STEP-BD in Context

- STEP-BD was a national public health initiative designed to examine the effectiveness of treatments and their impact on the course of bipolar disorder.
  - 4360 patients enrolled from 1999-2005
- The program was conceived in response to an NIMH request seeking a common intervention model for studies of treatment effectiveness.
- Used a hybrid research design to collect longitudinal data as patients made transitions between naturalistic studies and randomized clinical trials.
- Ensured wide representation by including the full spectrum of bipolar patients presenting for clinical care (mood states, diagnostic specifiers, and comorbidities).

STEP-BD = Systematic Treatment Enhancement Program for Bipolar Disorder; NIMH = National Institutes of Mental Health
Sachs GS et al. Biol Psychiatry; 2003; 53:1028-1042
Design of STEP-BD

Three randomized care pathways (RCPs) initially offered:
- Acute Depression Study
- Refractory Depression Study
- Relapse Prevention Study

Sachs GS et al. *Biol Psychiatry,* 2003; 53:1028-1042; CMF = Clinical Monitoring Form
Effectiveness of Adjunctive Antidepressant for Bipolar Depression

Study question: Does adjunctive antidepressant therapy reduce symptoms of bipolar depression without increasing risk of mania?

Method

Patients - Adults with bipolar depression

Study Design and Treatments

- Randomized, double-blind, placebo-controlled study within STEP-BD (up to 26 weeks)
- Mood stabilizer + adjunctive antidepressant therapy
- OR
- Mood stabilizer + placebo

Rates of Durable Recovery*

- 24% in the adjunctive antidepressant group
- 27% in the placebo group
- p = 0.40
- Rates of treatment-emergent affective switch were similar in the two groups

*Durable recovery was defined as 8 consecutive weeks of euthymia. Sachs GS et al. N Engl J Med; 356;17; Apr 2007
### After Other Approaches Fail: Effectiveness in Treatment-Resistant Bipolar Depression

<table>
<thead>
<tr>
<th>Method</th>
<th>Study Design and Treatments</th>
<th>Primary Outcome Measure: Rate of Recovery*</th>
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| Patients with Treatment-Resistant Bipolar Depression | Patients were randomly assigned to receive one of three refractory depression interventions for up to 16 weeks in addition to their current open-label treatment with mood stabilizer with active antidepressant:  
- Mood stabilizer  
- Vitamin B8 (inositol)  
- Antipsychotic | - 66 patients  
- No significant between-group differences were seen when any pair of treatments were compared, however recovery rates were highest with mood stabilizer (24%) compared with inositol (17%) and antipsychotic (5%)  
- Patients receiving mood stabilizer had lower depression ratings, lower CGI-Severity scores, greater GAF scores |

*Rate of recovery = no more than two symptoms meeting DSM-IV threshold criteria for a mood episode an no significant symptoms preset for 8 weeks. Nierenberg AA et al., Am J Psychiatry; 163:2, Feb 2006. CGI-Severity = Global Clinical Impression – Severity; GAF = Global Assessment of Functioning*
## Predictors of Recurrence

**Method**

For those who were symptomatic at study entry but subsequently achieved recovery, time to recurrence of a mood episode was examined.

1,469 patients symptomatic at study entry (observation period was up to 2 years)

**Findings**

- 58% achieved recovery
- 49% of these patients experienced recurrences:
  - 35% depressive recurrence
  - 14% manic, hypomanic, or mixed episode recurrence
- Majority of relapses were to depression. Ratio for depressive recurrences versus manic/hypomanic/mixed was 2.5:1

**Predictors of recurrence to depression**:
Residual depressive or manic symptoms at recovery; depression and anxiety in preceding year

**Predictors of recurrence to mania, hypomania, or mixed**:
- residual manic symptoms at recovery; proportion of days of elevated mood in preceding year

*Perlis RH et al. Am J Psychiatry; 163:2; Feb 2006*