

Fast Facts about the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE)

This summary provides details about the phases, design, and results of the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE). To learn more go to www.mentalhealthamerica.net/go/research/catie.

CATIE Background

- Funded by National Institutes of Mental Health; conducted from January 2001 - December 2004.
- Overseen by clinician team from University of North Carolina, Yale University, Duke University and Columbia University. Data analysis conducted by Quintiles.
- Study followed 1,460 participants with DSM-IV diagnosis of schizophrenia.
- Trials occurred at 57 sites in 23 states (e.g., mental health clinics, VA facilities, academic health centers).

Study Demographics

- Age: 18-65 years old (average age = 40)
- Gender: 74 % male; 26% female
- Race/Ethnicity:
 - 60% White/Caucasian
 - 35% African American/Black
 - 12% Spanish, Hispanic or Latino
 - 2% Asian
 - Less than 1% American Indian or Alaska Native
 - Less than 1% Native Hawaiian or other Pacific Islander
 - 2% identified as "two or more races"

- Employment status: 85% unemployed.
- Illness Severity:
- 75% of study participants termed "moderately ill" at beginning of study.
- One-third had experienced exacerbation of symptoms in previous three months
- Study excluded individuals experiencing first-episode or treatment-refractory schizophrenia

Study Design

CATIE was a three-phase study design with some additional treatment arms depending on patient experience during the trials. The details of each phase are outlined below, with demographic information, a summary of findings and links to further information.

Phase 1

- Participants randomly assigned to one of five medications, including one older-generation antipsychotic medication (perphenazine) and four atypical antipsychotics (olanzapine, risperidone, ziprasidone and quetiapine)
- Findings published in *New England Journal of Medicine*, September 22, 2005 (<http://content.nejm.org/cgi/content/abstract/353/12/1209>).
- Average discontinuation rates across all the study medications (for any reason) were 74%.

Olanzapine (64%)

Risperidone (74%)

Perphenazine (75%)

Ziprasidone (79%) - in later stage of recruitment

Quetiapine (82%)

- Across the medications, an average of 39% of participants discontinued treatment due to lack of efficacy or intolerability; 30% due to a decision by the participant or his/her advocate; and 5% for other reasons. The findings did not include the reasons why participants/patient advocates decided to discontinue treatment.

- Rates of discontinuation due to lack of efficacy were highest for quetiapine (28%) and lowest for olanzapine (15%).
- Rates of discontinuation due to intolerability were highest in olanzapine (18%) and lowest for risperidone (10%).
- Overall, Olanzapine was found to have the highest level of efficacy in reducing symptoms had the lowest rate of exacerbation of symptoms that required hospitalization. However, Olanzapine also had the highest incidence of discontinuation due to side effects related to weight gain and metabolic issues (9%).
- Perphenazine had the highest rate of discontinuation due to extrapyramidal side effects (EPS) - 8%. This was at least double the rate of any other study medication.

Phase 1B

- Of the 257 patients who were initially randomized to perphenazine in Phase 1, 192 discontinued the medication for various reasons, including ineffectiveness and intolerable side effects. Among those who discontinued, 114 agreed to be re-randomized to double-blind treatment with one of three newer antipsychotic medications- olanzapine, quetiapine or risperidone to determine if there were differences among the three treatments in effectiveness (time to discontinuation). Secondary outcomes were reasons for discontinuation and tolerability.
- Findings published in *American Journal of Psychiatry*, March 1, 2007 (<http://ajp.psychiatryonline.org/current.dtl>).
- The time to discontinuation for all causes was significantly longer for quetiapine (median 9.9 months) and olanzapine (median 7.1 months) than for risperidone (3.6 months).
- Quetiapine, and to some extent olanzapine, may be more effective than risperidone among patients who were originally taking, but had to discontinue, perphenazine-an older, first generation antipsychotic medication. NOTE: Although the phase 1B patients were very similar to those entering phase 1 of the study with regard to age, duration of illness, and symptom severity, all patients had received and not responded well to perphenazine. They may have represented a group of patients who are relatively unresponsive to or intolerant of the

higher affinity for the dopamine D2 receptor that is characteristic of older antipsychotic drugs. In this context, quetiapine is the least and risperidone the most like perphenazine, with olanzapine being intermediate.

- The patients assigned to olanzapine gained more weight than the patients who took the other drugs, with a mean gain of 1.6 pounds per month. A weight gain of more than 7% of the baseline body weight occurred in a larger proportion of patients taking olanzapine than patients taking risperidone or quetiapine. Olanzapine was associated with substantial increases in total cholesterol and triglyceride levels, while risperidone and quetiapine were associated with more modest increases in these measures, even after the duration of drug treatment was controlled for. Only risperidone was associated with a substantial increase in prolactin level.

- The study concluded that, "effectiveness and acceptability of antipsychotic drugs appears to vary considerably according to clinical circumstances."

- Demographics Phase 1B

N=114

- Gender: 77% male; 23% female
- Age: 18-65 years old (average age = 40.8)
- Race/Ethnicity for olanzapine:
 - 65% White/Caucasian
 - 33% African American/Black
 - 2 %Asian American
 - 14% Spanish, Hispanic or Latino

Phase 2

- Participants who decided to switch to another medication due to lack of efficacy were re-randomized to one of the other study drugs or clozapine in Phase 2E. If the switch was due to side effect problems (tolerability), patients were re-randomized to ziprasidone or another atypical antipsychotic (Phase 2T).

- Phase 2 findings published in *American Journal of Psychiatry*, April 1, 2006

(http://ajp.psychiatryonline.org/content/vol163/issue4/#IN_THIS_ISS)

UE)

- Of the 1,052 participants with DSM-IV diagnosis of schizophrenia who discontinued phase 1 treatment before 18 months, 509 left the study entirely, 99 participants entered the efficacy pathway (2E), and 444 entered the tolerability pathway (2T).

Phase 2E

- Participant Demographics Phase 2E (efficacy):
- Age: 18-65 years old (average age = 39.7)
- Race/Ethnicity:
 - 64% White/Caucasian
 - 33% African American/Black
 - 14% Spanish, Hispanic or Latino
 - 3% Other
- Results of efficacy pathway (Phase 2E):
- Clozapine was remarkably effective in this group of study participants and was substantially better than all the other atypical medications.
- 20 out of 45 patients (44%) who received clozapine were able to stay on clozapine for the rest of the study, whereas only eight out of 45 patients (18%) who received another atypical antipsychotic medication were able to stay on that medication to complete the study.
- Participants taking clozapine remained on it for an average of 10 months compared to an average of three months for those taking any of the three other medications.
- Those taking clozapine also had greater symptom reduction than those who took any of the other medications. Only one patient developed agranulocytosis (and was taken off clozapine).

Phase 2T

- Participant Demographics Phase 2T (tolerability):
- Age: 18-65 years old (average age = 40.8)
- Race/Ethnicity:
 - 66% White/Caucasian
 - 30% African American/Black

13% Spanish, Hispanic or Latino

4% Other

- Results of tolerability pathway (2T):
- About 35% of the participants who took olanzapine or risperidone were able to continue on their medication until the end of the 18 months of the study. This compares to only 23% of those who took ziprasidone and 16% of those who took quetiapine that were able to continue.

Phase 3

- Physicians could switch participants to any of eight medications, including the five previously-studied medications, fluphenazine, decanoate or aripiprazole, or introduce a second atypical antipsychotic. This phase has not yet been released.