se or observed by others).	
S3: Significant weight loss when not dieting or weight gain (e.g., a change of more than 5% of body weight in a month), or decrease or increase in appetite almost every day.	
S4: Insomnia or hypersomnia nearly every day.	
S5: Psychomotor agitation or retardation almost every day (noticed by other, not mere sensations of agitation or retardation).	
S6: Fatigue or loss of energy nearly every day	
S7: Feelings of worthlessness or excessive or inappropriate guilt (that can be delusional) almost every day (not simple self-reproach or guilt for being ill).	
S8: Diminished ability to think or concentrate, or indecisiveness, almost every day (whether subjective attribution or observation of others).	
S9: Recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide.	

The analysis of the concordance-discrepancy was made using the Kappa coefficient and its confidence intervals at 95% level, in the moment T0 to T6 and T0 to T12. This is done using a 5% significance level.

RESULTS

Most of the 741 patients included in the cohort were women (62.5%), had completed their primary studies (47.8%), were married (64.5%) and were working, whether as self-employed or hired (52.4%) and their mean age was 46.5±15.5 years (Table 2).

At six months of the study (76.5%) persons had completed the second interview, there being no statistically significant differences regarding the sociodemographic variables studied in relationship to the initial cohort. At 12 months, 492 subjects (66.4%) continued in the study and there was a statistically significant difference in the age variable regarding the initial cohort, which went from 46.5 years (SD 15.15) to 47.3 (ST 15.2) (p=0.028). No statistically significant differences were found in regards to the remaining sociodemographic variables studied (Table 3).

Regarding the diagnosis of depression, at the time of capture, 81 subjects (10.9%; 95% CI: 8.62 – 13.24%) suffered

depression according to the DSM-IV criteria. At six months, 25 (4.4%; 95% CI: 2.63-6.19%) persons had this diagnosis

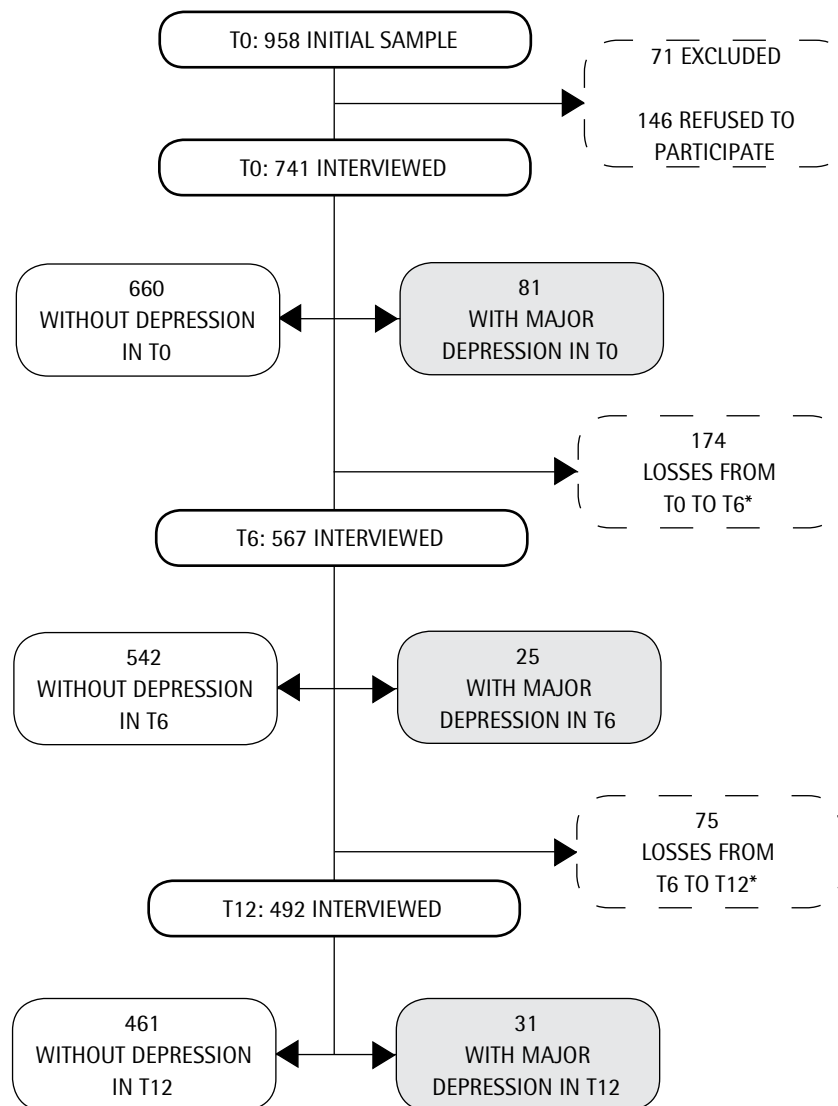
Table 2	Sample description based on sociodemographic variables	
	Number	Percentage
Gender (n=741)		
Woman	463	62.5
Man	278	37.5
Study level		
Read / Write	80	10.8
Primary	354	47.8
Secondary	196	26.4
Others (Doctorate, Degree, Diploma)	111	15.0
Civil Status (n=741)		
Single	192	25.9
Married	478	64.2
Other (Separated, widow(er), divorced)	71	9.6
Work Situation (n=741)		
Hired / Self-employed	388	52.3
Family and Home Caregiver	148	20.0
Retired	114	15.4
Others (Unemployed, disabled, student, ill/ long term, etc.)	91	12.3
Age (n=741)		
Mean (Standard Deviation)	46.5 (15.5)	

Table 3	Relation between sociodemographic variable and continuation in the study at 6 and 12 months				
	Initiate study N=741	Continue in T6 N=567		Continue in T12 N=492	
	N	N (%)	p-valor	N (%)	p-valor
Gender					
Woman	463	372 (80.3)	0.244	324 (69.8)	0.228
Man	278	195 (71)		168 (60.4)	
Study level					
Read / Write	80	59 (73.8)		57 (71.3)	
Primary	354	268 (75.7)	0.807	235 (66.1)	0.970
Secondary	196	149 (76.0)		126 (64.3)	
Others (Doctorate, Degree, Diploma)	111	91 (82.0)		74 (66.7)	
Civil Status					
Single	192	142 (74.0)	0.818	114 (59.4)	0.495
Married	478	375 (78.5)		333 (69.5)	
Other (Separated, widow(er), divorced)	71	50 (70.4)		45 (63.4)	
Work Situation					
Hired / Self-employed	388	293 (75.5)		237 (61.1)	
Family and Home Caregiver	148	121 (81.8)	0.228	114 (76.4)	0.460
Retired	114	79 (69.3)		77 (67.5)	
Others (Unemployed, disabled, student, ill/long term, etc.)	91	74 (81.3)		64 (70.3)	
Age					
Mean (Standard Deviation)	46.5 (15.5)	46.1 (15.2)	0.225	47.3 (15.2)	0.028

and at 12 months, there were 31 (6.3%; 95% CI: 4.05-8.55%). To understand the data better, the following flow chart on the evolution of the sample and their diagnoses is shown (Figure 1).

In order to know the incidence of depression in the follow-up year, subjects with depression at the onset of the study were excluded from the initial cohort, the risk population being obtained in this way. Following the DSM-IV criteria, the incidence was 6.9% (95% CI: 4.92-9.64%).

Regarding remission rates, in the first 6 months of the year, 43 (81.1%) cases of the 53 cases of depression diagnosed in T0 who continued in the study remitted in the first 6 months and 10 cases maintained depression from the onset of the study. In the second 6 months of the year, of the 21 cases of depression that existed at 6 months of the onset of the study and continued the follow-up until the last measurement at 12 months, 14 (63.6%) cases remitted in the second 6 months and 7 cases maintained the major depression.



* Majority Reasons for Drop-out: Not located 38% / Did not want 17%, Minority Reasons: Death 1% / Serious Disease 4%

Figure 1

Flow chart on the evolution of the sample and the diagnoses

Table 4		Concordance in the evolution (Appearance, Maintenance; Remission) of each symptoms and diagnosis of T0 to T6 based on DSM-IV				
SYMPTOM		DSM-IV DIAGNOSIS				Kappa 95% C.I.
		MA	A	R	MP	
S1: Depressed mood	MA	367	2	1	0	0.244
	A	24	0	13	1	
	R	78	37	0	0	0.199; 0.289
	MP	17	12	10	16	
S2: Anhedonia	MA	425	10	0	1	0.291
	A	22	0	19	4	
	R	42	30	0	0	0.241; 0.341
	MP	6	11	5	12	
S3: Weight	MA	4	1	0	2	-0.003
	A	2	0	2	1	
	R	8	1	1	4	-0.131; 0.125
	MP	5	10	7	10	
S4: Sleep	MA	3	0	2	0	0.076
	A	3	1	1	0	
	R	2	2	1	3	-0.044; 0.197
	MP	11	9	6	14	
S5: Agitation	MA	7	1	0	1	0.167
	A	2	2	0	3	
	R	2	1	2	1	0.011; 0.097
	MP	8	8	8	12	
S6: Fatigue	MA	0	0	0	0	-0.007
	A	3	0	1	0	
	R	2	0	0	1	-0.052; 0.038
	MP	14	12	9	16	
S7: Guilt and Inferiority	MA	4	0	0	0	0.166
	A	3	1	2	0	
	R	7	3	2	2	0.033; 0.299
	MP	5	8	5	14	
S8: Concentration	MA	1	0	0	0	0.037
	A	1	0	0	0	
	R	4	0	0	0	-0.020; 0.093
	MP	10	12	10	15	
S9: Death ideas	MA	5	5	4	5	0.050
	A	2	2	1	3	
	R	6	3	3	2	-0.109; 0.209
	MP	5	2	2	7	

MA: Maintained absence; A: Appearance; R: Remission; MP: Maintained Presence; CI: Confidence Interval

SYMPTOM	DSM-IV DIAGNOSIS				Kappa 95% C.I.	
	MA	A	R	MP		
S1: Depressed mood	MA	307	1	3	0	0.392 0.322; 0.463
	A	34	13	0	0	
	R	64	0	25	0	
	MP	21	8	9	19	
S2: Anhedonia	MA	344	11	8	0	0.379 0.295; 0.464
	A	28	7	1	2	
	R	34	2	19	3	
	MP	7	2	7	10	
S3: Weight	MA	6	1	1	0	0.118 -0.028; 0.265
	A	4	1	0	2	
	R	3	2	1	4	
	MP	8	4	7	13	
S4: Sleep	MA	5	0	0	0	0.214 0.061; 0.368
	A	0	4	1	0	
	R	2	0	1	3	
	MP	15	4	7	16	
S5: Agitation	MA	3	1	1	0	0.108 -0.017; 0.233
	A	6	2	3	3	
	R	5	1	0	1	
	MP	8	4	5	15	
S6: Fatigue	MA	4	0	0	0	0.147 0.025; 0.270
	A	2	1	0	0	
	R	1	0	1	1	
	MP	15	7	8	18	
S7: Guilt and Inferiority	MA	4	3	0	0	0.096 -0.029; 0.221
	A	6	1	0	0	
	R	1	0	0	3	
	MP	10	4	9	16	
S8: Concentration	MA	1	0	0	0	0.073 -0.023; 0.169
	A	0	1	1	1	
	R	5	1	0	0	
	MP	13	6	7	17	
S9: Death ideas	MA	9	4	5	3	0.015 -0.133; 0.163
	A	1	1	1	5	
	R	7	0	2	7	
	MP	4	3	1	4	

MA: Maintained absence; A: Appearance; R: Remission; MP: Maintained Presence; CI: Confidence Interval

As can be observed in tables 4 and 5, from the onset moment up to 6 months, concordance of the evolution of four symptoms with the diagnosis appears as significant. These four symptoms are depressed mood state (S1), decrease in interest or anhedonia (S2), agitation (S5) and feelings of guilt or inferiority (S7). From the onset until 12 month of follow-up, concordance of the evolution of the symptoms of depressed mood state (S1) and decrease in interest or anhedonia (S2) continue to be significant. However, during this period, concordance of the symptoms related with sleep (insomnia or hypersomnia) (S4) and fatigue or loss of energy (S6) also appear as significant. This concordance in the diagnosis means that when the symptom appear, in a significant percentage of cases, the diagnosis also appears. If the symptom remits in a significant number of cases, the diagnosis also remits. And if the symptoms are maintained (they either continue to be present or absent), the diagnosis is also maintained.

The remaining symptoms show an evolution, measured in appearance, maintained presence, maintained absence and remission, independent of the evolution of the diagnosis according to the DSM-IV.

DISCUSSION

In the existing literature, studies such as the Predict study can be found. These have performed an in-depth study on the risk factors to initiate or maintain a depressive episode.^{13,14} However, this study aims to complement this with the analysis of the symptoms that are present in the depressive episodes, residual or prodromic symptoms, to be considered in the possible evolution of a patient.

Although many studies attempt to analyze different aspects of the major depressive disorder, few have focused on the psychometric characteristics of the diagnostic symptoms, as has been recommended by some authors.¹⁵⁻¹⁹ In fact, there is no evidence of any study that analyzes the relationship between the evolution of the symptoms and the diagnosis according to the DSM-IV. Nonetheless, the results obtained are consistent with the literature regarding the depressive symptoms^{8,20,21} and can be useful for the clinical practice. In this sense, these results can provide a tool for clinicians to evaluate with greater certainty the prognosis of patients and adjust the treatment, focusing on the symptoms having greater weight to achieve a faster remission and to avoid new depressive episodes.

These results partially agree with studies showing a relationship of greater weight of some of these symptoms with the diagnosis compared with the rest of the symptoms.^{16-22,23} Among these symptoms are depressed mood state and anhedonia, which are considered "key" symptoms in the diagnosis since according to the DSM-IV criteria, a minimum of 5 symptoms out of a list of 9 are required (at least one part B will depressed mood state" or "lack of interest -anhedonia"), to have a positive diagnosis

of depression. Both symptoms have, according to Zimmerman,¹⁶ the strongest associations with the diagnosis, with odds ratios above 25. These two symptoms also have the largest β weight in the regression analysis.

Evolution of the "sleep alterations" symptom and its concordance with the evolution of the diagnosis of depression is supported by the demonstrated relation between the "sleep alterations" symptoms and the disorder widely stated in the scientific literature.²⁴⁻²⁷ Some studies even point to certain sleep variables as possible genetic biomarkers of the major depressive disorder.^{28,29}

On the contrary, other diagnostic symptoms in this study show some results that recommend continuing the investigation, since both the evolution of the "weight changes" symptom, "recurrent thoughts of death-suicide" and "thinking-concentration difficulties" are shown as independent of the evolution of the diagnosis both at 6 months as well as 12 months from the onset of the study. In fact, based on his studies, Zimmerman²² proposed the elimination of the "thinking-concentration-indecisiveness difficulties" symptoms and "weight gain or loss" due to their lack of impact on the major depressive diagnosis. Regarding the symptom "Recurrent thoughts of death-suicide" this author indicates¹⁶ that its presence is uncommon, so that this fact can explain its independence with the diagnosis of depression.

In spite of the existing literature that recommends going deeper into the study of the psychometric characteristics of the symptoms, the DSM-V³⁰ has not proposed any change in the diagnostic criteria of the major depressive episode. This manual once again proposes the 9 diagnostic symptoms, at least 5 of which the subjects should have, depressed mood state and/or anhedonia being essential for the diagnosis. The subjects should have the symptoms for at least 2 weeks, the greater part of the day, almost every day. However, some studies have questioned this criterion of a duration of 2 weeks when elaborating the diagnosis of depression.³¹

One limitation of this study may be the field work chronology. However, it is not considered that this can affect the results as it is an atemporal question and furthermore, the diagnostic criteria and symptoms of depression have been modified in the DSM-V. On the other hand, this is a sample selected in the Health Centers so that the results can be considered strictly representative of the outpatient population. Nonetheless, the aim this study has been to provide detection and alert tools to keep in consideration when a patient comes to the medical visit in the outpatient setting and that of the family doctor.

CONCLUSION

Within the Primary Care setting, it is important to know which symptoms are key in the evolution of the diagnosis of a major depression episode in order to achieve remission of

the depression. In this sense, it is also important that the concordance in symptoms such as depressed mood-sadness state, anhedonia and alterations of sleep-wake remit to achieve a remission of the disease. To do so, the family physician can establish a specific treatment for these symptoms (specific drug treatment, behavior modification techniques, sleep hygiene, etc.). It is also important to control the residual symptoms since these can give rise to prodromes of to depressive episodes.

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CONFLICTS OF INTERESTS

There are no conflicts of interests.

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