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Current Understanding and Pharmacological Management of Suicide Behavior in Clinical Setting

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Current understanding and Pharmacological management of suicide behavior in clinical setting.

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'Nearly half a century of routine clinical use of such treatments as, ADD, ECT, CBT, has not yielded evidence of reduction of long term suicidal risk ..., including from accidents, substance abuse, or stress-related cardiopulmonary distress'

Tondo, JCP, 2000

Learning objectives

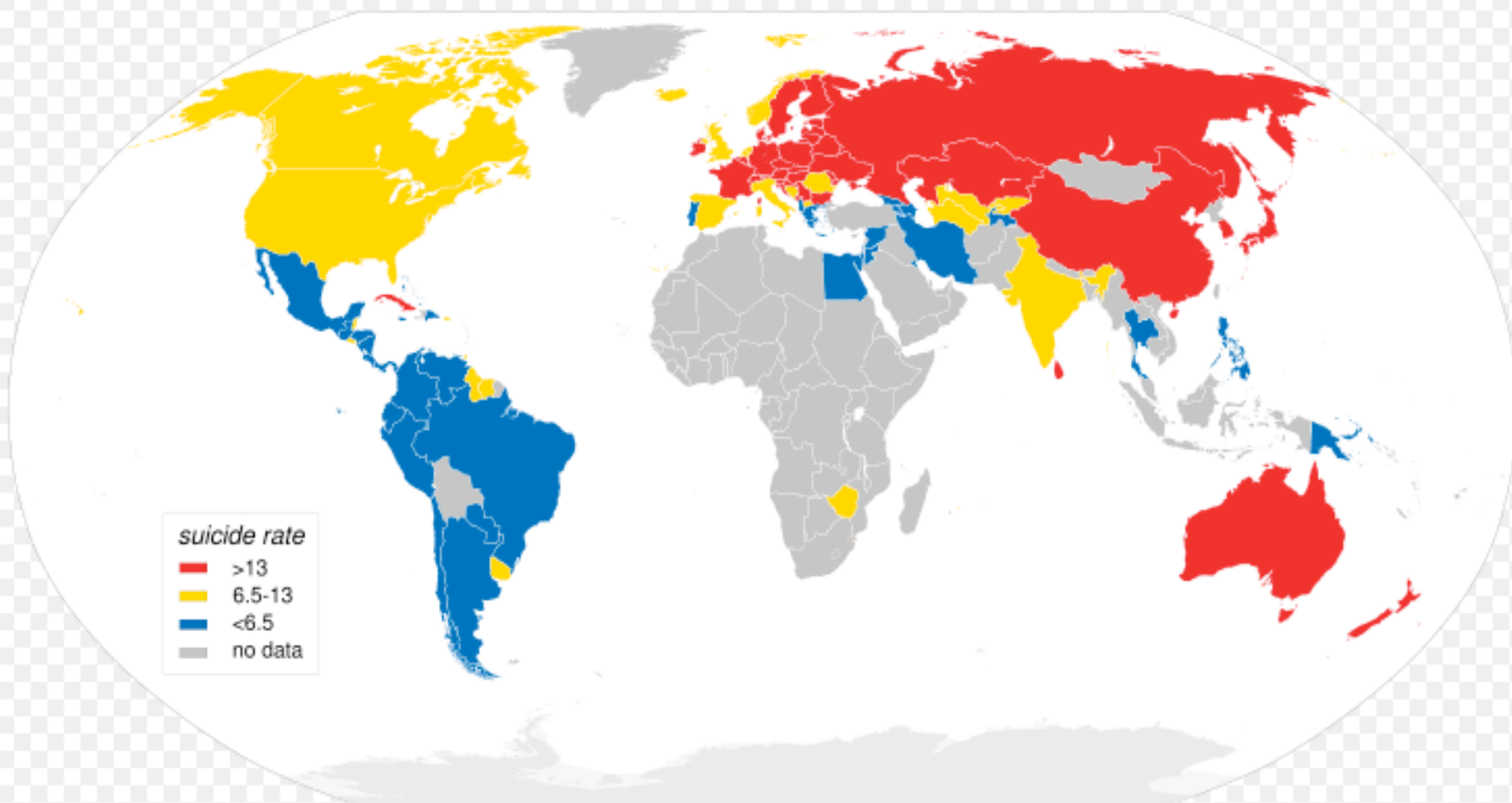
- Nature of problem in clinical settings.
- Current Understanding about suicide behavior (neurobiology)
- What can be done to deal with suicide in clinical settings
- Pharmacological management
 - Diagnosis
 - Pharmacological agents

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

Image

File history

Links



Suicide in clinical practice is NOT uncommon

- >50% - seen a physician in previous one month¹
- 50% of had experience in psychotherapy
- 1 of every 2 psychiatrists lose a patient to suicide across 20 years practice

Clinical issues and challenges

- Magnitude, Predictability
- Uncertain etiology
- Heterogeneous
- Unreliable Risk Assessment
- No specific treatment
- No evidence that it can be prevented

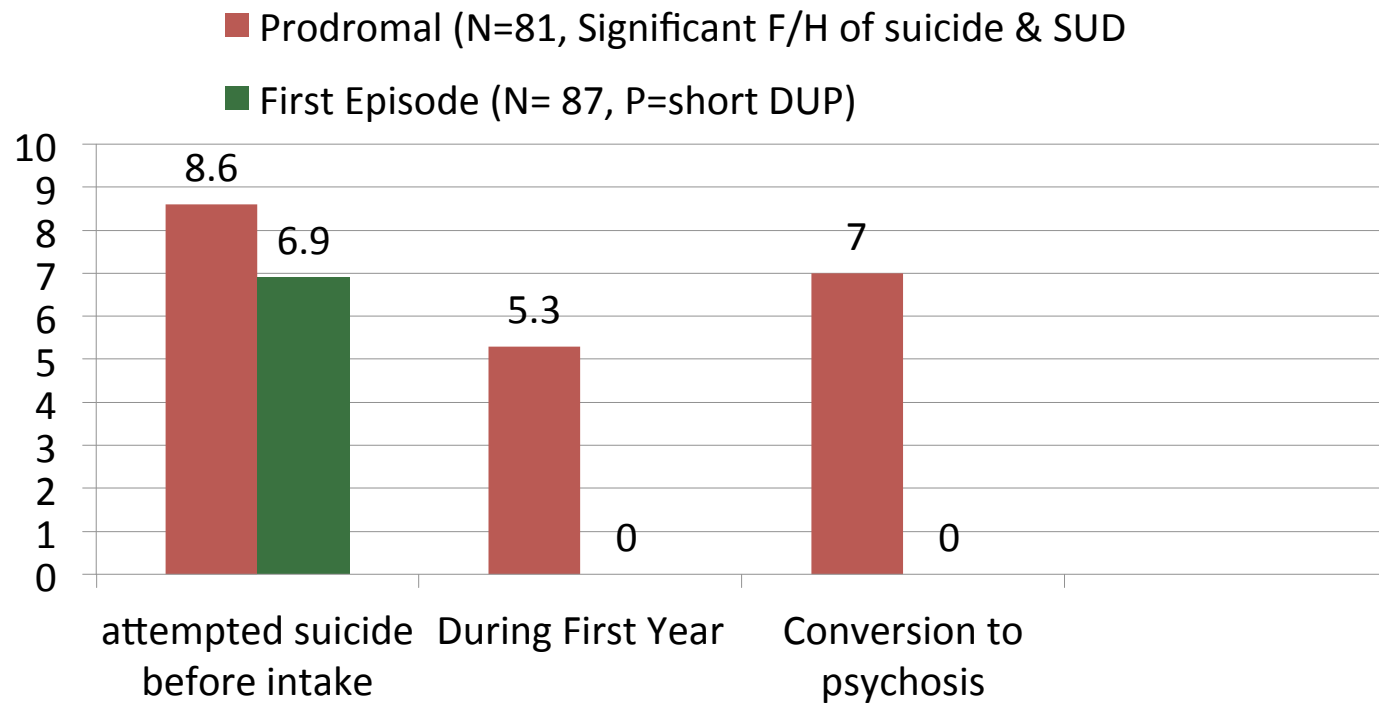
‘defeat depression’ program, UK.

US military using preventive program

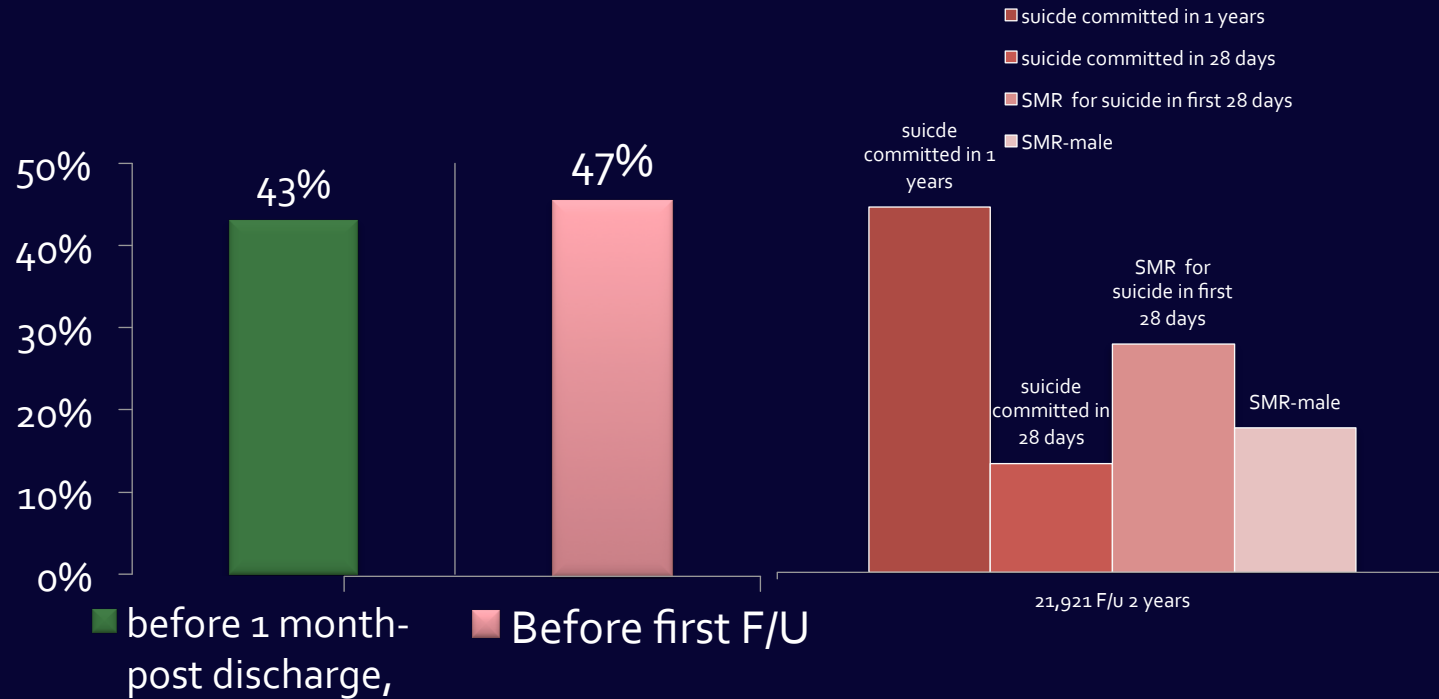
Magnitude of of death by suicide clinical settings ^{1,}

- 5-6.5% in hospital;
- 3 to 5.5% in psychiatric hospital and
- 2% in general hospital Inpatient. Rate
- 1% of all suicides in UK occurs in inpatients facility ²

Risk of suicide and suicidal ideation in psychosis & At-Risk clients: Italian study



Post discharge suicide



Current understanding of suicide behavior

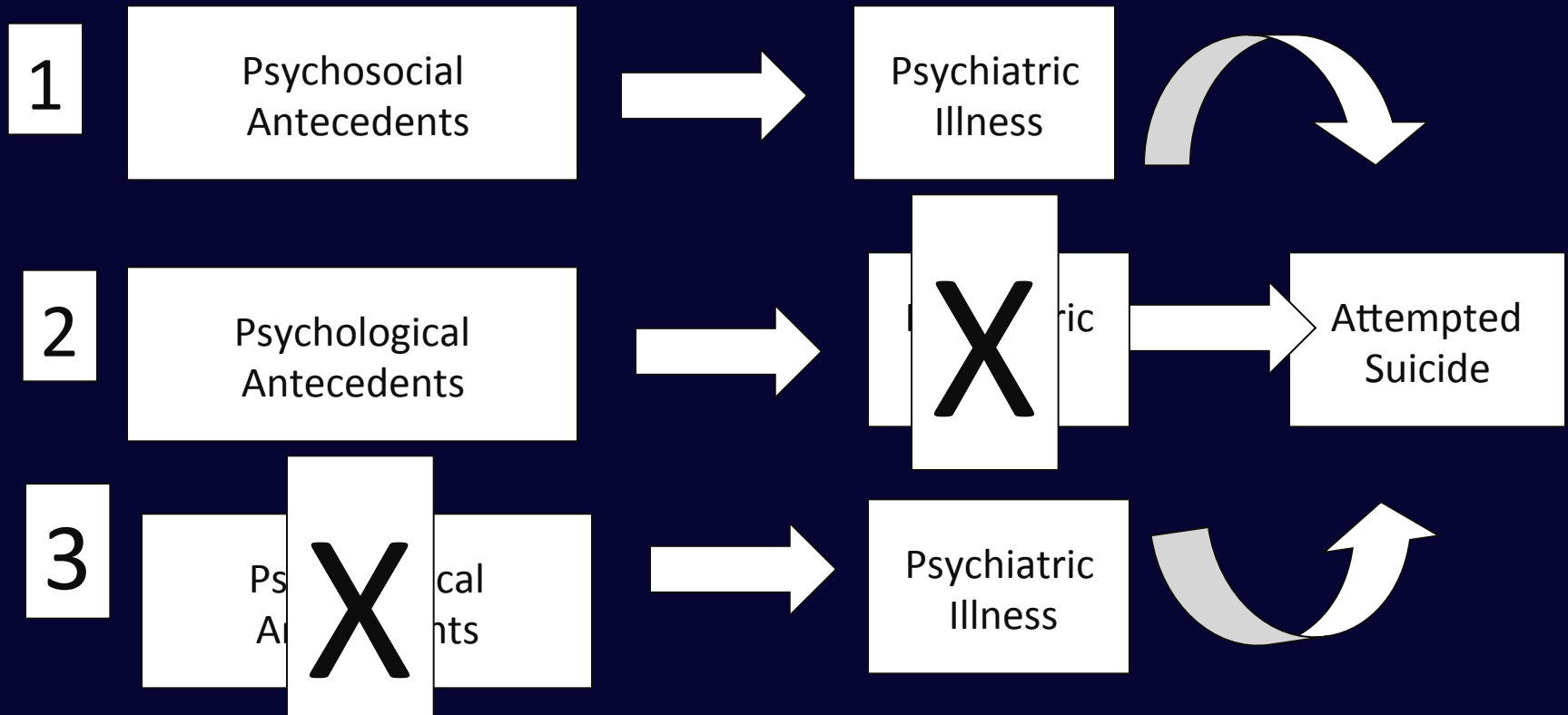
Paradigms in understanding of Suicidality

- Individuals At-risk
- Risk situation
- Risk factors
- ‘mental disorders’ >90% ¹
- >60-70% mentally ill experience Suicidality ²
- 20-35%-NO Mental Illness ^{3,4,5}

Suicide behavior is not necessarily a correlate of mental illness:

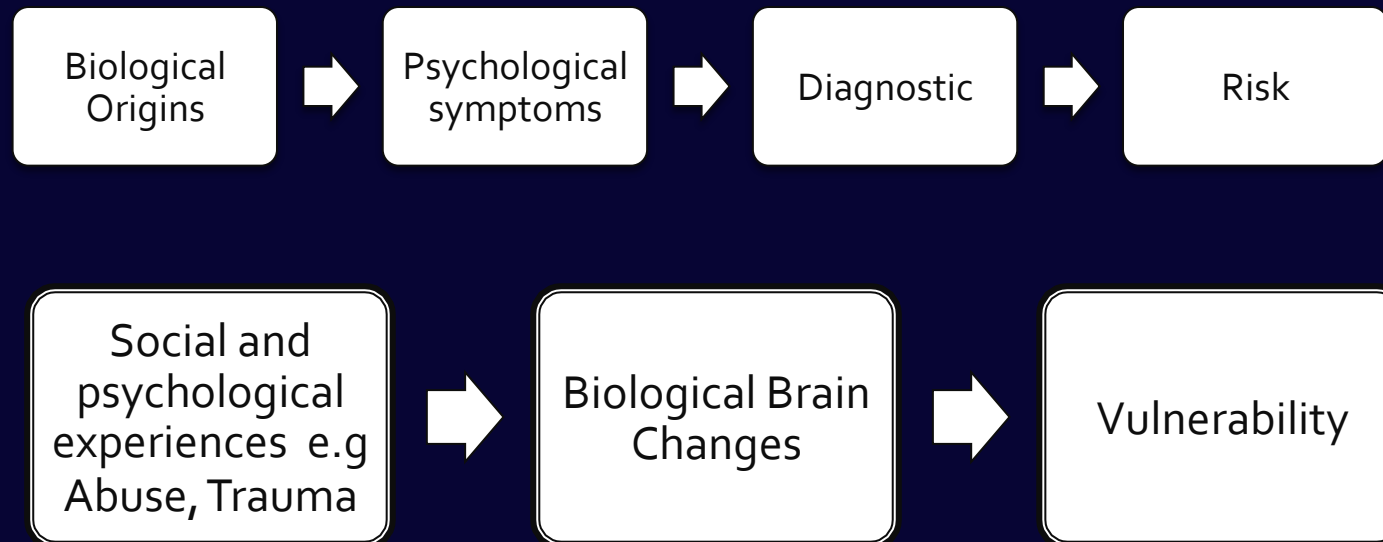
1. WHO, 2009; 2. Popali M 2006; 3. David Shaffer 1998, 4. Parkar 2009; 5. Shrivastava 2005

Re-organizing Pathways to Suicide

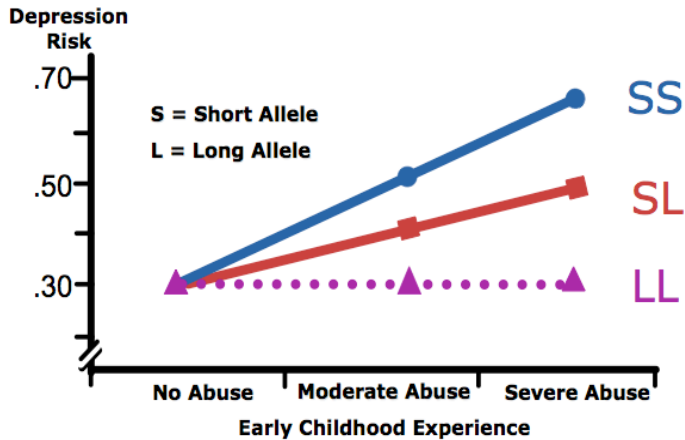


DSM-V, Axis II:
David Shaffer³

Paradigm shift in understanding of suicide behavior

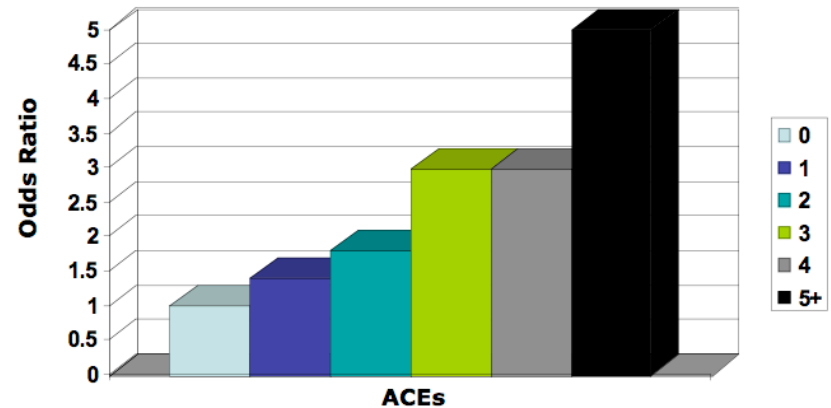


Serotonin Transporter as Model of Gene-Environment Interaction



Source: Caspi, 2003

Adverse Childhood Experiences and Adult Depression



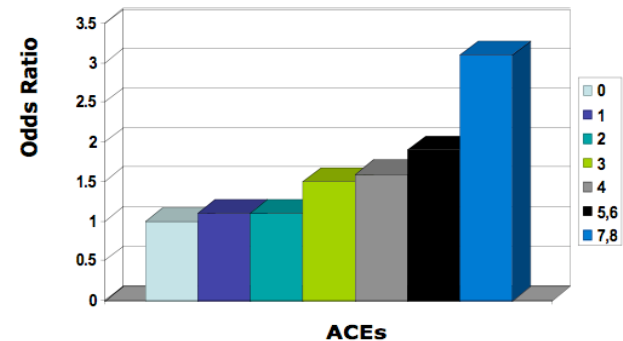
Source: Chapman et al, 2004

Public Health Thinking Should Extend Beyond Traditional Policy Boundaries

If we really want to promote better health outcomes, then we must apply the science of early childhood and early brain development to a broader range of policies ...

including child welfare services, adult mental health treatments, and workforce development programs for low income mothers, among others.

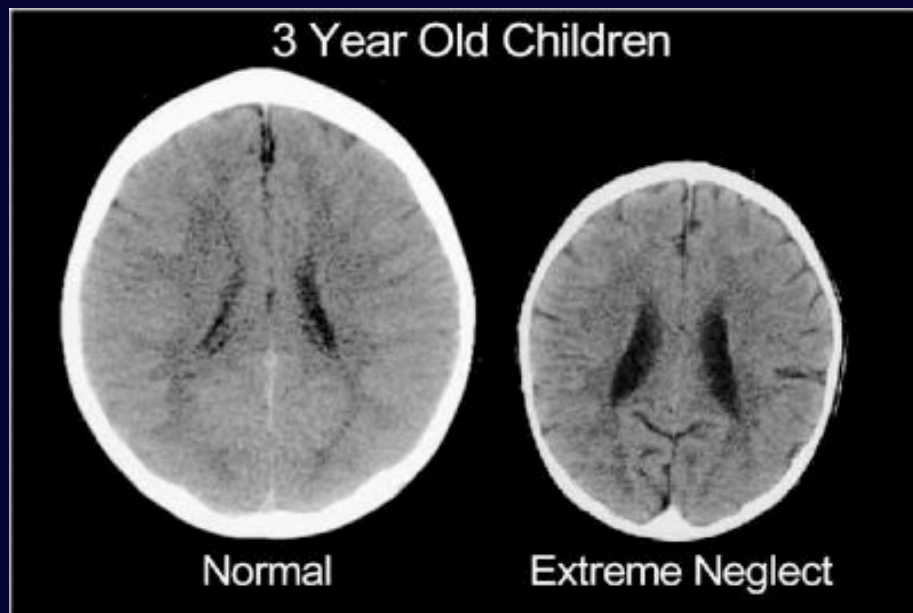
Adverse Childhood Experiences and Adult Cardiovascular Disease



Source: Dong et al, 2004

Neurobiology – child hood sex abuse

Childhood Experience & the Expression of Genetic Potential: What
Childhood Neglect Tells Us About Nature and Nurture?



CHILD ABUSE
Because daddy had a tough day at work.

1. Chen TJ, *Med Hypotheses*. 2006;66(5):1043-4.
2. Anda RF, *Eur Arch Psychiatry Clin Neurosci*. 2006 Apr;256(3):174-86. 2005

Suicide--Risk for Schizophrenia

- A cohort of 2759 of CSA
- Schizophrenia = 2.8% Vs. 1.4%

[Cutajar MC et al,, Archives Gen psychiatry 2010 Nov]

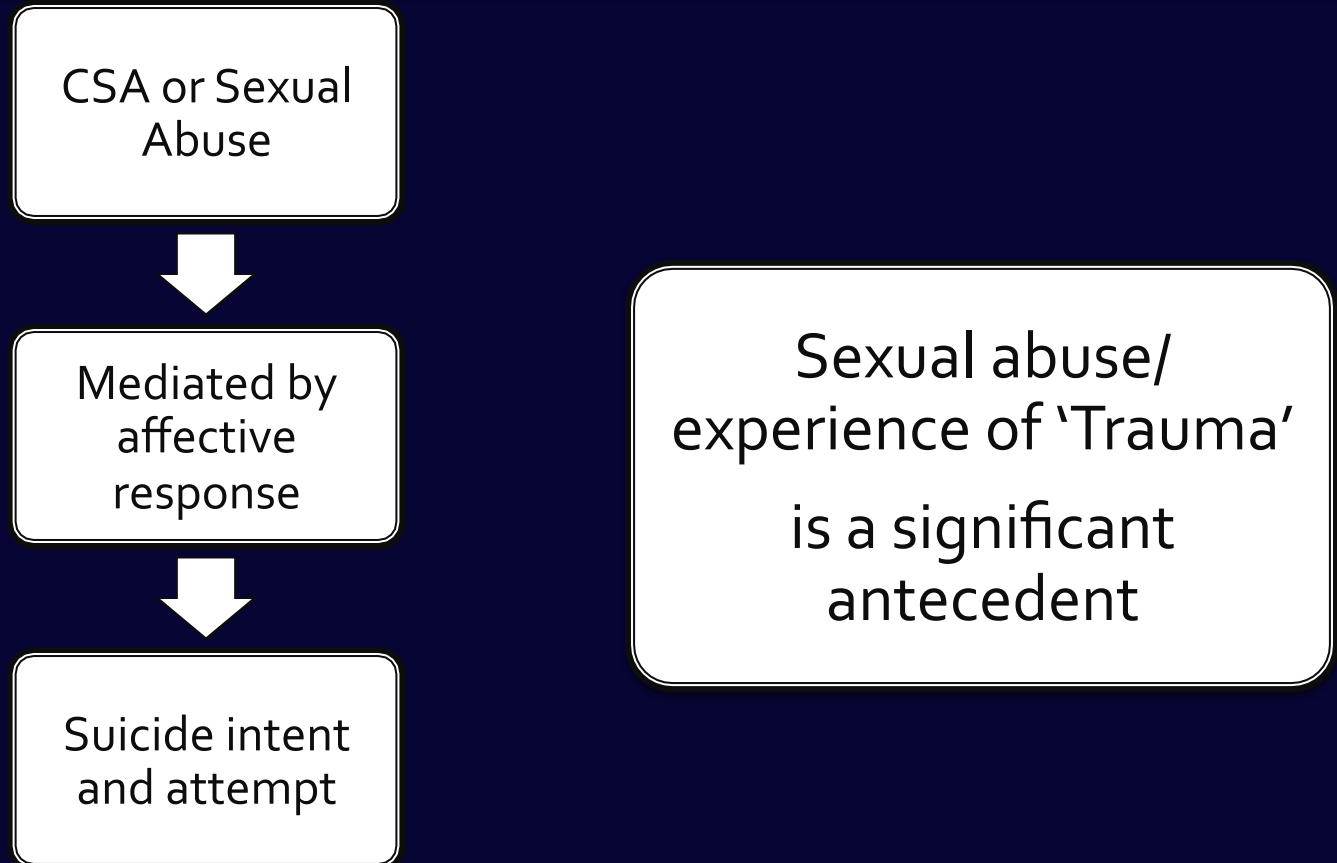
Impulsivity- Link with childhood experience and trauma

- Childhood sex abuse ^{1,2}
- Post traumatic stress disorder ³
- Childhood adversity ⁴
- Early prolonged trauma
- Chronic exposure to trauma,
- Neurobiology: Serotonin hypofunction, HPA Axis ⁵
- Overlap between neurobiology of SB and impulsivity

1. Maniglio R. The role of child sexual abuse in the etiology of suicide and non-suicidal self-injury. *Acta Psychiatr Scand.* 2010 Oct 11. doi: 10.1111/j.1600-0447.2010.01612.x; 2. Roy A. Combination of family history of suicidal behavior and childhood trauma may represent correlate of increased suicide risk. *J Affect Disord.* 2010 Oct 11; 4. Lentz V, Robinson J, Bolton JM. Childhood adversity, mental disorder comorbidity, and suicidal behavior in schizotypal personality disorder *J Nerv Ment Dis.* 2010 Nov;198(11):795-801.

Braquehais MD, Oquendo MA, Baca-Garcia E, Sher L. Is impulsivity a link between childhood abuse and suicide? *Compr. Psychiatry* 2010 Mar-Apr;51(2):121-129

Suicide attempts, gender, and sexual abuse: data from the 2000 British Psychiatric Morbidity Survey.2009



Suicide as an independent psychopathological axis: The evidence:^[a]

- Epidemiological,
- Phenomenological,
- Biological,
- Genetic,
- biochemistry

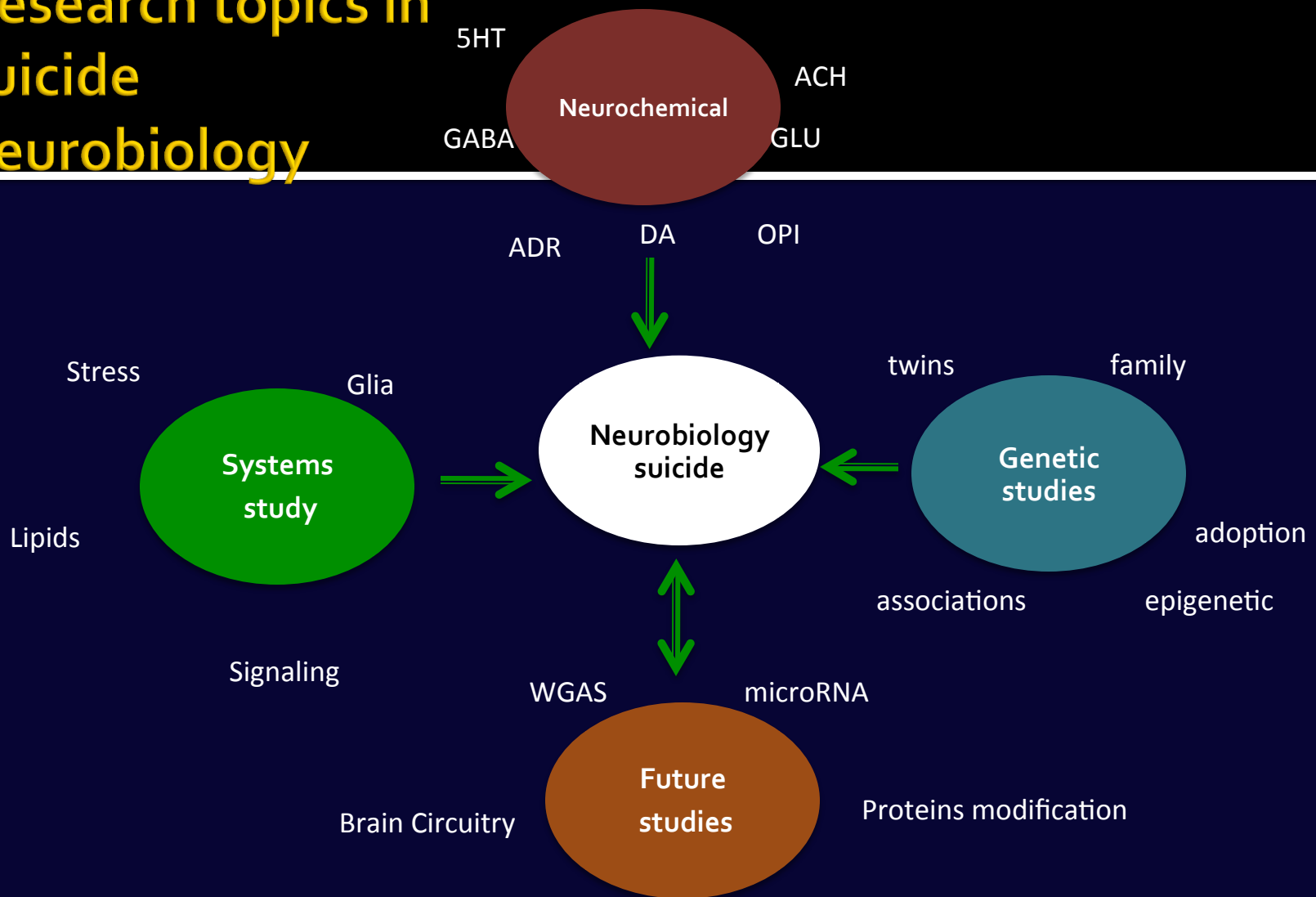
Supportive data for independent axis

- Psychopathology
- Impulsivity
- Across diagnosis
- No diagnosis
- Severity of illness Vs
Severity of attempt
- Cluster B
- Suicide:: subtype of
schizophrenia
- DSM-5

Implication: two treatment goal : 1.Treat mental illness,
2.Treat suicidality

(Meltzer & Okayli, 1995¹). (Hawton, et al., 2005)².

Research topics in suicide neurobiology



DA-dopamine, ADR-adrenaline, 5HT-serotonine,OPI – opiates, GLU-glutamate, WGAS-whole genome association study

Carl Ernst et al 'Suicide neurobiology, Progress in neurobiology 89 (2009) 315-333

Research n suicidology

Neurochemical,
5Ht, ACH, GABA, GLU,
ADR, DA, OPI

Genetics;
Twins, family, Adoption,
Association,
Epigenetics

Neurobiology

system study;
Glia, Stress, Lipids,
Signaling

Future study,
WAGS, micro RNA,
Proteins study, Brain
circuitry

Biological pathway; No simple method how to study neurobiology

- Uncovering markers
- Low sensitivity and predictability
- Environmental factors.
- No formal neurobiological consensus
- Indices of serotonergic NT and risk
- The 5 Ht association
 - 'unspecific;
- mRNA proteins, - dismissed,
- GABAergic and glutaminergic dysfunction
- Etiological heterogeneity
- Endophenotypes
- White matter volume

Nature and nurture in suicidal behavior, HPA response & NA response

Suicidal behavior and heredity

Genetic
investigation
of suicide
and suicide
attempt
(GISS)

Genes
implicated in
suicidality—
Serotonin

Change in
brain
structures

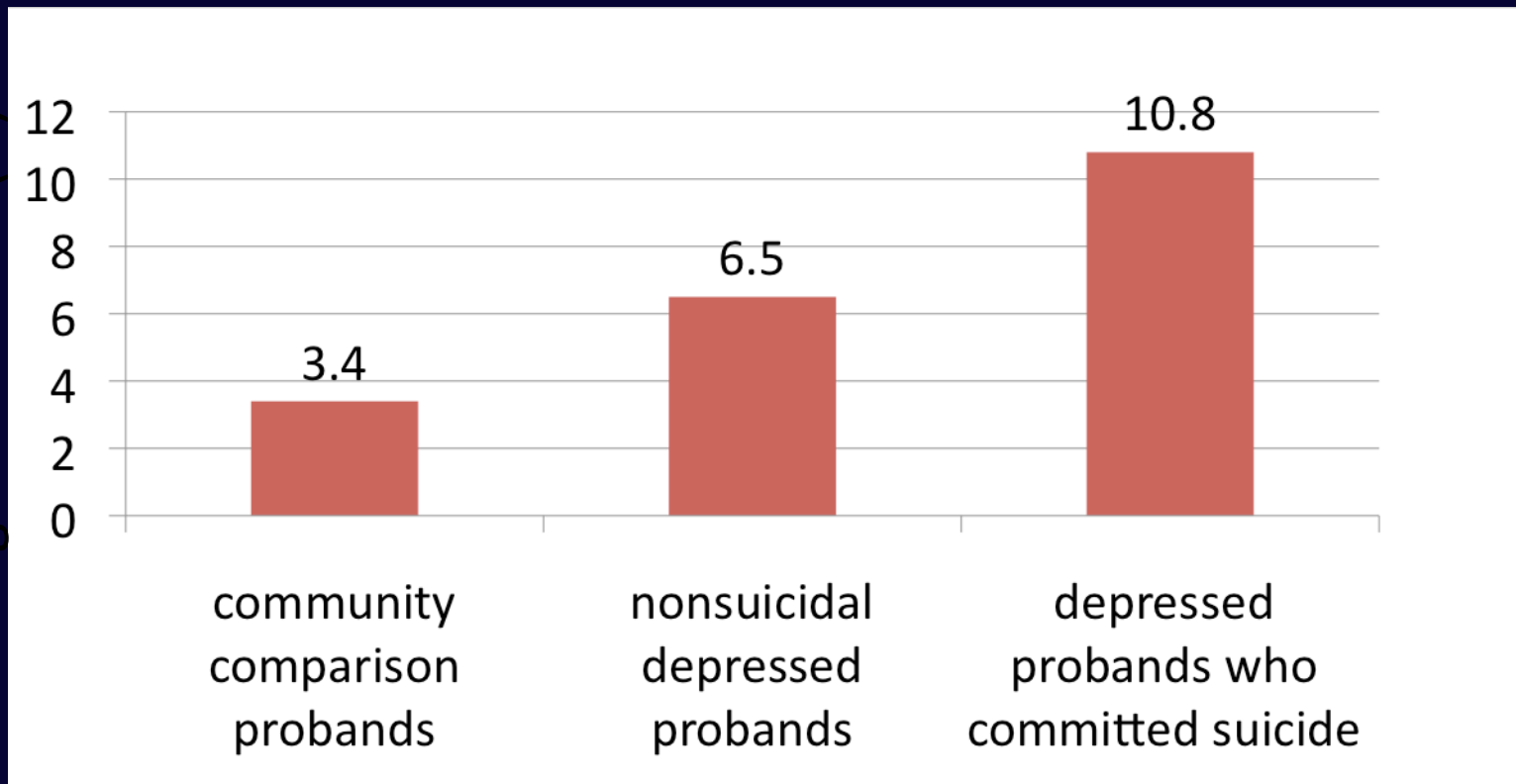
Risk and
protective
gene variants

Suicide behavior rate among First-degree relatives (%)

What is inherited?

- *Cluster B traits and impulsive behavior represent- intermediate phenotypes of suicide*

Suicide behaviour rate among First-degree relatives (%)



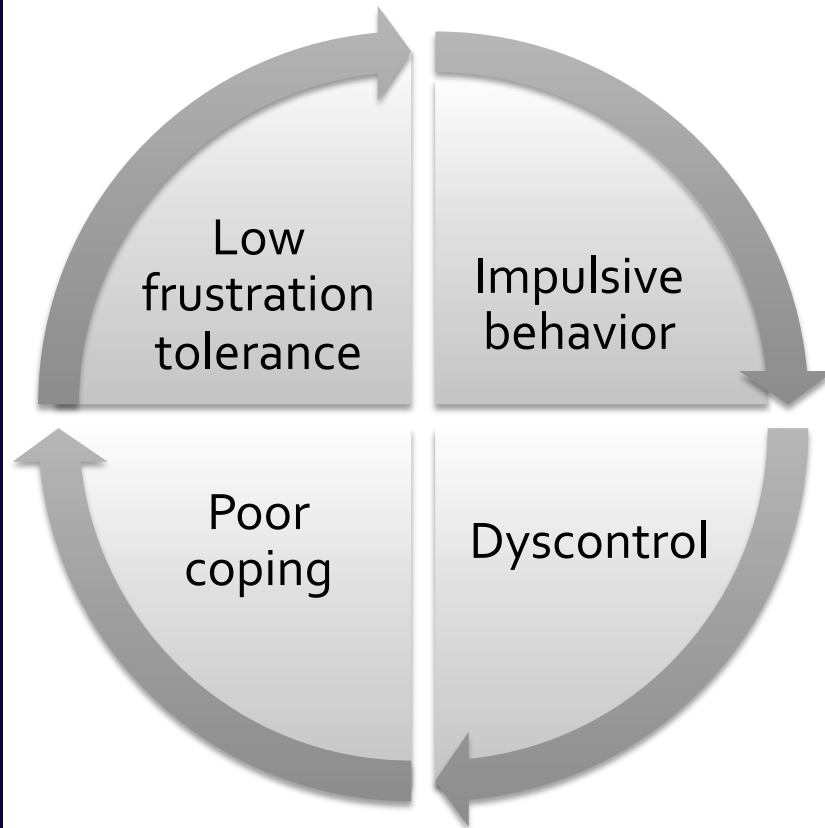
Genetics

- Additive genetic factors
- Estimated: 30% to 50% for a broad phenotype of suicidality that includes ideation, plans, and attempts
- Largely independent of the inheritance of psychiatric disorder ^[1]
- Heritability estimates of 17% to 45%- Nonfatal suicide attempts , even after controlling for psychiatric disorder ^[2]

Overlapping endophenotypes

Editorial

In Search of Endophenotypes for Suicidal Behavior



ed with psychiatric disorder, but the
neither attempt nor commit suicide.
ividuals who kill themselves from the
estion could improve our assessment

in vivo biological studies of suicide at-
t that among depressed individuals,
v a distinct biological and clinical pro-
central serotonin activity in the ven-

*“One candidate
endophenotype for
suicidal behavior
is... ‘impulsive
aggression.’”*

the elegant family study conducted by
o for Suicide Studies, was designed to

Endophenotypes: criteria^[1]

1. Association with illness in population;
2. Heritable (20% or greater);
3. Primarily state-independent;
4. Illness and endophenotype co-segregate within families (linkage of trait to gene variant); and
5. Found in nonaffected family members more frequently than in the general population

Proposed endophenotypes for suicide behavior

- Impulsive-aggressive traits,
- Early onset of major depression,
- Neurocognitive function,
- Heightened cortisol response to social stress.

Pharmacogenomics associations with polymorphisms in genes

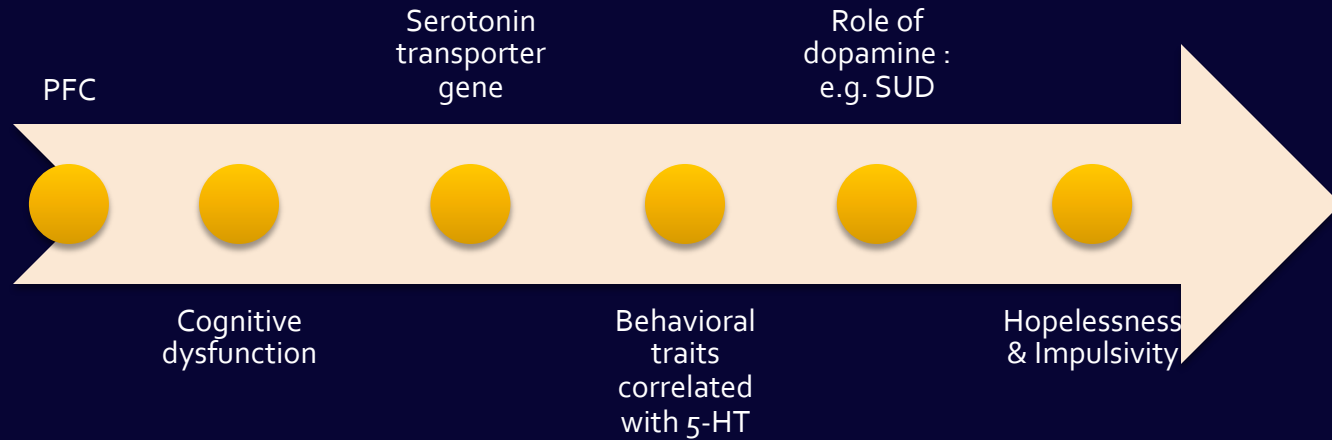
- Transcription
- Neuroprotection
- Glutamatergic and noradrenergic NT
- Stress and inflammatory responses
- Synthesis of glycoproteins
- Phenotypes of response and medication side effects,
- Biological pathways

Neuroprotective Proteins: Abnormal BDNF

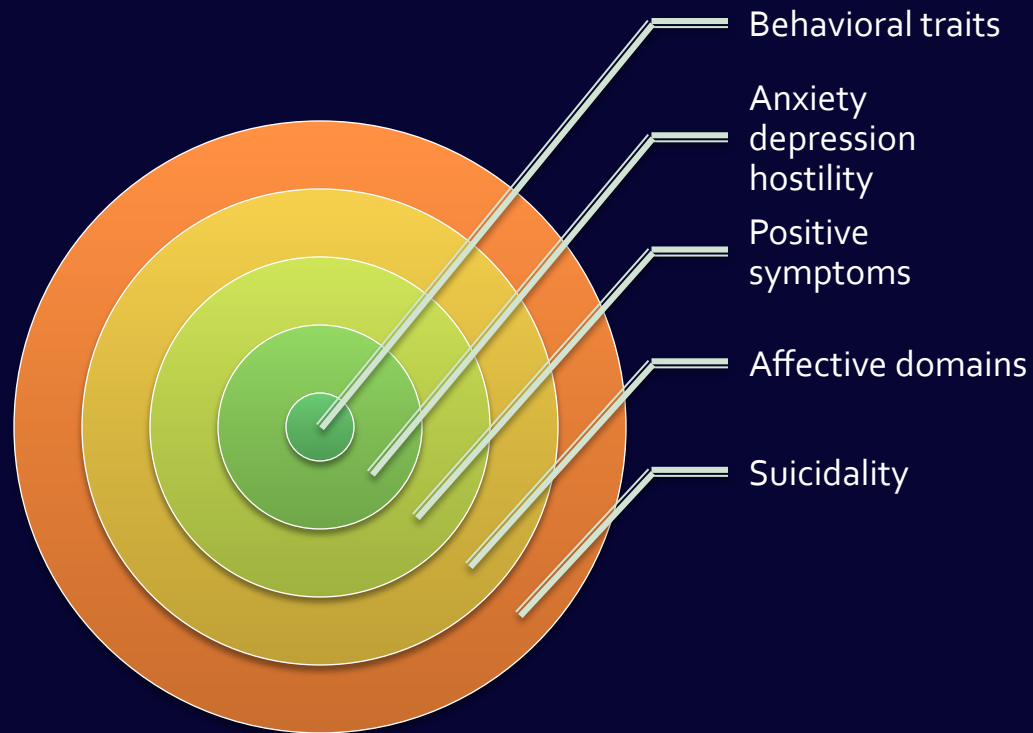
- Mood disorder, PTSD, SUD
- Suicide behavior [8],and Psychosocial stress [9]
- elevated suicidality independently of psychiatric diagnoses.
- biological marker [?] of suicidal
- increased BDNF due to Tx can facilitate neural integrity and prevent suicidal behavior

Sher L Brain-derived neurotrophic factor and suicidal behavior. QJM. 2010 Nov 4, De Luca V, Souza RP, Zai CC, Panariello F, Javaid N, Strauss J, et al. Parent of origin effect and differential allelic expression of BDNF Val66Met in suicidal behaviour. World J.Biol.Psychiatry. 2010 Aug 23, Dawood T, Anderson J, Barton D, Lambert E, Esler M, Hotchkin E, et al. Reduced overflow of BDNF from the brain is linked with suicide risk in depressive illness. Mol.Psychiatry 2007 Nov;12(11):981-983.

A neurobiological origin?



Current understanding in clinical phenomenology of psychosis



Predictors

- Past attempt
- Family history

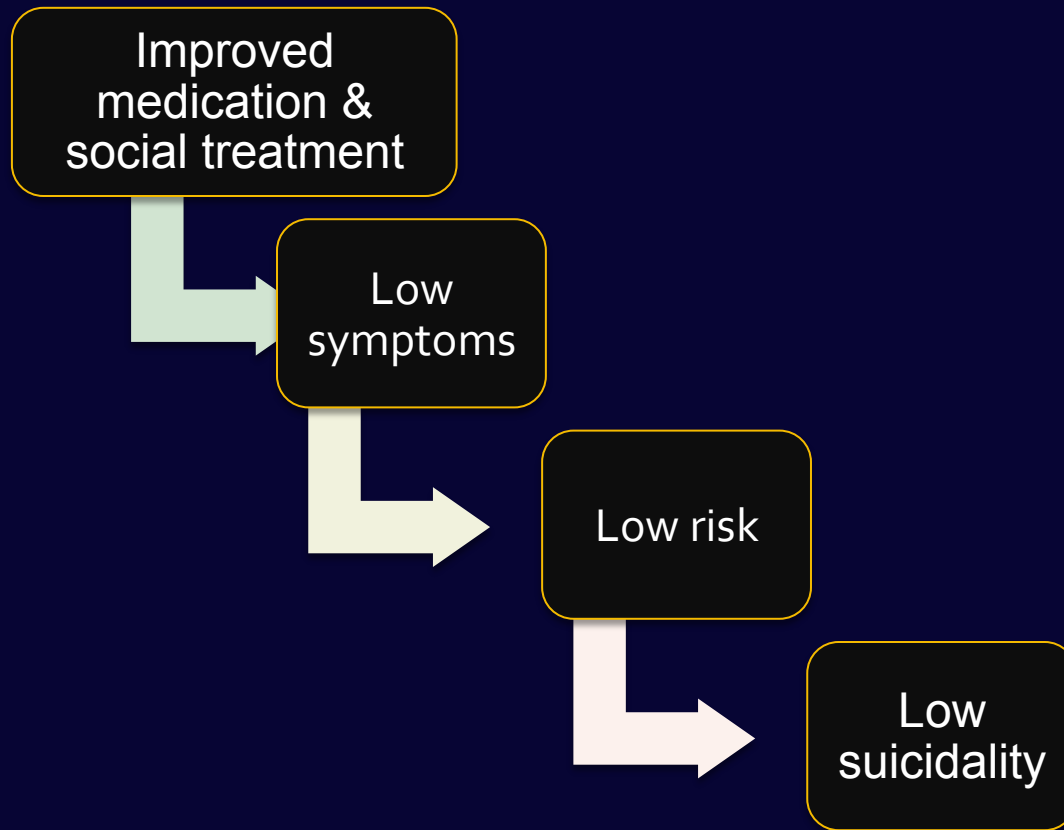
Pharmacological management

Approach to intervention and prevention

- Target Subgroups
- Comprehensive management,
- Risk assessment ,
- Continues community care
- Monitoring
- Resources

Need for Community based experiments in prevention

Pharmacological agents no specific 'suicido-cidal' drugs



Antidepressants

- No evidence of therapeutic benefit
- ADD Treatment emergent SD-polymorphism of genes :
 - Transcription, Neuroprotection, NT- Glum, NA
 - Stress inflammatory response

Lithium

- Neuroprotection
- Lithium responsive endophenotype
- Genetic predisposition (basis) of lithium response
- Gene-by- environment
- Risk was lower. ^[1] by 80% in 18 months and sustained. ^[2]

1.Tondo L, Hennen J, Baldessarini R J
Lower suicide risk with long-term lithium treatment in major affective illness: a meta-analysis. Acta Psychiatr Scand. 2001 Sep;104(3):163-72.

2.Baldessarini RJ, Tondo L, Davis P, Pompili M, Goodwin FK, Hennen J.
Decreased risk of suicides and attempts during long-term lithium treatment: a meta-analytic review. Bipolar Disord. 2006 Oct;8(5 Pt 2):625-39.

Effect of Lithium on Risk of Attempted or Completed Suicide

No. of Studies	N	Risk w/ Lithium*	Risk w/o Lithium*
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28	17,294	0.27	3.39
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- Apparent risk reduction : 9.20 fold
* % /Year

- *Tondo et al Neurobiology of Suicide 1997*

Mood stabilizers

- Less effective than lithium
- Anticonvulsants and suicide behavior

Clozapine

InterSePT, clozapine versus olanzapine (N=980)

- The mode of action is not known
- Antidepressant action,
- Cognitive functioning,
- Compliance,
- Insight,
- Negative symptoms
- Substance abuse,

(Meltzer, et al., 2003).

Clozapine

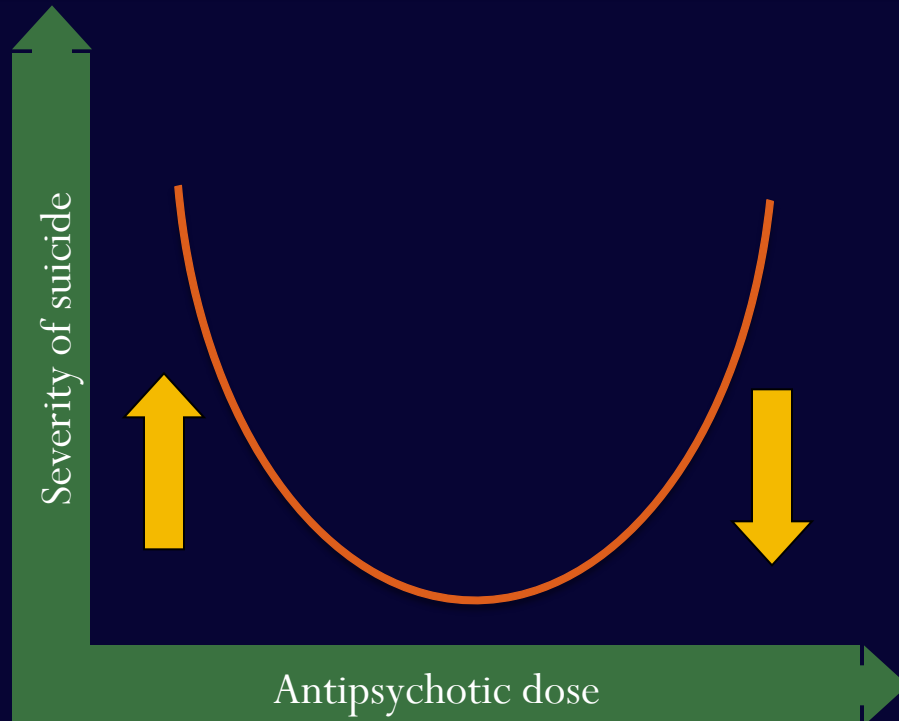
- Normalization of central 5-HT activity, in the prefrontal cortex, through down-regulation of central 5-HT_{2A}
- Increased availability of central 5-HT (Spivak, et al., 2003).

Clozapine versus other atypical antipsychotics for schizophrenia.

- A little more efficacious than zotepine and risperidone but (?)
- Differs more clearly in adverse effects from other SGA
- Most beneficial profile (Tiihonen et al., 2009
- [A critical appraisal of the FIN-11 study] ^[2]

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.

Antipsychotics and suicide: FGA and SGA

- Possible hypothesis: Decrease , Increase, Do not influence
- Several controlled studies have rejected a negative influence
- Reduce the risk of suicide and suicide attempts in schizophrenia.

Pharmacological management

Across diagnosis: outcome

- Good
 - Unipolar depression
 - bipolar disorder,
- Moderate
 - Schizophrenia
 - Eating disorder
 - dysthymia and common mental disorders
- Poor
 - Personality disorder
 - Substance abuse
 - comorbid conditions
 - organic mental disorder [case report]
 - PTSD

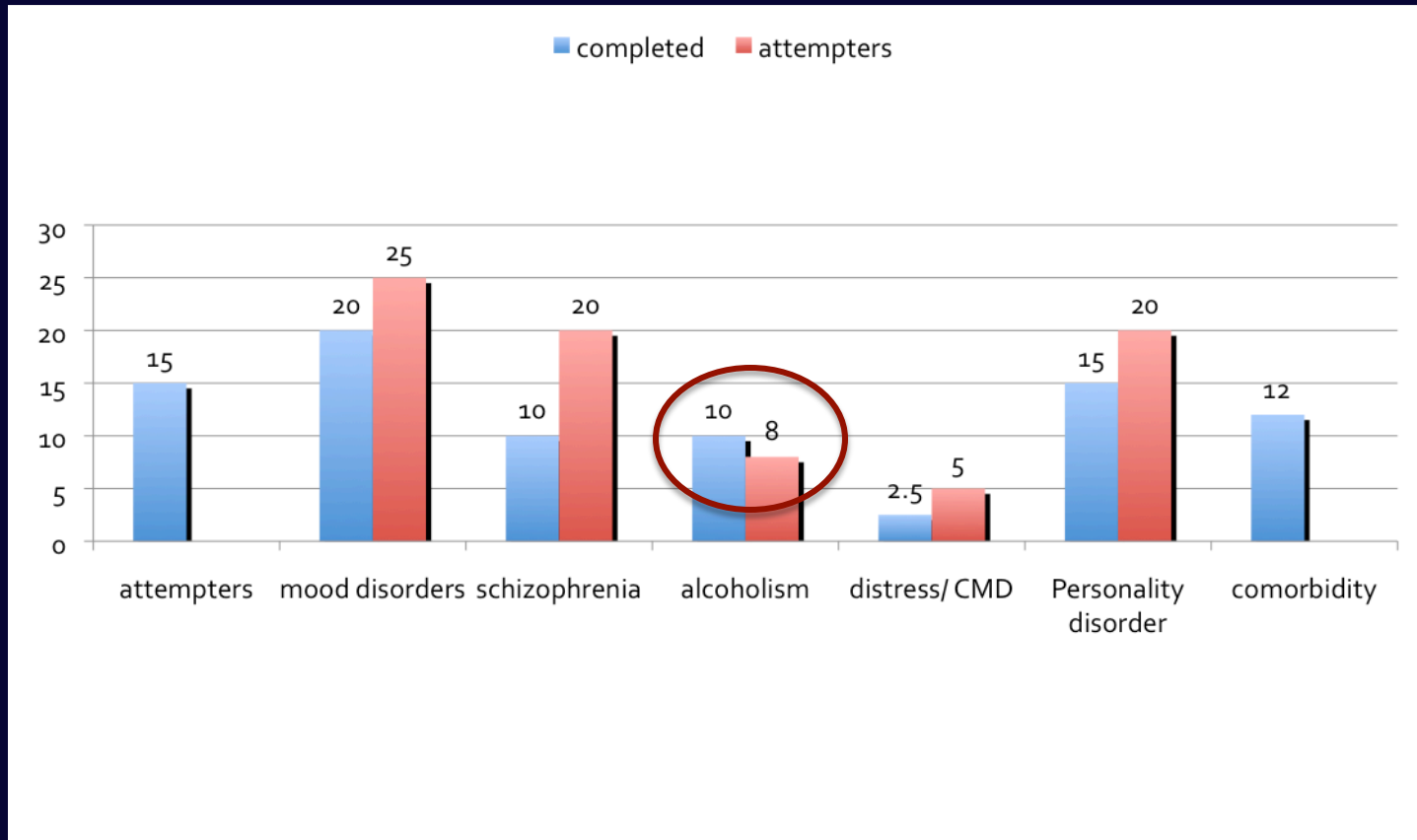
Electro Convulsive Therapy

Diagnosable psychiatric illness are found in 90% of all suicide based on 'psychological autopsies'

- Affective disorder 30% to 80%
- Substance use disorder 19 % to 60%
- Schizophrenia 2% to 14%

*In Both major depression and BPD ,
suicide account for 20% of death*

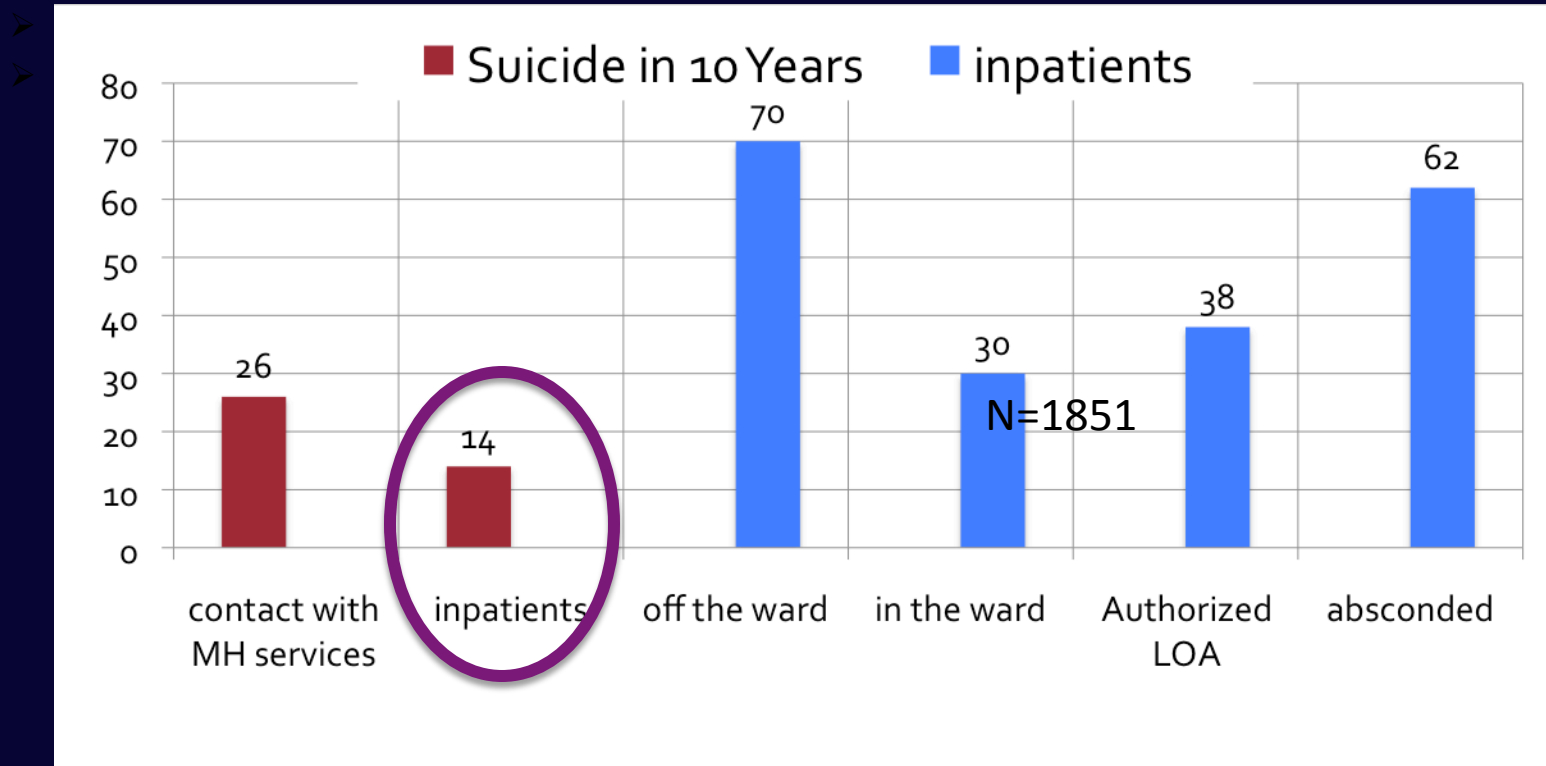
Rates suicide in psychiatric population



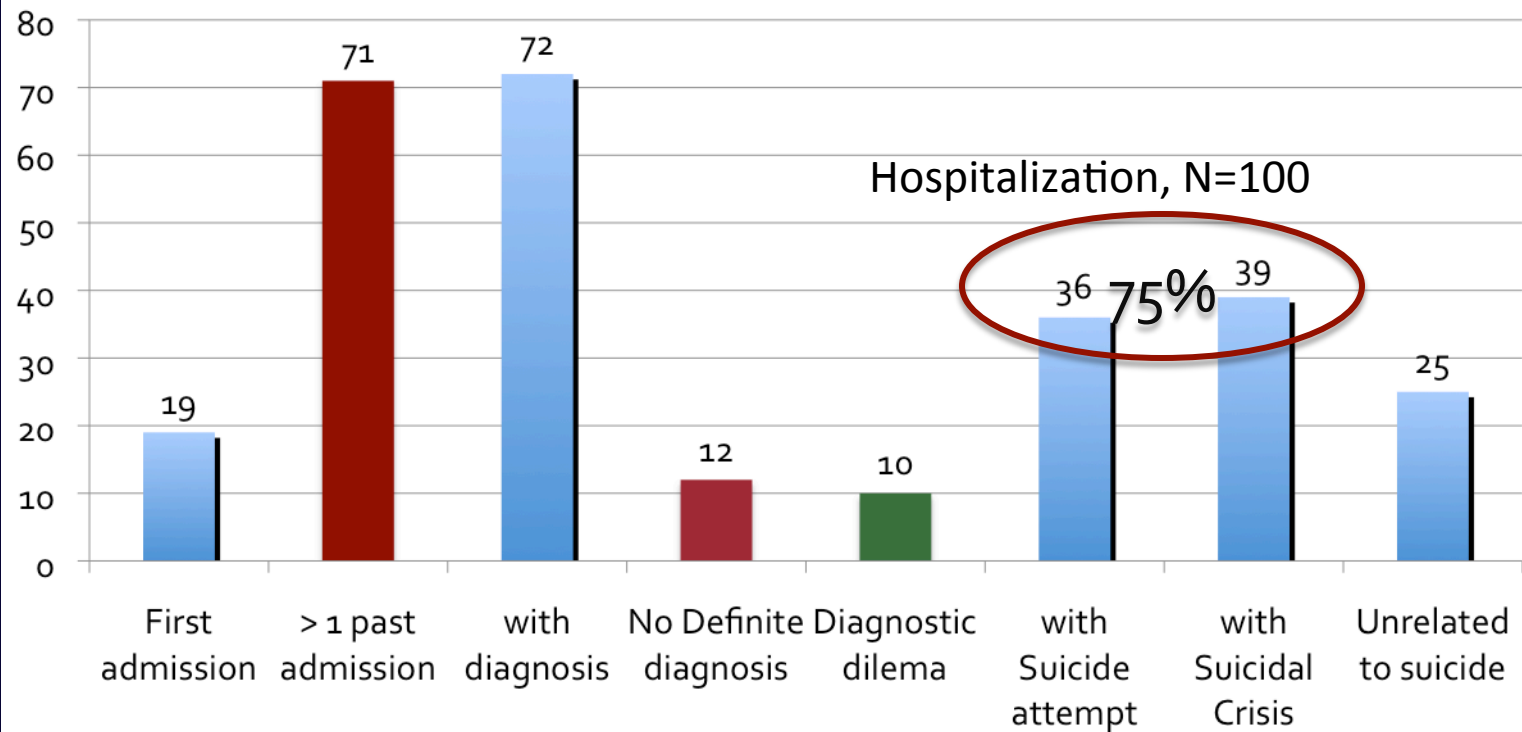
Suicide amongst psychiatric inpatient: a national clinical survey

➤ 50,352 cases in 10 years

services



Clinical Audit: Hospitalization



Some Preventive measures for inpatient suicide ^[1,2,3]

- Inpatient suicide reflects service quality ¹
- safe infrastructure, adequate monitoring,
- Regular risk assessment during recovery and prior to granting leave,
- staff training programs in management of risk,

1. Hunt IM, Kapur N, Webb R, Robinson J, Burns J, Turnbull P, Shaw J, Appleby L: Suicide in current psychiatric in-patients: a case-control study. *Psychol Med* 2007, 37:831-837.

2. Pompili M, Lester D, Innamorati M, del Casale A, Girardi P, Ferracuti S, Tatarelli R: Preventing suicide in jails and prisons: suggestions from experience with psychiatric in-patients. *J Forensic Sci* 2009, 54:1155-1162.24.

3. Tishler CL, Reiss NS: Inpatient suicide: preventing a common sentinel event. *Gen Hosp Psychiatry* 2009, 31:103-109.

Preventive measures

- Improved staff communication
- Observe ward exits; Improved observation methods;
- Increased engagement and support,
First few days are high risk

Mental health policy and its implementation

‘It is clearly challenging to achieve a balance between patient safety and patient autonomy, but the need to protect individuals from harm during a time when they are supposedly in a safe environment should be a principal objective of mental health services’ .

Dealing with inpatient suicide

- Assessment
- Setting the goals
- Level of monitoring
- Risk factors
- Physical environment
- Crisis intervention
- Psychological intervention

Dealing with inpatient suicide

- Pharmacotherapy
 - Aggressive management
 - Early introduction of Lithium or Clozapine
 - Optimizing the dosage
- Ward infrastructure

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

Prevention of Post-discharge Suicide :

- Discharge process
- Side effects
- Continuity of care
- Avoid typical antipsychotics
- Medication, dose, duration and compliance
- Identify risk & predictors

Conclusion

- Inpatient and post discharge suicide.
- Previous attempt and family history
- Psychopathological traits are inherited
- Not all suicide are due to mental illness

Conclusion

- Suicide as independent pathological dimension
- Epigenetics, neuroprotection, plasticity and serotonin are important
- Lithium and clozapine are good for treatment
- Treat both mental illness and suicidality

Need for paradigm shift in management of suicide behavior.

Thank you

