

# Treatment for depression: Emerging topics and Future Perspectives

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**Abstract:** Depression is a serious and common disorder that influences the feeling, interactions and thoughts of patients negatively. The prevalence and incidence of depression are really high, so it is necessary to find an effective treatment for depression. There are four major ways to treat depression: psychotherapy, TMS therapy, antidepressants, and meditation. To evaluate the effectiveness of each treatment, many data and studies can fulfill this purpose. The result indicated that each treatment has different results for people in different groups of age for different purposes. This review offers a summary of the effectiveness of treatment for depression which is a more straightforward and direct way to show the function and efficiency of different treatments for depression.

## 1. Introduction

Depression is a disorder that is considerably costly, disabling, and prevalent. It is connected to serious impacts to your body, including highly diminished life quality, mortality, satisfaction with medical care, body functioning and comorbidity. The prevalence of depression increases largely during these years. In 2014, there was from 7.2% 10.8% prevalence of depression [1]. However, due to COVID-19 in recent years, the prevalence of depression ranges from 7.45% to 48.30% [2]. Depression can lead to many weakening body functions, such as heart disease and increased heart attack. It even can result in suicide. Thus, depression is a very serious problem. For many decades, researchers have made huge progress and development to treat depression in many settings, such as primary care. There are two main types of treatment which are physical therapy and psychotherapy [3]. There are three approaches to psychotherapy consisting of cognitive therapy, systemic therapy and person-centred therapy. Physical therapy includes meditation, exercise, antidepressants, and TMS therapy. However, the effectiveness of physical therapy and that psychotherapy is still known. These approaches come from many fields, including psychological, behavioral and educational aspects. They aim to improve physical inactivity, smoking habits and unhealthy eating patterns to prevent more serious outcomes for patients [4]. In this review, each treatment's major strengths and weaknesses are compared and contrasted by researching different groups of ages. There is widespread concern about whether psychotherapy or physical therapy is more effective to treat depression. This review can show the effectiveness of the treatment for people with different groups of ages is different.

## 2. Psychotherapy

Psychotherapy is an efficient tool used for physiological intervention for a large number of behavioral, somatic and psychological problems, disorders and symptoms, so it can be referred to as the major way to manage somatic and mental health care. [5]. The rate at which different age groups of people use psychotherapy is significantly different. Psychotherapy is mainly classified into three categories, cognitive therapies, systemic therapies and person-centered therapy. Cognitive therapy focuses on the assumption in which representative cognition of patients' experiences affect how they act, feel and respond, and in which humans can metacognize, so to change and observe their beliefs and thinkings by practice and reflection, which results in a different perception of one's self, symptoms and social environment [6]. Systemic therapy mainly concentrates on a system structured by shared representations of realities, constructing a consensus on the way to explain the external and internal

environment. The emotional experiences of the patients of some systems can determine this collective perception largely. Person-centered therapy refers to a person's subjective experience, so the therapeutic concentration of the person-centered approach and its original point is based on the principle of humanistic psychology [5]. The technique of psychotherapy is that an expert forms a professional relationship with someone who has a disorder to modify or remove the existing symptoms, aiming to positive personality development and growth and moderating the weakened patterns of behavior. Thus, patients can establish a close relationship with the therapist. The treatment is also thorough and can last until the patient gets recovered or feels better completely.

However, psychotherapy is very time consuming which lasts for many years, and some patients don't want to share their past problems with the therapist, which is not beneficial for the treatment [7]. Moreover, psychotherapy can indeed prevent patients from full-blown major depression, but it is less effective to treat chronic depression by psychotherapy, especially for patients with subthreshold depression. Thus, in the future, there is a large room to improve psychotherapy. The first way to reduce the depression burden is to scale up the treatment and to improve the treatment in routine care. Another approach is to apply the model of stepwise treatment in which the cheapest and simplest treatment should be used first, followed by more intensive and complex therapies [8].

## 2.1 Psychotherapy for young children and adolescents

One study investigated Medicare beneficiaries who experienced depression during the study time. There were 2025 episodes of depression experienced by 1542 beneficiaries, including 1178 patients with one episode, 270 patients with two episodes and 94 patients with more than two episodes. In general, psychotherapy was used in the treatment for 25% of the episodes. People in the younger elderly group are more likely to be treated with people in the older group by multiple logistic regression [9].

Another study focused on psychotherapy as a treatment of depression for young children and adolescents. Data were chosen from 35 studies to figure out that the mean WLS ES for depression was 0.34. The ULS calculated in 35 studies was 0.40. Both measures were significantly different from 0. The mean influence of psychotherapy in the study was 0.34, which was too much smaller than this data from other similar studies. It showed a new finding on successful depression psychotherapy for young people. The analysis revealed that depression treatment for young people didn't develop so much but left behind treatments for other conditions for young people. But ES, which was significantly different from 0, suggested that this result was reliable [10].

Table 1. Traits of the psychotherapy as the treatment for adolescent and young children depression: 25 randomized trials

Variables	Results
children (C), adolescent (A) and mixed (CA) samples %	C=20, A=60, CA=20
No. of therapy hours	13.3
No. of depression outcome measures	2.0 <sup>a</sup>
No. of non-depression outcome measures	3.0 <sup>a.b</sup>

To learn about the effectiveness of psychotherapy for children, a related study was done by Deakin and Nunes in an outpatient place aimed at children aged from six to 11 years old in Brazil. The result revealed that after one year of treatment, treated children experienced a great reduction in overall internalizing and behavior problems. They also showed that affect modulation and better interpersonal relationships [11]. The Erica Process Outcome Study (EPOS) was conducted on children five years old to ten years old. The success of treating children with depression by psychotherapy was 80% [12]. In Anna Freud Centre retrospective study, there was the rate of 75% in which at the end of the treatment, children with depression showed they didn't have any symptoms by the intensive treatment,

which occurred more than once a week. Hence, the improvement was clinically reliable and significant [13].

## 2.2 Psychotherapy for adults

One study included 573 patients whose mean ages were 46 years old. SCL-20 refers to symptom checklist-20, which is the primary outcome of depression assessed. At baseline, the average SCL-20 depression score was 1.66, which meant that the severe depression was moderate and fit with SCL-20 scores in the primary care depression trials done previously. However, patients increased the mean SCL-20 score to 0.9 during 3 months since they made good responses. In general, psychotherapy is an effective treatment for depression among adults. The data in Table 2 shows that after 3 months of the treatment, there were a significant decrease in the mean of SCL-20, depression severity and major depression [14].

Table 2. Depression at baseline during 3 months

Measure	Baseline (N=573)	3 Months (N=501)
SCL-20, mean (SD)	1.66	0.91
Depression severity (SCL-20>1.3), N (%)	378	120
Major depression	418	162

## 2.3 Psychotherapy for older adults

According to Hummel et al., the effectiveness of psychotherapy for older adults with depression hospitalized for various acute conditions, consisting of neurological conditions, fractures, cardiovascular problems and falls. After four months, there was a significant improvement in physical functioning and depression severity for patients who received 15 sessions of psychotherapy. In contrast, people who didn't receive treatment of psychotherapy didn't change and even showed deterioration. As a result, older adults with depression should receive a psychotherapeutic intervention [15].

Moreover, a large number of psychotherapies are developed and examined for older adults with depression and cognitive disorders [16]. For example, a group used psychotherapy to treat depressed older adults with an executive impairment, which characterises starting, planning, and sequencing behaviors. Psychotherapy aims to improve executive skills, such as task initiation and planning. The result was better functioning and decreasing depression severity among depressed older adults who have executive dysfunction. Thus, it is notable that psychotherapy is an effective treatment for the group of older adults who are reluctant to experience pharmacotherapy. Researchers also showed that a new systematic review of cognitive-behavioural psychotherapies showed that psychotherapies had improved disability and depression for older adults [17].

## 3. Other important treatments for depression

There are three more important ways to treat depression. The first one is meditation, the modality as the science of life used in the natural and comprehensive health care system. The technique to treating depression by meditation promotes quality of duality and improves sensory perceptions [16]. The benefit is that it is more difficult for patients to give up the practice, but it is unknown for the true effect of meditation because of a lack of data. In the future, there should be more researches done to evaluate meditation [17]. The second approach is the antidepressant, a medication to treat depression and other mental disorders, including SSRIs, SNRIs, NASSAs, TCAs, and MAOIs. It is safe for almost everyone to use antidepressants, consisting of children and older adults sensitive to many medications. However, the dose of antidepressants is very restricted. Otherwise, there will be serotonergic effects. In the future, it is better to invent a kind of antidepressant that is effective and not dose-restricted [17].

The last one is TMS therapy which can stimulate the brain non invasively to form an electric current by the changing magnetic field to show the specific area of the brain. Patients are more likely to give response and remission through TMS therapy to reduce the severity of depression symptoms [18]. The side effect of TMS therapy may include headache, transient hearing changes and other local pains, but it is not fully investigated, which leaves a wide range of research in this field in the future [19].

### 3.1 Antidepressants for people with different groups of ages

One study done by the Committee on Safety of Medicines tested SSRIs, a kind of antidepressant, versus fluoxetine which is also a medication to treat depression in 2003. As a result, the rate of prescription for SSRIs dropped from 3.2 per 1,000 person-years at risk to 1.7 per 1,000 person-years at risk, which showed that the rate almost decreased by 50%. On the contrary, the rate of prescription for fluoxetine didn't change too much and almost remained stable. As a result, antidepressants were effective at treating depression for children [20].

Although antidepressants are a good approach to treat depression for children, they can't work for adults well. A placebo-controlled trial with SSRIs was conducted, and it showed the effect of antidepressants was too small to be considered clinically significant. The figure below showed that there was a minimum 12 point improvement in Hamilton score. The difference in the average change between placebo and drug groups was only one point. Another study showed that by using regression with mean, people who got more serious depression could at baseline be improved by antidepressants greatly [21]. Therefore, the antidepressant is not a good choice for adults to treat depression.

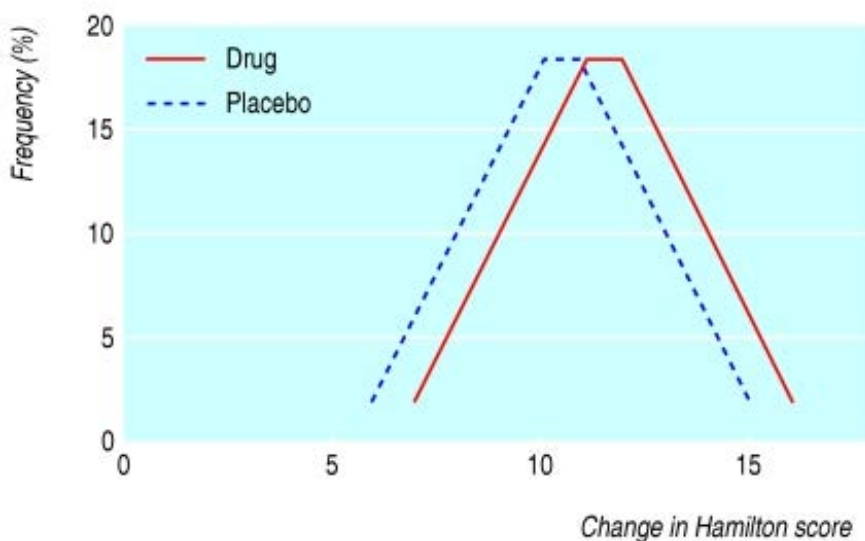


Figure 1. Normal distribution of scores for Hamilton rating scale for depression with the average score of 10.5 for placebo and 11.5 for an antidepressant

As the Hamilton score increases to a certain point, the frequency increases for both placebo and drug groups. After that point, as the Hamilton score increases, the frequency decreases for the two groups. There was a one-point difference in the change in Hamilton score between the drug group and the placebo group.

Among the population of older adults, there is a significant risk of suicide linked with depression which is about twice as frequent as that in populations of other ages. Antidepressant is an efficient approach to decrease the suicide rate significantly by changing the behavior and mind in older people who are more than 65 year old. Thus, depression is the most modifiable and noticeable risk factor for suicide, and effective treatment of antidepressants can be the most effective way to decrease suicide rates [22].

### 3.2 Meditation for people with different groups of age

Meditation can benefit older people with depression to a large extent because it can modify the feeling of social exclusion, stress, loneliness, anxiety and insomnia, which are the causes of depression.

In addition, there is a positive result of medication training on cognition, particularly for memory and attention, which is very sensitive to aging [23]. For young children and adults in the middle ages who experience depression, meditation can improve brain function and structure, especially in the limbic, insula and frontal structures. At a younger age, these structures are predominant for controlling the body. A study was conducted to show the relationship between brain function of the population from 24 to 77 years old and meditation. People who did meditation frequently had a less marked grey matter volume reduction as ages compared with people who didn't do meditation frequently. These results were potentially significant in the context of brain maintenance and reserve to prevent depression. Long-term meditation is an effective approach to maintaining brain function and structure, which can prevent progressive age-related decline. As a result, the brain's normal function can result in a reduced risk of depression and cognitive reserve [24].

### 3.3 TMS therapy for people with different groups of age

TMS therapy is an effective approach to manage depression clinically. There is a large proportion of people whose ages are larger than 65 received TMS therapy. About 70% study reported that TMS therapy was generally efficacious and safe used to treat depression. A study utilising two trials revealed a substantial benefit of TMS therapy in treating the elderly. One group conducted the trial with the stimulation intensity constant at or less than the motor threshold. On the contrary, the other group used a higher stimulation intensity. The result reported that the higher dose delivered to older people was more effective than that delivered to the younger people as the treatment for depression [25].

Table 3. Randomized Controlled Trials researching the antidepressant effect of TMS therapy in older adults (the mean age of the sample >60)

Trial	Age range	TMS parameters	Sample size	Results
Jorge et al. 2008 (Trial 1)	62.9+/-7.2	0 Hz; 110% MT; MRI-based target. Localization of left DLPFC; 1200 pulses/session; 10 sessions; no. of pulses=12000	30	Active treatment: Older adults showed better reactions with higher doses.
Jorge et al. 2008 (Trial 2)	64.3+/-9.4	10 Hz; 110% MT; MRI-based target. Localization of left DLPFC; 1200 pulses/session; 15 sessions; no. of pulses=18000	62	Active treatment: Older adults showed better reactions with higher doses.

For middle-aged adults, SF-36 and EQ-5D were measured to evaluate the improvement in depression. It was found that TMS therapy occurred with the ameliorated depressive symptoms at the same time, especially for patients who transferred from moderately severe to severe depression. The social functioning, mental health perceptions sub-scales, vitality and role-emotional perceptions sub-scales indicated a statistically significant improvement of 1.2-1.5 SDs. A more robust improvement was shown by remitters who reached the score close to the general population's norms and only a few SDs lower. On the contrary, non-remitters reported only a small improvement in statistics. However, this TMS therapy is not beneficial for patients who are severely depressed with a poor outcome. As a result, the role-physical, general health perceptions subscales, physical functioning and bodily pain indicated statistically significant for depressed middle-aged adults with mild symptoms [26].

A wide range of studies has indicated that TMS therapy is beneficial to treat adolescent depression. About 78% of studies showed that by using the Children’s Depression Rating Scale-Revised, the improvement of treating depression was captured. There were four multi-subject trials with pre- and post-CDRS-R scores, so the quantity of the change in depression was appreciated. These four trials revealed that young patients with moderate-to-severe depression fell into the range of moderate depression after the post-treatment. The promising outcomes were also indicated by the data from the Beck Depression Inventory, which is an adolescent self-report measure. In one study, the patients who experienced pre-treatment had the score from moderate to severe and then decreased to moderate and normal mood disturbance. In another study, the depression of four participants was improved significantly in statistics [27]. The intervention of TMS therapy also showed good clinical safety and effectiveness in adolescent depressed patients and a favorable side effect profile compared to other treatments of depression for young people. The most common side effect was a headache. Others were scalp pain, hearing loss, and seizures. No more than one per cent of healthy subjects showed TMS-precipitated convulsions. Cognition was not affected [28].

Table 4. Studies on efficacy and safety of TMS therapy in young children with depression

Study	N	Age range (average)	Number of TMS sessions	Session duration (min)	Frequency of stimulation (Hz)	results
Cristancho et al. (2014)	1	15	10	10	1	80
Wall et al. (2016)	10	15.9	30	(4,26)	10	80-120
Yang et al. (2014)	6	18.7	15	37.5	10	120
Mayer et al. (2012)	8	20.4	14	20	10	80
Bloch et al. (2008)	9	17.3	14	20	10	80

#### 4. Conclusion

All in all, depression is a common disorder that can occur in all age groups of people. It is harmful to people’s minds, body function and life quality. To treat depression, psychotherapy, meditation, TMS therapy, and antidepressants are the main approaches to relieve depressive symptoms. In general, almost all treatments are beneficial for patients with depression, but different treatments are more effective for people of different groups of ages. Studies have shown that psychotherapy and meditation are almost equally beneficial for people of all ranges of ages. Antidepressants are also effective in treating depression for middle-aged adults, older adults and young children, but the specific effects and purpose are different. TMS therapy can treat depression for people in all groups of ages as well, but the intensity and effect are different for middle-aged adults, older adults and young children. As a result, it is important to choose the treatment which is most suitable for different patients.

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