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Relapse Prevention In Schizophrenia

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Relapse Prevention In Schizophrenia

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Declaration

- Janssen Group
- Eli Lilly
- Astra Zeneca
- Nicholas Piramal-Rosch
- Sun Pharma- India
- Consultant
- Advisor
- Drug trial coordinator
- Research Investigator
- Reviewer
- Speaker
- Educational Groups

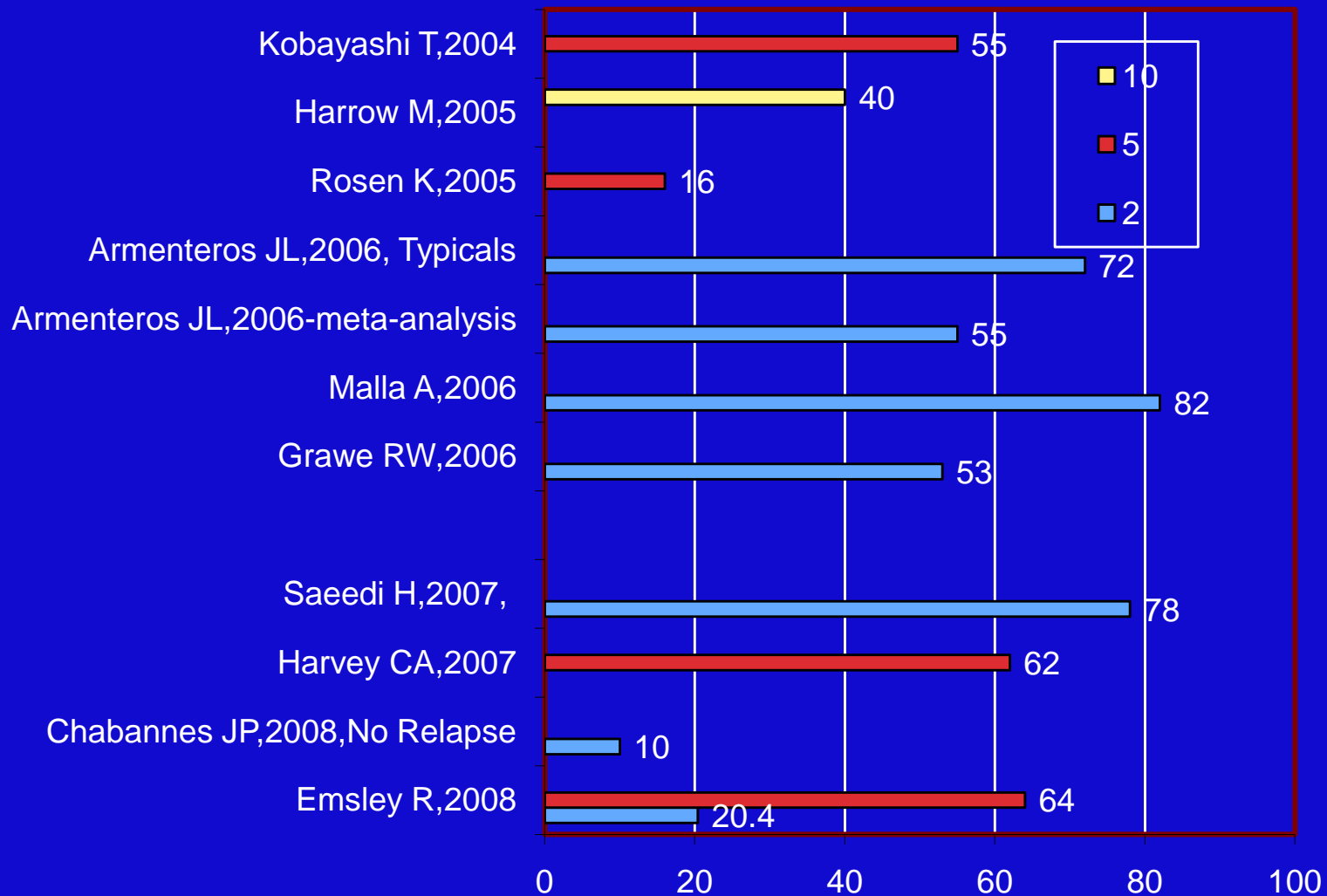
Relapse in schizophrenia: Current issues

- Nature of relapse
- What causes Relapse
- How to minimize
- What is beyond relapse prevention in improving outcome

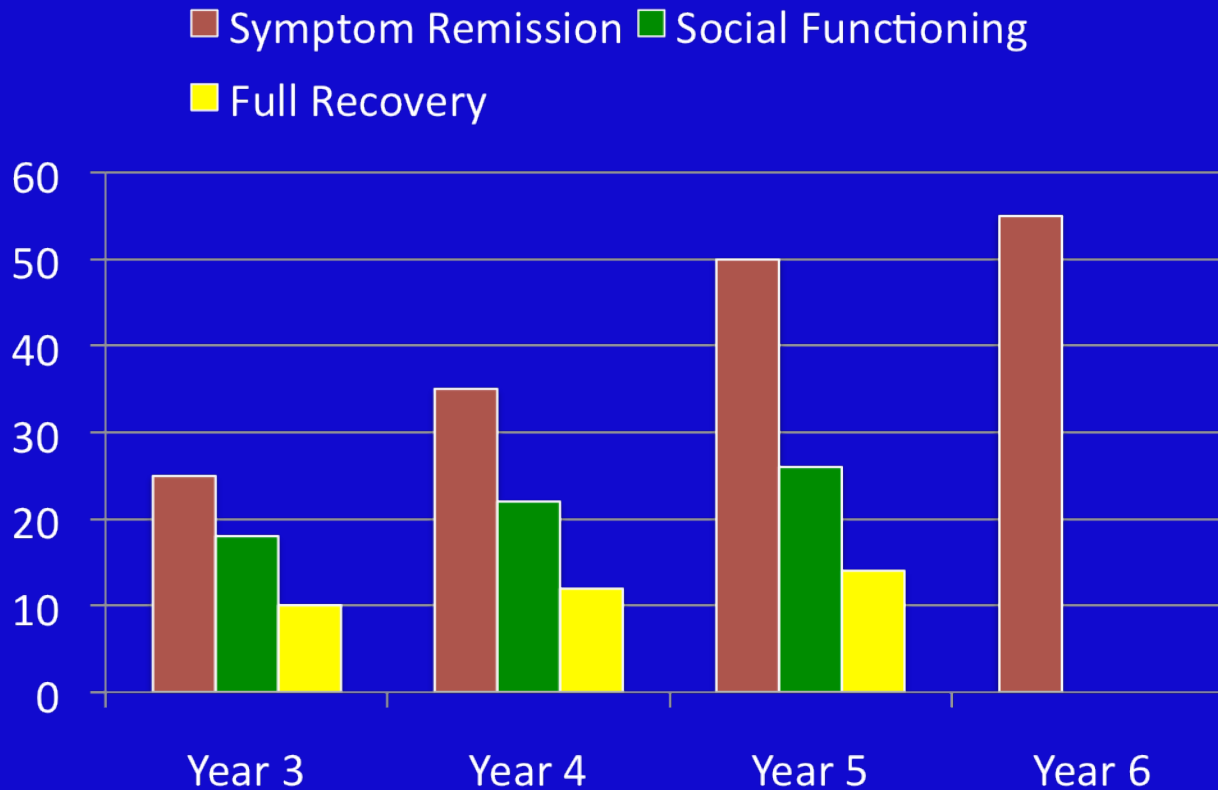
Relapse: 'Life is never the same again'

- Expected in 70% patients after First episode
- 70% of patients show an incomplete remission after first episode
- This includes Cognitive decline (in 55%)
- persistence of negative symptoms (in 41%),
- often associated with Social disabilities,
- Social Decline and a worsened QOL.
- Risk of relapse after an episode remained increased throughout the life.

Outcome-Recent Studies, Early Intervention

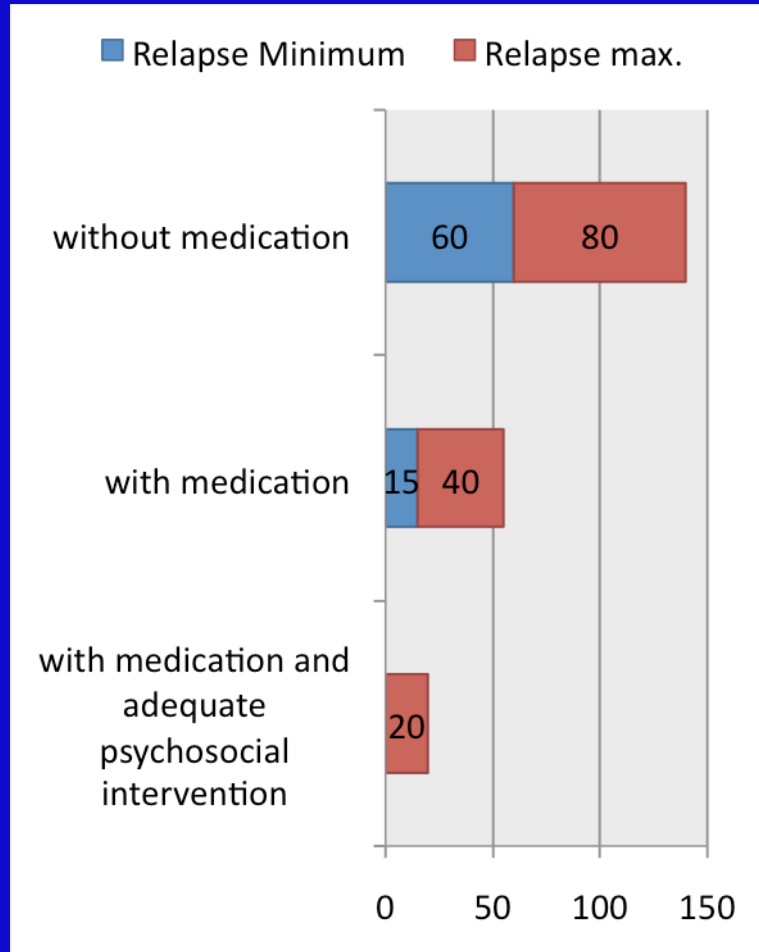
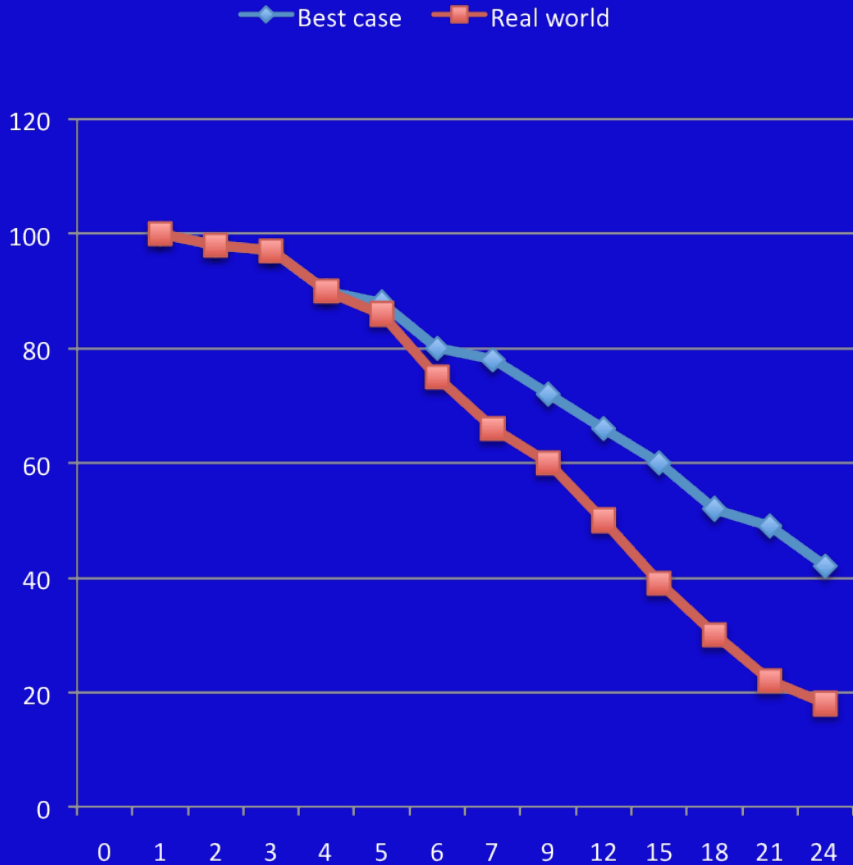


Cumulative Recovery Rate in First episode schizophrenia: Robinsons et al, JCP 2006



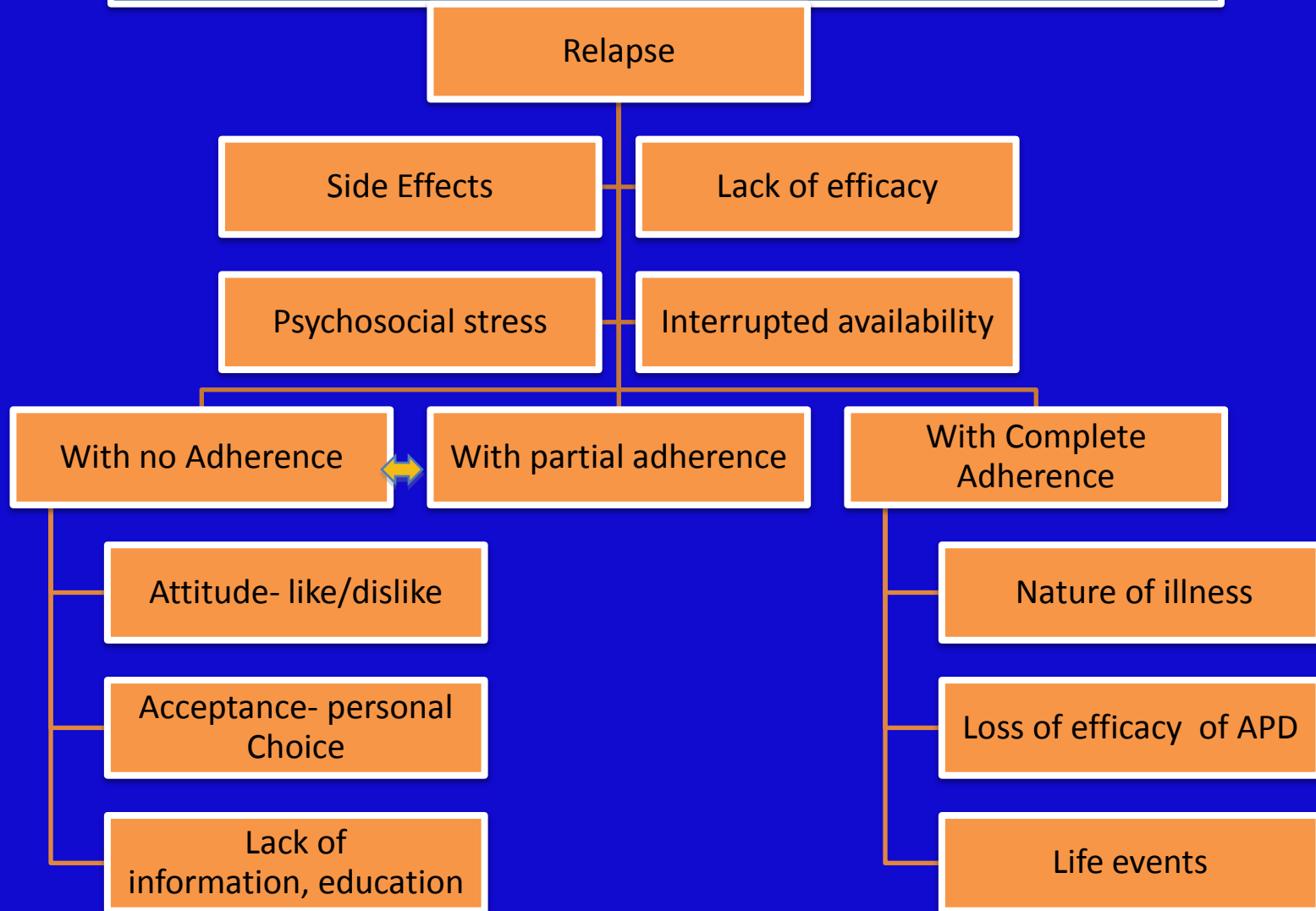
Schizophrenia Relapse rates

Survival Analysis of optimal NL dose and real world rehospitalization risk for multiepisodic NL responsive schizophrenia

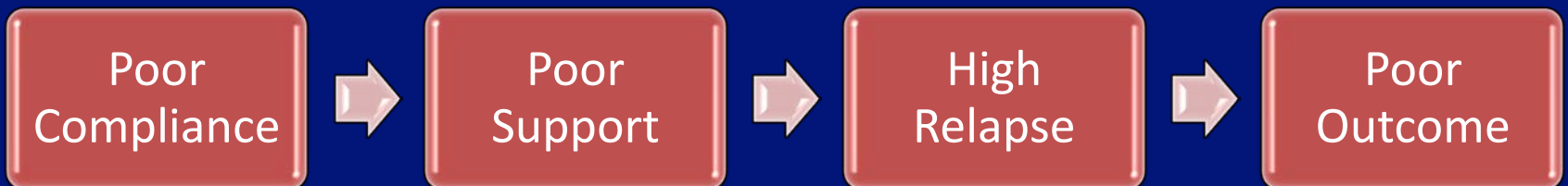


Cost of Relapse in Schizophrenia
 By Peter J. Weiden and Mark Oltson
 Schizophrenia Bulletin, Vol. 21, No. 3, 1995

Relapse : when and how it Occurs



**Concept of patient
responsiveness is a
continuum rather than
dichotomy of response &
nonresponse**



Relapse

Relapse is one of the outcome criteria



Underlying Neurobiology is poorly understood



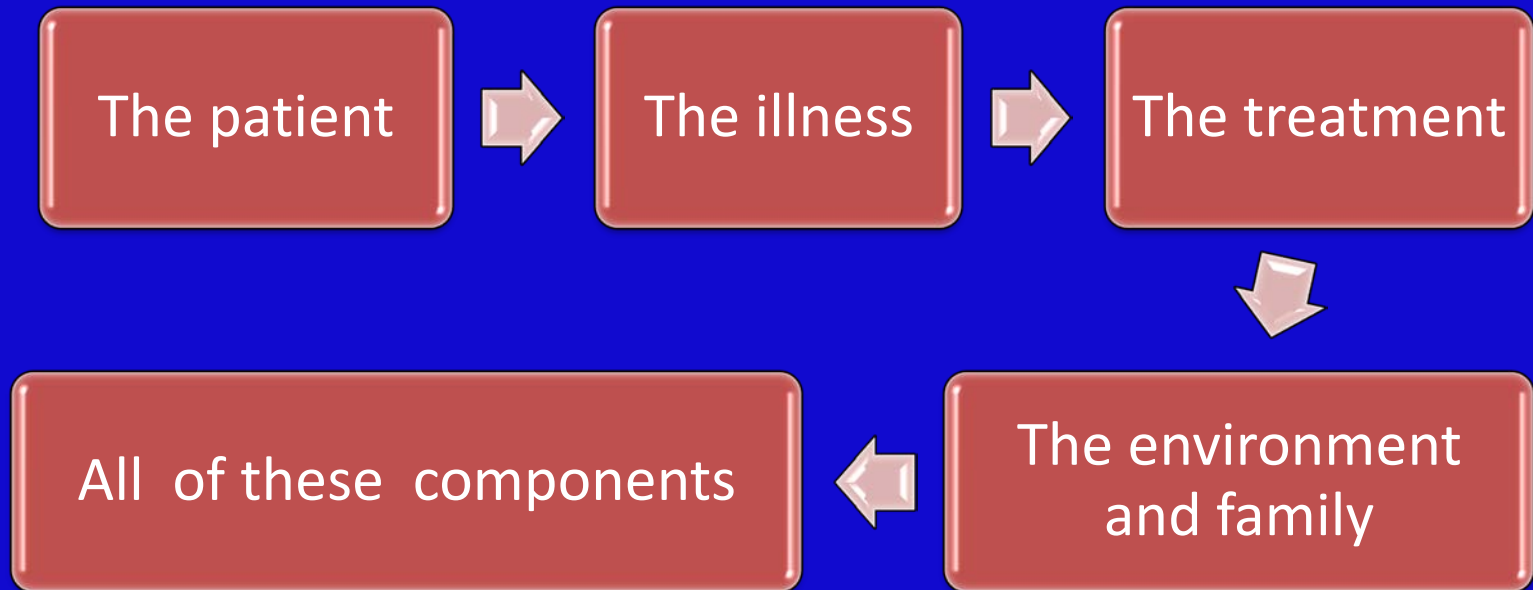
Fairly Common irrespective and independent of nature, age of onset, treatment given, monitoring



What relapses:
positive symptoms, depression and suicide, lack of self care, competency



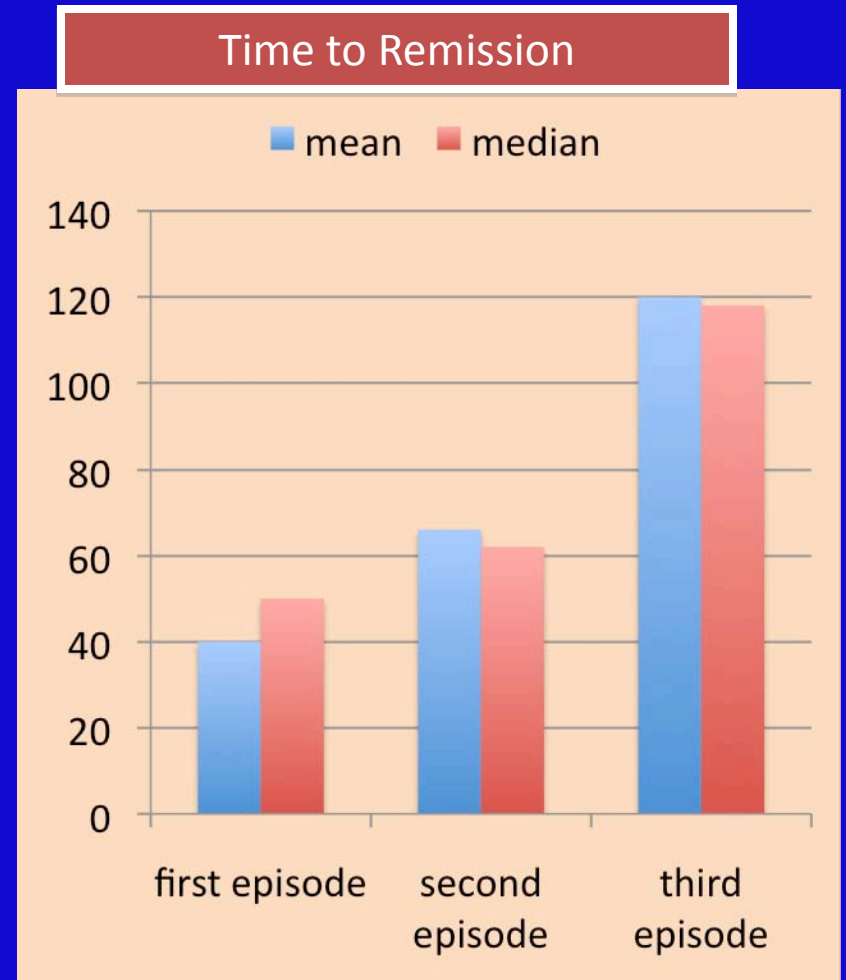
Not relapsed does not mean good functioning. Non-relapsing patients do have disability, dysfunction and poor QOL.



Determinants of Relapse

Risk factors

Possible
Mechanisms

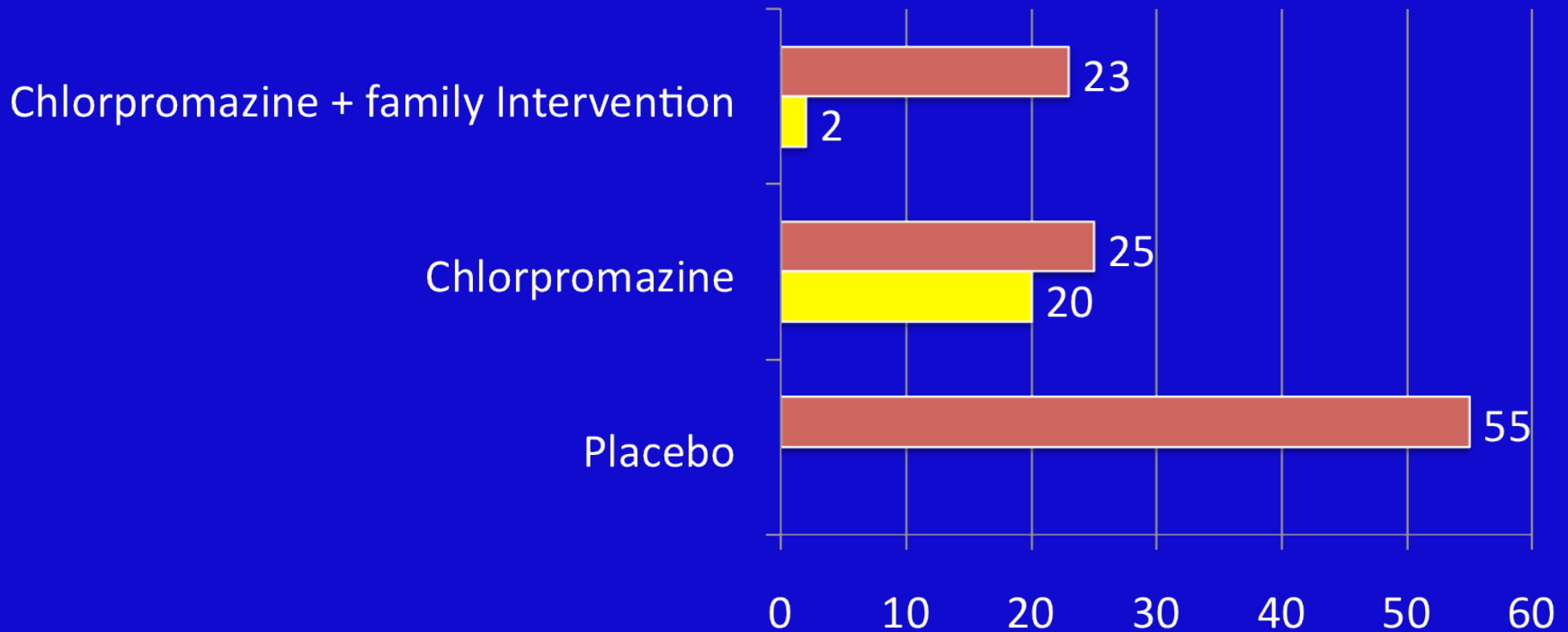


Protective Factors:

personal resource, good premorbid adjustment, a positive self concept & a competent social network

Effectiveness of intervention for Schizophrenia: Relapse rate

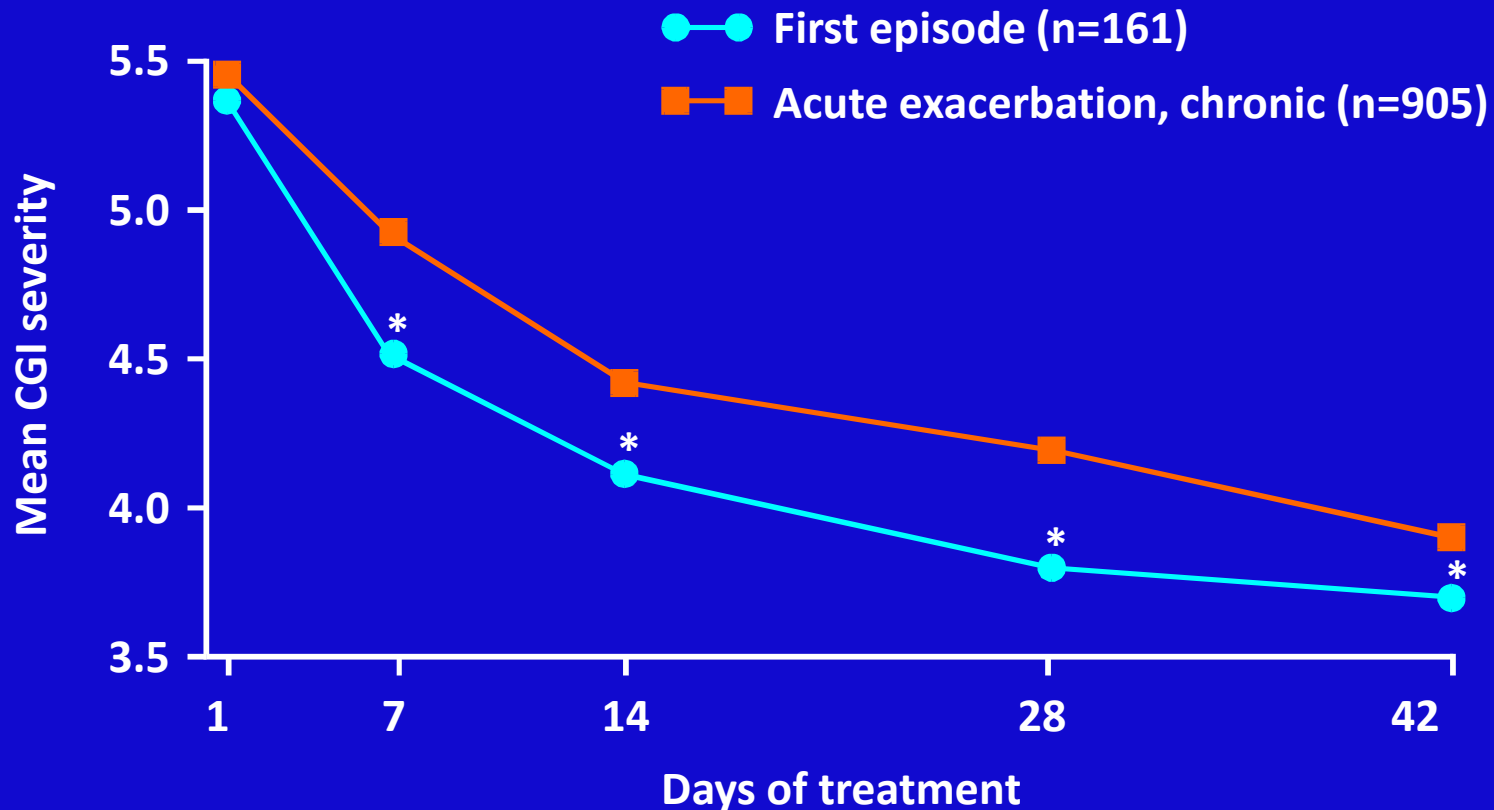
■ % Relapse after 1 year- Maximum ■ % of Relapse after One year



Dixon LB, Lehman AF (1996), Schizophrenia Bullatin, 21(2): 631-643
DixonLB et al (1995) Schizophrenia Bullatin, 21(4): 567-577,
World Health Report,WHO,2001

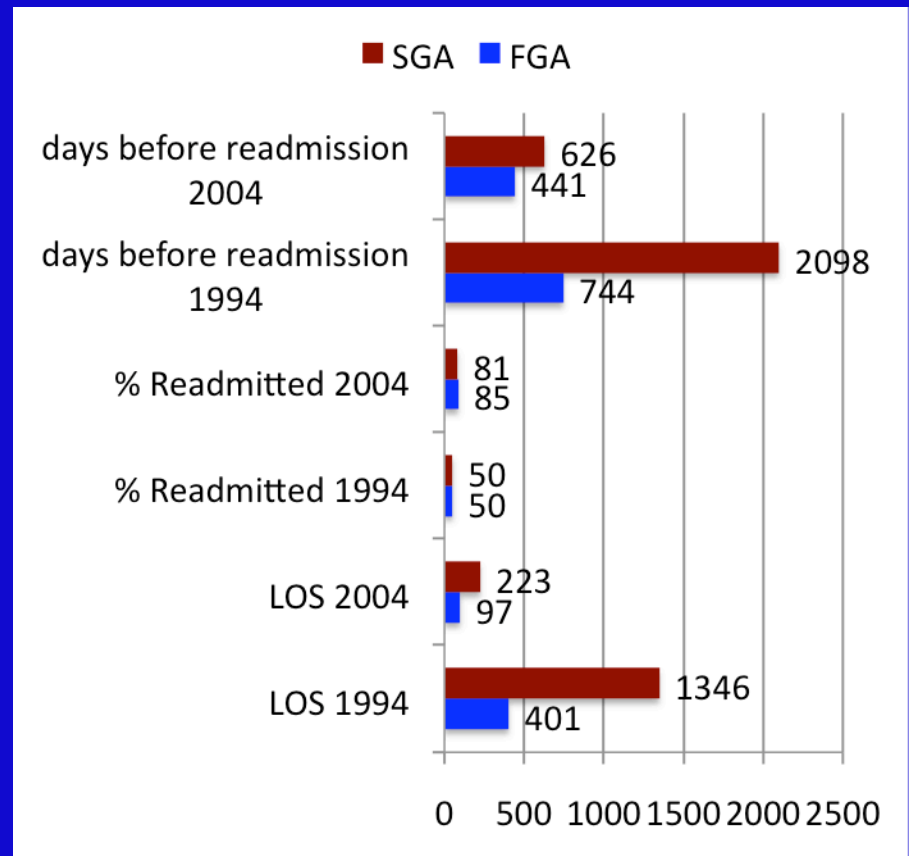
First-episode schizophrenia versus chronic schizophrenia treated with risperidone (2)

Clinical Global Impression (CGI)

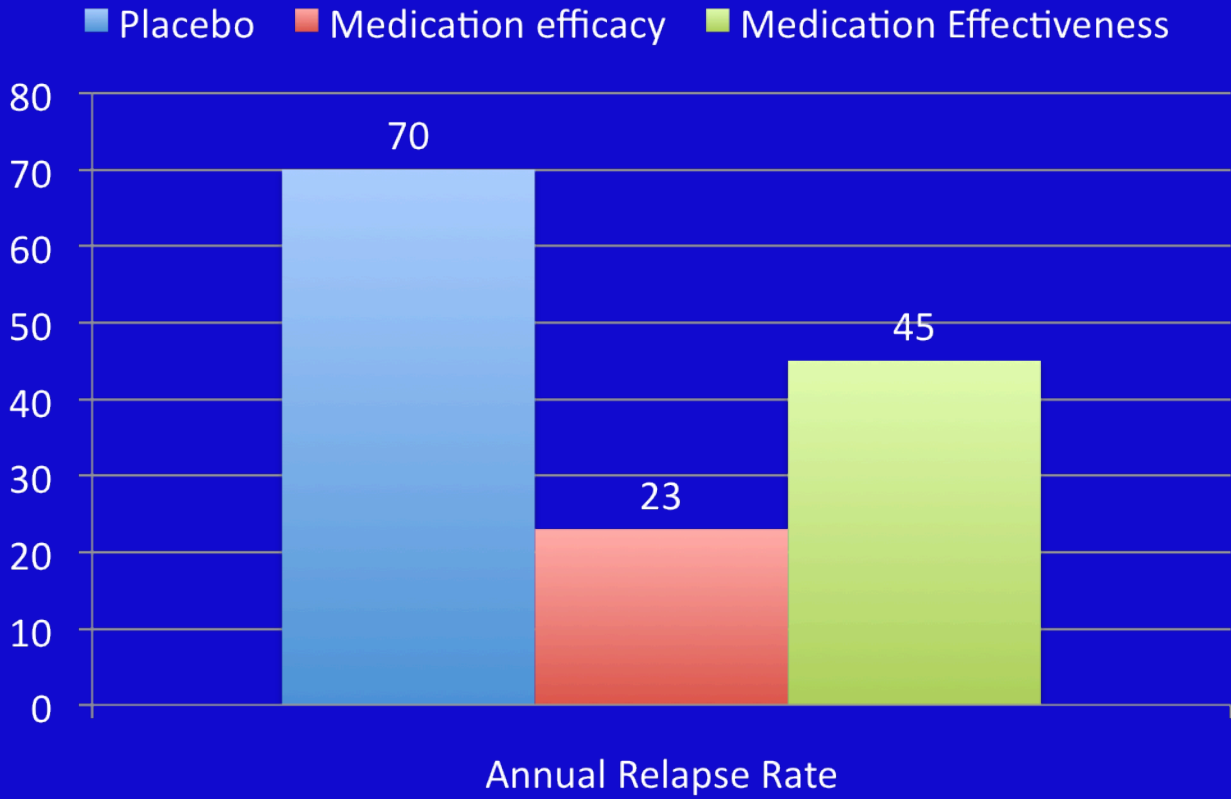


*p<0.05

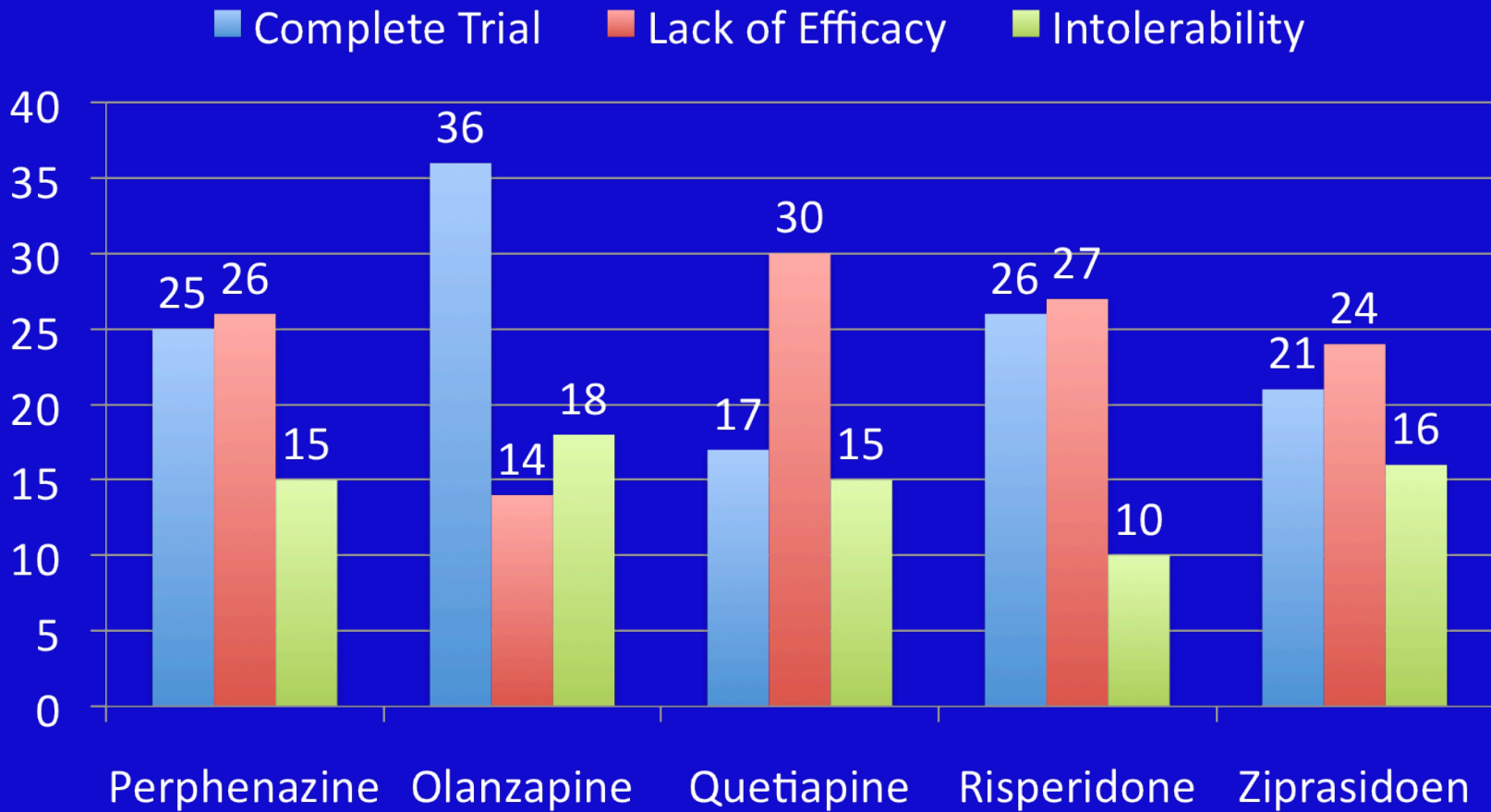
Rüther E, Klauder A. WCP, Hamburg, August 1999



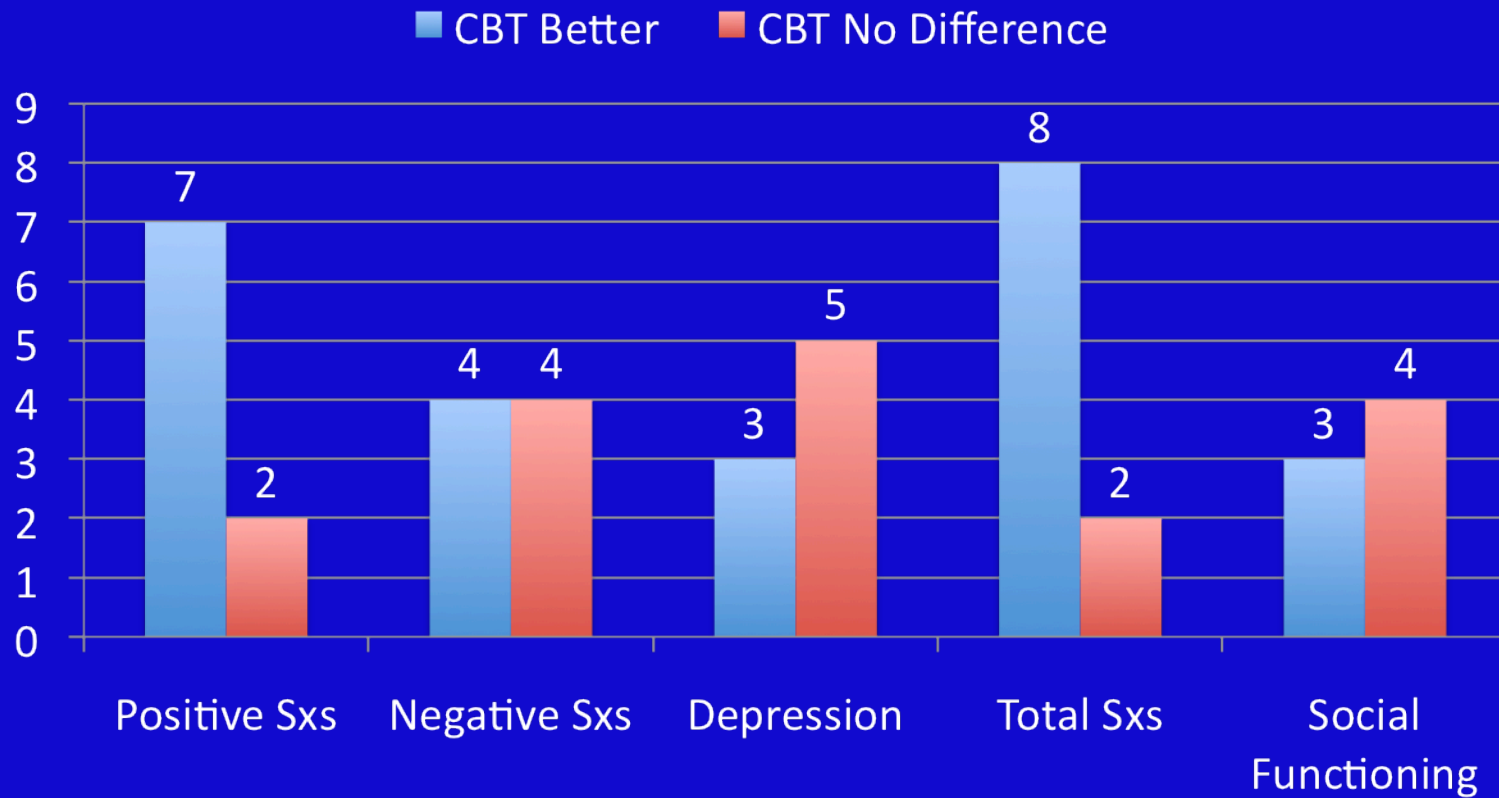
Efficacy and effectiveness of Antipsychotic Medications: Annual Relapse Rate



Effectiveness of Antipsychotic Dugs in Schizophrenia (Lieberman et al , 2005)



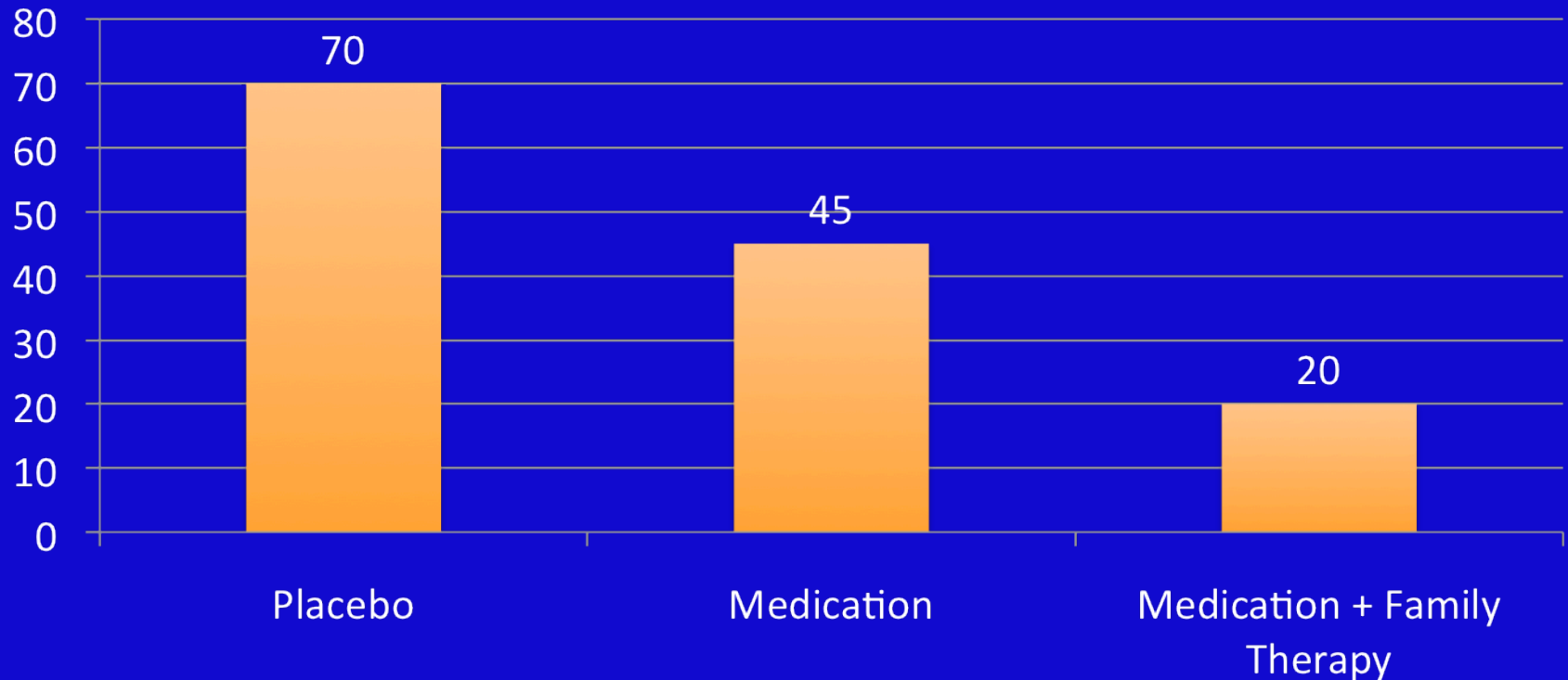
Cognitive behavior Therapy for residual symptoms in Schizophrenia Patients in Community (Dickerson & Lehman, 2005)



Combining Medication and Family Education in Schizophrenia; Relapse Rates

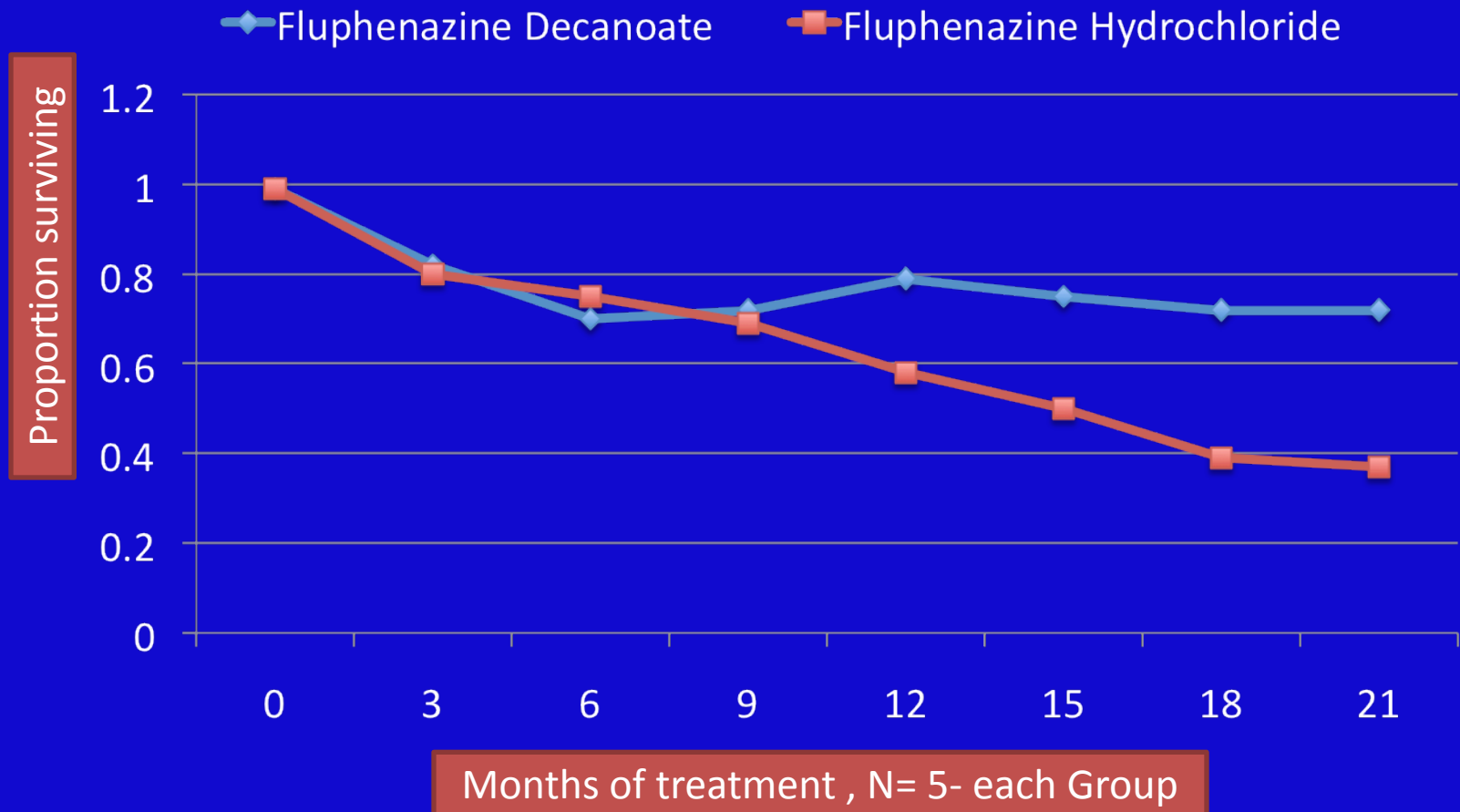
% of patients relapsed

■ % of patients relapsed



Relapse rate in 2 years

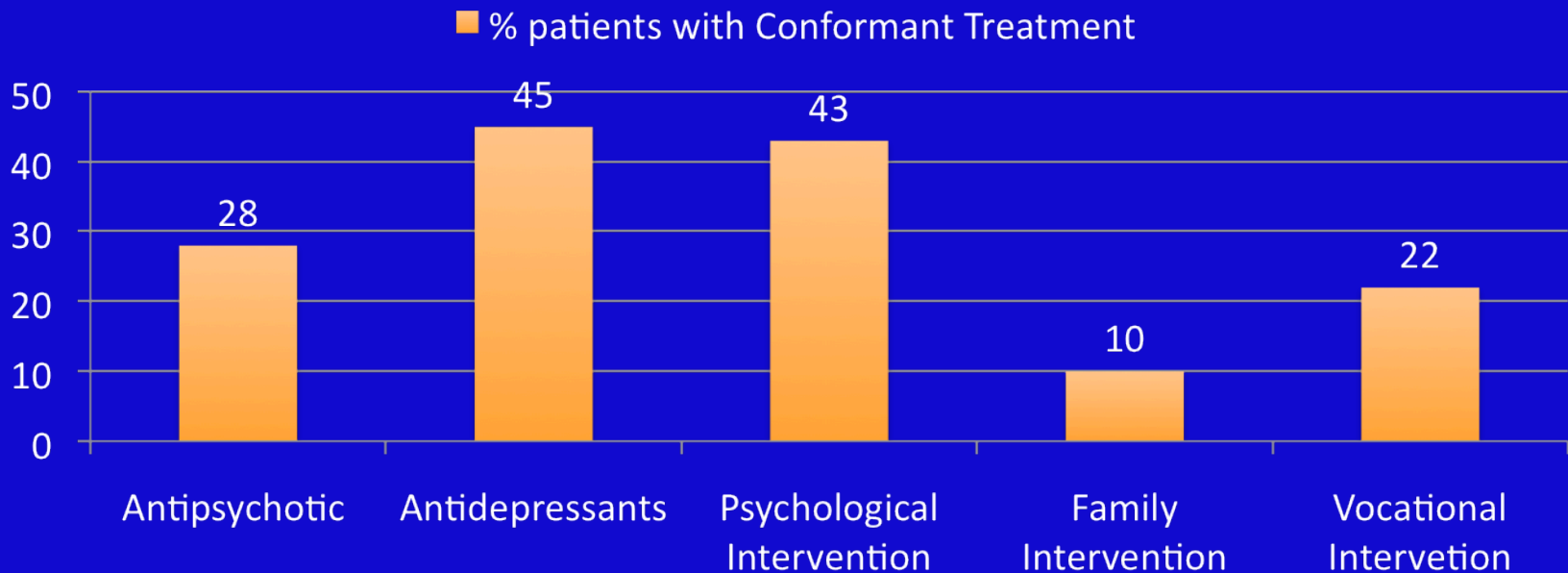
with Oral Vs LA Depot APD combined with psychosocial intervention, Scholar et al , 2006



Schizophrenia PORT

Current practices

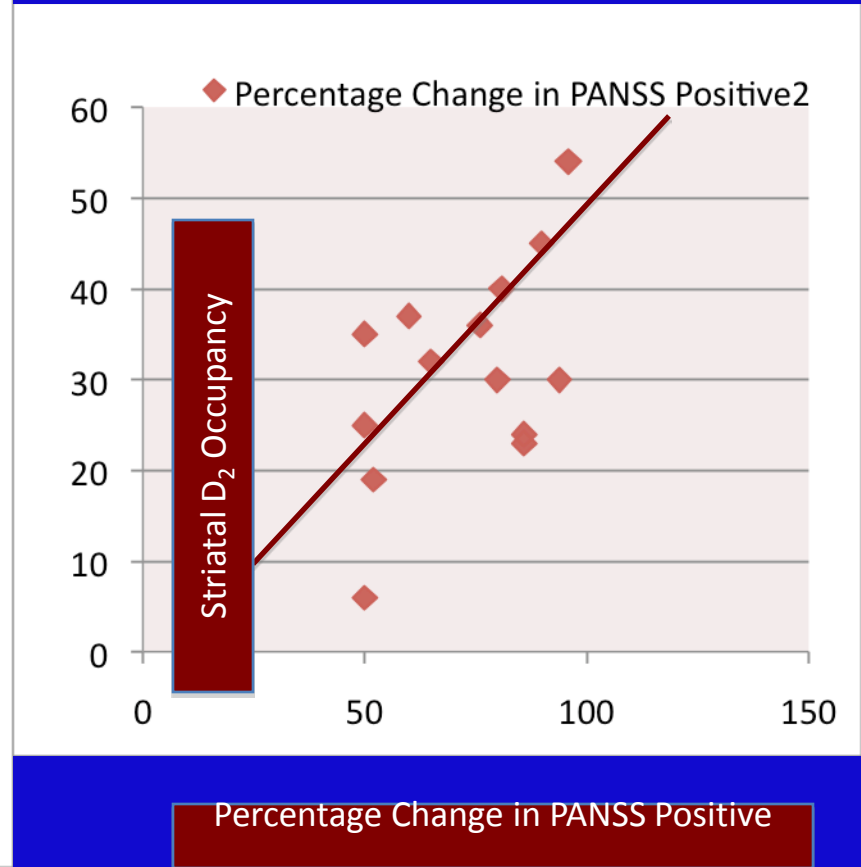
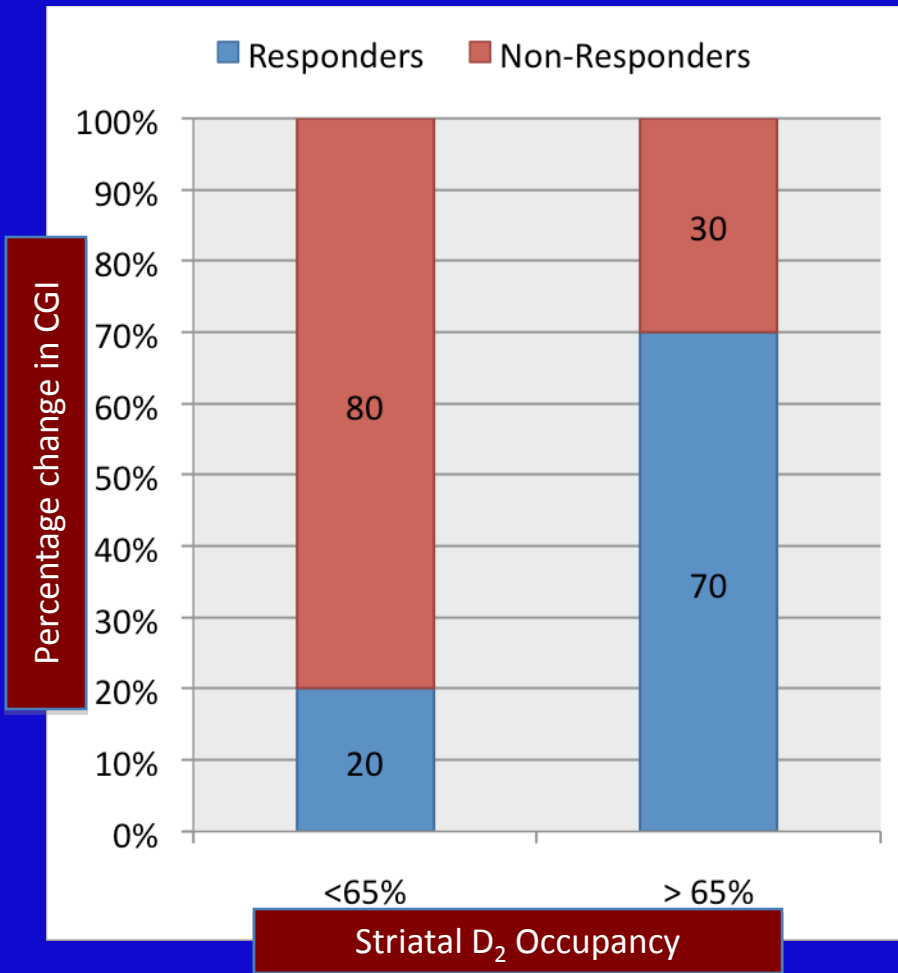
% patients with Conformant Treatment



Are Antipsychotics superior to psychosocial & cognitive behavioural therapies in relapse prevention of schizophrenia?

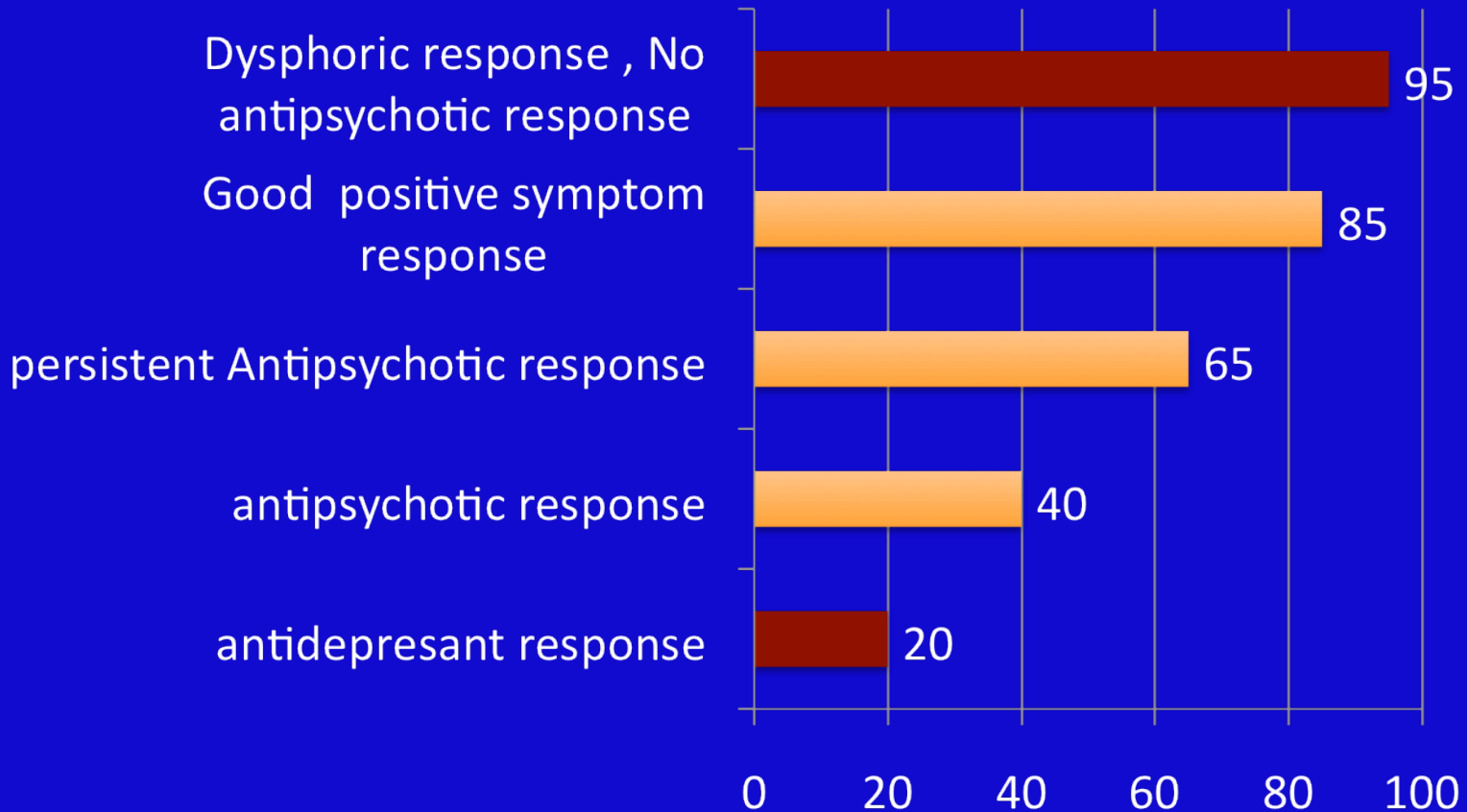
- Evidence is equivocal

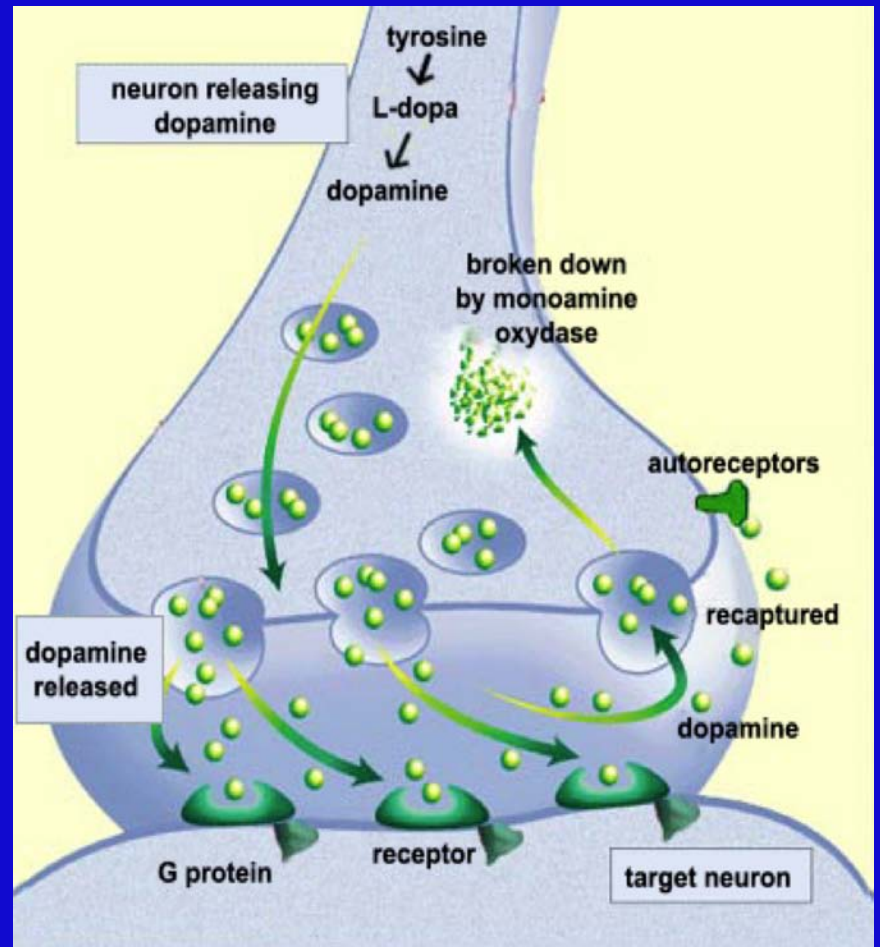
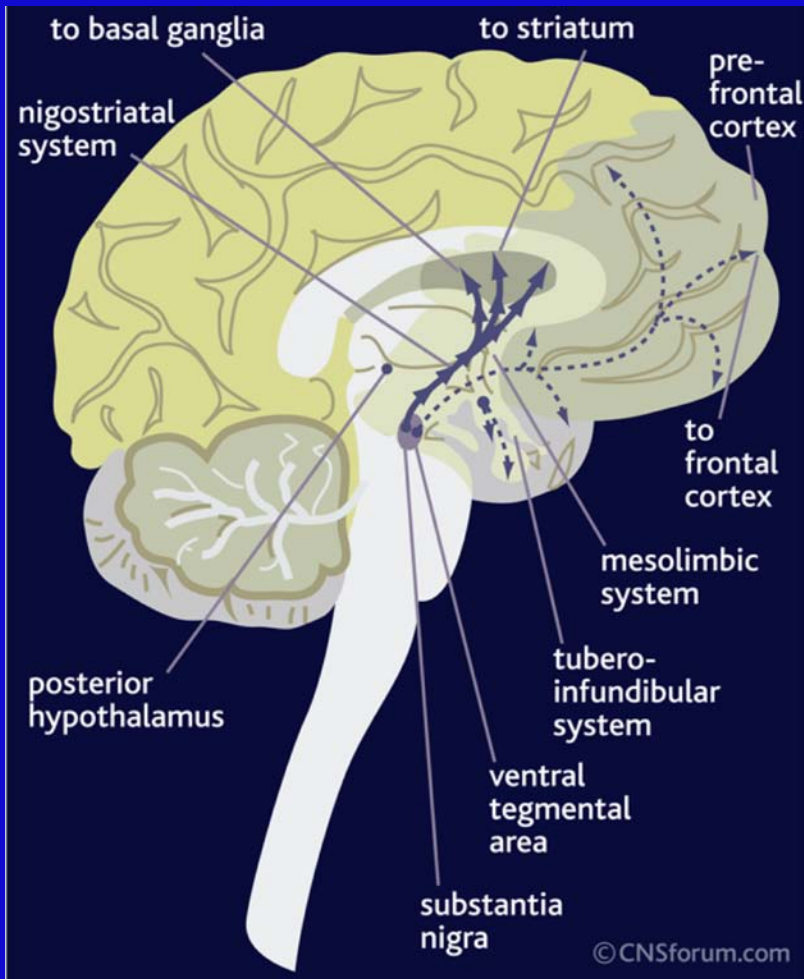
Thus ,there is a clear case for integrated and comprehensive therapy right from the day of the first contact; irrespective of the clinical settings; situations and alliances .



Antipsychotic Response is a function of 5HT2a & D2 blocking Ratio

D2 Receptor blocking % in Frontal Lobe





Genetics - Examples

- An example of how a genetic predisposition for schizophrenia can be triggered by environmental influences can be seen in a research study taken from Biological Psychiatry, Volume 57:
 - Indicates that people who had multiple copies of a version of the COMT gene and who smoked marijuana had a 1,000% increase in their risk of developing schizophrenia
- Another example from the British Journal of Psychiatry:
 - Indicates that adopted children with high genetic/biological risk for schizophrenia (their mother had schizophrenia) had an 86% lower rate of developing schizophrenia raised in a healthy vs. a dysfunctional family.
 - Only 6% of the children developed schizophrenia in the healthy family.
 - 37% of the children of the dysfunctional families developed schizophrenia

(as cited on www.schizophrenia.com).

Why does comorbidity develop??

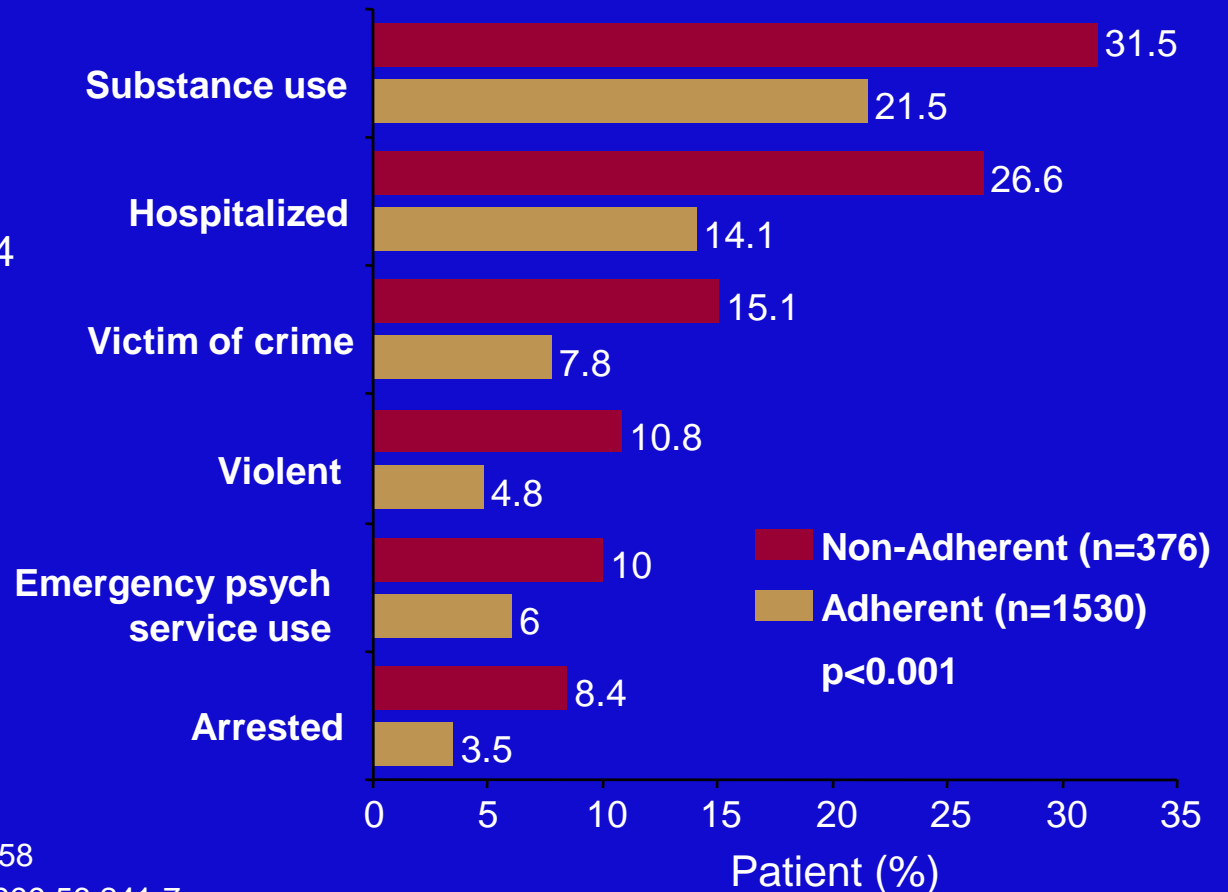
Why is Medication Not Sufficient?

- Neurodevelopmental dysfunction
- Subtle neurocognitive deficits from early childhood
- Diffuse system disruption
- Timing of first exacerbation disrupts adult socialization
- Residual primary and secondary negative symptoms

Impact of Non-Adherence

Non-adherence Associated with Poorer Functional Outcomes (n=1906)⁴

- ↓ Remission¹
- ↑ Relapse²
- ↑ Hospitalization^{3,4}
- ↓ Functional outcomes⁴



1. Malla et al. Psychol Med 2006;36:649-58

2. Robinson et al. Arch Gen Psychiatry 1999;56:241-7

3. Ward et al. Clin Ther 2006;28:1912-21

4. Ascher-Svanum et al. J Clin Psychiatry 2006;67:453-60

Negotiating Medications



Attitude, acceptance, Belief, culture



Team efforts, Education, Monitoring, Reinforcing Compliance as answer

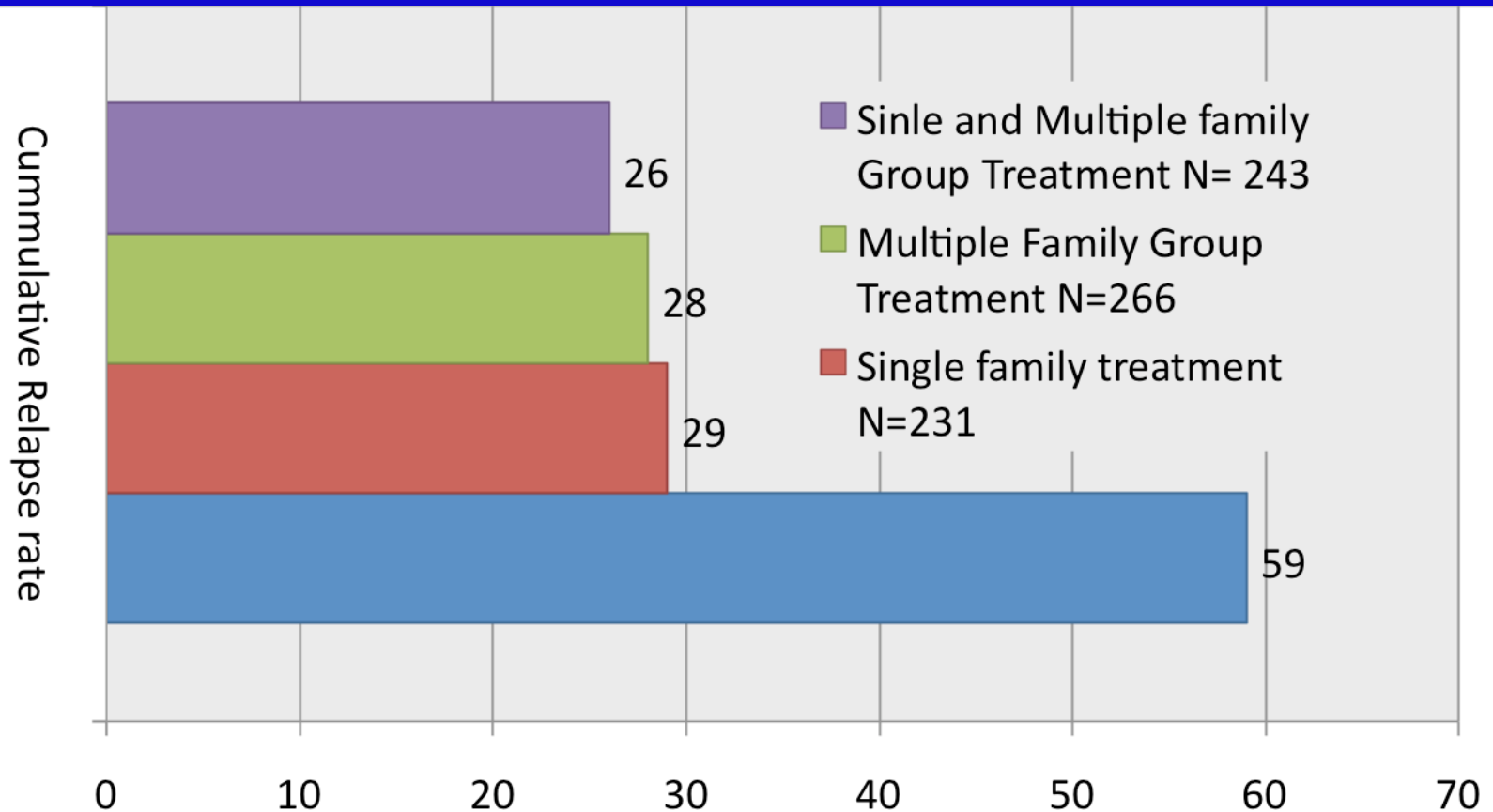


Nature of illness, Medication Effect & Side effects

Expressed emotion and psychiatric relapse: a meta-analysis.

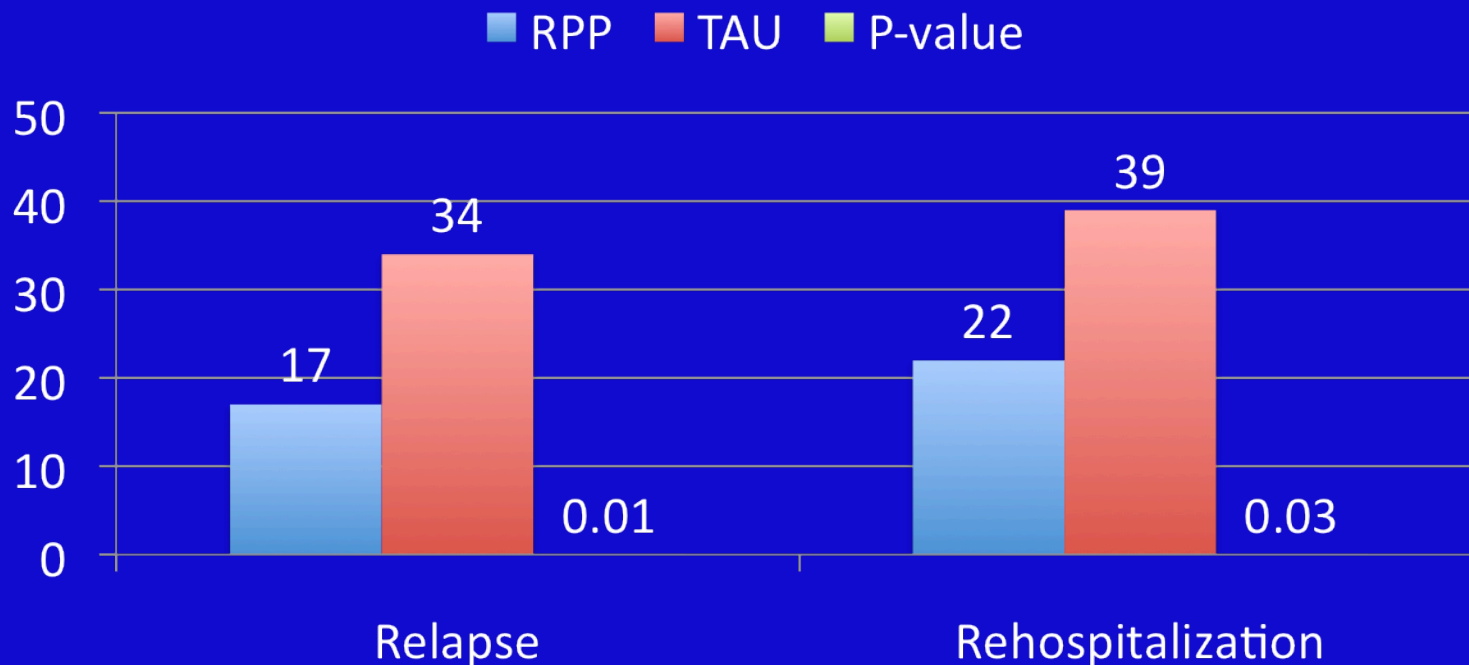
Community-Based Treatment of Schizophrenia and Other Severe Mental Disorders: Treatment Outcomes

cumulative relapse/rehospitalization rates during 18 to 24 months in randomized controlled trials of long-term family intervention for schizophrenia.



Specialized programs for relapse prevention are more effective in identifying prodromal episodes before frank relapse

'A Program for Relapse Prevention in Schizophrenia: A Controlled Study'

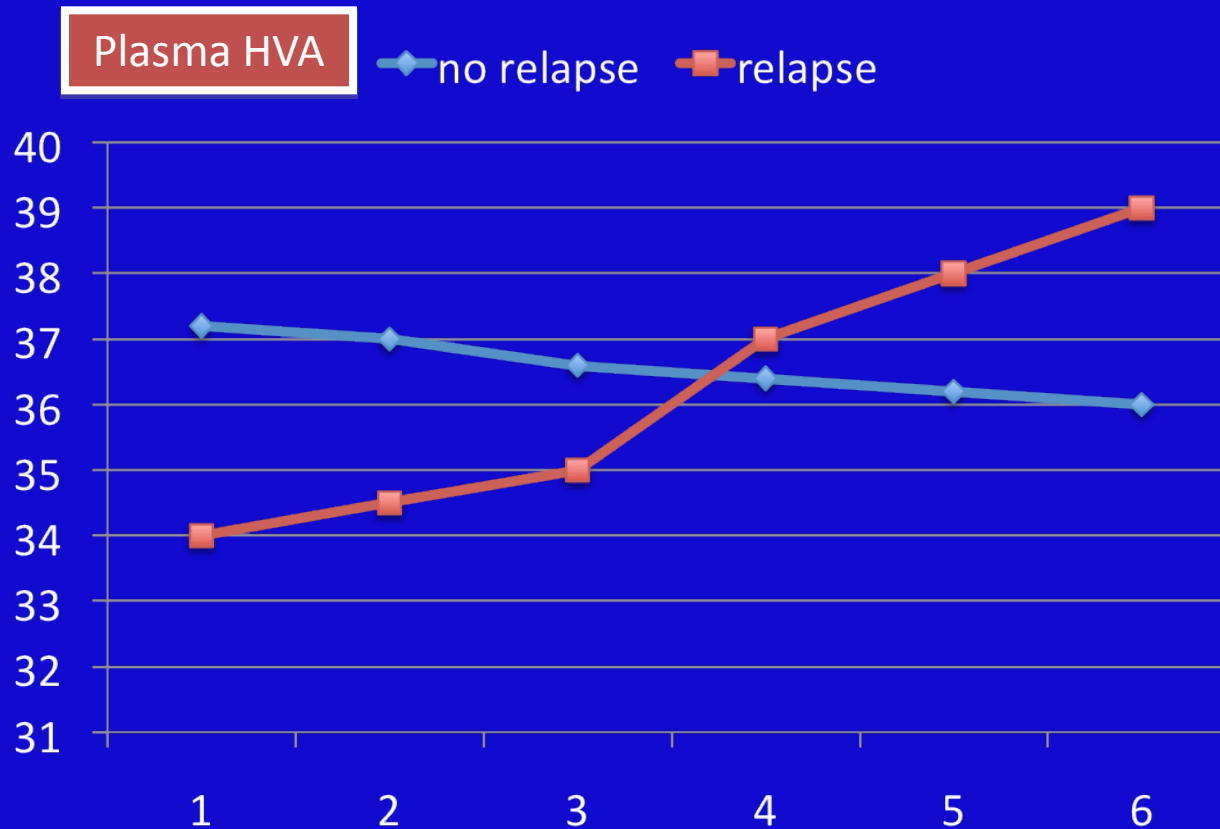


Nature of Illness as Determinants of Relapse

Biological mechanisms of relapse may not become fully elucidated before the mechanisms of the schizophrenic pathophysiology are clarified.

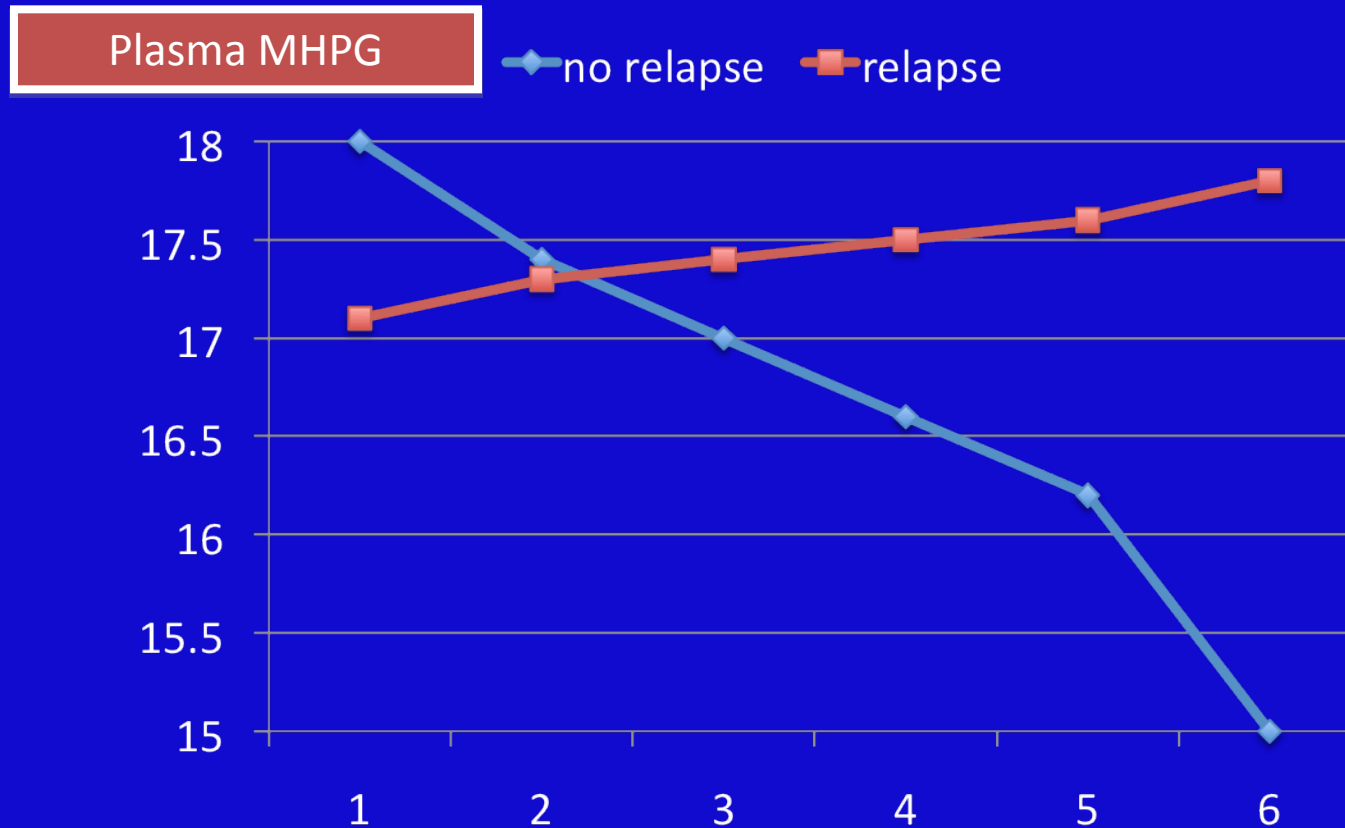
- low serotonergic and high dopaminergic neurotransmission are associated with a relapse,
- possibly high noradrenergic neurotransmission plays a role in short-term relapses.
- Role of Certain cytokines, which have rarely been studied to date, seem to have an even higher impact on schizophrenic relapse.

Biological studies and Relapse



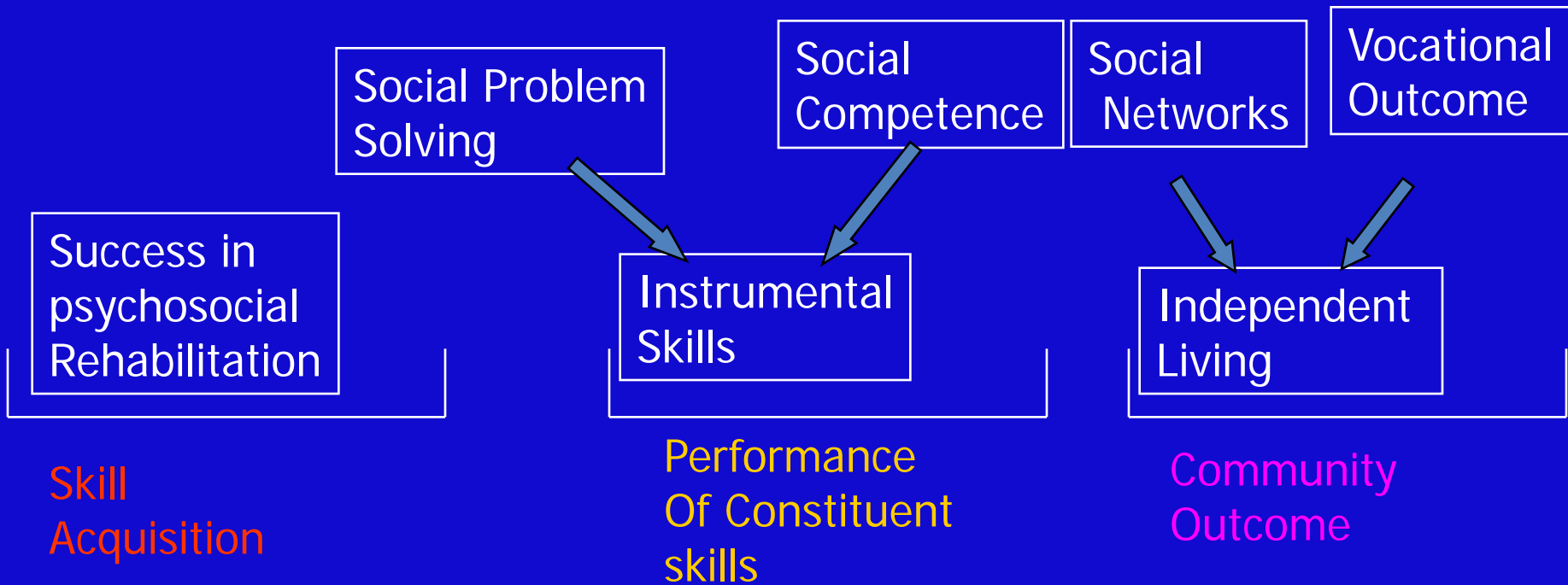
Week following haloperidol withdrawal model, likelihood ratio $p < 0.0005$

Biological studies and Relapse



Week following haloperidol withdrawal model, likelihood ratio $p < 0.0005$

Relevance of Neuro-cognitive deficits for functional outcome in schizophrenia

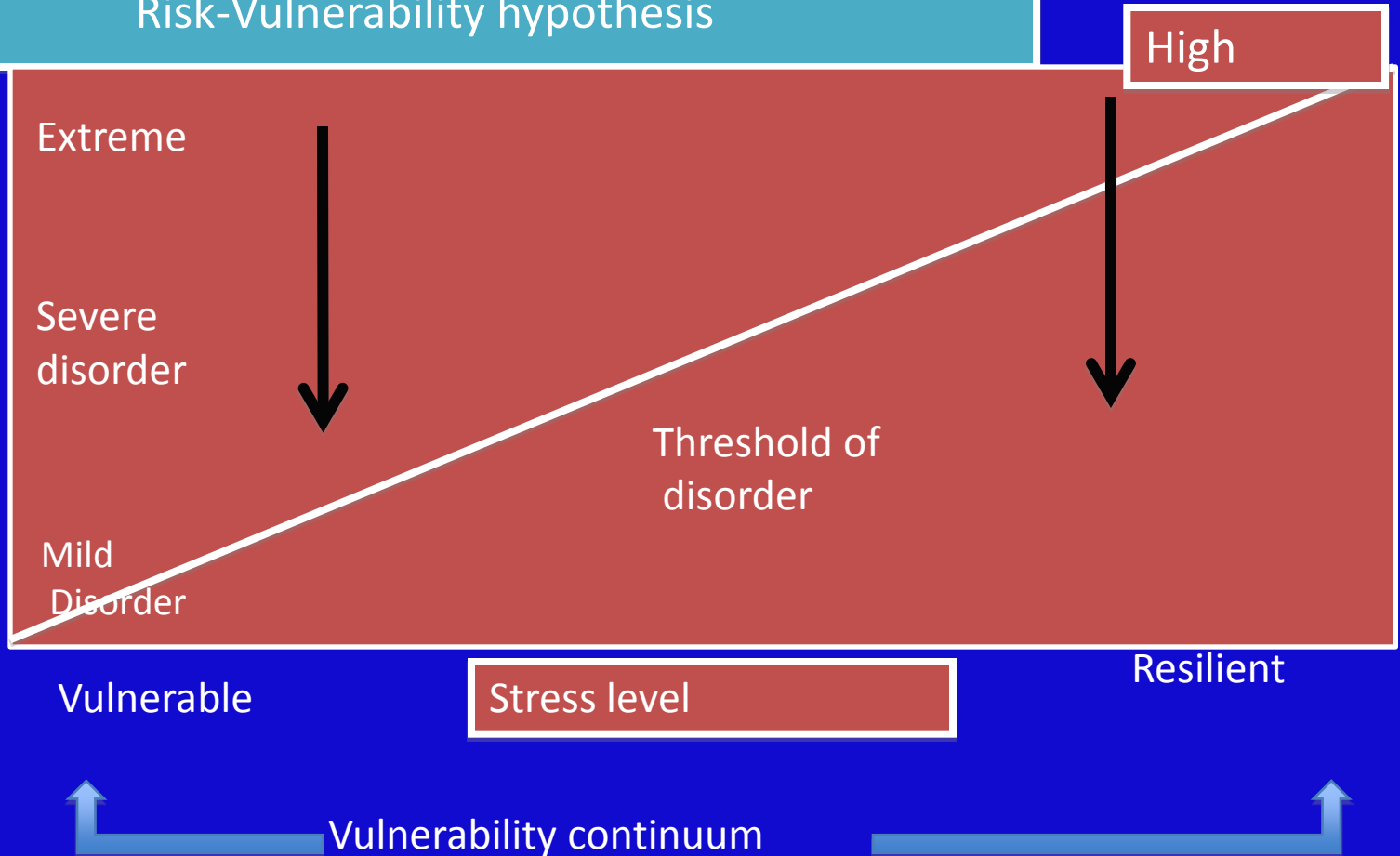


Can Neurocognitive Functioning Be
Improved with Psychosocial
Interventions?

Strategies for reducing
Cognitive Demands

Developmental and stress-related changes of neurotrophic factor gene expression in an animal model of schizophrenia

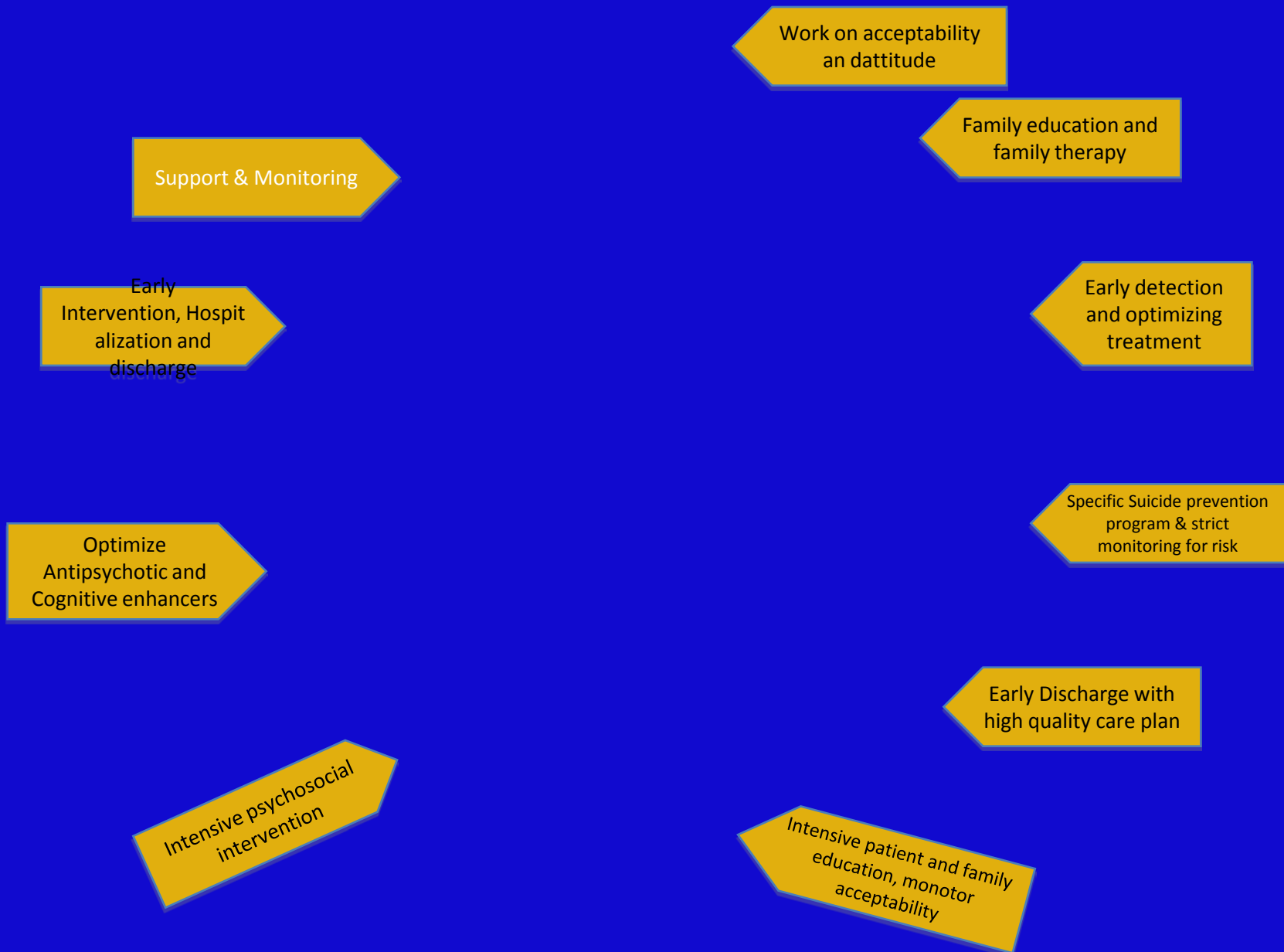
Stress-diathesis model forms the theoretical context of Risk-Vulnerability hypothesis



K. H. Nuechterlein¹ vulnerability/stress model of schizophrenic relapse: a longitudinal study;
Acta Psychiatrica Scandinavica Volume 89 Issue s382 ,58-64, 1994

15/03/2008

Maximizing outcome and preventing relapse : The necessary steps



What can a psychiatrist do?

Program based Intervention for psychosis: Advantages and Caution

- Much better than Treatment as usual
- Response, Recovery, outcome, Functioning & quality of life is better
- Relapse is less,
- Disability and morbidity due to side effect is reduced
- Caution : Continuity of care is clinical and ethical issue
- Discharging patients out of program is likely to compromise quality of care.
- Caution : discharge if remission has persisted for more than 5-7 years &
- subject has become over 40 years of age
- family is nor dysfunctional
- Genetic loading is not very high
- Low risk for suicide

Research needs for Relapse Prevention

Most Important ones :

- Biological Markers for
 - Course of psychosis
 - Responders Vs Non-responders
 - Endophenotypes of side effects of medications
 - Antipsychotic response
- Determinants of 'Insight' and 'awareness'
- Biological pathways for Cognitive dysfunction
- Markers for stress response in psychosis

Summary:

Relapse Can be effectively minimized

- Relapse is common and main issue in outcome
- It is part of biological nature of illness, mostly in first 5-7 years
- Treatment barriers and risk factors for relapse needs to be identified and dealt with.
- Early Intervention, Education, Enhancing Compliance, Qualitative assessments, Safety of medication, Optimization of treatments are necessary
- Optimum Dose and adequate duration is a must.
- Program based Comprehensive and multidisciplinary treatment needs to be managed