Treatment of Adolescent Depression in Primary Care

Brett Johnson, MD
Staff Psychiatrist
Rady Children's Behavioral Crisis Center
Assistant Clinical Professor (Voluntary), UCSD
March 17, 2011

Financial Disclosure

- I have no relationships to disclose

Off-Label Use of Medications

- This talk discusses the off-label use of medications
- Each off-label medication is clearly labeled in talk
- Clinical guidelines generally followed
  - Deviations from guidelines clearly discussed
- Discussion of off-label medications should not be construed as encouraging the use of these medications for other than FDA-indicated uses

Caveats

- Information and slides carefully reviewed prior to presentation
- Information presented here should not be assumed to be error-free
- Please consult standard references for full details regarding medications, doses, contraindications, etc.

Adolescent Depression

Depression: Epidemiology

- Prevalence of MDD
  - Children: 2.0%.
  - Children: males = females.
  - Adolescents: 8.3% (current) and around 20% throughout adolescence
  - Adolescents: females with 2x risk than males
- Dysthymic D/O
  - Children: 0.6-1.7%
  - Adolescents: 1.6-8%
  - Under recognized
  - Less clear gender differences

Major Depressive D/O: Symptoms*

- Depressed or irritable mood
- Anhedonia
- Appetite/wt change
- Sleep changes
- Psychomotor agitation/retardation
- Fatigue/loss of energy
- Worthlessness/guilt
- Trouble thinking, concentrating, making decisions
- Suicidal ideation

*Abbreviated/condensed from DSM-IV-TR which should be consulted for full diagnostic criteria

Major Depressive D/O: Symptoms*

- ***Depressed or irritable mood***
- Anhedonia
- ***Appetite/wt change***
- Sleep changes
- Psychomotor agitation/retardation
- Fatigue/loss of energy
- Worthlessness/guilt
- Trouble thinking, concentrating, making decisions
- Suicidal ideation

*Abbreviated/condensed from DSM-IV-TR which should be consulted for full diagnostic criteria

Major Depressive Disorder: Diagnosis

- Must have: depressed/irritable mood OR anhedonia for at least 2 weeks
- Need at least 5 out of 9 sx
- Impairment
- Cannot be better explained by:
  - Bereavement
  - Medical causes
  - Substance-induced
  - Another mental disorder

Depression in Kids

- Children
  - Irritability
  - Anxiety
  - Somatic sx
  - Psychotic sx
  - Conversion to bipolar d/o
- Adolescents
  - Sleep and appetite
  - Suicidality
  - More behavior problems (than adults)
  - Fewer neurovegetative sx (than adults)

Depression: Differential Dx

- Adjustment Disorder
- Bereavement
- Depression NOS
- Bipolar D/O
- Substance-induced mood d/o
- Medical causes

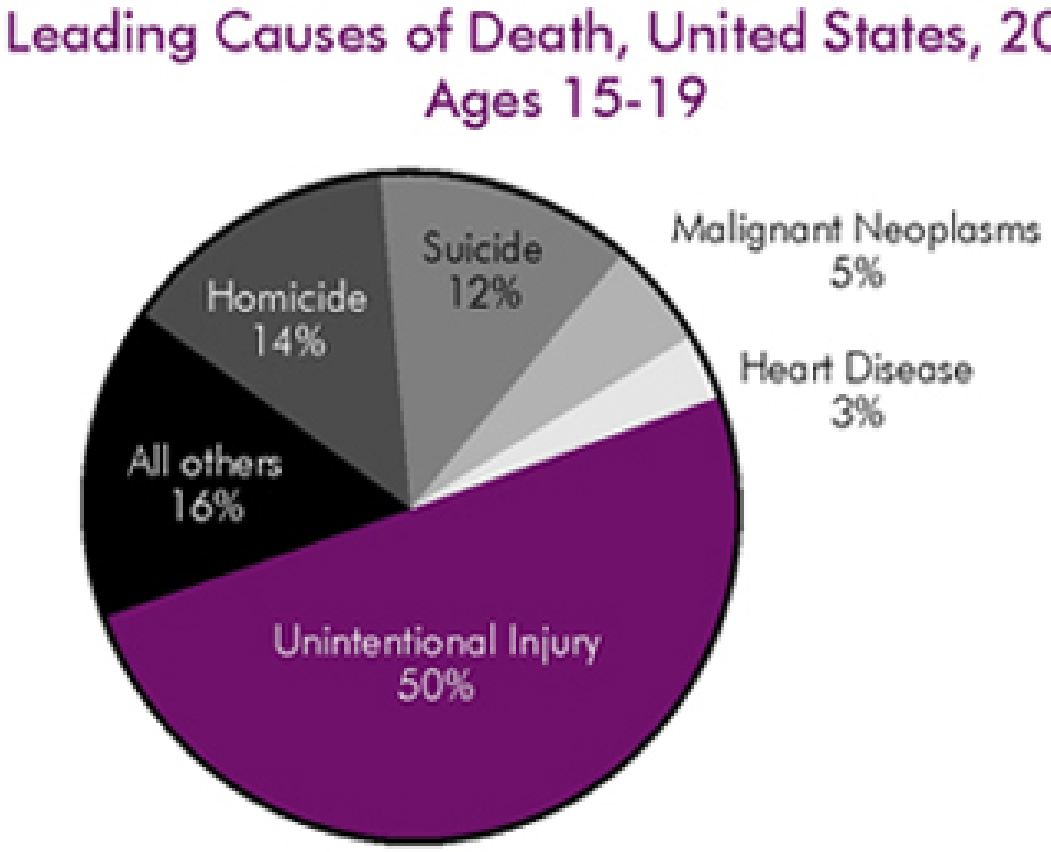
Depression: Impact on Society

A Major Cause of Disability Worldwide

Rank	1990	2020 (Estimated)
1	Lower respiratory infections	Ischemic heart disease
2	Perinatal conditions	Unipolar major depression
3	HIV/AIDS	Road traffic accidents
4	Unipolar major depression	Cerebrovascular disease
5	Diarrheal diseases	Chronic obstructive pulmonary disease

DALYs=disability adjusted life-years.
Murray CJL, Lopez AD, eds. *The Global Burden of Disease*; 1996.

Suicide: 3rd Leading Cause of Adolescent Death

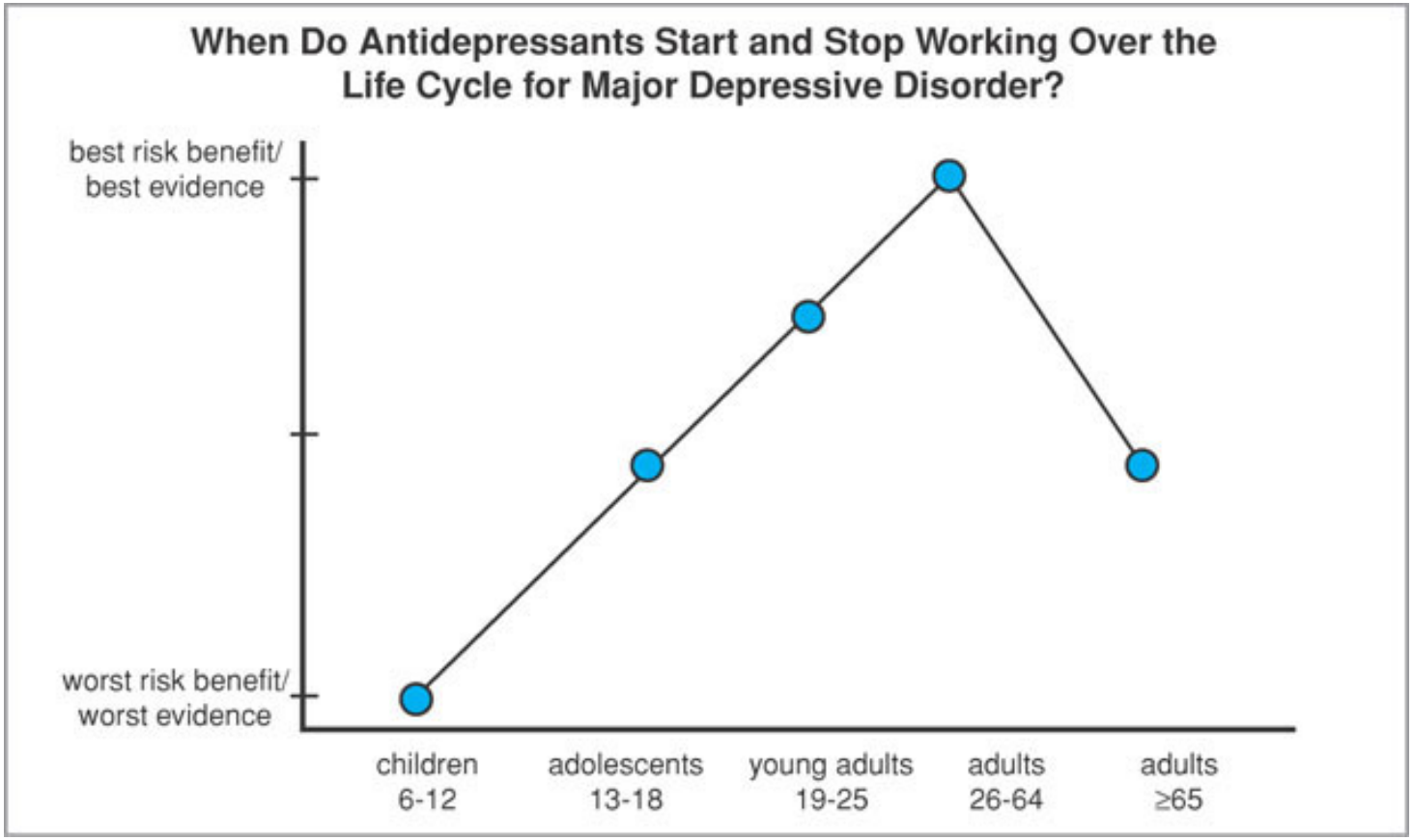


Untreated depression is by far the greatest risk factor for suicide

Depression: Treatment

- Therapy
  - Cognitive-Behavioral Therapy (CBT)
  - Interpersonal Therapy (IPT)
- Medications

Children: Poorer Response to Antidepressants



Therapy? Medications? Both?

TADS

- Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression: Treatment for Adolescents With Depression Study (TADS).
- **March, J. et al. JAMA. 2004 Aug 18;292(7):807-20.**

TADS: Participants

- 439 patients with MDD
- 12 to 17 years

- **March, J. et al. JAMA. 2004 Aug 18;292(7):807-20.**

TADS: Interventions

- Twelve weeks of
  - (1) fluoxetine alone (10 to 40 mg/d)
  - (2) CBT alone,
  - (3) CBT with fluoxetine (10 to 40 mg/d)
  - (4) placebo (equivalent to 10 to 40 mg/d).

- **March, J. et al. JAMA. 2004 Aug 18;292(7):807-20.**

TADS: Results

- Fluoxetine + CBT > Placebo (P =.001).
- Fluoxetine + CBT > fluoxetine alone (P =.02) and CBT alone (P =.01)
- Fluoxetine alone > CBT alone (P =.01).

- **March, J. et al. JAMA. 2004 Aug 18;292(7):807-20.**

TADS' Results: Suicidal Thinking

- Clinically significant suicidal thinking (29% at baseline), improved significantly in all 4 treatment groups.
- Fluoxetine with CBT showed the greatest reduction (P =.02). Seven (1.6%) of 439 patients attempted suicide; there were no completed suicides.

March, J. et al. JAMA. 2004 Aug 18;292(7):807-20.

TADS: Main Conclusion

- The combination of fluoxetine with CBT offered the most favorable tradeoff between benefit and risk for adolescents with major depressive disorder.
- **March, J. et al. JAMA. 2004 Aug 18;292(7):807-20.**

What If First-Line SSRI Doesn’t Work?

Treatment of SSRI-Resistant Depression In Adolescents (TORDIA)

- 12 Week trial of adolescents 12-18
- To determine how best to treat adolescents with depression that is "resistant" to the first SSRI antidepressant they have tried
- Participants received fluoxetine, venlafaxine, or citalopram either alone or with Cognitive-Behavioral Therapy (CBT)

Brent et al. Switching to Another SSRI or to Venlafaxine With or Without Cognitive Behavioral Therapy for Adolescents with SSRI-Resistant Depression: The TORDIA Randomized Controlled Trial. JAMA. 2008;299(8):901-913.

TORDIA CONCLUSIONS

- CBT + medication > medication alone after initial SSRI non-response.
- No difference between SSRI (fluoxetine or citalopram) and venlafaxine for second step.
- CBT added about 12% to clinical response.

FDA: Approvals and Warnings

- FDA approved for MDD:
  - Fluoxetine- ages 8 and up
  - Escitalopram- ages 12 and up
- Other antidepressants are off-label
- 2003: FDA recommended that paroxetine NOT be used in children and adolescents
- Greater risks with paroxetine/venlafaxine

FDA: Impact of FDA Warnings

- Decline in rates of MDD dx
- Decline in rates of antidepressant prescriptions
  - For PMDs, not psychiatrists
- Increase in suicide rate
  - Unclear if due to decreased antidepressant Rx

FDA Black Box Warning: More Recent Results.

- Comprehensive review of pediatric trials done between 1988 and 2006 suggested that the benefits of antidepressant medications likely outweigh their risks to children and adolescents with major depression and anxiety disorders.
- Bridge JA et al. *JAMA*. April 18, 2007;297:1683-1696

Guidelines for Adolescent Depression in Primary Care: GLAD-PC

- Of all adolescents with depression:
  - Only 50% diagnosed before adulthood
  - 2/3 are not identified by PCP as depressed
  - If diagnosed by PCP, only 1/2 receive appropriate treatment

Zuckerbrot et al. Guidelines for Adolescent Depression in Primary Care (GLAD-PC): I. Identification, Assessment, and Initial Management. *Pediatrics* 2007; 120; e1299-e1312.

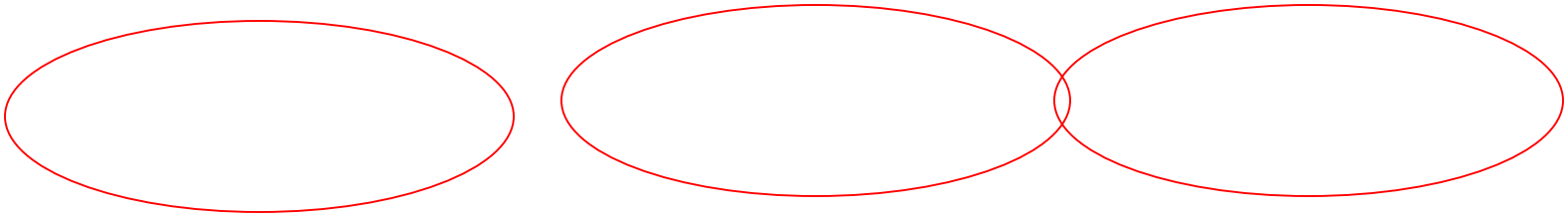
Cheung et al. Guidelines for Adolescent Depression in Primary Care (GLAD-PC): II. Treatment and Ongoing Management. *Pediatrics* 2007; 120;e1313-e1326.

Guidelines for Adolescent Depression in Primary Care: GLAD-PC

- Assist PCPs in recognizing and treating depression
- Ages 10-21

Zuckerbrot et al. Guidelines for Adolescent Depression in Primary Care (GLAD-PC): I. Identification, Assessment, and Initial Management. *Pediatrics* 2007; 120; e1299-e1312.

Cheung et al. Guidelines for Adolescent Depression in Primary Care (GLAD-PC): II. Treatment and Ongoing Management. *Pediatrics* 2007; 120;e1313-e1326.



QuickTime™ and a
decompressor
are needed to see this picture.

Conclusions: Treatment of MDD

- First episode, no SI, no HI, no psychotic symptoms: Try therapy treatment for at least 1-3 months.
- Screen for comorbid conditions
- If pt does not respond to supportive measures and therapy, consider adding antidepressant
  - Generally should be fluoxetine
  - Lexapro (escitalopram) is viable alternative
- More severe cases: consider concomitant trial of therapy and medications.

Conclusions: Treatment of MDD

- Continue treatment for 6-12 months after depression has remitted
- Remember: therapy + medication is better than either one alone
- Monitor closely for relapse

Antidepressants: Starting and Target Doses

- Start low, go slow
- Side effects emerge first
- May need 4-8 weeks at treatment doses for effect

QuickTime™ and a
decompressor
are needed to see this picture.

Depression: Monitoring Pts on Antidepressants

- FDA recommends:
  - Weekly face to face visits for 4 weeks
  - Biweekly face to face visits for 4 weeks
  - Monthly visits thereafter
  - But: start monitor plan over if raise dose
  - Phone check in acceptable as alternative if face to face appointment impossible
- No evidence that this reduces risk of adverse outcome
- Most clinicians cannot comply with recommendations

Active Monitoring

- Discourages a passive approach
- Useful for mild to moderate cases
  - Usually for 4-8 weeks
  - If no response, consider moving to more
- Also useful for more serious cases

Active Monitoring

- More frequent visits
- Phone check-ins
- Support groups
- Educational materials
- Exercise
- Sleep hygiene
- Self-management goals
- School support?
- Church support?

Resources

- Glad-pc.org for GLAD-PC toolkit
- Facts for Families (AACAP) for handouts on common mental health conditions www.aacap.org/cs/root/facts_for_families/facts_for_families
- National Alliance for the Mentally Ill (NAMI) nami.org

Conclusions: When to Refer

- Failure of 2 antidepressant trials
- Significant side effects such as:
  - Agitation
  - Worsened mood
  - Manic/hypomanic activation
- Psychotic sx
- Significant suicidal thoughts
- Complex comorbidity

Contact Information

- bljohnson@rchsd.org
- (760) 730-5900