

Depression in Primary Care Essentials of Primary Care 2009

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Educational Objectives:

By the end of the presentation, a participant will be able to:

- 1) State the prevalence of depression in the general population
- 2) Screen for depression by history taking or by use of the PHQ-9
- 3) Screen for bipolar disorder in depressed patients
- 4) Select appropriate antidepressant

See also National Institute for Health and Clinical Excellence (UK)
<http://www.nice.org.uk/nicemedia/pdf/CG23fullguideline.pdf>

Outline

- **Epidemiology**
- Assessment and Diagnosis
- Treatment



Depression in Primary Care:

Face-to-face household survey of 9090 Americans > age 17
(NCS-R study)

Prevalence: 1 year = **6.6%** (13.1-14.2 million)
lifetime = **16.2%** (32.6 – 35.1 million)
50% rated as severe or very severe
75% with co-morbid psychiatric dx

Impairment: Mean days out of work/role in past year:

Mild	2.8
Mod.	11.4
Severe	33.1
Very sev.	96.5

The Epidemiology of Major Depressive Disorder: Results
From the National Comorbidity Survey Replication (NCS-R).
Kessler, RC et al. *JAMA*. 2003;289:3095-3105.



Depression in Primary Care: The Depressing Reality



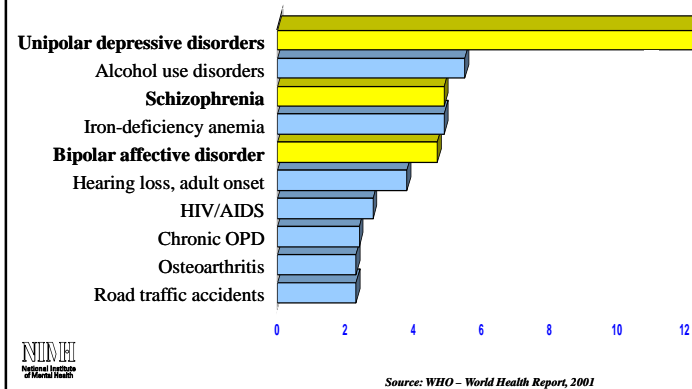
- **52%** of Community Cases Received any Treatment
- Treatment, when Received, was "Minimally Adequate" in only **42%**
- Thus, only **22%** of all Cases were Adequately Treated (ie, 42% of 52%)

The Epidemiology of Major Depressive Disorder: Results From the National Comorbidity Survey Replication (NCS-R). Kessler, RC et al. JAMA. 2003;289:3095-3105.

Disease Burden by Illness - DALY (Disability Adjusted Life Years)

United States, Canada and Western Europe, 2000

15-44 year olds



Depression: A Global Perspective

Leading cause of disability as measured by YLDs (Years Lived with Disability)

4th leading contributor to the global burden of disease (DALYs) in 2000.

By 2020, projected to reach 2nd place of the ranking of DALYs calculated for all ages, both sexes.

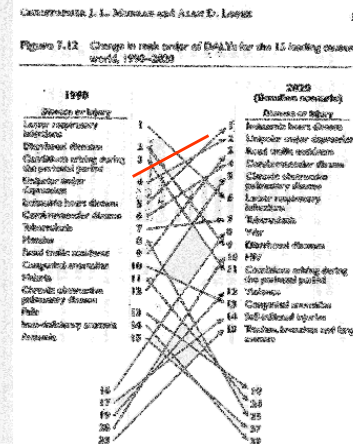
Currently, the 2nd cause of DALYs in the age category 15-44 years for both sexes combined.

http://www.who.int/healthinfo/global_burden_disease/2004_report_update/en/index.html

Global Burden of Disease

Major depression will have worldwide second rank order among the 15 leading causes of disability (DALY's) in 2020

Murray CJL & Lopez AD
WHO, Harvard SPH & Worldbank (1996)



Outline

- Epidemiology
- **Assessment and Diagnosis**
 - **Diagnostic criteria**
 - Screening techniques
 - Rule out bipolar disorder
- Treatment

Major Depressive Disorder –Diagnostic Criteria

Five or more of the following symptoms are present most of the day, nearly every day, during a period of **at least 2 consecutive weeks**

At least 1 of these 2 symptoms:

1. Depressed mood
2. Loss of interest or pleasure in all, or almost all, usual activities

Symptoms must cause clinically significant distress or impairment in social, occupational, or other important areas of functioning

DSM-IV-TR © 2000

Major Depressive Disorder –Diagnostic Criteria

Five or more of the following symptoms are present most of the day, nearly every day, during a period of **at least 2 consecutive weeks**

3. Significant weight loss or weight gain
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 think or concentrate or indecisiveness
9. Recurrent thoughts of death or suicide

DSM-

Major Depressive Episode: SIG E CAPS criteria

Depressed mood (or anhedonia), plus:

- **S** –Sleep symptoms
- **I** –Interest.
- **G** –Guilt
- **E** –Energy.
- **C** –Concentration.
- **A** –Appetite.
- **P** –Psychomotor changes
- **S** –Suicide

Case Vignette#1

A 41-year-old woman with recent diagnosis of systemic lupus erythematosus presents in your outpatient clinic with depression for 4 weeks. She reports 5 pound weight loss, little energy or interest in life, poor sleep, feelings of worthlessness/hopelessness, and thoughts of death and suicide.

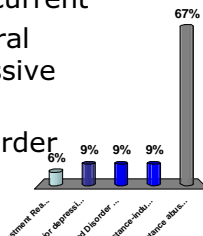
Case Vignette#1 (continued)

She has been taking prednisone 80mg daily for the past four weeks with partial improvement of her lupus symptoms. Her husband reports that her current depressive symptoms are very similar to the ones she experienced three years earlier when she was hospitalized for depression.

Case Vignette#1 (continued)

Which ONE of the following diagnoses is LEAST likely?

- a) Adjustment Reaction with Depressed Mood
- b) Major depressive disorder, recurrent
- c) Mood Disorder Due to a General Medical Condition with Depressive Features
- d) Substance-induced Mood Disorder with Depressive Features
- e) Substance abuse



Case Vignette#1 (continued)

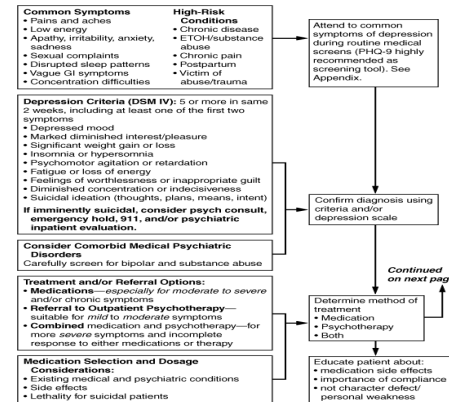
Discussion:

- a. Adj rxn – recent diagnosis of SLE
- b. MDD – this could be a recurrence
- c. Due to a General Medical Condition– SLE involves CNS
- d. Substance-induced Mood Disorder – corticosteroids generally cause euphoria, but can cause depression
- e. Substance abuse – common things are common

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Depression: Assessment



Depression in Primary Care:

2 Simple Screening Questions:

- “During the past 2 weeks, have you felt down, depressed or hopeless?”
- “During the past 2 weeks, have you felt little interest or pleasure in doing things?”

The US Preventive Services Task Force

JAMA, June 18, 2003- Vol 289 (23)

The Three S's of the Psychiatric Interview

- 1) S – Stressors/triggers
- 2) S – Suicidality
- 3) S – Substance Abuse

Diagnosis of Depression Key issues

- 1) Rule out Medical conditions causing psychiatric symptoms
- 2) Rule out Substance abuse or iatrogenic medications
- 3) Rule out Bipolar disorder (ie, screen for mania or hypomania)

Beyond the psychiatric interview

- Physical Health
Questionnaire-9, depression scale, aka PHQ-9
- Mood Disorder Questionnaire

Physical Health Questionnaire- 9, depression scale

- Nine (9) items
- Easy to score
- There are two components of the PHQ-9:
 - Diagnostic
 - Severity
- Google: "PHQ-9"

[http://www.depression-
primarycare.org/clinicians/toolkits/materials/forms/phq9/](http://www.depression-primarycare.org/clinicians/toolkits/materials/forms/phq9/)

Case Vignette#2

Three weeks ago, a 59yo Caucasian woman with a history of CHF, depression, and alcohol abuse presents to your office with three months of depressed mood. At that time, you started her on citalopram 20mg at bedtime.

She has been on hydrochlorothiazide and potassium supplements for over one year.

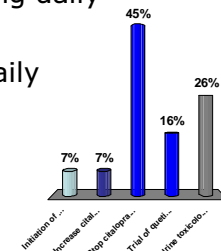
Case Vignette#2

Today in your office, she describes improved energy but significantly worsened irritability and insomnia, with new onset hyperactivity, racing thoughts, and impulsivity. She also endorses ruminative suicidal thoughts.

Case Vignette#2 Question

Which ONE of the following interventions is MOST appropriate?

- a) Initiation of divalproex 500mg qhs
- b) Increase citalopram to 40mg daily
- c) Stop citalopram
- d) Trial of quetiapine 50mg daily
- e) Urine toxicology screen



Case Vignette#2 Answers Discussed

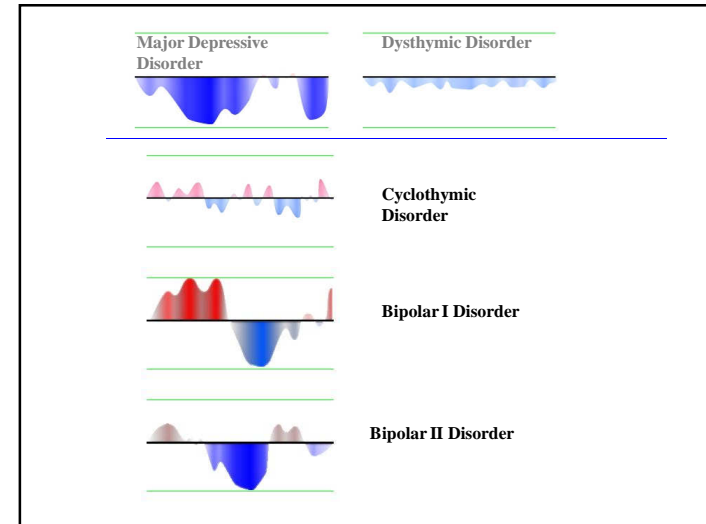
- a. Divalproex is the preferred treatment for bipolar disorder in patients with potential electrolyte and fluid shifts.
- b. If this patient is having a mixed episode, antidepressants may be the cause and are therefore contraindicated
- c. **Stopping citalopram is probably the most appropriate intervention**
- d. Low-dose atypical antipsychotics can target insomnia, racing thoughts, and agitation.
- e. Urine toxicology screen is indicated to rule out substance abuse.

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 - Diagnostic criteria
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 - **Rule out bipolar disorder**
- Treatment

Rule out Bipolar Disorder

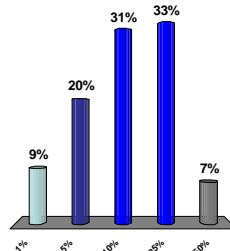
- Issue: antidepressants may worsen the course of bipolar disorder
- How common is bipolar disorder in primary care?
- Screen for mania or hypomania in all patients with depression



Bipolar Disorder in Patients with Anxiety and depression

A 56-year-old man comes to you with a chief complaint of anxiety and depression. What is the likelihood that he has bipolar disorder?

- a) 1%
- b) 5%
- c) 10%
- d) 25%
- e) 50%



Bipolar Disorder in Primary Care

- Of 108 consecutive anxious and depressed patients in primary care clinic,
- Using DSM-IV criteria in a semi-structured interview by family physician,
- **25%** were diagnosed with bipolar disorder: BP I (2.8%), BP II (18.5%), BP III (3.7%)

Manning JS et al. *Compr Psychiatry* 1997; 38: 102-108. On the Nature of Depressive and Anxious States in a Family Practice Setting: The High Prevalence of Bipolar II and Related Disorders in a Cohort Followed Longitudinally.

Bipolar Disorder: DIG FAST

- D – Distractibility
- I – Insomnia
- G – Grandiosity (or inflated self esteem)
- F – Flight of Ideas (or racing/crowded thoughts)
- A – Activities (increased goal directed activities)
- S- Speech (pressured)
- T- Thoughtlessness (impulsivity, ie, increased pleasurable activities with potential for negative consequences: sex, money, traveling, driving)

Mood Disorders Questionnaire

- Self-administered, one-page questionnaire
(see attached at end of syllabus)
- 7 or more positive responses is a positive screen

Hirschfeld RM et al. Validity of the Mood Disorder Questionnaire: A General Population Study. *(Am J Psychiatry 2003; 160:178–180)*

Hirschfeld RM et al. Development and Validation of a Screening Instrument for Bipolar Spectrum Disorder: The Mood Disorder Questionnaire. *(Am J Psychiatry 2000; 157:1873–1875)*

Antidepressants are generally contraindicated in bipolar disorder

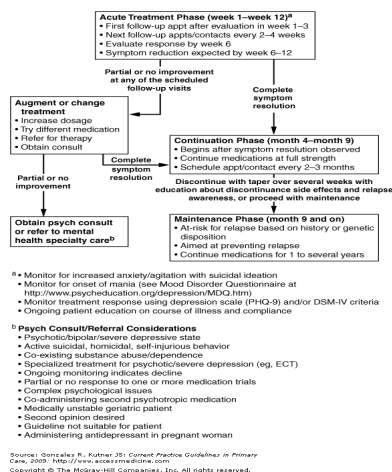
- Generally have NOT been shown to be effective in bipolar depression
- May trigger mania or hypomania
- May trigger rapid cycling or mixed episode

Sachs, GS et al. Effectiveness of adjunctive antidepressant treatment for bipolar depression. *NEJM 2007 356 17:1711 -22.*

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 - Psychotherapy
 - Medications

Depression Treatment Algorithm



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Psychotherapy of Depression

Psychodynamic psychotherapy

- unconscious content of a client's psyche causes depression
- more brief and less intensive than psychoanalysis
- relies on the interpersonal relationship between client and therapist

Psychotherapy of Depression

Interpersonal Psychotherapy (IPT)

- time-limited, manualized, supported by RCTs
- based on the belief that interpersonal factors contributes to depression
- focuses interpersonal problems

Psychotherapy of Depression

Behavior Therapy

Treatment is directed at having the individual desensitize to avoided stimuli through exposure and other behavioral interventions (behavioral activation, exercise)

Internal mental states are relatively unimportant.

Psychotherapy of Depression

Cognitive Therapy

Depression conceptualized as arising from cognitive distortions. Thus, treatment is directed at changing unproductive or intrusive thought patterns. The individual examines his or her feelings and learns to separate realistic from unrealistic thoughts.

Cognitive-Behavioral Therapy (CBT)

Combination of cognitive and behavior therapies.

Supported by RCTs

Self-Help Books for Depression Cognitive-behavioral

- Feeling Good, by David Burns
- Mind Over Mood, by Greenberger and Padefsky

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 - **Medications**
 - **Overview**
 - How to choose
 - Management

Medications

- SSRI's
- "Other"
Antidepressants
- Tricyclics
- MAOI's



SSRI's (selective serotonin reuptake inhibitors)

- First line
- Fairly safe in OD
- Recommend 9m minimum duration of treatment

Hx: 3-Phenoxy-3-phenylpropylamine, a compound structurally similar to diphenhydramine, was taken as a starting point to make a chemical compound that would inhibit serotonin reuptake

Fluoxetine (Prozac), sertraline (Zoloft), paroxetine (Paxil), fluvoxamine (Luvox), citalopram (Celexa), escitalopram (Lexapro)

SSRI: Side Effects

- long term:
 - Can be "deal-breakers"
 - Frequently do not resolve until medication is stopped
 - weight gain (moderate), sexual side effects (in around 35%)
- short term:
 - Generally more transient and mild, though occas. may be intolerable
 - nausea, diarrhea, headache, rash, insomnia, sweating

SSRI: Side Effects

serotonin syndrome: usually in combo with two or more serotonergic agents
-restlessness confusion, flushing, tremor progressing to hyperthermia, hypertonicity, rhabdomyolysis, death

suicide controversy: in 2004, black box on SSRI and other antidepressants warning of increased risk of suicidality in patients younger than 24.

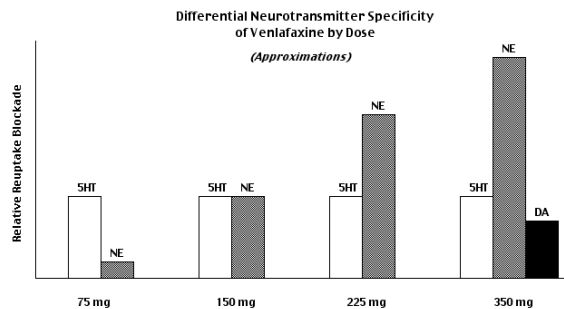
However, decrease in ssri prescriptions may have resulted in increased suicide rates in this population. [*Am J Psychiatry* **164** (9): 1356-63]

Other Antidepressants

- Bupropion (Wellbutrin):
 - low rate of sexual side effects or wt gain,
 - Assoc. w/ increased rate of seizures, not for pts w/ eating d/o or prior sz d/o
- Duloxetine (Cymbalta):
 - mixed NE and 5HT activity,
 - Alleviate pain of diabetic neuropathy and fibromyalgia?
- Mirtazapine (Remeron):
 - sedation and weight gain

Other Antidepressants

- Nefazodone (Serzone):
 - 5-HT₂ blocker, ?for anxious depression
 - black box for liver failure (1/250K pt-yrs)
 - low rate of sexual se's
- Trazodone (Desyrel):
 - usually prescribed as a hypnotic
 - Warn about priapism
- Venlafaxine (Effexor):
 - Mixed NE and 5HT activity
 - increases BP
 - similar side effect profile to ssri's
 - significant withdrawal syndrome



Note: Duloxetine, a newer "dual action" antidepressant, has more equal 5HT and NE effects across its dosage range.

Tricyclic Antidepressants (TCA's)

- NE reuptake inhibitors
- anticholinergic side effects, orthostatic hypotension, tremor, weight gain, sexual side effects,
- cardiac conduction delay (quinidine like effect)

Examples [not a complete list]: amitriptyline (Elavil), doxepin (Sinequan), imipramine (Tofranil), desipramine (Norpramin), nortriptyline (Pamelor, Aventyl), maprotiline (Ludiomil)

Monoamine-oxidase inhibitors (MAOIs)

Important: dietary restrictions! (b/o hypertensive crisis)

Also drug-drug interactions, including OTCs: ephedrine, pseudoephedrine, meperidine (Demerol)

Side effects: sedation, sexual side effects, weight gain

phenelzine (Nardil), tranylopramine (Parnate), [selegiline (Eldepryl) for Parkinson's]

MAOI Diet

- Avoid:
 - aged cheese
 - aged or cured meats (e.g., air-dried sausage);
 - any potentially spoiled meat, poultry, or fish;
 - broad (fava) bean pods;
 - Marmite concentrated yeast extract;
 - sauerkraut; soy sauce and soy bean condiments;
 - and tap beer.
- Wine and domestic bottled or canned beer are considered safe when consumed in moderation.
- Refer to article and give handout to patient

J Clin Psychiatry 1996 Mar;57(3):99-104 . **The making of a user friendly MAOI diet.**

Drugs to Avoid with MAOI's (Partial list)

Stimulants: Amphetamines, cocaine, MDMA, diet pills, methylphenidate, asthma inhalers

Sedatives: opiates, barbiturates, meperidine

Cold medications: decongestants & allergy medications

Certain antihypertensive medications: sympathomimetic amines (direct & indirect acting) including pseudoephedrine & ephedrine.

Other: levodopa, dopamine, carbamazepine,

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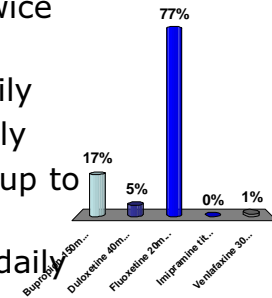
Case Vignette#3

A 34-year-old man with no prior psych history presents with depressed mood for the past six months. He endorses low energy, anhedonia, poor concentration, ruminative guilty feelings, low self-esteem. He denies h/o manic symptoms or past or present suicidal ideation.

Case Vignette#3

Which ONE of the following is the best medication intervention?

- Bupropion 150mg twice daily
- Duloxetine 40mg daily
- Fluoxetine 20mg daily
- Imipramine titrated up to 100mg at bedtime
- Venlafaxine 300mg daily



Choosing an Antidepressant is Not Based on Efficacy

Choosing a Therapy

"[T]he data indicate similar rates of response to all antidepressant drugs; therefore, the choice must be predicated on other factors. These include the drug's tendency to evoke a particular constellation of side effects, as well as specific factors related to the patient's psychiatric and medical history, family history of psychiatric disorder, and response to specific treatments."

---APA Practice Guideline for Major Depressive Disorder in Adults

See also: Gartlehner et al. *Ann Intern Med.* 2008;149:734-750. Comparative Benefits and Harms of Second-Generation Antidepressants: Background Paper for the American College of Physicians

Choosing an Antidepressant is Not Based on Efficacy?

"Clinically important differences exist between commonly prescribed antidepressants for both efficacy and acceptability **in favour of escitalopram and sertraline.**

Sertraline might be the best choice..."

Cipriani et al. *Lancet* 2009; 373: 746-58. Comparative efficacy and acceptability of 12 new-generation antidepressants: a multiple-treatments meta-analysis.

Rational Antidepressant Selection

1. History of response in pt (or family)
2. Patient preference
3. Clinician familiarity
4. Side effect profile

The Maze of Mood Medications

How do you choose?



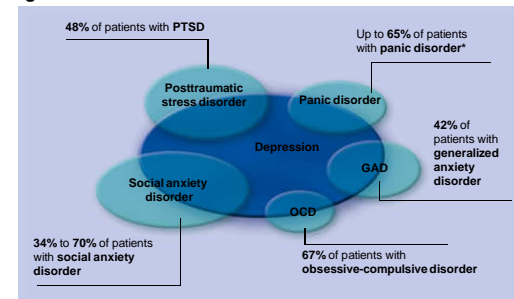
- Food
 - Fast
 - Good
 - Cheap
- Meds
 - Sedation
 - Weight gain
 - Sexual dysfunction
 - (Cheap)

Choosing an Antidepressant Side Effects

- Sedation/activation
- Weight gain
- Sexual dysfunction
- (Cost)

Choosing an Antidepressant: Comorbidities

Many patients with anxiety disorders have depression at some time during their lives



*Figures for panic disorder and depression not specified as lifetime in DSM-IV-TR™.



Kessler 1995; DSM-IV-TR™ 2000; Brawman-Mintzer 1993; Rasmussen 1992; Stein 2000; Van Ameringen 1991; Wittchen 1999.

FDA Approved Uses of SSRI's and SNRI's for Social Anxiety Disorder and Related Conditions

	Zoloft	Paxil/ Paxil CR	Effexor XR	Celexa/ Lexapro	Prozac	Luvox
MDD	✓	✓	✓	✓	✓	
Soc Anx	✓	✓	✓			
Gen Anx		✓	✓	✓ (L)		
Panic	✓	✓			✓	
OCD	✓	✓			✓	✓
PTSD	✓	✓				
PMDD	✓	✓			✓	


As of Oct., 2004

**Relative activation vs. Sedation
modern antidepressants***

Activating	psychostimulants Bupropion Fluoxetine, Sertraline	
Neutral or mixed	Venlafaxine, Escitalopram Citalopram	
Mildly to Moderately Sedating	Paroxetine, Fluvoxamine Nefazodone Tricyclics	
Strongly sedating	Trazadone Mirtazapine**	

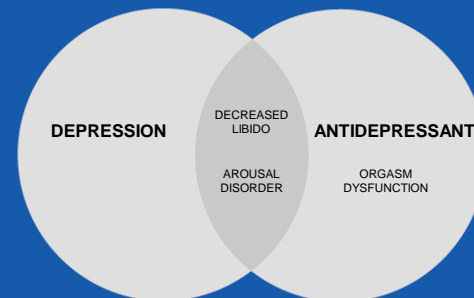
*based on personal experience, not clinically derived head-to-head data
**higher dosage may be less sedating

Impact on weight*

Weight loss (?)	psychostimulants Bupropion	
Neutral or mixed	Nefazadone	
mild to moderate	Ssri's (fluoxetine < paroxetine) Maoi's Tricyclics	
Significant	mirtazapine	

*based on personal experience, not clinically derived head-to-head data

SEXUAL DYSFUNCTION



Segraves. *J Clin Psychiatry Monogr.* 1993.

Effect on sexual functioning*

Increased?	Psychostimulants Bupropion
Neutral or mixed	Nefazadone Mirtazapine Duloxetine
Common	Tricyclics Maoi's Ssri's, Venlafaxine

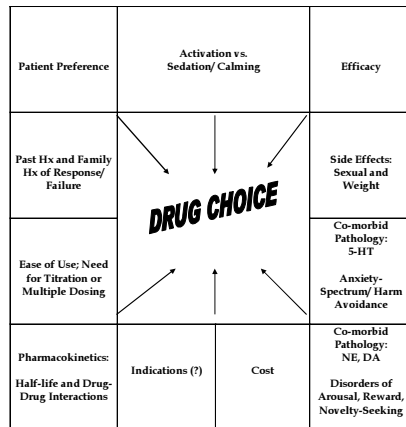
*based on personal experience, not clinically derived head-to-head data

Cost of some psychiatric meds

Drug & Strength	#	Cost	Unit cost
Budeprion SR 150MG Tabs	180	\$190.94	\$1.06
Wellbutrin SR 100MG Tab	180	\$587.60	\$3.26
Clonazepam 2MG Tab	90	\$23.99	\$0.27
Citalopram Hydrobromide 20mg Tab	90	\$89.97	\$1.00
Diazepam 5MG Tab	90	\$13.97	\$0.16
Escitalopram	90	\$257.98	\$2.87
Fluoxetine HCl 10MG Cap	90	\$26.97	\$0.30
Mirtazapine 15mg Tab	90	\$140.97	\$1.57
Sertraline HCl 100MG Tab*	90	\$29.97	\$0.33
Venlafaxine HCl 75mg Cap	90	\$299.99	\$3.33
Zolpidem Tartrate 10MG Tab	90	\$45.97	\$0.51

from Drugstore.com 7/19/09, prices subject to change, about 50% cheaper than local drugstore

*Descartes Li – Best Buy!



Wolkowitz, 3/13/00

Patient-Based Factors in Choosing an Antidepressant

Patient Characteristics:							
Anxiety	Insomnia	Atypical Dep ^{***}	Anhedonia ↓Cog-Att ⁿ	Cigarettes, ?Stimulant	Anxiety Spectrum*	*Broad Spectrum Sx? / ?Non-Remitters	On mult. meds
Serzone Paxil Remeron Celexa Lexapro Effexor Zoloft	Serzone Remeron Paxil Luvox	Wellbutrin Prozac Effexor	Wellbutrin ? Effexor	Wellbutrin	Paxil Zoloft Luvox Celexa Lexapro Prozac ? Effexor ? Serzone ? Remeron	Effexor Remeron SSRI+ Well Serzone TCA	Effexor Lexapro Celexa Remeron Zoloft Wellbutrin

*e.g., OCD, Panic, Social Phobia, PTSD, PMS (Serzone and Remeron may work less well than SSRIs for OCD)

** e.g., Hypersomnia, hyperphagia

Patient Concerned About*:			
Sexual Function	Weight Gain	Psychomotor Δ	GI Side Effects
Wellbutrin Serzone Remeron	Wellbutrin Serzone Lexapro Celexa Prozac Zoloft	Lexapro Celexa	Remeron Wellbutrin

* The medications listed here are generally less likely to cause these side effects.

(Note: These considerations are generalizations based on clinical experience rather than head-to-head studies or labeled indications. Medications are not necessarily listed in order of usefulness.)

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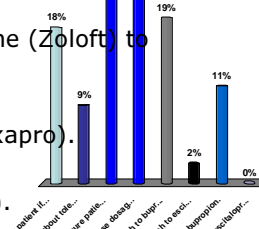
Case Vignette#4

28-year-old woman with 6 months of depressed mood has been on sertraline (Zoloft) 50mg for three weeks with no change in depressive symptoms. She is also concerned about weight gain.

Case Vignette#4

Which of the following are appropriate interventions? (more than one may be correct)

1. Ask patient if she has been taking medication regularly.
2. Ask about tolerability of weight gain.
3. Reassure patient and continue medication for another 1-3 weeks.
4. Increase dosage of sertraline (Zoloft) to 100mg daily
5. Switch to bupropion.
6. Switch to escitalopram (Lexapro).
7. Add bupropion.
8. Add escitalopram (Lexapro).



Case Vignette#4 answers

Which of the following are appropriate interventions? (more than one may be correct)

- a) Ask patient if she has been taking medication regularly.
- b) Ask about tolerability of weight gain.
- c) Reassure patient and continue medication for another 1-3 weeks.
- d) Increase dosage of sertraline (Zoloft) to 100mg daily
- e) Switch to bupropion.
- f) Switch to escitalopram (Lexapro).
- g) Add bupropion.
- h) Add escitalopram (Lexapro).

What if the antidepressant is NOT working?

First check that patient has been taking medication as prescribed
Consider increase in dosage
Switch to another antidepressant (monotherapy) – [in another class?]
Taper medication over a 4-week period
Discontinuation/withdrawal symptoms can include dizziness, nausea, paraesthesia, anxiety and headaches
Stopping drugs with a shorter half-life, such as *paroxetine* and *venlafaxine*, more likely to have withdrawal symptoms

End: Summary

- Epidemiology
 - Depression is common
- Assessment and Diagnosis
 - Diagnostic criteria – Ask about depression
 - Screening techniques: PHQ-9
 - Rule out bipolar disorder: Mood Disorder Questionnaire

End: Summary

Treatment

- Psychotherapy: Effective, but hard to deliver/access
- Medications
 - Overview – SSRI's, "Other", TCA's, MAOI's
 - How to choose – Sedation, Weight gain, Sexual dysfunction, (Cost)
 - Management -- adherence