Depressive Disorders

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Major Depressive Disorder (MDD)

DSM-5 criteria for Major Depressive Episode

A. **Five (or more)** of the following symptoms during the same **two week period** and represent a **change from previous functioning**, at least **one of the symptoms is (1) depressed mood or (2) loss of interest or pleasure**

1. **Depressed mood** most of the day, nearly every day
2. Marked **diminished interest or pleasure**
3. **Significant weight loss** when in all, or almost all, activities, most of the day, nearly every day.
4. **Insomnia or hypersomnia**
5. **Psychomotor agitation or retardation**
6. **Fatigue** or loss of energy
7. Feelings of **worthlessness or excessive or inappropriate guilt**
8. Diminished ability to **concentrate** or **indecisiveness**
9. Recurrent thoughts of **death**, recurrent **suicidal** ideation, suicide **attempt** or plan

B. The symptoms cause **significant distress or impairment** in functioning

C. The episode is **not attributable to** the physiological effects of a substance or another medical condition

D. The occurrence is **not better explained by another mental disorder**

E. There has **never been a manic episode or a hypomanic episode**

Notes

- Depressed **mood**, either;
  - **Subjective** report (sad, depressed, empty, hopeless, discouraged, down in the dumps) or
  - **Observed** by others (apparent tearful)

Other symptoms

- Boredom
- Tearful
- Irritability
- Anxiety or phobia
- Excessive worries about physical health
- Pain
- Menstrual problems
- Sexual dysfunction, decrease interest in sex

In children & adolescents

- Mood can be **irritable** mood
- Children may refer to depressive feelings in terms of **anger**, or feeling "**mad**" rather than sad
- Children tend to present with **somatic symptoms**
- Can have **failure to make expected weight gain** rather than weight loss

In elderly

- Symptoms of **depression are not part of normal aging**
- Symptoms compared to adult:
  - **Minimize** sadness
  - more **agitation**
  - **Higher rate of completed suicide** and **more lethal methods**

Specifiers

"With Psychotic Features" Specifier

Delusions and or hallucinations are present:

- **Mood-congruent psychotic features**: content of the delusions and hallucinations consistent with depressive themes (guilt, inadequacy, nihilism, etc.)
- **Mood-incongruent psychotic features**: does not involve typical depressive themes

"With melancholic features" Specifier

A. **One** of the following:
   1. **Loss of pleasure** in all or almost all activities.
   2. **Lack of reactivity** to usually pleasurable stimuli (does not feel better even temporarily when something good happens)

B. **Three (or more)** of the following:
   1. Distinct quality of mood (profound despondency, despair, empty mood)
   2. Depression is worse in the morning
   3. Early morning awakening (at least 2 hours before usual awakening)
   4. Marked psychomotor agitation or retardation
   5. Significant anorexia or weight loss
   6. Excessive or inappropriate guilt

- Melancholic features are more frequent in:
  - **Inpatients**
  - More **severe** depressive episodes
  - Those with **psychotic** features
  - **Older** individuals

"With atypical features" Specifier

A. Mood **reactivity** (mood brightens in response to positive events)
B. Two (or more) of the following:
    1. Significant weight gain or increase in appetite
    2. Hypersomnia
    3. Leaden paralysis (heavy, leaden feelings in arms or legs)
    4. Longstanding pattern of interpersonal rejection sensitivity causing functional impairment

C. Criteria are not met for "with melancholic features" or "with catatonia"

- Atypical features may be **more common in Bipolar Depression** than MDD

- Compared with patients with typical depression features, **the patients with atypical features are**;
  - found to have a **younger** age of onset
  - have **long-term course**
  - more frequent **coexisting diagnoses** of panic disorder, substance abuse or dependence, and somatization disorder

"With catatonia" Specifier

- 3 (or more) of the following symptoms:
  - Stupor (no psychomotor activity)
  - Catalepsy (passive induction of a posture held against gravity)
  - Waxy flexibility (slight resistance to positioning by examiner)
  - Mutism
  - Negativism (no response to instructions or external stimuli)
  - Posturing (spontaneous adoption of posture against gravity)
  - Mannerism (odd caricature of normal actions)
  - Stereotypy (repetitive, abnormal non-goal directed movements)
  - Agitation
  - Grimacing
  - Echolalia
  - Echopraxia (mimicking another's movements)

"With peripartum onset" Specifier

If mood symptoms occur **during pregnancy** or **in the 4 weeks following delivery**

Epidemiology

- MDD is **among the leading causes of global disability**

- Prevalence in adults:
  - Lifetime: approximately 10 to 17 %
  - 12-Month: approximately 4-7 %
  -
- Gender:
  - In adult: 1.5-3:1 **F**:M ratio
  - Age of Onset: Incidence **peaks in 20s,** likelihood increases markedly after puberty**,** but can still have first onset in late life (onset **later than for BAD**)

Differential Diagnosis

- **Medical Conditions:** especially
  - Hypothyroidism
  - Cushing's Disease or Addison's disease
  - Anemia, Vitamin B12 or Folate Deficiency
  - Infectious Etiology: Mononucleosis, HIV, etc.
  - Pancreatic cancer, brain tumors and other neoplasms
  - Epilepsy
  - CVA
  - Multiple Sclerosis
  - Parkinson's Disease

- **Substance Induced:**
  - Stimulants withdrawal: Amphetamine, MDMA, Cocaine
  - Sedatives: Alcohol, benzodiazepines, barbiturates
  - Medications induced

- **Normal Sadness**
- **Grief**
- **Adjustment Disorder with Depressed Mood**
- **Dysthymia**
- **Bipolar I and Bipolar II Disorder**
- **Schizoaffective Disorder**
- **ADHD (Attention deficit hyperactivity disorder)**
- In elderly: also consider: electrolyte imbalance, glucose abnormality, and pain

Grief vs. MDD

- In Grief:
  - Affect is **feelings of emptiness and loss**
  - **Dysphoria** likely **decrease in intensity over days to weeks**
  - Functional **impairment** is usually **transient**
  - May be accompanied by **positive emotions and humor**
  - In grief, **self-esteem is usually preserved**
  - If thoughts about death and dying, limited to **thoughts of joining the deceased** but **not on ending one's life because of worthlessness or pain of depression**
  - Survivor **does not have** morbid feelings of **guilt** and **worthlessness, suicidal ideation ,** or **psychomotor retardation**

Adjustment Disorder Vs. Major Depressive Disorder

- Adjustment disorder:
  - Some symptoms overlap
  - Doesn't involve as many of the physical and emotional symptoms of clinical depression
  - Less levels of severity

Schizoaffective Disorder Vs. MDD

DSM-5 criteria for schizoaffective disorder:

A. An uninterrupted duration of illness during which there is a **major mood episode (manic or depressive) in addition to criterion A for schizophrenia;** the major depressive episode must include depressed mood.

- Criterion A for schizophrenia is as follows: Two or more of the following presentations, each present for a significant amount of time during a 1-month period (or less if successfully treated). At least one of these must be from the first three below.
    1. Delusions
    2. Hallucinations
    3. Disorganized speech
    4. Grossly disorganized or catatonic behavior
    5. Negative symptoms

B. **Hallucinations and delusions for two or more weeks in the absence of a major mood episode** (manic or depressive) during the entire lifetime duration of the illness.

C. Symptoms that meet the criteria for a major mood episode are present for the majority of the total duration of the active as well as residual portions of the illness.

D. The disturbance is not the result of the effects of a substance (e.g., a drug of misuse or a medication) or another underlying medical condition.

ADHD vs. MDD

In ADHD:

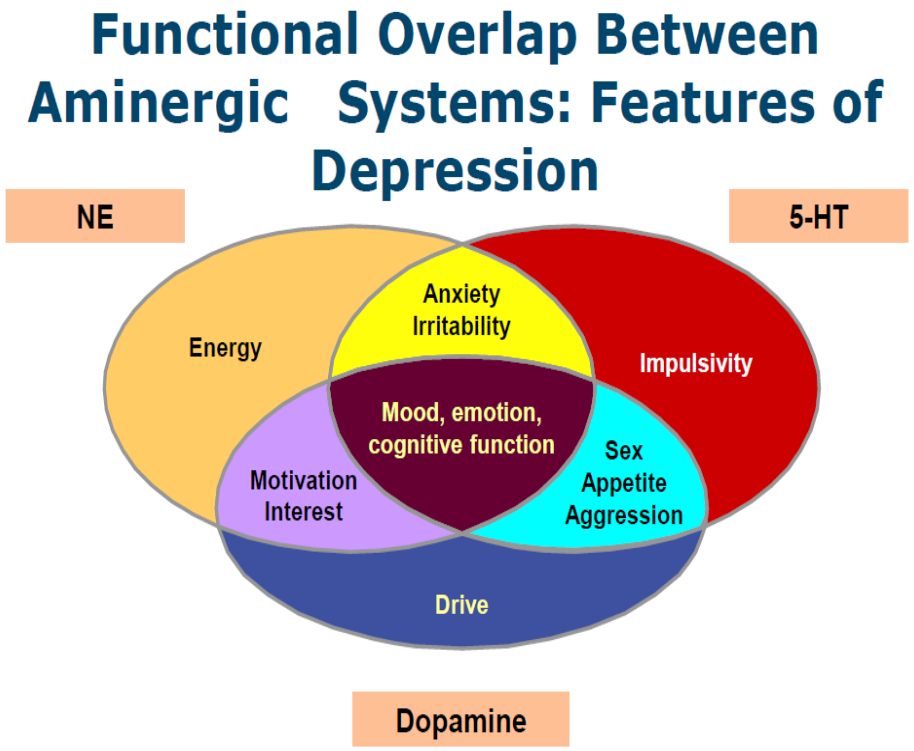
- Onset of clear-cut symptoms before age 7
- Onset of hyperactivity or disruptive behaviors
- Continuous
- Family history of disruptive disorders

Risk factors

Risk factors

- **Early-Onset Adversity**
- **Stressful Life Events**
- **Family History** (first degree relatives have 2-4x greater chance of having MDD)
- **Female** Gender
- **Neuroticism** (negative affectivity)
- Chronic **Medical Conditions**
- **Substance** use
- **Anxiety** Disorders
- Certain **personality disorders**

Depression & neurotransmitters



Courtesy of S.M. Stahl

Scales

Self-report scales, such as:

- Beck Depression Inventory II (BDI-II)
- Zung Self-Rating Depression Scale
- Patient Health Questionnaire (PHQ-9)
- Quick Inventory for Depressive Symptomatology, Self- Rated (QIDS-SR)

Clinician Rated Scale, such as:

- Hamilton Depression (HAM-D)
- Montgomery-Asberg Depression Assessment Scale (MADRAS)
- Inventory for Depressive Symptomatology (IDS)

Comorbidities

Comorbidities

- Substance Use Disorders
- Anxiety Disorders
- Eating Disorders
- Borderline Personality Disorder
- Attention-deficit/hyperactivity disorder (ADHD), Learning disabilities, oppositional defiant disorder, and conduct disorder

Men more frequently present with substance use disorders, *women more frequently present with comorbid anxiety and eating disorders*

Prognosis

- Untreated depressive episodes last 6 to 13 months, treated episodes last 3 months
- **Course is quite variable**, but 80% will recover within 1 year
- Can get both absenteeism and presenteeism at work
- **MDD increases the risk of** Type II diabetes and is an independent risk factor for cardiovascular disease and mortality
- Increased rates of emphysema, COPD, migraine, multiple sclerosis, back problems, cancer, epilepsy, asthma, stroke, thyroid disease, diabetes, and heart disease in patients with MDD

- Low recovery rates with:
  - Long duration of current episode
  - Symptom Severity
  - Psychotic features
  - Prominent anxiety
  - Personality Disorders

- Risk of Recurrence with:
  - Multiple prior episodes
  - Previous severe episode
  - Mild depressive symptoms persist during remission
  - Younger individuals

- Residual symptoms
  - **The least common residual symptoms are depressed mood, suicidality, and psychomotor retardation**

Depression and suicidality

- About **two-thirds** of all depressed patients **contemplate suicide** and **10 to 15 percent commit suicide**
- **Low concentrations of 5-HIAA (5-Hydroxyindoleacetic acid),** which is a serotonin metabolite, have been associated with suicidal behavior. Furthermore, low concentrations of 5-HIAA in the CSF also predicts the presence of future suicidal behavior.
- Several risk factors for suicide exist; **prior suicidality is the most significant risk factor.**

Management

Phases of treatment

Acute Phase

Goals:
remission of symptoms
restoration of functioning

Activities:
establish therapeutic alliance
educate and support
select and deliver evidence based treatment

Maintenance Phase

Goals:
return to full functioning and quality of life
prevention of recurrence

Activities:
educate
treat comorbidities
monitor for recurrence

Treatment Modalities

- Pharmacotherapy
- Psychotherapy
- Neurostimulation
- Others

Pharmacotherapy

Antidepressant choice based on multiple factors:

- Patient preference
- Past response
- Drug-drug interaction
- Comorbid Disorders
- Side-effect profile and tolerability
- Cost
- Availability

Length of Treatment:

- Risk factors supporting long-term (**2 years** to lifetime) antidepressant maintenance:
  - **Older** age
  - **Recurrent** episodes
  - **Chronic** episodes
  - **Psychotic** Episodes
  - **Severe** episodes
  - **Difficult to Treat** Episodes
  - Significant **Comorbidity** (psychiatric or medical)
  - **Residual** Symptoms
  - History of **recurrence during discontinuation** of antidepressant

Major medication classes

- **SSRI** (Selective serotonin reuptake inhibitors)
- **SNRI** (Serotonin–norepinephrine reuptake inhibitors)
  - VENLAFAXINE, DULOXETINE, and DESVENLAFAXINE
  - Might be associated with sexual side effects.
- **MAOIs** (Monoamine oxidase inhibitor)
- **TCA** (Tricyclic antidepressants)
- **Others**
  - Bupropion (norepinephrine-dopamine reuptake inhibitor) (less sexual side effects than SSRI and SNRI)
  - Mirtazapine (noradrenergic and specific serotonergic antidepressant) (less sexual side effects than SSRI and SNRI)
  - Trazadone (serotonin antagonist and reuptake inhibitor)
  - Other newer medications

- Adjunctive agents
  - Certain antipsychotics
  - Lithium
  - T_3
  - Stimulants
  - Others

SSRIs

- Selectively block reuptake of 5-HT
- Include:
  - Fluoxetine
  - Sertraline
  - Paroxetine
  - Fluvoxamine
  - Citalopram
  - Escitalopram
- Compared to MOIs and TCAs;
  - Less cardiotoxicity
  - More sexual dysfunction

- Side effects:
  - GI side effects (nausea, vomiting, diarrhea, appetite, weight)
  - headache
  - Insomnia
  - **Sexual dysfunction**
  - Agitation, restlessness, anxiety

- Other side effects:
  - Serotonin syndrome
  - Abnormal bleeding (Caution with anticoagulants, NSAIDs, ASA)
  - Cardiotoxicity (citalopram, escitalopram)
  - The syndrome of inappropriate antidiuretic hormone secretion (SIADH)

MAOIs

- Inhibit the metabolism of neurotransmitters DA, NE, 5-HT
- **Common uses:**
  - **Atypical depression**
  - Refractory patients
- **Most of the medications in this class, needs dietary monitoring**

Common side effects:

- Cardiovascular (orthostatic hypotension, peripheral edema)
- Weight gain
- Sexual side effects
- Neurological (headache, insomnia, sedation, paresthesias)
- Other (dry mouth, constipation, urinary hesitancy)

Other Side effects:

- **Hypertensive crisis**:
  - Hypertension, neurological symptoms, fever, nausea, palpitations, tachycardia, cardiac arrythmias, confusion
  - Possibly CVA and death
- **Serotonin syndrome**:
  - neurological symptoms, GI symptoms, restlessness, MSE changes, confusion, tachycardia, hypertension, fever
  - In severe form: Hyperthermia, rhabdomyolysis, renal failure, cardiovascular shock, coma, seizures, death

TCAs

- Affect multiple receptor systems
- Multiple side effects
- Several drug- drug interactions
- **Lethal in overdose** (**arrhythmias; seizures**)
- Helpful in cases of:
  - Pain
  - Fibromyalgia
  - Migraine
  - Sedative/hypnotic
  - Severe depression

- Side effects
  - Drowsiness, dizziness, falls, fracture
  - **Cardiac side effects**
  - Blurred vision, mydriasis (pupillary dilation)
  - Dry mouth
  - Constipation
  - Urinary retention
  - Memory impairment
  - Sexual dysfunction
  - Fever
  - Weight gain
  - Neurological side effects (myoclonus, confusional state, **seizure in overdose**)

Psychotherapy

- Several modalities exists

- Examples:
  - CBT (cognitive behavioural therapy)
  - IPT (interpersonal therapy)
  - Behavioural activation
  - Others

Neurostimulation

- Include:
  - ECT (electroconvulsive therapy)
  - rTMS (repetitive transcranial magnetic stimulation)
  - others

ECT

- A medical procedure that is delivered under controlled conditions. It involves the use of electrical stimulus to depolarize cerebral neurons thereby produce a generalized seizure

- **Helpful in;**
  - Elderly
  - Psychotic depression
  - Catatonia
  - Severe depression
  - Treatment resistant depression

  - **Important notes: ECT has other uses in psychiatry such as in schizophrenia**

rTMS

- Compared to ECT:
  - No anesthesia
  - No negative effects on neurocognitive functioning
  - No driving restrictions
- Used mainly for treatment resistant depression

Other therapies

- Exercise
- Light therapy
- Others: e.g.
  - St. John's Wort- mild to moderate depression
  - Thyroid hormone

Other Depressive Disorders

Persistent Depressive Disorder (Dysthymia)

A. **Depressed mood** for most of the day, for more days than not, as indicated by either subjective account or observation by others, **for at least 2 years**

B. **Presence, while depressed, of two (or more)** of the following:

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

C. During the 2-year period (1 year for children or adolescents) of the disturbance, the **individual has never been without the symptoms in Criteria A and B for more than 2 months at a time**

D. Criteria for a major depressive disorder may be continuously present for 2 years

E. There has **never been a manic episode or a hypomanic episode**, and criteria have **never been met for cyclothymic disorder**

F. The disturbance is **not better explained** by other mental illnesses such as schizoaffective disorder, etc.

G. The symptoms are **not attributable** to the physiological effects of a substance (e.g., a drug of abuse, a medication) or another medical condition (e.g., hypothyroidism).

H. The symptoms cause **clinically significant distress or impairment** in social, occupational, or other important areas of functioning.

Substance/ Medication-Induced Depressive Disorder

Diagnostic Criteria

A. A prominent & persistent disturbance in mood that predominates in the clinical picture and is characterized by depressed mood or markedly diminished interest or pleasure in all, or almost all, activities.

B. There is evidence from the history, physical examination, or laboratory findings of both (1) and (2):
   - The symptoms in Criterion A developed during or soon after substance intoxication or withdrawal or after exposure to a medication.
   - The involved substance/medication is capable of producing the symptoms in Criterion A.

C. The disturbance is not better explained by a depressive disorder that is not substance/medication-induced.

D. The disturbance does not occur exclusively during the course of a delirium.

E. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Depressive Disorder Due to Another Medical Condition

Diagnostic Criteria:

A. A prominent and persistent period of depressed mood or markedly diminished interest or pleasure in all, or almost all, activities that predominates in the clinical picture

B. There is evidence from the history, physical examination, or laboratory findings that the disturbance is the direct pathophysiological consequence of another medical condition

C. The disturbance is not better explained by another mental disorder

D. The disturbance does not occur exclusively during the course of a delirium

E. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning

- Examples;
  - Neurological: (stroke, Huntington's disease, multiple sclerosis, Parkinson's disease, traumatic brain injury)
  - Endocrinological: (Cushing's disease, hypothyroidism)
  - Others

Other Specified Depressive Disorder

This category applies to presentations in which symptoms characteristic of a depressive disorder that cause clinically significant distress or impairment in social, occupational, or other important areas of functioning predominate but **do not meet the full criteria for any of the disorders in the depressive disorders diagnostic class**. The other specified depressive disorder category is used in **situations in which the clinician chooses to communicate the specific reason that the presentation does not meet the criteria for any specific depressive disorder**

- Examples:
  - Short-duration depressive episode
  - Depressive episode with insufficient symptoms

Unspecified Depressive Disorder

This category applies to presentations in which symptoms characteristic of a depressive disorder that cause clinically significant distress or impairment in social, occupational, or other important areas of functioning predominate but **do not meet the full criteria for any of the disorders in the depressive disorders diagnostic class**. The unspecified depressive disorder category is used in **situations in which the clinician chooses not to specify the reason that the criteria are not met for a specific depressive disorder**, and includes presentations for which there is insufficient information to make a more specific diagnosis (e.g., in emergency room settings)

Summary

Major depressive disorder;

- is a **major psychiatric illness** that can affect several life domains
- in adults, it tends to occur more in **female** than males
- its onset is **later than for BAD (bipolar disorder)**
- **psychiatric and medical comorbidities** are common
- about **10 to 15 percent of depressed patients commit suicide**
- Several pharmacological and non-pharmacological treatments exist

Questions and Discussion

References

- DSM-5
- kaplan and sadock's synopsis of psychiatry
- CANMET Clinical Guildlines
- Others