

Integrated Care for Depression & Anxiety

Psychotropic Medication Management for Primary Care Providers

Los Angeles County
Department of Mental Health
September 20, 2011



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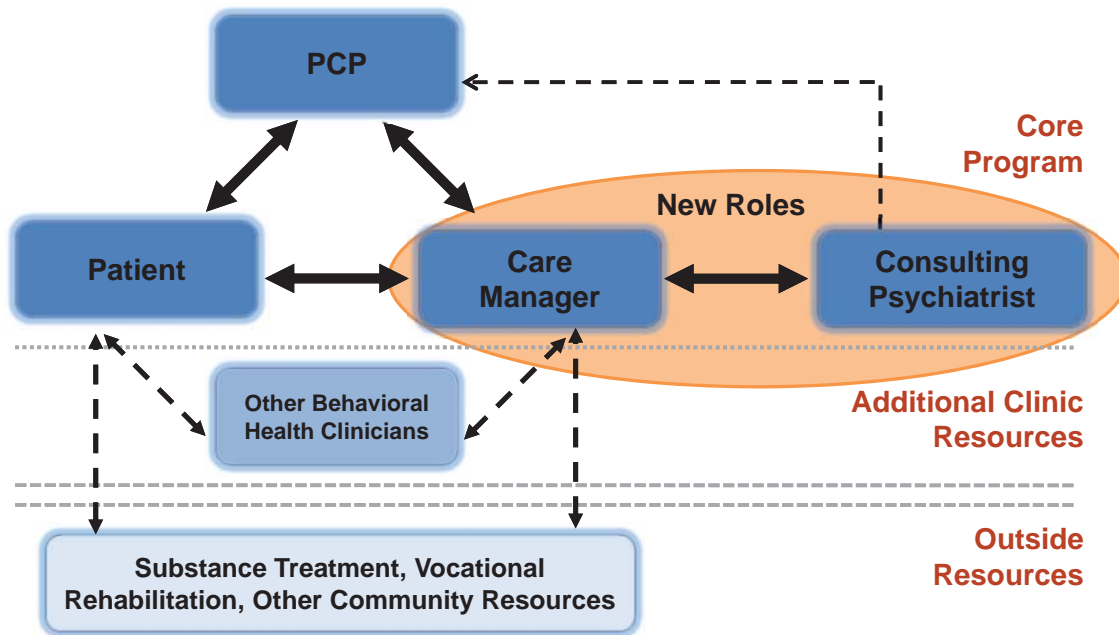
Medication Therapy for Depression and Anxiety

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Collaborative Team Approach



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Only a Minority of Patients Receive Effective Treatment

Almost 30 million Americans receive a prescription for an antidepressant in any given year

~ 20 - 30 %

Drop out of treatment too early

~ 25 - 50 %

Stay on ineffective treatments for too long

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Remember: Most Patients Need Treatment Adjustments

Over 30 – 50% of patients will have a complete response to initial treatment

50 – 70% will require at least one change in treatment to get better

Using Antidepressants

Key principles

- **Use antidepressants, not minor tranquilizers / benzodiazepine for depression and most anxiety disorders**
- **Use adequate doses for an adequate amount of time**
- **Start slow and work with side effects but titrate to an effective dose as needed**
- ***Change medication if not effective***
 - Usually after 8 – 10 weeks

FDA-Approved Antidepressants

Serotonin Reuptake Inhibitors (SSRIs)

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

Newer Antidepressants (atypical)

bupropion SR (Wellbutrin), mirtazapine (Remeron), venlafaxine XR (Effexor), desvenlafaxine (Pristiq), duloxetine (Cymbalta)

Tricyclics (TCAs)

**secondary amines: nortriptyline, desipramine
tertiary amines: imipramine, doxepin, amitriptyline**
Not recommended for older adults

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COMMONLY PRESCRIBED PSYCHOTROPIC MEDICATIONS			
NAME (Generic (Trade))	DOSAGE	Antidepressant Medications*	KEY CLINICAL INFORMATION
Antidepressant Medications*			
Dipropion (Wellbutrin)	Start: IR: 100 mg bid X 4d then ↑ to 100 mg bid. SR: 150 mg qam X 4d then ↑ to 150 mg bid. XL: 150 mg qam X 4d then ↑ to 300 mg qam. Range: 300-450 mg/d.	Contraindicated in seizure disorder because it decreases seizure threshold; stimulating; not good for treating anxiety disorders; second line TX for ADHD; abuse potential. ⚡ (R/SR), ⚡ (XL)	
Citalopram (Celexa)	Start: 10-20 mg qday. ↑ 10-20 mg qd-7d to 20-40 mg qday. Range: 20-60 mg/d.	Best tolerated of SSRIs; very low and limited CYP 450 interactions; good choice for anxious pt. ⚡	More GI side effects than SSRIs; tx neuropathic pain need to swallow BP; 2 nd line tx for ADHD. ⚡
Duloxetine (Cymbalta)	Start: 5 mg qday X 4-7d then ↑ to 10 mg qday. Range: 10-30 mg/d (3x potent vs. Celexa).	Best tolerated of SSRIs; very low and limited CYP 450 interactions. Good choice for anxious pt. ⚡	More activating than other SSRIs; long half-life reduces withdrawal (½ = 4-6 d). ⚡
Escitalopram (Lexapro)	Start: 10 mg qam X 4-7d then ↑ to 20 mg qday. Range: 20-60 mg/d.	Sedating and appetite promoting; Neurotoxicity risk (1 in 1000) so avoid in immunosuppressed patients. ⚡	Anticholinergic; sedating; significant withdrawal syndrome. ⚡
Mirtazapine (Remeron)	Start: 15 mg qhs X 4-7d then ↑ to 30 mg qhs. Range: 30-40 mg/d.	Fewest linked CYP 450 interactions; milky, activating. ⚡	More agitation & GI side effects than SSRIs; tx neuropathic pain above 150 mg qday; need to monitor BP; 2 nd line tx for ADHD. Significant withdrawal syndrome. ⚡ (R), ⚡ (SR)
Paroxetine (Paxil)	Start: 10 mg qhs X 4-7d then ↑ to 20 mg qday. Range: 20-60 mg/d.		
Sertraline (Zoloft)	Start: 25 mg qam X 4-7d then ↑ to 50 mg qday. Range: 50-200 mg/d.		
Venlafaxine (Effexor)	Start: IR: 37.5 mg bid X 4d then ↑ to 75 mg bid. XR: 75 mg qam X 4d then ↑ to 150 mg/d.		
*Warnings/precautions: (1) Potential increased suicidality in first few months; (2) Long-term weight gain likely (except fluoxetine & bupropion); (3) Sexual side effects common (except duloxetine & mirtazapine); (4) Withdrawal syndrome frequently occurs with abrupt cessation (especially with SSRIs and SNRIs); increased risk of bleeding with SSRIs and SNRIs (especially in combo with NSAIDs); (5) Risk for Serotonin Syndrome (avoid in combination with other serotonergic medications); (6) Hypotension sometimes seen with SSRIs and SNRIs.			
Anxiolytic and Sleep (Hypnotic) Medications			
Alprazolam (Xanax)	Start: 0.25 mg - 0.5 mg tid. Usual MAX: 4 mg/d.	Eqiv. dose: 0.5 mg. Onset: intermediate (1-2 hrs). TX: 11 hrs. More addictive than other benzos and has uniquely problematic withdrawal syndrome. Try to avoid as 1 st line tx. ⚡	
Chlordiazepoxide (Librium)	Start: 10-20 mg 3-4x daily. Usual MAX: 200 mg/d.	Eqiv. dose: 25 mg. Onset: intermediate (0.5-2 hrs). TX: 10-48 hrs (parent compound); 14-66 hrs (metabolites). Useful for treating withdrawal/ETOH withdrawal because of long half-life. ⚡	
Clonazepam (Klonopin)	Start: 0.25 mg bid or tid. Usual MAX: 3 mg/d.	Eqiv. dose: 0.25 mg. Onset: intermediate (1-4 hrs). TX: 40-50 hrs. Helpful in tx mania. ⚡	
Diazepam (Valium)	Start: 2-10 mg bid to qid with doses depending on symptoms severity. Usual MAX: 30-40 mg/d.	Eqiv. dose: 5 mg. Onset: immediate (highly lipophilic). TX: 20-90 hrs. Note: the presence of liver disease will significantly lengthen half-life. ⚡	
Lorazepam (Ativan)	Start: 0.5-1 mg bid to tid. Usual MAX: 6 mg/d. Insomnia: 0.5-2 mg qhs.	Eqiv. dose: 1 mg. Onset: intermediate. TX: 12 hrs. No active metabolites, so safer in liver dz. ⚡	
Risperidone (Risperal)	Start: 7.5 mg bid. Range: 10-30 mg bid.	Non-benzos SSRI-like drug FDA approved for anxiety. May take 4-6 weeks to become fully effective. ⚡	
Hydroxyzine (Vistaril)	Start: 25-100 mg 3-4x per day. Usual MAX: 400 mg per day.	Antihistamine/antemetic drug FDA approved for anxiety. Consider in pts w/ h/o substance abuse. ⚡	
Prazosin (Minipress)	Start: 1 mg qhs. Increase q 2-3 d until symptoms abate. Usual MAX: 10 mg qhs.	Old antihypertensive used to tx nightmares and night sweats of PTSD. Need to warn about orthostasis particularly in AM after first dose and after each new dosage change. ⚡	
Trazodone (Desyrel)	Start: 25-50 mg qhs. Range: 50-150 mg/d.	Commonly used as sleep aid. Inform about priapism risk in men. ⚡	
Temazepam (Restoril)	Start: 15 mg at bedtime. MAX: 45 mg qhs.	TX: 8.8 hrs. Older benzos hypnotic. No P450 metabolism. More potential for physical dependence than Ambien/Sonata. ⚡	
Zolpidem (Ambien)	Start: 5-10 mg qhs. MAX: 20 mg qhs.	TX: 2.6 hrs. Potential for sleep-eating and sleep-driving. ⚡ Available in longer acting form (CR). ⚡	
Mood Stabilizers			
Lithium	Start: 300 mg bid to tid. Target plasma level: acute mania & bipolar depression: 0.8-1.2 mEq/L. Maintenance: 0.6-0.8 mEq/L. Available as ER form dosed once daily (usually at HS, Lithobid & Eskalith). Plasma levels related to renal clearance.	Black box warning for toxicity. Teratogenic (cardiac malform.) and will need to inform women of childbearing age of this risk. Check TSH and BUN before starting and q 6-12 months thereafter. Abuse pt. about concurrent use of NSAIDs and HTN meds as can decrease renal clearance. Lithium strongly anti-suicidal. ⚡ (Lithium carbonate, citrate & SR). ⚡ (Lithobid, Eskalith)	
Divalproex (Depakote)			

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Serotonin Reuptake Inhibitors (SSRIs)

Common side effects in all SSRIs (>10 %): GI distress (nausea, diarrhea), insomnia, restlessness, agitation, fine tremor, headache, dizziness, sexual dysfunction.

*mg

Drug name	Unit doses avail.*	Therapeutic dose*	Usual dose*	Starting dose*	Comments
Fluoxetine	10, 20	10-60	20	10 daily	Long half-life
Sertraline	50, 100	25-200	50-100	25 daily	
Citalopram	20, 40	10-40	20	10 daily	Few drug interactions
Escitalopram	5, 10, 20	10-20	10	10 daily	Few drug interactions
Paroxetine	10, 20, 30, 40	10-50	20-30	10 daily	Dry mouth, constipation

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New Antidepressants: SNRIs

*SNRI side effects: GI distress (NAUSEA, diarrhea), insomnia, restlessness, agitation, fine tremor, headache, dizziness, constipation, decreased appetite, sexual dysfunction.
Small risk of elevation of blood pressure at higher doses => check BP.*

* mg

Drug name	Unit doses avail.*	Therapeutic dose*	Usual dose*	Starting dose*
Venlafaxine	25, 37.5, 50, 75, 100	12.5-150 bid	25-100 bid	25 daily
	XR 37.5, XR 75, XR 150	37.5-225 daily (XR)	75-225 daily (XR)	37.5 daily (XR)
Comments	Once daily dosing with XR preparation.			
Desvenlafaxine (no generic)	50, 100	50 – 100	50 daily	50 daily
Comments	Active metabolite of venlafaxine; similar side effect profile.			

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New Antidepressants: SNRIs – II

*SNRI side effects: GI distress (NAUSEA, diarrhea), insomnia, restlessness, agitation, fine tremor, headache, dizziness, constipation, decreased appetite, sexual dysfunction.
Small risk of elevation of blood pressure at higher doses => check BP.*

** mg*

Drug name	Unit doses avail.*	Therapeutic dose*	Usual dose*	Starting dose*
Duloxetine	20, 30, 60	40 – 60 daily	40 – 60 daily	30 daily

Comments Nausea, dry mouth, constipation, decreased appetite, fatigue, sweating, sexual dysfunction.
Enteric coated. **DO NOT break tablets!**

Mirtazapine

Drug name	Unit doses avail.*	Therapeutic dose*	Usual dose*	Starting dose*
Mirtazapine	15, 30	15-45 qhs	15-30 qhs	7.5 -15 qhs

Comments Sedation, weight gain.
Minimal sexual side effects.
May help with anxiety / nausea.

**mg*

Bupropion

Drug name	Unit doses avail.*	Therapeutic dose*	Usual dose*	Starting dose*
Bupropion	75,100 SR 100, 150 XL 150, 300	75-150 tid 100-200 bid (SR) 150-450 daily (XL)	75-150 tid 100-200 bid (SR) 150-300 daily (XL)	75 daily 100 daily (SR) 150 daily (XL)

Comments

- TID dosing with regular preparation.
- BID dosing with SR. Daily dosing with XL.
- Insomnia, agitation, tremor.
- Anorexia; no weight gain.
- Risk of seizures at high doses.
- Minimal sexual side effects.
- Perhaps less mania induction in bipolars
- Not good for anxiety.

*mg

Secondary Amine Tricyclics (TCAs)

Common side effects in all TCAs (>10 %): arrhythmias (particularly with pre-existing conduction defects), dry mouth, constipation, blurry vision, orthostatic hypotension, and weight gain.

*mg

Drug name	Unit doses avail.*	Therap dose*	Usual dose*	Starting dose*	Side effects
Nortriptyline	10, 25, 50, 75	40-150	50-100	10 qhs	Weakness/fatigue
Desipramine	10, 25, 50, 75, 100, 150	75-200	100-200	25 daily	Tachycardia, insomnia, agitation

Choosing Antidepressants

Prior treatment history in patient/family members

Patient preferences

Expertise of prescribing provider

Side effect profile

Safety in overdose

– 10 days of a TCA can be a lethal overdose

Availability and costs

Drug-drug interactions

When and How to Stop Antidepressants?

Treat all adults for 6-9 months after initial response

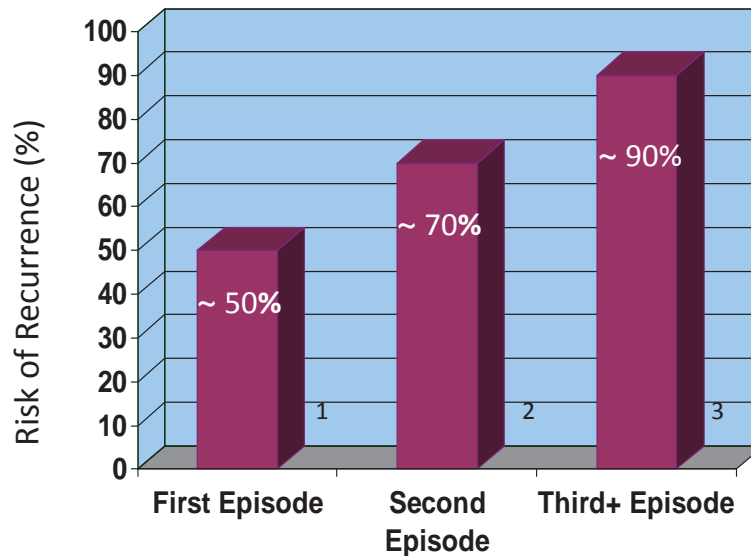
Treat those at high risk for relapse for 2 years or longer. Some may need lifetime treatment

Maintenance treatment should be at full dose

Make a relapse prevention plan

Taper antidepressants slowly to avoid discontinuation syndrome

Maintenance Therapy on Basis of Episodes



¹ Judd LL et al., *Am J Psychiatry*, 2000

² Mueller TI et al., *Am J Psychiatry*, 1999

³ DSM-IV-TR. Washington, DC: American Psychiatric Association, 2000

Problems Early in Treatment

Nonadherence

Medical and psychiatric comorbidity

Side effects

Unmasking bipolar disorder

Activation and suicidal ideation

Incomplete response

General Office Strategies for Optimizing Adherence

- Provide rationale for use**
- Careful attention to side-effects (see below)**
- Counter demoralization**
- Address fear of dependence and loss of control**
- Enlist family/spousal support**
- Address concerns in relation to patient's or significant other's prior experience with medication**
- Increase contact with brief phone check-ins**
- Specific instructions (take regardless of symptom change, don't stop on own)**
- Use symptom scale (e.g., PHQ-9)**

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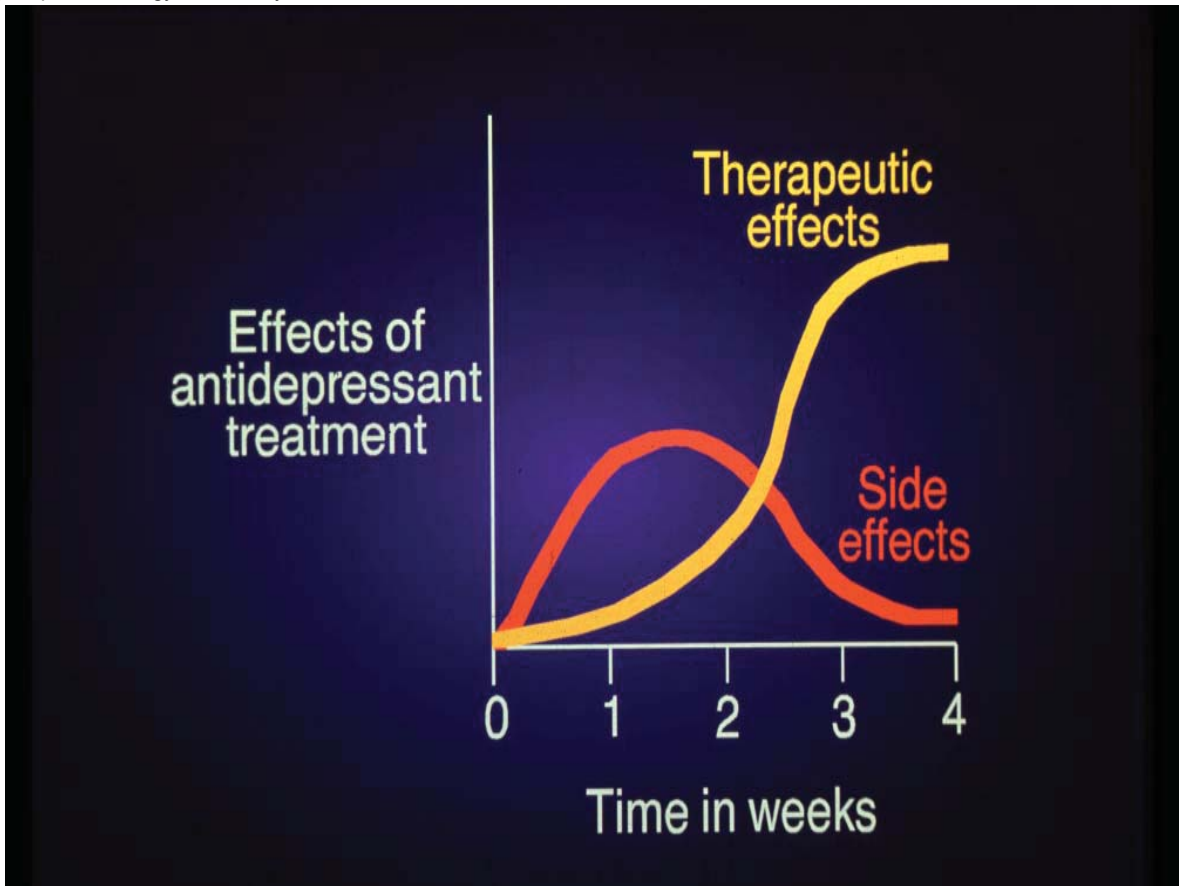
Is Patient at Maximum Therapeutic Dosage?*

Fluoxetine	60mg
Paroxetine	60mg
Escitalopram	20mg
Citalopram	60mg
Sertraline	200mg
Venlafaxine	300mg
Desvenlafaxine	100mg
Duloxetine	60mg
Bupropion SR	450mg
Mirtazapine	60mg
Nortriptyline	150mg (check serum level)
Despramine	300mg (check serum level)

*Consider titrating to these doses unless patient does not tolerate them 'maximum doses' due to side effects.

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Managing Side Effects

Consult with pharmacist / team psychiatrist

- Are side effects 'physical' or 'psychological'?

Short term strategies

- Wait and support (e.g., GI side effects of SSRIs)
- Adjust medication timing (e.g., take sedating meds at bedtime)
- Consider temporary dose reduction
- Treat side effects (if drug effective)

Change to a different antidepressant

Change to or add PST-PC

Common Side Effects

Short term:

- **GI upset / nausea**
- **Jitteriness / restlessness / insomnia**
- **Sedation / fatigue**

Long term:

- **Sexual dysfunction (up to 33%)**
- **Weight gain (5 to 10%)**

Orgasmic Dysfunction

25 – 33% of SSRI-treated patients

Change to

- **Bupropion**
- **Mirtazapine**

Augment

- **Bupropion SR 100mg PO BID**
- **Buspirone 15mg PO BID to 30mg PO BID**

Weight Gain

5 to 10% of SSRI treated patients

Rx – Bupropion, Fluoxetine

Drug-Drug Interactions

Antidepressants are metabolized by the P450 isoenzyme system in the liver. They can

- **change blood levels of other drugs that are metabolized by the same hepatic enzymes**
- **displace other protein-bound drugs**

Rule of thumb: if a patient is on a drug with a narrow therapeutic window (e.g., digoxin, warfarin, theophylline, antiarrhythmics, lithium, TCAs, anticonvulsants), check a serum level of that drug when a steady state of the antidepressant is reached or if there are side effects

Consult pharmacist

Good Reasons to Stop a Medication

Intolerable side effects

Dangerous interactions with necessary medications

The medication was not indicated to start with (e.g., bipolar depression)

Medication has been at maximum therapeutic dose without improvement for 4-8 weeks

What if Patients Don't Improve?

Is the patient adhering to treatment?

Is the dose high enough?

– **See max dose guidelines**

Is the diagnosis correct?

– ? **Bipolar depression**

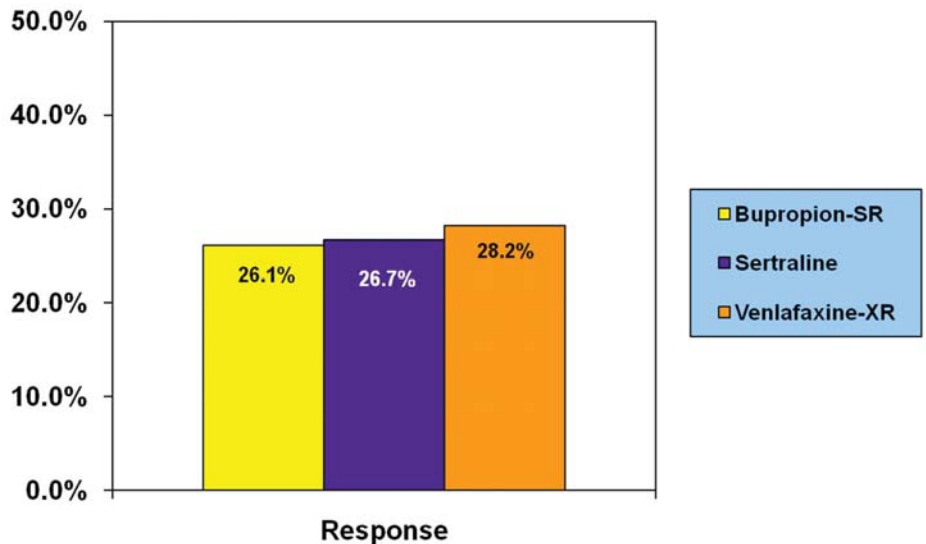
– ? **Medical conditions (hypothyroidism, sleep apnea, pain)**

– ? **Meds: steroids, interferon, hormones**

– ? **Withdrawal: stimulants, anxiolytics**

Are there untreated comorbid conditions / life stressors?

Bupropion-SR, Sertraline or Venlafaxine-XR after Failure of SSRIs for Depression



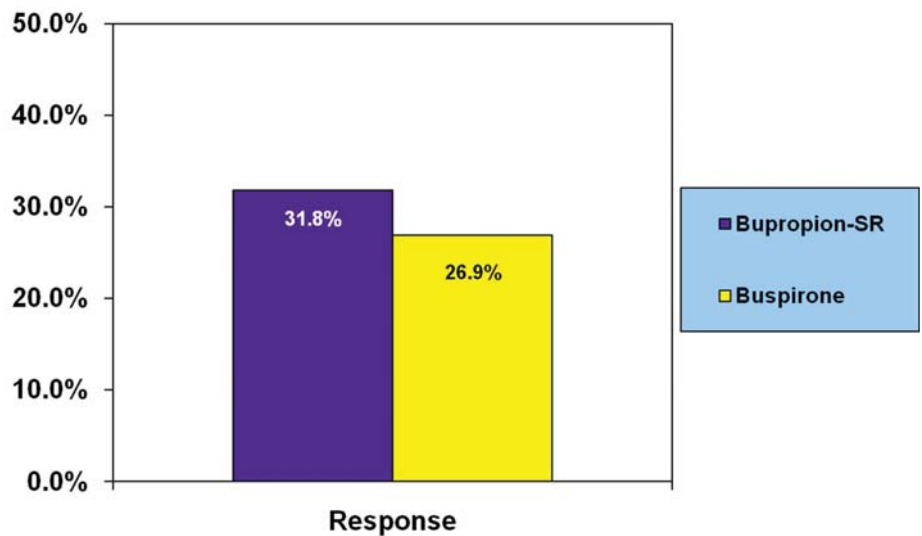
About one in four patients had a response after switching to a new antidepressant with no differential effect

Rush et al., *NEJM*, 2006

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Medication Augmentation after the Failure of SSRIs for Depression



No differences in response rates, but bupropion was associated with greater reduction in depressive symptoms and lower dropout from side-effects than buspirone

Trivedi et al., *NEJM*, 2006

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CBT in STAR-D

Switch from citalopram to CBT or augmentation of citalopram with CBT

– **Only 26% accepted CBT as an option at 'level 2'**

Remission over 12 weeks not significantly different from medication comparators

– **25 and 23%**

CBT took longer but had fewer side effects

STAR-D Remission Rates Based on Number of TREATMENT STEPS

First Step:	36.8%
Second Step:	30.6%
Third Step:	13.7%
Fourth Step:	13.0%

Bottom line: 1/3 respond with initial treatment but almost all patients respond eventually

Caveat: those requiring more Rx steps had higher relapse rates during naturalistic follow-up

Antidepressant Summary

There are over 30 FDA-approved antidepressants

- Each is effective in ~ 40 – 50% of patients
- It may take several trials until an effective medication is identified
- Patients need support during this time (work with care manager)

If medications are not effective after 8 – 10 weeks at a therapeutic dose

- Is patient taking medication as prescribed?
- Consider substance abuse, bipolar disorder, anxiety disorders, cognitive impairment. Ask every patient about suicidal ideation
- Consult with team psychiatrist and change treatment (medications, other somatic treatments, psychotherapy)

Overview of Medication Therapy for PTSD & Anxiety

Psychopharmacology for PTSD & Anxiety Disorders

**More similarities than differences among
common anxiety disorders**

– PD, GAD, SAD, PTSD

**SSRIs and SNRIs are equally efficacious for
anxiety and depression**

**Medications targeting arousal symptoms
(e.g., insomnia) important**

Why Antidepressants for PTSD & Anxiety?

**Most antidepressants are efficacious for
PTSD / anxiety disorders**

Comorbid depression common

No risk of abuse

Anxiety Psychopharmacology Initial Medication Choice

No prior history: start with SSRI

No evidence that one SSRI is better than another

If patient has had a definite prior response to a non-SSRI and patient prefers this, may use SNRI, mirtazapine, or TCA

Be careful about assuming prior medication trials were ineffective—must confirm that optimal dose (top doses) and durations (12 week minimum) were used

Titration of Medication Treatment

START LOW, GO SLOW to avoid excessive activation and side effects – but titrate to therapeutic dose over 4-6 week period

Titrate partial responders after 4-6 weeks to higher doses if tolerated: try to get to maximum doses AND durations

Evidence-based Medication for PTSD & Anxiety

**SSRI (fluoxetine/Prozac, sertraline/Zoloft,
paroxetine/Paxil, citalopram/Celexa)**

**SNRI (venlafaxine/Effexor,
duloxetine/Cymbalta)**

**Prazosin & trazadone/Desyrel targeting
arousal symptoms (e.g., sleep)**

Care Manager Role in Supporting Medication Therapy

Supporting Medication Therapy

Become familiar with commonly used antidepressant and other psychotropic medications and medication doses

Provide basic patient education about medications commonly prescribed in primary care

Support medication adherence

Know when treatment is 'not working' and alert the rest of the team to facilitate a change

Supporting Medication Therapy

Help patients and providers identify...

- **Potentially inadequate doses**
- **Ineffective treatment (e.g., persistent symptoms after adequate duration of medication trial)**
- **Side effects**

Facilitate patient-provider (e.g., PCP) communication about medications

Consult with PCP and team psychiatrist about medication questions

Patient Education About Antidepressants

Key messages

- **How do these medications work?**
 - By restoring a chemical imbalance in the brain
- **There are many options (over 30 available medications)**

Anticipate

- **Patient concerns about medications**
- **Side effects (these can be managed)**
- **Problems with adherence**

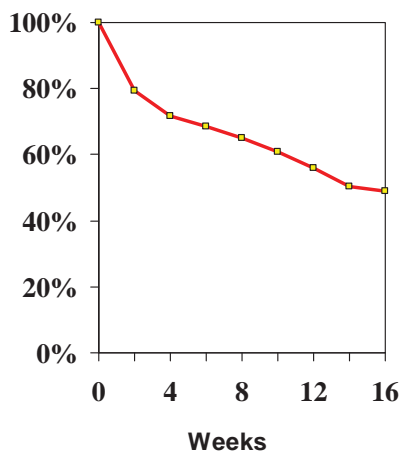
Reinforce

- **Need for continuation or maintenance treatment to prevent relapse even after the patient feels better**

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Antidepressant Adherence



Key messages:

- **Take medication daily**
- **Wait 2-4 weeks for effect**
- **Side effects can occur, but often resolve in 1-2 weeks**
- **Keep taking medication even if better**
- **Check with MD before stopping**
- **Not addicting**

Lin EH., *Med Care* 1995;33:67

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