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Challenges in Managing Depression in Clinical Practice: Result of a Global Survey

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Abstract: Background/Objectives: Despite improved knowledgebase, effective intervention, and guidelines, many patients with depression do not get adequate treatment; and treatment discontinuation and nonresponse are common. It was intended to explore the challenges clinicians face while managing depression in their clinical practice and their suggestions for solutions. **Methods**: It was an online survey of 137 psychiatrists in 18 countries including both high and low economies, using a pre-designed questionnaire; with both quantitative and qualitative measures. **Results**: Antidepressant prescribing appeared close to the evidence-based guidelines. There was frequent use of other medications alongside antidepressants since treatment initiation. There were many challenges in managing depression such as treatment non-response, resistance and discontinuation, side effects mostly sexual problems, inadequate psychological intervention, availability and affordability of treatment modalities, comorbidities especially substance use and personality disorders, stigma, and lack of education and training. Suggested approaches for solutions included personalized treatment, quicker follow-up, psychoeducation, blending psychological intervention into routine clinical practice, improving continuity of care, and preventing treatment discontinuation. Support from governments, improving access, making interventions affordable, and providing socio-occupational support are essential. Training and development of professionals; and public education providing information, and dealing with stigma are still relevant. **Conclusions**: The results indicated a need for reviewing current practices in managing depression, optimizing it with available resources, and preventing treatment discontinuation, and non-response. Making treatment available and affordable, public education fighting stigma to improve treatment acceptability, and research addressing gaps in interventions, especially for treatment resistance and psychotherapy are other approaches that may improve depression management.

Keywords: antidepressants; bipolar depression; depression; medication nonadherence; psychiatry; side effects; treatment resistant depressions

1. Introduction

Depressive disorders are a major public health concern worldwide. These are highly prevalent in the general population, and in both primary and secondary care settings. Globally an estimated 3.8% of the population suffers from depression, which includes 5% of adults and 5.7% of older adults above 60 years [1]. Among the mental illnesses, depression accounts for the largest proportion of disability-adjusted life-years (DALYs) [2]. A study in 18 countries suggested average lifetime (14.6%) and 12-month (5.5%) prevalence of major depressive episodes in 10 high-income countries (HIC), compared to 11.1% and 5.9% respectively in eight low-income countries [3].

It appears as if the depression prevalence is increasing over the years and during stressful situations, e.g. in the UK, it was 5% in the general population in 1994 [4], 7.5% in 2014 [5], which increased to 32% during COVID-19 pandemic; which was a 27.9% increase from pre-pandemic 4.1% [6]. Globally there was an increase of 27.6% in cases of major depressive disorder during the COVID pandemic [7].

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Depression is common in primary care with reported prevalence rates around 4 to 16%;[8–10] and most of the depressed patients are treated there. Reported proportions of patients with depression in psychiatric outpatients vary, and have been reported from 19.3% [11] to 54.4% [12]. Rates up to 55.2% in general hospital outpatient departments have been reported [13]. In the general hospital inpatient settings involving medicine and surgery departments the prevalence of major depression has been reported between 5% to 34% [14,15], suggesting that this is a widespread condition. When depression and depressive symptoms are taken together the prevalence figures in different specialties varied from 17% to 53%.[16] Besides clinical settings, depression is common in educational [17–20], and occupational environments [21], and a major reason for impairment in functioning. This is associated with poorer scholastic achievement; and a leading cause of sickness absences.

Depression is commonly associated with physical illnesses as a comorbid condition. Many physical illnesses are etiologically linked with depression. Commonly associated physical illnesses with depression are diabetes, thyroid disorders, adrenal disorders, hypercalcemia, hyponatremia, cerebrovascular accident, multiple sclerosis, subdural hematoma, epilepsy, Parkinson's disease, Alzheimer's disease, malignancies, infectious diseases such as HIV and syphilis nutritional deficiencies such as vitamin D, B12, B6 deficiency, iron or folate deficiency etc. Depression is also associated with medication or substances of abuse such as steroids, antihypertensives, anticonvulsants, antibiotics, sedatives, hypnotics, alcohol, stimulant withdrawal, etc. [22].

Patients with depression get hospitalized mostly for physical illnesses such as endocrine, musculoskeletal, and vascular diseases, rather than psychiatric disorders [23]. Depression increases the risk of treatment noncompliance for physical illnesses by three times [24,25]. Association of depression with physical illnesses increases the burden, functional impairment, health service utilization, non-psychiatric hospital admission, cost of care; worsens prognosis, and increases mortality [26,27]. This highlights that identification and treatment of depression should be a priority in both primary and secondary care [28,29]. As evident, depressive disorders and these conditions are prevalent in primary, secondary, and tertiary medical care settings and contribute to suffering as a comorbid condition and worsen the prognosis of associated illnesses [28,29]. Despite these concerns, there is a chance that in the primary and secondary care settings depression is missed as a diagnosis or is not adequately treated [33,34].

Besides single and recurrent major depressive episodes, there are various other kinds of depression such as persistent depressive disorder (dysthymia), mixed depressive and anxiety disorder, disruptive mood dysregulation disorder in children and adolescents, premenstrual dysphoric disorder, substance/medication-induced depressive disorder, depressive disorder due to another medical condition and unspecified depressive disorder [30,31]. Besides physical comorbidities, psychiatric comorbidities are common in depressive disorders, such as alcohol and other substance use disorders, anxiety disorder, panic disorder, social anxiety disorder, obsessive-compulsive disorder, personality disorders, etc. [32].

It is known that untreated depression may continue for around 6-12 months, a good proportion of these become recurrent and chronic. Suicidal attempts and death are commonly linked to depression [35], and there is usually an eight-fold increase in suicide [32], while 2/3rd contemplate suicide, 10-15% die by suicide. Comorbidities increase the risk of suicide [32]. Besides suicidal death, all-cause mortality is higher in depressed patients as well [32].

Management approaches for depression involve psychotherapies, antidepressants, adjuncts or augmenting drugs, electroconvulsive therapy, other neuromodulation, and lifestyle modifications. Antidepressants have a robust evidence base for their effectiveness. In primary care, the numbers needed to treat (NNT) for tricyclic antidepressants range from 7 to 16 (median 9) and for selective serotonin reuptake inhibitors (SSRI) from 7 to 8 (median 7) [36]. Among the SSRI, sertraline has been reported to be significantly better in efficacy and acceptability [37]. Combined treatment with psychotherapy improves the efficacy with clinically meaningful outcomes [38].

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Despite massive prevalence, pervasive presence in various settings, being present as a common comorbid condition of many physical illnesses, and relatively ease in identifying symptoms and making a diagnosis, it is common to see that depression is missed in various clinical settings such as primary care even in HIC [39–41], emergency departments and secondary care [42].

In addition, although there are many available treatment options, a considerable proportion of patients with depression are not treated; for example, more than 75% of people in low- and middle-income countries receive no treatment [1,43]. Among those who are treated a proportion of them do not receive adequate treatment and there is less than adequate response to treatment. Despite the evidence base of efficacious interventions, only 18% of patients experience a 50% or greater decrease in symptoms after 6 months [32]. Inadequate or nonresponse is common in depression and that adds a huge clinical, psychosocial, and occupational burden. In this context, it was intended to explore the challenges clinicians face while managing depression in their clinical practice and their suggestions for solutions.

2. Results

There were 137 responses from the 18 countries, 70 (51.1%) from HIC and 67 (48.9%) from low and middle income countries (LAMIC). Most of them (99, 72.3%) were in public (government, university, etc.), 34 (24.8%) in private hospital set up; and 4 (2.9%) in others. More LAMIC respondents were in private organizations (35.8% v 14.3%) and fewer in public sector 62.&% v 81.4%) compared to HIC (8.97, $p < 0.05$). Most of the respondents (98, 71.5%) were from teaching organizations. There were 57.7% consultant psychiatrists including professors, 21.9% psychiatrists (senior residents, associate specialists, etc.), 14.6% psychiatry trainees, and 5.8% doctors who were not in psychiatry but managed psychiatric patients; with 35.8% having 0-9 years of clinical psychiatry experience, 24.1 % with 10-19 years and 40.1% had 20 or more years.

2.1. Common Challenges in Managing Depression

At the beginning of the survey, the most common challenges faced by psychiatrists in their clinical practice managing depression were enquired about. The responses were analyzed qualitatively and provided below as major themes and sub-themes (Table 1).

Table 1. Themes and subthemes of common challenges managing depression in clinical practice.

Themes and subthemes
• Managing treatment-resistant depression (TRD) (persistent partial or non-response to medication, difficulty deciding appropriate person-specific augmentation)
• Patient adherence to treatment (both for medications and psychotherapy, frustration at tardy response to treatment, hesitancy for medication, amotivation)
• Managing side effects (sexual, gastrointestinal, agitation, leading to non-adherence)
• Challenges with psychological services (limited availability, inadequate access especially early in treatment, long waiting, lack of resources)
• Stigma (associated with psychiatric illnesses and treatment, using medications, being labeled, perceived social consequences)
• Medication availability (hospital pharmacies especially in the government sector, guidelines, affordability)
• Comorbidities (substance use disorders, personality disorders)
• Psychosocial issues (family attitude, denial, social isolation)
• Clinical challenges (diagnosis, deciding person-specific treatment strategy, recurrent episodes, managing suicidality)
• Treatment challenges (inadequate response, resistance to change treatment after nonresponse, delay in holistic intervention, augmentation strategies, polypharmacy, lack of newer modalities of treatment such as neuromodulation)
• Continuity of care issues (lack of appropriate follow-up, patient motivation, and engagement)

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- Education and awareness (lack of public awareness, delayed help-seeking, reluctance to use medication, erroneous belief of getting addicted to medications)

2.2. Identification of Depression

Regarding depression being identified in primary or secondary care physicians or by significant others, 13.9% of respondents were not at all confident, 58.4% were somewhat, and only around a quarter (27.7%) were confident. There was a significant difference among respondents from LAMIC reporting no confidence (23.9% v 4.3%) compared to those from HIC ($p < 0.005$).

2.3. Psychological Intervention

The majority of the respondents (65.7%) reported having facilities for psychological intervention, 7.3% did not, and 27.0% had limited facilities (NS). Considering the availability of specific psychotherapies, the responses were: cognitive-behavioral therapy (CBT) (93.4%), problem-solving therapy, (43.8%), behavioral activation, (38.7%), interpersonal therapy (38.0%), mindfulness-based psychotherapy (37.2%), brief psychodynamic therapy (18.2%), and other (6.6%). A higher proportion of respondents from LAMIC reported having the availability of interpersonal therapy (43.3% v 32.9%), behavioral activation (50.7% v 27.1%), and problem-solving therapy (59.7% v 28.6%) compared with HIC, whereas CBT was more available in HIC (98.6% v 88.1%). In clinical practice, the most common challenges related to psychotherapy reported by the respondents were availability (62.8%), long waiting list (56.2%), accessibility (45.3%), and affordability (30.7%).

2.4. Antidepressant Medications

The specific antidepressant prescribed as the first choice was sertraline (51.1%), however, it was more (64.3%) in HIC, compared to LAMIC (37.3%) where the first choice was escitalopram (47.8%). The first choice as second-line antidepressant was venlafaxine including desvenlafaxine (32.1%) (HIC: 34.3%, v LAMIC: 29.9%), followed by mirtazapine 22.6 % (HIC: 25.7%, LAMIC: 19.4%).

Based on the overall responses involving three choices, the ranks of first-line antidepressants were sertraline (75.2%), fluoxetine (44.5%), escitalopram (43.8%), mirtazapine (21.2%), venlafaxine (18.2%), citalopram (13.1%), and desvenlafaxine (5.1%). Similarly, overall ranks of second-line antidepressants were mirtazapine (49.6%), venlafaxine (42.3%), duloxetine (14.6%), bupropion (11.7%), amitriptyline (10.9%), desvenlafaxine (9.5%), vortioxetine (8.8%), fluoxetine (8.0%), escitalopram (5.8%), paroxetine (5.8%), and sertraline (5.1%).

2.5. Medications Prescribed Alongside Antidepressants

While initiating antidepressant drugs, respondents reported prescribing benzodiazepines (40.5%), second-generation antipsychotic drugs (13.7%), anxiolytics (29.0%), and no other medication only in 16.8% (131 responses). There was a significant difference in LAMIC where 53.8% use benzodiazepines in contrast to 27.3% in HIC and no additional medication in 6.2% v 27.3% respectively ($p < 0.005$).

2.6. Augmenting Agents

Considering augmenting agents, lithium (17.5%) was the first choice followed by olanzapine (11.7%), quetiapine (10.2%), aripiprazole (8.8%), and mirtazapine (8.0%). However, considering all three choices provided, the order of preference for the commonly prescribed augmenting agents was: lithium (36.5%), quetiapine (28.5%), olanzapine (23.4%), aripiprazole (19.7%), mirtazapine (11.7%), and lamotrigine (7.3%).

2.7. Type of Depression

The survey specifically enquired regarding management strategies for TRD and bipolar depression. The average percentage of patients who were perceived to have TRD by the respondents

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(132 responses) was 21.0 ± 14.6 (median 20); with no significant difference between HIC (20.8 ± 15.5) and LAMIC (21.2 ± 13.8). Common treatment strategies in managing TRD used by the respondents are given in Table 2. There was no response for vagus nerve stimulation (VNS) and only one response for transcranial direct current stimulation (tDCS) from LAMIC. Common strategies for managing bipolar depression in clinical practice are given in Table 3.

Table 2. Common strategies reported for managing TRD.

Management strategies	HIC n (%)	LAMIC n (%)	Total n (%)
Antidepressants with second-generation antipsychotics	51 (72.9)	54 (80.6)	105 (76.6)
Switching antidepressants	56 (80.0)	47 (70.1)	103 (75.2)
Two antidepressants	45 (64.3)	45 (67.2)	90 (65.7)
Antidepressant and lithium	39 (55.7)	49 (73.1)	88 (64.2)
Psychotherapy	46 (65.7)	42 (62.7)	88 (64.2)
Electroconvulsive therapy	33 (47.1)	48 (71.6)	81 (59.1)
Increased trial length of antidepressant	29 (41.4)	25 (37.3)	54 (39.4)
Antidepressant and valproate/carbamazepine/lamotrigine	27 (38.6)	24 (35.8)	51 (37.2)
intravenous ketamine or intranasal esketamine	8 (11.4)	18 (26.9)	26 (19.0)
Antidepressant with thyroid hormone	5 (7.1)	21 (31.3)	26 (19.0)
Bupropion	8 (11.4)	17 (25.4)	25 (18.2)
Transcranial magnetic stimulation	8 (11.4)	8 (11.9)	16 (11.7)

Table 3. Strategies used for managing bipolar depression.

Strategy	HIC n (%)	LAMIC n (%)	Total n (%)
Lithium and antidepressant	48 (68.6)	45 (67.2)	93 (67.9)
Atypical antipsychotic and antidepressant	46 (65.7)	45 (67.2)	91 (66.4)
Lamotrigine and antidepressant	33 (47.1)	37 (55.2)	70 (51.1)
Valproate and antidepressant	22 (31.4)	31 (46.3)	53 (38.7)
Psychotherapy	19 (27.1)	21 (31.3)	40 (29.2)
Two mood stabilisers	10 (14.3)	17 (25.4)	27 (19.7)
No antidepressant	12 (17.1)	10 (14.9)	22 (16.1)
Others	4 (5.7)	11 (16.4)	15 (10.9)

2.8. Common Reasons for Treatment Discontinuation

Considering the reasons for patients discontinuing medications, it was observed that the most common first responses were impaired insight (43.1%) and side effects (40.1%). However, considering all the responses, the overall ranks were: side effects (73.0%), lack of response to treatment (53.3%), impaired insight (46.7%), lack of psychoeducation (46.7%0, stigma (35.8%), and the inability of afford treatment (27.0%). Side effects posing a challenge to treatment adherence are given in Table 4. Among the sexual problems, 36.5% did not specify the nature of the problem, except that decreased libido (5.1%) and erectile dysfunctions (4.4%) were specifically mentioned in a few. Challenges for continuity of care are summarised in Table 5.

Table 4. Side effects posing a challenge to treatment adherence.

	HIC n (%)	LAMIC n (%)	Total n (%)
Sexual problems	31 (44.4)	32 (47.8)	63 (46.0)
Weight gain	26 (37.1)	23 (34.3)	48 (35.0)
Sedation	15 (21.4)	30 (44.8)	43 (31.4)
Gastrointestinal side effects	19 (27.1)	22 (32.9)	41 (29.9)
Agitation	9 (12.8)	9 (13.4)	17 (12.4)
Insomnia	4 (5.7)	6 (9.0)	10 (7.3)
Fatigue	3 (4.3)	2 (3.0)	5 (3.6)

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Other	14 (20.0)	12 (17.9)	26 (19.0)

2.9. Continuity of Care Issues

Review of the patients after initial assessment was done within less than a month in 43.1%, within one to two months in 49.6%, and in more than two months (7.3%). Although more than half (57.7%) of the respondents reported no problem in arranging laboratory investigation (to rule out organic cause or monitoring e.g. lithium) for the treatment, 21.2% reported definite challenges and another 21.2% faced it to an extent. The challenges in continuing the care are mentioned in Table 5.

Table 5. Challenges to continuity of care.

Challenges	HIC n (%)	LAMIC n (%)	Total n (%)
Non-adherence	54 (77.1)	59 (88.1)	113 (82.5)
Unresolved psychological stress	41 (58.6)	50 (74.6)	91 (66.4)
Missed appointments	42 (60.0)	45 (67.2)	87 (63.5)
Personality disorders	49 (70.0)	37 (55.2)	86 (62.8)
Substance use	47 (67.1)	36 (53.7)	83 (60.6)
Physical comorbidities	40 (57.1)	29 (43.3)	69 (50.4)
Other psychiatric comorbidities	35 (50.0)	26 (38.8)	61 (44.5)
Other	3 (4.3)	4 (6.0)	7 (5.1)

2.10. Treatment Availability

Interestingly, almost half (46.7%) of the respondents from both HIC (41.4%) and LAMIC (52.2%) reported that they were not able to prescribe treatment as it was not available or was difficult to procure (NS); it was mostly rTMS (18.2%). There are availability issues in organizational formulary (6.6%) or government pharmacy (5.1%) for the medications. Most respondents (73.7%) reported access to electroconvulsive therapy (ECT), and repetitive transcranial magnetic stimulation (rTMS) (20.4%). However, 23.4% had no access to ECT, rTMS, or VNS. In the previous year, 59.1% of respondents had used ECT, 16.1% rTMS, 1.5% VNS, and 35.8% had used none.

2.11. Treatment Cost

Most respondents (64.2%) from LAMIC in contrast to 24.3% of HIC reported that patients face a challenge about affordability of the treatment cost of depression ($p < 0.001$). More than half the patients (57.4%) get the treatment free, according to respondents; however, it was 70.0% for HIC and 43.9% for LAMIC. In addition, 40.9% of respondents from LAMIC reported that patients bear all the treatment costs in contrast to 5.7% from HIC ($p < 0.001$). In a minority (13.2%) of cases patients bear part of the costs and in 2.9% insurance pays full and in 3.7% insurance pays in part.

2.12. Suggestions for Solutions

At the end of the survey, suggestions were invited regarding solutions for all the challenges of managing depression. The suggestions are summarised in Table 6.

Table 6. Themes and subthemes of solutions provided by clinicians to manage the challenges in treating depression in clinical practice.

• Psychoeducation (public education, schools, workplace, families, family caregivers, patients, regarding illness, treatment, and stigma)
• Improving access to treatment (ensuring availability of affordable, accessible medications and psychotherapies, reducing waiting time; community-based services, online platform for consultation, prescription, and service delivery)

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• Personalized treatment (provided appropriate medication and psychotherapy based on individual requirement)
• Training and development of healthcare providers (training for early detection and treatment of depression, supporting healthcare professionals to provide psychological interventions, interdisciplinary collaboration)
• Managing stigma (prioritizing mental health in public awareness programmes, improving cultural perceptions about mental illness and treatment, improving acceptance of mental health care seeking behavior, multiagency work involving government and media de-stigmatizing depression)
• Improving continuity of care (enhanced communication between professionals, primary and secondary care, rapid access to comprehensive holistic care for depression including both medications and psychological intervention, supporting regular follow-up and monitoring progress)
• Government and policy support (funding for medications and other treatment modalities, increased insurance cover, policy-making depression treatment more accessible and affordable)
• Research and innovation (research on new treatment modalities, biomarkers for treatment response, management for comorbidities, long-term effects of current treatments)
• Social support (peer-led support groups for emotional support, community outreach, social networks for support, encouraging family involvement in the treatment process)
• Medication management (optimise medication to avoid polypharmacy, reduce side effects, regular reviews to check response, effectiveness, and adjustment, ensure availability of a range of antidepressants for improved flexibility in treatment, explore non-medicinal interventions (e.g. neuromodulation))
• Sustaining long-term recovery (ongoing support following improvement, long-term lifestyle changes, addressing relapses early, proactive follow-ups)

3. Discussion

This survey of psychiatrists was about the challenges they face in managing depression in clinical practice. The sample was spread across various grades in different work settings from government, academic, and private sectors in HIC and LAMIC. Major themes about the challenges managing depression, ground realities observed and the solutions suggested by the psychiatrists in the clinical frontline are discussed below.

3.1. Identifying Depression

It is evident from the responses that psychiatrists are not confident if depression is being identified in primary or secondary care clinicians, which suggests improving the education and training on mental illness for other professionals e.g. for medical and nursing students, general practitioners (GP), and other doctors in secondary care. It is probably better to arrange the training periodically; as most clinicians do not get any training following their graduation.

Possibility of depression can be suspected by clinical judgment; or positive answers to either screening questions such as 'often being bothered by feeling down, depressed, or hopeless' and 'having little interest or pleasure in doing things during the last month' [44,45]. Similarly, screening with the first 2 items of the Patient Health Questionnaire (PHQ)-9 (termed the PHQ-2) [46], and a score of 2 or higher has 86% sensitivity and 78% specificity for diagnosing major depression; which was 74% and 91% respectively for score 10 of PHQ-9 [47]. Diagnostic criteria provided by the classificatory systems help diagnose depression by primary care clinicians [30,31,48] who can easily ascertain the somatic symptoms and syndrome associated with depression [49]. In addition, there are

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many commonly used patient-rated e.g. Beck Depression Inventory [50], Zung Self-Rating Depression Scale [51], etc. or clinician-rated scales e.g. Hamilton's Rating Scale for Depression [52], and Montgomery-Asberg Depression Rating Scale [53], etc. to identify and grade the severity of depression.

Mild depression can be managed in primary care [45], and there is a need to identify and manage depression associated with physical illnesses in both primary and secondary care [54]. Along with clinical settings, it is essential to improve the identification of depression in the general public, educational (schools and colleges), and work environments. Specific information about identifying signs and symptoms, and supportive measures to the public, teachers, and managers may be helpful.

3.2. Medicinal Treatment

Results from this survey indicated that while a wide range of antidepressants is considered in clinical practice, SSRIs are commonly considered as the first-line as most guidelines suggest. In the second-line mirtazapine and venlafaxine are considered mostly. A huge proportion of patients (83.2%) are prescribed additional medications while starting antidepressants reflecting the current practice to deal with associated symptoms, mostly benzodiazepines, second-generation antipsychotic drugs, and anxiolytics. This area needs further research, as even the combination of antidepressant and antipsychotic drugs for psychotic depression is under-studied [55]. It was observed that lithium was still the first choice as an augmenting agent, followed by second-generation antipsychotics (SGA). There is a suggestion of two antidepressants being combined in this regard as mirtazapine was used by many.

3.3. Availability of Treatment Modalities

Many respondents from both HIC and LAMIC reported the issue of the availability of the drugs. Besides availability in the market, some of the medications are not available in government pharmacies in LAMIC that provide them free to patients. In HIC, some of the medications are not available in hospital pharmacies for various reasons, including cost, supportive guidelines, etc. The non-availability may indirectly impact patient care limiting the resources of the clinicians. Interestingly many respondents (46.7%) reported that they were not able to prescribe a treatment as it was not available or difficult to procure; however, these included mostly rTMS, medications in hospital or government pharmacies, or periodic shortages.

3.3. Challenges in Continuity of Care

The psychiatrists reported many challenges during the follow-up of the patients; major issues observed were non-adherence to treatment, missed appointments, comorbid personality, substance use, other psychiatric disorders, and unmet psychological needs. All these impact the continuity of care, and outcome.

Less than half the patients could be seen within one month of treatment initiation, however, most were seen within two months. In minority patients (7.3%) the medication review happened more than two months after the initiation of treatment; this might affect the timely dose optimization, which may secondarily impact response, perception of non-effectiveness of medications, and discontinuation/non-adherence. Being in contact in person or over the phone/online might help, where access, travel, and cost impact on the follow-up visits. Facilities for earlier follow-ups may help in identifying early signs of nonresponse and optimizing treatment.

3.4. Treatment Nonadherence

Medication non-adherence is common in patients with depression [56]. Various reasons were reported for treatment non-adherence, besides side effects, lack of response to treatment, impaired insight, and lack of psychoeducation were cited as major causes. Stigma and affordability were other reasons. Most of these reasons can be addressed satisfactorily, some through treatment approaches,

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others through patient and public education. Psychoeducation of the patients addressing their possible reasons for non-adherence and the risks associated is recommended [57].

3.5. Side Effects Leading to Discontinuation

As observed, side effects were the most common (73.0%) reason for discontinuation of medications. Amongst them, sexual side effects were most frequently cited. There is a need to manage this side effect, through proactive assessment, counseling, and the use of appropriate medicinal strategies including antidepressants [58,59]. Other commonly reported side effects were weight gain, sedation, gastrointestinal problems, and agitation, which need to be addressed as well. Specific guidelines/training about managing these side effects, making them a priority focus during clinical reviews is essential. Improving adherence to medications might be able to deal with many pseudo-nonresponses to treatment [60].

3.6. Challenges of Managing TRD

In this study, the average proportion of patients considered by the respondents as TRD was 21%; which is lower than many reported rates; which is usually considered to be at least 30% [61,62]. However many patients considered TRD could be pseudo-resistant due to the inadequacy of treatment trials or non-adherence to treatment [60]. The respondents reported various strategies to manage TRD, most of which are well known; although the evidence regarding extending antidepressant trials, medication switching, and combining antidepressants has been reported to be mixed for TRD [60]. The reported strategies of managing depression appeared similar in the initial steps of starting with an SSRI and switching to another SSRI or venlafaxine, or augmenting with thyroid hormone, but the approaches of using bupropion, buspirone, tranylcypromine as used in the Sequenced Treatment Alternatives to Relieve Depression (STAR*D) trial [63], were not reported.

Some second-generation antipsychotics (e.g., aripiprazole, brexpiprazole, cariprazine, quetiapine XR) are proven effective as adjunctive treatments to antidepressants in partial responders, but only the olanzapine-fluoxetine combination has been studied in FDA-defined TRD.[60] Similarly, while the role of ECT is fairly established; evidence is becoming more robust for rTMS which is reported to be as effective [60]. Intravenous ketamine and intranasal esketamine (co-administered with an antidepressant) are established as efficacious, and around 19% of respondents mentioned this.

The availability of ECT and neuromodulation was not uniform, based on the results. Around a quarter (26.9%) of respondents reported no access to ECT in their clinical practice; while the rest had, only 59.1% used ECT in the previous year. ECT is regarded as an effective acute and maintenance intervention in TRD [60], however it appears it is underused. Access to rTMS was present for 20.4%, and its role in TRD has been established as an adjunct [64].

3.7. Challenges of Managing Bipolar Depression

Common approaches to managing bipolar depression observed in this survey were similar to the guidelines, in certain aspects. Interestingly some respondents used two mood stabilizers (19.7%) and considered no antidepressant (16.1%) while managing bipolar depression. The suggestions from NICE guidelines in the UK include CBT, interpersonal therapy, behavioural couples therapy; fluoxetine-olanzapine combination, or quetiapine, and if there is no response to consider lamotrigine. It advocates optimizing the dose of lithium or valproate if the patient is already on them and adding other medications [65]. A few SGA (quetiapine, lurasidone, cariprazine, lumateperone, and olanzapine with fluoxetine) are effective and approved by the FDA for bipolar depression [66]. However as observed in the study, challenges in managing bipolar depression remain and require further study in different resource-scant areas.

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3.8. Depression with Comorbidities

Another area of challenges reported by the psychiatrists was managing comorbidities, primarily personality disorders and substance use disorders; which are commonly associated [32]. They are known to affect the outcome of depressive disorder, complicating the progress. Most of the time, these comorbidities are not addressed because of a lack of intervention facilities; and these pose a challenge during follow-ups. Strategies and resources for managing these comorbidities are vital in achieving remission in depressive disorders.

3.9. Psychological Intervention

It was a concern to observe that the continuity of care was impacted in a huge proportion of cases, for unresolved psychological stress issues, more frequently in LAMIC (Table 5). Similarly, patients with personality disorder and substance use had challenges during follow-up. These would need psychological interventions.

Major themes related to psychotherapy for depression across the HIC and LAMIC were accessibility and affordability of psychotherapy; and where it is available; there is a long waiting list. While there are many psychotherapy approaches such as counseling, CBT, IPT, behavioral activation, problem-solving therapy, brief psychodynamic therapy, mindfulness-based psychotherapy, etc. with higher efficacy compared to the usual care [32]often these are not available or not affordable. Improving the availability of psychological intervention is a foregone conclusion.

Besides increasing the workforce, and making services available nearer to patients and more affordable, there are few other options. Using technologies such as internet-based therapy, therapy over the phone and video, etc. are already in place, effective, and can be easily adapted to different settings [67,68]. Psychotherapies can be blended into the circumstances improving their use. Short-duration psychotherapies can be easily provided in the usual clinical setup where resources for psychological intervention are scarce. There are examples of techniques with less therapist time being non-inferior to standard CBT [69], fewer sessions of CBT [70], and brief interventions that can be delivered during outpatient visits [71].

Various measures of psychological intervention can be included in routine clinical practices such as psychoeducation. Psychoeducation has been reported to be effective in improving the clinical course, treatment adherence, and psychosocial functioning of depressive patients [72]. Family psychoeducation has been noted to have a small but significant effect on depression in the short and long term [73]. It also helps in the prevention of depression, more so in children, adolescents, and younger adults [74]. Similarly, problem-solving therapy and behavioral activation can be a part of usual clinical intervention [45]. In resource-scant areas, and with large patient populations, group therapies may be a better option than individual one-to-one sessions. In addition, guided self-help, lifestyle advice [75,76], and exercise [77], can be routine parts of clinical management.

3.10. Affordability of the Treatment Cost

Depression has a high economic burden not only on patients and families but also on nations due to clinical and work-related costs [78,79]. A little over half the patients with depression get the treatment free; however, more proportion of patients in HIC got it free compared to LAMIC; and a significantly higher proportion of patients or their families in LAMIC bear the total cost of the care. This might indirectly influence the adherence and continuity of treatment for a proportion of patients. One of the ways of managing a huge number of patients with depression is supporting more tele-mental-health service facilities, with assessment, prescriptions, psychotherapy, follow-ups, and even emergency contact. These may improve the access to treatment. The cost of care may be decreased through government planning, monitoring the cost of the medications and other treatment modalities; and appropriate resource allocation prioritizing the treatment of depression.

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3.11. Managing Stigma

Another major theme that contributed to seeking and continuing treatment was stigma. It is common worldwide and impacts help-seeking as a barrier [80]. Along with the patients, education for the family members and the general public is consistently needed. While mental health professionals may lead this process, it is essential that health, social welfare, media, and governmental agencies play their roles effectively. This aspect needs to be particularly prioritized and addressed during clinical reviews.

3.12. Limitations

There are several limitations of this study. The sample size is relatively small and the coverage of countries is limited. The findings are from the practising clinicians; however, the views of patients, their caregivers, and the health authorities may be different. Any confounding factors influencing the responses from the participants are not known.

4. Materials and Methods

4.1. Setting

It was an online survey based on a pre-designed questionnaire.

4.2. Participants

Participants included psychiatrists and other doctors who were managing psychiatric patients, working in various clinical settings such as government hospitals, private set-ups; and teaching or non-teaching organizations.

4.3. Recruitment

The online link and information about the survey were circulated in different countries by colleagues supporting the project, in September 2024, among participants with a request to share the link with the interested colleagues. Two reminders were given to participants to complete the survey.

4.4. Questionnaire

The questionnaire asked for the most common challenge clinicians face in managing depression in their clinical practice. Other questions included: their confidence level about depression being identified in primary and secondary care, facility for psychological intervention, commonly available psychotherapy, challenges faced for psychotherapy, first and second-line antidepressants, common additional medications, augmenting drugs, strategies for treating TRD, bipolar depression, common reasons for discontinuation of treatment by the patients, side effects affecting adherence, affordability of treatment cost and its provider. Challenges the clinicians encountered in arranging laboratory investigations, follow-up appointments, and access to ECT and other neuromodulation, were checked. Suggestions for the solutions for the challenges in managing depression were also enquired about. The questionnaire needed around 10-12 minutes to complete.

4.5. Ethical Aspects

Information about the survey was provided to participants on the online link, and consent was taken electronically. The respondents had the option not to participate, terminate the participation at any point, and not submit the form. It was an anonymous survey; no identifiable details of the respondents were collected. All the data was confidential. There was an option to contact the research team for any further information about the survey.

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4.6. Analysis

The quantitative data was analyzed using using SPSS version 28. Missing data was not included in the analysis. The themes and subthemes from the qualitative information from the open-ended questions were derived.

5. Conclusions

The result of the survey from psychiatrists highlighted that there are many challenges in managing depression which can be summarised as: treatment non-response, resistance, and discontinuation, side effects mostly sexual in nature, inadequate psychological intervention, availability of treatment and affordability, comorbidities, especially substance use and personality disorders, stigma, and lack of education and training. Approaches to intervention may change the scenario, e.g. personalized treatment; quicker follow-up, psychoeducation, blending psychological intervention into routine clinical practice, and improving continuity of care to prevent treatment discontinuation. Policy support from governments, improving access, making treatment affordable, and providing socio-occupational support for the patients appear essential. Training and development of professionals especially those who are not in psychiatry and public education sharing information about depression and its treatment along with dealing with stigma are needed.

This survey highlighted a few areas which may be a focus of research. Methods of providing effective psychological interventions, especially in resource-scant situations; developing and checking the effectiveness of briefer therapy sessions and culturally adapted therapies that can be provided during outpatient appointments, management of depression in the presence of complicating comorbid conditions; and methods that can improve the long-term outcome of depression, decreasing non-response or resistance are some of the areas. These might help update the currently available guidelines to the clinicians.

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Informed Consent Statement: Informed consent was obtained from all subjects involved in the study.

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Abbreviations

The following abbreviations are used in this manuscript:

HIC	High-income countries
LAMIC	Low and middle income countries
COVID	Corona virus disease

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NNT	Numbers needed to treat
SSRI	Selective serotonin reuptake inhibitors
TRD	Treatment resistant depression
CBT	Cognitive behavioral therapy
VNS	Vagus nerve stimulation
ECT	Electroconvulsive therapy
rTMS	Repetitive transcranial magnetic stimulation
tDCS	Transcranial direct current stimulation
PHQ	Patient health questionnaire

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