



Computational Psychiatry Course 2019

Clinical Psychiatry

Helen Schmidt



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Alika



independent.co.uk



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Situation



youtube



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Bipolar affective disorder

Manic and depressive episodes



thatsmaths.com



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Manic symptoms

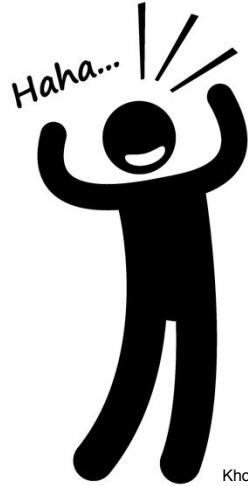


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elevated, expansive mood



Khoon Lay Gan © 123RF.com

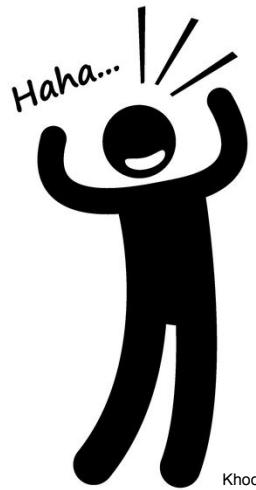


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increased energy

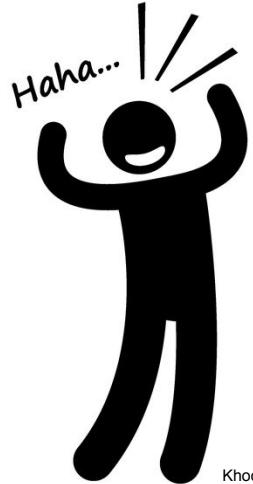


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increased energy



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talkative



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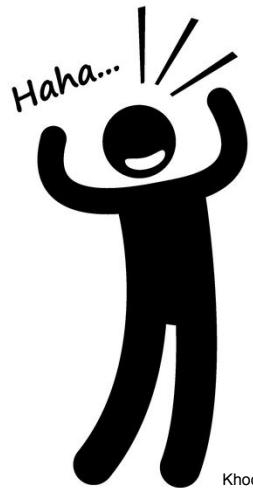


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Racing thoughts



adapted by lecture
UKE Hamburg, Prof. Lambert



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spending money

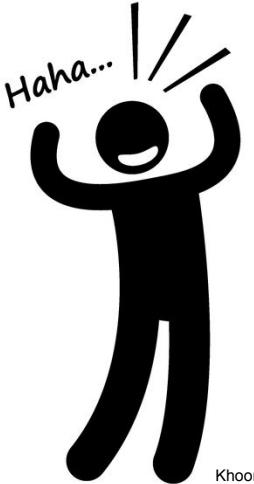


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spending money



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high-risk behavior



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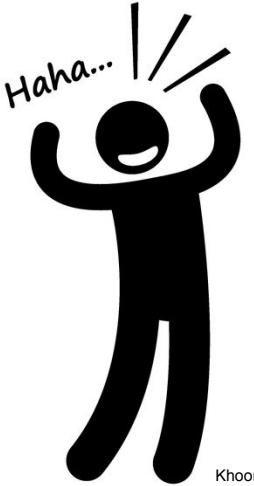


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increased libido



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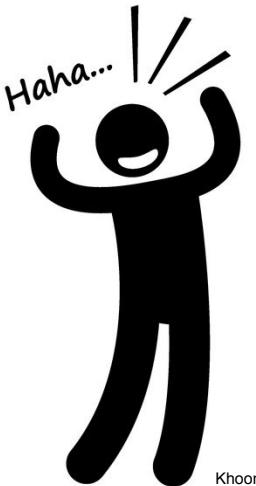


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racing thoughts



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spending money



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high-risk behavior



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increased libido



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inflated self-esteem



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psychotic symptoms



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auditory hallucination



pa/united archives

psychotic symptoms



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auditory hallucination



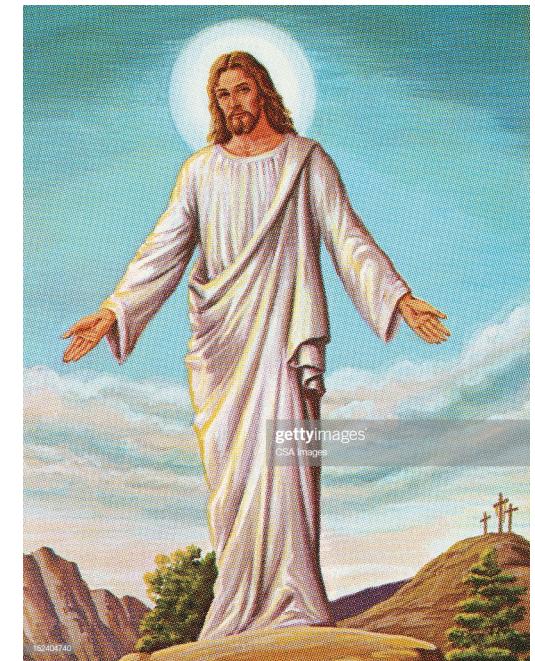
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psychotic symptoms



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grandiose delusion



“Jesus-Syndrome”



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Manic episode (ICD-10 F31.1-F31.2)

A) Elevated expansive/ irritable mood	B) More than 3 symptoms:
Increased activity or energy for 1 week	inflated self-esteem or grandiosity
	decreased need for sleep
	talkative
	flight ideas (thoughts racing)
	distractibility
	increase in goal-directed activity psychomotoric agitation
	activities with high potential for painful consequences
	severe mood disturbance in social/occupational functioning



Hypomanic episode (ICD-10 F31.0)

„milder“ version of manic: increased energy, elevated mood

episode duration: 4 days

no psychotic or delusional symptoms

without social consequences



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Hypomanic episode (ICD-10 F31.0)

The New York Times

Just Manic Enough: Seeking Perfect Entrepreneurs



**“If you’re manic, you think you’re Jesus.
If you’re hypomanic, you think you are
God’s gift to technology investing.”**

John D. Gartner, psychologist and author of
“The Hypomanic Edge”



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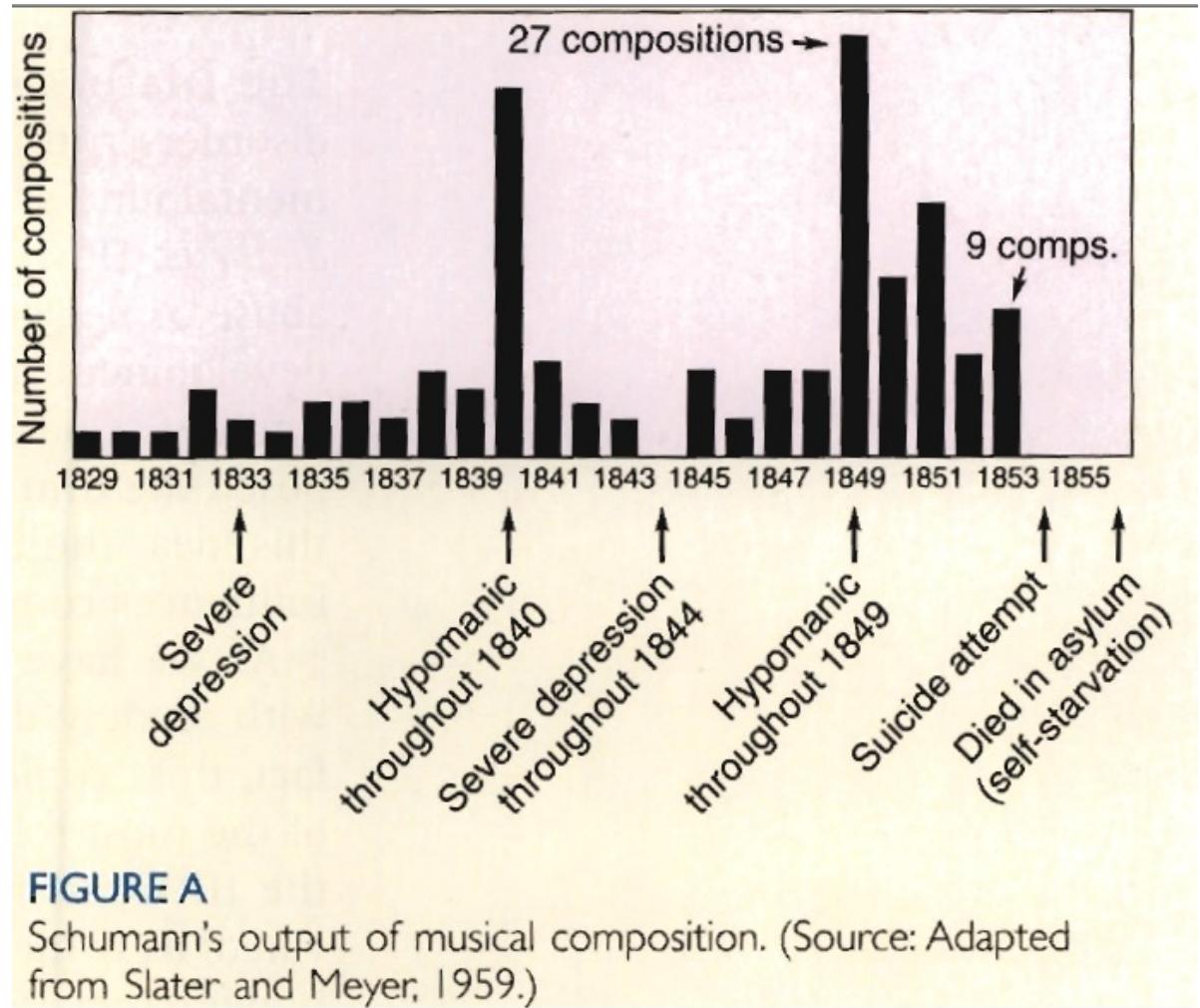
Hypomanic episode (ICD-10 F31.0)

Robert Schumann (1810-1856, composer)



© Public Domain

„melancholia with delusion“



Depressive episode



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ICD-10 F31.1-F31.5 : bipolar depression

Key symptoms

Persistent sadness or low mood

Loss of interests or pleasure

Fatigue or low energy

Additional symptoms

Low self-confidence

Guilt or self-blame

Suicidal thoughts or acts

Poor concentration or indecisiveness

Agitation or slowing of movements

Disturbed sleep

Poor or increased appetite

Diagnosis

F31.3- depressive episode

F31.3 mild

F31.3 moderate

F31.4 severe without psychotic

F31.5 severe with psychotic

adapted by Gina's talk



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F31.3- depressive episode

F31.3 mild

F31.3 moderate

F31.4 severe without psychotic

F31.5 severe with psychotic

adapted by Gina's talk



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Bipolar depression vs. unipolar depression

caution: antidepressant medication can lead to a “switch”
into a manic episode

20% with depression develop a bipolar disorder



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mania



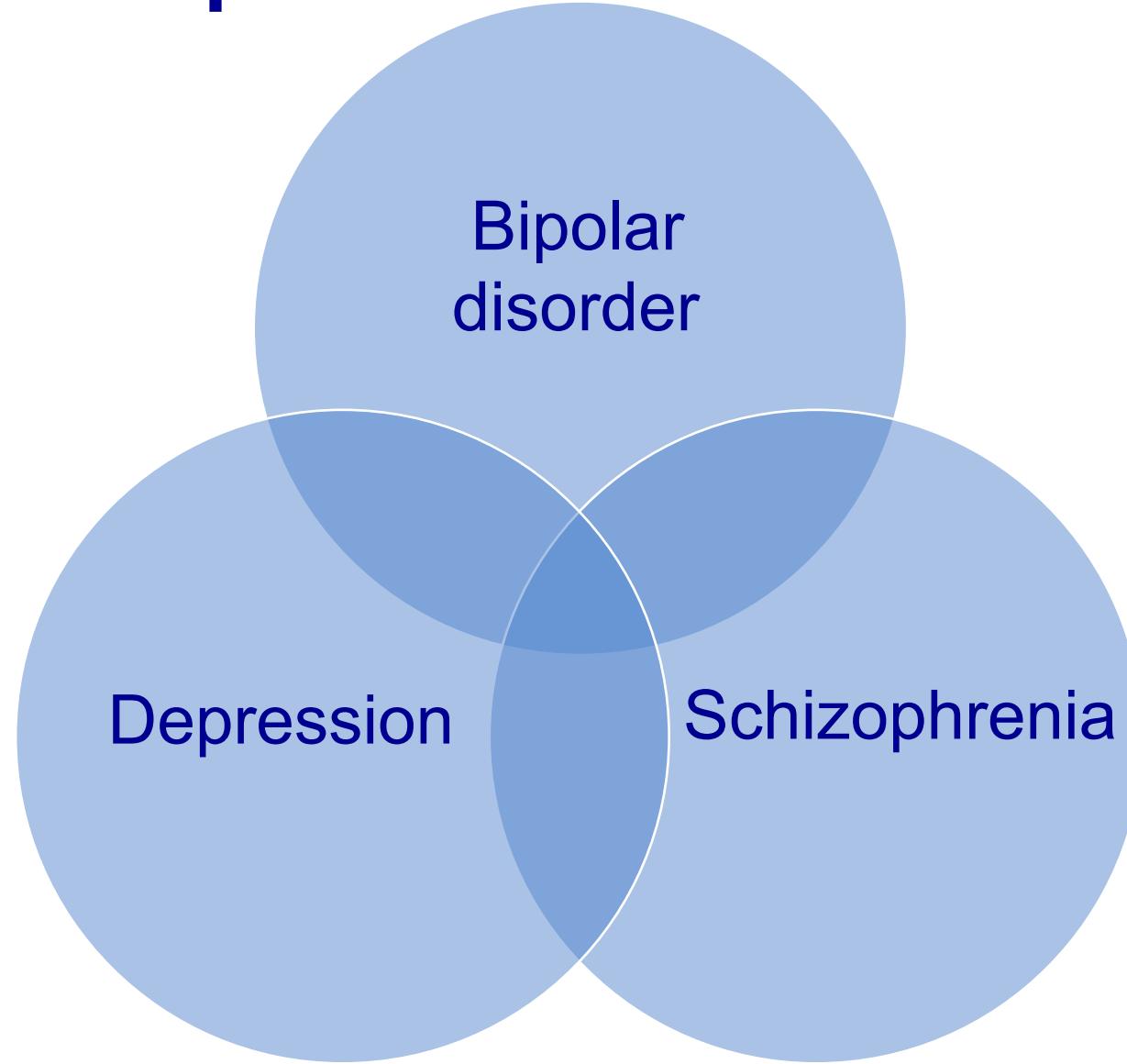
depression

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Symptoms overlap



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Progression



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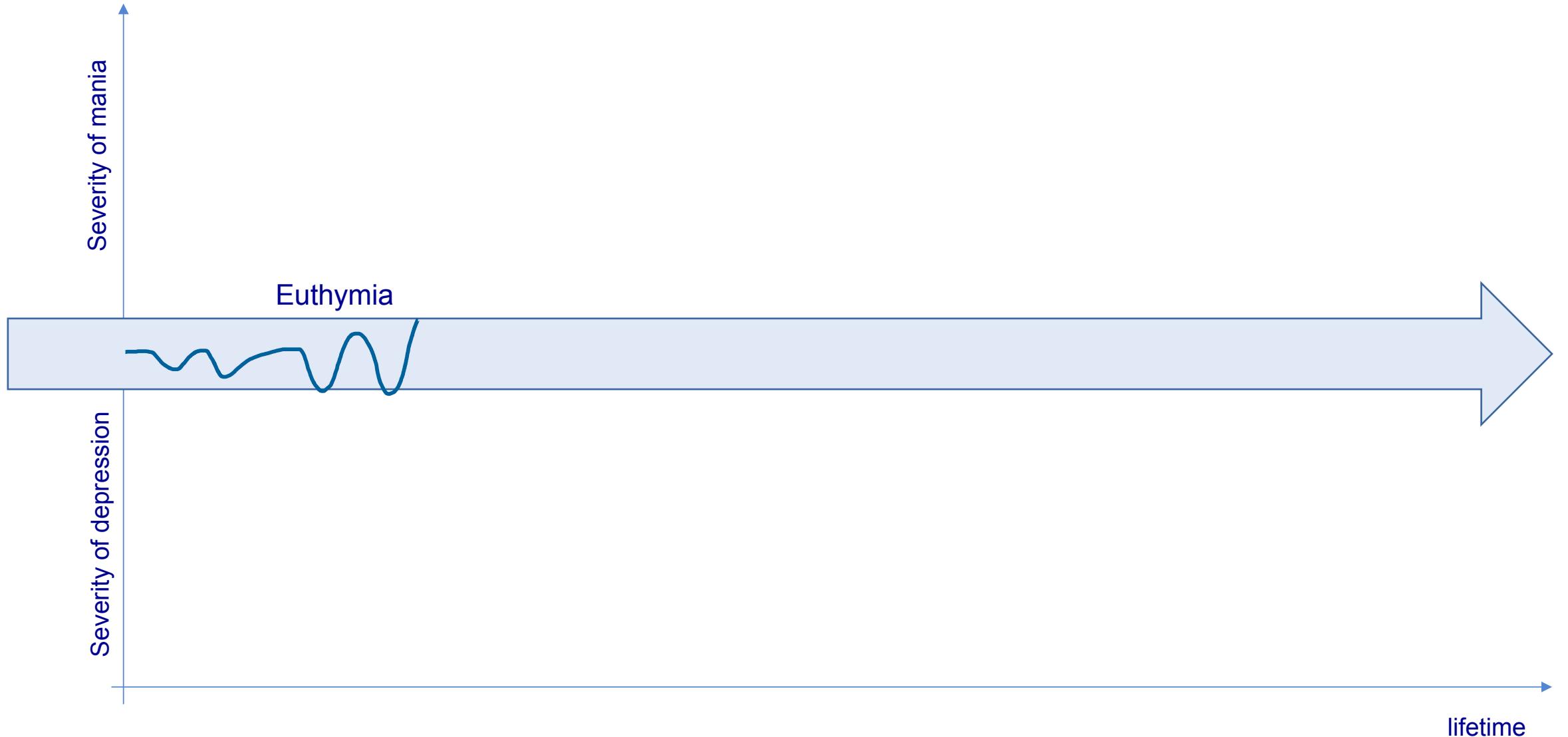
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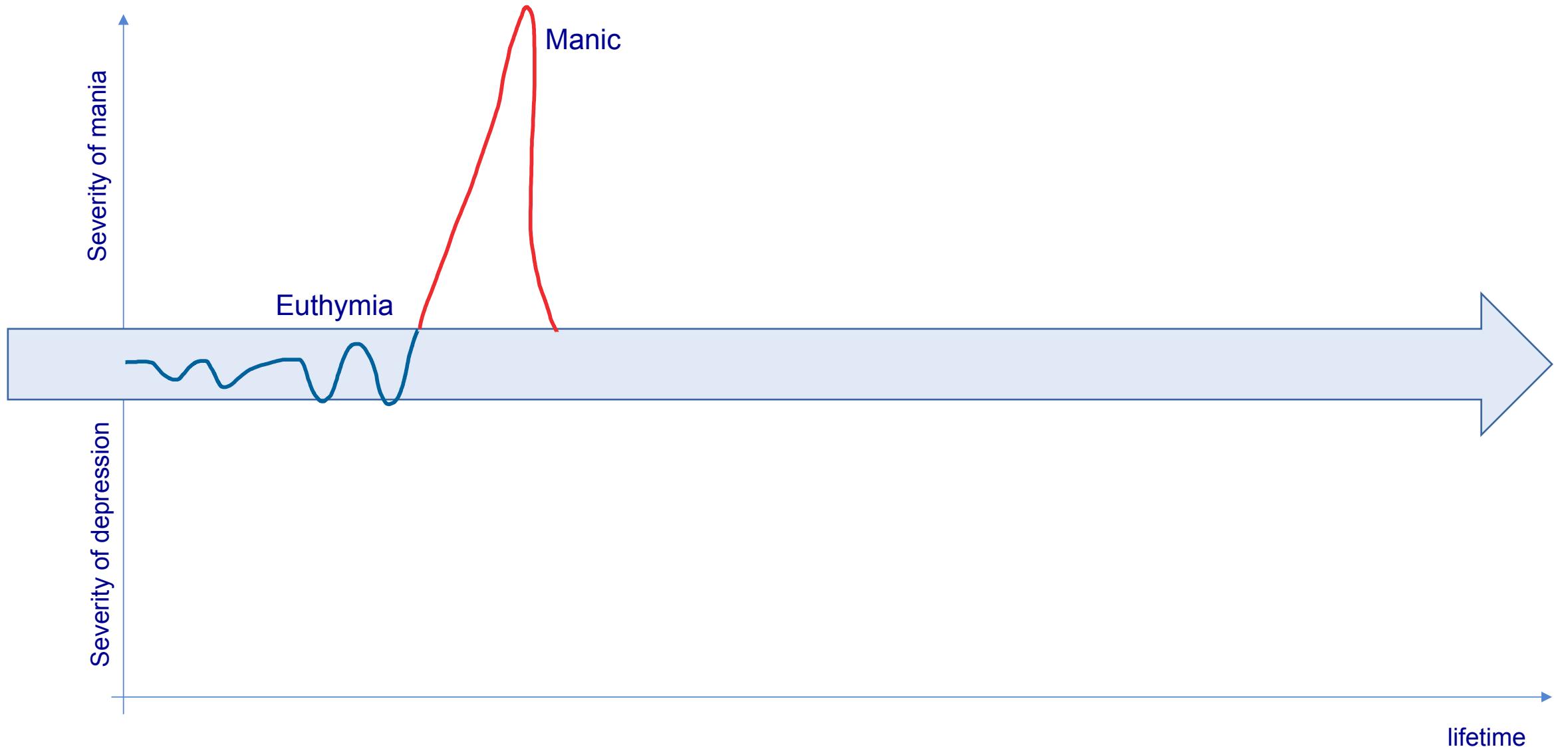
Adapted by Grande et al. *The Lancet*, 2016

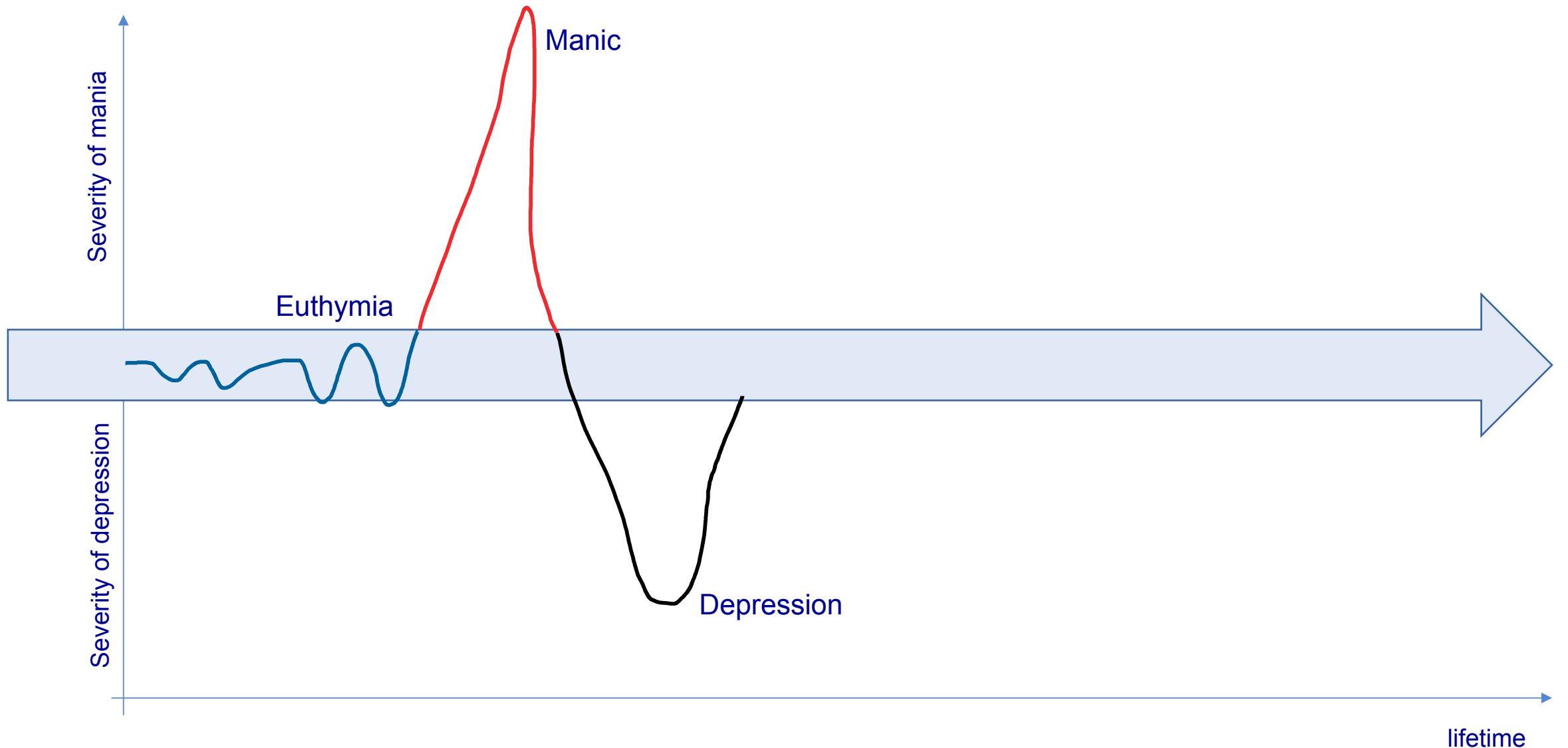


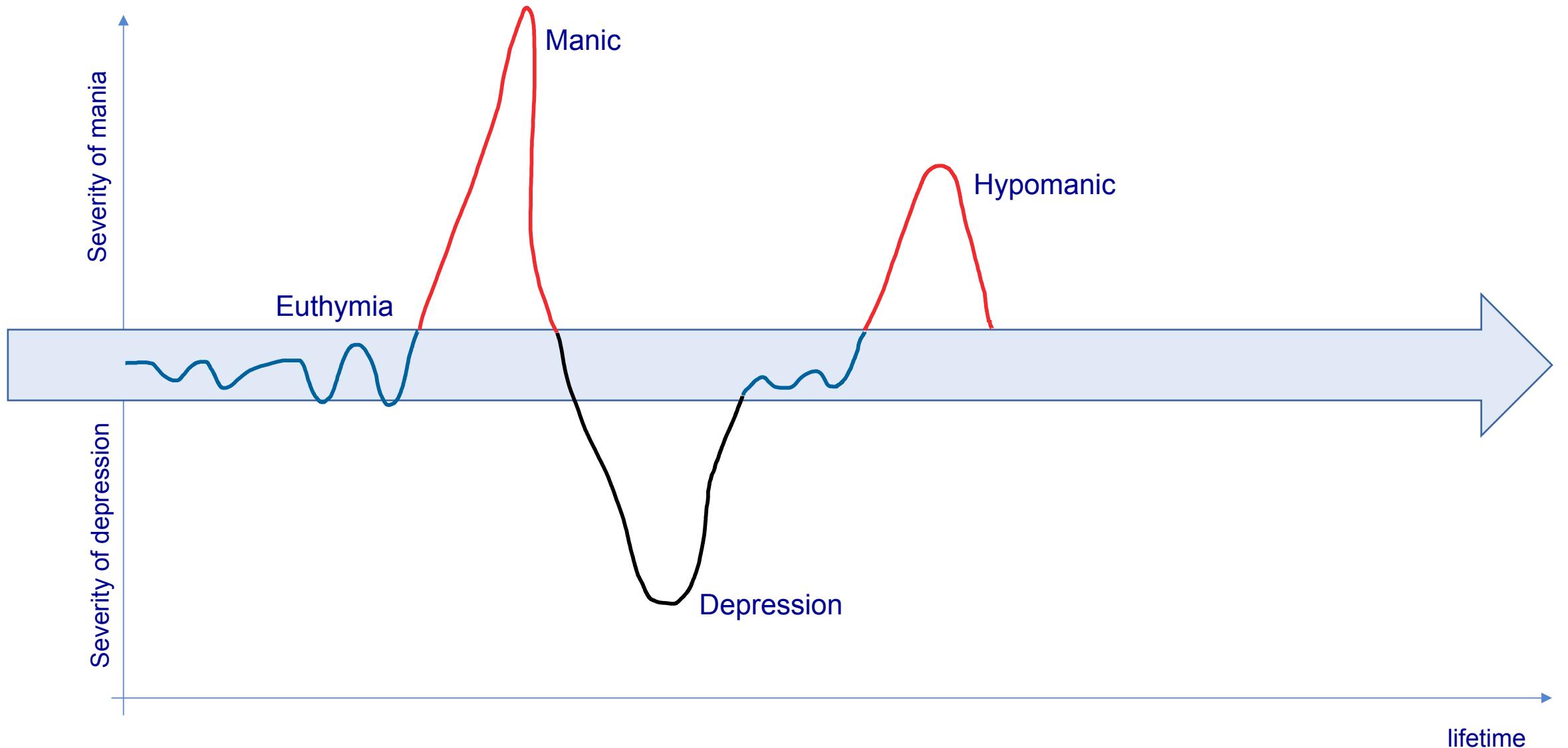
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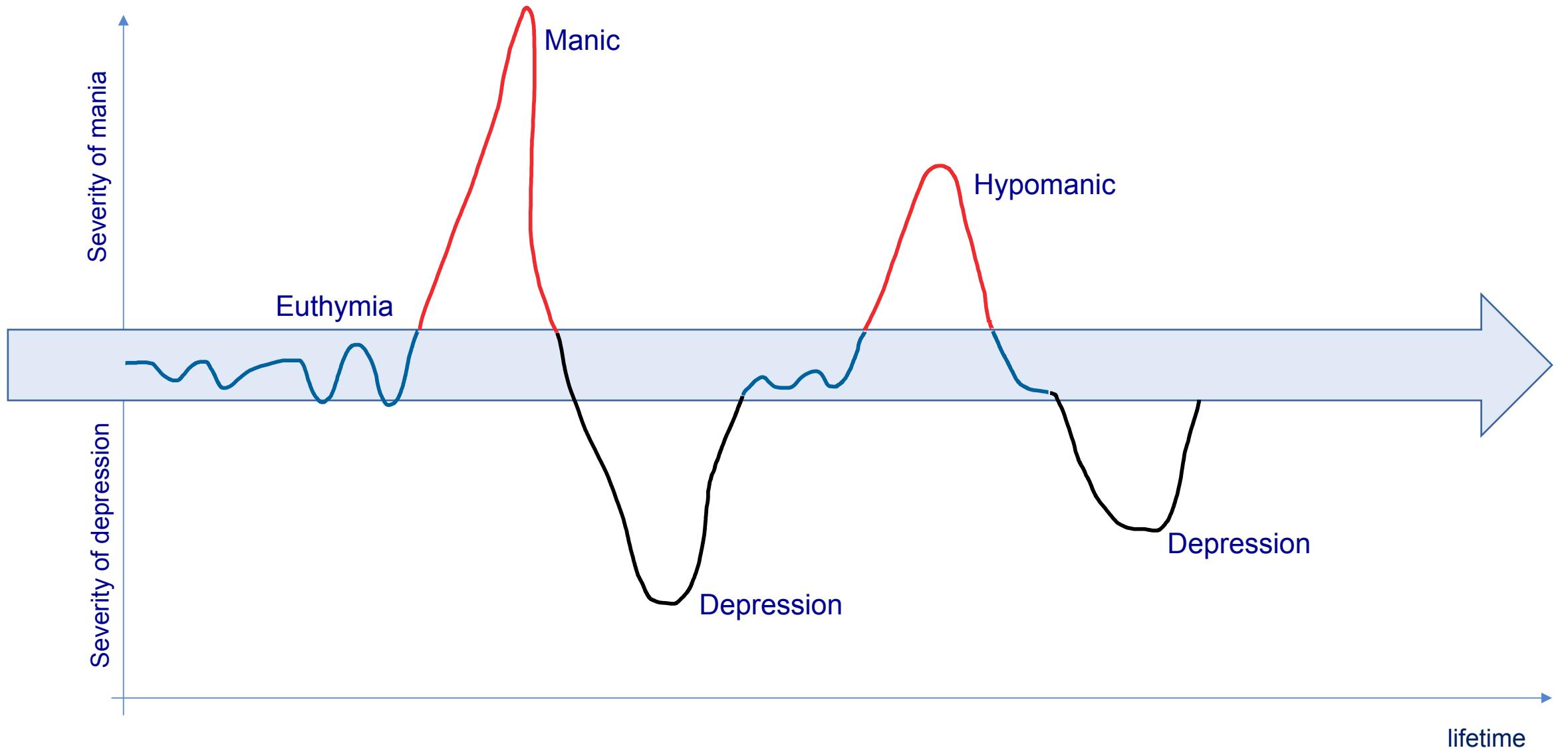


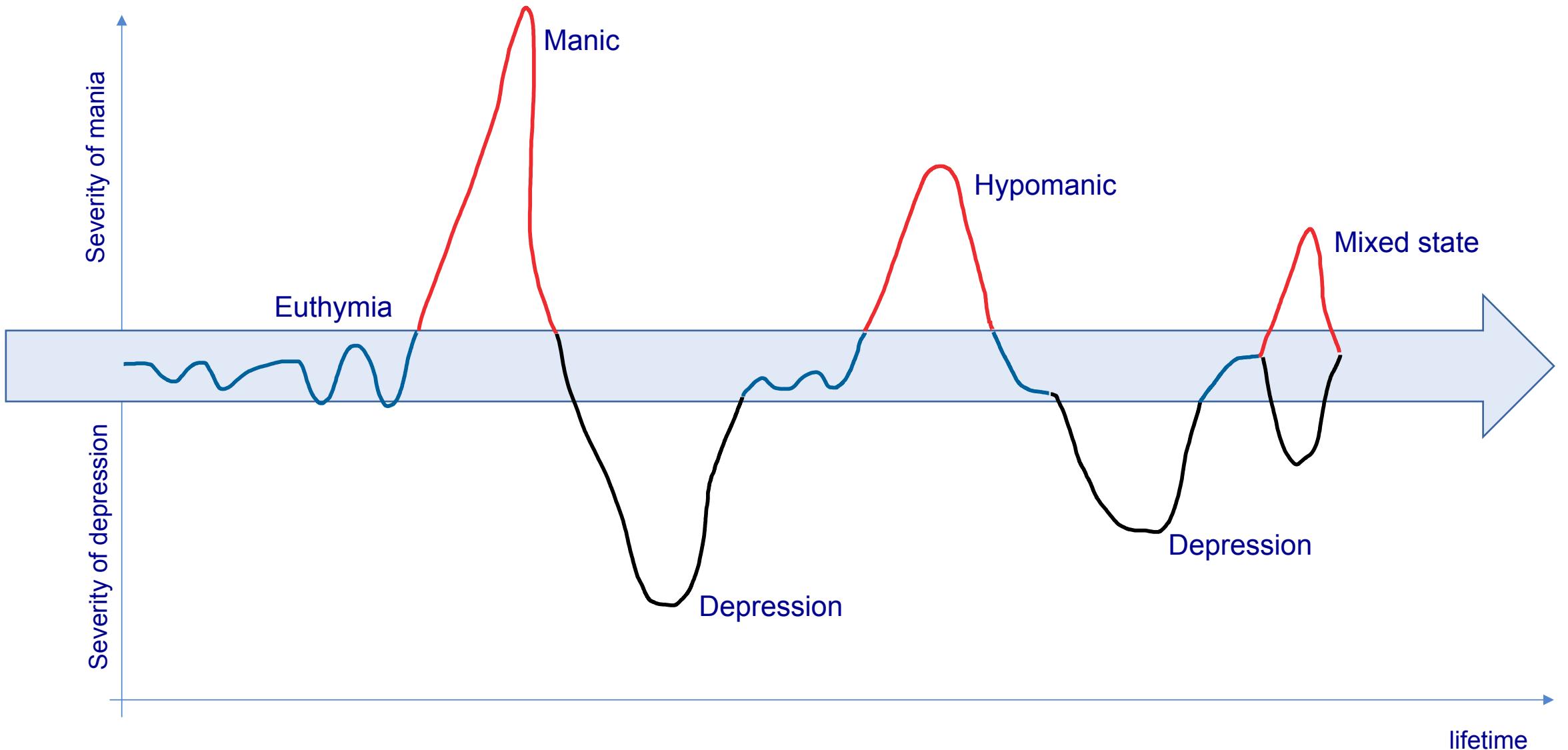
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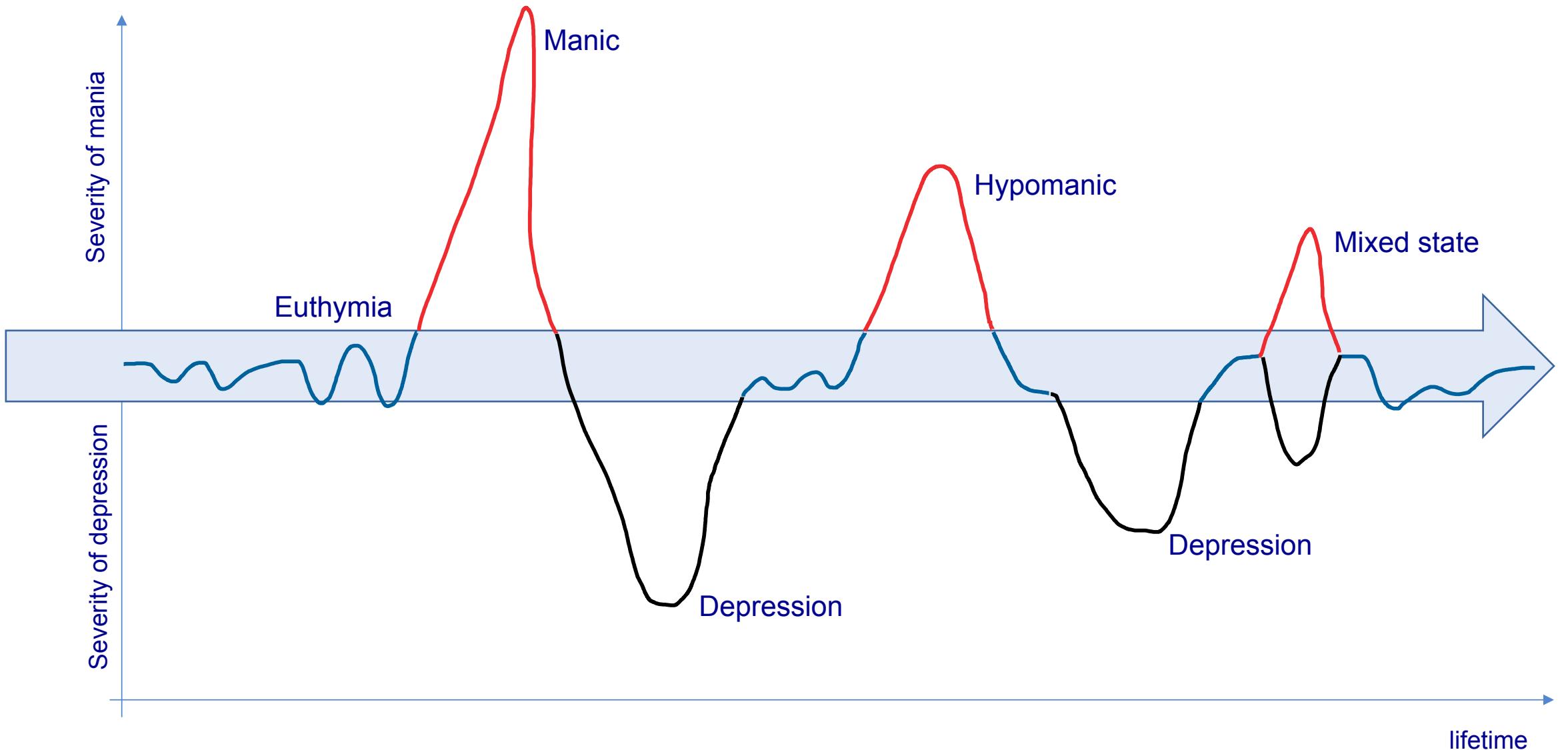












Diagnostics



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Diagnostics

Clinical Evaluation (ICD-10, DSM-5)

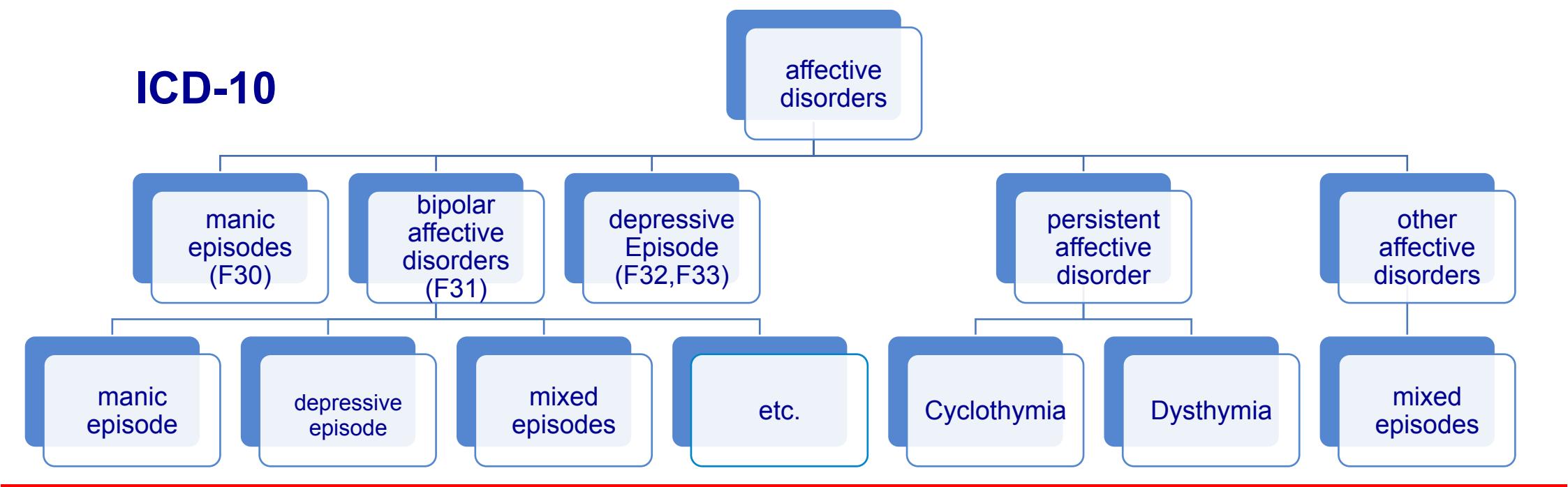
Self-report/ indirect anamnesis

Positive family history

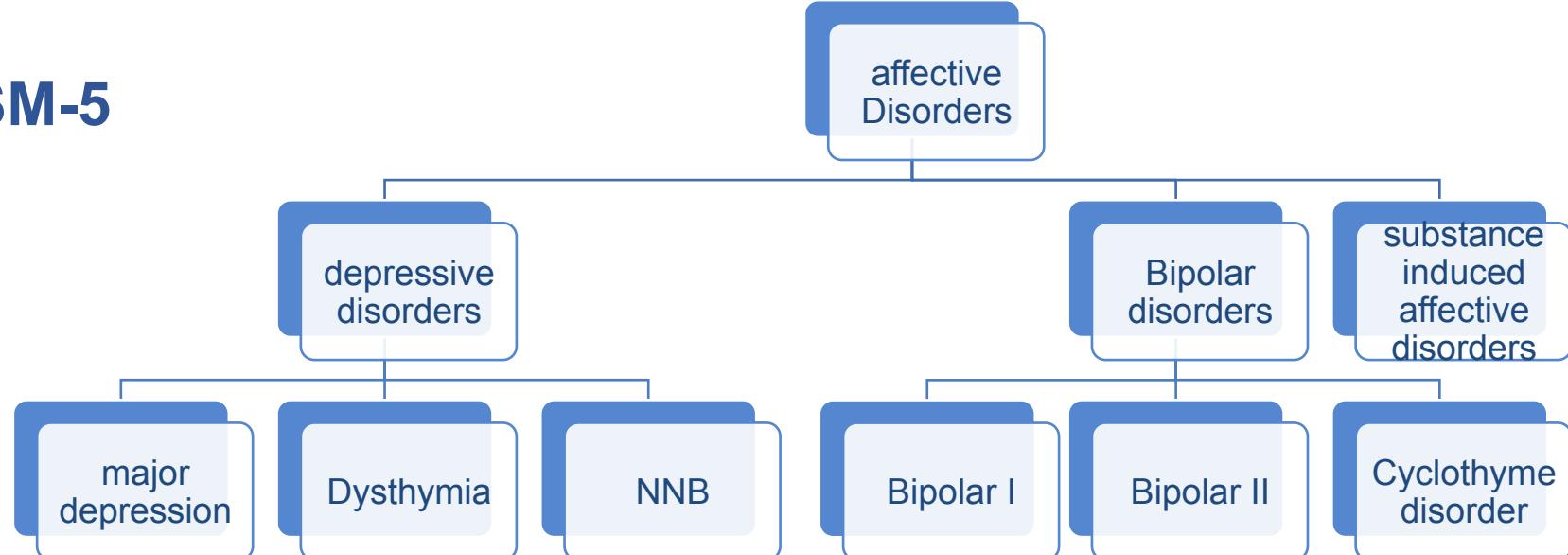
MRI, EEG, laboratory tests



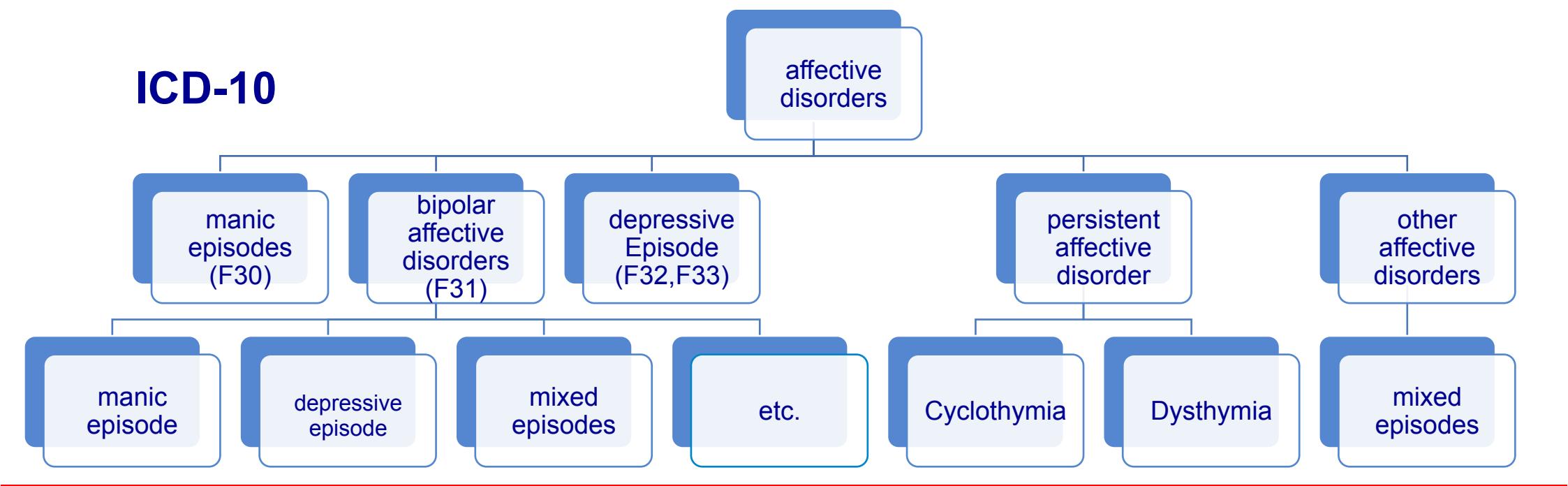
ICD-10



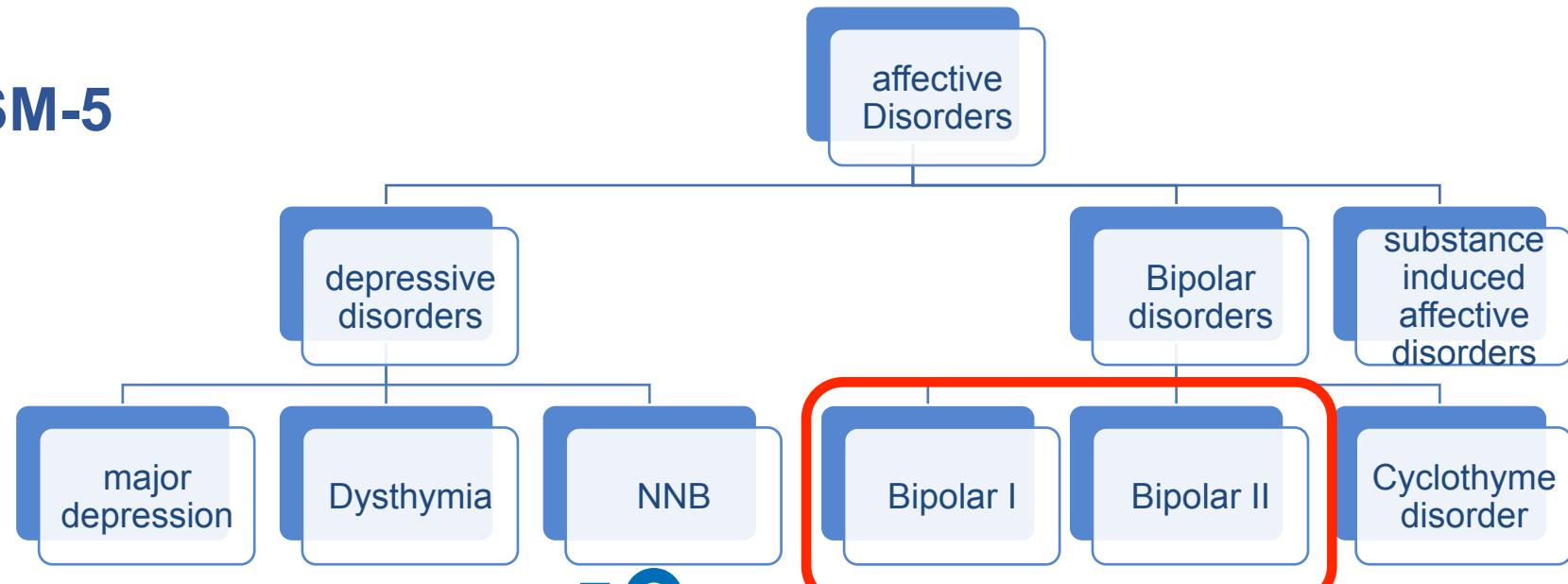
DSM-5



ICD-10



DSM-5



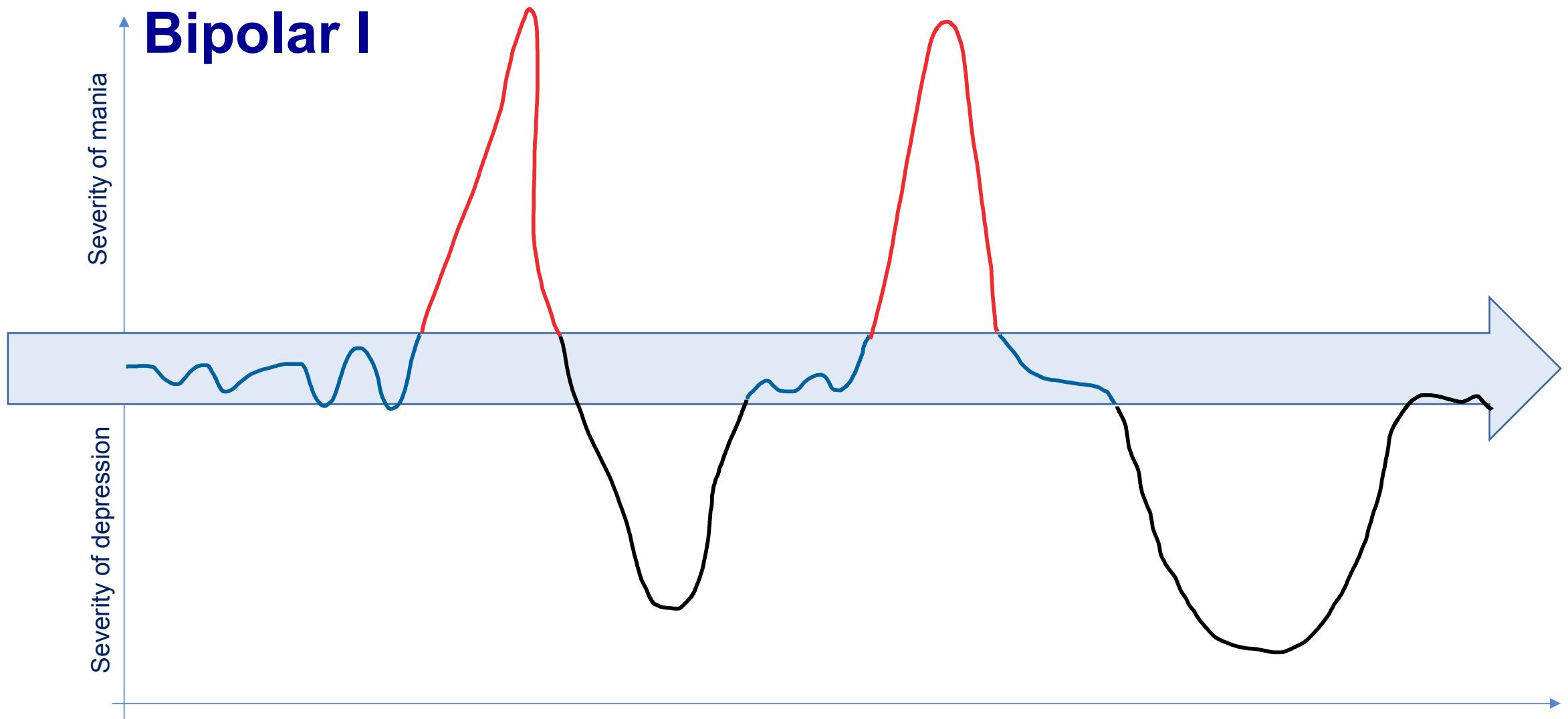
Progression of subgroups



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Bipolar I

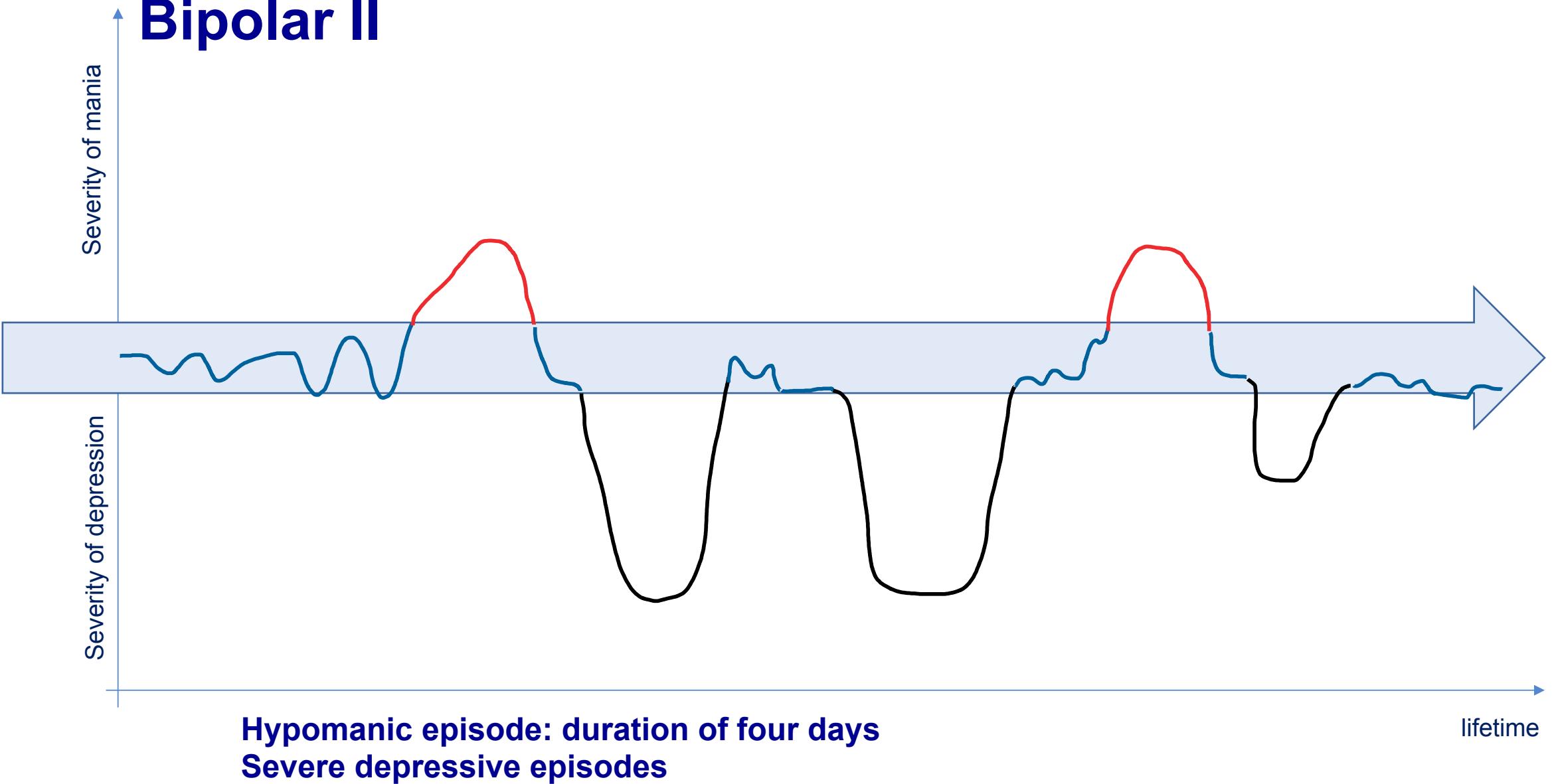


Manic (and depressive episode)
Duration > one week
90% relapse rate



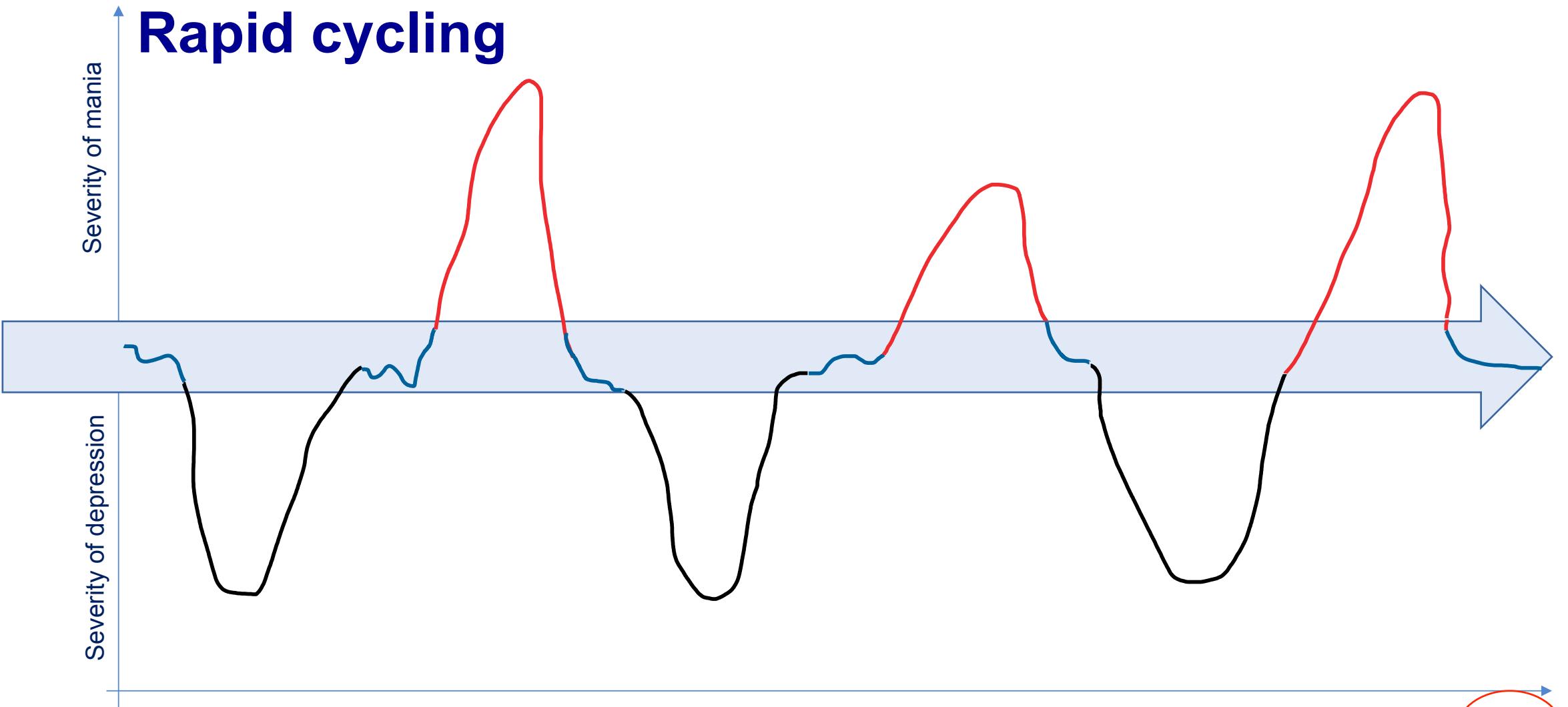
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Bipolar II



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Rapid cycling



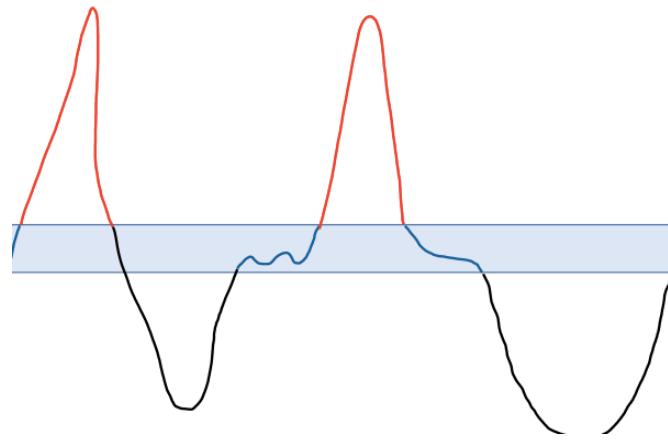
Minimum of 4 episodes each year
20% of BD develop rapid cycling
90% women



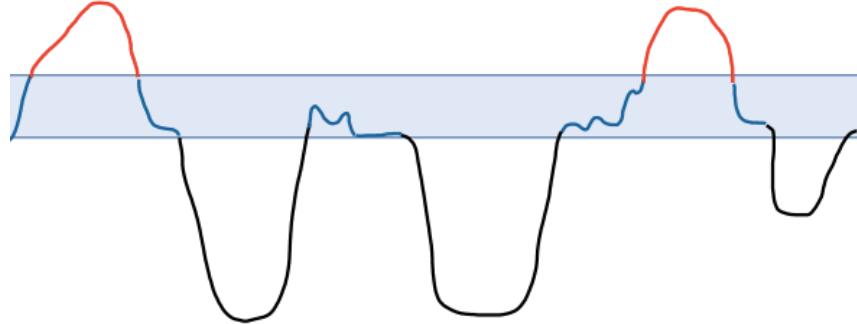
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Summary of bipolar spectrum disease

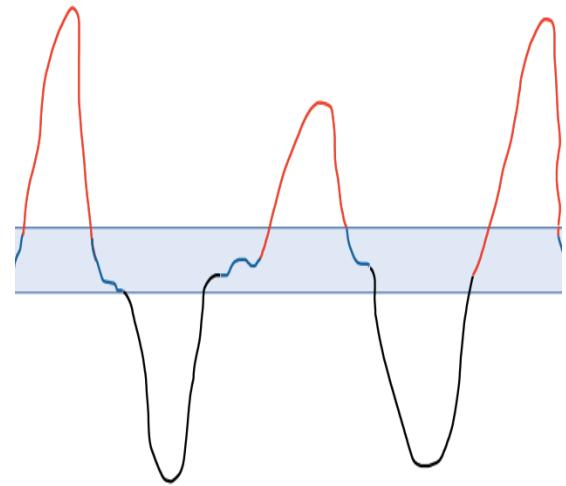
BD I



BD II



Rapid cycling



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Differential diagnosis



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Differential diagnosis

Diagnosis	common symptoms	differences
Schizophrenia	-positive symptoms: psychotic symptoms, delusion	-without circadian fluctuation -pronounced cognitive impairment
Unipolar depression	-depressive symptoms	-without (hypo-)manic symptoms -Medication: antidepressant
Schizoaffective disorder	-psychotic symptoms -mood swings	simultaneous psychotic symptoms and mood swings Medication: antipsychotics
Personality disorder: Borderline disorder	-high-risk behaviour -impulsive	-cause: childhood trauma -persistent symptoms: emotional regulation, unstable relationships, interactive problems -treatment: CBT (DBT)
Attention Deficit Hyperactivity Disorder (ADHD)	-problems in focussing -impulsive -distractibility -comorbidity: addition	-treatment: support in education, trainings for concentration, mindfulness - Medication: methylphenidate (Ritalin®)
Somatic diseases: brain tumor/infection Endocrinology dysf.	-eg. psychotic symptoms	-cause-related treatment: eg. Operation, Infection medication, Hormone substitution

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Epidemiology



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Epidemiology

2-4% lifetime prevalence

No. 6 leading cause of disability (worldwide)

annual health costs of US \$30 billion (indirect costs US \$>120 billion)

59-85% heritability

Age at onset: 18-23 years

4-20% commit suicide



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Epidemiology

psychiatric comorbidities

40-56% anxiety

30-70% substance abuse

30-50% personality disorders

10% Attention Deficit Hyperactivity Disorder (ADHD)

somatic comorbidities

cardio-/cerebrovascular disease

3-fold increased HIV prevalence



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Pathomechanism

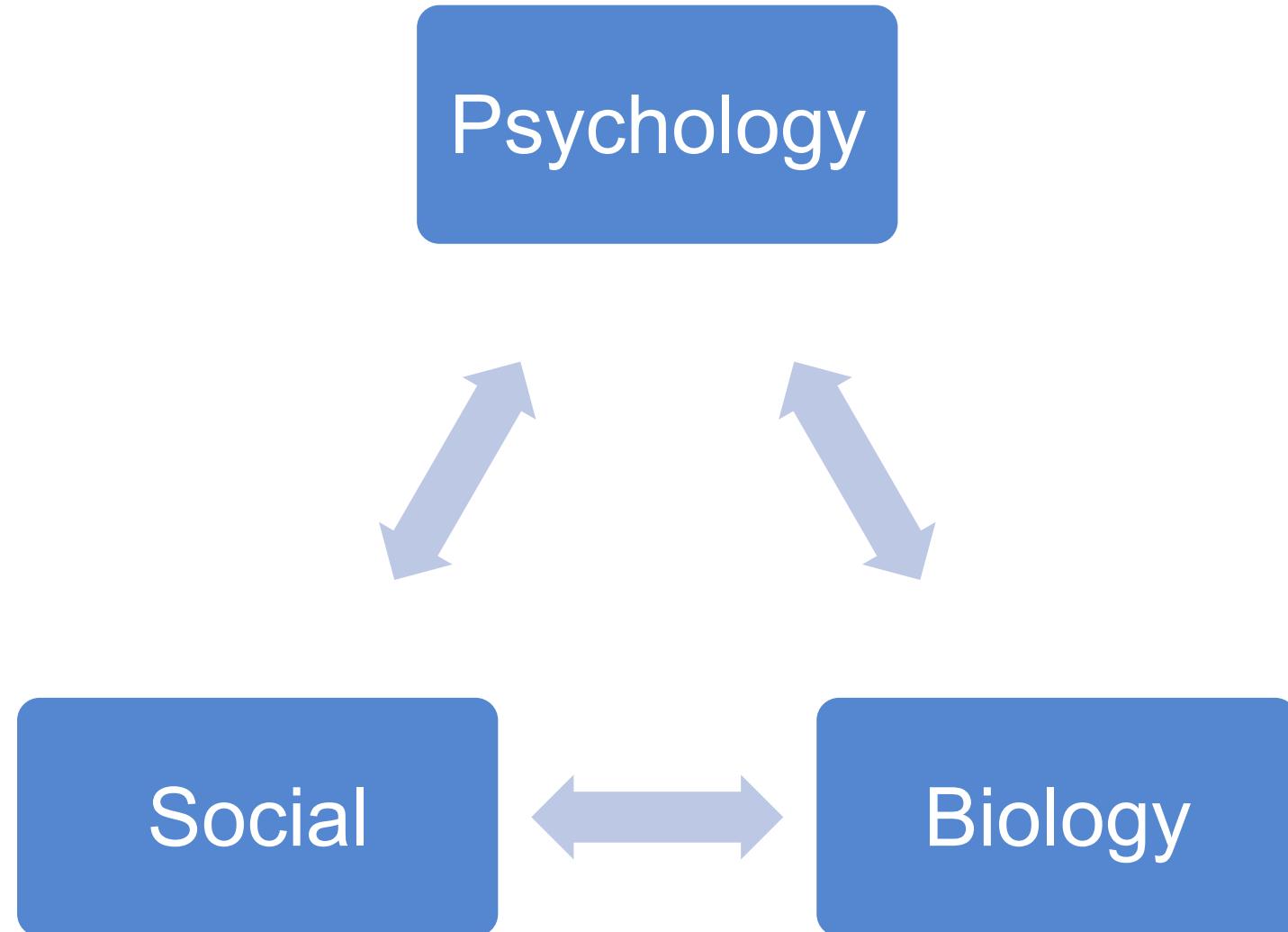


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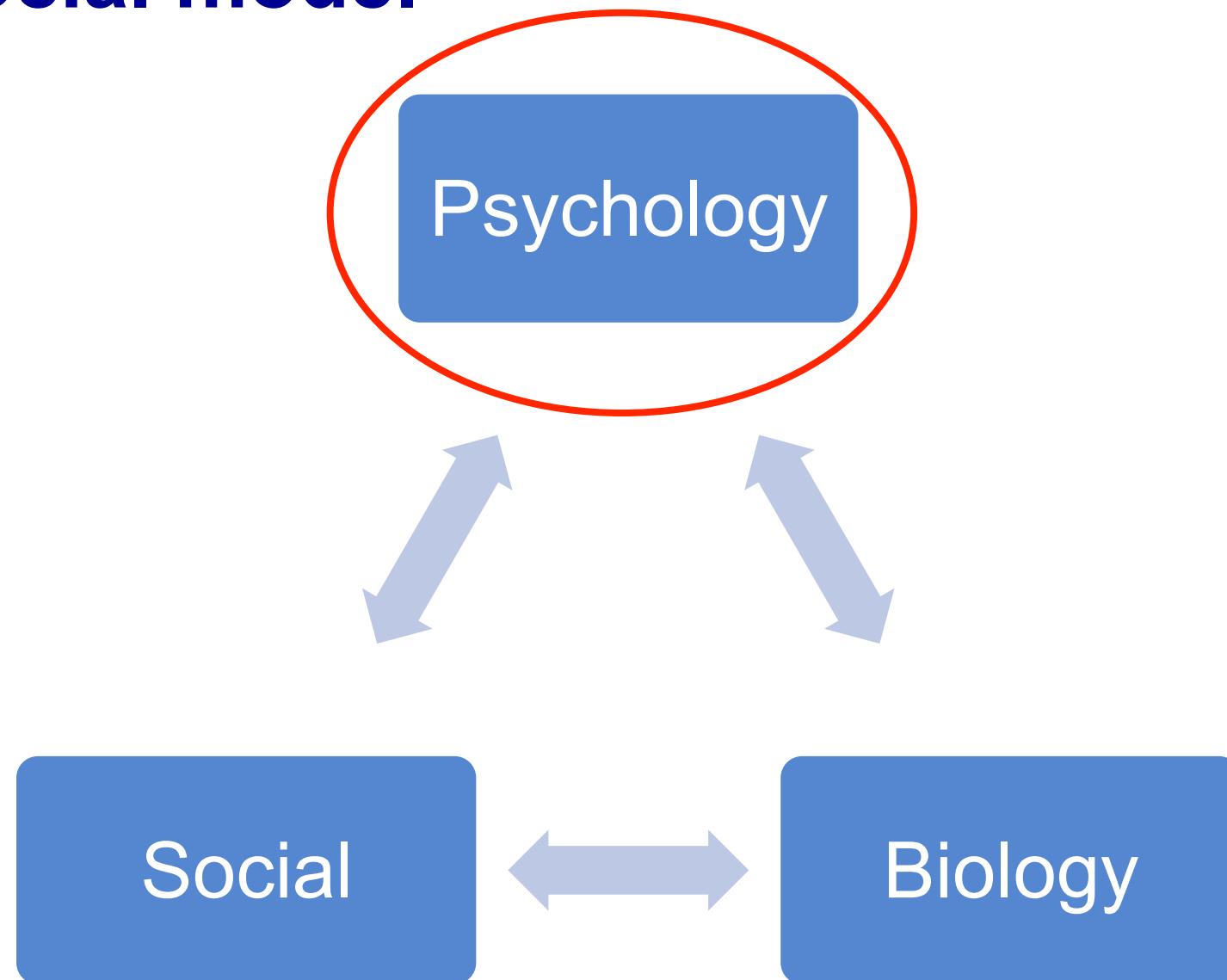


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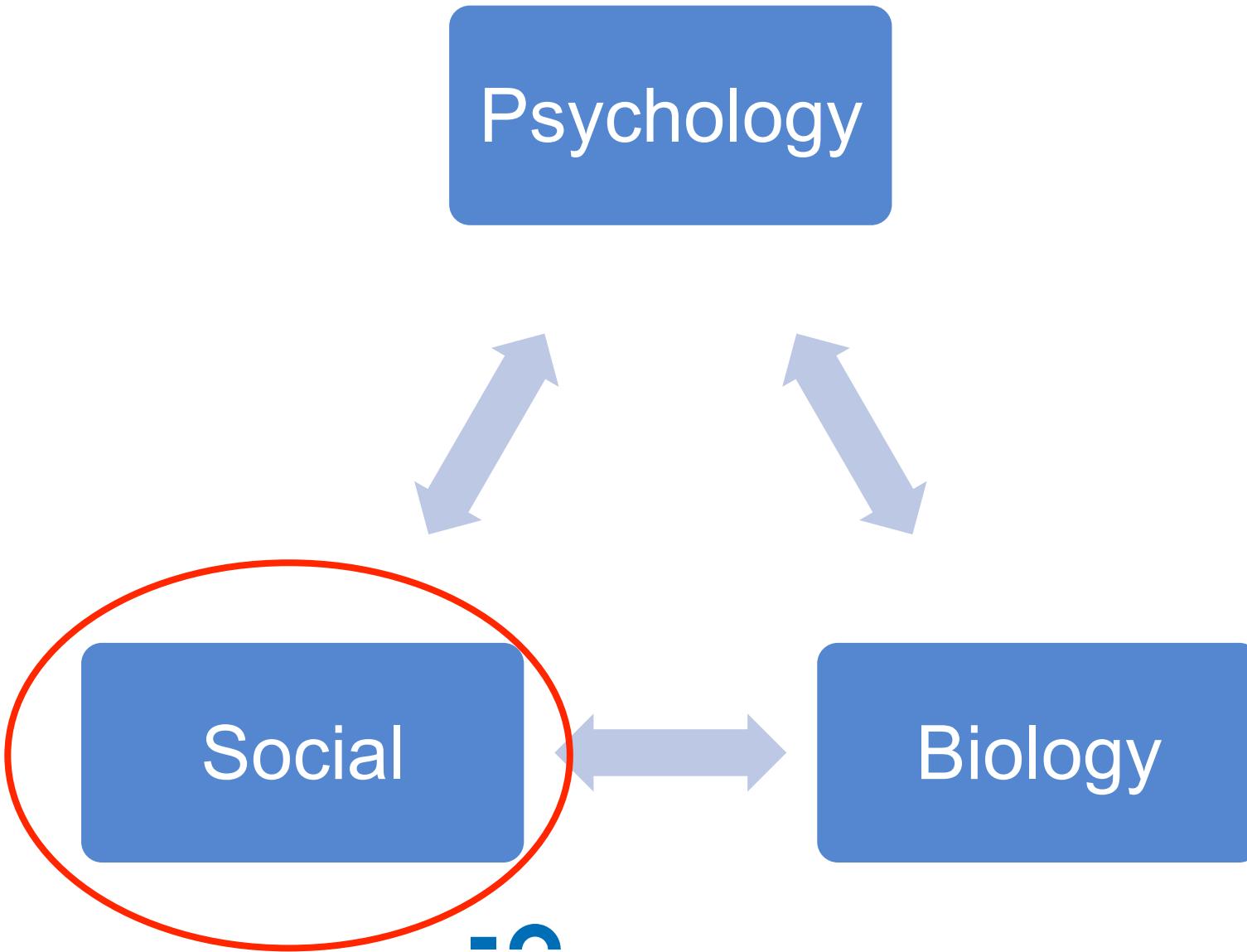
Biopsychosocial model



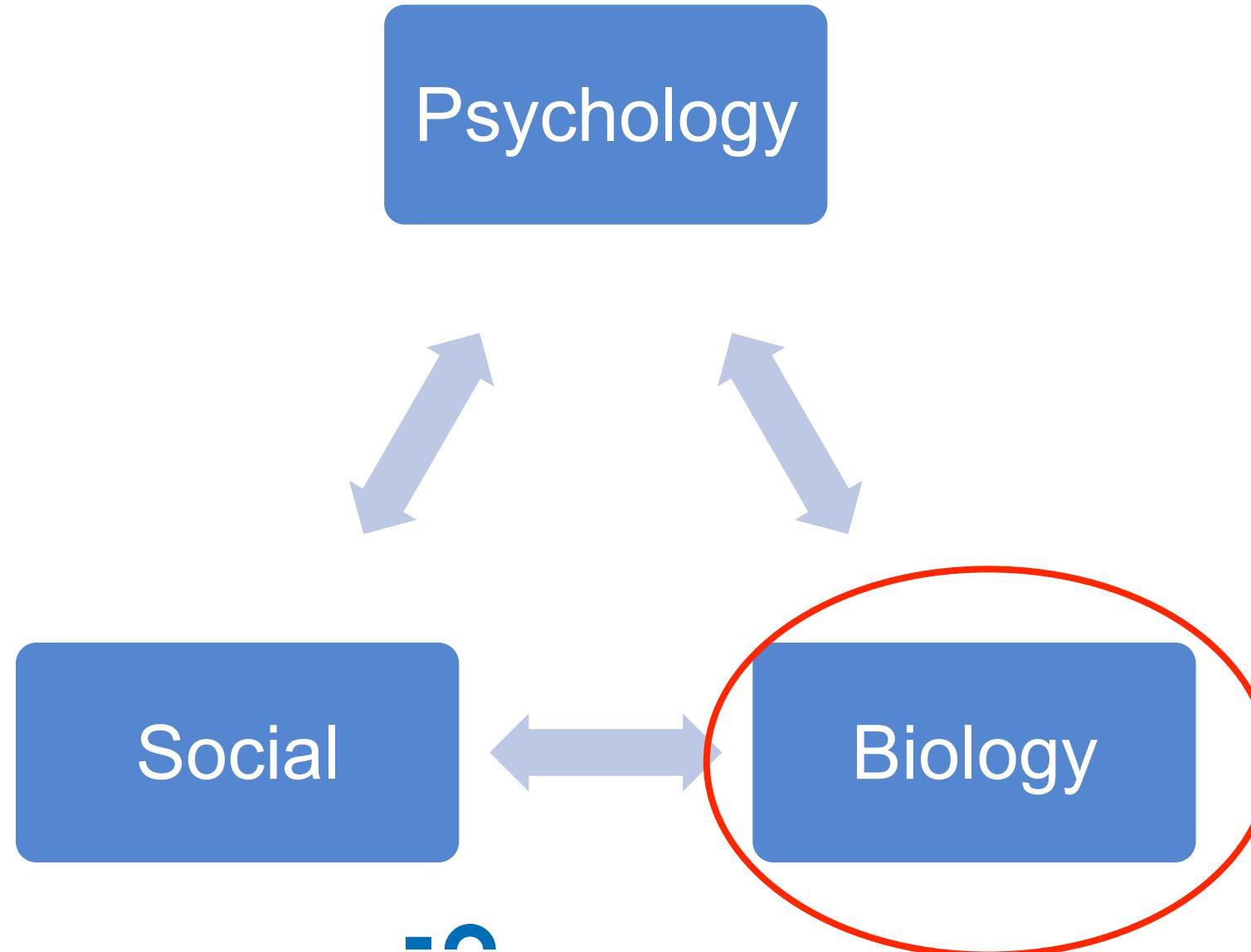
Biopsychosocial model



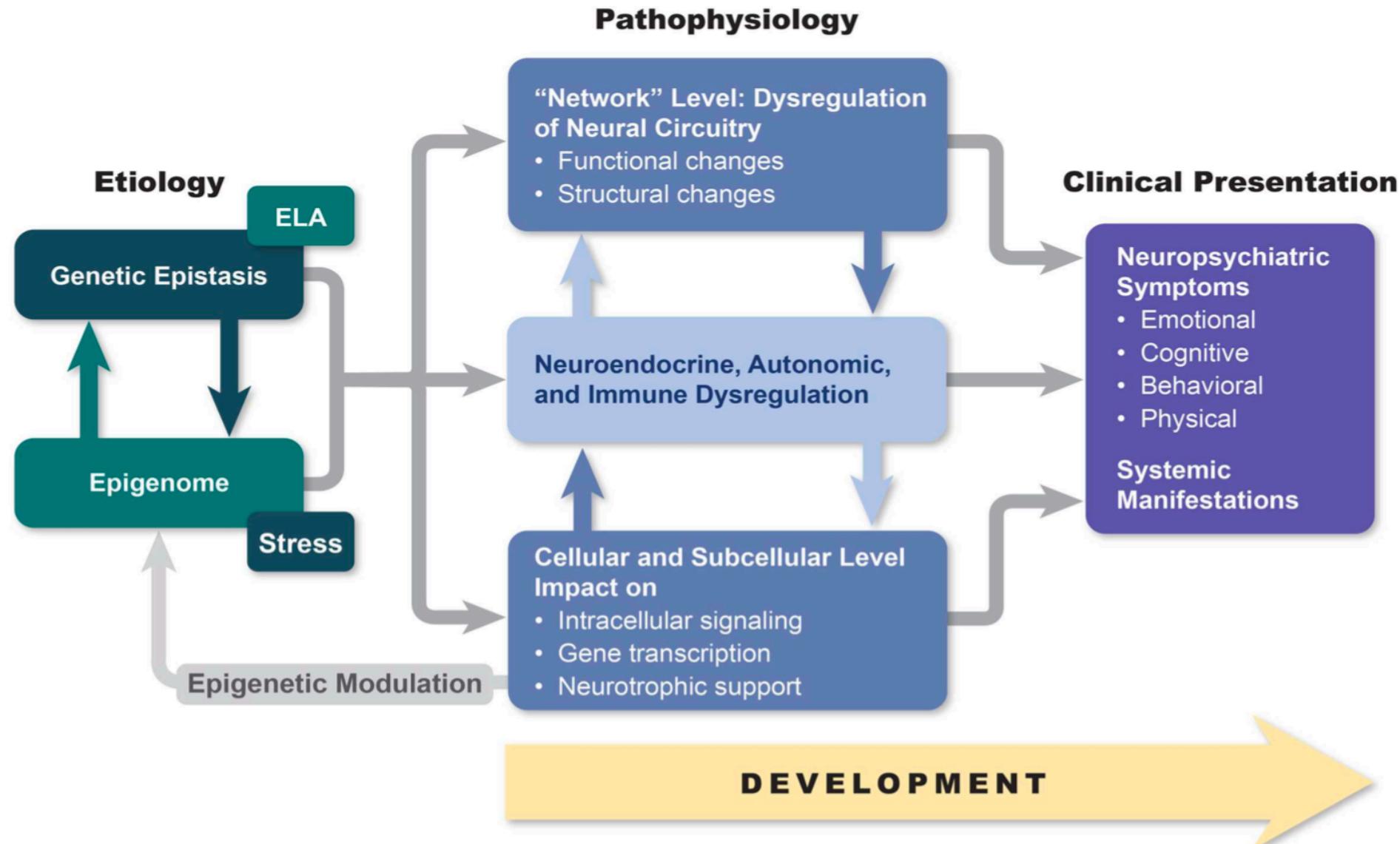
Biopsychosocial model



Biopsychosocial model



Multilevel approach

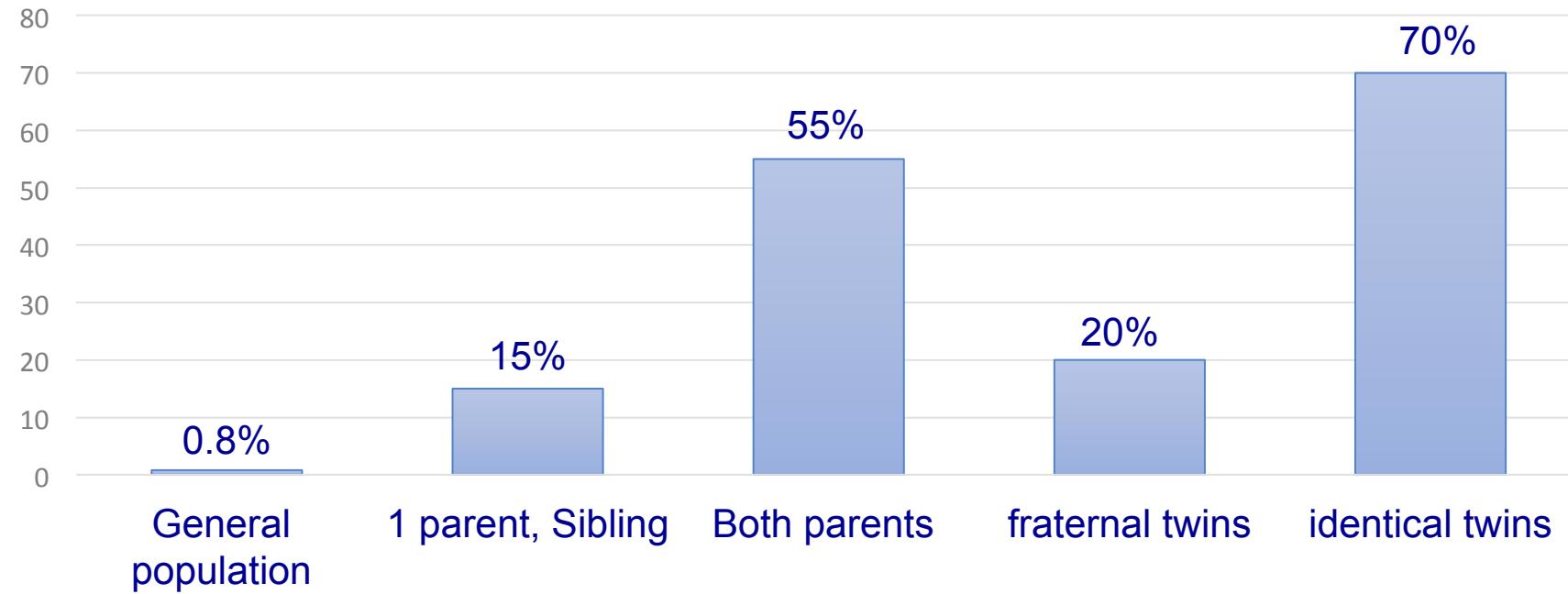


Maletic and Raison, *frontiers in Psychiatry*, 2014



Heritability

Risk of bipolar disorder for relatives

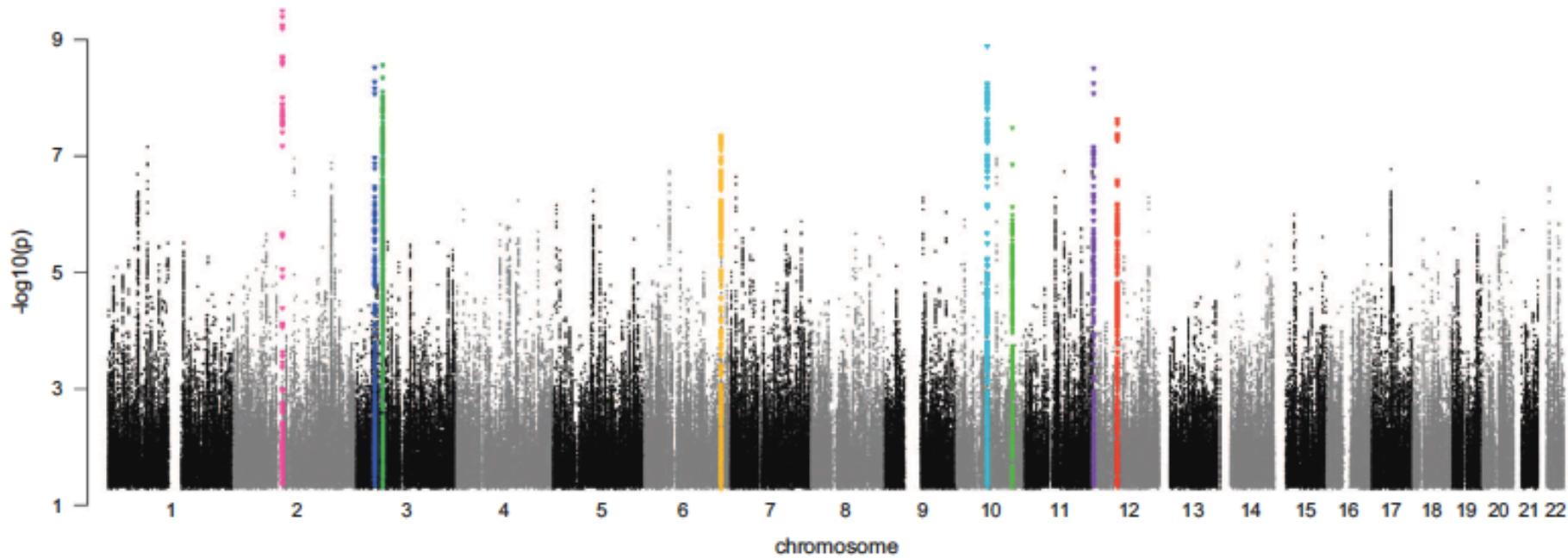


adapted by Lieb, Intensivkurs Psychiatrie und Psychotherapie



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Genetics

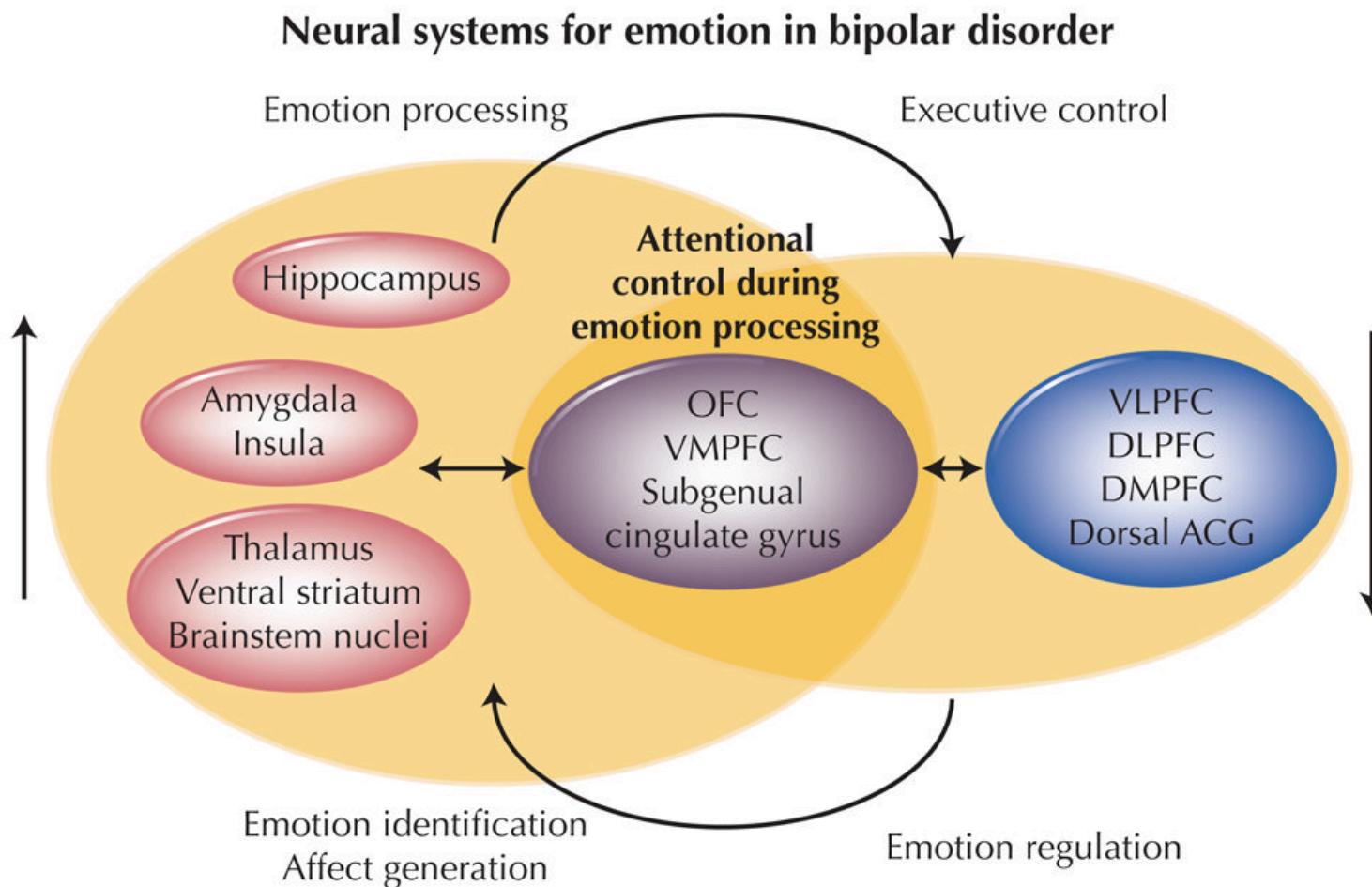


Locus information					ICCBBD		PGCBD		ICCBBD-PGCBD		Strongest previous association				
Chr	SNP	Position	Allele	Genes in LD ^a	p-value	OR	p-value	OR	p-value	OR	p-value ^b	SNP	Position	R ^c	Reference
2	rs56361249	97380229	T	LMAN2L, FERIL5, CNNM4	4.12 x 10 ⁻⁵	1.10	4.71 x 10 ⁻⁷	1.14	3.19 x 10 ⁻¹⁰	1.12	2.20 x 10 ⁻¹⁰	rs2271893	97,405,440	0.82	26
3	rs9834970	36856030	T	TRANK1	1.87 x 10 ⁻⁷	0.89	5.75 x 10 ⁻⁶	0.90	1.59 x 10 ⁻¹⁰	0.90	1.48 x 10 ⁻¹²	rs9834970	36,856,030	1.00	26
3	rs2302417	52814256	T	many genes	4.46 x 10 ⁻⁵	1.10	2.80 x 10 ⁻⁶	1.12	2.75 x 10 ⁻⁹	1.11	1.64 x 10 ⁻⁹	rs7618915	52,279,594	0.16	26
6	rs1203233	152714606	G	SYNE1	1.83 x 10 ⁻³	0.93	4.48 x 10 ⁻⁸	0.88	4.46 x 10 ⁻⁸	0.91	4.33 x 10 ⁻⁹	rs9371601	152,790,573	0.47	24
10	rs10994299	62076628	C	ANK3	1.64 x 10 ⁻³	0.86	2.42 x 10 ⁻¹⁰	0.73	1.28 x 10 ⁻⁹	0.81	7.00 x 10 ⁻¹¹	rs10994415	60,562,276	0.23	27 ^d
10	rs10884920	111774807	A	ADD3, LOC100505933, XPNPEP1	1.20 x 10 ⁻⁸	1.17	0.02	1.07	3.28 x 10 ⁻⁸	1.12	0.01	rs62843660	111,768,533	0.76	24 ^d
12	rs4765913	2419896	A	CACNA1C family	3.05 x 10 ⁻⁵	1.12	4.40 x 10 ⁻⁶	1.14	3.12 x 10 ⁻⁹	1.13	1.82 x 10 ⁻⁹	rs4765913	2,419,896	1.00	24
12	rs10459221	49466994	C	many genes	1.87 x 10 ⁻³	0.93	6.98 x 10 ⁻⁸	0.88	2.33 x 10 ⁻⁸	0.91	9.39 x 10 ⁻⁹	rs7296288	49,479,968	0.57	24

Charney et al., Translational Psychiatry, 2017



Neuroimaging findings



Keener, and Phillips, Curr Psychiatry Rep, 2009



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Therapy



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Therapy



- **Manic symptoms**

- psychiatric emergency (endangering others/self)
- Stimulus control (reducing stress): own room, rebalancing the sleep-wake-rhythm
- Medication: combination of antipsychotics, mood-stabilizers (ms): Lithium, other ms: anticonvulsive medication: e.g. Valproat, tranquilizers

- **Depressive symptoms**

- Mood-stabilizers: Lithium, other ms: anticonvulsive medication
- cave: Antidepressive Medication can lead to “switching” into a manic episode

- Relapse of symptoms within 6-12 months (75% risk)

- Medication intake for 12 months with full dosage
- Psychoeducation: red-flags symptoms, integration of partners/family etc., precaution
- Psychotherapy (CBT)

- Prevention of recurrence

- Indication > 2 episodes within 5 years or severe form
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Acute phase

Manic symptoms

Psychiatric emergency

Medication:

combination of antipsychotics, tranquilizers and

“mood-stabilizers”(ms): Lithium, other ms: anticonvulsive medication (Valproat)

Stimulus control (reducing stress, rebalancing sleep-wake-rhythm)



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Lithium

1817 discovery “allrounder“ medication

1949 J. Cade: antimanic medication

1950s 7UP

2019 effect uncertain

Effect:

Mood-stabilizer

anti-suicidal

neuroprotective (frontal atrophy)



wikimedia.org



flashbak.com

Treatment regime: side effects, tight therapeutic range, highly toxic

Adherence required: lifestyle adaption, regular blood testings of lithium-level



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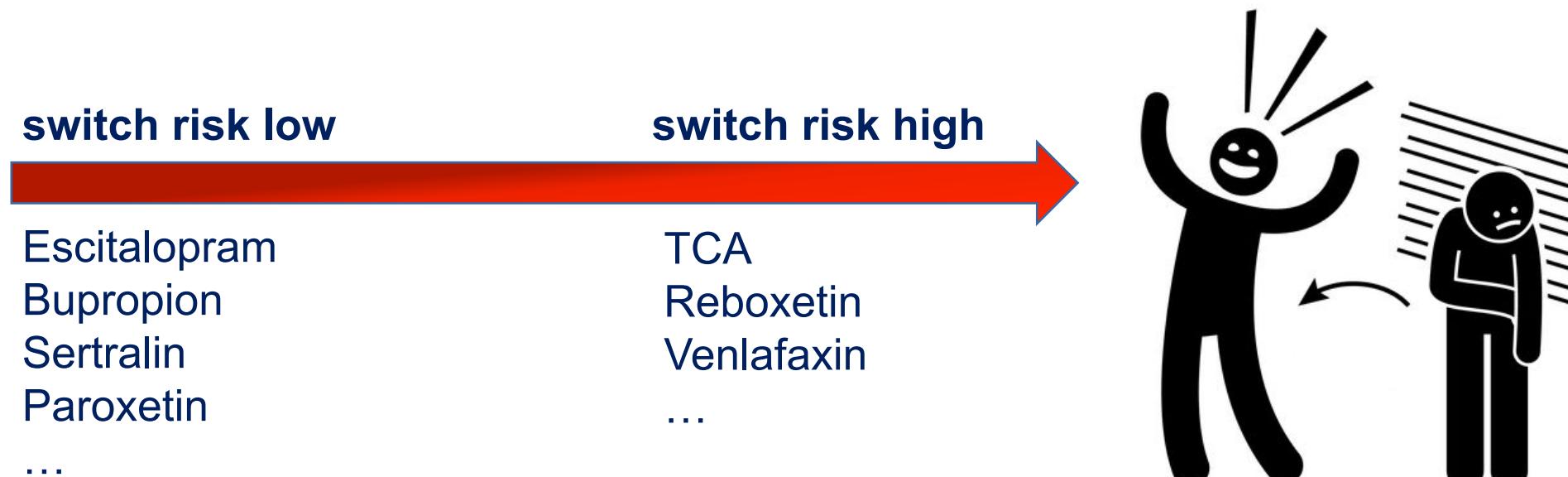
Acute phase

Depressive symptoms

mood-stabilizers: eg. Lithium

caution: antidepressant medication (AD) can lead to switch into a manic episode

If AD necessary: just in combination with mood-stabilizer



Khoon Lay Gan © 123RF.com

Continuation therapy

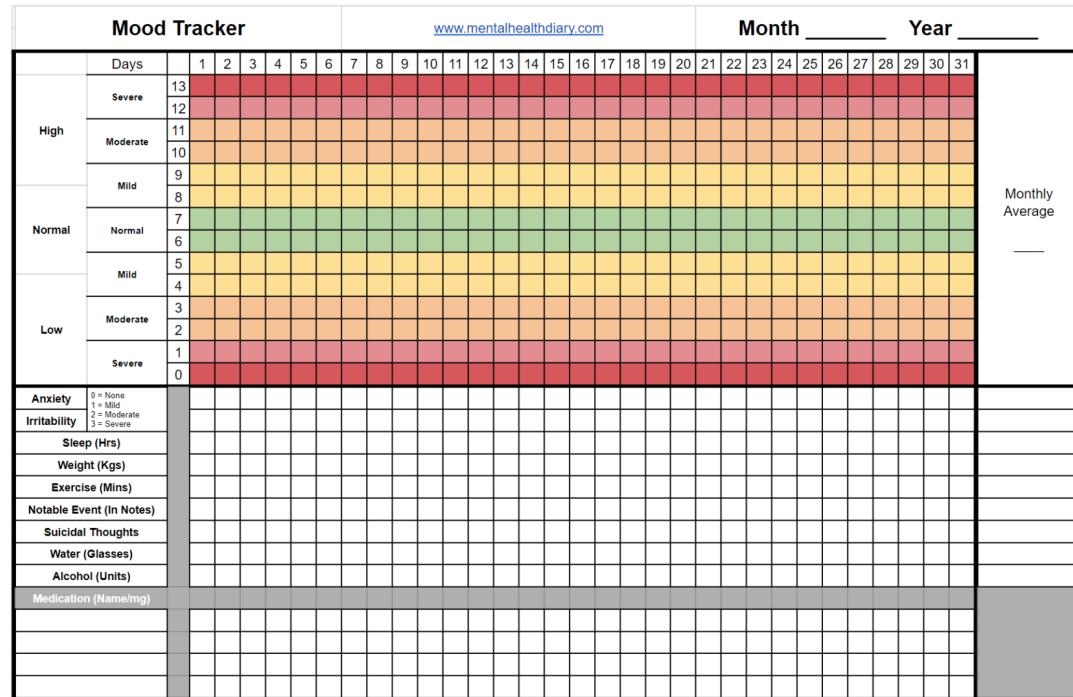
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[mentalhealthdiary.com](http://www.mentalhealthdiary.com)



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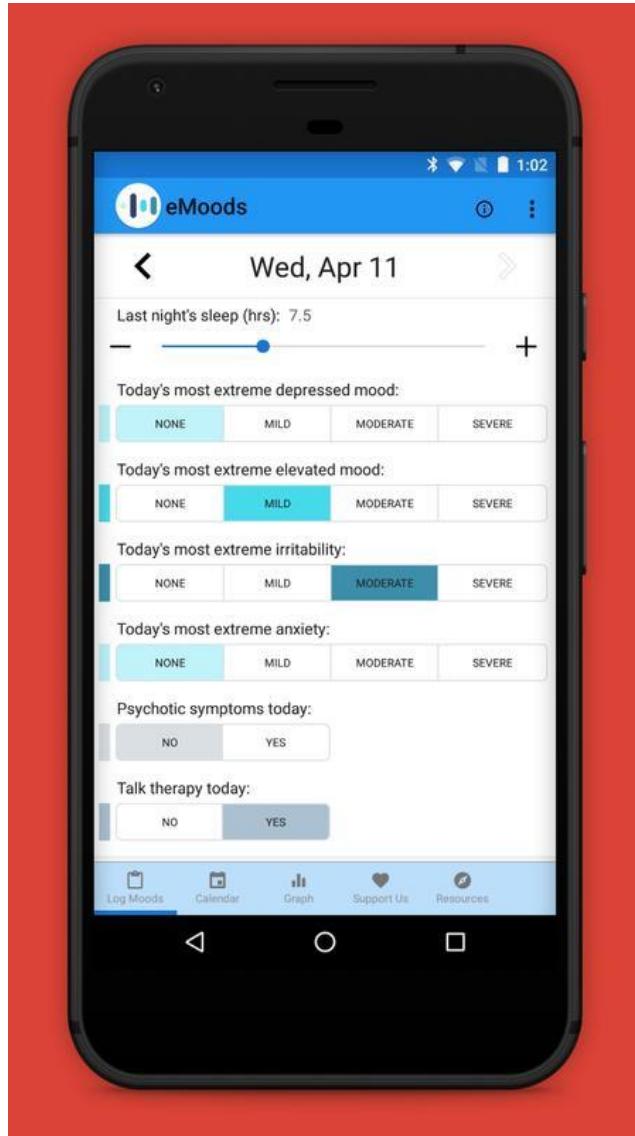
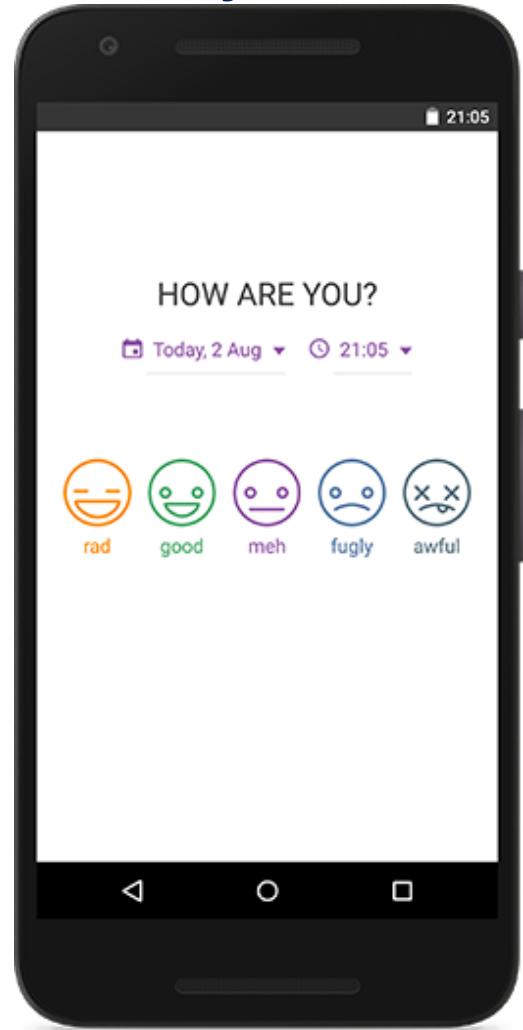
Mood Tracker							www.mentalhealthdiary.com														Month _____						Year _____							
	Days	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31		
High	Severe	13																																
		12																																
	Moderate	11	X																															
		10																																
	Mild	9																																
		8	X																															
	Normal	7																																
		6																																
	Mild	5																																
		4																																
Low	Moderate	3																																
		2																																
	Severe	1																																
		0																																
	Anxiety	0 = None 1 = Mild 2 = Moderate 3 = Severe																																
Irritability	Sleep (Hrs)																																	
	Weight (Kgs)																																	
	Exercise (Mins)																																	
	Notable Event (In Notes)																																	
	Suicidal Thoughts																																	
	Water (Glasses)																																	
	Alcohol (Units)																																	
	Medication (Name/mg)																																	

mentalhealthdiary.com

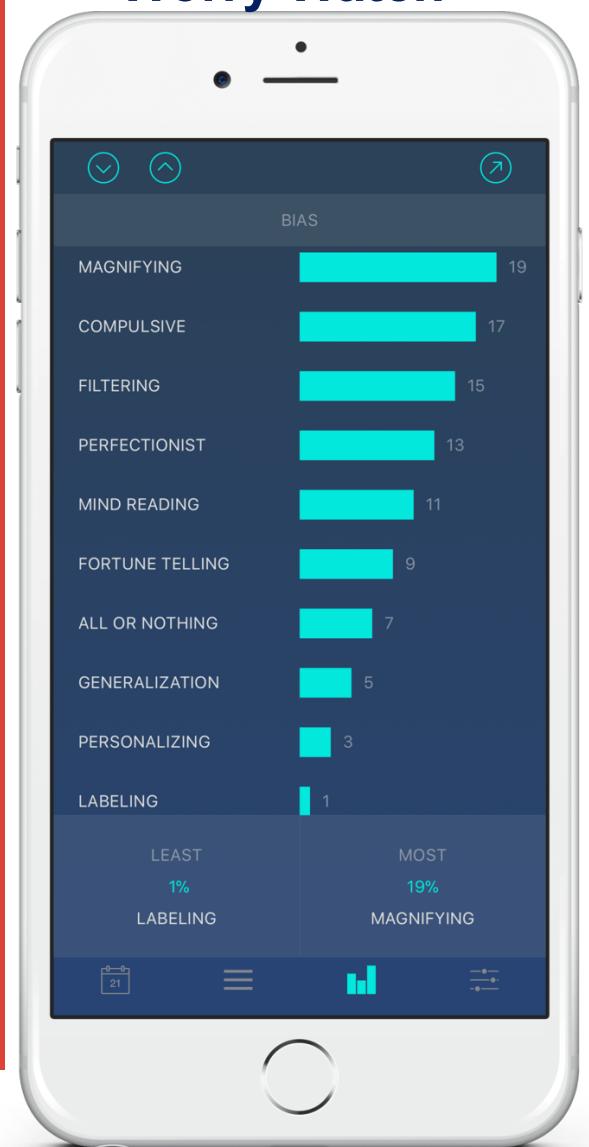


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Daylino



Worry Watch



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Continuation therapy

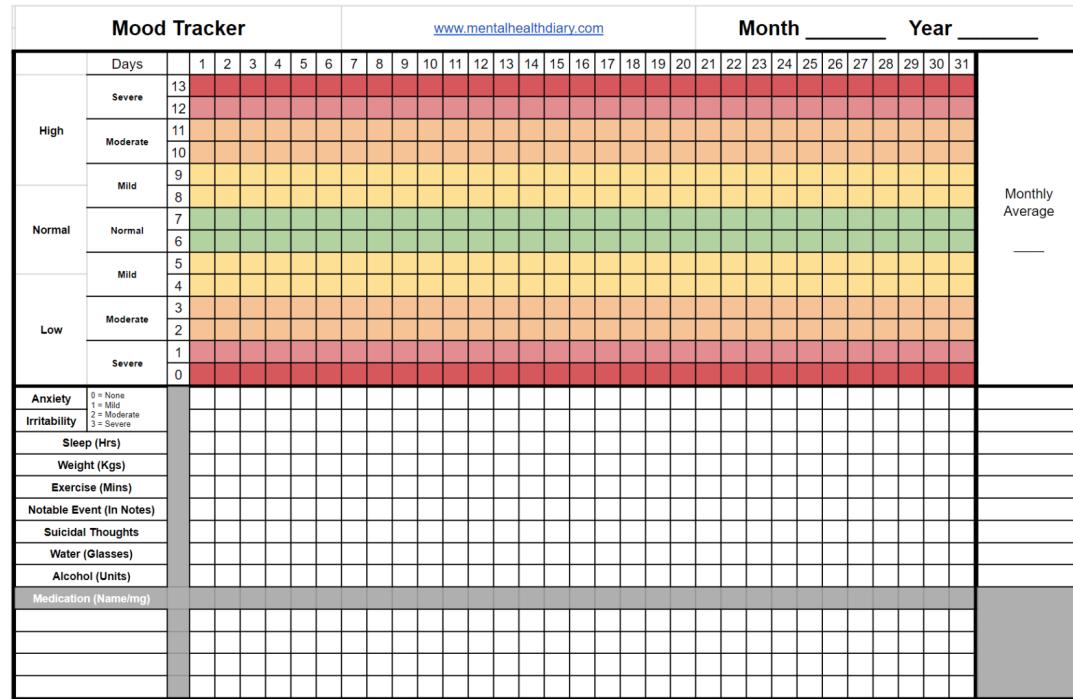
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Maintenance therapy

Prevention of recurrence

Indication: >2 episodes within 5 years or severe form

Medication intake for years or lifelong

Lithium as “Goldstandard”

Psychotherapy (CBT)



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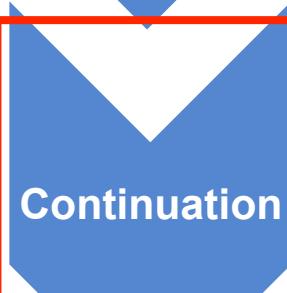
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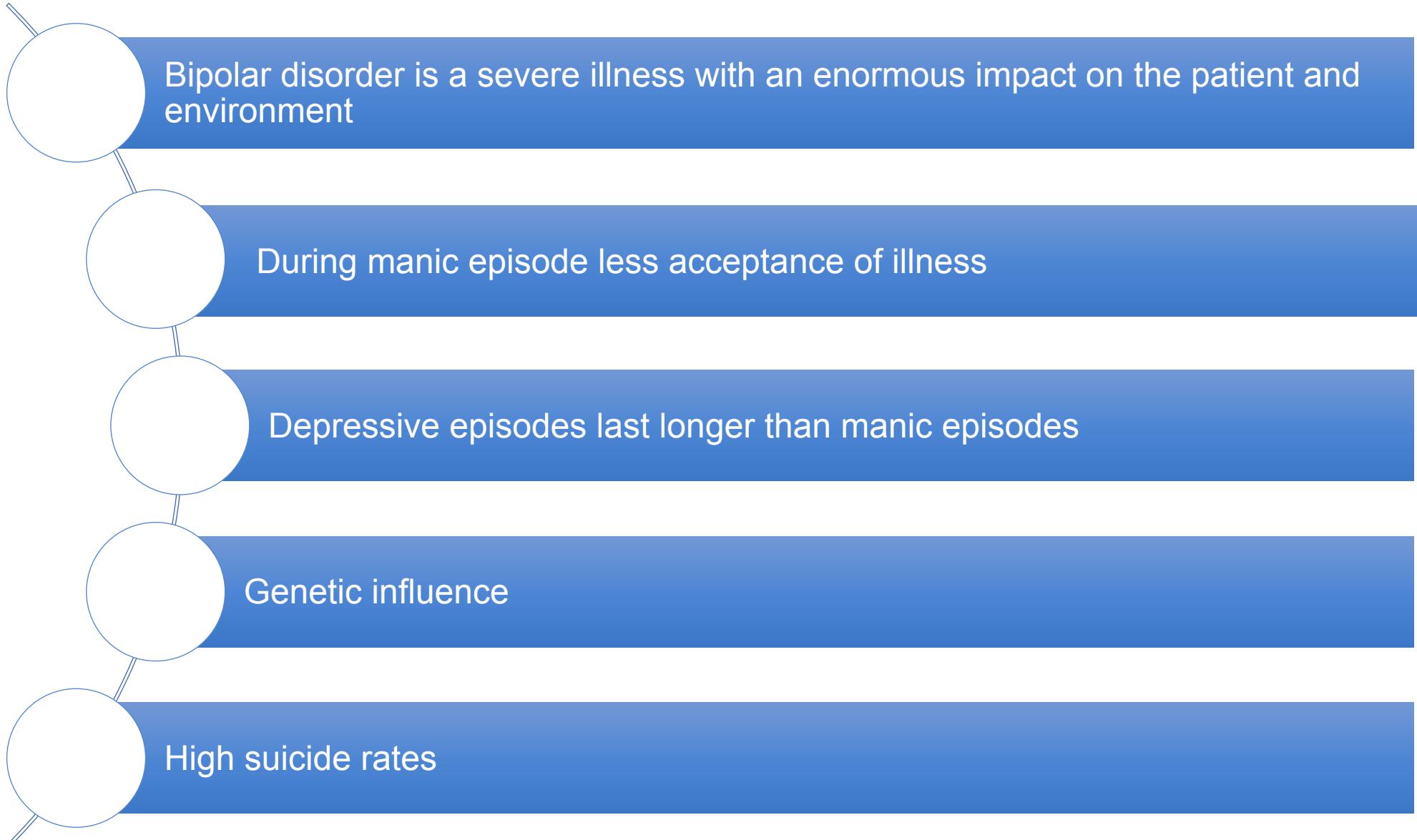
Résumé



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Summary



Future directions

Differential diagnosis

Mechanism

Episode
prediction

Treatment



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Identify differential diagnosis

Different treatment regimes (unipolar vs. bipolar depression)

Assumption: Different mechanisms

Early diagnostic detection
for people at high-risk developing a bipolar disorder:
reduce suffering, avoid long-term consequences

Understanding the mechanisms

Differentiate subgroups

Improve treatment options

Focus above the affective disorder spectrum (divers symptoms)



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For patients: capability to predict an episode

“Red-flags“ and mood diary not sufficient enough

Avoid acute episodes with long-term consequences



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Improve treatment

Treatment prediction on the individual level:
diverse combinations of different medications

Does everyone need a maintenance therapy (medication)?

In depression: shorten the duration of the episode
identify those antidepressants that will not lead to a switch



Future directions

Differential diagnosis

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