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Should Schizoaffective Disorder Be Dropped from DSM V

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Should schizoaffective disorder be dropped from DSM V

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Lecture.reginal.Mental.Health care.St.Thomas.

Declaration

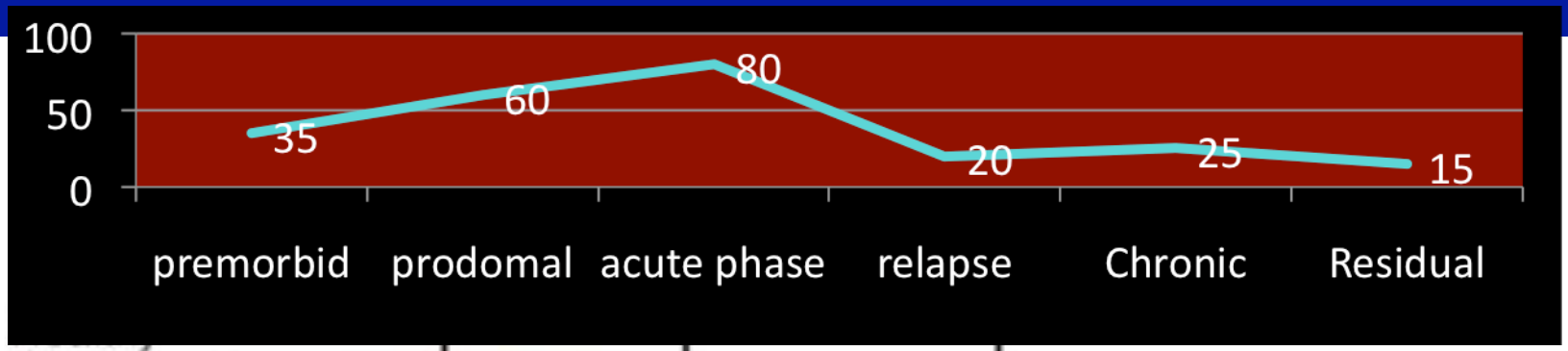
- Janssen Group
- Eli Lilly
- Astra Zeneca
- Nicholas Piramal-Rosch
- Pfizer
- Sun Pharma- India

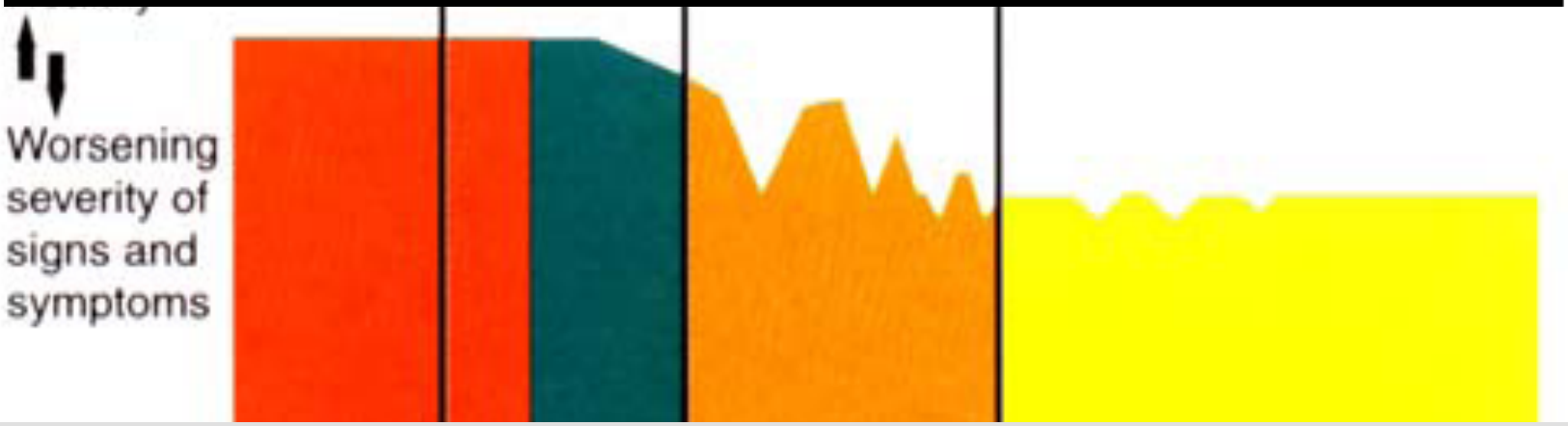
- Consultant
- Advisor
- Drug trial coordinator
- Research Investigator
- Reviewer
- Speaker
- Educational Groups

Objectives

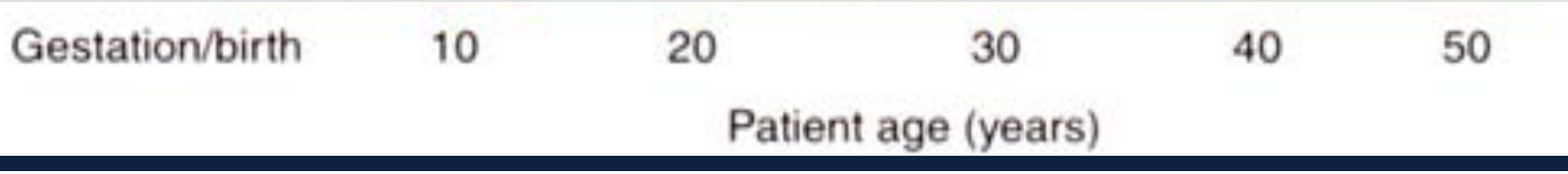
- To discuss the historical arguments for a diagnostic category.
- Why are we raising this issue now?
- Does schizoaffective disorder qualify as a diagnosis for any classification?

Prevalence of mood symptoms across longitudinal course of schizophrenia (from different studies)





Depression occurs across the course of schizophrenia



Emergence of new diagnosis: Jacob kasonin 1933

- **Jacob Kasonin 1933:**
- **Relatively good pre-illness psychosocial adjustment**
- **Abrupt emotional presentation**
- **Less social withdrawal or passivity**
- **A shorter course of illness**
- **A relatively good recovery**

Positioning of schizoaffective psychosis

- Leonard 1961 : third psychosis”
- ICD 9 : subsumed under schizophrenia
- In RDC : it was kept separate entity
- Separate entity was continued up to DSM-III R
- In DSM IV : with schizophrenic disorder
- Draft of ICD 10 in 1986: with affective disorder
- Final draft of ICD 10 : placed alongside of schizophrenic disorder

DSM

DSM IV and ICD 10 both insist on exclusion

An uninterrupted period of illness during which,

at some time there is either:

(1) A Major Depressive Episode

(2) A Manic Episode, or

(3) A Mixed Episode concurrent with symptoms that meet

(4) Criterion A for Schizophrenia.

- Schizoaffective
  - Bipolar
  - Depressive

Utilizes - Categorical approach

Two major neurobehavioral dimensions:

thought &

Mood

Schizoaffective disorders: ICD 10

- Episodic disorders in which both affective and schizophrenic symptoms are prominent but
- do not justify diagnosis of either
- schizophrenia or depressive or manic episodes.
- Mood-incongruent psychotic symptoms in affective disorders : DO NOT

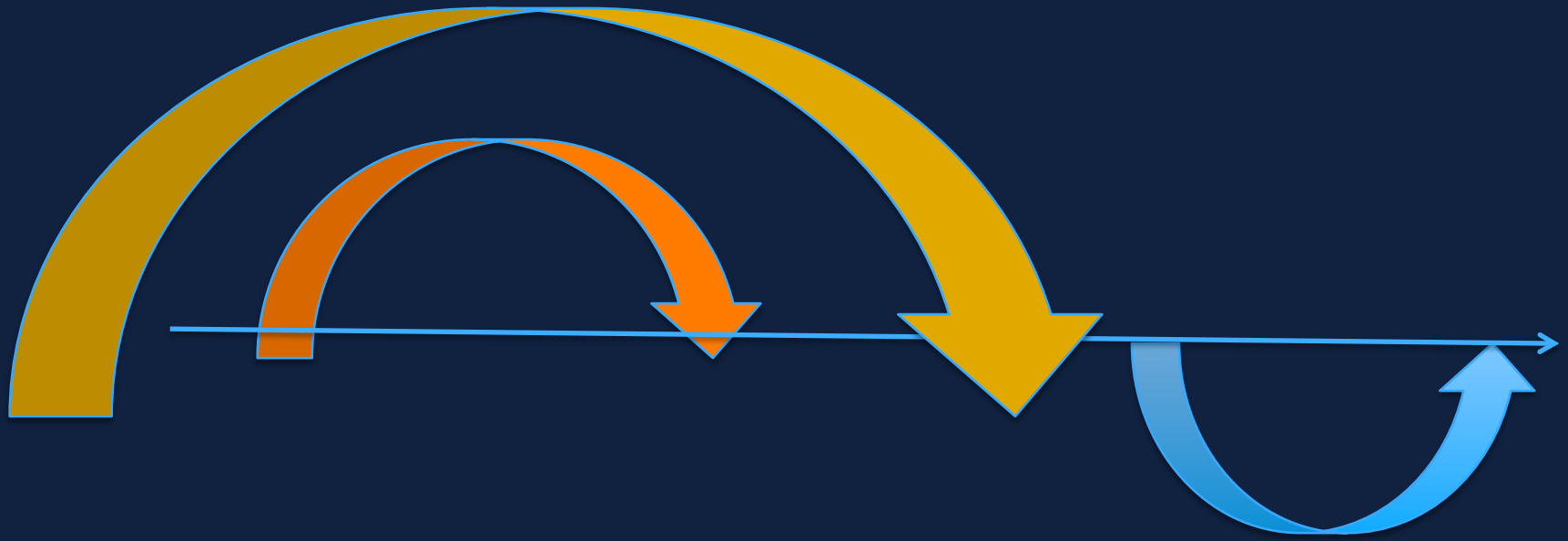
Schizoaffective disorders: ICD 10

F25.0 Schizoaffective disorder, manic type

- F25.1 Schizoaffective disorder, depressive type
- F25.8 Other schizoaffective disorders
- F25.9 Schizoaffective disorder, unspecified

Commonly seen co-occurrence of symptoms:

Representation of depressive cluster & psychotic cluster in relation to its appearance during psychotic episode.



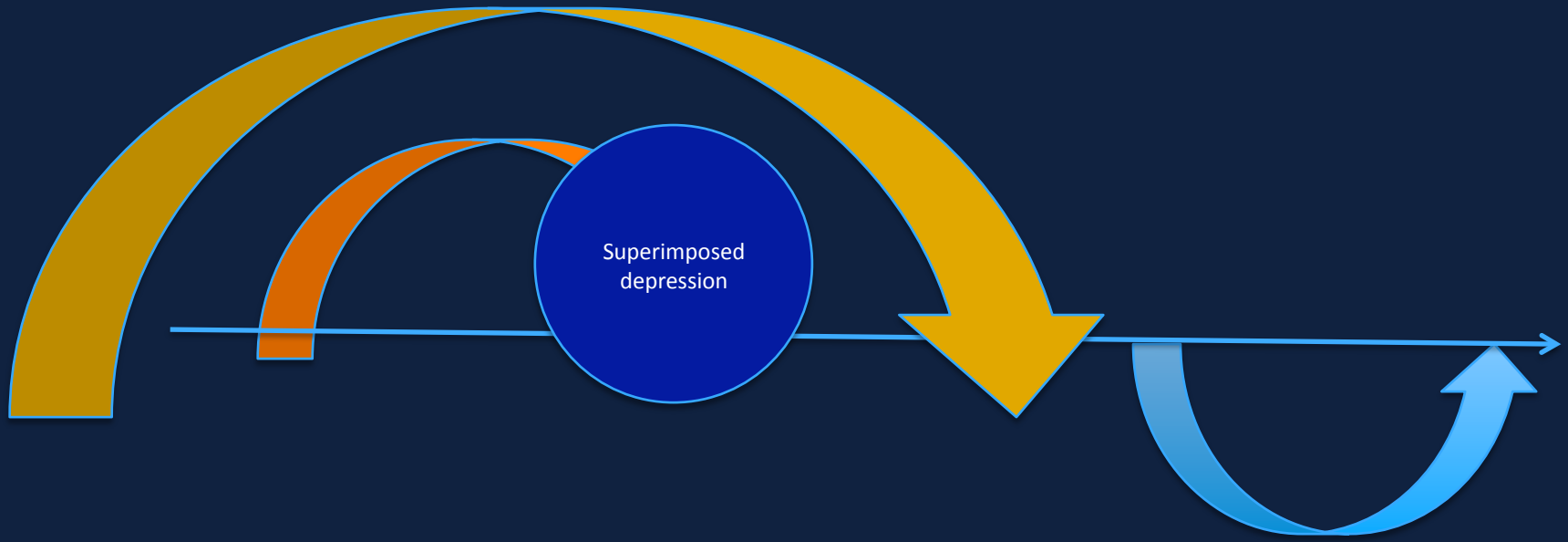
A psychotic episode

Psychosis domain

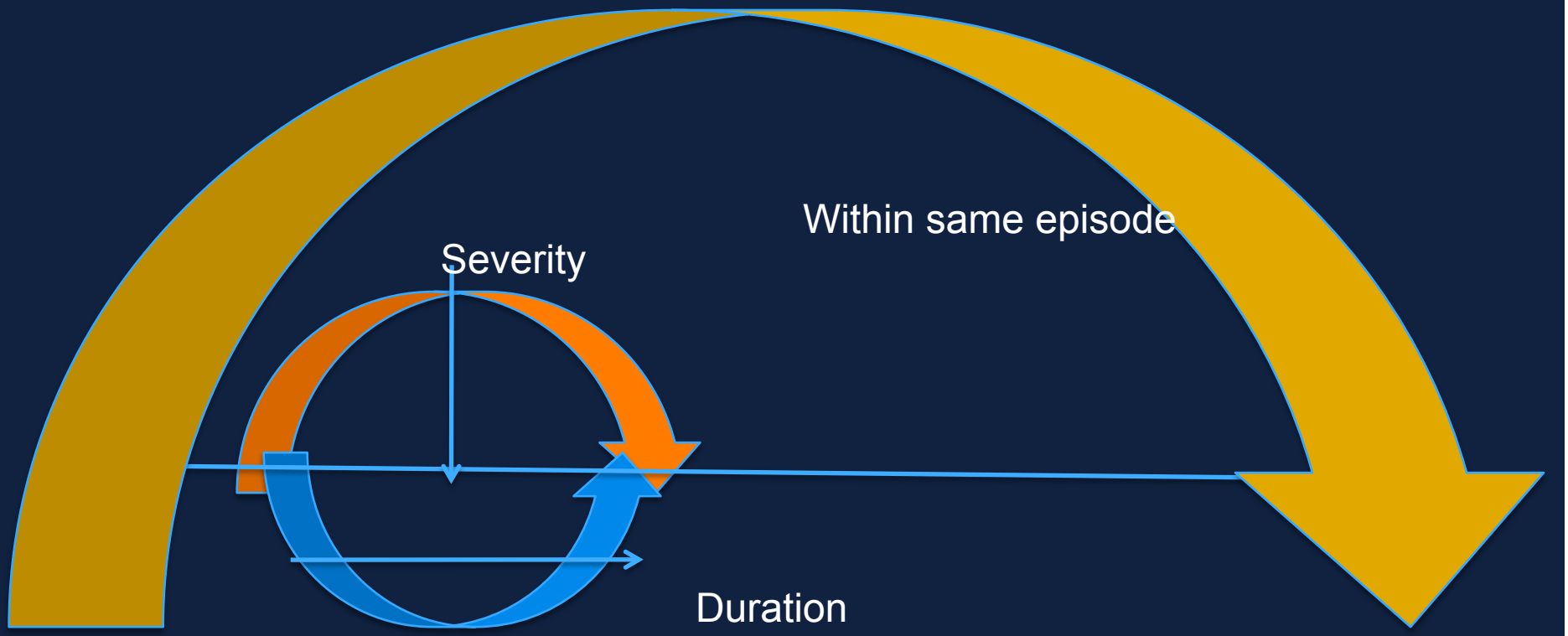
Depressive domain

The term should not be applied to patients who exhibit schizophrenic symptoms and affective symptoms only in different episodes of illness.

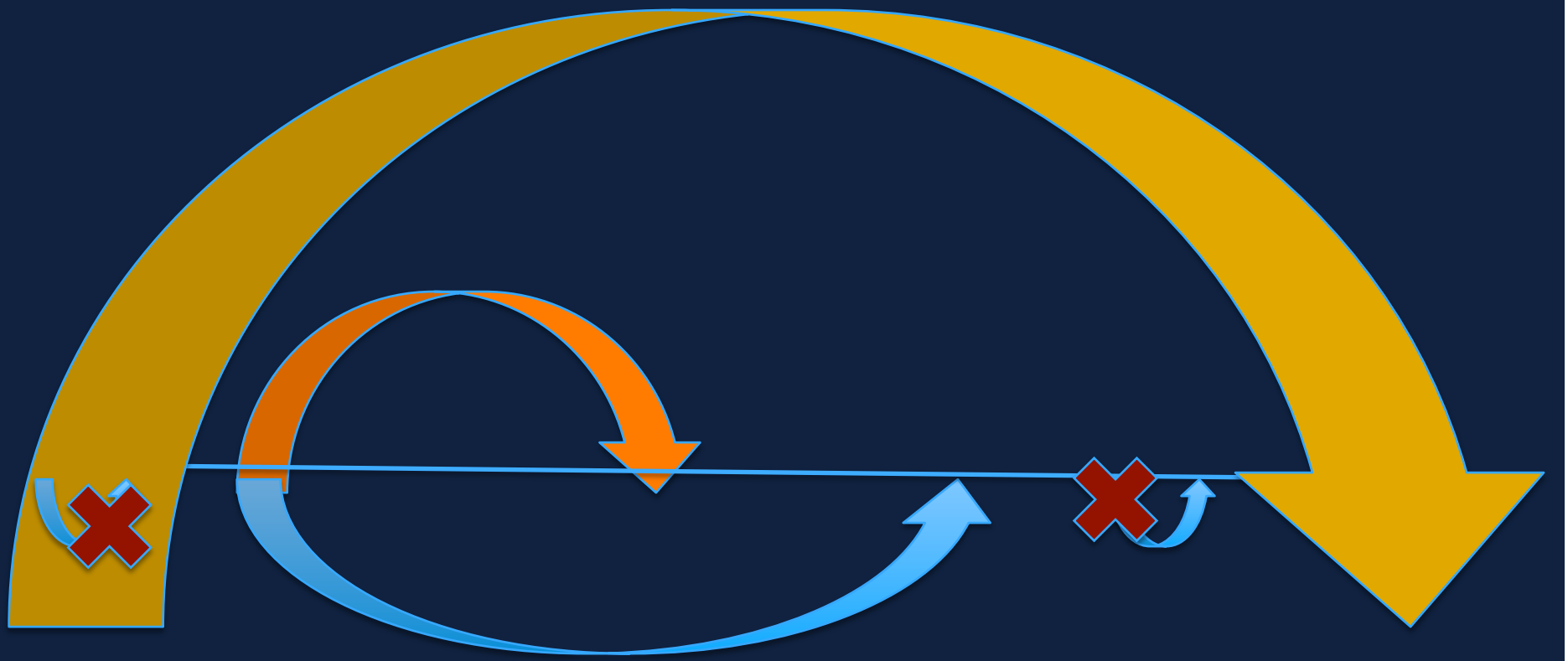
Superimposed secondary depression is not a schizoaffective disorder



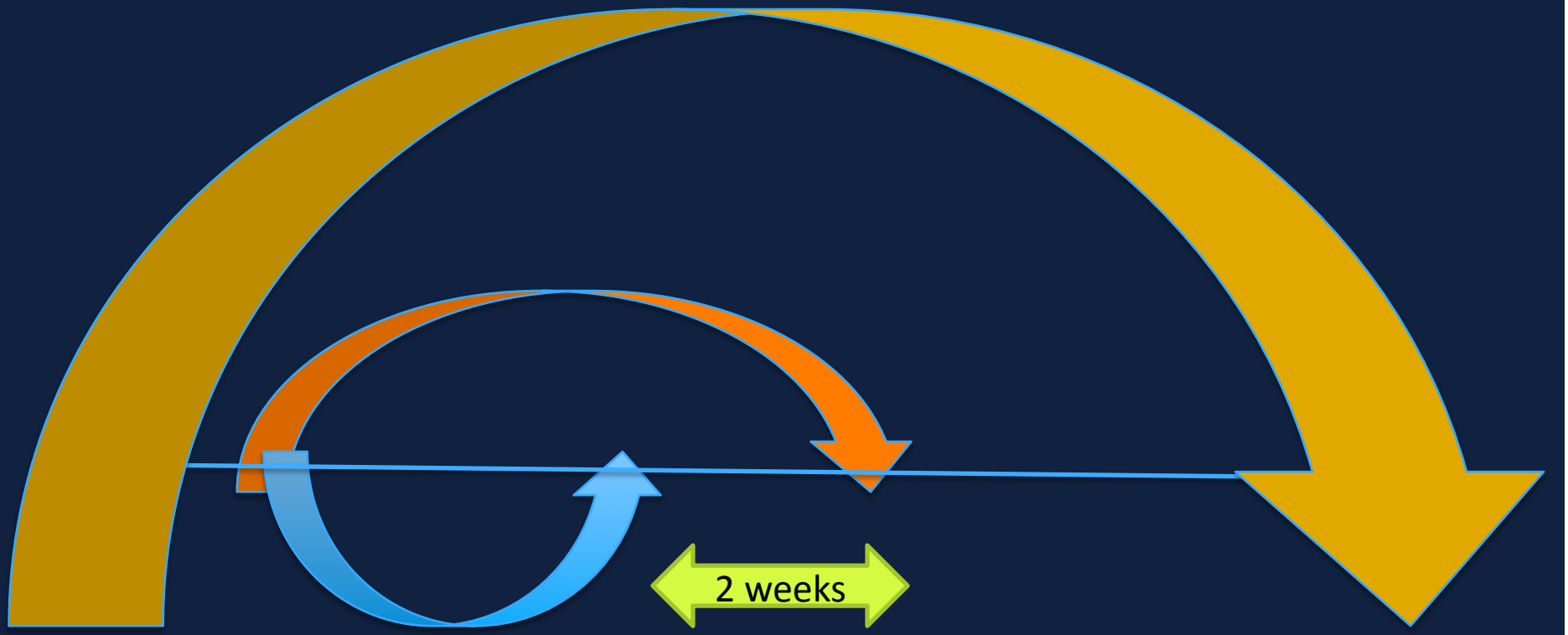
Other conditions in which affective symptoms are superimposed on a pre-existing schizophrenic illness, or co-exist or alternate with persistent delusional disorders of other kinds, are classified under F20-F29.



Booth clusters of psychosis and depression should occur within same episode with reasonable equivalence in severity and duration for a diagnosis of SAD

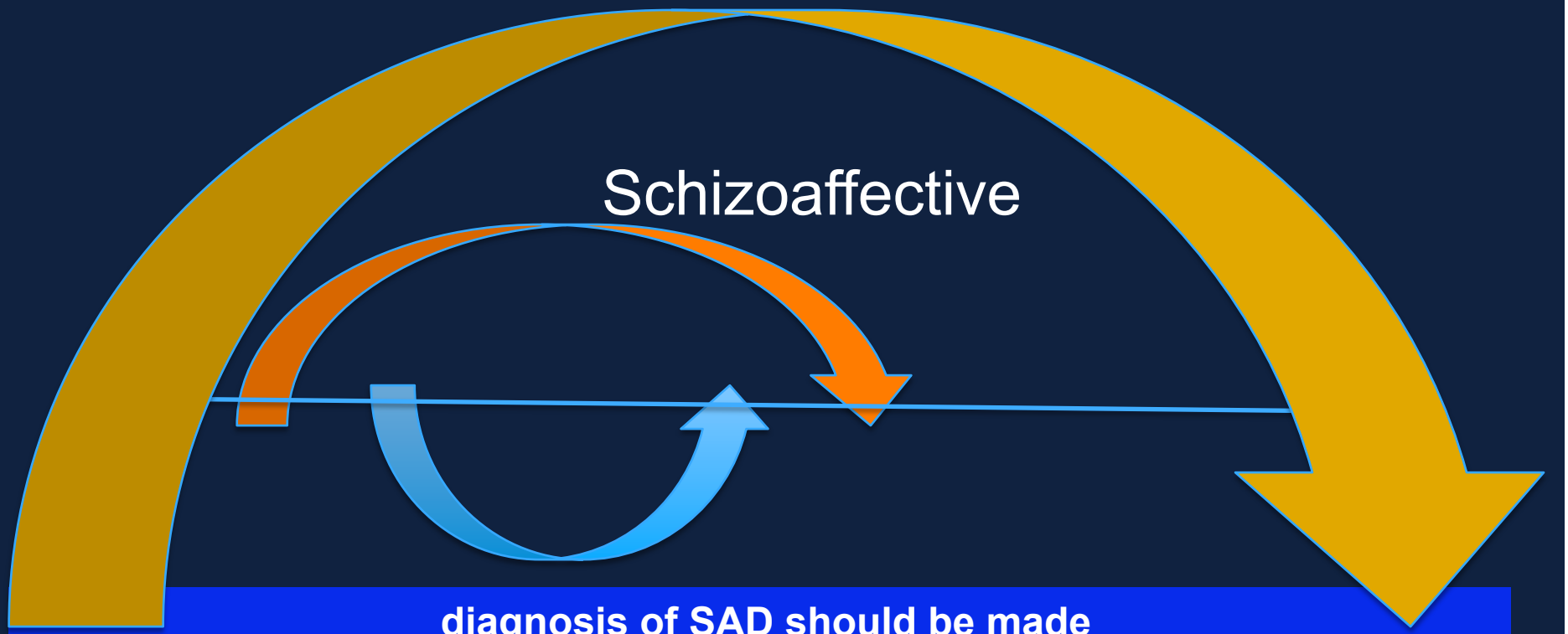


DSM-IV:
presence of mood symptoms for
Substantial portion
of total duration of the episode for diagnosis of SAD is required.



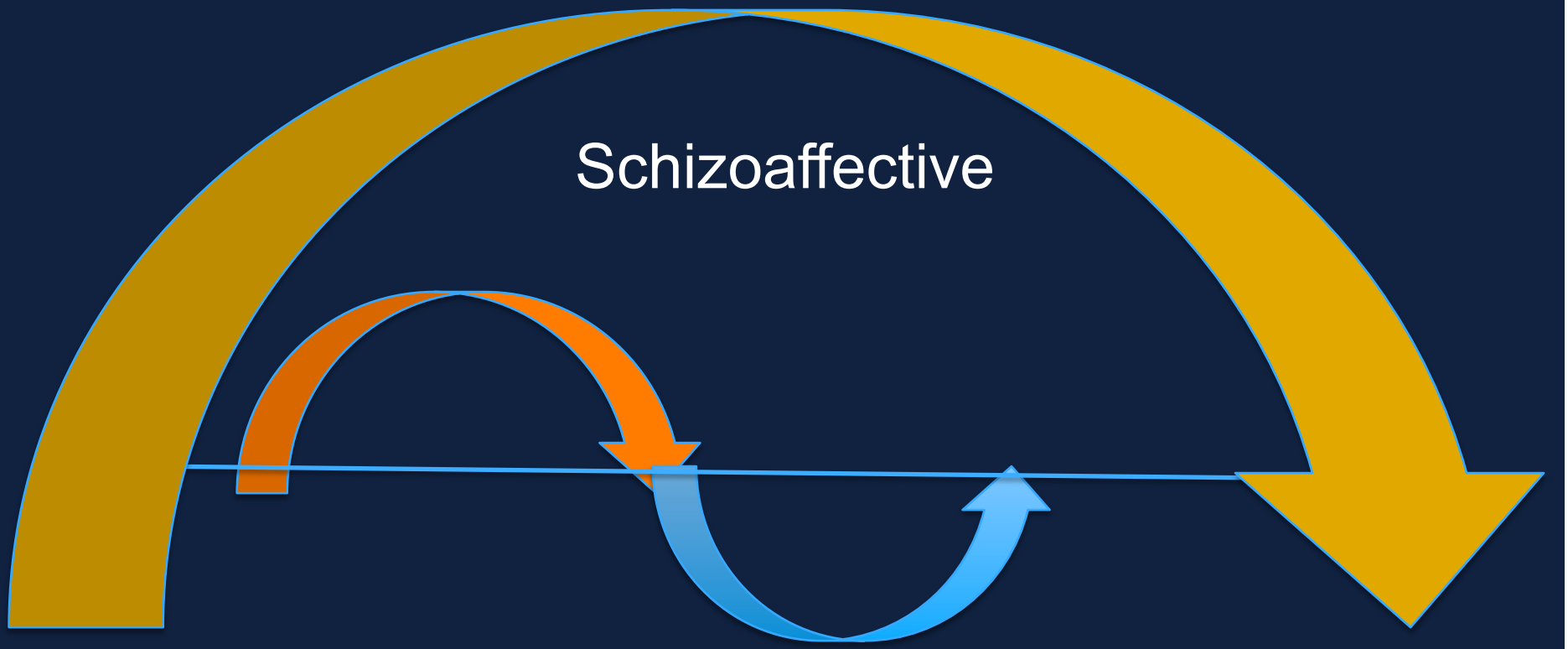
Schizoaffective

Persistence of psychotic symptoms for at least 2 weeks beyond the resolution of mood symptoms: DSM –III-R



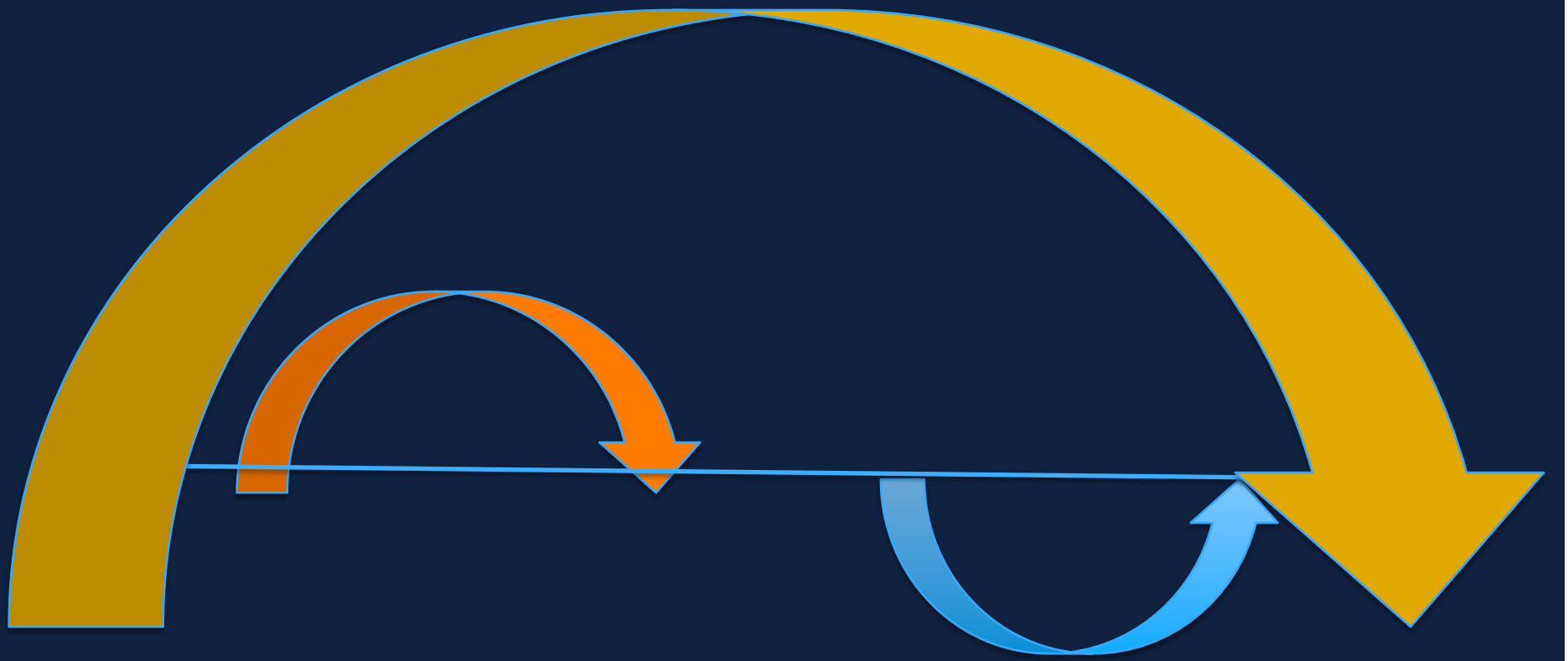
diagnosis of SAD should be made only when both definite schizophrenic and definite affective symptoms are prominent simultaneously, or within a few days of each other, within the same episode of illness,

and when, as a consequence of this, the episode of illness does not meet criteria for either schizophrenia or a depressive or manic episode.

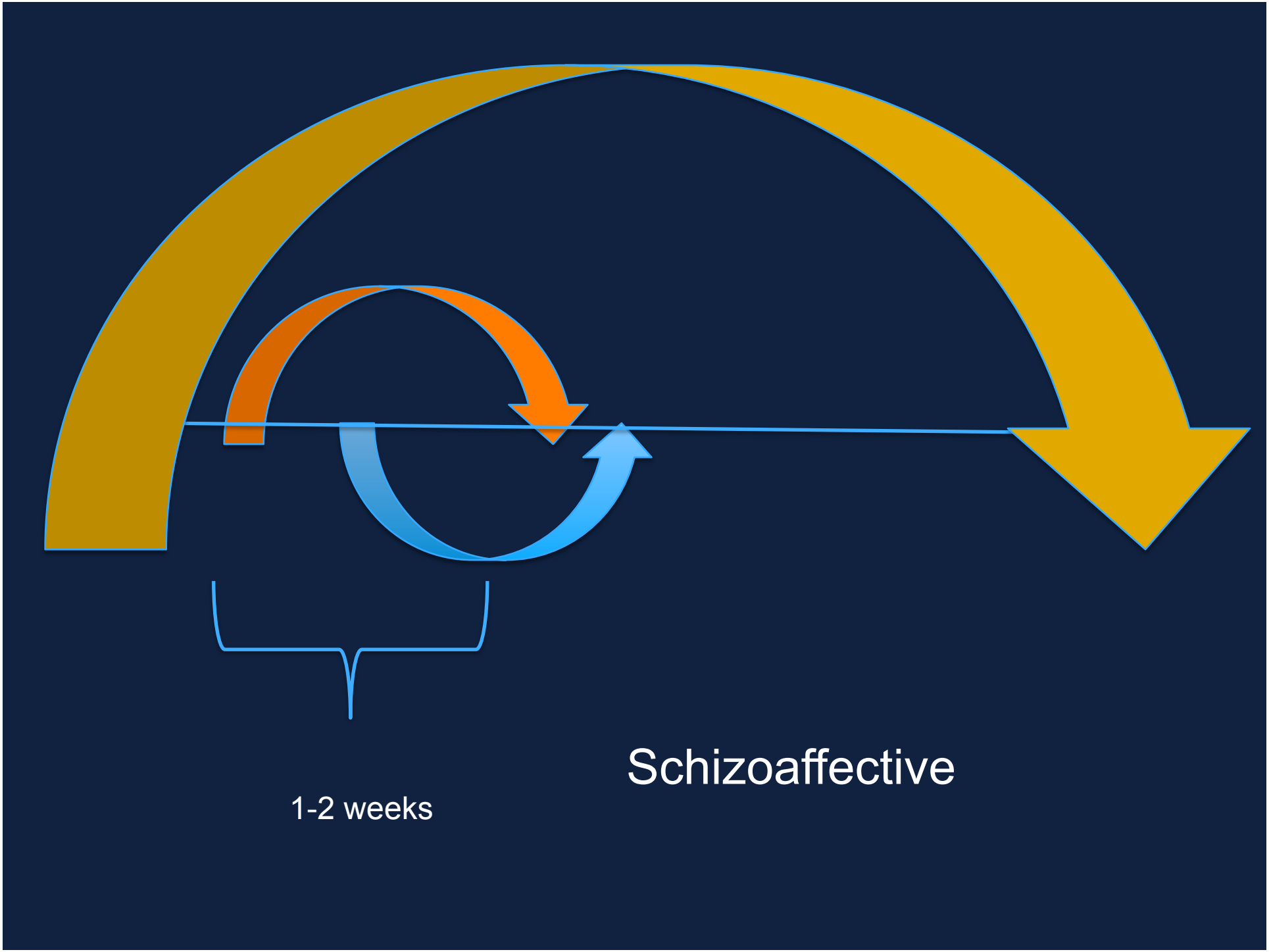


It is common, for example, for a schizophrenic patient to present with depressive symptoms in the aftermath of a psychotic episode.

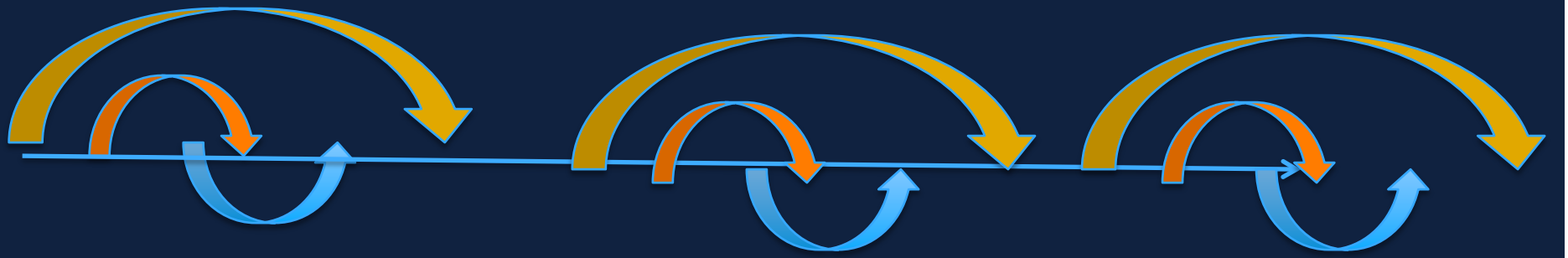
The 'Post-psychotic depression or mania is NOT SAD



Schizoaffective

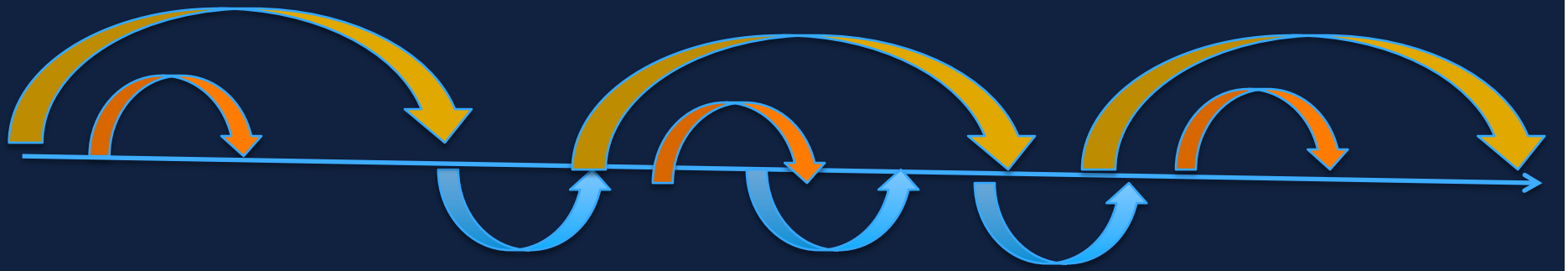

1-2 weeks
Schizoaffective

Recurrent Schizoaffective



Some patients have recurrent schizoaffective episodes, which may be of the manic or depressive type or a mixture of the two. In this case, schizoaffective disorder is the appropriate diagnosis.

Bipolar affective



Others have one or two schizoaffective episodes interspersed between typical episodes of mania or depression.

The occurrence of an occasional schizoaffective episode does not invalidate a diagnosis of bipolar affective disorder or recurrent depressive disorder if the clinical picture is typical in other respects

Does schizoaffective disorder really exist?

middle point of a continuum between SCH and MD.

J Affect Disord. 2008 Mar

Schizoaffective disorder merges schizophrenia and bipolar disorders as one disease-

-There is no schizoaffective disorder

Curr Opin Psychiatry. 2007 Jul;.

Schizoaffective disorders are psychotic mood disorders; there are no schizoaffective disorders.

Psychiatry Res. 2006 Aug

Why is this argument being made?

Objections & DSM V

- Subgroup of schizophrenia
- Severe form of mood disorder (MMD or BAD)
- Co-occurrence of the two
- Diagnostic instability influences outcome & prognosis

Objections & DSM V

- Lack of consensus
  - Conceptually
  - Clinical aspects
- Dimensional approach recognize disturbance
  - thought &
  - mood
  - Would avoid categorizing into either mood or psychosis

Diagnostic instability

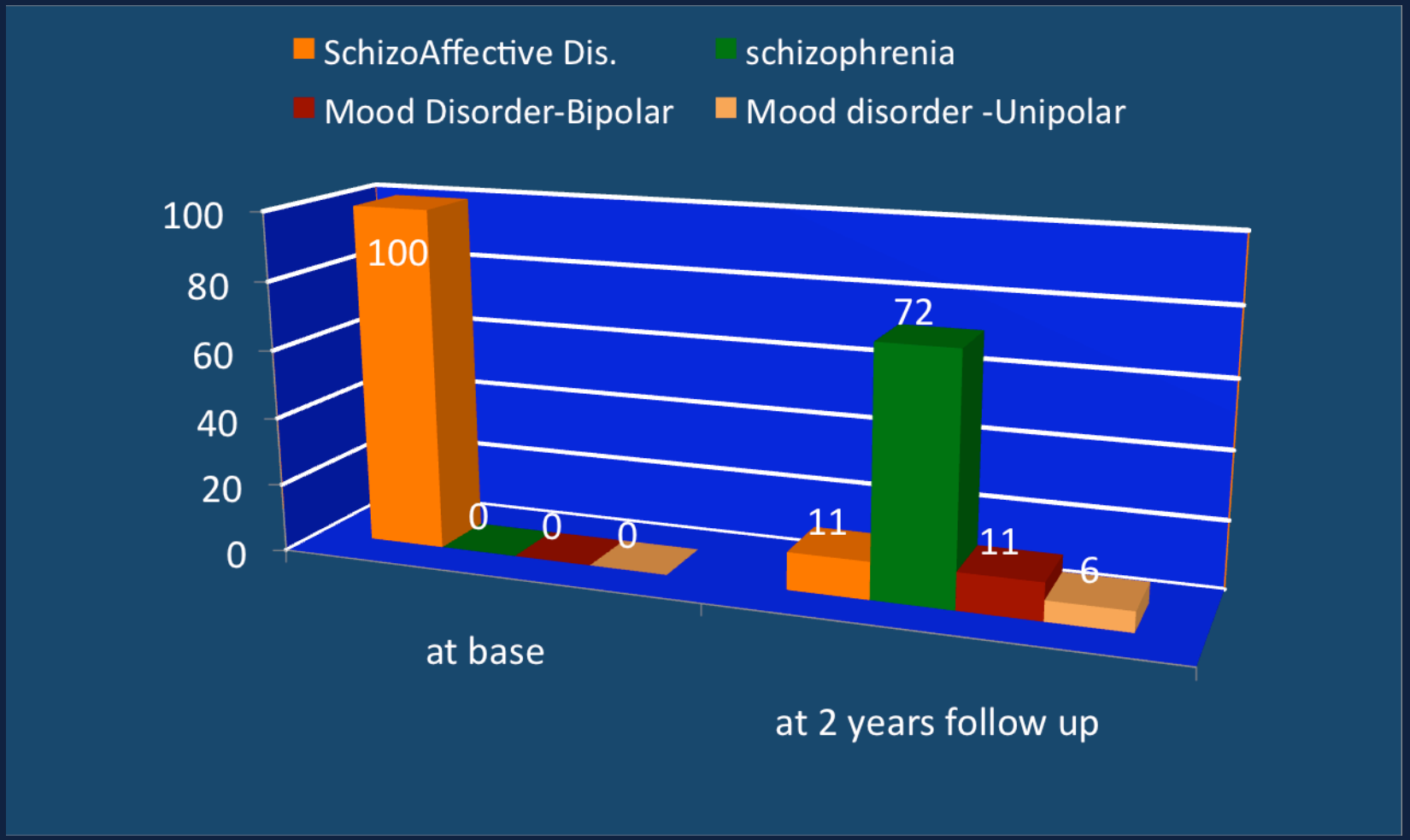
- Poor inter-rater reliability for SAD (Mario 2000),
- 0% reconfirmation of discharge diagnosis of SAD (Vollmer-Larsen 2006)

Diagnostic instability

- Schwartz et al stability of diagnosis at 6 & 24 months
  - 92% schizophrenia
  - 83% Bipolar disorder
  - 74% major Depression
  - 44% psychosis NOS
  - 36% Schizoaffective
  - 27% Brief psychotic Disorder

‘Diagnostic Validity of Schizoaffective disorders’

Shrivastava A, Rao, S. IJP.1997

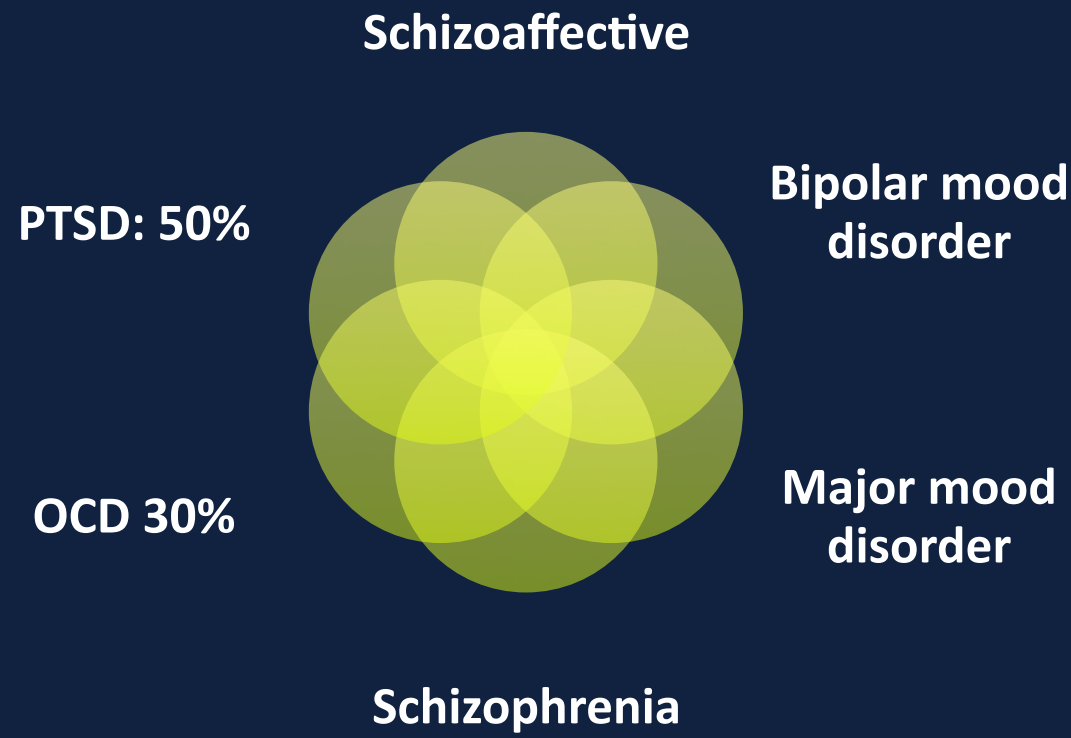


‘Diagnostic Validity of Schizoaffective disorders’

Shrivastava A, Rao, S. IJP.1997

- 82.5% patients diagnosis of schizoaffective disorder in Changed at the endpoint of 2 years
- 70% qualify for a diagnosis of schizophrenia in 2 years time

Co morbidity in Categorical approach would need to be coded on different axis



Utility of diagnosing these condition away from main disorder is questionable

Byerly, 2004, 2005, Strauss et al 2006

Does it qualify as a diagnosis to be in any classification?

Literature review also failed to indicate a clear cut distinction between SAD and SCH or MD.

DISCUSSION: Present analysis indicated that

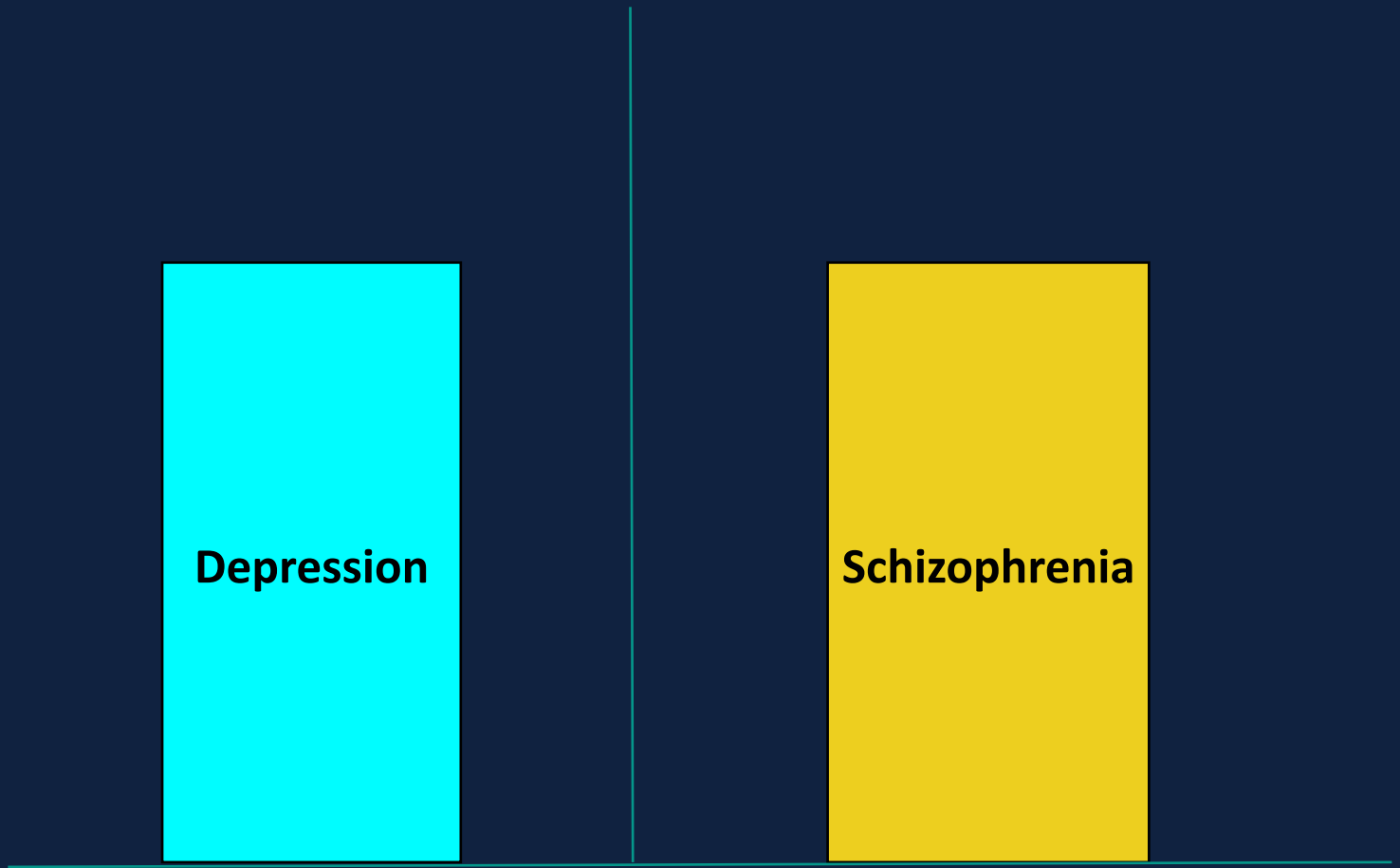
1. SAD cannot be interpreted as atypical forms of SCH or MD.
2. SAD also does not appear to represent a SCH and MD comorbidity or
3. yet an independent mental disorder.
4. It is argued that SAD might constitute a heterogeneous group composed by both SCH and MD patients or
5. a middle point of a continuum between SCH and MD.

J Affect Disord. 2008 Mar

Criteria for classification Evidence

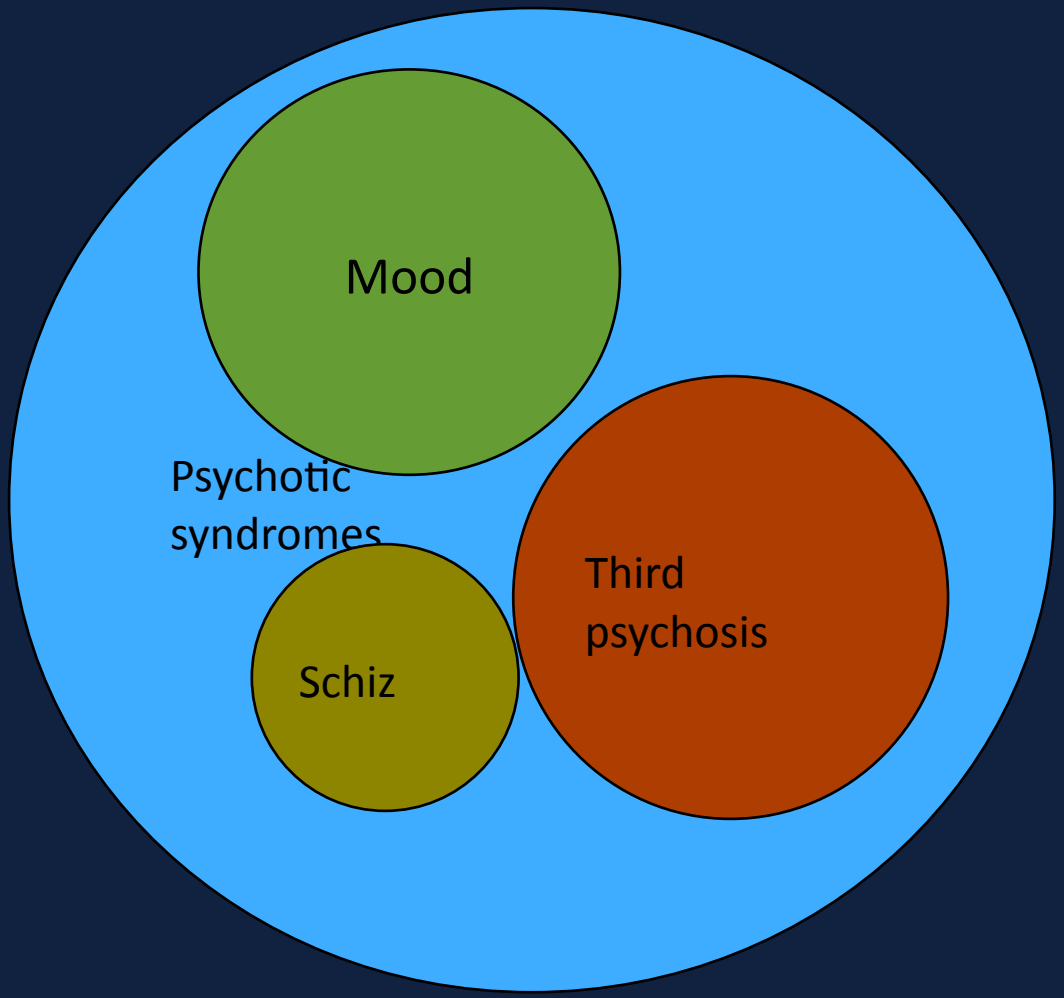
Included	Excluded
• **Origin**	• Severity
• **Manifestation**	• Co morbidity
• **Course**	• Sub-types
• **Outcome**	• Aetiopathological
• **Response to treatment**	• Biological
	• Genetics
	• Heritability

Categorical approach

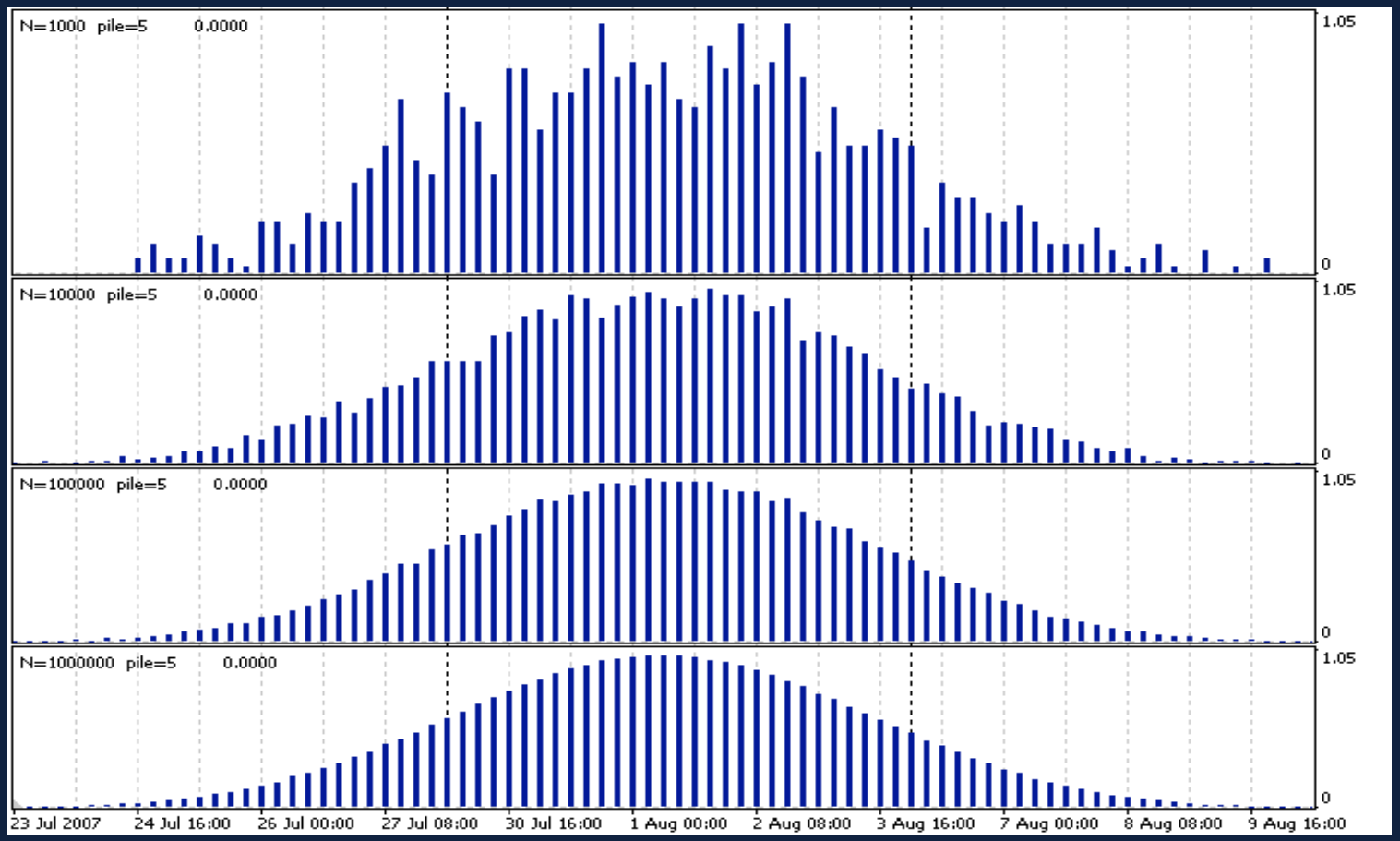


Independent origin , course, outcome , response to treatment

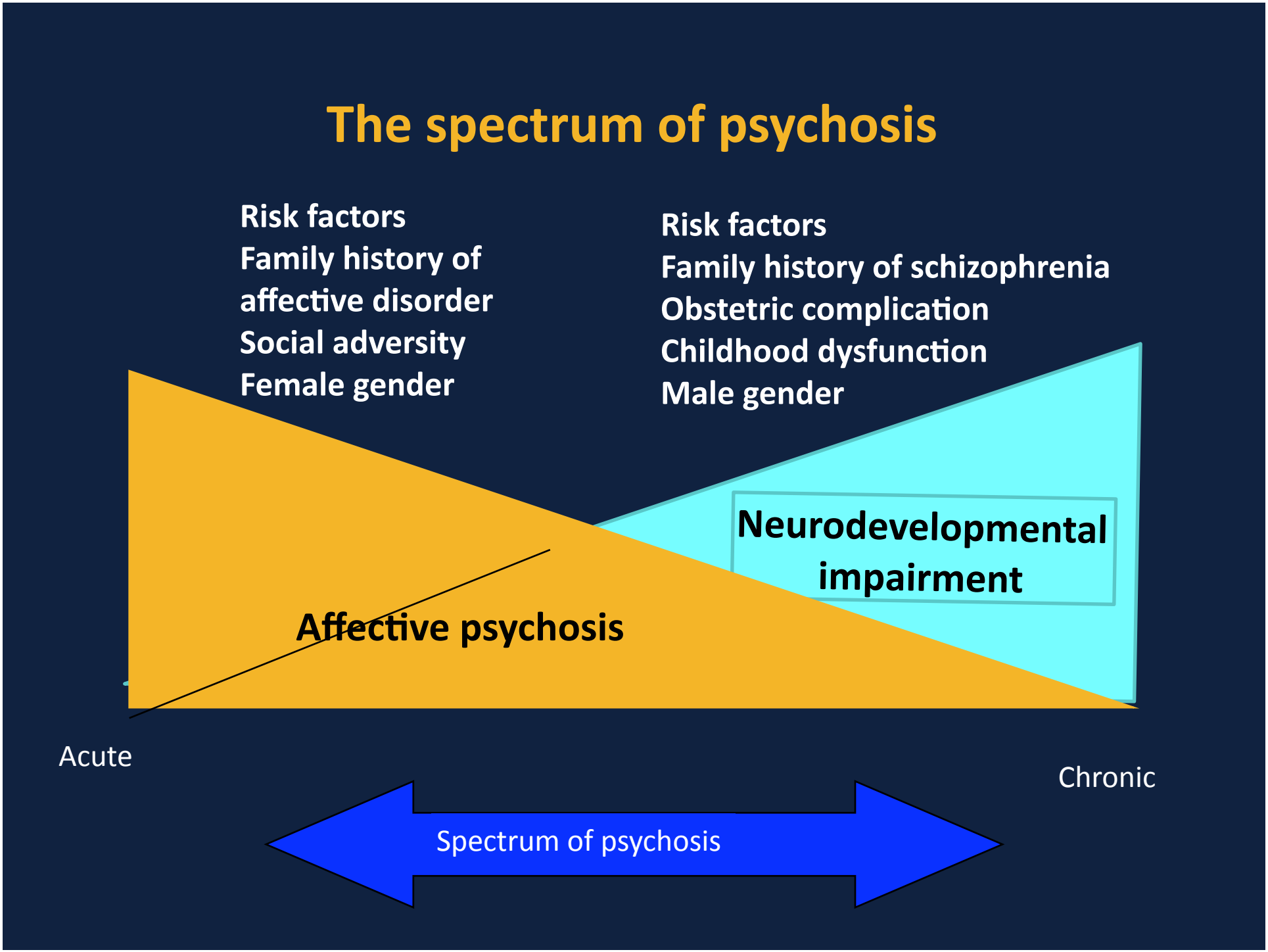
Categorical approach



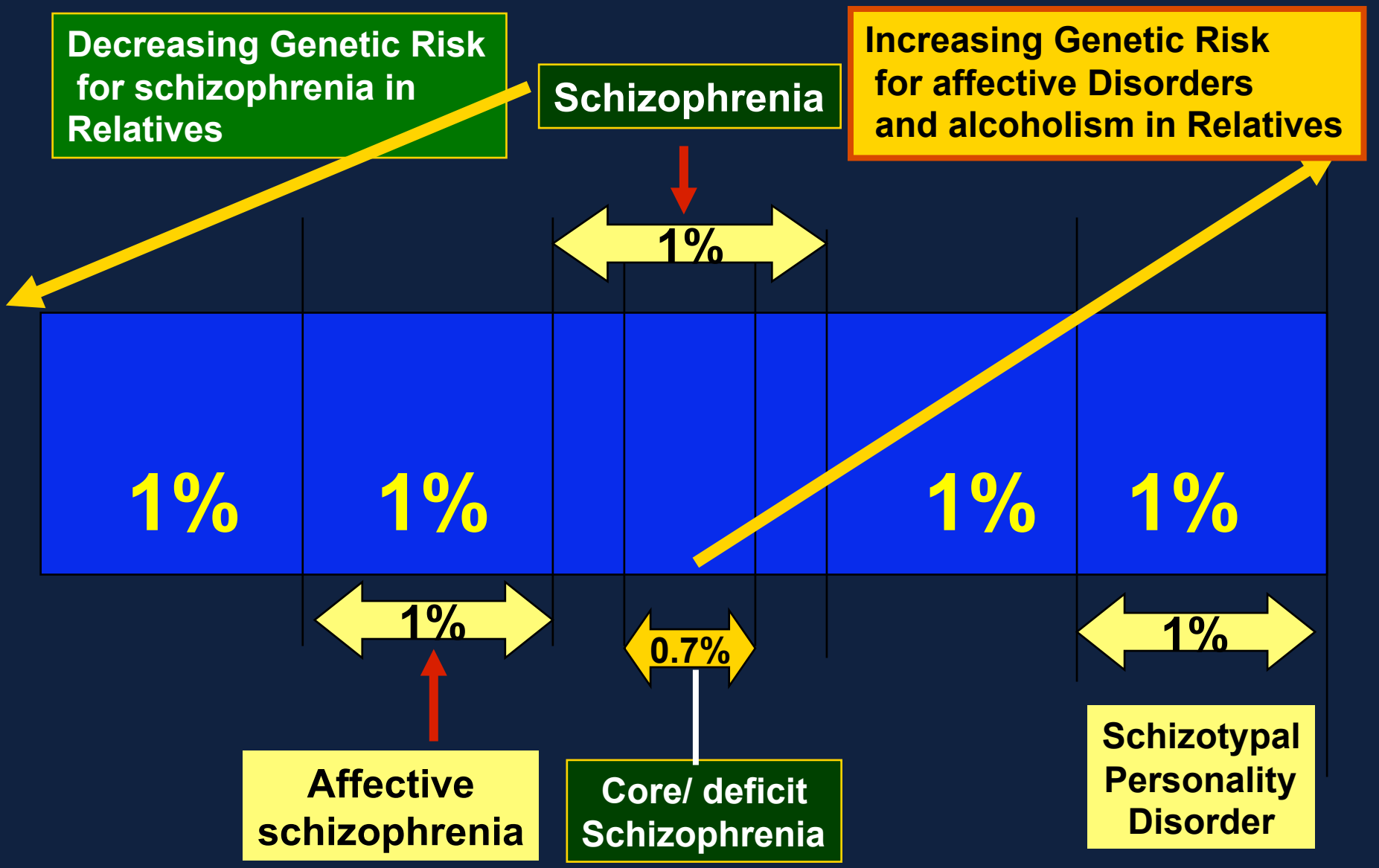
Dimensional approach
Spectrum

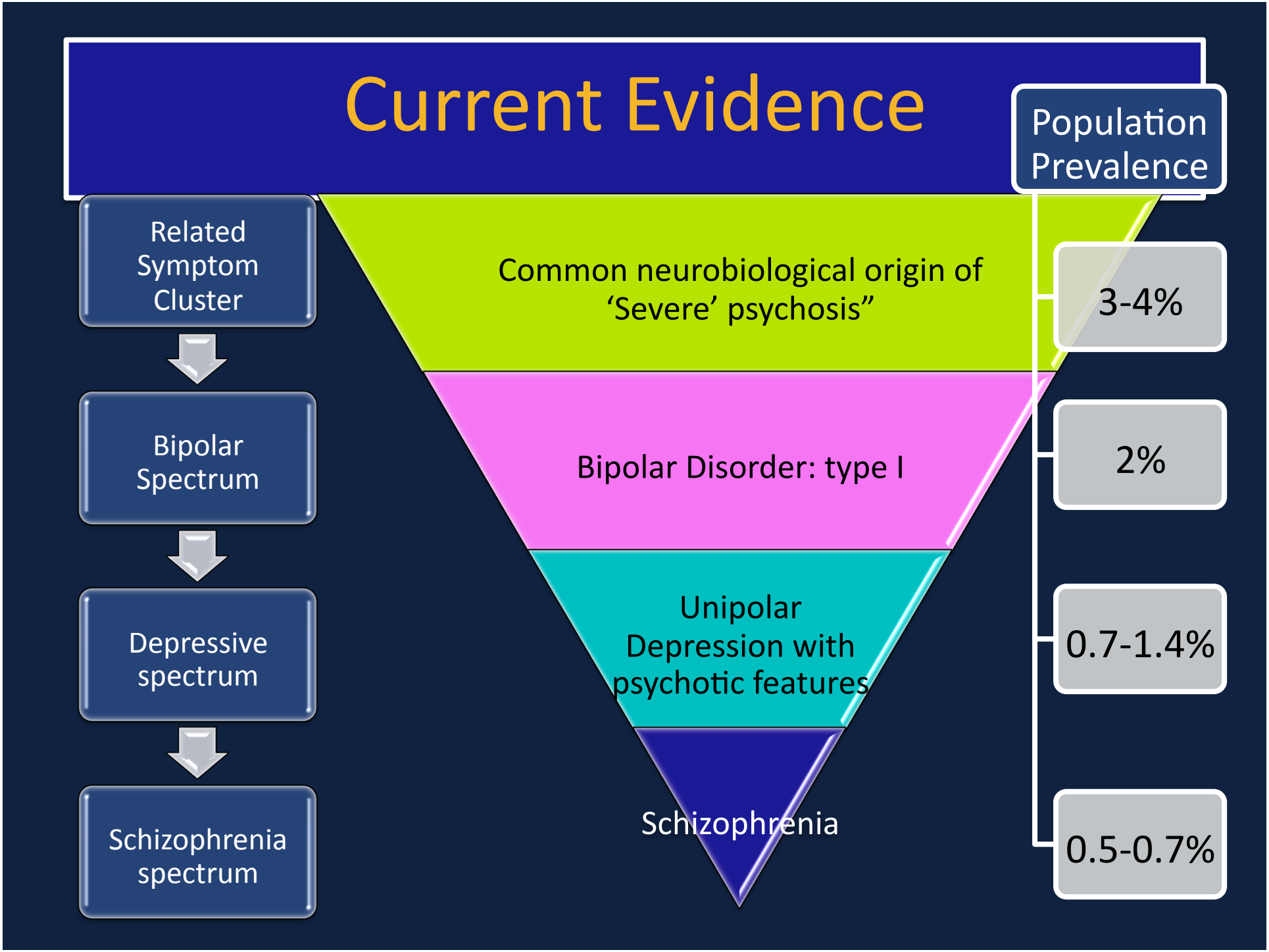


The spectrum of psychosis

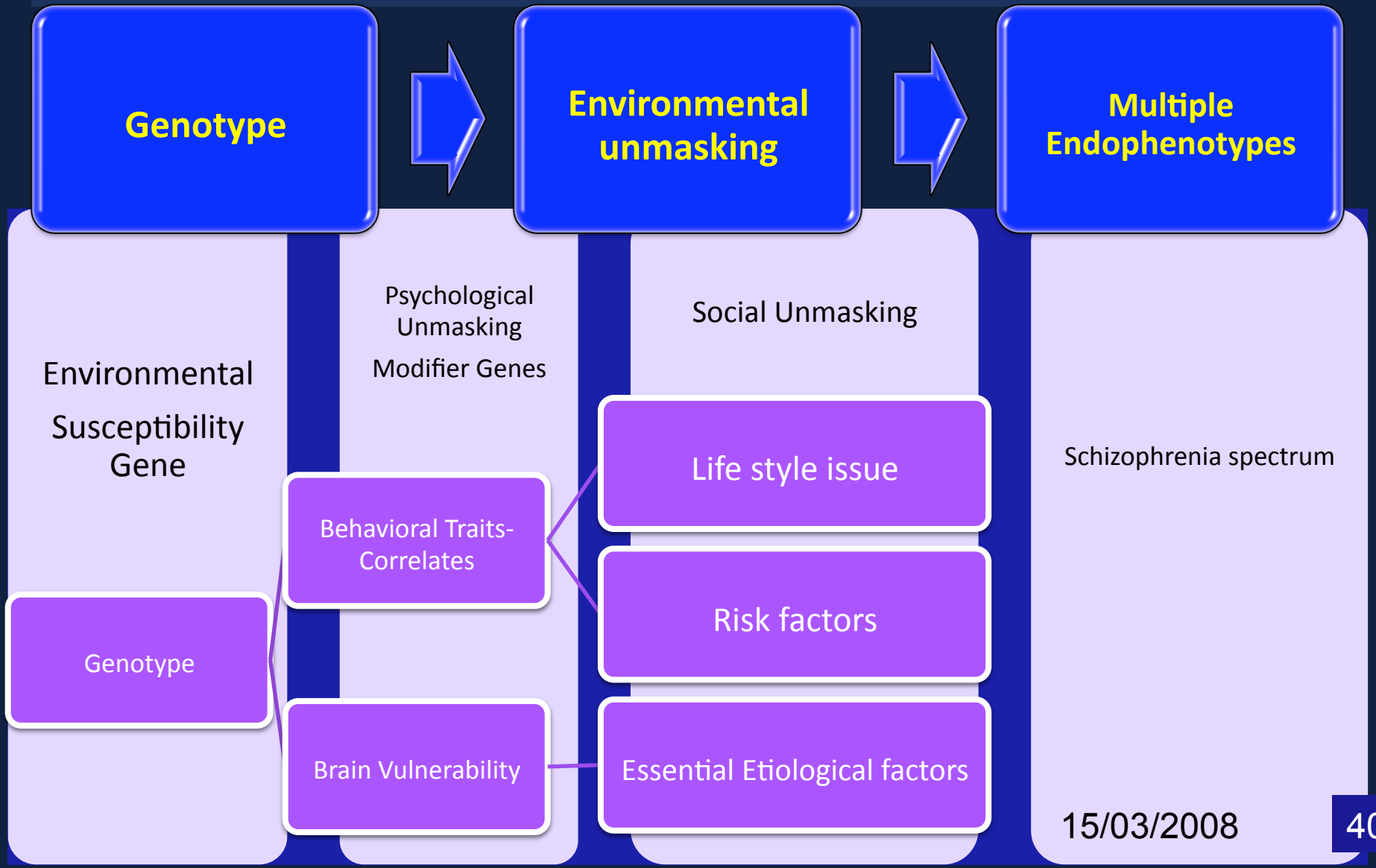


Schizophrenia and spectrum Disorder: Genetic phenomenology




Current Evidence
Population Prevalence
Related Symptom Cluster
Bipolar Spectrum
Depressive spectrum
Schizophrenia spectrum
Common neurobiological origin of 'Severe' psychosis"
Bipolar Disorder: type I
Unipolar Depression with psychotic features
Schizophrenia
3-4%
2%
0.7-1.4%
0.5-0.7%

An Endophenotype of Schizophrenia



Current position & Evidence to drop from DSM V

Reviewing and contrasting categorical & dimensional approach to approach

Clinical description

Neurobiology

Treatment.

Aetiologic overlap between schizophrenia, schizoaffective disorder, and bipolar disorder

- Growing evidence
- Investigated 'magnitude of the overlap' over a 35-year period based on the entire Danish population. followed from 1970 to 2006.
- A register-based prospective cohort study > 2.5 million persons born in Denmark after 1954.
- A new comorbidity index, CI
- Schizophrenia N = 12,734,
- Bipolar disorder N = 4,205 with
- Schizoaffective disorder N = 1,881
- SAD & BD = 103.
- SAD & SCH = 80
- SCH & BD = 20.
- Similar large indexes were found for men as well

J Clin Psychiatry. 2009 Jun 16. Laraun TM et al

Aetiologic overlap between schizophrenia, schizoaffective disorder, and bipolar disorder

- Substantial comorbidity index
- This study supports the existence of an overlap between bipolar disorder and schizophrenia and thus challenges the strict categorical approach used in both DSM-IV and ICD-10 classification systems.

J Clin Psychiatry. 2009 Jun 16. Laraun TM et al

Outcome is better than schizophrenia and worse than mood disorder: Benabarre 2001, del Rio 1990, 1992

Symptomatic & long term function is stable like schizophrenia

Tsuang 1993, Harrow 2000, Benabarre 2001

Better symptomatic and functional outcome of SAD< MMD< SCHIZ:

Marneros 1989, Tohen 2000

Long-term outcome: Is it any different

- 1934 and 1944 : 30- to 40-year outcome study.
- Patients with schizoaffective disorders had a significantly better outcome
- A significantly poorer outcome than those with affective disorders and surgical conditions.

Arch Gen Psychiatry. 1979 Nov;36(12):1302-4. **Long-term outcome of major psychoses. II. Schizoaffective disorder compared with schizophrenia, affective disorders, and a surgical contro group Tsuag MT Dempsey GM**

Long-term outcome: Is it any different

- 4-5 years after hospitalization
- Overall, schizoaffective patients showed some similarities to both schizophrenic and bipolar manic patients.
- Somewhat better overall post hospital functioning.
- LS Grossman, M Harrow, JF Goldberg and CG Fichtner 1991

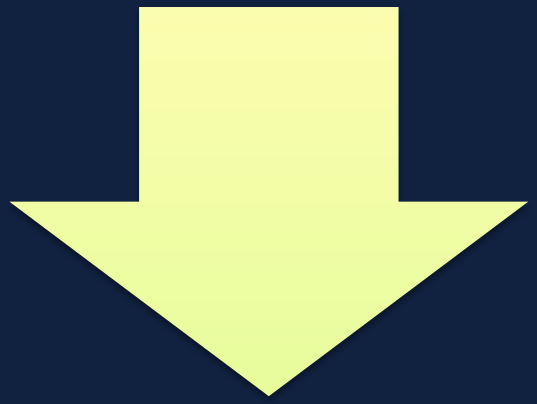
Response to Treatment: Does it distinguish?

- Treatments echo dimensional approach
- There is no specific treatment
- Symptom-guided treatments are advocated
- Response to any approach of treatment does not distinguish this diagnostic entity
- SAD: better responsive schizophrenia
- Poor responding mood disorder

Epidemiology

As prevalent as schizophrenia but less than Bipolar disorder

Similar to SCH, as per one criteria: 'information processing'



Less than SCH if 2 Criteria information processing + emotional regulation

Epidemiology

As prevalent as schizophrenia but less than Bipolar disorder

- Prevalence < schizophrenia as DSM-IV TR
- Life time prevalence: 0.2%-1.1%(Zarate 1997, Marneros 2003)
- 9% among hospitalized psychiatric inpatients(Scully 2004)
- SAD & SCH half as common as Bipolar I (Benaberre 2001)
- Rare among psychotic children (Werry 1991)
- Diagnostic challenge in Co morbidity of LD, SUD (Freidlander 2004, Malla 2000)

Age of onset

- Broad range
- 1/3 between 25-35 years
- 1/3 Prior to 25
- 1/3 after 35
- Early age onset: SAD with Depressed & Bipolar subtype
- Adult onset: ‘pure’ Mood disorder

Gender:

F < M : 2/3:1/3

Angst 1995, Dell’osso 1993,

Neurobiology

studies are 1-or-2 domain specific

- All 3 are manifestation of disturbance in several domains of NB
- Neuropsychology
- Neuroimaging,
- Electrophysiological
- Neurochemical
- Genetic

Neurobiology

studies are 1-or-2 domain specific

‘dysfunction of information processing’ → **‘indistinguishable’ from any other psychiatric disorder**

Emotional regulation → **Indistinguishable from mood disorder**

Neuropsychology : 16 studies

- Changes similar to schizophrenia
- Impairments in frontally mediated cognition, including
  - working memory,
  - alteration attention,
  - information recall,
  - category generation,
  - abstraction, Motor
  - planning

Neuropsychology : 16 studies

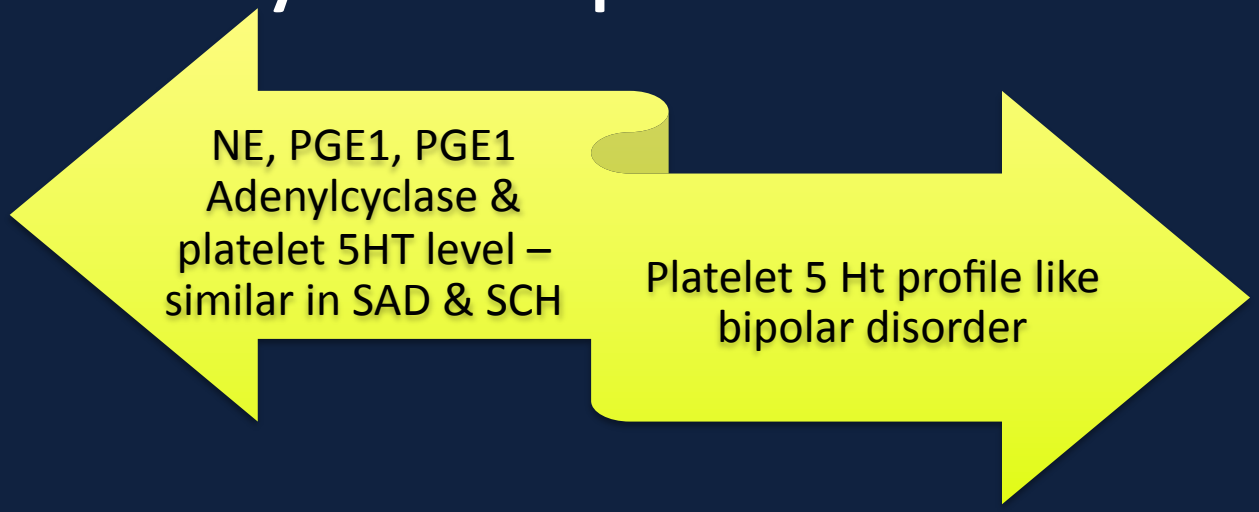
- **Better performance in 2 studies (Glodstein 2005, Strip 2005)**
- **SCH itself is heterogeneous**
- **Sub typing of SCH based on domains of neurobehavioral dysfunction may result in distinct subgroup.**
- **Basic dysfunction : Cognition- information processing**

Structural neuroimaging: CT & MRI: 12 studies.

- Reduction in cerebral volumes particularly temporal & frontal regions
- Both white & grey matter loss
- Most consistent area of abnormality : hippocampus & parahymppocampal gyri
- Indistinguishable from either SCH or Bipolar
- Distinguishable from Normal controls
- Subtle differences are present

Neurochemical: 16 studies

- CSF or Serum NT or metabolite
- 'Similar pattern of NT abnormality in SCH, SAD & BAD' (Meltzer 1984)recent studies also observed 'no difference'
- Neurochemistry is symptom specific rather than disease or syndrome specific



Neuroendocrine:
Evidence for a neuromodulatory role for TRH

CSF thyrotropin-releasing hormone concentrations differ in patients with schizoaffective disorder from patients with schizophrenia or mood disorders, :

Charles B. Nemeroffc Journal of Psychiatric Research
Volume 35, Issue 5, September-October 2001,

Genetics

- Studies have generally failed to distinguish SAD from either SCH or BAD on the basis of genetic underpinnings
- DISC 1 abnormality on Chromosome 1q42
- A role in neurodevelopment process
- Preferentially expressed in forebrain.
- DISC 1 is regarded as risk factor for both SCH & bipolar

Familial

- To test whether schizoaffective disorder is a variant
- Number of ADSA and SASC pairs were compared against the expected numbers.
- No significant differences were found,
- Suggests that schizoaffective disorder is genetically heterogeneous,
- With at least two subtypes,
  - one a variant of affective disorder,
  - the other a variant of schizophrenia

Summary

Current evidence in favor of Schizoaffective

Clinical- Course & Outcome Negative

Neurochemistry: Equivocal

Neuroimaging: Negative

Genetics: Negative

Treatment Response: Negative

Kraepelin is not dead

“It is increasingly becoming clear that we can not distinguish satisfactorily between these two illnesses and this brings home the suspicion that our formulation of the problem may be incorrect”
Kraepelin .E.

Future recommendations.

- Schizoaffective disorder is a prototypic boundary condition
- Epitomizes the pitfalls of the current categorical classification system.
- Future revisions to the DSM should consider:
- (i) SAD is a co morbid set of symptoms that occur as a by-product of two separate disorders (SCZ and BD) or, that
- (ii) SAD exists as the mid-point on a continuum between SCZ and BD,

Malhi GS, **Green M**, **Fagiolini A**, **Peselow ED** **Kumari V**
Bipolar Disord. 2008 Feb;10(1 Pt 2):215-30

DSM V

- Incorporation of these two disorders onto one dimension may be a suitable alternative.
- Hence the category SAD should be omitted in future revisions of DSM, allowing the development of meaningful nomenclature that…..
- …..rests upon further rigorous investigation of differences and similarities between disorders.

Management of Mood symptoms in schizophrenia: Beyond Diagnostic ambiguity.

- Pharmacological management of Mood symptoms and that of ‘suicidality’ in schizophrenia goes hand –in-hand.
- Effective strategy
- Optimizing antipsychotic treatment and atypical antipsychotics prove to be most effective
- Adjunctive antidepressants may be useful for patients who are not acutely ill
- Careful longitudinal assessment is required to ensure identification of primary mood disorders

How to treat schizoaffective disorder?.. Cochrane review June 2009

- Aim: to review treatment studies for schizoaffective disorder and draw conclusions for clinical decision making.
- Method: : Thirty-three studies , 14 randomized controlled trials.
- The studies reviewed do not permit consistent recommendations as to whether SAD should be treated primarily with
- antipsychotics,
- mood stabilizers or combinations of these drugs.
- The relevance of diverse subtypes .. for treatment recommendations is unclear.
- Conclusion:. The lack of conclusive recommendations is related to issues of nosological status, plurality of diagnostic criteria and validity of the concept.

Jäger M, Becker T, Weinmann S, Frasch K.Department of Psychiatry II, Ulm University, Günzburg, : Treatment of schizoaffective disorder - a challenge for evidence-based psychiatry. *Acta Psychiatr Scand. 2009 Jun 30.*

Current evidence: Anti Depressant Drugs

Use of antidepressant drugs in schizophrenic patients with depression Encephale. 2006

- **The results provide weak evidence for the efficacy of antidepressants in patients with schizophrenia and depression.**
- **The only SSRI tested in the treatment of depression in schizophrenic patients is sertraline.**
- **In meta-analysis, No difference between the 2 treatment groups was demonstrated**

Electroconvulsive therapy for schizophrenia
2009 The Cochrane Collaboration. 26 trials with 50 reports.

1. Efficacy.

1. ECT is compared with placebo or sham ECT,
2. ECT resulted in less relapses in the short term and a greater likelihood of discharge
3. No significant drop out compared with sham ECT .

2. Sustain the efficacy.

1. No evidence - advantage is maintained - medium to long term.

3. Combination APD

1. Compared with antipsychotic drug - favour the medication group
2. Limited evidence - ECT combined with antipsychotic drugs > greater improvement than with antipsychotic drugs alone.
3. When continuation ECT was added to antipsychotic drugs, the combination was superior to the use of antipsychotics alone.

Prathap Thyhan , Schizophrenia Cochrane group 2009.

Electroconvulsive therapy for schizophrenia
2009 The Cochrane Collaboration. 26 trials with 50 reports.

4.Memory

1. Very limited data indicated that visual memory might decline after ECT compared with sham ECT
2. Verbal memory tests were equivocal.
3. One small study suggested more memory impairment with ECT combined with antipsychotics than with antipsychotics alone , though this proved transient.

5. Type

1. Unilateral and bilateral ECT were equally effective in terms of global improvement

6.Numbers.

1. One trial showed a significant advantage for 20 treatments over 12 treatments for sustenance of remission

Current evidence : Mood Stabilizers

- Lithium
- Carbamezapine
- Valproic acid
- Lamotregene
- Toperamate
- Gabapentine
- Calcium channel blockers

Carbamazepine for schizophrenia
2009 The Cochrane Collaboration,
Studies 10, N= 258

Based on currently available randomized trial-derived evidence, carbamazepine cannot be recommended

Valproate for schizophrenia
2009 The Cochrane Collaboration,
7 studies, 6 RCT, N=519

There is some evidence for positive effects on aggression and tardive dyskinesia,

Adding Lithium or Anticonvulsants to Antipsychotics for the Treatment of Schizophrenia: Useful Strategy or Exercise in Futility? June 2009 JCP

- Lithium is perhaps the best-known mood stabilizer,
- Although early studies showed adjunctive lithium to be some- what useful, later and better-designed trials did not.
- A Cochrane review of RCTs concluded that, despite some evidence supporting the efficacy of lithium augmentation among 11 studies testing this,
- Overall results were inconclusive.

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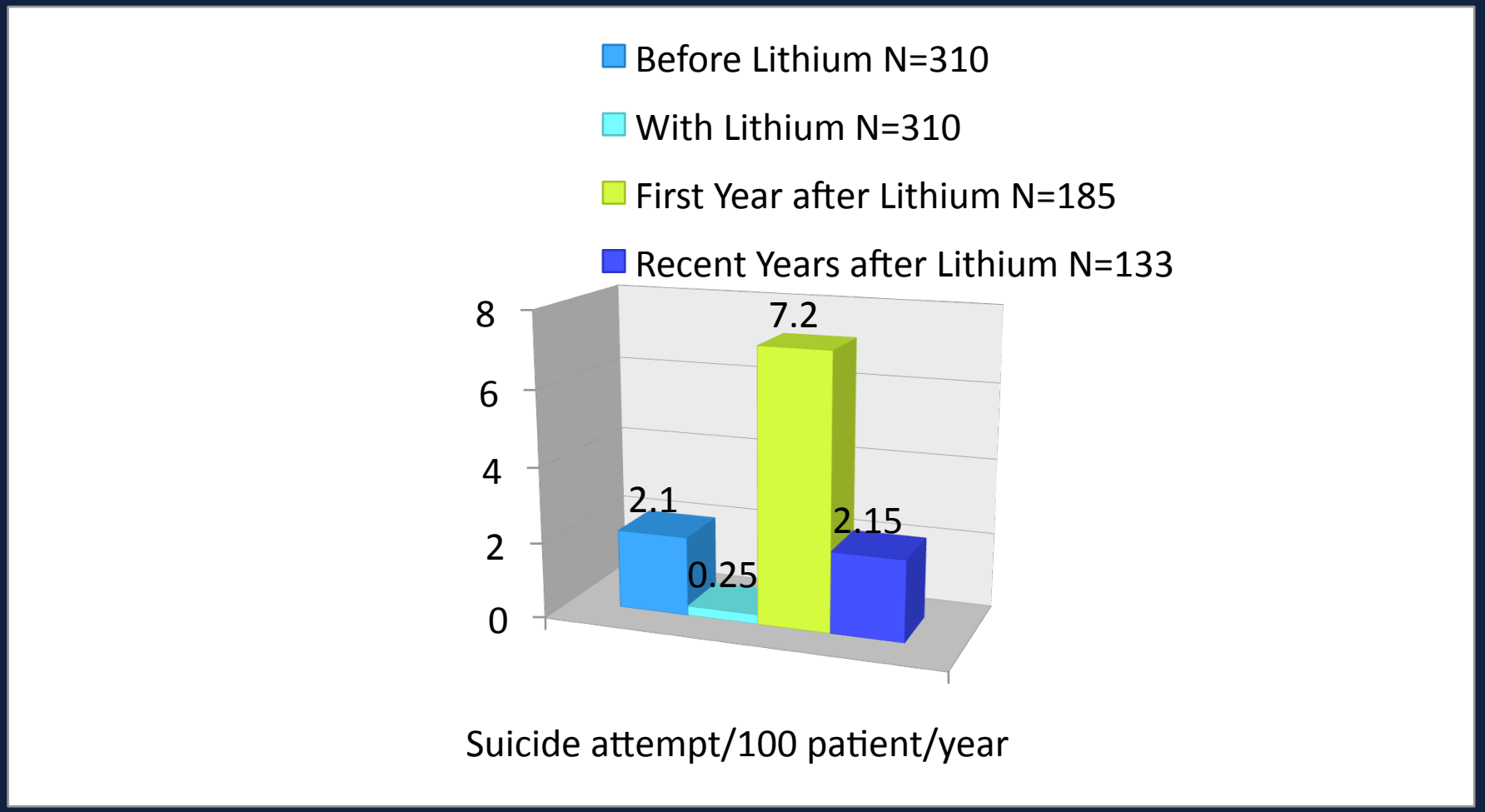
Adding Lithium or Anticonvulsants to Antipsychotics for the Treatment of Schizophrenia: Useful Strategy or Exercise in Futility? June 2009 JCP



Meltzer e Baldessarini, 2003

Are atypical neuroleptics mood stabilisers?

- Are they effective beyond psychotic affective states?
- Are they effective against the depressive phase of bipolar disorder?
- Do they induce mania?
- Do they work in mixed states?
- Do they work in rapid cycling?
- Can they prevent suicide?

How do we explain?

Why do Atypical antipsychotics have Antidepressant action?

A: Regional distribution of 5-HT System in the Brain??

B. Effect of metabolites (norquetiapine)

Relative Efficacy of AAPD for mood symptoms and suicidality in Schizophrenia

Clozapine and Suicide

- Itersept
- CATIE
- SOHO
- Cultass
- BORAS
- Phase III trials
- Individual studies,
- RCT

- Clozapine
- Olanzapine
- Aripiprazole
- Quetiapine
- Amisulpiride
- Ziprasidone
- Paliperidone
- Risperidone

Does quetiapine have mood altering properties?

- A combination of Non-quetiapine and quetiapine has been found to have antidepressant property in MMD, thus FDA approved now.
- Supported by a data base of 1900 patients.
- An ability to elevate mood while controlling psychoses would be helpful in the treatment of post-psychotic and bipolar depression.
- Its clinical importance in the control of manic episodes, for which atypical antipsychotics are used increasingly, is uncertain.

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

Prevention of Suicide in Psychotic Disorders: General principles and strategies.

What is specific to suicide in schizophrenia disorder? Demographic, clinical and behavioural dimensions.

Elevated levels of impulsive-aggressive personality traits, and behaviours
(Schizophrenia research 2008)

Post-diacharge suicide is high

- Term ‘Discharge’ is a misnomer.
  It is actually ‘transfer of Care from Hospital to Community’
  It is a dynamic Process’ .

Review: Assessment, Outcome, Care Plan, Discharge Plan, Risk Management & Transfer of care

Documentation

Conclusions:
Schizoaffective disorders.

There are many unanswered questions

- Schizoaffective disorder is a severe psychotic disorder with disability, burden and complications.
- Schizoaffective Disorder is an inconsistent condition and does not deserve an independent diagnosis
- We are moving towards unitary theory for single-severe-psychotic-disorder, based on clinical and biological evidences

Conclusions:
Schizoaffective disorders.
There are many unanswered questions

- Treatment appears inadequate and unclear, but optimizing atypicals APD appears best option.
- Quetiapine is an effective and approved atypical APD for MMD, Bipolar & schizophrenia