4. Definition and diagnosis of major depression

- Would screening improve the results in major depression?
- Are there suicide risk factors in patients with major depression?

4.1. Definition

Major depression is a syndrome or grouping of symptoms where there is a predominance of affective symptoms (pathological sadness, lassitude, irritability, subjective feeling of distress and impotence in the face of life's demands), although to a greater or lesser extent, symptoms of a cognitive, volitional or even somatic type are present, wherefore we could also talk about an overall impairment of the psychic life, with special emphasis on the affective sphere. The basis for distinguishing these pathological changes from ordinary changes is given by the persistence of the clinical symptoms, their severity, the presence of other symptoms and the degree of functional and social impairment that accompanies it.

Many cases of depression are clearly noticeably in clinical practice, although it is rarely easy to establish its separate diagnosis with respect to other psychopathological situations. For example, there is high association between depressive disorder and anxiety, and with different combinations in its manifestations. Depression can also occur simultaneously with alcohol abuse or the abuse of other toxic substances and with some cerebral organic and systemic diseases[1].

Even though the causes of depression remain unknown, various factors could take part in its origin, such as certain genetic factors, childhood experiences and current psychosocial adversities (social context and personality aspects). Difficulties in social relations, gender, socio-economic status or cognitive dysfunctions could also play an important role as risk factors in the development of depression, although it is most likely that it is an interaction of biological, psychological and social factors[25,26].

4.2. Diagnosis

The diagnostic possibility of a depressive disorder can be approached based on scarcely-specific observational factors, such as deterioration of personal appearance and look, psychomotor retardation, low tone of voice, sad facies, easy or spontaneous weeping, decreased attention, verbalisation of pessimistic ideas, hypochondriacal ideas, alterations of sleep and non-specific somatic complaints.

Even though the initial age of major depression varies in different studies, it can be established between 30 and 40 years of age, and it reaches a maximum peak of incidence between 18 and 44[27]. The illness can appear differently according to age; thus, young people show fundamentally behavioural symptoms while the elderly have a greater frequency of somatic symptoms[28].

There are several, reliable diagnostic instruments, such as the MINI self-evaluation scale (*Mini International Neuropsychiatric Interview*)[29, 30], which allow identifying those individuals who show depressive symptoms and make it possible for a clinician to carry out a diagnostic interview. Many of these instruments are useful at Primary Care centres.

The first episode of a major depression can occur at any time, and in some cases during the first months of appearance patients can experience a set of symptoms such as anxiety, phobias, minimal depressive symptoms and panic attacks[21]. The tendency towards recurrence is very frequent in this pathology[31]. A severe depressive episode may or may not also be accompanied by psychotic symptoms, in which delusional ideas, hallucinations or stupor appear, in addition to the criteria established for defining a severe depressive episode.

Depressive symptoms can be assessed and ordered according to operational diagnostic criteria, and those used the most – both in the clinic and in research studies – are the ICD-10[32] and DSM-IV[33] classifications. Their importance stems from using uniform diagnostic criteria among different professionals.

Table 2. General diagnostic criteria of a depressive episode according to ICD-10

A. The depressive episode should last for at least two weeks.
B. The episode is not attributable to psychoactive substance use or to any organic mental disorder.
C. Somatic Syndrome: some depressive symptoms are widely regarded as having special clinical significance, and in other classifications they are called melancholic or endogenomorphic ~ Marked loss of interest or pleasure in activities that are normally pleasurable ~ Lack of emotional reactions to events that normally produce a response ~ Waking in the morning 2 hours or more before the usual time ~ Depression worse in the morning ~ Evidence of psychomotor retardation or agitation ~ Marked loss of appetite ~ Weight loss of at least 5% in the last month ~ Marked loss of libido
Source: Adapted from WHO. Tenth Revision of the International Classification of Diseases. ICD-10. Mental and behavioural disorders. Madrid: Meditor 1992.

The ICD-10 uses a list of 10 depressive symptoms and divides the major depression into mild, moderate or severe (with or without psychotic symptoms) (Tables 2 and 3). In any of these cases, at least two of the three symptoms considered typical of depression must always be present: depressive mood, loss of interest and ability to enjoy and increase in fatigability, and the episode must last at least two weeks.

The DSM-IV uses a list of 9 depressive symptoms, it also requires that the episode last at least two weeks, and it divides the major depressive table into mild, moderate or severe, with specific codes for partial/full remission or unspecified remission. The diagnosis is established with the presence of at least five of the symptoms, and one of them must be a depressive mood state or the loss of interest or ability for pleasure.

Table 3. Severity criteria of a depressive episode according to ICD-10

A. General criteria for depressive episode 1. The depressive episode should last for at least two weeks 2. The episode is not attributable to psychoactive substance use or to any organic mental disorder
B. Presence of at least two of the following symptoms: 1. Depressed mood to a degree that is definitely abnormal for the individual, present for most of the day and almost every day, largely uninfluenced by environmental circumstances and sustained for at least two weeks. 2. Marked loss of interest or ability to enjoy activities that were previously pleasurable. 3. Decreased energy or increased fatigability.
C. An additional symptom or symptoms from the following list should be present, to give a total of at least four: 1. Loss of confidence and self-esteem and feelings of inferiority 2. Unreasonable feelings of self-reproaches or excessive and inappropriate guilt 3. Recurrent thoughts of death or suicide or any suicidal behaviour 4. Complaints or evidence of diminished ability to concentrate or think, accompanied by indecisiveness or vacillation 5. Change in psychomotor activity, with agitation or inhibition 6. Sleep disturbance of any type 7. Changes in appetite (decrease or increase), with corresponding weight change
D. There may or may not be the somatic syndrome*
Mild depressive episode: Two or three of the symptoms of criteria B are present. A person with a mild episode is probably capable of continuing with the majority of their activities. **Moderate depressive episode**: At least two of the symptoms of criteria B are present, in addition to symptoms of criteria C until there is a minimum total of 6 symptoms. A person with a moderate episode will probably have difficulties continuing with their ordinary activities. **Severe depressive episode**: There must be 3 symptoms of criteria B, in addition to symptoms of criteria C until there is a minimum of 8 symptoms. People with this type of depression have symptoms that are marked and distressing, mainly the loss of self-esteem and feelings of guilt or worthlessness. Suicidal thoughts and acts are common, and a number of somatic symptoms are present. Psychotic symptoms can appear, such as hallucinations, delusions, psychomotor retardation or severe stupor. In this case, it is called a severe depressive episode with psychotic symptoms. The psychotic phenomena such as hallucinations or delusion may or may not be mood-congruent.
Source: WHO. Tenth Revision of the International Classification of Diseases. ICD-10. Mental and behavioural disorders. Madrid: Meditor 1992.

This clinical practice guideline assumes the classification and definitions of depression included in the tenth edition of the International Classification of Diseases (Mental and Behavioural Disorders), ICD-10[32], with codes F32 (depressive episodes) and F33 (recurrent depressive disorder), and by the *American Psychiatric Association* (DSM- IV)[33], with codes 296.2X (depressive disorder) and 296.3X (depressive disorder, recurrent).

4.3. Risk factors

Major depression is a multi-factor and complex process whose probability of development depends on a broad group of risk factors, and to date it has not been possible to establish neither the totality thereof or the multiple interactions existing between them. The weight of each factor in relation to the circumstances and to the moment in life in which they develop is unknown.

Variables that increase the risk of depression include personal, cognitive, social, family and genetic factors[34]. Poverty, chronic illnesses (both physical and mental[21]), the possible association with the consumption of alcohol and tobacco and work circumstances have been highlighted within the role attributed to personal or social circumstances, given that the unemployed, the disabled and people on sick leave due to illness or maternity show signs of depression with greater frequency[5]. Civil status and chronic stress seem to be related to a greater likelihood of developing depression[21], and it has been observed that exposure to adversities throughout life is involved in the onset of depressive and anxiety disorders[36].

The offsprings of patients with depression constitute a high-risk group, for both somatic and psychiatric illnesses, which begin at an early age and persist throughout adult life[37]. Thus, first-degree relatives of patients with a major depressive disorder have double the possibility of showing depression than the general population[38], a proportion that is also considerable in second-degree relatives[39]. The pattern of how the symptoms are presented can also be different, and an anxiety disorder has been found as the earliest sign[40]. However, these family studies cannot, by themselves, establish what amount of risk comes from genetic factors and what amount comes from the shared family environment. Moreover, with the progressive knowledge of the human genome, it has become possible to identify the chromosomic location of genes that determine vulnerability for disorders such as major depression. One factor that could have an influence on its development is the presence of a polymorphism of the gene that codes the serotonin transporter, thereby causing a decrease in the transport of this neurotransmitter[41].

The neurotic traits of the personality are associated with a greater incidence of cases and relapses of major depression[42, 43], and this personality trait probably lends greater susceptibility to developing depression when faced with the adversities of life[44]. In general, anxiety disorders are risk factors for the development of the first episode of major depression[41, 42], and dysthymia has also been seen as an important predictor of the subsequent development of major depressive symptoms. Furthermore, it has been observed that patients, mainly males, with previous panic attacks, had a greater risk of developing major depression. This correlation has not been found with other psychiatric disorders[46]. An association between migraines and depression has been described, such that patients with major depression showed a greater risk of suffering from migraines, and in turn those who had migraines (and not another type of headache) had a greater risk of major depression[47]. Also, the presence of heart disease and various endocrine illnesses such as diabetes, hypo or hyperthyroidism, Cushing's syndrome, Addison's disease and hyperprolactinemic amenorrhea seem to increase the risk of depression[21].

Finally, and in order to create a predictive model of depression, a prospective study is being carried out in various European countries, based on taking surveys focussed on depression risk factors in Primary Care[48].

4.4. Depression screening

A high percentage of patients with depression are neither diagnosed nor treated[11, 49, 50], wherefore some authors propose screening of the population in order to assure that everyone is identified and receives suitable treatment.

It is important to question if screening improves the results in patients with major depression and if it should be done broadly (all the general population, all patients who go to a doctor's appointment) or in a limited manner (only those patients for whom there is a specific type of risk).

In a recent meta-analysis[51], performed to evaluate the diagnostic validity of the questionnaires in depression screening, the authors observed that the tests of a single question have a sensitivity of 32% and a specificity of 96%, with a positive predictive value (PPV) of 56% and a negative predictive value (NPV) of 92%, while the tests of two or three questions have a sensitivity and specificity of 74%, with a PPV of 38% and an NPV of 93%. The authors conclude that the ultra-short tests (between one and four questions) seem to be, in the best of cases, a method for excluding the diagnosis of depression and should be used only when there are sufficient resources for a second analysis of initially positive cases.

In the NICE[21] Depression CPG, the depression screening section is based on two systematic reviews. The first one summarises the work of the *U.S. Preventive Services Task Force* and identifies 14 randomised clinical trials in which the effect of routine screening of depression in adults was evaluated[52]. The second reviews a group of nine trials similar to the previous one, although not identical[53]. The NICE conclusions were the following:

~ Routine screening for depression may be effective in identifying an increased number of cases but there is only limited evidence that screening alone may have any beneficial effect on depressive symptomatology, even when integrated into an accessible treatment programme.

~ For screening, a questionnaire with two questions is as effective as a more elaborate questionnaire, and it adapts better to the characteristics of Primary Care.

~ None of the reviewed studies specifically handled people considered to be at high risk for developing depression.

~ And its recommendations for clinical practice were the following:

~ Screening of depression should be undertaken in Primary Care for risk groups, such as those with a past history of depression, significant physical illnesses causing disability or other mental problems such as dementia.

~ Healthcare professionals should bear in mind the potential physical causes of depression and the possibility that depression may be caused by medication and consider screening if appropriate.

~ Depression screening should include the use of at least two questions referring to a person's mood and to the ability to enjoy.

~ Research is needed into the cost-effectiveness of routine screening of populations known to be at high risk of depression.

In 2004, the *Canadian Task Force on Preventive Health Care*[53] published an update of their recommendations after a review by Pignone *et al*[52]. This task force recommends screening for major depression in adults in Primary Care, as long as it is linked to effective treatment and follow-up. Finally, the Cochrane Collaboration published a review on the subject in 2001

(updated in 2005[54, 55]), although it only contributes one trial with respect to the NICE depression CPG[21]. The authors conclude that screening questionnaires have a minimum impact on the detection, treatment or outcome of depression, and this strategy should not be adopted alone.

Summary of the evidence

1+	Tests with more than one question (between two and three) are the most suitable for depression screening. (51).
1-	The studies currently available show that while there are valid instruments for identifying or excluding cases of depression, there are insufficient trials on their ability to favourably modify the evolution and prognosis of the illness (21, 52, 53).
1-	The screening of major depression without a programme of accessible treatment and suitable follow-up does not seem to be effective (21, 52, 53).

Recommendations

✓	In general, screening of depression is not recommended, given that there are reasonable doubts about its effectiveness to modify the course of the illness if it is not accompanied by follow-up measures.
✓	The possibility of a depressive pathology in persons with risk factors must be taken into account.
B	The questionnaires used should include at least two questions referring to the person's mood and ability to enjoy.

4.5. Risk of suicide

Depression is one of the factors most-related to suicidal behaviour[56], which is the result of a confluence of a large number of situations and factors that combine together to generate a range that would go from a simple passing thought to actually committing suicide. There are many variables that intervene in causing suicidal behaviour, and they include biological factors as well as sociodemographic, psychiatric and psychosocial variables[57-59].

One of the main problems that arises when interpreting the findings of studies about suicidal behaviour is their low representativity, given that suicide is an infrequent behaviour.

The NICE guideline includes the importance of the severity of the major depressive episode as a suicide risk factor, whereas other authors point out the importance of hopelessness[60]. Two prospective studies with 18-24 months of follow-up observed different percentages of attempted suicide or suicide completion, varying between 8%[61] and 16.6%[62], without therein specifying the severity of the depressive disorder. In the first study[61], the risk of suicide was significantly greater in periods of partial remission and during the episode than in the period of full remission. After a multivariate analysis, the most important factors were the duration of the depressive episode, suicide attempts and not having a partner. The second study took on the risk factors associated with suicidal behaviour, thereby observing that a family history of previous suicides, a background of drug addiction

or tobacco use, borderline personality disorders and family separation at an early age multiply the risk of suicidal acts by three in men with major depression. In women, the risk of suicide was greater in those who had made previous attempts and those with suicidal ideation, and the risk of suicide increased by three with each previous attempt.

Table 4. Suicide risk factors in people with major depression

~ History of previous suicide attempts. ~ History of familial suicide. ~ Axis II comorbidity (diagnosis by DSM-IV axes): Borderline personality disorder. ~ Impulsiveness. ~ Hopelessness. ~ Traumatic early life events. ~ Life stress. ~ Low social-couple support. ~ Masculine sex. ~ Abuse of – dependence on alcohol or other drugs.
Source: own preparation.

Impulsive and aggressive behaviour as a suicide risk factor was studied in a case-control study (male depressed suicide completers compared to living depressed male subjects). The authors observed that abuse of or dependence on alcohol or other drugs and that the borderline personality disorder increase the risk of suicide in patients with major depression, in addition to high levels of impulsiveness and aggressiveness[63].

Finally, a retrospective study with 21 years of follow-up that included 785 patients with depression found that the only significant predictor variables of suicide after a univariate analysis were suicidal tendency, assessed with 7 points in the *Schedule for Affective Disorders and Schizophrenia* (SADS), and a history of previous suicide attempts[64].

Summary of the evidence

3	The risk of suicide increases during the major depression episode and during the period of partial remission (61).
3	Prior attempts to inflict self-harm by a patient are significantly associated with the probability of a future, completed suicide (61, 62, 64).
3	The abuse of or dependence on alcohol or other drugs, the borderline personality disorder and high levels of impulsiveness and aggressiveness increase the risk of suicide in males with a major depressive disorder (63).
3	Even though the clinical information is scarce and heterogeneous, there is evidence that suggests that there is a difference in the suicide risk factors in patients with major depression with respect to sex, age, severity and duration of the episode, civil status and comorbidity (alcoholism or drug addiction) (62).

Recommendations

✓	In any patient with a major depressive disorder, it is advisable to explore ideas of death and the intention to inflict self-harm.
✓	The clinical history of a patient with major depression must always include previous attempts to inflict self-harm.
✓	In patients with a high risk of suicide, it is advisable to seek frequent, additional support and to assess sending them urgently to a mental health specialist.
✓	Hospitalisation should be considered for patients with a high risk of suicide.