Spectrum of Depression & Bipolar: Diagnoses & Conceptual Aspects

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Disclosures: Dr. Roger McIntyre

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Dr. Roger McIntyre is a CEO of Braxia Scientific Corp.

Therapeutic Objectives in Bipolar Disorder

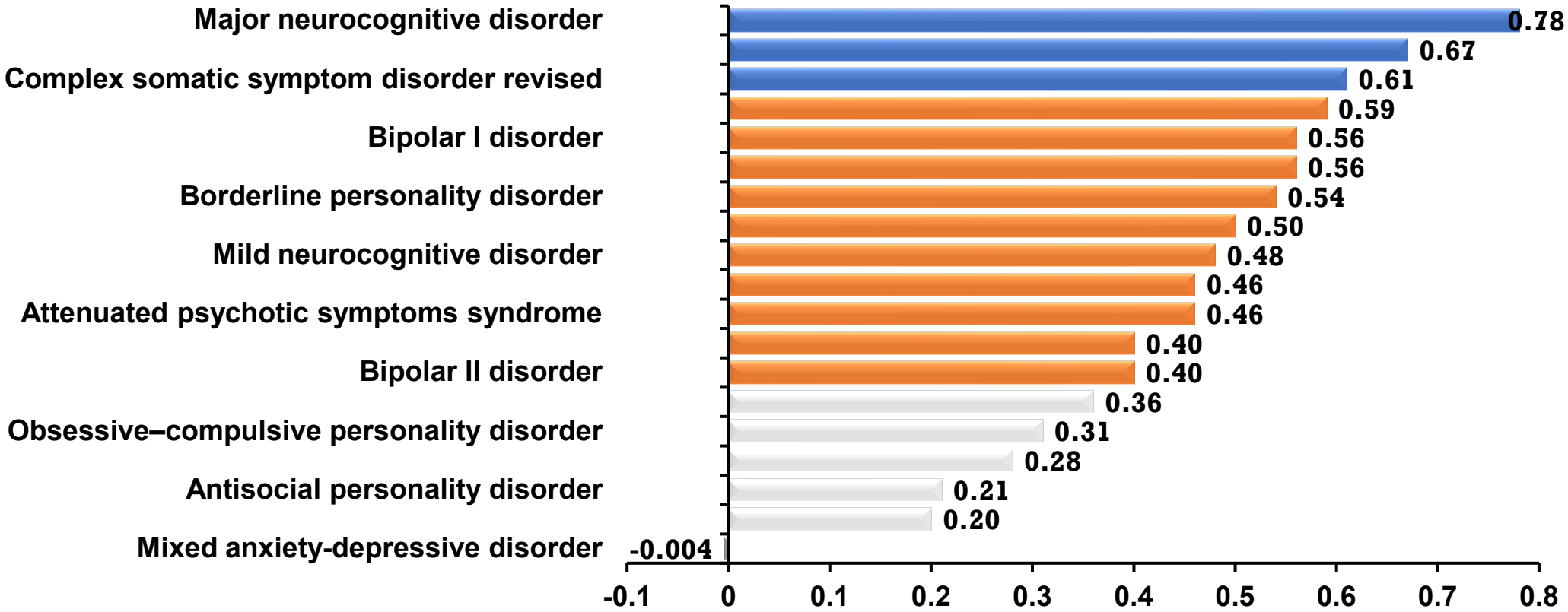
The therapeutic objectives in bipolar disorders are the:

- Prevention and treatment of syndromal hypomania, mania, and depression
- Abatement of interepisodic depressive symptoms
- Normalization of circadian disturbances (eg, in sleep)
- Improvement and preservation of cognitive function
- Treatment and prevention of psychiatric and medical comorbidity
- Improvement of patient-reported outcomes (eg, quality of life)
- Reduction of suicidality

McIntyre et al. Lancet. 2020;396:1841.

Barriers – diagnosis

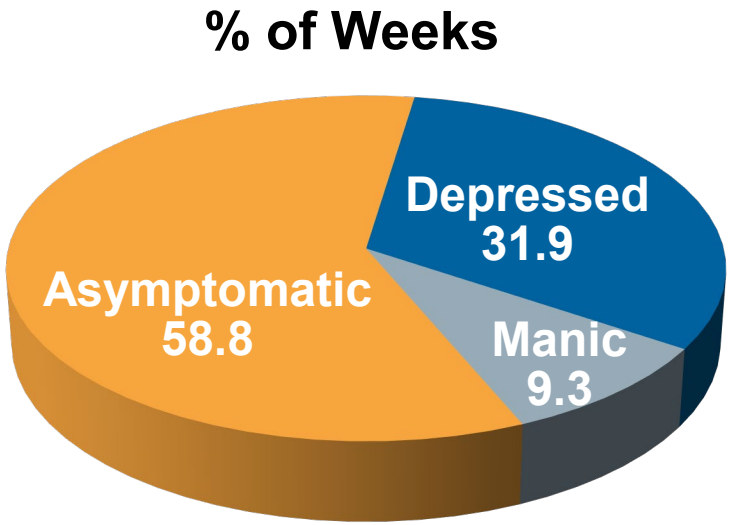
DSM-5: Inter-rater reliability of diagnoses from the initial field trials (adult diagnoses)



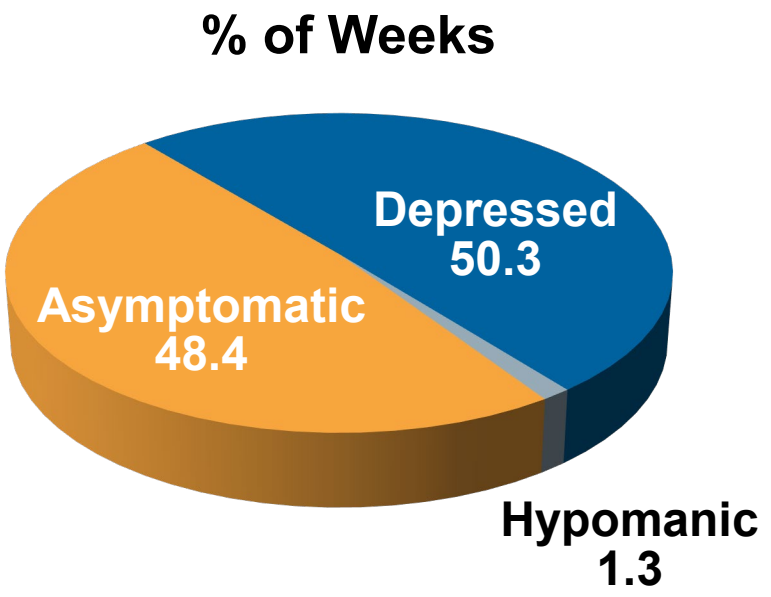
Pooled data presented from DSM-5 field trial sites, except for the diagnosis of complex somatic symptoms disorder revised, hoarding disorder, binge eating disorder, schizoaffective disorder, attenuated psychotic symptoms syndrome, bipolar II disorder, obsessive–compulsive disorder, antisocial personality disorder, and generalized anxiety disorder

Regier DA, *et al. Am J Psychiatry.* 2013;170:59–70; Freedman R, *et al. Am J Psychiatry.* 2013;170:1–5;
American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders.* 5th ed. Arlington, VA: American Psychiatric Association; 2013.

Time Spent Depressed: BD-I vs BD-II



BD-I
Depression:Mania 3:1 (N=146)

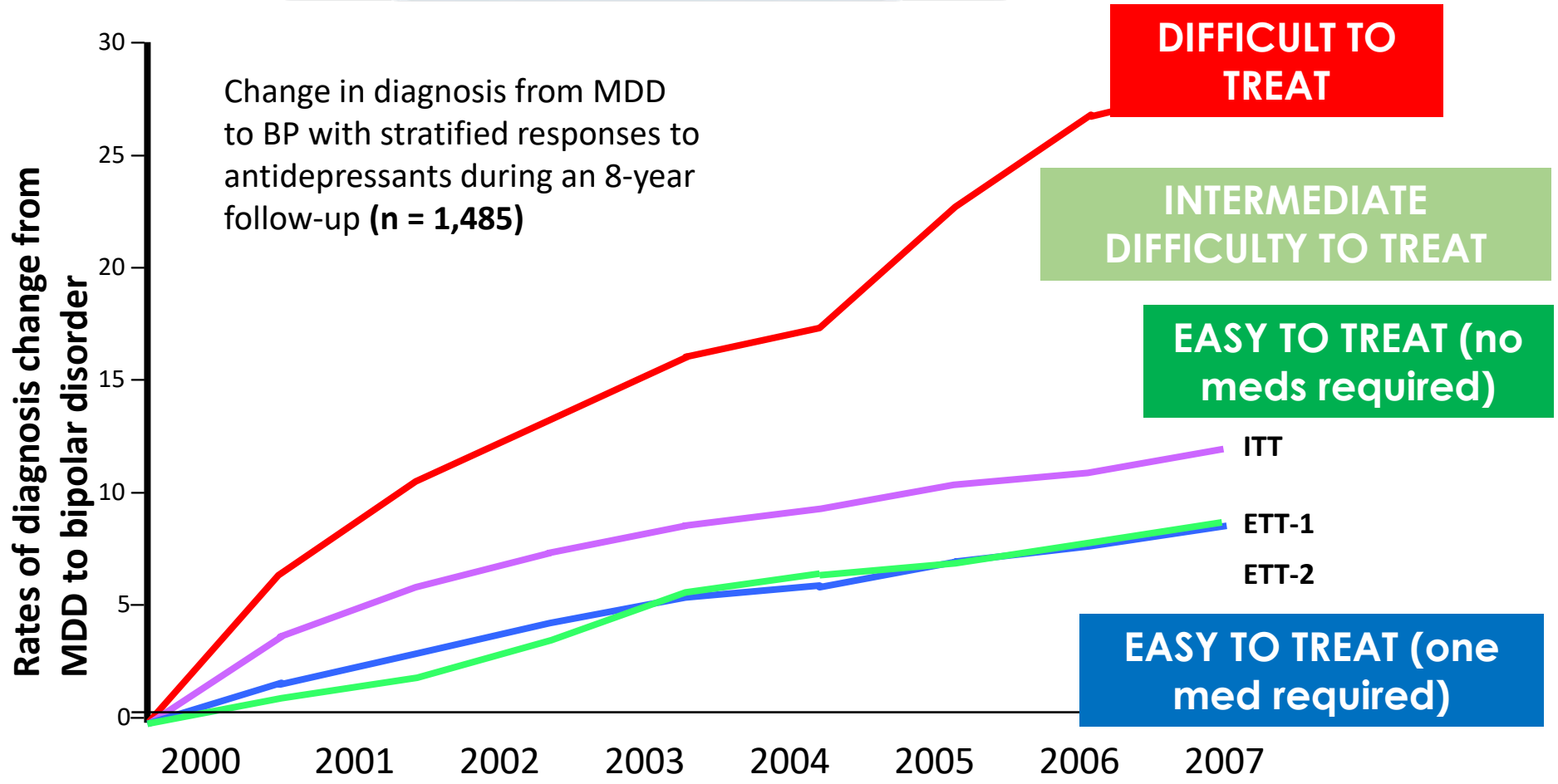


BD-II
Depression:Hypo-Mania 37:1 (N=71)
Higher Morbidity, Chronicity

BD-I = bipolar I disorder; BD-II = bipolar II disorder; NIMH = National Institute of Mental Health.

Judd LL, et al. *Arch Gen Psychiatry*. 2002;59(6):530-537. Judd LL, et al. *Arch Gen Psychiatry*. 2003;60(3):261-269.

Is Antidepressant Resistance a Predictor of Bipolar Disorder?



Participants with medication-resistant history (difficult-to-treat group [DTT]) without any antidepressant use (easy-to-treat group 1 [ETT-1]) or those without any change in antidepressant (easy-to-treat group 2 [ETT-2]). Participants who changed antidepressant just once, after an adequate antidepressant trial (intermediate level of difficulty to treat [ITT])

MDD = major depressive disorder

Li CT, et al. Br J Psychiatry 2012; 200(1):45-51.

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Adults with Bipolar Disorder: A Pilot Study

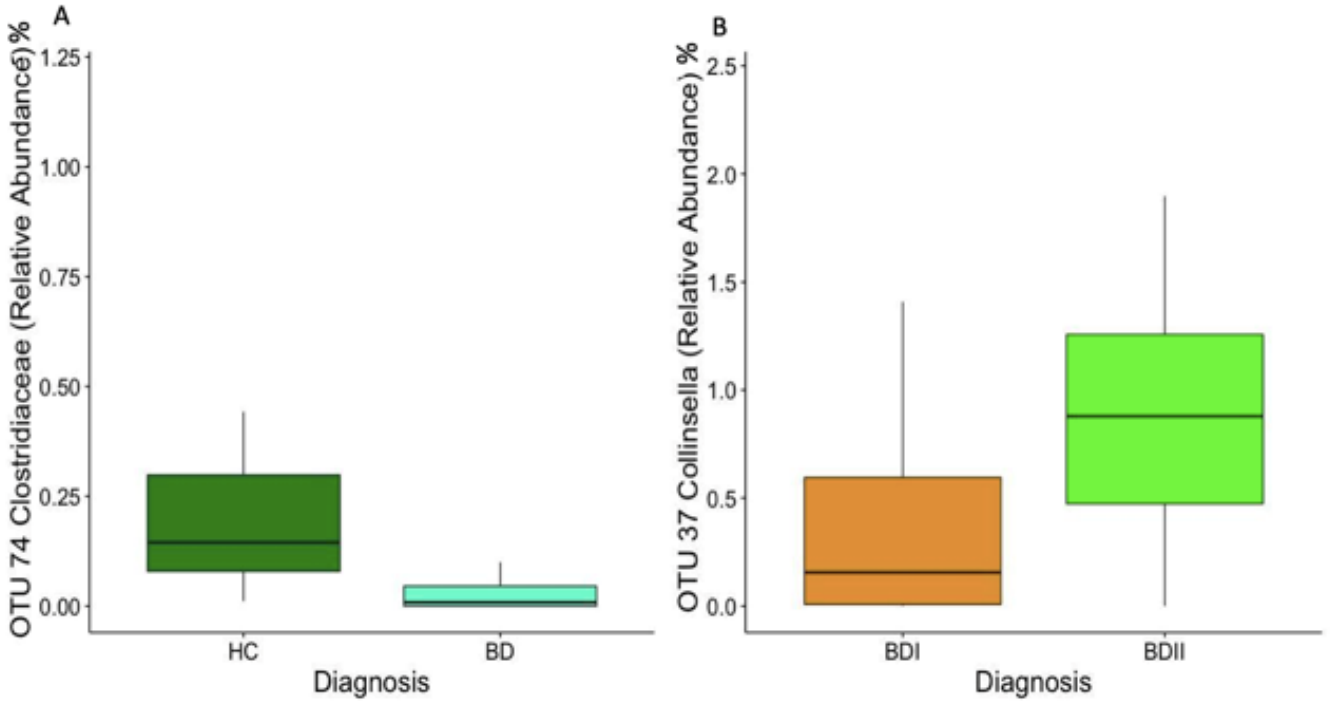
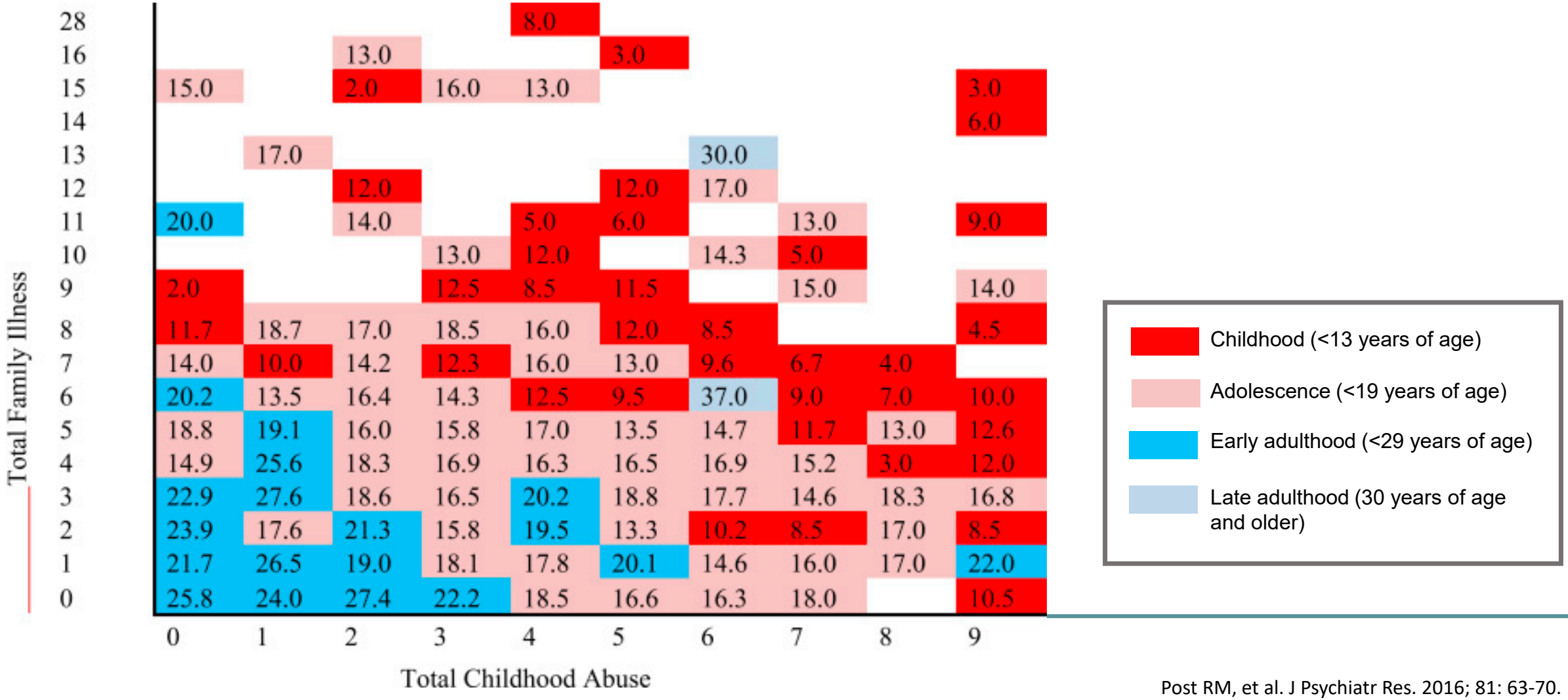


Figure 3: Boxplots comparing the relative abundance of the family and genera whose abundance was found to differ significantly when comparing BD patients to healthy volunteers (*Clostridiaceae*) and BD I and BD II patients (*Collinsella*). The abundance of these OTUs was identified as being significantly different between participant groups at a level of $p < 0.05$ following Bonferroni multiple testing correction.

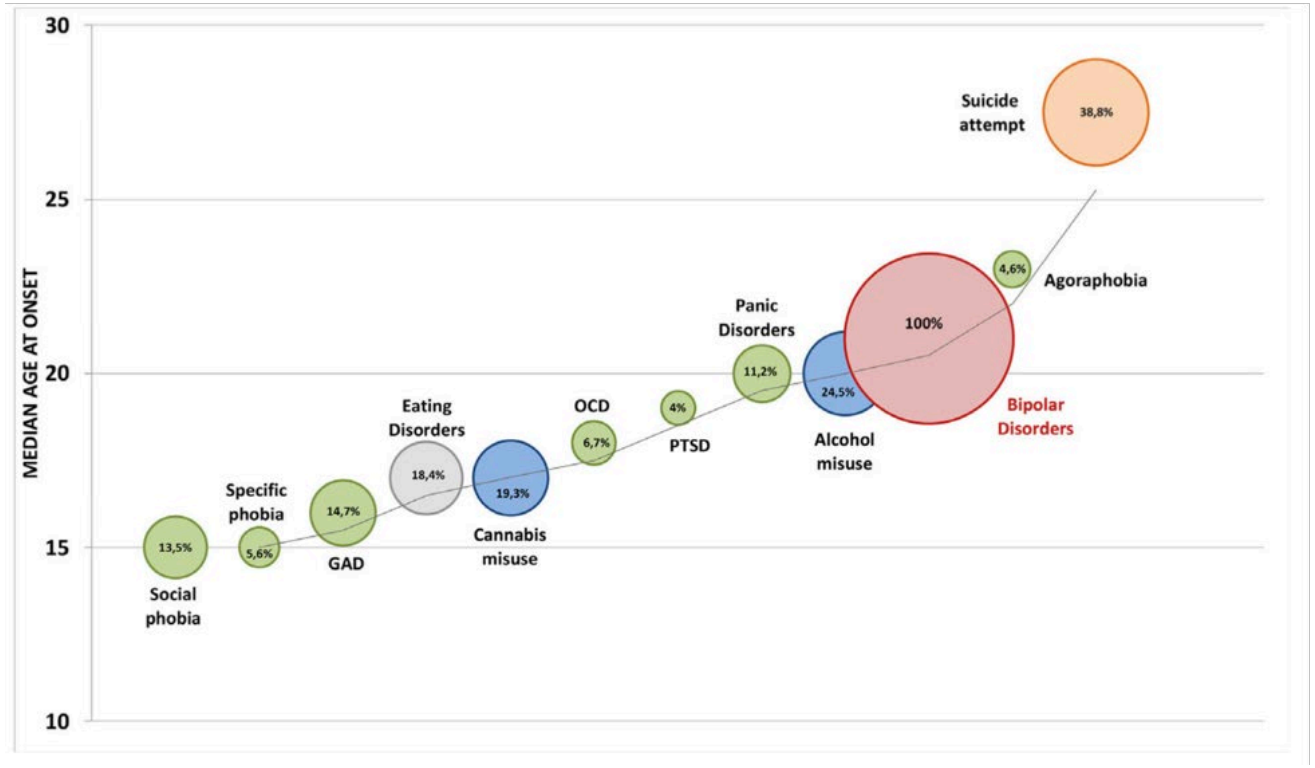
Young Age of Onset of Affective Instability Especially in Context of Trauma Should Raise Suspicions of Bipolar Spectrum



Post RM, et al. J Psychiatr Res. 2016; 81: 63-70.

Influence of Childhood Maltreatment on Prevalence, Onset, and Persistence of Psychiatric Comorbidities and Suicide Attempts in Bipolar Disorders

Diagrammatic Representation of the Prevalence and Age at Onset (AAO) of Disorders



The location of the bubble on the vertical axis indicates the median AAO of each disorder. The size of each bubble is proportional to the prevalence of the disorder (e.g., the size of the bubble for bipolar disorders corresponds to 100%), with each percentage being indicated inside the bubble. Red: bipolar disorder; Blue: substance (alcohol and cannabis) use disorders; Green: anxiety disorders; Gray: eating disorders; and Orange: suicide attempts. GAD, generalized anxiety disorder; OCD, obsessive–compulsive disorder; PTSD, post-traumatic stress disorder.

Grillault Laroche D, et al. Eur Psychiatry. 2022;65(1):e15.

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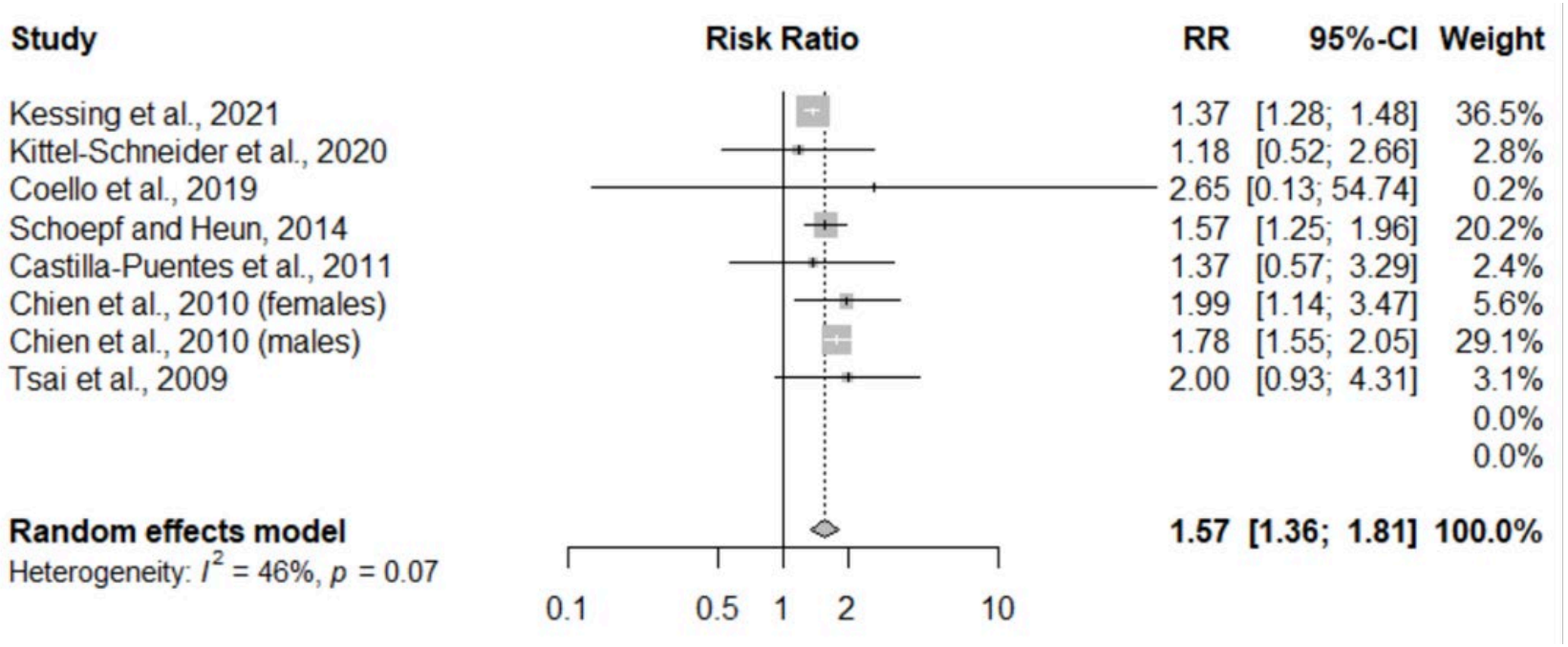
Prevalence of Type 2 Diabetes Mellitus, Impaired Fasting Glucose, General Obesity, and Abdominal Obesity in Patients with Bipolar Disorder: A Systematic Review and Meta-Analysis

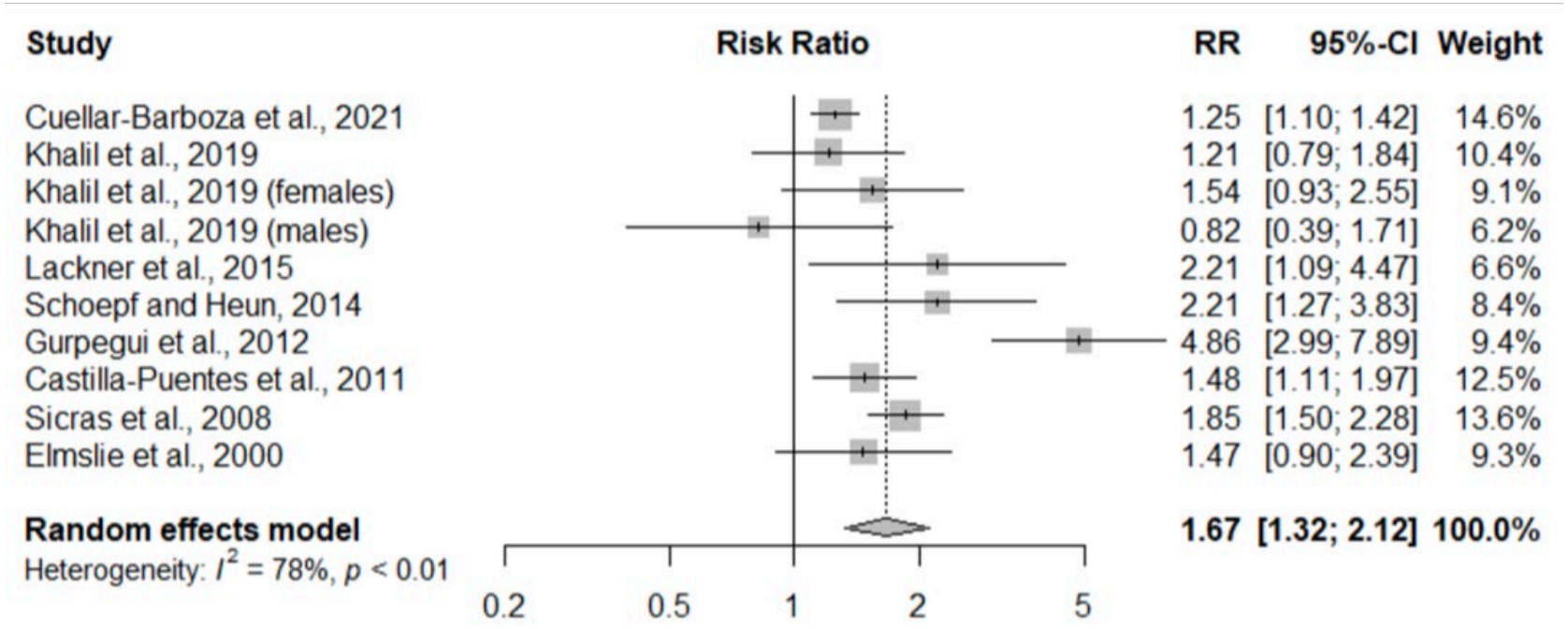
Relative risk of developing type 2 diabetes mellitus in bipolar patients and age- and gender-matched non-bipolar populations



Liu YK, et al. J Affect Disord. 2021 Dec 26;S0165-0327(21)01427-0.

Prevalence of Type 2 Diabetes Mellitus, Impaired Fasting Glucose, General Obesity, and Abdominal Obesity in Patients with Bipolar Disorder: A Systematic Review and Meta-Analysis

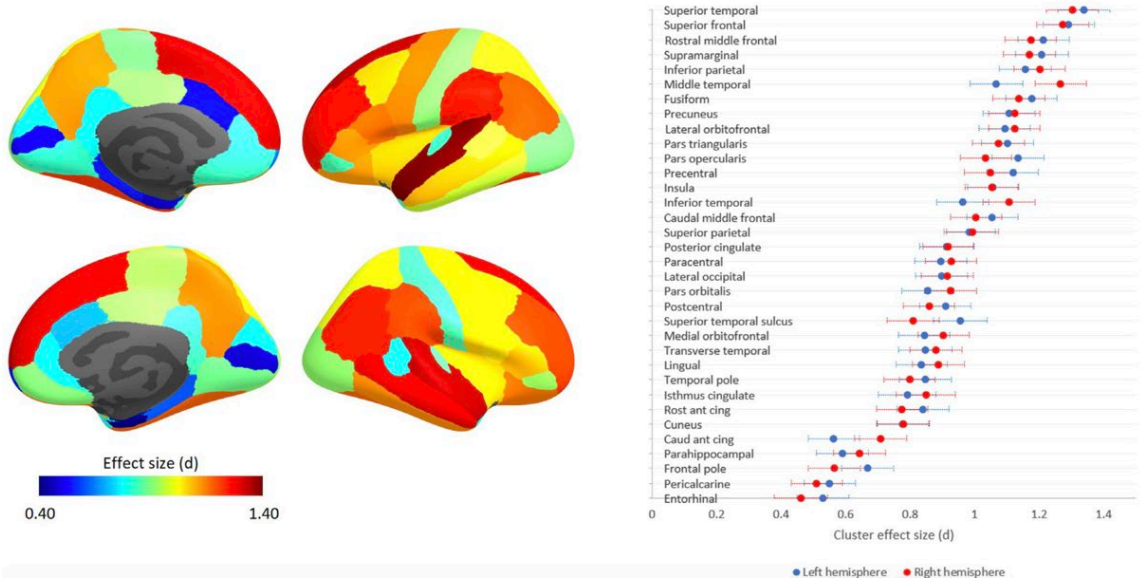
Relative risk of developing general obesity in bipolar patients and age- and gender-matched non-bipolar populations



Liu YK, et al. J Affect Disord. 2021 Dec 26;S0165-0327(21)01427-0.

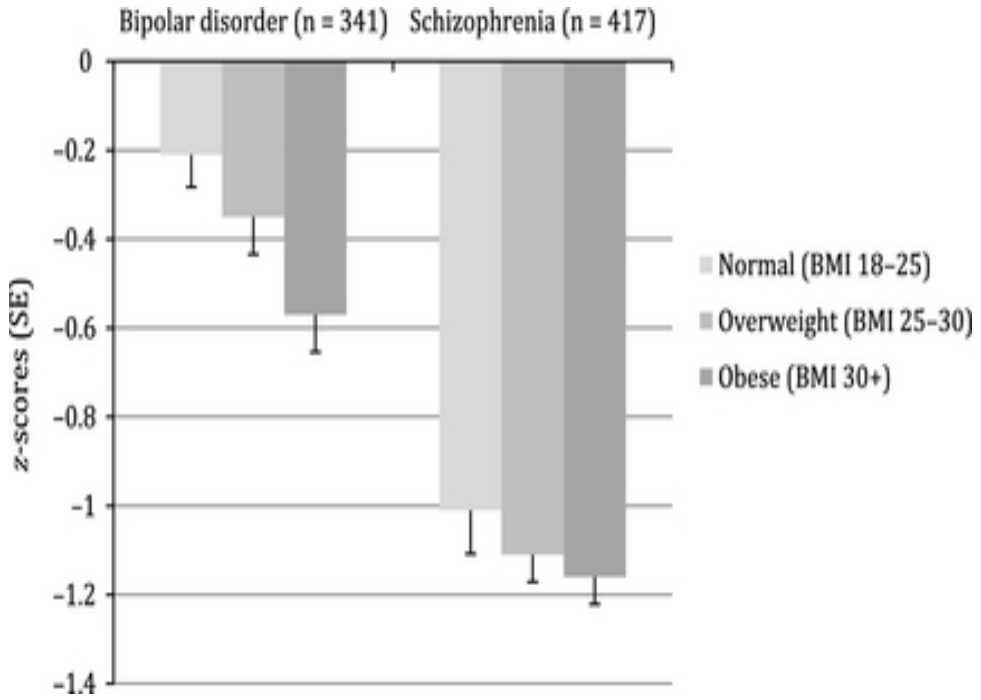
Diagnosis of Bipolar Disorders and Body Mass Index Predict Clustering Based on Similarities in Cortical Thickness-ENIGMA Study in 2436 Individuals

Effect Size (d) of Cortical Thickness Differences between Clusters in Each Brain Region



McWhinney SR, et al. Bipolar Disord. 2021. Online ahead of print.

Association of Obesity and Treated Hypertension and Diabetes with Cognitive Ability in Bipolar Disorder and Schizophrenia



Global cognitive ability by body mass index (BMI) level clustered by diagnosis. Error bars are standard errors (SE). Group comparisons: bipolar disorder: $F(2,338) = 5.2$, $p = 0.006$ [adjusted for education, Positive and Negative Syndrome Scale *negative* score, atypical antipsychotic use, and residential status: $F(2,320) = 18.2$, $p = 0.035$]; Tukey post hoc normal > obese; schizophrenia: $F(2,413) = 0.70$, $p = 0.482$. Effect size from lowest to highest BMI in bipolar disorder is Cohen's $d = 0.43$ compared to $d = 0.16$ for schizophrenia.

Depp, CA. et al. *Bipolar Disorders*. 2014; 16: 422-431.

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Expression of Insulin and Dopamine Genes in the Prefrontal Cortex Altered in Individuals who are Obese: Implications for Cognition and Reward

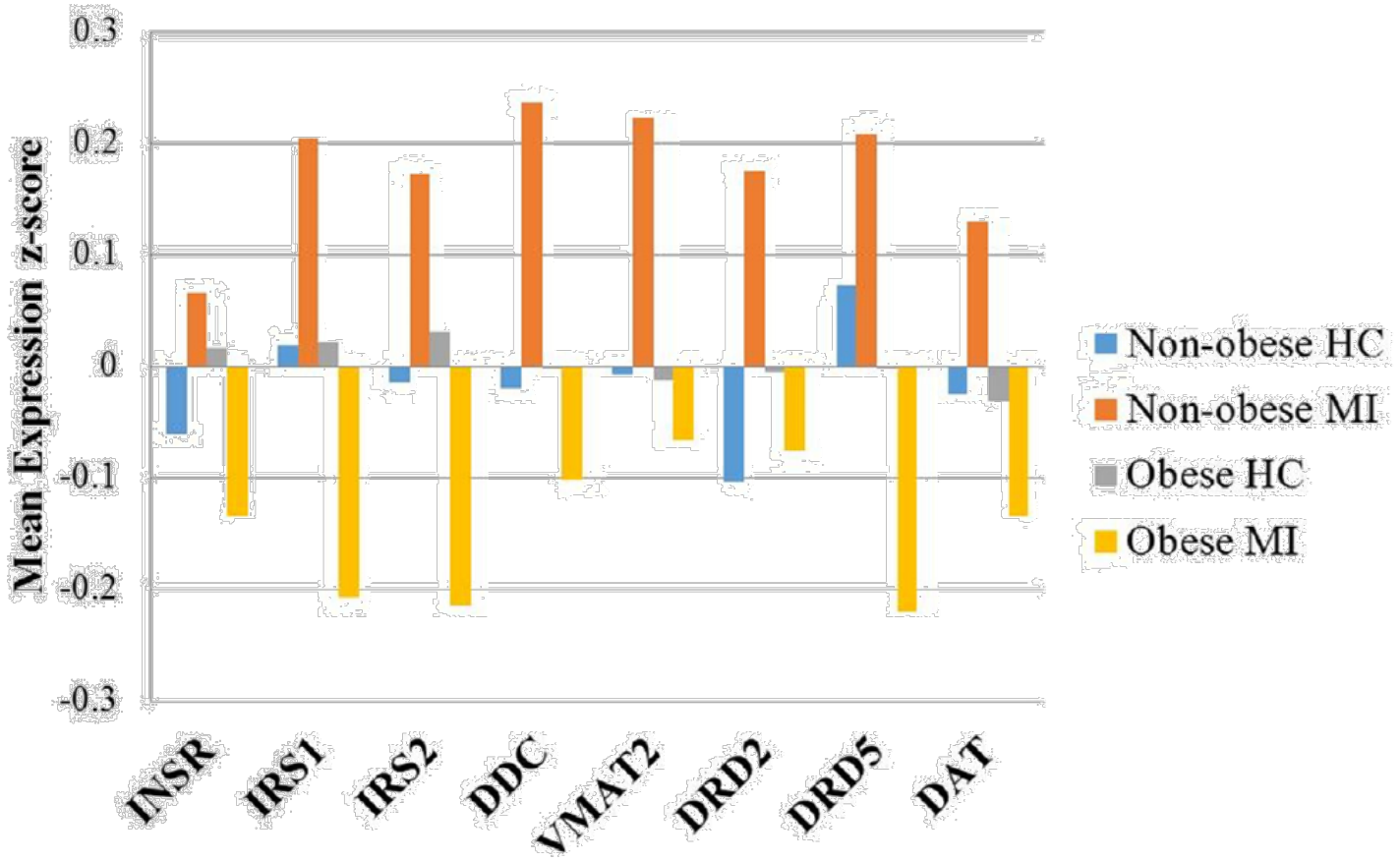

Fig. 1. Gene Expression in the Dorsolateral Prefrontal Cortex. Mean standardized expression values of insulin and dopamine signaling genes in the dorsolateral prefrontal cortex, according to group (HC vs. MI) and BMI. For illustration purposes, BMI was dichotomized as obesity (BMI ≥ 30 kg/m2) and non-obesity (BMI < 30 kg/m2). HC: healthy controls; MI: mental illness.

Mansur, R. B., Fries, G. R., Subramaniapillai, M., Frangou, S., Felice, F. G., Rasgon, N et al . (2018). *Journal of Psychiatric Research,107*, 128-135. doi:10.1016/j.jpsychires.2018.10.020

Canadian Rapid Treatment Center of Excellence

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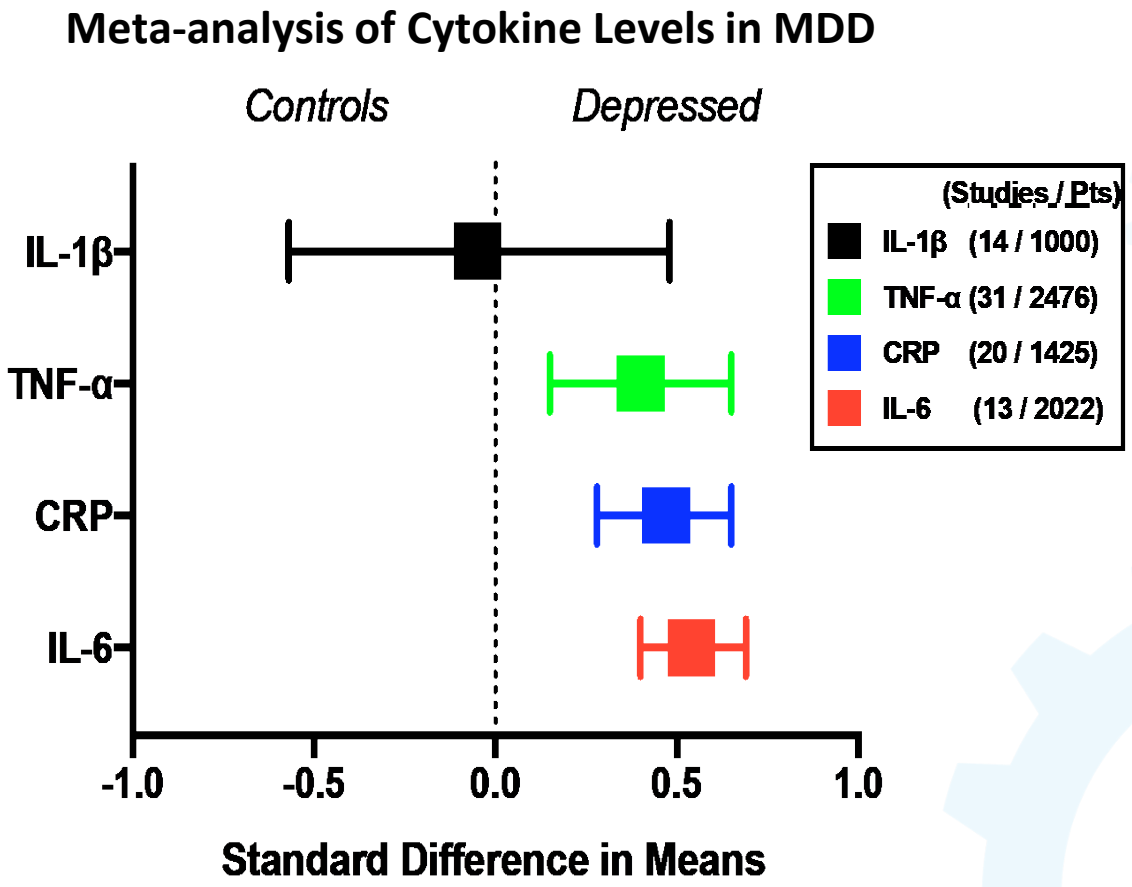
High Prevalence of Inflammation in Depression

- Cytokines = non-antibody proteins released by cells on contact with antigens
- Cytokines induce depressive symptoms and HPA axis activation
- Depressed patients have high levels of cytokines



Dunn AJ et al. *Neurosci Biobehav Rev*. 2005.
Yirimya R et al. *Ann NY Acad Sci*. 2000.
Haapkoski et al. *Brain Behav Immun.* 2014.

In vivo Phenotyping of Bipolar Disorder: Salient Domains

1. Psychopathological components of mania/hypomania
2. Psychopathological components of depression
3. Suicidality
4. Clinical subtypes
5. Onset and clinical course
6. Neurocognition
7. Social functioning
8. Clinical staging
9. Temperament and personality
10. Other antecedent and concomitant psychiatric conditions
11. Physical comorbidities
12. Family history
13. Early environmental exposures
14. Recent environmental exposures and relapse triggers
15. Protective factors and resilience
16. Internalized stigma

McIntyre RS, et al. World Psychiatry. 2022 Oct;21(3):364-387.

Misdiagnosis of Bipolar I Disorder

In a patient survey, 70% of patients with bipolar disorder reported being initially misdiagnosed.[1]

Because most patients with bipolar disorder seek care during a depressive episode, MDD is the most common misdiagnosis.[1]

Over half of patients who had been previously misdiagnosed had a delay of 5 years or more between seeking treatment and receiving the correct diagnosis; and over one third of patients had a delay of 10 years or more.[1,2]

MDD = major depressive disorder.

1. Hirschfeld MA, et al. *J Clin Psychiatry.* 2003;64(2):161-174. 2. Lish JD, et al. *J Affect Disord*. 1994;31(4):281-294.

Timely and Accurate Diagnosis of Bipolar Disorder Is Critical: Screening Using the Rapid Mood Screener www.rapidmoodscreener.com

Item	Response	
1. Have there been at least 6 different periods of time (at least 2 weeks) when you felt deeply depressed?	Yes	No
2. Did you have problems with depression before the age of 18?	Yes	No
3. Have you ever had to stop or change your antidepressant because it made you highly irritable or hyper?	Yes	No
4. Have you ever had a period of at least 1 week during which you were more talkative than normal with thoughts racing in your head?	Yes	No
5. Have you ever had a period of at least 1 week during which you felt any of the following: unusually happy; unusually outgoing; or unusually energetic?	Yes	No
6. Have you ever had a period of at least 1 week during which you needed much less sleep than usual?	Yes	No

Highest estimated accuracy was observed with ≥4 "yes" responses

- RMS sensitivity was 0.88 and specificity was 0.80; concordance index 0.87
- MDQ sensitivity was 0.86 and specificity was 0.78; concordance index 0.82

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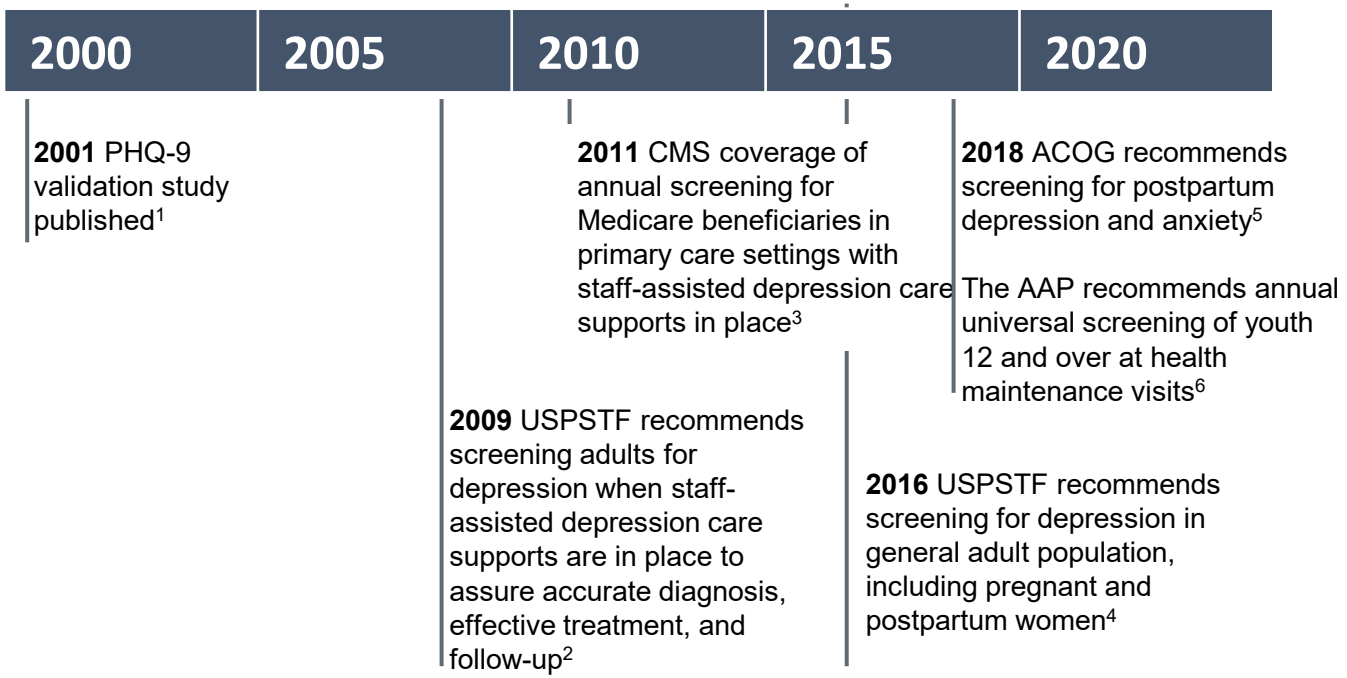
McIntyre RS et al. Curr Med Res Opin 2021;37(1):135-44.

Brain and Cognition DISCOVERY FOUNDATION

Widespread Implementation of PHQ-9 Screening for Depression Following the US Preventative Health Task Force Recommendation



- Since CMS recognition of depression screening as a quality measure, many health systems/ACOs are implementing or enhancing screening in primary care settings[7]
  - 59% of patients had ≥1 screen with the PHQ-2 or PHQ-9 following implementation of a systematic depression screening initiative in a large health system[8]

While use of the PHQ-2 and PHQ-9 are growing, these assess for the presence of current depressive symptoms that may be associated with a major depressive episode, and **do not distinguish between bipolar disorders from major depressive disorder.**[9]

AAP = American Academy of Pediatrics; ACO = Accountable Care Organization; ACOG = American College of Obstetricians and Gynecologists; CMS = Centers for Medicare & Medicaid Services; PHQ = Patient Health Questionnaire; USPSTF = U.S. Preventive Services Task Force.

1. Kroenke K, Spitzer RL, Williams JBW. *J Gen Intern Med*. 2001;16:606-613. 2. USPSTF. *Ann Intern Med*. 2009;151(11):784-792. 3. CMS. https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?ncdid=346&ncdver=1. Effective October 14, 2011. Accessed August 30, 2022. 4. Siu AL, USPSTF. *JAMA*. 2016;315(4):380-387. 5. ACOG Committee Opinion No. 757. *Obstet Gynecol*. 2018;132(5):e208-e212. 6. Zuckerbrot RA, Cheung A, Jensen PS, et al. *Pediatrics*. 2018;141(3):e2017408. 7. Fullerton CA, Henke RM, Crable EL, Hohlbauch A, Cummings N. *Health Aff* (Millwood). 2016;35(7):1257-1265. 8. Pfoh E, Janmey I, Anand A, et al. *J Gen Intern Med*. 2020;35(11):3141-3147. 9. Hirschfield RM. *J Affect Disord*. 2014;169 Suppl 1:S12-S16.

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14. Recent environmental exposures and relapse triggers
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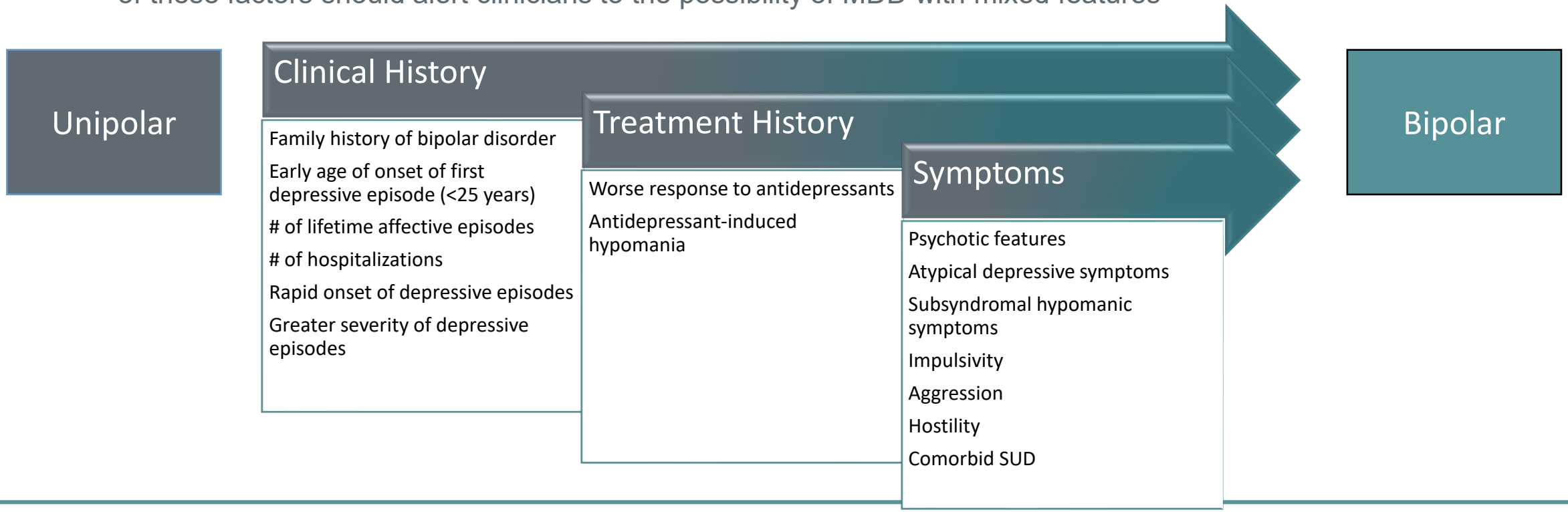
16. Internalized stigma

McIntyre RS, et al. World Psychiatry. 2022 Oct;21(3):364-387.

Probabilistic Approach to Diagnosis

- A ‘probabilistic’ approach may help identify patients who are more likely to have bipolar mood disorders
  - Many factors are more common in BPD than in unipolar depression
  - The presence of any of these probabilistic factors is not necessarily indicative of mixed states, but accumulation of these factors should alert clinicians to the possibility of MDD with mixed features



McIntyre RS, et al. *Lancet* 2020: S0140-6736(20)31544-0.

The “4 As” Increase Suspicion of Mixed Features

Mixed episode

- Described in the DSM-IV-TR
- Requires an individual to simultaneously meet the criteria for a major depressive episode and a manic episode

Mixed features specifier

- Described in the DSM-5
- Can be applied to episodes of major depression, mania, and hypomania
- Requires the presence of at least 3 manic or hypomanic non-overlapping symptoms during a major depressive episode
- Requires the presence of at least 3 depressive non-overlapping symptoms during a hypomanic or manic episode

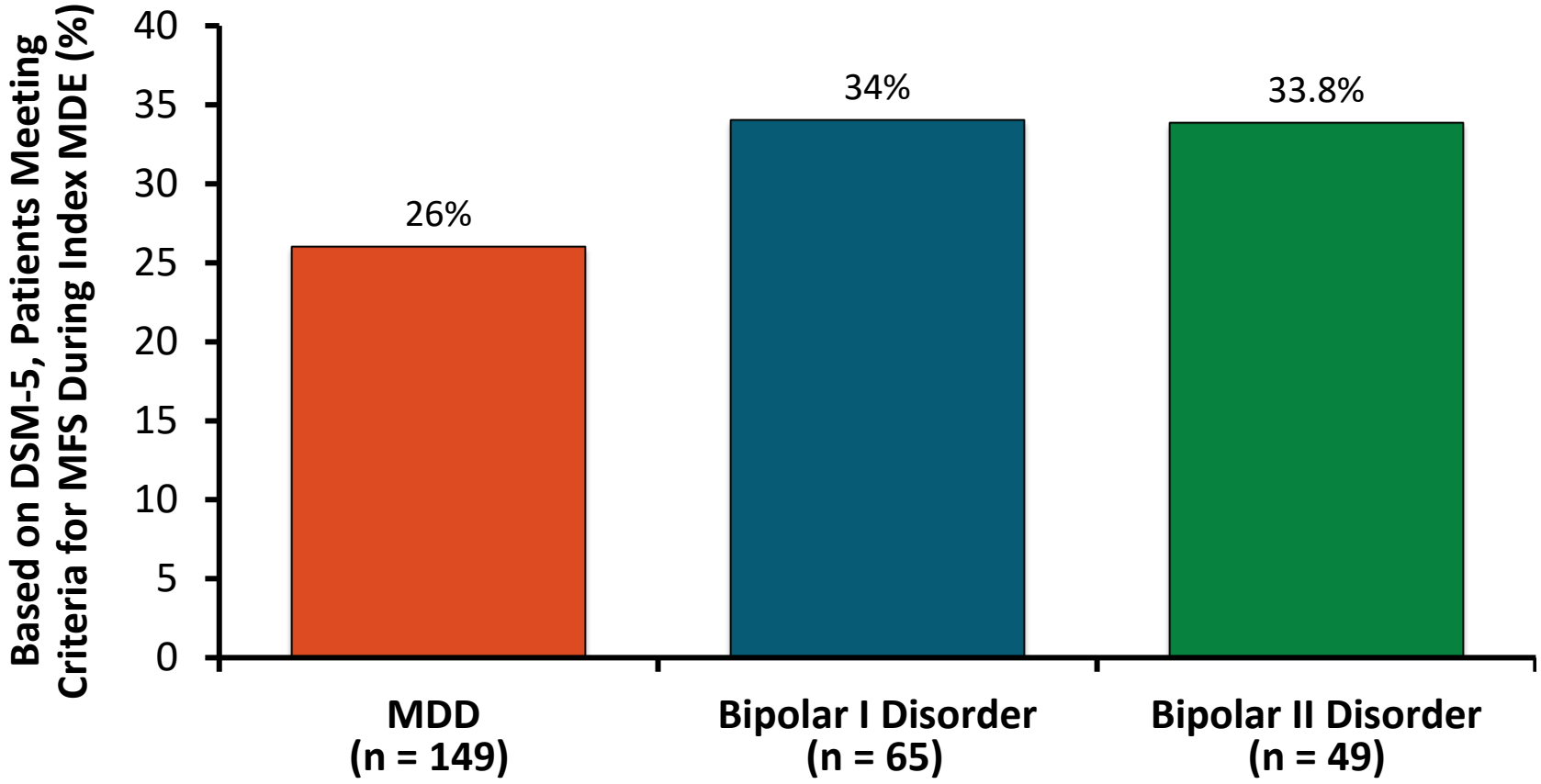
Healthcare professionals should be aware of the **“4 As”**:

- Anxiety
- Agitation
- Anger/irritability
- Attentional disturbance-distractibility

These symptoms are highly suggestive of mixed features in individuals with mood disorders

McIntyre et al. Lancet. 2020;396:1841.

Prevalence of Mixed Features in Mood Disorders



N = 852 patients who met criteria for a current mood episode as part of MDD or bipolar disorder. MFS was defined as a score ≥1 on 3 or more items on YMRS or ≥1 on 3 items of the MADRS or HAM-D-17 during an index MDE.

McIntyre et al. J Affect Disord. 2014;12:259.

Treatments Reported to Be Efficacious Across the Various Phases of Bipolar Disorder

ACUTE BIPOLAR DEPRESSION

Treatments APPROVED by the FDA

- Cariprazine
- Lumateperone
- Lurasidone
- Quetiapine
- Olanzapine/fluoxetine

Treatments not approved by the FDA

- Lithium
- Lamotrigine
- Antidepressants
- Electroconvulsive therapy
- Repetitive transcranial magnetic stimulation (rTMS)

ACUTE MANIA

All treatments APPROVED by the FDA, except for*

- Lithium
- Divalproex
- Carbamazepine
- Aripiprazole
- Asenapine
- Cariprazine
- Chlorpromazine
- Haloperidol*
- Olanzapine
- Olanzapine Samidorphan
- Paliperidone*
- Quetiapine
- Risperidone
- Ziprasidone
- Combination treatment with either aripiprazole, asenapine, olanzapine, quetiapine, or risperidone, and lithium or divalproex

MAINTENANCE

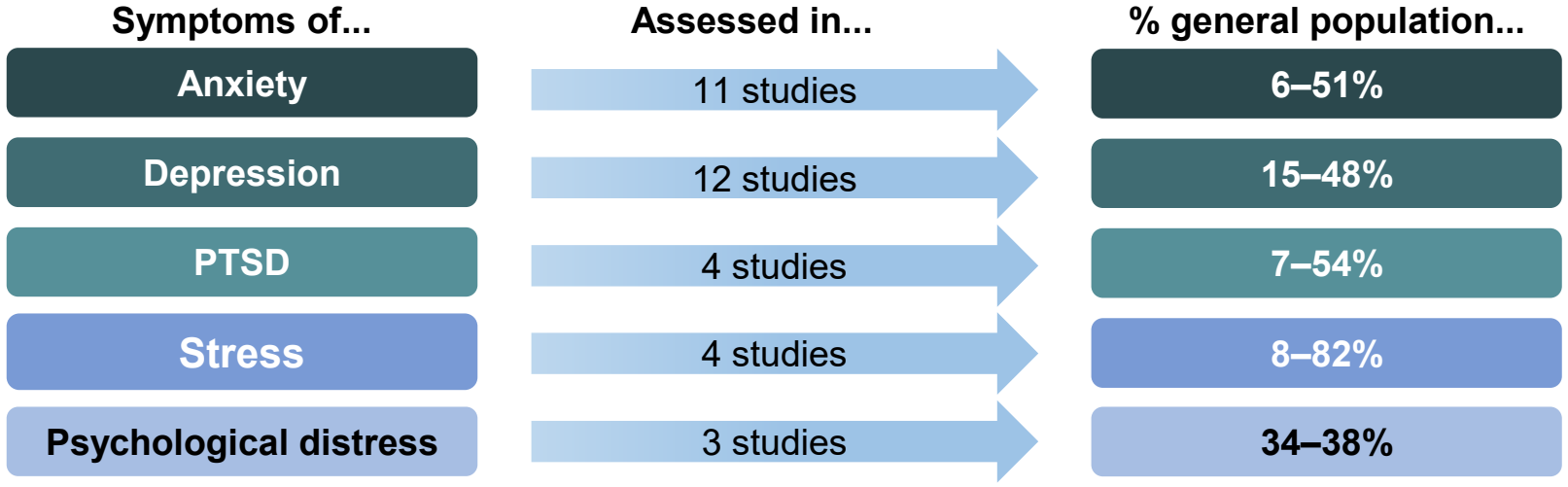
All treatments APPROVED by the FDA, except for*

- Lithium
- Aripiprazole (oral and long-acting injectable)
- Asenapine
- Lamotrigine
- Paliperidone*
- Quetiapine (adjunctive)
- Olanzapine
- Olanzapine Samidorphan
- Risperidone (long-acting injectable)

McIntyre RS et al. Lancet 2020;396(10265):1841-56.

COVID-19 Is Associated With Significant Increase in the Rate of Mental Disorders in the General Population

In a systematic review of 19 studies in 8 countries*, the COVID-19 pandemic is associated with psychological distress in the general population to the extent that would often meet the threshold for clinical relevance



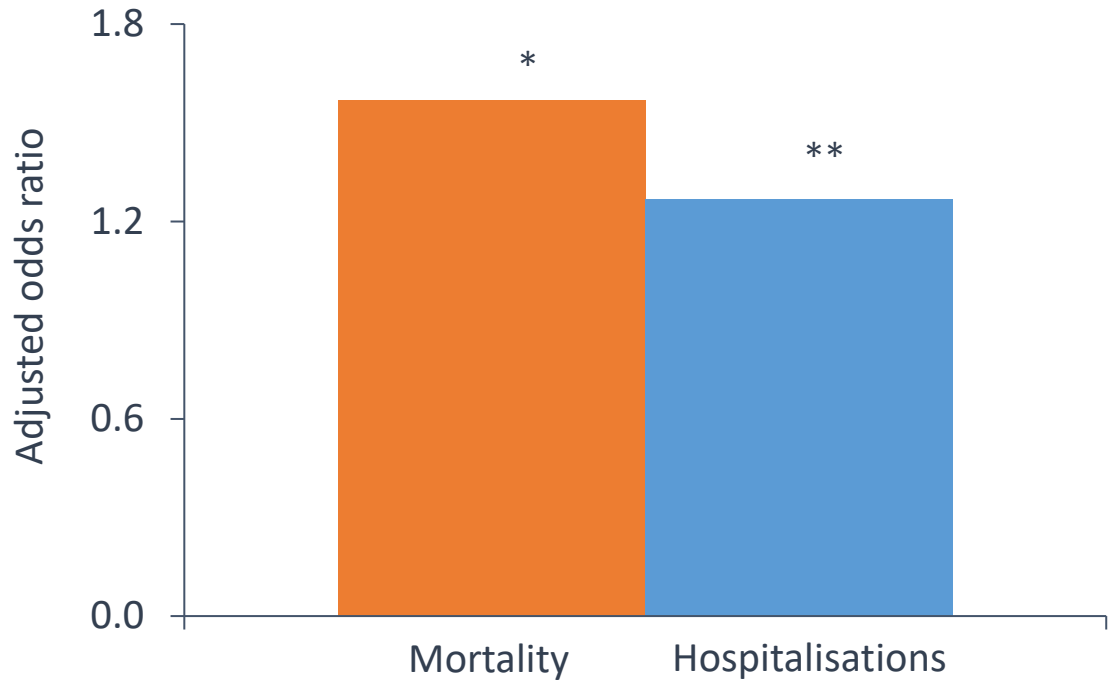
Mitigating the hazardous effects of COVID-19 on mental health is an international public health priority

Xiong J et al. J Affect Disord 2020;277:55-64.

*China, Denmark, Iran, Nepal, Spain, Turkey, US and Nepal.
COVID-19, coronavirus disease 2019; PTSD, post-traumatic stress disorder.

Individuals with Pre-existing Mood Disorders are at Higher Risk of COVID-19 Hospitalisation and Death

Odds ratios for COVID-19 hospitalisations and mortality in mood disorders



Adapted from: Ceban F, *et al. JAMA psychiatry*. 2021;78(10):1079–1091.

These results suggest that **individuals with mood disorders**, like persons with other pre-existing conditions (e.g., obesity), **should be categorised as an at-risk group** on the basis of a pre-existing condition.

*Statistically significant odds ratio (p<0.001)
**Statistically significant odds ratio (p=0.002)

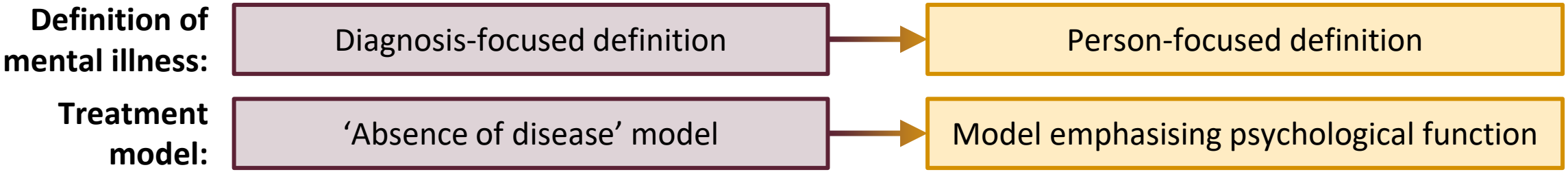
This Systematic Review and Meta-analysis included 21 studies with more than 91 million individuals to assess whether preexisting mood disorders are associated with a higher risk of COVID-19 susceptibility, hospitalization, severe complications, and death

COVID-19: Coronavirus disease 2019.

Ceban F, *et al. JAMA psychiatry*. 2021;78(10):1079–1091.

Definitions of ‘mental health’ have evolved over time[1]

- Definitions of wellness and illness have changed from the mid-20th century to the present day[1]



- In recent decades, measures of **psychological functioning, well-being and hope have emerged[1]**
- Recently, psychological well-being has been investigated in many studies, demonstrating that **the absence of mental distress does not guarantee the presence of well-being[1]**

1- Manderscheid RW, Ryff CD, Freeman EJ, McKnight-Eily LR, Dhingra S, Strine TW. Evolving definitions of mental illness and wellness. Prev Chronic Dis. 2010 Jan;7(1):A19. Epub 2009 Dec 15. PMID: 20040234; PMCID: PMC2811514.

Patient-Reported Outcome Measures for Life Engagement in Mental Health: A Systematic Review

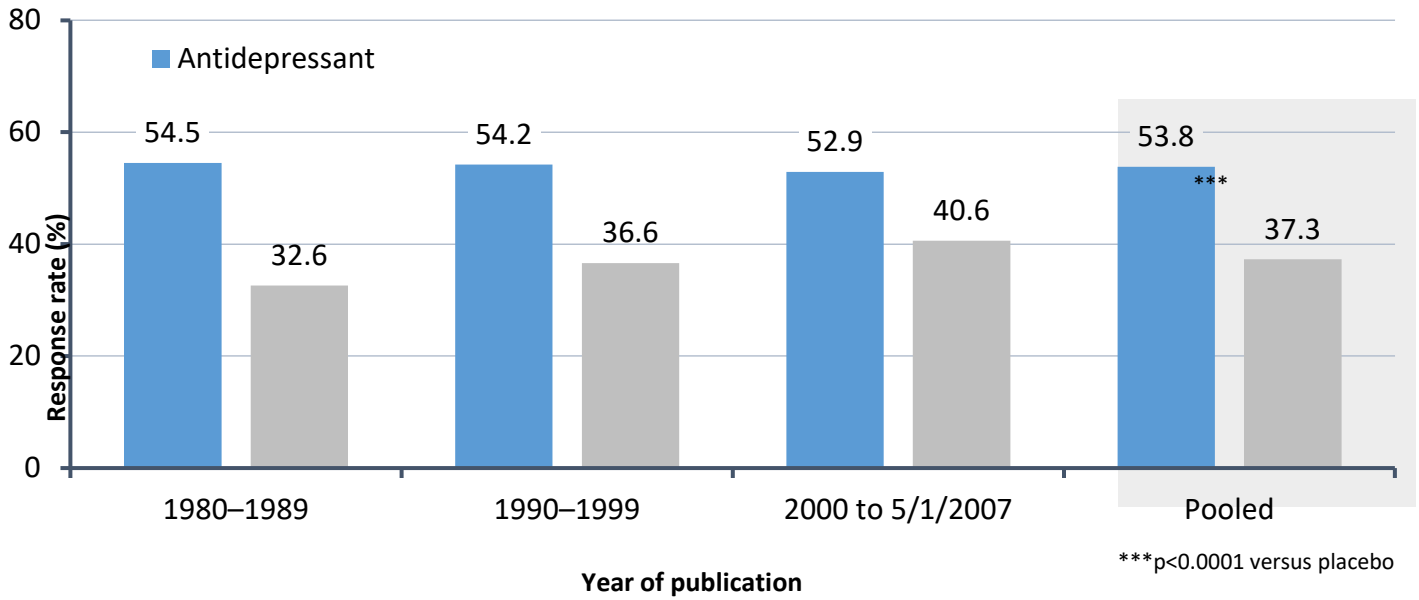
Concept/theme	Name of PRO [primary source]	Number of hits
Life engagement	Engaged Living Scale (ELS)	1
	Life Engagement Test (LET)	1
Work/occupation engagement/vigor	Utrecht Work Engagement Scale (UWES) Short version (UWES-9)	7
	Profles of Occupational Engagement in Severe mental illness—Productive occupations (POES-P	3
	Shirom–Melamed Vigor Measure (SMVM)	1
Motivation/reward/ energy–apathy	Behavioral Activation System (BAS) scale	28
	Apathy Evaluation Scale Self-report (AES-S) Short version	14
	Motivation and Pleasure Scale—Self-Report (MAP-SR)	7
	Sensitivity to Reward (SR) scale	4
	Rewarding Events Inventory (REI)	3
	Motivation and Energy Inventory (MEI)	1
	Environmental Reward Observation Scale (EROS)	1
	Motivational Trait Questionnaire (MTQ)	1
	Reward Responsiveness (RR)	1
	Work Extrinsic and Intrinsic Motivation Scale (WEIMS)	1
	MacCarthy Task Motivation Scale (MCTMS)	1
Pleasure–anhedonia	Revised Chapman Physical and Social Anhedonia Scales (PAS/SAS)	36
	Snaith–Hamilton Pleasure Scale (SHAPS)	33
	Temporal Experience of Pleasure Scale (TEPS)	29
	Fawcett–Clarke Pleasure Capacity Scale (FCPCS)	6
	Anticipatory and Consummatory Interpersonal Pleasure Scale (ACIPS)	5
	Hedonic Defcit & Interference Scale (HDIS)	2
	Dimensional Anhedonia Rating Scale (DARS)	2
	Domains of Pleasure Scale (DOPS)	1
	Specifc Loss of Interest and Pleasure Scale (SLIPS)	1

Concept/theme	Name of PRO [primary source]	Number of hits
Attention/alertness	Attentional Control Scale (ACS)	14
	Mindful Attention Awareness Scale (MAAS)	3
	Everyday Life Attention Scale (ELAS)	2
	Emotional Attentional Control Scale (eACS) (adaptation of ACS)	1
	Toronto Hospital Alertness Test (THAT)	1
Connectedness/social well-being	Keyes Social Well-Being (SWB) scale	3
	Social Connectedness Scale—Revised (SCS-R)	2
	Autonomy–Connectedness Scale, 30-item version (ACS-30)	1
Mental/psychological well-being	Warwick–Edinburgh Mental Well-Being Scale (WEMWBS)	16
	Short version (SWEMWBS)	
	WHO (Five) Well-Being Questionnaire (WHO-5)	14
	Ryf's scales of Psychological Well-Being (PWB)	12
	Mental Health Continuum Short Form (MHC-SF)	3
	Flourishing Scale (FS)	3
	Comprehensive Inventory of Thriving (CIT)	1
	Psychological General Well-Being Index (PGWBI)	1
	Inventory of General Life Functioning (GLF) (adaptation of PGWBI)	1
Life satisfaction/ meaning	Satisfaction With Life Scale (SWLS)	16
	Personal Well-being Index (PWI)	3
	Meaning in Life Questionnaire (MLQ)	2
Calmness–arousal	Stress Arousal Checklist (SACL)	1
Rumination	Ruminative Response Scale (RRS) Revised version	20
	Ruminative Thought Style Questionnaire (RTSQ)	4
	Leuven Adaptation of the Rumination on Sadness Scale (LARSS)	1
	Mini Cambridge–Exeter Repetitive Thought Scale (Mini-CERTS)	1

McIntyre RS, et al. J Patient Rep Outcomes. 2022 Jun 10;6(1):62.

Monoaminergic Antidepressant Response Rates Have Not Improved Over Many Years: Innovative Treatments Urgently Required

Antidepressant response rates over time

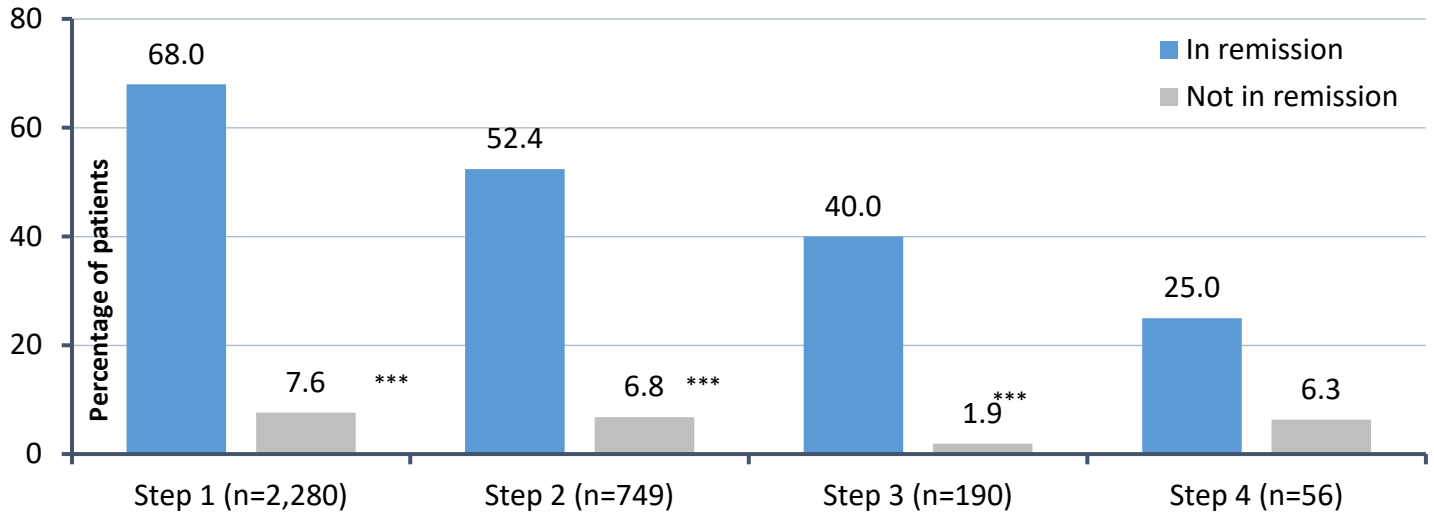


Additionally, in 2015, it was reported that antidepressant clinical trials had an effect size of only 0.3[3]

Han et al. Expert Rev Neurother 2013;13(7):851–870; 2. Papakostas & Fava. Eur Neuropsychopharmacol 2009;19(1):34–40; 3. Khan & Brown. World Psychiatry 2015;14(3):294–300

Monoaminergic Antidepressants Exerts Insufficient Effects on Quality of Life

Percentage of patients achieving a normal quality of life



***p<0.001 versus patients in remission; 'normal' quality of life defined as Q-LES-Q short-form score within 10% of community norms (≥70.47); remission defined as a QIDS-SR score ≤5

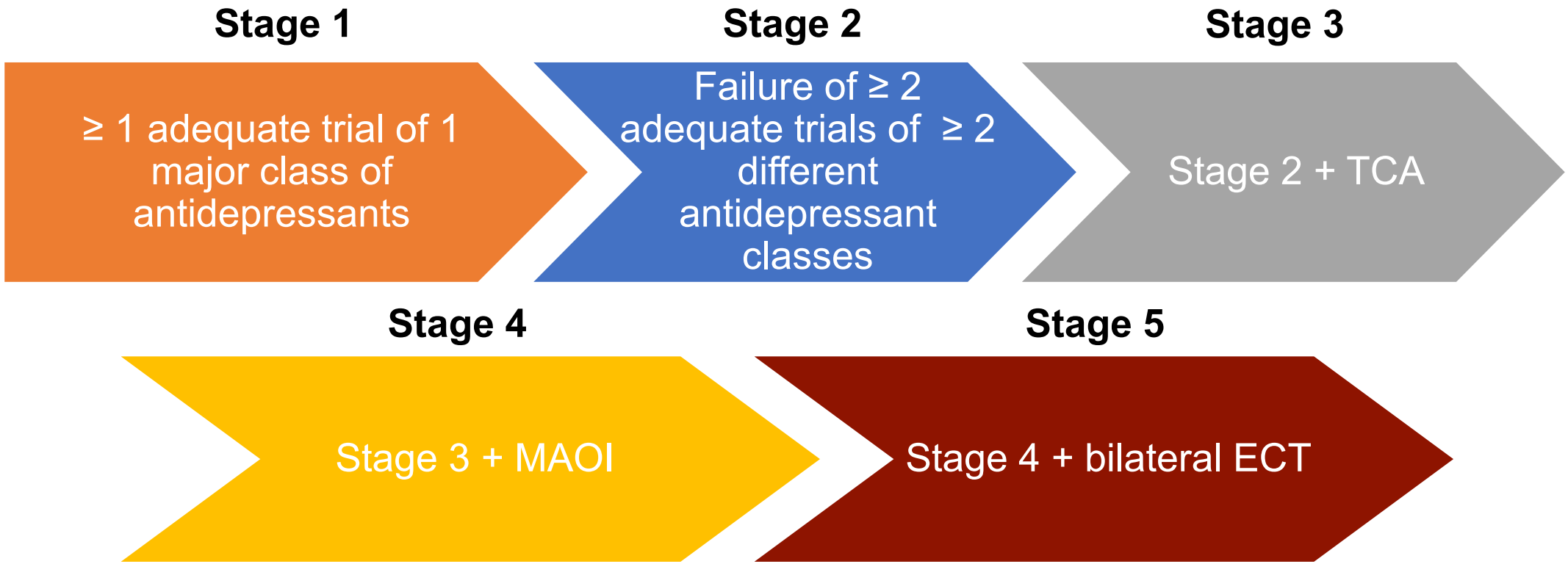
QIDS-SR=Quick Inventory of Depressive Symptomatology-Self Report; Q-LES-Q=Quality of Life, Enjoyment, and Satisfaction Questionnaire; STAR*D=Sequenced Treatment Alternatives to Relieve Depression

In the STAR*D study, patients who did not achieve remission were less likely to achieve a normal quality of life – even with multiple treatment steps

IsHak et al. Acta Psychiatr Scand 2015;131(1):51–60

Thase and Rush System for Staging Resistance to Antidepressants

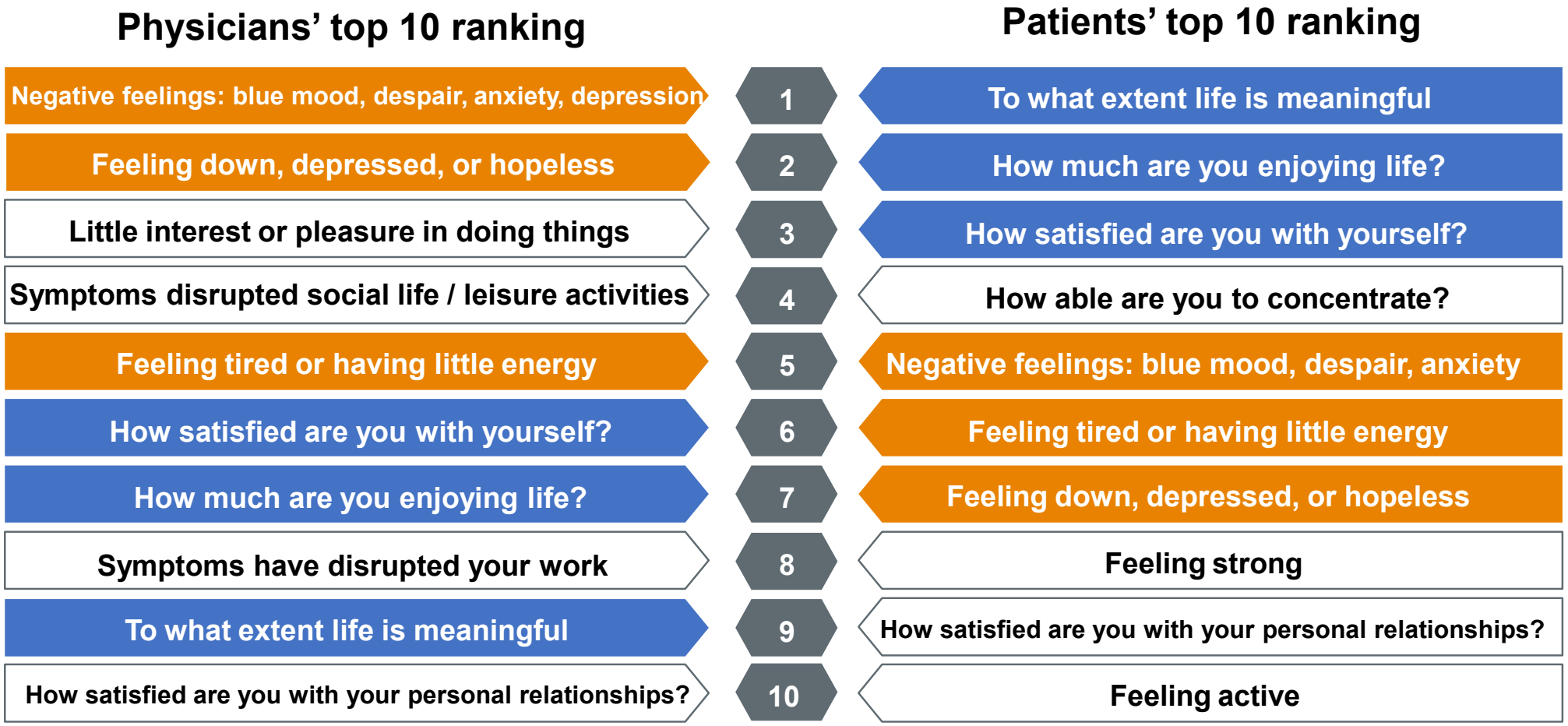
Stages of resistance after failures of different classes and types of treatment



ECT: electroconvulsive therapy; MAOI: monoamine oxidase inhibitor; TCA: tricyclic antidepressant.

Thase ME, Rush AJ. J Clin Psychiatry 1997;58(Suppl 13):23-9.

HCPs Mainly Focus on Alleviation of Depressive Symptoms, Whereas Patients Focus on the Restoration of Positive Affect



Demyttenaere K et al. J Affect Dis 2015;174:390-6.

Positive affect items Depressive items

HCPs: healthcare practitioners

CRTCE

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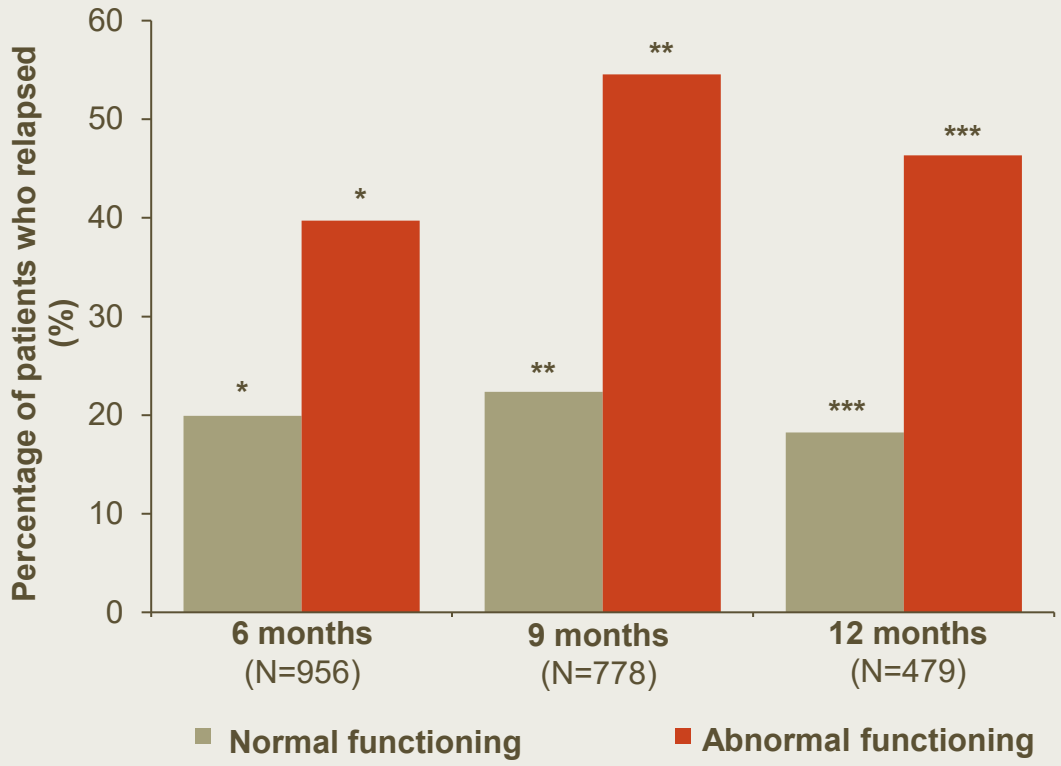
Brain and Cognition DISCOVERY FOUNDATION

A relevant challenge: Functional recovery achievement
Patients who do not achieve substantial functional recovery at remission are likely to relapse



Created from Ishak WW, et al. 2013

- **Patients who report themselves as having abnormal functioning** are at a **2.5–4.1x greater risk of relapse**
- In instances when patients exhibit **abnormal functioning**, even after depressive symptom reduction, **treatment optimisation should be considered** to improve the level of functioning

*p=0.0006; **p=3.7^10^{-6}; ***p=0.00056. †Data based on an analysis of adult (18–75 years old) citalopram treated remitted patients with a primary diagnosis of MDD enrolled in Level 1 of the STAR*D trial, at six, nine and twelve months. Relapse was defined as QIDS-SR score >7, remission was defined as QIDS-SR score ≤5 and normal functioning was defined as WSAS <10. Prescribing information for citalopram can be found at the end of this slide deck. MDD = major depressive disorder; QIDS-SR = Quick Inventory of Depressive Symptomatology-Self Report; STAR*D = Sequenced Treatment Alternatives to Relieve Depression; WSAS = Work and Social Adjustment Scale. Ishak WW, et al. J Affect Disord. 2013;151(1):59-65.

CERTICE

BRAXIA ACADEMY

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Anhedonia is common after recovery from COVID-19 and is correlated with fatigue

- Cross-sectional observational study (N=200) investigated post-COVID-19 anhedonia
- Across the group, high scores on **all subtypes of the self-assessment anhedonia scale** were reported
- There was a positive statistically significant correlation between **anhedonia and fatigue**

COVID-19, coronavirus disease 2019.

El Sayed S, et al. Neuropsychopharmacol Rep. 2020;10.1002/npr2.12154.

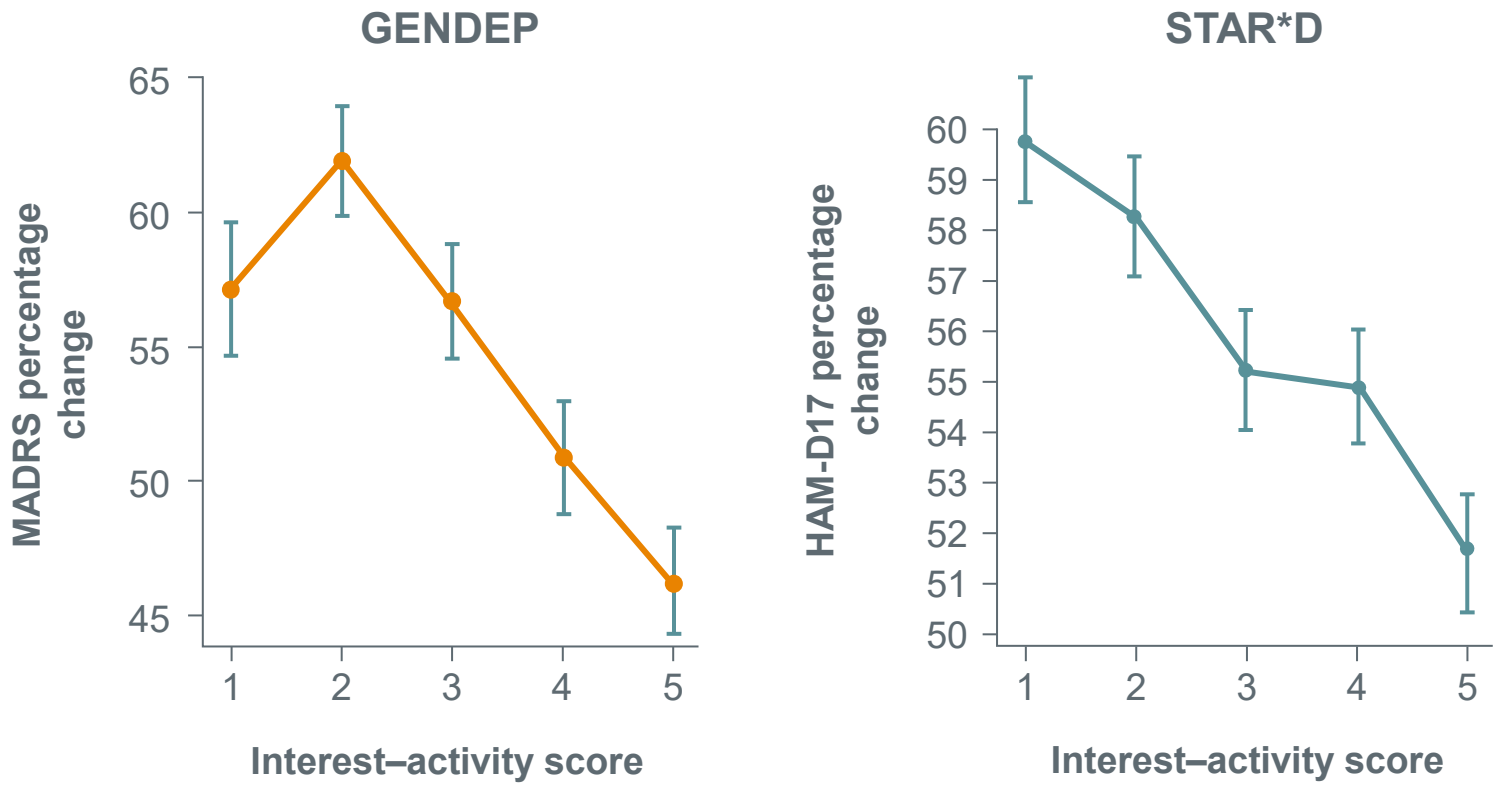
Identified Phases of Reward Processing

Reward Phase	Associated Symptom	Translational Term	Example Experimental Task
Prediction	Anticipatory anhedonia	Reward/loss anticipation	Monetary incentive delay task
Decision	Impaired decision making	Choice	Iowa gambling task
Action	Low energy	Effort expenditure	Effort expenditure for rewards task
Experience	Consummatory anhedonia	Reward/loss feedback	Monetary incentive delay task

Keren H et al. Am J Psychiatry. 2018;175(11):1111-1120.

Anhedonia Strongly Predicts Poor Antidepressant Outcomes in Patients with MDD

Association between interest–activity score and percentage improvement over 12 weeks



Low interest–activity, reflecting reduced enjoyment in addition to interest and activity, strongly predicted poor antidepressant outcome, as assessed by MADRS and HAM-D17

GENDEP = Genome-based Therapeutic Drugs for Depression; HAM-D17 = 17-item Hamilton Depression Rating Scale; MADRS = Montgomery–Åsberg Depression Rating Scale; MDD = major depressive disorder; STAR*D = Sequenced Treatment Alternatives to Relieve Depression.

Uher R, et al. Psychol Med. 2012;42:967–980.

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Brain and Cognition DISCOVERY FOUNDATION

Pay People to Take Their Antidepressants!?

Outcomes at 6 Weeks of Adult Patients With Depression in Primary Care, by Incentive Group

Outcome	No. (%)			*P* value		
	Escalating group	Deescalating group	Control group	Escalating vs deescalating[a]	Escalating vs control	Deescalating vs control
Antidepressant adherence at 6 wk[b]						
Antidepressant adherence percentage, mean (SD), %	90.7 (14.6)	83.4 (22.8)	74.9 (23.6)	.09	<.001	.12
Antidepressant adherence (≥80%)	35 (87.5)	26 (68.4)	18 (47.4)	.04	<.001	.06
PHQ-9 score at 6 wk[c]						
Depression symptom response[d]	26 (65.0)	24 (63.2)	14 (40.0)	.87	.03	.048
Depression symptom remission[e]	14 (35.0)	10 (26.3)	3 (8.6)	.41	.01	.048
Financial incentives provided, mean (SD), $	163 (5.3)	168 (5.3)	NA	.53	NA	NA

Abbreviations: NA, not applicable; PHQ-9, Patient Health Questionnaire-9.

[a] Post hoc comparison.

[b] The escalating group had 40 participants in this analysis; the deescalating group, 38; the control group, 38.

[c] The escalating group had 40 participants in this analysis; the deescalating group, 38; the control group, 35.

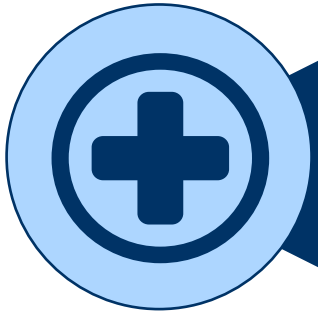
[d] Symptom response denotes 50% or greater decrease in score from screening.

[e] Symptom remission denotes PHQ-9 score of 0 to 4 at 6 weeks.

Marcus SC et al. JAMA Psychiatry 2021;78(2):222-4.

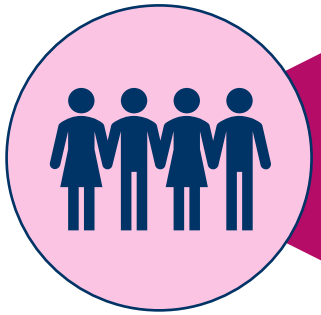
What is emotional dysregulation?

- Rapid and intense shifts in mood[1,2]
- Overdramatic affective expression[1]
- Excessive emotional reactivity[1]



use

Associated with suicidal thinking, poorer patient outcomes, and greater of healthcare services and medications[2]

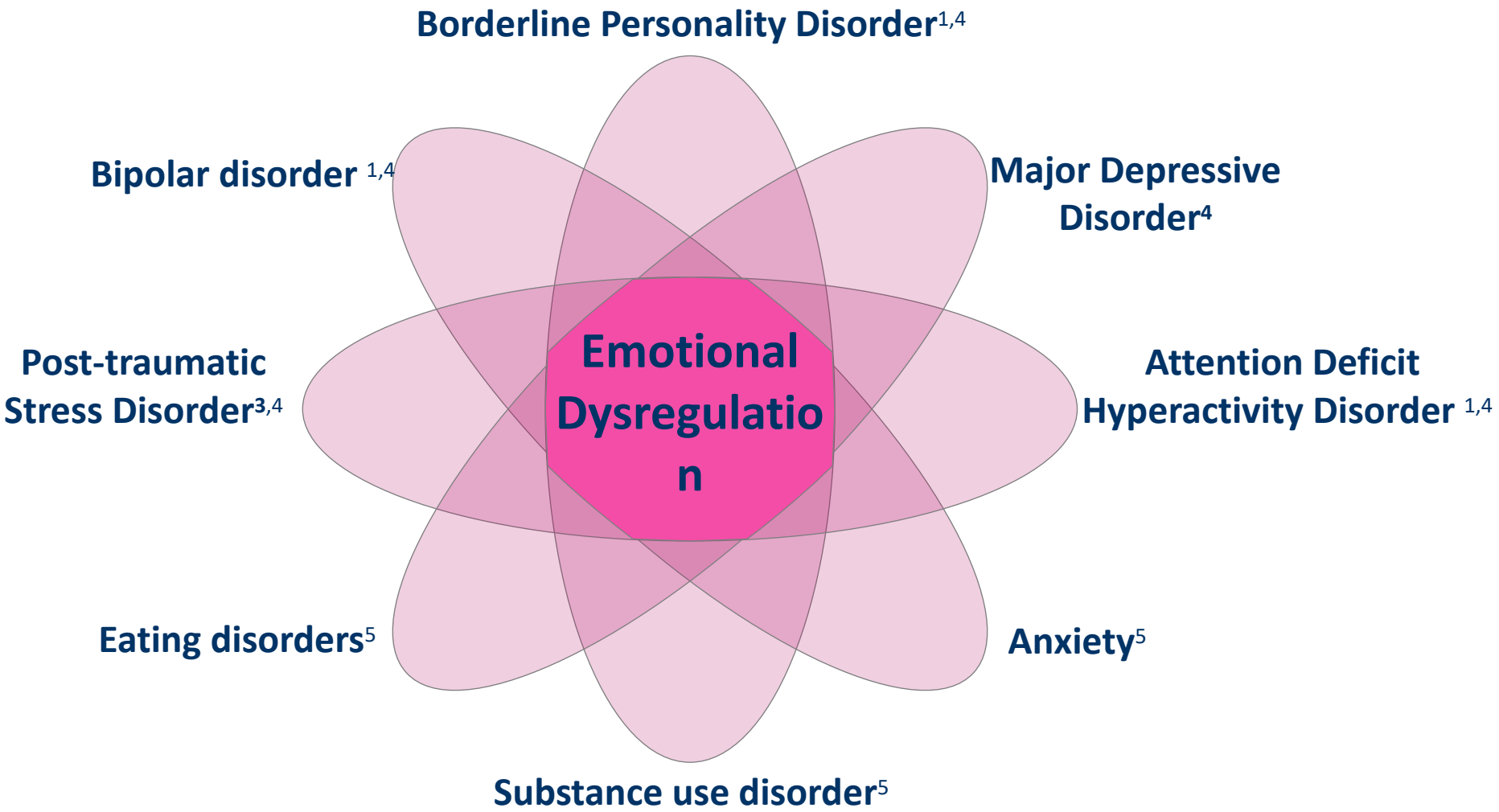


- Symptom of many psychiatric disorders[1]
- Estimated prevalence in the general population is **14%**[2]

Boehringer Ingelheim

1. Broome MR, et al. Neurosci Biobeh Rev 2015;51:243-254. 2. Marwaha S, et al. J Affect Disord Rep 2018;241:492-498.

Emotional dysregulation is a transdiagnostic symptom



1. Kebets V, et al. Transl Psychiatry. 2021;11:1-8; 2. Dadomo H et al., Frontiers. 2016; 7:1987. 3. Weiss et al., Psychol Trauma. 2020;12(3):219-226. 4. Broome et al, Neurosci Biobeh Rev. 2015;51:243-254. 5. Wolff J. Eur Psychiatry .2019;59:25-36.

Spectrum of Depression & Bipolar: Diagnoses & Conceptual Aspects

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