

# **Bipolar Disorders: Therapeutic Options**

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Revised October 2011<sup>1</sup>

# **Part 2: Treatment of Acute Bipolar Depression**

**Revised October 2011**

# Teaching Points

- 1. Treatment algorithms and guidelines rely on both data and expert opinion.**
- 2. Olanzapine/fluoxetine combination and quetiapine are the only FDA-approved products for acute bipolar depression (as of October 2011 )**
- 3. The role that antidepressants should play or not play in bipolar depression continues to be debated.**

# Outline

**I. Recognition and Diagnosis**

**II. Treatment Approaches**

**A. Lithium**

**B. Antiepileptics**

**C. Atypical Antipsychotics**

**D. Antidepressants**

**E. Innovative Drugs**

**F. Psychotherapies**

# **Pre-Lecture Exam**

## **Question 1**

- 1. Which of the following is more common in bipolar depression than in major depressive disorder?**
  - a. Insomnia**
  - b. Later age of onset**
  - c. Agitation**
  - d. Higher number of episodes**
  - e. Agitation**

## Question 2

2. As October 2011, which of the following is FDA-approved treatment for acute bipolar I and II depression?
- a. Lithium
  - b. Lamotrigine
  - c. Quetiapine
  - d. Bupropion
  - e. Duloxetine

## Question 3

- 3. Which of the following was the most commonly used antidepressant in the STEP 500 survey?**
- a. Bupropion**
  - b. Citalopram**
  - c. Venlafaxine**
  - d. Sertraline**
  - e. Paroxetine**

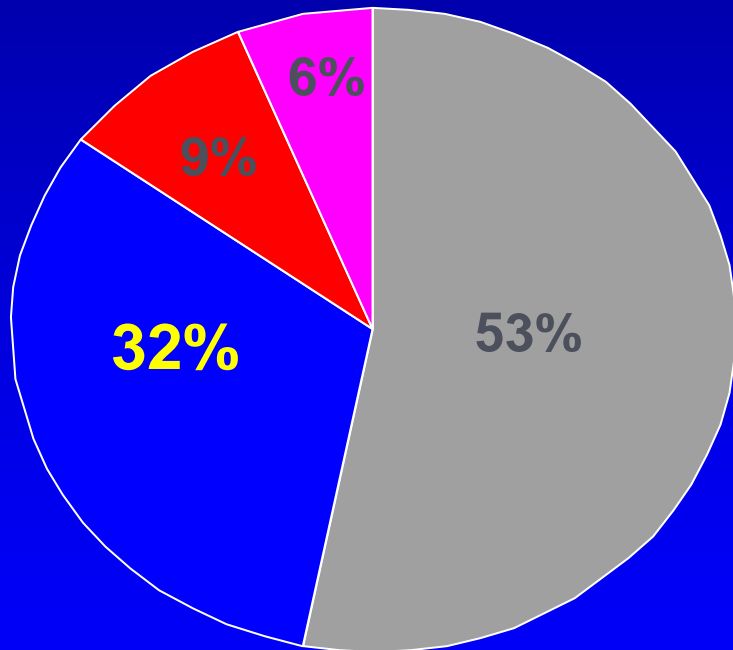
# Question 4

- 4. Which antidepressant appears to have the highest switch rate when used to treat bipolar depression?**
- a. Bupropion**
  - b. Sertraline**
  - c. Venlafaxine**

# Bipolar Depression

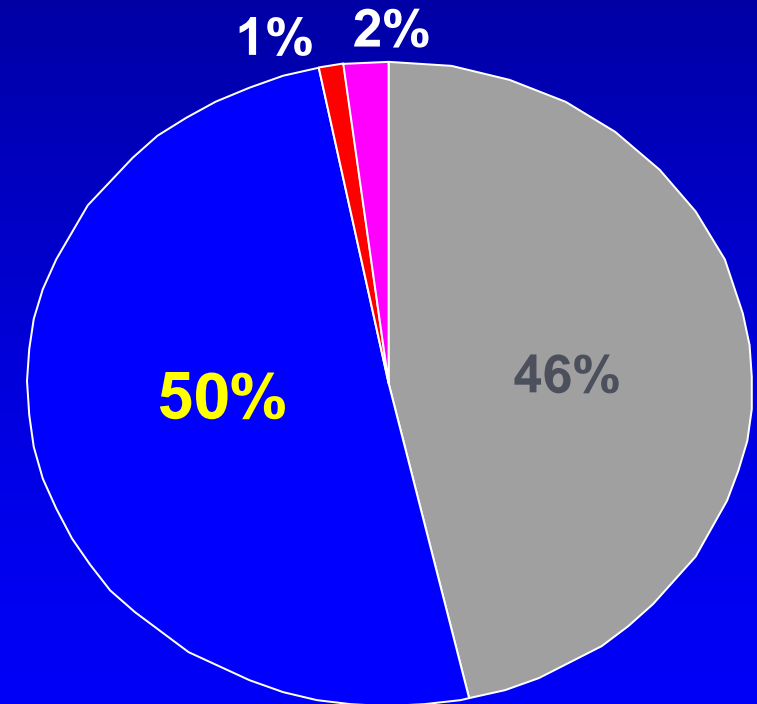
# Bipolar Disorder Symptoms: Chronic and Predominantly Depressive

146 Bipolar I Patients  
followed 12.8 yrs



Judd et al, 2002

86 Bipolar II Patients  
followed 13.4 yrs



Judd et al, 2003

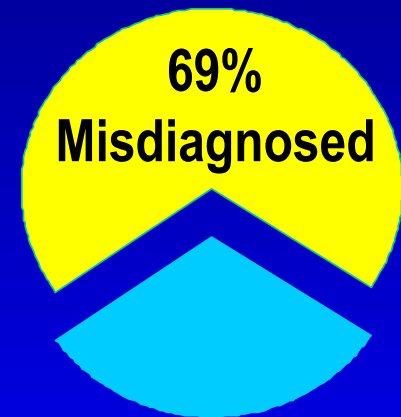
Judd LL, et al. *Arch Gen Psychiatry*. 2002;59:530-537.

Judd LL, et al. *Arch Gen Psychiatry*. 2003;60:261-269.

# Misdiagnosis

## 2000 NDMDA Bipolar Survey

- **Most frequent misdiagnosis:  
unipolar depression**

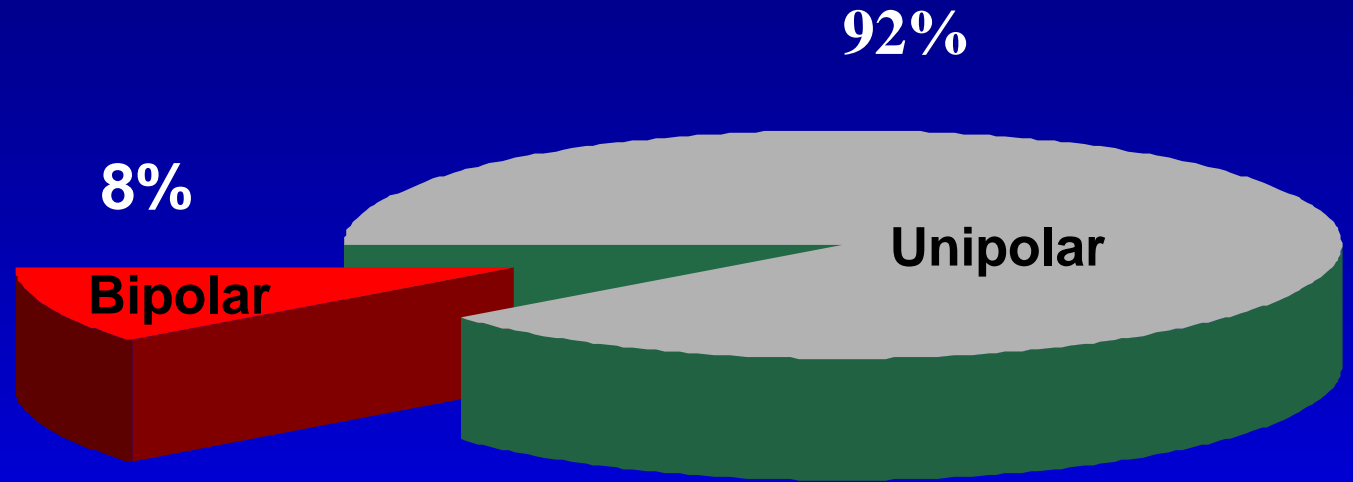


**35% Were Symptomatic for More Than  
10 Years Before Correct Diagnosis**

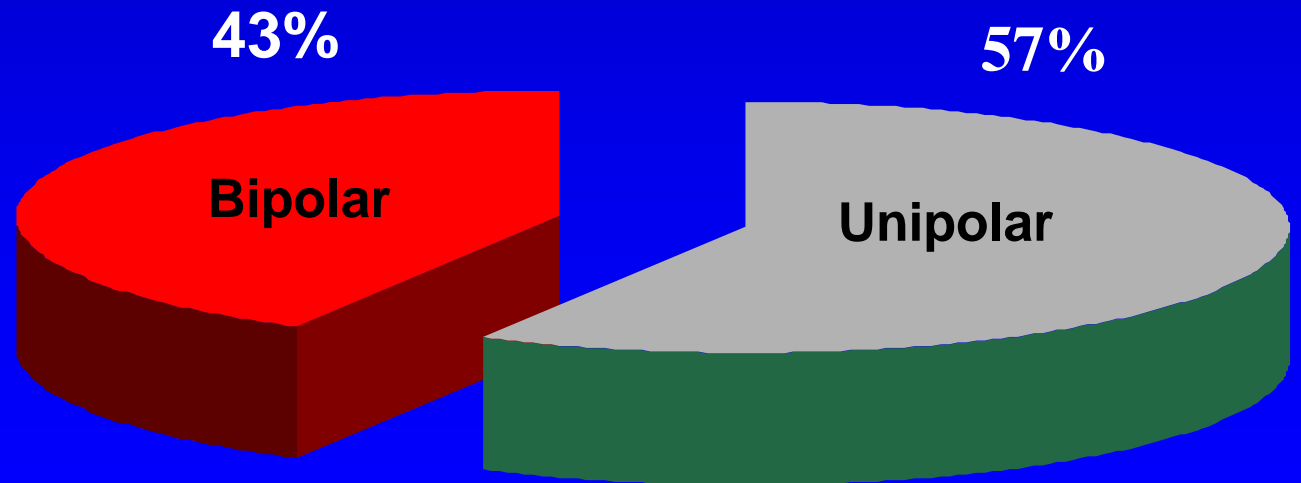
**10+ Years**

# Unipolar or Bipolar Disorder

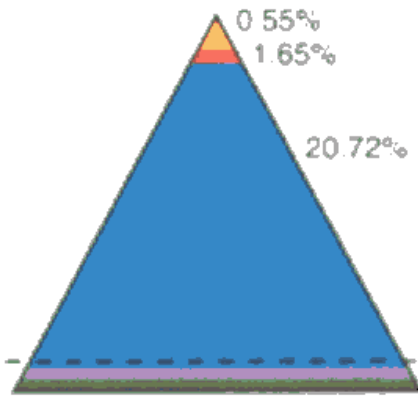
**At Clinic Entry**



**At 30-Yr Follow-up**



DSM-IV



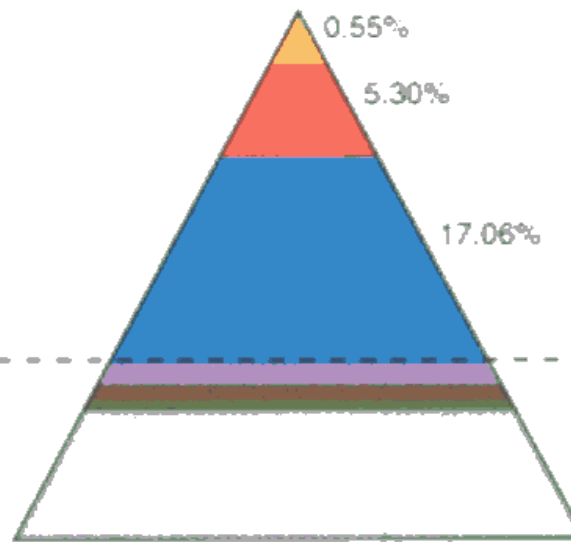
Major depressive episodes

Minor depressive episodes

Total prevalence 25.7%

Ratio of MDD vs BP-I or BP-II 9.4

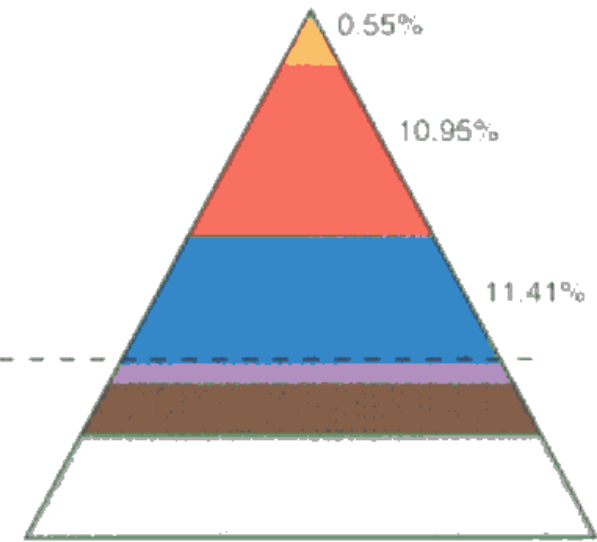
Zurich strict criteria



49.5%

2.9

Zurich broad criteria



49.5%

1.0



# Bipolar Spectrum

# Zurich Study Hypomania Criteria

## Strict

**3 or more DSM-IV criteria**

**Minimum duration 1 day**

**Consequences**

## Loose

**2 or more DSM-IV criteria**

**No minimum duration**

**No consequences**

# More Common in Bipolar Than Unipolar Depression

- **Hypersomnia**
- **Psychomotor retardation**
- **Family history of mania**
- **Earlier age of onset**
- **Greater number of episodes**
- **Greater proportion of time ill**
- **Postpartum episodes**
- **Poor response to antidepressants**

**20-30% of youth with major  
depression will go on to have  
manic episodes**

Geller et al., 1994; Rao et al., 1995; Strober and Carlson, 1982

# **Detecting Bipolar Patients Presenting With Depression**

- **Ask about history of mania and hypomania**
- **Ask about family history of BD**
- **Involve family members or significant others**
- **Administer a bipolar screening instrument, such as the MDQ**

# Mood Disorders Questionnaire (MDQ)

- **Bipolar disorders screening**
- **13 yes/no questions**
- **Correctly identified**
  - 7 of 10 with bipolar disorder (sensitivity)**
  - 9 of 10 without bipolar disorder (specificity)**
- **What about predictive value?**

# Predictive Value of the MDQ

The **positive predictive value** of the MDQ in a community sample would be about 26%  
(about 3 of 4 cases would be false positives)

The **negative predictive value**, however, would be quite high (very few false negatives)

# Treatment

# Lithium

# Lithium for Acute Bipolar Depression

- **WFSBP 2009: Category of evidence D  
(inconsistent results)**
- **CANMAT 2009: Bipolar I- First-line  
Bipolar II- Second-line**
- **BAP 2009: “the actual evidence for acute  
efficacy ... is disappointing”**

**WFSBP: World Federation of Societies of Biological Psychiatry  
CANMAT: Canadian Network for Mood and Anxiety Treatments  
BAP: British Association for Psychopharmacology**

# **Lithium Beneficial for Spinach**

- **Lithium decreased cold-induced microtubule depolymerization of spinach mesophyll cells**

**Bartolo and Carter. Plant Physiology 1992;99:1716-1718**

# Lamotrigine

# Lamotrigine for Bipolar Depression (5 multicenter, placebo-controlled studies)

- Lamotrigine did **not** separate from placebo on the primary endpoint of any of the 5 studies
- But a meta-analysis found “consistent evidence of a mild to modest, but clinically worthwhile benefit for lamotrigine that is unlikely to be due to chance.”\*
- Benefit greater in more severely depressed\*\*

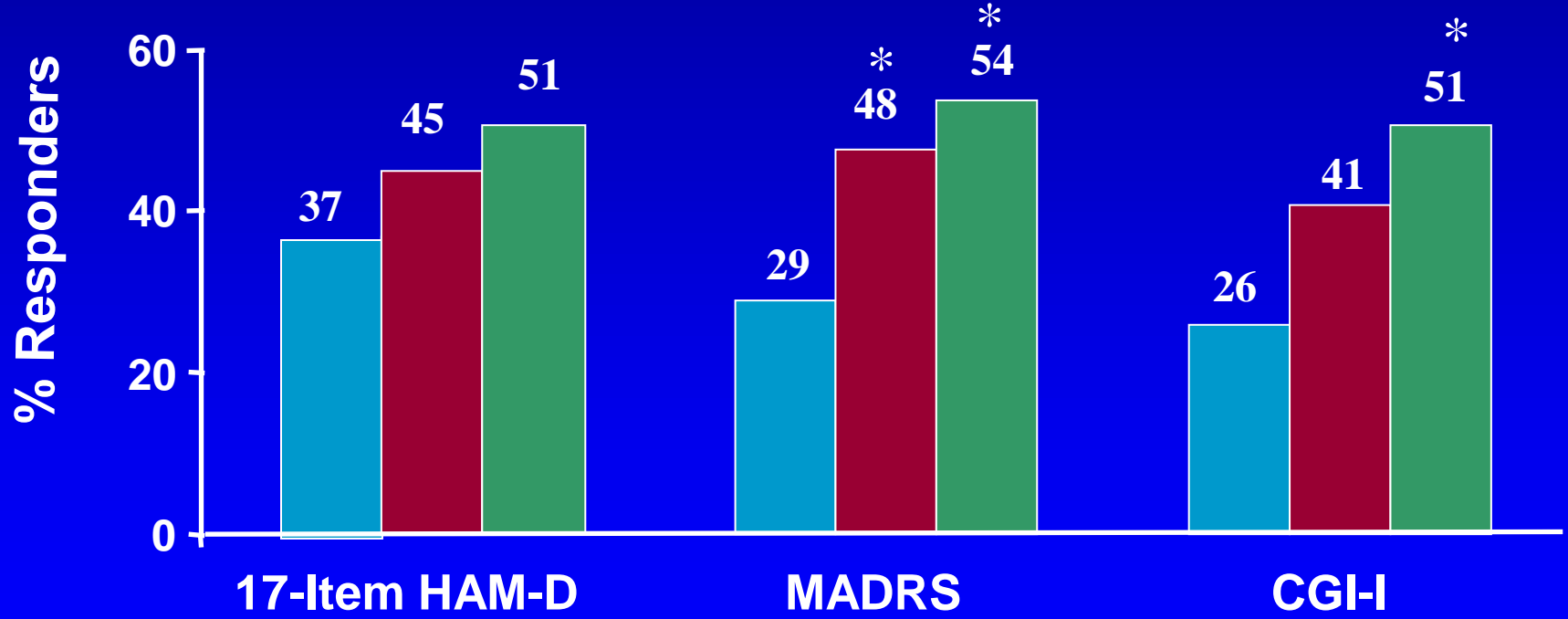
\*Geddes et al., NCDEU Annual Meeting poster I-64, June 2007

\*\*Geddes et al. Br J Psychiatry 2009;194:4-9

Calabrese et al. Bipolar Disorders 2008;10:323-333

# Lamotrigine Monotherapy for Bipolar I Depression (7 weeks, n=192)

■ Placebo    ■ Lamotrigine 50 mg/d    ■ Lamotrigine 200 mg/d



Calabrese et al. J Clin Psychiatry 1999;60:79-88

\*p<0.05

# **Lamotrigine for Bipolar Depression**

**(meta-analysis and meta-regression of individual patient data from 5 randomized trials)**

- **3 trials- bipolar I only, 1 trial- bipolar II only, 1 trial- bipolar I and II**
- **Response: NNT on HAM-D 11, on MADRS 13 (both significant)**
- **Response significant only with baseline HAM-D >24**
- **Remission: HAM-D not significant, MADRS significant (NNTs not provided)**

# Lamotrigine Add-On to Lithium for Bipolar Depression

**(8-week, double-blind, placebo-controlled, n=124)**

- **Dose: maximum 200 mg/day**
- **LTG > PBO on MADRS change (p=.024)**  
**MADRS response (51.6% vs. 31.7%) (p=.030)**
- **No remission data**
- **Well tolerated (1 severe rash—on placebo)**

# Divalproex

# Divalproex for Acute Bipolar Depression

- 4 small double-blind studies
- **Positive results:** Ghaemi et al. J Clin Psychiatry 2007;68:1840-1844 (n=18); Davis et al. J Affect Dis 2005;85:259-266 (n=25); Muzina et al. NCDEU poster, May 2008 (n=54)
- **Negative results:** Sachs et al. ACNP poster, December 2001 (n=45)

# **Divalproex for Acute Bipolar Depression (Systematic Review and Meta-Analysis)**

- **4 small double-blind studies (2 unpublished)**
- **Total sample size: n=142**
- **Response: DVPX 39.3%, PBO 17.5%**
- **Remission: DVPX 40.6%, PBO 24.3%**
- **Conclusion: “...preliminary evidence that divalproex is efficacious in the treatment of BD depression”**

# **Divalproex for Acute Bipolar Depression**

- **6-week monotherapy vs. placebo, n=54, bipolar I, n=20; bipolar II, n=34**
- **DVPX > PBO: sig. ↓MADRS and response (38.5% vs. 10.7%), but not remission**
- **Subgroup analysis: Only > PBO for bipolar I**

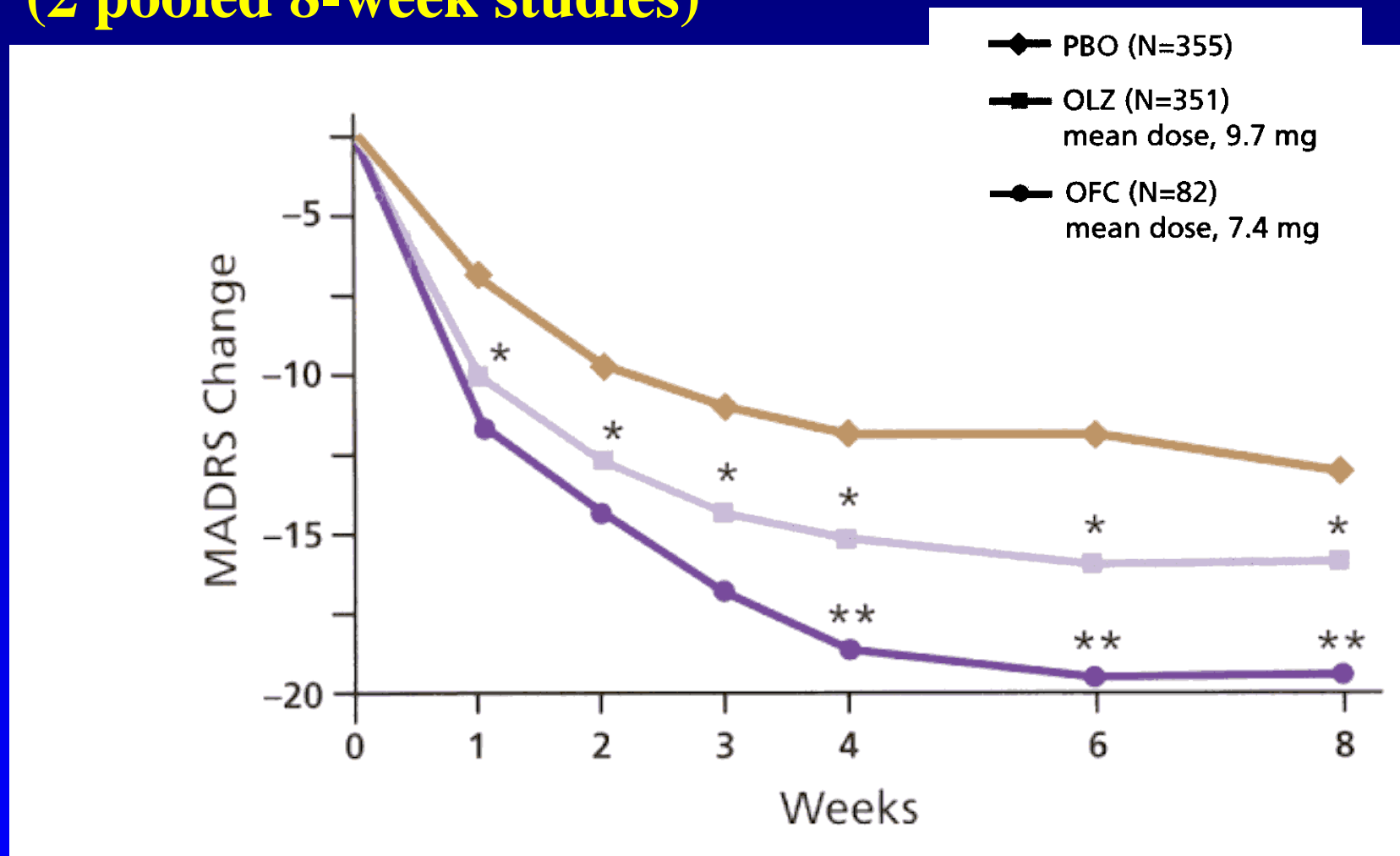
# *Atypical Antipsychotics*

# **Bipolar Depression: FDA Approval**

- **Olanzapine/fluoxetine combination  
2003 for bipolar I depression**
- **Quetiapine  
2006 for bipolar I and II depression**

# Olanzapine/Fluoxetine

# Olanzapine/OFC for Bipolar I Depression (2 pooled 8-week studies)



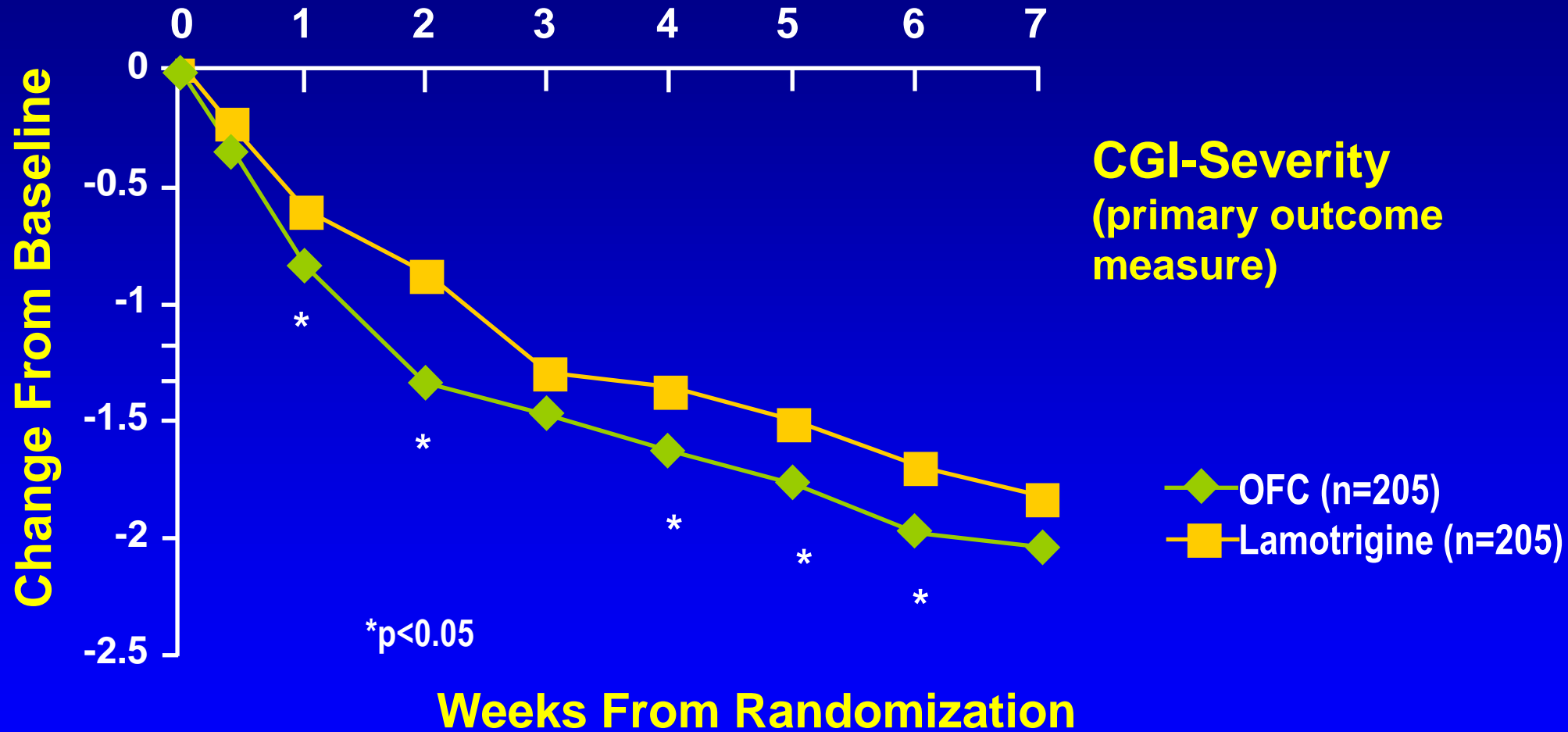
MMRM=Mixed Modal Repeated Measures,  
OFC=Olanzapine-Fluoxetine Combination

Tohen et al. APA 5/02 Full article AGP 60:1079-1088, Nov 2003

# Bipolar I Depression: Weight Change Over 8 Weeks

	<u>Kg</u>	<u>≥7%</u>
• Placebo	- 0.5	0.3%
• Olanzapine	+2.6	18.7%
• OFC	+2.8	19.5%

# OFC vs. Lamotrigine in Bipolar I Depression (N=410)



MMRM = mixed model repeated measures analysis of variance

Brown et al. J Clin Psychiatry 2006;67:1025-1033

# **OFC vs. LTG for Bipolar I Depression (7-week, double-blind, n=410)**

- **Results favored OFC (Clinical significance?)**
- **AEs favored LTG: weight, lipids, prolactin, somnolence, dry mouth, tremor**
- **Weight  $\geq 7\%$  OLZ: 23%, LTG: 0%**
- **Serious AEs (wide variety): OLZ 1.0%, LTG 5.4%**

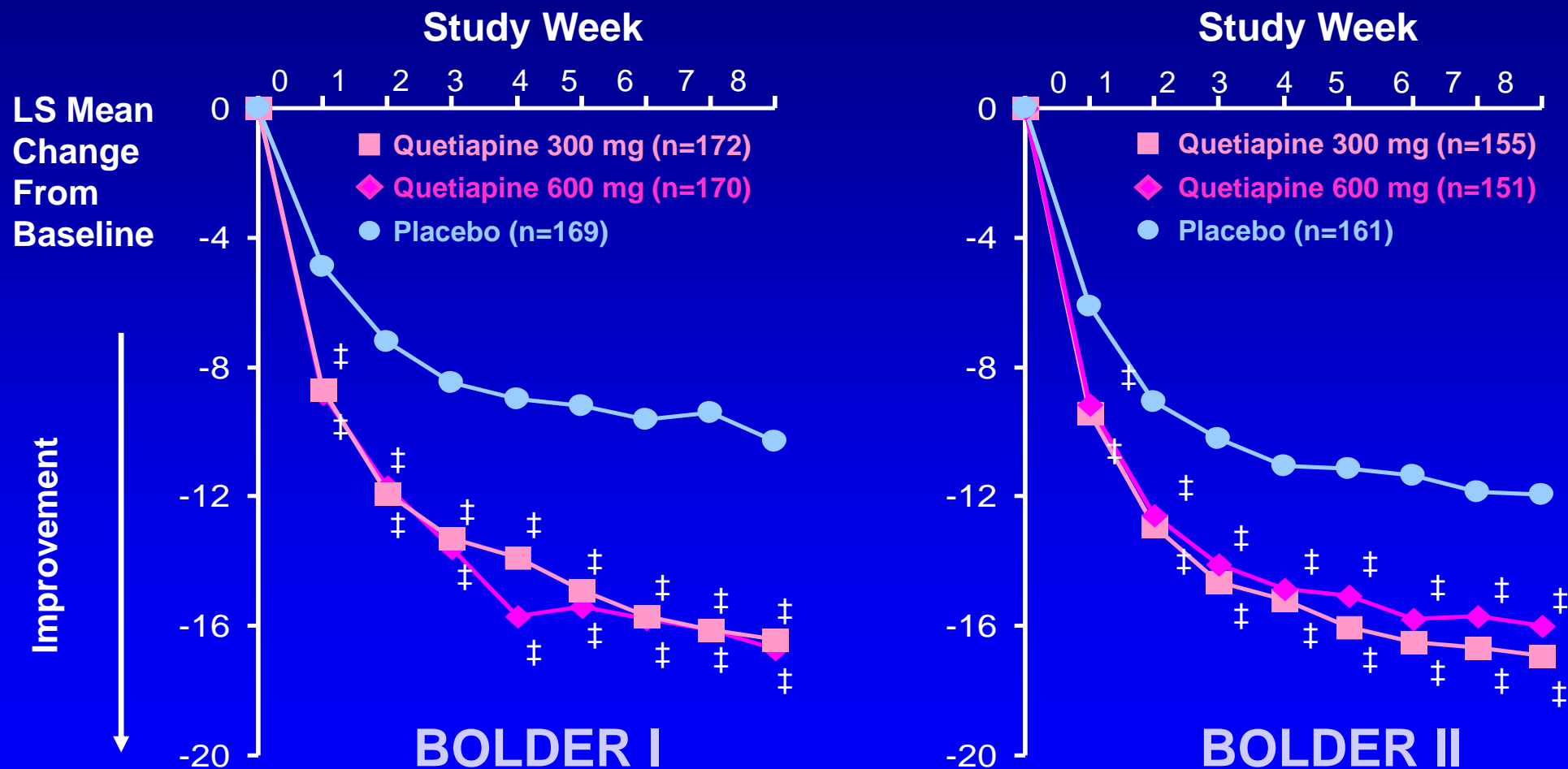
# **OFC vs. LTG for Bipolar I Depression (25-week analysis)**

- **Results favored OFC (Clinical significance?)**
- **Primary efficacy measure: CGI-S (MMRM)  
OFC > LTG at weeks 1,2,4,5,6, and 17 (p<0.05)**
- **No sig. difference in response, remission, relapse**
- **AEs favored LTG: weight, lipids, prolactin, HgA1c, somnolence, dry mouth, tremor, edema**
- **Weight  $\geq$  7%: OLZ: 33.8%, LTG: 2.1%**

# Quetiapine

# Quetiapine for Bipolar I and II Depression

## MADRS Total Score



Calabrese et al. Am J Psychiatry 2005;162:1351-1360  
 Thase et al. J Clin Psychopharmacol 2006;26:600-609

‡p<0.001 vs placebo

ITT, LOCF

# Quetiapine for Bipolar I and II Depression

## Adverse Event Dropouts

	<b>BOLDER I*</b>	<b>BOLDER II**</b>
<b>Quetiapine 600 mg</b>	<b>26.1%</b>	<b>11.2%</b>
<b>Quetiapine 300 mg</b>	<b>16.0%</b>	<b>8.1%</b>
<b>Placebo</b>	<b>8.8%</b>	<b>1.2%</b>

\*Calabrese et al., Am J Psychiatry 2005;162:1351-1360

\*\*Thase et al., J Clin Psychopharmacol 2006;26:600-609

# Quetiapine for Bipolar I and II Depression

## Weight Gain $\geq 7\%$

	BOLDER I*	BOLDER II**
Quetiapine 600 mg	9.0%	8.6%
Quetiapine 300 mg	8.5%	3.9%
Placebo	1.7%	2.8%

\*Calabrese et al., Am J Psychiatry 2005;162:1351-1360

\*\*Thase et al., J Clin Psychopharmacol 2006;26:600-609

# Quetiapine vs Lithium and Placebo for Bipolar I/II Depression (EMBOLDEN I) (8-week, double-blind, n=794)

- ↓ MADRS: QTP 300 mg = QTP 600 mg  
> Lithium (0.6-1.2 meq/l) = placebo
- Remission at week 8 (MADRS ≤ 12)

QTP 300 mg	69.8%	(p<0.01)	(NNT=7)
QTP 600 mg	70.3%	(p<0.01)	(NNT=7)
Lithium	62.5%	(n.s.)	(NNT=13)
Placebo	55.0%		

# Quetiapine vs Paroxetine and Placebo Monotherapy for Bipolar I/II Depression (EMBOLDEN II) (8-week, double-blind,, n=740)

- **↓ MADRS: QTP 300 mg = QTP 600 mg  
>Paroxetine = placebo**

- **Remission at week 8 (MADRS ≤ 12)**

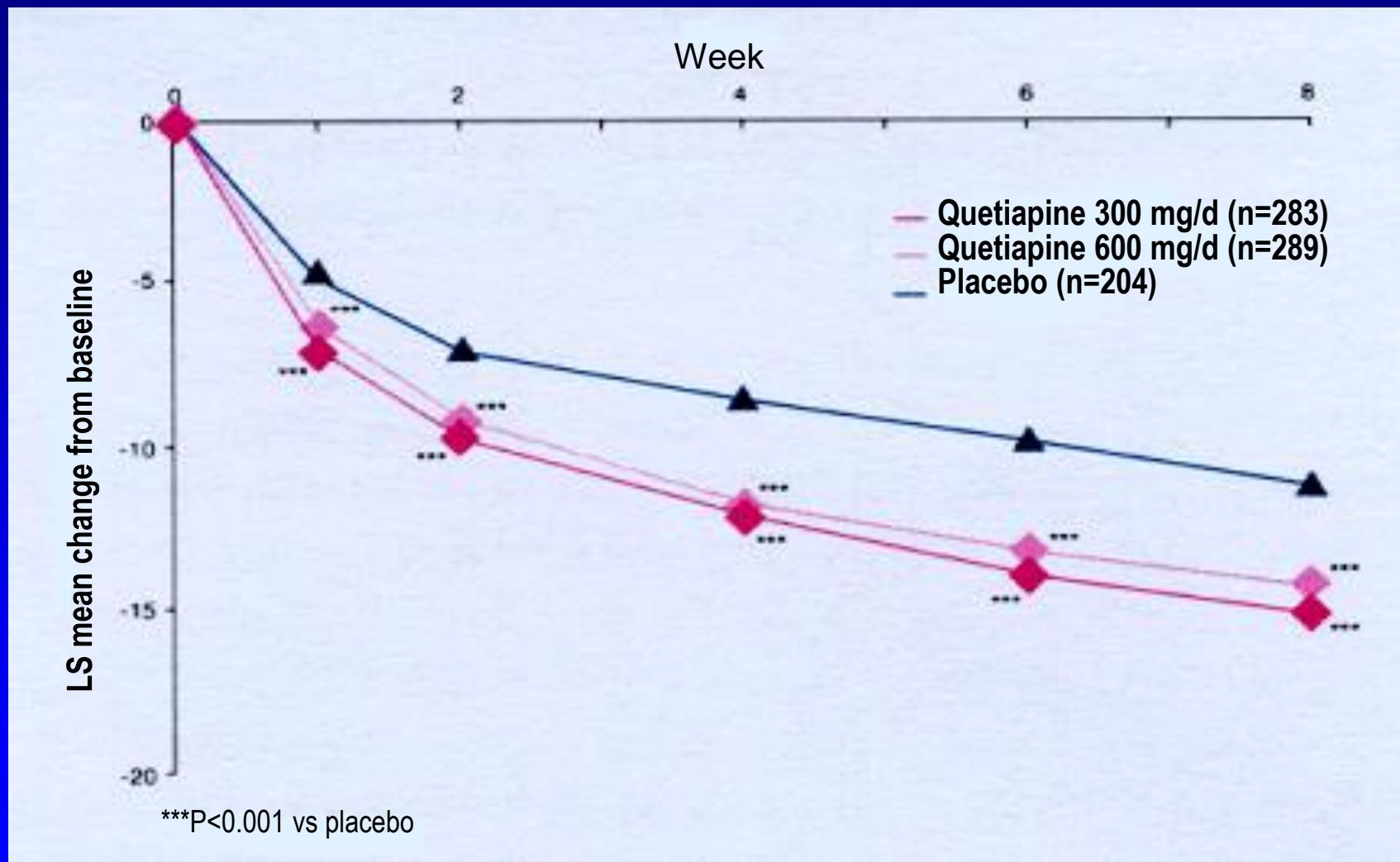
<b>QTP 600 mg</b>	<b>68.5%</b>	<b>(p&lt;0.05)</b>	<b>(NNT=8)</b>
<b>QTP 300 mg</b>	<b>64.6%</b>	<b>(n.s.)</b>	<b>(NNT=11)</b>
<b>Paroxetine</b>	<b>56.8%</b>	<b>(n.s.)</b>	<b>(NNT=71)</b>
<b>Placebo</b>	<b>55.4%</b>		

# Quetiapine Monotherapy for Bipolar II Depression: Combined Data From 4 Double-Blind, 8-Week Studies

- **↓ MADRS: QTP 300 mg = QTP 600 mg > placebo beginning at week 1**
- **Remission at week 8 (MADRS ≤ 12)**

<b>QTP 300 mg</b>	<b>65.0%</b>	<b>(p&lt;0.01)</b>	<b>NNT 5</b>
<b>QTP 600 mg</b>	<b>61.9%</b>	<b>(p&lt;0.01)</b>	<b>NNT 6</b>
<b>Placebo</b>	<b>46.1%</b>		

# Quetiapine Monotherapy for Bipolar II Depression: Combined Data From 4 Double-Blind, 8-Week Studies



# **Quetiapine Monotherapy for Acute Bipolar I Depression in Adolescents**

- **8-week, double-blind, placebo-controlled, n=32**
- **Dose: 300-600 mg/day**
- **No significant difference in primary  
(↓ CDRS-R) or secondary efficacy measures**

# Aripiprazole

# **Aripiprazole Monotherapy for Acute Bipolar I Depression**

- **Two identical 8-week, double-blind, placebo-controlled studies (total n=749)**
- **Flexible dose: start 10 mg (range 5-30 mg)**
- **Primary endpoint: MADRS (LOCF)**  
**No significant difference in either study**

# Ziprasidone

# **Ziprasidone Monotherapy for Acute Bipolar I Depression**

- **Two similar 6-week, double-blind, placebo-controlled studies (total n=928)**
- **Flexible dose: Study 1- 40-80 mg/day or 120-160 mg/day; study 2- 40-160 mg/day\***
- **Primary endpoint: MADRS (MMRM)**

**No significant difference in either study!**

Sachs et al. NCDEU Poster II-13, 49<sup>th</sup> Annual Meeting, June 29-July2, 2009

\*Sachs et al. J Clin Psychiatry 2011 May 3 (Epub ahead of print)

# **Antidepressants**

# Antidepressants for Bipolar Depression

- **TIMA**-“Although ... in common use, controlled studies ... in patients with BDI are limited”  
Therefore Stage 4
- **WFSBP**-“... antidepressants are probably the most efficacious..., whereas mood stabilizers are the safest or most conservative ...”
- **Expert Consensus Guideline**-First line: Li, LTG, or antidepressant plus Li or LTG
- **CANMAT**-First line includes Li or DVPX + SSRI or bupropion; OLZ+SSRI

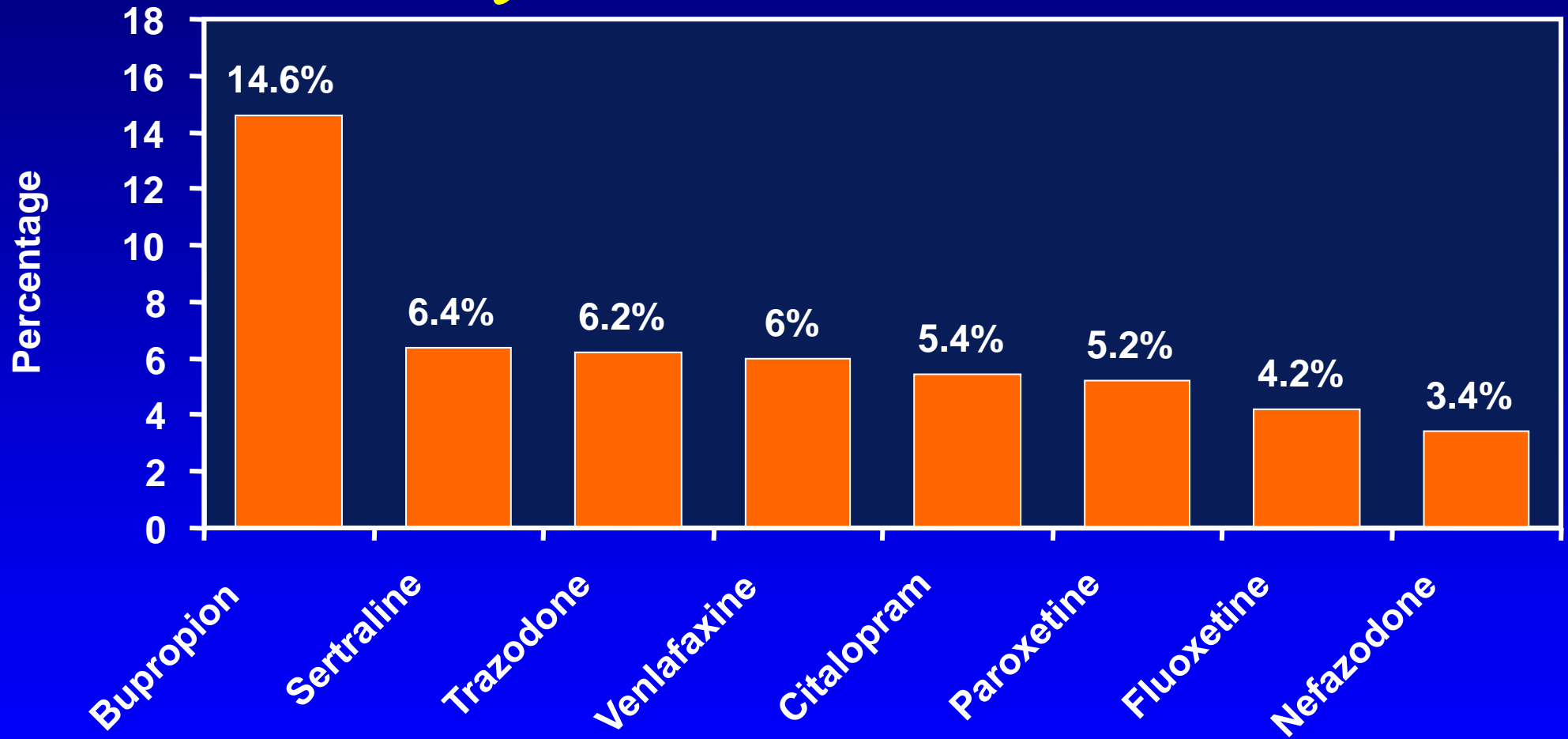
# Antidepressants in Bipolar Disorder

- **Disadvantages<sup>1</sup>**
  - **Poor response**
  - **Manic switches**
  - **Cycle acceleration**
  - **Late response loss**
- **Advantages<sup>2</sup>**
  - **An exceptional subgroup**

<sup>1</sup>Ghaemi SN et al. (2004), Am J Psychiatry 161(1):163-165; <sup>2</sup>Altshuler L et al. (2003), Am J Psychiatry 160(7):1252-1262

# *Antidepressant Use at STEP-BD Study*

## *Entry: First 500 Patients*



# **Adjunctive Antidepressant for Bipolar I or II Depression (STEP-BD)**

**(26-Week, double-blind, N=366)**

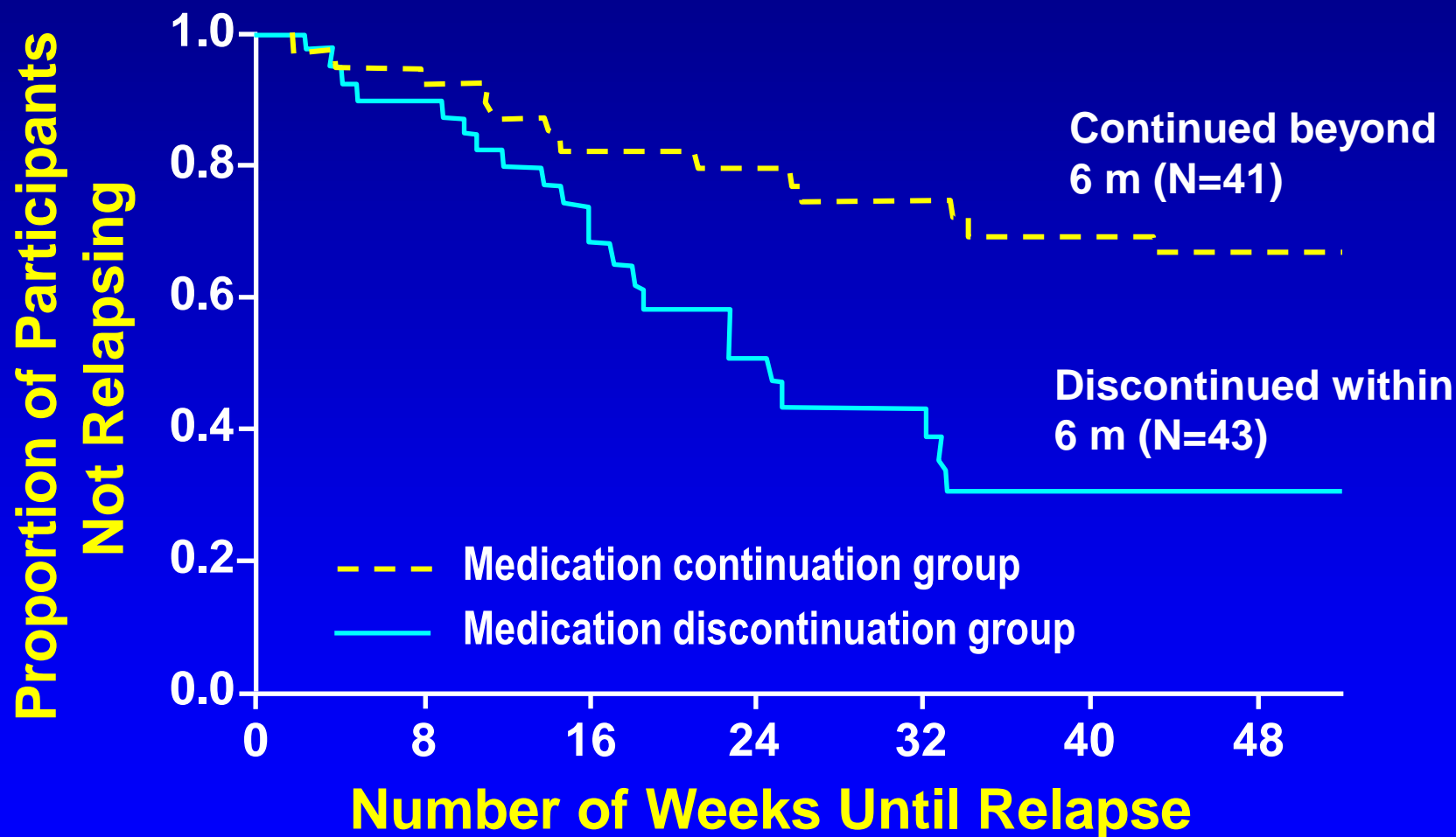
- **Bupropion, paroxetine or placebo**
- **Primary outcome: 8 consecutive euthymic weeks**
- **Results: NO DIFFERENCE**

<b>Mood stabilizer + antidepressant</b>	<b>23.5%</b>
<b>Mood stabilizer + placebo</b>	<b>27.3%</b>
- **Affective switch: no difference**

Sachs et al., N Eng J Med 2007;356:1711-1722

Belmaker (editorial) N Eng J Med 2007;356:1771-1772

# Antidepressants in Bipolar Disorder: Continue or Discontinue?



Altshuler L et al. (2003), Am J Psychiatry 160(7):1252-1262.

Similar findings: Joffe et al. Acta Psychiatr Scand 2005;112:105-109

# **Antidepressants for Bipolar Depression: Systematic Review- 12 Randomized, Controlled Trials**

- **Effective short-term (longest was 10 weeks)**
- **Switching not common**
- **Prefer SSRIs, MAOIs over TCAs**
- **To prefer bupropion or paroxetine moves  
“beyond the evidence”**

# Antidepressants in Bipolar Depression

## An Updated Review (18 RCTs, n=2515)

- Antidepressants exert some efficacy in some populations
- Increased switch rate associated with substance abuse, many previous episodes, depression with manic/hypomanic features

# **Antidepressants for Acute Bipolar Depression**

## **Systematic Review and Meta-Analysis**

- **15 randomized, double-blind studies with either placebo or active comparator (n=2373)**

# **Antidepressants for Acute Bipolar Depression**

## **Systematic Review and Meta-Analysis**

- **15 randomized, double-blind studies with either placebo or active comparator (n=2373)**
- **Antidepressants NOT statistically better**

# **Antidepressants for Acute Bipolar Depression**

## **Systematic Review and Meta-Analysis**

- **15 randomized, double-blind studies with either placebo or active comparator (n=2373)**
- **Antidepressants NOT statistically better**
- **Antidepressants NOT associated with increased switch rate**

# **Antidepressants for Acute Bipolar Depression**

## **Systematic Review and Meta-Analysis**

- **15 randomized, double-blind studies with either placebo or active comparator (n=2373)**
- **Antidepressants NOT statistically better**
- **Antidepressants NOT associated with increased switch rate**
- **“...present findings suggest that antidepressant medications offer little in the acute treatment of bipolar depression”**

# **Antidepressants for Acute Bipolar Depression**

## **Systematic Review and Meta-Analysis**

### **HOWEVER:**

- **Relatively “few high quality RCTs”**
- **Methodological limitations reduce validity of existing studies.**
- **“The results of this meta-analysis are far from conclusive.”**

# Quetiapine vs Paroxetine and Placebo Monotherapy for Bipolar I/II Depression (EMBOLDEN II) (8-week, double-blind,, n=740)

- ↓ MADRS: QTP 300 mg = QTP 600 mg  
>Paroxetine = placebo

- Remission at week 8 (MADRS ≤ 12)

QTP 600 mg	68.5%	(p<0.05)	(NNT=8)
QTP 300 mg	64.6%	(n.s.)	(NNT=11)
Paroxetine 20 mg	56.8%	(n.s.)	(NNT=71)
Placebo	55.4%		

# **Adjunctive Paroxetine vs. Venlafaxine for Bipolar Depression (6-week, single-blind, n=60)**

- **No significant difference on HAM-D change, response or remission rates**
- **Mania/hypomania switch rates:**

<b>Paroxetine</b>	<b>3%</b>	<b>(1/30)</b>
<b>Venlafaxine</b>	<b>13%</b>	<b>(4/30)</b>

**Do Antidepressants Cause  
Mania/Hypomania?**

# **Do Antidepressants Cause Mania/Hypomania?**

**Maybe**

# **Quetiapine vs Paroxetine and Placebo Monotherapy for Bipolar I/II Depression (EMBOLDEN II) (8-week, double-blind, n=740)**

- Mania/hypomania**

<b>QTP 600 mg</b>	<b>4.1%</b>
<b>QTP 300 mg</b>	<b>2.1%</b>
<b>Paroxetine 20 mg</b>	<b>10.7%</b>
<b>Placebo</b>	<b>8.9%</b>

# **Antidepressant Switch Rate in Bipolar II Disorder (NIMH-CDS)**

- **Antidepressant      3.6% switch**
- **No antidepressant   3.5% switch**

# Bipolar Depression Switch Rates

10-week, adjunctive, db (mostly), n=174

- Equal response and remission rates

- Switch rates

	CGI-BP-M	YMRS
Bupropion	10%	4%
Sertraline	9%	7%
Venlafaxine	29%	15%

- ↑ Venlafaxine risk in rapid cyclers

# **Do Antidepressants Cause Rapid Cycling?**

# **Do Antidepressants Cause Rapid Cycling?**

**Maybe**

# **The Role of Antidepressants or the Lack Thereof in Bipolar Disorder Continues to Be Debated**

**But there is agreement that  
antidepressants should not be used as  
monotherapy for Bipolar I depression**

**Is antidepressant monotherapy safe  
and effective for bipolar II  
depression?**

# Is antidepressant monotherapy safe and effective for bipolar II depression?

Maybe

Amsterdam and Brunswick. *Bipolar Disorders* 2003;5:388-395  
Agosti and Stewart. *Int Clin Psychopharmacol* 2007;22:309-311

# Venlafaxine vs. Lithium Monotherapy for Bipolar II Depression (12-week, open-label, n=83)

- **VEN: mean daily dose 185.6mg**  
**Lithium: mean serum level 0.64 meq/l**
- **VEN > Lithium ↓HAM-D28**  
**Response 60.4% vs. 20%**  
**Remission 44.2% vs. 7.5%**
- **Young Mania Rating Scale: No significant increase**

# **Fluoxetine vs. Lithium Monotherapy for Bipolar II Depression (50-week, double-blind, n=81)**

- **Remission after open-label FLX**
- **Then randomized to FLX, Li, or PBO**
- **Mean time to relapse/recurrence, %**
  - FLX: 249.9 days (32.1%)**
  - Li : 156.4 days (57.7%)**
  - PBO: 186.9 days (51.9%)**
- **No increased mania/hypomania**

# Odds and Ends

# Adjunctive Modafinil for Bipolar I or II Depression (6-week, double-blind, n=85)

- **Dose: 100 mg x 1 week, then 100 mg bid  
(mean 174 mg/day)**
- **Reponse ( $\downarrow$  IDS  $\geq 50\%$ ):**

<b>MOD</b>	<b>43.9%</b>	<b>(P=0.038)</b>
<b>PBO</b>	<b>22.7%</b>	
- **Remission (IDS < 12):**

<b>MOD</b>	<b>39%</b>	<b>(P=0.033)</b>
<b>PBO</b>	<b>18%</b>	

# Adjunctive Armodafinil for Bipolar I Depression (8-week, double-blind, n=247)

- **Dose: 150 mg/d or placebo**
- **Primary efficacy: IDS-C<sub>30</sub> change**  
    **ARM: -15.8**  
    **PBO: -12.8**      (ANOVA: p=.044)
- **Secondary efficacy: No sig. diff on response, remission, QIDS-SR, MADRS, etc.**
- **Further studies needed**

# Adjunctive Pramipexole for Bipolar Depression (6-week, double-blind)

- Study 1: n=22, dose- start 0.125 mg bid, max 5 mg, mean 1.7 mg/day  
Response **Pram 67%, PBO 20%**
- Study 2: n=21 (BP II), dose- start 0.125 mg tid max 4.5 mg, mean 1.7 mg/day  
Response **Pram 60% PBO 9%**

# Treatment-Resistant BP Depression STEP-BD Equipoise Randomization (open-label, up to 16 weeks, n=66)

**Lamotrigine:** target 150-250 mg/day, n=21  
Recovery 23.8%

**Inositol:** target 10-25 gm/day, n=23  
Recovery 17.4%

**Risperidone:** up to 6 mg/day, n=22  
Recovery 4.6%

**NO SIGNIFICANT DIFFERENCES IN RECOVERY**  
(post-hoc analyses favored lamotrigine)

# **Omega-3 Fatty Acid Augmentation For Bipolar Depression**

- **Two double-blind, placebo-controlled studies**
- **“Adjunctive ethyl-EPA is an effective and well-tolerated intervention in bipolar depression.”<sup>1</sup>**
- **“Overall, there were no significant differences on any outcome measure between the EPA and placebo groups.”<sup>2</sup>**

**1 Frangou et al. Br J Psychiatry 2006;188:46-50**

**2 Keck et al Biol Psychiatry 2006;60:1020-1022**

# Adjunctive Riluzole for Bipolar Depression (8-week, open-label, n=14)

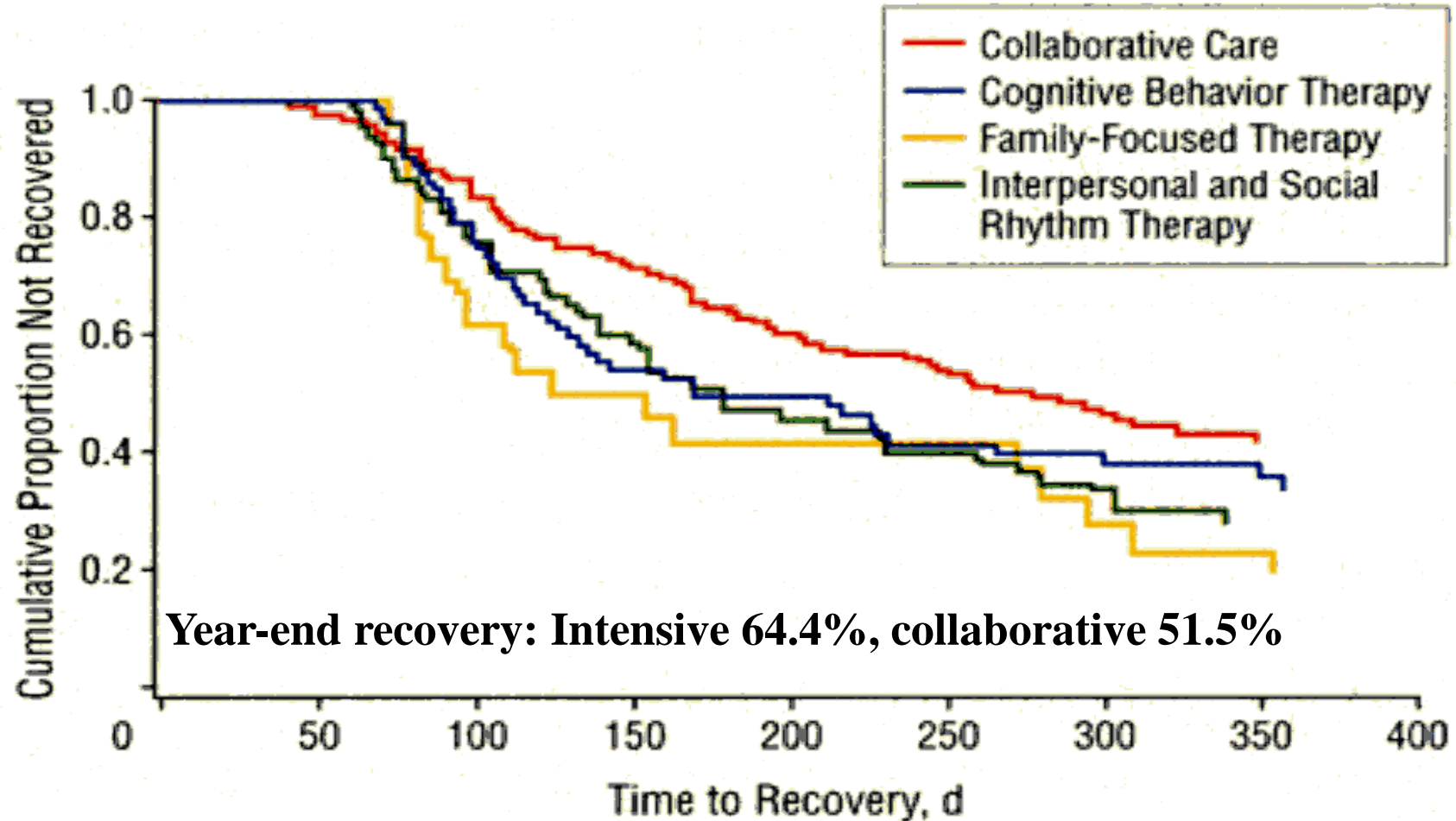
- Approved for ALS
- Anti-glutamergic, sodium channel blocker
- 50-200 mg/day added to lithium:
  - significant on MADRS at weeks 5-8
- 57% completion
- AE dropouts 14%
- No manic switches

# Adjunctive N-Acetyl Cysteine (NAC) for Subthreshold Bipolar Depressive Symptoms (24-week, db, PBO-controlled, n=75)

- Glutathione: antioxidant substrate
- NAC: glutathione precursor (2 gm/day)
- MADRS: Significant ↓ **at week 20** and after
- Time to mood episode: Not significant
- Cheap, safe, OTC, but how effective?

# STEP-BD: Adjunctive Psychosocial Treatments for Bipolar Depression

Higher recovery rates and shorter time to recovery



# Recent Summaries

# Acute Bipolar I Depression: CANMAT

- **First Line:** Lithium, LTG, QTP, QTP XR, Li or DVPX + SSRI, Li + DVPX, Li or DVPX + bupropion
- **Second Line:** QTP + SSRI, DVPX, Li or DVPX + LTG, adjunctive modafinil
- **Third Line:** Many combinations
- **Not Recommended:** Gabapentin monotherapy, aripiprazole monotherapy

# **WFSBP\* 2009: Bipolar Depression Efficacy**

- **Clear evidence: quetiapine**
- **Strong evidence: olanzapine/fluoxetine combo**
- **Fair evidence: antidepressants in combo with antimanic drug**
- **Efficacy in a post-hoc pooled analysis in more severely depressed: lamotrigine**
- **Evidence not as good, but consider as add-on: modafinil and pramipexole**

\*World Federation of Societies of Biological Psychiatry

Grunze et al. World J Biol Psychiatry 2010;11:81-109

# **Acute Bipolar II Depression: Current Evidence**

- **Quetiapine: Compelling evidence**
- **Lithium, antidepressants, pramipexole:  
Preliminary support for efficacy**
- **Lamotrigine: Mixed support**

# Conclusions

- **Bipolar depression: common, under-diagnosed, misdiagnosed**
- **Treatment: two FDA-approved treatments**
- **Treatment: data vs. expert opinion**
- **Treatment: role of antidepressants?**
- **Treatment: need for more research**

# **Pre-Lecture Exam**

## **Question 1**

- 1. Which of the following is more common in bipolar depression than in major depressive disorder?**
  - a. Insomnia**
  - b. Later age of onset**
  - c. Agitation**
  - d. Greater number of episodes**
  - e. Agitation**

## Question 2

2. As October 2011, which of the following is FDA-approved treatment for acute bipolar I and II depression?
- a. Lithium
  - b. Lamotrigine
  - c. Quetiapine
  - d. Bupropion
  - e. Duloxetine

## Question 3

- 3. Which of the following was the most commonly used antidepressant in the STEP 500 survey?**
- a. Bupropion**
  - b. Citalopram**
  - c. Venlafaxine**
  - d. Sertraline**
  - e. Paroxetine**

# Question 4

- 4. Which antidepressant appears to have the highest switch rate when used to treat bipolar depression?**
- a. Bupropion**
  - b. Sertraline**
  - c. Venlafaxine**

# Answers to Pre & Post Lecture Exams

1. d

2. c

3. a

4. c