

Child and Adolescent Depression

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Disclosure

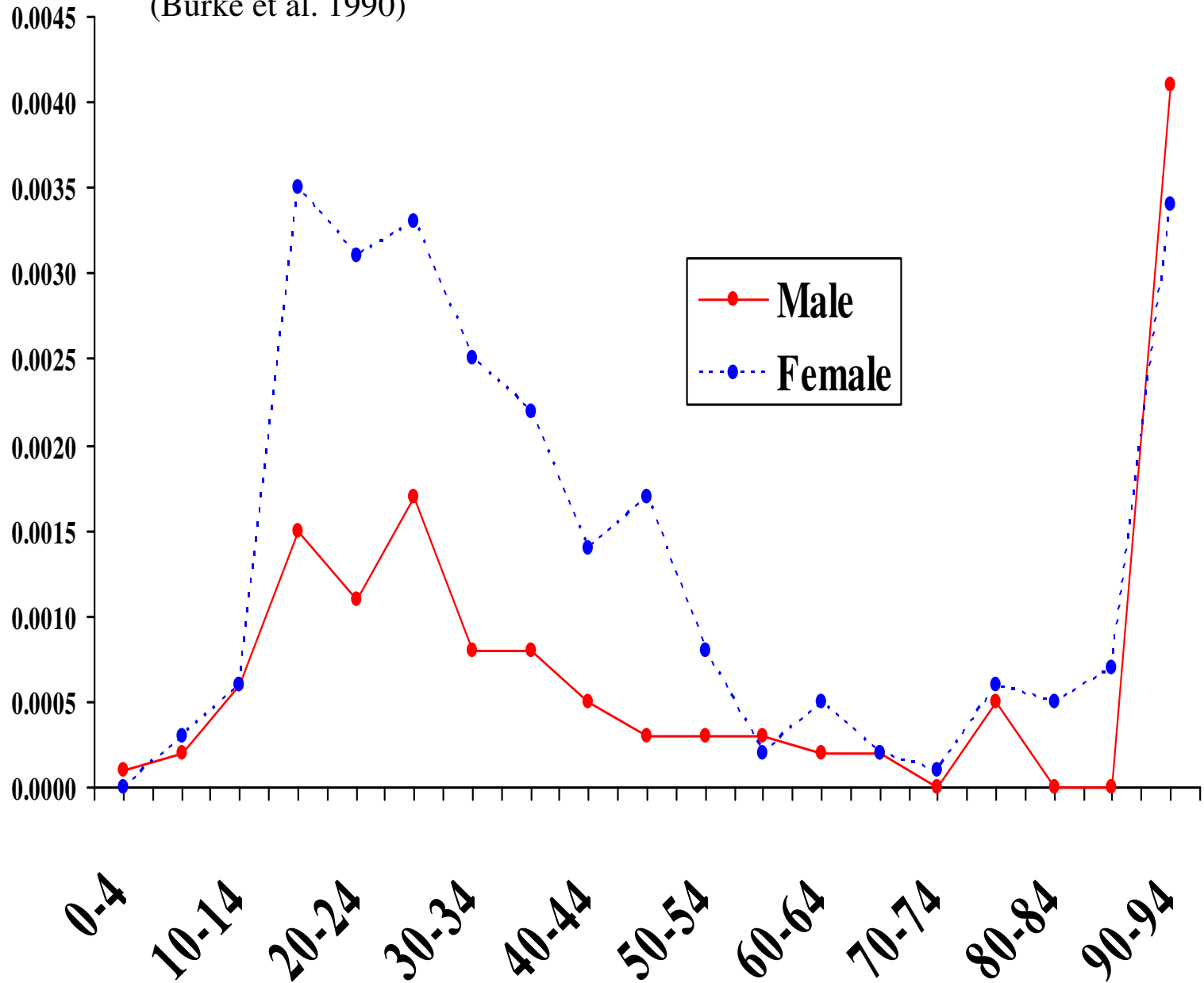
- I have no financial relationships with pharmaceutical companies
- I work at the NIMH/NIH, but the views here presented should not be construed as official statements of the NIMH/NIH

Major Depression: Prevalence

- Prepubertal children: 2%
 - Same rate in boys as in girls
- Adolescents: 4-6%
 - Twice as common in girls
- By age 18, 20% will have experienced at least one episode (cumulative incidence)

Age at Onset of Major Depression: Hazard Rate

(Burke et al. 1990)



Age of onset of mood disorders

(Kessler et al., 2005)

MDD In 25% of cases, onset by age 19
 In 10% of cases, onset by age 14
 In 5% of cases, onset by age 12

Bipolar In 25% of cases, onset by age 17
 In 10% of cases, onset by age 13
 In 5% of cases, onset by age 11

Depression: course of illness

- Episodic
- Protracted course (7-9 months)
- Tends to remit
- 70% recurrence within five years
- Increases risk for substance abuse, suicide attempts, and suicide

Most common reasons for hospitalization

Age 10-14 yr:

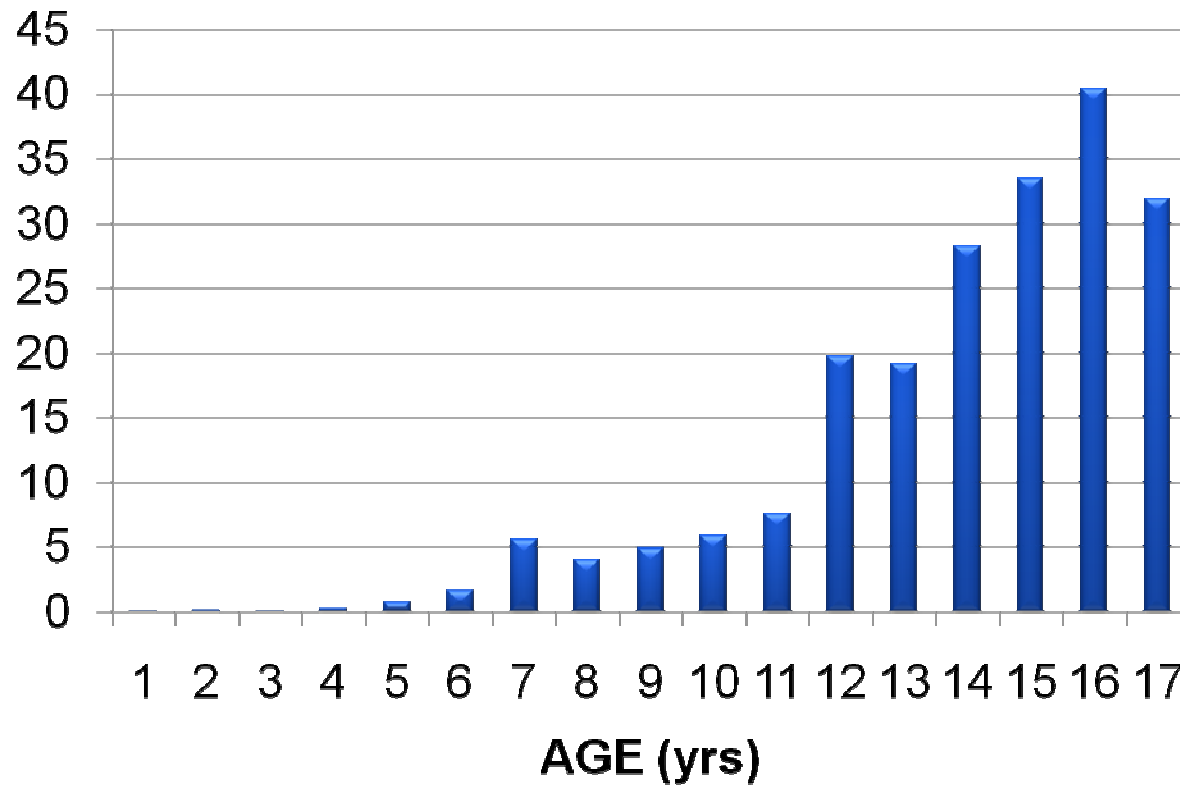
1. Appendicitis
2. **Mood disorders**
3. Asthma

Age 15-17 yr:

1. **Mood disorders**
2. Obstetrics
3. Traumas

Hospitalizations with primary dx of mood disorder by age group

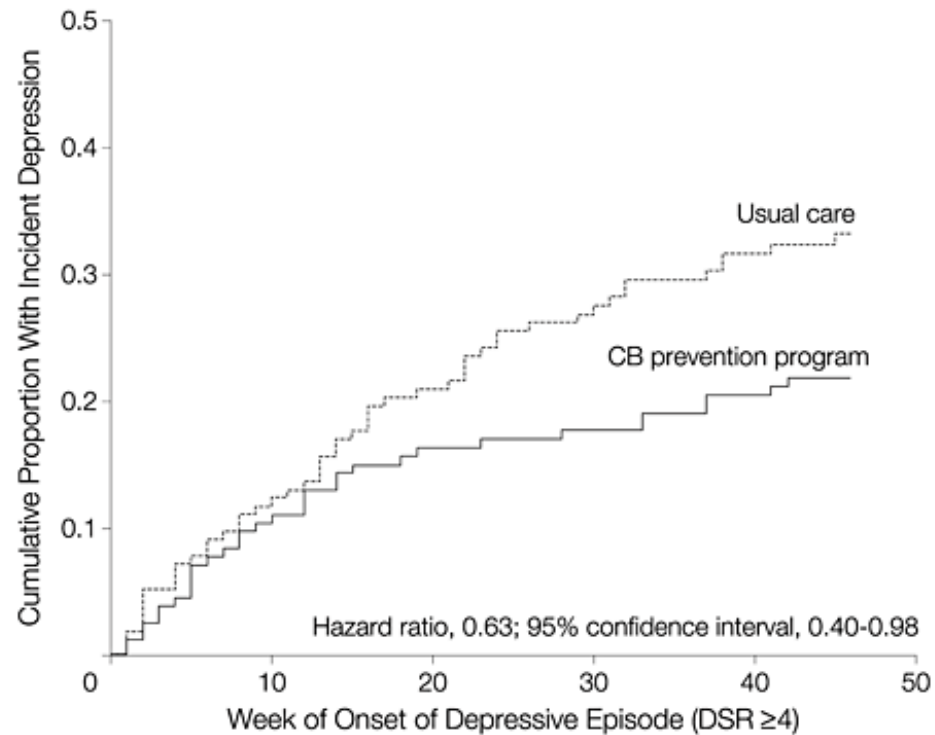
(per 10,000 U.S. population - 2006)



Effective treatments exist

- Psychotherapy:
 - cognitive behavioral therapy (CBT)
 - Interpersonal therapy (IPT)
- Pharmacotherapy:
 - SSRIs
 - fluoxetine
 - escitalopram

Adolescent depression can be prevented



No. at risk	0	10	20	30	40
Usual care	157	134	120	109	93
CB prevention program	159	137	123	121	112

Garber, J. et al. JAMA 2009;301:2215-2224.

Treating depressed youths: 12 years of progress.....

- 1997: efficacy of fluoxetine and of CBT
- 2001: fluoxetine efficacy confirmed
- 2004: TADS primary results
- 2008: TORDIA primary results
- 2009 TADS long-term outcomes

.... and controversy:

- Do antidepressants trigger suicidal behavior in children and adolescents?
- Are antidepressants effective in treating depressed children and adolescents?

FDA Meta-analysis of Suicidality in Pediatric Trials of Antidepressants (2004)

Pooled data from 26 clinical trials of 9 antidepressants (N=4,400)

- Major Depressive Disorder (MDD) – 16 trials
- Anxiety Disorders – 8 trials
- Attention Deficit Hyperactivity Disorder – 2 trials

(Hammad et al. Arch Gen Psychiatry, 2006)

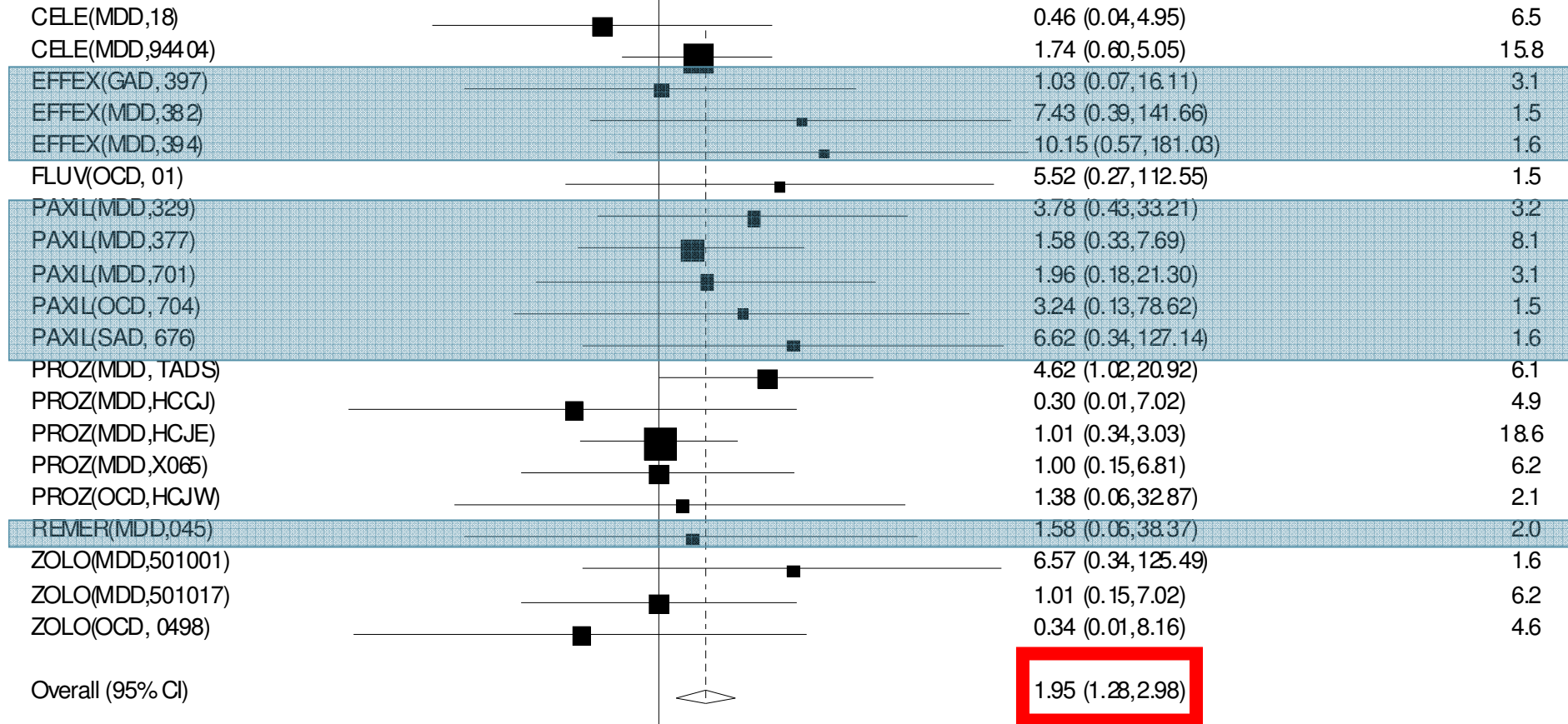


All trials, all indications
(Fixed effect model)

Risk ratio
(95% CI)

% Weight

Study



.01 .1 1 10 100
Risk ratio

Suicidal Behavior or Ideation [codes 1, 2, & 6]

Across all clinical trials (N=4,400 children and adolescents)

No suicide occurred

Rate of “suicidality” (suicidal thinking or behavior):

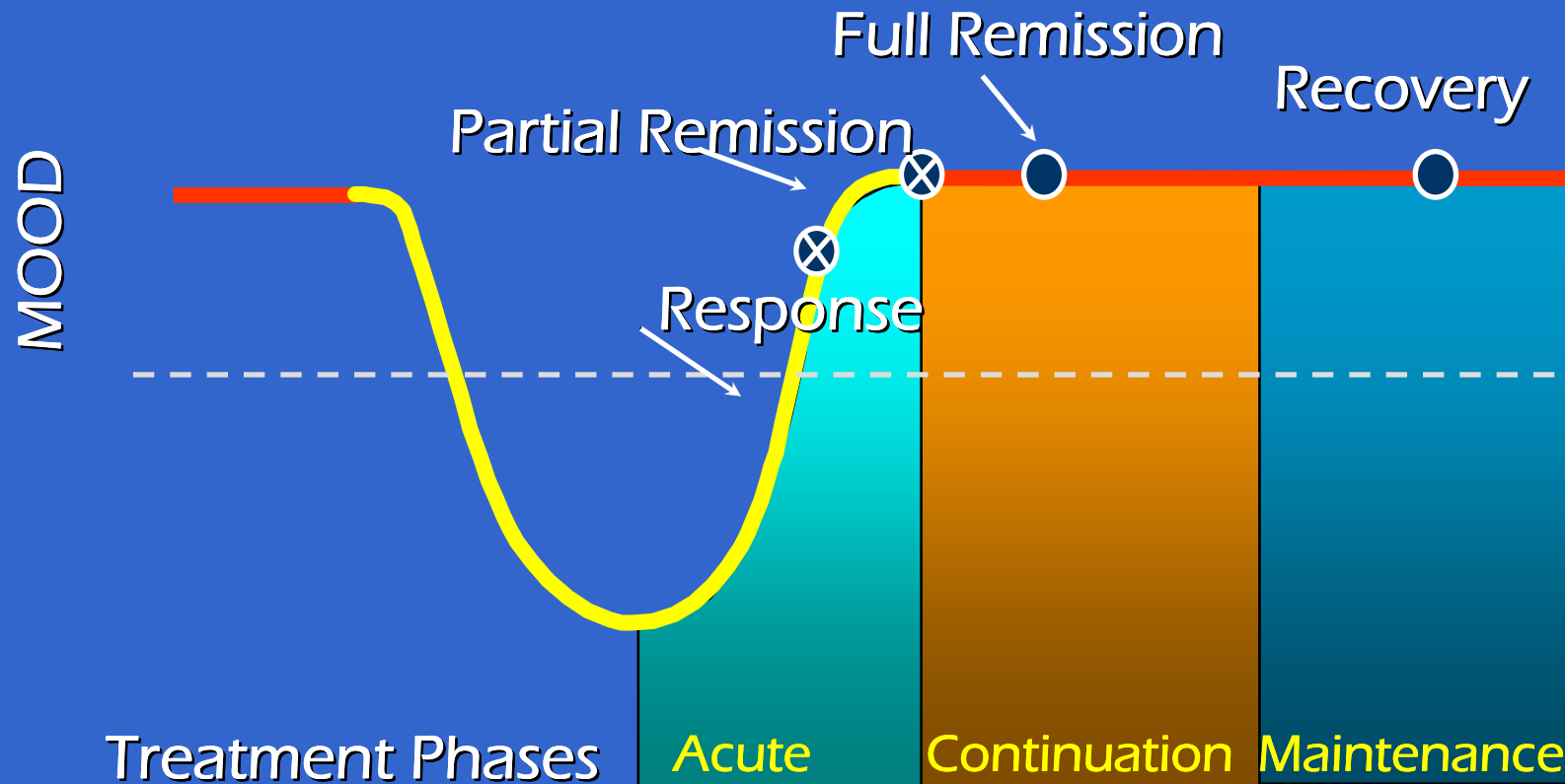
2% on placebo

4% on antidepressant

Antidepressants in children and adolescents

- How effective?
 - Symptomatic improvement
 - Remission
 - Functional recovery
- How safe?
 - Suicidality
 - Suicide

RESPONSE → REMISSION → RECOVERY
[resistance] [relapse] [recurrence]



Efficacy of antidepressants in child/adolescent depression

Meta-analysis of 13 clinical trials:

- Effect size: 0.25 (95% C.I. 0.16-0.34)
- Response rate: 61% (95% C.I. 0.58-63%)
placebo 50% (95% C.I. 47-53)
→ NNT=10

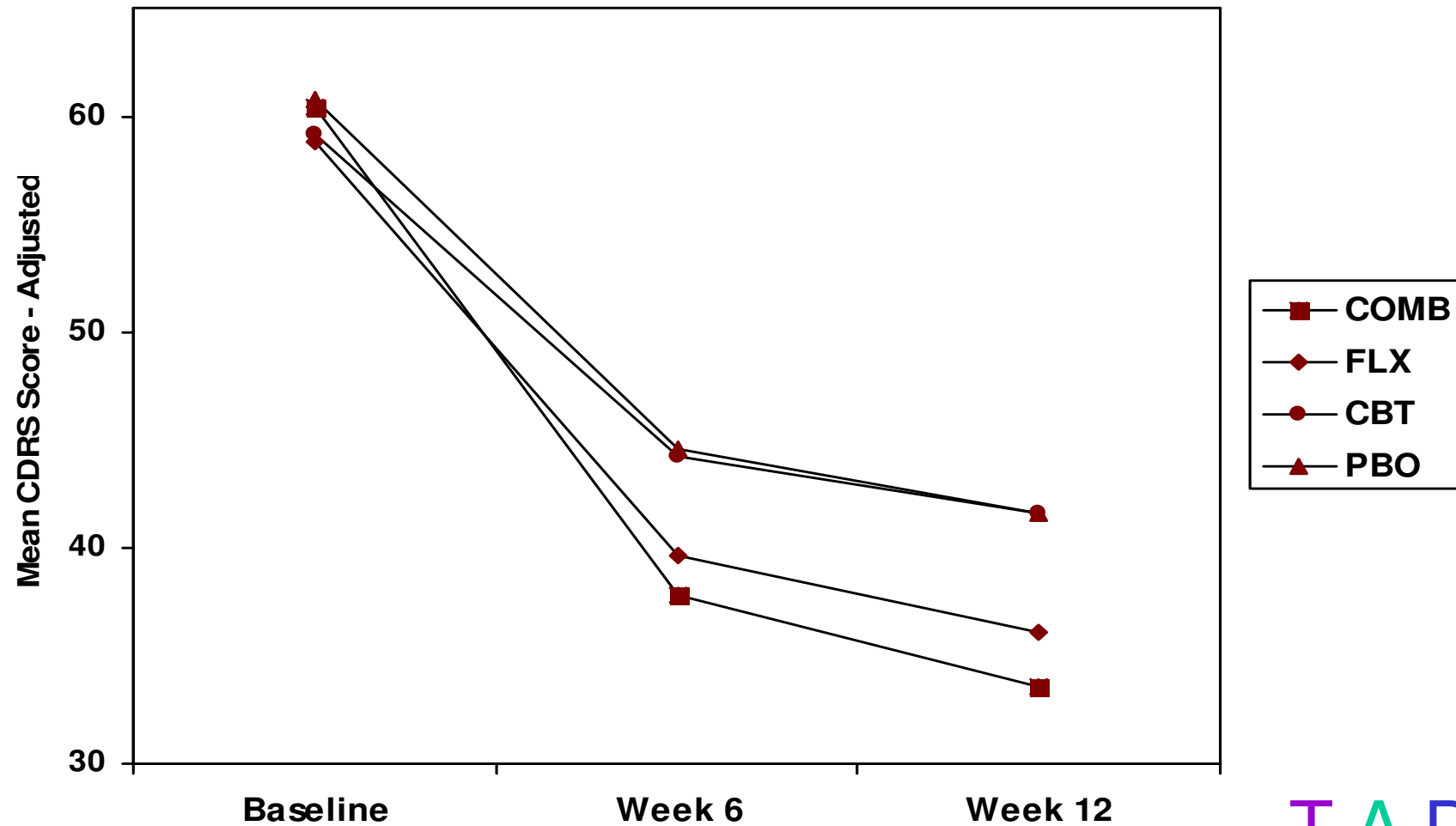
[Bridge et al. 2007]

The Treatment for Adolescents with Depression Study

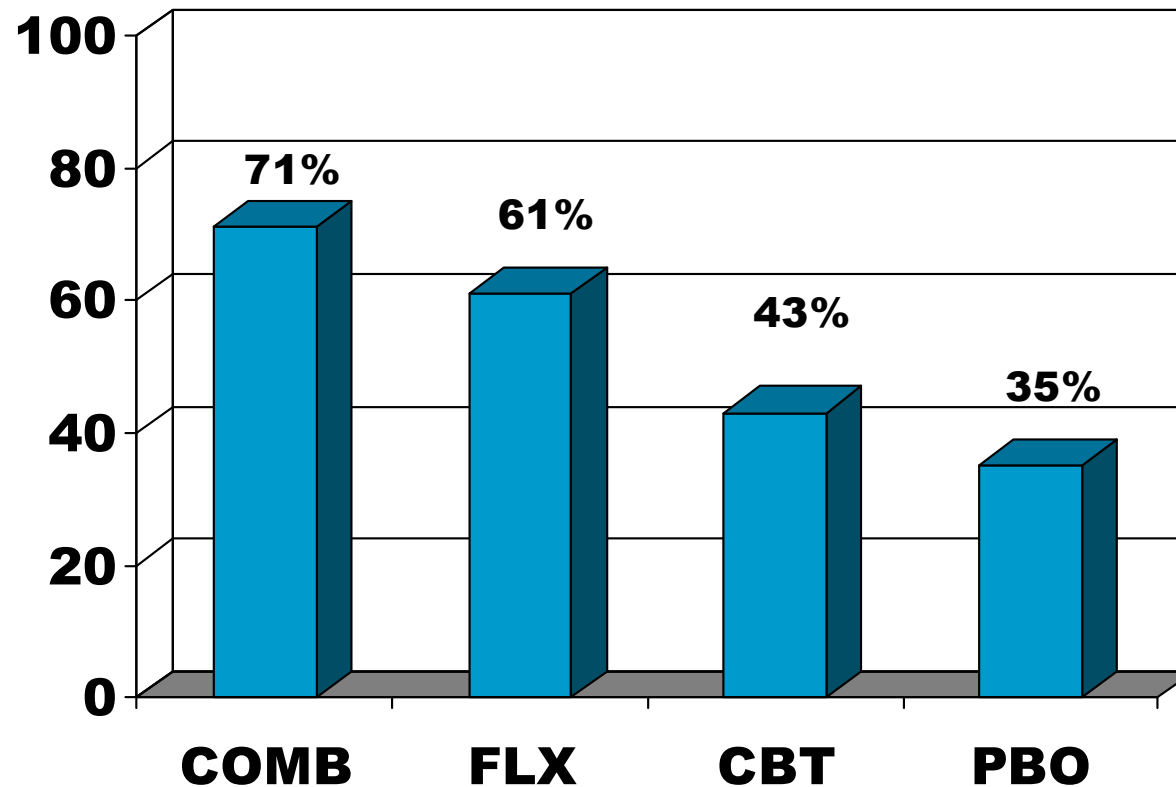


T A D S

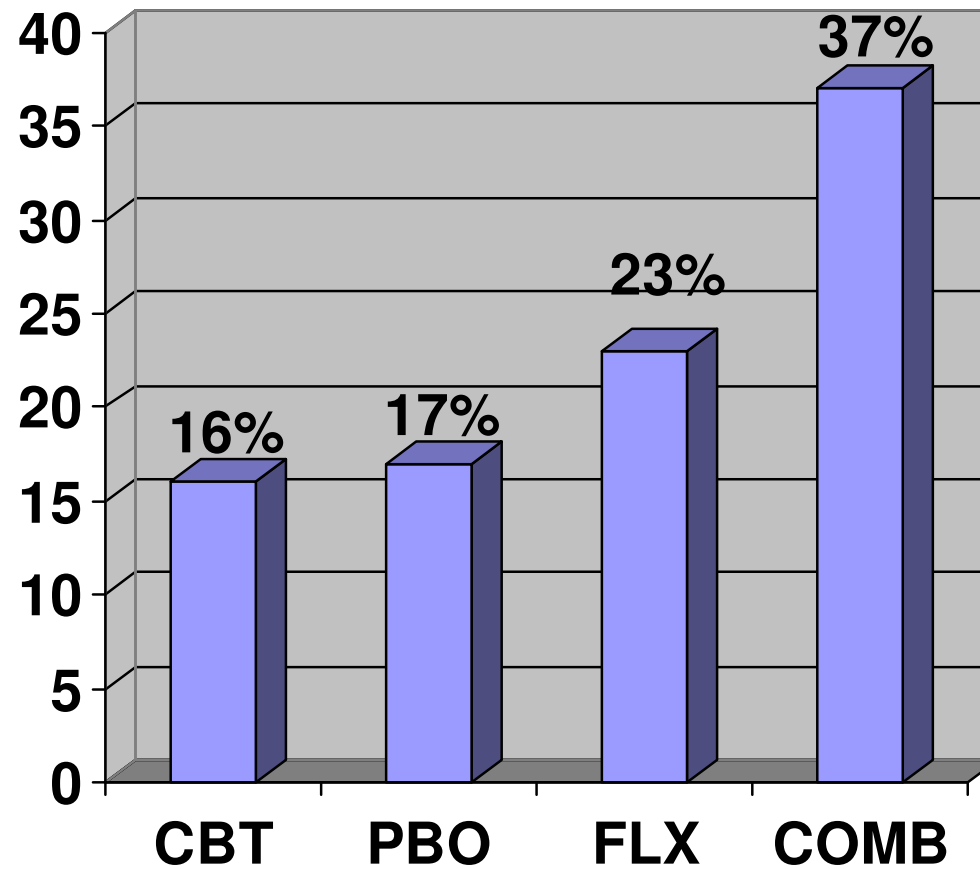
Depression symptoms



Treatment Response: Week 12

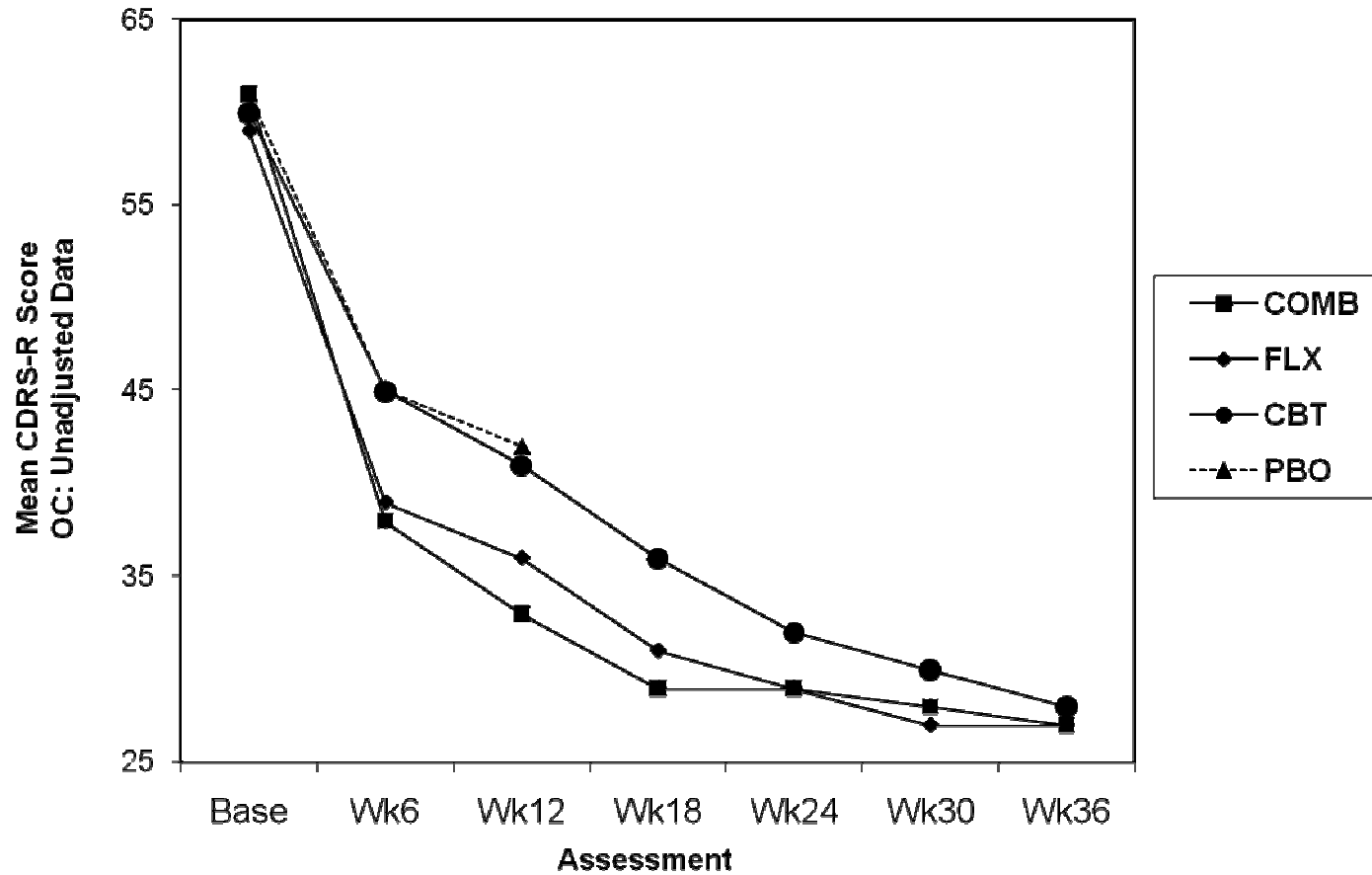


Remission (CDRS \leq 28)

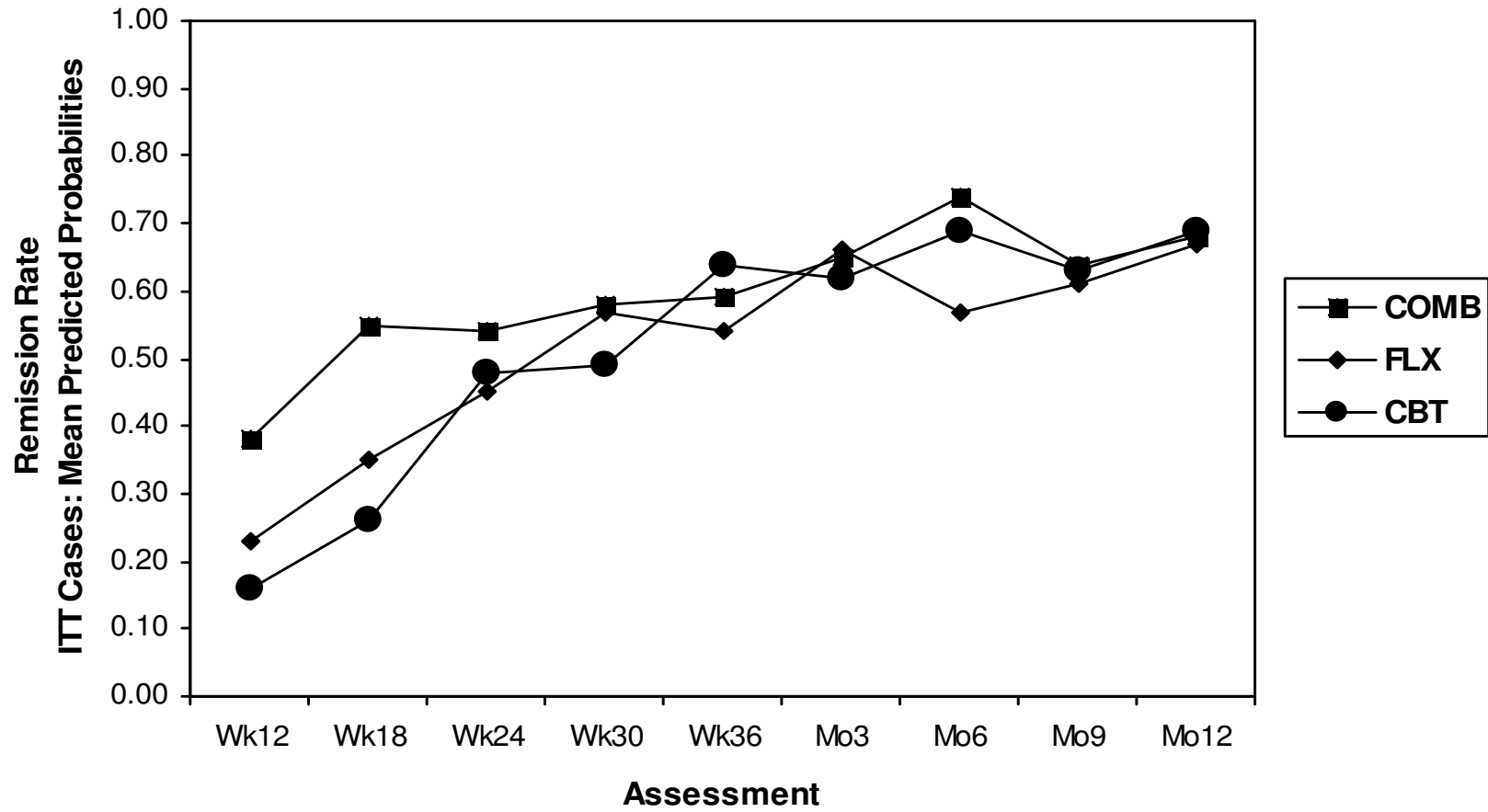


Depression Scores Over 9 Months

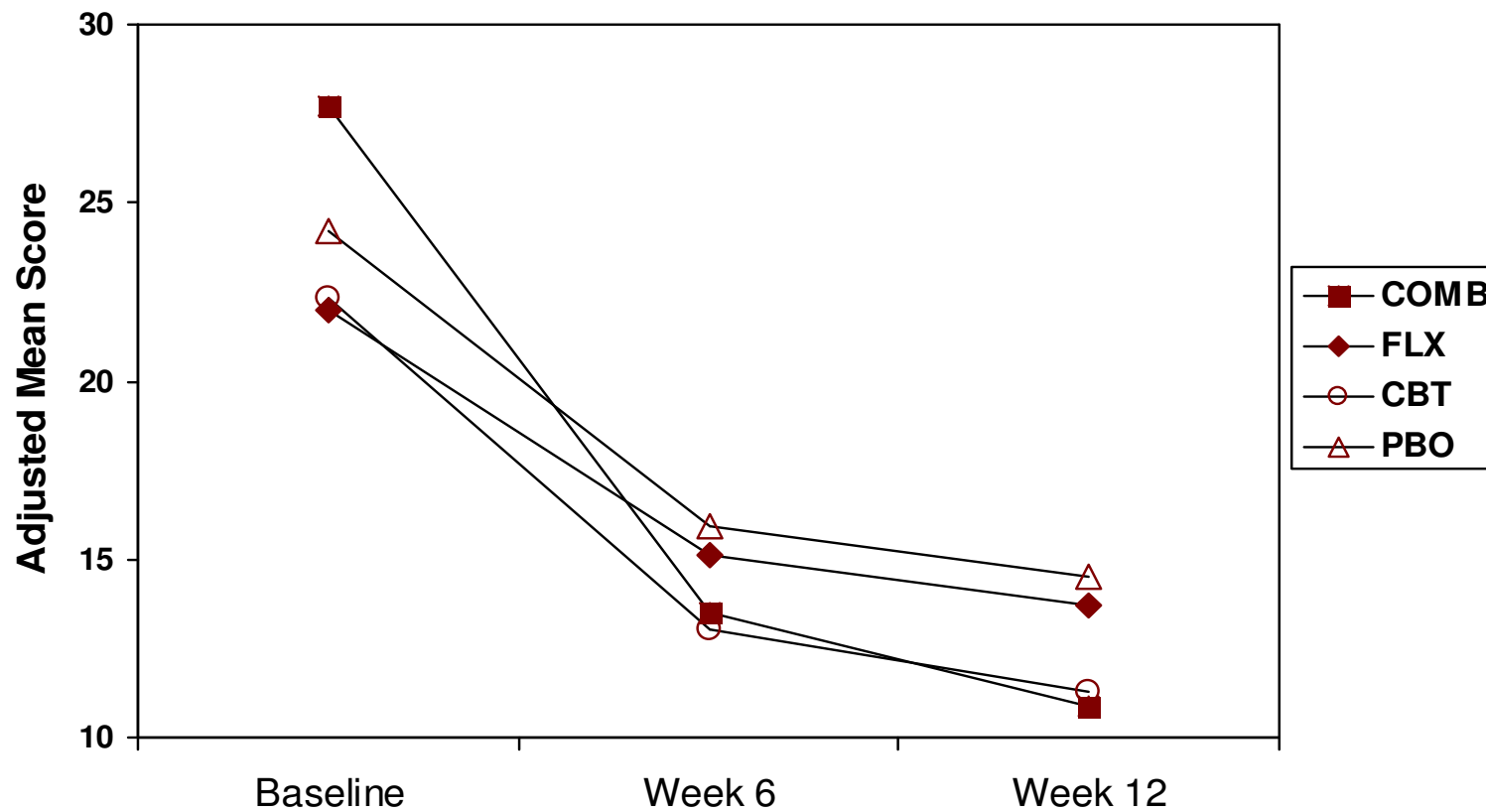
TADS



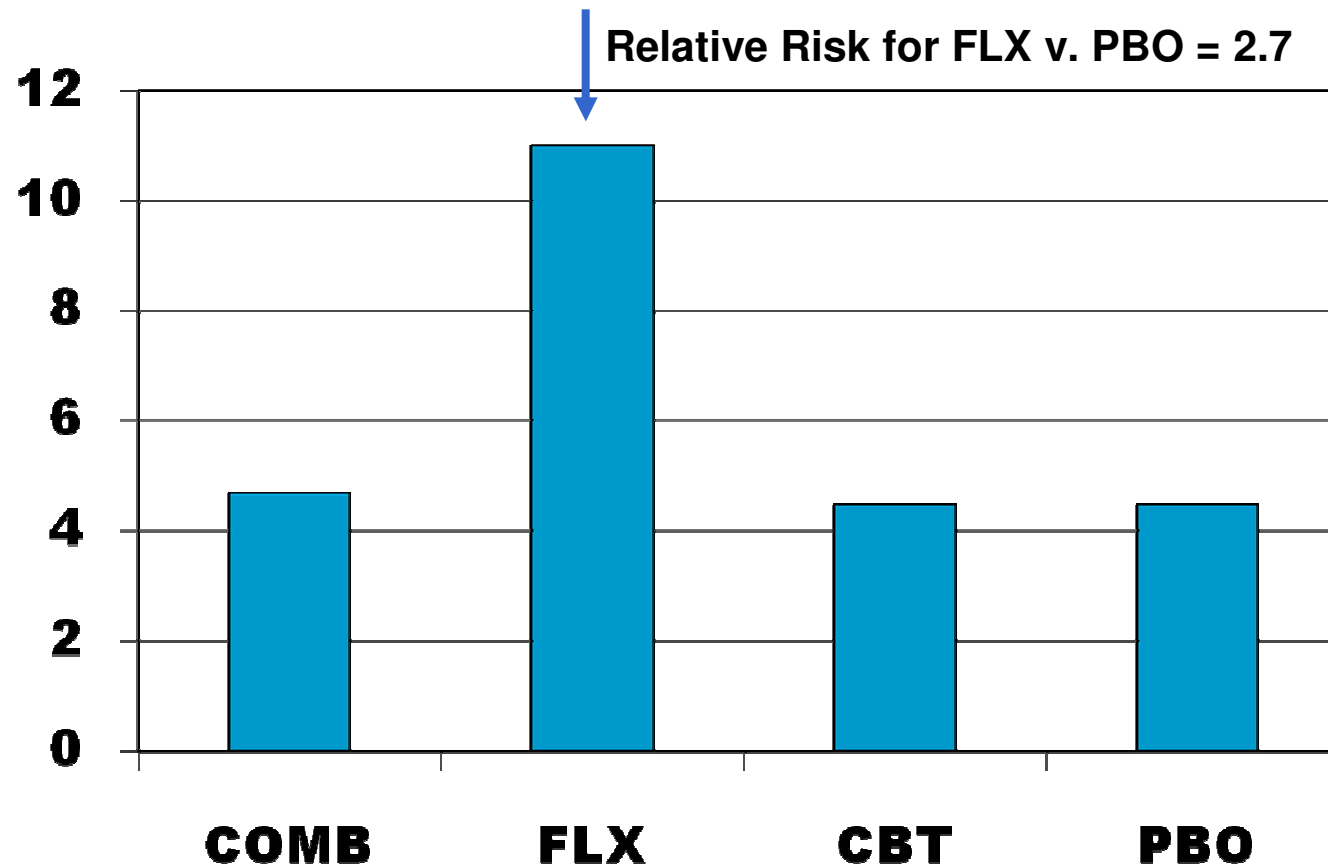
Remission rate



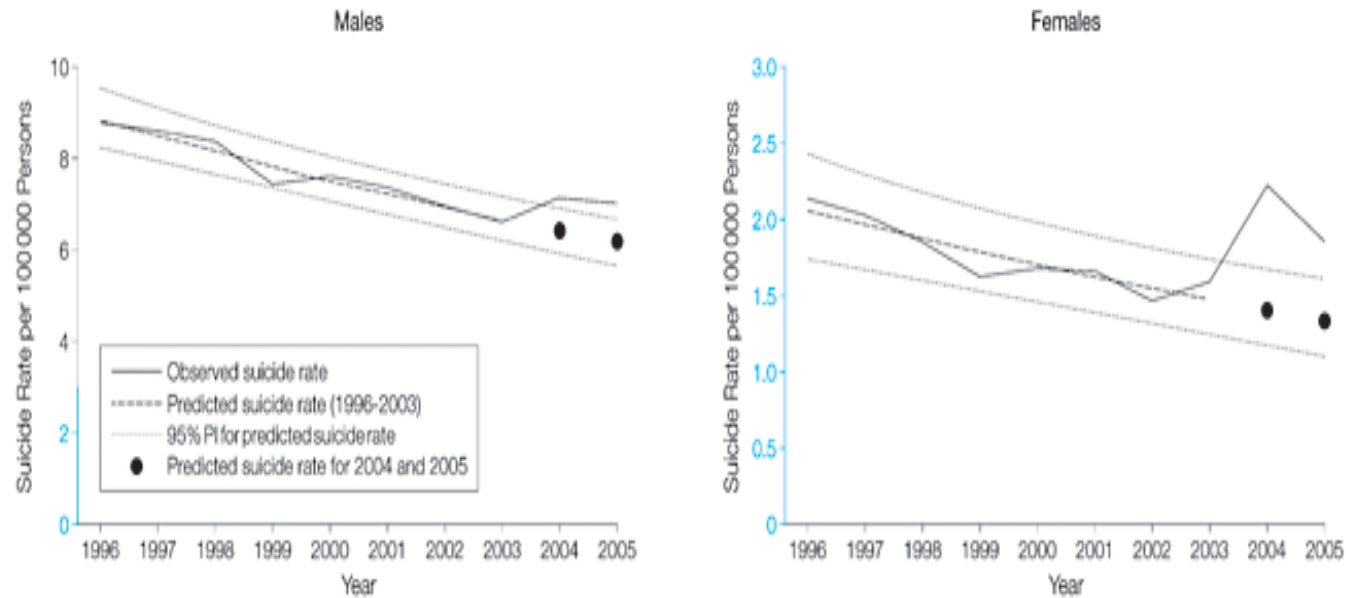
Suicidal Ideation Questionnaire (adjusted means)



TADS: Rate of Suicidality (% of patients with an event)



Annual Suicide Rates for Males and Females Aged 10 to 19 Years in the United States, 1996-2005



Bridge et al. JAMA 2008;300:1025-1026.

SSRIs in children & adolescents

- Better than placebo (and CBT) at speeding-up improvement
 - but with a small effect size, NNT=10
 - Few patients reach remission after 3 months
- 1/3 of pts improves with non-specific tx (placebo)
 - 1/3 does not improve at all

Still unanswered questions

- Does early treatment improve the course of illness/long-term prognosis?
- What is the impact of treatment on suicide risk?
- What is the mechanism of the apparent antidepressant-induced suicidality?
- What subtypes of depression are more responsive to medications vs. psychotherapy?