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# Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD)

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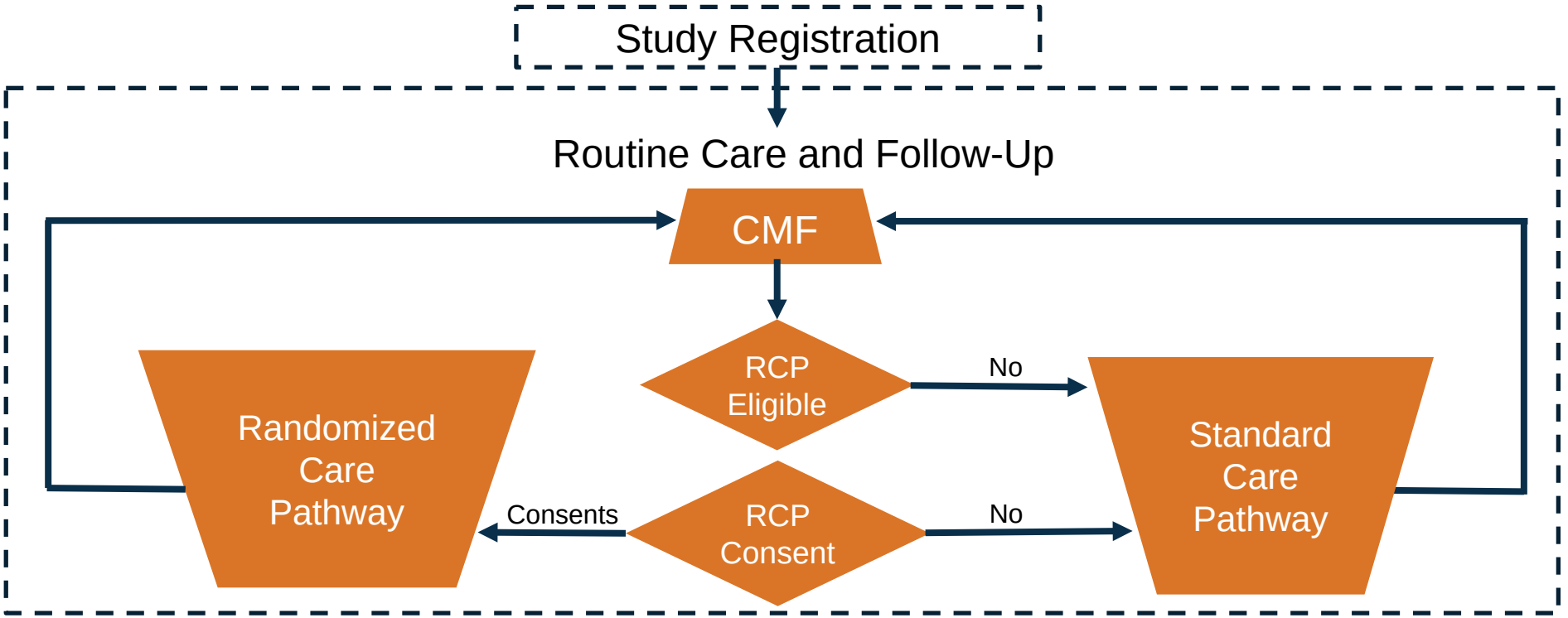
# STEP-BD in Context

- 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



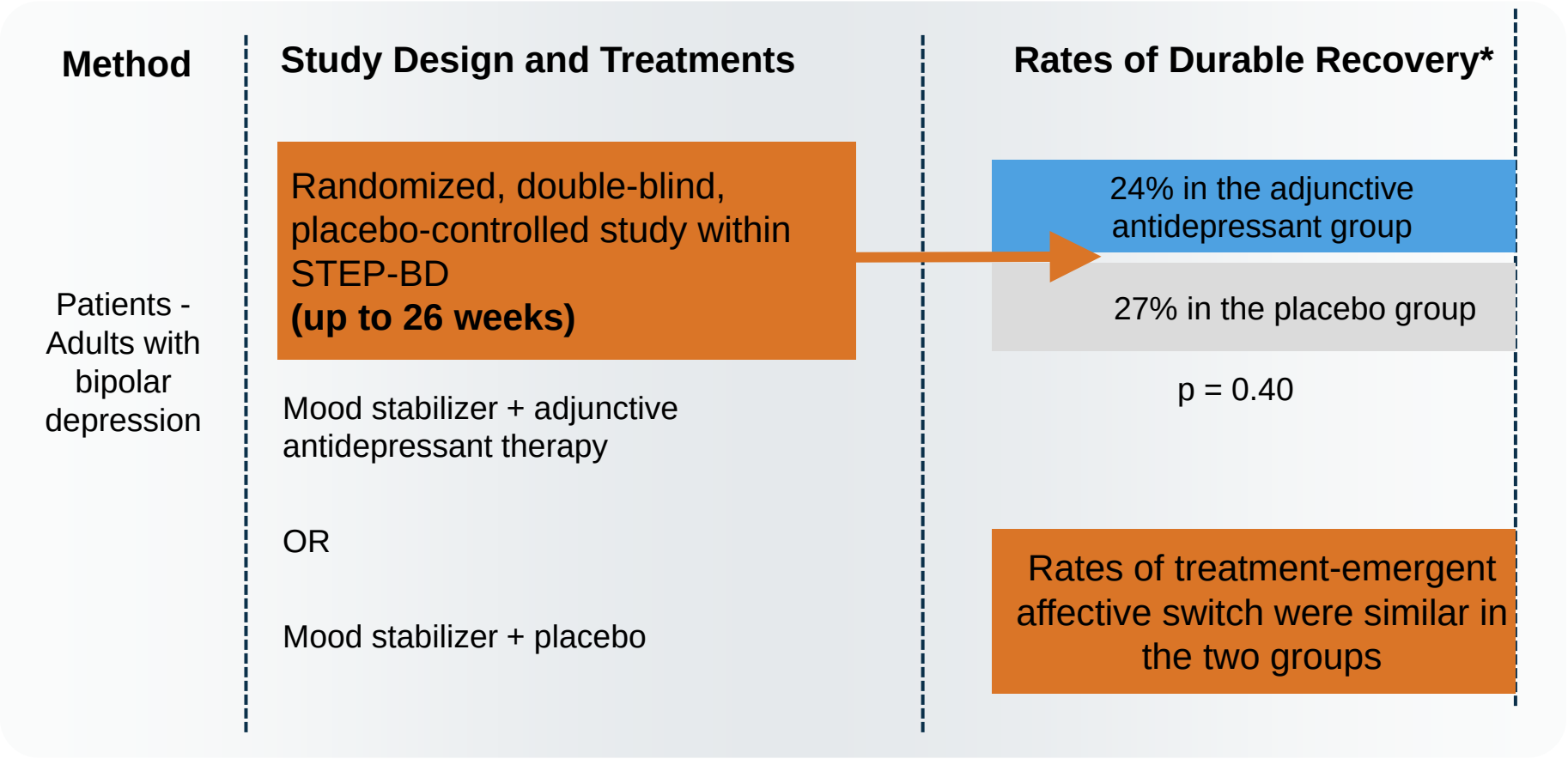

Three randomized care pathways (RCPs) initially offered:

- 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?**




*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

**Method**

Patients with Treatment-Resistant Bipolar Depression

**Study Design and Treatments**

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

**Primary Outcome Measure: Rate of Recovery***

- 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