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Major Depressive Disorder (MDD) - Diagnosis

- Depressed mood (irritable mood in children or adolescents) and/or reduced interest or pleasure (core symptoms) lasting for at least 2 weeks AND

- Presence of 4 or more other symptoms – SIG: E CAPS (Rx for energy capsules)
  - S – insomnia or hypersomnia
  - I – reduced interest or pleasure
  - G – excessive guilt or feelings of worthlessness
  - E – reduced energy or fatigue
  - C – diminished ability to concentrate or make decisions
  - A – loss or increase of either appetite or weight
  - P – psychomotor agitation or retardation
  - S – thoughts of suicide or death or suicidal behavior

- Chronic depression = syndrome present for more than 2 years

- Minor depression = depressed mood and 3 or fewer symptoms
Dysthymia

- Depressed mood (may be irritable mood in children and adolescents)
  - Most of the day when present
  - Present more days than not
  - Occurring continuously for at least 2 years

- Presence of at least 2 of the following symptoms:
  - Poor appetite or overeating
  - Insomnia or hypersomnia
  - Low energy or fatigue
  - Low self esteem
  - Poor concentration or difficulty making decisions
  - Feelings of hopelessness

- Symptoms cause **significant impairment** of daily functioning

- Symptoms are **not due directly due to a medical condition or substance/drug**

- Symptoms are **not due to another condition** (bipolar, psychosis, MDD)
Major Depressive Disorder (MDD)

- Median age of onset is 32
- Prevalence levels are high in the general population
  - Cross sectional – 2.3% - 4.9%
  - 12 month – 6.6%
  - Lifetime – 13.3% - 17.1%, average around 16% in the US
- More common in the setting of medical illness
  - Primary care – 10%
  - Nursing homes – 15% - 20%
  - Medically ill patients – 22% - 33%

- Majority of individuals are treated by a primary care physician
- Chronic Condition
  - Recurrence rate = 50% after a single episode
  - Recurrence rate = 70% after a two episodes
  - Recurrence rate = 90% after a three episodes
Major Depressive Disorder (MDD) – Risk Factors

- **Gender**
  - Twice as common in women as in men

- **Genetics**
  - Aggregates in families
    - Up to 3-4 times more common in first degree relatives of individuals with MDD

- **Prior history of depression**

- **Stressful life events** – especially in childhood
  - Divorce, death of loved one, job loss, trauma or abuse in childhood

- **Substance abuse**

- **Chronic medical conditions**

- **Certain medications**

- **Certain personality traits**
  - Overly dependent, self critical, predisposition to emotional upset under stress
# Severity by Depression Scales

<table>
<thead>
<tr>
<th>Severity</th>
<th>Hamilton Rating Scale (HAM-D-17)</th>
<th>Beck Depression Inventory (BDI)</th>
<th>Inventory of Depressive Symptoms (IDS)</th>
<th>Zung Self Rating Depression Scale (Zung SDS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None-Minimal</td>
<td>0-7</td>
<td>0-9</td>
<td>0-13</td>
<td>0-49</td>
</tr>
<tr>
<td>Mild</td>
<td>8-13</td>
<td>10-16</td>
<td>14-22</td>
<td>50-59</td>
</tr>
<tr>
<td>Moderate</td>
<td>14-18</td>
<td>17-29</td>
<td>22-30</td>
<td>60-69</td>
</tr>
<tr>
<td>Severe</td>
<td>19-22</td>
<td>≥ 29</td>
<td>30-38</td>
<td>≥ 69</td>
</tr>
<tr>
<td>Very Severe</td>
<td>≥ 23</td>
<td></td>
<td>≥ 38</td>
<td></td>
</tr>
<tr>
<td>Score</td>
<td>Interpretation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---------</td>
<td>-------------------------------------------------------------------------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>91-100</td>
<td>Superior function, no symptoms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>81-90</td>
<td>Good function, absent or minimal symptoms</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>71-80</td>
<td>Symptoms are transient, slight impairment of function</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>61-70</td>
<td>Mild symptoms, some difficulty, generally functions well</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>51-60</td>
<td>Moderate symptoms or moderate difficulty in functioning</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>41-50</td>
<td>Serious symptoms or serious difficulty in functioning</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>31-40</td>
<td>Impaired reality testing or communication or seriously impaired functioning</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>21-30</td>
<td>Behavior considerably influenced by psychotic symptoms or inability to function in almost all areas</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11-20</td>
<td>Some danger of hurting self or others or occasionally fails to maintain hygiene</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-10</td>
<td>Persistent danger of hurting self or others, serious suicidal act or inability to maintain hygiene</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0</td>
<td>Inadequate information</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## Practical Application of GAF Score

<table>
<thead>
<tr>
<th>Score</th>
<th>Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>None - Minimal</td>
<td>80 or more</td>
</tr>
<tr>
<td>Mild</td>
<td>71-80</td>
</tr>
<tr>
<td>Mild - Moderate</td>
<td>61-70</td>
</tr>
<tr>
<td>Moderate</td>
<td>51-60</td>
</tr>
<tr>
<td>Moderate - Severe</td>
<td>41-50</td>
</tr>
<tr>
<td>Severe</td>
<td>40 or lower</td>
</tr>
</tbody>
</table>
Major Depressive Disorder – Risk Factors for Recurrence

- Early age of onset
- Presence of prior episodes
- Severity but not duration of first episode
- Presence of dysthymia
  - “Double Depression” – dysthymia + MDD
- Presence of an accompanying anxiety disorder
- History of alcohol or drug abuse
- Presence of bipolar disorder
- Family history of psychopathology – especially depression
- Recurrent life stressors
- Poor social support network
Depression – General Treatment Principles

- All depression, including dysthymia should be treated aggressively
- Only about 60%-70% of individuals at most respond to first line therapy
- The combination of medical therapy and cognitive-behavioral therapy works better than either alone
- For mild to moderate depression there is no particular advantage in efficacy for one drug over another
  - Choice of meds is based more on side effect profiles and presence of other medical conditions
  - Tricyclic drugs may work better for severe depression
  - Use of MAO inhibitors is usually discouraged as first line therapy due to risk of side effects
Depression – General Treatment Principles

- A response to medical therapy takes at least 2-3 weeks
  - Could take up to 6-8 weeks
- Duration of therapy for a first episode of depression should be at least 6-12 months after remission is achieved
- Maintenance therapy is recommended for certain situations
  - Two episodes with the presence of risk factors for recurrence
  - Three or more episodes
- Cessation of medication is NOT always a good thing
### Selective Serotonin Reuptake (SSRI) and Serotonin and Noradrenaline Reuptake Inhibitors (SNRI) Drugs

<table>
<thead>
<tr>
<th>Generic - SSRI</th>
<th>Brand Name - SSRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citalopram</td>
<td>Celexa</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>Lexapro, Cipralex</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>Prozac, Sarafem, Pexeva</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>Luvox, Faverin</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>Paxil</td>
</tr>
<tr>
<td>Sertraline</td>
<td>Zoloft</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Generic - SNRI</th>
<th>Brand Name - SNRI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Desvenlafaxine</td>
<td>Pristiq</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>Cymbalta</td>
</tr>
<tr>
<td>Milnacipran</td>
<td>Savella</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>Effexor</td>
</tr>
</tbody>
</table>
### Tricyclics

<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amitryptyline</td>
<td>Elavil, Endep, Levate</td>
</tr>
<tr>
<td>Amoxapine</td>
<td>Ascendin</td>
</tr>
<tr>
<td>Clomipramine</td>
<td>Anafril</td>
</tr>
<tr>
<td>Desipramine</td>
<td>Norpramin, Pertofrane</td>
</tr>
<tr>
<td>Doxepin</td>
<td>Adapin, Sinequan</td>
</tr>
<tr>
<td>Imipramine</td>
<td>Tofranil</td>
</tr>
<tr>
<td>Maprolootinine</td>
<td>Deprilept, Ludiomil</td>
</tr>
<tr>
<td>Nortriptyline</td>
<td>Pameler</td>
</tr>
<tr>
<td>Protriptyline</td>
<td>Vivactil</td>
</tr>
<tr>
<td>Trimipramine</td>
<td>Surmontil</td>
</tr>
</tbody>
</table>
# MAO Inhibitors

<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isocarboxazid</td>
<td>Marplan</td>
</tr>
<tr>
<td>Phenelzine</td>
<td>Nardil</td>
</tr>
<tr>
<td>Tranylcypromine</td>
<td>Parnate</td>
</tr>
<tr>
<td>Selegiline</td>
<td>Emsam (transdermal)</td>
</tr>
</tbody>
</table>
### Others

<table>
<thead>
<tr>
<th>Generic</th>
<th>Brand Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bupropion</td>
<td>Budeprion, Welbutrin</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>Remeron</td>
</tr>
<tr>
<td>Nefazadone</td>
<td>Nefadar, Serzone</td>
</tr>
<tr>
<td>Trazadone</td>
<td>Desyrel, Oleptro</td>
</tr>
<tr>
<td>Vilazadone</td>
<td>Viibryd</td>
</tr>
</tbody>
</table>
Depression – Treatment Resistant

- Not staying on medication long enough
- Not using high enough dosage
- Skipping doses
- Side effects of medications
- Resistance to the chosen medication
- Drug interactions
- Genetic effects
- Contributing medical conditions
  - Cancer, heart disease
- Presence of other psychiatric conditions
- Substance abuse
Depression – Options for Treatment Resistant Disease

- Maximize dose for adequate duration of time
- Change to alternative drug
- Use a combination of drugs
- Augmentation of therapy - Use drugs that are not antidepressants but enhance antidepressant effect
  - Lithium
  - Thyroid hormone
  - Atypical antipsychotic drugs
    - Olanzepine (Zyprexa)
    - Risperidone (Risperdal)
    - Aripiprazole (Abilify)
    - Quetiapine (Seroquel)
Depression – Somatic Therapies for Resistant Disease

- **Electroconvulsive therapy (ECT)**
  - Most consistently effective therapy for resistant disease
  - Effective in 50%-70% of cases
  - Less effective with bipolar type, mania, less severe depression, long duration
- **Deep brain stimulation**
- **Repetitive transcranial magnetic stimulation**
- **Vagus nerve stimulation**
- **Transcranial direct current stimulation**
Red Flags for Depression

- Prior suicide attempt
- Suicide ideation, especially with intent and definite plan
- Psychosis
- Substance abuse
- Use of somatic therapy
  - ECT and others
- Use of mood stabilizers
- Use of MAO inhibitors
Red Flags for Depression

- Worsening symptoms with use of an antidepressant
  - Suggests bipolar disease
- Concomitant severe anxiety disorder
- Non-compliance
- Failure to use maintenance therapy despite repeated episodes
- Concurrent severe medical conditions
Dysthymia

- Reduced quality of life
- Difficulty in effective functioning
- Degree of morbidity due more to the duration than the number and severity of the symptoms
- 70% of patients go on to develop major depressive disorder
- Double depression = recurrent episodes of major depression superimposed on an underlying dysthymic disorder
Anxiety Disorders

- Panic Disorder
- Agoraphobia
- Social Anxiety
- Obsessive Compulsive Disorder
- Post Traumatic Stress Disorder (PTSD)
- Generalized Anxiety Disorder
Anxiety Disorders - Epidemiology

- Most common mental health problem in the US
  - 18.1% of the general population in a given year
  - 28.8% of adults at some point during their lifetime
  - Estimated cost $42 billion per year

- Factors that separate normal anxiety from pathology
  - Excessiveness – out of proportion to situation
  - Intensity – markedly increased level
  - Duration or chronicity
  - Impairment – interferes with social, occupational, daily functioning
Anxiety Disorders – Risk Factors
Combination of Genetic Predisposition and Environment

- Past history of an anxiety disorder
- Family history of an anxiety disorder
- Recent increase in stressful life events
- Ineffective emotional coping strategies
- Female sex
- Adverse events in childhood
- Having a chronic pain condition
- History of substance abuse
- Poor social support
Panic Attack

- Discrete period of intense fear or discomfort with 4 or more of the following symptoms that develop abruptly
  - Palpitations, pounding heart, rapid heart rate
  - Sweating
  - Trembling/shaking
  - Sensations of shortness of breath or smothering
  - Feeling of choking
  - Chest pain or discomfort
  - Nausea or abdominal distress
  - Feeling dizzy, unsteady, lightheaded or faint
  - Feelings of unreality or depersonalization
  - Fear of losing control
  - Fear of dying
  - Paresthesias
  - Chills or hot flushes
Panic Disorder

- Recurrent, unexpected panic attacks
- At least one of the attacks is followed by 1 month (or more) of one or more of the following
  - Persistent concern about having additional panic attacks
  - Worry about the consequences of the attack(s)
  - A significant change in behavior related to the attacks
- Presence or absence of agoraphobia (avoiding certain situations due to fear of the possible attacks)
- Attacks not due to substances or other medical conditions
- Symptoms not due to other mental disorders
Post Traumatic Stress Disorder

- Person has been exposed to a traumatic event with the following characteristics
  - Events that involved actual or threatened death or serious injury to self or others
  - The person’s response involved intense fear, helplessness or horror
- Traumatic event is persistently re-experienced
- Persistent avoidance of stimuli associated with the trauma and numbing of general responsiveness (not present before the trauma)
- Persistent symptoms of increased arousal
General Anxiety Disorder

- Excessive anxiety and worry present more days than not for at least 6 months about a number of events or activities
  - Person finds it difficult to control the worry
  - Anxiety and worry are associated with 3 or more of the following symptoms:
    - Restlessness or feeling keyed up or on edge
    - Being easily fatigued
    - Difficulty concentrating or mind going blank
    - Irritability
    - Muscle tension
    - Sleep disturbance

- Symptoms are not related to another mental disorder
- Symptoms cause significant distress with impairment of functioning
- Symptoms are not due to a substance or other medical condition
Anxiety Disorders - Treatment

► Education about the condition and what triggers it is a key
► Psychotherapy – especially cognitive-behavioral therapy (CBT) is helpful
► A combination of medical therapy and CBT works best
► Selective serotonin reuptake inhibitors (SSRIs)
  • Work the best for the common anxiety disorders
  • Usually takes 3-4 weeks to show improvement
► Benzodiazepines (alprazolam – Xanax, clonazepam – Klonapin, others)
  • Used to be used more commonly
  • Cessation of use can cause rebound anxiety
  • Best application is as a bridge until SSRI drugs reach maximum effect
Red Flags for Anxiety Disorders

- Early age of onset
- More severe functional impairment
- Comorbidity with other mental illnesses
- Substance abuse
- Chronic pain
- Comorbidity with other medical illnesses
Depression & Anxiety are Associated with Poor Health Behavior

- Increased risk of smoking
- Increased alcohol use
- Reduced physical activity
- Poor diet
- Social isolation
- Poor compliance with medical therapies
Mortality Risk with Depression – General Comments

Data is somewhat mixed - study by Wulsin et al in 1999 – reviewed literature from 1966-1996
- 51% of studies showed a positive association
- 23% of studies showed a negative association
- 26% of studies showed a mixed association

Criteria differ on how to diagnose depression
- Depressive symptoms versus clinical depression

Difficult to study because of comorbid factors and conditions – studies vary in how they adjust for these
- Medical conditions can lead to depression
- Depression can exacerbate medical risks
- Psychiatric and substance abuse comorbidities are common
- Age, sex, smoking and socioeconomic factors also are significant
Mortality Risk with Depression – General Comments

- Risk appears to increase with severity
- Risk persists in older ages
- Data on minor depression is mixed
  - Some show an effect, others do not
  - Part of the problem in general with the literature is the mixture of major and minor depression in studies
The Mortality Risk with Depression is due to Medical and Non-Medical Causes
Overall Mortality Risk with Depression – VA Study

Years of Potential Life Lost (YPLL) for Depressed v Non-Depressed Patients

- Depressed
- Non-Depressed

Mortality Risk with Depression

Multiple Studies

Relative Risk

- Finland 1: 1.97
- Finland 2: 1.68
- Meta-Analysis: 1.58
- Norway: 1.37
- Review: 1.7
- MRFIT Males: 1.15
- US Male Veterans: 0.92
- Vietnam Veterans: 1.55
- ACL Study: 1.13
Mortality by Severity of Depression - Finland

Severity Gauged by Beck Depression Inventory (BDI)

Relative Risk

Mortality by Severity of Depression - Norway

Severity Gauged by Hospital Anxiety and Depression Scale (HADS-D)

Relative Risk

Mortality with Depression in the Elderly

Relative Risk of Mortality by Various Studies – Multivariate Adjusted

Relative Risk

- Netherlands: 1.8
- UK: 1.6
- US: 1.4
- Older Women: 1.2

Relative Risk
Mortality Risk with Minor Depression

Relative Risk

- Meta Analysis: 1.3
- Netherlands Men: 1.4
- Netherlands Women: 0.8
- UK: 1.2
- Finland 2: 1.6
Mortality Risk with Anxiety

- Far fewer studies than with depression
- Data is very mixed and difficult to evaluate
- Comorbidities drive much of the risk
  - Comorbid depression and other psychiatric conditions
  - Comorbid medical conditions
  - Especially comorbid substance abuse
- Risk, if present, is clearly smaller than with major depression
Anxiety May be More of a Morbidity Risk and a Modifier of Mortality Risk in Conjunction with Other Factors
Mortality Risk with Anxiety

Relative Risk in Representative Articles

Relative Risk

- Finland: 1.2
- Texas Older: 1.52
- Netherlands Men: 1.78
- Neth Women: 0.89
- Panic Disorder: 1.9
- Norway Severe: 0.96
- Vietnam Veterans: 1.68
Mortality Risk by Severity of Anxiety

Relative Risk

Post Traumatic Stress Disorder (PTSD)

- Can appear at any age
  - More common in young adults
- Women are twice as likely as men to develop PTSD
- More likely with a preexisting psychiatric condition
- Occurrence depends on the nature and severity of the inciting event
- Associated with a personality prone to over reaction and negative emotions
  - Neuroticism
- High degree of associated comorbidity
  - Depressive disorder – 48%
  - Alcohol abuse – 40%
  - Drug abuse – 31%
  - Social phobia – 28%
  - Panic disorder – 9%
Mortality with PTSD

- PTSD does not increase the risk of suicide in the absence of significant comorbidity.
- There is little evidence to suggest an overall increase in the risk of mortality with PTSD alone in multivariate controlled studies.
- PTSD may increase the risk of cardiovascular disease and coronary calcium scores even when controlling for risk factors.
- PTSD is associated with chronic pain and excessive opioid use.
Mortality Risk Associated with PTSD

Multivariate Adjusted Relative Risk – 2 Different Studies

PTSD and Risk of Coronary Artery Disease

Relative Risk of Death by Calcium Score – PTSD v No PTSD

Relative Risk

- 0
- 1-100
- 101-400
- > 400

Relative Risk

- 1.04
- 1.23
- 1.51
- 1.81
Suicide

- 11th leading cause of death, > 30,000 deaths per year
  - 3rd leading cause of death in adolescents
- Overall there are 8-10 attempts per completed suicide
- Success rates vary with the means used
  - Guns are the most common means of completed suicide
  - Drug overdose is the most common means of attempted suicide
- Rates vary by race
  - Caucasians have twice the risk of African-Americans
  - American Indians and Alaskan natives have 1.7 times the risk in Caucasians
- Rates vary with age
  - Highest rate is in the elderly (1.5-2 times higher)
  - Elderly are more likely to complete an attempt
  - Adolescent suicide rates tripled between 1950 and 1990
Suicide Risk Factors

- **Psychiatric illness** – present in 90%-95% of cases
  - Affective illness – 50%
  - Substance abuse – 25%
  - Schizophrenia – 10%
- **Male sex** (3-4:1 risk of completed suicide)
  - Women are more likely to attempt suicide (3-4:1)
- **Older age**
  - Elderly Caucasian males are highest risk group
- **Marital status** (widowed, divorced, separated are higher risk)
- **Living alone**
- **Recent personal loss or unemployment, including retirement**
- **Financial or legal difficulties**
  - Policy year 3 effect in life insurance
- **Family history** of suicide or psychiatric illness
Suicide Risk Factors

► Previous suicide attempt
  • Very important risk factor for mortality

► Recent hospitalization for a suicide attempt
  • Especially in the first month after discharge

► Presence of guns in the house

► Comorbid medical illnesses
  • Especially chronic or disabling medical illnesses
  • Chronic pain is a factor for increased suicide risk
  • Presence of medical illnesses is more common in older individuals
Suicide in Depression

- About 15% of people with major depressive disorder complete suicide
  - 30 times more common than the general population
  - Usually occurs during a depressive episode
- Feeling of hopelessness is more important than measures of severity of depression
- Risk is variable with psychosis
- Risk is higher at earlier phases of the disease
  - Higher sooner after initial diagnosis, earlier in the lifetime course of the illness, earlier in recovery, earlier in the course of a hospitalization, in the first month after discharge
- Starting or changing therapy may increase risk
- Comorbid anxiety increases the risk
- Comorbid personality disorder
- Comorbid substance abuse
Suicide in Anxiety

- As with data on mortality – evidence is mixed on anxiety and suicide
  - Some studies show risk similar to depression, others do not
- Some data suggests risk is increased, especially with panic disorder
- Evaluation is complicated by comorbidities
  - Depression
  - Substance abuse
- Use of anti-anxiety medications, especially with comorbid depression may be a red flag
- Risk may be increased in some situations
  - Panic disorder
  - Generalized anxiety disorder
- Risk does not appear to be increased with PTSD in the absence of other comorbid conditions
Risk of Mortality in Those with a Prior Suicide Attempt

Risk by Standardized Mortality Ratio (SMR) in Veterans

Risk of Completed Suicide after a Suicide Attempt

Relative Risk by Psychiatric Diagnosis Over the Long-Term

Tidemalm D, BMJ, 2008; 337: Published Online.
Risk of Completed Suicide by Comorbid Depression & Anxiety

By Specific Anxiety Diagnosis

Odds Ratio

Panic Disorder
GAD
Anxiety NOS
PTSD
Antianxiety Med
High Dose AA Med

Odds Ratio

Pfeiffer PN, Depress Anxiety, 2009; 26:752-757