Where to from Here? Evidence-Based Strategies for Treatment of Refractory Depression

Part 2: Beyond STAR*D

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Learning Objectives

Attendees will:

- recognized the importance of medication dose and duration in the treatment of depression;
- know and be able to screen for alternative or comorbid diagnoses that may be associated with treatment resistant depression;
- identify evidence-based augmentation strategies for treatment resistant depression.

Case History

- Mr G is a 37-yr-old man with a 2-year history of major depression unresponsive to trials of 2 SSRIs, an SNRI, augmentation with T3, and a combination of venlafaxine and mirtazapine. He could not tolerate a TCA. He is not interested in CBT.

Treatment Refractory Depression

- Depression has not responded to at least 3 standard treatments
- STAR*D steps have been followed
- Patient could not tolerate or did not respond to treatment

Question 1

What should I do now?

1. Switch to bupropion
2. Augment with aripiprazole
3. Switch to quetiapine
4. Review his history and symptoms
5. Refer for ECT

Question 2

Is there any way to predict which of these might be most appropriate for this patient?

1. Yes
2. No

Treatment Dose and Duration

Is the dose high enough?

- Only 25% of treated patients receive an adequate dose of antidepressant
- Use at least a moderate dose for all medication trials
- If tolerated, titrate the medication to the highest recommended dose

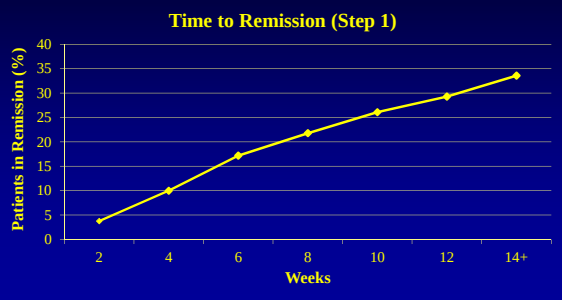
Treatment Dose and Duration

Has it been long enough?

- Some response is usually seen within 3-5 days
- Most treatment trials are 4-6 weeks
- Average response time is 6-7 weeks
- Remission rate increases for >14 weeks

STAR*D

Step 1 Outcomes



Trivedi MH, et al. Am J Psychiatry 2006;163:28

Is the Diagnosis Correct?

Consider other forms of depression

- Bipolar depression
- Depression with psychotic features
- Substance induced mood disorder
- Personality disorder

Bipolar Depression

- 3% of population
- Bipolar I patients spend 2x more time in depressive episodes than in mania or hypomania
- Bipolar II patients spend 10x more time in depressive episodes than in hypomania
- Poor response to antidepressants alone

Bipolar Depression

Screening questions

- Have you experienced any periods of at least a few days during which your mood was elevated, you did not need to sleep, and your activity level increased?
- Do any family members have bipolar disorder?
- Do you have psychotic symptoms when depressed?

Bipolar Depression

Diagnosis

- Diagnosis requires a manic or hypomanic episode
- Positive screening questions raise the index of suspicion
- Positive screening questions may justify addition of mood stabilizing medication

Bipolar Depression

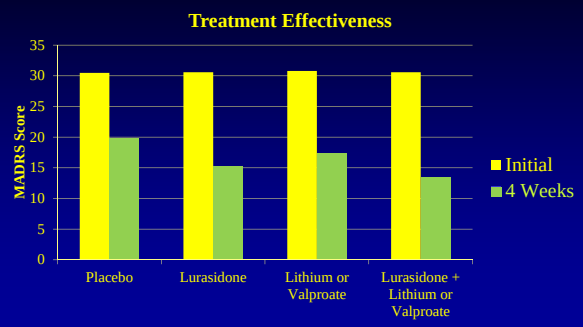
FDA-approved treatment options

- Acute treatment
  - Lurasidone (Latuda)
  - Olanzapine+fluoxetine (Symbiax)
  - Quetiapine (Seroquel)
- Maintenance treatment only
  - Lamotrigine (Lamictal)

Bipolar Depression

- FDA-approved treatments are generally combined with a mood stabilizer
- FDA-approved treatments are often combined with an antidepressant
- Data on these approaches are limited
- Treatment outcomes are fair

Bipolar Depression



Loebel A, et al. Am J Psychiatry 2014; 171:160; Loebel A, et al. Am J Psychiatry 2014; 171:169

Depression with Psychotic Features

- 1-2% of population
- Delusions or hallucinations only when depressed
- Poor response to antidepressant monotherapy

Depression with Psychotic Features

Screening questions

- At any point during your illness have you seen or heard things other people could not see or hear?
- Have you been concerned about other people following you, spying on you, or trying to hurt you?
- Have there been special messages just for you from the TV, recorded music, or reading material?

Depression with Psychotic Features

Screening questions

- Have you felt that there are strange changes in your body, such as your insides rotting or being eaten by worms?
- Do you believe that you are intentionally being punished for something you have done wrong?

Depression with Psychotic Features

Treatment

- No medication has an FDA indication
- Fair-good response (50%) to antidepressant + antipsychotic
- Excellent response to ECT (80-90%)

Substance Induced Mood Disorder

- Depression caused by persistent substance abuse
  - Alcohol
  - Barbiturates
  - Cannabis
- Requires reduction in substance use
- May also require antidepressant medication

Substance Induced Mood Disorder

Screening questions

- CAGE
  - Cut down
  - Annoyance
  - Guilt
  - Eye-opener
- T-ACE
  - Tolerance
  - Annoyance
  - Cut down
  - Eye-opener

Personality Disorders

- Personality disorders are associated with high rates of depression
  - Dependent
  - Avoidant
  - Borderline
  - Antisocial
- Although a “depressive personality” has been proposed, it is not widely accepted

Personality Disorders

- Success rates are lower than in general population
- Concurrent treatment of personality symptoms may be helpful
  - Dependent – supportive therapy
  - Avoidant – CBT and anxiolytics
  - Borderline – DBT and mood stabilizers or low-dose antipsychotics
  - Antisocial – transfer to structured environment (eg, jail)

Personality Disorders

Screening questions

- What are your relationships like?
- How stable is your mood now? How stable when you are not depressed?
- What sorts of things tend to trigger your depression?

Augmentation Beyond STAR*D

Other Evidence-based Augmentation

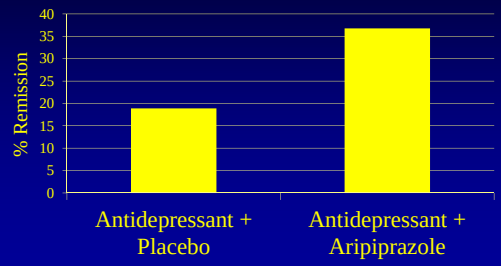
- Mirtazapine* (Remeron)
- Atypical antipsychotics
  - Aripiprazole (Abilify)
  - Lurasidone (Latuda)
  - Quetiapine (Seroquel)

*Medication is not FDA-approved for augmentation

Lopes Rocha F, et al. J Affective Disorders 2013;144:1

Antipsychotic Augmentation

Aripiprazole Augmentation Following Failed Antidepressant Monotherapy (8 weeks)



Berman RM, et al. CNS Spectrums 2009:14:197

Severe Treatment-Refractory Depression

Electroconvulsive Therapy (ECT)

- Effective in 70-80% of cases
- Generally well tolerated, even in older patients
- Primary side effect is short-term memory loss
- Outpatient maintenance treatment is available
- Primary limitation is cost

Recommendations

- Make sure the diagnosis is correct
- Address comorbid symptoms
- Use additional augmentation strategies
- Consider ECT