INTRODUCTION

Depression is a common psychiatric disorder with a reported lifetime prevalence rate between 8-16 per cent. It is associated with increased healthcare cost and disability. In primary care, it is more common in women, with the ratio varying from 1.5:1 to 2.6:1. However, recent trends show that the rates of depression are increasing with an earlier age of onset and some narrowing of the sex difference. The prevalence in pre-pubertal children is equal in boys and girls and increases to a 2:1 female-to-male ratio in adolescents. In Malaysia, a rural survey on psychiatric illness showed that depressive disorders were the commonest psychiatric illnesses identified with a point prevalence rate of 3.6%. The prevalence of depression among the elderly, when assessed using rating scales, was reported as 6.3 per cent and 13 per cent. The prevalence was also noted to be higher in the presence of underlying physical problems and during the post partum period.

CLINICAL SPECTRUM OF DEPRESSION

The core symptoms of depressive disorder include depressed mood, inability to experience pleasure, a sense of helplessness, hopelessness, guilt and inhibition of behaviour and thinking. Other features that impair the social and occupational functioning include fatigue, anxiety, apathy and sometimes hostility towards self or others. In many patients, somatic symptoms are common; these are changes in sleep (either increased or decreased), appetite (increased or decreased), weight (increased or decreased) and loss of libido. Table 1 summarises the Diagnostic and Statistical Manual fourth edition (DSM-IV-TR) criteria for different types of depression in adults.

Some people with depression may experience unexplained pain, which is one of the reasons they go to their primary care physicians complaining of physical symptoms (e.g. musculoskeletal pain and fatigue) instead of saying that they are depressed. This is perceived as a more acceptable and less stigmatised reason to seek help. Therefore somatic complaints are ways of communicating any underlying distress.

Major depressive disorder

Major depressive disorder can be classified as mild, moderate or severe. Mild major depressive disorder refers to a condition where few symptoms present and result in minor impairment in social or occupational functioning.
Severe major depressive disorder would have several symptoms and these symptoms markedly interfere with social and occupational functioning. Presence of psychotic features and suicidal ideation or attempts indicates severe major depressive disorder. The clinical features and functional impairment of moderate major depressive disorder fall in between mild and severe.

**Adjustment disorder**

Adjustment disorder is a common condition with a prevalence between 12-23 per cent and is usually characterised by mild depressive symptoms, anxiety symptoms, traumatic stress symptoms or a combination of these. The commonest is adjustment disorder with depressed mood which is self-limiting, once the stressor is over. If the stressor lasts for several years, there is a risk of developing more serious psychiatric disorder such as major depressive disorder, schizophrenia, schizoaffective disorder, bipolar disorder, alcohol dependence and drug use disorder within five years. Among the disorders, major depressive disorder and alcohol dependence are common and the co-morbidity of these two conditions is high. Hence, adjustment disorder may represent a sub-threshold clinical syndrome or a precursor to a more severe psychiatric disorder.

### Table 1: Clinical features of depressive disorders based on DSM-IV-TR criteria

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Clinical features</th>
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<tbody>
<tr>
<td>Adjustment disorder with depressed mood</td>
<td>Depressed mood, tearfulness or feelings of hopelessness occurring within 3 months of the onset of the stressor. May present with impairment in social or occupational functioning.</td>
</tr>
</tbody>
</table>
| Major depressive disorder       | Five or more of the following symptoms have been present during the same 2 week period representing a change from previous functioning:  
  1. Depressed mood  
  2. Loss of interest or pleasure  
  3. Insomnia or hypersomnia  
  4. Significant weight loss or weight gain  
  5. Psychomotor agitation or retardation  
  6. Fatigue or loss of energy  
  7. Feelings of worthlessness or inappropriate guilt  
  8. Diminished ability to think or concentrate  
  9. Recurrent thoughts of death or suicide attempts   
  Either (1) or (2) must be present. Severe major depressive disorders would present with suicidal ideation and/or psychotic features.  
  Melancholic features include loss of pleasure, lack of reactivity to usually pleasurable stimuli, depressed mood and depression regularly worse in the morning, early morning awakening (at least 2 hours before usual time of awakening), marked psychomotor retardation or agitation, significant anorexia or weight loss and excessive or inappropriate guilt.  
  Atypical features include mood reactivity (i.e. mood brightens in response to potential positive events), increase in appetite, weight gain, hypersomnia, leaden paralysis (heavy feelings in arms and legs) and a long-standing pattern of interpersonal rejection sensitivity (not limited to episodes of mood disturbance) that results in significant social or occupational impairment. |
| Dysthymia                       | Depressed mood for most of the days for at least a 2-year duration. Two or more of the following symptoms present while depressed:  
  1. poor appetite or overeating  
  2. insomnia or hypersomnia  
  3. low energy or fatigue  
  4. low self esteem  
  5. poor concentration or difficulty making decisions  
  6. feelings of hopelessness   
  In children or adolescents, mood can be irritable and the duration must be at least for 1 year. |
| Bipolar disorder: Most recent episode depressed | Currently fulfils the criteria for major depressive disorder and there has been at least one episode of mania in the past. |
| Postpartum onset                | Onset of depressive episode within 4 weeks postpartum. May be associated with psychotic features. |

### Depression in children and adolescents

In children and adolescents, depression is frequently unrecognised and the presentation varies with age. Preschoolers express feelings of sadness in their behaviour such as apathy, being withdrawn or failure to thrive without any organic cause. School-aged children would display poor...
academic achievements, low self esteem, somatic complaints, anxiety symptoms and behavioural problems. Adolescents would exhibit more anhedonia, hypersomnia, weight change and substance abuse.\(^5\)

**Depression in elderly**

Depression in the elderly can be difficult to detect because some of the symptoms overlap with symptoms of physical illness and at times, the clinical presentation is atypical and vague.\(^14\) Another possible reason is our own age-related bias especially among young physicians who often view depression in the elderly as a normal reaction to serious illness or disability.\(^14\) e.g. it is understood to feel depressed when an elderly person is sick, which makes the case seem as a ‘normal’ depression rather than ‘clinical’ depression. As a result, no proper assessment would be made.

**Other types of depression**

DSM-IV-TR mentions other types of depression and these are briefly mentioned below. In dysthymia, there are fewer symptoms than major depressive disorder but the duration is for more than one year for an adolescent and two years for adults. If a patient had at least one episode of mania in the past, and is currently depressed, then the diagnosis of bipolar disorder in depressed phase is made. Diagnosis of postpartum depression is made if the onset of depression is within 4 weeks of postpartum. Clinical features are similar to depression and guilt concerning babies is common.

**Grief reaction**

Another condition which shares some of the major depressive disorders features is grief reaction. Grief can be due to the death of loved ones or reaction towards terminal illness.\(^15\) Grief reaction in the terminally ill patient where the patient is preparing himself for his final separation from this world is known as preparatory grief or anticipatory grief reaction.\(^15\) Grief and depression can be differentiated clinically although some symptoms overlap.\(^16\) There will be a temporal variation of mood in grief, i.e. a mixture of ‘good and bad’ days, in contrast to persistent dysphoria in depression. Guilt feelings in grief will be focused on certain issues and not generalised as in depression. A disturbed self esteem or sense of hopelessness is not typically seen in grief and hope in a grieving patient may shift but not be lost. Therefore, the desire for an early death or suicidal ideation is highly suggestive of depression. In a grieving person, social support helps in providing acceptance and assistance. In depression, social support is helpful in some depressed patients but it will not resolve depression. The inability to feel pleasure (anhedonia) is characteristic of depression and it is absent in grief reaction.

**Case vignettes**

The following case vignettes illustrate the different presentation of depression.

**Case 1**

Ms A, a 26-year-old ex-clerk, was admitted to hospital with a four-month history of feeling low after she broke up with her boyfriend. She became increasingly sad and unable to concentrate on her work. She felt tired easily and was unable to get up in the morning. She finally quit her job two months ago. She lost about eight kg within four months. She had lost interest in most things. Her mother noticed that whenever she was alone, she would just stare and appeared blank. She had been quieter and lately she refused to come out from her room. She needed supervision for her personal hygiene and her mother had to coax her to eat. For the past two weeks, she repeatedly told her mother that “I am going to die. My body has no blood and the heart is getting weaker”.

**Case 2**

Ms B, a 30-year-old hairdresser had been referred to the clinic after she had broken down in tears in front of her clients for the third time in a week. Three weeks ago, her boyfriend of four years decided to break off their relationship. She said that she was in a state of shock for three days and gradually managed to pull herself together. She still thinks about her boyfriend and finds it difficult to focus on her work. She felt constantly on the verge of crying. She had some difficulty falling asleep but her appetite remained the same. Her main fear was the prospect of being alone.

**Case 3**

Mrs C, a 35-year-old lady complained of frequent episodes of headache and back pain for the past four years. It started after her husband left her. The pain became worse last year after her eldest son left the house. She experienced the pain almost everyday and she was not able to work. She also had poor sleep due to pain. She could not carry out household chores as she felt tired easily. She spent most of her time lying on the bed. She was seen by a number of doctors of different specialty and thorough investigations were made. There was no organic cause for the headache and back pain. Her pain was not relieved by analgesics. On further questioning, she fulfilled the criteria of major depression.

**Case discussion**

Although all patients develop depression following a break off in their relationships, the presenting features are not the same. Ms A fulfils the criteria for severe major depression with psychotic features as she presented with nihilistic delusion. She could not function socially as well as occupationally. On the other hand, Ms B presents with depressive features which are not severe enough to qualify the diagnosis of major depression and since her functioning is affected, a diagnosis of adjustment disorder with depressed mood is warranted. Ms B can progress to major depression if she continues having a maladaptive reaction to the situation. Mrs C presented with somatic complaints
which had no organic cause. Mrs C is more likely to be suffering from major depression and the diagnosis was missed when she first presented to the clinic. In a primary care setting, presenting complaints of depression are more likely to be somatic such as back pain, chest pain, shortness of breath, heart palpitations, problems with sleep or appetite and fatigue.17

SCRENNING FOR DEPRESSION

Clinical interviews are important in assessing depression. A good interview will retrieve information for further action and at the same time establishes a good doctor-patient relationship.18 The assessment must include finding symptoms to diagnose depression and the impact it has on the patient's life.

Screening questions for depression6 include:

- How have you been feeling recently?
- Have you been low in spirits?
- Have you been able to enjoy the things you usually enjoy?
- Have you had your usual level of energy, or have you been feeling tired?
- How has your sleep been?
- Have you been able to concentrate on newspaper articles or television or radio programmes?

The final step would be focusing on the patient’s personality and excluding other conditions which may affect the outcome. Some cases may not be clear-cut. Perhaps a few specific questions at the end of the interview may help further clarify the diagnosis of depression18 such as:

- Do you have any trouble with your nerves, sleep or appetite?
- Does your mood fluctuate during the day?
- Do you still gain enjoyment from life?
- Do you still take an interest in everyday events?
- Are you inclined to ruminate?
- Do you find it difficult to make decisions?

Another simple way to assess would be a careful inquiry into the mnemonic SIGECAPS – Sleep, Interest, Guilt, Energy, Concentration, Appetite, Psychomotor Function and Suicide.19 Symptoms such as poor sleep, low energy or poor appetite are non-specific as they can be seen in patients with underlying medical problems. Therefore, any positive answer should be probed further. If depression is confirmed or suspected, further assessment of suicide risk must be made. The expression of a ‘wish to die’ is the best indicator of high suicide risk. Other indicators include previous attempts, family history of suicide, a suicide plan, recent attempts and leaving a suicide note or if it was carefully prepared with precautions against discovery and/or highly lethal. In addition, other factors that increases the risks include older age, male gender, unemployment, social isolation and chronic medical illnesses.

Apart from questioning, rating scales can be used to screen for depression. Table 2 summarizes the different types of questionnaires that are easy to administer in primary care clinics.

### Table 2. Screening tools for depression

<table>
<thead>
<tr>
<th>Tools</th>
<th>Address12</th>
<th>Rating / Purpose</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Health Questionnaire (PHQ)</td>
<td>Dr Robert L. Spitzer, Columbia University, 1051 Riverside Drive, New York, NY 10032, USA</td>
<td>Self-report. To screen for depression in primary care.</td>
<td>Adults and adolescents</td>
</tr>
<tr>
<td>Patient Health Questionnaire 9 (PHQ-9)</td>
<td><a href="http://www.pfizer.com/phq-9">www.pfizer.com/phq-9</a></td>
<td>To screen for depression in primary care.</td>
<td>Adults</td>
</tr>
<tr>
<td>Hamilton Depression Rating Scale (HDRS or Ham-D)13</td>
<td>Public Domain</td>
<td>Clinician rated. To assess severity of depression and change in symptoms.</td>
<td>Adults</td>
</tr>
<tr>
<td>Geriatric Depression Scale (GDS)16</td>
<td>Dr Jerome Yesavage, Stanford University School of Medicine, Stanford, CA 94305-5548, USA</td>
<td>Self report. To assess depression in older adults.</td>
<td>People aged ≥65 years</td>
</tr>
</tbody>
</table>

**Patient Health Questionnaire**

Patient Health Questionnaire 9 (PHQ-9) is useful in screening for depression. It is a self report questionnaire and consists of nine items looking at depressives symptoms over the previous two weeks plus one question concerning functional impairment20. A shorter version is known as Patient Health Questionnaire 2 (PHQ-2) which consists of two items with ‘yes’ or ‘no’ response. It can be used as a screening tool for depression and intended for use with PHQ-9 if PHQ-2 is ‘positive’ (‘yes’ to either question).21 The Malay version is also available and validated but the sensitivity and specificity of the tool is quite low. The possible explanation
is the different understanding and cultural variation of depression between the study sample and Western population.\textsuperscript{23}

**Hamilton Depression Rating Scale**
The Hamilton Depression Rating Scale (HDRS) is a clinician-administered scale to assess the severity of depressive symptoms. The original version has 17 items\textsuperscript{14} and a later version has 21 items which include the subtype of depression. The limitation of this scale is that it does not assess the atypical symptoms of depression e.g. hypersonnia or hyperphagia. Other versions include HDRS-29, HDRS-8, HDRS-6, HDRS-24 and HDRS-7.\textsuperscript{22}

**Geriatric Depression Scale**
Geriatric Depression Scale (GDS) is a simple self report scale to assess depression in the elderly.\textsuperscript{25} The original version has 30 items with 'yes' or 'no' response. Other shorter versions are GDS 15, GDS 10 and GDS 4.\textsuperscript{22} The Malay version (M-GDS-14) is translated from GDS 15. However, it only has 14 items as item-9 from the Malay version was omitted as it does not have discriminatory value in differentiating cases from non-cases.\textsuperscript{26}

If the same rating scale is administered repeatedly to the same patient, it can be used to assess that patient's progress.

**Co-morbidity**
Depression is often seen in patients with chronic medical problems, e.g. chronic pain, sleep disorders, diabetes, stroke, malignancies, endocrine problems particularly thyroid disorders and other psychological disorders such as anxiety,\textsuperscript{12} eating disorders, dementia and schizophrenia. More than 75 per cent of patients diagnosed with depression in a primary care setting also suffer from anxiety disorder\textsuperscript{17} which could be one of the following:

- Patient fulfils the criteria for major depressive disorder but suffers subsyndromal levels of anxiety symptoms.
- Patient fulfils the criteria for anxiety disorder but suffers subsyndromal levels of depressive symptoms.
- Patient fulfils the criteria for both, i.e. anxiety and depressive disorders.
- Patient presents with both symptoms but these symptoms are not severe enough to fulfill the criteria.

Apart from that, co-morbidity with substance abuse is also common. Treatment for the underlying medical disorders can contribute to the development of depression as well. Some of the medications that may cause or worsen depression\textsuperscript{27} include beta-blockers, interferons, phenytoin, calcium channel blockers, corticosteroids, indomethacin, histamine-2 blockers, narcotics, cytotoxic drugs, etc. Screening for underlying medical problems is important for late onset depression especially in the absence of family history.\textsuperscript{27}

Depression can precipitate and exacerbate chronic illness, and vice versa.\textsuperscript{28} Presence of a psychosocial stressor for depression in a medical patient should never mitigate treatment; as Stewart JT quoted in his paper "this is similar to withholding morphine for severe chest pain once a myocardial infarction was diagnosed".\textsuperscript{14} Generally, depressive disorders assume an important role in the aetiology, course and outcome associated with chronic disease.\textsuperscript{29}

**References**

Rosiglitazone and cardiovascular risks: three meta-analyses from three journals

The DREAM trial\(^1\) showed that rosiglitazone substantially reduced risk of diabetes among adults with impaired fasting glucose or impaired glucose tolerance. The publication of this trial in 2006 raised many questions about the potential cardiovascular risk of rosiglitazone. By the end of 2007, at least three meta-analyses have examined this issue. The gists of the findings are:

- Rosiglitazone was associated with an increased risk of myocardial infarction (OR 1.43, 95% CI 1.03 to 1.98; p=0.03).\(^2\)
- Thiazolidinediones (rosiglitazone and pioglitazone) were associated with an increased risk for development of congestive heart failure (RR 1.72, 95%CI 1.21 to 2.42, p=0.002).\(^3\)
- Rosiglitazone significantly increased the risk of myocardial infarction (RR 1.42, 95%CI 1.06 to 1.91, p=0.02) and heart failure (RR 2.09, 95%CI 1.52 to 2.88, p<0.001).\(^4\)

There are some differences in the methodology in the above three meta-analyses (number of included studies were 42, 7 and 4, respectively). Interestingly, none of them found an increase in cardiovascular mortality for rosiglitazone.

1. The DREAM Trial Investigators. Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial. Lancet. 2006;368(9541):1096-105
Appendix 1: Hamilton Depression Rating Scale

<table>
<thead>
<tr>
<th>Patient Name: _________________________</th>
<th>Date: (dd/mm/yy) ___ / ___ / ____</th>
<th>Rater: _________________________</th>
</tr>
</thead>
</table>

1. Depressed Mood
   0. Absent
   1. These feeling states indicated only on questioning.
   2. These feeling states spontaneously reported verbally.
   3. Communicates feeling states non-verbally, i.e. through facial expression, posture, voice, and tendency to weep.
   4. Patient reports virtually only these feeling states in his spontaneous verbal and non-verbal communication.

2. Work and Activities
   0. No difficulty
   1. Thoughts and feelings of incapacity, fatigue or weakness related to activities, work or hobbies.
   2. Loss of interest in activities, hobbies or work-either directly reported by patient, or indirect in listlessness, indecision and vacillation (feels he has to push self to work or activities).
   3. Decrease in actual time spent in activities or decrease in productivity. In hospital rate 3 if patient does not spend at least three hours a day in activities (hospital job or hobbies) exclusive of ward chores.
   4. Stopped working because of present illness. In hospital rate 4 if patient engages in no activities except ward chores, or if patient fails to perform ward chores unassisted.

3. Genital Symptoms
   0. Absent.
   1. Mild.
   2. Severe.

4. Somatic Symptoms – GI
   0. None.
   1. Loss of appetite but eating without staff encouragement. Heavy feelings in the abdomen.
   2. Difficulty eating without staff urging. Requests or requires laxatives or medication for bowels or medication for GI symptoms.

5. Loss of Weight
   0. No weight loss.
   1. Probable weight loss associated with present illness.
   2. Definite (according to patient) weight loss.

6. Insomnia – Early
   0. No difficulty falling asleep.
   1. Complains of occasional difficulty falling asleep, i.e. more than ½ hour.
   2. Complains of nightly difficulty falling asleep.

7. Insomnia – Middle
   0. No difficulty.
   1. Patient complains of being restless and disturbed during the night.
   2. Waking during the night – any getting out of bed rates 2 (except for purposes of voiding).

8. Insomnia – Late
   0. No difficulty.
   1. Waking in early hours of the morning but goes back to sleep.
   2. Unable to fall asleep again if he gets out of bed.

9. Somatic Symptoms
   0. None.
   1. Heaviness in limbs, back or head. Backaches, headache, muscle aches. Loss of energy and fatigability.

10. Feelings of Guilt
    0. Absent.
    1. Self reproach, feels he has let people down.
    2. Ideas of guilt or rumination over past errors or sinful deeds.
    3. Present illness is a punishment. Delusions of guilt.
    4. Hears accusatory or denunciatory voices and/or experiences threatening visual hallucinations.

11. Suicide
    0. Absent.
    1. Feels life is not worth living.
    2. Wishes he were dead or any thoughts of possible death to self.
    3. Suicide ideas or gestures.
    4. Attempts at suicide.

12. Anxiety – Psychic
    0. No difficulty.
    1. Subjective tension and irritability.
    2. Worrying about minor matters.
    3. Apprehensive attitude apparent in face or speech.

13. Anxiety - Somatic
    0. Absent.
    1. Mild.
    2. Moderate.
    3. Severe.
    4. Incapacitating.

14. Hypochondriasis
    0. Not present.
    1. Self-absorption (bodily).
    2. Preoccupation with health.
    3. Frequent complaints, requests for help, etc.
    4. Hypochondriacal delusions.

15. Insight
    0. Acknowledges being depressed and ill.
    1. Acknowledges illness but attributes cause to bad food, climate, over work, virus, need for rest, etc.
    2. Denies being ill at all.

16. Motor Retardation
    0. Normal speech and thought.
    1. Slight retardation at interview.
    2. Obvious retardation at interview.
    3. Interview difficult
    4. Complete stupor

17. Agitation
    0. None.
    1. Fidgetiness.
    2. Playing with hands, hair, etc
    3. Moving about can’t sit still.
    4. Hand wringing, nail biting, hair pulling, biting of lips.

17-item HDRS TOTAL: __ __

Score of 0-7: within normal or in clinical remission
Score of 20 or above: at least moderate severity and usually required medication
P/s: Please cover the score and the interpretation when administer this questionnaire.