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Approval Process

	Name	Title	Institution	Date	Signature
Written by	Badriya Al Ghammari	Senior Staff Nurse	Al Masarra Hospital	26.7.22	
	Dr. Thuraya Al Hashme	Psychiatrist	Al Masarra Hospital	1.8.2022	
	Dr.Fathyia Abd Elazeim Elhofy	Psychiatrist	Al Masarra Hospital	1.8.2022	
Reviewed by	Local Clinical Guidelines Committee	Committee	Al Masarra Hospital	26/7/22	DR. Nawal Mohammed Al Zadjali Specialist Psychiatry Al Masarra Hospital
Validated by	Kunooz Al Balushi	Document Manager	Al Masarra Hospital	July 2022	
Approved by	Dr. Bader Al Habsi	Hospital Director	Al Masarra Hospital	25/7/22	

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Acronyms

AMRH	Al Masarra Hospital
(ABG)	arterial blood gas.
ADHD	Attention Deficit Hyperactivity Disorder
B12	Vitamin B12
Ca2+	Calcium
CBT	cognitive behavioral therapy
CT	Computerized Tomography
e.g.	Example
ECT	Electroconvulsive Therapy
EEG	Electro encephalo gram
ESR	Erythrocyte Sedimentation Rate
FBC	Full Blood Count
Gl	Gastro Intestinal
Hz	Hertz
LFTs	Liver Function Tests
MAOI	Monoamine Oxidase Inhibitors
Ml	Myocardial infection
MRI	Magnetic Resonance Imaging
OCD	Obsessive-compulsive disorder
rTMS	Repetitive Transcranial Magnetic Stimulation
SAD	Seasonal Affective Disorder

SSRI	Selective serotonin reuptake inhibitors
T3	Triiodothyronine
TCAs	Tricyclic Antidepressant
TFTs,	Thyroid Function Tests
U&Es	Urea and Electrolytes
VDRL	Veneral disease research lab
WHO	World Health Organization

Clinical Guideline for the Diagnosis and Treatment Of Major Depressive Disorder

1. Introduction

This guideline addresses the management of major depressive disorder (MDD) in adults with a target audience of psychiatrists and other mental health professionals in Al-Masarra Hospital. It provides clear and comprehensive evidence based recommendations incorporating the latest international guidelines and practices in the treatment of MDD.

Major Depression is a common disorder, which often leads to poor quality of life and impaired role functioning. It is known to be a major contributor to the global burden of diseases and according to World Health Organization (WHO), depression is the fourth leading cause of disability worldwide, it will be the second most common leading cause of disability . Major Depression is also associated with high rates of suicidal behavior and mortality. When major depression occurs in the context of medical morbidity, it is associated with increased health care cost, longer duration of hospitalization, poor cooperation in treatment, poor treatment compliance and high rates of morbidity.

2. Scope

This guideline is applicable to psychiatrists and other mental health professionals in Al Masarra Hospital (AMRH).

3. Purpose

3.1. To providing information, promoting the health worker on, diseases and their management.

3.2. To improve the general practice of & increase awareness of a disease or diagnosis and to provide health educational information on that disease and its management.

3.3. To provide Evidence-based recommendations on diagnosis and management on MDD.

3.4. To provide all health care professionals who are involved in the management of patients with depression with updated and reliable information.

4. Definitions

4.1. Depression: Major Depressive Disorder is a broad and heterogeneous diagnosis. Central to it is depressed mood and/or loss of pleasure in most activities. Severity of the disorder is determined by the number and severity of symptoms, as well as the degree of functional impairment. To diagnose MDD the symptoms must be present for at least two weeks.

4.1.1. A formal diagnosis using the ICD-10 classification system requires at least four out of ten depressive symptoms, whereas the DSM-V system requires at least five out of nine (decrease or increase in appetite with change in weight e.g. more than 5% of body weight in a month , Insomnia or hypersomnia , Psychomotor agitation or retardation, Fatigue or loss of energy ,Feelings of worthlessness , excessive or inappropriate guilt , poor concentration or indecisiveness, Recurrent thoughts of death , recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan) for a diagnosis of major depression .Both diagnostic systems require at least one (DSM-V) or two (ICD-10) key symptoms (low mood, loss of interest and pleasure) to be present.

4.1.2. Depression presents with of symptoms of depressed mood, loss of interest or pleasure, decreased energy and fatigue, reduced concentration and attention, reduced self-esteem and self-confidence, ideas of guilt and unworthiness, bleak and pessimistic views of the future, ideas or acts of self-harm or suicide, disturbed sleep and diminished appetite.

5. Procedure

5.1. Assessment

5.1.1. Patients should receive a thorough diagnostic assessment in order to establish the diagnosis of major depressive disorder, identify other psychiatric or general medical conditions that may require attention, and develop a comprehensive plan for treatment.

5.1.2. Assessment generally includes a history of the present illness and current symptoms; a psychiatric history, including identification of past symptoms of mania, hypomania, or mixed episodes and responses to previous treatments; a general medical history; a personal history including information about psychological development and responses to life transitions and major life events;

a social, occupational, and family history (including mood disorders and suicide); review of the patient's prescribed and over-the-counter medications; a review of systems; a mental status examination; a physical examination; and appropriate diagnostic tests as indicated to rule out possible general medical causes of depressive symptoms .

5.1.3. Thorough assessment also ought to focus on evaluation for co morbid substance abuse/dependence. Careful history of substance intake need to be taken to evaluate the relationship of depression with substance intoxication, withdrawal and abstinence. Whenever required appropriate tests like, urine or blood screens (with prior consent) may be used to confirm the existence of comorbid substance abuse/dependence.

5.1.4. Many physical illnesses are known to have high rates of depression. In some situations the physical illnesses have causative role in development of depression, whereas in other situations the relationship/co-occurrence is due to common etiology.

5.1.5. When depression occurs in relation to physical illness attempt may be made to clearly delineate the symptoms of depression and physical illness.

5.1.6. Further, while reviewing the treatment history to kept in mind medication induced depression, as many medications are known to cause depression.

5.1.7. It is always important to take the longitudinal life course perspective into account to evaluate for previous episodes and presence of symptoms of depression amounting to dysthymia.

5.1.8. Evaluation of history also takes into consideration the relationship of onset of depression with change in season (seasonal affective disorder), peripartum period and phase of menstrual cycle. Further, the longitudinal course approach may also take into account response to previous treatment and whether the patient achieved full remission, partial remission or did not respond to treatment.

5.1.9. An important aspect of diagnosis of depression is to rule out bipolar disorder. Many patients with bipolar disorder present to the clinicians during the depressive phase of illness and do not spontaneously report about previous hypomanic or manic episodes.

5.1.10. Careful history from the patient and other sources (family members) often provide important clues for the bipolar disorder. It is often useful to use standardized

scales like mood disorder questionnaire to rule out bipolarity. Treating a patient of bipolar depression as unipolar disorder can increase the risk of antidepressant induced switch. Presence of psychotic features, marked psychomotor retardation, reverse neurovegetative symptoms (excessive sleep and appetite), irritability of mood, anger, family history of bipolar disorder and early age of onset need to alert the clinicians to evaluate for the possibility of bipolar disorder.

5.1.11. Area to be covered in assessment include symptom dimensions, symptom-severity, comorbid psychiatric and medical conditions, particularly comorbid substance abuse, the risk of harm to self or others, level of functioning and the socio-cultural milieu of the patient.

5.1.12. In case patient has received treatment in the past, it is important to evaluate the information in the form of type of antidepressant used, dose of medication used, compliance with medication, reasons for poor compliance, reasons for discontinuation of medication, response to treatment, side effects experienced etc. If the medications were changed, then the reason for change is also to be evaluated.

5.1.13. Wherever possible, unstructured assessments need to be supplemented by ratings on appropriate standardized rating scales.

5.1.14. A careful and ongoing evaluation of suicide risk is necessary for all patients with major depressive disorder. Such an assessment includes specific inquiry about suicidal thoughts, intent, plans and behaviors. Identification of factors that may increase the likelihood of acting on suicidal ideas (e.g. presence of psychosis, severe anxiety, co morbid substance use or general medical conditions ,past and, particularly, recent suicidal behavior; presence of stressors). Identification of potential protective factors (e.g., positive reasons for living, strong social support); and identification of any family history of suicide or mental illness.

5.1.15. As part of the assessment process, impulsivity and potential for risk to others should also be evaluated, including any history of violence or homicidal ideas, plans, or intentions.

5.1.16. In addition it is important to assess the patient's level of self-care, hydration, and nutrition, each of which can be compromised by severe depressive symptoms.

5.1.17. Depending on the need, investigations need to be carried out. The use of neuroimaging may be indicated in those with first-episode of depression seen in

late or very late age; those have neurological signs, those having treatment resistant depression.

5.1.18. Besides, patients, information about the illness need to be obtained from the caregivers too and their knowledge and understanding of the illness, their attitudes and beliefs regarding treatment, the impact of the illness on them and their personal and social resources need to be evaluated

5.2. Types of depression

There are different types of depressive disorders. Symptoms can range from relatively minor (but still disabling) through to very severe. The American Psychiatric Association's Diagnostic Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) (1) classifies the depressive disorders as disruptive mood deregulation disorder, major depressive disorder (including major depressive episode), persistent depressive disorder, premenstrual dysphoric disorder, Substance/Medication-Induced Depressive Disorder, depressive disorder due to another medical condition, and Other Specified Depressive Disorder which include; Recurrent brief depression, Short-duration depressive episode (4-13 days), Depressive episode with insufficient symptoms.

5.2.1. Major depression Disorder

Major depressive disorders may be further categorized by specifiers that include peripartum onset, seasonal pattern, melancholic features, mood-congruent or mood-incongruent psychotic features, anxious distress, and catatonia. When diagnosing Major Depressive episode you need to specify:

- If it's single or recurrent (For an episode to be considered recurrent, there must be an interval of at least 2 consecutive months between separate episodes in which criteria are not met for a major depressive episode).
- Level of severity: Mild, Moderate, and Severe with or without psychotic features.
- Remission level : in partial remission , in full remission , unspecified

5.2.1.1. **Mild depressive episode:** Two or three symptoms of Depression are usually present. The patient is usually distressed by these but will probably be able to continue with most activities.

5.2.1.2. **Moderate depressive episode:** Four or more symptoms of depression are usually present and the patient is likely to have great difficulty in continuing with ordinary activities.

5.2.1.3. **Severe depressive episode without psychotic symptoms:** An episode of depression in which several symptoms are marked and distressing, typically loss of self-esteem and ideas of worthlessness or guilt. Suicidal thoughts and acts are common and a number of "somatic" symptoms are usually present.

5.2.1.4. **Severe depressive episode with psychotic symptoms:** as described in Severe depressive episode without psychotic symptoms but with presence of hallucinations, delusions, psychomotor retardation, or stupor.

5.2.1.5. **Melancholia:** Characterizes by one of the following: Loss of pleasure in almost all activities, Lack of reactivity to usually pleasurable stimuli. In addition to three (or more) of the following; depressed mood characterized by profound despondency and despair. Depression that is regularly worse in the morning. Early-morning awakening (i.e., at least 2 hours before usual awakening). Marked psychomotor agitation or retardation. Significant anorexia or weight loss. Excessive or inappropriate guilt.

5.2.1.6. **With anxious distress:** defined as the presence of at least two of the following symptoms during the majority of days of a major depressive episode ; feeling keyed up or tens, feeling unusually restless, difficulty concentrating because of worry, fear that something awful may happen, feeling that the individual might lose control of himself or herself. High levels of anxiety have been associated with higher suicide risk, longer duration of ill ness, and greater likelihood of treatment nonresponse.

5.2.1.7. **With mixed features:** At least three of the following manic/hypomanic symptoms are present nearly every day during the major depressive episode; elevated, expansive mood, inflated self-esteem or grandiosity, more talkative than usual , flight of ideas or subjective experience that thoughts are racing, increase in energy or goal-directed activity, Increased or excessive involvement in activities that have a high potential for painful consequences, decreased need for sleep.

5.2.1.8. **With atypical features:** Characterize by mood reactivity and significant weight gain or increase in appetite, hypersomnia, leaden paralysis, long-standing pattern of interpersonal rejection sensitivity. These features predominate during the majority of days of the current or most recent major depressive episode.

5.2.1.9. **With péripartum onset:** This specifier can be applied if full criteria are met for a major depressive episode and onset of mood symptoms occurs during pregnancy or in the 4 weeks following delivery. Women with péripartum major depressive episodes often have severe anxiety and even panic attacks. Infanticide is most often associated with postpartum depression with psychotic symptoms.

5.2.1.10. **With seasonal pattern:** This applies to recurrent major depressive disorder. There has been a regular temporal relationship between the onset of major depressive episodes and a particular time of the year with full remissions occurs at a characteristic time of the year.

5.2.2 Persistent Depressive Disorder (Dysthymia):

The essential feature of persistent depressive disorder (dysthymia) is a depressed mood that occurs for most of the day, for more days than not, for at least 2 years, or at least 1 year for children and adolescents. The symptoms of dysthymia are similar to those of major depression but are less severe. Early onset Dysthymia if onset is before age 21 years and late onset if onset is at age 21 years or older.

5.2.3 Premenstrual Dysphoric Disorder

To diagnose PMDD at least five of the following, present to a marked degree, in the week before menstruation for most months of the previous year: depressed mood , emotional lability , irritability and anger ,poor concentration , tension and anxiety ,loss of interest in usual activities ,altered eating habits or food cravings ,disturbed sleep patterns, lethargy and fatigue, feeling overwhelmed or out of control, physical symptoms such as headache, breast tenderness, weight gain and feeling bloated. The features must include at least one mood or anxiety symptom and should severely interfere with social and occupational functioning.

5.2.2. Recurrent brief depression:

Characterized by depressed mood and at least four other symptoms of depression for 2-13 days at least once per month (not associated with the menstrual cycle) for at least 12 consecutive months. Patient has never met criteria for any other depressive or bipolar disorder and does not currently meet active or residual criteria for any psychotic disorder.

5.2.3. Short-duration depressive episode (4-13 days):

Characterized by depressed mood and at least four of the other eight symptoms of a major depressive episode associated with clinically significant distress or impairment that persists for more than 4 days, but less than 14 days, in an individual whose presentation has never met criteria for any other depressive or bipolar disorder

5.2.4. Depressive episode with insufficient symptoms:

Characterize by depressed mood and at least one of the other eight symptoms of a major depressive episode associated with clinically significant distress or impairment that persist for at least 2 weeks in an individual whose presentation has never met criteria for any other depressive or bipolar disorder.

5.2.5. Depressive Disorder Due to another Medical Condition:

Characterized by a prominent and persistent period of depressed mood or markedly diminished interest that is thought to be related to the direct physiological effects of another medical condition. A careful and comprehensive assessment of multiple factors is necessary to make this judgment. One consideration is the presence of a temporal association between the onset, exacerbation, or remission of the general medical condition and that of the mood disturbance. A second consideration is the presence of features that are atypical of primary Mood Disorders (e.g., atypical age at onset or course).

5.2.6. Substance/Medication-Induced Depressive Disorder:

Characterized by symptoms of a depressive disorder, such as major depressive disorder; however, the depressive symptoms are associated with the ingestion, injection, or inhalation of a substance. Depressive disorder should have developed during or within 1 month after use of a substance. In addition, the diagnosis is not better explained by an independent depressive disorder e.g the depressive disorder preceded the onset of ingestion or withdrawal from the substance; the depressive

disorder persists beyond a substantial period of time after the cessation of sub¬ stance use.

5.3. Management of depression

Treatment options for management of depression can be broadly be divided into Pharmacotherapy {typical antidepressants, atypical antidepressants} Psychotherapy, electroconvulsive therapy (ECT) and psychosocial interventions. Physical therapy other less commonly used treatment or treatments used in patients with treatment resistant depression include repetitive transcranial magnetic stimulation (rTMS).

5.3.1. Pharmacotherapy:

5.3.1.1. **Medications vs. no medications**

5.3.1.1.1. Antidepressants may be considered where there is:

5.3.1.1.1.1 History of moderate or severe depression

5.3.1.1.1.2 Mild depression that have been present for more than two years (dysthymia).

5.3.1.1.1.3 Mild depression that persists after other interventions.

5.3.1.1.2. For mild depression: usually no need for use of antidepressants. Psychotherapeutic treatments are advised.

5.3.1.1.3. For moderate or severe depression: combine antidepressant medications and a high intensity psychotherapeutic intervention.

5.3.1.2. **Selective Serotonin Reuptake Inhibitors**

SSRIs have the advantage of ease of dosing and low toxicity in overdose. SSRIs are greatly preferred over the other classes of antidepressants for the treatment of children and adolescents, and they are also the first-line medications for late-onset depression. This recommendation is supported by the 2011 APA guideline. Ease of dosing; better tolerated than TCAs, less cardio toxic, fewer anticholinergic side-effects, low toxicity in overdose.

5.3.1.2.1. **Side Effects**

5.3.1.2.1.1. Serotonin reuptake inhibition (leads to increase 5-HT in synaptic cleft).

5.3.1.1.1.2 .5-HT1A agonism: antidepressant, anxiolytic, anti-

obsessive, antibulimic effects.

5.3.1.2.1.3 . 5-HT2 agonism: agitation, akathisia, anxiety/panic, insomnia, sexual dysfunction.

5.3.1.2.1.4 .5-HT3 agonism: nausea, GlT upset, diarrhea, headache.

5.3.1.2.2 **Adverse Effects**

5.3.1.2.2.1 The adverse-effect profile of SSRIs is less prominent than that of some other agents, which promotes better compliance. Common adverse effects include gastrointestinal effects {upset,nausea, diarrhea, constipation, vomiting,}**,** sexual dysfunction, and changes in energy level (fatigue, restlessness) and insomnia.

5.3.1.2.3 **Contraindication**

5.3.1.2.3.1 Manic episode, concomitant use of MAOIs.

5.3.1.2.4 **Caution**

5.3.1.2.4.1 Variable and significant inhibitory effects on hepatic P450 (particularly CYP2D6) enzymes. Hence, take care when co-prescribing with drugs that undergo extensive liver metabolism and have a narrow therapeutic range.

5.3.1.2.4.2 Significant interactions :(variable for different agents):alcohol, anticoagulants, anticonvulsants, antipsychotics, BDZs, B-blockers, bupropion, buspirone, cimetidine, cyproheptadine, hypoglycemic, lithium, methadone, MAOIs, morphine, smoking, TCAs, theophylline, warfarin.

5.3.1.2.5 **Medications**

5.3.1.2.5.1 Citalopram

5.3.1.2.5.2 Escitalopram

5.3.1.2.5.3 Fluoxetine

5.3.1.2.5.4 Fluvoxamine

5.3.1.2.5.5 Paroxetine

5.3.1.2.5.6 Sertraline

5.3.1.2.5.7 Vilazodone

5.3.1.2.5.8 Vortioxetine

5.3.1.3 **Serotonin/norepinephrine reuptake inhibitors**

SNRIs has greater potency for norepinephrine reuptake inhibition than for serotonin reuptake inhibition without directly affecting the uptake of dopamine or other neurotransmitters. **SNRIs** also have an important role as second-line agents in patients who have not responded to SSRIs. The safety, tolerability, and side-effect profiles of SNRIs include those of the SSRIs, as well as noradrenergic side effects, such as hypertension

5.3.1.3.2 **Medications**

5.3.1.3.2.1 Venlafaxine

5.3.1.3.2.2 Desvenlafaxine

5.3.1.3.2.3 Duloxetine

5.3.1.3.2.4 Levomilnacipran

5.3.1.4 **Atypical antidepressant**

Atypical Antidepressants have all been found to be effective in monotherapy in major depressive disorder and may be used in combination therapy for more difficult to treat depression. This group also shows low toxicity in overdose.

5.3.1.4.2 **Medications**

5.3.1.4.2.1 Bupropion

5.3.1.4.2.2 Mirtazapine

5.3.1.4.2.3 Nefazodne

5.3.1.4.2.4 Trazodone

5.3.1.5 **Serotonin-Dopamine Activity Modulators**

SDAMs act as a partial agonist at 5-HT1A and dopamine D2 receptors at similar potency, and as an antagonist at 5-HT2A and noradrenaline alpha1B/2C receptors. This mechanism of action is unique from other atypical antipsychotic drugs.

5.3.1.5.2 **Medications**

5.3.1.5.2.1 Brexpiprazole

5.3.1.5.2.2 Aripiprazole

5.3.1.6 **Tricyclic Antidepressants**

TCAs have a long record of efficacy in the treatment of depression. They are used less commonly because of their side-effect profile and their considerable toxicity in overdose.It is good practice to monitor cardiac and liver function, U&Es, FBC, and weight during long-term therapy.

5.3.1.6.2 **Medications**

5.3.1.6.2.1 Amitriptyline

5.3.1.6.2.2 Clomipramine

5.3.1.6.2.3 Desipramine

5.3.1.6.2.4 Doxepin

5.3.1.6.2.5 Imipramine

5.3.1.6.2.6 Nortriptyline

5.3.1.6.2.7 Protriptyline

5.3.1.6.2.8 Trimipramine

5.3.1.6.3 **Side Effects**

5.3.1.6.4 **Serotonin/noradrenaline** (and dopamine) reuptake inhibition: antidepressant effects.

5.3.1.6.5 **Anticholinergic** (antimuscarinic—Ml): dry mouth, blurred vision, constipation, urinary retention, drowsiness, confusion/memory problems (particularly in the elderly), palpitations-tachycardia.

5.3.1.6.6 **Adrenergic antagonism**: drowsiness, postural hypotension (occasionally syncope), tachycardia, sexual dysfunction.

5.3.1.6.7 **5-HT2 antagonism**: anxiolytic reduced sexual dysfunction, sedation.

5.3.1.6.8 **Antihistaminergic (HI):** drowsiness, weight gain.

5.3.1.6.9 **Contraindications**

5.3.1.6.9.1 Acute Ml,

5.3.1.6.9.2 Heart block,

5.3.1.6.9.3 Arrhythmias,

5.3.1.6.9.4 IHD

5.3.1.6.9.5 Severe liver disease

5.3.1.6.9.6 Pregnancy

5.3.1.6.9.7 Lactation

5.3.1.6.10 **Cautions**

5.3.1.6.10.1 Cardiovascular, liver, renal disease; endocrine disorders (hyperthyroidism, adrenal tumors, diabetes); urinary retention/prostatic hypertrophy; constipation; glaucoma; epilepsy; psychotic disorders; patients with thoughts of suicide; elderly (use lower doses).

5.3.1.7 **Monoamine oxidase inhibitors:**

These agents are widely effective in a broad range of affective and anxiety disorders. Because of the risk of hypertensive crisis, patients on these medications must follow a low-tyramine diet. Other adverse effects can include insomnia, anxiety, orthostatic hypotension, weight gain, and sexual dysfunction

5.3.1.7.2 **Medications**

5.3.1.7.2.1 Isocarboxazid

5.3.1.7.2.2 Phenelzine

5.3.1.7.2.3 Selegiline

5.3.1.7.2.4 Tranylcypromine

5.3.1.8 **N-methyl-D-aspartate antagonists.**

The N-methyl-D-aspartate (NMDA) receptor antagonist has been shown to improve treatment-resistant depression in conjunction with an oral antidepressant. The precise mechanism by which esketamine elicits its antidepressant effect is not fully understood.

5.3.1.8.2 **Medication**

5.3.1.8.2.1 Esketamine Intranasal

5.3.2 Comparative effectiveness of antidepressants

5.3.2.2 The Agency for Healthcare Research and Quality (AHRQ) compared the effectiveness of the following 12 second-generation antidepressants :

5.3.2.1.1 Bupropion

5.3.2.1.2 Citalopram

5.3.2.1.3 Duloxetine

5.3.2.1.4 Escitalopram

5.3.2.1.5 Fluoxetine

5.3.2.1.6 Fluvoxamine

5.3.2.1.7 Mirtazapine

5.3.2.1.8 Paroxetine

5.3.2.1.9 Sertraline

5.3.2.1.10 Trazodone

5.3.2.1.11 Venlafaxine

5.3.2.2 The AHRQ found that average effectiveness of those 12 antidepressants appeared similar, but the studies reviewed were not designed to test variation among patients' responses to individual drugs. However, the AHRQ did find moderately strong evidence of differences among individual second-generation antidepressants with respect to onset of action and some measures (eg, sexual functioning) that could affect health-related quality of life.

5.3.2.3 The combination of sustained-release bupropion and escitalopram was more effective at reducing suicidal ideation than sustained-release venlafaxine plus mirtazapine

5.3.3 Available antidepressants in AMRH

5.3.3.1 **Selective serotonin reuptake inhibitors (SSRIs)**

5.3.3.1.1 Available agents in the Hospital: Citalopram, Fluoxetine, Paroxetine.

5.3.3.2 **Tricyclic/tetracyclic Antidepressants**

5.3.3.2.1 Available agents in the Hospital: Amitriptyline, Clomipramine, Imipramine. Maprotiline.

5.3.4 Outpatient vs. inpatient treatment

5.3.4.1 Usually pharmacological treatment can be initiated on an outpatient basis, severe cases may require admission.

5.3.4.2 Indications for hospital admission

5.3.4.2.1 Serious risk of suicide.

5.3.4.2.2 Serious risk of harm to others.

5.3.4.2.3 Significant self-neglect.

5.3.4.2.4 Severe depressive symptoms.

5.3.4.2.5 Severe psychotic symptoms

5.3.4.2.6 Lack or breakdown of social supports.

5.3.4.2.7 Initiation of ECT.

5.3.4.2.8 Treatment-resistant depression (where inpatient monitoring may be helpful).

5.3.4.2.9 A need to address comorbid conditions (e.g. physical problems, other psychiatric conditions, inpatient detoxification).

5.3.5 Key aims for follow-up

5.3.5.1 Establishing and maintaining a therapeutic alliance.

5.3.5.2 Monitoring the patient's psychiatric status.

5.3.5.3 Providing education regarding depressive disorder and the treatment options.

5.3.5.4 Enhancing treatment compliance.

5.3.5.5 Monitoring side-effects of medication.

5.3.5.6 Identifying and addressing any significant comorbidity.

5.3.5.7 Promoting regular patterns of activity and rest.

5.3.5.8 Identifying unmet needs for specific (practical) support, counseling, (bereavement, stress management), or psychotherapy.

5.3.5.9 Promoting understanding of and adaptation to the psychosocial effects of symptoms.

5.3.5.10 Identifying new episodes early.

5.3.5.11 Reducing the morbidity and squeal of depressive disorder.

5.3.6 Baseline investigations

5.3.6.1 No specific tests for depression.

5.3.6.2 Investigations focus on the exclusion of treatable causes, or other secondary problems (e.g. loss of appetite, alcohol misuse). Standard tests: FBC, ESR, B12/folate, U&Es, LFTs, TFTs, glucose, Ca2+.

5.3.6.3 Focused investigations, only if indicated by history and/or physical signs:

5.3.6.3.1 Urine or blood toxicology.

5.3.6.3.2 Breath or blood alcohol.

5.3.6.3.3 Arterial blood gas (ABG).

5.3.6.3.4 Thyroid antibodies.

5.3.6.3.5 Antinuclear antibody.

5.3.6.3.6 Syphilis serology.

5.3.6.3.7 Additional electrolytes—e.g. phosphate, magnesium, zinc.

5.3.6.3.8 Dexamethasone suppression test (Cushing's disease).

5.3.6.3.9 Cosyntropin stimulation test (Addison's disease).

5.3.6.3.10 Lumbar puncture (VDRL, Lyme antibody, cell count, chemistry, protein electrophoresis).

5.3.6.3.11 CT/MRI, EEG.

5.3.7 Basic principles of prescribing medication in depression

5.3.7.1 Discuss with the patient choice of drug and utility/availability of other, non- pharmacological treatments.

5.3.7.2 Discuss with the patient likely outcomes, such as gradual relief from depressive symptoms over several weeks.

5.3.7.3 Prescribe a dose of antidepressant (after titration, if necessary) that is likely to be effective.

5.3.7.4 For a single episode, continue treatment for at least 6-9 months after resolution of symptoms (multiple episodes may require longer).

5.3.7.5 Withdraw antidepressants gradually; always inform patients of the risk and nature of discontinuation symptoms mainly when used short half-life antidepressant.

5.3.8 First-line treatment

5.3.8.1 Antidepressant drugs are effective in 65-75% of patients.

5.3.8.2 For mild-moderate episodes or where antidepressants are contraindicated (e.g. recent Ml), CBT or other psychotherapies may have a role.

5.3.8.3 The combination of psychotherapeutic approaches and pharmacotherapy may be synergistic, but in severe cases treatment—at least initially—is almost exclusively pharmacological or physical (e.g. ECT).

5.3.9 Choosing an antidepressant

5.3.9.1 The decision about which antidepressant to choose will depend upon:

5.3.9.1.1 Patient factors: age, sex, comorbid physical illness (cardiac, renal, liver, neurological, previous response to antidepressants).

5.3.9.1.2 Tolerability

5.3.9.1.3 Symptomatology: sleep problems (more sedative agent), lack of energy/ hypersomnia (more adrenergic/stimulatory agent), mixed (e.g. with anxiety/panic—SSRI/imipramine), OCD symptoms, (clomipramine/ SSRI), risk of suicide (avoid TCAs).

5.3.10 Adequate trial

5.3.10.1 Generally, an adequate trial of an antidepressant is defined as at least 4wks of the highest tolerated dose.

5.3.11 Suicide risk

5.3.11.1 The risk of suicide may be increased in the early stages of antidepressant treatment. Often patients with previous marked psychomotor retardation have been unable to act upon their thoughts of self-harm. Partial treatment response may 'free' them to do this, hence careful monitoring is critical (and admission to hospital may be indicated).

5.3.12 Treatment failure—second-line treatment

5.3.12.1 Failure of an adequate trial of an antidepressant may occur in ~25% of cases.

5.3.12.2 A similar number of patients will experience unacceptable side effects, leading to the withdrawal of the agent without completing an adequate trial.

5.3.12.3 For these patients, second-line treatment is with an alternative agent usually from a different class of antidepressant, or from the same class but with a different side-effect profile.

5.3.13 Maintenance therapy

5.3.13.1 **First episode**

5.3.13.1.1 A collaborative approach with the patient should emphasize compliance (even when feeling 'better') with advice to continue the effective treatment for 6mths to 1yr after remission.

5.3.13.1.2 Discontinuation should be gradual and if there is recurrence of symptoms revert to effective dose with further attempt at

withdrawal after at least a further 4-6months.

5.3.13.1.3 Often patients wish to continue medication indefinitely (particularly after a severe episode) and reassurance should be given that there is no evidence of any specific long-term problems with such a course of action.

5.3.13.2 **Recurrent episodes**

5.3.13.2.1 If period between episodes is less than 3yrs, or with severe episodes (esp. with marked suicidal thought/actions) prophylactic treatment should be maintained for at least 5yrs (often indefinitely—risk of relapse if medication stopped is 70-90% within 5yrs).

5.3.14 Treating depressive illness with psychotic features

5.3.14.1 **ECT** is advocated by most guidelines for the treatment of psychotic depression as being at least equally as effective as the suggested pharmacological first-line treatment. Only NICE, RANZCP, and DNSC place ECT as a third and final option to be used when other treatments have failed, or if acute response is required due to medical comorbidities or suicidality.

5.3.14.2 Combination treatment (antidepressant plus antipsychotic): There is no clear evidence for any particular combination of medication being more efficacious, but the available evidence supports use of an atypical antipsychotics.

5.3.14.3 Newer medications (selective serotonin reuptake inhibitor or serotonin-norepinephrine reuptake inhibitor +second-generation antipsychotic)

5.3.14.3.1 Venlafaxine plus quetiapine

5.3.14.3.2 Sertraline plus olanzapine

5.3.14.3.3 Fluoxetine plus olanzapine

5.3.14.4 Older medications (tricyclic antidepressant +first-generation antipsychotic)

5.3.14.4.1 Amitriptyline plus haloperidol, trimipramine

5.3.14.4.2 Nortriptyline plus perphenazine

5.3.14.4.3 Amoxapine, Amitriptyline plus perphenazine

5.3.14.4.4 Amitriptyline plus perphenazine

5.3.14.5 Additional practice points:

5.3.14.5.1 Symptoms ought to be carefully monitored, as antipsychotic side-effects may mask improvement in depressive symptoms—hence use of lowest effective dose is advocated.

5.3.14.5.2 Combinations of antidepressant/antipsychotic may worsen side-effects common to both (e.g. sedation, anticholinergic effects) and careful dose titration is necessary.

5.3.14.5.3 Once acute psychotic symptoms have resolved, a lower dose of antipsychotic (or withdrawal) may be indicated, particularly when patients begin to manifest side-effects (which were not seen in the acute stages, even with higher doses)—with careful monitoring for recurrence of psychotic symptoms.

5.3.15 Treatment resistant depression

5.3.15.1 Commonly defined as 'failure to respond to adequate (dose and duration for at least 4 weeks) courses of 2 antidepressants, or 1 antidepressant and ECT.

5.3.15.2 The consequences of resistant depression include reduced quality of life, excessive strain on relationships (which may lead to break-up of families), significant personal economic impact, increased physical comorbidity, increased risk of suicide, therapeutic alienation (making further interventions difficult due to difficulties forming a therapeutic alliance), and high use of psychiatric services (without clear benefit).

5.3.15.3 It is important to distinguish actual treatment resistance from chronicity of symptoms. Apparent treatment failure may also occur due to: incorrect initial diagnosis (i.e. not depressive disorder in the first place), inadequate initial treatment, poor compliance, incomplete formulation (esp. role of maintaining factors), and issues of comorbidity (both physical and other psychiatric disorders).

5.3.16 Management of resistant depression

5.3.16.1 Review diagnostic formulation: is diagnosis correct? Are there any unaddressed maintaining factors (e.g. social, physical, and psychological) *Note: a proportion of individuals with chronic, refractory depression will have unrecognized bipolar disorder.*

5.3.16.2 Check patient understanding/compliance: serum levels may help.

5.3.16.3 Continue mono therapy at maximum tolerable dose: may mean exceeding BNF guidelines (esp. if there has been partial benefit)

5.3.16.4 Consider change in antidepressant: try different class of antidepressant.

5.3.16.5 Consider augmentation with a mood stabilizer: e.g. lithium.

5.3.16.6 Consider additional augmentative agents: e.g. T3, tryptophan.

5.3.16.7 Consider combining antidepressants from different classes: cautionis advised, due to possible serious adverse reactions.

5.3.16.8 Consider use of ECT: esp. if severe biological features or psychotic symptoms).

5.3.16.9 Consider possibility of psychosurgery or other advanced intervention.

5.3.17 Depression during pregnancy

5.3.17.1 There are many different factors that can increase risk of developing depression during your pregnancy. These risks can include:

5.3.17.1.1 Having a history of depression or premenstrual dysphoric disorder (PMDD).

5.3.17.1.2 Your age at time of your pregnancy — the younger you are, the higher the risk.

5.3.17.1.3 Living alone.

5.3.17.1.4 Having limited social support.

5.3.17.1.5 Experiencing marital conflict.

5.3.17.1.6 Feeling ambivalent about your pregnancy

5.3.17.2 Some antidepressants are considered safer for pregnant women than others. Antidepressants that are considered safer include:

5.3.17.2.1 Fluoxetine

5.3.17.2.2 Citalopram

5.3.17.2.3 Sertraline

5.3.17.2.4 Amitriptyline

5.3.17.2.5 Desipramine

5.3.17.2.6 Nortriptyline

5.3.17.2.7 Bupropion

5.3.17.3 **Postpartum Depression Treatment**

5.3.17.3.1 Principles of treatment of postpartum major depressive disorder are the same as for depression during any other time of life. Earlier initiation of treatment is associated with better prognosis.

5.3.17.3.2 Postpartum blues are typically mild and resolve spontaneously; no specific treatment is required, other than support and reassurance.

5.3.17.3.3 For first episodes of depression in postpartum women, 6-12 months of treatment is recommended.

5.3.17.3.4 For women with recurrent major depression following pregnancy, long-term maintenance treatment with an antidepressant is indicated.

5.3.17.3.5 Antidepressants remain the first line of treatment. However, there are preliminary data to suggest that estrogen, alone or in combination with an antidepressant, may be beneficial.

5.3.17.4 **Medications used for postpartum depression**

5.3.17.4.1 Selective serotonin reuptake inhibitors (SSRIs) are first-line agents and are effective in women with postpartum depression.

5.3.17.4.2 Serotonin/norepinephrine reuptake inhibitors (SNRIs) such as venlafaxine (Effexor) 75-300mg/day or duloxetine are also highly effective for managing depression and anxiety.

5.3.17.4.3 Tricyclic antidepressants (TCAs) (eg, nortriptyline 50-150mg/day) may be useful for women with sleep disturbance, although some studies suggest that women respond better to the SSRI drug category.

5.3.17.4.4 **Brexanolone:** The first drug to be approved by the FDA for the treatment of postpartum depression. The mechanism by which brexanolone works for postpartum depression is not fully understood, but it is believed to be related to positive allosteric modulation of both synaptic and extrasynaptic GABA-A receptors.

5.3.17.5 **Antidepressants and Breast-feeding**

5.3.17.5.1 The use of TCAs, fluoxetine (Prozac), sertraline (Zoloft), and paroxetine (Paxil) during breast-feeding are encouraging, and serum antidepressant levels in the breast-fed infant are either low or undetectable.

5.3.17.5.2 Reports of toxicity in breast-fed infants are rare.

5.3.17.6 **Additional points**

5.3.17.6.1 There is little definitive evidence to support any specific augmentative regime.

5.3.17.6.2 Spontaneous remission is possible.

5.3.17.6.3 Psychological and social interventions, particularly when psychosocial factors appear paramount, may be important aspects of management.

5.3.18 Physical therapy:

5.3.18.1 **Electroconvulsive therapy (ECT)**

5.3.18.1.1 A highly effective treatment for depression (particularly with psychotic symptoms).

5.3.18.1.2 May act more rapidly than antidepressant medication.

5.3.18.1.3 **Indications:**

5.3.18.1.3.1 Depressive episode: severe episodes, need for rapid antidepressant response (e.g. due to failure to eat or drink in depressive stupor; high suicide risk), failure of drug treatments, patients who are unable to tolerate side-effects of drug treatment, previous history of good response to ECT, patient preference.

5.3.18.1.3.2 Other indications: treatment-resistant psychosis and mania (50-60% effective), schizoaffective disorder, catatonia, neuroleptic malignant syndrome, neurological crises (e.g. extreme Parkinsonian symptoms: on-off phenomena), intractable seizure disorders (acts to raise seizure threshold).

5.3.18.1.4 **Contrindications:**

5.3.18.1.4.1 There are no absolute contraindications.

5.3.18.1.4.2 Use of ECT should be limited for patients with cerebral aneurysm, recent Ml, cardiac arrhythmias, intracerebral hemorrhage, acute/ impending retinal detachment, pheochromocytoma, high anaesthetic risk, and unstable vascular aneurysm or malformation.

5.3.18.1.4.3 Other considerations: -Time-limited action: benefit from ECT tends to dissipate after a couple of weeks. There is a need for a clear maintenance plan to be in place before the course of ECT finishes. ECT should not be considered the only treatment—except in very rare cases when continuation/ maintenance treatment is indicated.

5.3.18.1.5 **Consent:** guidelines on ECT vary between legislatures concerning use of capacity legislation/Mental Health Act. Decisions rest on assessment of capacity, informal/formal status, active (or advance statement) refusal, potential as a life-saving intervention.

5.3.18.1.6 **Side-effects:** ECT does cause potential side-effects and the administration of ECT will always be a balance of risk and benefit. Of particular note is the potential to cause cognitive problems and this may dictate electrode positioning.

5.3.18.2 **Repetitive trans cranial magnetic stimulation (rTMS)**

5.3.18.2.1 The rationale for treatment is either to increase activity in the left dorsolateral prefrontal cortex (using high-frequency stimulation, e.g. 20Hz) or to reduce activity in the right dorsolateral prefrontal cortex (using low- frequency stimulation, e.g. 1Hz).

5.3.18.2.2 **Adverse effects:** Minimal, but patients often report headache or facial discomfort; rarely seizure induction.

5.3.18.2.3 **Indications:** Experimental treatment for treatment-resistant depression; possible use in treatment of treatment-resistant auditory hallucinations; negative symptoms of schizophrenia;

OCD; panic disorder.

5.3.18.2.4 **Contraindications:** History of stroke, brain tumor, or epilepsy.

6. Responsibility

6.1 Psychiatrists

6.1.1 Adhere to safe management according to depression guidelines.

6.1.2 Take full history including all necessary information from relevant

6.1.3 Accomplish Mental State Examination on admission

6.1.4 Ensure full physical assessment carried out including necessary investigation

6.1.5 Perform initial risk assessment

6.1.6 Provisional diagnosis and information of care plan including observation and treatment

6.1.7 Referral to other multidisciplinary team for assessment

6.1.8 Finalize diagnosis with comprehensive risk assessment by the multidisciplinary team

6.1.9 Implement integrated team intervention

6.1.10 Monitor progress.

6.2 Nurses

6.2.1 **Establishing Trust and rapport**

6.2.1.1 Tell your name to the patient and call him by name.

6.2.1.2 Expect the patient to put you through a rigorous testing period before he shows the evidence of trust. Don't tease or joke with him.

6.2.1.3 Don't touch the patient without first telling exactly what you are going to do.

6.2.1.4 If necessary postpone the procedures that require physical contact until the patient is less suspicious.

6.2.1.5 Use an accepting and consistent approach.

6.2.1.6 Don't avoid or overwhelm the patient.

6.2.1.7 Make repeated contacts until trust is been established.

6.2.1.8 Use clear, unambiguous language.

6.2.1.9 Maintain a sense of hope for possible improvement and convey this to the patient

6.2.2 **Ensuring Safety**

6.2.2.1 Maintain a safe environment with minimal stimulation.

6.2.2.2 Monitor the patient's nutritional status, weigh him regularly.

6.2.2.3 If the patient expresses suicidal thoughts, institute suicide precautions.

6.2.2.4 If he expresses homicidal thoughts, initiate homicidal precautions and notify the doctor.

6.2.3 **Maximizing the level of functioning**

6.2.3.1 Assess the patient ability to carry out activities of daily living.

6.2.3.2 Avoid promoting dependence.

6.2.3.3 Reward positive behavior

6.2.4 **Promoting Social skills**

6.2.4.1 Encourage the patient to engage in meaningful interpersonal relationships.

6.2.4.2 Provide support to assisting him to learn social skills

6.2.5 **Promoting Compliance and monitoring Drug therapy**

6.2.5.1 Administer prescribed drugs to manage depression symptoms

6.2.5.2 Encourage the patient to comply with the medication regimen to prevent relapse**.**

6.2.5.3 Regularly assess the patient for adverse side effects.

6.3 Occupational Therapist

6.3.1 The scope of Initial assessment should include but not limited to the following:

6.3.1.1 Treatment approach should be flexible and multiple approaches may be used for different patients, functioning at different level.

6.3.1.2 The realistic and achievable short term and long term treatment goals should be set.

6.3.1.3 Patient is involved in variety of sessions focusing on.

6.3.2 Daily living skills: Encourage attention and motivation to personal hygiene, including bathing, grooming & dressing

retraining of self-care activities through modeling, group discussion & education,

chaining and self-awareness programs.

Increase functional skills in independent living such a small preparation,

6.3.3 Self-concept, coping skills and adaptive strategies, social skills, social support system: Decrease inappropriate expression of sadness by vigorous physical exercise, games, work, group session and creative art.

6.3.4 Increase self-esteem and positive self-image through individual accomplishment with expressive activities like, painting, drawing, poem or story writing.

Provide opportunities for graded, structured verbalization by event narrating, storytelling, singing, and sharing

6.3.5 Provide one- to –one approach for individual who are withdrawn or too psychotic to benefit from group approach

6.4 Psychologists

6.4.1 Obtain CBT ,behavior modification

6.4.2 Psycho –education (1-3 session) :

6.4.2.1 Clinical interview ,gathering full information ,history taking and identify patient symptoms through intake form.

6.4.2.2 Psycho –education patient about causes ,symptoms ,triggers and medication through broachers ,set homework and verbal explanation

6.4.3 Family Psycho –education (1-2 session) :

6.4.3.1 Psycho –education about the illness , psycho education about the triggers and how to deal with it ,how to deal with patient relapse and support him in correct way

6.4.4 Individual therapy (6-15 session) depending on patient response :

6.4.4.1 Social skills communication skills and interactive with others through weight out pros and cons , role play and thought record sheet

6.4.4.2 Coping skills: adjust with illness and accept it , adjust with life change ,cope with life stressor ,anger management strategist and problem solving skills through calming skills (breathing technique ,counting backward) given situational and examples.

6.4.4.3 Activation behavioral therapy through daily activity schedule, setting goals, outline hobbies and interest.

7. Document History and Version Control

Document History and Version Control			
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1	Initial Release	Clinical pathway formulations	2021
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Written By	**Reviewed By**	**Approved By**	
Dr.Tharaya Al Hashemi Dr.Fatehyia Abd Elazeim Abd Elatif	Local Clinical Guideline Committee	Dr. Bader Al Habsi	

8. Related Document

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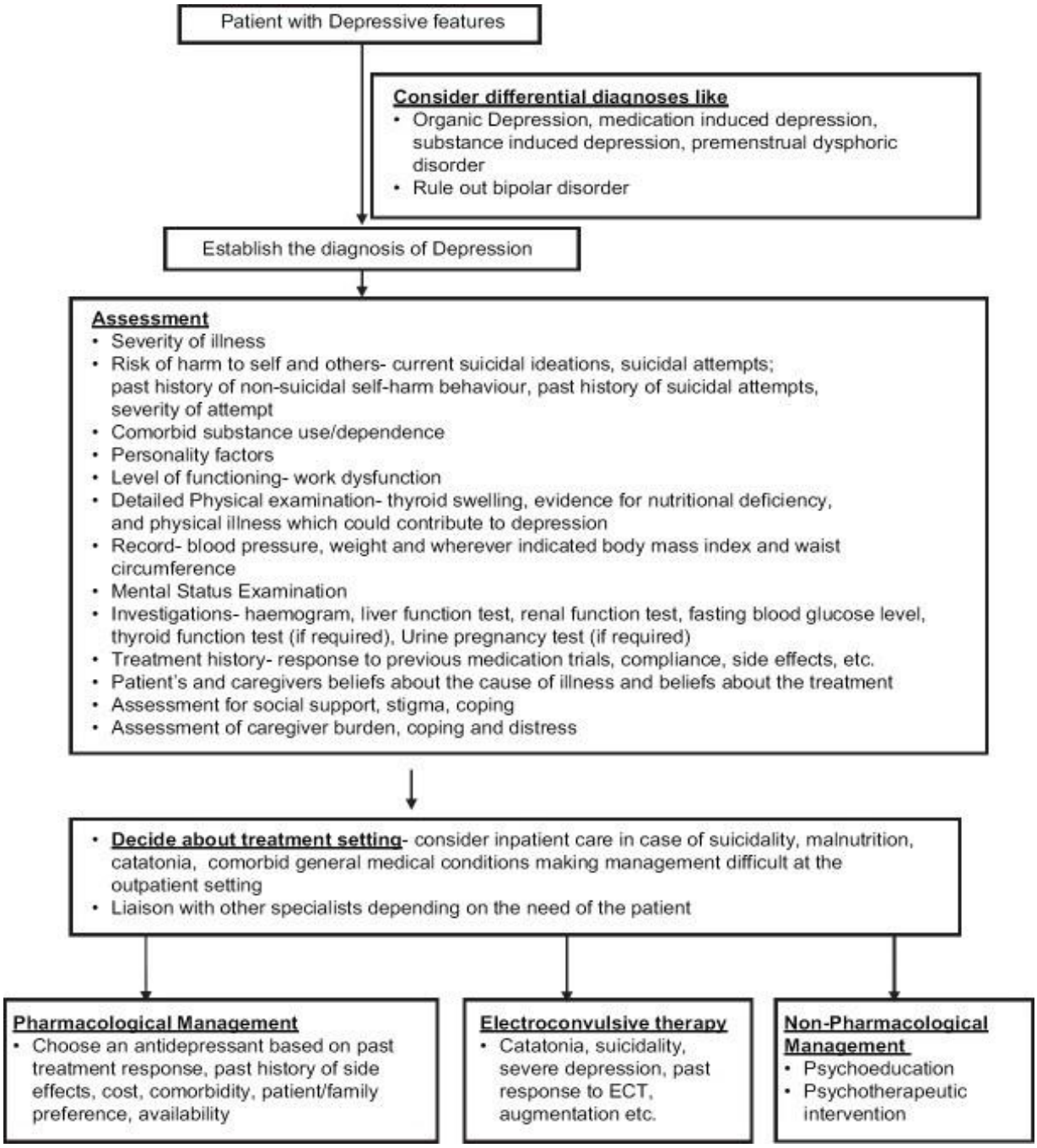
Esketamine Nasal Spray for Rapid Reduction of Major Depressive Disorder Symptoms in Patients Who Have Active Suicidal Ideation With Intent: Double-Blind, Randomized Study (ASPIRE I).	Fu DJ, Ionescu DF, Li X, Lane R, Lim P, Sanacora G, et al.	2020	9-15
Esketamine Nasal Spray May Rapidly Reduce Suicidal Thoughts. *Medscape Medical News*..	Davenport L.	2019	

10. Appendices

10.1. Appendix 1. Formulating a Treatment Plan



10.2. **Appendix 2.** Audit Tool

S.N	Audit process	Standard / Criteria	Yes	Partial	No	N/A	Comment
1.	Interview	Does health care provider are aware about P&P of depression.					
		Assessment					
2.	Interview observation	Are all patients assessed on admission to identify patient who are depressed with risk of suicidal**.**					
3.	Interview observation Document Review	Does doctor Take full history including all necessary information , Initial risk assessment for the patient with depression , depression Hamilton scales , Mental state examination and Ensure full physical assessment carried out including necessary investigation.					
		Management of depression					
4.	Interview Document Review	Dose the psychiatrist's implementation of a management/care plan appropriate to the risk factor identified.					
5	Document Review	Dose the doctor provisional diagnosis and information of care plan including observation and treatment and referring the patient to other multidisciplinary team for assessment.					
6.	Interview	Dose the psychiatrists has knowledge about Treatment options for management of depression (First-line treatment and Second line treatment.					
7	observation	Does assigned nurse took appropriate action to make the environment safe to promote the safety of service users/ patients.					
8	Interview observation Document	Does assigned nurse Monitor the depression patient’s nutritional status, weigh him regularly.					

	Review						
9	Interview observation Document Review	Does assigned nurse maximizing the level of functioning Assess the patient ability to carry out activities of daily living and promoting Social skills.					

Department: _____

Date: _____

10.3. Appendix 3. Document Request Form

Document Request Form			
Section A: Completed by Document Requester			
1. Requester Details			
Name	Dr. Thuraya Al Hashme	Date of Request	July 2022
Institute	Al Masarra Hospital	Mobile	—
Department	Psychiatry	Email	—
The Purpose of Request			
☐ Develop New Document	■ Modification of Document	☐ Cancelling of Document	
1. Document Information			
Document Title	Clinical Guideline for the Diagnosis and Treatment of Major Depressive Disorder		
Document Code	AMRH/PSY/GUD/001/Vers.02		
Section B: Completed by Document Controller			
■ Approved	☐ Cancelled	☐ Forward To:……..	
Comment and Recommendation:			
Name	Kunooz Al BAlushi	Date	July 2022
Signature		Stamp	

10.4. Appendix 4. Document Validation Checklist

Document Validation Checklist					
Document Title:	Clinical Guideline for the Diagnosis and Treatment of Major Depressive Disorder	**Document Code :** AMRH/PSY/GUD/001/Vers.02			
No	Criteria	**Meets the Criteria**			**Comments**
		Yes	**No**	**N/A**	
1.	**Approved format used**				
1.1	Clear title – Clear Applicability	✓			
1.2	Index number stated	✓			
1.3	Header/ Footer complete	✓			
1.4	Accurate page numbering	✓			
1.5	Involved departments contributed	✓			
1.6	Involved personnel signature /approval	✓			
1.7	Clear Stamp	✓			
2.	**Document Content**				
2.1	Clear purpose and scope	✓			
2.2	Clear definitions	✓			
2.3	Clear policy statements (if any)			✓	
3.	**Well defined procedures and steps**				
3.1	Procedures in orderly manner	✓			
3.2	Procedure define personnel to carry out step	✓			
3.3	Procedures define the use of relevant forms			✓	
3.4	Procedures to define flowchart	✓			
3.5	Responsibilities are clearly defined	✓			
3.6	Necessary forms and equipment are listed	✓			
3.7	Forms are numbered	✓			
3.8	References are clearly stated	✓			
4.	**General Criteria**				
4.1	Policy is adherent to MOH rules and regulations	✓			
4.2	Policy within hospital/department scope	✓			
4.3	Relevant policies are reviewed	✓			
4.4	Items numbering is well outlined	✓			
4.5	Used of approved font type and size	✓			
4.6	Language is clear, understood and well structured	✓			
Recommendations..... ~~.....~~ For implementation ..... More revision ..... To be cancelled					
Reviewed by: Kunooz Al Balushi		**Reviewed by: Irwin S. Rio**