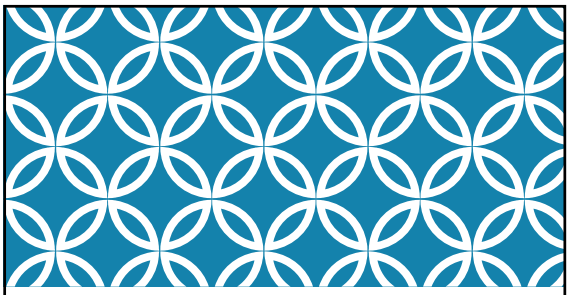

DIAGNOSIS AND TREATMENT OF ANXIETY AND DEPRESSIVE DISORDERS IN PRIMARY CARE

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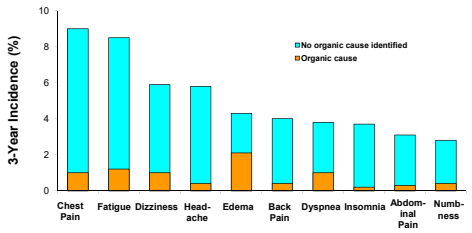
LEARNING OBJECTIVES

- Describe the epidemiology of Depression
- List the diagnostic criteria for Depression
- Recognize comorbid conditions and a differential diagnosis of Depression
- Identify screening tools for use in Depression diagnosis
- Acquire an approach to assessing and approaching suicidality
- Recognize treatment options for Depression
- List the prevalence of anxiety and related disorders
- Identify comorbid psychiatric diagnoses
- Perform a quick screen for anxiety and related disorders
- Apply general pharmacologic approaches to the treatment of anxiety disorders

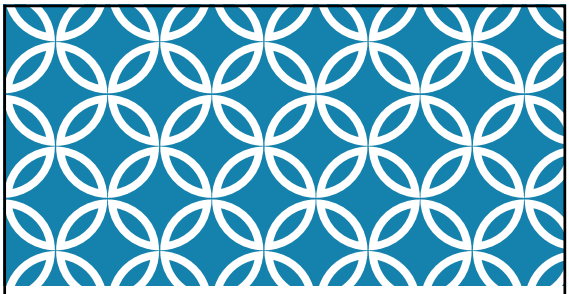
MENTAL DISORDERS IN PRIMARY CARE

- 25% of patients have a mental disorder
- 88% of patients with mental disorder seek primary care first
- Diagnosis missed half the time for depression
- 83% of depressed patients presented with
  - SOMATIC complaints
- The three most common primary care presenting symptoms for depression? (Preboth 2000)
  - Sleep disturbance
  - Fatigue
  - Pain

PHYSICAL COMPLAINTS ARE OFTEN NOT ORGANIC



Kroenke K, Mangelsdorff AD. *Am J Med.* 1989;86:262-266



DEPRESSIVE DISORDERS

DEPRESSIVE DISORDERS

Disruptive Mood Dysregulation Disorder

Major Depressive Disorder

Persistent Depressive Disorder (Dysthymia)

Premenstrual Dysphoric Disorder

Substance/Medication-Induced Depressive Disorder

Depressive Disorder Due to Another Medical Condition

Other Specified Depressive Disorder

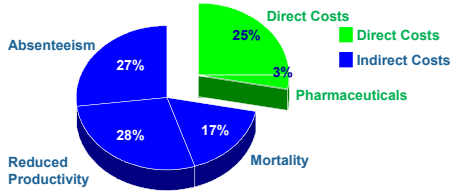
Unspecified Depressive Disorder

DEPRESSION -EPIDEMIOLOGY

- Major depressive disorder affects approximately 14.8 million American adults, or about 6.7 percent of the U.S. population age 18 and older (Archives of General Psychiatry, 2005 Jun; 62(6): 617-27)
- The median age at onset is 32. (U.S. Census Bureau Population Estimates by Demographic Characteristics, 2005)
- As many as one in 33 children and one in eight adolescents have clinical depression. (Center for Mental Health Services, U.S. Dept. of Health and Human Services, 1996)

THE BURDEN OF DEPRESSION

Total costs = $44 billion per year in 1990 dollars
Direct costs = *$12.4* billion per year in 1990 dollars



Greenberg et al. *J Clin Psychiatry.* 1993;54:405-418.

THE PERSONAL PRICE OF DEPRESSION

Mental anguish

Poor physical functioning

Poor social and occupational functioning

Pain, somatic symptoms

Family frustration

Suicide and other mortality risks

Wells et al. *JAMA.* 1989;262:914-919.

DIAGNOSTIC CRITERIA FOR MAJOR DEPRESSIVE DISORDER-DSM V

- A. Five or more of the following for at least 2 weeks
  - Depressed mood*
  - Loss of interest or pleasure*
  - Appetite/weight change
  - Sleep disturbance
  - Psychomotor disturbance
  - Fatigue or low energy
  - Feelings of worthlessness or inappropriate guilt
  - Impaired ability to think or concentrate
  - Recurrent thoughts of death or suicide

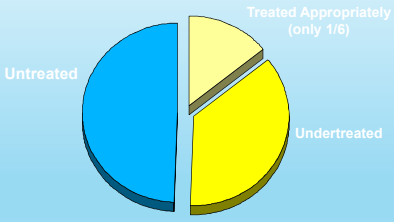
*At least one of these symptoms must be present.

SIGECAPS symptoms

DIAGNOSTIC CRITERIA FOR MAJOR DEPRESSIVE DISORDER-DSM V

- B. The symptoms cause clinically significant distress or impairment in social, occupational or other important areas of functioning.
- C. The symptoms are not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition (e.g. hypothyroidism).

DEPRESSION FREQUENTLY UNTREATED OR UNDERTREATED IN PRIMARY CARE



Hirschfeld et al. JAMA. 1997;277:333-340.

RISK FACTORS FOR DEPRESSION

- Family History
  - Depression
  - Bipolar disorder
  - Alcohol abuse
  - Other psychiatric illness
- Patient History
  - Gender
  - Periods of significant depression in the past
  - Previous episodes of other psychiatric disorder(s)

DIFFERENTIAL DIAGNOSIS OF DEPRESSION

- Rule out underlying medical conditions (eg. CNS disease, hypothyroidism)
- Rule out medications causing depression
- Screen for substance abuse
- Screen for other psychiatric disorders

DIFFERENTIAL DIAGNOSIS OF DEPRESSION

Medical Conditions

- Anemia
- Diabetes
- Drug abuse
- Epilepsy
- Chronic headache
- Brain injury
- Mononucleosis
- Lyme's disease
- Renal disease
- Hypothyroidism

Medications/Substances

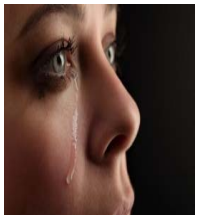
- Antihypertensives: e.g. beta blockers
- Sedatives: e.g. barbiturates, benzos
- Hormones: steroids, corticosteroids, BCP. progesterone
- Anticonvulsants: e.g. Tegretol
- Analgesics: e.g. opiates, codeine, ibuprofen
- H-2 blockers: e.g. Tagamet, Zantac
- Stimulant withdrawal: speed, cocaine
- Dopamine agonists: e.g. Levodopa
- Tamoxifen, NSAIDs, Accutane, reserpine
- Alcohol, cannabis, hallucinogens, etc. etc.

(Leon 2003 JFP)

DEPRESSION AND COMORBIDITY

Prevalence of Depression as a Concomitant Condition

- Cancer: 25%
- Diabetes: 32.5%
- Postpartum: 10%–20%
- Post stroke: 32%
- Post-myocardial infarction: 16%



Massie, Holland. *J Clin Psychiatry*, 1990. Lustman et al. *Diabetes Care*, 1988.
Dobie and Walker. *J Am Board Fam Pract*, 1992. Morris et al. *Int J Psychiatry Med*, 1990.
Frasure-Smith et al. *Circulation*, 1995.

SCREENING: A MUST!

- The USPSTF recommends screening of adolescents (12-18 years of age) for major depressive disorder (MDD) when systems are in place to ensure accurate diagnosis, psychotherapy (cognitive-behavioral or interpersonal), and follow-up.
- The USPSTF recommends screening adults for depression when staff-assisted depression care supports are in place to assure accurate diagnosis, effective treatment, and follow-up.

SCREENING: TESTS

2-Question Screen-PHQ2

"During the past month, have you often been bothered by
- 1. feeling down, depressed or hopeless?"
- 2. little interest or pleasure in doing things?"

"As effective as other instruments in detecting depression" (Whooley 1997)

SCREENING: TESTS

PATIENT HEALTH QUESTIONNAIRE-9 (PHQ-9)

Over the last 2 weeks, how often have you been bothered by any of the following problems? *(Use ✔ to indicate your answer)*

	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself — or that you are a failure or have let yourself or your family down	0	1	2	3
7. Trouble concentrating on things, such as reading the newspaper or watching television	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite — being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3
9. Thoughts that you would be better off dead or of hurting yourself in some way	0	1	2	3

FOR OFFICE CODING ___0___ + _____ + _____ + _____
=Total Score: _____

If you checked off any problems, how difficult have these problems made it for you to do your work, take care of things at home, or get along with other people?

Not difficult at all	Somewhat difficult	Very difficult	Extremely difficult
☐	☐	☐	☐

SUICIDE

Lifetime risk by patient category (Bostwick 2001)
- 8.6% for patients hospitalized for attempt
- 4% for hospitalized general psych patients
- 2% for outpatients treated for depression
- 1% for general population

Highest Risk profile
- Prior suicide attempt
- Suicidal plan
- Alcohol abuse
- Access to firearms/weapons
- Refuse psychiatric help
- Sudden lift in mood

ASSESSING SUICIDAL IDEATION

Studies show that more than 70% of suicide victims visit a physician within 2 months preceding their death

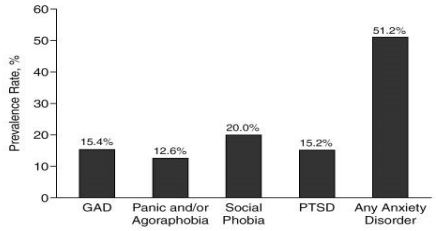
Evaluate suicidal potential if during evaluation patient admits to suicidal ideation by considering:

- Degree of hopelessness about situation
- Any reason to stay alive (e.g., for children)
- Thoughts of a specific method of suicide
- Personal or family history of suicide attempts

If there is significant suicidal potential refer to inpatient psychiatry/ER

Spitzer et al. *JAMA*. 1994;272:1749-1756.

DEPRESSION AND COMORBIDITY



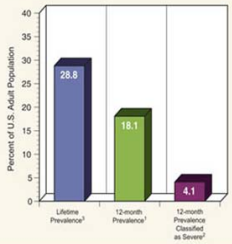
[a]Data from Kessler et al.[15] Values based on 12-month comorbid prevalence data. Abbreviations: GAD = generalized anxiety disorder, PTSD = posttraumatic stress disorder.

Percentage of Patients With Major Depression Who Also Suffer From a Current Anxiety Disorder

ANXIETY DISORDERS

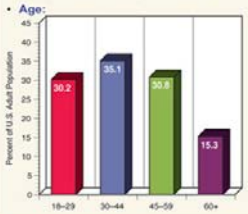
Prevalence

- **12-month Prevalence:** 18.1% of U.S. adult population[1]
- **Severe:** 22.8% of these cases (e.g., 4.1% of U.S. adult population) are classified as "severe"[2]



Demographics (for lifetime prevalence)[5]

- **Sex:** Women are 60% more likely than men to experience an anxiety disorder over their lifetime
- **Race:** Non-Hispanic blacks are 20% less likely, and Hispanics are 30% less likely, than non-Hispanic whites to experience an anxiety disorder during their lifetime
- **Age:**



Average Age-of-Onset: 11 years old[4]

ANXIETY DISORDERS

Separation Anxiety Disorder

Selective Mutism

Specific Phobia

Social Anxiety Disorder (SAD)

Panic Disorder (PD)

Agoraphobia

Generalized Anxiety Disorder (GAD)

Anxiety Disorder Due to a General Medical Condition

Substance-Induced Anxiety Disorder

Other Specified Anxiety Disorder

Unspecified Anxiety Disorder

COMORBID DIAGNOSES

Once an anxiety disorder is diagnosed it is essential to screen for other psychiatric diagnoses since it is very common for other diagnoses to be present and this can impact both treatment and prognosis.

What characteristics of primary anxiety disorders predict subsequent major depressive disorder. J clin psychiatry 2004 may;65(5):618-25

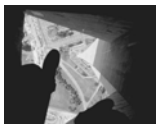
SPECIFIC PHOBIA

Marked or persistent fear (>6 months) that is excessive or unreasonable cued by the presence or anticipation of a specific object or situation

- Anxiety must be out of proportion to the actual danger or situation
- It interferes significantly with the persons routine or function

Treatment

- Systematic desensitization



SOCIAL ANXIETY DISORDER (SAD)

Marked fear of one or more social or performance situations in which the person is exposed to the possible scrutiny of others and fears he will act in a way that will be humiliating

- Exposure to the feared situation almost invariably provokes anxiety
- Anxiety is out of proportion to the actual threat posed by the situation
- The anxiety lasts more than 6 months
- The feared situation is avoided or endured with distress
- The avoidance, fear or distress significantly interferes with their routine or function

Treatment

- Social skills training, behavior therapy, cognitive therapy
- Medication – SSRIs, SNRIs, MAOIs, benzodiazepines, gabapentin

Incidence of social anxiety disorders and the consistent risk for secondary depression in the first three decades of life. Arch gen psychiatry 2007 mar(4):221-232

PANIC DISORDER

Recurrent unexpected panic attacks and in addition a one month period or more of:

- Persistent worry about having additional attacks
- Worry about the implications of the attacks
- Significant change in behavior because of the attacks

50-60% have lifetime major depression

- One third have current depression

20-25% have history substance dependence

Treatment

- Education, reassurance
- Elimination of caffeine, alcohol, drugs, OTC stimulants
- Cognitive-behavioral therapy
- Medications – SSRIs, venlafaxine, tricyclics, MAOIs, benzodiazepines, valproate, gabapentin

A PANIC ATTACK IS:

A discrete period of intense fear in which 4 of the following Symptoms abruptly develop and peak within 10 minutes:

Palpitations or rapid heart rate
Sweating
Trembling or shaking
Shortness of breath
Feeling of choking
Chest pain or discomfort
Nausea
Chills or heat sensations
Paresthesias
Feeling dizzy or faint
Derealization or depersonalization
Fear of losing control or going crazy
Fear of dying

A panic attack ≠ panic disorder

GENERALIZED ANXIETY DISORDER

Excessive worry more days than not, for at least 6 months, about a number of events, and difficulty in controlling the worry.

3 or more of the following symptoms:

- Restlessness or feeling keyed up or on edge
- Easily fatigued
- Difficulty concentrating
- Irritability
- Muscle tension
- Sleep disturbance

Causes significant distress or impairment

90% have at least one other lifetime Mood or Anxiety Disorder

66% have another current Mood or Anxiety disorder

Treatment

- Medications: buspirone, benzodiazepines, antidepressants (SSRIs, venlafaxine, imipramine)
- Cognitive-behavioral therapy

TREATMENT

GENERAL TREATMENT APPROACHES

Pharmacotherapy

- Antidepressants
  - SSRI
  - SNRI
  - TCA
  - MAOI
  - Atypical AD
- Anxiolytics
  - B blockers
  - Antihistamines
  - Benzodiazepines
  - Azapirones
- Antipsychotics (1st, 2nd, and 3rd generation)
- Mood stabilizers
  - Antiepileptics
  - Lithium
  - 2nd and 3rd gen AP)

Psychotherapy

- Cognitive Behavior Therapy
- Systematic Desensitization
- Social Skills Training
- Psychoeducation

DRUG TREATMENT GUIDELINES

- Treatment response is around 70% in most drug studies.
- Psychotherapy also has good response rates.
- Largest study (STAR-D) showed 67% remission rate with sequential approach.
- There is little to no comparative efficacy data to base initial choice on for medicine
- Titrate agent to achieve therapeutic dose or remission
- Full effect may take 4-6 weeks
- Treat for 4-12 months after full remission
- Continue medication indefinitely for recurrent depression

CRANK UP THE SEROTONIN

Cornerstone of treatment for depression and anxiety disorders is increasing serotonin

DRUG SELECTION – GENERAL CONSIDERATIONS

- History of previous response/familial response
- Impact of antidepressant on concurrent medical conditions
  - Bupropion with epilepsy
  - Venlafaxine with severe hypertension
  - Nefazodone with liver disease
- Safety in overdose
- Effect of medication on person's symptoms/beneficial side effects
- Potential for drug interactions
- Pregnancy
- Ease of administration
- Cost

SEROTONIN AGENTS

Advantages
- Safety
- Less orthostatic hypotension, anticholinergic side effects, adverse cardiac effects
- Increased patient satisfaction

Disadvantages
- Potential for interactions with other drugs
- Lack of sedation
- Development of serotonin syndrome
- Some distressing side effects

SEROTONIN SYNDROME

Medical emergency

Signs & symptoms:
- Mental status change, agitation, confusion
- Flushing, sweating, diarrhea, nausea, vomiting
- Muscle twitching/jerking/rigidity, tremor
- Fever, fast heart rate

If medication is not stopped, further serious complications may occur:
- Metabolic acidosis
- Respiratory failure
- Muscle breakdown (rhabdomyolysis)

SSRI

Mechanism: inhibition of reuptake of serotonin in neurons

Generally well tolerated

Safer if taken in overdose than other classes

"Black box warning" for increased suicidal thinking in adolescents & young adults

Potential for serotonin syndrome

Common side effects: headache, insomnia, diarrhea, nausea, sweating, tremor, sexual dysfunction

Common reason for patient discontinuation is sexual side effects (sexual side effects occur in 20% of patients on SSRIs)

Effective dosage to treat anxiety tends to be higher than dosage to treat depression

Some benefit seen at 2 weeks. Full effect in 4-6 weeks

SNRI

Mechanism: inhibition of reuptake of both serotonin and norepinephrine in neurons

Generally well tolerated

Not as safe as SSRIs if taken in overdose

Have "Black box warning" for increased suicidal thinking in adolescents & young adults

Can cause serotonin syndrome

Side Effects: dizziness, headache, insomnia, sedation, nausea, diarrhea, decreased appetite, vomiting, abdominal pain, dry mouth, sexual dysfunction, paresthesia.

Associated with hypertension & seizures in some patients

TRICYCLIC ANTIDEPRESSANTS

Mechanism of action: Increase levels of serotonin and norepinephrine

Can be fatal due to cardiac arrhythmias if therapeutic levels get too high or if taken in an intentional overdose

Anticholinergic side effects—dry mouth, constipation, urinary retention, weight gain

Interactions with many medications

Requires EKG at baseline and periodic monitoring

Serum levels can measured for most TCAs

ATYPICAL ANTIDEPRESSANTS

Norepinephrine-dopamine reuptake inhibitor (NDRI)—bupropion
- Mechanism of action: inhibits reuptake of dopamine and norepinephrine
- Indications: MDD, SAD, smoking cessation

Tetracyclic antidepressant (TeCA)—Mirtazpine
- Mechanism: inhibits serotonin reuptake, blocks histamine and boosts serotonin and norepinephrine
- Indications: MDD

Serotonin agonist and reuptake inhibitor (SARI)—Trazodone
- Mechanism: serotonin agonist and serotonin reuptake inhibitor
- Indications: MDD

BENZODIAZEPINES

Mechanism: Agonist at GABA-a receptor

Indications: panic disorder, insomnia

Known to cause long-term problems with memory and cognition, especially chronic use

Alprazolam is most addictive due to short-half life and quick onset of action

If used, longer acting formulations are preferred and for short term use only

Contraindications: History or current addiction, concomitant opiate pain medication use, liver dysfunction

BETA BLOCKERS

Mechanism: antagonist (blocker) at beta receptors

Indications: high blood pressure, irregular heart rate, essential tremor, performance anxiety, prevention of migraine headaches

Contraindications: asthma, COPD, heart block, bradycardia or low blood pressure

Side effects: dizziness, sedation (should take first time when not needing to drive), occasional nausea, abdominal pain, constipation

ANTIHISTAMINES

Mechanism: CNS depressant, antihistaminic and antiemetic activity. Blocks histamine-1 receptors.

Indications: treatment of anxiety, pre-op sedation, antiemetic, antipruritic

Common side effects: drowsiness, dry mouth

AZAPIRONES

Mechanism: binds to Serotonin 1-A receptors Indications: GAD, anxiety related to depression

Contraindications: Liver or kidney dysfunction

Side effects: dizziness, sedation, headache, nausea, restlessness

ADDITIONAL TREATMENTS

If adequate trials of 2 or more medications from different classes have been taken regularly at the maximum dose for more than 6 months without treatment response, refer to psychiatry

Use of MAOIs, mood stabilizers, antipsychotics, and off label use of medication should be reserved for treatment refractory cases, often referred to psychiatry for evaluation.

ECT, TMS, and other nueromodulation strategies are available, referral to psychiatry for evaluation

PSYCHOTHERAPY

- Multiple studies demonstrate efficacy of psychotherapy alone (Norcross 2004)
- Only two modalities validated
  - Cognitive-Behavioral Therapy [60-90% of the research]
  - Interpersonal Psychotherapy (Antonuccio 1995; Norcross 2004)

COGNITIVE BEHAVIORAL THERAPY

- Multiple studies demonstrate efficacy of psychotherapy alone (Hofmann 2004)
- Helps to change thinking patterns that support fears
- Change the reaction to anxiety-provoking situations
- Often lasts about 12 weeks
- May be conducted individually or in groups
- Group therapy particularly helpful in patients with social phobia
- "Homework" is often assigned between sessions
- Benefits may last longer than those of medication for patients with panic disorder, and possibly social phobia
- If a disorder recurs, CBT can be successfully used again
- In mild to moderate depression CBT = medication
- In severe depression CBT + medication

FOLLOW UP

- Assess every 2-4 weeks until remission
- Assess side effects
- Titrate dose for total remission
- Maintain effective dose for 4-12 months
- Consider maintenance therapy

TAKE HOME POINTS

- Anxiety and depressive disorders are common and disabling.
- Diagnosis missed half the time or more.
- High prevalence and associated disability make strong argument for routine screening.
- Screening questions can help identify or rule out diagnoses.
- There is a huge amount of suffering associated with these disorders.
- There are many effective treatments including psychotherapy and psychopharmacology
- Referral to psychiatry for treatment refractory cases or diagnostic uncertainty

QUESTIONS