

PHENOMENOLOGY, OCCUPATIONAL DISABILITY, AND SOCIAL BURDEN OF BIPOLAR DISORDER

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Hosted by
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BIPOLAR DISORDER

- Bipolar I
- Bipolar II
- Bipolar NOS
- Cyclothymic disorder
- Rapid cycling
- mixed states/dysphoric manias

ETIOLOGIES

- Genetics
- Neurotransmission
- Circadian rhythm disturbances
- Nature - nurture

SCREENING FOR BIPOLAR ILLNESS

- Mood elevation or irritability plus:
 - Distractibility
 - Indiscretions
 - Grandiosity
 - Flight of ideas/racing thoughts
 - Activity level increase
 - Sleep needs decrease
 - Rate of speech increase (too much talk)

MOOD DISORDERS QUESTIONNAIRE (MDQ)

- 13-item self-administered screen
- Psychometrically validated
- High sensitivity/specificity
- Suggests bipolar spectrum features in 3-5% of population

VARIABLE PRESENTATIONS OF BIPOLAR ILLNESS

- Mania
- Depression
- Mixed states
- agitation
- Rapid cycling
- psychosis
- impulsivity
- aggression/violence
- Attention/concentration problems
- Interpersonal problems
- substance abuse
- anxiety
- sleep disorders
- suicidality
- No problems

PREVALENCE AND COURSE OF ILLNESS

- Lifetime prevalence 0.8-1.6% ¹
- Men ~ women 1:1 ²
- Recurrent episodes in > 90% ²
- Number of episodes may influence treatment response ^{3,4}
- Persistent subsyndromal symptoms in >half of patients ⁵
- Frequent comorbidity ⁶

¹ Regier et al., *Arch Gen Psychiatry* 1984; ² Goodwin & Jamison, *Manic Depressive Illness*, 1990;

³ Gelenberg et al., *N Engl J Med*, 1989; ⁴ Swann et al., *Am J Psychiatry* 1999

⁵ Judd et al., *Arch Gen Psychiatry* 2002; ⁶ McElroy et al., *Am J Psychiatry* 2001

COMORBIDITIES

Any - about 2/3 of patients ¹

- Substance abuse or dependence: 60-70%
lifetime prevalence ^{2,3}
- anxiety disorders
- eating disorders
- posttraumatic stress disorder
- personality disorders
- medical

¹ McElroy et al., Am J Psychiatry 2000

² Regier et al., JAMA 1990

³ Kessler et al., Arch Gen Psychiatry 1992

RAPID CYCLING

- >4 episodes/year
- about 20% of bipolar patients
- 70% are women
- poorer response to lithium
- May be caused by antidepressant overuse

DELAYS TO DIAGNOSIS AND TREATMENT INITIATION

- 8-10 year delay from symptom onset to diagnosis ^{1,2}
- Misdiagnosis of unipolar depression in up to 40% of depressed patients ³
- 1st mental health contact 2 years after symptom onset but 1st mood stabilizer 8 years afterward ²
- Heightened risk for suicide attempts, multiple hospitalizations, poorer outcome with delayed mood stabilizer initiation ²

¹ Lish et al., *J Affect Disord*, 1992

² Goldberg & Ernst, *J Clin Psychiatry* 2002

³ Ghaemi et al., *J Clin Psychiatry* 2000

WRONG TREATMENTS

- Use of antidepressants rather than mood stabilizers at illness onset does not reduce risk for suicide attempts or multiple relapses ²
- Antidepressants may induce manias or accelerate cycle frequency in 1/4 - 1/3 of bipolar patients ²
- Some mood stabilizers (eg, lithium) may work better when initiated early in illness course ³

¹ Goldberg & Ernst, *J Clin Psychiatry* 2002

² Altshuler et al., *Am J Psychiatry* 1995

³ Franchini et al., *Eur J Psych Neurosci*, 1993

SUICIDE RISK

- 15x mortality ratio ¹
- attempts in 25-50% of patients ²
- completions in nearly 20% ²
- Risk profile: male, early age at onset, prior attempts, multiple depressions, mixed states, substance abuse comorbidity ³
- Attempts may be especially common in women with BP II disorder ⁴
- Lithium may be protective

¹ Harris & Barraclough, *Br J Psychiatry*, 1997

² Goodwin & Jamison, *Manic Depressive Illness*, 1990

³ Goldberg et al., *J Clin Psychiatry*, 2001

⁴ Rihmerr et al., *Psych Clin N Amer* 1999

ECONOMIC COSTS

- \$44 billion in 1990
- Direct costs ~ 17% (\$7.6 billion/year)
 - inpatient/nursing home costs, crime, substance abuse, suicide, medications, shelters
- Indirect costs ~ 83%:
 - worker absenteeism, diminished productivity, lost wages, family/caregiver burden, institutional costs, assisted living

INCIDENCE-BASED COST ESTIMATES OF BIPOLAR DISORDER

- Total lifetime costs: \$24 billion
- Average cost per case: \$252,212
 - single episode/stable course: \$11,720
 - chronic/treatment nonresponsive: \$624,785

OCCUPATIONAL DISABILITY IN BIPOLAR DISORDER

- In 1990, bipolar disorder accounted for 289 million days of worker absenteeism ¹
- 6 months after a manic episode, only 43% were employed; 80% were symptomatically recovered, yet only 21% were functioning at expected levels ²

¹ Greenberg et al., *J Clin Psychiatry* 54: 405-418, 1993

² Dion et al., *Hosp & Commun Psychiatr* 39: 652-657, 1988

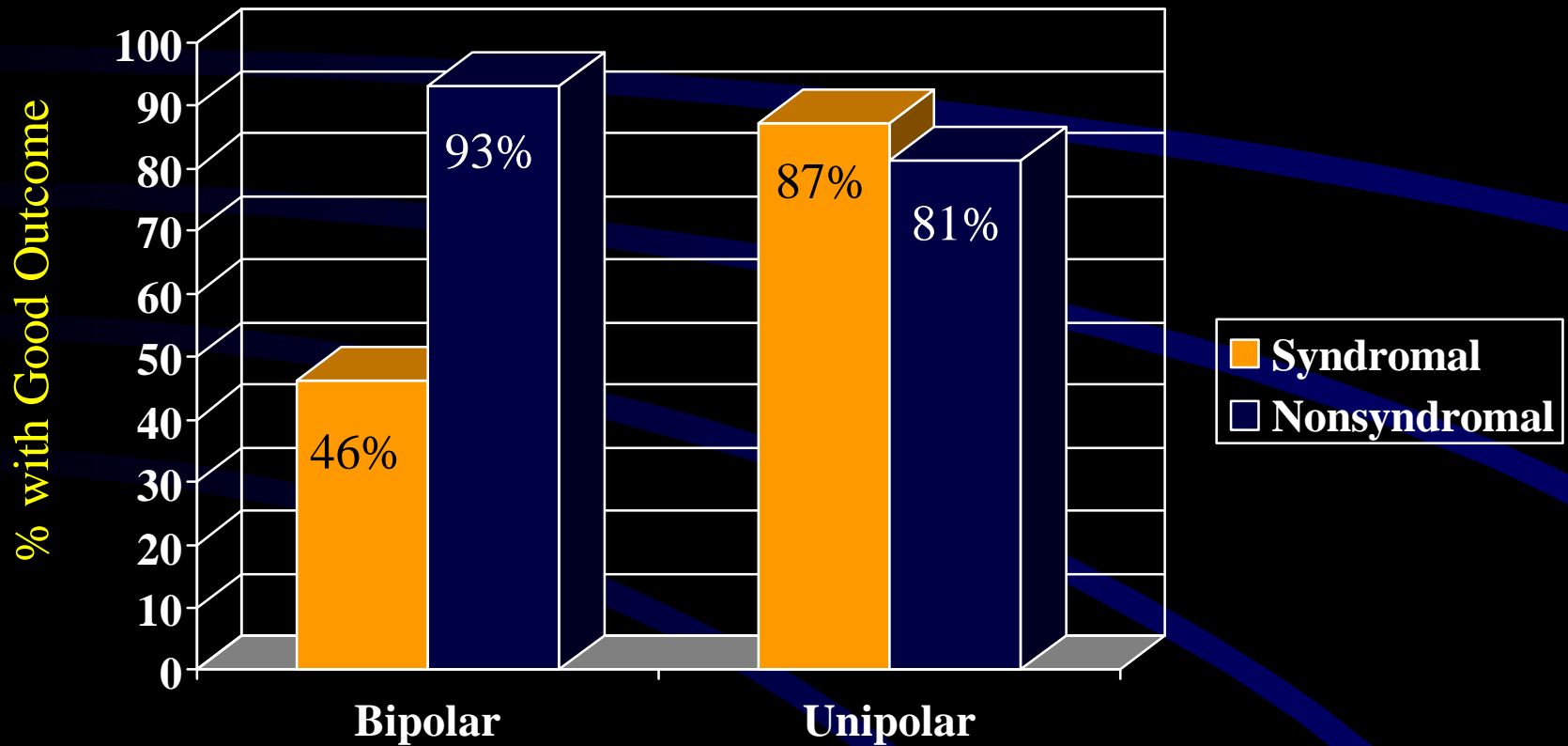
SERVICE UTILIZATION

- “Bipolar illness accounts for 90% of inpatient psychiatric costs, yet parity of mental health insurance would increase overall health care costs by only 6%”¹
- Higher service utilization if a history of childhood/physical abuse²

¹ Simon & Unutzer, *Psych Serv* 50: 1303-1308, 1999

² Bauer et al., *J Affect Disord* 44: 159-168, 1997

FUNCTIONAL IMPAIRMENT IN SYNDROMAL BIPOLAR VS. UNIPOLAR PATIENTS AT 5-YEAR FOLLOW-UP



AVERAGE TIME TO RECOVERY

- Mania: 10 weeks
- Depression: 19 weeks
- Mixed states: 36 weeks

- Probability of successful return to work within 1 week after hospitalization for manic episode: zero

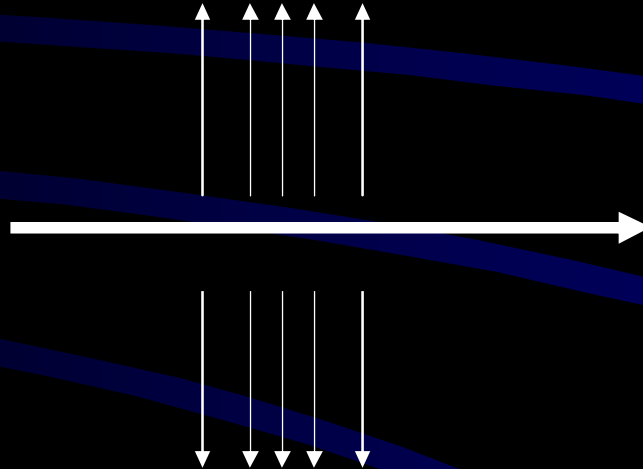
PSYCHOSOCIAL AND FAMILY BURDEN

- Significant family/caregiver burden in over half of partners or parents
- 80% of bipolar marriages end
- May weaken social supports, impair community functioning, contribute to relapse
- Role of negative expressed emotion (EE)

RISK FACTORS FOR RELAPSE

- Multiple episodes
- comorbid substance abuse
- medication nonadherence
 - lack of insight, missing highs, stigma/illness denial, medication side effects
- poor social support/negative expressed emotion

MOOD STABILIZATION

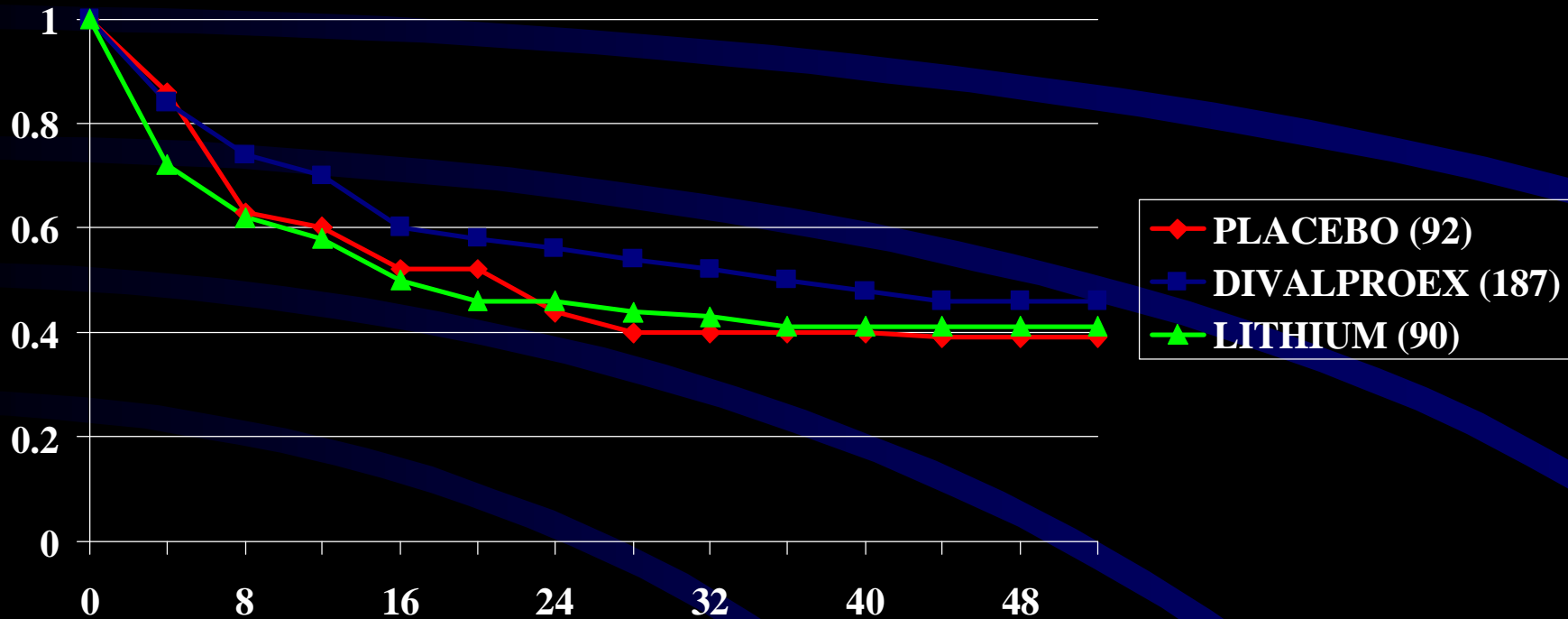


TREATMENTS FOR BIPOLAR DISORDER: ANTICONVULSANTS

- Divalproex (Depakote)
- carbamazepine (Tegretol)
- oxcarbazepine (Trileptal)
- gabapentin (Neurontin)
- topiramate (Topamax)
- Lamotrigine (Lamictal)
- tiagabine (Gabitril)
- zonisamide (Zonegran)
- levetiracetam (Keppra)
- pregabalin

LITHIUM, DIVALPROEX OR PLACEBO FOR 1-YEAR BIPOLAR RELAPSE PREVENTION

Kaplan-Meier Survival Estimate: Time to Depressive or Manic Episode



Divalproex vs. Placebo $p=.33$; Divalproex vs. Lithium $p=.08$; Lithium vs. Placebo $p=.31$

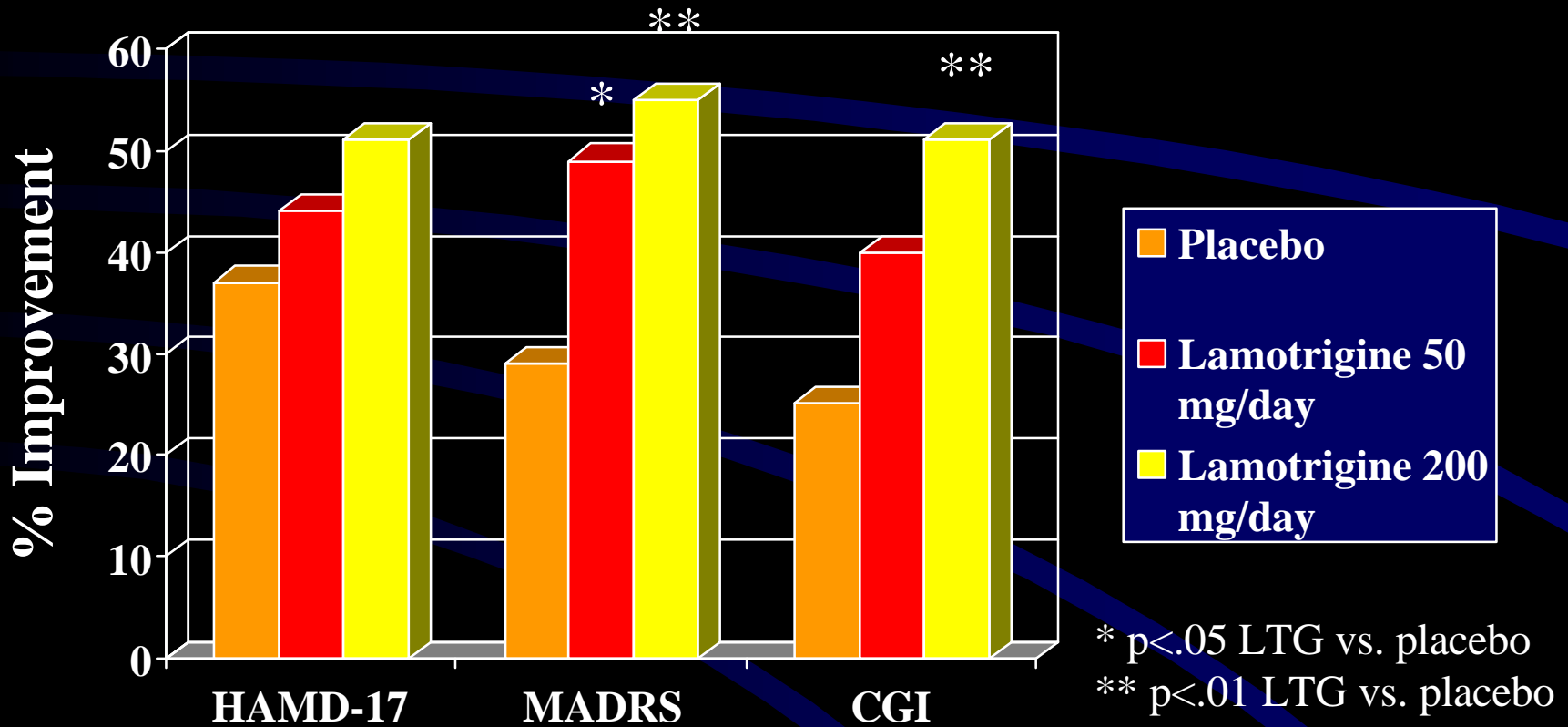
TREATMENTS FOR BIPOLAR DISORDER: ATYPICAL ANTIPSYCHOTICS

- Clozapine (Clozaril)
- olanzapine (Zyprexa)
- risperidone (Risperdal)
- quetiapine (Seroquel)
- ziprasidone (Geodon)
- aripiprazole (Abilify)

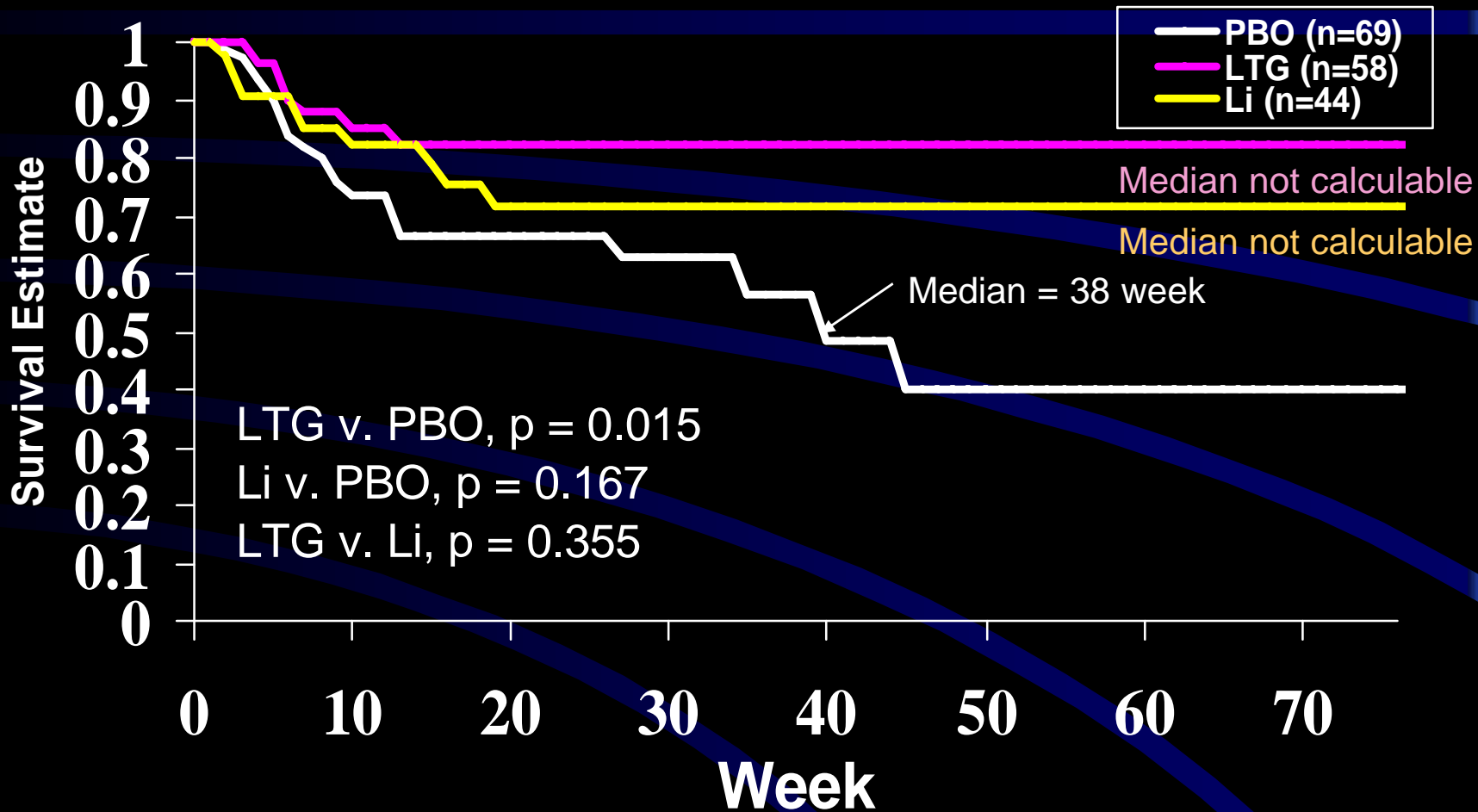
STANDARD ANTIDEPRESSANTS FOR BIPOLAR DEPRESSION

- Randomized Trials:
 - Bupropion
 - Paroxetine
 - fluoxetine
 - venlafaxine
 - Tranylcypromine
- Open Trials:
 - Citalopram

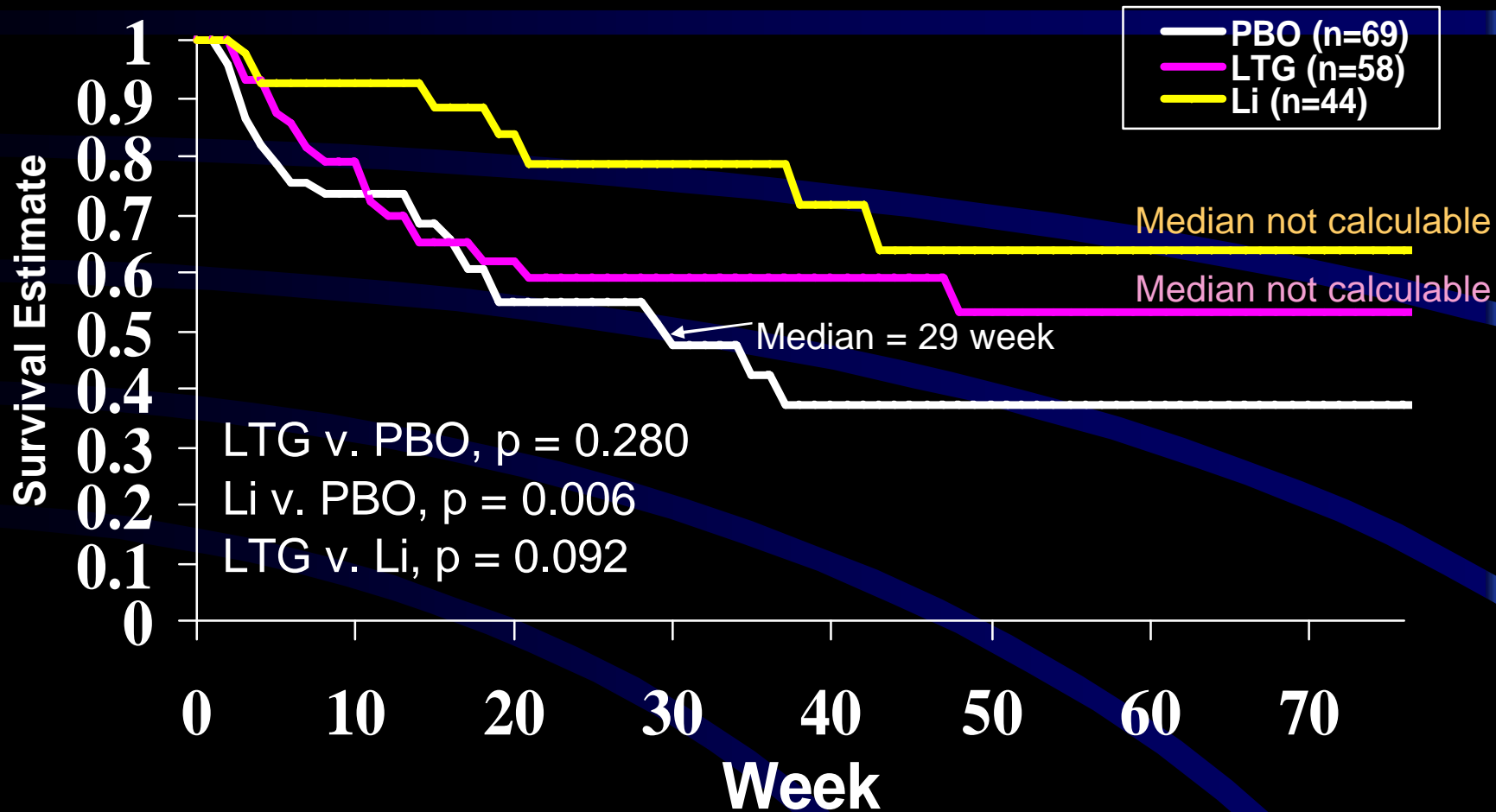
LAMOTRIGINE IN BIPOLAR DEPRESSION: RESPONDER ANALYSIS ($\geq 50\%$ IMPROVEMENT FROM BASELINE)



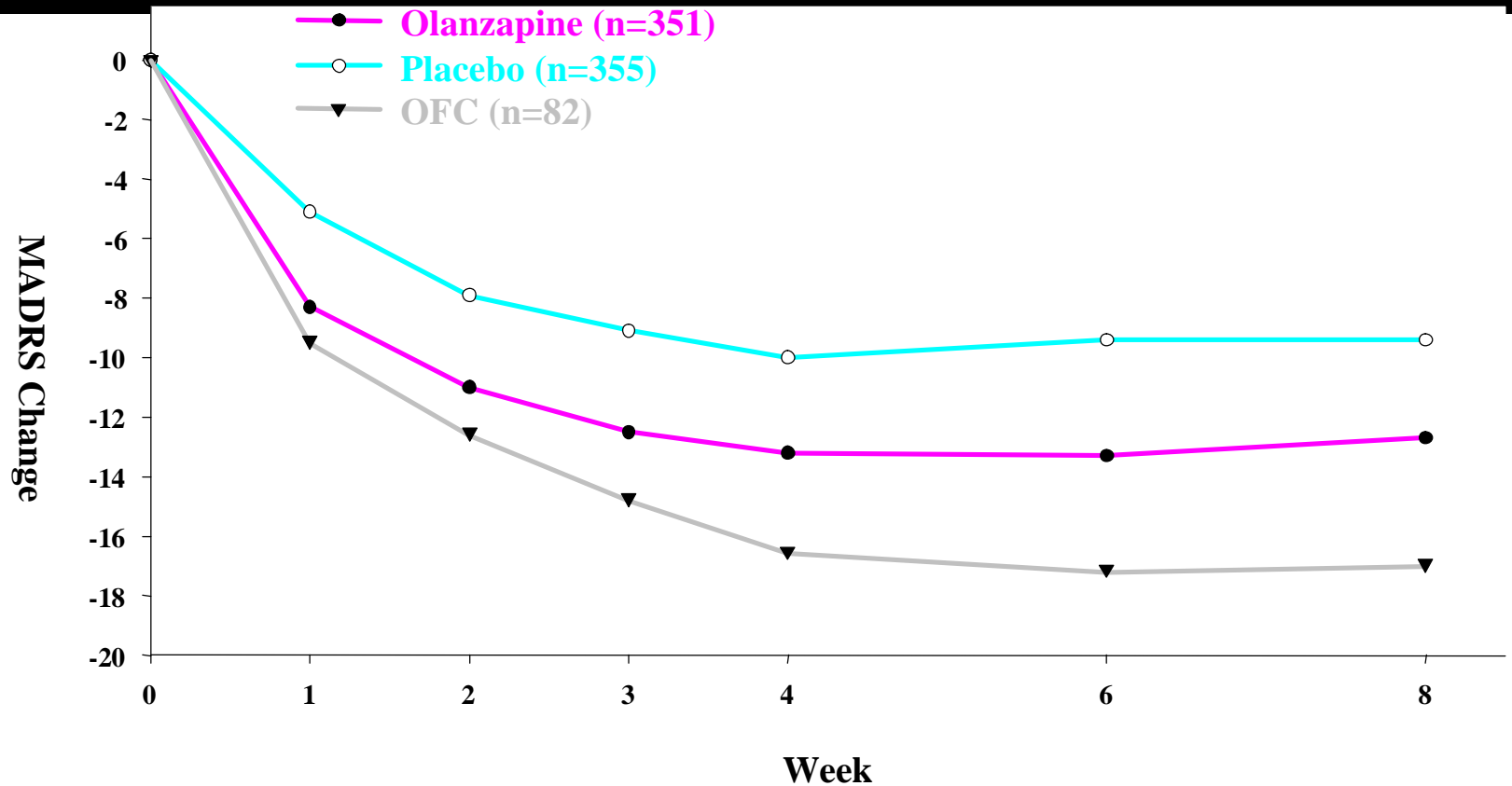
LAMOTRIGINE v. LITHIUM v. PLACEBO: TIME TO INTERVENTION FOR DEPRESSION



LAMOTRIGINE v. LITHIUM v. PLACEBO: TIME TO INTERVENTION FOR DEPRESSION



OLANZAPINE v. PLACEBO v. OLANZAPINE + FLUOXETIN FOR BIPOLAR DEPRESSION



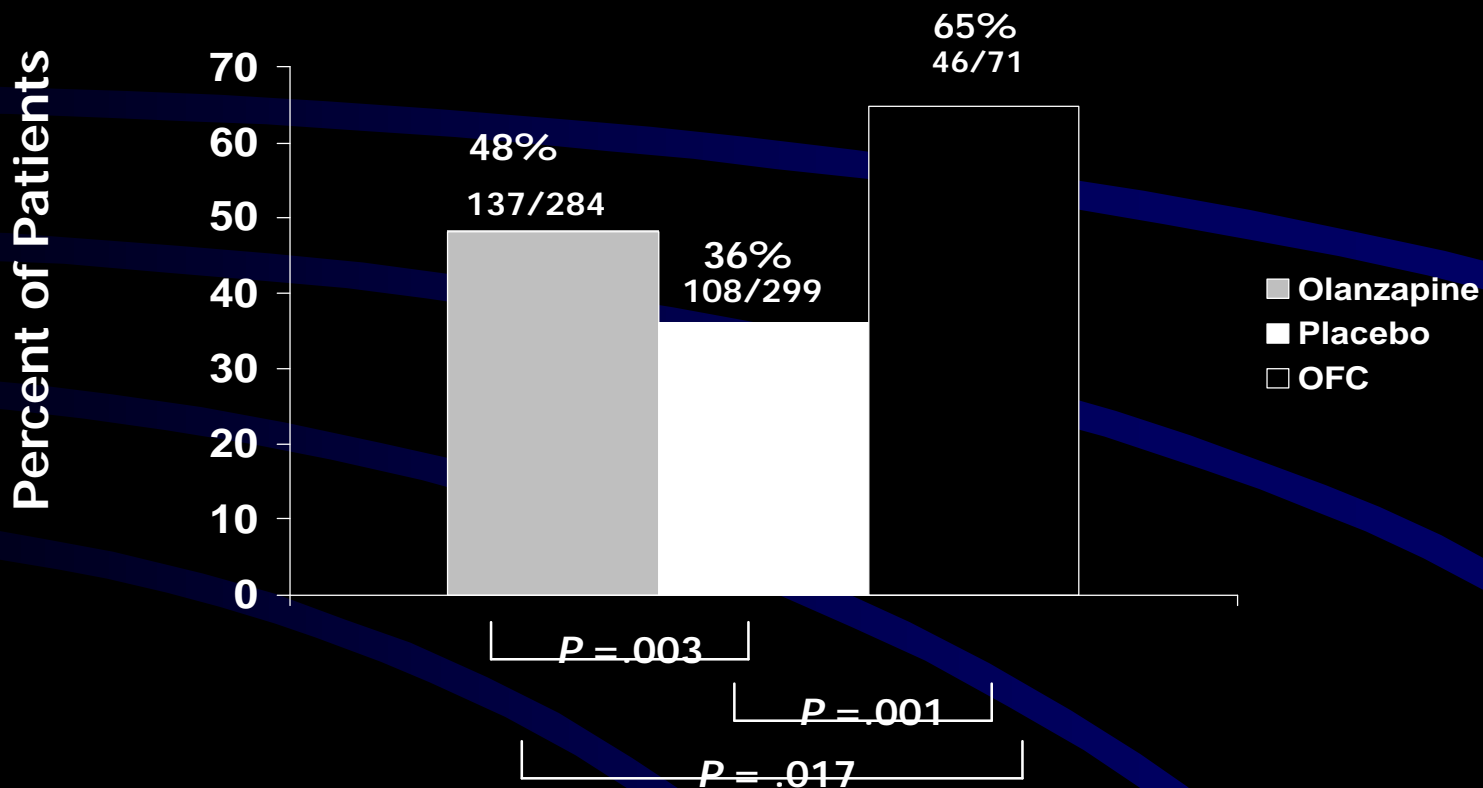
Olanzapine separates statistically from placebo at every Week (1, 2, 3, 4, 6 and 8) post-baseline.

OFC separates statistically from placebo at Weeks 1, 3, 4, 6 and 8 post-baseline.

OFC separates statistically from Olanzapine at Weeks 4, 6 and 8 post-baseline.

OLANZAPINE v. PLACEBO v. OLANZAPINE + FLUOXETINE FOR BIPOLAR DEPRESSION

50% decrease in MADRS Total Score

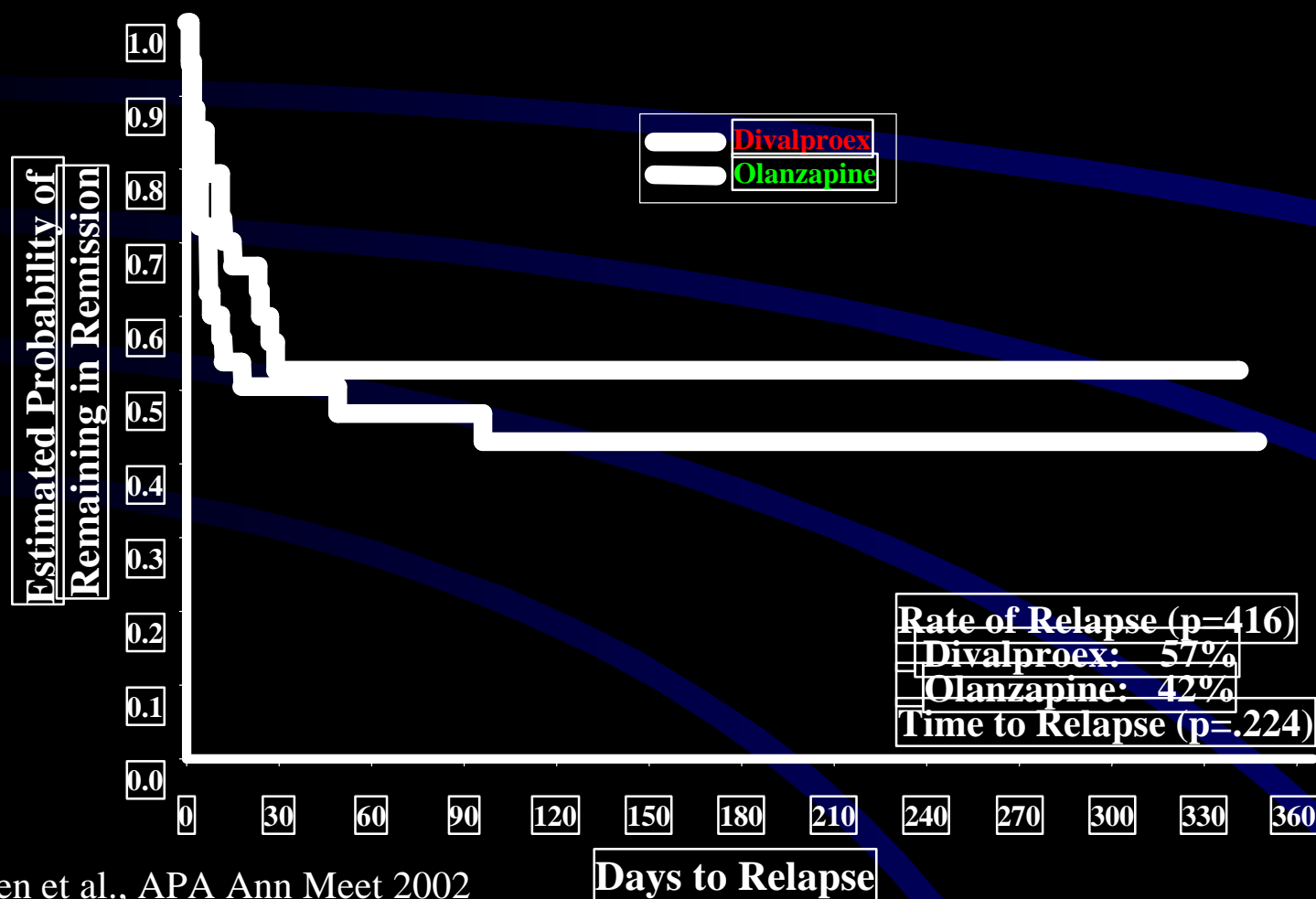


RELAPSE PREVENTION

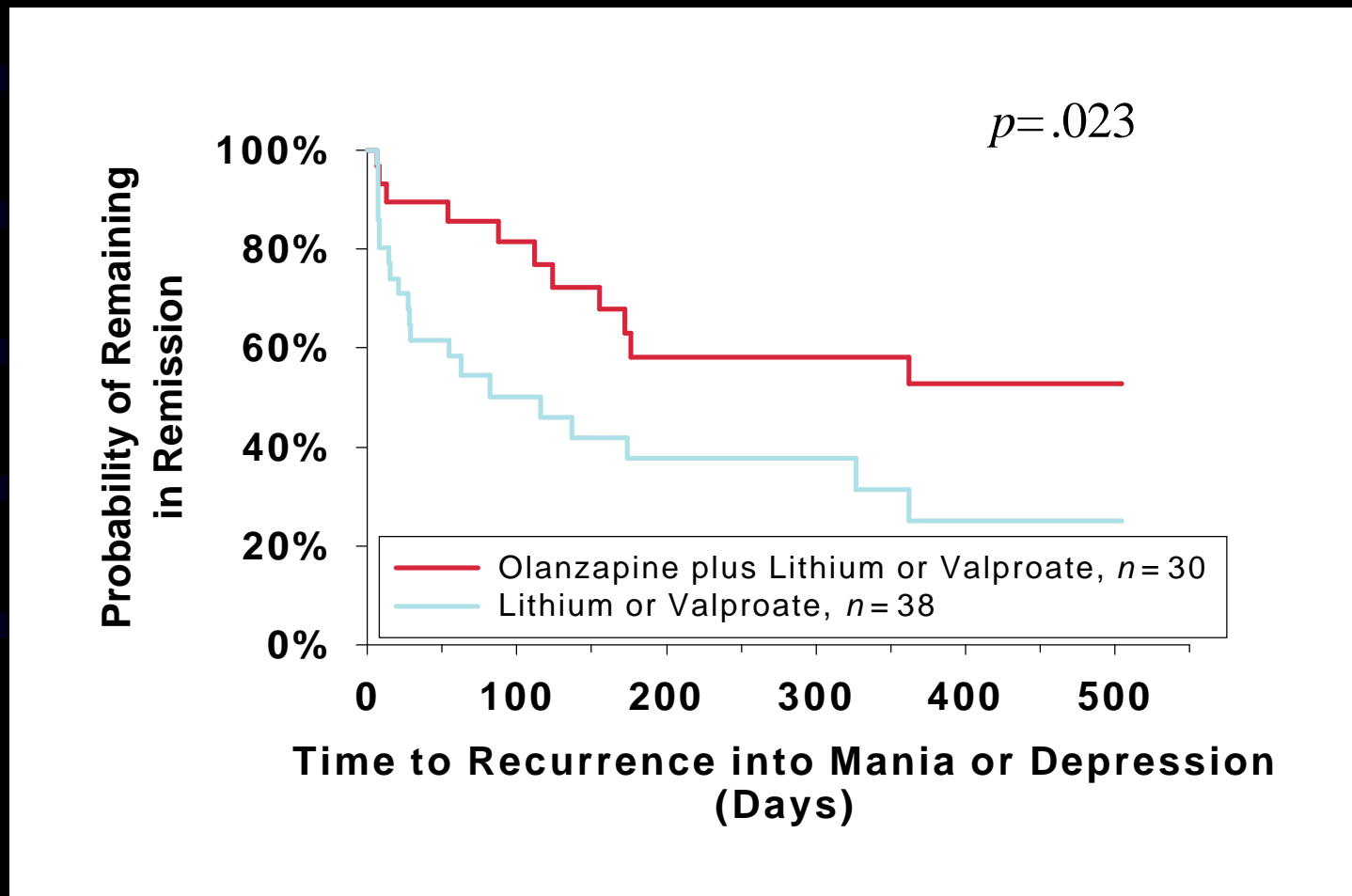
- Detect prodromal symptoms
 - psychoeducation models
- sleep hygiene
- avoiding mood destabilizers
- Impact of stress/life events

RANDOMIZED COMPARISON OF OLANZAPINE OR DIVALPROEX: SYMPTOMATIC RELAPSE OF BIPOLAR DISORDER

Y-MRS or HAM-D ≥ 15 after remission



TIME TO SYMPTOMATIC RECURRENCE OF MANIA OR DEPRESSION AFTER REMISSION OF MANIA AND DEPRESSION



Time to recurrence into either pole following symptomatic remission of mania (YMRS ≤ 12) and depression (HAMD-21 ≤ 8), was significantly longer for the olanzapine cotherapy group compared to the monotherapy group (estimated 25th percentile 124 vs 15 days, respectively).

Tohen et al., APA Ann Meet 2002

PRINCIPLES FOR MANAGEMENT OF BIPOLAR DISORDER

- Accurate diagnosis, including bipolar spectrum
- Recognize comorbidities
- Appropriate referral and management for target symptoms
- Treatment focus on medications that stabilize mood
- Avoiding mood destabilizers
- Lifelong management, medical model