Malaysian Family Physician
Official Journal of the Academy of Family Physicians of Malaysia
and Family Medicine Specialist Association of Malaysia

CPG UPDATE

Case scenario: Management of major depressive disorder in primary care based on the updated Malaysian clinical practice guidelines

Uma Visvalingam, Umi Adzlin Silim, Muhammad Muhsin Ahmad Zahari, Firdaus Abdul Gani, Noormazita Mislan, Noor Izuana Redzuan, Peter Kuan Hoe Low, Sing Yee Tan, Masseni Abd Aziz, Aida Syarinaz Ahmad Adlan, Suzaily Wahab, Aida Farhana Suhaimi, Nurul Syakilah Embok Raub, Siti Mariam Mohtar, Mohd Aminuddin Mohd Yusof

Visvalingam U, Silim UA, M Muhsin AZ, et al. Case scenario: Management of major depressive disorder in primary care based on the updated Malaysian clinical practice guidelines. *Malays Fam Physician.* 2022;17(1);71–77. https://doi.org/10.51866/cpg1328

Keywords:
Depression, major depressive disorder, primary care, screening, treatment

Authors:

Mohd Aminuddin Mohd Yusof
(Corresponding author)
MD (UKM), MPH (Epidemiology) (Malaya)
Malaysian Health Technology Assessment Section (MaHTAS)
Ministry of Health Malaysia
Putrajaya, Malaysia
Email: am2dr@yahoo.com

Uma Visvalingam
MBBS (MAHE), Master of Medicine (Psychiatry) (UKM)
Department of Psychiatry and Mental Health, Hospital Putrajaya, Putrajaya, Malaysia

Umi Adzlin Silim
MD (UKM), M. Med (Psychiatry) (UKM)
Department of Psychiatry and Mental Health, Hospital Serdang, Serdang Selangor, Malaysia

Muhammad Muhsin Ahmad Zahari
MB., BCh., BAO (UCD, Ireland)
M. Psych Med (Malaya)
Department of Psychological Medicine, Faculty of Medicine
Universiti Malaya, Kuala Lumpur
Malaysia

Abstract
Major depressive disorder (MDD) is a common but complex illness that is frequently presented in the primary care setting. Managing this disorder in primary care can be difficult, and many patients are underdiagnosed and/or undertreated. The Malaysian *Clinical Practice Guidelines (CPG) on the Management of Major Depressive Disorder (MDD)* (2nd ed.), published in 2019, covers screening, diagnosis, treatment and referral (which frequently pose a challenge in the primary care setting) while minimising variation in clinical practice.

Introduction
MDD is one of the most common mental illnesses encountered in primary care. It presents with a combination of symptoms that may complicate its management.

This mental disorder requires specific treatment approaches and is projected to be the leading cause of the disease burden in 2030.[1] Patients experiencing this ailment are at elevated risk for early mortality from physical disorders and suicide.[2] In Malaysia in particular, MDD contributes to 6.9% of total Years Living with Disability.[3]

Ensuring full functional recovery and prevention of relapse makes remission the targeted outcome for treatment of MDD. In contrast, non-remission of depressive symptoms in MDD can impact functionality[4] and subsequently amplify the economic burden that the illness imposes.

About the new edition
The highlights of the updated CPG MDD (2nd ed.) are as follows:

- emphasis on psychosocial and psychological interventions, particularly for mild to moderate MDD
- inclusion of all second-generation antidepressants as the first-line pharmacotherapy
- introduction of new emerging treatments, ie. intravenous ketamine for acute phase and intranasal esketamine for next-step treatment/treatment-resistant MDD
- improvement in pre-treatment screening and monitoring of treatment
- integration of mental health into other health services with emphasis on collaborative care
- addition of 2 new chapters on special populations (pregnancy and postpartum, chronic medical illness) and table on safety profile of pharmacotherapy in pregnancy and breastfeeding
- comprehensive, holistic biopsychosocial-spiritual approaches addressing psychospirituality

Details of the evidence supporting the above statements can be found in *Clinical Practice Guidelines on the Management of Major Depressive Disorder* (2nd ed.) 2019, available on the following websites: http://www.moh.gov.my (Ministry of Health Malaysia) and http://www.acadmed.org.my (Academy of Medicine). Corresponding organisation: CPG Secretariat, Health Technology Assessment Section, Medical Development Division, Ministry of Health Malaysia; contactable at htamalaysia@moh.gov.my.

Statement of intent
This is a support tool for implementation of CPG Management of Major Depressive Disorder (2nd ed.).

Firdaus Abdul Gani
MBBS (Malaya) M.Med (Psy) (USM)
CMIA (NIOSH)
Department of Psychiatry and Mental Health, Hospital Sultan Haji Ahmad Shah, Temerloh, Pahang, Malaysia

Noormazita Mislan
MB, BCh, BAO (Ireland), M Med. (Psychiatry) (UKM)
Department of Psychiatry and Mental Health,Hospital Tuanku Ja'afar Seremban, Negeri Sembilan Malaysia

Noor Izuana Redzuan
MBBS (Malaya), Dr in Psychiatry (UKM)
Department of Psychiatry and Mental Health, Hospital Raja Permaisuri Bainun, Ipoh, Perak, Malaysia

Peter Kuan Hoe Low
MB, BCh, BAO (Ireland), M.Psych Med (UM)
Department of Psychiatry and Mental Health, Hospital Kuala Lumpur
Kuala Lumpur, Malaysia

Sing Yee Tan
MBBS (Malaya), M.Med (Family Med) (UM)
Klinik Kesihatan Jenjarom, Jenjarom Selangor, Malaysia.

Masseni Abd Aziz
MD (USM) M Med (Fammed) USM
Klinik Kesihatan Umbai, Merlimau Melaka, Malaysia

Aida Syarinaz Ahmad Adlan
MBBS (Malaya), M. Psych Med (UM), PostGrad.Dip. (Dynamic Psychotherapy) (Mcgill University)
Department of Psychological Medicine Faculty of Medicine, Universiti Malaya Kuala Lumpur, Malaysia

Suzaily Wahab
MD (UKM), MMed Psych (UKM)
Hospital Canselor Tuanku Muhriz UKM Kuala Lumpur, Malaysia.

Healthcare providers are advised of their responsibility to implement this evidence-based CPG in their local context. Such implementation will lead to capacity building to ensure better accessibility of psychosocial and psychological services. More options in pharmacotherapy facilitate flexibility in prescribing antidepressants among clinicians. Further integration of mental health into other health services, upscaling of mental health service development in perinatal and medical services, and enhancement of collaborative care will incorporate holistic approaches into care.

Case Scenario

Tini is a female college student aged 24 years old. She comes to the health clinic accompanied by a friend and complains of several symptoms that she has experienced over the past 4 weeks. She reports:

- difficulty falling asleep, feeling tired after waking up in the morning and experiencing headaches
- difficulty staying focused during classes. These symptoms have led to deterioration in her study and prompted her to seek advice from the doctor.

Question 1
Will you screen her for depression?

Answer 1
Yes, because the patient presents with multiple vague symptoms and sleep disturbance.[5]
(Refer to Subchapter 2.1, page 3 in CPG.)

Question 2
What tools are used to screen for depression?

Answer 2
Screening tools for depression are:

- Beck Depression Inventory (BDI)
- Depression Anxiety and Stress Scale (DASS)
- Patient Health Questionnaire-9 (PHQ-9)
- Hospital Anxiety and Depression Scale (HADS)
- Whooley Questions

Screening for depression using Whooley Questions in primary care may be considered in people at risk.[5]
(Refer to Subchapter 2.1, pages 3 and 4 in CPG.)

- Whooley Questions on depression:
  - "During the past month, have you often been bothered by feeling down, depressed or hopeless?"
  - "During the past month, have you often been bothered by having little interest or pleasure in doing things?

The doctor decides to use Whooley Questions, and Tini answers "yes" to both questions.

Question 3
How would you proceed from here to further assess for depression?

Answer 3
Assessment of depression consists of:

- detailed history taking
  (Refer to Subchapter 2.2, page 4 in CPG.)
- mental state examination (MSE), including evaluation of symptom severity, presence of psychotic symptoms and risk of harm to self and others
- physical examination to rule out organic causes
- investigations where indicated – biological and psychosocial investigations

Upon further assessment, Tini reveals that she feels overwhelmingly sad. She is frequently tearful and reports feeling excessively guilty, blaming herself for not performing well enough in her studies. Her postings on social media have been revolving around themes of self-defeat. Despite feeling low, she still strives to attend classes and complete her assignments. However, her academic performance has exhibited a marked deterioration. There is no history to suggest hypomanic, manic or psychotic symptoms. She denies using any illicit substances or alcohol. Her menstrual cycle is normal and does not correspond to her mood changes.

MSE reveals a young lady who appears to be in distress. Rapport is easily established, but her eyes are downcast. Her speech is relevant, with low tone. She describes her mood as sad; she is tearful while talking about her poor results, with appropriate affect. She harbours multiple unhelpful thoughts, eg. "I'm a failure" and "I'm useless". She exhibits no suicidal ideations, delusions or hallucinations. Her concentration is poor, and insight is partial.

Physical examination reveals no recent self-harm scars, and examination of other systems is unremarkable. Biological investigations such

Aida Farhana Suhaimi
B. Psych (Adelaide), M. Psych (Clin. Psych) (Tasmania), PhD (Psychological Medicine) (UPM)
Department of Psychiatry and Mental Health, Hospital Putrajaya, Putrajaya Malaysia

Nurul Syakilah Embok Raub
BPharm (Hons) (CUCMS), MPH (Malaya)
Pharmacy Enforcement Branch
Selangor Health State Department
Shah Alam, Selangor, Malaysia

Siti Mariam Mohtar
BPharm (UniSA)
Malaysian Health Technology Assessment Section (MaHTAS)
Ministry of Health Malaysia
Putrajaya, Malaysia

as full blood count and thyroid function test are within normal range. Corroborative history is taken from accompanying person to verify the symptoms.

Question 4
How would you arrive at the diagnosis and severity?

Answer 4
Diagnosis of depression can be made using the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) or the 10th revision of the International Statistical Classification of Disease and Related Health Problems (ICD-10).[5]
(Refer to Appendix 3 and 4, pages 73-76 in CPG.)[6,7]

In the last 2 weeks, Tini has been experiencing:
i. low mood
ii. insomnia
iii. poor concentration
iv. lethargy
v. excessive guilt

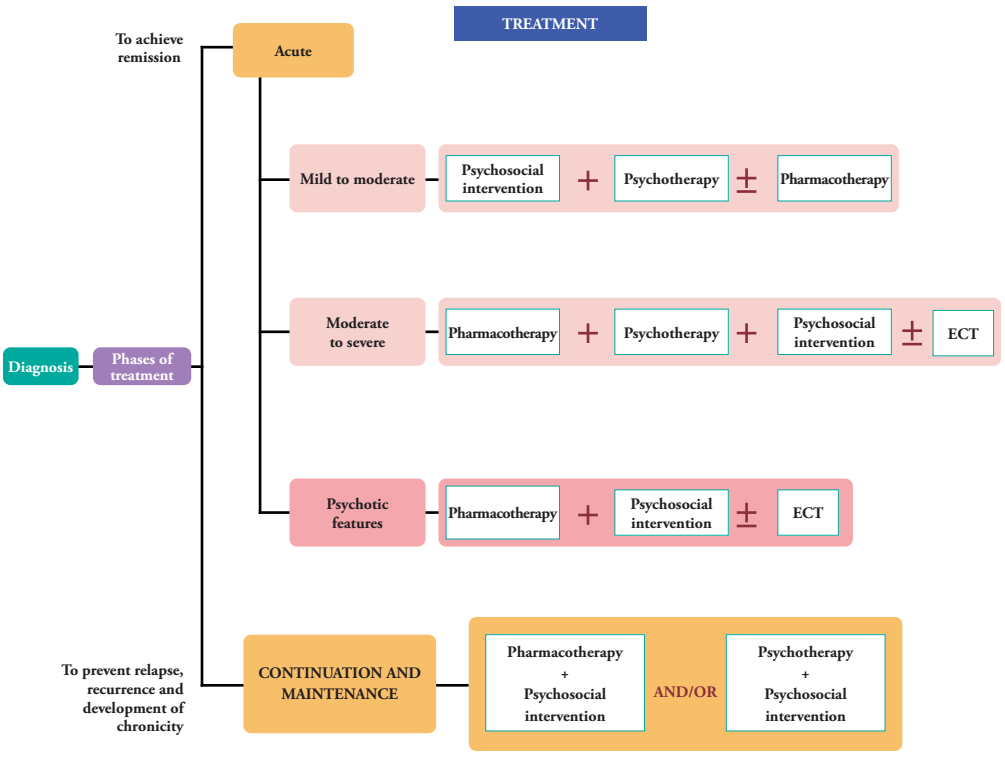
These symptoms have caused marked impairment in her academic functioning. Thus, she is diagnosed as having MDD with mild to moderate severity in acute phase and can be treated in primary care.

Severity according to DSM-5
- Mild depression
  - Five or more symptoms are present, which cause distress but are manageable
  - Result in minor impairment in social or occupational functioning
- Moderate depression
  - Symptom presentation and functional impairment between 2 severities
- Severe depression
  - Most of the symptoms are present with marked impairment in functioning

Question 5
What can be offered to this patient?

Answer 5
Psychosocial interventions and psychotherapy with or without pharmacotherapy.[5]
(Refer to Algorithm 1. Treatment of Major Depressive Disorder, page xii in CPG)

ALGORITHM 1. TREATMENT OF MAJOR DEPRESSIVE DISORDER



ECT = electroconvulsive therapy

Psychosocial interventions include the following:

a. Psychoeducation is an important part of psychosocial intervention. It consists of topics on[5]:
   - symptoms and course of depression
   - biopsychosocial model of aetiology
   - pharmacotherapy for acute phase and maintenance
   - drug side effects and complications
   - importance of medication adherence
   - early signs of recurrence
   - management of relapse and recurrence

b. Other components of psychosocial intervention include[5]:
   - counselling/non-directive supportive therapy – aims to guide the person in decision-making and allow to ventilate their emotions
   - relaxation – a method to help a person attain a state of calmness, eg. breathing exercise, progressive muscle relaxation, relaxation imagery
   - peer intervention – eg. peer support group
   - exercise – activity of 45-60 minutes per session, up to 3 times per week, and prescribed for 10-12 weeks
   - psychospiritual intervention – to address this treatment as part of biopsychosocial and spiritual model

   (Refer to subchapter 4.1.1, pages 9-12 in CPG.)

However, the doctor may choose to start antidepressant medication as an initial measure in some situations, for example:
- past history of moderate to severe depression
- patient's preference
- previous response to antidepressants
- lack of response to non-pharmacotherapy interventions

Question 6
What are the types of psychotherapy that can be offered in mild to moderate MDD, and what factors should be considered before starting psychotherapy?

Answer 6
Psychotherapy for the treatment of MDD has been shown to reduce psychological distress and improve recovery through the therapeutic relationship between the therapist and the patient.

In mild to moderate MDD, psychosocial intervention and psychotherapy should be offered, based on resource availability, and may include but are not restricted to the following[5]:
- Cognitive behavioural therapy (CBT)
- Interpersonal therapy
- Problem-solving therapy
- Behavioural therapy
- Internet-based CBT

The type of psychotherapy offered to the patient will depend on various factors, including[5]:
- patient preference and attitude
- nature of depression
- availability of trained therapist
- therapeutic alliance
- availability of therapy

(Refer to Subchapter 4.1.1, page 17 in CPG.)

After shared-decision making, Tini receives psychosocial intervention, that includes:
- psychoeducation
- non-directive supportive therapy
- exercise
- lifestyle modification, e.g. restoring healthy sleep hygiene and adopting healthy eating habits
- relaxation, e.g. progressive muscle relaxation, imagery and breathing technique

Tini will benefit from CBT due to her multiple unhelpful thoughts, for example, "I'm a failure" and "I'm useless".

CBT helps improve understanding of the impact of a person's unhelpful thoughts on current behaviour and functioning through cognitive restructuring and a behavioural approach. By learning to correctly identify these negative thinking patterns, Tini can then challenge such thoughts repeatedly to replace disordered thinking with more rational, balanced and healthy thinking. However, she is not able to commit to regular sessions of CBT due to a demanding academic schedule and upcoming final examination. After further discussion, Tini opts for pharmacotherapy.

Question 7
What are the options for pharmacotherapy?

Answer 7
The choice of antidepressant medication will depend on various factors, including

efficacy and tolerability, patient profile and comorbidities, concomitant medications and drug-drug interactions, cost and availability, as well as the patient's preference. Taking into account efficacy and side effect profiles, most second-generation antidepressants, namely selective serotonin reuptake inhibitors (SSRIs), serotonin noradrenaline reuptake inhibitors (SNRIs), noradrenergic and specific serotonergic antidepressants (NaSSAs), melatonergic agonist and serotonergic antagonist, noradrenaline/dopamine-reuptake inhibitors (NDRIs) and a multimodal antidepressants may be considered as the initial treatment medication, while the older antidepressants such as tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs) may be subsequently considered for a later choice.[5] (Refer to Subchapter 4.1.2, page 18 in CPG.)

Since Tini is being seen at a health clinic, the widely available SSRIs are sertraline and fluvoxamine. Sertraline has fewer gastrointestinal side effects and drug interactions compared with fluvoxamine. TCAs are not the treatment of choice due to prominent side effects. Tini is put on tablet sertraline 50 mg daily and educated on the anticipated onset of response and possible side effects. Short-term and low dose benzodiazepine, eg. alprazolam or lorazepam, may be offered as an adjunct to treat her insomnia. (Refer to Subchapter 4.1.2, page 24 in CPG.) Tini is given tablet lorazepam 0.5 mg at night for 2 weeks. She is asked to come in for a follow-up.

Question 8
What is her follow-up and monitoring plan?

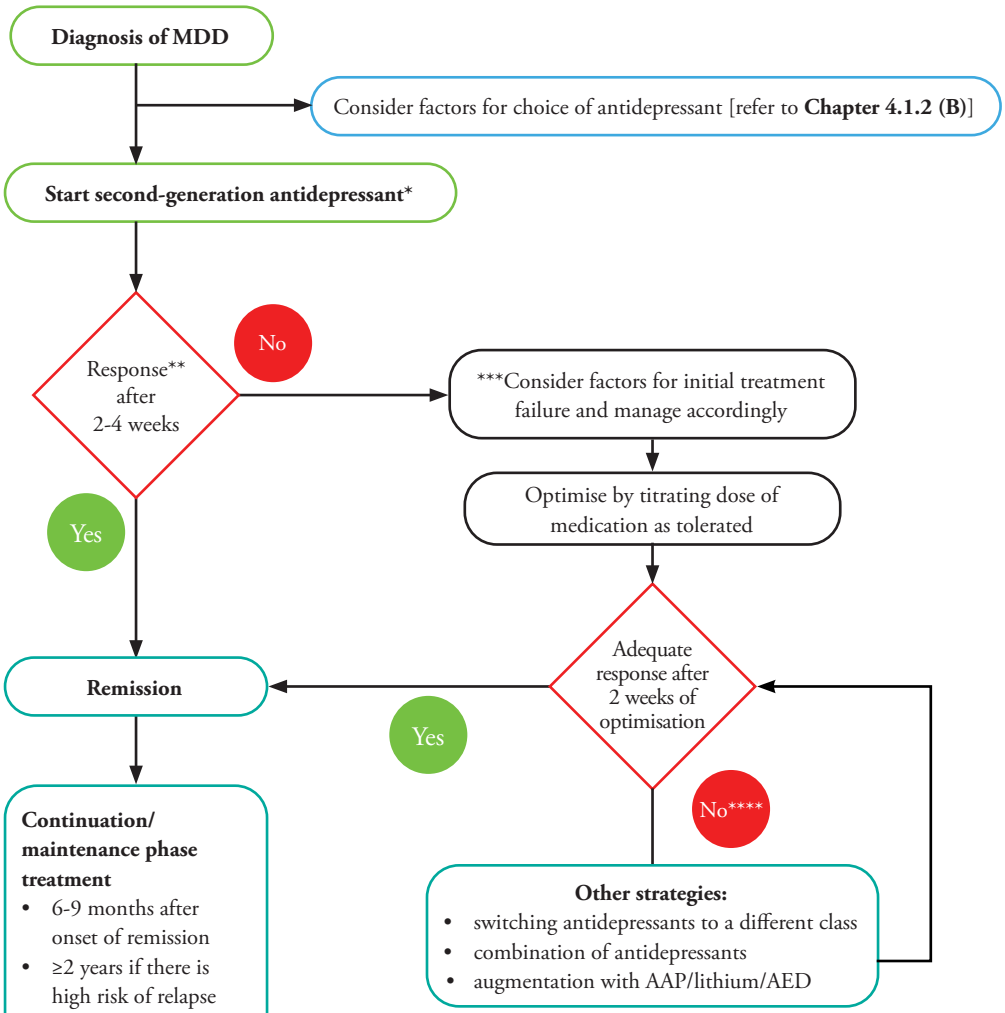
Answer 8
The following should be done:

- Review response and tolerability on follow-up within 2 weeks (Refer to Appendix 8, page 81 in CPG.)
- Titrate up by 50 mg within 1-2 weeks (but may be done earlier based on clinical judgement)
- Monitor biological parameters if indicated (Refer to Table 5. Ongoing monitoring during treatment of MDD, page 57 in CPG.)

During follow-up at 2 weeks, she is noted to show partial response despite being compliant with good tolerability. She is not experienceing nausea, diarrhoea, headache, constipation, dry mouth or somnolence. She reports being less tearful. Her sleep and ability to focus have improved. Tini has started engaging in regular exercise and practises relaxation, especially before sleep. Tablet sertraline is optimised to 100 mg daily, while tablet lorazepam is reduced to 0.5 mg PRN.

Tini is reviewed again within 4 weeks; during this subsequent follow-up, she achieves full remission. Tablet lorazepam is stopped. She is then advised to continue tablet sertraline for at least 6-9 months in maintenance phase. The aim in this phase is to prevent relapse and recurrence of MDD. In view of her young age, no comorbidities and good tolerability, repeated electrolyte monitoring is not indicated.
(Refer to Algorithm 2. Pharmacotherapy for Major Depressive Disorder, page xiii in CPG.)

ALGORITHM 2. PHARMACOTHERAPY FOR MAJOR DEPRESSIVE DISORDER



*Second-generation antidepressants: SSRIs, SNRIs, NaSSAs, melatonergic agonist and serotonergic antagonist, multimodal antidepressants and NDRIs
Refer to **Chapter 3
***Consider:
- Incorrect diagnosis (e.g. failure to diagnose bipolar disorder)
- Psychotic depression
- Organic conditions (e.g. anaemia or hypothyroidism)
- Co-morbid psychiatric disorder (e.g. substance abuse or dependence, panic disorder, obsessive-compulsive disorder and personality disorder)
- Adverse psychosocial factors
- Non/poor compliance

****Consider referral to psychiatrist

MDD = major depressive disorder
AAP = atypical antipsychotics
AED = antiepilectic drugs
SSRIs = selective serotonin reuptake inhibitors
SNRIs = serotonin norepinephrine reuptake inhibitors
NaSSAs = noradrenergic and specific serotonergic antidepressants
NDRI = norepinephrine/dopamine-reuptake inhibitors

References

1. World Health Organization. The global burden of disease: 2004 updated. 2008. Jan 19, 2021. https://apps.who.int/iris/bitstream/handle/10665/43942/9789241563710_eng.pdf

2. Kessler RC, Bromet EJ. The epidemiology of depression across cultures. Annu Rev Public Health. 2013;34:119-138. doi:10.1146/annurev-publhealth-031912-114409

3. World Health Organization. Depression and other common mental disorders: global health estimates. Geneva: WHO; 2017.

4. Judd LL, Akiskal HS, Zeller PJ, et al. Psychosocial disability during the long-term course of unipolar major depressive disorder. *Arch Gen Psychiatry*. 2000;57(4):375–380. doi:10.1001/archpsyc.57.4.375

5. Ministry of Health, Malaysia. CPG management of major depressive disorder. 2nd ed. Putrajaya: MoH; 2019.

6. American Psychiatric Association. Diagnostic and statistical manual of mental disorders (DSM-5). 5th ed. Arlington: American Psychiatric Association; 2013.

7. World Health Organization. ICD-10 classification of mental and behavioural disorders: clinical descriptions and diagnostic guidelines. Geneva: WHO; 1992.