UPDATE ON THE ASSESSMENT AND TREATMENT OF EATING DISORDERS
Learning Objectives

• Identify the diagnostic criteria for binge eating disorder, bulimia nervosa, and anorexia nervosa

• Implement evidence-based treatment in the management of patients with eating disorders

• Incorporate a multidisciplinary approach in the management of patients with eating disorders
# Eating Disorders: DSM-IV-TR vs. DSM-5

## Consolidation Into One Section, Inclusion of Binge-Eating Disorder

### DSM-IV-TR

<table>
<thead>
<tr>
<th>Code</th>
<th>Disorder</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>307.52</td>
<td>Pica</td>
<td>Feeding and Eating Disorders of Infancy or Early Childhood (71)</td>
</tr>
<tr>
<td>307.53</td>
<td>Rumination Disorder</td>
<td></td>
</tr>
<tr>
<td>307.59</td>
<td>Feeding Disorder of Infancy or Early Childhood</td>
<td></td>
</tr>
</tbody>
</table>

### DSM-5

**Feeding and Eating Disorders (169)**

The following specifiers apply to Feeding and Eating Disorders where indicated:

a. Specify if: In remission
b. Specify if: In partial remission, In full remission
c. Specify current severity: Mild, Moderate, Severe, Extreme

<table>
<thead>
<tr>
<th>Code</th>
<th>Specifier</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>307.52</td>
<td>Picaa (169)</td>
<td>In children</td>
</tr>
<tr>
<td></td>
<td>(F98.3)</td>
<td>In adults</td>
</tr>
<tr>
<td>307.53</td>
<td>Rumination Disordera (169)</td>
<td></td>
</tr>
<tr>
<td>307.59</td>
<td>Avoidant/Restrictive Food Intake Disordera (170)</td>
<td></td>
</tr>
</tbody>
</table>

- **Anorexia Nervosa**
  - (F50.01) Specifier if: Restricting type
  - (F50.02) Specifier if: Binge-eating/purging type

- **Bulimia Nervosa**
  - (F50.2) Specifier if: Binge-eating/purging type

- **Other Specified Feeding or Eating Disorder**
  - (F50.9) Unspecified Feeding or Eating Disorder (176)
What is anorexia nervosa?

• Characterized by an intense fear of weight gain and a disturbed body image, which motivate severe dietary restriction or other weight loss behaviors such as purging or excessive physical activity

• Adolescent girls and young adult women are particularly at risk

• Cognitive and emotional functioning are markedly disturbed

• Serious medical morbidity and psychiatric comorbidity are the norm

• Commonly has a relapsing or protracted course

• Levels of disability and mortality are high, especially without treatment

• Quality of life is poor and the burden placed on individuals, families, and society is high

How do we diagnose anorexia nervosa?

• *DSM-5* highlights:
  – **Restriction** of energy intake leading to a significantly low bodyweight
  – **Intense fear of gaining weight** or of becoming fat, or persistent behavior that interferes with weight gain, even though at a significantly low weight
  – **Disturbance** in the way one’s bodyweight or shape is experienced

• Amenorrhea is no longer required
How do we treat anorexia nervosa?

• Assessments include both psychological and physical evaluations
• Psychological and behavioral interventions are core
• Nutritional interventions are necessary
• Pharmacological interventions have a limited role, other than treating comorbidities

Table 4: Behavioural treatments in adolescent and adult patients with anorexia nervosa

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Evidence</th>
<th>Effect (evidence level)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adolescent anorexia nervosa³⁷⁸¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family-based treatment (FBT)</td>
<td>Strong*</td>
<td>+++ (1)</td>
</tr>
<tr>
<td>Maudsley family therapy (MFT)</td>
<td>Strong*</td>
<td>+++ (1)</td>
</tr>
<tr>
<td>Family system therapy (FST)</td>
<td>Moderate*</td>
<td>++ (2)</td>
</tr>
<tr>
<td>Adolescent focused therapy (AFT)</td>
<td>Moderate*</td>
<td>++ (2)</td>
</tr>
<tr>
<td>Cognitive behavioural treatment (broad; CBT-b)</td>
<td>Weak/moderate</td>
<td>−/+ (4)</td>
</tr>
<tr>
<td>Cognitive behavioural treatment (enhanced; CBT-E)</td>
<td>Moderate*</td>
<td>+ (4)</td>
</tr>
<tr>
<td>Adult anorexia nervosa¹²</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cognitive behavioural therapy (CBT)</td>
<td>Weak</td>
<td>+</td>
</tr>
<tr>
<td>Cognitive behavioural therapy (enhanced; CBT-E)</td>
<td>Moderate*</td>
<td>++</td>
</tr>
<tr>
<td>Behavioural therapies (BT)</td>
<td>Weak</td>
<td>−/+</td>
</tr>
<tr>
<td>Interpersonal psychotherapy (IPT)</td>
<td>Weak</td>
<td>+</td>
</tr>
<tr>
<td>Psychodynamic therapy (PT)</td>
<td>Weak</td>
<td>+</td>
</tr>
<tr>
<td>Cognitive analytic therapy (CAT)</td>
<td>Weak</td>
<td>+</td>
</tr>
<tr>
<td>Focal psychodynamic psychotherapy</td>
<td>Moderate*</td>
<td>++</td>
</tr>
<tr>
<td>Maudsley model of anorexia nervosa treatment for adults (MANTRA)</td>
<td>Moderate*</td>
<td>++</td>
</tr>
<tr>
<td>Specialist supportive clinical management (SSCM)</td>
<td>Moderate*</td>
<td>++ (+)</td>
</tr>
</tbody>
</table>

Evidence grades are weak, moderate, or strong. Effect grades are: − for no beneficial effect; −/+ for mixed result or still inconsistent result; + for slight beneficial effect; +/+ for moderate beneficial effect; ++ for moderate and lasting beneficial effect (further improvement shown in follow-up); and +++ for strong beneficial effect (superiority demonstrated in primary outcome of randomised trial). Evidence levels are: 1 for well established, 2 for probably efficacious, and 4 for experimental. *At least one multicentre randomised trial or more than one randomised trial.

More Common Than Anorexia Nervosa are Bulimia Nervosa, and, Especially, Binge Eating Disorder

- Nationally representative sample of US adults using data from the 2012–2013 National Epidemiologic Survey on Alcohol and Related Conditions (NESARC-III) comprising of over 36,000 respondents

<table>
<thead>
<tr>
<th>Disorder</th>
<th>12-Month Prevalence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anorexia nervosa</td>
<td>0.05%</td>
</tr>
<tr>
<td>Bulimia nervosa</td>
<td>0.14%</td>
</tr>
<tr>
<td>Binge-eating disorder</td>
<td>0.44%</td>
</tr>
</tbody>
</table>

- Caveat: There are reports of higher prevalence rates from older data, and lifetime prevalence rates are also higher
**Bulimia Nervosa and Binge Eating Disorder - Similar but different: DSM-5 diagnostic criteria**

<table>
<thead>
<tr>
<th>Clinical Symptom</th>
<th>Bulimia Nervosa</th>
<th>Binge Eating Disorder</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of control</td>
<td>Binge eating with loss of control</td>
<td>Binge eating with loss of control</td>
</tr>
<tr>
<td>Presence of compensatory behaviors</td>
<td>Regular compensatory behaviors</td>
<td>No regular compensatory behavior</td>
</tr>
<tr>
<td>Overconcern with shape and weight</td>
<td>Overconcern about shape and weight required for diagnosis</td>
<td>Not part of diagnostic criteria, although often present</td>
</tr>
<tr>
<td>Behavioral indicators for binge eating</td>
<td>Not part of diagnostic criteria</td>
<td>Required for diagnosis</td>
</tr>
<tr>
<td>Distress about binge eating</td>
<td>Not part of diagnostic criteria</td>
<td>Marked distress about binge eating</td>
</tr>
<tr>
<td>Binge eating frequency</td>
<td>Binge eating occurs at least once weekly</td>
<td>Binge eating occurs at least once weekly</td>
</tr>
<tr>
<td>Duration of binge eating</td>
<td>Duration of at least 3 months</td>
<td>Duration of at least 3 months</td>
</tr>
</tbody>
</table>

Psychopathology Across Eating Disorders

How do we treat bulimia nervosa and binge eating disorder?

• Similar psychological and behavioral interventions: CBT

• Pharmacological interventions differ
  – Fluoxetine is the only FDA-approved medication for bulimia nervosa; higher doses used than for MDD
  – Lisdexamfetamine is currently the only FDA-approved medication for binge eating disorder
  – In contrast, there are no FDA-approved medication treatments for anorexia nervosa
Deeper Dive: Binge Eating Disorder

The most commonly encountered eating disorder in YOUR clinical practice!
What is binge eating disorder (BED)?

• *DSM-5* defines BED as recurrent episodes of binge eating:
  • Eating, in a discrete period of time, an amount of food larger than most people would eat in a similar amount of time under similar circumstances
  • A sense of *lack of control* overeating during the episode
  • Occurring at least once a week for 3 months
  • Associated with marked distress
DSM-5 Associated Features

Binge episodes are also associated with ≥ 3 of the following:

1. Eating more rapidly than usual
2. Eating until feeling uncomfortably full
3. Eating large amounts of food when not feeling physically hungry
4. Eating alone because of feeling embarrassed by how much one is eating
5. Feeling disgusted with oneself, depressed, or guilty afterwards

Not unusual for all 5 features to be present

**DSM-5 Severity**

- Levels of severity are based on the **number of weekly binge eating episodes**:
  - **Mild**: 1–3
  - **Moderate**: 4–7
  - **Severe**: 8–13
  - **Extreme**: ≥ 14

- Severity level can be increased to reflect other symptoms and functional disability

- Validity of *DSM-5* severity indicators uncertain

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Binge Eating Disorder Diagnostic Caveats

- Although overvaluation of shape or weight is often seen (40%)…
  - it is not part of the DSM-5 criteria for BED

- BED vs bulimia nervosa?
  - BED is not associated with regular compensatory behaviors such as purging or excessive exercise, or with dietary restriction, although frequent dieting may be reported

- Since it is often a secretive behavior and associated with embarrassment or shame…
  - It is not ordinarily revealed unless the clinician makes a direct inquiry regarding eating patterns

Context is Important

• An excessive amount of food for a typical meal might be considered normal during a celebration or holiday meal
• A single episode of binge eating ≠ one setting
  • i.e., from office to car to home
• The food consumption must be accompanied by a sense of lack of control
  • e.g., not unusual for an individual to continue binge eating if the phone rings
• Types of foods consumed can also be “healthy”
  • e.g., fruits, yogurt

Etiology of Binge Eating Disorder

- Multiple neurobiological explanations, including:
  - Dysregulation in reward center and impulse control circuitry
  - Potentially related disturbances in dopamine signalling ("wanting food") and endogenous μ-opioid signalling ("liking food")

- Additionally, there is interplay between genetic influences and environmental stressors
  - Functional polymorphisms of the dopamine D₂ receptor gene and of the μ-opioid gene may influence proneness to BED
  - Antecedents to binge eating include negative affect; interpersonal stressors; dietary restraint; negative feelings related to body weight, body shape, and food; and boredom
Binge Eating Disorder is the Most Common Eating Disorder

• Estimated lifetime prevalence of 0.85% among US adults
  • BED > bulimia nervosa and anorexia nervosa

• Lifetime prevalence for BED:
  • 0.42% for men and 1.25% for women

• Important caveats:
  • Although many people with BED are obese (BMI \( \geq 30 \text{ kg/m}^2 \)), roughly half are not (yet)
  • Odds Ratio BED with severe obesity (BMI > 40) is 4.61

BMI = body mass index

Binge Eating Disorder is the Most Common Eating Disorder (cont’d)

• Roughly comparable across ethnic/racial groups:
  • Non-Latino white (0.94%)
  • Latino (0.75%)
  • African-American (0.62%)

• The onset of BED occurs at a later median age (21 years) than anorexia nervosa (17 years) or bulimia nervosa (16 years), and with a much wider distribution

• The mean persistence of BED is about 16 years

Binge Eating Disorder: The “Invisible Disorder”

• BED is often a secret disorder – spouse and children often unaware
• BED is often shameful – reluctance to bring it up
• BED is an unknown disorder to patients – many have not heard of it
• BED is an under-recognized disorder to clinicians
  • Among the 22,397 respondents to an Internet survey:
    • 344 participants (1.5%) met the DSM-5 criteria for BED in the past 12 months
    • Of these 344 respondents with BED, only 11 (3.2%) had ever been diagnosed with BED by a health care provider

Every clinician has patients with unrecognized BED: They come for treatment of other disorders!

How to ask?

*Make it Routine*

- We already ask about disturbances in appetite and change in weight, both up and down – a barometer for general health.

- **How** a person eats is not always a subject for discussion:
  - **ASK:** “Have you ever eaten more than you intended?”
  - **Follow up with:** “Did you feel like it wasn’t possible to stop?”

There is often miscommunication about the severity of binge-eating episodes, as well as judgment, bias, and shame surrounding BED.

BE=binge-eating

How to ask? Preferred Words

Preferred Words?

• Preferred obesity-related terms
  • “weight”
  • “BMI”

• Preferred binge-related descriptions
  • “kept eating even though not physically hungry and loss of control”

Words to Avoid?

• “fatness”
• “excess fat”
• “large size”
• “heaviness”
• “obesity”
• “willpower”

Share the Binge Eating Disorder Criteria With Your Patient

• The *DSM-5* criteria are a useful educational tool

• If asked, patients will endorse that they have the symptoms

• They will feel validated that these symptoms “are real”

• They will feel validated that this is a “real” disorder

• They will be more open to share their thoughts and feelings about this “shameful secret” they have kept to themselves for years
Comorbidities

- Comorbidities bring the patient in for treatment → associated BED often goes unrecognized

- Typical physical comorbidities (even with normal BMI, include a heightened risk for metabolic syndrome):
  - Sleep disturbances
  - Pain (musculoskeletal, headaches)
  - Gastrointestinal conditions
  - Menstrual irregularities
  - Shortness of breath
  - Diabetes
  - Low health-related quality of life

Comorbidities (cont’d)

• Psychiatric comorbidities are ubiquitous…
  • Mood disorders
  • Anxiety disorders
  • Substance use
  • Attention deficit disorder

  80% of patients with BED will meet criteria for other psychiatric disorders

• Suicide attempt risk is elevated in individuals with BED, even after accounting for the presence of major depressive disorder

• Psychiatric comorbidity is linked to the severity of binge eating and not to the degree of obesity

Prevalence of Psychiatric Comorbidities

Rate of comorbidity by specific illness
Data from the National Comorbidity Survey Replication (N=9282)

MDD = major depressive disorder
GAD = generalized anxiety disorder
PTSD = posttraumatic stress disorder
OCD = obsessive-compulsive disorder
ADHD = attention-deficit/hyperactivity disorder

Hudson JI et al. Biol Psychiatry. 2007;61(3):348-358;
Figure adapted from: Citrome L. J Clin Psychiatry. 2017;78 Suppl 1:9-13.
Burden of Binge Eating Disorder: Functional Impairment

Role Impairment Associated with BED
Data from the National Comorbidity Survey Replication (N=9282)

Hudson JI et al. Biol Psychiatry. 2007;61(3):348-358;
Figure adapted from: Kornstein SG. J Clin Psychiatry. 2017;78 Suppl 1:3-8.
Psychological Treatments for Binge Eating Disorder

• Cognitive behavioral therapy (CBT) and interpersonal psychotherapy (IPT) can reduce binge-eating behavior
  • Access to such treatments may be limited because of local availability and/or cost
  • 33-50% of patients with BED do not appear to benefit completely or sufficiently from psychological and behavioral treatment
  • Generally little to no weight loss, although successfully eliminating binge eating can protect against future weight gain

CBT = cognitive-behavioral therapy; IPT = interpersonal psychotherapy

## Psychological Treatments for Binge Eating Disorder (cont’d)

### Effect of therapist-led CBT on abstinence from binge eating

<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>RR (95% CI)</th>
<th>Events, n/N</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Treatment</td>
<td>Placebo</td>
</tr>
<tr>
<td>Dingemans <em>et al</em>, 2007</td>
<td>3.48 (1.39–8.81)</td>
<td>19/30</td>
</tr>
<tr>
<td>Peterson <em>et al</em>, 1998</td>
<td>7.56 (1.13–50.45)</td>
<td>11/16</td>
</tr>
<tr>
<td>Peterson <em>et al</em>, 2009</td>
<td>5.09 (2.42–10.71)</td>
<td>31/60</td>
</tr>
<tr>
<td>Tasca <em>et al</em>, 2006</td>
<td>6.17 (2.37–16.06)</td>
<td>29/47</td>
</tr>
<tr>
<td>Overall</td>
<td>4.95 (3.06–8.00)</td>
<td>90/153</td>
</tr>
</tbody>
</table>

Pharmacologic Treatments for Binge Eating Disorder

- Antidepressants (SSRIs, SNRIs, NDRIs)
  - Can reduce BE frequency
  - Not effective for weight loss
  - May increase appetite
- Anticonvulsants (topiramate)
  - Efficacious in reducing BE and weight
  - Negative impact on cognitive function
- Anti-obesity/anorectic agents that target appetite and weight (sibutramine)
- Medications for addictive disorders (naltrexone)
- ADHD medications (lisdexamfetamine)
- Dual-acting dopamine and norepinephrine reuptake inhibitor (dasotraline)

None indicated for BED
- Falls short in terms of robustness of effect, tolerability, or both

Sole agent approved for BED
- Phase 3 for BED

SSRI = selective serotonin reuptake inhibitor; SNRI = serotonin–norepinephrine reuptake inhibitor; NDRI = norepinephrine–dopamine reuptake inhibitor

**Pharmacologic Treatments for Binge Eating Disorder**

Effect of lisdexamfetamine, 50 mg/day or 70 mg/day (top), and Second-Generation Antidepressants (bottom) on Abstinence from Binge Eating

![Diagram showing effect of treatments on abstinence from binge eating]

**Events, n/N**

<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>RR (95% CI)</th>
<th>Treatment</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>McElroy et al, 2015</td>
<td>2.11 (1.28–3.48)</td>
<td>60/130</td>
<td>14/64</td>
</tr>
<tr>
<td>SPDB489-343, 2015</td>
<td>2.84 (1.92–4.19)</td>
<td>77/192</td>
<td>27/191</td>
</tr>
<tr>
<td>SPDB489-344, 2015</td>
<td>2.73 (1.83–4.09)</td>
<td>71/195</td>
<td>26/195</td>
</tr>
<tr>
<td>Overall</td>
<td>2.61 (2.04–3.33)</td>
<td>208/517</td>
<td>67/450</td>
</tr>
</tbody>
</table>

**Events, n/N**

<table>
<thead>
<tr>
<th>Study, Year (Reference)</th>
<th>RR (95% CI)</th>
<th>Treatment</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>McElroy et al, 2015</td>
<td>3.11 (0.75–12.87)</td>
<td>15/42</td>
<td>11/43</td>
</tr>
<tr>
<td>McElroy et al, 2000</td>
<td>1.40 (0.73–2.68)</td>
<td>7/18</td>
<td>2/16</td>
</tr>
<tr>
<td>McElroy et al, 2003</td>
<td>2.25 (0.84–6.06)</td>
<td>9/19</td>
<td>4/19</td>
</tr>
<tr>
<td>White and Grillo, 2013</td>
<td>1.57 (0.76–3.24)</td>
<td>13/31</td>
<td>8/30</td>
</tr>
<tr>
<td>Overall</td>
<td>1.67 (1.24–2.26)</td>
<td>83/208</td>
<td>49/208</td>
</tr>
</tbody>
</table>

More Details about Lisdexamfetamine

• Lisdexamfetamine is indicated for the treatment of moderate to severe BED and is not indicated for weight loss
• Cardiac disease and risk of abuse must be assessed when prescribing
• Recommended starting dose 30 mg/day
• Titrated in increments of 20 mg at approximately 1 week intervals to achieve the recommended target dose of 50–70 mg/day
• Lisdexamfetamine is taken once daily in the morning with or without food
  • Afternoon doses are to be avoided because of the potential for insomnia
Lisdexamfetamine Clinical Trials

• One 11-week, Phase II, proof-of-concept, placebo-controlled study that tested fixed doses of lisdexamfetamine (30, 50 and 70 mg/day)

• Two 12-week, Phase III, placebo-controlled studies examining lisdexamfetamine (50-70 mg/day)

• Statistically significant reductions in binge eating days/week, the primary outcome measure, were observed at doses of 50 and 70 mg/day with large effect sizes

• Large effects were observed on reductions in the Yale-Brown Obsessive Compulsive Scale modified for binge eating
Phase 3 Acute Studies

- Two 12-week, randomized, double-blind, multi-center, parallel-group, placebo-controlled dose-optimization studies (N=374; 350)
- In both studies, LDX was superior to placebo in reducing binge days/week (primary outcome)
- LDX was also superior to placebo for global improvement, 4-week binge eating cessation rates, and reduction of obsessive-compulsive binge eating symptoms

LDX, lisdexamfetamine dimesylate; PBO, placebo; SD, standard deviation

## Lisdexamfetamine and Specific Adverse Events

Number and percentage of participants with common adverse events and NNH vs. placebo and 95% CIs from the Phase 2 or 3 double-blind, 11- to 12-week placebo-controlled trials of lisdexamfetamine in adults with BED

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>Lisdexamfetamine (all doses) (N=569)</th>
<th>Placebo (N=435)</th>
<th>NNH (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry mouth</td>
<td>207 (36.4%)</td>
<td>32 (7.4%)</td>
<td>4 (3–5)</td>
</tr>
<tr>
<td>Decreased appetite</td>
<td>70 (12.3%)</td>
<td>13 (3.0%)</td>
<td>11 (8–17)</td>
</tr>
<tr>
<td>Insomnia</td>
<td>79 (13.9%)</td>
<td>21 (4.8%)</td>
<td>11 (8–18)</td>
</tr>
<tr>
<td>Headache</td>
<td>81 (14.2%)</td>
<td>39 (9.0%)</td>
<td>19 (11–75)</td>
</tr>
<tr>
<td>Constipation</td>
<td>35 (6.2%)</td>
<td>6 (1.4%)</td>
<td>21 (15–40)</td>
</tr>
<tr>
<td>Feeling jittery</td>
<td>30 (5.3%)</td>
<td>2 (0.5%)</td>
<td>21 (15–35)</td>
</tr>
<tr>
<td>Nausea</td>
<td>47 (8.3%)</td>
<td>22 (5.1%)</td>
<td>32 (16–696)</td>
</tr>
<tr>
<td>Irritability</td>
<td>36 (6.3%)</td>
<td>23 (5.3%)</td>
<td>97 (ns)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>31 (5.4%)</td>
<td>21 (4.8%)</td>
<td>162 (ns)</td>
</tr>
</tbody>
</table>

NNH = number needed to harm; ns = not significant.

Lisdexamfetamine Maintenance

- A 39-week, long-term maintenance of efficacy study of lisdexamfetamine for BED, N=275 randomized
- During the 26-week, double-blind, randomized-withdrawal phase of the study, lisdexamfetamine demonstrated superiority over placebo on time to relapse

Observed relapsed rates for lisdexamfetamine vs placebo were 3.7% vs 32.1%, resulting in an NNT of 4

NNT = number needed to treat

LDX Clinically Relevant Outcomes

**RESPONSE**
- LDX: 86.0% (N = 556)
- Placebo: 47.9% (N = 422)

**REMISSION**
- LDX: 39.6% (N = 553)
- Placebo: 14.7% (N = 421)

**UNACCEPTABILITY**
- LDX: 4.6% (N = 569)
- Placebo: 2.3% (N = 435)

- Responder rate (CGI-I = 1 or 2)
- Remission rate (No BE in last four weeks)
- Discontinuation rate due to AEs

NNT = 3
NNT = 4
NNH = 44

LDX Clinically Relevant Outcomes

**Likelihood to be Helped or Harmed**

- LHH for response vs. discontinuation because of an AE is 44/3 = 14.7
  - LDX is about 15 times more likely to result in response than in discontinuation because of an adverse event
- LHH for remission vs. discontinuation because of an AE is 44/4 = 11
  - LDX is 11 times more likely to result in remission than in discontinuation because of an adverse event

**NNT**
- RESPONSE: 3
- REMISSION: 4
- UNACCEPTABILITY: 44

Tips for Rx Lisdexamfetamine for Binge Eating Disorder

• Explain that the goal is to decrease the frequency of binge episodes and that lisdexamfetamine is not being Rx’d for weight loss or for obesity
  – Weight loss will probably occur and you should continue with weighing the patient at every visit

• Warn that dry mouth will probably occur

• Ask that you be told right away if they experience being “revved up” or irritable, or otherwise feeling not themselves

• Be open-minded about dosing
  – The clinical trials compared groups of patients, but we treat individuals
In the Pipeline: Dasotraline

• Selective norepinephrine-dopamine reuptake inhibitor
  • Does not directly stimulate dopamine release

• Being developed for BED

• Two positive pivotal studies in BED
  • Shown to reduce binge eating behavior as well as obsessive-compulsive features of binge eating and body weight

• Generally well-tolerated

• Most common adverse events were insomnia, dry mouth, and decreased appetite
Dasotraline Flexible Dose Study

• In a randomized, double-blind, placebo-controlled, 12-week trial in adults with moderate to severe BED, flexibly dosed dasotraline 4–8 mg/day demonstrated meaningful improvement in BED symptoms vs. placebo

• Change from baseline in:
  • Number of binge days per week
  • BE-CGI-S score
  • Y-BOCS-BE total score
  • 4-week cessation from binge eating in 47% of the dasotraline group vs. 21% of the placebo group

BE-CGI-S = Binge Eating Clinical Global Impression-Severity; Y-BOCS-BE = Yale-Brown Obsessive Compulsive Scale Modified for Binge Eating
Dasotraline Flexible Dose Clinical Trial: Secondary Outcomes

• Y-BOCS-BE obsessions

Figure 1. LS Mean Change From Baseline in Y-BOCS-BE Obsessions Subscale Score

Dasotraline Flexible Dose Clinical Trial: Secondary Outcomes (cont’d)

• Y-BOCS-BE compulsions

Figure 2. LS Mean Change From Baseline in Y-BOCS-BE Compulsions Subscale Score

- Dasotraline demonstrated significant efficacy in reducing both obsessional thoughts and compulsive behaviors related to binge eating, with onset of efficacy within the first 2 weeks of treatment. At week 12, effect sizes were comparably large on both Y-BOCS-BE Obsessions and Compulsions subscales (0.95 and 0.87)

Dasotraline Fixed Dose Clinical Trial

- A second randomized, double-blind, placebo-controlled, 12-week trial in adults, with a fixed dose design
- Statistically significant decrease in number of binge days per week from baseline to Week 12 in the group treated with 6 mg/day vs placebo, but not for 4 mg/day
- Both dose groups showed statistically significant improvement vs. placebo in BE-CGI-S score and Y-BOCS-BE total score

Dasotraline Fixed Dose Clinical Trial (cont’d)

• Discontinuation rates due to adverse events in the 4 mg/day, 6 mg/day, and placebo groups were 8.6%, 14.1%, and 1.2%

• Reasons for early discontinuation consisted of:
  • Adverse events (8.6%, 14.1%, and 1.2%)
  • Withdrew consent (3.1%, 11.0%, and 9.0%)
  • Lost to follow-up (7.4%, 8.0%, and 7.8%)
  • Other reasons (4.9%, 1.8%, and 3.0%)

• Most common (≥ 10%) adverse events in either dose group were insomnia, dry mouth, headache, decreased appetite, nausea, and anxiety
What about combination therapy: CBT+Rx?

- Adding pharmacotherapy to CBT failed to enhance binge eating outcomes in 6 of 7 published studies testing a variety of medications

- One study with statistical advantage for a combined approach: topiramate + CBT
  - Produced better outcomes than placebo + CBT for reducing both binge eating and weight

- CBT plus lisdexamfetamine has not been tested

Binge Eating Disorder: Summary

• BED is different from overeating and requires the presence of distinguishing features, notably and specifically **loss of control**, marked distress, and strong feelings of shame and guilt

• Psychiatric and somatic co-occurrences are very common, as are functional impairments

• **BED may go undiagnosed** for many years because patients are not always specifically asked about their eating behaviors

• BED occurs in **both men and women** across racial and ethnic groups, and although BED is frequently associated with obesity, many adults with BED are of healthy weight or overweight

• Effective treatment modalities include certain specific psychotherapy (**CBT, IPT, behavioral weight loss**) and pharmacologic approaches, of which **lisdexamfetamine** has received regulatory approval, and **dasotraline** is in Phase 3 of clinical development
Eating Disorders: Summary

• Anorexia nervosa, bulimia nervosa, and binge eating disorder are distinct from one another but share some similarities on psychopathology

• All three can be treated with psychological/behavioral therapies

• Medication treatments have been established for bulimia nervosa (fluoxetine) and binge eating disorder (lisdexamfetamine, and possibly dasotraline in the near future), but not for anorexia nervosa

• Anorexia nervosa and bulimia nervosa are associated with behaviors that are more difficult to hide than binge eating disorder, so that persons with binge eating disorder are often unrecognized and untreated
Posttest Question

Which of the following is FDA approved for bulimia nervosa?

1. Fluoxetine
2. Lisdexamfetamine
3. Topiramate
4. 1 and 2
5. None of the above
Posttest Question

Which of the following is FDA approved for binge-eating disorder?

1. Fluoxetine
2. Lisdexamfetamine
3. Topiramate
4. 1 and 2
5. None of the above
Posttest Question

Which of the following is FDA approved for anorexia nervosa?

1. Fluoxetine
2. Lisdexamfetamine
3. Topiramate
4. 1 and 2
5. None of the above