

Adolescent Depression: Research to Practice

Graham J. Emslie, MD
University of Texas Southwestern Medical Center at Dallas
And Children's Medical Center

Childhood Depression

- Prevalence rate of up to 8%.
- High rates of comorbid psychiatric diagnoses.
- Relapse and recurrence rates from 34-75%.
- Pediatric depression leads to long-term consequences with school and work performance, substance abuse, suicide attempts, legal difficulties, etc.

US vs. Hong Kong Adolescents

| | US | Hong Kong | References |
|-------------------|------------------------------|----------------------------|--|
| MDD | 2.2% | 2.2% | Stewart et al., 2002 |
| Suicide attempts | 12% 19% girls 16% boys | 6%* 9% girls 3% boys | Stewart et al., 2006 |
| Suicidal ideation | 33% girls 35% boys | 42% girls 34% boys | Lam et al., 2004; Stewart, Lam, et al., 1999 |

* $p < 0.001$ (US vs. Hong Kong; girls vs. boys)

PHQ-9A

Directions: Circle the appropriate number in answer to the following question:
 ****Have you had any of the following problems during the LAST TWO WEEKS?

1. Little interest or pleasure in doing things?
 3. Yes: Nearly everyday in the past 2 weeks
 2. Yes: A few days in the past 2 weeks.
 1. No
2. Feeling down, depressed, irritable or hopeless?
 3. Yes: Nearly everyday in the past 2 weeks
 2. Yes: A few days in the past 2 weeks.
 1. No
3. Trouble falling asleep, staying asleep, or sleeping too much?
 3. Yes: Nearly everyday in the past 2 weeks
 2. Yes: A few days in the past 2 weeks.
 1. No
4. Feeling tired or having little energy?
 3. Yes: Nearly everyday in the past 2 weeks
 2. Yes: A few days in the past 2 weeks.
 1. No
5. Poor appetite, weight loss, or overeating?
 3. Yes: Nearly everyday in the past 2 weeks
 2. Yes: A few days in the past 2 weeks.
 1. No
6. Feeling bad about yourself-or feeling that you are a failure, or that you have let yourself or your family down?
 3. Yes: Nearly everyday in the past 2 weeks
 2. Yes: A few days in the past 2 weeks.
 1. No
7. Trouble concentrating on things like school work, reading, or watching TV?
 3. Yes: Nearly everyday in the past 2 weeks
 2. Yes: A few days in the past 2 weeks.
 1. No
8. Moving or speaking so slowly that other people have noticed? Or the opposite—being too fidgety or restless that you were moving around a lot more than usual?
 3. Yes: Nearly everyday in the past 2 weeks
 2. Yes: A few days in the past 2 weeks.
 1. No
9. In the past 2 weeks, have you been so sad, down, irritable, or depressed that it has been difficult to do your work, take care of things at home, or get along with other people?
 1. not difficult at all
 2. a little difficult
 3. quite difficult
 4. very difficult
 5. extremely difficult

QUICK INVENTORY OF DEPRESSIVE SYMPTOMATOLOGY - ADOLESCENT (17 ITEM) - SELF REPORT
(QIDS-A₁₇-SR)

Name: _____ Today's Date: ____/____/____

Please circle the one description for each question that best describes you for the past seven days.

1. Falling Asleep:

- 0 I always fall asleep in less than 30 minutes.
- 1 I take at least 30 minutes to fall asleep, less than half the time.
- 2 I take at least 30 minutes to fall asleep, more than half the time.
- 3 I take more than 60 minutes to fall asleep, more than half the time.

2. Sleep During the Night:

- 0 I do not wake up at night.
- 1 I toss and turn a lot on some nights.
- 2 I wake up at least once in the middle of the night, but I go back to sleep easily.
- 3 I wake up many times in the middle of the night and usually stay awake for 20 minutes or more on most nights.

3. Waking Up Too Early:

- 0 Most of the time, I wake up no more than 30 minutes before I need to get up.
- 1 More than half the time, I wake up more than 30 minutes before I need to get up.
- 2 I almost always wake up at least one hour or so before I need or want to, but I go back to sleep eventually.
- 3 I wake up at least one hour before I need or want to, and can't go back to sleep.

4. Sleeping Too Much:

- 0 I sleep no longer than 7-8 hours each night, without napping during the day.
- 1 I sleep no longer than 10 out of 24 hours a day including naps.
- 2 I sleep no longer than 12 out of 24 hours a day including naps.
- 3 I sleep longer than 12 out of 24 hours a day including naps.

5. Feeling Sad:

- 0 I do not feel down, unhappy, sad, or miserable.
- 1 I feel down, unhappy, sad, or miserable less than half the time.
- 2 I feel down, unhappy, sad or miserable more than half the time.
- 3 I feel really down, unhappy, sad, or miserable pretty much all the time.

6. Feeling Irritable:

- 0 I do not feel crabby, grouchy, or cranky.
- 1 I feel crabby, grouchy, or cranky less than half the time.
- 2 I feel crabby, grouchy, or cranky more than half the time.
- 3 I feel crabby, grouchy, or cranky nearly all of the time.

1

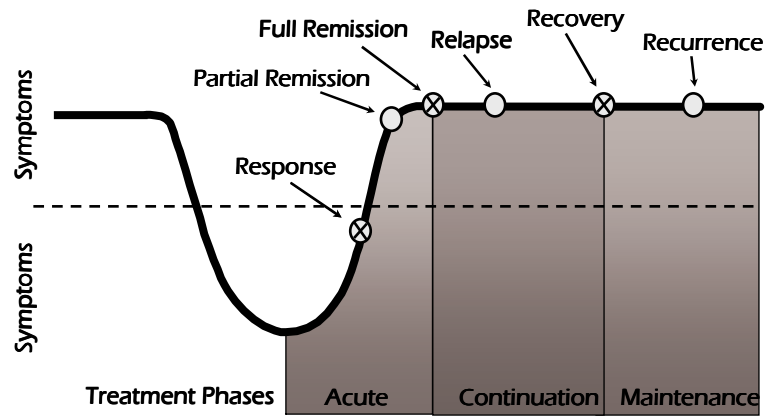
Version 12/12/2006

Adolescent Report vs. Clinician Rating

- Adolescents tend to report themselves as slightly worse overall than clinician report.
 - Only “general interest” was significantly different.
- Clinicians scores were more pathological than adolescent ratings for concentration, self-view, and restlessness/agitation.

Based on QIDS-SR and QIDS-C (adolescent interview)

RESPONSE, REMISSION, RECOVERY, RELAPSE, RECURRENCE

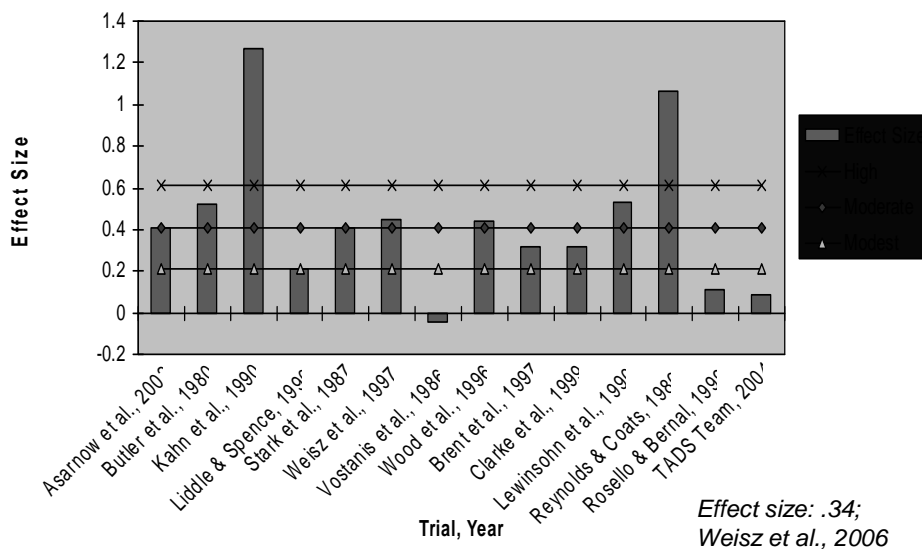


ACUTE TREATMENT

Compton SN, March JS, Brent D, Albano AM 5th, Weersing R, Curry J. Cognitive-behavioral psychotherapy for anxiety and depressive disorders in children and adolescents: an evidence-based medicine review. J Am Acad Child Adolesc Psychiatry 43:930-59, 2004.

Weisz JR, McCarty CA, Valeri SM. Effects of psychotherapy for depression in children and adolescents: a meta-analysis. Psychol Bull 132:132-49, 2006.

Why use CBT? Acute CBT Trials in Youth with MDD





ANTIDEPRESSANT STUDIES

SSRIs

- FLUOXETINE
 - Emslie et al., 1997, 2002; TADS 2004
- CITALOPRAM
 - Von Knorring et al., 2006; Wagner et al., 2004
- SERTRALINE
 - Wagner et al., 2003
- PAROXETINE
 - Berard et al., 2006; Emslie et al., 2006; Keller et al., 2001
- ESCITALOPRAM
 - Wagner et al., 2006
 - Emslie et al., 2008

NON-SSRIs

- MIRTAZAPINE
 - Reviewed in Cheung et al., 2005
- NEFAZODONE
 - Reviewed in Cheung et al., 2005
- VENLAFAXINE
 - Emslie et al., 2007

Bridge JA, Iyengar S, Salary CB, Barbe RP, Birmaher B, Pincus HA, Ren L, Brent DA. Clinical response and risk for reported suicidal ideation and suicide attempts in pediatric antidepressant treatment: a meta-analysis of randomized controlled trials. JAMA 297:1683-1696, 2007.

Cheung AH, Emslie GJ, Mayes TL. Review of the efficacy and safety of antidepressants in youth depression. J Ch Psychology and Psychiatry 46:735-754, 2005.

Antidepressant Meta-Analysis

- 27 MDD trials
- Pooled risk differences (benefit vs. risk) favored antidepressants for MDD.
- Efficacy was moderated by age, duration of depression, and number of sites in the trial.
- In children younger than 12, only fluoxetine showed benefit over placebo.

(Bridge et al., 2007)

Combination Treatment

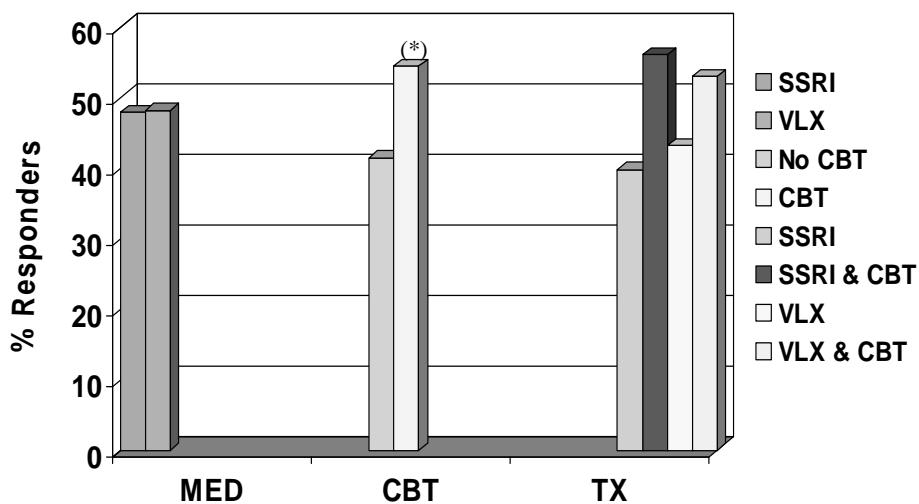
| | Intervention | Results |
|----------------------|------------------------------|------------------------------|
| Clarke et al., 2005 | Comb vs. Med | Comb=Med |
| Goodyer et al., 2007 | Comb vs. Med | Comb=Med |
| Melvin et al., 2006 | Comb vs. CBT vs. Med | Comb=monotherapy; CBT>Med |
| TADS Team, 2004 | Comb vs. CBT vs. Med vs. Pbo | Comb=Med>CBT=Pbo |

**TREATMENT
RESISTANT
DEPRESSION**

SUBJECTS

- Adolescents (age 12-18) with MDD or dysthymia (N=334)
- Currently not responding to a SSRI
- Alternate SSRI vs. venlafaxine vs. alternate SSRI plus CBT vs. venlafaxine plus CBT
 - 12-weeks acute treatment
 - 12-weeks continuation treatment for responders (or open treatment for non-and partial responders)

CLINICAL RESPONSE BY TREATMENT GROUP



CBT: $P = .018$

TORDIA CONCLUSIONS

- CBT + medication superior to medication alone for second step after SSRI non-response
- No difference between SSRI and Venlafaxine for second step and no interaction with CBT

CONTINUATION TREATMENT

APA Guidelines for Adults

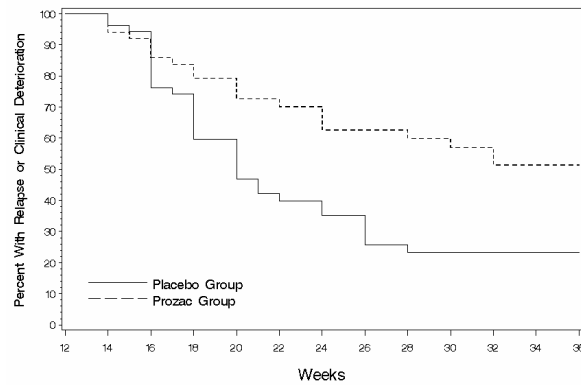
- Continuation treatment for 4-9 months following complete remission.
- Same dose of antidepressant.
- Visits every 1-3 months

STUDY DESIGN

- Outpatients 7-18 years with MDD
- 12 weeks open-label fluoxetine (n=168)
 - Visits weekly for 4 weeks, every other week until week 12
- 6 months double-blind continuation treatment (n=102)
 - 1:1 randomization
- Relapse
 - One time CDRS \geq 40 with history of 2 wks of clinical deterioration as determined by patient report, parent report, or clinician history.
 - Or
 - If physician believes patient has experienced relapse sufficient to warrant discontinuation from study, but not met criteria for relapse.

* Emslie et al., 2008

RELAPSE

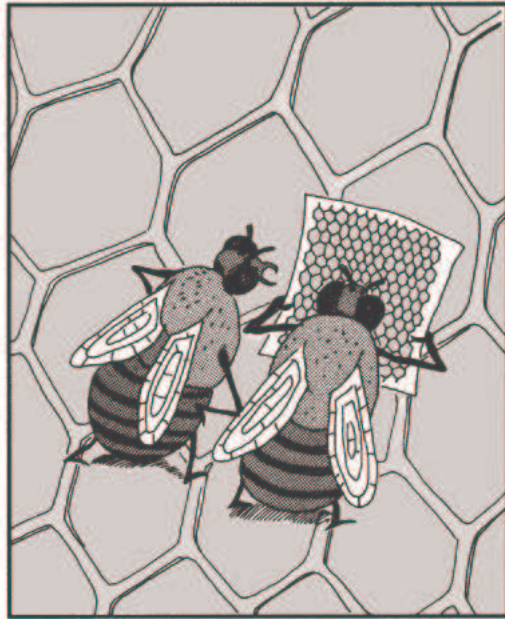


| | Fluoxetine (n=50) | Placebo (n=52) | P |
|----------------|------------------------------|---------------------------|----------|
| Relapse | 42.0% (21/50) | 69.2% (36/52) | .005 |

Residual symptoms are associated with relapse.

| | No Residual Symptoms | Residual Symptoms | p |
|------------|----------------------|-------------------|------|
| Fluoxetine | 5/20 (25.0%) | 16/30 (53.3%) | 0.05 |
| Placebo | 19/28 (67.9%) | 17/24 (70.8%) | 0.82 |

NOTE: Based on full relapse, 0/20 subjects on fluoxetine with no residual symptoms relapsed, compared to 11/28 (39.3%) on placebo.



So, Where are we exactly?

Implementing Evidence Based Medicine In Community Practice

| | |
|--|---|
| | <h2>Evidence Based Decision-Making</h2> |
| | <ul style="list-style-type: none">■ Evidence-based medicine (EBM) is the integration of best research evidence with clinical expertise and patient values. |

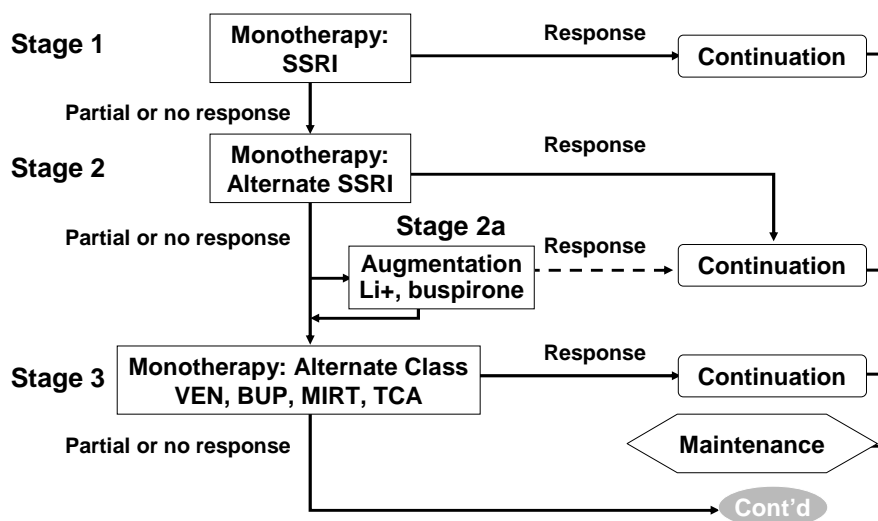
| | |
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| | <h2>TMAP/CMAP Algorithm Philosophy</h2> |
| | <ul style="list-style-type: none">■ Goal of treatment should be remission■ Most efficacious/safest treatments first<ul style="list-style-type: none">– (i.e., evidence based)■ Simplest interventions first■ Subsequent interventions tend toward increased complexity and increased risk■ Multiple options when appropriate■ Patient/family preference |

Algorithm Development Process

- Review of the evidence on a specific topic
- Consensus panel process
 - Academic content experts
 - Practicing clinicians
 - Consumers/family members
- Present research evidence
- Reaction panels
- Discuss evidence & develop algorithms
- Review and revise

Crismon ML, et al. *J Clin Psych* 1999; Suppes T, et al. *J Clin Psych* 2002; Miller AL, et al. *J Clin Psych* 2004

Guidelines for Treatment of Pediatric Depression*



*Note: Any stage(s) can be skipped depending on the clinical picture
 Hughes CW, et al. *J Am Acad Child Adolesc Psychiatry*. 1999;38:1442-1454.

| | |
|--|---|
| | |
| | <p>Emslie GJ, Hughes CW, Crismon ML, et al. A feasibility study of the Childhood MDD Medication Algorithm: The Texas Children's Medication Algorithm Project (CMAP). <u>J Am Acad Ch Adolesc Psychiatry</u>. 2004; 43(5):519-27.</p> |

| | |
|--|--|
| | <h2>Results</h2> |
| | <ul style="list-style-type: none"> ■ 4 MHMR Centers in Texas. ■ ALGO: 39 subjects (24 depressed; 15 depressed plus ADHD). ■ 114 TAU: 114 (74 depressed; 40 depressed plus ADHD). ■ 4-month follow-up. ■ CGI-I of 1 or 2: <ul style="list-style-type: none"> – 40% Algo vs. 22.8% TAU (p=.04) ■ CGI Severity: <ul style="list-style-type: none"> – Algo: 5.7 to 3.7 – TAU: 5.8 to 4.8 (p=<.003) |

| | |
|--|--------------------------------|
| | |
| | Treatment Interventions |

| | |
|--|---|
| | GOALS OF TREATMENT |
| | <ul style="list-style-type: none">■ Shorten the acute episode■ Limit the amount of dysfunction caused by the episode■ Remission of depression■ Normalization of functioning■ Prevent recurrence |

Diagnosis

- MDD Only.
- Interviews conducted with child and parent separately.
- Evaluate comorbid diagnoses
- Assess psychosocial stressors.
- Utilize diagnostic and severity scales.
- Non-Medication Treatment Alternatives
- Evaluation lasts 1-3 weeks

Non-Specific Interventions

- Many children respond to non-specific treatment interventions.
- Duration of evaluation?
- Depression in youth is more influenced by psychosocial factors (Hammen et al., 1999).

| | |
|--|---|
| | <h2>Clinical Management</h2> |
| | <ul style="list-style-type: none">■ Individual problem-focused care■ Family psychopathology■ School intervention■ Social skills deficits |

| | |
|--|---|
| | <h2>Guidelines for Choosing Treatment</h2> |
| | <ul style="list-style-type: none">■ Severity of depression■ Psychosocial stressors■ Past medication response■ Past psychotherapy trial■ Family history of response■ Availability■ Cost■ Patient preference |

| | |
|--|--|
| | <h2>Tactics</h2> |
| | <ul style="list-style-type: none">■ Involvement of patient and family in decision-making.■ Goal of treatment is REMISSION.■ Monotherapy■ Slow/low |

| | |
|--|--|
| | <h2>Tactics cont.</h2> |
| | <ul style="list-style-type: none">■ Visit frequency: FDA warning recommends that patients treated with antidepressants be observed closely, and that "such observation would generally include at least weekly face-to-face contact with patients or their family members or caregivers during the first 4 weeks of treatment, then visits every other week for the next 4 weeks, then at 12 weeks, and as clinically indicated beyond 12 weeks." |

Tactics cont.

■ Visit frequency:

- However, visit frequency for specific patients may vary based on multiple factors
 - Presence of suicidal behaviors, severity of illness, severity of psychosocial stressors, development of therapeutic alliance, level of family support, and progress in treatment.
- Patients and families should be encouraged to contact the clinician if depression worsens, the patient demonstrates suicidal behavior or verbalizations, or if medication side effects occur.

Changes in Visit Frequency

- Following FDA advisory, no changes in visit frequency were noted.
- Less than 5% met the requirements put forth by the FDA.
- Only 60% of all youth had at least 3 visits in 3 months.

* Morrato et al., 2008

Tactics cont.

- Monitor for improvement.
- Monitor for suicidal ideation and behavior.
- Monitor for other behavioral AEs: anxiety, agitation, panic attacks, insomnia, irritability, hostility, impulsivity, akathisia, hypomania, and mania.
- Critical points (Weeks 4, 6, 8, 12).
- Duration of treatment.

Guidelines

- Involve practicing clinicians and patients/parents during development stages.
- Provide a synthesis of what is known and not known.
- Provide a clinical framework from which clinicians can deviate.
- Provide support for clinicians in an era of increased regulatory concerns.

Conclusions

- Recognition and identification of depression
- Public health significance
- Research to practice
- Implementation