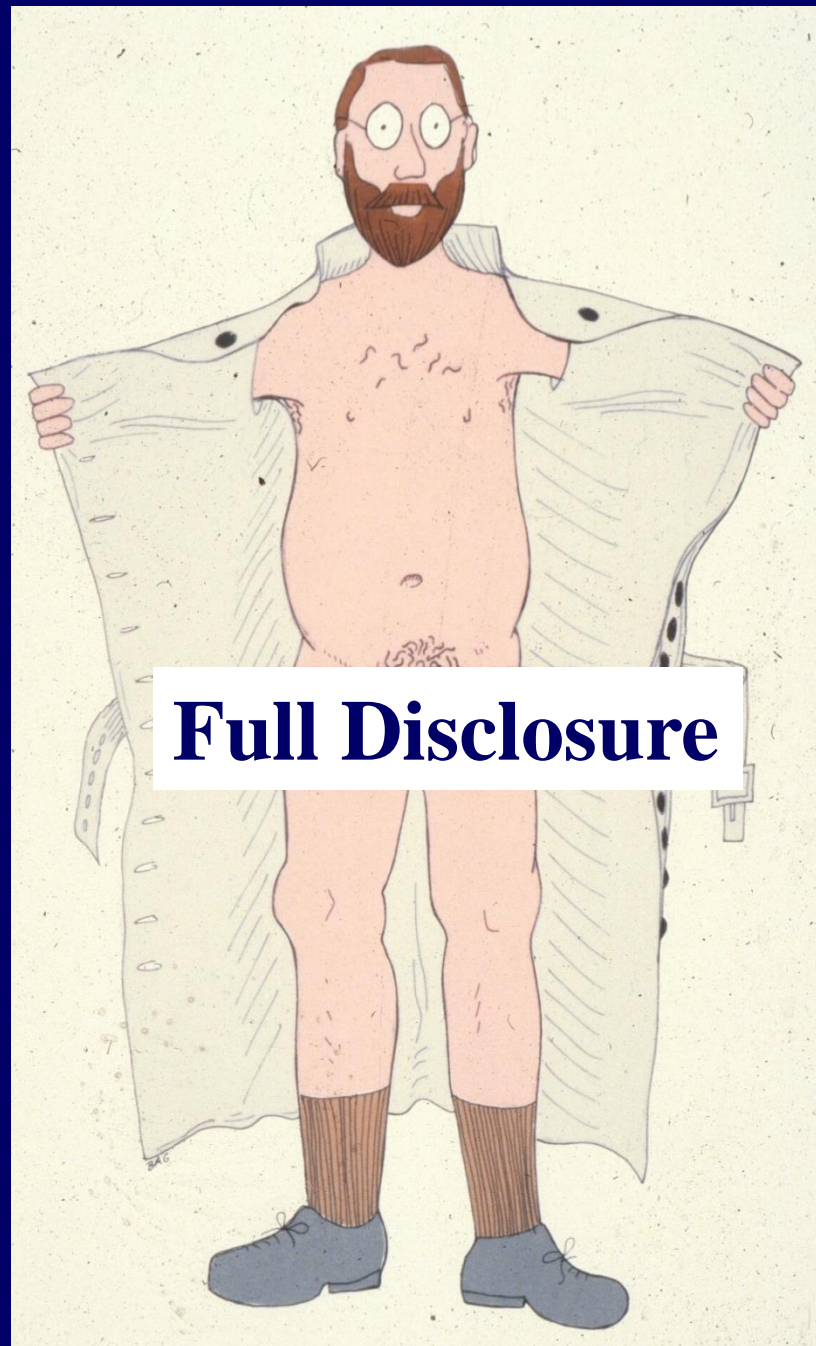


Mastering the Mysteries of Bipolar Disorder: Diagnosis and Evaluation

James W. Jefferson, MD
Clinical Adjunct Professor
of Psychiatry
University of Wisconsin
School of Medicine and
Public Health



Full Disclosure

**(Stolen from
me by John
Greist)**

Learning Objectives:

1. Appreciate the evolution of bipolar diagnosis from the first DSM to DSM-5
2. Become familiar with DSM-5 Bipolar Specifiers
3. Understand the Bipolar Spectrum concept
4. Recognize the complexities of bipolar comorbidities

Pre-Test Question #1

1. The results of a survey of the general population found that the most common association with Bipolar Disorder was:
 - A. Psychiatric illness
 - B. Bad weather front
 - C. Melting of polar ice caps

Pre-Test Question #2

2. In what version of the DSMs did Bipolar Disorder replace Manic-Depressive Disorder?

- A. DSM-II
- B. DSM-III
- C. DSM-IV
- D. DSM-5

Pre-Test Question #3

3. How many Bipolar Specifiers are in DSM-5?

- A. 6
- B. 8
- C. 10
- D. 12
- E. 14

Pre-Test Question #4

4. The most common Bipolar Disorder comorbidity is which of the following?
- A. Anxiety Disorders
 - B. Migraine
 - C. Major Depression
 - D. Substance Abuse
 - E. OCD

Pre-Test Question #5

5. Concerns about the overdiagnosis of Bipolar Disorder in children led to the creation of which of the following diagnoses in DSM-5?
- A. Depression Protracted by hypomania
 - B. Unspecified Bipolar and Related Disorder
 - C. Illness Anxiety Disorder
 - D. Disruptive Mood Dysregulation Disorder
 - E. Unspecified Disruptive, Impulse-Control and Conduct Disorder

What is Bipolar Disorder

German Telephone Survey (n=1006)

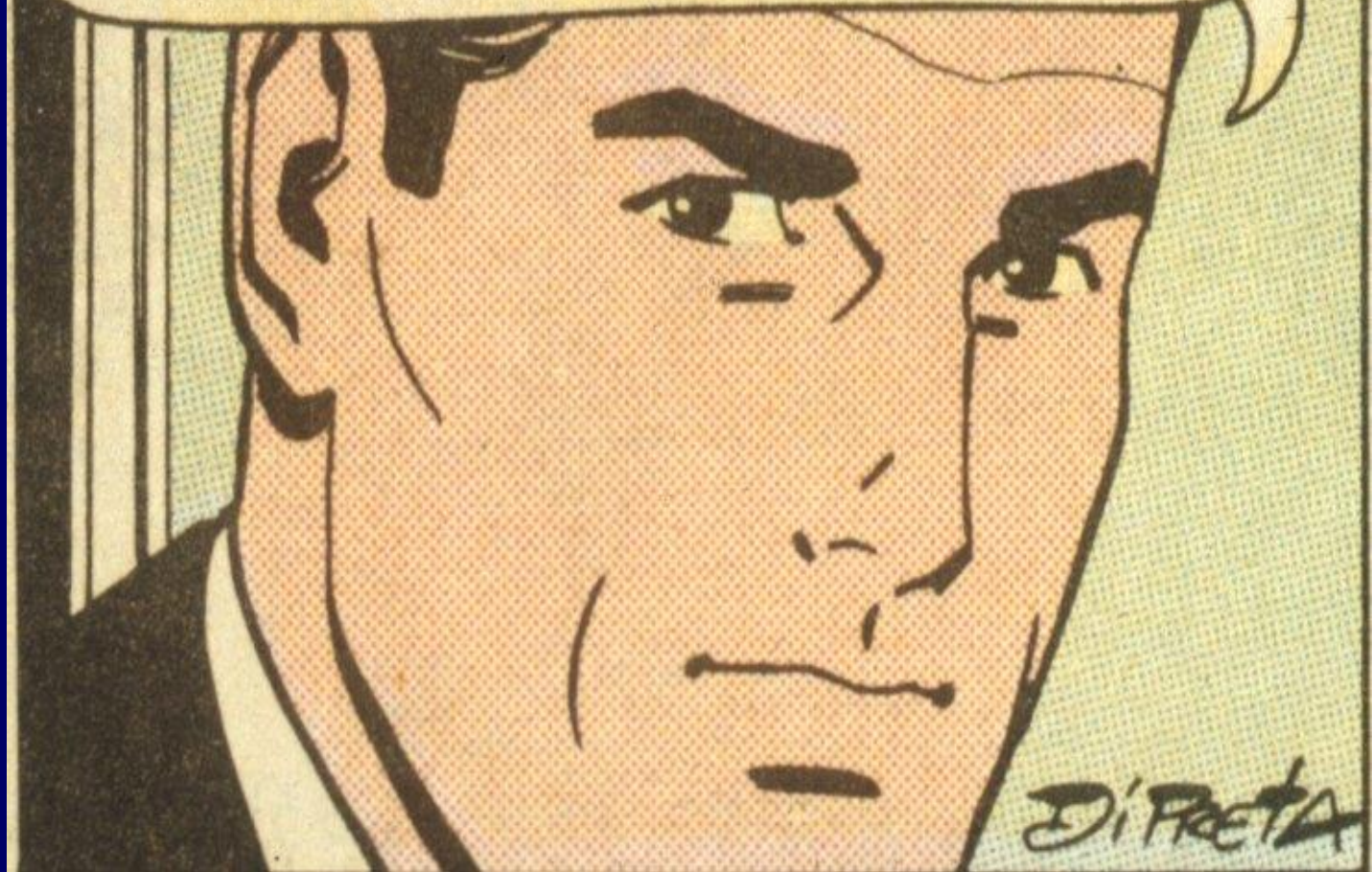
- **Psychiatric illness**
- **Bad weather front**
- **Melting of polar ice caps**

What is Bipolar Disorder

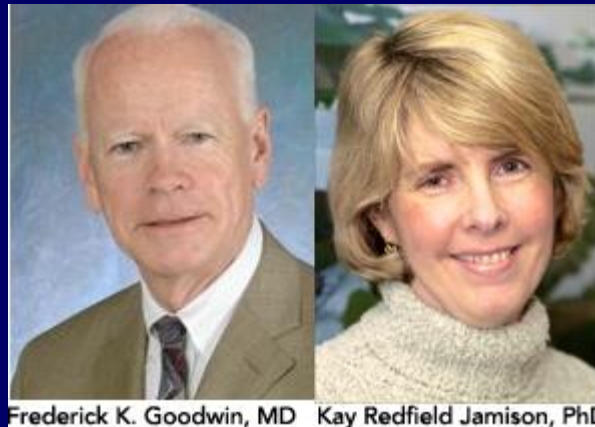
German Telephone Survey (n=1006)

- **Psychiatric illness** **4.6%**
- **Bad weather front** **17%**
- **Melting of polar ice caps** **61%**

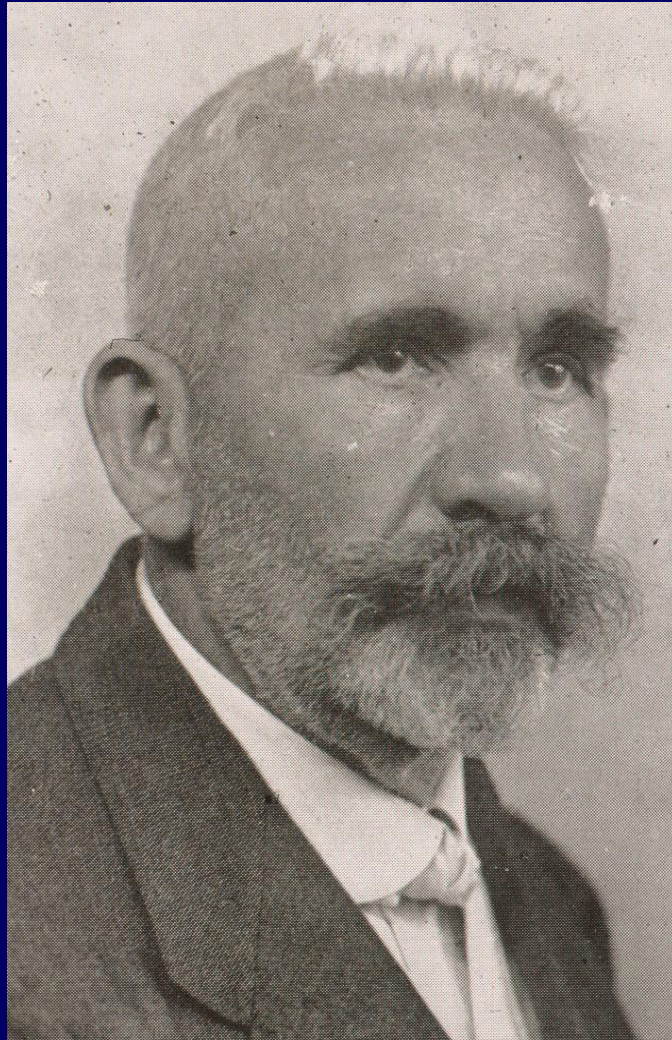
THEY HAVE AN ILLNESS
WHICH SOMETIMES CAUSES
THEM TO GET VERY HIGH
OR VERY DEPRESSED!



“The history of psychiatric diagnosis has been notable for its confusion, reflected in the myriad of overlapping systems for classifying and subdividing depressive disorders.”

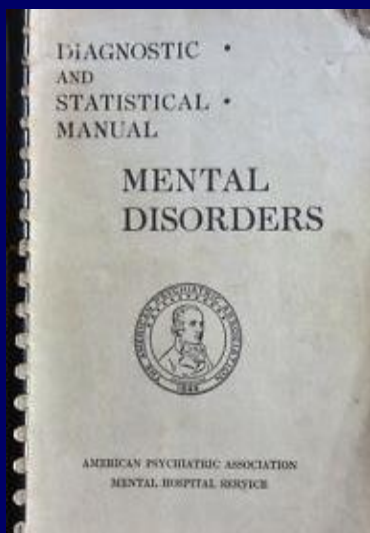


Goodwin and Jamison, 2nd ed. Manic-Depressive Illness, 2007, p 89



Emil Kraepelin
(1856 - 1926)

**Distinguished between
manic-depressive illness
and
dementia praecox
(schizophrenia)**



Diagnostic and Statistical Manual of Mental Disorders (1952)

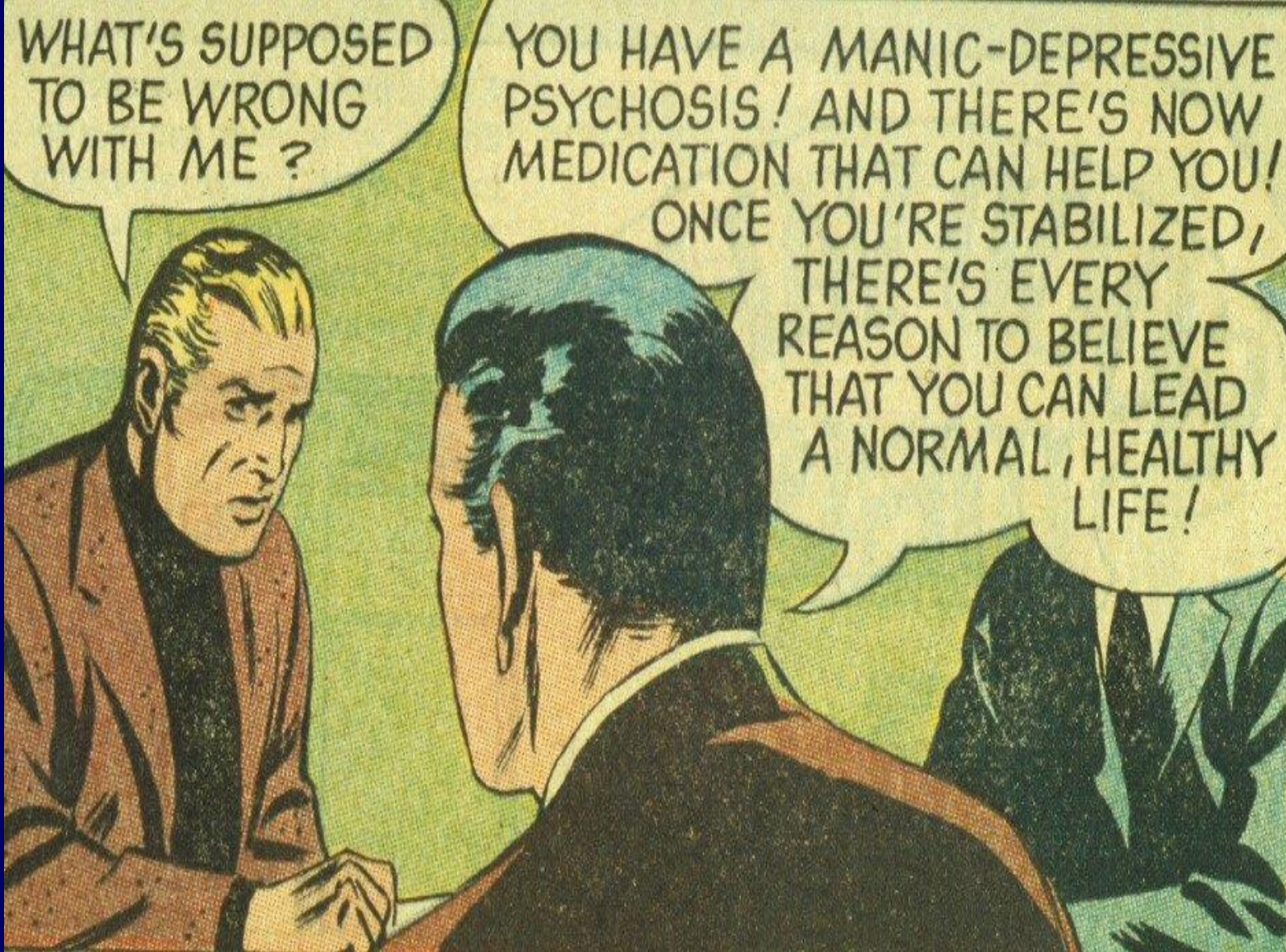
Manic-Depressive Reactions

- **Manic type**
- **Depressive type**
- **Other**

**EVEN A TRACE OF
SCHIZOPHRENIA
IS STILL SCHIZOPHRENIA**

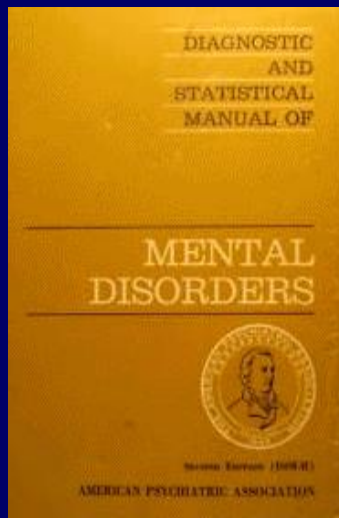
Nolan D.C. Lewis (1954)

The first practicing American psychoanalyst



WHAT'S SUPPOSED
TO BE WRONG
WITH ME ?

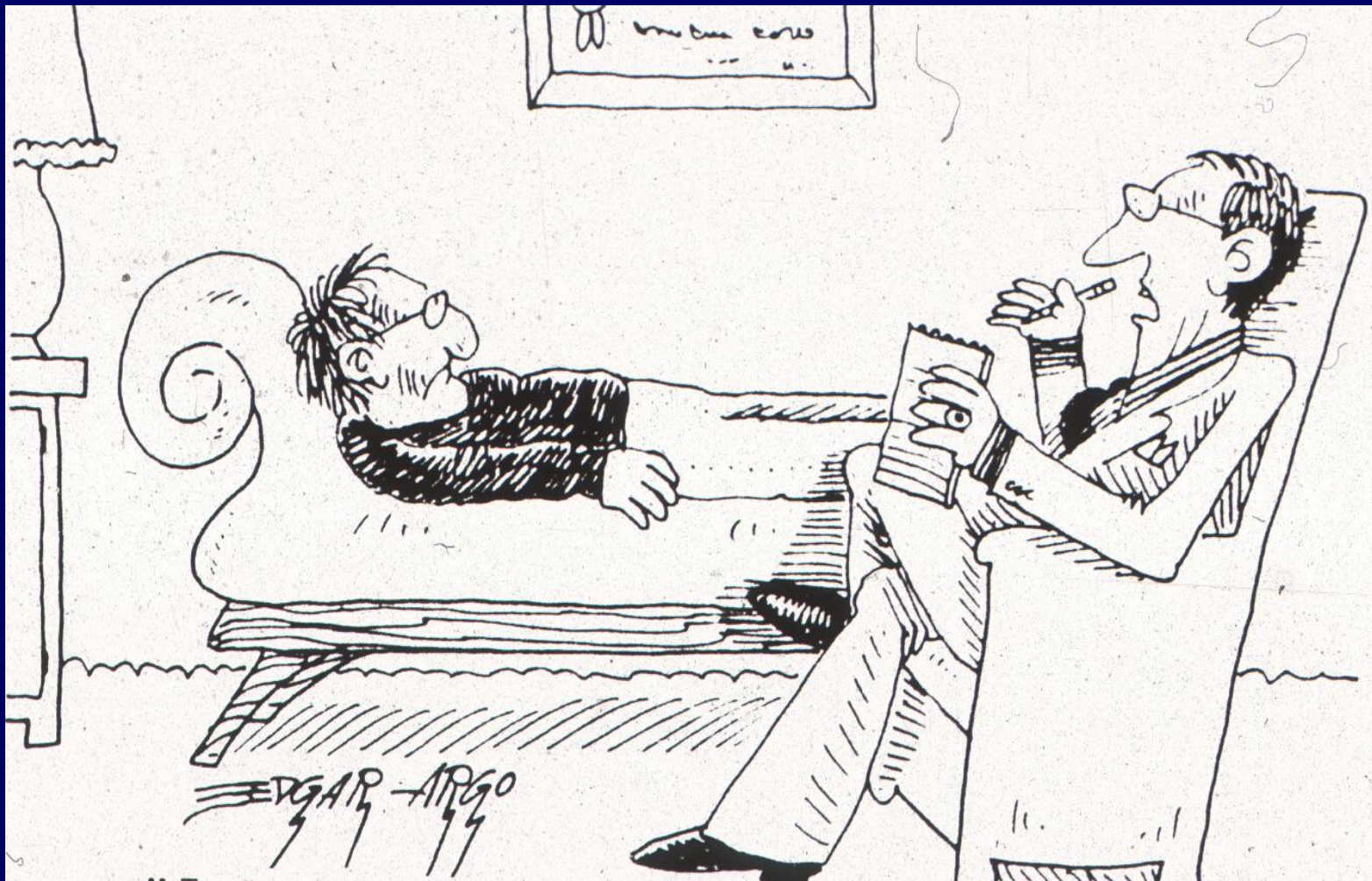
YOU HAVE A MANIC-DEPRESSIVE
PSYCHOSIS ! AND THERE'S NOW
MEDICATION THAT CAN HELP YOU !
ONCE YOU'RE STABILIZED,
THERE'S EVERY
REASON TO BELIEVE
THAT YOU CAN LEAD
A NORMAL , HEALTHY
LIFE !



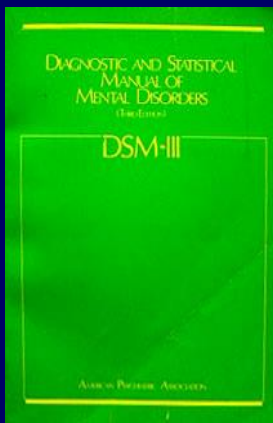
DSM-II (1968)

Affective Psychoses

- **Involucional melancholia**
- **Manic-depressive psychoses**
 - **manic type**
 - **depressive type**
 - **circular type**

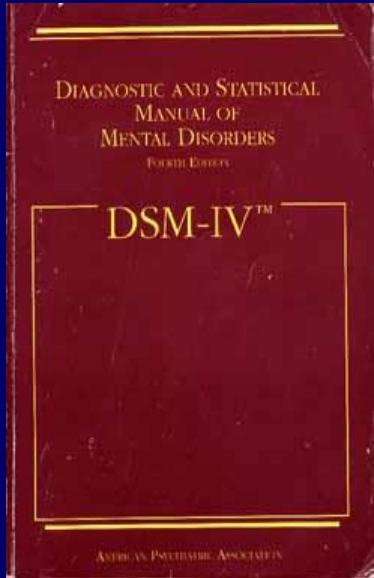


**“I haven’t exactly cured you, but
sanity standards have changed a lot
in the last 12 years”**



DSM-III (1980)

- **Separate categories for Bipolar and Major Depressive disorders**
- **Depressive neurosis became Dysthymic Disorder**
- **Cyclothymia became an affective disorder rather than a personality disorder**



DSM-IV (1994)

Bipolar Disorders

- **Bipolar I Disorder**
- **Bipolar II Disorder**
- **Cyclothymic Disorder**
- **Bipolar Disorder NOS**
(Not Otherwise Specified)

I assume that all of you have mastered Bipolar Disorders in DSM-IV, but what about DSM-5?



Bipolar Disorders in DSM-5?



DSM-IV

Bipolar Disorders

DSM-5

**Bipolar and
Related
Disorders**

Pretty Much the Same in IV and 5

**Bipolar I, Bipolar II
Cyclothymic Disorder
Due to General Medical Condition
Substance Induced**

**But what about Bipolar Disorder
NOS??**

Say Goodbye to NOS and Hello to:

- **Other Specified Bipolar and Related Disorder**
- **Unspecified Bipolar and Related Disorder**

Bipolar and Related Disorders: DSM-5

Other Specified Bipolar and Related Disorder

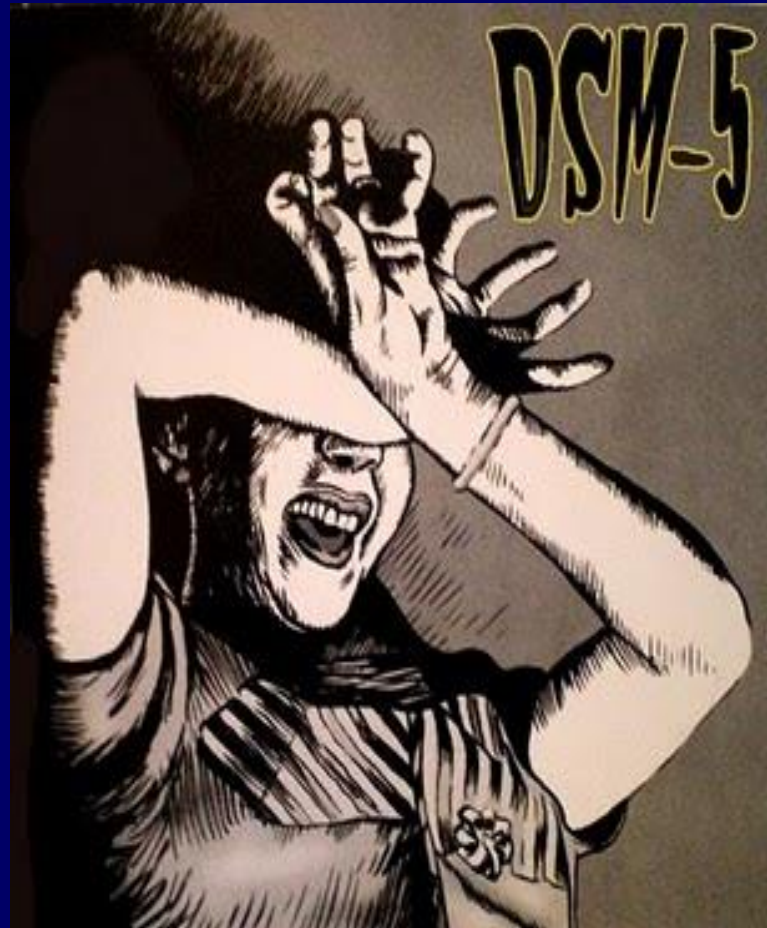
- **Characteristic Bipolar symptoms that do not meet full diagnostic criteria**
- **eg. Short duration hypomanic episodes**
- **eg. Hypomania without MDE**
- **eg. Cyclothymia < 24 months**
- **Sounds like NOS (can we call it OSBaRD?)**

Bipolar and Related Disorders: DSM-5

Unspecified Bipolar and Related Disorder

- Symptoms characteristic of Bipolar Disorder that do not meet full criteria, but “the clinician chooses *not* to specify” why criteria are not met.
- Also sounds like good old NOS
(Can we call it UBaRD?)

Next Come Ten Specifiers



Specifiers: Bipolar and Related Disorders

- **With anxious distress**

Specifiers: Bipolar and Related Disorders

- **With anxious distress**
- **With mixed features**

Specifiers: Bipolar and Related Disorders

- With anxious distress
- With mixed features
- **With rapid cycling**

Specifiers: Bipolar and Related Disorders

- With anxious distress
- With mixed features
- With rapid cycling
- **With melancholic features**

Specifiers: Bipolar and Related Disorders

- With anxious distress
- With mixed features
- With rapid cycling
- With melancholic features
- **With atypical features**

Specifiers: Bipolar and Related Disorders

- With anxious distress
- With mixed features
- With rapid cycling
- With melancholic features
- With atypical features
- **With psychotic features**

Specifiers: Bipolar and Related Disorders

- With anxious distress
- With mixed features
- With rapid cycling
- With melancholic features
- With atypical features
- With psychotic features
- **With catatonia**

Specifiers: Bipolar and Related Disorders

- **With anxious distress**
- **With mixed features**
- **With rapid cycling**
- **With melancholic features**
- **With atypical features**
- **With psychotic features**
- **With catatonia**
- **With seasonal pattern**

Specifiers: Bipolar and Related Disorders

- With anxious distress
- With mixed features
- With rapid cycling
- With melancholic features
- With atypical features
- With psychotic features
- With catatonia
- With seasonal pattern
- **In partial or full remission**

Specifiers: Bipolar and Related Disorders

- With anxious distress
- With mixed features
- With rapid cycling
- With melancholic features
- With atypical features
- With psychotic features
- With catatonia
- With seasonal pattern
- In partial or full remission
- **Mild, Moderate or Severe**

How do Bipolar and Depressive Disorder Specifiers Differ?

Specifiers

- **Bipolar Disorder has Rapid Cycling, but lacks With Peripartum Onset**
- **Yet Bipolar Disorder can have Peripartum Onset and Depressive Disorders can have Rapid Cycling**
- **We need an NOS specifier**

DIAGNOSTIC AND STATISTICAL
MANUAL OF
MENTAL DISORDERS

FIFTH EDITION

DSM-5

**Open for all
the gory details**

AMERICAN PSYCHIATRIC ASSOCIATION

**That was easy, now let's take
a look at some real issues**

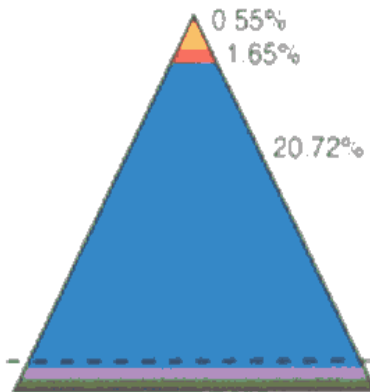


**“I tell you, a playpen is just plain worthless –
what we need around here is a good cardboard box.”**

“Our data suggest that every depressive individual manifesting signs of hyperactivity, irritability, euphoria, or mood irritability could well be bipolar.”

Angst and Gamma. Clin Approaches in Bipolar Disorders 1:10-14, 2002

DSM-IV



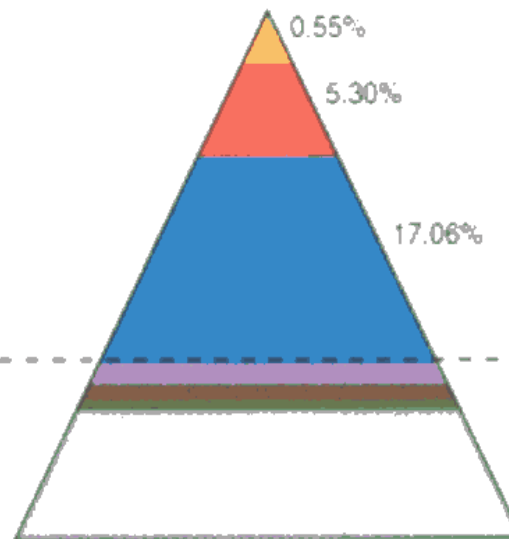
Major depressive episodes

Minor depressive episodes

Total prevalence 25.7%

Ratio of MDD vs BP-I or BP-II 9.4

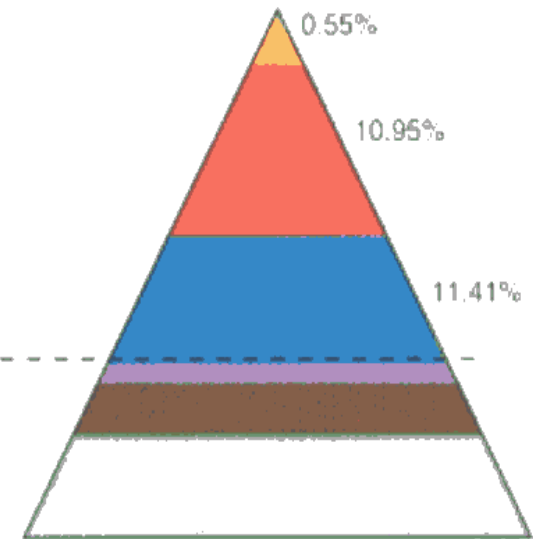
Zurich strict criteria



49.5%

2.9

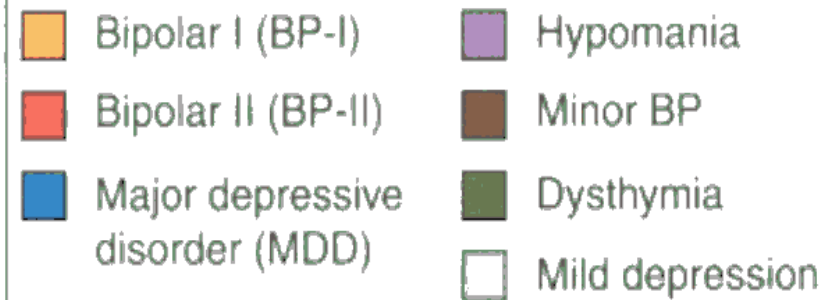
Zurich broad criteria



49.5%

1.0

Bipolar Spectrum



Zurich Study Hypomania Criteria

- **Strict**

3 or more DSM-IV criteria

Minimum duration 1 day

Consequences

- **Broad**

2 or more DSM-IV criteria

No minimum duration

No consequences

Hagop Akiskal

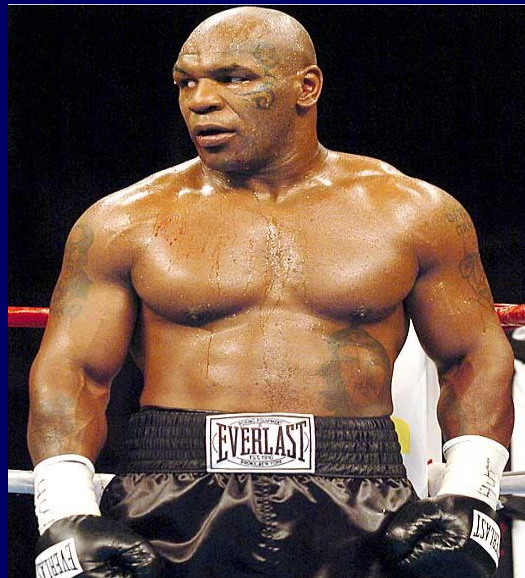


The Bipolar Spectrum According to Akiskal

- **Bipolar 1/2 Schizobipolar**
- **Bipolar I Manic-depressive illness**
- **Bipolar I 1/2 Depression, protracted hypomania**
- **Bipolar II Depression, discrete hypomania**
- **Bipolar II 1/2 Depression on cyclothymic temperament**
- **Bipolar III Depression, hypomania due to somatic Rx**
- **Bipolar III 1/2 Depression, mood swings, hypomania due to substance abuse**
- **Bipolar IV Depression on hyperthymic temperament**
- **Bipolar V Recurrent depressions (≥ 5 episodes)**

Thursday, September 22, 1988, The Anchorage Times

Tyson suffers from 'manic depression'



Eventually, it may be easier to assume that everyone is bipolar, and then exclude the few who aren't

The BIPOLAR SPECTRUM



- **Concerns about Bipolar Over-Diagnosis in Children Resulted in the Creation of Disruptive Mood Dysregulation Disorder in DSM-5**

- **“Everything we hear is an opinion, not a fact. Everything we see is a perspective, not the truth.”**

Marcus Aurelius (121-180 AD)

Subthreshold Bipolarity

- It is a risk factor for future bipolar disorder

Zimmerman M, J Clin Psychiatry 2012;73:437-443

Subthreshold Bipolarity

- It is a risk factor for future bipolar disorder
- **But, if diagnostic criteria are broadened, false positives will exceed true positives**

Subthreshold Bipolarity

- It is a risk factor for future bipolar disorder
- But, if diagnostic criteria are broadened,
f false positives will exceed true positives
- **Resulting in inappropriate exposure to
psychiatric drugs**

Mood Disorder Questionnaire (MDQ)

The Mood Disorder Questionnaire

INSTRUCTIONS: Please answer each question as best you can. YES NO

1. Has there ever been a period of time when you were not your usual self and...

...you felt so good or so hyper that other people thought you were not your normal self or you were so hyper that you got into trouble?	<input type="checkbox"/>	<input type="checkbox"/>
...you were so irritable that you shouted at people or started fights or arguments?	<input type="checkbox"/>	<input type="checkbox"/>
...you felt much more self-confident than usual?	<input type="checkbox"/>	<input type="checkbox"/>
...you got much less sleep than usual and found that you didn't really miss it?	<input type="checkbox"/>	<input type="checkbox"/>
...you were much more talkative or spoke much faster than usual?	<input type="checkbox"/>	<input type="checkbox"/>
thoughts raced through your head or you couldn't slow your mind down?	<input type="checkbox"/>	<input type="checkbox"/>
...you were so easily distracted by things around you that you had trouble concentrating or staying on track?	<input type="checkbox"/>	<input type="checkbox"/>
...you had much more energy than usual?	<input type="checkbox"/>	<input type="checkbox"/>
...you were much more active or did many more things than usual?	<input type="checkbox"/>	<input type="checkbox"/>
...you were much more social or outgoing than usual, for example, you telephoned friends in the middle of the night?	<input type="checkbox"/>	<input type="checkbox"/>
...you were much more interested in sex than usual?	<input type="checkbox"/>	<input type="checkbox"/>
...you did things that were unusual for you or that other people might have thought were excessive, foolish, or risky?	<input type="checkbox"/>	<input type="checkbox"/>
... spending money got you or your family in trouble?	<input type="checkbox"/>	<input type="checkbox"/>

2. If you checked YES to more than one of the above, have several of these ever happened during the same period of time? YES NO

3. How much of a problem did any of these cause you - like being unable to work; leaving family, money, or legal troubles; getting into arguments or fights?
Please circle one response only.

No problem	Minor problem	Moderate problem	Serious problem
------------	---------------	------------------	-----------------

- Bipolar screening
- 7 of 13 yes/no questions
- Several at same time
- Moderate or serious problem
- Correctly identified
- 7 of 10 with bipolar (sensitivity)
- 9 of 10 without bipolar (specificity)

Hirschfeld et al. Am J Psychiatry. 2000;157:1873-1875. (14 years old)

Predictive Value of the MDQ

The **positive predictive value** of the MDQ in a community sample would be about 26%
(about 3 of 4 false positives)

The **negative predictive value**, however, would be quite high
(very few false negatives)

Comorbidity Can Cause Diagnostic Confusion





Bipolar Disorder Comorbidity

- Substance abuse: up to 60%¹
- Anxiety: 42%²
- Social phobia: 18-40%¹
- OCD: 7.4-35.0%¹
- Eating disorders: 5%²
- Migraine: 8.6-44.0%^{3, 4}

¹Cassano GB et al. (2000), J Affect Disord 59(suppl 1):S69-S79; ²McElroy SL et al. (2001), Am J Psychiatry 158(3):420-426; ³Fasmer OB (2001), Cephalalgia 21(9):894-899; ⁴Robbins L, Ludmer C (2000), Am J Pain Management 10(4):167-170

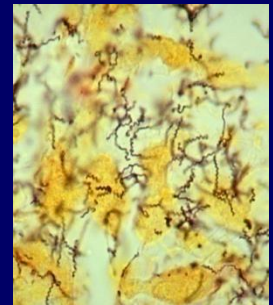
Where to From Here?

**General paralysis of the insane
(dementia paralytica, paresis)**

> 10% of mental hospital admissions until...

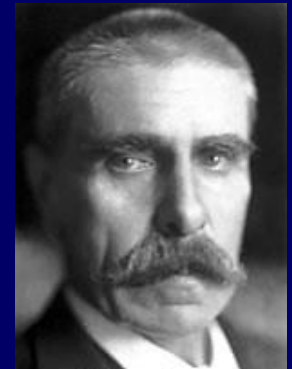


- **1913 - Noguchi and Moore found syphilitic spirochetes in the brains of paretics**



- **1917 – Malaria treatment (pyrotherapy) by Wagner-Jauregg effective for general paresis**

- **1927 – He gets the Nobel prize**



Where to From Here in 2014?

The search for the etiology of bipolar disorder continues



The Bipolarity Virus

- **Herpes simplex and bipolar disorder are clinically episodic illnesses**

The Bipolarity Virus

- Herpes simplex and bipolar disorder are clinically episodic illnesses
- **Lithium has antiviral activity**

The Bipolarity Virus

- Herpes simplex and bipolar disorder are clinically episodic illnesses
- Lithium has antiviral activity
- **Lithium has antibipolar activity**

The Bipolarity Virus

- Herpes simplex and bipolar disorder are clinically episodic illnesses
- Lithium has antiviral activity
- Lithium has antibipolar activity
- **Therefore, a virus causes bipolar disorder**

Post-Test Question #1

1. The results of a survey of the general population found that the most common association with Bipolar Disorder was:
 - A. Psychiatric illness
 - B. Bad weather front
 - C. Melting of polar ice caps

Post-Test Question #2

2. In what version of the DSMs did Bipolar Disorder replace Manic-Depressive Disorder?

- A. DSM-II
- B. DSM-III
- C. DSM-IV
- D. DSM-5

Post-Test Question #3

3. How many Bipolar Specifiers are in DSM-5?

- A. 6
- B. 8
- C. 10
- D. 12
- E. 14

Post-Test Question #4

4. The most common Bipolar Disorder comorbidity is which of the following?
- A. Anxiety Disorders
 - B. Migraine
 - C. Major Depression
 - D. Substance Abuse
 - E. OCD

Post-Test Question #5

5. Concerns about the overdiagnosis of Bipolar Disorder in children led to the creation of which of the following diagnoses in DSM-5?
- A. Depression Protracted by hypomania
 - B. Unspecified Bipolar and Related Disorder
 - C. Illness Anxiety Disorder
 - D. Disruptive Mood Dysregulation Disorder
 - E. Unspecified Disruptive, Impulse-Control and Conduct Disorder

Post Test Answers

- 1- Ans: C (Melting of polar ice caps 64%,
Bad weather front 17%, Psychiatric illness
4- 6%)
- 2- Ans: B (DSM-III)
- 3- Ans: C (10)
- 4- Ans: D (Substance Abuse)
- 5- Ans: D (DMDD)

Where to From Here?

- The search for the bipolarity virus is underway
- Will neuroimaging unlock the door to diagnosis?
- **At present, diagnosis by committee is the best we have**

DIAGNOSTIC AND STATISTICAL
MANUAL OF
MENTAL DISORDERS

FIFTH EDITION

DSM-5

**Open cover,
read, and
diagnose**

AMERICAN PSYCHIATRIC ASSOCIATION



After the break
I'LL BE BACK!