

7. Other treatments

- Is electroconvulsive therapy effective for the treatment of major depression?
- Is guided self-help effective for any sub-group of patients?
- Are support groups effective for patients with major depression?
- Is physical exercise effective for patients with major depression?
- Is acupuncture effective for patients with major depression?
- Is treatment with St John's Wort effective?

7.1 Electroconvulsive therapy

Electroconvulsive therapy (ECT) induces, for a therapeutic purpose, generalised seizure activity through electrical stimulation of the central nervous system. Even though years ago it was a reviled and even prohibited technique, today it is performed under certain circumstances, under anaesthetic control and with muscle relaxation, wherefore secondary effects have been reduced to the point where they are comparable to those of general anaesthesia.

Even though electroconvulsive therapy has been used in clinical practice for more than 50 years, there continues to be controversy about the pathologies for which it could be indicated, as well as its efficacy, how it is administered, the possible complications and its indication as maintenance treatment. Despite all this, ECT has proven its efficacy in various studies, and it is used in severe depressive episodes, with or without psychotic symptoms, and in resistant depression. It should also be considered as first-line treatment in acute situations of suicidal risk or for patients who have severely deteriorated medically^{21, 132}.

There are no absolute contraindications for electroconvulsive therapy, although there are situations of relative risk, such as the presence of brain injuries that occupy space (tumours or haemorrhages) or any other situation in which intracranial pressure is high; recent cardiovascular problems (such as acute myocardial infarction or vascular malformations); treatment with MAOIs or lithium; and the existence of increased risk for general anaesthesia¹³³. Regarding side effects, they depend basically on the patient's previous conditions, their personal susceptibility, the technique used (bilateral or unilateral), the number of sessions used and the frequency of administration. These side effects can be immediate (mental confusion, amnesia and headache) or more persistent (euphoria and cognitive disorders)¹³².

In 1999, the Sociedad Española de Psiquiatría [*Spanish Society of Psychiatry*] promoted the formulation of a Spanish consensus on electroconvulsive therapy, in which it was agreed that maintenance ETC could benefit 10-15% of patients with severe affective disorders in which relapses occur (even with adequate drug treatments) during the 6 months following the ECT¹³⁴.

The ECT section of the NICE²¹ Depression CPG is based on a systematic review prepared by the University of Sheffield and subsequently published in 2005^{21, 135}, and it in turn includes two systematic reviews of quality randomised clinical trials. The first, prepared by the Cochrane Collaboration, studied the efficacy and safety of ECT in schizophrenia¹³⁶, and the second, performed by the *UK ECT Group*, studied the efficacy of ECT on the depressive illness¹³⁷. It also included a systematic review of non-randomised studies on

the patients' point of view about this technique¹³⁸; two clinical studies in which ECT was compared with transcranial magnetic stimulation; ten studies in which ECT combined with drugs was compared to ECT plus placebo; a prospective cohort study in which patients of advanced age who had received ECT were compared to those who had not received it¹³⁹; and a systematic review of a series of cases on using ECT during pregnancy^{140, 141}. The NICE CPG considers ECT to be an effective treatment for depression in adults and it reaches the following conclusions:

- ~ Real ECT is more effective than sham ECT, although the parameters of the electrical stimulus have an important influence on efficacy.
- ~ Bilateral ECT is more effective than unilateral ECT, and unilateral ECT at a low dose is not more effective than sham ECT.
- ~ ECT has the risk that side effects of the cognitive type may appear. Even though the evidence is limited, it seems that the duration of these effects does not go beyond six months, although there are no longer-term studies.
- ~ ECT is probably more effective than short-term pharmacotherapy, although the evidence of this affirmation is based on studies of inadequate variable quality and doses.
- ~ The combination of ECT with pharmacotherapy was not shown to have a greater short-term effect than ECT alone.
- ~ There is limited information to the effect that ECT is more effective than repetitive transcranial magnetic stimulation.
- ~ Certain data suggest that tricyclic antidepressants could improve the effect of ECT and that the continuation of treatment associated with lithium reduces the rate of relapses in patients who have responded to ECT after an acute episode.
- ~ Finally, the meta-analysis prepared by Kho *et al*¹⁴² and based on 16 clinical trials included in most of the preceding reviews supports the aforementioned conclusions.

Summary of the evidence

1+	There are numerous controlled studies that demonstrate that electroconvulsive therapy is an effective and safe treatment in adult patients with severe major depression (133, 135, 140).
1+	The parameters of the electrical stimulus have a major influence on the efficacy of the technique, and bilateral ECT is more effective than unilateral ECT (133, 135, 140).
1+	ECT is a safe technique, and its side effects on memory are usually slight and temporary (133, 135, 140).
1+	ECT is more effective in the short-term than pharmacotherapy, and the combination of ECT with pharmacotherapy has not shown to have a greater short-term effect than ECT alone (133, 135, 140).

1+	Tricyclic antidepressants improve the effect of ECT, and continuing with antidepressant treatment associated with lithium could reduce the rate of relapses in patients who have responded to ECT after an acute episode (133, 135, 140).
----	---

Recommendations

A	Electroconvulsive therapy should be considered as a therapeutic alternative in adults with severe major depression.
✓	ECT is especially indicated for patients with severe major depression (with a high risk of suicide or severe physical impairment), in resistant depression and by informed choice of the patient.

7.2 Guided self-help

Guided self-help is an ambiguous term that includes self-help as such and guided self-help. Self-help is directed at improving the clinical outcome by training patients on the pertinent skills for overcoming and managing their health problem. It includes the use of written materials (bibliotherapy), computer programmes or material recorded in audio/video format so that, for the purpose of modifying their attitudes and behaviour, they successfully solve or improve their problems.

In turn, guided self-help is more complete and uses these self-help materials in conjunction with minimum guidance offered by a professional “to monitor progress, clarify the procedures, respond to general questions or provide general support or stimulus”¹⁴³.

Reading the existing literature on this subject brought several questions to light:

- ~ First of all, the self-help material for depression is scarce, it is in English, and it always alludes to two texts of reference: *Feeling Good, The New Mood Therapy*, by David Burns, whose version in Spanish is called *Sentirse bien*¹⁴⁴; and *Managing anxiety and depression*¹⁴⁵, which has been translated into Spanish under the title of *Manejando su ansiedad y depresión*. A single article refers to a third book titled *Control your depression*¹⁴⁶. We are unaware if these books have been validated in Spanish and if they are actually used as bibliotherapy material in consultations.
- ~ Most studies refer to the fact that the therapist is the one to deliver the reading material, with minimum intervention. Moreover, there was considerable variation in the range of patients to whom bibliotherapy was offered.
- ~ There is considerable heterogeneity about the diagnosis and classification of depression, and on many occasions neither criteria nor scales considered to be of reference in this guideline are used.
- ~ The use of different nomenclatures and, occasionally, combinations of techniques was observed, which limits the assessment.

NICE assessed guided self-help through nine randomised clinical trials, and it concluded that guided self-help generates a significant clinical reduction of depressive symptoms in comparison to non-intervention. In patients with mild or moderate depression, it could be as effective as some forms of individual therapy and more effective than group psychotherapy, although there isn't

sufficient data to the effect that this benefit is maintained in the long term²¹. The recommendations that it makes are the following:

- ~ In patients with mild depression, health professionals should recommend guided self-help programmes based on cognitive behavioural therapies.
- ~ Guided self-help, in addition to providing suitable written material, must include support and follow-up by health professionals for six to nine weeks.

Bibliotherapy in the treatment of depression was assessed in a meta-analysis¹⁴⁷, and it was observed that using bibliotherapy translated into at least a 25% reduction in scores of depression tests when compared to non-treatment, although there was no significant relationship between the maintenance time of the treatment and the final clinical outcome. Up to now, there are no clinical trials that demonstrate that bibliotherapy is helpful in patients with severe depression.

A randomised controlled trial¹⁴⁸ examined if the fact that adding self-help material (books, brochures, algorithms, etc.) to the standard treatment of depression using antidepressants by primary care physicians was associated with any additional improvement of the clinical outcomes. The outcomes showed no significant reduction between the patients treated only with antidepressants and those who also received self-help. However, significant differences were observed in favour of the intervention group with respect to knowledge of the treatment, of the illness, of how to make changes in their lives and of the effects of the medication. The patients were shown to be satisfied with receiving self-help, and most general physicians found it to be useful.

Summary of the evidence

1+	Compared to non-intervention, guided self-help is effective at reducing the symptoms of mild to moderate depression, although its long-term effect is unknown (21).
1+	No significant differences were observed when the pharmacological treatment of depression was compared to adding or not adding self-help (146).

Recommendations

✓	In general, guided self-help is not recommended for patients with severe major depression.
B	However, for patients with mild or moderate depression, professionals could consider recommending guided self-help programmes based on cognitive behavioural therapy.

7.3 Support groups

A **mutual support group** is understood as a group specifically created to help its members face a critical life situation, such as chronically mental ill persons, and to inform, guideline and support families, thereby offering resources for supporting the anxiety and bearing the prejudices linked to the ignorance of certain illnesses. These “non-professional” groups and networks work autonomously and arise in society when formal healthcare organisations do not satisfy certain needs. The most well-known examples are alcoholics anonymous groups and self-help programmes for food disorders. These groups are considered to be mainly self-sufficient and usually have no professional interference.

Conversely, **support groups** tend to be called together by a professional and are composed of people who share some type of problem that alters or modifies aspects of their normal functioning. Belonging to these groups provides new links and social relationships for their members, thereby allowing interaction with people who have common problems, deficiencies and/or experiences. A group can begin by being a support group and over time become a mutual support group that operates autonomously, although this group may likewise and occasionally require the help of a professional or of an institution and operate for a certain period of time like a support group.

Occasionally, these groups can be guided by **paraprofessionals** who are trained or supervised by professionals. They are defined as mental health workers, paid or volunteers, without training regarding psychological treatment for anxiety and depression, and who substitute professionals in treating patients with these disorders¹⁴⁹.

In this section, the NICE²¹ guideline only included one randomised clinical trial that used befriending of women with depression. It consisted of especially trained volunteers who got to know, speak with and accompany women with depression for at least one hour a week, which women were also allowed another type of treatment. The outcomes showed that friendship is significantly effective at achieving the remission of depressive symptoms in comparison with controls. NICE concludes with the recommendation that in patients with chronic depression, friendship could be considered an adjuvant to pharmacological or psychological treatment.

In a prospective cohort study not included by NICE¹⁵⁰, the use of depression support forums through the Internet was assessed. The patients that customarily used these forums (more than five hours a week) showed a better resolution of their depressive symptoms. However, the high probability of skewing of this study must be considered, given that it used patients who had different states and who were socially isolated.

Support and socialisation groups seem to constitute protector factors in older persons with depression, while sensory limitations, such as blindness and deafness, the absence of a home and low financial income behave like depression risk factors¹⁵¹. Finally, a satisfaction study showed that up to 64% of the participants in depression support groups declared that this type of therapy met their expectations¹⁵².

Summary of the evidence

	Studies about support and self-help groups are scarce and of insufficient quality to determine if they can be beneficial or not in patients with major depression.
--	--

Recommendations

✓	Participation in support groups is not considered an effective treatment measure in patients with the major depressive disorder, either alone or combined with other therapeutic measures.
---	--

7.4 Physical exercise

It is well-known that exercise improves the mood and the general sensation of well-being, wherefore it has been attempted to determine up to what point it can be useful as treatment in patients with major depression. A depressed patient who exercises regularly successfully develops his self-esteem and develops better and greater support from others, which favours his relationships with the environment.

NICE²¹ performed a systematic review on the likelihood of remission, reduction of symptoms and adherence to treatment in patients with depression who took exercise, versus not exercising and versus different available treatments (pharmacological, psychotherapeutic, social support and meditation), thereby including a total of nine clinical trials. In general, the exercise programmes used had a relatively high frequency (at least 3 times per week), lasting from 45 minutes to one hour and in periods of 10 to 12 weeks. The conclusions were that in subjects with depression, in particular mild or moderate depression, structured and supervised exercise had a clinically significant impact on improving the symptoms, even though there was no evidence of long-term benefits for preventing relapses or of the utility of maintenance exercise programmes. There also was insufficient evidence to assess its usefulness as an alternative or in combination with other treatments, although a recent study – with few patients – points out that endurance exercise associated with antidepressant drugs is better than antidepressant drugs alone¹⁵³.

One trial with considerable methodological limitations (small sample size, poor definitions of exercise time and intensity, low number of participants among those potentially eligible and no assessment of comorbidities) and not included in the NICE guideline compared physical exercise to educational activities in patients without clinical improvement after six weeks of pharmacological treatment at suitable doses¹⁵⁴. The authors observed that exercise twice a week provides a greater reduction of depressive symptoms, even though the exercise may be light.

Another systematic review¹⁵⁵, which only included three studies with patients with major depression, observed that physical exercise programmes significantly reduce the symptoms of depression, although the conclusions are limited by the heterogeneity of the three assessed studies and their methodological limitations.

The efficacy of exercise in patients with mild and moderate major depression and their dose-response ratio was evaluated in a trial in which only 5% of the potentially eligible patients initiated it¹⁵⁶. The authors conclude that aerobic exercise at the traditionally recommended doses (17 kcal/kg/week, taken 3 to 5 times per week) improves the symptoms of depression, while exercise at low doses (7 kcal/kg/week) has no effect at all.

Finally, in patients over 60 years of age, intense exercise also seems to be more effective than low intensity exercise or the usual care by the primary care physician¹⁵⁷.

Summary of the evidence

2++	For patients with major depression, in particular mild to moderate depression, a structured and supervised programme of exercise could be effective intervention, with significant clinical impact on depressive symptoms (21).
2+	Although the acceptance rate of exercise programmes is low, once one is started, adherence is similar to other types of therapies, and short-term benefits are detected (21).
2++	The greatest beneficial effect of exercise is obtained when it is given in association with pharmacological or psychotherapeutic treatment (151).
	No evidence has been found about the usefulness of exercise for maintenance therapy or for the prevention of relapses.

Recommendations

C	Programmes of structured and supervised exercise of moderate intensity, with a frequency of 2-3 times per week, with a duration of 40-45 minutes and for a period of 10 to 12 weeks should be recommended to patients with mild-moderate depression.
---	--

7.5 Acupuncture

Acupuncture is a technique that consists of inserting thin needles in various parts of the body, and it is based on traditional Chinese medicine. There are a wide variety of techniques, which include the classic or traditional, auricular, trigger points and single points.

The use of acupuncture was not discussed in the NICE²¹ CPG. We identified three systematic reviews and one subsequent clinical trial with which we used to deal with the question. The first review¹⁵⁸ included 7 randomised clinical trials, six of which included only patients with major depression (a total of 466 patients). The second review, published by the Cochrane Collaboration¹⁵⁹, included seven randomised clinical trials (a total of 517 patients), five of which were included in the first¹⁵⁸. A final review¹⁶⁰ included nine randomised clinical trials, eight of which included only patients with major depression (614 patients). All the clinical trials of the first review¹⁵⁸ were included in the latter, and only one from the Cochrane review¹⁵⁸ was not included.

The inclusion criteria considered in the reviews were randomised clinical trials that compared acupuncture (specific for depression or not) to simulated acupuncture, pharmacological treatment or no treatment, and all the trials included in the three reviews were considered to be poor quality.

In general, the reviews coincide in that there is insufficient scientific evidence to determine if specific acupuncture for depression is more effective than non-specific acupuncture or no treatment, or if acupuncture plus medication is more effective than acupuncture plus placebo. Moreover, the aforementioned methodological aspects mean that the outcomes must be interpreted with caution.

A final, double-blind, randomised clinical trial not included in the previous reviews and performed on 151 patients diagnosed with major depression compared traditional Chinese acupuncture to manual stimulation and to a control group¹⁶¹. It concluded that, even though acupuncture seems to improve the treated patients with respect to the wait-list patients, there are no data as to different efficacy between the two types of acupuncture, and it concluded that acupuncture with manual stimulation is not effective as monotherapy in major depression.

Summary of the evidence

	The available trials lack suitable methodological rigour, wherefore it is not possible to determine if acupuncture, whether specific for depression or not, alone or in combination with other treatments, has a beneficial effect in patients with symptoms of major depression.
--	---

Recommendations

✓	The existing scientific evidence does not allow recommending the use of acupuncture as a treatment for major depression.
---	--

7.6 St John's Wort

The extract of *hypericum perforatum*, commonly called St John's Wort, is a product that has been used for centuries, and it has at least seven components that can contribute to its pharmacological effects¹⁶². Their action mechanism is not entirely clear¹⁶³. Easy access, its low cost and the general belief that it has no side effects¹⁶⁴ have caused a considerable increase in the use of herbal products for treating depression.

The NICE²¹ CPG on managing depression selected forty trials pertaining to the use of St John's Wort in treating depression, out of which only 19 finally met the criteria for inclusion. The comparison groups were the placebo (10 articles), tricyclic antidepressants (four articles), serotonin reuptake inhibitors (six articles) and antidepressants related to tricyclics (one article). The conclusions were that St John's Wort seems to be more effective than the placebo at obtaining a response, both in moderate depression and in severe depression, and there are no differences when compared to other antidepressants. Despite the fact that St John's Wort could be beneficial in cases of mild and moderate depression, the authors of the guideline recommend that health professionals do not prescribe it due to the uncertainty of the appropriate dose, the variation in the nature of the existing preparations and the potential interactions with other drugs, such as oral contraceptives, anticoagulants and anticonvulsants. Moreover, patients who may be receiving St John's Wort should be suitably informed about the aforementioned.

A subsequent Cochrane review identified 37 trials that compared St John's Wort with placebo or with other antidepressants¹⁶⁵. This review includes most of the trials of the NICE review²¹. In adults with mild to moderate depression, St John's Wort improved symptoms more than placebo and than standard antidepressants. When jointly analysing the six most recent trials, all of large size, with an improved design and including only patients with major depression, the observed benefits of *hypericum* over placebo were minimal. This leads to considering a possible over-estimation of the effect in the older studies and in those of a smaller sample size. The authors conclude that the comparison of St John's Wort to placebo only seems to have fewer benefits in patients with major depression, that there possibly is no benefit in patients with prolonged depression and that there is no evidence as to its effectiveness on major depression. A third systematic review¹⁶⁶ in which the outcomes of two meta-analyses were compared, one that included 15 studies published between 1979 and 2000 and the second in which three new studies are added to the previous ones, does not contribute relevant data to the review prepared by the Cochrane Collaboration¹⁶⁵.

Summary of the evidence

	St John's Wort or <i>hypericum perforatum</i> is an herbal product frequently used for treating depression due to its easy access and low cost. However, there is uncertainty about the appropriate dose, and complications can appear when using it due to the variation of the nature of the existing preparations and to the potential interactions with other drugs (160).
1+	Current scientific information about the efficacy of St John's Wort for treating depression is heterogeneous, and there may be an over-estimation of its effect. In patients with major depression, only minor benefits would be obtained, and possibly none in patients with a prolonged duration of their depression (21, 163).

Recommendations

B	The use of St John's Wort is not recommended as a treatment option for patients with major depression.
✓	Health professionals should inform patients who consume it about the possible risks and benefits.