#### **Free Webcasts!**

Treating Depression in Primary Care Presented by: Ryan Shackelford, MD Nov 18, 2010 12:30 pm - 1:30 pm

Treating Anxiety in Primary Care Presented by: Nicole Lanouette, MD Dec 16, 2010 12:30 pm – 1:30 pm



No need to travel – you can access the webcasts from your personal computer.

Both webcasts will be recorded for on-demand access for those that can't attend the live sessions.



Please RSVP to Marty madelman@ccc-sd.org PSYCHIATRY FOR PRIMARY CARE: DEPRESSION

**Ryan Shackelford** 

Family Medicine/Psychiatry Combined Program November 18th, 2010

#### DEPRESSIVE DISORDERS

Pathophysiology Video Case Studies: STAR D Trial, Lancet, Impact, JAMA AD Treatment Algorithim Rating Scales Treatment Scenarios

#### PRIMARY CARE DOCS ARE THE MOST IMPORTANT PIECE!

- Depressive illness 2<sup>nd</sup> leading cause of disability worldwide by 2020<sup>4</sup>
- <5% of clinical instruction for 20-33% of primary care practice<sup>3</sup>
- In 2008, >50% antidepressant Rx's from PCP's, 20% by Psychiatrists<sup>6</sup>

# MOOD STATES

Depressive Episode
Dysthymia
Hypomanic Episode
Manic Episode
Mixed Episode

#### MDD PREVALENCE

Leading cause of disability in the United States for ages 15-44<sup>1</sup> Affects approximately 14.8 million American adults or 6.7% of the U.S. adult population in a given year<sup>2</sup>

#### PATHOPHYSIOLOGY OF DEPRESSION

**Deficiency in active neurotransmitters:** 

- Serotonin (Raphe Nucleus)
- •Dopamine (Nucleus Accumbens/Ventral Tegmentum)
- •Norepinephrine (Locus Ceruleus)

\*\*\*Meds increase concentration of these substances but also <u>receptor</u> <u>upregulation</u>



#### MAJOR DEPRESSION (MDD) <u>SIG-E-CAPS</u>

- 5 of 9 symptoms lasting at least 2 weeks:
  - Sleep: Insomnia/Hypersomnia
  - Interest: Diminished Interest or Pleasure
  - Guilt: Feelings of Worthlessness or Excessive Guilt
  - <u>Energy</u>: Fatigue/Loss of Energy
  - <u>Concentration</u>: Diminished/Indecisiveness
  - Appetite: Weight Loss or Change in Appetite
  - Psychomotor Agitation or Retardation
  - Suicide: Recurrent Thoughts of Death/SI/SA
  - Sadness: Depressed Mood (irritability in child/teen)

# DYSTHYMIA

- Low mood state for most of the time over at least a 2year period
- 2 or more of the following while depressed:
  - Appetite change (poor or overeating)
  - Insomnia or Hypersomnia
  - Fatigue or low energy
  - Low Self-esteem
  - Poor concentration or difficulty with decisions
  - Feelings of hopelessness



20yo female w/ depressive symptoms for several months comes into your office for help.



http://picasaweb.google.co m/ZisCalendar/Video#

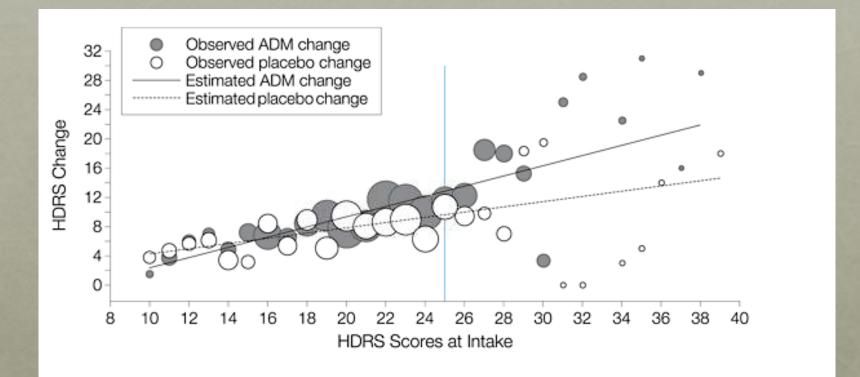
# WHAT ELSE DO YOU NEED TO KNOW?

- Severity of the depressive episode.
- Suicidal thoughts?
- Mania/hypomania
- Psychotic features.

# WHAT IS YOUR PRIMARY TREATMENT?

Anti-depressant
 Therapy
 Lifestyle Modification
 Hospitalization

# AD EFFECTIVENESS BY SEVERITY



Observed and Estimated Change in HDRS Scores Following Treatment With ADM and Placebo

JAMA Jan 6, 2010. Vol 303 No. 1

# WHAT MED DO YOU Start with?

- 1. Effexor (Venlafaxine)
- 2. Zoloft (Sertraline)
- 3. Prozac (Fluoxetine)
- 4. Wellbutrin (Buproprion)
- 5. Lexapro (Escitalopram)

- Anti-Depressant Medications
  - General Considerations:
    - Increased risk of suicide attempt
    - GI s.e. (nausea, diarrhea), acclimation period
    - Sexual s.e. (delayed ejaculation, *low libido*, anorgasmia)
      Exception Wellbutrin
    - Serotonin Syndrome (any serotonergic meds in combination e.g. demerol, SSRI, TCA, MAOI, Tramadol)
    - Induction of Hypomania

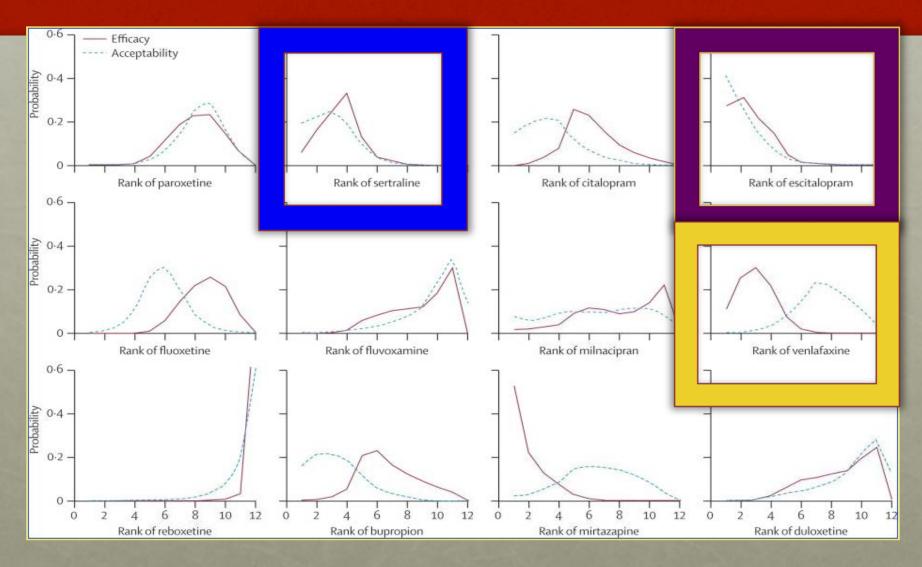
- Selective Serotonin Reuptake Inhibitors (SSRI)
  - Fluoxetine (Prozac):
    - longest half-life (t1/2 5-7days), activating, many drugdrug interactions
  - Paroxetine (Paxil):
    - weight gain and sedation common, w/d effects, many ddi
  - Sertraline (Zoloft):
    - data supports best efficacy to se ratio, some dopamine RI

- Selective Serotonin Reuptake Inhibitors (SSRI)
  - Citalopram (Celexa):
    - anecdotally best tolerated
    - low ddi
    - safe choice but often need high doses (failure = 60mg)
  - Escitalopram (Lexapro AKA Celexa):
    - active enantiomer of Citalopram

- Serotonin Norepinephrine Reuptake Inhibitor
  - Venlafaxine (Effexor, Effexor XR):
    - potent SRI at all doses/225-375mg SNRI
    - taper to avoid "shocking" w/d symptoms
    - can severely elevate BP at doses >150mg
    - contraindicated in heart dz
  - Duloxetine (Cymbalta):
    - "weak" antidepressant
    - equal SNRI at therapeutic doses
    - stress incontinence/fibromyalgia/neuropathy
  - Desvenlafaxine (Pristiq, AKA Effexor):

- Dopamine Norepinephrine Reuptake Inhibitor
  - Bupropion (Wellbutrin IR/SR/XL, Zyban):
    - reverse SSRI sexual dysfunction/apathy, nicotine dep, se include anxiety/agitation/seizures (IR)
- Alpha 2-Antagonist
  - Mirtazapine (Remeron):
    - boosts SNRI's through alpha 2 antagonism, H1 histamine antagonism, se sedation (low dose=more) and weight gain

#### AD EFFECTIVENESS



Lancet 2009 Vol 373, issue 9665, pg 746-58.

WHAT MED DO YOU START WITH?

A) Zoloft (Sertraline) B) Effexor (Venlafaxine) C) Prozac (Fluoxetine) D) Wellbutrin (Buproprion) E) Lexapro (Escitalopram)

#### AMY

### No Better. No SE. Increase Dose? Switch Meds?

Augment?



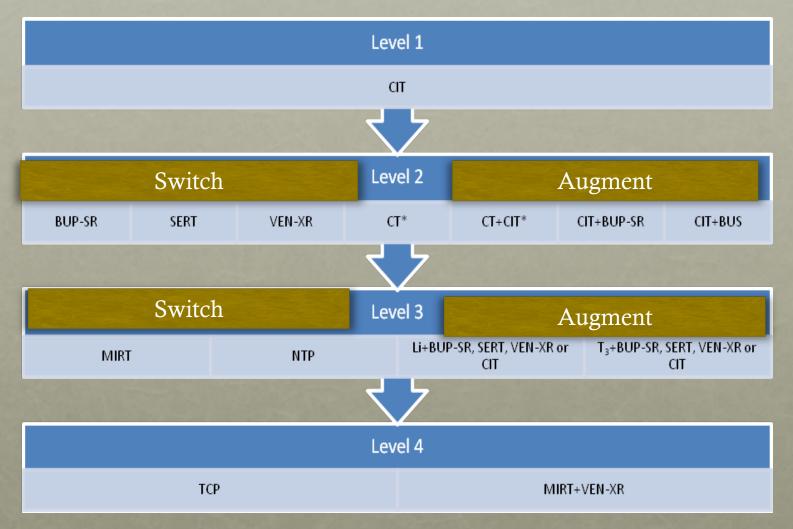
# STAR\*D TRIAL

• <u>Sequenced Treatment Alternatives to Relieve</u> <u>Depression</u>.

• **Goal**: Assess the effectiveness of depression treatments for MDD.

• **Participants**: 4,041, ages 18-75, 41 clinical sites in U.S. Broad range of SES and ethnic groups.

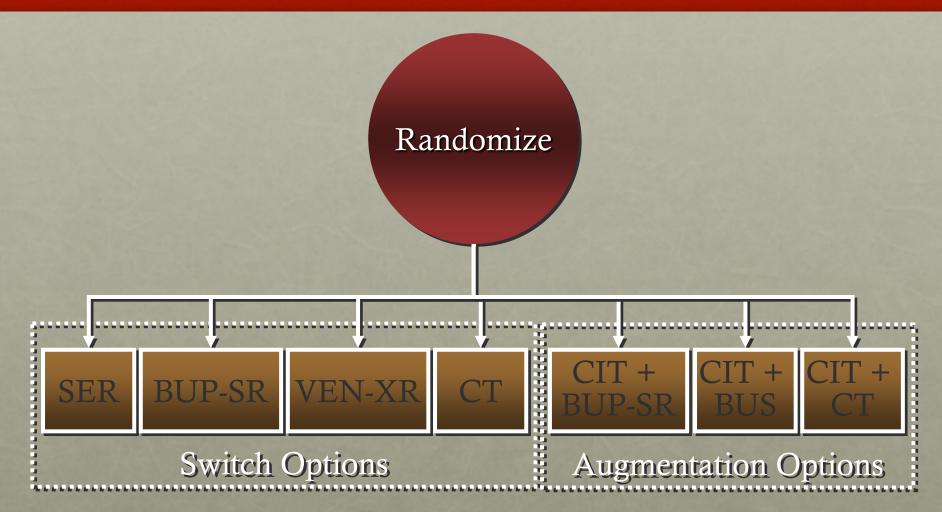
# TREATMENT LEVELS IN STAR\*D



# CONCLUSIONS FROM LEVEL 1

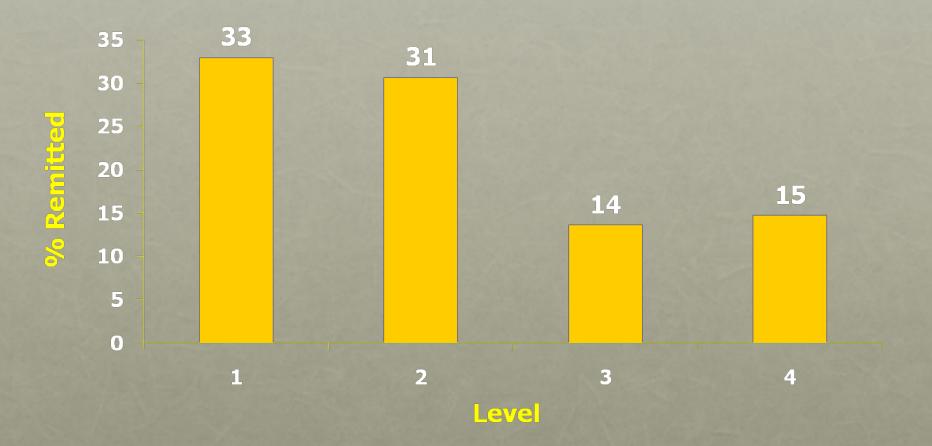
- About 1/3 will remit
- Of those who remit, remission occurs in almost 1/2 AFTER 6 weeks
- Effective treatment reduces suicide risk
- 40% will relapse within 1 year

# LEVEL 2 FINDINGS



Rush AJ, et al. Am J Psychiatry 2003;160:237.

## REMISSION RATES BY TREATMENT LEVEL (QIDS-SR<sub>16</sub>)



# LEVEL 1-2 CONCLUSIONS

- Cumulative remission rate is over 50% with first 2 steps
  - Relapse rate and drop out rates also high
- Patient preference plays a big role in strategy selection
- Pharmacological distinctions do not translate into large clinical differences
  - Therefore, other factors (eg, expected side effects and patient preferences) should help guide treatment decisions
- Switching or augmenting with CT about as effective as switching to medications

# MANAGING MDD IN THE CLINIC

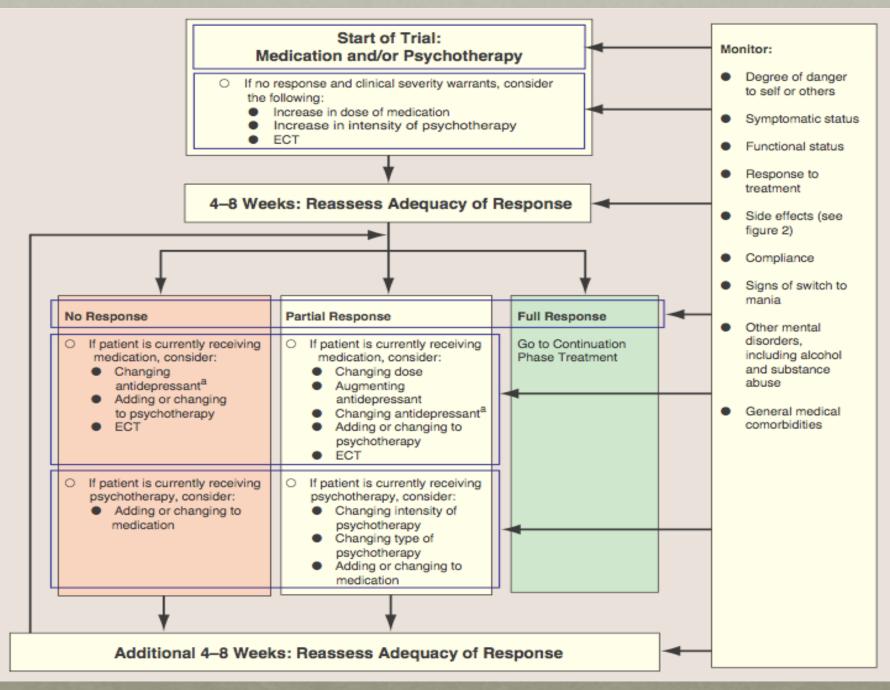
- IMPACT: Collaborative Stepped Care Project
- RCT in pts 60yrs+ w/ MDD or dysthymia
- Randomly assigned to IMPACT intervention (n=906) or to usual care (n=895)
- Intervention group had a depression care manager supervised by psychiatrist and PCP
  - Gave education, care management and support of AD management by PCP or a brief psychotherapy
- Assessed at 3, 6, 12mos for depression, satisfaction w/ care, functional impairment and QOL

# MANAGING MDD IN THE CLINIC

#### • Results IMPACT Study:

- At 12mos 45% of pts had a 50% or greater reduction in depressive symptoms from baseline compared with 19% of usual care patients p<.001
- Also had greater rates of depression treatment, satisfaction w/ care, lower depression severity, less functional impairment and greater QOL than usual care patients
- Cost Effectiveness Average cost IMPACT program was \$580/pt, <1\$pmpm. \$3,300 less overall medical cost on average for 4yr period

JAMA. 2002; 288:2836-2845



#### APA Practice Guidelines, 2010

# DOSING STRATEGIES

**Initiate Pharmacotherapy:** 

- Re-eval in 4-6wks (2<sup>nd</sup> visit)
  - If no or mild improvement and tolerating, increase dose
- Re-eval in 4-6wks (3rd visit)
  - If no improvement, switch medications
  - If mild/mod improvement, increase dose again or augment (different classes)
  - If at or near remission, maintenance mode
    - continue medication for 4-6months
    - consider indefinite treatment for tx resistant or multiple relapses.

# RATING SCALES

• Hamilton Depression Inventory (HAM-D)

• BECK Depression Inventory (BDI)

• Quick Inventory of Depression (QIDS)

• Patient Health Questionnaire (PHQ-2, PHQ-9)

# TAKE HOME

- Depression is very common, disabling and treatable.
- Therapy is first line for mild depression.
- Meds and therapy for severe depression.
- Give the medication time to work.
- Remember to screen for (hypo)mania/psychosis/SI.
- You can trust the patient self-rating scales to guide tx.
- Collaborative care approach is the ideal to strive for.

# TREATMENT SCENARIO

- 42yo male w/ MDD currently in mild depression. On Zoloft 200mg. Prominent anhedonia, anergia, low libido. No drugs/etoh, +tobacco
  - Questions?
    - (Situational? Relationship Prob?)
  - Medical r/o's?
    - Fatigue w/u TSH/Test/CBC/CMP/RPR
  - Medication vs. Therapy vs. Lifestyle?
  - Med Choices?
    - Increase Zoloft, Augment w/ Wellbutrin, Switch Meds

# TREATMENT SCENARIO

- 24yo female college student, THC abuse, with 2<sup>nd</sup> MDE, one prior hosp and SA. Predominent irritability, h/o episodes were she is super productive and "sped up".
  - Questions?
    - r/o BAD
  - Medical r/o's?
    - **RPR/UPT/utox**
    - Medication vs. Therapy?
    - Med Choices Initially?
      - Weary of BAD especially if mania worsens or made "worse" by anti-depressant.

# TREATMENT SCENARIO

- 80yo female w/ advanced ovarian CA, depressed w/ cachexia and insomnia.
  - Questions?
  - Medical r/o's?
  - Medication vs. Therapy?
  - Med Choices?

# **On-line Survey**

Please complete the <u>very short</u> 4 question survey regarding this training at: <u>http://www.surveymonkey.com/s/QYGR578</u>

# INTRO CITATIONS

- 1. The World Health Organization. The World Health Report 2004: Changing History, Annex Table 3: Burden of disease in DALYs by cause, sex, and mortality stratum in WHO regions, estimates for 2002. Geneva: WHO, 2004.
- 2. Kessler RC, Chiu WT, Demler O, Walters EE. Prevalence, severity, and comorbidity of twelve-month DSM-IV disorders in the National Comorbidity Survey Replication (NCS-R). *Archives of General Psychiatry*, 2005 Jun;62(6):617-27.
- 3. Eisenberg, Leon. Treating Depression and Anxiety in the Primary Care Setting. *The New England Journal of Medicine* (16 April 1992): 1080–1084.
- 4. Piglione, M et al. U.S. Preventive Services Task Force. Screening for Depression in Adults: Summary of the Evidence. *Ann Intern Med 2002;136(10):765-76.*
- 5. Simon GE, VonKorff M. Recognition, management, and outcomes of depression in primary care. *Arch Fam Med 1995;4:99-105.*
- 6. Cascade, E et al. Antidepressant Prescribing by Specialty and Treatment of PMDD. *Psychiatry MMC*. 2008 Dec; 5(12): 14-15.

# MDD CITATIONS

- 1. Cognitive therapy versus medication in augmentation as switch strategies in second step treatments: a STAR\*D report. *American Journal of Psychiatry*. 2007 May; 164(5):739-52.
- Evaluation of outcomes with Citalopram for depression using measurement based care in STAR\*D: Implications for clinical practice. *American Journal of Psychiatry*. 2006 Jan; 163(1):28-40.
- 3. Bupropion-SR, sertraline, or venlafaxine-XR after failure of SSRIs for depression. *New England Journal of Medicine*. 2006 March; 354(12):1231-42.
- 4. Medication augmentation after the failure of SSRIs for depression. *New England Journal of Medicine*. 2006 March; 354(12):1243-52.
- 5. A comparison of mirtazapine and nortriptyline following two consecutive failed medication treatments for depressed outpatients: a STAR\*D report. *American Journal of Psychiatry*. 2006 July; 163(7): 1161-72.

# MDD CITATIONS

- 6. A comparison of lithium and T(3) augmentation following two failed medication treatments for depression: a STAR\*D report. *American Journal of Psychiatry*. 2006 Sep; 163(9): 1519-30.
- 7. Tranylcypromine versus venlafaxine plus mirtazapine following three failed antidepressant medication trials for depression: a STAR\*D report. *American Journal of Psychiatry*. 2006 163(9): 1531-41.
- 8. Cipriani A, et al. Comparative efficacy and acceptability of 12 newgeneration antidepressants: a multiple-treatments meta-analysis. Lancet 2009 Vol 373, issue 9665, pg 746-58.
- 9. IMPACT: Collaborative Stepped CareUnutzer J, et al. Collaborative Care Management of Late-Life Depression in the Primary Care Setting: A Randomized Controlled Trial. JAMA. 2002; 288:2836-2845.
- 10. Fournier JC et al. Antidepressant Drug Effects and Depression Severity. JAMA Jan 6, 2010. Vol 303 No. 1

# MDD CITATIONS

- 11. Rush AJ, et al. The 16-Item Quick Inventory of Depressive Symptomatology (QIDS), clinician rating (QIDS-C), and self-report (QIDS-SR): a psychometric evaluation in patients with chronic major depression. Biologic Psychiatry 2003 Sep 1; 54(5):573-83.
- 12. Rush AJ, et al. The 16-Item quick inventory of depressive symptomatology (QIDS), clinician rating (QIDS-C), and self-report (QIDS-SR): a psychometric evaluation in patients with chronic major depression. Biological Psychiatry **1 September 2003 Vol. 54, Issue 5, Page 573-583.**
- 13. Kroenke K, et al. The PHQ-9: validity of a brief depression severity measure. J General Internal Medicine 2001 Sep ;16(9):606-13.
- Arroll B, et al. Validation of PHQ-2 and PHQ-9 to screen for major depression in the primary care population. Annals of Family Medicine 2010 Jul-Aug;8(4):348-53.