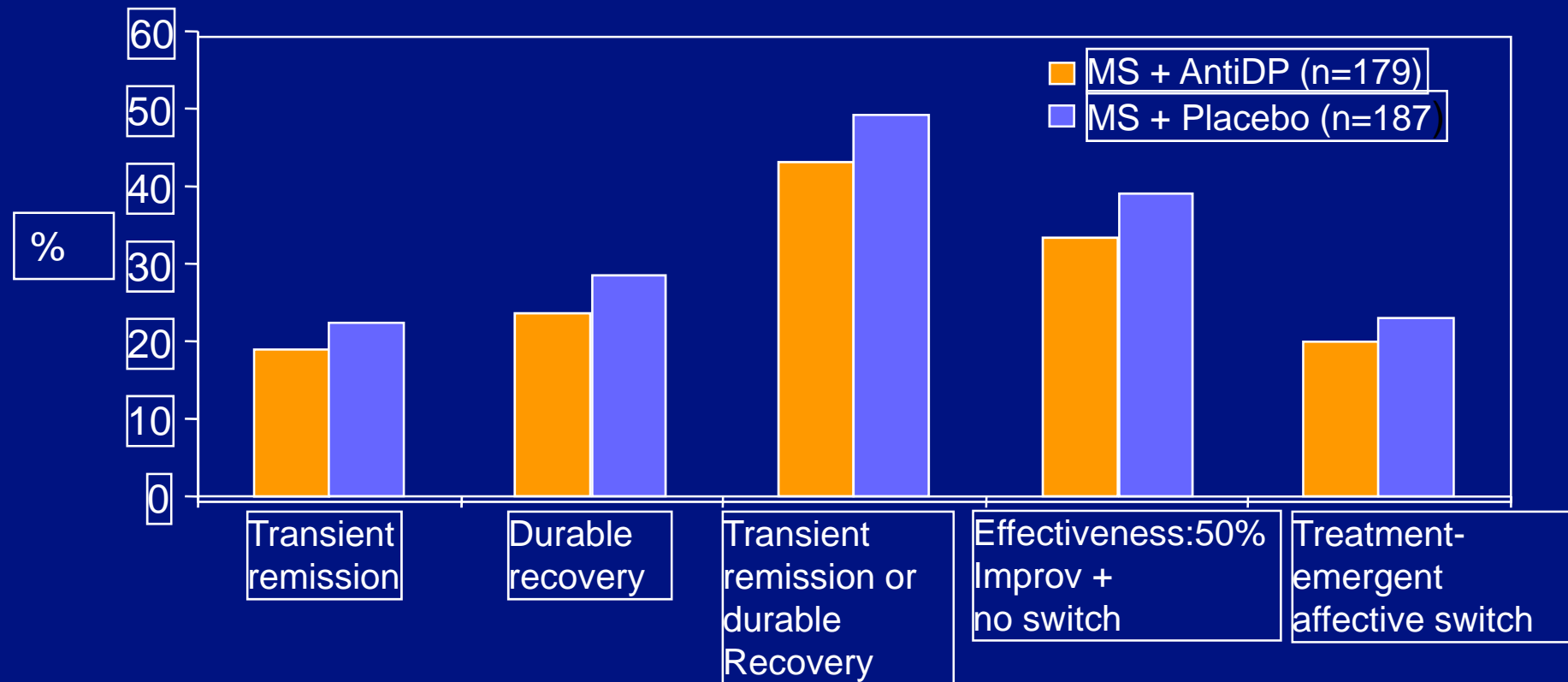


Treatment of Bipolar Depression: Discussion

Charles L. Bowden MD.

**Karren Endowed Chair of Psychiatry
Clinical Professor of Psychiatry
and Pharmacology
University of Texas Health Science Center
at San Antonio**

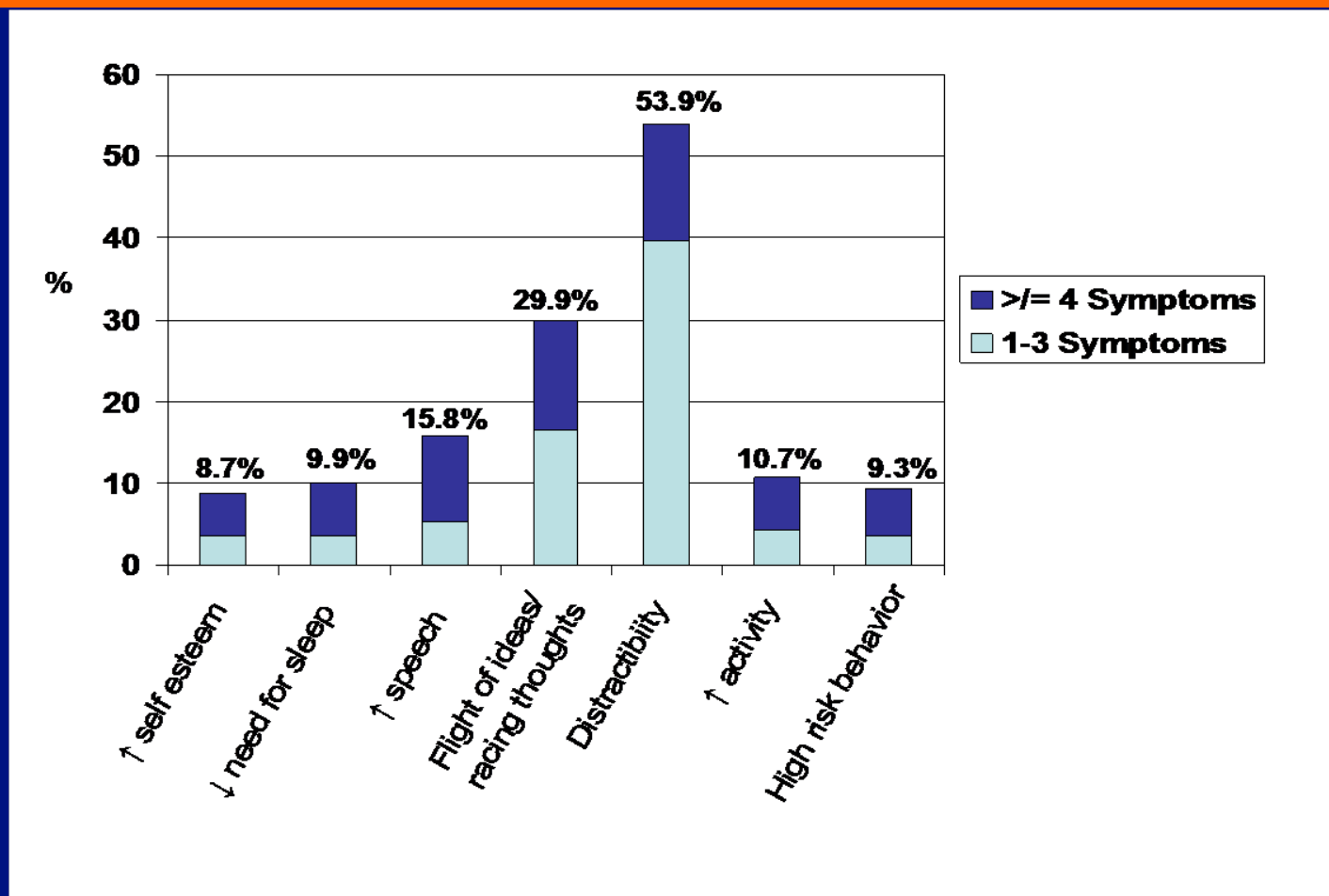
Effectiveness of Adjunctive Antidepressant Treatment for Bipolar Depression in 26 wk. Randomized Blinded Study



MS, mood stabilizers; AntiDP, antidepressants; Durable=8 consecutive wks of euthymia

Sachs G, et al. N Engl J Med 2007;356: 1711–22 (ClinicalTrials.gov number, NCT00012558.)

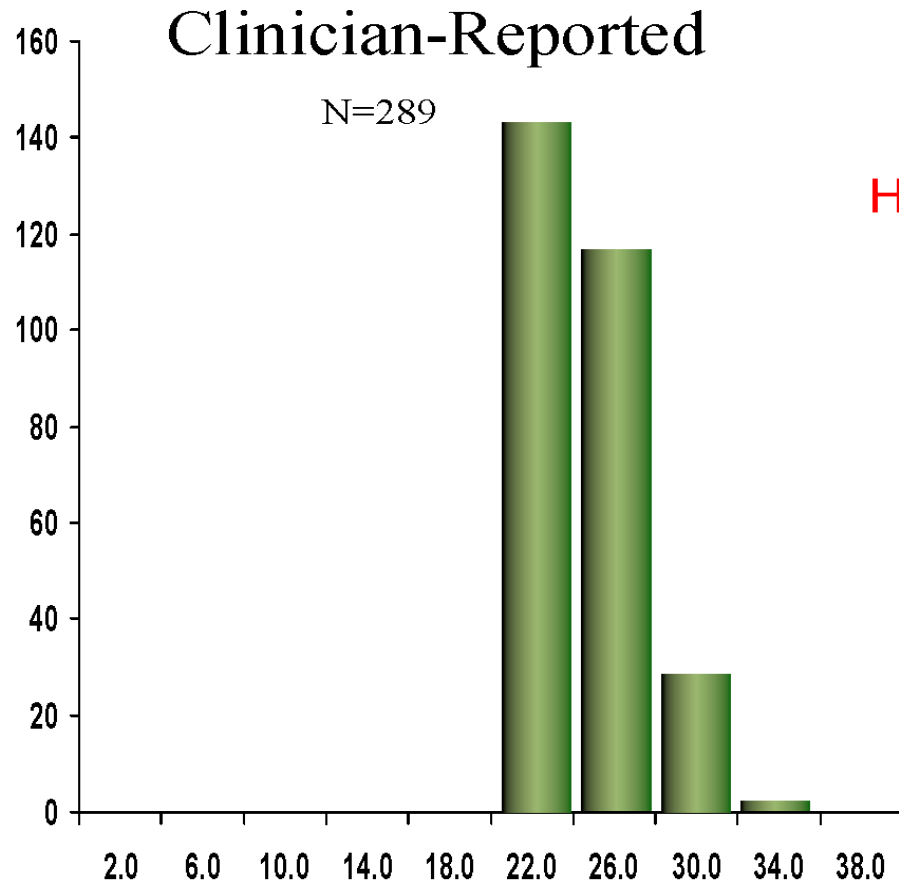
Symptoms of Mania During an Index Bipolar Depressive Episode in the NIMH STEP BD



31% had no manic symptoms. Neither elation or grandiosity were elevated

Antidepressant RCT: Baseline HAM-D Ratings

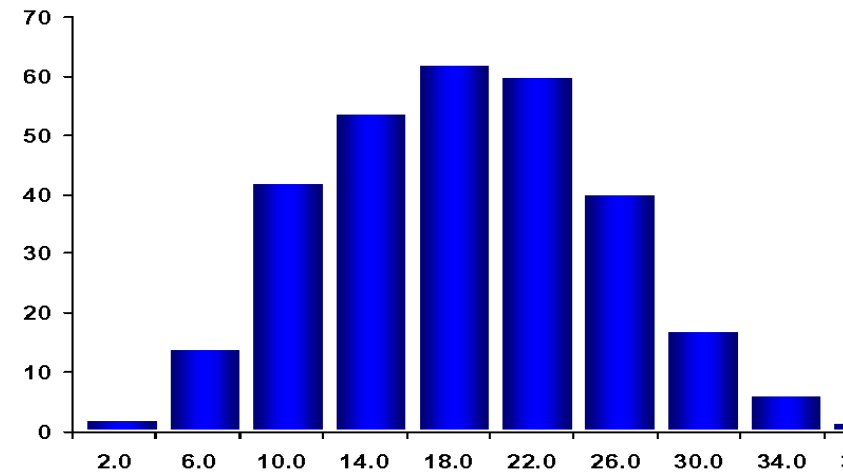
Evidence of Baseline Inflation



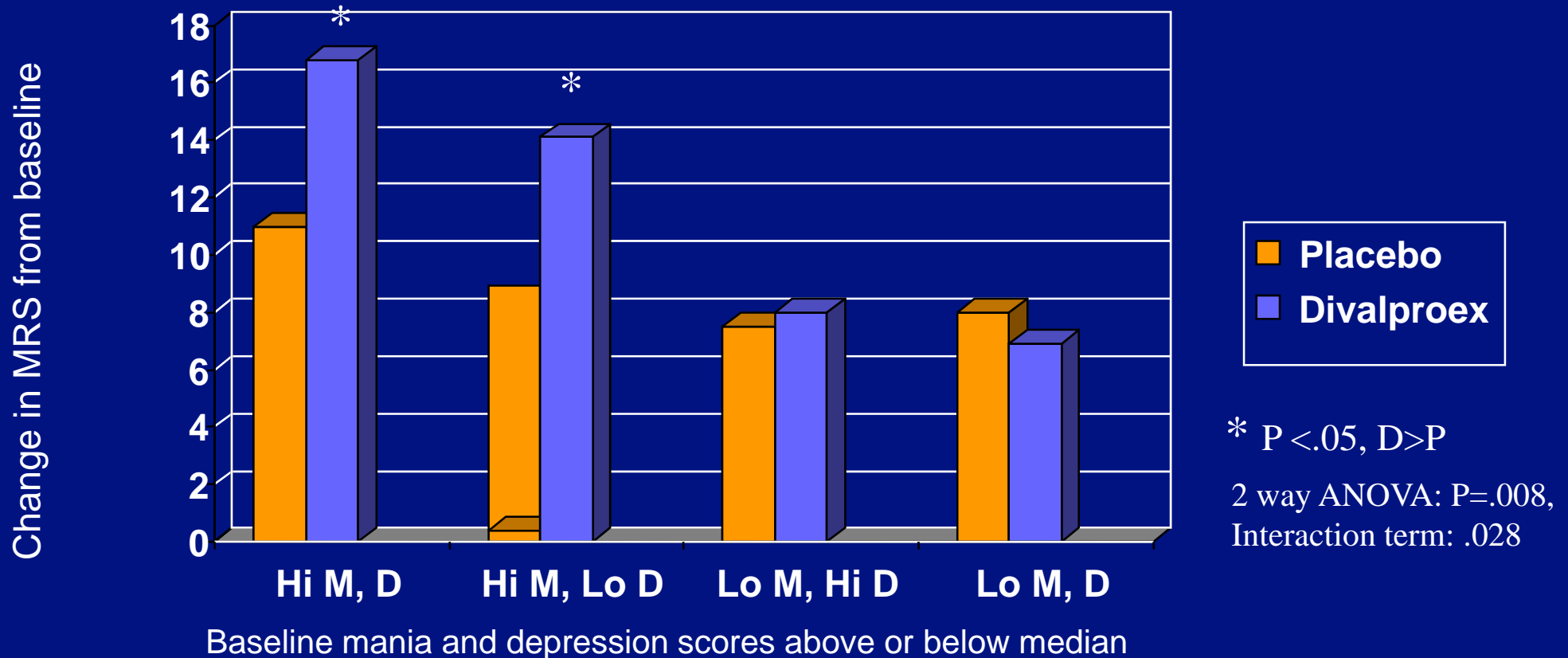
Patient-Reported (IVR)

N=289

Half the subjects had scores inflated by an average of 10 points

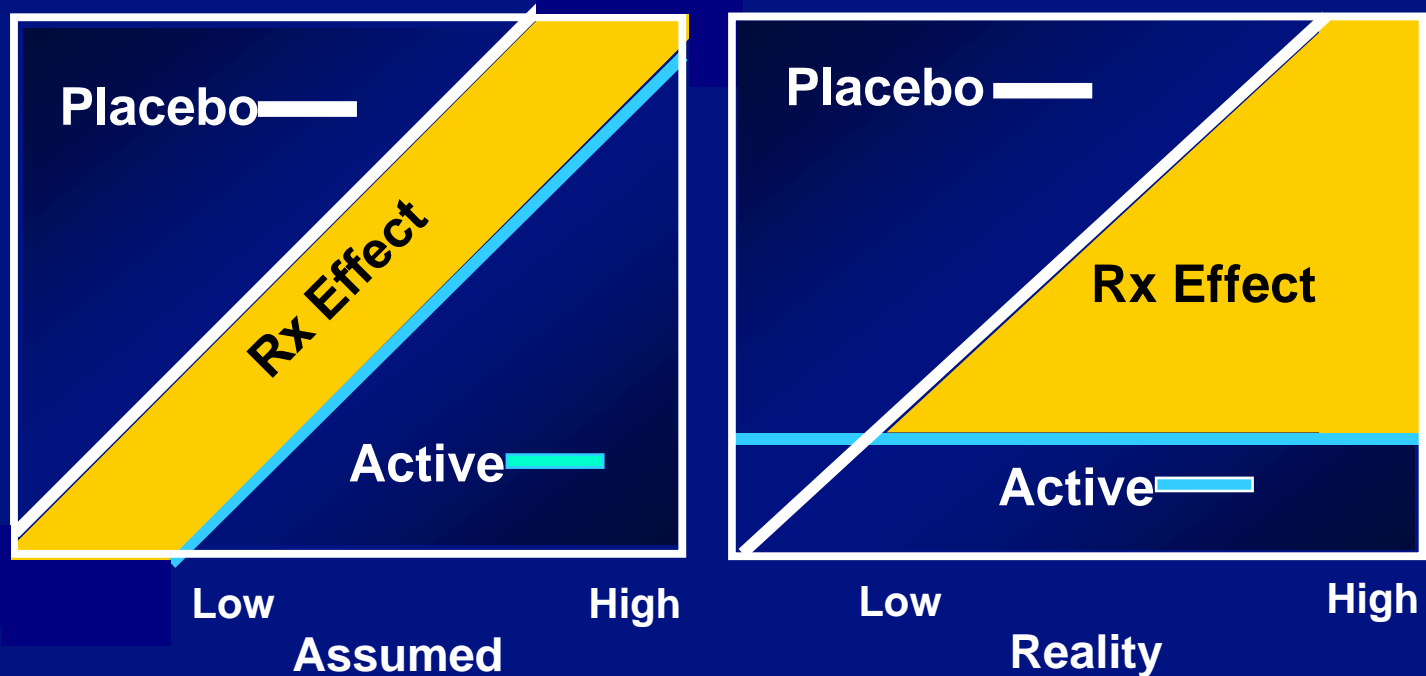


Consequence of Enrollment of Patients with Mild vs Severe Manic Symptoms



Effect of Initial Illness Severity on Drug-Placebo Difference

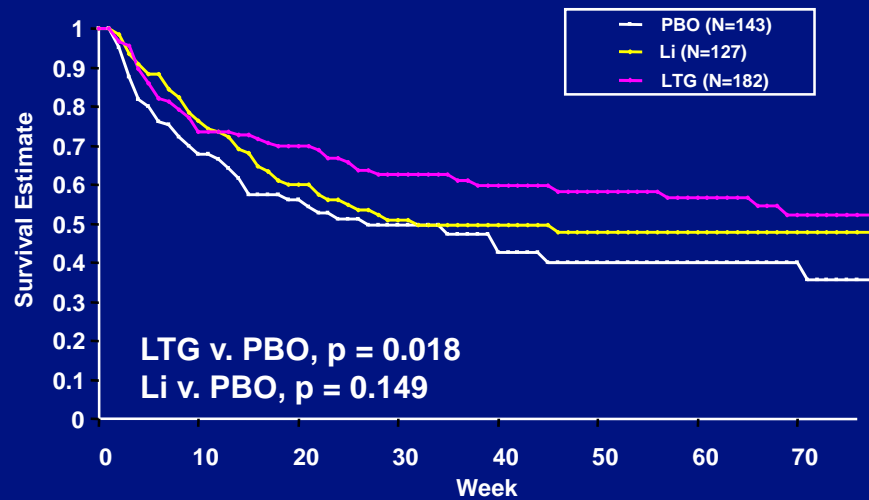
Post-Treatment
Severity



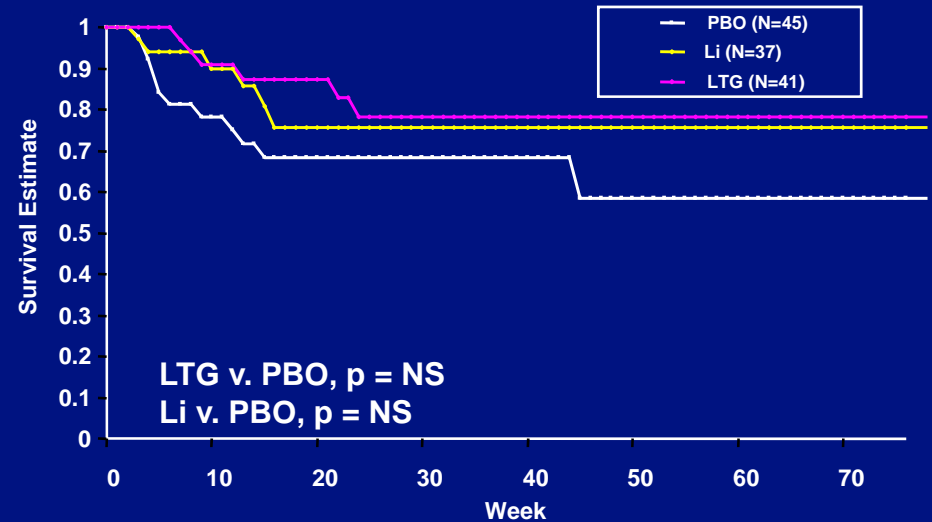
Pre-Treatment Severity

Uhlenhuth et al Psychopharm Bull 1997 33:31-9, Fisher et al, Psychopharmacologia 1965 7:57-60, Benjamin LS Psychosom Med 1963, 25:556-566

Time to Intervention for Depression in 18 Month Randomized Blinded Treatment



Polytherapy in acute, open phase



Lamotrigine only in acute, open phase

Effect of Acute Phase Treatment on Early Termination in 1 Yr. Trial of Divalproex vs Placebo

Open phase	Divalproex %	Placebo %	P
Divalproex	58.6	86.8	.002
Placebo	63.2	66.7	NS

Conclusions and Implications for Study Designs

- **Bipolar disorders are multidimensional**
- **Profiles of behavior domains reveal more than global measures of mania, depression**
- **Anxiety inadequately addressed in BD ratings and diagnosis**
- **Psychopathology of BD likely to be more effectively revealed by phenomics.**
- **More effective treatments likely to be discovered through profiling symptom areas benefited and those not benefited, effectiveness, and durable benefit.**