

عیش شخصی یا کم شخصی:

کدامیک در مدیریت اختلال دوقطبی غالب است؟

دکتر امیر شعبانی

گروه روانپزشکی دانشگاه علوم پزشکی ایران، گروه پژوهشی اختلالات دوقطبی

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# New Trend

The rare  
Cinderella psychiatric disorder

1990s-2000s

24% soft and softest bipolarity



# Bipolar & Bipolar Spectrums

<b>Klerman</b>	<b>Recurrent unipolar mania; Depression + family history of BD</b>
<b>Kraepelin</b>	<b>Recurrent depression on the spectrum of manic depressive illness</b>
<b>Leonhard, 1950s</b>	<b>Bipolar and unipolar recurrent psychoses</b>
American researchers (headed at the <b>Washington University</b> of St. Louis) (1960s-70s)	<b>Bipolar illness and unipolar depressive illness</b>
<b>Research Diagnostic Criteria (RDC), 1970s</b>	<b>Bipolar with mania/Bipolar with hypomania/MDD</b>
<b>DSM-III, 1980</b>	<b>Bipolar/Cyclothymic/Major depression/Dysthymic</b>
<b>Goodwin and Jamison, 1990</b>	<b>Recurrent or treatment-refractory depression on the bipolar spectrum</b>
<b>Akiskal</b>	<b>Subtyping and temperaments</b>
<b>Ghaemi, Goodwin, Ko, 2002</b>	<b>Categorical bipolar spectrum illness</b>
<b>Angst, 2003</b>	<b>Minor bipolar disorder</b>
<b>Angst, Gamma, et al., 2003</b>	<b>Softest bipolarity (between BD and normality, 13%)</b>
<b>Sachs, 2004</b>	<b>Bipolarity Index</b>
<b>Koukopoulos</b>	<b>Mixed states</b>

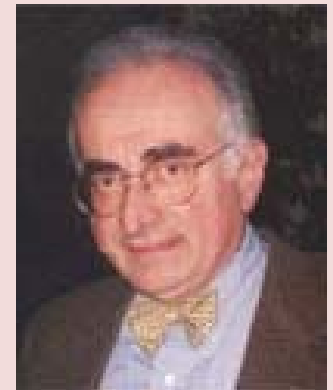
# Bipolar Spectrum is a Clinical Reality

- 1) no sharp **boundaries** exist between mania or depression and **normal** experience
- 2) current understanding about **risk factors** for BD
- 3) the diathesis-stress model and the role of **temperament**
- 4) mounting empiric evidence from epidemiologic and clinical studies that **spectrum presentations** of BD exist, fall along a continuum, and are often associated with profound **impairment**.

- **More recent efforts examining cross-diagnostic categories have determined that there appears to be a higher genetic correlation between **BD-schizophrenia** than between **BD-MDD**.**

(Cross-Disorder Group of the Psychiatric Genomics Consortium, et al., 2013)

- Concern that BD was becoming **overdiagnosed** first arose more than a decade ago.



**ROSS J. Baldessarini**

(Baldessarini RJ. A plea for integrity of the bipolar disorder concept. *Bipolar Disord.* 2000;2(1):3-7)

**Overdiagnosis:**

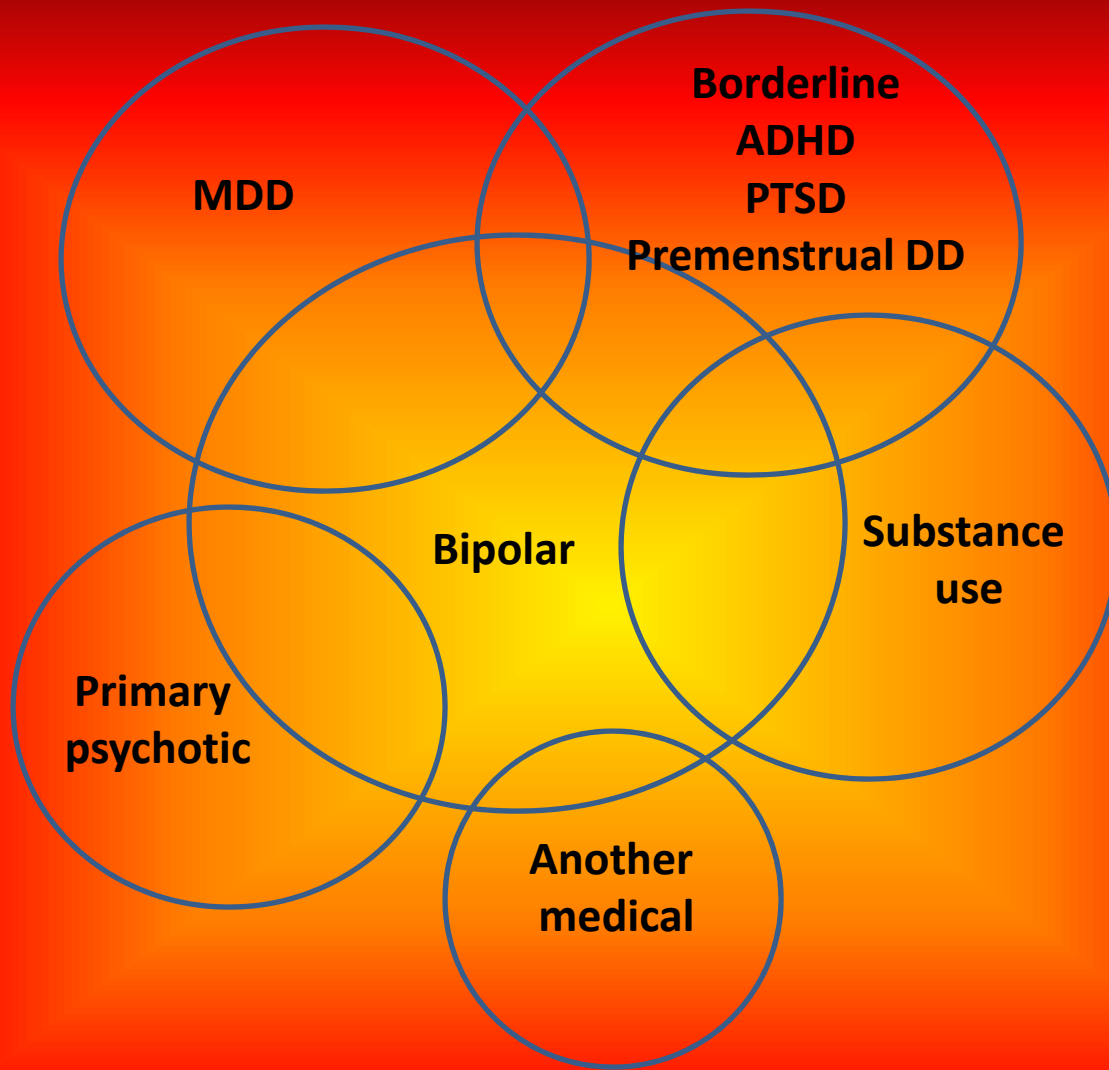
**Is it a real?**

Author/year	Sample	Gold standard	Findings
Ghaemi et al. (2000) [9]	Outpatients	SCID	Clinician-based diagnosis of BD: PPV of 34% and NPV of 95%
Stewart and El-Mallakh (2007) [10]	Outpatients from substance abuse treatment program	DSM-IV criteria	Only 42.9% of patients diagnosed with BD actually met diagnostic criteria Only 33% of patients diagnosed with BD actually met criteria for that condition.
Goldberg et al. (2008) [11]	Dual diagnosis inpatients	SCID	Misdiagnosis associated with cocaine and polysubstance abuse
Zimmerman et al. (2008) [8]	Outpatients	SCID	Clinician-based diagnosis of BD: PPV of 37% and NPV of 95%
Ruggero et al. (2010) [12]	Outpatients	SCID	40% of patients with borderline personality disorder mistakenly diagnosed with BD
Zimmerman et al. (2010) [13]	Outpatients	SCID	Patients overdiagnosed with BD were significantly more likely to receive disability payments
Chilakamarri et al. (2011) [14]	Child outpatients	DSM-IV criteria	Minimum number of patients misdiagnosed with BD; underdiagnosis was common



# Potential reasons for overdiagnosis

- 1) Bipolar spectrum model/ Looser criteria**
- 2) Unipolar phobia**
- 3) The textbook for psychiatry training**
- 4) Inclination to diagnose a potentially medication-responsive dis.**
- 5) Cluster B PD/ Substance abuse/ ADHD/ PTSD**
- 6) Irrational use of screening tools; Insufficient diagnostic rigor**
- 7) Poor education for psychology students**
- 8) Secondary gain associated with receiving disability payments**



(Koenigsberg, 2010; Swann et al., 1987; Swann et al., 2001; Manuck et al., 1998; Paris, 2007; Parker G., 2011)	<b>Bipolar</b>	<b>Borderline Personality</b>
<b>Personality</b>	No distinctive style	Ongoing emotional dysregulation
<b>Course</b>	Unstable instability	Stable instability
<b>Onset</b>	Usually distinctive	No clear
<b>Age at onset</b>	Early or late	Early
	Mood swings	Emotional dysregulation
<b>Mood lability</b>	Autonomous/More sustained	Triggered/Less sustained
<b>Severity of impulsivity</b>	Lower	Higher
<b>Impulsiveness</b>	Attentional	Non-planning
<b>Impulsivity features</b>	State/Noradrenergic	Trait/Serotonergic
<b>Depression</b>	More melancholic	More non-melancholic
<b>Mood dis. in Family</b>	Higher rate	Lower rate
<b>Attribution style</b>	View episodes as 'their' problem (BIID)	Usually blame another person as the cause
<b>Treatment outcome</b>	Remission	No remission

# BD & BPD



**Borderline is not a personality disorder:**

1- An ensemble of personality disorders; 2- bipolar disorder

There has been a rush to judgment about the bipolar spectrum. **BPD and BDs do not exist on a spectrum** but the data allow for the possibility of partially overlapping etiologies.



Distinguishing between BIID and BPD is valid.

The bipolar spectrum is a disease-process; **BPD is a clinical picture, but not a disease.** BPD is our culture's interpretation of what used to be called "**hysteria**".



# Screening instruments



Robert M.A. Hirschfeld

**Mood Disorders Questionnaire**

**Bipolar Spectrum Diagnostic Scale**



S. Nassir Ghaemi

The screening instruments have become widely available on the **Internet**, further contributing to **widespread self-diagnosis** among members of the general public, with an associated tendency to **romanticize** this condition.

**Overdiagnosis:**

**Is it a real?**

**Is it worth paying attention?**

# Potential risks of overdiagnosis

- 1) **Overtreatment or inappropriate treatment**
- 2) **Unnecessary adverse medication effects**
- 3) **Wrongful maintenance pharmacotherapy**
- 4) **Increasing stigma**
- 5) **Excessively diluting samples**
- 6) **Limiting discovery**
- 7) **Misleading clinicians into misdiagnosing relatives as having BD** (Shabani, 2007)
- 8) **Potential for diagnostic oversimplification, with consequent diagnostic deskilling and loss of credibility for the psychiatric profession** (Mitchell, 2012)

**Overdiagnosis:**

**Is it a real?**

**Is it worth paying attention?**

**Does it prevail over underdiagnosis?**



## Zimmerman, et al., 2010 [MIDAS project]

- **N=700 outpatients**

Table 2. Current DSM-IV Axis I Diagnoses of 700 Psychiatric Outpatients

DSM-IV Diagnosis	N	%
Major depressive disorder	374	53.4
Bipolar disorder	90	12.9
Dysthymic disorder	64	9.1
Generalized anxiety disorder	125	17.9
Panic disorder	149	21.3
Social phobia	179	25.6
Specific phobia	72	10.3
Obsessive-compulsive disorder	45	6.4
Posttraumatic stress disorder	131	18.7
Adjustment disorder	47	6.7
Schizophrenia	3	0.4
Eating disorder	66	9.4
Alcohol abuse/dependence	85	12.1
Drug abuse/dependence	45	6.4
Somatoform disorder	58	8.3
Attention-deficit disorder	43	6.1
Impulse-control disorder	92	13.1

## Zimmerman, et al., 2010 [MIDAS project]

- N=700 outpatients
- Bipolar disorders: **13%**, 90/700  
29% BID; 46% BIID; 23% BD-NOS; 2% Cyclothymic
- Previous bipolar diagnosis: **21%** (145/700): **43% true bipolar** (SCID)

Table 3. Association Between the Diagnosis of Bipolar Disorder Based on the Structured Clinical Interview for DSM-IV (SCID) and Patient Report of Previous Diagnosis of Bipolar Disorder

Self-Reported Prior Diagnosis of Bipolar Disorder	SCID Bipolar Disorder Diagnosis		
	Present	Absent	Total
Yes	63	82	<b>13.4% over-</b>
No	<b>30% under-</b>	528	555
Total	<b>90</b>	<b>610</b>	700

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Sensitivity	Specificity	PPV	NPV
70%	87%	43%	95%
Underdiagnosis	Overdiagnosis		
30% $\times 90 = 30$	13% $\times 610 = 79$		

**Over-/Under-=2.6**

(Phelps, Ghaemi, 2012)

# Overdiagnosis/Underdiagnosis

- **Burden?**
- **Reversibility?**

## **Overdiagnosis:**

**Is it a real?**

**Is it worth paying attention?**

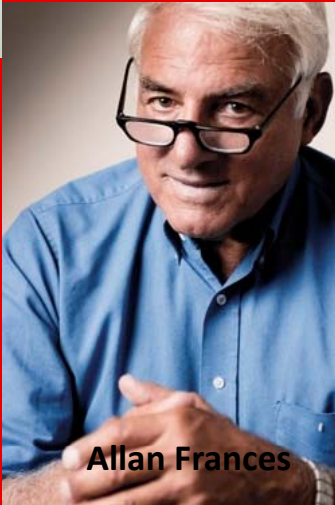
**Does it prevail over underdiagnosis?**

**The focus of attention?**

# Bipolar spectrum critics



Philip B. Mitchell



Allan Frances



Mark Zimmerman



Joel Paris



David Healy



Jules Angst



Athanasios Koukopoulos

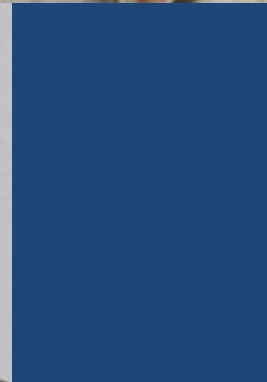
# Bipolar spectrum proponents



James Phelps



Hagop Akiskal



S. Nassir Ghaemi

# Critiques

1. Lack of widely accepted **definitions**
2. The difficulty in **reliably** identifying subsyndromal presentations
3. **Operationalizing** subthreshold bipolarity
4. Differentiating subthreshold bipolarity from **BPD**
5. Bipolar spectrum might subsume cases with **non-bipolar** Disorders.
6. Uncertainties about optimal **interventions** for subthreshold
7. More diagnosis of bipolar spectrum may increase **aggressive pharmacotherapy**.

# Critiques

1. **Diagnostic creep:** Capturing the borders of bipolar phenomenology
2. **Assimilating** other disorders into the bipolar rubric
3. **Diagnostic Encroachment**
4. **Disease mongering:** pathologizing presentations within normal **limits** (Healy D: The latest mania: selling bipolar disorder; 2006)
5. **Imperialism of bipolar disorder** (Alan Francis)
6. **Weakening** or trivializing the core concept of **BD** (Baldessarini, 2000)

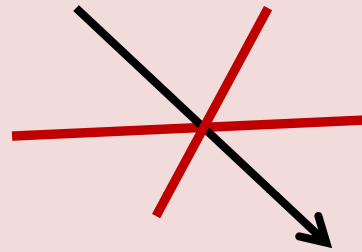


# No Class, but confusing effect!

- **Lithium** is effective in unipolar depression, not just BD. (Prien, et al, 1974)
- The presumed strong efficacy of **antidepressants** in MDD was thrown into doubt with the discovery of a large number of negative unpublished studies. (Turner, et al, 2008)
- **Atypical antipsychotics** showed efficacy for depressive episodes, not limited to BD but even in MDD with some agents. (Nelson, et a, 2009)
- **Aripiprazole** does not seem to be efficacious in bipolar depression, but is apparently effective in unipolar depression.
- **Antidepressants** may protect patients with BD but not unipolar depressive disorder from **suicidal** behavior. (Leon, et al, 2014)
- An anticonvulsant, **lamotrigine**, were much more effective in preventing depression rather than mania. (Goodwin, et al, 2004) And an antipsychotic, **lurasidone**, is FDA approved for treating bipolar depression, and not mania.
- There are no class effect for antidepressants in treating MDD (Cipriani, et al, 2009) and BD, and for mood stabilizers/antipsychotics in treating BD.
- There is **very little research** on exactly which treatments are most effective among the neuroleptics and mood stabilizers, at which doses, and for how long.

# No Class, but confusing effect!

- **Bipolar spectrum**

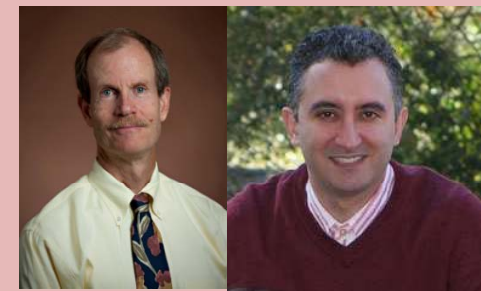


**Standard treatment of bipolar disorder**

# “two-step diagnostic process”

(Phelps, Ghaemi, 2012)

- Solving the problem of overdiagnosis by tightening diagnostic criteria is virtually impossible.
- For diagnoses that are **relatively uncommon** in the general population, for example, 1–5% frequencies, unless a diagnostic instrument is nearly perfect, the **inevitable false positives** will outnumber the true positives.



# “two-step diagnostic process”

(Phelps, Ghaemi, 2012)

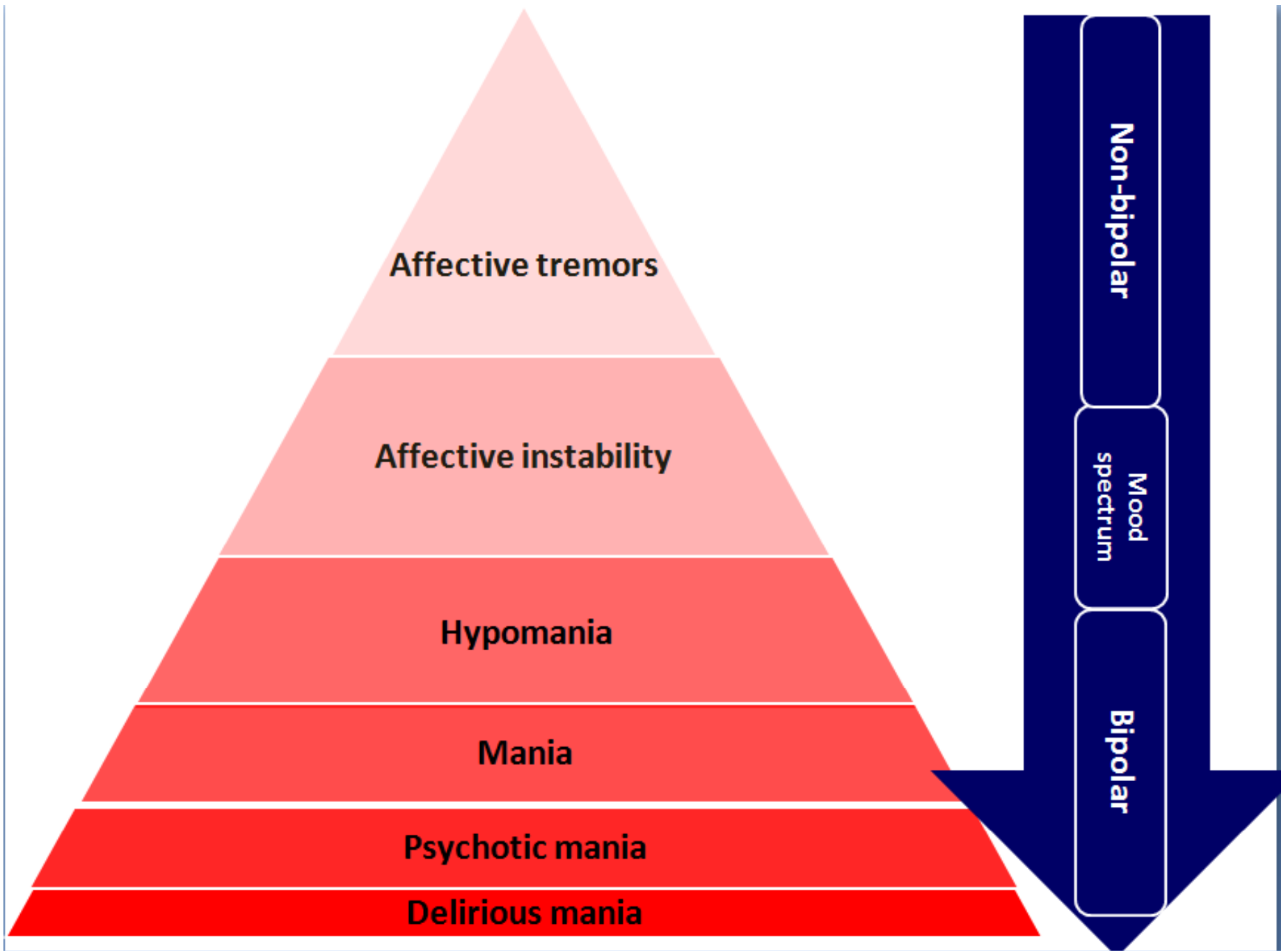
- 1) Needs to be tested: like any other approaches
- 2) Unknown and probably low reliability/validity of clinical diagnosis of bipolar features: FH\* of BID/BIID; temperaments; ...
- 3) Various directions of misdiagnosis:  
MDD/BPD/Schizophrenia/ADHD/PTSD/Substance-induced/Another medical condition
- 4) Originality of main criteria vs. second hand bipolar features
- 5) Early onset is in favor of which one: BPD>BD>MDD?
- 6) The more bipolar indices, the more bipolar diagnosis!
- 7) There is no any index for MDD! And no concern for that!
- 8) Irreversibility of bipolar diagnosis; contrary to MDD
- 9) Prior probability: setting-dependent
- 10) Low reliability of BIID and unknown reliability for soft bipolars
- 11) Understandable reluctance by primary care clinicians to diagnose and manage these complex and challenging patients

# “two-step diagnostic process”

- **Validity of family history** : Subjects with **BD I**, **BD II**, and **MDE** with subthreshold hypomania described (in response to a simple single question) rates of a family history of mania in a relative of **70%**, **68%**, and **76%**, respectively—extraordinarily high rates.

(Angst J, Cui L, Swendsen J, et al. Major depressive disorder with subthreshold bipolarity in the National Comorbidity Survey Replication. Am J Psychiatry. 2010; 167( 10): 1194-1201.)

- While BD is characterized by a **younger age at onset** and greater diagnostic **comorbidity** than non-bipolar depression, the same differences would be predicted to differentiate depressed patients with and without a personality disorder.



# Diagnosing Bipolar

- 1) **Criteria:** systematically assessing
- 2) **Multiple** associated features/screening tools
- 3) **Differential** diagnoses of affective instability
- 4) **Multiple contacts** with the patient
- 5) **Patience** and follow