



Management of Eating Disorders

Webcast
Tuesday, July 18, 2006
2:00 – 4:00 p.m., EST





Moderator :

Sabrina Matoff-Stepp, HRSA
OWH





Management of Eating Disorders

Welcome/Opening Remarks

Peter van Dyck, M.D., M.P.H.
Associate Administrator for Maternal
and Child Health
Health Resources and Services
Administration
U.S. Department of Health and Human
Services



Management of Eating Disorders

Presenting Authors:

Cynthia M Bulik, PhD
University of North Carolina at Chapel Hill

Nancy D Berkman, PhD
RTI International





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RTI-UNC EPC Eating Disorders Report Authors

- Nancy D Berkman, PhD
- Cynthia M Bulik, PhD
- Kimberly A Brownley, PhD
- Kathleen Lohr, PhD
- Jan A Sedway, PhD
- Adrienne Rooks, BA
- Gerald Gartlehner, MD

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Sponsors and Disclaimer

- Nominators of Report
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 - Health Resources and Services Administration (HRSA)
- The RTI-UNC authors are solely responsible for content
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Anorexia Nervosa (AN)

- Refusal to maintain body weight
- Intense fear of gaining weight or becoming fat
- Disturbance in the way one's weight or shape is experienced, undue influence on self-evaluation, or denial of seriousness of illness
- Amenorrhea of at least 3 months
- Restricting or binge-eating/purging type
- Sex ratio: 9 women: 1 man
- Prevalence 0.1–1.0% (average 0.3%)
- Subthreshold conditions more prevalent

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Bulimia Nervosa (BN)

- Recurrent binge-eating
- Feeling out of control
- Compensatory behaviors
 - Vomiting
 - Laxative abuse
 - Excessive exercise
 - Fasting
- Self-evaluation unduly influenced by shape and weight
- Purging and nonpurging types
- Occurs at all body weights
- Prevalence 1–3%
- Subthreshold conditions more common
- Sex ratio: 9 women: 1 man

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Eating Disorder Not Otherwise Specified (EDNOS)

- All criteria for AN except amenorrhea
- All criteria for AN except weight loss, weight is in the normal range
- All criteria for BN except that binge eating and compensatory behaviors at a lower frequency or duration
- Regular inappropriate compensatory behavior after eating small amounts of food, normal weight
- Repeatedly chewing and spitting out food

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Binge Eating Disorder (BED)

- Recurrent episodes of binge eating
- 3 or more of: eating more rapidly than normal, eating until uncomfortably full, eating large amount of food when not hungry, eating alone because of embarrassment or disgust, depressed or guilty after overeating
- Marked distress regarding binge eating
- On average at least 2/week X 6 months
- Not associated with regular use of inappropriate compensatory behaviors
- Provisional diagnostic criteria
- Prevalence: 0.7–4% in non-patient community samples
- Prevalence in obese populations: 5–8%
- Sex ratio approximately equal

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Abbreviations Used in this Presentation

- **AN** – Anorexia Nervosa
- **BN** – Bulimia Nervosa
- **BED** – Binge Eating Disorder
- **EDNOS** – Eating Disorder Not Otherwise Specified

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Key Questions — Treatment

- KQ1. What is the evidence for the efficacy of treatments or combination of treatments for each of the following eating disorders: AN, BN, and BED?
- KQ2. What is the evidence of harms associated with the treatment or combination of treatments for each of the following eating disorders: AN, BN, and BED?
- KQ3. What factors are associated with the efficacy of treatment among patients with the following eating disorders: AN, BN, and BED?
- KQ4. Does the efficacy of treatment for AN, BN, and BED differ by sex, gender, age, race, ethnicity, or cultural group?

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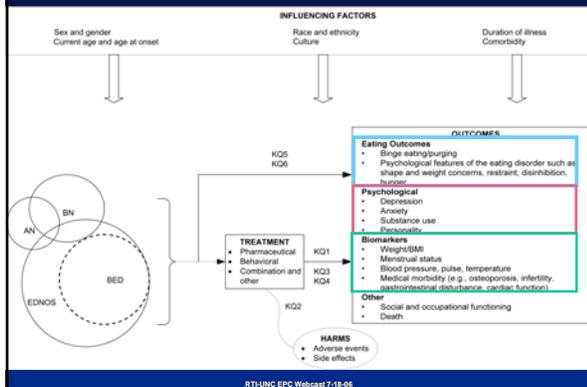
Key Questions — Outcomes

KQ5. What factors are associated with outcomes among individuals with the following eating disorders: AN, BN, and BED?

KQ6. Do outcomes for AN, BN, and BED differ by sex, gender, age, race, ethnicity, or cultural group?

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Analytic Framework



Methods

- Searches in:
 - MEDLINE®
 - Cumulative Index to Nursing and Applied Health (CINAHL)
 - PsycINFO
 - Educational Resources Information Center (ERIC)
 - National AGRICultural OnLine Access (AGRICOLA)
 - Cochrane Collaboration libraries
- Dual abstract and full article review for inclusion or exclusion
- Dual abstraction of data into evidence tables

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Methods (continued)

- Ongoing input from Technical Expert Panel (TEP)
- Grading of articles and the strength of the evidence
- Peer review of draft report
- Revisions and response to comments

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Inclusion and Exclusion Criteria

Category	Criteria
Study population	Humans All races, ethnicities, and cultural groups 10 years of age or older.
Study settings and geography	All nations
Time period	Published from 1980 to the present
Publication criteria	All languages Articles in print Excluded articles: published in nonpeer reviewed journals "gray literature" or unobtainable during review period

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Inclusion and Exclusion Criteria (continued) Admissible Evidence

- Original research studies with sufficient detail regarding methods and results to allow for analysis
- Diagnostic criteria
 - **Anorexia Nervosa:** DSM III, DSM III-R, DSM IV, ICD-10, Feighner or Russell criteria
 - **Bulimia Nervosa:** DSM III-R, DSM IV, ICD-10
 - **BED:** DSM IV

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Inclusion and Exclusion Criteria *(continued)*
Outcomes of Interest

- Eating related
- Psychiatric or Psychological
- Biomarker measures

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Inclusion and Exclusion Criteria *(continued)*
Eligible Designs: Treatment Studies

- Randomized Controlled Trials (RCTs)
 - Double blinded, single blinded, and cross-over designs (prior to first cross-over)
- AN:** 10 or more participants, followed for any length of time
- BN:** 30 or more participants, followed for a minimum of 3 months
- BED:** 10 or more participants, followed for any length of time

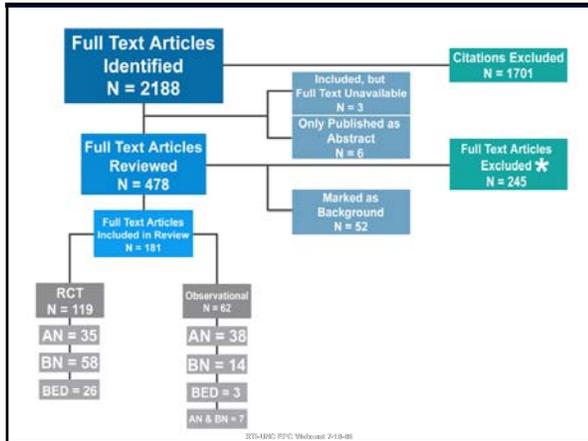
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Inclusion and Exclusion Criteria *(continued)*
Eligible Designs: Outcome Studies

- Observational studies
 - Prospective and retrospective cohort
 - Case series
 - With and without comparison groups

Disease population must be followed for a minimum of one year and must include 50 participants at the time of the analysis.

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* Full Text Articles Excluded

- 78 Sample size too small
- 52 Wrong study design
- 22 Wrong outcome or no outcome
- 21 Does not focus on AN, BN or BED
- 20 Used DSM-III definition for BN
- 12 Insufficient statistical analysis to make comparisons
- 10 No control or comparison group
- 12 Does not follow individuals for at least 1 year
- 9 No original data (e.g., letters, editorials, reviews)
- 3 RCT does not follow BN individuals for 3 months
- 3 Wrong year (e.g., outside of 1980–2005)
- 1 Drug no longer on the market
- 1 Not published in a peer-reviewed journal

Grading Criteria for Treatment Articles

Graded Parameters

- research aim/study question
- study population
- randomization
- blinding
- interventions
- outcomes
- statistical analysis
- results
- discussion
- external validity
- funding/sponsorship

Grading Criteria for Outcomes Articles

Graded Parameters

- research aim/study question
- study population
- eating disorder diagnosis method
- study design
- statistical analysis
- results/outcome measurement
- external validity
- discussion

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Rating the Strength of the Evidence

- I. Strong evidence base.** Studies of strong design; results clinically important and consistent with minor exceptions; results free from serious doubts about generalizability, bias, or flaws in design. Studies with negative results are adequately powered.
- II. Moderate evidence base.** Studies of strong design, uncertainty due to inconsistencies or concern about generalizability, bias, design flaws, or sample size. Or, consistent evidence derived from studies of weaker design.
- III. Weak evidence base.** Limited number of studies of weaker design. Studies with strong design either have not been done or are inconclusive.
- IV. No evidence base.** No published literature.

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Anorexia Nervosa Outcomes and Treatment

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AN: Factors Associated with Eating Related Outcomes

- Moderately strong evidence (II); 45 articles
- Eating related outcomes
 - For some, AN diagnosis persists over time
 - For many, AN diagnosis changes to other eating disorder diagnoses over time
 - Approximately 1/4 have no eating disorder diagnosis at followup
- Factors associated with diagnostic outcomes
 - Longer duration of disorder
 - Psychiatric/Psychological characteristics
 - Other factors

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AN: Psychiatric/Psychological Outcomes

- Depression
- Anxiety disorders
- Substance abuse
- Asperger and autism spectrum disorders

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AN: Factors Associated with Biomarker and Mortality Outcomes

- Biomarker measured outcomes
 - Lower weight/BMI
 - Regular or cyclical menstruation less likely
- Mortality outcomes
 - Increased risk overall
 - Increased risk of suicide
- Factors associated with mortality outcomes
 - Alcohol and substance abuse
 - Greater severity of eating disorder

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AN: Outcome Differences by Sex, Gender, Age, Race, Ethnicity or Cultural Group

- Weak evidence related to diversity (III)
 - Differences by age: findings mixed
 - Differences by sex: no data
 - Differences by race/ethnicity/cultural group: no data

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AN Treatment: Overview

- 32 studies reported in 35 articles
- 13 excluded due to poor rating
- Medications: tricyclic antidepressants, 2nd generation antidepressants, hormones, nutritional supplements
- No study reported race/ethnicity, one did not report sex
- One study used intention to treat
- Sample size: 15–72 (average 23)
- Total studied: 319 women, 1 man
- Drop out: 0–66%

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AN: Types of Studies

- 8 Medication only
- 0 Medication plus psychotherapy
- 6 Behavioral: adult (≥ 18)
- 4 Behavioral: adolescent only
- 1 Behavioral: (adolescent + adult)

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Source, Treatment	Age, Sample Size (Dropout %)	Significant Differences Between Groups
Attia, 1998 Fluoxetine vs. placebo	Age range: 16–45 Enrolled: 33 (3%)	At endpoint: Not reported Change over time: None
Kaye, 2001 Fluoxetine vs. placebo	Fluoxetine: 23 (9) Placebo: 22 (6) Enrolled: 39 (66%)	At endpoint: None Change over time: None
Halmi, 1986 Amitriptyline vs. cyproheptadine vs. placebo	Age range: 13–36 Enrolled: 72 (25%)	At endpoint: Cyproheptadine associated with fewer days to target weight, higher caloric intake, and less depressed mood than placebo. Change over time: Not reported
Biederman, 1985 Amitriptyline vs. placebo	Age range: 11–27 Enrolled: 25 (0%)	At endpoint: None Change over time: Not reported

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Source, Treatment	Age, Sample Size (Dropout %)	Significant Differences Between Groups
Miller, 2005 Testosterone vs. placebo	Age range: 18–37 Enrolled: 38 (13%)	At endpoint: Testosterone associated with less depressed mood. Change over time: Depressed mood increased less in testosterone group.
Hill, 2000 Growth hormone (rhGH) vs. placebo	Age range: 12–18 Enrolled: 15 (0%)	At endpoint: rhGH associated with fewer days to restoration of normal orthostatic response compared with placebo. Change over time: Not reported
Klibanski, 1995 Estrogen/progestin vs. nonmed control	Age range: 16–43 Enrolled: 48 (8%)	At endpoint: None Change over time: None
Birmingham 1994 Zinc vs. placebo	Age range: ≥15 Enrolled: 54 (35%)	At endpoint: None Change over time: Zinc superior in rate of body mass index increase.

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AN: Behavioral Studies Adults

- **Cognitive Behavioral Therapy** (focus on cognitive and behavioral features associated with maintaining eating pathology)
 - vs. nutritional counseling after weight restoration, decreased relapse risk and increased likelihood of good outcomes
 - vs. NSCM or IPT, NSCM greater global good outcomes than IPT with CBT intermittent
- **Cognitive Analytic Therapy** (based on psychodynamic and behavioral principles)
 - No advantage over educational behavioral or family treatment
- **Family Therapy**
 - Less effective for adults and those with chronic illness

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AN: Behavioral Studies Adolescent

- **Family Therapy** (focus on initial parental control of renutrition)
 - Advantage to conjoint versus separated delivery
 - Superior to ego-oriented individual therapy in increasing BMI and restoring menstruation
 - No differences between short (10 sessions over 6 months) or long (20 sessions over 12 months); more severe eating-related obsessions and non-intact families may benefit from longer

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AN: Treatment Harms

- Most common—need for hospitalization due to weight loss
- Second-generation antidepressants nausea, headache, diarrhea, constipation, dizziness, fatigue, sweating, and sexual side effects; rarely hyponatremia, suicidality, and seizures
- Unknown if harms are greater in underweight state
- Harms rarely reported in behavioral intervention trials

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Factors Associated with AN Treatment Outcomes

- No consistent factors associated with better or poorer treatment outcome across studies
- Subgroup analyses not planned *a priori*, had very small samples, and conclusions must be viewed with extreme caution

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AN: Treatment Efficacy by Sex, Gender, Age, Race, Ethnicity, or Cultural Group

- No information exists regarding differential efficacy of pharmacotherapy or behavioral interventions for AN by sex, gender, race, ethnicity, or cultural group
- Scant evidence (1 study) shows that interventions involving the family have greater efficacy for individuals below the age of 15 than for patients above that age

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AN: Treatment Summary

- Medication: literature sparse and inconclusive
- Combination medication and behavioral: no studies
- CBT may reduce relapse risk for adults with AN after weight restoration
- Insufficient evidence to determine whether CBT is effective in the underweight state
- Family therapy with focus on parental control of renutrition is efficacious for AN in adolescents in terms of weight gain and psychological change
- Family therapy as currently conceptualized does not appear to be effective with adults with AN with longer duration of illness

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AN: Strength of Evidence Concerning Four Treatment Key Questions

	Efficacy KQ 1	Harms KQ 2	Factors KQ 3	Diversity KQ 4
Interventions				
Medication and Medication plus Behavioral Interventions				
Adults	III	III	III	IV
Adolescents	III	III	III	IV
Behavioral Interventions				
Adults	III	IV	III	IV
Adolescents	II	IV	III	IV

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Bulimia Nervosa: Outcomes and Treatment

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BN: Factors Associated with Eating Related Outcomes

- Moderately strong evidence (II); 21 articles
- Eating related outcomes
 - Approximately 1/2 have no eating disorder diagnosis at followup
- Factors associated with BN diagnostic outcomes
 - Depression
 - Substance abuse
 - Age at onset generally not a predictor

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BN: Psychiatric/Psychological Outcomes

- Depression
- Mood disorder
- Substance use and abuse

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BN: Factors Associated with Biomarker and Mortality Outcomes

- Biomarker measured outcomes
 - Weight/BMI improved over time
- Mortality outcomes
 - No significantly increased risk

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BN: Outcome Differences by Sex, Gender, Age, Race, Ethnicity or Cultural Group

- No evidence related to diversity (IV)

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BN Treatment: Overview

- 47 studies reported in 58 articles
- 10 excluded due to poor rating
- Medications: second-generation antidepressants, tricyclic antidepressants, an anticonvulsant, monoamine-oxidase inhibitors (MAOIs), and a 5HT₃ antagonist
- 31 studies failed to report ethnicity
- Sample size: 31–398 (average 93)
- Total studied: 3,334 women, 69 men
- Drop-out: 0–87%

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BN: Types of Studies

- 12 Medication only
- 6 Medication plus psychotherapy
- 13 Psychotherapy only
- 4 Self-help
- 3 Other

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BN: Medication Treatment

- **Fluoxetine** (60 mg/day) (6 to 18 weeks) has been shown in several included trials to reduce binge eating, purging, and psychological features of BN in the short term
- 60 mg performs better than 20 mg dose
- Considerable evidence for 60 mg/day of fluoxetine to treat BN in the short term. Evidence for the long-term effectiveness of relatively brief medication treatment does not exist
- Optimal duration of treatment and the optimal strategy for maintenance of treatment gains are unknown

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BN: Medication Treatment (continued)

- Preliminary evidence of the efficacy of **trazodone** and **fluvoxamine**, and **topiramate**
- One preliminary trial of **ondansetron**, a 5HT3 antagonist and antiemetic, led to an intriguing decrease in binge eating and vomiting when patients could self-administer when they had urges to binge or purge
- One trial of **brofaromine**, an MAOI, showed a significantly greater effect on reducing vomiting than placebo
- Abstinence: medication treatment leads to abstinence in a minority of individuals—although bulimia symptoms improve, they nonetheless persist
- Drop out: zero to 51 percent

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BN: Medication + Behavioral Treatment

- Combined medication plus behavioral intervention studies provide only preliminary evidence regarding the optimal combination of medication and psychotherapy or self-help
- Given the variety of designs used and lack of replication, evidence remains weak

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BN: Behavioral Treatment

- **Cognitive Behavioral Therapy** (focus on cognitive and behavioral features associated with maintaining eating pathology)
- A large number of included trials provide evidence that CBT (individually or in group) is effective in reducing binge eating, purging, and psychological features of BN in both the short and the long term
- CBT may act more quickly than interpersonal psychotherapy
- Individual CBT may confer no advantage over the more economical group CBT approach; although this finding is important for service delivery, it requires replication
- **Dialectical Behavior Therapy** may be effective and is worth additional study

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BN: Treatment Harms

- **Second-generation antidepressants:** nausea, headache, diarrhea, constipation, dizziness, fatigue, sweating, and sexual side effects; rarely hyponatremia, suicidality, and seizures—consistent with those observed in other disorders
- **MAOI:** nausea, sleep disturbance, and dizziness. No hypertensive crises reported, although this danger should always be considered in patients who experience uncontrollable eating episodes
- Harms rarely reported in behavioral or self-help intervention trials

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Factors Associated with BN Treatment Outcomes

- **Medication trials:** greater concern for body shape and weight and longer duration of illness had more favorable treatment responses
- **Behavioral trials:** high frequency of binge eating and longer duration of illness associated with poorer outcome
- **Self-help:** (preliminary) higher perfectionism, higher compulsivity scores, higher intimacy problem scores, and lower cognitive behavior knowledge scores associated with better outcome

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BN: Treatment Efficacy by Sex, Gender, Age, Race, Ethnicity, or Cultural Group

- No information exists regarding differential efficacy of *medication only* or *combined medication plus behavioral interventions* for BN by sex, gender, age, race, ethnicity, or cultural group
- No data exist regarding differential efficacy of *behavioral only* interventions for BN by sex, gender, age, race, ethnicity, or cultural group

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BN: Treatment Summary

- **Fluoxetine** (60 mg/day) (6–18 weeks): decreased short-term binge eating, purging, and psychological features
- 60 mg better; prevention of relapse at 1 year. Long-term effectiveness unknown. Optimal duration of treatment and strategy for maintenance unknown
- Combined drug and behavioral interventions: only preliminary evidence of impact of combination of medication and psychotherapy or self-help
- **CBT** (individual or group): decreased binge eating, purging, and psychological features in short and long term
- Further evidence is required to establish the role for self-help in reducing bulimic behaviors
- How best to treat individuals who do not respond to CBT or fluoxetine remains a major shortcoming of the literature

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BN: Strength of Evidence Concerning Four Treatment Key Questions

	Efficacy	Harms	Factors	Diversity
	KQ 1	KQ 2	KQ 3	KQ 4
Interventions				
Medication and Medication plus Behavioral Interventions				
All ages	I	I	III	IV
Behavioral Interventions				
All ages	I	IV	II	IV
Self-help				
All ages	III	IV	III	IV
Other				
All ages	III	IV	III	IV

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**5 Minute
BREAK**



**Binge Eating Disorder:
Outcomes and Treatment**

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BED: Factors Associated with Outcomes

- Weak evidence (III), 3 articles
- Eating related outcomes
 - Approximately ¼ have no eating disorder diagnosis and 6% have BED at 6 year followup
 - Cluster B personality disorders associated with greater number of binge days at 1 year followup
- Psychiatric/Psychological outcomes
 - Depression, anxiety, and obsessionality improved
- Biomarker outcomes
 - No data

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BED: Outcome Differences by Sex, Gender, Age, Race, Ethnicity or Cultural Group

- No evidence related to diversity (IV)

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BED Treatment: Overview

- 26 studies
- 6 excluded due to poor rating
- Medications: second-generation antidepressants, tricyclic antidepressants, an anticonvulsant, sibutramine, orlistat
- 6 studies failed to reported race/ethnicity
- Sample size: 20–162 (average 62)
- Total studied: 984 women, 87 men, 61 unknown
- Drop out: 0–40%
- Two critical outcomes: binge eating and weight

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BED: Types of Studies

- 9 Medication only
- 4 Medication plus behavioral intervention
- 8 Behavioral
- 3 Self-help
- 2 Other

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BED: Medication Only Treatments

- **SSRIs:**
 - Reduction in target eating, psychiatric and weight symptoms, and severity of illness
 - Abstinence rates unclear
 - Persistence of effects unknown
- **Low-dose imipramine**
 - augmenting standard dietary counseling and psychological support associated with decreases in binge eating and weight that persist after discontinuation of medication
- **Sibutramine and Topiramate**
 - clinically significant reductions in BMI over the short term
- **Drop out:** 7–40% ; **Placebo** response high

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BED: Medication + Behavioral Treatments

- **Fluoxetine, orlistat, desipramine + CBT**
- Combining medication and CBT may improve both binge eating and weight loss
- Optimal combinations unknown
- Optimal duration of medication treatment for sustained reductions in binge eating and maintenance of weight loss has not yet been addressed empirically

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BED: Behavioral Treatments

- **CBT** (12 weeks–5 months)
- Effective in reducing number of binge days or number of binge episodes
- CBT associated with greater abstinence than waiting list—persists for 4 months
- CBT improves the psychological aspects of BED (restraint, hunger, and disinhibition)
- Unclear whether CBT improves depression
- CBT did not lead to decreases in weight
- DBT worthy of further study

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BED: Self-Help Treatments

- **Self-help** (three trials) is efficacious in decreasing binge days, binge eating episodes, and psychological features associated with BED
- Leads to greater abstinence from binge eating vs. waiting list control condition
- Short-term abstinence rates approximate those seen in face-to-face psychotherapy trials
- Self-help not associated with decreased depression or weight

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BED: Treatment Harms

- **SSRIs**: (side-effects similar to BN trials)
- **Topiramate**: headache, parasthesias, and amenorrhea.
- **Sibutramine**: significantly more constipation than placebo.
- **Orlistat**: significantly more gastrointestinal than placebo
- Harms rarely reported in behavioral intervention trials

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Factors Associated with BED Treatment Outcomes

- No consistently replicated factors associated with outcome

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BED: Treatment Efficacy by Sex, Gender, Age, Race, Ethnicity, or Cultural Group

- No information exists about differential efficacy of *pharmacotherapy* interventions for BED by sex, age, gender, race, ethnicity, or cultural group
- No data exist regarding differential efficacy of *psychotherapeutic* treatment for BED by sex, age, gender, race, ethnicity, or cultural group.

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BED: Treatment Conclusions

- Outcomes: binge eating and decrease in weight
- **SSRIs**: superior on eating, psychiatric, and weight measures than placebo. Unknown if changes persist after drug discontinuation.
- **Medication + CBT**: may improve both binge eating and weight loss outcomes.
- **CBT (group or individual)**: decreased binge eating; greater abstinence than waiting list. Improves psychological features. Mixed results on depression. Little impact on weight.
- **Self-help**: decreased binge eating and psychological features. Greater abstinence than waiting list; short-term abstinence rates approximate those seen in face-to-face psychotherapy trials.

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BED: Strength of Evidence Concerning Four Treatment Key Questions

	Efficacy	Harms	Factors	Diversity
	KQ 1	KQ 2	KQ 3	KQ 4
Interventions				
Medication and Medication plus Behavioral Interventions				
Adult	II	I	III	IV
Behavioral Interventions				
Adult	II	IV	III	IV
Self-help				
Adult	III	IV	III	IV
Other				
Adult	III	IV	III	IV

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Conclusions: Treatment

- AN, BN, and BED is of highly variable quality—AN weakest
- Future in AN
 - large samples and multiple sites
 - appropriate biomarker outcomes
 - clear delineation of the age of participants
- Future in BN
 - novel treatments for the disorder and enhancements to CBT
 - optimal duration of intervention
 - optimal approaches for CBT & medication nonresponders
- Future in BED
 - two outcomes: binge eating and weight control
 - optimal duration of intervention
 - effective strategies for relapse prevention

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Conclusions: Treatment (continued)

- For AN, BN and BED
 - explore additional treatment approaches
 - attention to factors influencing outcomes and harms associated with treatment

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Conclusions: Outcomes

- Prospective cohort studies
- Inclusion of comparison groups
- Use of appropriate multivariate statistical techniques
- Tracing outcomes across diagnoses (crossover)
- Age and lifespan orientation—differential outcomes by age
- Most studies outside of US, little data on racial/ethnic groups within the US
- Greater attention to medical outcomes

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Conclusions: Global

- Increase cross-talk between treatment and outcome research
- Replication critical
- Develop consensus definitions of remission, recovery, and relapse for all disorders
- Standardize and consolidate outcome measures
- Attend to disease presentations currently grouped under EDNOS
- Attention to efficacy and outcome by sex, gender, age, race, ethnicity, or cultural group

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Contributors

<p>Project Staff UNC-RTI EPC</p> <ul style="list-style-type: none"> ▪ Timothy S. Carey, MD MPH ▪ B. Lynn Whitener PhD ▪ Leah Randolph, MA ▪ Laura Morgan, MA ▪ Loraine Monroe, EPC ▪ Jennifer Best, PhD ▪ Jennifer McDuffie, PhD ▪ Thomas Ranev, PhD ▪ Lauren Reba, BA ▪ Jennifer Shapiro, PhD ▪ Hemal Shroff, PhD ▪ Kelly Beth Bowker ▪ Michele Crisafulli 	<p>Technical Expert Panel</p> <ul style="list-style-type: none"> ▪ Lisa Begg, DrPH, RN ▪ Mark Chavez, PhD ▪ Mary Gee ▪ Craig L. Johnson, PhD ▪ Richard E. Kreipe, MD ▪ James Lock, MD, PhD ▪ Marsha D. Marcus, PhD ▪ Cheryl L. Rock, PhD, RD ▪ Mary Tantiilo, PhD, RN ▪ B. Timothy Walsh, MD ▪ Joel Yager, MD
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<http://www.ahrq.gov/downloads/pub/evidence/pdf/eatingdisorders/eatdis.pdf>

Agency for Healthcare Quality and Research: www.ahrq.gov

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Management of Eating Disorders

Closing Remarks

Vivian W. Pinn, M.D.
Associate Director for Research on Women's Health
& Director, Office of Research on Women's Health
National Institutes of Health
U.S. Department of Health and Human Services