

Medication Approaches to Reduced Hospitalization

Scott Stroup, MD, MPH

Clozapine – renewed interest

- Newer antipsychotic medications have not matched clozapine's effectiveness for people with treatment-resistant schizophrenia
- Continued lack of evidence for alternative strategies, including antipsychotic polypharmacy

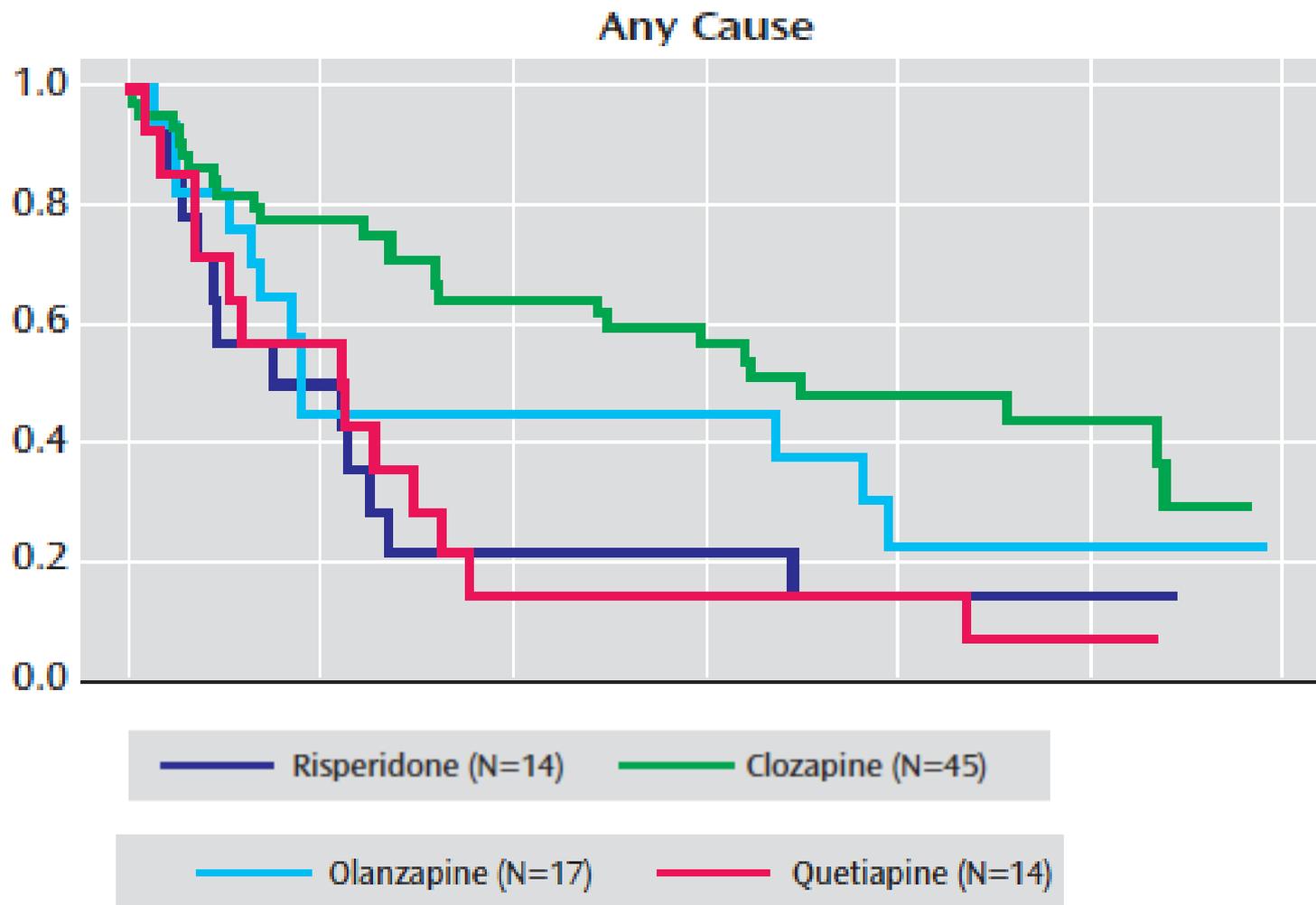
Randomized trial of clozapine versus usual care

- Long-term patients in Connecticut's state hospitals (N = 227) were followed for 2 years.
- Clozapine was associated with significantly greater reductions in hospitalization
- No difference symptoms or improving quality of life
- No difference in likelihood of discharge; once discharged, clozapine patients were less likely to be readmitted.

Clozapine Indications

1. “Treatment resistance”—Management of severely ill schizophrenic patients who fail to respond adequately to standard drug treatment for schizophrenia, either because of insufficient effectiveness or the inability to achieve an effective dose due to intolerable adverse effects.
2. Suicidal behaviors—Reducing the risk of recurrent suicidal behavior in patients with schizophrenia or schizoaffective disorder who are judged to be at chronic risk for re-experiencing suicidal behavior, based on history and recent clinical state.

Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Phase 2E: Time to Discontinuation



Factors Associated with Clozapine Use Among New York State (NYS) Medicaid Recipients

- Aim: To identify factors associated with initiating clozapine versus initiating other antipsychotic medications
- Sample included 7,035 Medicaid recipients
- Eligibility criteria
 - Schizophrenia or schizoaffective disorder
 - At least one clinic service and had an antipsychotic prescription filled in 2009
 - Medicaid eligible 2008-2009
- Logistic regression: initiation of clozapine (n=144, 2%) versus other antipsychotics (n=6,891, 98%)

What Factors are Related to Clozapine Initiation in NYS Medicaid?

	Odds Ratio	95% CI
Age	.96 ^{***}	.94 – .97
Male	1.32	.93 – 1.89
Race/ethnicity ^a		
Black, non-Hispanic	.57 ^{**}	.38 – .86
Hispanic	.47 [*]	.24 – .91
Other	.81	.52 – 1.26
State auspice	2.28 ^{***}	1.46 – 3.56
# different antipsychotics, past year	1.13 [†]	.98 – 1.31
Substance use disorder, past year	.46 ^{***}	.30 – .71
Inpatient hospital admissions, past year ^b		
1-2 admissions	1.64 [*]	1.05 – 2.59
3+ admissions	1.88 [*]	1.03 – 3.45
Psychiatric costs, past year	1.46 ^{***}	1.27 – 1.69

***p≤.001, **p ≤.01, *p≤.05, †p≤.10

^aReference group = white, non-Hispanic

^bReference group = no inpatient hospital admissions

Summary of clozapine evidence

- Consistently the most effective medicine for people with “treatment-resistant” schizophrenia
- No clear advantages in “all comers” or first episode schizophrenia
- CATIE: clozapine better than other “Second Generation Antipsychotics (SGAs)” after treatment discontinuation due to inefficacy
- Lower readmission rates in state hospital study

Argument for improved clozapine prescribing

- Best available treatment for certain situations
 - (treatment-resistance, persistent suicidality)
- Widely underused
- Disparities in use
- Unproven, more expensive approaches are much more common
- Potential for decreased readmissions because the best available treatment for severely ill individuals

Long-acting Injectable
(Depot)
Antipsychotic Medications

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Long-acting Injectable (LAI) (Depot) Antipsychotic Medications

- Schizophrenia Patient Outcomes Research Team (PORT) 2009 recommendation:

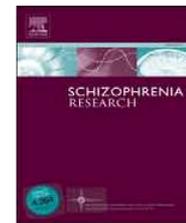
“LAI antipsychotic medication should be offered as an alternative to oral antipsychotic medication for the maintenance treatment of schizophrenia when the LAI formulation is preferred to oral preparations.”

PORT Summary of Evidence

- Significant gaps in the evidence base
- No clear evidence that LAI antipsychotic medications reduce the risk of relapse in comparison to oral antipsychotic agents
- No data to support their use over orals as first-line treatments
- Current evidence is insufficient to recommend a specific LAI antipsychotic agent over another



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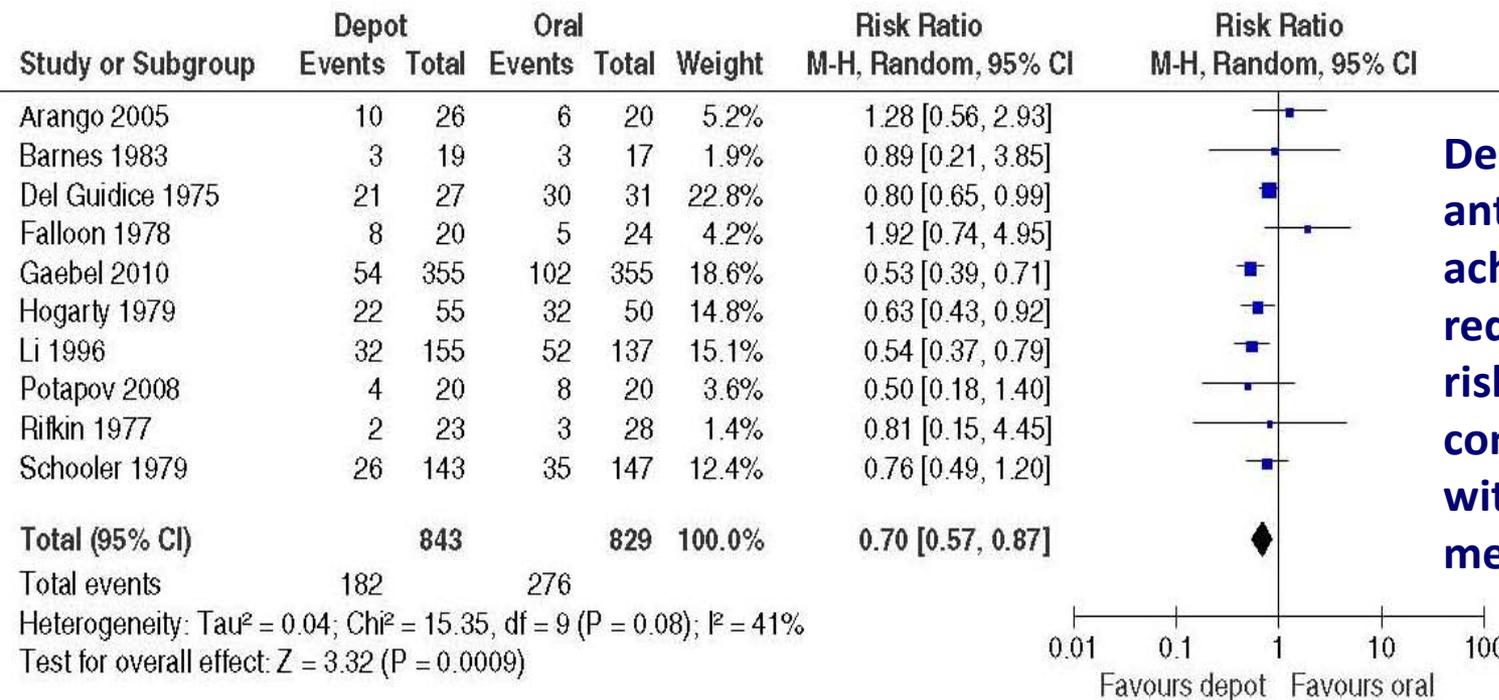
Oral versus depot antipsychotic drugs for schizophrenia—A critical systematic review and meta-analysis of randomised long-term trials

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Veteran Affairs (VA) Study 555

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Long-Acting Risperidone and Oral Antipsychotics in Unstable Schizophrenia

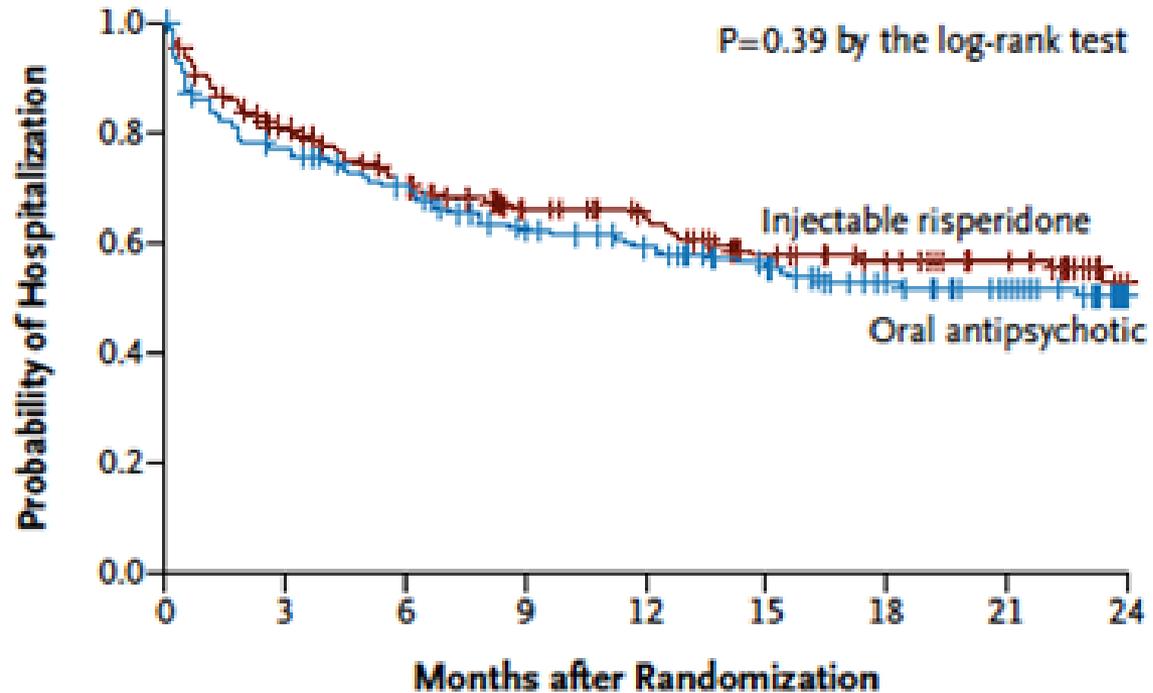
Robert A. Rosenheck, M.D., John H. Krystal, M.D., Robert Lew, Ph.D.,
Paul G. Barnett, Ph.D., Louis Fiore, M.D., M.P.H., Danielle Valley, M.P.H.,
Soe Soe Thwin, Ph.D., Julia E. Vertrees, Pharm.D.,
and Matthew H. Liang, M.D., M.P.H., for the CSP555 Research Group*

N ENGL J MED 364;9 NEJM.ORG MARCH 3, 2011

VA Study 555

- 369 participants with schizophrenia or schizoaffective disorder
- Hospitalized within last 2 years or at imminent risk of hospitalization
- Randomized to risperidone microspheres 25-50 milligrams (mg) every 2 weeks OR psychiatrist's choice of oral antipsychotic
- Primary outcome: Hospitalization
- Up to 2 years of follow-up

VA Study 555



No. at Risk

Oral antipsychotic	182	136	116	96	84	71	58	49	28
Injectable risperidone	187	136	110	92	82	65	53	45	37

VA Study 555

- Psychiatric symptoms, quality of life, scores on the Personal and Social Performance scale of global functioning, and neurologic side effects were not significantly improved with long-acting injectable risperidone as compared with control treatments.
- **CONCLUSION:** Long-acting injectable risperidone was not superior to a psychiatrist's choice of oral treatment

Conclusions

- Limited evidence on best medications to reduce re-hospitalizations
- Clozapine the best available antipsychotic for treatment-resistant schizophrenia
- Long-acting injectable medications logical and promising but research evidence is not strong, possibly due to methodological challenges