The Society for Clinical Child and Adolescent Psychology (SCCAP): Initiative for Dissemination of Evidence-based Treatments for Childhood and Adolescent Mental Health Problems

With additional support from Florida International University and The Children’s Trust.
Keynote
Evidence-based Medication Treatment for Anxiety and Depression in Young People

Gabrielle A. Carlson, MD
Professor of Psychiatry and Pediatrics
Director, Child and Adolescent Psychiatry
Stony Brook University School of Medicine
Evidence based medication treatment of depression and anxiety in young people

Gabrielle A. Carlson, MD
Professor of Psychiatry and Pediatrics
Director, Child and Adolescent Psychiatry
Stony Brook University School of Medicine
# Disclosure – 2011

<table>
<thead>
<tr>
<th>Company</th>
<th>Research Support/Honoraria/SAB</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMS</td>
<td>Research</td>
</tr>
<tr>
<td>GSK</td>
<td>Research</td>
</tr>
<tr>
<td>FIU</td>
<td>This presentation</td>
</tr>
</tbody>
</table>
What I will cover

• How to make sense of antidepressant drug trials
• Recently published studies in the treatment of major depression (MDD)
  - (I am concentrating on MDD because findings are more controversial than for anxiety disorders but will mention those too)
• Psychiatric adverse events (aka side effects)
• How I put the information together
Ways of determining drug response

- **Statistical significance**: If sample size is large enough, a minor change may be statistically significant. That may have public health implications but may not have strong clinical implications for single patient.

- **Effect size**: Tx group minus Change in Placebo or Control group, (i.e., differential change) divided by standard deviation at baseline; http://web.uccs.edu/lbecker/Psy590/escalc3.htm
  - >0.8 = large E.S.
  - 0.5 to 0.7 = medium E.S.
  - 0.2 to 0.4 = small E.S.

- **Absolute Treatment Benefit**: % drug response minus % placebo response

- **Change from baseline in rating scale used**

- **% patients who respond/recover/no longer meet criteria for disorder**
Ways of determining drug response e.g. Depression: Response vs. Remission


CDRS-r Scores

40

28

Depression

• **Response/Partial Response** is 50% reduction in baseline CDRS score

• **Remission**: Reduction in CDRS-r to ≤28 regardless of baseline score

• lower risk of relapse

• improved physical and social functioning
APPROVAL STATUS FOR DRUGS USED FOR INTERNALIZING DISORDERS
Positive studies are more numerous than FDA approvals for anxiety disorders

<table>
<thead>
<tr>
<th>Drug</th>
<th>Approved for kids</th>
<th>Published PBO controlled</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoxetine/PROZAC</td>
<td>MDD 8-17 OCD</td>
<td>MDD=4; Anx=2 OCD=2</td>
</tr>
<tr>
<td>Paroxetine/PAXIL</td>
<td>NO</td>
<td>MDD =3 SoPH=1 OCD=1</td>
</tr>
<tr>
<td>sertraline/ZOLOFT</td>
<td>OCD</td>
<td>MDD=2; OCD=2 GAD=2</td>
</tr>
<tr>
<td>Citalopram/CELEXA</td>
<td>NO</td>
<td>MDD=2</td>
</tr>
<tr>
<td>Bupriopion/WELLBUTRIN</td>
<td>NO</td>
<td>ADHD</td>
</tr>
<tr>
<td>Mirtazepine/REMERON</td>
<td>NO</td>
<td>Study done</td>
</tr>
<tr>
<td>Escitalopram/LEXAPRO</td>
<td>MDD-12-17</td>
<td>MDD=1</td>
</tr>
<tr>
<td>Venlafaxine/EFFEXOR</td>
<td>NO</td>
<td>MDD=1 (2); Anx=1</td>
</tr>
</tbody>
</table>
Tricyclic Antidepressants (TCAs)

- Meta-analysis of the 6 studies using TCAs in children and/or adolescents (n=196):
  - None found TCA were superior to placebo
  - High placebo response rates (21% to 70% across studies) or low drug/placebo response rates
  - Stringency of response higher than in current trials
  - **Effect size -0.15 in children, 0.47 in teens**

- Fear of cardiovascular side effects (and the “c.y.a.” of EKGs) However, comparison between PBO in and IMI in the paroxetine/IMI trial (Keller et al., 2001) also negative
### Controlled Industry Pediatric Depression Trials

<table>
<thead>
<tr>
<th>Medication</th>
<th>Ages</th>
<th>Number of Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td><em><em>Positive</em> Studies</em>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>8-17</td>
<td>1 (2 NIMH sponsored)</td>
</tr>
<tr>
<td>Sertraline</td>
<td>6-17</td>
<td>2 (a priori pooled analysis)**</td>
</tr>
<tr>
<td>Citalopram</td>
<td>7-17</td>
<td>1</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>12-17</td>
<td></td>
</tr>
<tr>
<td><em><em>Negative</em> Studies</em>*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Citalopram</td>
<td>13-18</td>
<td>1</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>6-17</td>
<td>1</td>
</tr>
<tr>
<td>Mirtazapine</td>
<td>7-18</td>
<td>2</td>
</tr>
<tr>
<td>Nefazadone</td>
<td>7-17</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>12-17</td>
<td></td>
</tr>
<tr>
<td>Paroxetine</td>
<td>7-17</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>12-18</td>
<td></td>
</tr>
<tr>
<td></td>
<td>13-18</td>
<td></td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>7-17</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>7-17</td>
<td></td>
</tr>
</tbody>
</table>

* On primary outcome measure

Absolute Benefit Increase* that can be attributed to antidepressants using various response outcomes

Bridge, Ann Med, 2005

(*difference between percent responded and placebo response)

number in ( ) = number of studies

![Bar chart showing absolute benefit increase for various treatments and adult populations.](chart.png)
Effect sizes based on CDRS (mostly)
RECENTLY COMPLETED randomized MDD TRIALS (non-industry-14 sites)

- TADS: Treatment of Adolescent Depression Study- 12 wk with 6, 12 month f-u (any rx after 12 wks); CBT/FLX, FLX, CBT, PBO; March et al., JAMA, 2004; JAACAP
- ADAPT: Adolescent Depression Antidepressant Psychotherapy Trial-28wk, CBT/FLX, FLX; Goodyer et al., BMJ, 6/2007 (on line) [6 sites]
- TORDIA: Treatment of Resistant Depression in Adolescence; next treatment after 1st SSRI failure; Brent et al., presented at ISRCAP, June, 2007
% Remission (CDRS<28), response (CGI-I 1 or 2), CGAS ≥ 70 and no MDD criteria in TADS at 12 weeks
Moderators and Mediators in TADS 12 wks

Mild to moderate depression: COMB>FLUOX>CBT=PBO
Moderate to severe depression: COMB=FLUOX>CBT=PBO
Poor response = Indicators of ↑ depression severity:
  - Higher scores in depression scales
  - Long duration
  - Suicidal ideation/attempts
  - ↑Hopelessness
  - Poor functioning
Poor response (psychological predictors)
  - ↓ expectations to treatment benefits
  - ↓ Coping skills
  - ↓ Socio-economic Status
  - ↑ Comorbid disorders
  - ↑ Family conflict and dysfunction
  - ↑ Exposure to negative events (e.g., abuse)
FIGURE 1. Depression Scores From Baseline to End of Naturalistic Follow-Up for 327 Adolescents With Major Depression Disorder Treated With Fluoxetine, Cognitive-Behavioral Therapy (CBT), or a Combination

Adjusted Predicted Mean Score on Children's Depression Rating Scale—Revised (intention-to-treat analysis)*

* Derived from the random coefficients regression model with adjustments for fixed and random effects.

Study entrance remission

TADS Team, Am J Psychiatry 2009; 166:1141-1149
At what point can you determine that response/remission is likely?

N=168 - Open label Fluoxetine

At week 4, a CDRS-R reduction of ~50% best discriminates remitters from non-remitters; as effective with children as teens; + Fam hx a predictor;  

Outcomes in ADAPT – A UK study of Flx and CBT; no placebo

% CGI very much or improved but CDRS-R never ≤28

Goodyer et al., Br. J. Psychiatry, 2008
## COMPARISON OF ADAPT AND TADS TRIALS

<table>
<thead>
<tr>
<th></th>
<th>ADAPT N=208 r 6 sites Age 11-17</th>
<th>TADS N=439 r 13 sites 12-17</th>
</tr>
</thead>
<tbody>
<tr>
<td>% comorbid</td>
<td>89</td>
<td>52</td>
</tr>
<tr>
<td>X HoNOSCA</td>
<td>25</td>
<td>17</td>
</tr>
<tr>
<td>X CDRS</td>
<td>59</td>
<td>60</td>
</tr>
<tr>
<td>X CGAS</td>
<td>41</td>
<td>50</td>
</tr>
<tr>
<td>% suicidal</td>
<td>47%</td>
<td>27%</td>
</tr>
<tr>
<td>3, ~ 6mo resp</td>
<td>41% 53%</td>
<td>71% 80%</td>
</tr>
<tr>
<td>3, ~6mo Honosca</td>
<td>17 15</td>
<td>10.6 (7.9)</td>
</tr>
<tr>
<td>12 mo CDRS</td>
<td>Dropped 1.5 sds</td>
<td>Dropped 2 sds</td>
</tr>
</tbody>
</table>

**HoNOSCA** = Health and Social Functioning Scale
Age related Antidepressant response in MDD

Bridge et al., JAMA 297:1683, 2007
Safer, Pediatrics, 2007

P values

0.08 <.001 <.001

Children Teens total

AD PBO

P values
Reasons for modest response rate

- High placebo response rates; rates children > teens > adults (Bridge et al., JAMA 297:1683, 2007; Safer, Pediatrics, 2006, 118(3):1248-51)
- Increasing placebo response with year of study (Walsh, 2003)
- Pharmacokinetics differ a little in young people (Findling et al., JCAP 2006)
- In MDD trials, decrease in the magnitude of antidepressant treatment effects as the number of study sites increased. (Bridge et al., 2007)
- In 9 of 15 MDD trials less efficacy with longer duration of illness. (Bridge et al., 2007)
- Some think that higher rate of child BP decreases response rate but lithium treatment in putatively bipolar depressed children had no effect (Geller et al.,)
- Duration of trials aren’t long enough (ADAPT Study) though recent data indicate most response is evident by 4-6 weeks (Tao et al., 2009)
- Drugs just aren’t effective enough (Carlson, now)
Predictors of placebo response in internalizing disorders
Cohen et al., JCAP 20:39-47, 2010

- Lower placebo response rate associated with
  - Caucasian race
  - Male gender
  - Washout period in the study
  - Longer illness duration
  - Type of internalizing disorder: OCD 31% (range 4-41%) < Anxiety disorder 39.6% (9-53%) < MDD 49.6% (17-90%)
  - RULE OF THUMB: When placebo response <33%, drug superior; when >40%, placebo superior
TORDIA  
(Brent et al., JAMA 2008; 299:901–913)

next treatment after 1st SSRI failure

- 7 years to complete
- 334 teens – no or incomplete response to adequate trial of 1 SSRI (investigators continued this 2 more wks, raised dose 2 weeks before starting – only 6% of original sample responded)
- Randomized to another SSRI (paroxetine, citalopram, sertraline), SNRI (venlafaxine), or CBT added to either 2nd antidepressant or venlafaxine
- Blinded treatment for 12 weeks, then open treatment for 12 wks then naturalistic follow up
- 6 sites
TORDIA data at 24 months
Emslie et al., Am J Psychiatry, 2010

61.6% of whose who’d remitted
At 24 months had shown a clinical
Response by wk 12 (vs 18.3%).

Type of AD or CBT
Did not impact time
To remission or
Time to relapse

Response – CGI ≤2 or 50% drop on CDRS; Remission- 3 wks of ≤1 dep symptom; Relapse-2wks of definite or probable depression.
Cumulative REMISSION rate
12 wks - 17.7%
24 wks – 38.9%
48 wks - 50%
72 wks - 61.1%

Median time to remission - 25 wks

~30% of remitters still had low self esteem, irritability, fatigue

Remission predictors:
• Lower depression scores (CDRS, BDI etc)
• Shorter episode
• Lower CGI-severity
• Higher CGAS
• Less NSSI
• Less SUD

Demographic variables and comorbidity were not predictors
TORDIA-Naturalistic follow up
Vitiello et al., J Clin Psychiatry, 2010

- Relapse between 24 and 72 weeks was 25.4%
- Type of treatment (med only, CBT, SSRI or venlafaxine) didn’t matter
- Correlation between CDRS-R and CGAS was $r = -0.66$
- Suicidality declined but those on venlafaxine showed less decline ($p<0.03$)
Long term outcome of TORDIA sample

Vittiello et al., J. Clinical Psychiatry, 2010

Figure 3. Trajectories of Depression Symptoms (Children’s Depression Rating Scale–Revised Version [CDRS-R]) by Remission Status at Week 72

A. Raw Mean Score

- No remission
- Remission

B. Estimated Mean Score

- No remission
- Remission

At week 6, remitters had lower CDRS-R scores (39.5 ± 12.7) than nonremitters (49.9 ± 3.6), t_{331} = 7.15, P < .001. Error bars: 95% confidence interval.
Long term outcome of TORDIA sample

Vittiello et al., J. Clinical Psychiatry, 2010

Symptoms present in remitters and non-remitters

**B. Remitters and Nonremitters**

- Low Self-Esteem
- Sleep
- Depressed Feelings
- Irritability
- Fatigue
- Schoolwork
- Social Withdrawal
- Difficulty Having Fun
- Physical Complaints
- Appetite
- Excessive Weeping
- Guilt
- Morbid Ideation
- Suicidal Ideation
- Facial Affect
- Hypoactivity
- Lisless Speech

**CDRS-R Item**

*Percentage of participants assessed at 72 weeks (n = 173) endorsing (score of 3 or above) specific symptoms of the CDRS-R. Percentage of participants assessed at 72 weeks who had reached remission (n = 138) or not (n = 35) in TORDIA, endorsing (score of 3 or above) specific symptoms of the CDRS-R. Remission is defined as at least 3 consecutive weeks without clinically significant depressive symptoms, corresponding to a score of 1 on the A-LIFE.*

Abbreviations: A-LIFE = adolescent version of the Longitudinal Interval Follow-Up Evaluation, CDRS-R = Children's Depression Rating Scale-Revised Version, TORDIA = Treatment of Selective Serotonin Reuptake Inhibitor (SSRI)–Resistant Depression in Adolescents study.
Maintenance Treatment for Adolescent Depression

<table>
<thead>
<tr>
<th>Phase</th>
<th>Sertraline (n = 93)</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Phase</td>
<td>12 weeks</td>
<td></td>
</tr>
<tr>
<td>Continuation Phase</td>
<td>(n = 51)</td>
<td></td>
</tr>
<tr>
<td>Maintenance Phase</td>
<td>(n = 13)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Sertraline (n = 9)</td>
<td>Placebo</td>
</tr>
<tr>
<td></td>
<td>24 Weeks</td>
<td></td>
</tr>
<tr>
<td></td>
<td>52 Weeks</td>
<td></td>
</tr>
</tbody>
</table>

Maintained Response (No Recurrence) at 52 Weeks

- Sertraline: 38%
- Placebo: 0%

Summary of treatment studies of adolescent depression-CBT
Walkup editorial, Am J Psychiatry, 2010

- CBT and medication > medication alone on some outcomes (e.g. suicidality) in TADS but not ADAPT or TORDIA
- CBT doesn’t add much in severe depression.
- In the TORDIA acute phase, the groups getting combined treatment had an approximately 10% greater response rate, but this between-group difference did not persist to week 24.
- TORDIA, like ADAPT, did not find a signal for the protective effects of CBT.
- Depression is different from anxiety in this regard, as well as in response to SSRIs
Summary of treatment studies of adolescent depression-Meds

Walkup editorial, Am J Psychiatry, 2010

- Clinic visits were weekly and dose adjustments brisk.
- Data suggest that doses should be adjusted quickly and to use adequate doses.
- For complex or treatment resistant cases, find that out soon.
- How long to wait before switching antidepressants is not fully established, but remitters usually demonstrate improvement by 8–10 weeks.
- Minimal response or failure to respond by 8–10 weeks does not preclude later improvement, but clinicians should be prepared for the management of resistant depression early in treatment.
Treatment of TEEN (vs child) depression

• Investigator-initiated studies such as TADS, APADT, and TORDIA (as opposed to industry-sponsored studies which have high placebo response rates) suggest that treatment for teen depression that includes medication is effective and can be implemented safely.

• It is important to make sure that teens get to the clinic and get there early in their course of illness.
Bottom line benefit for MDD in children and adolescents

• Drug produces some improvement in 61% of children and adolescents; placebo works in half (50%) of the participants. Bridge et al., JAMA 297:1683, 2007

• The teen response is more robust than the child response. Bridge et al., JAMA 297:1683, 2007

• Teen response > child response because placebo response lower. Bridge et al., JAMA 297:1683, 2007

• In general, efficacy was inversely proportional to duration and severity of depression. Bridge et al., JAMA 297:1683, 2007; Goodyer et al., BMJ 2007

• CBT OK in mild depression; may add to treatment resistant depression (TORDIA)

• Close follow up with attentive treatment is needed

• Algorithm: SSRI → SSRI+CBT → 2\textsuperscript{nd} SSRI/SNRI + CBT
Proportion (CGI-I) responders (intention-to-treat population) for children and adolescent subgroups and total -week 16 LOCF for ANXIETY disorders

Same drug and dose; different conditions

SOCIAL PHOBIA

MAJOR DEPRESSION


Emslie et al; JAACAP, 45:709, 2006
Same drug and dose; different conditions

GENERALIZED ANXIETY DISORDER

MAJOR DEPRESSION

Venlafaxine ER in GAD

Venlafaxine ER in MDD; Emslie et al., JAACAP 46: 479-488, 2007
Efficacy of CBT, SSRI and both in anxiety disorders in youth
Walkup et al., NEJM, 2008

No difference
Combo 3X better
Issues with adverse events

• How elicited?
  – Spontaneous or by rating scale
  – How thorough is the rating scale
  – Do rating/spontaneous reports agree with each other
• Determined a priori like efficacy?
• If present, how serious?
  – Did it cause study drop out
  – Was the symptom present but not troubling
  – Can you tell if it is a symptom of the condition or the treatment
Suicidality in TADS-note different measures
Emslie et al., JAACAP, 2007

- A=> 31 on Suicidal Ideation Questionnaire
- B=Suicidality item on the CDRS-1 point
- C=5 point CDRS increase
- D=Any spontaneous report/Vetted through the Columbia rating
CDRS-r Suicidal ideation item

13. SUICIDAL IDEATION

☐ 1. Understands the word "suicide" but does not apply the term to himself/herself

☐ 2. Sharp denial of suicidal thoughts

☐ 3. Has thoughts about suicide, or hurting himself/herself (if he/she does not understand the concept of suicide), usually when angry

☐ 4

☐ 5. Has recurrent thoughts of suicide

☐ 6

☐ 7. Has made a suicide attempt within the last month or is actively suicidal
Absolute Suicidal Behavior Increase* that can be attributed to intervention using various response outcomes 
(*difference between percent drug and placebo response) 
number in ( ) = number of studies
Suicidality Risk with Drug Treatment by Age

Adult and Pediatric Studies

Odds Ratio

Age

Behavior or Ideation

Behavior

Suicidality Risk with Drug Treatment by Age
Suicidal Ideation/Suicide Attempts in Placebo-Treated Participants

(Bridge et al., JAMA, 2007)

- Among participants treated with placebo, the risk of suicidal ideation/suicide attempt was greater in MDD trials compared with non-OCD anxiety disorders trials (odds ratio, 9.9; 95% CI, 1.6 to 406.3) and OCD trials (odds ratio, 5.8; 95% CI, 0.9 to 237.3).
- These effects were limited to adolescent participants. There was no evidence of a treatment x indication x suicidal ideation/suicide attempt interaction ($P = .53$).
EFFECT OF ANTI-DEPRESSANTS ON OVERALL SUICIDE RATE ISN’T CLEAR

Milane et al
PLOS Medicine
3(6) e 90
June 2006
www.plosmedicine.org
Relative Risk of Activation
(note: confidence intervals very wide; * means statistically significant)
Age effects on behavioral toxicity

- Number Needed to Harm (NNH) for Mood Stabilizer use after 3 months of Antidepressant use (Martin et al., 2004)
  - Ages 5-9, nnh 13; Ages 25-29 nnh 29
- Review of SSRI trials (Safer and Zito, 2006) child average 10.7% (32 of 298) for active drug and 3.4% (10 of 294) for placebo; adolescents average 2.1% (13 of 622) for SSRIs and 1.9% (10 of 538) for placebo.
- Rates of disinhibition in children < age 8 significantly higher than those over age 8 (Carlson and Mick, 2003)
- >350 teens have been enrolled in carefully done med trials with up to 1 year follow up. < 5 cases of mania – if that.
Bottom line re: overall adverse events

- Somatic effects not that different from placebo
- Usually <10%
- The AEs of greatest psychiatric relevance and concern are behavioral activation and suicidal behavior
  - Activation rates vary widely from 2-26%
  - Younger children are more vulnerable
  - Children with developmental disabilities are more vulnerable
Bottom line on Suicidality (so far)

- The suicidal behavior rate (mostly ideation and threat, few attempts, no suicides) is low but always higher on medication.
- “emergence” of suicidal behavior on meds is about 3-4% compared to ~1-2% in placebo treated kids.
- There is a relationship between age and suicidal behavior; rates are higher in younger people-up to age 25 in fact.
- There is a relationship between disorder and suicidality; rates are higher in young people treated for depression.
- The number of 6-17 year olds one needs to see to get a response is about 10; the number to see before seeing suicidal behavior is about 112.
- While primary outcomes were established a priori, measures of suicidal behavior were not.
# Internalizing disorders medication treatment score card

(Bridge et al., JAMA, 2007)

<table>
<thead>
<tr>
<th></th>
<th># studies</th>
<th># patients</th>
<th>AntiD resp</th>
<th>Pbo Resp Prd*</th>
<th>NNT</th>
<th>SuiB AD SuiB Pbo Prd</th>
<th>NNH</th>
<th>E.S.</th>
</tr>
</thead>
<tbody>
<tr>
<td>MDD</td>
<td>13/2910</td>
<td></td>
<td>61%;50%</td>
<td>11%</td>
<td>10</td>
<td>3%; 2% 1%</td>
<td>112</td>
<td>.25</td>
</tr>
<tr>
<td>OCD</td>
<td>6/705</td>
<td></td>
<td>52%;32%</td>
<td>20%</td>
<td>6</td>
<td>1%; 0.3% .5%</td>
<td>200</td>
<td>.48</td>
</tr>
<tr>
<td>Anxiety</td>
<td>6/1136</td>
<td></td>
<td>69%;39%</td>
<td>30%</td>
<td>3</td>
<td>1%; 0.2% 0.7%</td>
<td>143</td>
<td>.69</td>
</tr>
</tbody>
</table>

Prd=Pooled risk difference like Absolute Treatment Benefit
SSRI Rx Rates in USA, 2002–2005, Stratified by Age Group -Expressed as a % of the 2003 Rate

Largest national database of longitudinal Integrated health care claims from 1999-2007; 1° care-44% decrease for kids, 29% adults; no substitute care to offset in kids

Libby et al., AGP 2009; 66:633-39

Suicide Rate in Children and Adolescents (Ages 5–19 Years) in the United States, 1988–2004

Editorial: How Can We Know Whether Antidepressants Increase Suicide Risk? Gregory E. Simon, M.D.

What to tell patients:

“The Food and Drug Administration requires a warning that antidepressant medications can sometimes cause or increase thoughts of suicide. That is because studies in children, adolescents [and young adults] have shown that antidepressants can increase suicidal thoughts. However, other studies have shown that the overall risk of attempting suicide goes down after starting antidepressant medication. Even if antidepressants help most people who take them, some people may have very negative reactions. Thus, it is important that we have regular contact over the next few weeks. If you have thoughts about suicide or about harming yourself, please contact me right away.”
My Summary of Data for Pediatric Depression and Anxiety

- Benefit of most antidepressants in children and adolescents for depression (outside of fluoxetine) is often modest.
- Benefit in anxiety disorders is better in part because placebo responses are lower.
- Risks of suicidal behavior and activation are small but consistently associated with antidepressant medication and in younger patients.
- Given the morbidity of mood and anxiety disorders in children and adolescents treatment should be vigorously pursued.
- It is just necessary to be honest about both the benefits and risks.
Severe depression is a deep hole; we need better ways to get out of it.
For more information, please go to the main website and browse for workshops on this topic or check out our additional resources.

**Additional Resources**

**Online resources:**

**Selected Peer-reviewed Journal Articles:**
Peer Reviewed Journal Articles:


TADS Team(2004). Fluoxetine, cognitive-behavioral therapy, and their combination for adolescents with depression: Treatment for Adolescents with Depression Study (TADS) randomized controlled trial. *JAMA*, 292, 807-820.


