A Review of Risk Factors for Suicide in Bipolar Disorder

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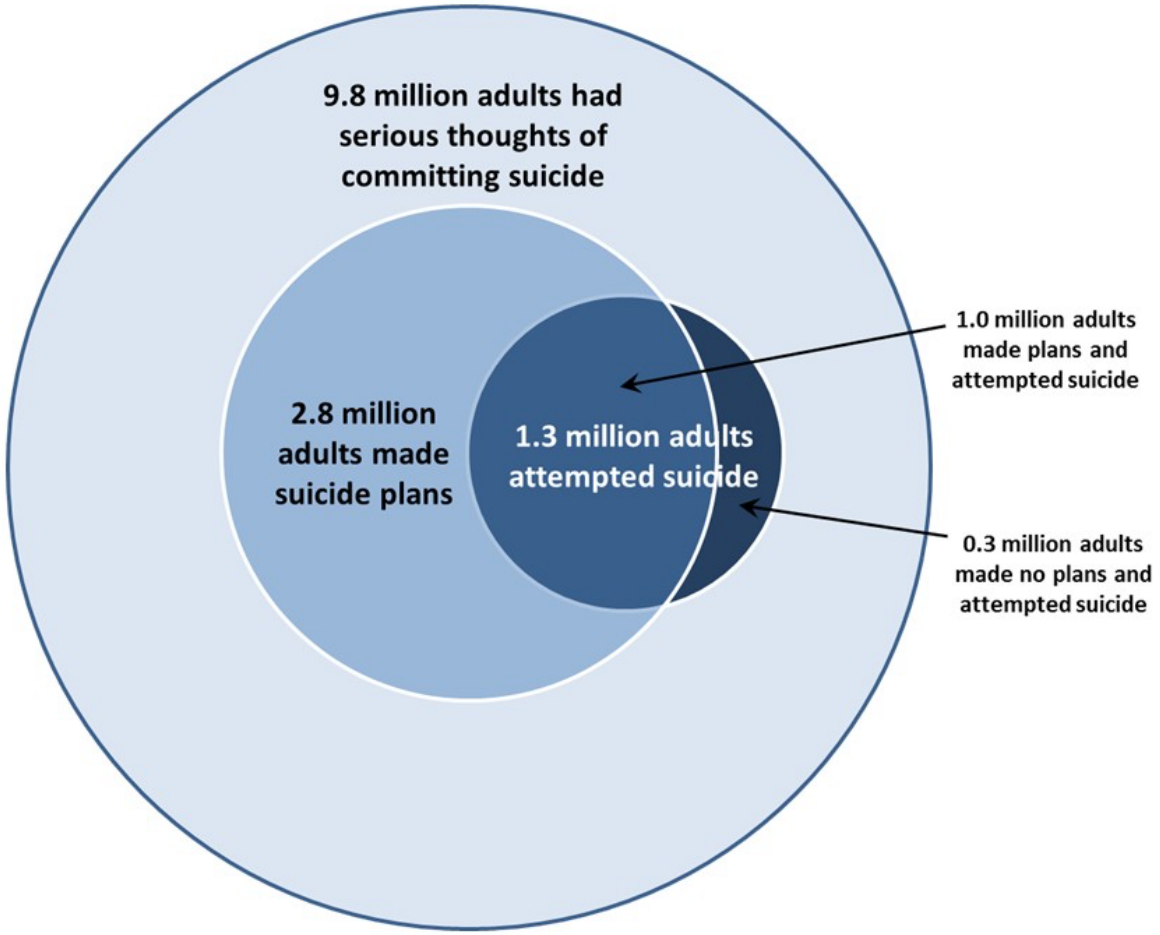
Objectives

- Review epidemiology of suicide and bipolar disorder
- Discuss risk factors for suicide in bipolar disorder
- Review clinical and pharmacological interventions for managing suicide risk in bipolar disorder

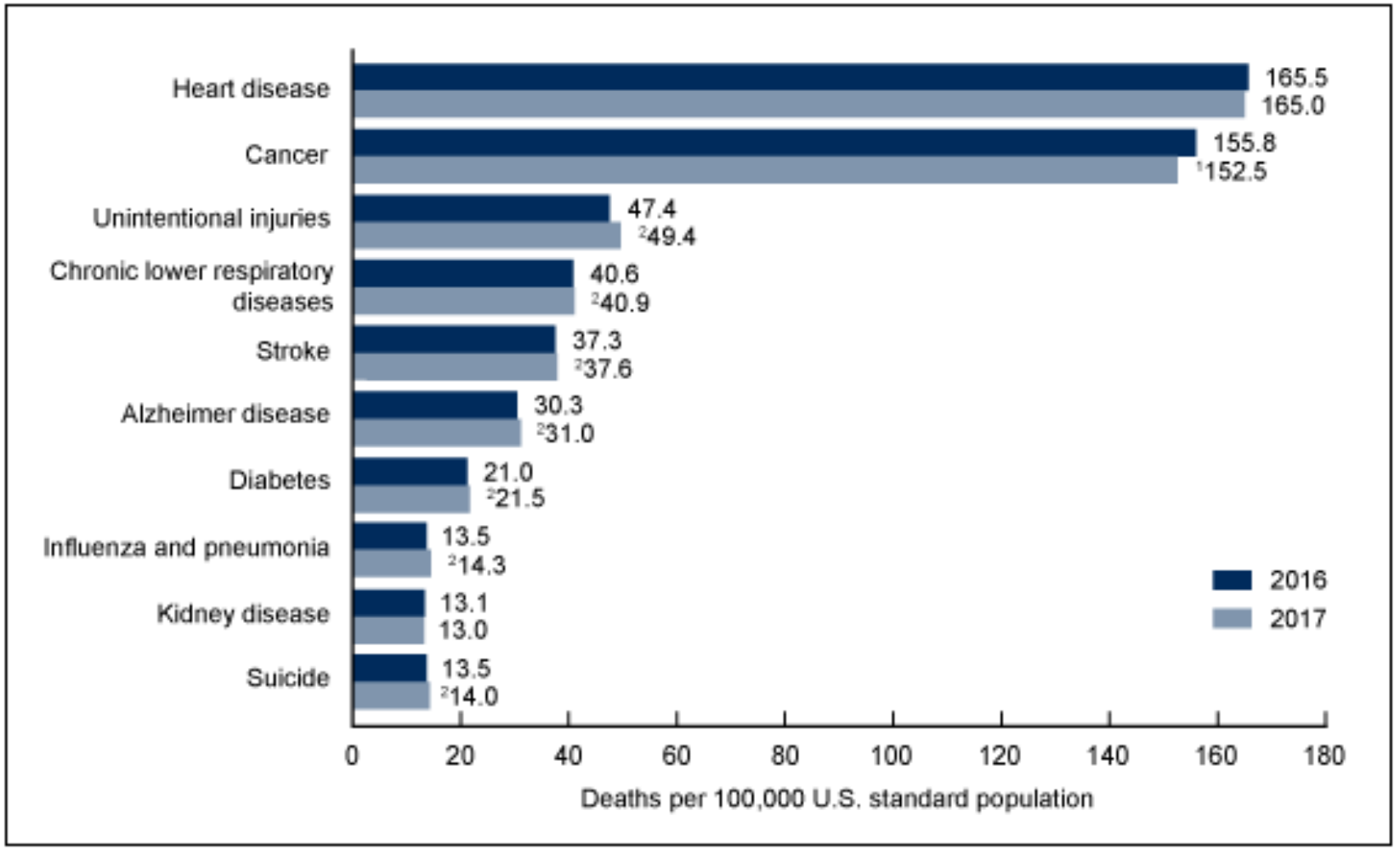

In the U.S., every 12.8 minutes, someone dies by suicide.
Make time to help a loved one.
Always stay with someone who is in crisis. If you or a friend is in danger, call the National Suicide Prevention Lifeline, 1-800-273-TALK (8255).
AMERICAN ASSOCIATION OF SUICIDOLOGY
WWW.SUICIDOLOGY.ORG

Suicide Statistics



https://www.nimh.nih.gov/health/statistics/suicide.shtml

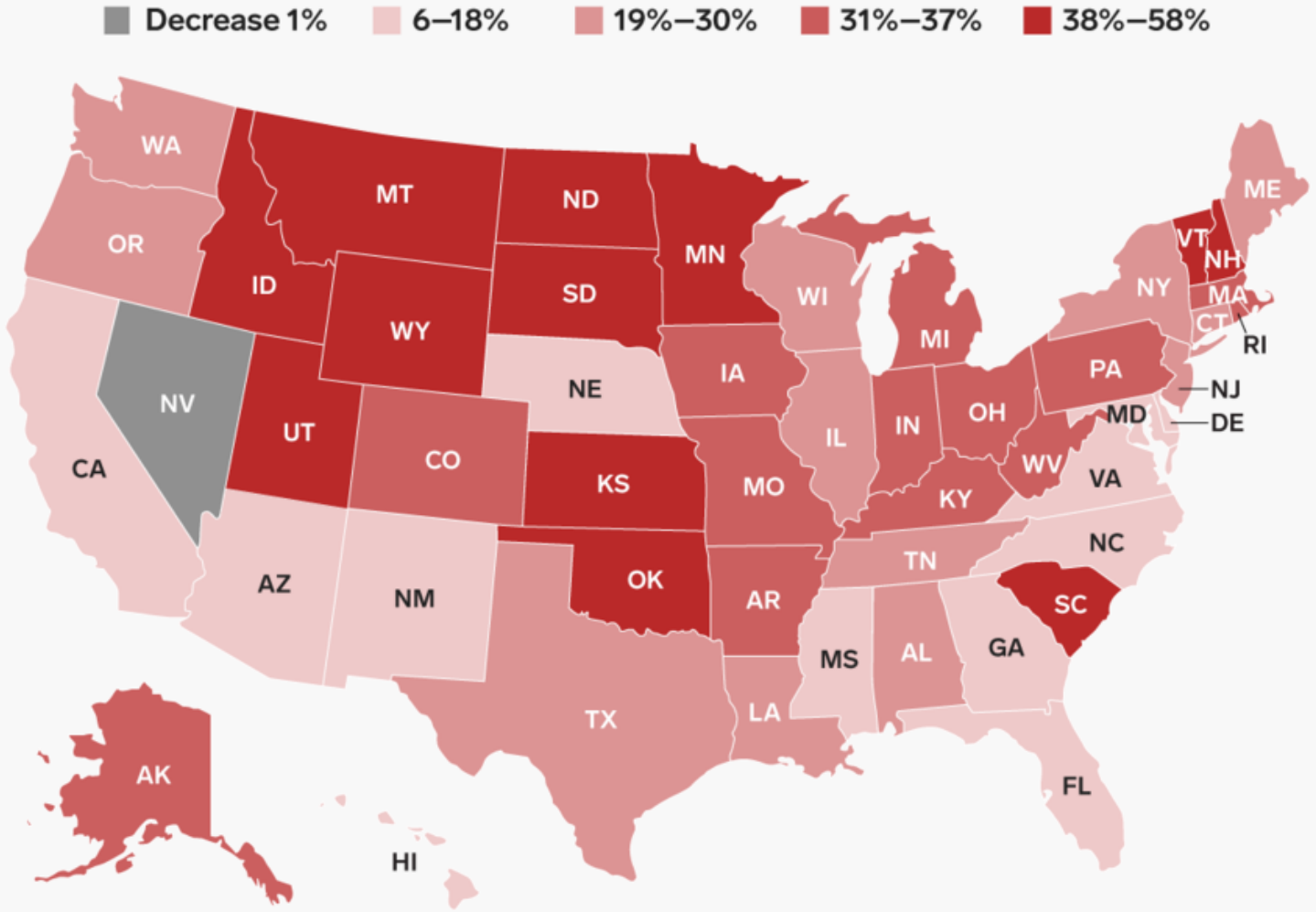
Figure 4. Age-adjusted death rates for the 10 leading causes of death: United States, 2016 and 2017



[1]Statistically significant decrease in age-adjusted death rate from 2016 to 2017 ($p < 0.05$).

[2]Statistically significant increase in age-adjusted death rate from 2016 to 2017 ($p < 0.05$).

Suicide rates have risen significantly since 1999



Source: CDC Note: Suicide rate is per 100K population, age-adjusted to 2000 US standard population. Insider Inc.

Suicide Statistics

- Suicide is the 10th leading cause of death in the US
- Worldwide almost 1 million die by suicide each year
- On average, there are 129 completed suicides a day
- In 2017, firearms accounted for 50% of all suicide deaths
- Rate of suicide is highest in middle-aged white men
- Adult females reported suicide attempt 1.4 times as often as males

Bipolar Disorder Statistics

- Almost 3% of US adults have been diagnosed with bipolar disorder
- Over 80% of those individuals with bipolar disorder have serious impairment
- Average age of onset is about 25
- Bipolar disorder affects men and women equally
- In adolescents, the prevalence is higher for females than males

Risk factors for Suicide in Bipolar Disorder

- Socio-demographics
- Family history of suicide
- Genetic associations
- Early onset of illness
- Rapid cycling bipolar disorder
- Concurrent substance use disorders

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Epidemiology, neurobiology and pharmacological interventions related to suicide deaths and suicide attempts in bipolar disorder: Part I of a report of the International Society for Bipolar Disorders Task Force on Suicide in Bipolar Disorder

Ayal Schaffer[1], **Erkki T Isometsä**[2], **Leonardo Tondo**[3], **Doris H Moreno**[4], **Mark Sinyor**[5], **Lars Vedel Kessing**[6], **Gustavo Turecki**[7], **Abraham Weizman**[8], **Jean-Michel Azorin**[9], **Kyooseob Ha**[10], **Catherine Reis**[11], **Frederick Cassidy**[12], **Tina Goldstein**[13], **Zoltán Rihmer**[14], **Annette Beautrais**[15], **Yuan-Hwa Chou**[16], **Nancy Diazgranados**[17], **Anthony J Levitt**[5], **Carlos A Zarate Jr**[18], and **Lakshmi Yatham**[19]

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A review of factors associated with greater likelihood of suicide attempts and suicide deaths in bipolar disorder: Part II of a report of the International Society for Bipolar Disorders Task Force on Suicide in Bipolar Disorder

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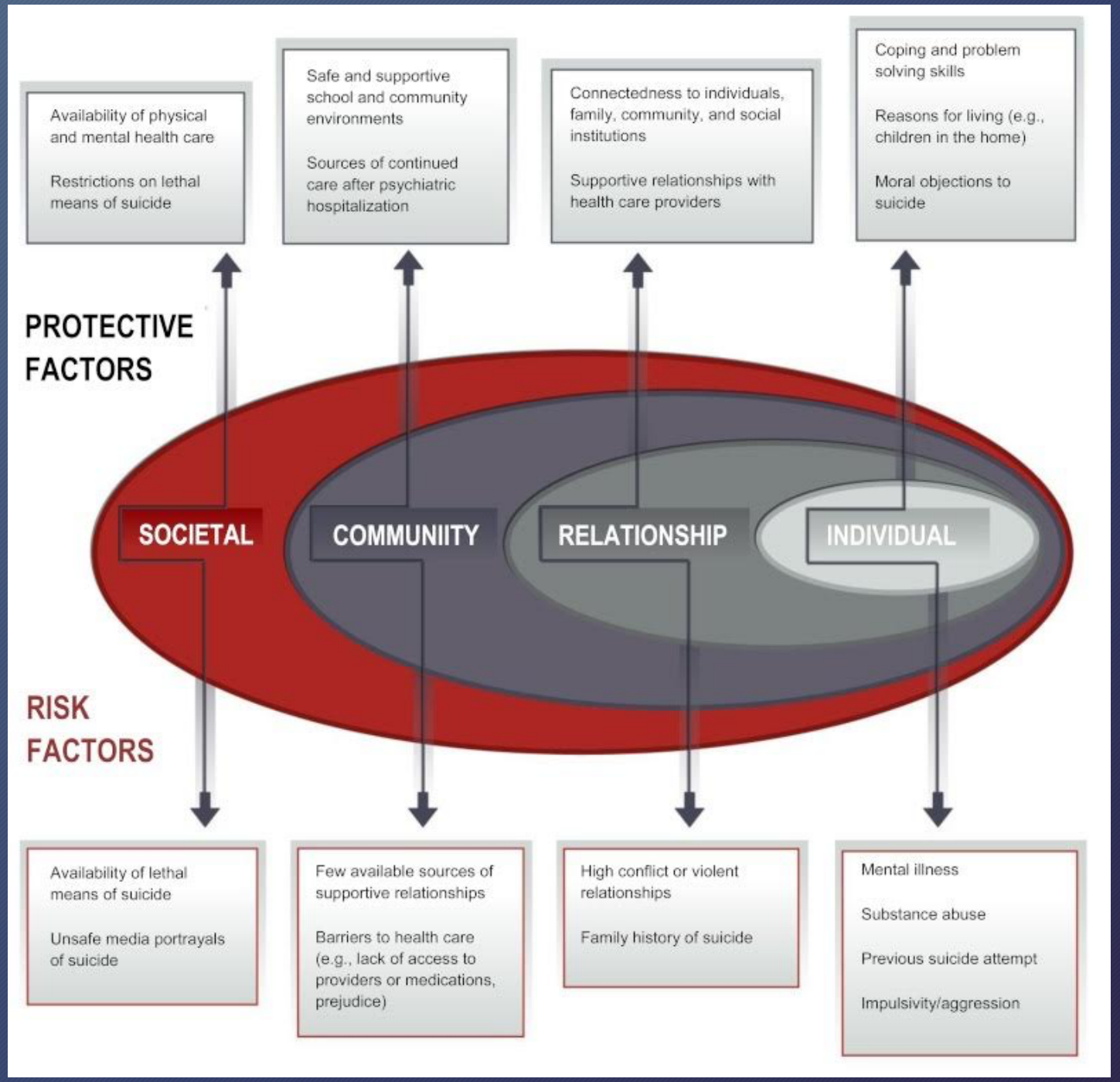
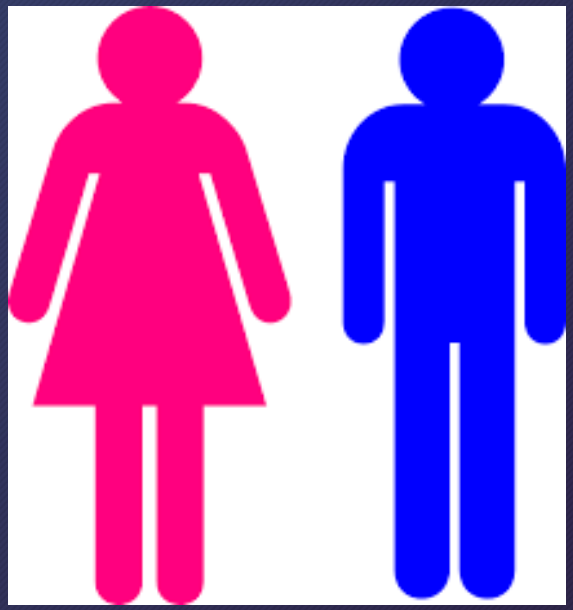

Availability of physical and mental health care
Restrictions on lethal means of suicide
Safe and supportive school and community environments
Sources of continued care after psychiatric hospitalization
Connectedness to individuals, family, community, and social institutions
Supportive relationships with health care providers
Coping and problem solving skills
Reasons for living (e.g., children in the home)
Moral objections to suicide
PROTECTIVE FACTORS
SOCIETAL
COMMUNIITY
RELATIONSHIP
INDIVIDUAL
RISK FACTORS
Availability of lethal means of suicide
Unsafe media portrayals of suicide
Few available sources of supportive relationships
Barriers to health care (e.g., lack of access to providers or medications, prejudice)
High conflict or violent relationships
Family history of suicide
Mental illness
Substance abuse
Previous suicide attempt
Impulsivity/aggression

Gender as a Risk Factor for Suicide in Bipolar Disorder

- Impact of illness on risk of suicide is greater in women than men
- Women more likely than men to attempt suicide
- However, men have higher rates of suicide completion
- Women less likely to attempt suicide by violent methods



Age as a Risk Factor for Suicide in Bipolar Disorder

- Ages 20-29 has highest risk of suicide attempt
- Older age individuals have higher lethality of suicide attempt
- Individuals with bipolar disorder were significantly younger at the time of death compared to non-BD suicides

Race/Ethnicity

- Non-Hispanic whites who died of suicide had higher rate of bipolar disorder (6.1%) than non-Hispanic blacks (2.6%) and Hispanics (2.3%)
- Not enough evidence to suggest that ethnicity influences risk of suicide attempts in patients with bipolar disorder

Marital and Family Status

- Single/divorced individuals have higher rates of lifetime suicide attempts
- Family support is a protective factor for suicide

Religious Affiliation

- Religious or moral objections to suicide appear to decrease suicidal behavior
- Negative religious coping may have an increase in suicide risk
- Hyper-religious beliefs during manic phase can increase suicidal behavior

Altitude of residence

- Suicide victims with bipolar disorder had significantly higher average altitude of residence compared to other suicide victims
- Possible role of mitochondrial dysfunction as a contributor to suicidal behavior in bipolar disorder as they may have elevated rates of depressive symptoms
- Possible increased metabolic stress due to hypoxia
- Lower concentration of lithium in ground and drinking water at higher altitudes

Family History of Suicide

- First-degree family member suicide increases likelihood of suicide attempt in patients with bipolar disorder
- Estimated that heritability of suicide is 40%
- Additive effect especially if patient reports a history of childhood abuse
- Increased likelihood of earlier age of first suicide attempt and greater number of lifetime attempts

Genetic Associations

- Suicide behavior associated with an alteration in serotonergic neurotransmissions
- Impulsivity linked to dysregulation of serotonergic and dopaminergic systems
- Post-mortem study detected reduced mRNA levels of BDNF gene in the prefrontal cortex and hippocampus of suicide subjects
- Conflicting evidence with need to investigate further

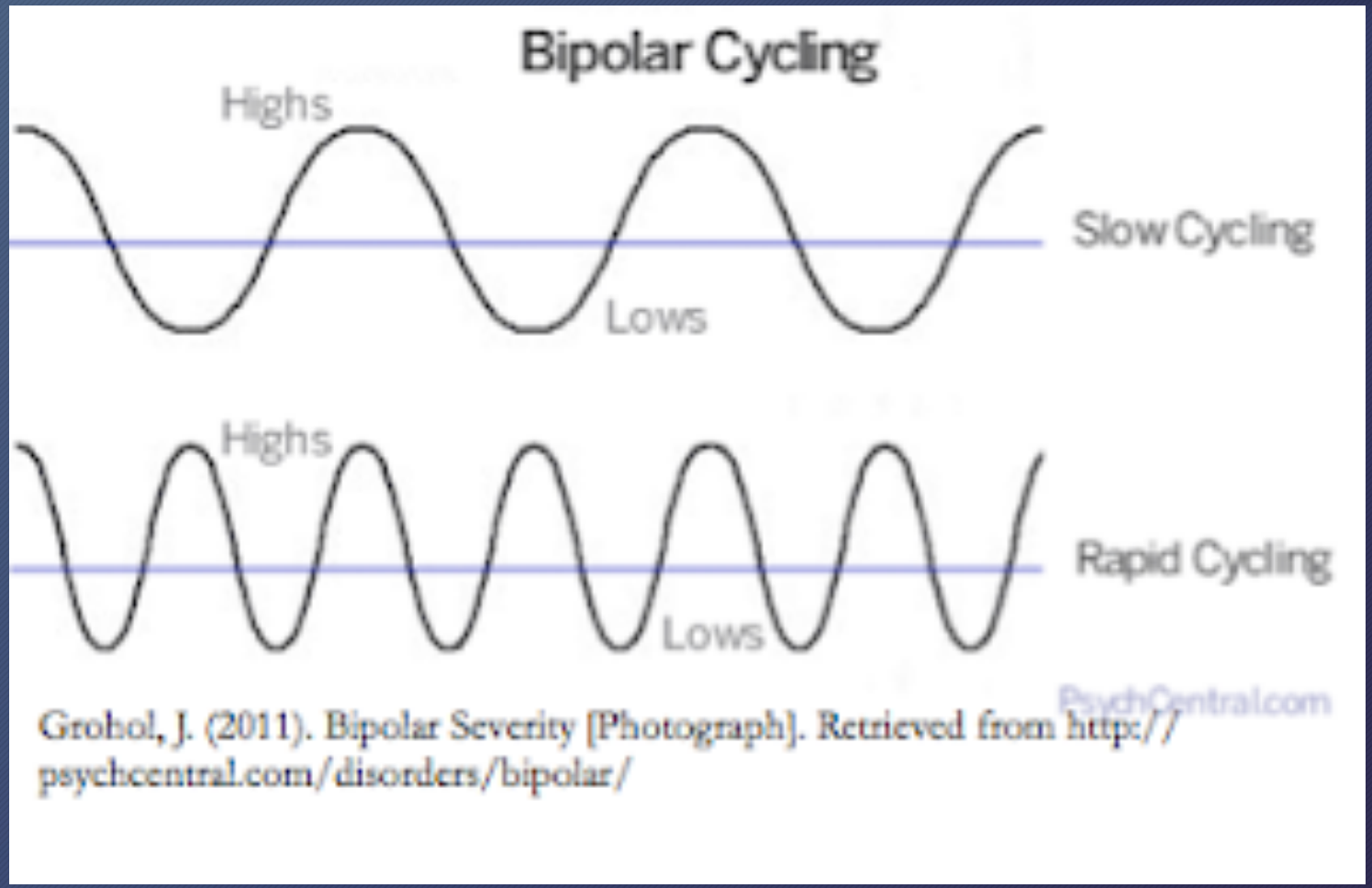
Early Onset of Bipolar Disorder

- Earlier age of illness onset is associated with increased likelihood of suicide attempts
- Age of onset defined as age when patient first fulfilled DSM-5 criteria for major mood episode (depressive, manic/hypomanic, mixed)
- Earlier age of onset also associated with rapid cycling course of disease

Rapid Cycling Bipolar Disorder

- Rapid-Cycling Specifier
  - Can be Bipolar I or II
  - 4 or more mood episodes in 12 month period (i.e. depressive, manic, mixed, or hypomanic)
  - Can be in any order or combination
  - Demarcated by a period of full remission OR switch to an episode of t opposite polarity

Rapid Cycling Bipolar Disorder



Grohol, J. (2011). Bipolar Severity [Photograph]. Retrieved from http://psychcentral.com/disorders/bipolar/

Rapid Cycling Bipolar Disorder

- Rapid-cyclers experience more weeks with manic or hypomanic symptoms
- Twice as likely other bipolar disorder patients to have a history of severe suicide attempts
- No difference in completed suicide outcomes

Manic Episode Risk Factors

- Lower rates of suicidal behavior compared to those with depressive episodes and mixed states
- Grandiosity during mania may be a protective factor for suicide, but may lead to high risk accidental death
- Individuals with a first episode of mania are more likely to attempt suicide by violent means than those with a first depressive episode

Depressive Episode Risk Factors

- Depressive first episode has 8-fold higher association with suicide attempts compared to individuals with a manic first episode
- Longer and more frequent depressive episodes may increase risk of suicide attempts in bipolar patients
- Initial depressive episode may lead to misdiagnosis and mismanagement

Mixed States in Bipolar Disorder

- Full criteria is met for a depressive episode with 3 or more manic/hypomanic symptoms
- Full criteria is met for a manic/hypomanic episode with 3 or more depressive symptoms
- Increased suicide risk attributed to depression-predominant course of illness

Concurrent Use with Cannabis

- Cannabis is the most common illicit drug used in bipolar disorder and up to 38% of affected individuals use it
- Chronic cannabis use is associated with higher severity of illness and greater noncompliance to treatment
- Earlier age at onset associated with misuse
- Increased risk of mania, duration of manic symptoms, incidence of psychotic symptoms and increased suicide risk

Concurrent Use with Alcohol

- Lifetime alcohol use disorder is present among 46-58% of those who meet criteria for Bipolar I Disorder (19-39% for Bipolar II Disorder)
- Alcohol associated with increased lifetime rate of attempted suicide
- High severity of illness may lead to self-medication with substances/alcohol and increased suicide attempts
- Alcohol impairs decision-making and can increase impulsivity

Concurrent Use with Stimulants**

- Substances foster impulsivity and aggression and increase chance to act on suicidal thoughts
- Methamphetamine increases psychotic symptoms and severity of manic symptoms

Clinical Interventions for Managing Suicide Risk in Bipolar Disorder

Pharmacological Interventions – Lithium carbonate

- Lithium associated with a reduced risk of suicidal behavior
- Potent mood-stabilizer and decreases aggression and impulsivity
- Requires close monitoring for therapeutic levels and adverse effects
- Rebound suicidality associated with discontinuation of lithium

Pharmacological Interventions - Anticonvulsants

- Divalproex Sodium (Depakote®)
  - Treatment of manic episodes or acute manic or mixed episodes with or without psychotic features
- Carbamazepine (Equetro®)
  - Treatment of acute manic or mixed episodes associated with Bipolar I Disorder
- Lamotrigine (Lamictal®)
  - Maintenance treatment of bipolar I disorder to delay the time to occurrence of mood episodes

Pharmacological Interventions - Anticonvulsants

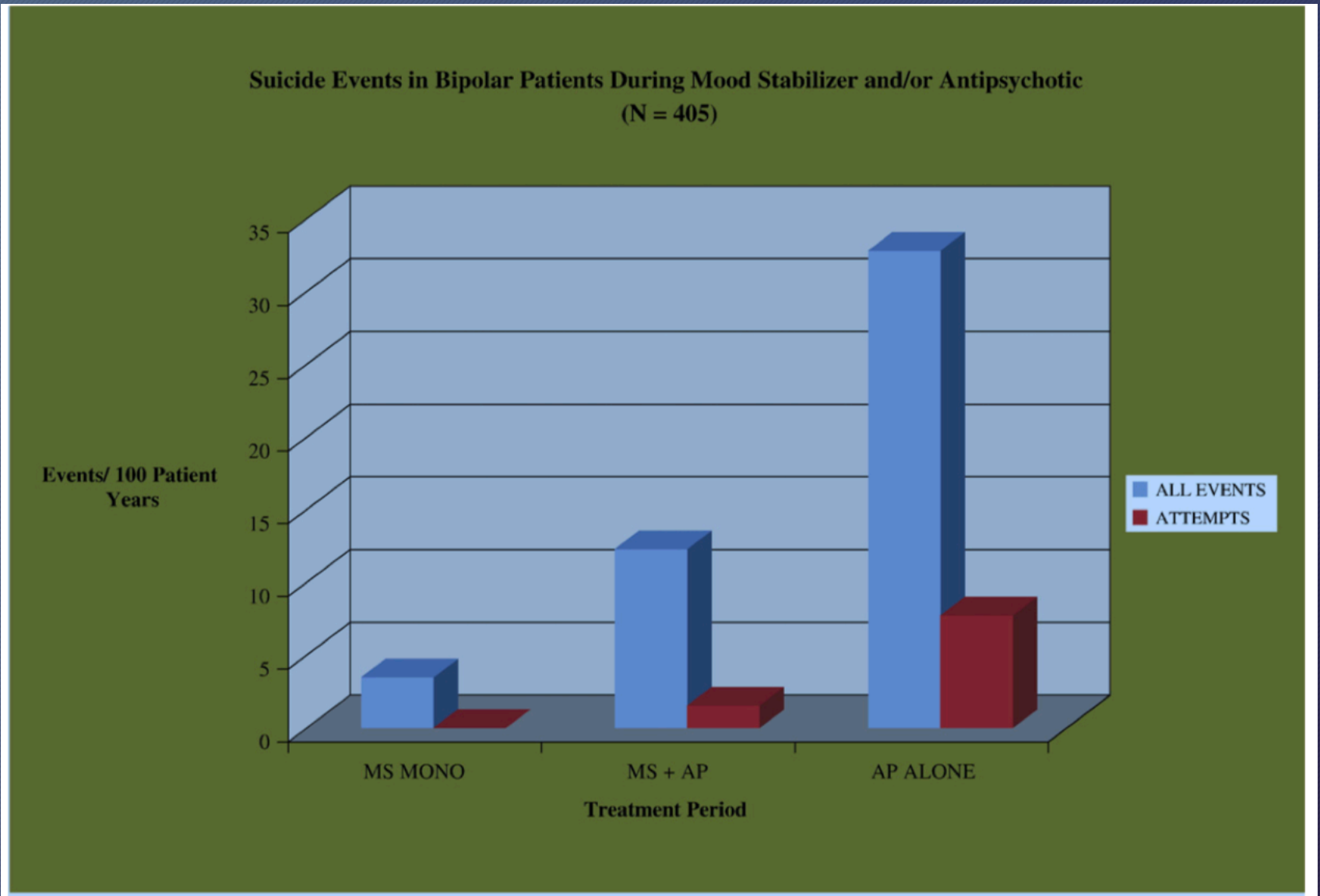
- In 2008, FDA published a warning that 11 anticonvulsants carry an increased risk of suicidal thoughts or actions and patients should be closely monitored
- Very little evidence to suggest role of anticonvulsants in the prevention of suicide
- Increased suicidal risk in months following discontinuation of Carbamazepine and Divalproex

Pharmacological Interventions – Antipsychotics

- Aripiprazole (Abilify®)
- Asenapine (Saphris®)
- Cariprazine (Vraylar®)
- Fluoxetine + Olanzapine (Symbyax®)
- Olanzapine (Zyprexa®)
- Quetiapine fumarate (Seroquel®)
- Risperidone (Risperdal®)
- Ziprasidone (Geodon®)

Pharmacological Interventions – Antipsychotics

- Relative effects of different antipsychotics in bipolar disorder are largely unknown
- Higher risk of suicidal behavior associated with antipsychotic treatment than with mood stabilizer monotherapy
- Study demonstrated antipsychotic treatment has been associated with increased rate of non-lethal suicidal behavior



MS MONO = Monotherapy with mood stabilizer (lithium, divalproex or carbamazepine); MS + AP = mood stabilizer + antipsychotic; AP Alone = treatment with antipsychotic alone. Event Rates are from Table 4.

Pharmacological Interventions – Clozapine

- FDA indication for suicidal behavior in schizophrenia or schizoaffective disorder
- Off-label use in treatment resistant bipolar disorder with mania or psychosis
- Anti-suicidal effect may extend beyond schizophrenia, however not well studied

Pharmacological Interventions – Antidepressants

- Antidepressant monotherapy has 6-10fold increase in suicidal behavior than mood stabilizer monotherapy
- Bipolar patients treated with an antidepressant alone are at very high risk for suicidal behavior
- Unrecognized bipolar disorder may be mismanaged with antidepressant monotherapy
- Can use in conjunction with mood stabilizers or antipsychotics

Clinical Risk Assessment

- Take a good history!
- Important to note family history and history of prior suicide attempts
- Age at onset of first mood episode or hospitalization
- Characteristics of bipolar disorder – mixed episodes, rapid-cycling, etc.
- Assess for concurrent substance use
- Pharmacotherapy
- Use clinical judgment!

Take home points

- Risk of suicide in individuals with bipolar disorder 20-30 times higher than the general population
- 1 in 15 individuals with bipolar disorder will commit suicide
- Rapid-cycling and mixed episode bipolar disorder have increased suicidal behavior
- Depressive first episode has 8-fold higher association with suicide attempt
- Earlier age of onset associated with increased severity of illness
- Concurrent substance use has increased risk of suicidal behavior
- Lithium only mood-stabilizer with proven reduced risk of suicidal behavior
- Use caution with all pharmacological interventions with close monitoring

Questions?

Works Cited

- Leite RT, Nogueira Sde O, do Nascimento JP, et al. The Use of Cannabis as a Predictor of Early Onset of Bipolar Disorder and Suicide Attempts. *Neural Plast*. 2015;2015:434127. doi:10.1155/2015/434127
- Muhtadie L, Johnson SL, Carver CS, Gotlib IH, Ketter TA. A profile approach to impulsivity in bipolar disorder: the key role of strong emotions. *Acta Psychiatr Scand*. 2013;129(2):100–108. doi:10.1111/acps.12136
- Chesin M, Stanley B. Risk assessment and psychosocial interventions for suicidal patients. *Bipolar Disord*. 2013;15(5):584–593. doi:10.1111/bdi.12092
- Huber RS, Coon H, Kim N, Renshaw PF, Kondo DG. Altitude is a risk factor for completed suicide in bipolar disorder. *Med Hypotheses*. 2014;82(3):377–381. doi:10.1016/j.mehy.2014.01.006
- Coryell W, Solomon D, Turvey C, et al. The Long-term Course of Rapid-Cycling Bipolar Disorder. *Arch Gen Psychiatry*. 2003;60(9):914–920. doi:10.1001/archpsyc.60.9.914
- Ryu V, Jon DI, Cho HS, et al. Initial depressive episodes affect the risk of suicide attempts in Korean patients with bipolar disorder. *Yonsei Med J*. 2010;51(5):641–647. doi:10.3349/ymj.2010.51.5.641
- https://s3.amazonaws.com/academia.edu.documents/45953446/j.jad.2007.05.01820160525-10524-dh16kg.pdf?AWSAccessKeyId=AKIAIWOWYYGZ2Y53UL3A&Expires=1556242259&Signature=%2BKDUjggUXHsZGwL791TYvT5Onrl%3D&response-content-disposition=inline%3B%20filename%3DBipolar_pharmacotherapy_and_suicidal_beh.pdf
- L. Plans, C. Barrot, E. Nieto, J. Rios, T.G. Schulze, S. Papiol, M. Mitjans, E. Vieta, A. Benabarre, Association between completed suicide and bipolar disorder: A systematic review of the literature, Journal of Affective Disorders, Volume 242, 2019, Pages 111-122, ISSN 0165-0327, https://doi.org/10.1016/j.jad.2018.08.054. (http://www.sciencedirect.com/science/article/pii/S0165032718305147)
- Tasha D Cate Carter, Emanuela Mundo, Sagar V Parikh, James L Kennedy, Early age at onset as a risk factor for poor outcome of bipolar disorder, Journal of Psychiatric Research. Volume 37, Issue 4, 2003, Pages 297-303, ISSN 0022-3956, https://doi.org/10.1016/S0022-3956(03)00052-9. (http://www.sciencedirect.com/science/article/pii/S0022395603000529)
- Leite RT, Nogueira Sde O, do Nascimento JP, et al. The Use of Cannabis as a Predictor of Early Onset of Bipolar Disorder and Suicide Attempts. *Neural Plast*. 2015;2015:434127. doi:10.1155/2015/434127