Neuere Entwicklungen in der Therapie von Anorexia Nervosa

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"Extraordinary claims require extraordinary evidence."
- Carl Sagan

Collaborators

- Daniel le Grange, Ph.D
- W. Stewart Agras, MD
- Helena Kraemer, Ph.D
- Booil Jo, Ph.D
- Susan Bryson, MS
- Judy Beenhakker, MS
- Subjects and therapists

Adolescent AN Treatment Studies

Uncontrolled Studies

- Minuchin et al (1978)
- Dare (1983)
- Martin (1984)
- Stierlin & Weber (1987; 1989)
- Mayer (1994)
- Herscovici & Bay (1996)
- Le Grange & Gelman (1998)
- Lock & Le Grange (2001)
- Wallin & Kronwall (2002)
- Le Grange et al (2005)
- Lock, Le Grange et al (2006)
- Loeb et al (2007)

Controlled Studies

- Russell et al (1987)
- Eisler et al (1997)

- Le Grange et al (1992)
- Eisler et al (2000)
- Eisler et al (2007)

- Robin et al (1994)
- Robin et al (1999)

- Lock et al (2005)
- Lock et al (2006)

- Gowers et al (2007)*
- Lock et al. (2010)

"The patients should be fed at regular intervals, and surrounded by persons who would have moral control over them; relatives and friends being generally the worst attendants."

Sir William Gull
(1816-1890)

“It is necessary to separate both children and adults from their father and mother, whose influence, as experience teaches, is particularly pernicious”

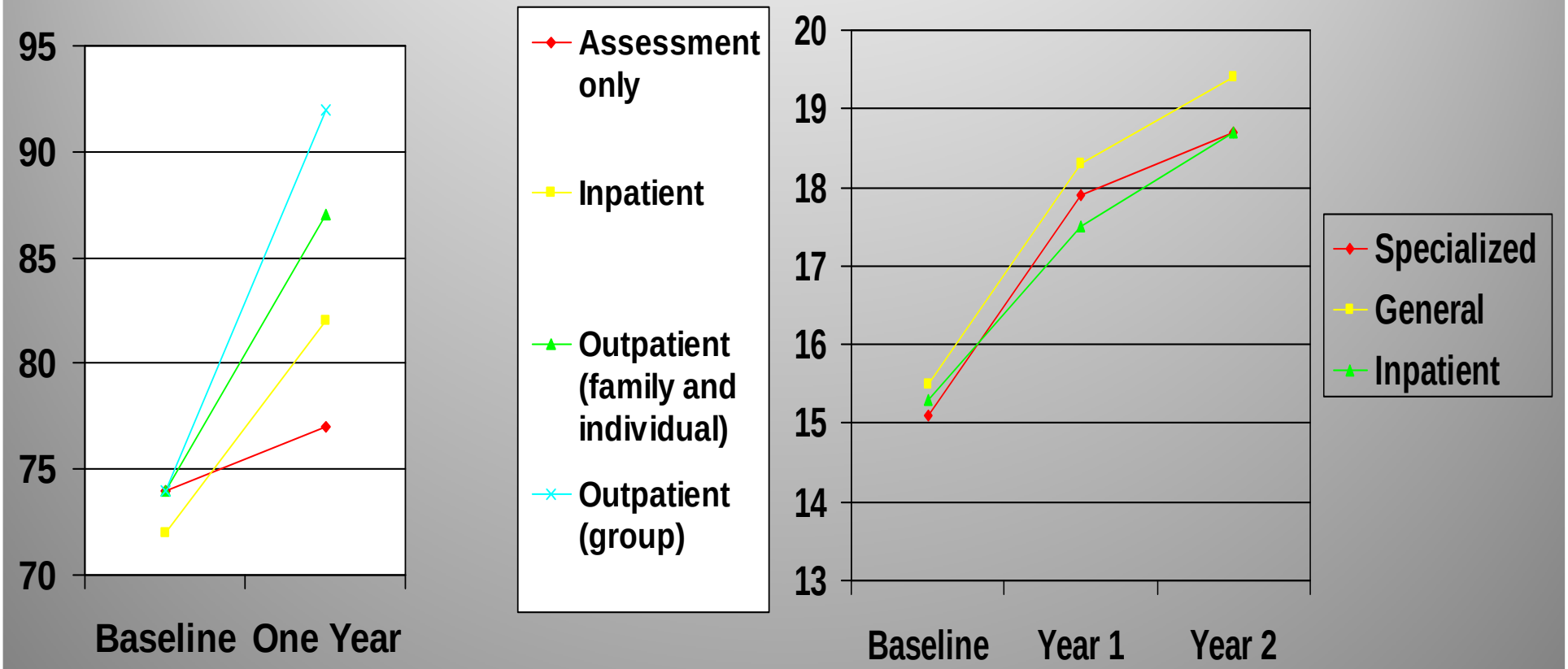
Jean Martin Charcot

(1825-1893)

But just how well does this work?

Hospitalization for Adolescent AN

Crisp et al 1991



Gowers et al 2007

What about outpatient treatments?

- “excessive concern with the body and its size, and the rigid control over eating, are late symptoms in the development of youngsters who have been engaged in a desperate fight against feeling enslaved and exploited, not competent to lead a life of their own.”

- “The avoidant position in anorexia nervosa is therefore a profoundly psychosomatic one, rooted in the seemingly miraculous and certainly unique capacity to reverse pubertal process and hence all of its social and psychological impacts.”

Family-Based Treatment

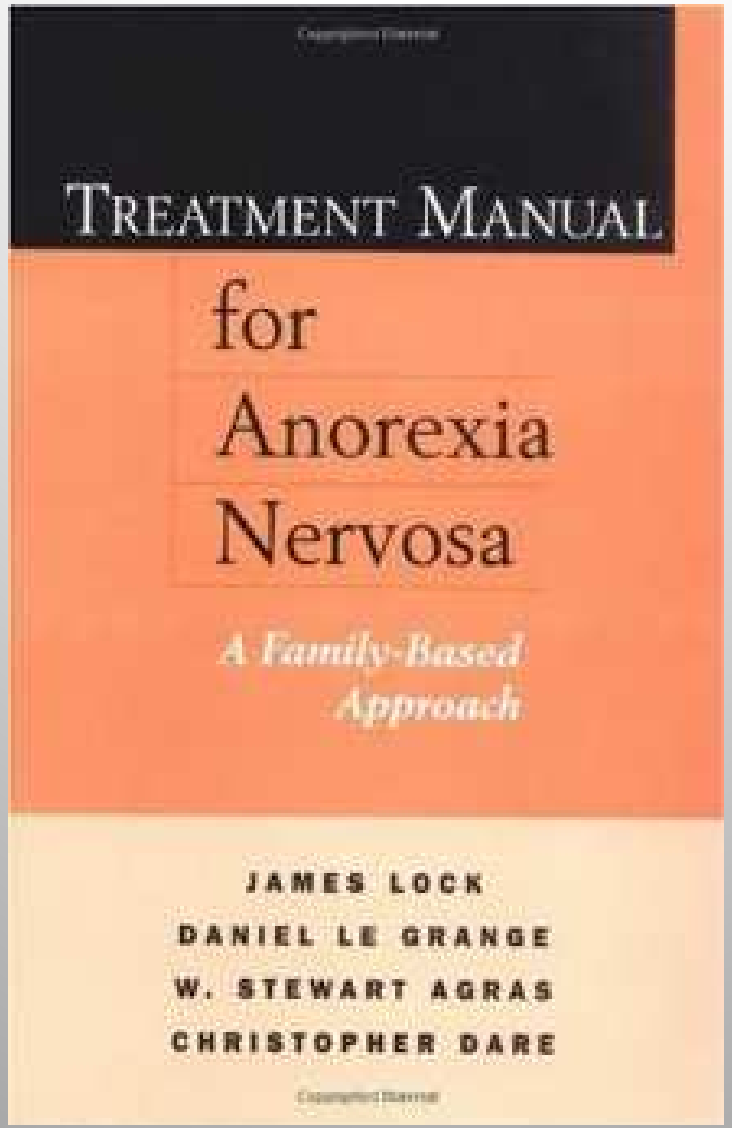
- **Developed at the Maudsley Hospital in London in the 1980s**
- **Refined at the Stanford University and The University of Chicago**
- **Takes key strategies or interventions from a variety of Schools of Family Therapy**
  - **Minuchin – Structural Family Therapy**
  - **Selvini-Palozzoli – Milan School**
  - **Haley – Strategic Family Therapy**
  - **White – Narrative Therapy**

Family-Based Treatment

- **Theoretically agnostic – no assumptions about the origin of the disorder, focus on what can be done**
- **Parents are a resource with no blame directed to either the parents or the ill adolescent**
- **Siblings play supportive role and protected from the job assigned to the parents**
- **FBT is a team approach, i.e., primary therapist, child & adolescent psychiatrist, pediatrician**

Three Phases of FBT

Phase 1 (Sessions 1-10)	• Parents in charge of weight restoration
Phase 2 (Sessions 11-16)	• Parents hand control over eating back to the adolescent
Phase 3 (Sessions 17-20)	• Discuss adolescent developmental issues


TREATMENT MANUAL
for
Anorexia
Nervosa
A Family-Based Approach
JAMES LOCK
DANIEL LE GRANGE
W. STEWART AGRAS
CHRISTOPHER DARE

RCT Comparing FBT to Individual Therapy

(Lock, Le Grange et al 2010)

Rationale

- Two of the predominant models for treating adolescent AN are
  - Family-Based Treatment (FBT), a family therapy aimed at symptom management by parents early in treatment
  - Adolescent Focused Therapy (AFT) a primarily individual therapy aimed at promoting self-efficacy, self-esteem, and self-management of eating problems.

Design

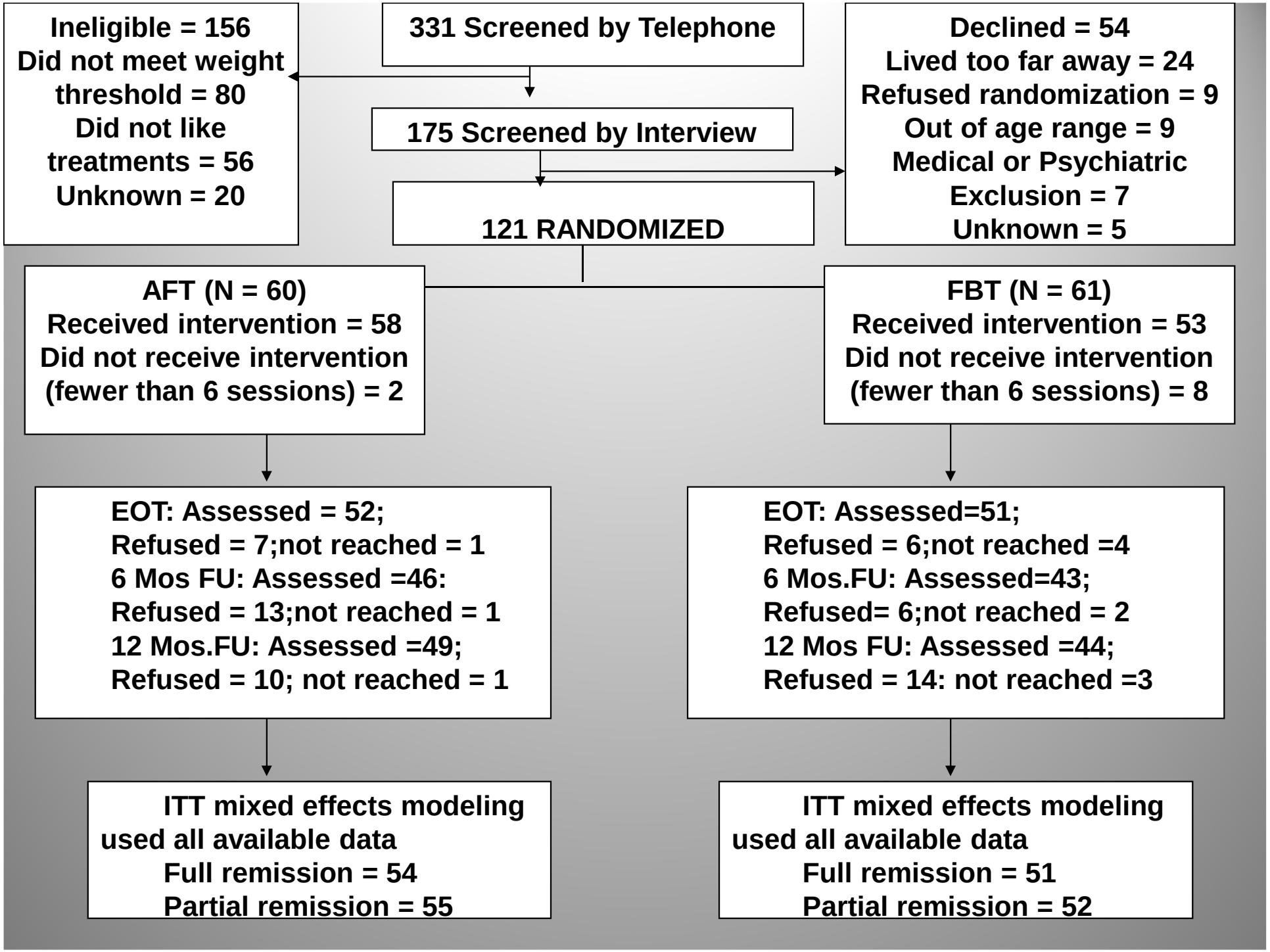
Hypothesis: FBT is more effective than AFT in promoting full remission and partial remission; Medication use will moderate outcome

Randomized 121 medically stable adolescents with AN (excluding amenorrhea requirement) with parents or guardian to either FBT or AFT. Two month medication on stable dose still meeting entry criteria.

12 months of treatment (24 contact hours/ 24-1 hour sessions in FBT and 32- 45 minute sessions in AFT including collaterals with parents alone)

Primary Outcomes: Full Remission and Partial Remission

Independent assessments of weight, EDE at BL, EOT, 6 and 12 month follow-up


Ineligible = 156
Did not meet weight threshold = 80
Did not like treatments = 56
Unknown = 20
331 Screened by Telephone
175 Screened by Interview
121 RANDOMIZED
Declined = 54
Lived too far away = 24
Refused randomization = 9
Out of age range = 9
Medical or Psychiatric Exclusion = 7
Unknown = 5
AFT (N = 60)
Received intervention = 58
Did not receive intervention (fewer than 6 sessions) = 2
FBT (N = 61)
Received intervention = 53
Did not receive intervention (fewer than 6 sessions) = 8
EOT: Assessed = 52;
Refused = 7;not reached = 1
6 Mos FU: Assessed =46:
Refused = 13;not reached = 1
12 Mos.FU: Assessed =49;
Refused = 10; not reached = 1
EOT: Assessed=51;
Refused = 6;not reached =4
6 Mos.FU: Assessed=43;
Refused= 6;not reached = 2
12 Mos FU: Assessed =44;
Refused = 14: not reached =3
ITT mixed effects modeling used all available data
Full remission = 54
Partial remission = 55
ITT mixed effects modeling used all available data
Full remission = 51
Partial remission = 52

Outcome—Clinically Significant

Primary Outcome: Full Remission (weight to 95% IBW weight for height and age according to CDC norms and EDE 1SD with community norms)

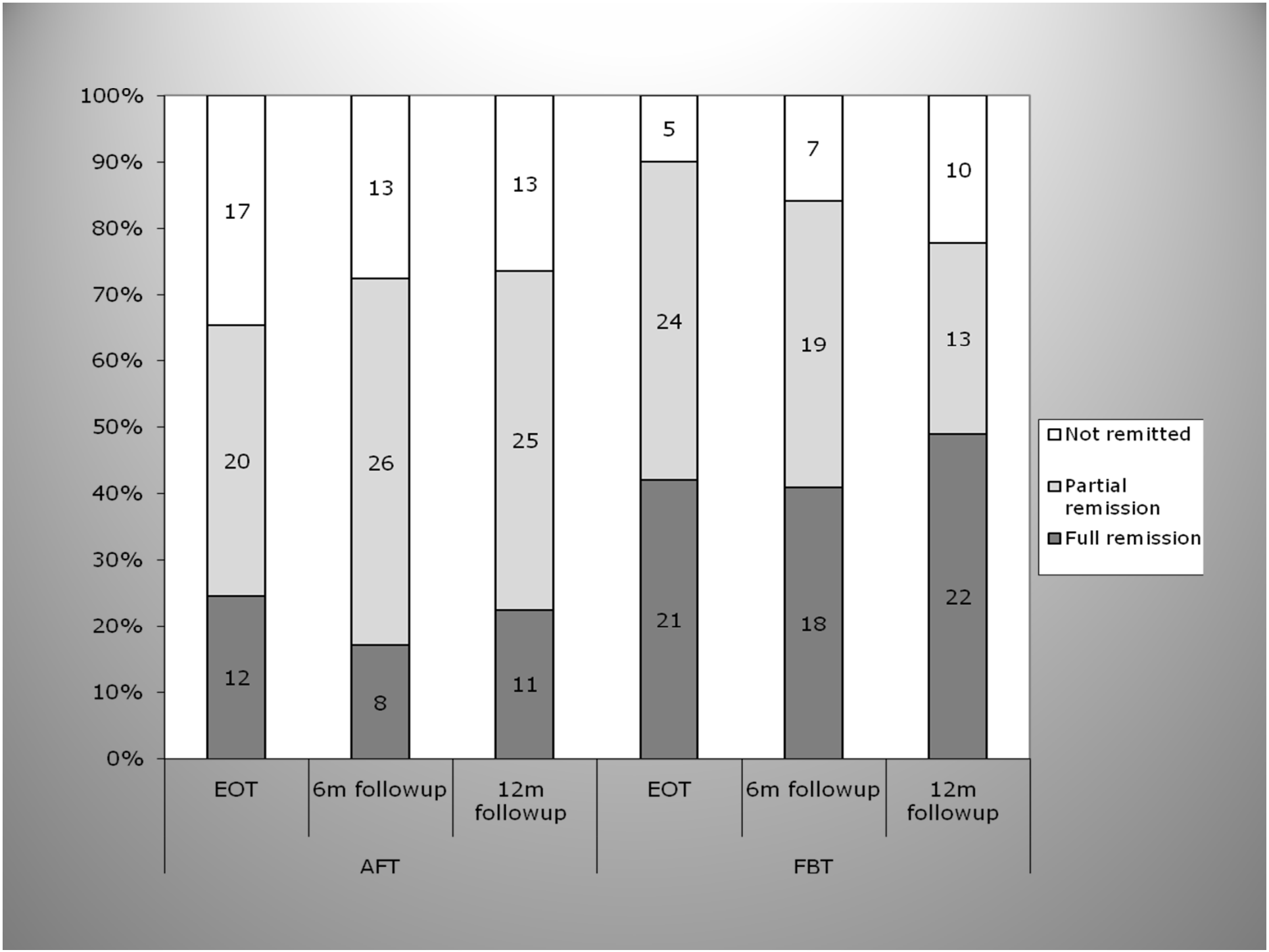
--weight threshold approximates weight needed for return to full physical health in young adolescents and to address growth, bone health, and hormonal function

--EDE threshold is in the normal range for community sample and addresses minimization common in adolescent AN

Outcome—Clinically Significant

- Secondary Outcome is partial remission defined as weight greater than 85%IBW age for height using CDC norms.
  - This threshold approximates common cut point for good/intermediate outcome in many studies using Morgan Russell Outcome Criteria.

	Chicago		Stanford		TOTAL	
	AFT	**FBT**	**AFT**	**FBT**	**AFT**	**FBT**
Age[1]	14.7(1.6)	14.4(1.8)	14.8(1.4)	13.8(1.6)	14.7(1.5)	14.1(1.7)
Comorbidity	31%	12%	32%	28%	32%	20%
Duration of illness (in months)	8.9 (7.8)	11.6 (8.5)	11.6 (9.5)	13.0 (8.6)	10.3 (8.7)	12.3 (8.5)
Ethnicity						
Asian	0 (0%)	1(3%)	6(19%)	6(21%)	6(10%)	7(12%)
Black	0 (0%)	0(0%)	1(3%)	0(0%)	1(2%)	0(0%)
Caucasian	27(93%)	27(84%)	20(64%)	18(62%)	47(78%)	45(74%)
Hispanic	1(3%)	3(9%)	2(6%)	3(10%)	3(5%)	6(10%)
Other	1(3%)	1(3%)	2(6%)	2(7%)	3(5%)	3(5%)
% minority	2 (7%)	5(16%)	11(35%)	11(38%)	13(22%	16(26%)
Gender % male	10%	12%	3%	10%	7%	11%
Intact family	79%	94%	74%	66%	77%	80%
Medication use	31%	28%	6%	3%	18%	16%
Parent education (years)	17.8(2.6)	16.3(2.6)	16.1(3.3)	17.1(2.6)	17.0(3.1)	16.7(2.6)
Previous Hospitalizations	24%	19%	71%	66%	48%	41%
Sample Size	29	32	31	29	60	61


100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
17
20
12
13
26
8
13
25
11
5
24
21
7
19
18
10
13
22
Not remitted
Partial remission
Full remission
EOT
6m followup
12m followup
EOT
6m followup
12m followup
AFT
FBT

Measure	Baseline Adjusted Estimated Mean and Standard Error		Baseline Adjusted Mean Difference (FBT-AFT) and 95 % Confidence Intervals	T-values	P	Number Needed To Treat (Effect Size)
	AFT	FBT				
BMI percentile for age and gender						
End of Treatment	23.4(2.8)	31.4(2.8)	8.0(0.1,15.9)	t(117)= 2.0	**.048**	5
6 month F/U	29.1(3.4)	31.4 (3.5)	2.3 (-7.4,12.0)	t(117)=0.5	.640	19
12 month F/U	29.0(3.4)	32.2(3.4)	3.2(-6.4,12.8)	t(117)=0.7	.510	14
EDE						
End of Treatment	1.20(0.15)	0.71(0.16)	-0.49(-0.93,-.06)	t(117)=-2.2	**.027**	4
6 month F/U	1.01(0.16)	0.78(0.17)	-0.24 (-0.70, 0.22)	t(117)=-1.0	.307	10
12 month F/U	1.04(0.16)	0.79(0.16)	-0.25(-0.69,0.19)	t(117)=1.1	.263	9

Maintenance of Remission

- Relapse from full remission at post treatment was 10% for FBT and 45% for AFT by 12 month follow-up.
- Relapse from partial remission at post treatment was 17% for FBT and 6% from AFT by 12 month follow-up.
- The percent of participants that were partially remitted who later achieved full remission from AFT was 19% and from FBT was 25%.

Other Findings

Dropout, though low in both treatments, no differences between the two groups.

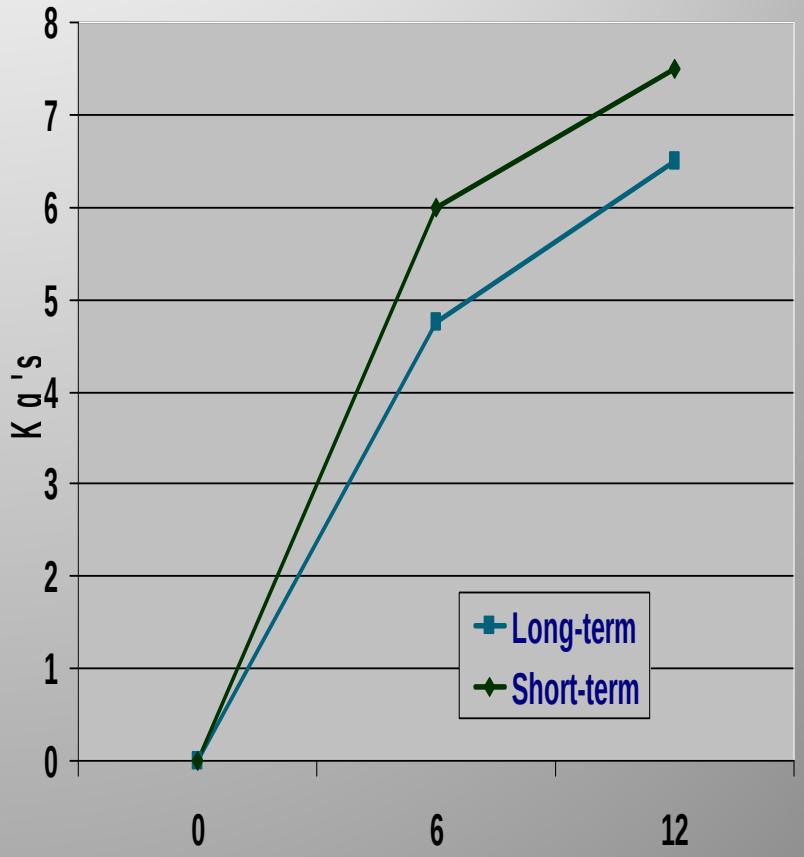
By 3 months 38% (N = 23) of FBT participants had reached 95% IBW vs 20% (N = 12) in AFT $F(1,105)=5.5$ $p=.021$)

Hospitalization rates during treatment were 18% in FBT and 31% in AFT

How much FBT is needed?

Stanford Dosage Study

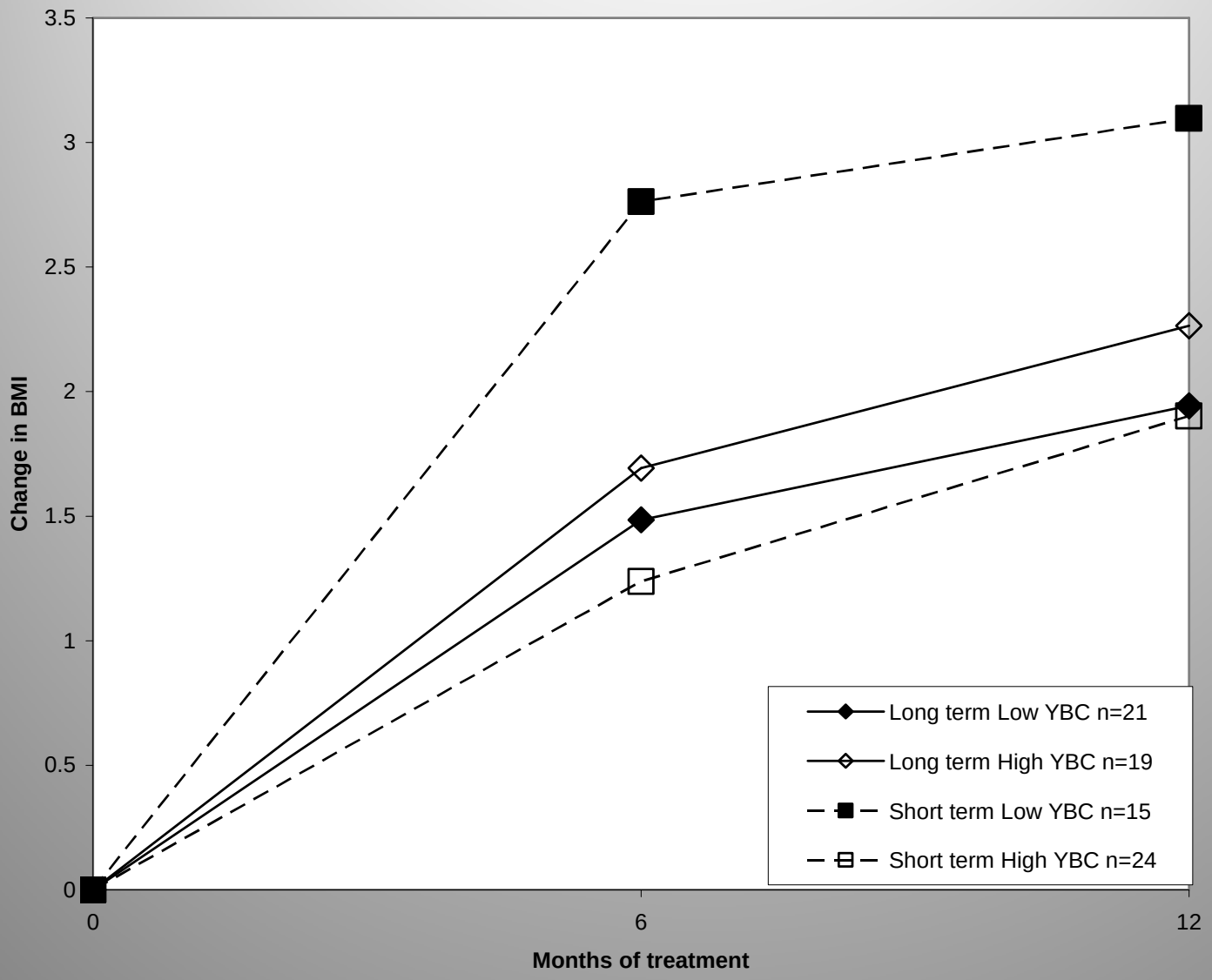
- 86 adolescents with AN
- Long-term FBT
- Short-term FBT



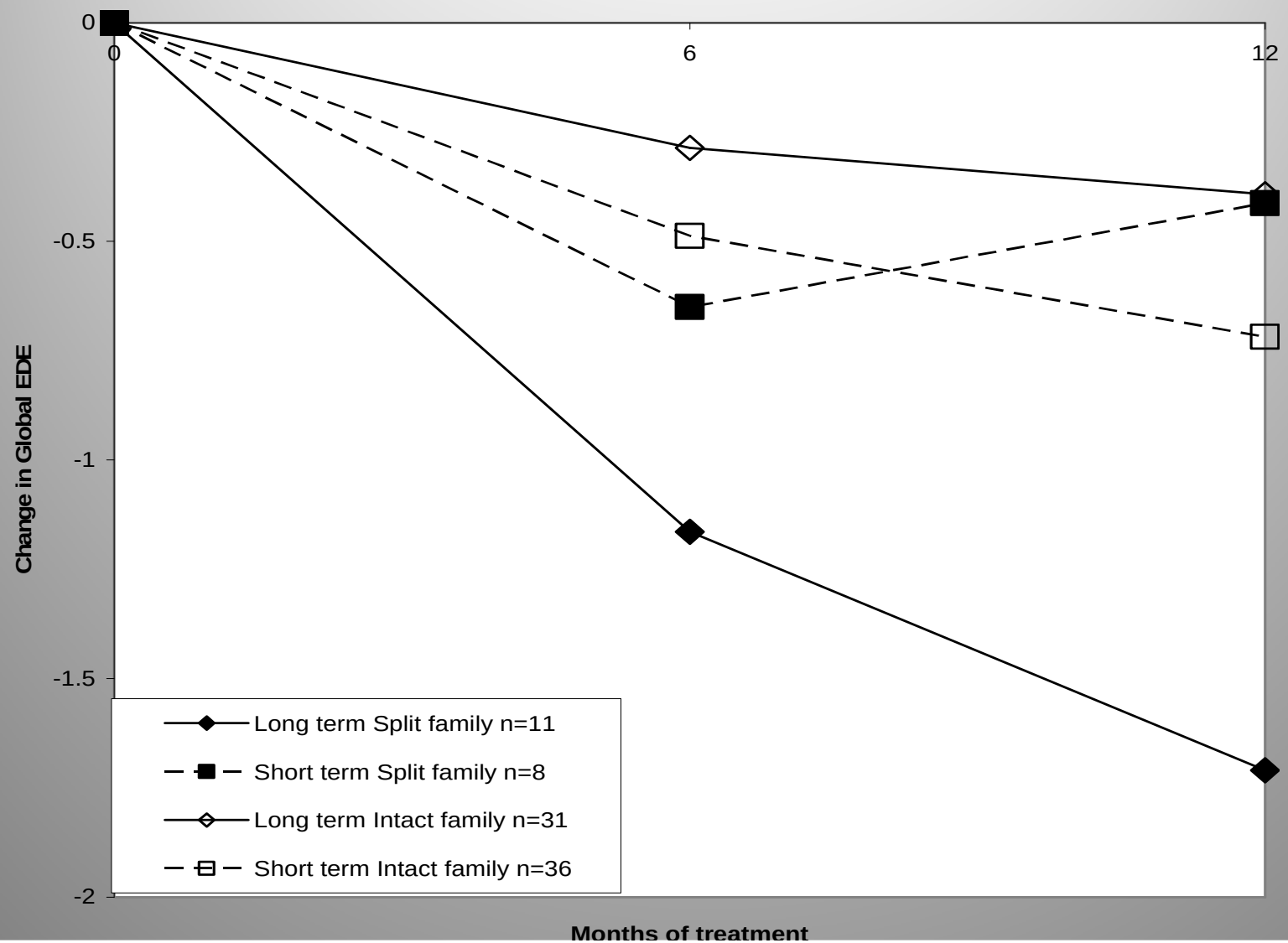
Lock et al. (2005)

Moderators of Outcome

Moderators of Treatment Outcome



Moderators of Treatment Outcome



Family Criticism

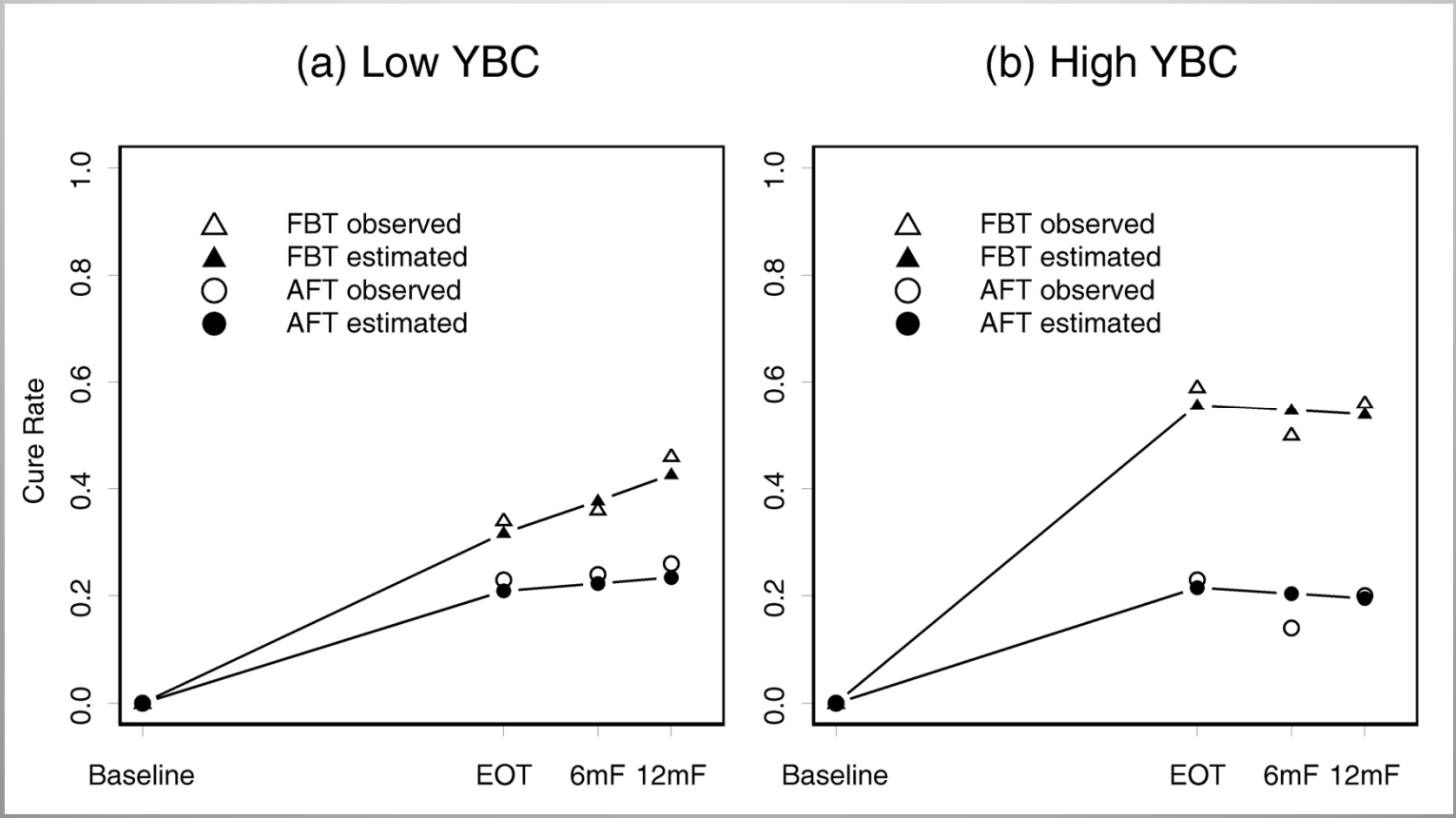
- Separated vs Conjoined FBT compared in two studies controlling for family criticism
  - No differences overall in outcomes (most did well)
  - Family criticism moderated outcome; those with higher levels of criticism did better with separated FBT in both studies
  - 2 year (Le Grange) and 5 year (Eisler) follow-up showed similar pattern

  (Le Grange 1992; Eisler et al 2000)

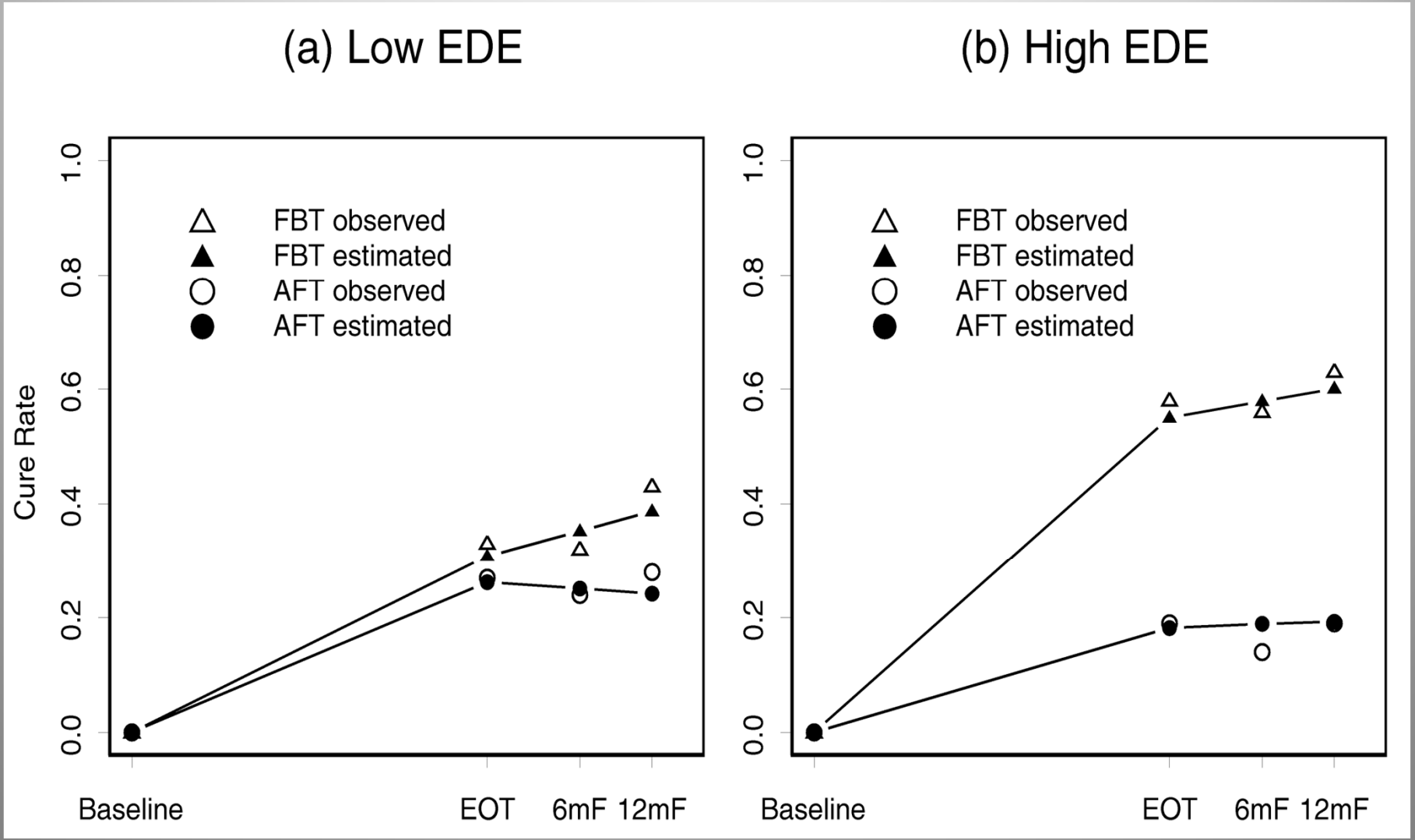
Moderators of Remission

- Patients with higher EDE scores did better in FBT
- Patients with higher YBC-ED scores did better in FBT
- Patients with binge purge subtype did better in FBT

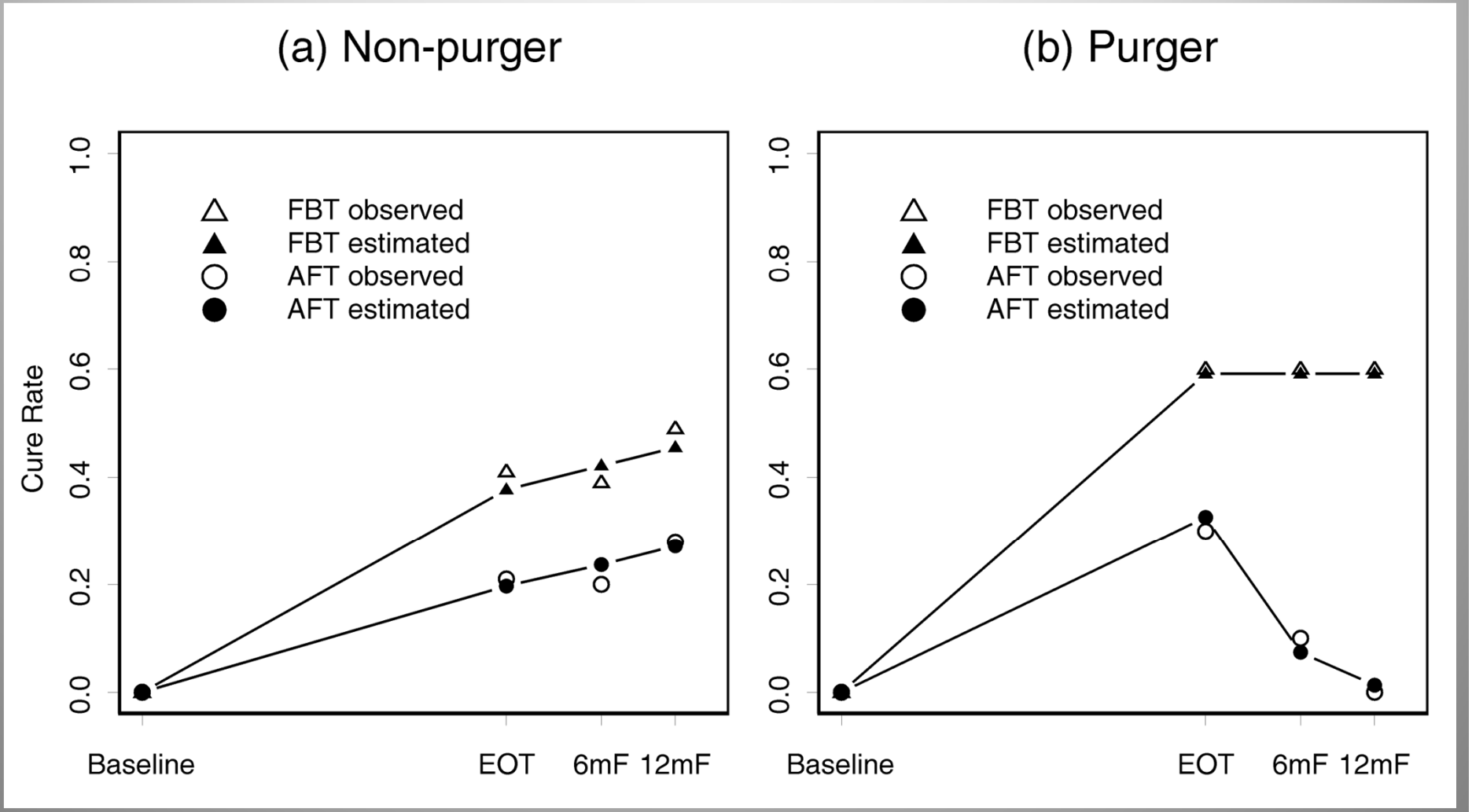
YBC-ED


(a) Low YBC
(b) High YBC
Cure Rate
0.0
0.2
0.4
0.6
0.8
1.0
FBT observed
FBT estimated
AFT observed
AFT estimated
Baseline
EOT
6mF
12mF

EDE Score

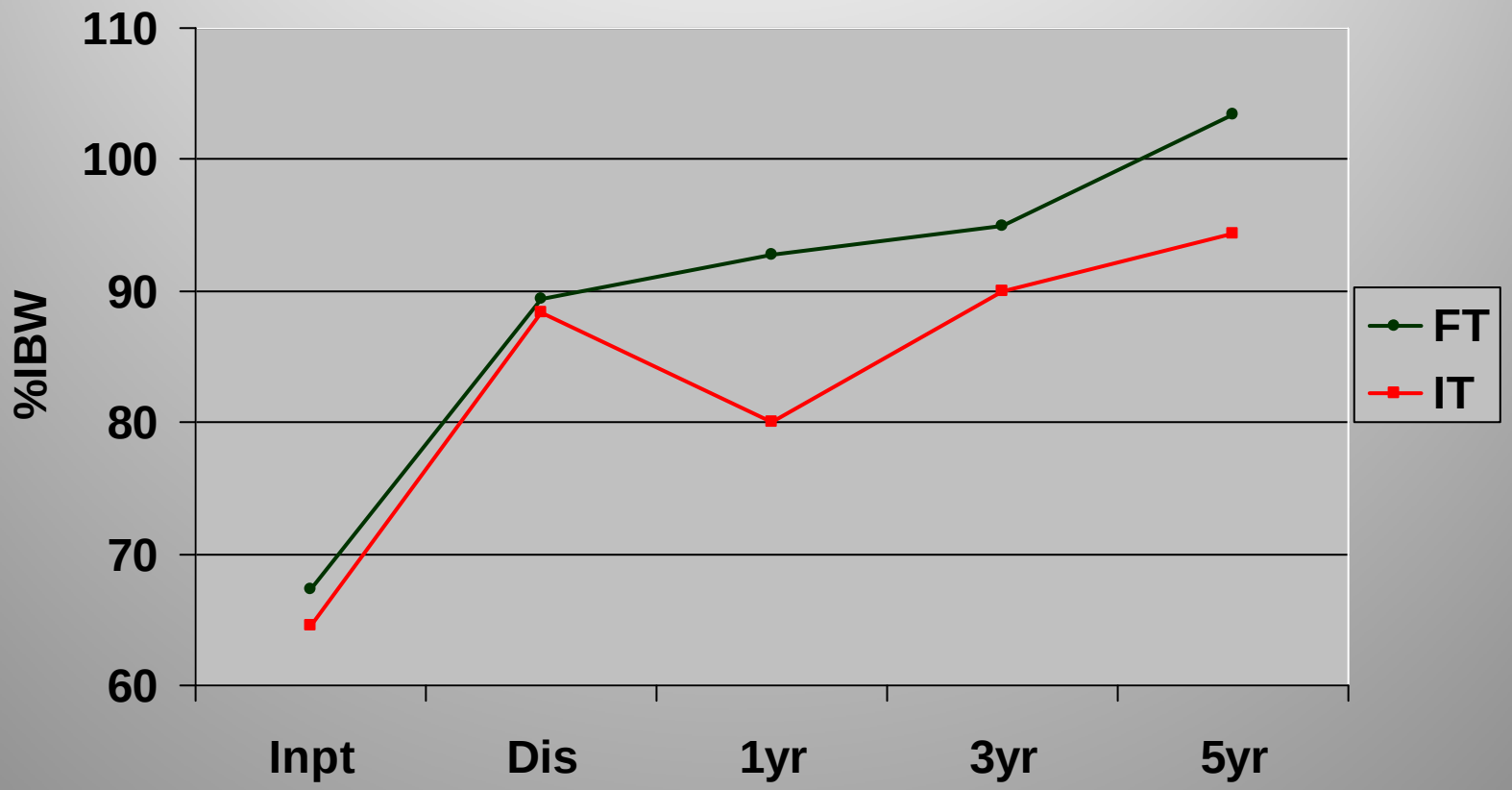

(a) Low EDE
(b) High EDE
Cure Rate
0.0
0.2
0.4
0.6
0.8
1.0
FBT observed
FBT estimated
AFT observed
AFT estimated
Baseline
EOT
6mF
12mF

Binge-Purge sub-type



How do patients treated with FBT do over time?

Weight Chart for Patients in Subgroup 1 (Five Year Follow-up)

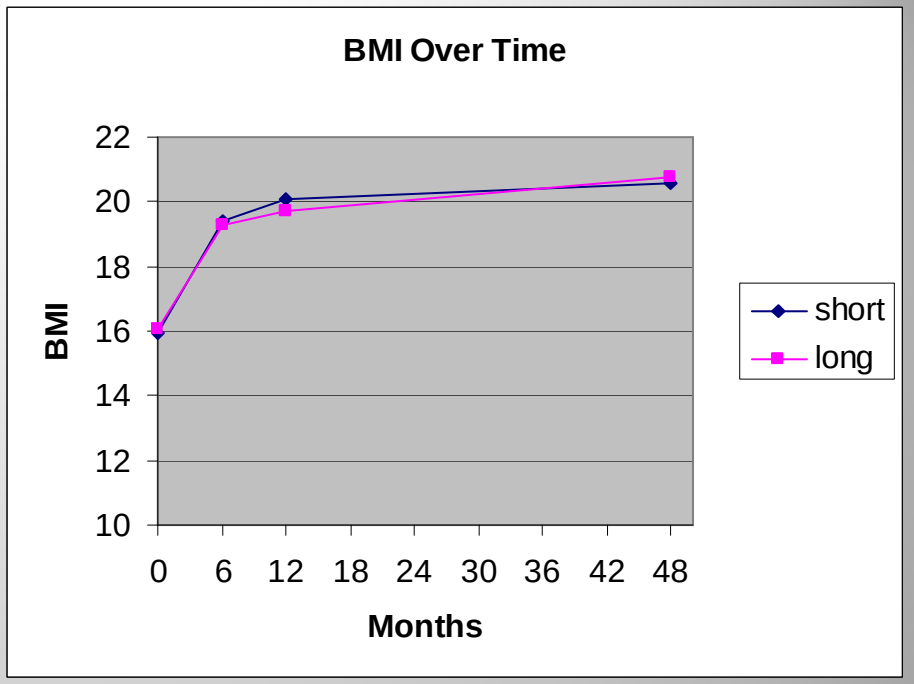


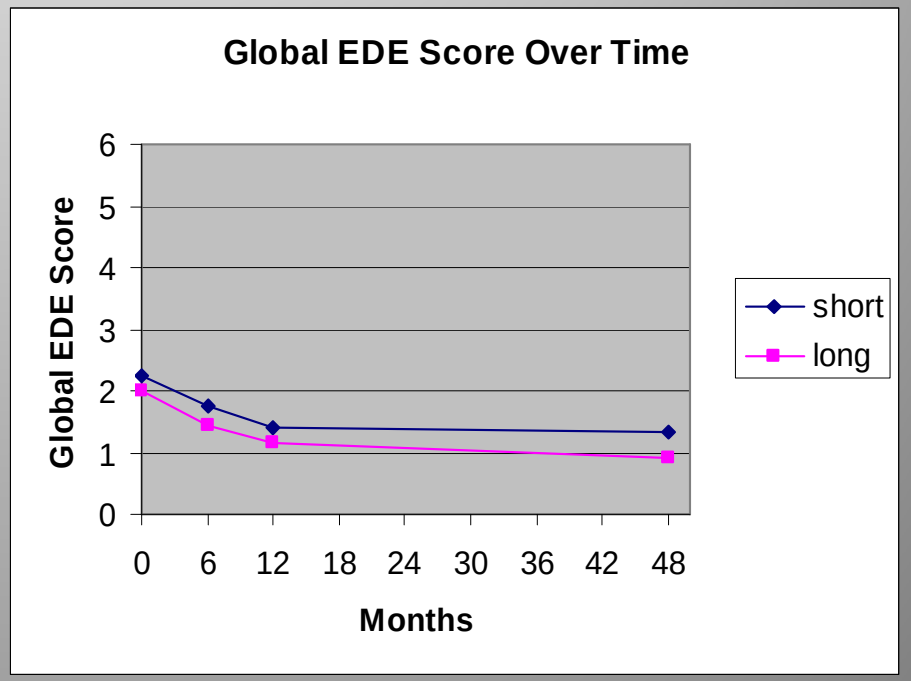
Eisler I, Dare C, Russell G, Szmukler G, Le Grange D, & Dodge E. (1997)

Stanford Dosage Study

48 Month Follow-up

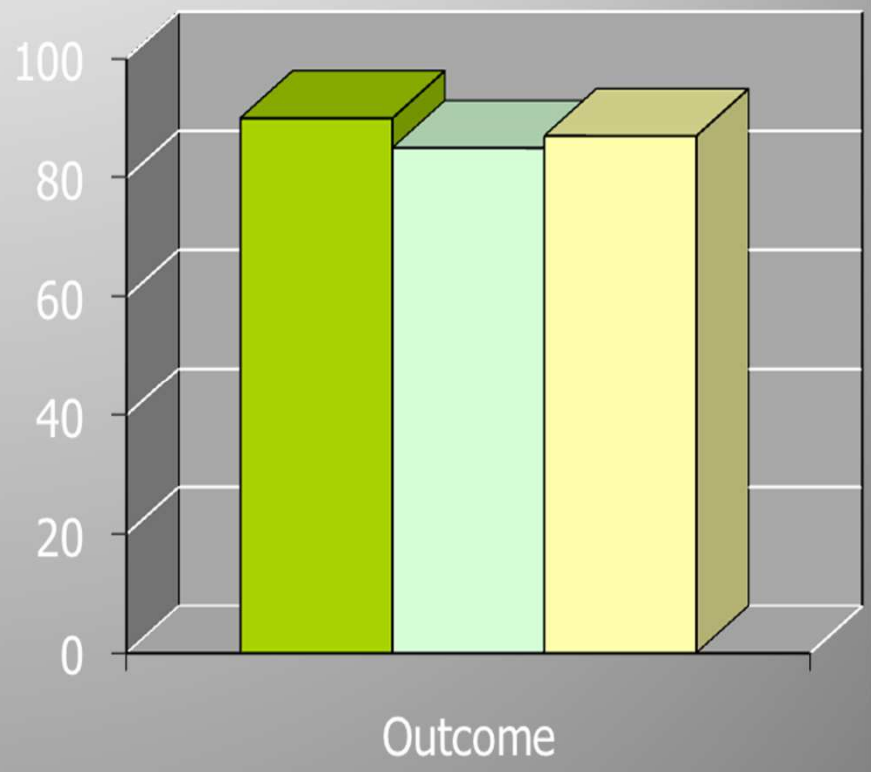
Lock et al. (2006)





Long-term Follow-up in FBT

- Eisler et al. (1997)
- Lock et al. (2006)
- Eisler et al. (2007)



Patient and Family Satisfaction

Patient Satisfaction

- Therapeutic rapport on 5-point scale (mother = 4.71; father = 4.19; adolescent = 4.18)
- Success of treatment on 5-point scale (mother = 4.40; father = 4.10; adolescent = 3.97)

Krautter T, Lock J (2004), Journal of Family Therapy 26(1):66-82

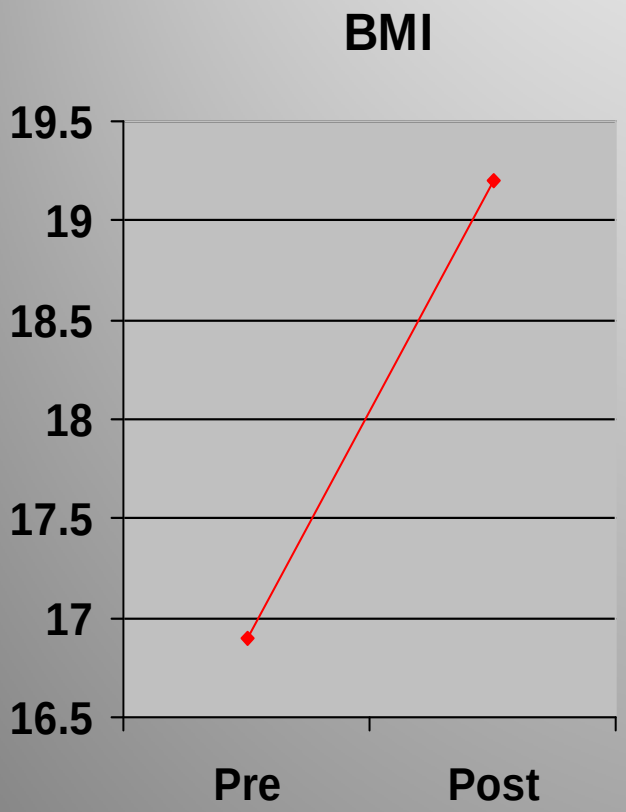
Therapeutic Alliance

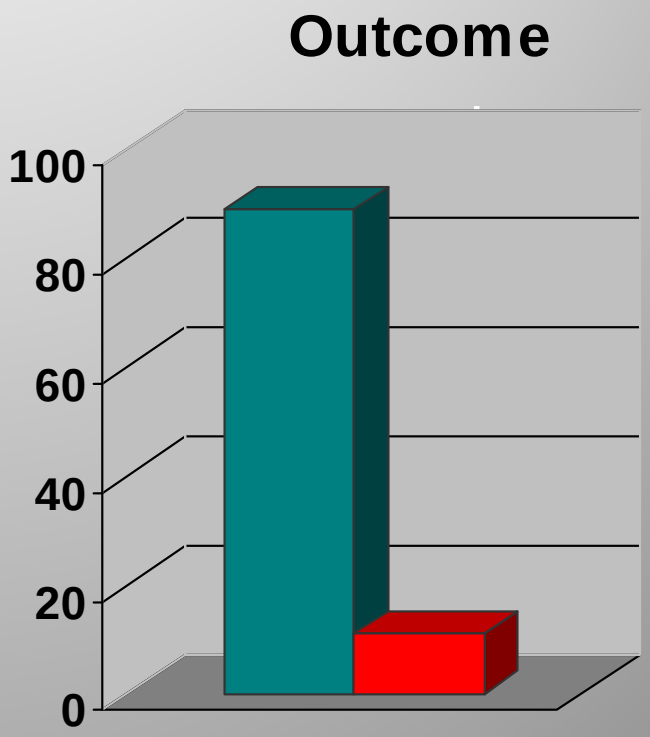
- Therapeutic alliances were strong for both adolescents and parents were strong throughout treatment
- Early patient therapeutic alliance (bond) predicted early weight gain
- Early parental therapeutic alliance predicted staying in treatment
- Early weight gain predicted end of treatment EDE scores and therapeutic alliance
- Late parental alliance predicted overall weight gain

Pereira T et al. (2006), Int J Eat Disord 39(8):677-684

Dissemination Studies

Chicago Case Series





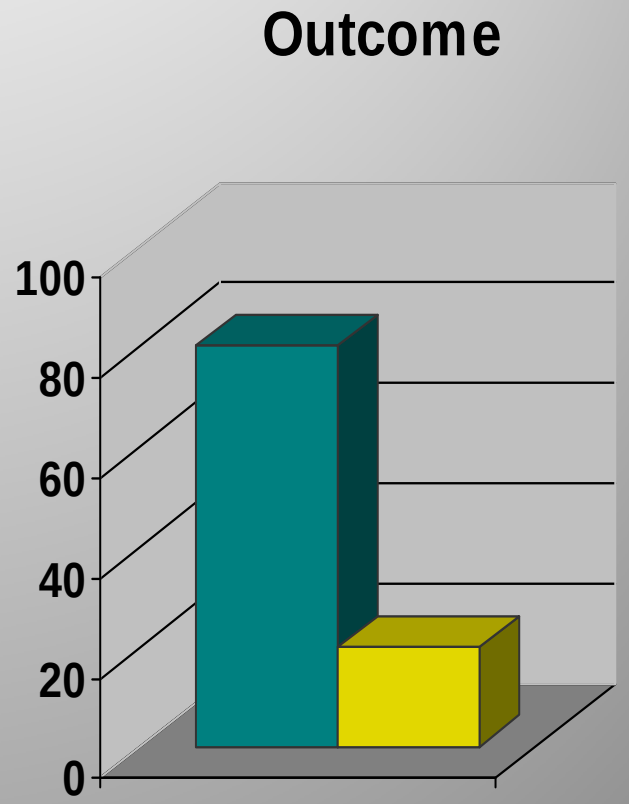
* t(44)-8.153, p<.001

Le Grange et al. (2005)

Columbia Open Trial

Tx Response

- 75% completed full course of treatment
- 67% menstruating by end of treatment
- %IBW changed from 81.9 to 94.1 (p=.000)
- Sign changes in EDE Res, EC, binge/purge, and BDI



Loeb et al. (2007)

Canadian Study (Couturier et al, 2010)

- 14 Adolescents Treated Using Manual:

Effectiveness

  - Weight – 86% were above 85% at final session, 57% were above 95%
  - Psychological symptoms – 54% were within 2 sd of normal on the EDE
  - Menses – 8/9 regained menstrual function,
  - Two continued to have BP behaviours
- Fidelity – “Considerable – 5/7 or more” 72% of the time in phase I, 47% in phase II, and 54% in phase III
- Acceptability - high

Brazilian Study (Turkiewicz, et al, 2010)

11 adolescents with AN offered FBT

- 9 (82%) agreed (12-17 years, mean 14.64)
- 78% completed treatment (11 sessions over 6 months)
- Mean BMI 16.39 baseline, 19.0 at end of treatment; 86% reached target weight at EOT
- 6 month follow-up mean BMI 20.8; no patients met criteria for an eating disorder

Status of Current Knowledge

- FBT for children and adolescent AN patients with short duration illness is effective
- FBT is more effective than psychodynamic developmentally oriented individual therapy
- Most patients respond favorably after relatively few outpatient treatment session
- The beneficial effects of FBT are sustained at 4-5 year follow-up
- Pilot studies suggest that FBT can be disseminated

Arthur Schopenhauer once said:

"All truth passes through three stages: First, it is ridiculed, second it is violently opposed, and third, it is accepted as self-evident."

What we don't know: research directions

- FBT vs. Strategic Family Therapy (NIH)
- FBT post medical stabilization vs. long term hospital for adolescent AN (Westmead Children's Hospital, Sydney, Australia)
- FBT for sub-syndromal AN (Mt. Sinai Hospital)(NIH)
- Multi-family Group FBT vs. FBT (Maudsley Hospital, London)
- FBT vs. Family FBT (Duke University) (NIH)
- Prevention of AN (pilot) using FBT, Germany (Jacobi)