Suicide, schizophrenia and antipsychotics: Perspectives

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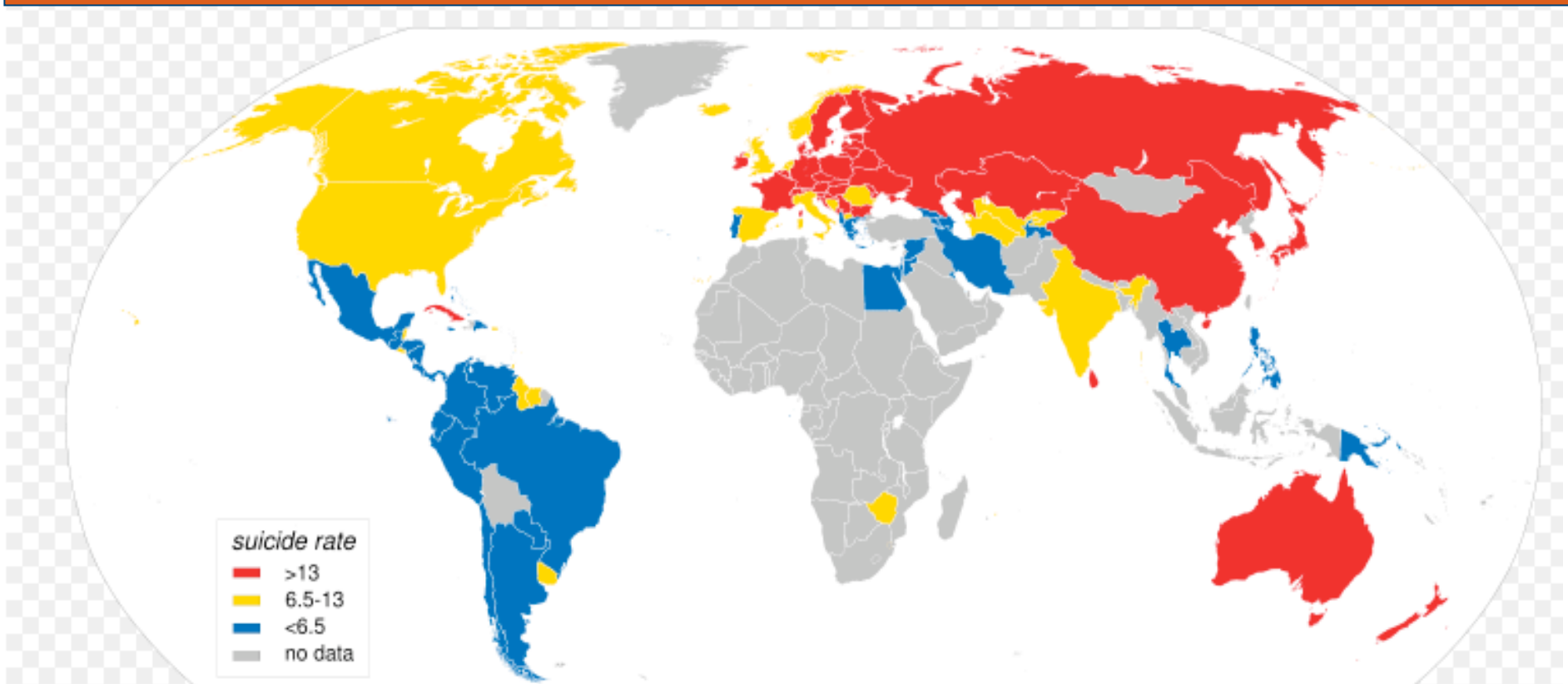
Objectives:

- Since antipsychotic treatment is the mainstream of the treatment of schizophrenia, we should know whether and how these drugs influence suicidal behaviour.
- What can be done to reduce suicide in schizophrenia?

>50% patients committing suicide have seen a doctor in preceding one month of their death (David Lester, 2004)

Suicide is a global public health problem, affecting more than a million people every year



In Canada Suicide Rate has tripled in 40 years, Male : female = 3:1

3200 per year, Rate 10-12/100,000

Source: statistics Canada 2003, Suicide in Canada (1994), Mental Health Division, Health Services Directorate, Health Canada

In clinical practice suicide is not uncommon

Despite advancement in psychosocial and pharmacological interventions, suicide rates in general have not decreased

- 1 in 6 completed suicides are patients in psychotherapy ,
- 1 of every 2 psychiatrists will lose a patient to suicide across (mean) 19.3 years practice
- 30% psychiatric residents across 4 years' residency
- 1 of every 4 psychologists will lose a patient to suicide across (mean) 18.5 years practice

- Formulation of 'mental disorders' >90% [1]
- >60-70% mentally ill experience & >20-30% attempt Suicidality [2]
- 20-35%-NO Mental Illness [3,4,5]

1.WHO, 2009; 2. Popali M 2006; 3.David Shaffer 1998, 4. Parkar 2009; 5. Shrivastava 2005

Case

- 17 male. acute psychosis from 100 Km
- Admitted - 8 weeks.
- Discharged with follow up after 4 weeks,
- No family physician Link
- On day 7; killed himself (under the train)

Case 2

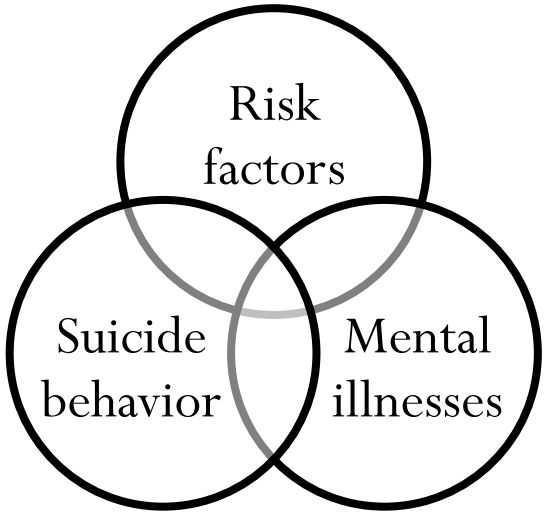
- NF, 52 years , FES, Hospitalized x 3 months
- Discharged on clozapine 175 me/day, CMHA and family support
- Good improvement, started going to school for second language, independent living, asymptomatic x 8 months
- Re-emergence of suicidal thoughts since 3-4 weeks, 'I can manage to push away these thoughts and want to stay home'.
- Re-admitted as involuntary patient
- Why this happened and What to do?

Case 3

- BM, 32 yr. Psychosis with aggressive personality, H/o suicidality and homicdal ideas, violence, admitted x 2 months, discharged with family support and psychiatric f/u. on quetiapine XR 600 mg/day and risperidone consta 37.5 mg Q 2 weeks.
- Recovery was moderate in terms of symptoms and functioning.
- After 3 months approached crisis with 'feeling suicidal and unsafe' , MSE showed depressed mood, and moderate to severe level of ideas
- Re-admitted

Paradigms in management of Suicidality

- Individuals: at-risk
- Risk situation
- Risk factors



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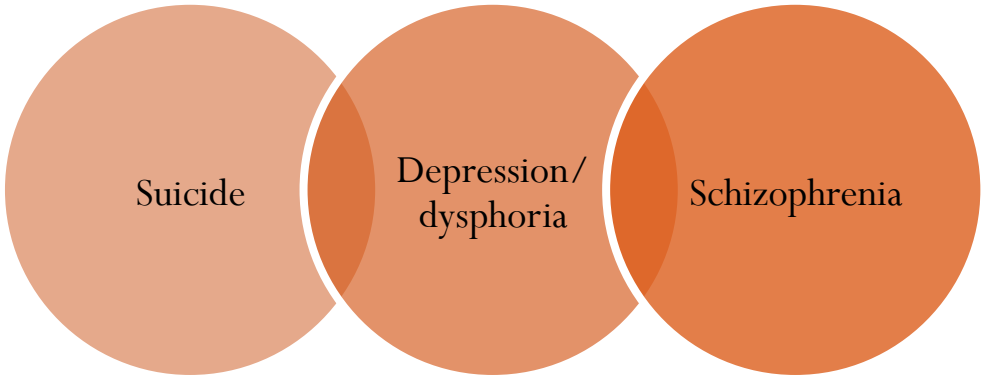
The Lifetime Risk of Suicide in Schizophrenia A Reexamination

- 9- 13% died due to suicide
- 50% suicide ideation / suicidality, 25% suicide attempt
- Data has been challenged (4.9%)
- Suicide rates in schizophrenia have increased (despite FGA or SGA
  - Healy, et al. (2006) *Number of suicides in 5 years follow up in the 1994–1998 cohort was considerably higher than 1875-1925 Explained by*
  - Deinstitutionalisation, brief admissions and, abrupt discontinuation of antipsychotic treatment

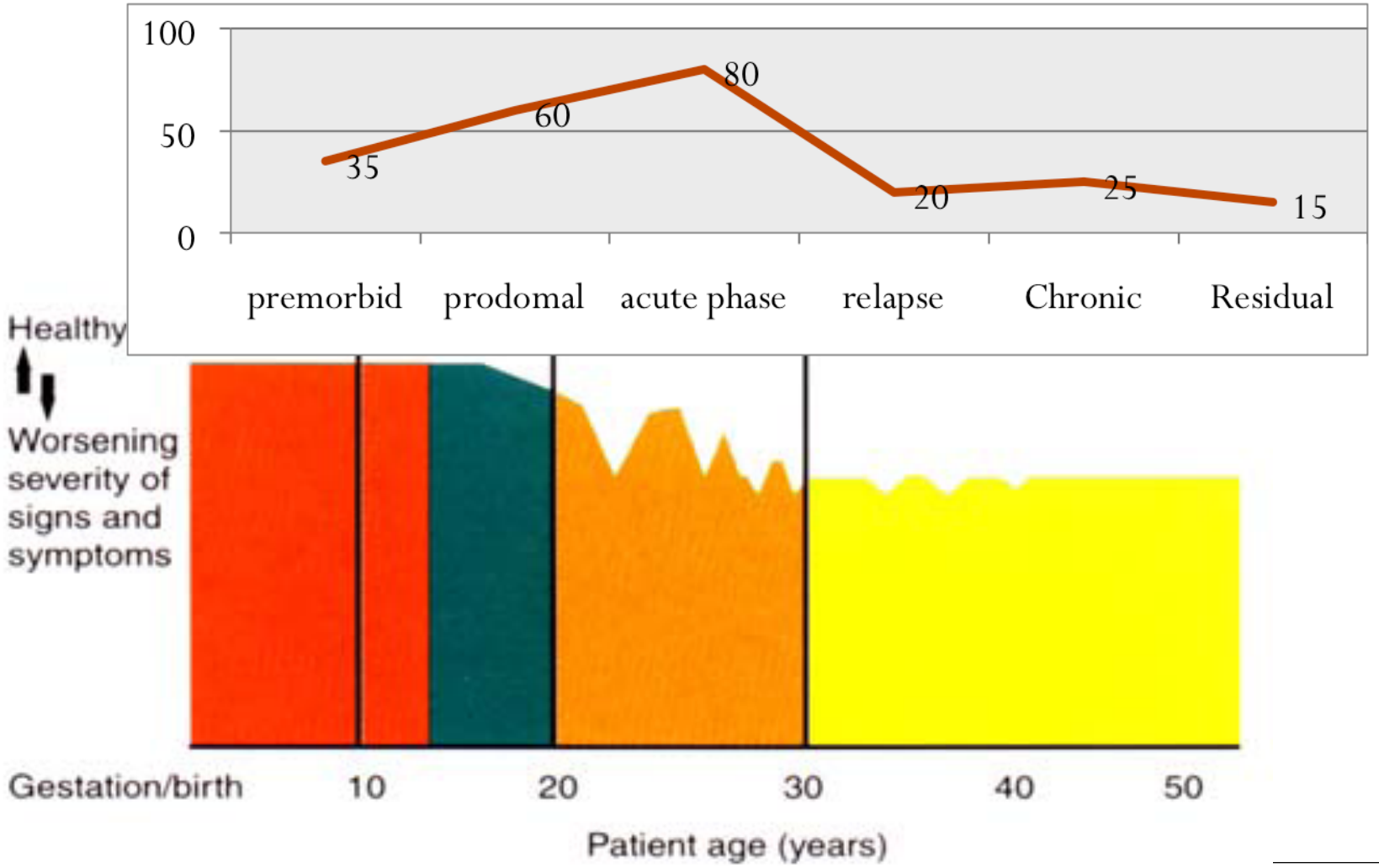
Brian A. PalmerThe Lifetime Risk of Suicide in Schizophrenia, A Reexamination Arch Gen Psychiatry. 2005;62:247-253

‘Suicidality’: Clinical situations

- Acute onset/ illness
- Maintenance phase
  - Episodes of Suicidality
  - Re-emergence of Suicidality
  - Persistent Suicidality
- Chronic Suicidality



Depression occurs across the course of schizophrenia



Guidelines and Management

- Assessment of suicide risk/ severity
- Prediction
- Safety
- Crisis intervention
- Psychosocial interventions
- Psychopharmacology ????????
- ECT ??

Suicide as first contact

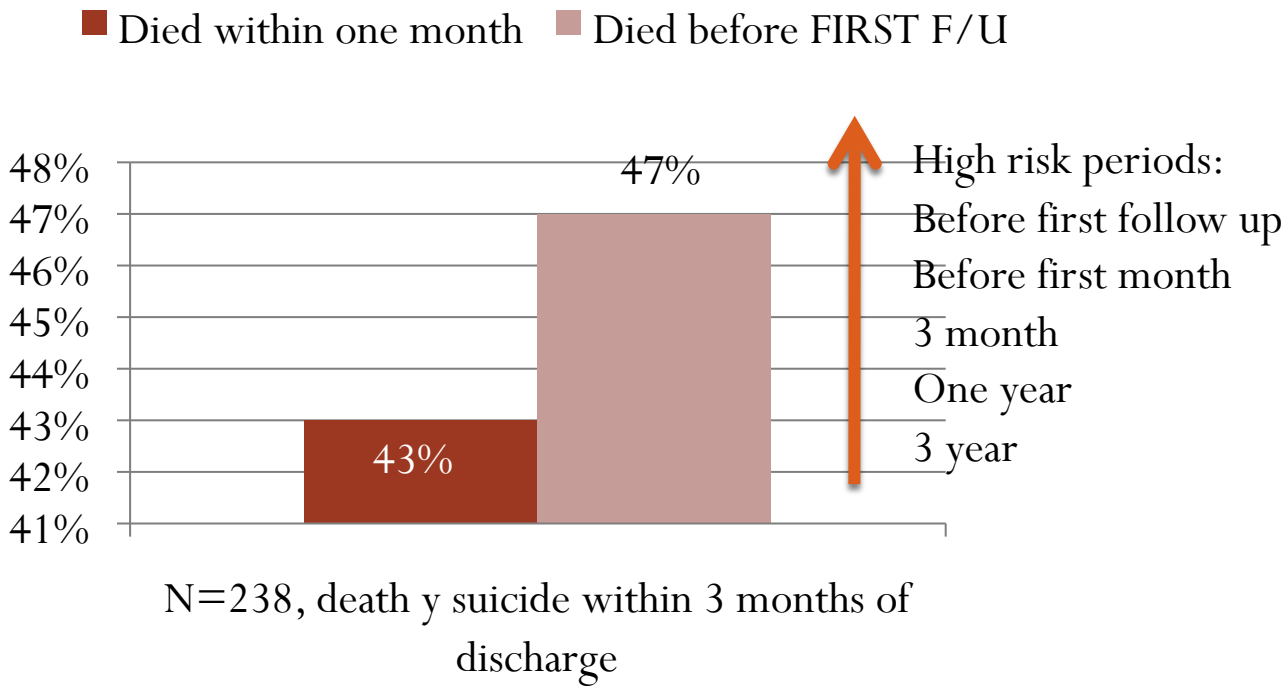
Studies	Attempt Prior to contact	Attempt During treatment	Death
Aust.NZ.J.2009	4.3%	8.7%	0.4%
Act.Psych.Scand.2004	15%	2.9%	
BJP, 2008	4.3%	8.7%	
BJP, 2007	4.5%		12.2%
Can.J. Psychiatry, 2006	18.8%		

Risk syndrome and early phase of schizophrenia

The staging model of psychosis

Mc Gorry.P.D.et all

High suicide in recently discharged patients [1]



N=238, death y suicide within 3 months of discharge

Majority of suicide: in first 3 years[71%]

Long –term follow up: 13 years f/u Study showed SMR as 48.9, [2]

1. Alaraisanen A , Suicide rate in schizophrenia in the Northern Finland 1966 Birth Cohort. Soc.Psychiatry Psychiatr.Epidemiol. 2009 Dec;44 (12):1107-1110
2. Ajdacic-Gross V,In-patient suicide - a 13-year assessment. Acta Psychiatr Scand. 2009

Heritability / family History

- Overlapping endophenotypes of suicide and schizophrenia
- *Cluster B traits and impulsive behavior represent intermediate phenotypes of suicide*
- Issue of family history raises question about What is inherited?
  - Impulsive behaviour
  - Dyscontrol
  - Poor coping
  - Low frustration tolerance
- Suicide in a subtype of schizophrenia

  (Meltzer & Okayli, 1995). (Hawton, et al., 2005).

Psychological dimensions of schizophrenia contributing to suicide

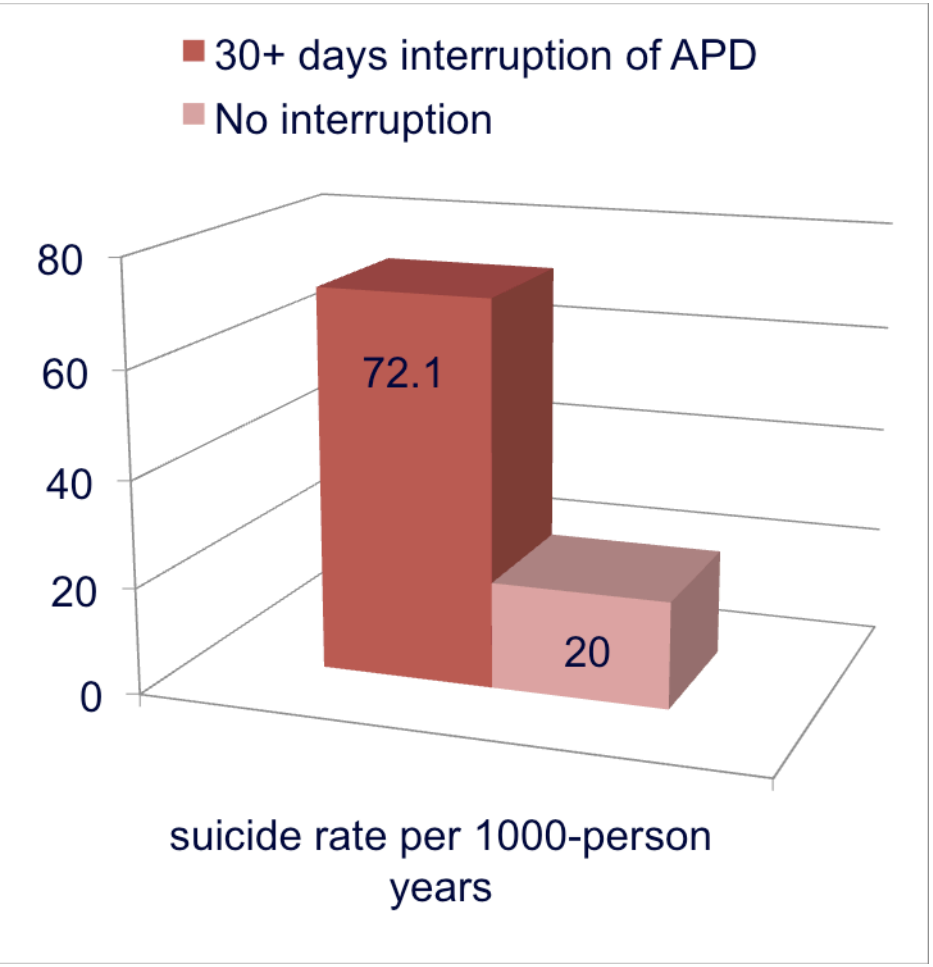
- Anxiety
- Hostility
- Impulsivity
- Aggression
- depression,
- Psychotic symptoms
- Dysphoria

APD side effects and suicide

- EPS
- TD
- Dysphoria
- Depression
- Akathesis
- Akinesia

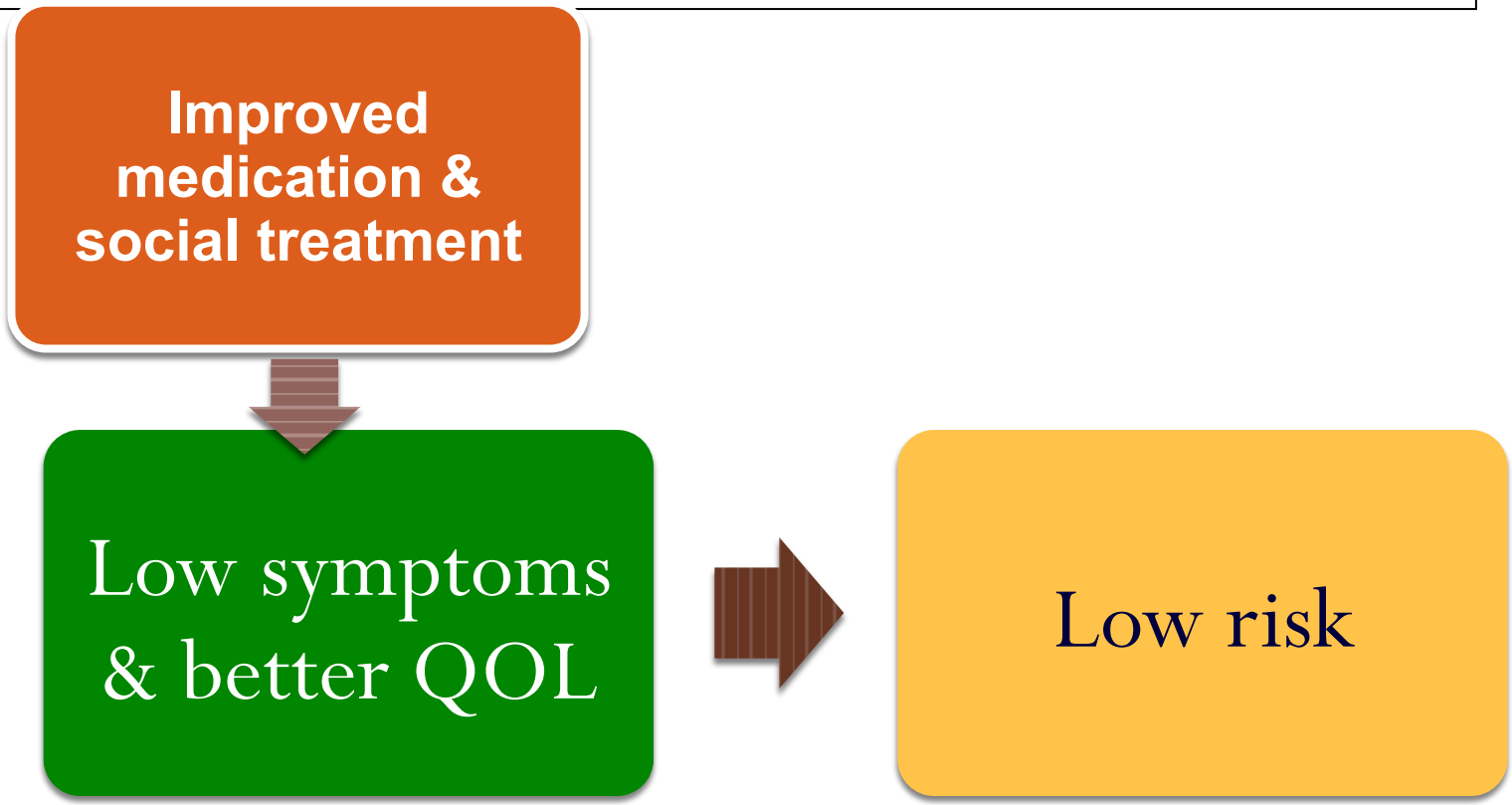
Suicide Attempt increases when Atypical Antipsychotic Therapy is Interrupted.

- A study by Herings and Erkens (2003) has demonstrated a four-fold increase in suicide attempts for patients who interrupt or stop treatment with olanzapine or risperidone.



Herings RM, Erkens JA Pharmacoepidemiol Drug saf. 2003;12;423-424

How does it work?



Antipsychotics and suicide: FGA and SGA

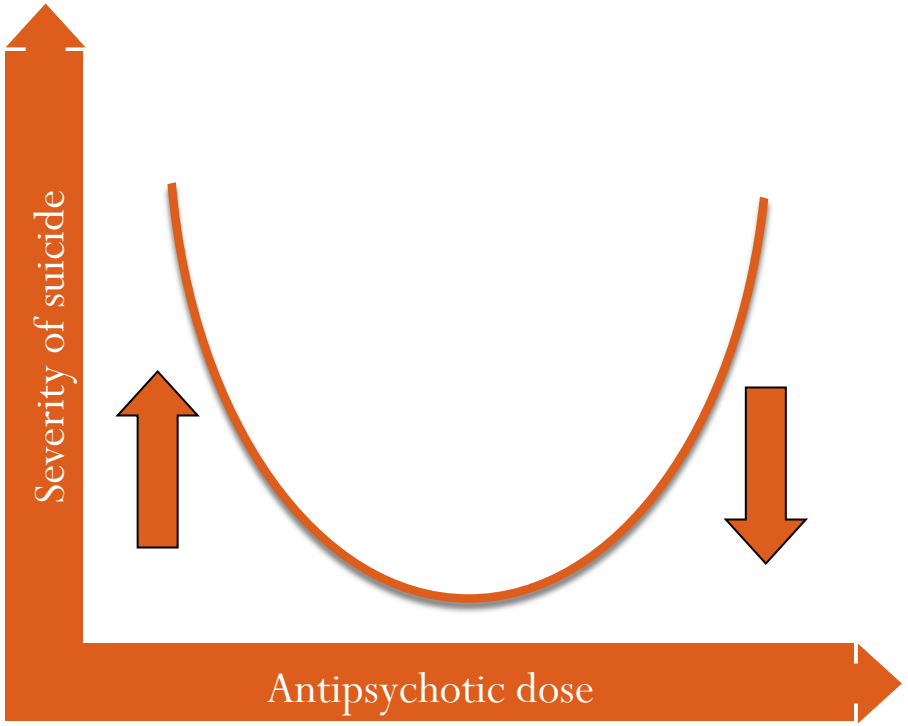
- Decrease Suicidality
- Increase Suicidality
- Do not influence Suicidality
- Several controlled studies have rejected a negative influence
- Reduce the risk of suicide and suicide attempts in schizophrenia.
- Evidence suggests that not all antipsychotics have the same potential for preventing suicide.

Options in optimization

- Antipsychotics
  - Decrease
  - Increase
  - Discontinue
  - Adjunct
- Adjuncts
  - BZ
  - ADD
  - Mood stabilizers
    - Lithium
    - antiepileptic

Antipsychotic dosage and Suicidality

- Exacerbation of psychosis
- Neurological and other side effects
- Suicide behavior



- It could also be that antipsychotics do not help to prevent suicidal behaviour because suicide may be a partially independent illness.
-

Clozapine

- InterSePT (Meltzer, et al., 2003). –
- compared clozapine versus olanzapine in 980 patients
- The mode of action of clozapine in preventing suicide
- is not known.
- Possible mechanisms are
  - a direct antidepressant action,
  - an indirect effect through the improvement of
  - cognitive functioning,
  - compliance,
  - insight,
  - negative symptoms and
  - substance abuse,

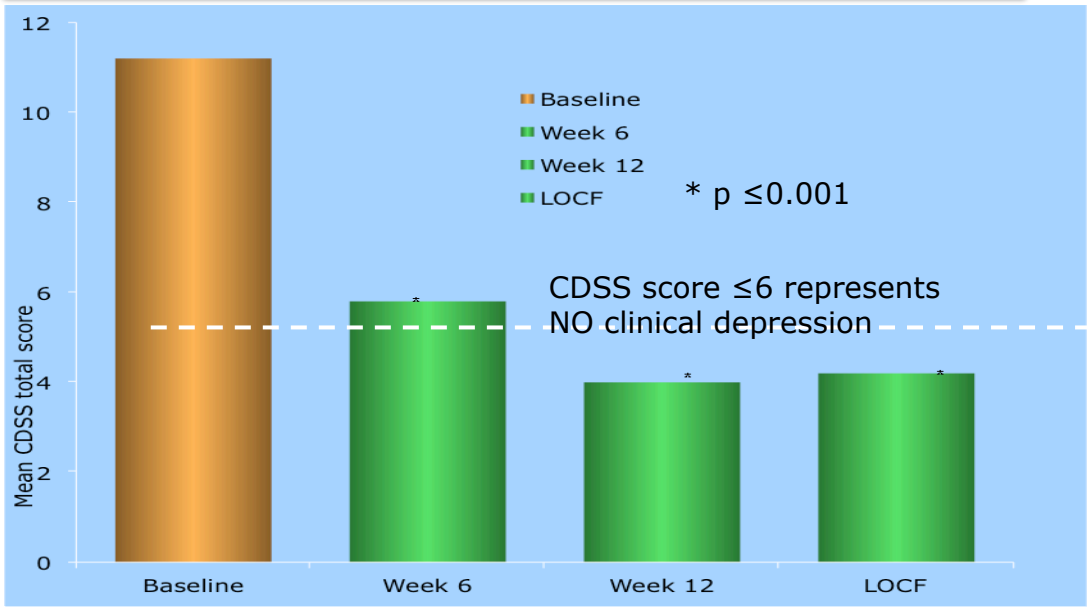
Other SGA & Clozapine : mechanism for reduction in Suicidality

- Specific effects on neurotransmitters and serum lipid levels
- Lower rates of akathisia and tardive dyskinesia.
- Action through normalizing serotonergic function
- Both its antidepressive effect and its specificity on suicidal behaviour can be mediated by
  - an increased central availability of norepinephrine and dopamine,
  - along with a normalization of central 5-HT activity, especially in the prefrontal cortex, through down-regulation of central 5-HT_{2A} and increased availability of central 5-HT (Spivak, et al., 2003).

Quetiapine

SPECTRUM, 12-wk, open trial in patients with schizophrenia switched to quetiapine (n=509)

Subgroup with clinically significant depressive symptoms at baseline



- 69% of patients who switched from previous antipsychotic to quetiapine had a clinical improvement
- Improvements after switching in both group of patients
  - poor efficacy
  - intolerable SEs with previous therapy

CDSS: Calgary Depression Scale for Schizophrenia

1. De Nayer *et al*. *Int J Psych Clin Pract* 2003;7:59-66.

Selecting antipsychotics in view of reduction in Suicidality

- Second generation
- High efficacy
- Low EPS
- Effective of anxiety , depression, hostility, impulsivity and aggression
- High compliance
- Fewer relapses
- Fewer dysphoria

Quetiapine

- Anxiety-hostility
- Impulsivity
- Depression-dysphoria
- Psychosis
- Sedation aggression
- Low EPS
- Acute suicidal crisis
- Long term maintenance
- Relapse prevention

Benefits of switching

Figure 2. Potential Side Effect Benefits When Switching Between Antipsychotic Medications[a,b]

Preswitch Antipsychotic	Postswitch Antipsychotic: Aripiprazole	Olanzapine	Quetiapine	Risperidone	Ziprasidone
Haloperidol	↓↓ EPS ↓↓ Prolactin ↓ Akathisia ↓ Sedation	↓↓ Akathisia ↓↓ EPS ↓↓ Prolactin	↓↓↓ Akathisia ↓↓↓ EPS ↓↓ Prolactin	↓ Akathisia ↓ EPS	↓↓ EPS ↓↓ Prolactin ↓ Akathisia ↓ Sedation
Aripiprazole		↓ Akathisia ↓ Insomnia	↓↓ Akathisia ↓ EPS ↓ Insomnia	↓ Insomnia	↓ Akathisia ↓ Insomnia
Olanzapine	↓↓↓ Dyslipidemia ↓↓↓ Weight ↓↓ Sedation ↓ Prolactin		↓ Akathisia ↓ Dyslipidemia ↓ EPS ↓ Prolactin ↓ Weight	↓ Dyslipidemia ↓ Sedation ↓ Weight	↓↓↓ Dyslipidemia ↓↓↓ Weight ↓↓ Sedation
Quetiapine	↓↓ Sedation ↓ Dyslipidemia ↓ Orthostatic Hypotension ↓ Weight	↓ Orthostatic Hypotension		↓ Sedation	↓↓ Sedation ↓ Dyslipidemia ↓ Orthostatic Hypotension ↓ Weight
Risperidone	↓↓↓ Prolactin ↓ Dyslipidemia ↓ EPS ↓ Orthostatic Hypotension ↓ Sedation ↓ Weight	↓↓ Akathisia ↓↓ EPS ↓↓ Prolactin ↓ Orthostatic Hypotension	↓↓↓ Akathisia ↓↓↓ EPS ↓↓↓ Prolactin		↓↓ EPS ↓↓ Prolactin ↓↓ Weight ↓ Dyslipidemia ↓ Orthostatic Hypotension ↓ Sedation
Ziprasidone	↓ Prolactin ↓ Sedation	↓ Akathisia ↓ Insomnia	↓ Akathisia ↓ EPS ↓ Insomnia	↓ Insomnia	

[a]Reprinted with permission from Weiden.[6]

Program based intervention

	Community with EI	Community without EI
Rates of suicidal ideation & attempt	56%	39%
Previous attempt	16%	5%
Decrease in Rates after first clinical contact	Similar	Similar
SUD	High	Low
Suicidal behaviors	Low	High

Clinical practice

- Awareness
- Ongoing Assessment
- Recognizing suicidogenic psychological factors
- Selection of antipsychotics
  - Anxiety
  - Aggression
  - Hostility
  - Impulsivity
  - Dysphoria /depression

Prevention of Suicide in Psychotic Disorders:

- Discharge when fit
- Assess suicidality and while discharging
- Address comorbidity; alcohol, drug abuse
- Offer comprehensive management
- Medications
- Psychosocial intervention is mandatory
- Identify level of acceptance of 1.illness, 2. treatment
- Identify risk & predictors
- Tighten the gap in planning and implementation
- Use measurements and quantification tools
- Be sensitive to 'Change' in patients life

Prevention of Suicide in Psychotic Disorders:

- Do not discharge if there is
  - Current Risk , Symptoms, Side effects
  - Transitional state of syndromes
  - Poor after care
- Deal with side effects and monitor
- Avoid typical antipsychotics
- Be careful about 'EPS-Depression-Dysphoria' complex
- Do not reduce dosage prematurely (Minimum 12 months remission)
- Be watchful for switch to mania with TCA & SSRIs
- Don't reduce the quality of care package without very thorough assessment

Need for paradigm shift in management of suicide behavior.

Breaking the barriers for identification

1. at-risk individuals
2. Risk factors
3. Risk situations

From mental disorders to RISK for mental disorders