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Antipsychotics and Outcome in Schizophrenia

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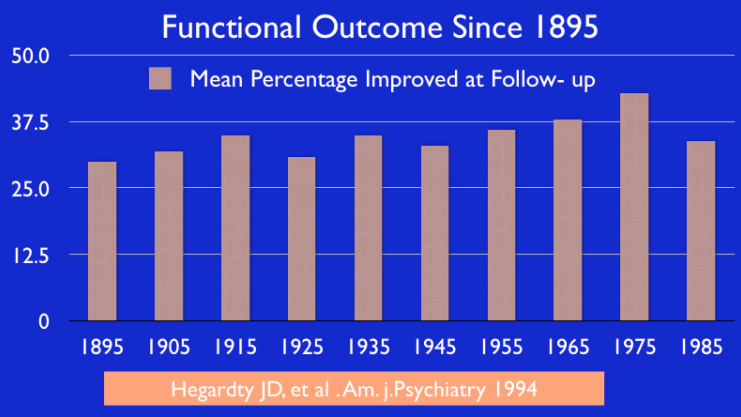
International pilot study of schizophrenia (IPSS): Agra centre, India

- Multicentre, WHO at 2 and 5 years
- 76% followed at 2 years (n=1,202)
- Consistent finding at 2 and 5 years was that schizophrenia in developing countries has better outcome

Indian Council of Medical Research (ICMR)

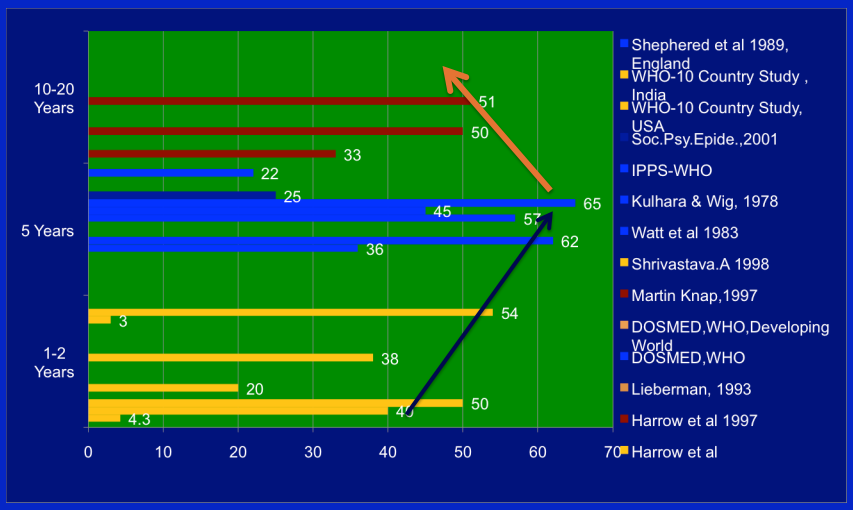
Government of India multicentre study on course and outcome of schizophrenia

- Time spent in psychotic state
  - 15% or less: 62%; 75% or more: 4%
- Best pattern of course: 45%; worst course: 10%
- Impairment of occupational functioning
  - nil: 40%; severe: 18%
- Social impairment
  - nil: 34%; severe: 12 %
- Overall outcome
  - favourable: 66%; intermediate: 30%; unfavourable: 4%



- Change In QLS Total Score With Change in Memory Function - positive linear correlation; Buchanan RW et al Biol.Psychiatry 1994;36

Complete Remission as Outcome status in Schizophrenia



'Real World' Comparison of First- and Second- Generation Antipsychotics in Regard to Length of Inpatient Hospitalization and Number of Re-hospitalizations(2008)

Claire Advokat Æ Benjamin D. Hill Æ Joseph E. Comaty Psychiatr Q (2008) 79:55–64

Antipsychotics

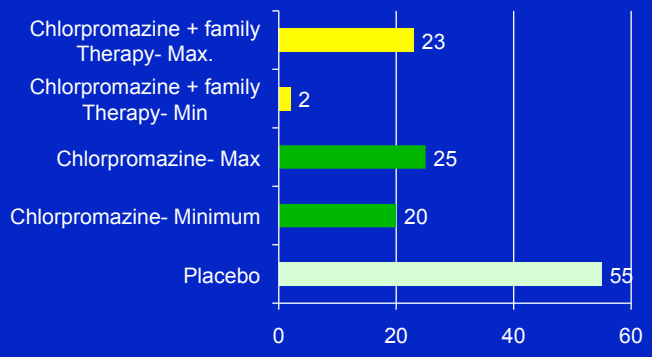
Whether to treat schizophrenia with antipsychotic? Banglore Study

- OBJECTIVE: To compare disability in schizophrenia patients receiving antipsychotics and untreated
- Untreated: unchanged Mean disability scores
- Continued to receive and initiated APD: showed a significant decline disability.
- The proportion of patients classified as 'disabled' declined significantly in the treated group ($P < 0.01$), but remained the same in the untreated group

Thirthalli J, Venkatesh BK, Kishorekumar KV, Arunachala U, Venkatasubramanian G, Subbakrishna DK, Gangadhar BN.
Prospective comparison of course of disability in antipsychotic-treated and untreated schizophrenia patients.
Acta Psychiatr Scand. 2009 Mar;119(3):209-17

Treatment effectiveness in Schizophrenia (World Health report 2001, WHO)

% of relapse after 1 Year



Dixon LB, Lehman AF (1995). Family interventions for schizophrenia. Schizophrenia Bulletin, 21(4): 631–643.

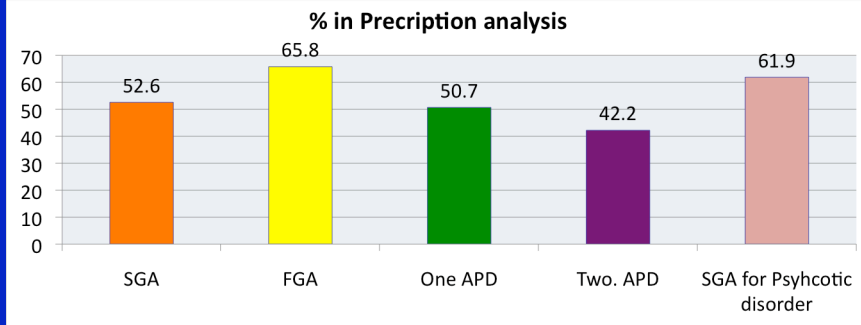
Dixon LB et al. (1995). Conventional antipsychotic medications for schizophrenia. Schizophrenia Bulletin, 21(4): 567–577.

CATIE – Phase 3, Symptom response

Drugs	ARIP	CLOZ	COMB	FLU-D	OLAN	PERP	QUET	RISP	ZIPR	P-value
PANSS – 3 months	0.506	0.002 ✓	0.002	0.005 ✓	0.002 ✓	0.084	0.013	0.044	0.045	0.832 ✖
PANSS -6	<0.001 ✔✔	0.006	<0.001 ✔	0.43	0.003 ✔	0.018	0.100	0.009	0.371	0.515 ✖

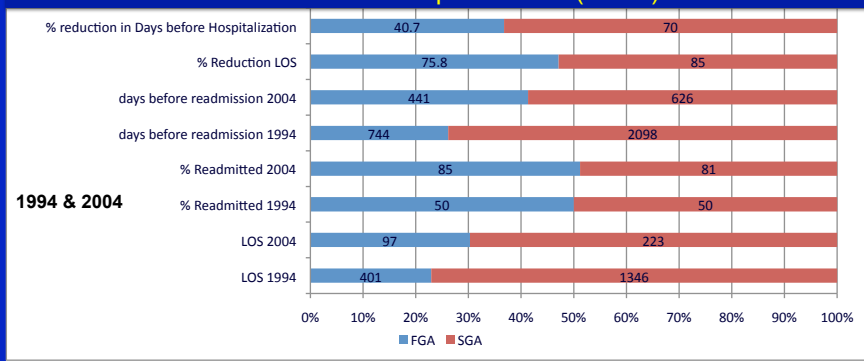
What is the prescribing pattern

SGAs have become the first-line treatment for psychiatric disorders.



Bret P, Bret MC, Queuille E. Prescribing patterns of antipsychotics in 13 French psychiatric hospitals.Encephale. 2009 Apr;35(2):129-38.

'Real World' Comparison of First- and Second- Generation Antipsychotics in Regard to Length of Inpatient Hospitalization and Number of Re-hospitalizations(2008)



- % reduction for SGA in number of days before relapse was significantly more impressive
- During both time periods, patients on FGAs had significantly shorter LOS than those receiving SGAs
- Inpatients receiving SGAs were hospitalized longer than those receiving FGAs.
- Conversely, patients receiving SGAs were significantly less likely to be re-admitted

Claire Advokat Æ Benjamin D. Hill Æ Joseph E. Comaty Psychiatr Q (2008) 79:55–64

Second-generation versus first-generation antipsychotic drugs for schizophrenia: a meta-analysis

Stefan Leucht, Caroline Corves, Dieter Arbter, Rolf R Engel, Chunbo Li, John M Davis

Summary

Background Because of the debate about whether second-generation antipsychotic drugs are better than first-generation antipsychotic drugs, we did a meta-analysis of randomised controlled trials to compare the effects of these two types of drugs in patients with schizophrenia.

Lancet 2009; 373: 31–41
Published Online
December 5, 2008
DOI:10.1016/S0140-

150 DB, N= 21 533,

4 Drugs amisulpride clozapine, olanzapine risperidone were better than FGA, with small to medium ES.:

The other SGA were not more efficacious than the FGA, even for negative symptoms.

With the exception of aripiprazole and ziprasidone, SGA drugs induced more weight gain

The CATIE and CUtLASS studies in schizophrenia: results and implications for clinicians.

- CATIE and CUtLASS suggest that SGAs do not live up to all the previous expectations.
- However, even if most of these advantages are debatable, the lower risk of Tardive dyskinesia and the better subjective effects should be strong enough reasons to favour these drugs.
- There is no single antipsychotic that is best for every schizophrenia patient, as individual responses differ markedly.
- For successfully individualized treatment, a multitude of antipsychotic options are needed.

Naber D, Lambert M.The CATIE and CUtLASS studies in schizophrenia: results and implications for clinicians.
CNS Drugs. 2009 Aug 1;23(8):649-59.

Lessons to take home from CATIE.

- Rather than selecting drugs on the basis of unfounded expectations of superior efficacy, clinicians can focus on selecting drugs and optimizing dosages to minimize adverse effects without sacrificing efficacy.
- Tardive dyskinesia may be a good reason to avoid a high dosage of first-generation antipsychotics,
- although the evidence for differential risk is less compelling for a modest dosage of low-affinity first-generation antipsychotics.
- Similarly, the metabolic effects of some second-generation antipsychotics can be decisive in considering risks.
- In either case, the clinician should detect earliest signs and take action while dyskinetic or metabolic effects are most reversible.

Carpenter WT, Buchanan RW. Lessons to take home from CATIE. Psychiatr Serv. 2008 May;59(5):523-5.

Bottom line: the dichotomy between first- and second-generation antipsychotics was not supported by efficacy data (and now, is not supported effectiveness data).

Only clozapine has documented superiority in treatment-resistant cases.

Lessons to take home from CATIE.

Carpenter WT, Buchanan RW. Lessons to take home from CATIE. Psychiatr Serv. 2008 May;59(5):523-5.

Do Atypical Antipsychotics Differ in Determining Long-term Outcome of First Episode Schizophrenia? A Naturalistic Outcome Study in India

Amresh Srivastava[1], Nilesh Shah[2], Megan Johnston[3], Larry Stitt[4],
Meghana Thakar[5], Gurusamy Chinnasamy[6],
& Anukant Mital[7]

INTRODUCTION

- Antipsychotic medications form the mainstream of treatment in schizophrenia
- These drugs have several short term as well long term advantages
- It is not known if atypical antipsychotics have the long-term effect of improving outcome and meeting expectations (1,2,3)

The present study examined the usage of antipsychotics drugs and their associations with clinical outcome in a long-term naturalistic study

METHODS AND MATERIALS

- • First episode hospitalized schizophrenia patients (diagnosed according to DSM-IIIR criteria) were followed for ten years
- • After ten years, diagnosis was re-confirmed (using DSM-IV criteria) and outcome was assessed
- • Outcome was assessed using Clinical Global Impression Scale (CGIS)
- • CGIS scores were correlated with key antipsychotic drugs used in the preceding 12 months

Multiple outcome criteria in schizophrenia

Thirteen criteria

- Psychopathology (positive symptoms, negative symptoms and disorganisation)
- Cognitive function (attention, executive function, working memory, recall memory, semantic memory, storage memory)
- Interpersonal social function
- Work–school function
- Extrapyramidal function (parkinsonism, akathisia, tardive dyskinesia)

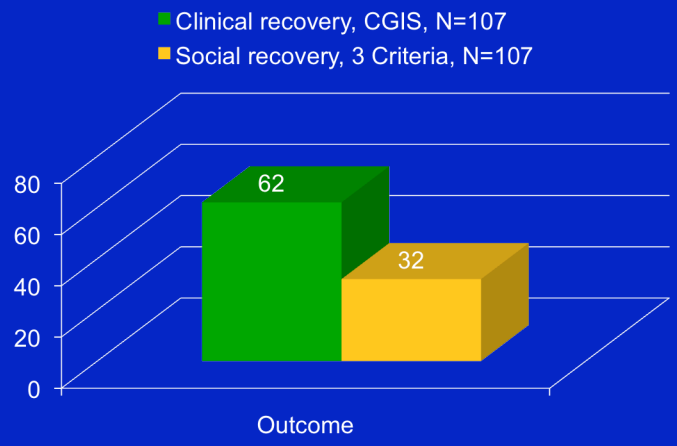
Meltzer HY. Eur Psychiatry 1995;10(Suppl. 1):19S–25S

Multiple outcome criteria in schizophrenia (cont'd)

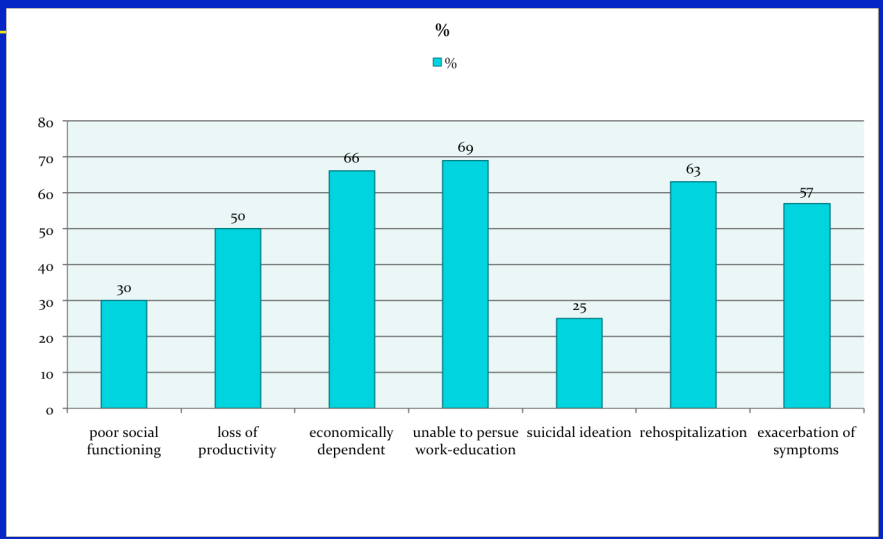
- Independent living
- Aggression
- Quality of life
- Compliance
- Hospitalisation
- Family burden
- Social burden
- Suicidality

Meltzer HY. Eur Psychiatry 1995;10(Suppl. 1):19S–25S

Re-assessed outcome at 10 years



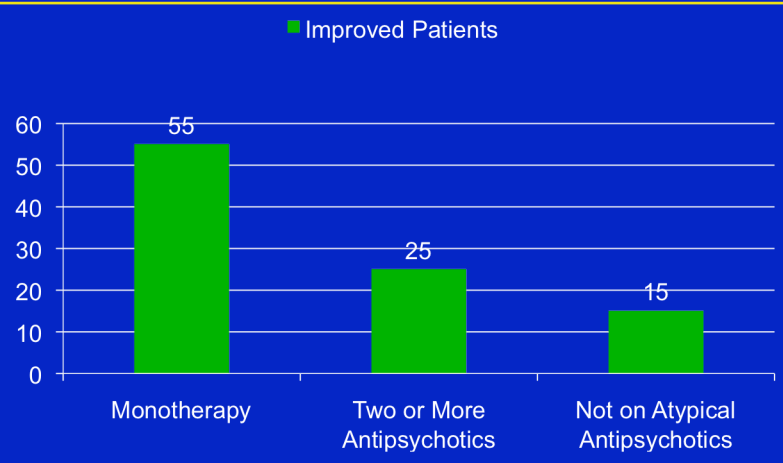
Global Social outcome



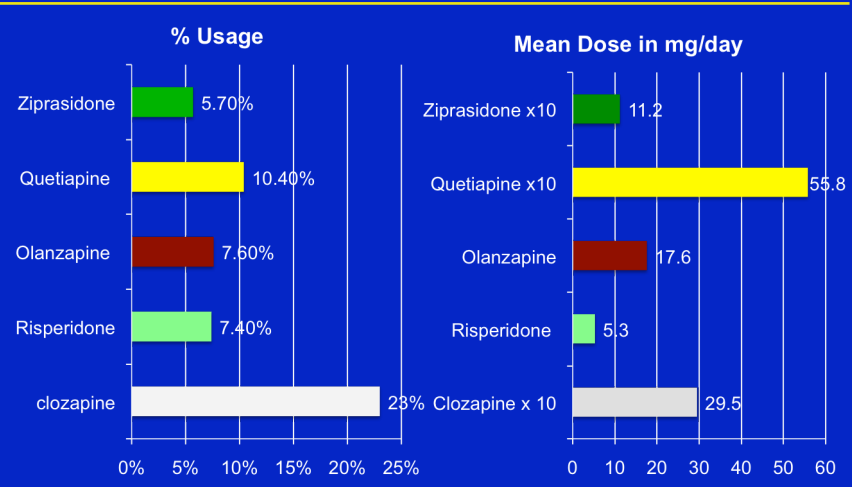
RESULTS

- Only 62.6% improved significantly in a cohort of 101 patients after ten years
- 85% patients were maintained on atypical antipsychotics

Improved Patients



Percentage usage pattern and per day mean dosage in mg at end point:



Cognition

- Significant decrease in visuo-spatial function.
- (p=.002, Paired t),
- % of patients with abnormal value on BG increased but not significantly (p=.114, McNemar's Chi-square test)
- Memory decreased (WMS) significantly (p=.003, Paired t)
- % of patient with abnormal values increased but not significantly (p=.144, McNemar's Chi-square test)

Correlation between BG & WMS (Cognition) at Baseline and other Baseline Variables

Correlation between BG & WMS (Cognition) at Baseline and other Baseline Variables				
	BG		WMS	
	r	P	r	P
PANSS	-0.210	.104	0.204	.115
NS	0.070	.593	-0.164	.206
PS	-0.006	.966	-0.150	.249
Duration	-0.051	.695	0.350	.006
Age at Intake	-0.014	.918	-0.088	.504
Sex	.243	.059	-0.047	.717

Association between Baseline Cognition (BG/WMS) and outcome parameters at 10 Year Outcomes

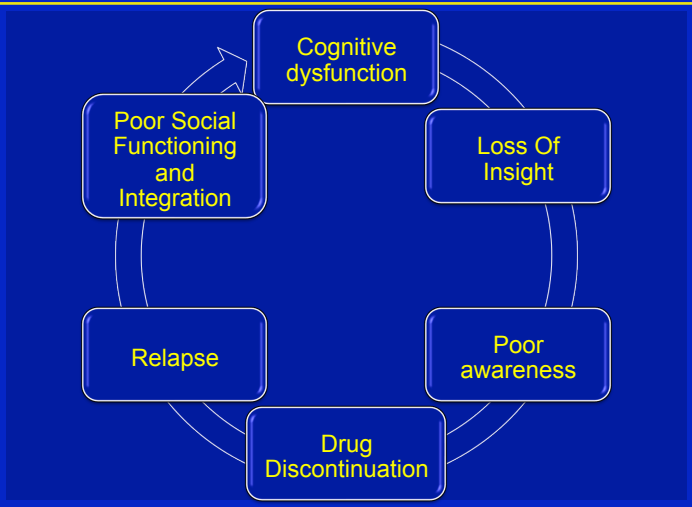
Association between Baseline Cognition (GB/WMS) at baseline and 10 Year Outcomes				
	BG		WMS	
10 Year Outcomes	Parameter Estimate (se)	P value	Parameter Estimate (se)	P value
PS	-0.042 (0.037)	.260	0.012 (0.039)	.766
NS	-0.052 (0.072)	.474	-0.029 (0.076)	.699
GP	0.133 (0.122)	.279	0.087 (0.129)	.503
HDRS	0.071 (0.054)	.196	-0.079 (0.054)	.146
GAF	0.176 (0.117)	.137	0.045 (0.124)	.721
QOL	-0.203 (0.109)	.067	0.112 (0.116)	.340
CGIS-I	0.0005 (0.0048)	.913	0.004 (0.005)	.487

Conclusion

Long-term Outcome of first episode schizophrenia does NOT differ across atypical antipsychotics

What decides quality of life of patients with schizophrenia?

Pathway for poor Outcome



Weiden et al. *Psych Services*, 2004

Determinants of outcome in schizophrenia

Illness Related

- illness loses its intensity [Dube K.C]
- definitions did not reveal significant variability [, Kulhara.P]
- Short duration of illness [vergese.et al]
- longer time spent in psychosis [Thara R]
- short-term course [Varma V.K.]
- Sexual, religious and grandiose delusions and flat affect [Thara, R]
- DUP, [Tirupati,, Yanos PT]
- Relapse [Yanos PT]
- Comorbidity
- negative syndrome
- cognitive functioning [Altamura AC]
- Premorbid level of functioning
- violence,
- severity of illness [Wittorf A]

Patient related

- absence of economic difficulties, Verghese A
- increase in religious activities Verghese A
- a non-schizoid pre-morbid personality [Verghese A]
- Male [DubeK.C.]

Family related

- Positive attitudes of relatives and neighbours, [Verghese A]
- EE
- Psycho-education [Kulhara P.]

Treatment related (nature)

- consistent compliance
- Reduced levels of membrane essential polyunsaturated fatty acids (EPUFAs),[Arvindakshan M,
- Rehabilitation [Chatterjee S]
- limited efficacy for specific domains of psychopathology of current treatments; [Yanos PT]

Treatment settings

- Developing country , [Dube.K.C., Varma.V.K. Dragomirecká E, Patel V, Kulhara.P
- Rural background, (Verghese A]

Environment related

- Mean environmental temperature [Gupta,S
- Bias [Thirthalli J]
- Transcultural factors [Kulhara.P]

Measures to maximise the outcome

- Early psychosis programme
- Cognitive enhancement and preservation
- Improvising insight, awareness and compliance
- Minimising EPS
- Minimising drop-outs and discontinuation
- Psycho-education
- Psychosocial intervention
- Cognitive behavioural
- Minimising hospital stay
- Relapse prevention

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