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## Expert opinion on the management of major depressive disorder in Indian settings

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### Abstract

**Background:** Major depressive disorder (MDD) is a widespread mental health condition in India, affecting people across various age groups and backgrounds. Various studies suggest that millions of Indians are living with this condition, and it significantly contributes to the country's overall disease burden.

**Methodology:** A cross sectional, questionnaire-based study was conducted to collect opinion among doctors in neurology and psychiatry practiced in India between June 2022 and December 2022. Convenient sampling method was used.

**Results:** Out of 138 booklets sent, 127 filled booklets received were assessed. The target respondents see on an average of 25-30% of their patients suffer from MDD in their clinical setup. In total, 40 percent of doctors see patients with MDD, while 25-50% of their patients suffer from bipolar disorders, which affects 10-25% of patients, PDD affects 0-10% of patients, and post-traumatic disorder is most common among 25-50% of patients, reported most by 34 percent of doctors. Vortioxetine (22%) is the third most preferred molecules as first line treatment for managing depression. On an average, 10-25% of men suffered from depressive disorders. The study reveals that 10-25% of side effects usually observed with the use of anti-depressants by 57% of doctors. The study reports 54% of doctors consider vortioxetine suitable for patients with MDD.

**Conclusion:** This study provided significant understanding into MDD and the perspectives of doctors on management. Further, more than half of the clinicians preferred vortioxetine for the management of patients with MDD.

**Keywords:** Depression, MDD, vortioxetine, treatment, pharmacotherapy, neuropsychiatry

### Introduction

According to the World Health Organization (WHO) estimates, major depressive disorder (MDD) will rank first by 2030, placing it as the third leading cause of disease burden worldwide in 2008. It is identified when a person exhibits symptoms such as a chronically low or depressed mood, anhedonia, or a diminished interest in enjoyable activities, feelings of worthlessness or guilt, lethargy, difficulty concentrating, changes in appetite, agitation or psychomotor retardation, insomnia, or suicidal thoughts. A person can be diagnosed with major depressive disorder (MDD) if they meet five criteria listed in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5). Among these criteria is a low mood or anhedonia that interferes with social or professional functioning. It is necessary to rule out any history of manic or hypomanic episodes <sup>[1]</sup>. Major Depressive Disorder (MDD), often referred to simply as depression, is a debilitating mental health condition characterized by persistent sadness, loss of interest or pleasure in activities, and a range of physical and cognitive symptoms. In India, as in many parts of the world, MDD represents a significant public health concern. MDD is chronic, recurrent or episodic psychiatric illness. Lifetime prevalence of MDD is about 5 to 17 percent, with the average being 12 percent. Despite the considerable advances in the understanding of the pathophysiology of MDD, a large proportion of depressed patients, up to 1/3 of patients with major depressive disorder (MDD) do not achieve a complete response. New treatment methods are needed to manage MDD while not affecting the patient's quality of life by adverse effects.

Depression is a common mental illness that frequently results in a low quality of life and functional impairments. The goal of treatment during a major depressive episode's acute phase is to assist the patient in going into remission and ultimately returning to their baseline

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level of functioning. Pharmacotherapy, notably selective serotonin reuptake inhibitors antidepressants, remains the most frequent option for treating depression during the acute period, but other potential pharmacological approaches are still fighting for the attention of practitioners. The second most popular method for assisting patients in enduring the acute phase, keeping their remission, and avoiding relapses is depression-focused psychotherapy. In certain circumstances, electroconvulsive therapy is the most effective somatic therapy for depression; in the meantime, other approaches have drawbacks, and their precise indications are currently being researched [2].

Serotonergic signaling is recognized as an important therapeutic target for the treatment of mental illnesses, particularly depression, where it is shown to play a critical role. For the treatment of depression, serotonergic signaling inhibitors, particularly selective serotonin reuptake inhibitors (SSRI) or serotonin and norepinephrine reuptake inhibitors (SNRI), are widely chosen as first-line therapy. These inhibitors increase norepinephrine by blocking serotonin/norepinephrine reuptake, which in turn increases activity [3]. Augmentation of SSRIs best fit in MDD management. The strongest support was seen for atypical antipsychotics, specifically, aripiprazole and quetiapine extended-release, when it comes to augmenting SSRI treatment in MDD. Nonetheless, it is wise to think about different medications for first-line augmentation therapy due to the severe side effects of atypical antipsychotics; medications should be selected based on best practices and scientific data. Supplements offer less side effects and an increasing body of research supports their use, despite not being usually thought of as enhancement choices [4].

Better pharmacotherapeutics approaches to treating depression have long been the focus of MDD research, and developing medications with several modes of action has attracted a lot of attention. These agents can be divided into three main groups. The clinical efficacy and/or tolerance of antidepressants can be enhanced by one of three strategies: monoaminergic mechanisms that selectively target monoaminergic neurocircuitry; non-monoaminergic targets; or monoaminergic mechanisms that also impact non-monoaminergic pathways. With their focus on the monoaminergic route, none of the drugs now on the market have consistently demonstrated greater efficacy when compared to the older antidepressants [5]. This study explores the prevalence, treatment approaches, pharmacotherapy, epidemiology, prescription behavior, and the latest developments in the management of MDD in India.

### Methodology

A cross sectional, multiple-response questionnaire based survey among doctors specialized in neurology and psychiatry in the major Indian cities from June 2022 to December 2022.

### Questionnaire

The questionnaire booklet titled VORSERO study was sent to the doctors who were interested to participate. The VORSERO study questionnaire included questions aimed at gathering prevalence, treatment approaches, pharmacotherapy, epidemiology, prescription behaviour, and the latest developments in the management of MDD in India. The study was performed after obtaining approval

from Bangalore Ethics, an Independent Ethics Committee which was recognized by the Indian Regulatory Authority, Drug Controller General of India.

### Participants

An invitation was sent to professionals across India based on their expertise and experience in treating MDD in the month of March 2022 for participation in this Indian survey. About 127 clinicians from major cities of all Indian states representing the geographical distribution shared their willingness to participate and provide necessary data. They were explicitly instructed to provide individual responses without consulting their colleagues. Before commencing the study, written informed consent was obtained from all survey participants.

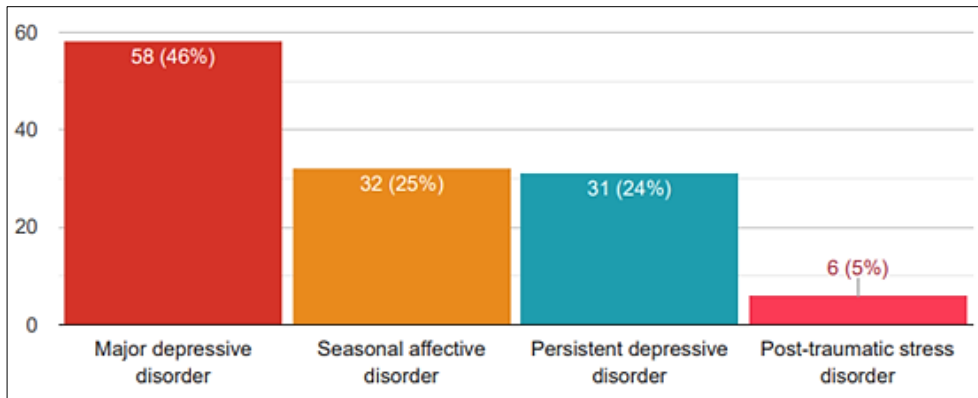
### Statistical Methods

The data were analyzed using descriptive statistics. Categorical variables were presented as percentages to provide a clear understanding of their distribution. The frequency of occurrence and the corresponding percentage were used to represent the distribution of each variable. To visualize the distribution of the categorical variables, pie, and bar charts were created using Microsoft Excel 2013 (version 16.0.13901.20400).

### Results

A total of 138 questionnaire booklets were distributed and response rate was 93% (N=127). Completed questionnaires were collected personally by study coordinators after 4 weeks. As per the responses obtained, 40% of doctors said that 25-50% of their patients are suffering from MDD while another 37% of doctors said as 10-25% of their patients are MDD. The study observed the prevalence of bipolar disorder as at 10-25% by 46% of the doctors. About 31% of doctors indicate it is as high as 25-50% in their practice and 4% expressed it is 50% to 60%. Also, it was observed that 36% of doctors mentioned the prevalence of persistent depressive disorder (PDD) was at 0-10% while another 34% of doctors mentioned the prevalence is at 10-25%. Further, 24% of doctors said that PDD cases were observed in the range of 25-50%. Even 6% of the respondents indicated that 50-60% of their patients were suffering from PDD. The prevalence of post traumatic disorder as indicated by 34% of doctors was 25-50%, while another 34% said it was 10-25% while 24% of doctors reported that their post traumatic disorder cases ranged from 25-50% and 6% said that 50-60% of their patients suffer from PDD.

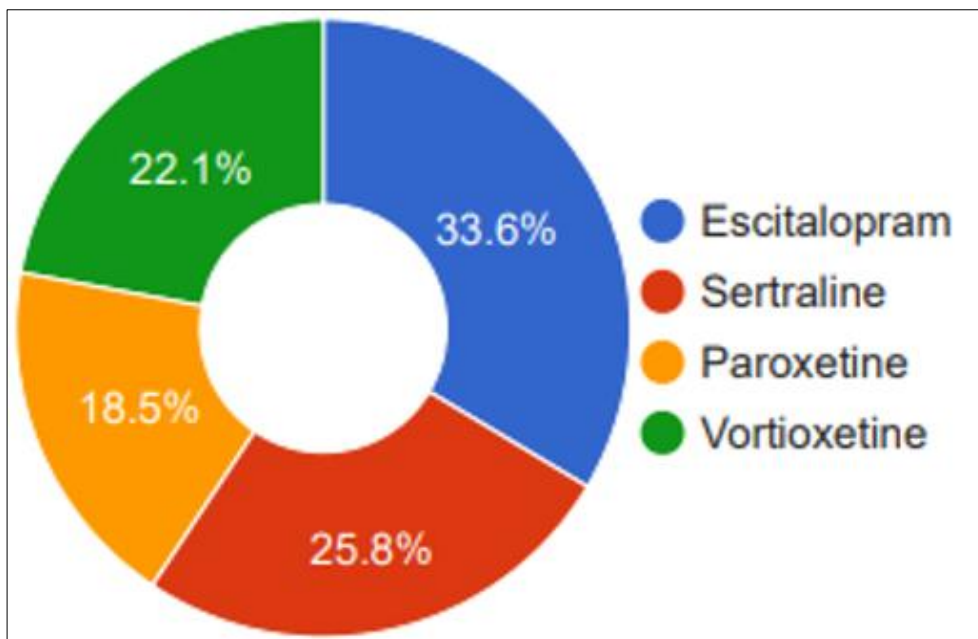
The responses on factors take into consideration by practitioners while choosing right antidepressants were ranked according to priority as being highest priority and 5 as least priority. The respondents unanimously reported tolerability as key considerations compared to other factors. Atypical antidepressants were reported to be commonly prescribed with SNRI for MDD, with a significant 61% of respondents identifying this condition. Followed by seasonal affective disorder by 13% of respondents, persistent depressive disorder to the extent of 17%, post-traumatic stress disorder to 8% of the respondents. Atypical antidepressants were used for the major conditions like major depressive disorder by 46% of respondents, followed by seasonal affective disorder 25%, persistent depressive disorder 24% and post-traumatic stress disorder 5% (Figure 1).



**Fig 1:** Distribution of preference of atypical anti-depressants in various depressive disorders among clinicians

The doctors were enquired for the most preferred molecule as a first line treatment for managing depression and the responses were ranked accordingly with score 1 for the most preferred to 5 as the least preferred. Escitalopram (34%),

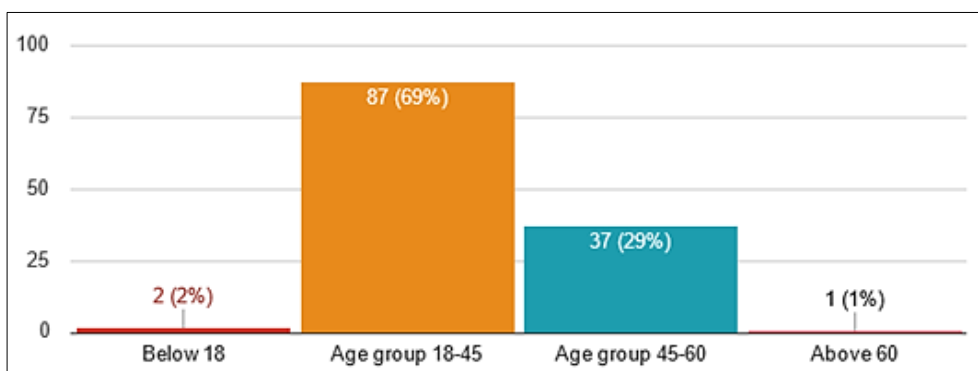
sertraline (26%), paroxetine (9%) and vortioxetine (22%) were the most preferred molecules of the respondents as prescribed for first line treatment for managing depression (Figure 2).



**Fig 2:** Distribution of preference of first line agent for managing depression among clinicians

On an average, 10-25% of men suffered from depressive disorders as reported by 60% of doctors while another 28% of doctors reported as 25-50% of men suffer from depressive disorders. Similarly, the doctors conveyed that 25-50% of women suffered from depressive disorders as reported by 48% of doctors while another 32% of doctors

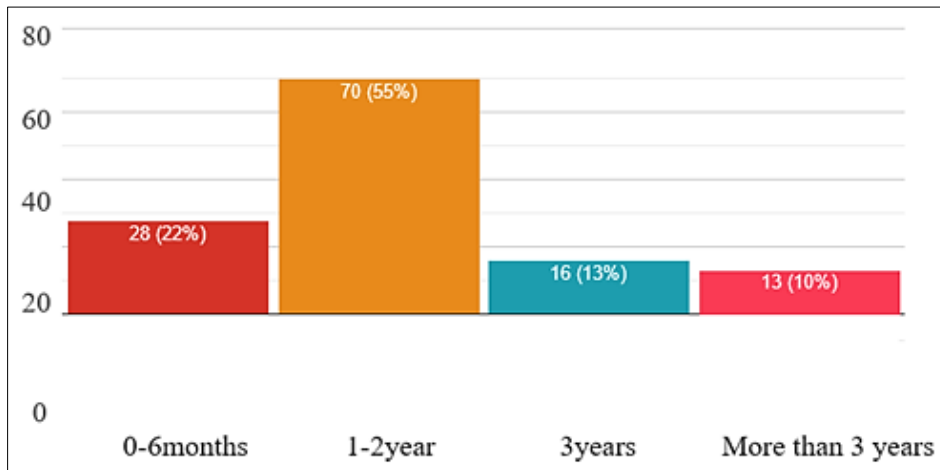
reported as 10-25% of men suffer from depressive disorders. The study reported that the age group of 18-45 suffered from depressive disorders as answered 69% of doctors, followed by the age group of 45-60 with 29% as the second most important category (Figure 3).



**Fig 3:** Distribution of prevalence of depressive disorders in different age groups

It was observed that 49% of doctors found the patient adherence to medication and counselling was good while another 32% of doctors reported as excellent. The study also revealed that 91% of doctors agreed that counselling played an important role in the management of MDD while the rest did not agree with. Seemingly, 38% of doctors suggested monthly counselling for MDD patients while another 31% suggested counseling fortnightly. The responses were suggestive of sexual dysfunction as the most common drawback by 28.6% of doctors, followed by nausea by 23.8% of

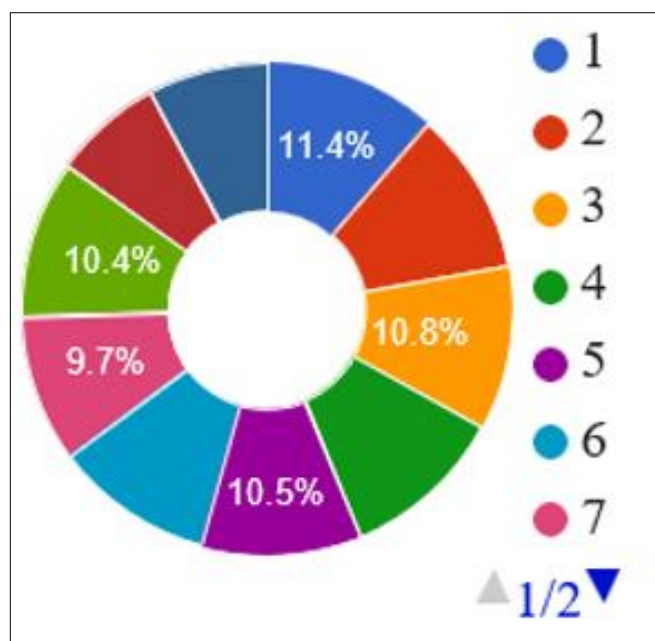
doctors and another 23.8% mentioned fatigue as the next major drawback usually seen with SSRI/SNRI/Paroxetine/Sertraline. Weight gain was represented by 19% of the doctors as well. It was observed that the treatment tenure/duration for patients associated with depressive disorders were 1 to 2 years as said by 55% of doctors. Followed by 0-6 months by 22% of respondents. Only 22% of doctors conveyed 3 years and above as duration for treating patients associated with depressive disorders (Figure 4).



**Fig 4:** Distribution of physician’s perspectives on the duration for treating patients associated with depressive disorders

It was evident that 57% of doctors unveiled that 10-25% of their patients experienced adverse effects while 32% of doctors said that the side effects were seen among 2-50% of their patients. The study also reports 10-25% of patients taking SSRI/SNRIs class of drugs suffered from cognitive decline as informed by 38% of the doctors followed by 33% of doctors saying 0-10% of patients taking SSRI/SNRIs class of drugs suffered from cognitive decline. Nearly, 25% expressed 25-50% of patients with cognitive decline and only 4% said 50-75% had the effect. The study reports 90% of doctors prescribed vortioxetine in newly diagnosed patients with depression disorders and only 10% left without

prescribing the drug. The responses revealed that 54.4% of doctors found vortioxetine suitable for patients with MDD, 31% of doctors considered the drug as suitable for patients consuming other antidepressants but with partial responses to therapy. Significant size of doctors does consider vortioxetine for patients having relapse post therapy and for patients who have withdrawn previous therapy and anxiety/panic disorder as well. The preference of doctors to recommend vortioxetine for treating depression disorders were scored on a scale of 1 to 10. It was observed that more than 40% respondents have rated 6+ rating on 10-point scale.



**Fig 5:** Distribution of physician’s preference on vortioxetine on 10-point scale

## Discussion

The survey's response rate was robust, with 127 completed questionnaires collected out of 138 distributed, resulting in a 93% response rate. This high response rate enhances the reliability of the findings. The study examined the prevalence of various psychological conditions among patients. Major depressive disorder, bipolar affective disorder, persistent depressive disorder and post-traumatic stress disorder were the frequently prevalent conditions as per the responses. However, the prevalence rate of the disorders varied. According to the systematic review conducted by Math SB *et al.*, the prevalence rates of psychiatric diseases in India range from 9.5 to 370/1000 people. These differing rates of mental disorder prevalence are not exclusive to Indian studies; they are also observed in other foreign investigations. The available data from the Indian studies indicates that roughly 20% of the adult population in the community was afflicted with one or more psychiatric disorders, despite variances in study design<sup>[6]</sup>.

MDD emerged as a significant mental health concern, with 77% of doctors reporting that a substantial portion of their patients suffered from this condition. This highlights the burden of MDD in clinical practice, underlining the importance of effective treatment strategies. Arvind *et al.* discussed the prevalence and socioeconomic impact of depressive disorders in India and reported that almost 23 million persons would require care for MDD at any one moment. Since the group that is most productive is impacted, MDD has a significant socioeconomic impact on both the individual and the family. The results are similar to the responses of the current study. This is a clear call to action for all relevant parties to increase the scope of services provided by the National Mental Health Program in India and to integrate MDD care with other active national health initiatives<sup>[7]</sup>.

Bipolar disorder was reported to be prevalent, with 81% of doctors indicating its presence in their clinical practice. This suggests that bipolar disorder is a substantial area of focus for mental healthcare professionals. Studies on epidemiology and course and outcome of BD from India are scarce. In epidemiological studies, lifetime prevalence rates are 0.1% for bipolar spectrum disorders and 0.5% for BD<sup>[8]</sup>. Approximately 70% of doctors reported the presence of persistent depressive disorder in their patients. This finding underscores the relevance of addressing this form of depression in clinical practice. Post-Traumatic Stress Disorder (PTSD) was identified as a concern by 74% of doctors, further emphasizing the significance of recognizing and treating this condition. Studies from India have shown its presence as a psychiatric morbidity after various natural as well as man-made disasters, though to a variable extent<sup>[9]</sup>.

The survey revealed that tolerability was the primary consideration when choosing the right antidepressant, ranking higher than other factors. This underscores the importance of patient comfort and adherence when selecting treatment options. Rahman *et al.* on factors influencing antidepressant activity unveiled that health professionals would consider efficacy (64%) and tolerability (24%) to be the most important factors in choice of antipsychotics for themselves while efficacy (56%) and cost (24%) would be considered important factor while prescribing drugs to the patient<sup>[10]</sup>. Atypical antidepressants, particularly SNRIs, were commonly prescribed for various conditions. This

indicates the versatility of these medications in addressing different forms of depression, with MDD being the primary indication. The treatment of depressive illness does not stop with treatment of acute episodes, and has to be envisaged as a continuous therapeutic intervention, of which we are still not able to determine the optimal duration of treatment and the moment that it should be ceased<sup>[11]</sup>.

The responses on preferred molecules for depression management varied among respondents. Escitalopram emerged as the most preferred molecule for first-line treatment, followed by sertraline, paroxetine, and vortioxetine. These preferences reflect the prescribing patterns among healthcare professionals. The results were consistent with other Indian studies as in Tripathi *et al.* with SSRIs as the most common group and escitalopram was the most common medication used<sup>[12]</sup>. Varying perceptions of the prevalence of depressive disorders among men and women were observed. A significant percentage of doctors reported that both genders experienced depressive disorders at different rates. However, the female: male ratio of global disability from major depression remained unchanged at 1.7:1<sup>[13]</sup>. The age group most associated with depressive disorders was identified as 18-46 years, as reported by 69% of doctors. This finding highlights the importance of considering age-related factors in treatment planning. Kesslet *et al.* discuss that prevalence of mental disorders decreasing with age, comorbidity of hierarchy-free MDD with these disorders was either highest among the elderly or unrelated to age<sup>[14]</sup>.

Most clinicians reported good to excellent patient adherence to medication and counseling, indicating the effectiveness of treatment strategies in promoting patient engagement. Medication adherence is crucial in MDD management. As observed by Tamburrino *et al.* non-adherent patients reported being more careless about taking their medications, were more worried about side effects, were less satisfied with their physicians, were under the age of 40 years, and were more likely to have asked for a specific antidepressant. Non-adherent patients also indicated being at lower stages of change<sup>[15]</sup>. An overwhelming majority (91%) of doctors acknowledged the importance of counseling in the management of MDD, affirming its integral role in holistic care. Patient counseling undoubtedly helps in improving medication adherence. Most doctors reported that 10-25% of their patients experienced side effects with antidepressant use, emphasizing the need for careful monitoring and management.

Common drawbacks associated with SSRIs/SNRIs, including sexual dysfunction, nausea, fatigue, and weight gain, were identified by healthcare professionals. Gastrointestinal (GI) disturbances are the most frequently reported side effects. During long-term SSRI therapy, the most troubling adverse effects are sexual dysfunction, weight gain, and sleep disturbance<sup>[16]</sup>. Cognitive decline was reported in a subset of patients taking SSRI/SNRI medications, with 10-25% of patients affected, highlighting the importance of assessing cognitive function during treatment. The use of SSRIs in patients with depression or OCD, can cause cognitive dysfunction in the acute phase of treatment in M. Sayyad *et al.*, which in turn favors our statement<sup>[17]</sup>.

The study found varying opinions on the treatment duration for patients with depressive disorders, with 55% of doctors suggesting long-term treatment. The results are in

inclination to the duration of illness where most of the respondents agreed 1 to 2 years as duration of illness. The study found that 90% of doctors had used vortioxetine in newly diagnosed patients with depression disorders, indicating its acceptance in clinical practice. Vortioxetine was considered suitable for various patient profiles, including those with MDD and patients with partial responses to previous therapy. More than 40% of respondents expressed a high likelihood of recommending vortioxetine for treating depression disorder, suggesting a favourable view of its efficacy. The randomized controlled trial of vortioxetine implies the beneficial effect of vortioxetine on cognition is largely a direct treatment effect. No safety concern emerged with vortioxetine. Vortioxetine significantly improved objective and subjective measures of cognitive function in adults with recurrent MDD and these effects were largely independent of its effect on improving depressive symptoms.

### Conclusion

The survey findings highlighted the information about the frequency of different psychological disorders, the barriers preventing people from using antidepressants, and the prescription practices of medical experts. In clinical practice, major depressive disorder, bipolar disorder, persistent depression, and post-traumatic stress disorder are important issues. When choosing an antidepressant, tolerability is a key consideration. Atypical antidepressants, particularly SNRIs, are essential for treating certain problems. Further, more than half of the clinicians preferred vortioxetine for the management of patients with MDD.

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