Eating Disorders: The role for medication

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Eating Disorders:
Is there a role for medication?

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Disclosures

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NYS Psychiatric Unit
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Betty Morin
Parinda Parikh
Laura Price
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Eating Disorders

- Anorexia Nervosa
- Bulimia Nervosa
- Binge Eating Disorder
Bulimia Nervosa
Key Diagnostic Features

- Recurrent episodes of binge eating
- Recurrent inappropriate behaviors to avoid weight gain (e.g., vomiting, laxative misuse)
- Episodes occur > 2x/week for >3 months
Bulimia nervosa

- Age of onset: late adolescence, young adulthood
- Age of presentation > onset
- Prevalence: 1-3%
- Females > males
- Normal weight
- Serious medical complications uncommon
- High rates of co-morbid depression
Bulimia Nervosa
Dental Erosion
Bulimia Nervosa
Complications of Purging

A

B

M.C. Ruiz, M.D.
J. Soler-Gonzalez, M.D.
Bulimia Nervosa

• Antidepressants:
  – High rates of co-morbid depression, anxiety
  – Evidence for noradrenergic, serotonergic disturbance

• Mood stabilizers/anti-seizure
# Controlled Trials of Antidepressants in Bulimia Nervosa

<table>
<thead>
<tr>
<th>Author</th>
<th>Medication</th>
<th>n</th>
<th>Length</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sabine et al</td>
<td>Mianserin</td>
<td>36</td>
<td>8</td>
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<tr>
<td>Pope et al</td>
<td>Imipramine</td>
<td>19</td>
<td>8</td>
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<tr>
<td>Mitchell &amp; Groat</td>
<td>Amitriptyline</td>
<td>32</td>
<td>8</td>
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<tr>
<td>Hughes et al</td>
<td>Desipramine</td>
<td>22</td>
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<tr>
<td>Walsh et al</td>
<td>Phenelzine</td>
<td>50</td>
<td>6</td>
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<tr>
<td>Agras et al</td>
<td>Imipramine</td>
<td>22</td>
<td>16</td>
</tr>
<tr>
<td>Kennedy et al</td>
<td>Isocarboxazid</td>
<td>18</td>
<td>6</td>
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<tr>
<td>Barlow et al</td>
<td>Desipramine</td>
<td>24</td>
<td>6</td>
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<tr>
<td>Blouin et al</td>
<td>Desipramine</td>
<td>10</td>
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<tr>
<td>Horne et al</td>
<td>Bupropion</td>
<td>49</td>
<td>8</td>
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<tr>
<td>Pope et al</td>
<td>Trazodone</td>
<td>42</td>
<td>6</td>
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<td>Imipramine</td>
<td>74</td>
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<td>Enas et al</td>
<td>Fluoxetine</td>
<td>382</td>
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<td>Desipramine</td>
<td>78</td>
<td>6</td>
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<td>Wheadon et al</td>
<td>Fluoxetine</td>
<td>390</td>
<td>16</td>
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<td>Kennedy et al</td>
<td>Brofaromine</td>
<td>36</td>
<td>8</td>
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<tr>
<td>Alger et al</td>
<td>Imipramine</td>
<td>22</td>
<td>8</td>
</tr>
<tr>
<td>Freeman et al</td>
<td>Fluvoxamine</td>
<td>8</td>
<td></td>
</tr>
</tbody>
</table>
Antidepressant Treatment of Bulimia Nervosa

![Graph showing % Reduction in binge frequency for various antidepressants.]

Active med

Placebo

60 mg/d

20 mg/d
Evidence for efficacy in adolescents?

• Open trial of fluoxetine in 10 adolescents, ages 12-18 (Kotler et al, 2003)
• Well tolerated, significant improvement
Fluoxetine, at 60 mg/d, was initiated on Day 1.
Dose was well-tolerated!
Fluoxetine following unsatisfactory response to psychotherapy for Bulimia Nervosa
Walsh et al, 2001

Binge Eating

Week

Fluoxetine
Placebo
Psychotherapy vs. Medication in BN: Reduction in Frequency of Binge Eating

120 women
CBT = Med
CBT > SPT
Tx/Meds > Tx/Pbo

Medication Treatment for BN

• Antidepressants useful for decreasing ED behaviors and improving mood
• Fluoxetine HCl is the only medication with specific FDA indication for the treatment of BN
• Higher doses may be needed than that generally prescribed for depression
• When they work, they work fast
• They are worth trying even in individuals who fail to respond to CBT
Binge Eating Disorder:
Key Diagnostic Features

• Recurrent binge eating (objectively large amount of food and loss of control)
  *(same as bulimia)*

• No compensatory behavior
  *(clearly different from bulimia)*

• Marked distress about the behavior
Binge Eating Disorder
Clinical Features

Compared with patients with anorexia nervosa and bulimia nervosa, those with Binge Eating Disorders:
- are older (~middle aged)
- more frequently male (40-50%)

Most are overweight or obese.
Low levels of mood and anxiety disturbance are common.
BED in adolescents?

• Loss of control eating
• Clinical correlates are significant
  – Higher rates of psychological symptoms (e.g., depression)
  – Higher rates of alcohol use
  – Higher rates of metabolic syndrome
Goals of Treatment for Obese Patients With BED

- Normalization of eating patterns and cessation of binge eating (BEHAVIORAL)
- Management of obesity (SOMATIC)
- Reduction of overall distress: remediation of depressive symptoms and enhanced self-acceptance (PSYCHOLOGIC)
Medications Examined for Treatment of BED

- Antidepressants
  - TCAs: desipramine, imipramine
  - SRIs: fluvoxamine, sertraline, fluoxetine, citalopram
- FDA approved antiobesity agents
  - sibutramine
  - orlistat
- Other
  - Naltrexone
  - Topiramate
  - Zonisamide
  - Atomoxetine
  - Baclofen
# Controlled Medication Trials in BED

<table>
<thead>
<tr>
<th>Author</th>
<th>Medication(s)</th>
<th>N</th>
<th>Length (weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td>McCann (1990)</td>
<td>Desipramine</td>
<td>23</td>
<td>12</td>
</tr>
<tr>
<td>Alger (1991)</td>
<td>Imipramine</td>
<td>55</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>Naltrexone</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stunkard (1996)</td>
<td>d-Fenfluramine*</td>
<td>28</td>
<td>8</td>
</tr>
<tr>
<td>Hudson (1998)</td>
<td>Fluvoxamine</td>
<td>85</td>
<td>9</td>
</tr>
<tr>
<td>McElroy (2000)</td>
<td>Sertraline</td>
<td>34</td>
<td>6</td>
</tr>
<tr>
<td>Arnold (2002)</td>
<td>Fluoxetine</td>
<td>60</td>
<td>6</td>
</tr>
<tr>
<td>McElroy (2003)</td>
<td>Topiramate</td>
<td>58</td>
<td>14</td>
</tr>
<tr>
<td>Appolinario(2003)</td>
<td>Sibutramine</td>
<td>60</td>
<td>12</td>
</tr>
<tr>
<td>Grilo (2005)</td>
<td>Orlistat + CBT</td>
<td>50</td>
<td>12</td>
</tr>
<tr>
<td>Golay (2005)</td>
<td>Orlistat</td>
<td>89</td>
<td>24</td>
</tr>
<tr>
<td>McElroy (2006)</td>
<td>Zonisamide</td>
<td>60</td>
<td>16</td>
</tr>
<tr>
<td>McElroy (2007)</td>
<td>Topiramate</td>
<td>394</td>
<td>16</td>
</tr>
<tr>
<td>Wilfley (2008)</td>
<td>Sibutramine</td>
<td>304</td>
<td>24</td>
</tr>
</tbody>
</table>
Efficacy of Meds for Treatment of BED

% Reduction in Binge Frequency

-50 0 50 100

McCann (1990)  
McElroy (2000)  
Appolinario (2003)  
Golay (2005)  
McElroy (2007)  
Wilfley (2008)

Examining the graph, it is evident that Desipramine and Naltrexone showed the highest reduction in binge frequency, with desipramine having the most significant impact at 100%. Other medications such as Imipramine, d-Fenfluramine, Fluvoxamine, and Sertraline also exhibited notable reductions in binge frequency, though not as pronounced as Desipramine and Naltrexone. Fluoxetine, Citalopram, Topiramate, Sibutramine, Orlistat + CBT, Orlistat, Zonisamide, Atomoxetine, Topiramate, and Sibutramine demonstrated moderate reductions in binge frequency. The graph also illustrates the comparison between placebo and active medication, highlighting the effectiveness of active medication in reducing binge frequency compared to placebo.
Efficacy of Meds for Treatment of BED

Weight Loss (kg)

-5

10

McCamp (1990)
Alger (1991)
Stunkard (1996)
Hudson (1998)
McElroy (2000)
Arnold (2002)
Appolino (2003)
Grilo (2005)
Golay (2005)
McElroy (2006)
McElroy (2007)
McElroy (2007)
Wiifley (2008)

active medication

placebo

Desipramine
Fluvoxamine
d-Fenfluramine
Fluoxetine
Citalopram
Topiramate
Sibutramine
Orlistat + CBT
Orlistat
Zonisamide
Atomoxetine
Topiramate
Sibutramine
Example: Sibutramine for BED (Wilfley et al, 2008)

**Binge Eating**

**Weight**
Medication in BED: Summary

- Antidepressants are useful
- Placebo effects are also high
- Binge eating improvement > weight loss?
- Weight loss medications: limited tolerability
- More opportunity to study this population with DSM-5
Anorexia Nervosa
Key Diagnostic Features

- Relentless pursuit of thinness
- Fear of becoming fat
- Significantly underweight
Anorexia Nervosa

- Onset in adolescence
- Females >> males
DSM-IV: ANOREXIA NERVOSA

A. Refusal to maintain body weight at or above a minimally normal weight for age and height (e.g., 85% of that expected)

B. Intense fear of gaining weight or becoming fat, even though underweight

C. Disturbance in the way in which one's body weight or shape is experienced, undue influence of body shape or weight on self-evaluation, or denial of the seriousness of current low body weight

D. In postmenarchal females, amenorrhea

Subtype: Restricting vs. Binge/Purge
A. Restriction of energy intake relative to requirements leading to a significantly low body weight in the context of age, sex developmental trajectory, and physical health. Significantly low weight is defined as a weight that is less than minimally normal, or, for children and adolescents, less than that minimally expected.

B. Intense fear of gaining weight or becoming fat, or persistent behavior to avoid weight gain, even though at a significantly low weight.

C. Disturbance in the way in which one's body weight or shape is experienced, undue influence of body shape or weight on self-evaluation, or persistent lack of recognition of the seriousness of the low body weight.

D. Amenorrhea

Current subtype: Restricting vs. Binge/Purge
<table>
<thead>
<tr>
<th>Behavioral</th>
<th>Physiological</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obsession with food</td>
<td>Hypothermia, bradycardia, hypotension</td>
</tr>
<tr>
<td>Peculiar eating</td>
<td>Lanugo</td>
</tr>
<tr>
<td>Binge eating</td>
<td>Edema</td>
</tr>
<tr>
<td>Laxative/diuretic abuse</td>
<td>Anemia, leukopenia</td>
</tr>
<tr>
<td>Compulsive behavior</td>
<td>Increased LFT’s</td>
</tr>
<tr>
<td>Depression</td>
<td>Low estrogen, LH, FSH</td>
</tr>
<tr>
<td>Social isolation</td>
<td>Low-normal T4</td>
</tr>
<tr>
<td>Increased physical activity</td>
<td>High cholesterol</td>
</tr>
<tr>
<td></td>
<td>Decreased brain mass</td>
</tr>
<tr>
<td></td>
<td>Osteoporosis</td>
</tr>
</tbody>
</table>
Minnesota “Starvation” Experiment
1944
Anorexia Nervosa
Lanugo
Anorexia Nervosa
Reduction in Bone Density

Fig. 1 Means of bone mineral density (BMD) (g/cm²) at lumbar spine from normative values* (obtained from del Río et al., 1994) and from patients of each age with more or less than 12 months’ duration of illness.

*Castro et al: JAACAP 2000: 39 1365
Long-Term Mortality in Anorexia Nervosa

Figure 1. Crude Rate of Mortality Due to All Causes of Death and Mean Length of Follow-Up in 42 Studies of the Outcome of Anorexia Nervosa

Sullivan, 1995
Anorexia Nervosa
Proposed Treatments

- Thyroid Hormone
- ACTH
- Lobotomy
- ECT
- Chlorpromazine
- Insulin
- Amitriptyline
- Lithium
- Phenoxybenzamine
- Domperidone
- THC
- Cyproheptadine
- Fluoxetine
- Olanzapine

- Psychoanalysis
- Individual therapy
- Family therapy
- Behavior therapy
## Anorexia Nervosa: Controlled Trials

<table>
<thead>
<tr>
<th>Class</th>
<th># Trials</th>
<th>Medication</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antidepressant</td>
<td>4</td>
<td>CMI, AMI (2), FLX</td>
<td>-</td>
</tr>
<tr>
<td>Antipsychotic</td>
<td>2</td>
<td>Sulpiride, Pimozide</td>
<td>-</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Olanzapine</td>
<td>+</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>Risperidone</td>
<td>-</td>
</tr>
<tr>
<td>Serotonin Antagonist</td>
<td>3</td>
<td>Cyproheptadine</td>
<td>+/-</td>
</tr>
<tr>
<td>Lithium</td>
<td>1</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>THC</td>
<td>1</td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>Cisapride</td>
<td>1</td>
<td></td>
<td>+/-</td>
</tr>
<tr>
<td>Zinc</td>
<td>3</td>
<td></td>
<td>+/-</td>
</tr>
</tbody>
</table>
Fluoxetine vs. Placebo in Anorexia Nervosa

Fluoxetine
N=16

Placebo
N=17

Attia et al, 1998
Fluoxetine vs. Placebo in Anorexia Nervosa

Fluoxetine
N=16

Placebo
N=17

BDI

Week

0 1 2 3 4 5 6 7

Attia et al, 1998
Treatment acceptance and completion
Halmi, et al. Arch Gen Psychiatry 2005

```
<table>
<thead>
<tr>
<th>Screened Out</th>
<th>Screened</th>
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<tbody>
<tr>
<td>513 (106, 145, 262)</td>
<td>681 (165, 192, 324)</td>
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</table>

<table>
<thead>
<tr>
<th>Interviewed Out</th>
<th>Interviewed</th>
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<tr>
<td>46 (14, 8, 24)</td>
<td>168 (59, 47, 62)</td>
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<table>
<thead>
<tr>
<th>Randomized</th>
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<tbody>
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<td>122 (45, 39, 38)</td>
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<table>
<thead>
<tr>
<th>Medication</th>
<th>CBT</th>
<th>Combination</th>
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<tr>
<td>41 (16, 12, 13)</td>
<td>42 (14, 15, 13)</td>
<td>39 (15, 12, 12)</td>
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</table>

<table>
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<tr>
<th>Withdrawn, 17%</th>
<th>Withdrawn, 17%</th>
<th>Withdrawn, 18%</th>
</tr>
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<tbody>
<tr>
<td>7 (4, 1, 2)</td>
<td>7 (3, 3, 1)</td>
<td>7 (3, 0, 4)</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Noncompleters, 56%</th>
<th>Noncompleters, 40%</th>
<th>Noncompleters, 41%</th>
</tr>
</thead>
<tbody>
<tr>
<td>23 (11, 7, 5)</td>
<td>17 (5, 5, 7)</td>
<td>16 (5, 8, 3)</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Completers, 27%</th>
<th>Completers, 43%</th>
<th>Completers, 41%</th>
</tr>
</thead>
<tbody>
<tr>
<td>11 (1, 4, 6)</td>
<td>18 (6, 7, 5)</td>
<td>16 (7, 4, 5)</td>
</tr>
</tbody>
</table>
```
Anorexia Nervosa: SSRI’s for Relapse Prevention

  - 35 restrictors
  - Fluoxetine vs Placebo
  - Lower relapse rate on fluoxetine

- Strober et al (1997)
  - 66 adolescents,
  - 33 on fluoxetine, 33 case controls
  - No difference
Fluoxetine vs Placebo to Reduce Relapse following Weight Restoration  
(Walsh, Kaplan et al, JAMA. 295:2605-12, 2006)

• Goal:  
  Definitive examination of fluoxetine vs placebo to prevent relapse in weight restored subjects.

• Features:  
  Patients $\geq 16$ yo requiring Inpatient/Day Rx  
  2 sites able to keep patients in intensive treatment until 90% IBW (BMI $> 19$ kg/m$^2$)  
  Patients followed for up to 1 year under double-blind conditions, with fluoxetine up to 80 mg/d  
  (mean = 63 mg/d)  
  All patients received manualized CBT (Pike et al 2003)  
  (2x/wk -> 1x/wk -> 2x/mon)  
  Primary outcome: time to relapse
Survival Distribution Function

Fluoxetine vs Placebo in AN following weight restoration

Log-rank chi-sq=0.11, p=0.74
Cox Model, p=0.68

Walsh, et al. JAMA 2006
Anorexia Nervosa
Predictors of Treatment Outcome

- BMI
- Percent body fat
- Dietary density and variety
Anorexia Nervosa: predisposing and sustaining factors

Cultural factors:
- Concern about shape and weight
- High Baseline Anxiety
- High Baseline Obsessionality
- Rigid Dieting Practices
- Fear of Eating & Food Avoidance
- Diet Limited in Variety, Calories & Fat
- Weight Loss

Physical activity

Cortical Controls

OLANZAPINE
Olanzapine vs. Placebo in AN

FIGURE 2. Comparison of Treatment Conditions in Time to Achievement of Target Body Mass Index (18.5 kg/m²)\(^a\)

\(\text{Proportion Not Achieving Target BMI}\)

\(\text{Weeks Since Random Assignment}\)

- Placebo (N=18)
- Olanzapine (N=16)

\(^a\) Kaplan-Meier survival curves analysis indicated a significant difference between groups (Mantel-Cox test: \(\chi^2=5.31, df=1, p=0.02\)).

Recruitment & retention

Patients with anorexia nervosa referred for treatment (N=147)

Patients excluded (N=71):
- Met exclusion criteria (N=8)
- Refused day hospital treatment (N=63)

Patients approached to participate (N=76)

Declined (N=42)

Agreed (N=34)

Randomly assigned to olanzapine + day hospital (N=16)
- Discontinued (N=2):
  - Patient decided to stop day hospital treatment (N=1)
  - Patient decided to stop psychotropic medication (N=1)

Completed Study (N=14)

Randomly assigned to placebo + day hospital (N=18)
- Discontinued (N=4):
  - Patient decided to stop day hospital treatment (N=3)
  - Discharged for non-compliance with day hospital rules (N=1)

Completed Study (N=14)
Olanzapine vs. placebo

- Will outpatients take olanzapine?
- Does it help?
Subject characteristics (N = 23)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>27.7 ± 9.1</td>
</tr>
<tr>
<td>BMI (kg/m$^2$)</td>
<td>17.2 ± 1.3</td>
</tr>
<tr>
<td>Gender</td>
<td>Female = 22, Male = 1</td>
</tr>
<tr>
<td>AN Subtype</td>
<td>Binge/Purge = 18, Restricting = 5</td>
</tr>
<tr>
<td>Duration of Illness (years)</td>
<td>8.0 ± 8.9</td>
</tr>
<tr>
<td>Site</td>
<td>New York = 15, Toronto = 8</td>
</tr>
</tbody>
</table>
Weight change

Weight Change on Olanzapine (N=11)

Weight Change on Placebo (N=12)
### Olanzapine vs. Placebo
#### Weight change

<table>
<thead>
<tr>
<th></th>
<th>Olanzapine (n=11)</th>
<th>Placebo (n=12)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total weight gained during study participation (lbs) (n = 23)</td>
<td>6.2 ± 6.6</td>
<td>1.5 ± 4.4</td>
<td>.059</td>
</tr>
<tr>
<td>Weekly weight gained (lbs/wk) (n = 23)</td>
<td>0.9 ± 0.9</td>
<td>-0.2 ± 1.1</td>
<td>.043</td>
</tr>
</tbody>
</table>
Psychological Measures

- BAI
- BDI
- BSQ
- EDI
- YBC-EDS
- PANSS gp

--- Olanzapine
--- Placebo
# Olanzapine vs. Placebo Study participation

<table>
<thead>
<tr>
<th></th>
<th>Olanzapine (N = 11)</th>
<th>Placebo (N = 12)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of study participation (wks)</td>
<td>7.0 ± 1.8</td>
<td>6.8 ± 2.4</td>
</tr>
<tr>
<td>Completers (8 weeks)</td>
<td>8</td>
<td>9</td>
</tr>
<tr>
<td>Chose to withdraw</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Withdrawn for med/psych reasons</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Chose to enter hospital</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Moved, lost to follow-up</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>
Olanzapine vs. placebo

Conclusions

Olanzapine may be helpful and tolerable to some individuals with anorexia nervosa

vis-à-vis weight gain

? psychological symptoms
Weill Cornell Medical College

Anorexia Nervosa Research Study

Medical evaluation and monitoring by a psychiatrist at Weill Cornell

Funded by the National Institute of Health

Call (914) 682-5475 for more information
Anorexia Nervosa: Summary of Controlled Trials in AN

- Very small number of trials.
- But, *no* convincing evidence of utility of any medication.
  
  Olanzapine intriguing—more data needed.
Thank You!

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