



Computational Psychiatry Course 2020

Clinical Psychiatry

Helen Schmidt



Universität
Zürich^{UZH}

Bipolar affective disorder



thatsmaths.com



Universität
Zürich^{UZH}



Translational Neuromodeling Unit



Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

3 case studies

Sophie, 34

Steve, 29

Michael, 52



**Universität
Zürich^{UZH}**

3 case studies

Sophie, 34

Steve, 29

Michael, 52



**Universität
Zürich^{UZH}**

SOPHIE, 34

SITUATION

Involuntary hospitalisation, acute psychiatric unit

BACKGROUND

- Arrested by police: Protesting (naked) in front of federal building
- Inappropriate behavior

CHIEF COMPLAINT

„I was trying to save the world from wearing masks.
COVID-19 does not exist. Bill Gates wants to kill the fun
in the world“



Getty Images, Unsplash



Purecostumes.com



Universität
Zürich^{UZH}



Translational Neuromodeling Unit

ETH

Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

MENTAL STATUS EXAMINATION

APPEARANCE

In bathingrobe, intense make-up;
laughing & smiling
Increased energy & activity



CONCENTRATION AND ATTENTION

Easily distracted (focus on details)

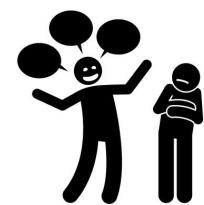


THOUGHT PROCESS AND CONTENT

Fast speech, flight of ideas, talkative

"Was chosen to rescue humankind from all the fear, gifted with love and harmony."

→ **delusional, psychotic symptoms**



MOOD

Elevated, Overanimated



→ **No insight**



Universität
Zürich^{UZH}

SOPHIE, 34

Married, 2 children, lost her part-time job



INFORMATION FROM HUSBAND

- Bipolar disorder for 10 years
- 3rd Manic episode: since June (no sleep, restless, intensive fears about future), Since 2 weeks: disinhibited behavior

PAST PSYCHIATRIC HISTORY / FAMILY HISTORY

- 2x Manic episodes (2010, 2013; sexual promiscuity, high-risk behavior)
- Major Depression after mother's death (Bipolar disorder, suicide in 2008)
- Comorbidity: Generalized anxiety since youth

MEDICAL HISTORY

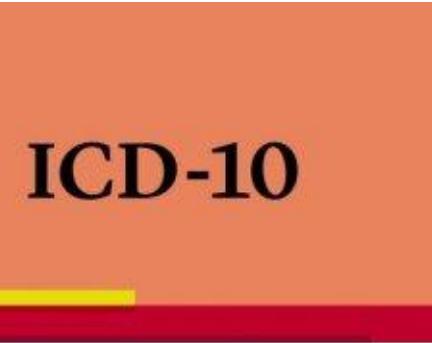
- Lithium therapy after 2nd manic episode
- Since August: stop medication



Universität
Zürich^{UZH}

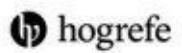
Manic episode: Bipolar disorder (ICD-10 F31.1-F31.2)

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



Horst Dilling
Harald J. Freyberger
(Hrsg.)
Taschenführer zur
ICD-10-Klassifikation
psychischer Störungen

Nach dem Pocket Guide von J. E. Cooper
9., aktualisierte Auflage entsprechend
ICD-10-GM



→ +/- psychotic symptoms: delusion; hallucination



Universität
Zürich ^{UZH}

3 case studies

Sophie, 34

Steve, 29

Michael, 52



**Universität
Zürich^{UZH}**

STEVE, 29

SITUATION

In the Office of the Company physician

BACKGROUND

- Supervisor is worried: restless, slightly euphoric & cranky, work is lacking for the last week
- Usually calm and exact person

CHIEF COMPLAINT

“ I am busy, but in an excellent shape and mood. Sleep is overrated. “



© Bildagentur PantherMedia/ Roger Jegg



Universität
Zürich^{UZH}



Translational Neuromodeling Unit

ETH

Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

MENTAL STATUS EXAMINATION

Increased activity



CONCENTRATION AND ATTENTION

Troubles to listen, several questions have to be repeated

THOUGHT PROCESS AND CONTENT

Fast, "head is on the run and I can't stop" +
"I have a lot of ideas how to restore the company."



© Bildagentur PantherMedia/ Roger Jegg

MOOD

Slightly elevated and irritated



Universität
Zürich^{UZH}



Translational Neuromodeling Unit

ETH

Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

STEVE, 29

IT specialist, extreme sports: downhill-biking, climbing

PAST PSYCHIATRIC HISTORY / FAMILY HISTORY

- „hyperactive“ during youth (compensation with sports)
- „2 phases of feeling sad“: teenager, after graduation
→ no treatment
- No positive family history
- No drugs/alcohol

MEDICAL HISTORY

- None



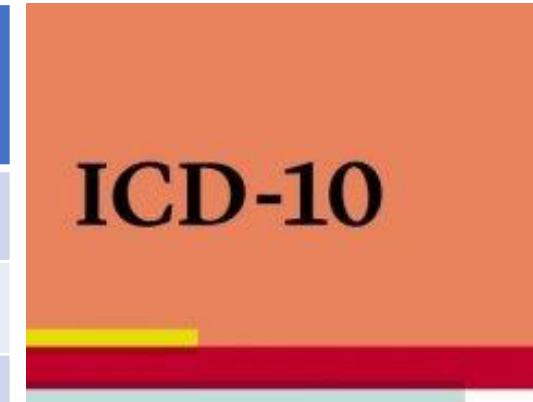
© Bildagentur PantherMedia/ Roger Jegg



Universität
Zürich^{UZH}

Hypomanic episode: Bipolar disorder (ICD-10 F31.0)

A) Elevated expansiv or irritable mood	Increased energy or activity B) More than 3 symptoms:
Duration: min. 4 days	inflated self-esteem
	talkative
	decreased need for sleep
	distractibility
	increase in goal-directed activity psychomotoric agitation
	Involvement in activities with high potential for painful consequences

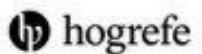


Horst Dilling
Harald J. Freyberger
(Hrsg.)

Taschenführer zur
ICD-10-Klassifikation
psychischer Störungen

Nach dem Pocket Guide von J. E. Cooper

9., aktualisierte Auflage entsprechend
ICD-10-GM



- No psychotic or delusional symptoms
- Without social consequences
- In the past: depressive, hypomanic or manic episodes



Universität
Zürich^{UZH}

Hypomanic episode (ICD-10 F31.0)

The New York Times

Just Manic Enough: Seeking Perfect Entrepreneurs



Matthew Cavanaugh for The New York Times

**“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”



Universität
Zürich^{UZH}



Translational Neuromodeling Unit

ETH

Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Hypomanic episode (ICD-10 F31.0)

Robert Schumann (1810-1856, composer)



© Public Domain

„melancholia with delusion“

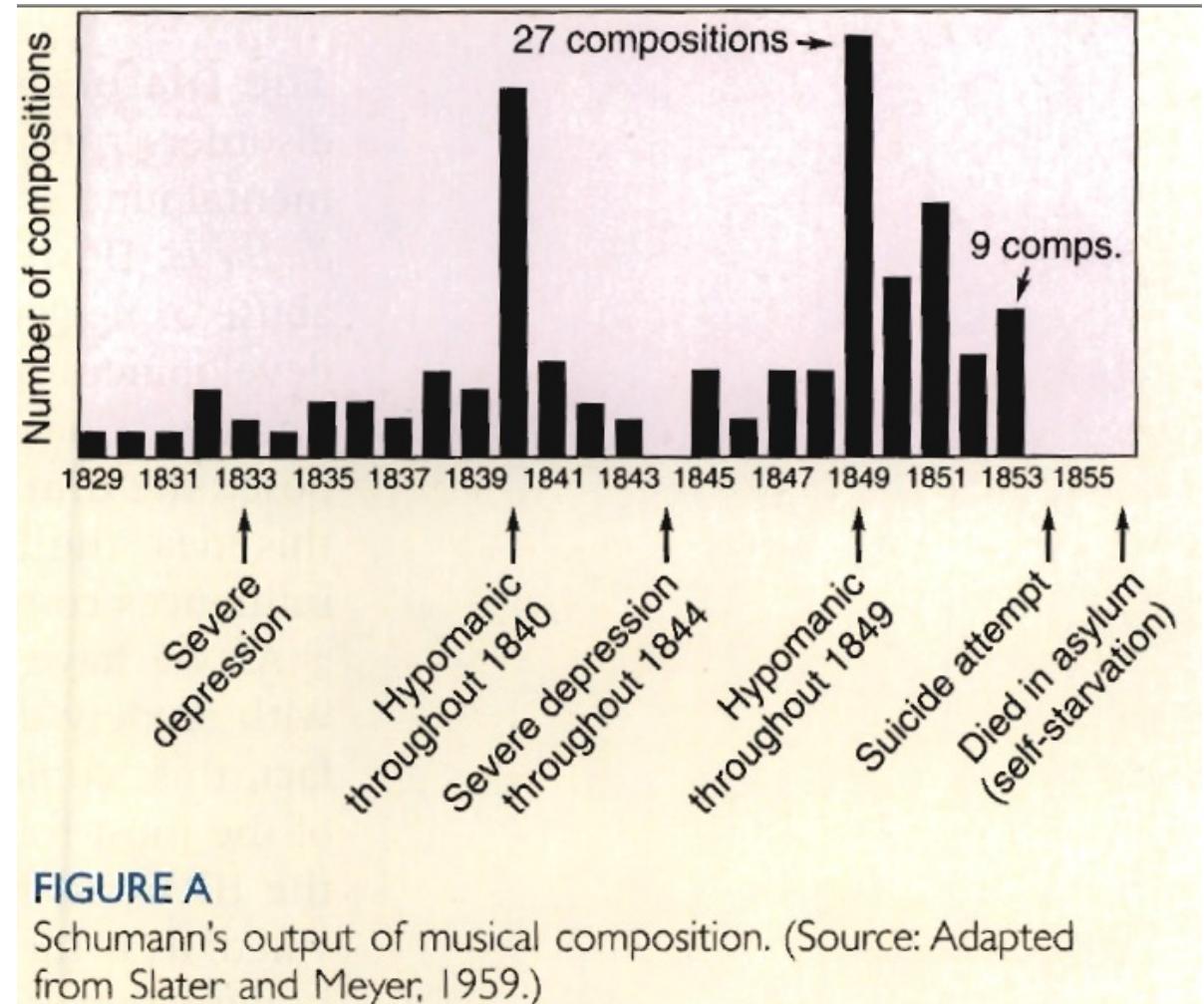


FIGURE A

Schumann's output of musical composition. (Source: Adapted from Slater and Meyer, 1959.)

3 case studies

Sophie, 34

Steve, 26

Michael, 52

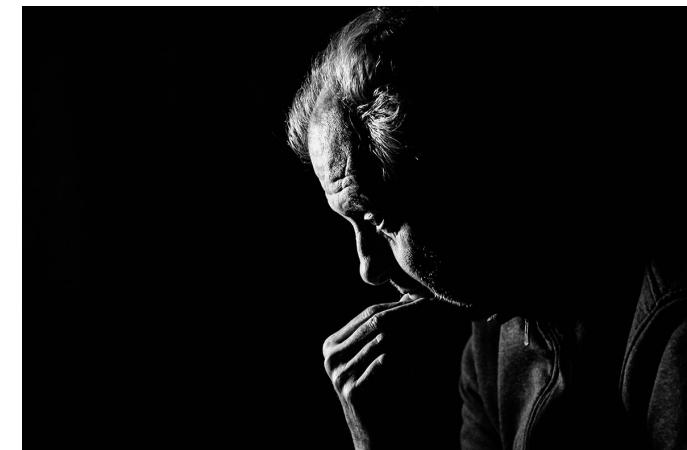


**Universität
Zürich^{UZH}**

MICHAEL, 52

SITUATION

Voluntary hospitalisation, acute psychiatric unit



shutterstock/Andrew Stripes

BACKGROUND

- Emergency: Suicide attempt (car crash with medication and alcohol)
- Severe depressive symptoms for 3 weeks: after positive HIV test-result

CHIEF COMPLAINT

„I have no hope. Nothing makes sense to me. I want to die.“



Universität
Zürich^{UZH}



Translational Neuromodeling Unit

ETH

Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

MENTAL STATUS EXAMINATION

ATTENTION

Restricted to HIV infection



shutterstock/Andrew Stripes

THOUGHT PROCESS AND CONTENT

Slow speech, pauses

Less energy, fatigue

Guilty and ashamed about HIV infection



MOOD

Depressed, no swings



SUICIDAL THOUGHTS

Recurrent suicidal thoughts



Universität
Zürich^{UZH}



Translational Neuromodeling Unit

ETH

Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

MICHAEL, 52

PAST PSYCHIATRIC HISTORY

- Bipolar disorder for 24 years, several severe episodes
- Comorbidity: alcohol abuse



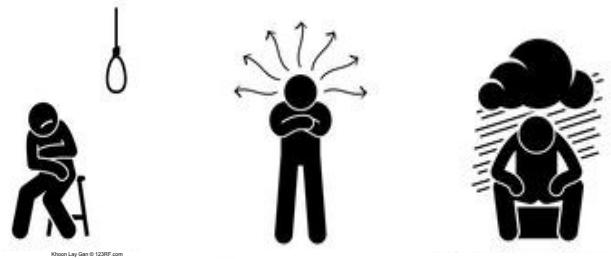
shutterstock/Andrew Stripes

FAMILY HISTORY

- Adoption
- No information about biological parents

MEDICAL HISTORY

- First episode: Lithium → intoxication: one kidney
 - Antipsychotics: less adherence because of side-effects
 - Depressive episode: Antidepressant medication triggered a manic episode
- No stable medication over the last years



Universität
Zürich^{UZH}



Translational Neuromodeling Unit



Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Depressive episode: Bipolar disorder (ICD-10 F31.44)

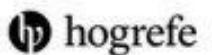
A) Depressed mood or loss of interest	B) More than 5 symptoms:	ICD-10
Duration: 2 weeks	Fatigue	
	Low self-confidence	
	Guilt/ self-blame	
	Suicidal thoughts or action	
	Insomnia	
	Psychomotoric agitation	
	Reduce concentration	
	Increase/decrease in appetite	

Horst Dilling
Harald J. Freyberger
(Hrsg.)

Taschenführer zur
ICD-10-Klassifikation
psychischer Störungen

Nach dem Pocket Guide von J. E. Cooper

9., aktualisierte Auflage entsprechend
ICD-10-GM



Universität
Zürich ^{UZH}



Translational Neuromodeling Unit

ETH

Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

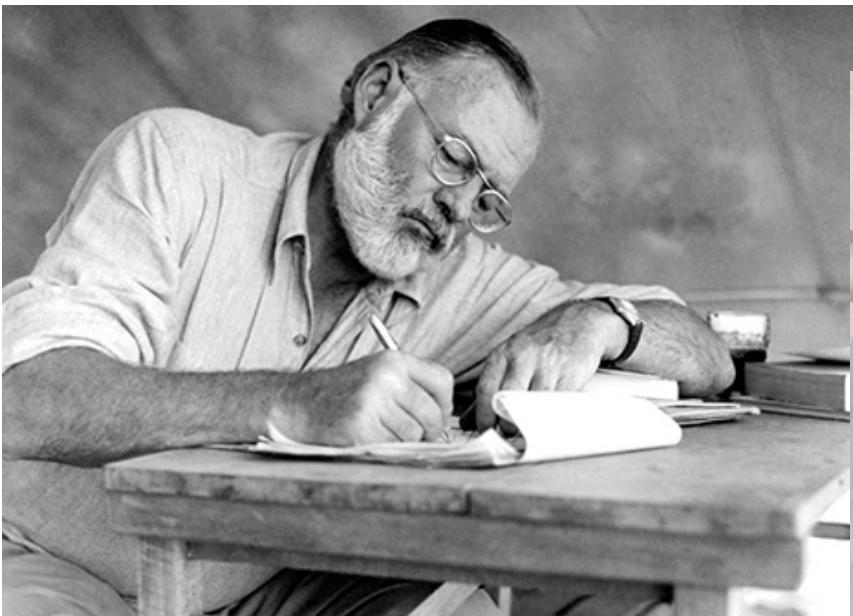
Unipolar Depression vs. Bipolar Depression

- Symptoms
- Psychiatric history
- Treatment



15-20% commit suicide

Highest suicide rate in all psychiatric disorders



Ernest Hemmingway



Lee Thompson Young



Kurt Cobain

Miller, J. N. and D. W. Black (2020). "Bipolar Disorder and Suicide: a Review." *Curr Psychiatry Rep* 22(2): .



Universität
Zürich^{UZH}



Translational Neuromodeling Unit



Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

mania

depression



adapted from jugglux.ch



**Universität
Zürich^{UZH}**

Trajectory of symptoms



Universität
Zürich^{UZH}

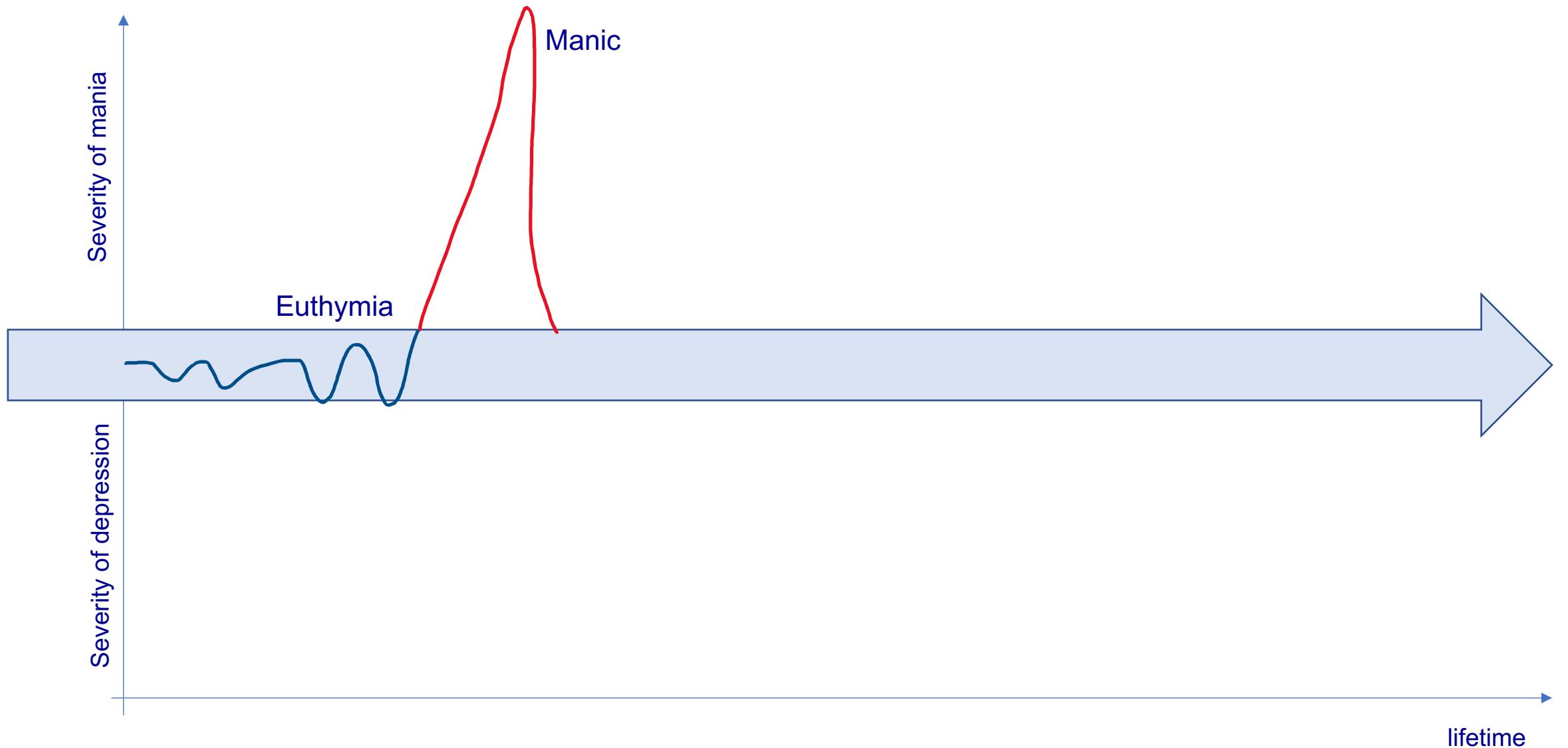


ETH
Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

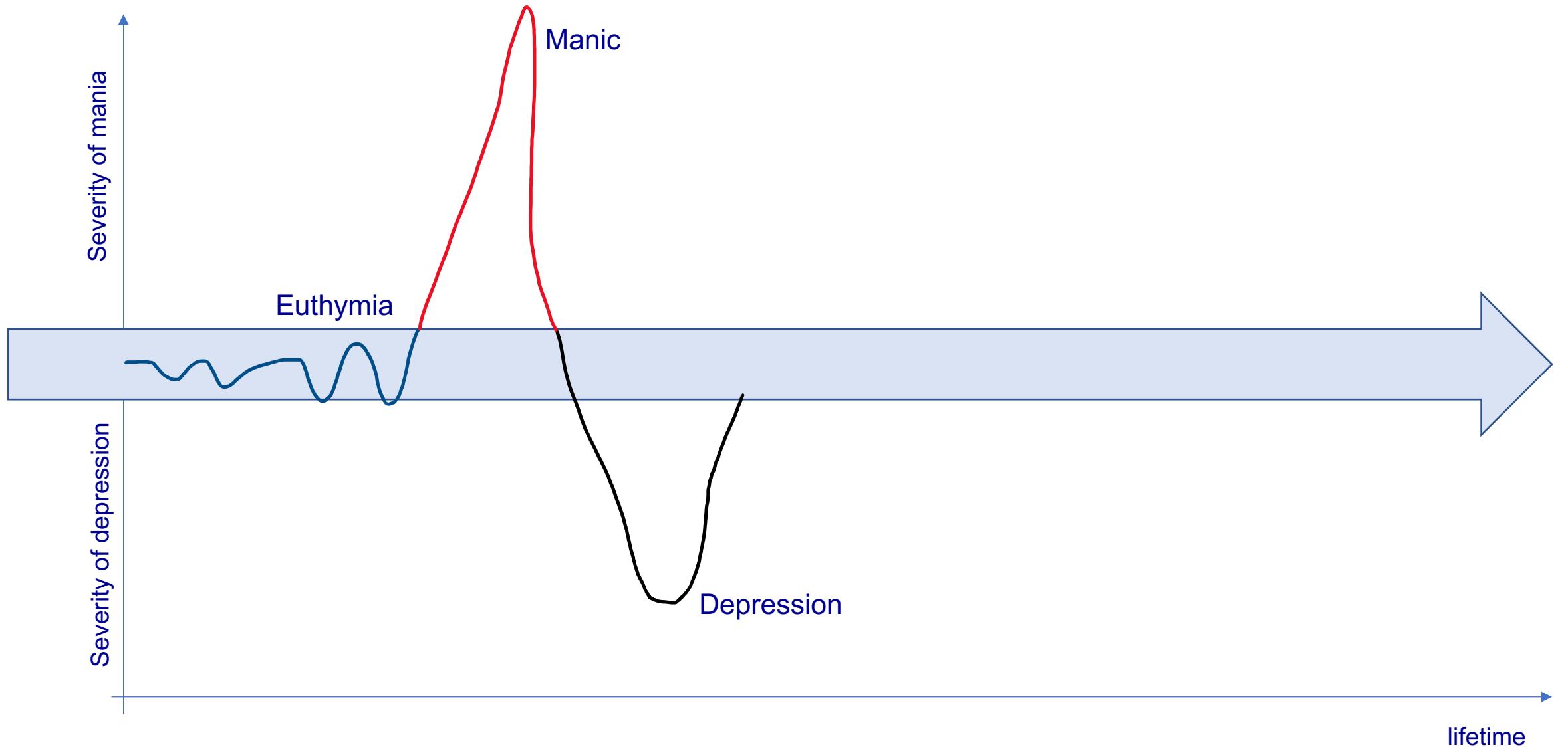


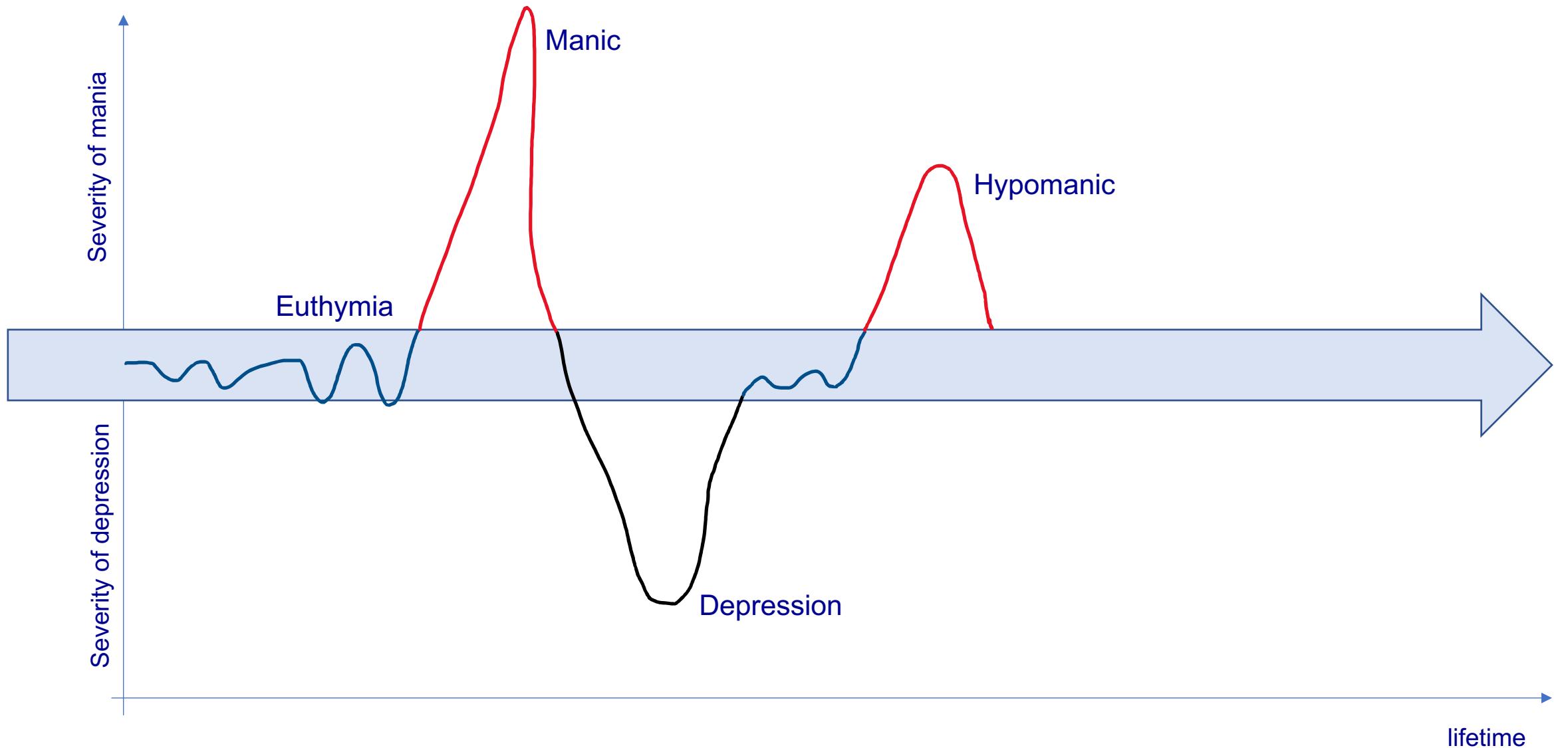
Adapted from Grande et al. *The Lancet*, 2016

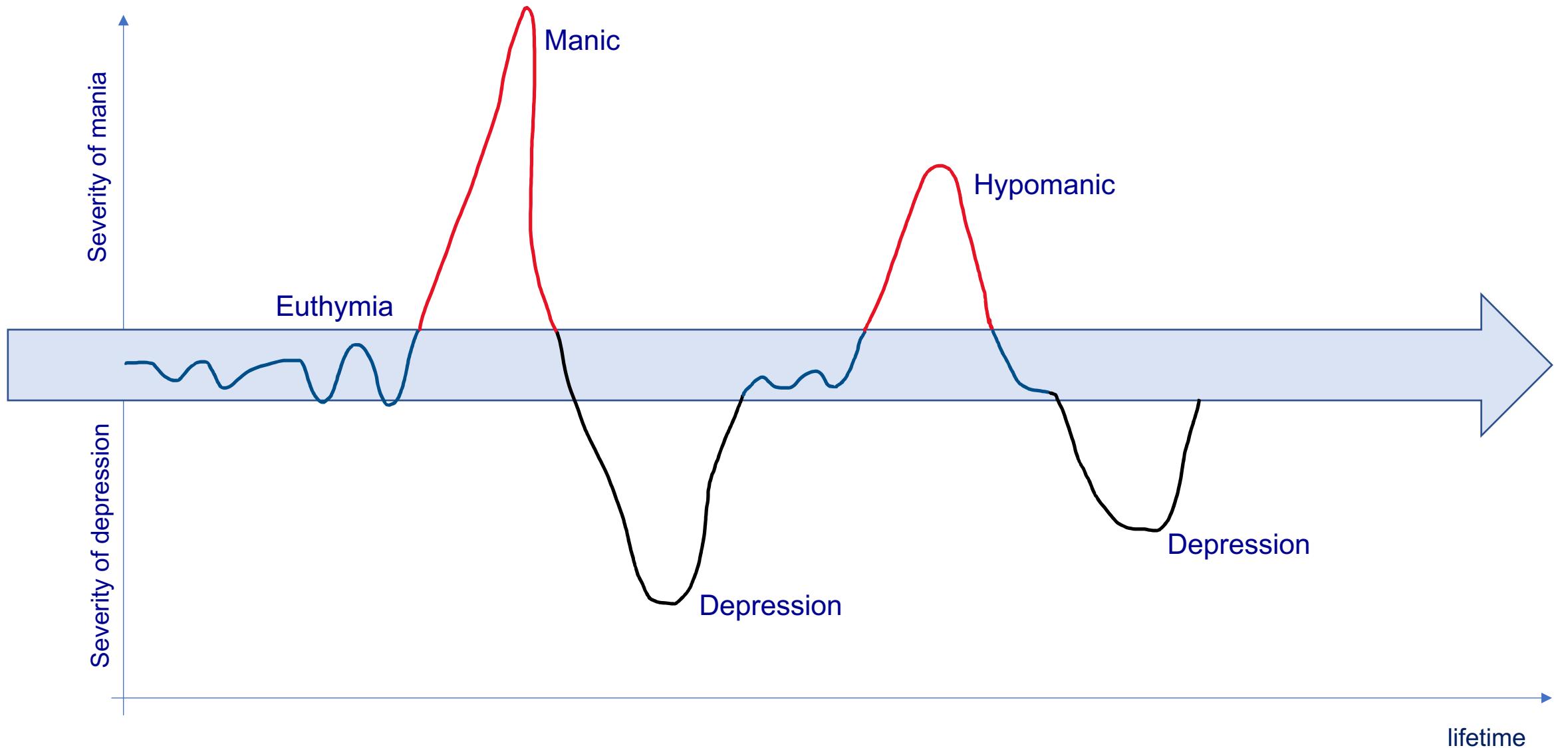


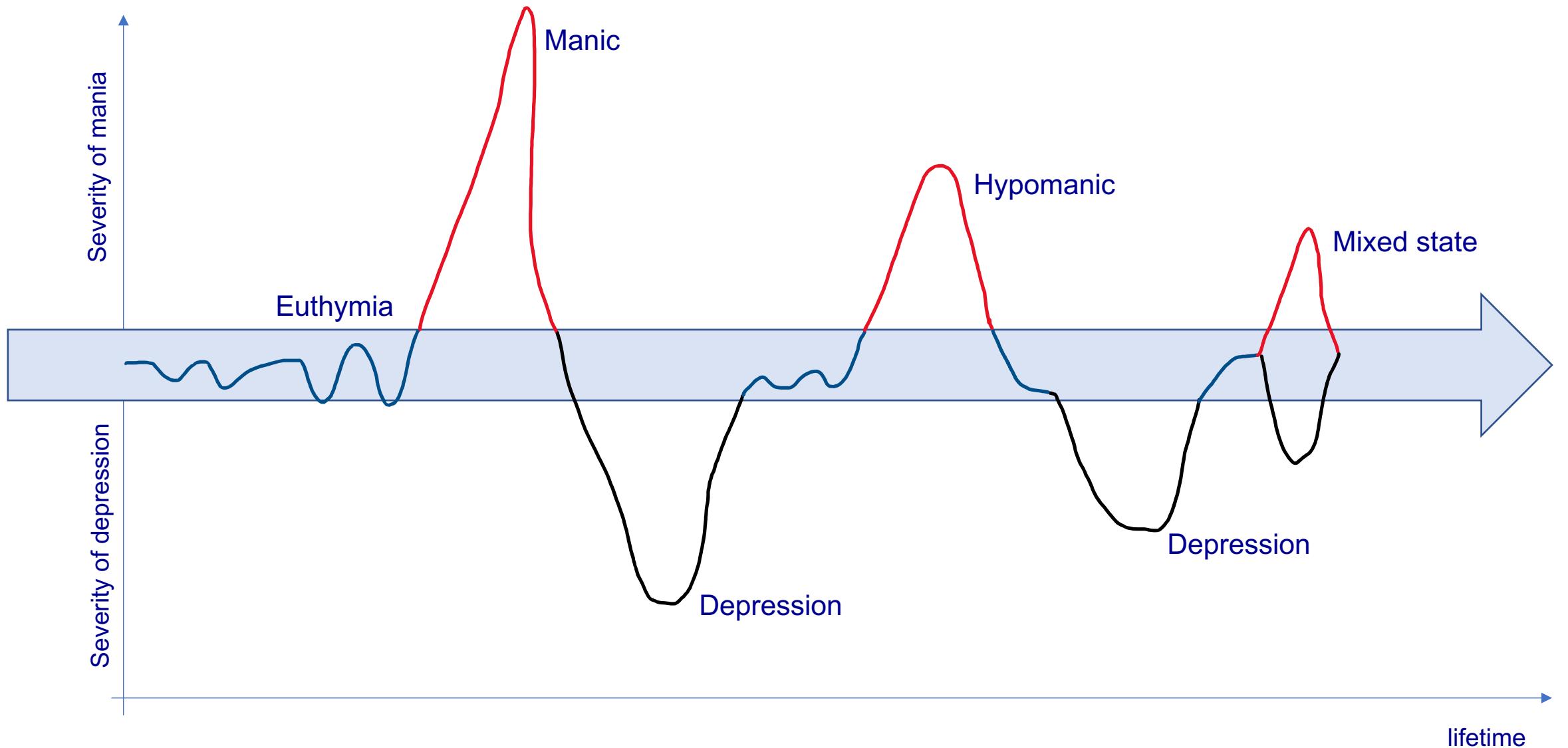


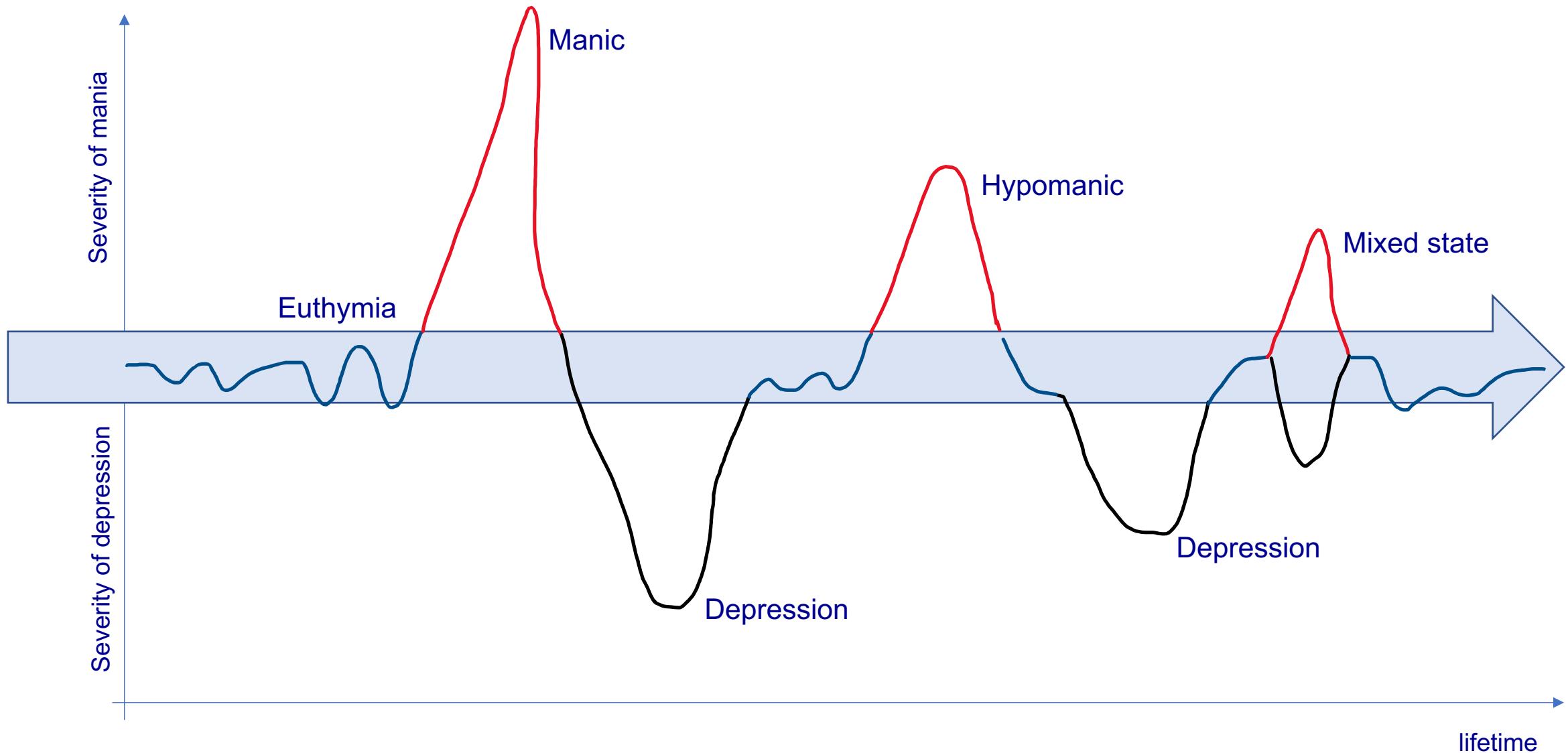
Universität
Zürich^{UZH}











Diagnostics



Universität
Zürich^{UZH}



Translational Neuromodeling Unit

ETH

Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Diagnostics

Clinical Evaluation (ICD-10, DSM-5)

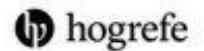


Horst Dilling
Harald J. Freyberger
(Hrsg.)

Taschenführer zur
ICD-10-Klassifikation
psychischer Störungen

Nach dem Pocket Guide von J. E. Cooper

9., aktualisierte Auflage entsprechend
ICD-10-GM



MRI, EEG, laboratory tests



Universität
Zürich^{UZH}



Translational Neuromodeling Unit



Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Diagnostics

Clinical Evaluation (ICD-10, DSM-5)

10-15 years
of latency
until

MRI, EEG, laboratory tests

final
diagnosis
is identified

Phillips, M. L. and D. J. Kupfer (2013). "Bipolar disorder diagnosis: challenges and future directions." *Lancet* **381**(9878): 1663-1671.



Universität
Zürich^{UZH}



Translational Neuromodeling Unit



Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Differential diagnoses

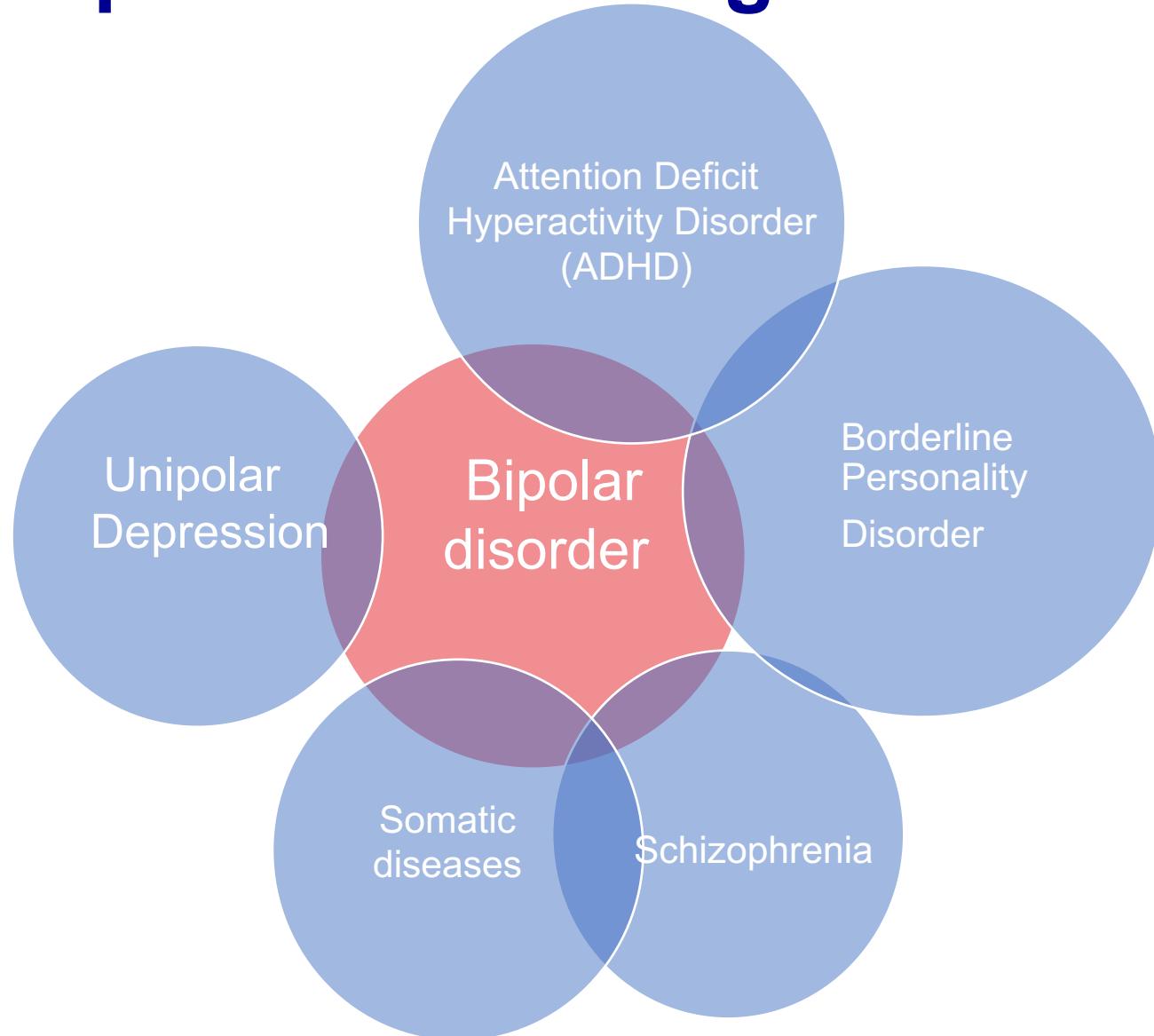


Universität
Zürich^{UZH}



ETH
Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Symptoms overlap with other diagnoses



Comorbidities

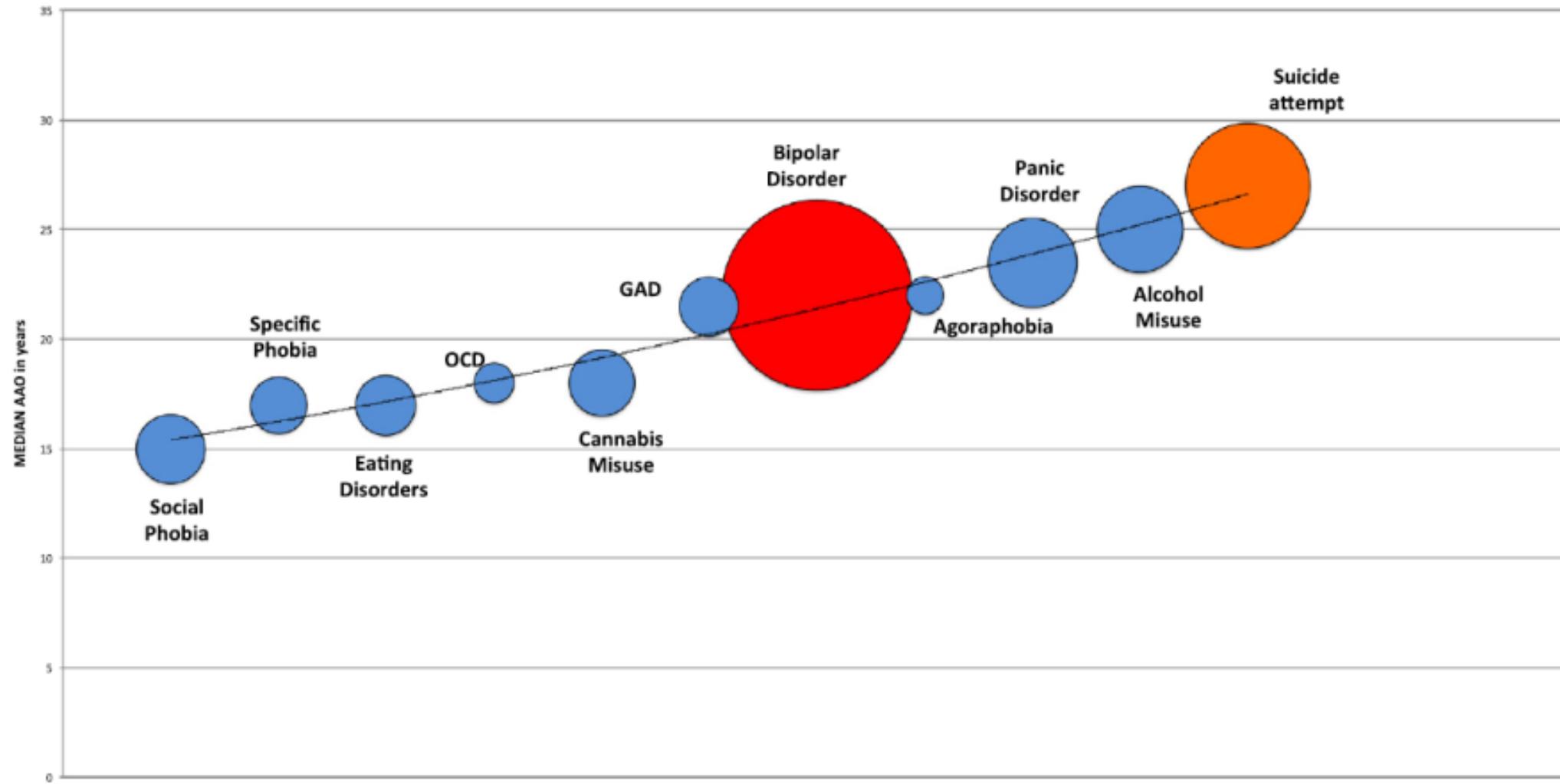


Universität
Zürich^{UZH}



ETH
Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Comorbidities



Loftus, J et al. (2020). "Psychiatric comorbidities in bipolar disorders: An examination of the prevalence and chronology of onset according to sex and bipolar subtype." *Journal of Affective Disorders* **267**: 258-263.

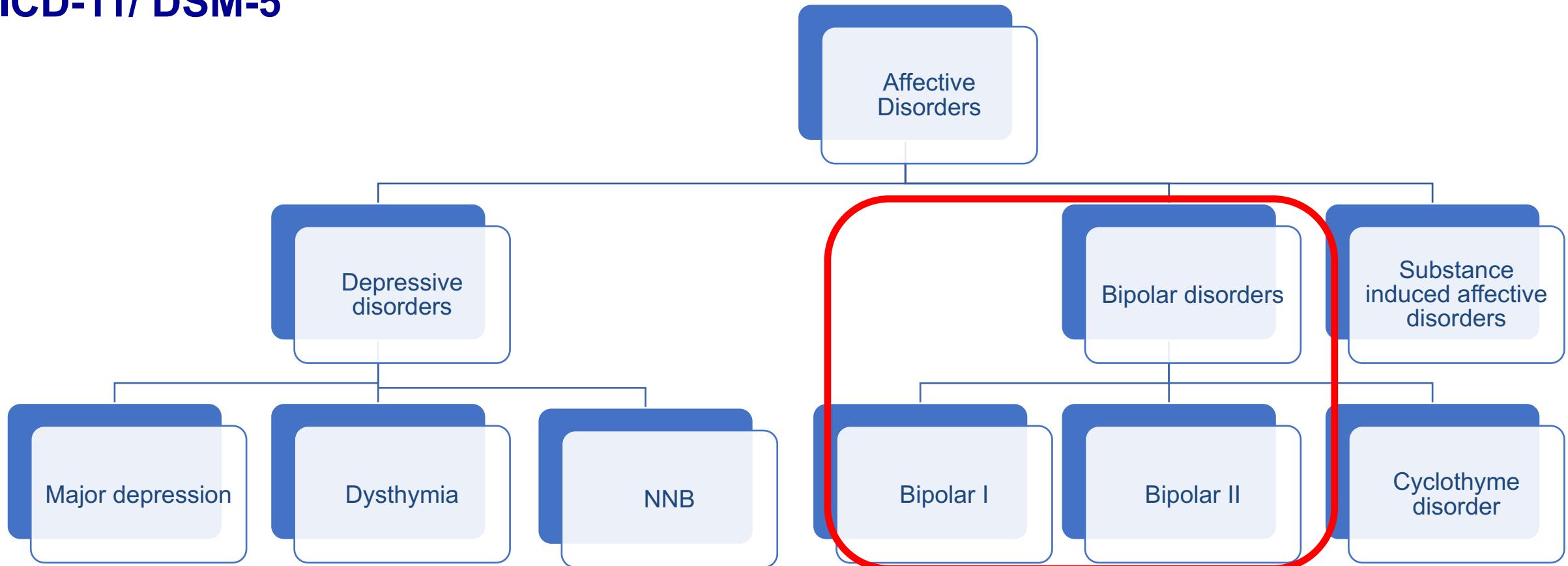


Bipolar Spectrum Disorder: Subgroups

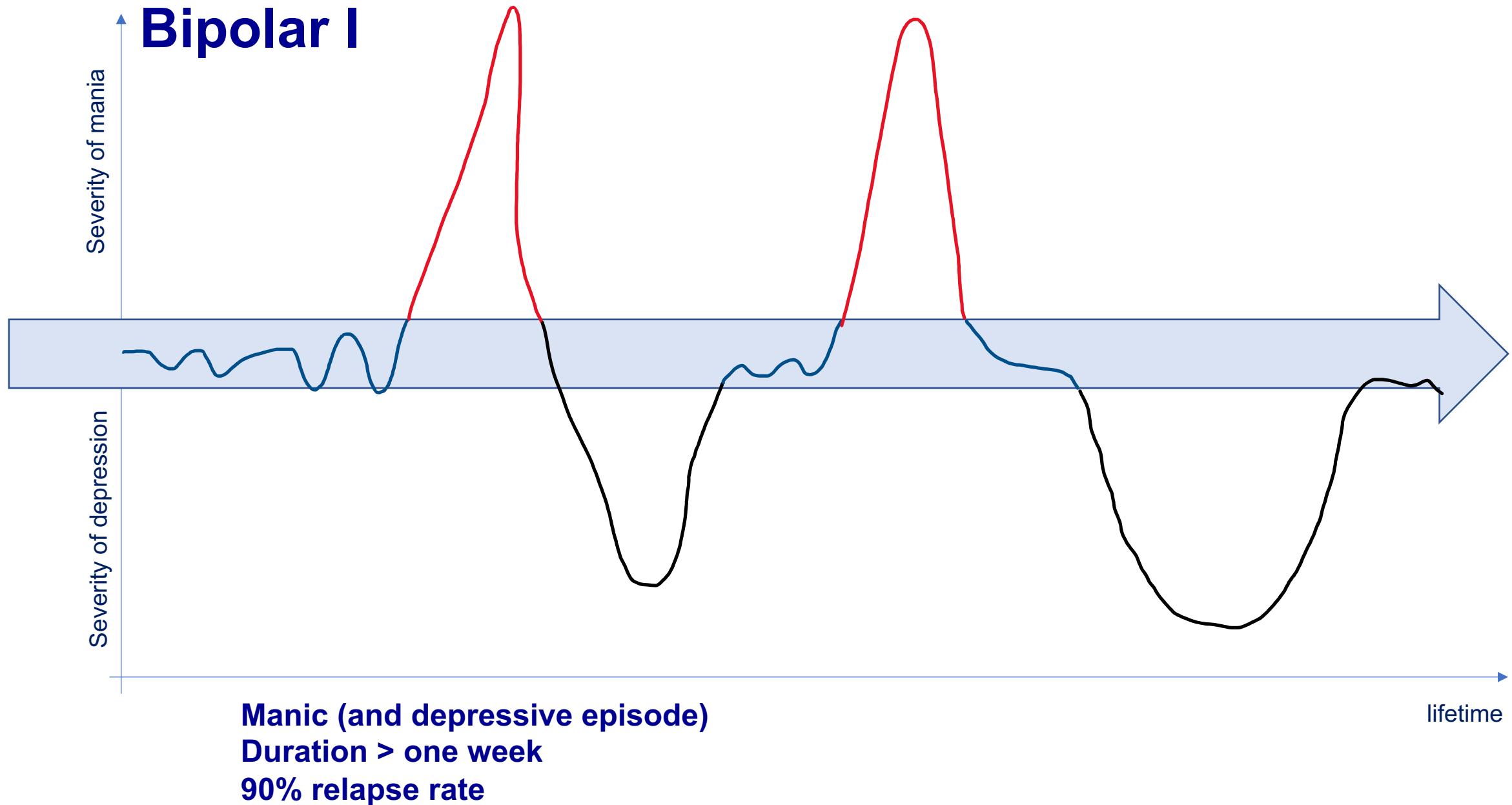


Universität
Zürich^{UZH}

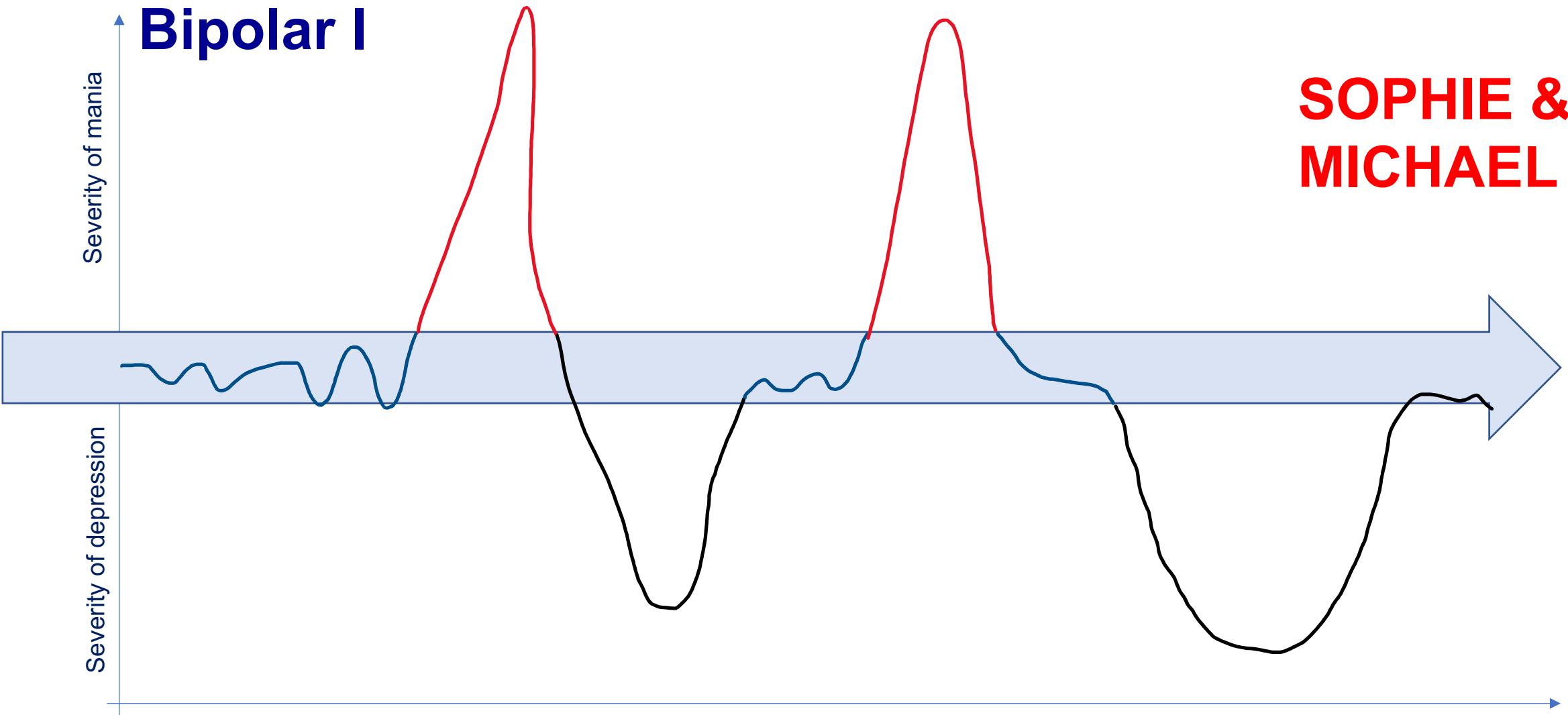
ICD-11/ DSM-5



Bipolar I



Bipolar I



SOPHIE &
MICHAEL

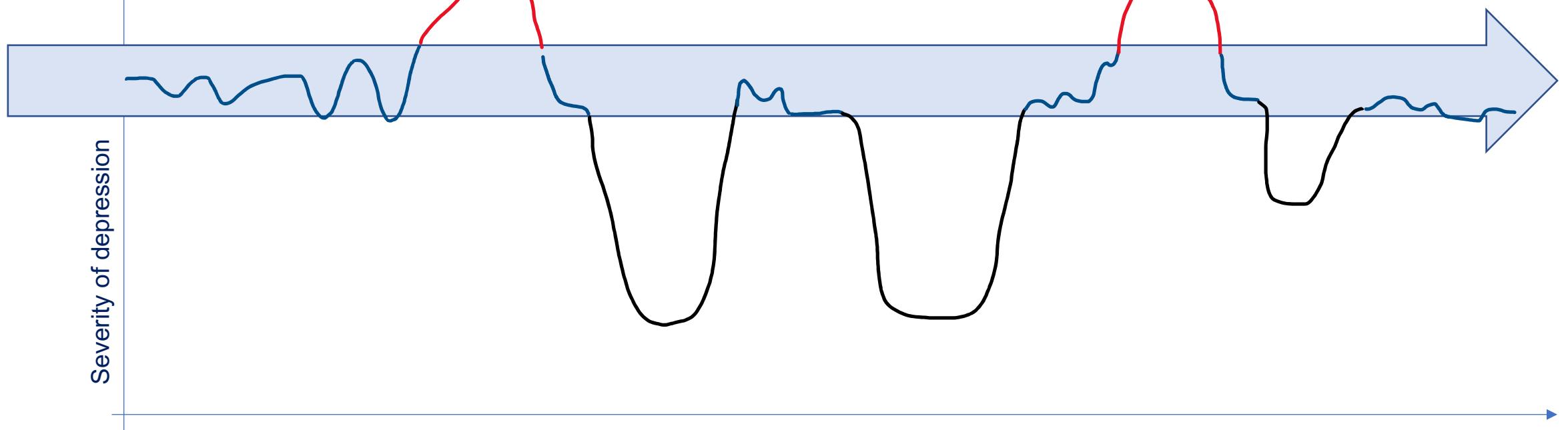
Manic (and depressive episode)
Duration > one week
90% relapse rate



Universität
Zürich^{UZH}

Bipolar II

Severity of mania



Hypomanic episode
Severe depressive episodes



Universität
Zürich^{UZH}



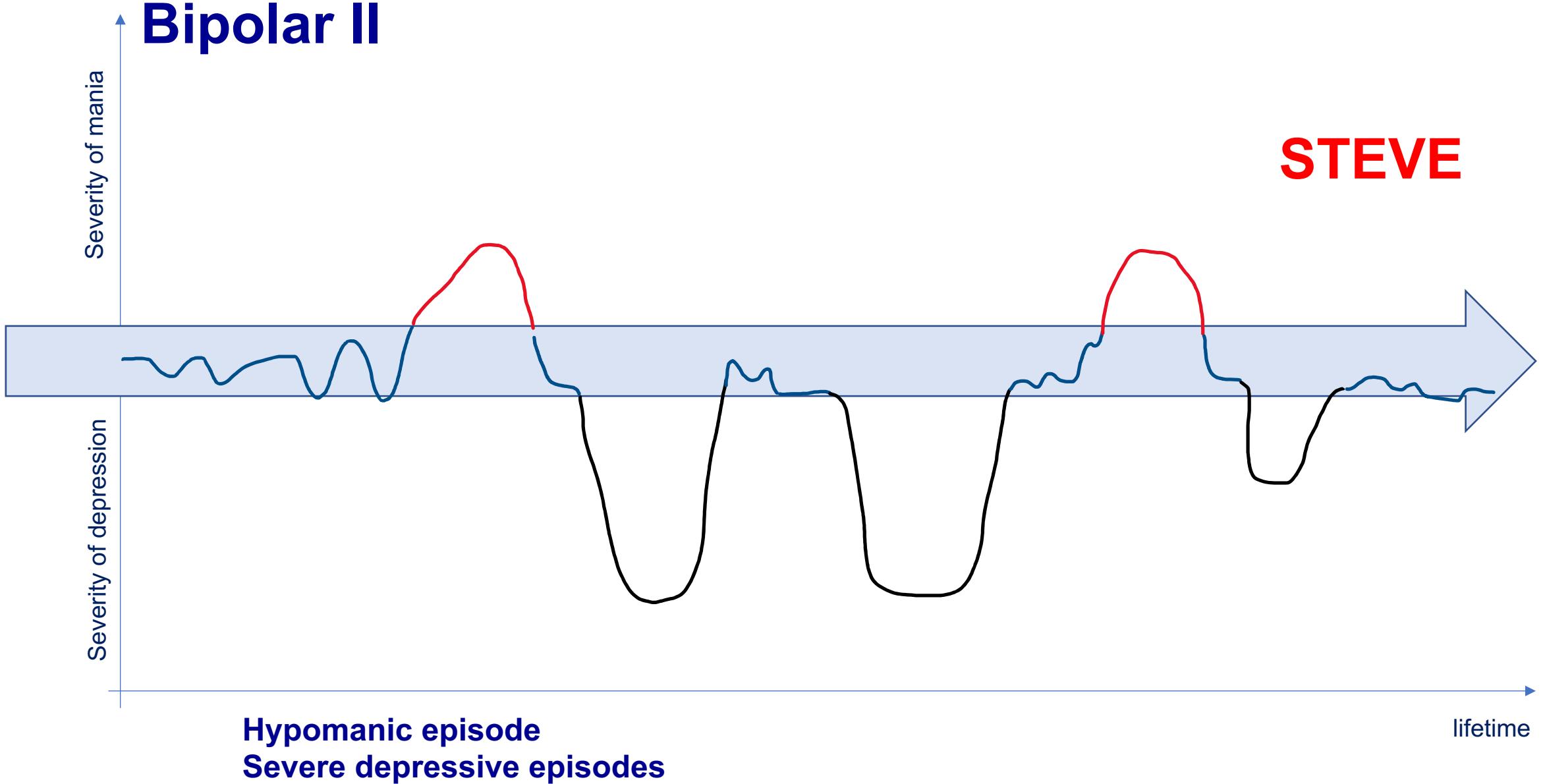
Translational Neuromodeling Unit

ETH

Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

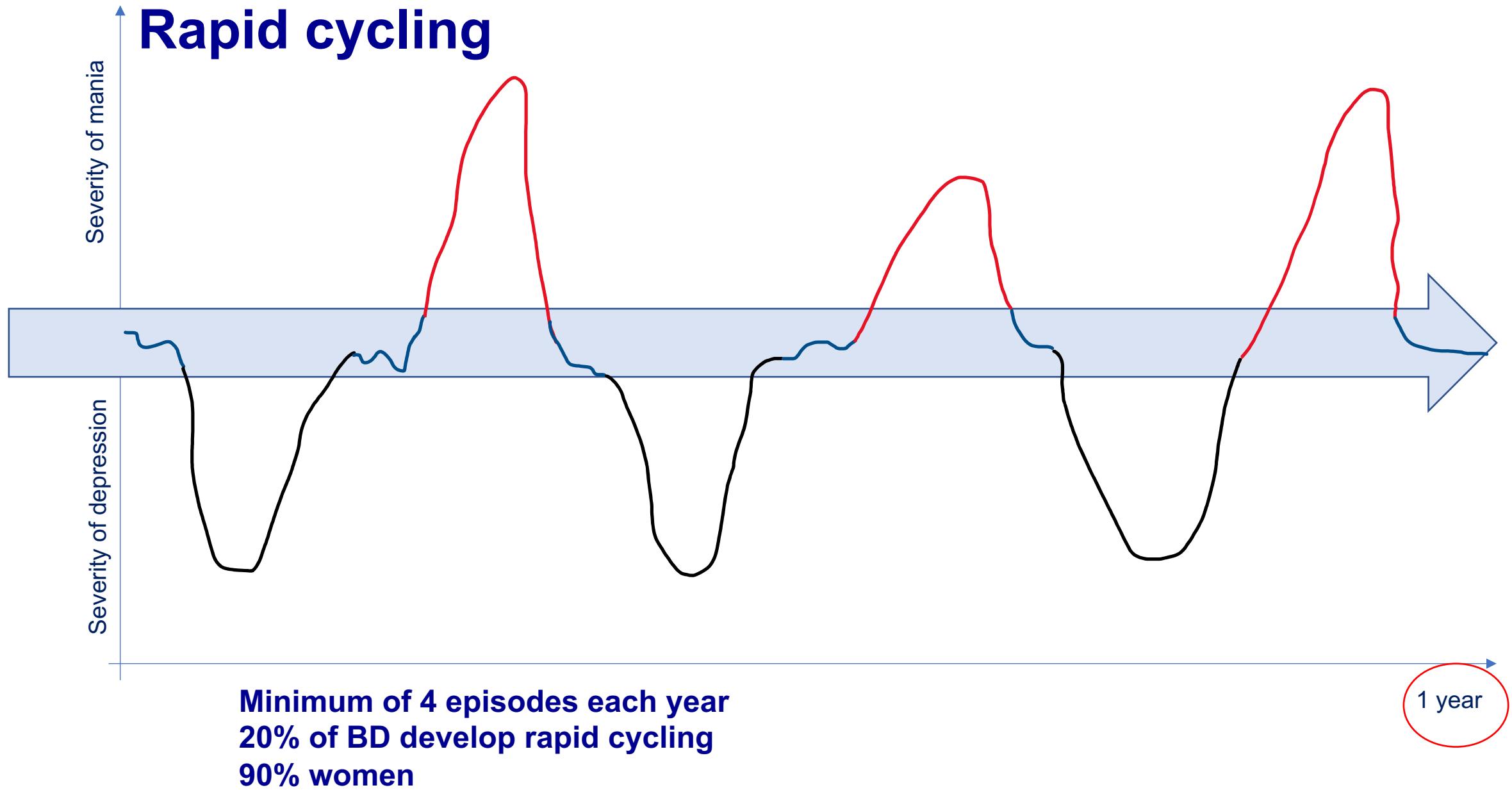
Bipolar II

STEVE



Universität
Zürich^{UZH}

Rapid cycling



Universität
Zürich^{UZH}

Pathomechanisms

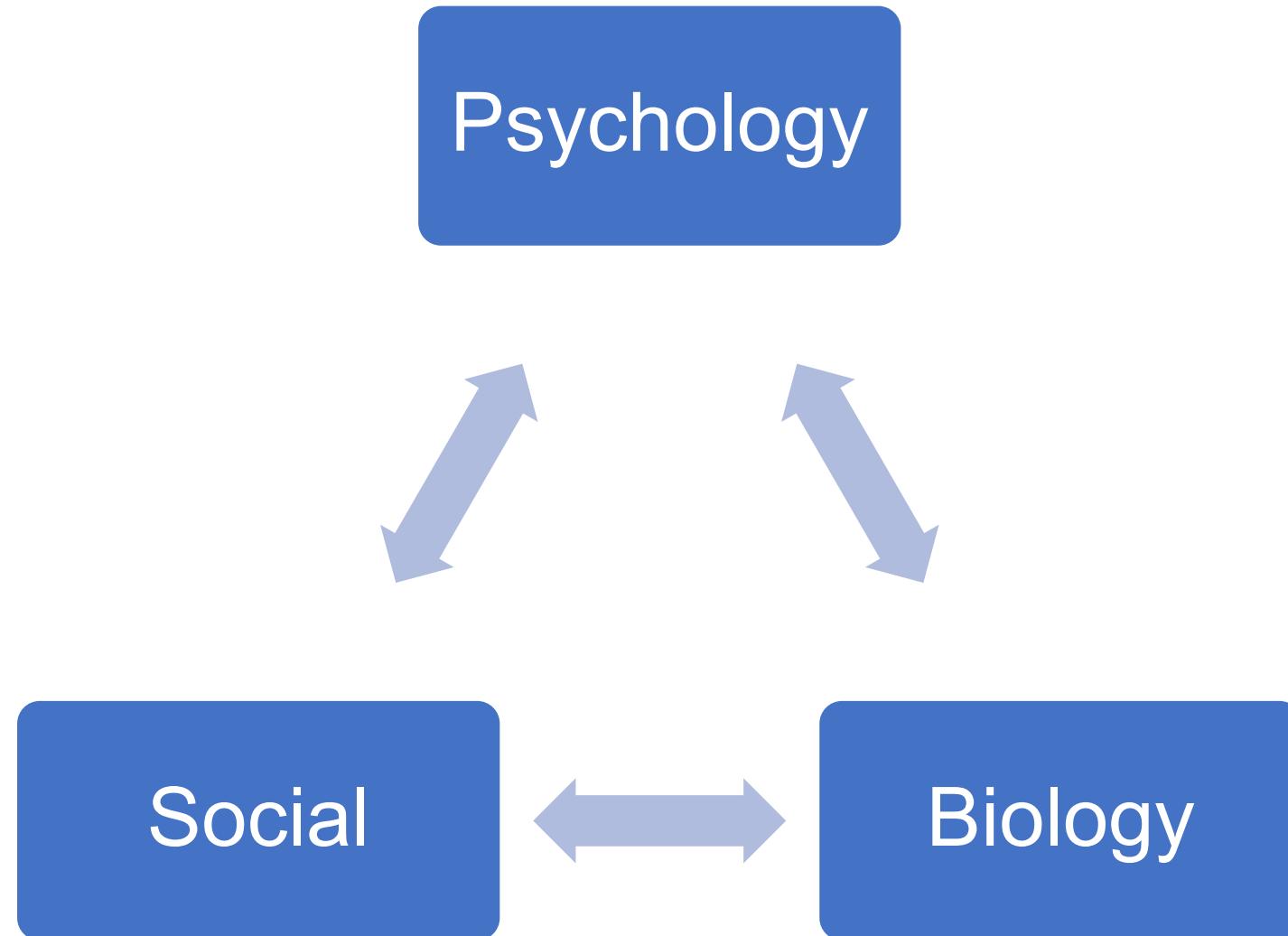


Universität
Zürich^{UZH}

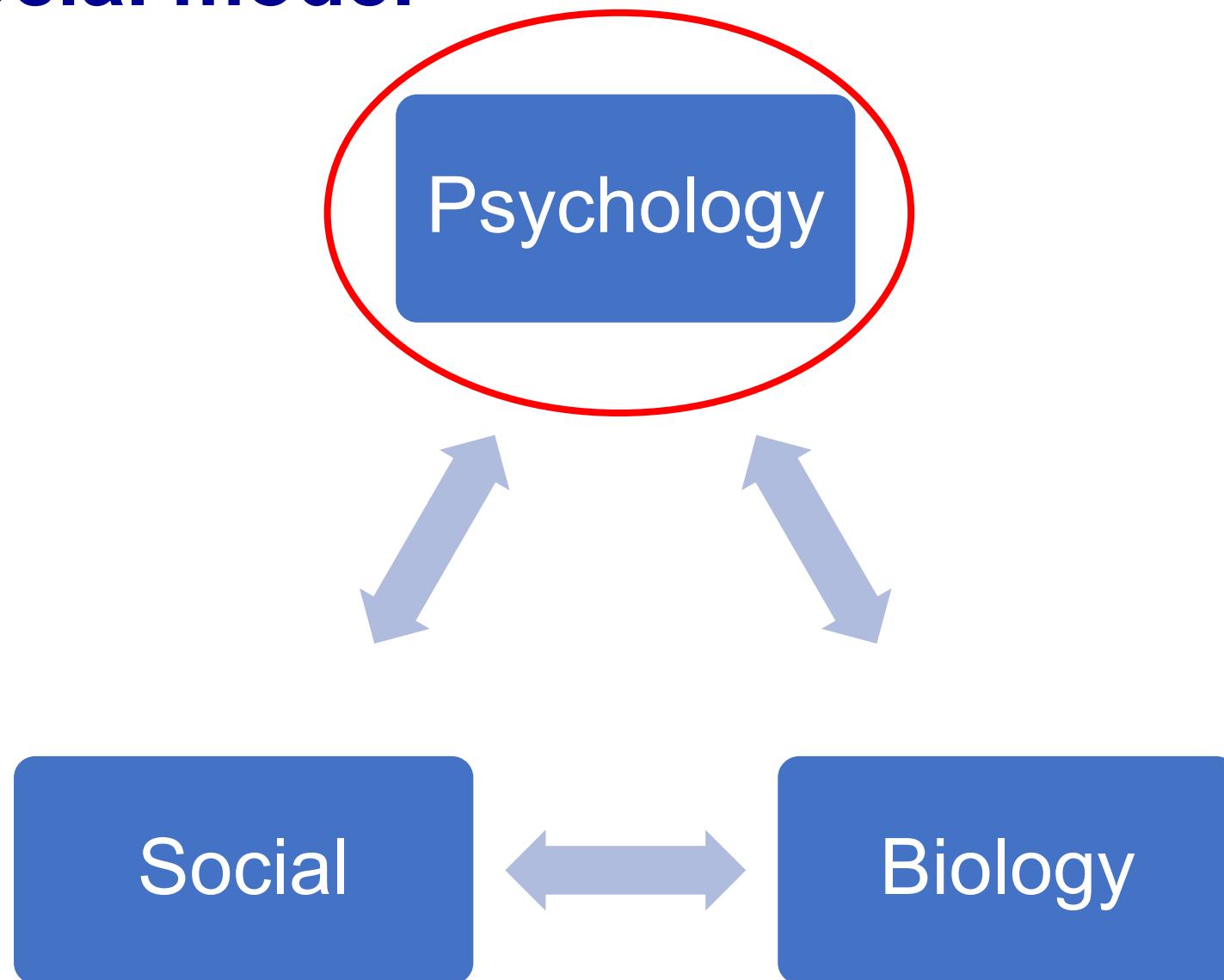


ETH
Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

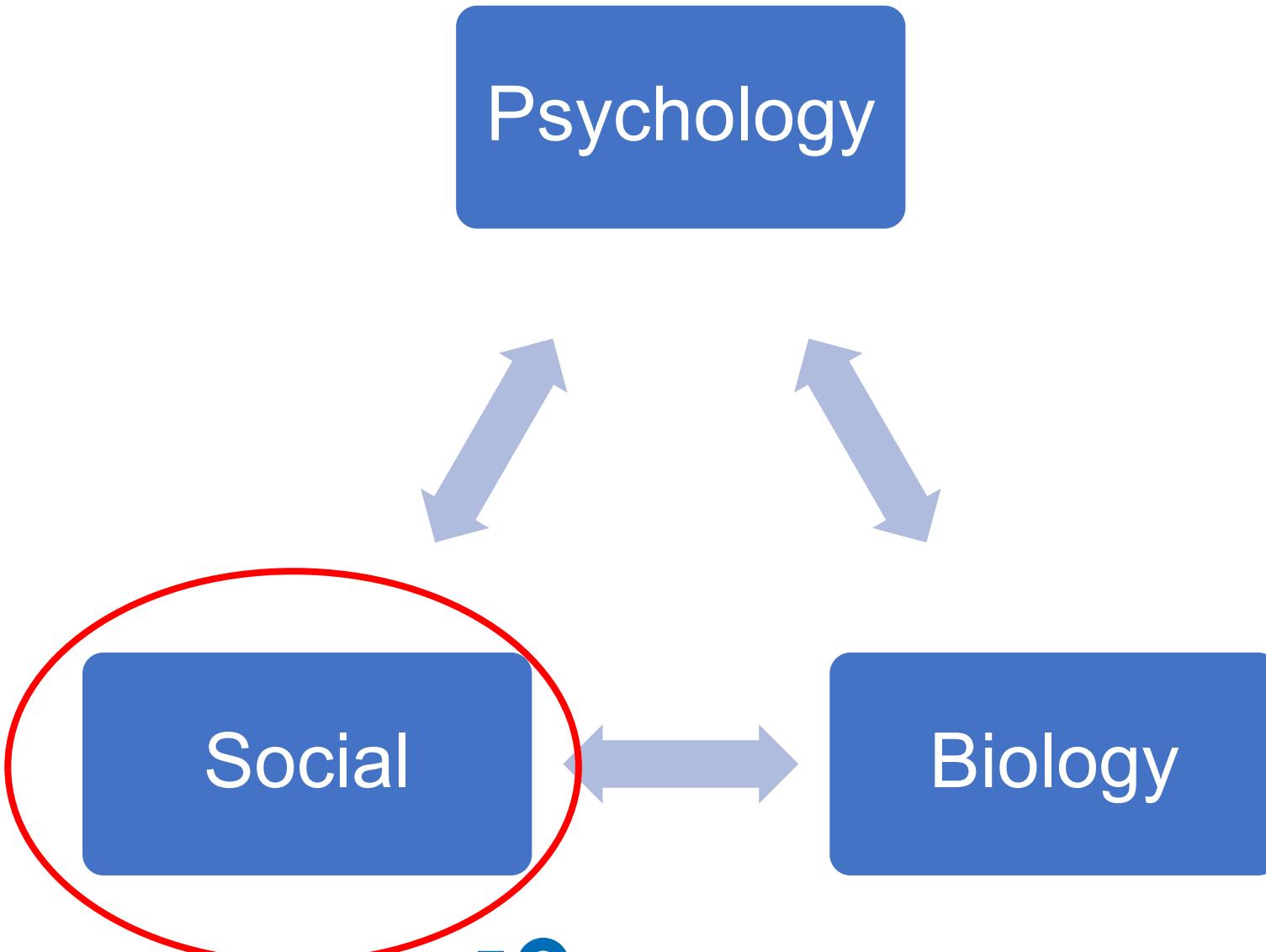
Biopsychosocial model



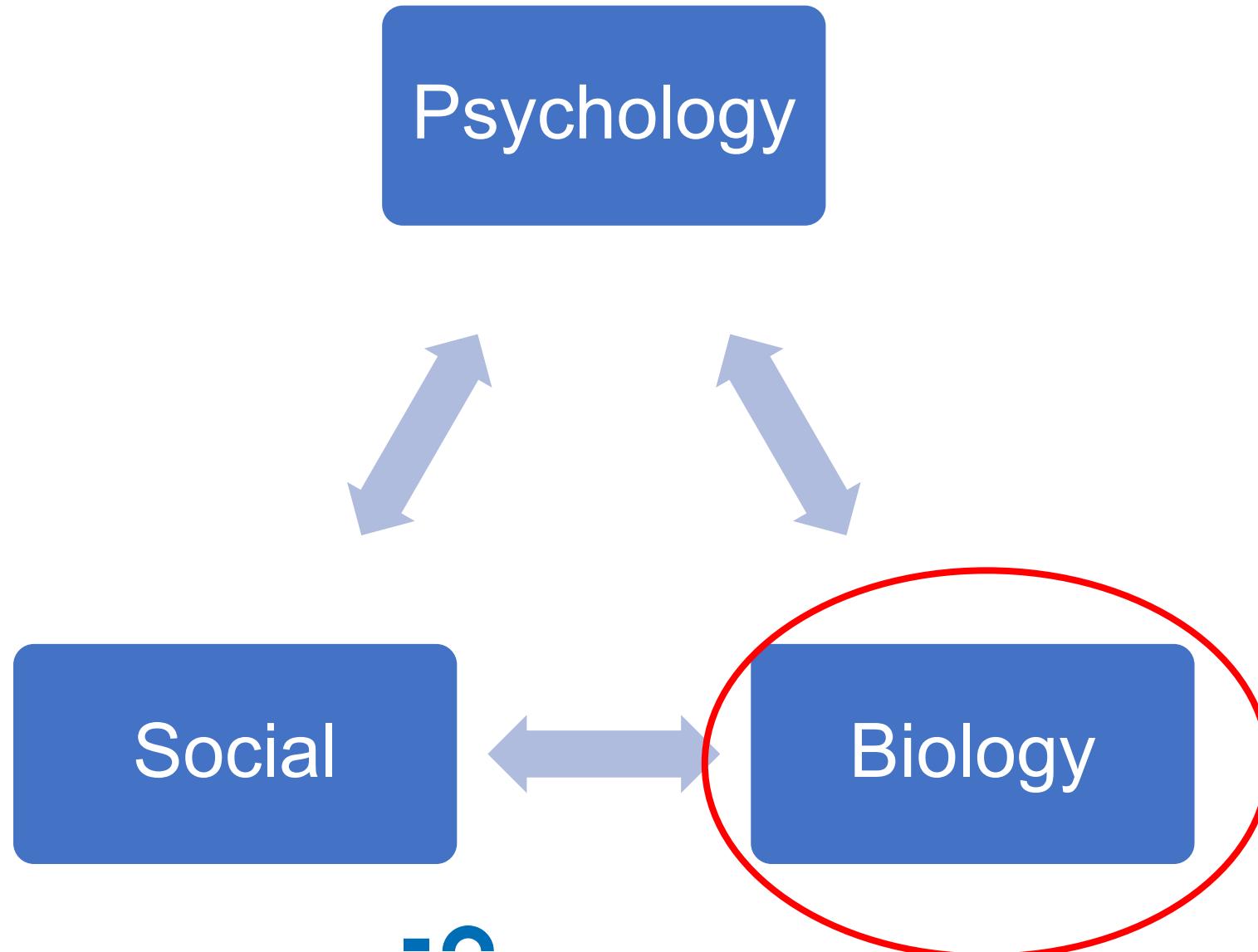
Biopsychosocial model



Biopsychosocial model

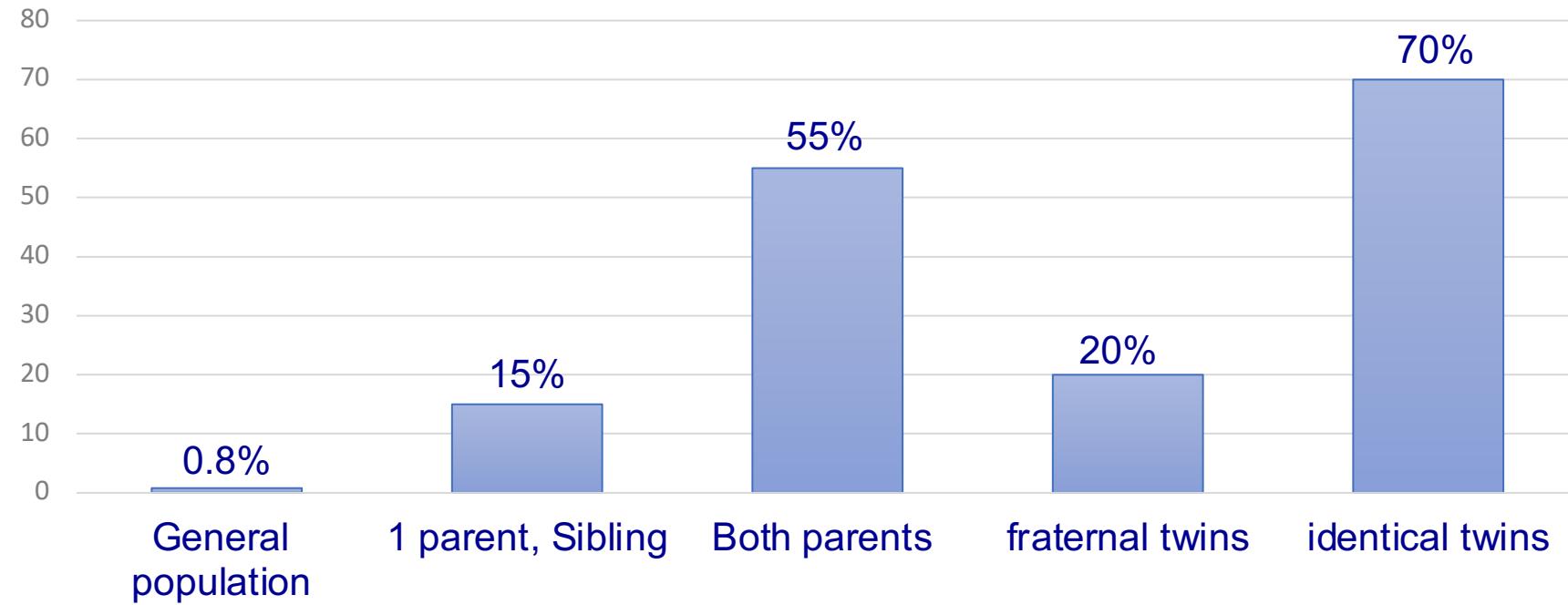


Biopsychosocial model



Heritability

Risk of bipolar disorder for relatives

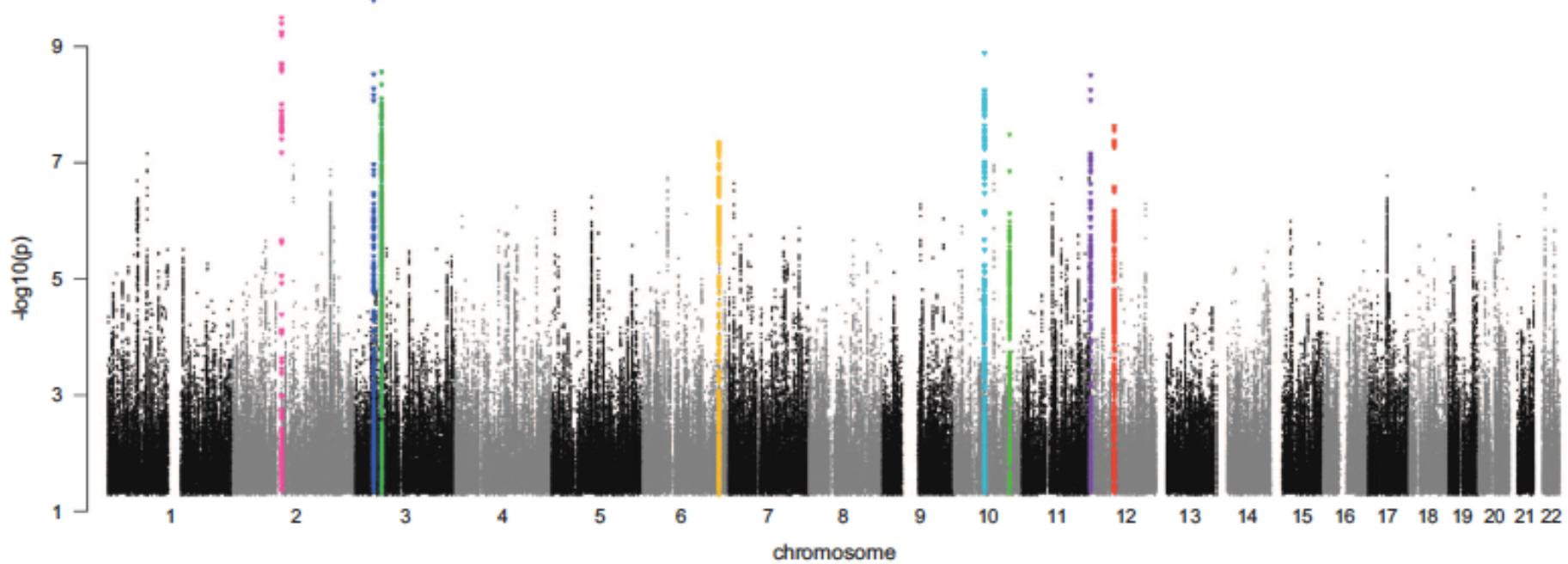


adapted from Volderholzer, Therapie psychischer Erkrankungen



Universität
Zürich^{UZH}

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 ^c
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



Treatment

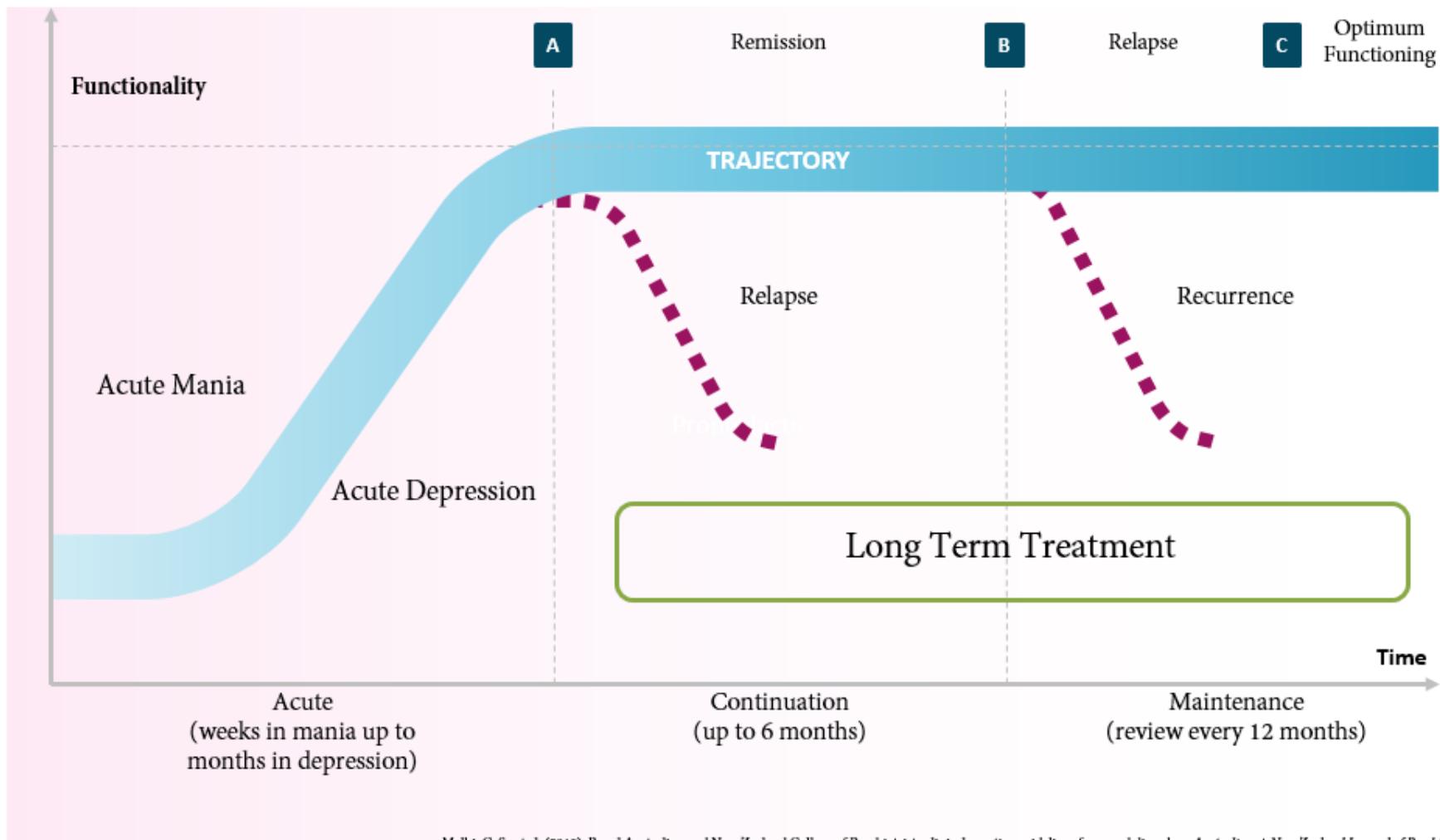


Universität
Zürich^{UZH}

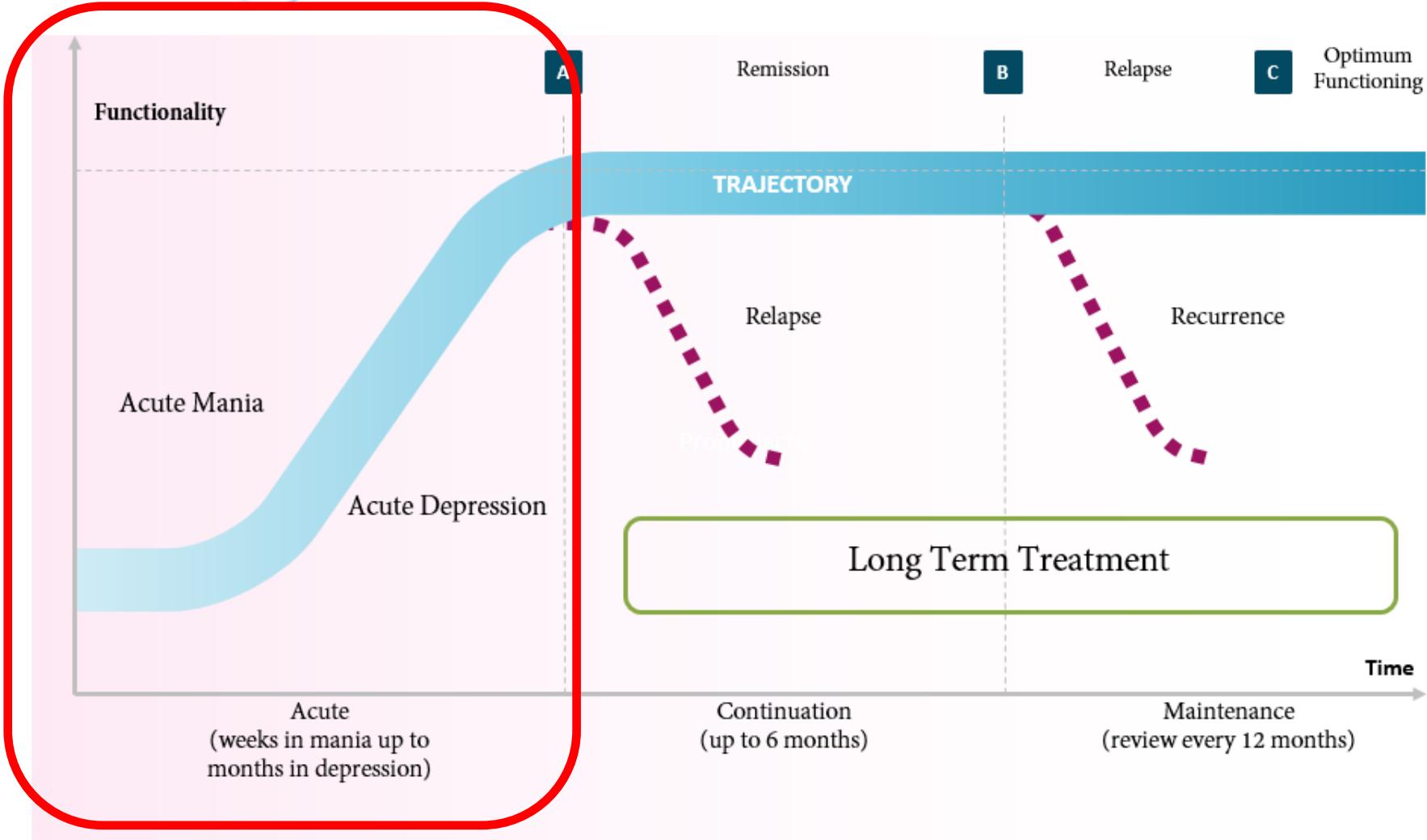


ETH
Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

PHASES OF TREATMENT



PHASES OF TREATMENT



Acute manic episode (Sophie)



Universität
Zürich^{UZH}



ETH
Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Acute manic episode

Psychiatric emergency

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

Medication*:

*German Guidelines 2019

Monotherapy:

- “Mood-stabilizers”(ms): Lithium, other ms: anticonvulsive medication (Valproat)
- *Antipsychotics*

Combination therapy:

- Mood-stabilizer + antipsychotics
- tranquilizers



Universität
Zürich^{UZH}



Translational Neuromodeling Unit

ETH

Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Lithium

- 1817 “allrounder“ medication
- 1949 J. Cade: antimanic medication
- 1950s 7UP
- 2020 effect uncertain

Effect:

- Mood-stabilizer
- Anti-suicidal



wikimedia.org



flashbak.com

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

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

Acute hypomanic episode (Steve)



Universität
Zürich^{UZH}



Translational Neuromodeling Unit

ETH
Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Acute hypomanic episode

- Diagnostics!
- Wait & observe
- Outpatient-psychiatrist : Psychoeducation
- If necessary: medication (sleep)



Acute depressive episode (Michael)



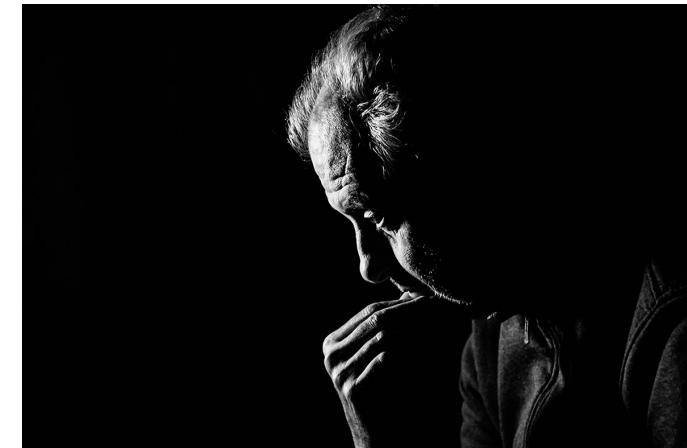
Universität
Zürich^{UZH}



ETH
Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Acute depressive episode

- Antidepressant monotherapy?
- Caution: Antidepressant medication (AD) may induce a manic episode («switch»)
- If AD necessary: just in combination with mood-stabilizer



Low switch risk

High switch risk

Escitalopram
Bupropion
Sertraline
Paroxetine
...

TCA
Reboxetine
Venlafaxin
...



Acute depressive episode

Mood-stabilizer: eg. Lithium

Antipsychotics: Quetiapine



Non-pharmacological treatment:

Electroconvulsive therapy (ECT)

- Induce generalized seizures (6-12 treatments)
→ Coordinated activity of nerve cells
- Indication: severe depressive bipolar/
treatment-resistant
- High response rate



muehlenkreiskliniken.de



Universität
Zürich^{UZH}



Translational Neuromodeling Unit

ETH

Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Continuation therapy

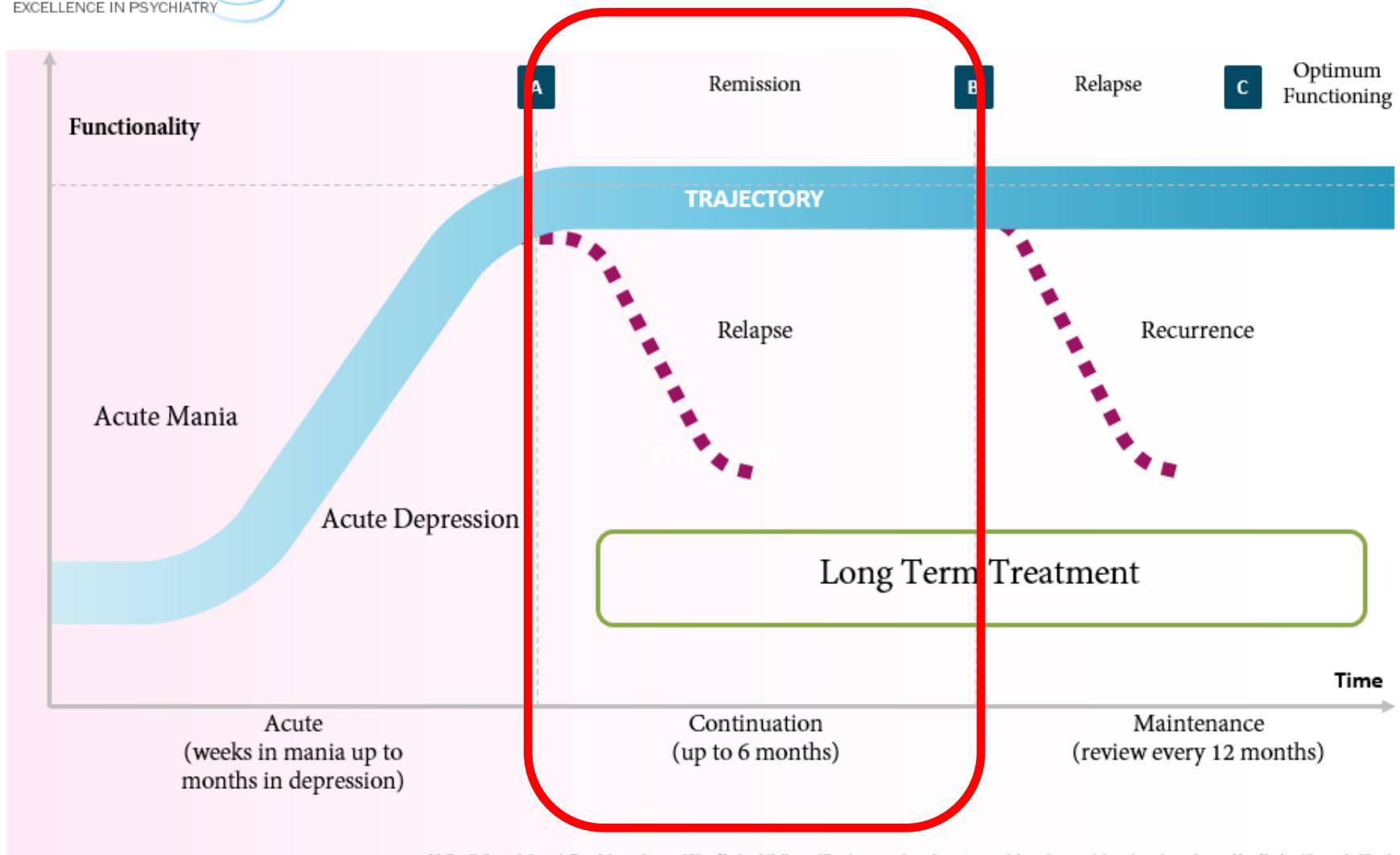


Universität
Zürich^{UZH}



ETH
Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

PHASES OF TREATMENT



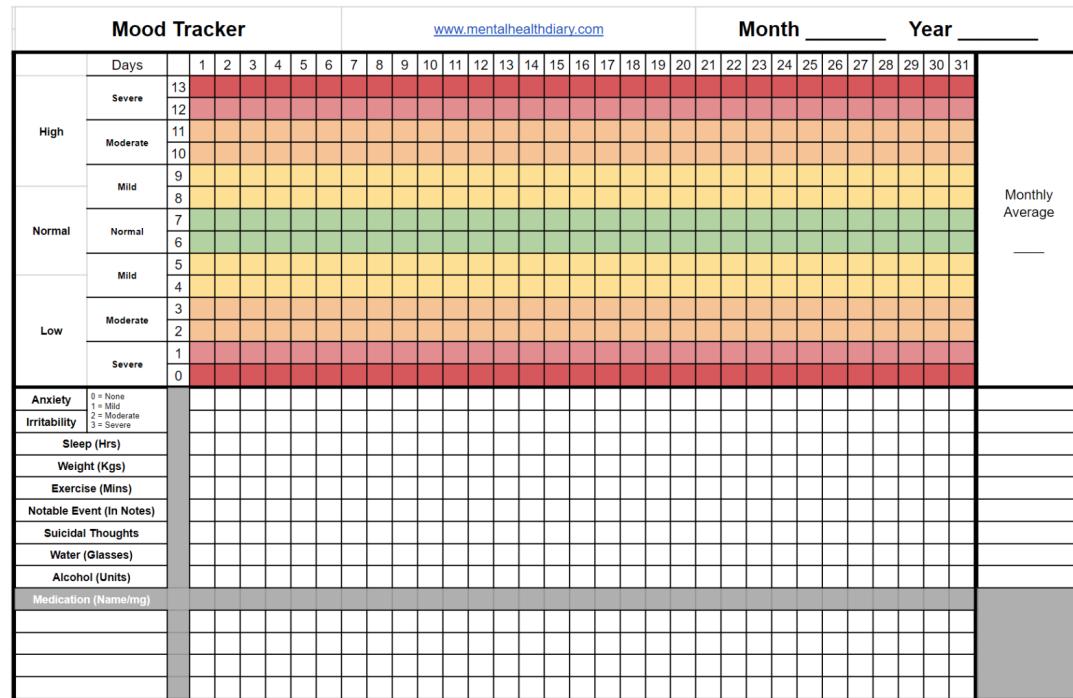
Malhi, G. S., et al. (2015). Royal Australian and New Zealand College of Psychiatrists clinical practice guidelines for mood disorders. *Australian & New Zealand Journal of Psychiatry*, 49(12), 1087-1206.

Continuation therapy

- Goal: prevention of relapse
- 75% relapse risk within 6-12 months
- Medication intake for 12 months in full dosage (alternative: ECT)
→ incl. laboratory & somatic monitoring

Psychosocial Interventions

- Psychotherapy (CBT) and Psychoeducation:
“Red-flag symptoms”, mood diary
- Integration of partner/family, precaution



www.mentalhealthdiary.com



financer.com



Universität
Zürich ^{UZH}



Translational Neuromodeling Unit

ETH

Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Maintenance therapy

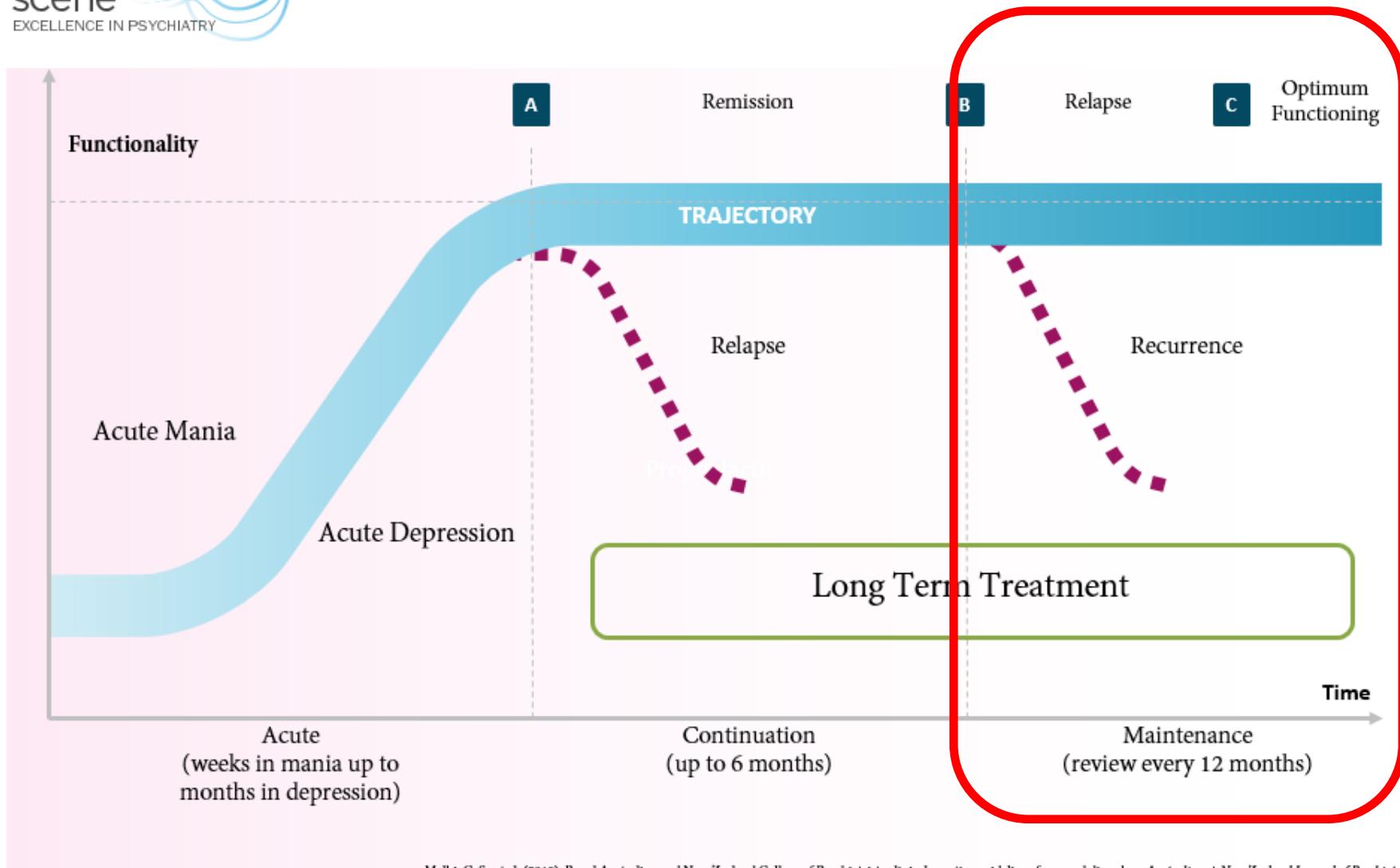


Universität
Zürich^{UZH}



ETH
Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

PHASES OF TREATMENT



Maintenance therapy

- Goal: Prevention of recurrence
 - Medication intake for years or lifelong
 - Lithium: first-line treatment
- Indication: severe form or >2 episodes within 5 years

Psychosocial Interventions

- Psychotherapy (CBT)
- Supported employment



Universität
Zürich^{UZH}

Future directions

Faster & reliable
diagnostic tools

Understanding
Pathomechanisms

Early
Episode
prediction

Treatment
Prediction



Universität
Zürich^{UZH}



Translational Neuromodeling Unit



Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Future directions

- Differential diagnoses
- Identify & Co-treatment of comorbidities
- high-risk people

Faster & reliable diagnostic tools

Understanding Pathomechanisms

Early
Episode
prediction

Treatment
Prediction



Future directions

- Differential diagnosis
- Identify & Co-treatment of comorbidities
- high-risk people

Faster & reliable diagnostic tools

Understanding Pathomechanisms

Early Episode prediction

Treatment Prediction

- Identify subgroups
- Individual treatment options



Universität
Zürich^{UZH}



Translational Neuromodeling Unit

ETH

Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Future directions

- Differential diagnosis
- Identify & Co-treatment of comorbidities
- high-risk people

Faster & reliable diagnostic tools

Understanding Pathomechanisms

- Avoid/ weaken acute symptoms

Early Episode prediction

Treatment Prediction

- Identify subgroups
- Individual treatment options



Universität
Zürich^{UZH}



Translational Neuromodeling Unit

ETH

Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Future directions

- Differential diagnosis
- Identify & Co-treatment of comorbidities
- high-risk people

Faster & reliable diagnostic tools

- Avoid/ weaken acute symptoms

Early Episode prediction

Understanding Pathomechanisms

- Identify subgroups
- Individual treatment options

Treatment Prediction

- Precise medication
- Prevention of polypharmacy
- Shorten episodes
- Long-term treatment outcomes



Universität
Zürich^{UZH}



Translational Neuromodeling Unit

ETH

Eidgenössische Technische Hochschule Zürich
Swiss Federal Institute of Technology Zurich

Thank you



Khoon Lay Gan © 123RF.com



Universität
Zürich^{UZH}