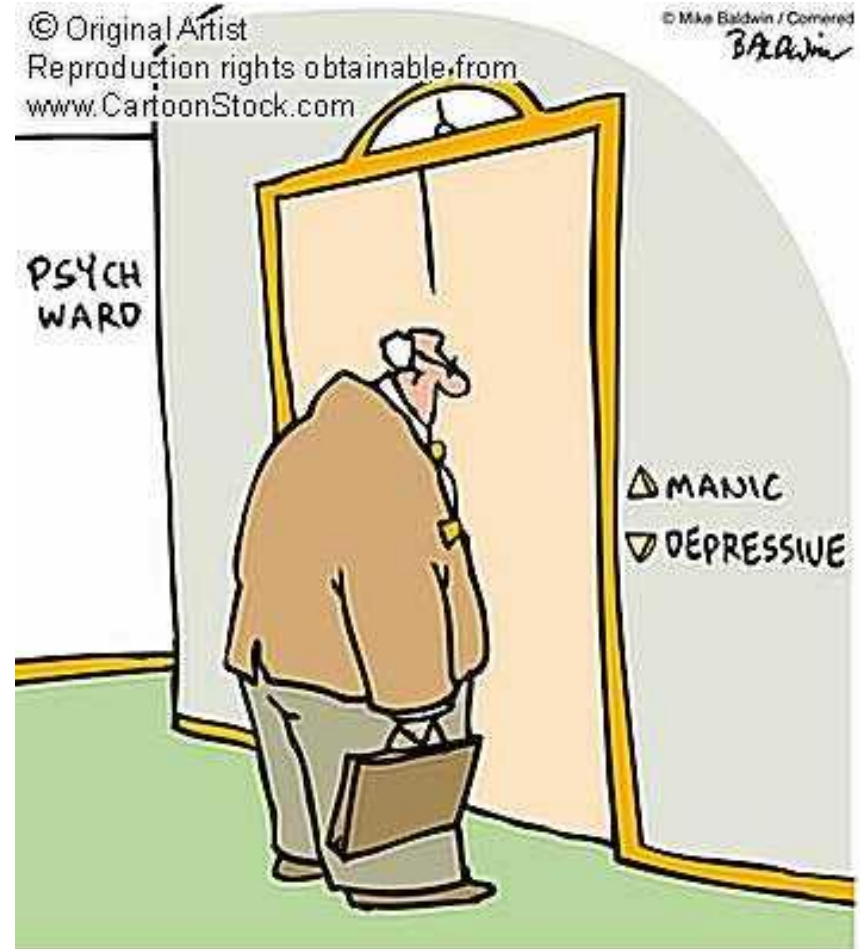


# Bipolar disorder

Paz García-Portilla



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# BD I: Epidemiology

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- Life-time prevalence
  - 1% (0.7 – 1.8%)
  - 30% with diagnosis and without treatment, or with erroneous diagnosis (major unipolar depression, borderline PD)
- Age at onset
  - Adolescence – young adulthood
  - If positive family history: higher likelihood of early onset
  - BD II: something later
  - Depression at the onset, > age > likelihood of mania at the onset
- Gender ratio
  - BD I: 1:1
  - Increased risk in women of BD II, rapid cycling and mixed episodes



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# BD I: Epidemiology

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- Marital status
  - Unmarried (never married, separated or divorced, widowed)
- Working status
  - Unemployed (bidirectional)
- Socioeconomic status
  - Higher than schizophrenia and unipolar depression
- High burden of disease



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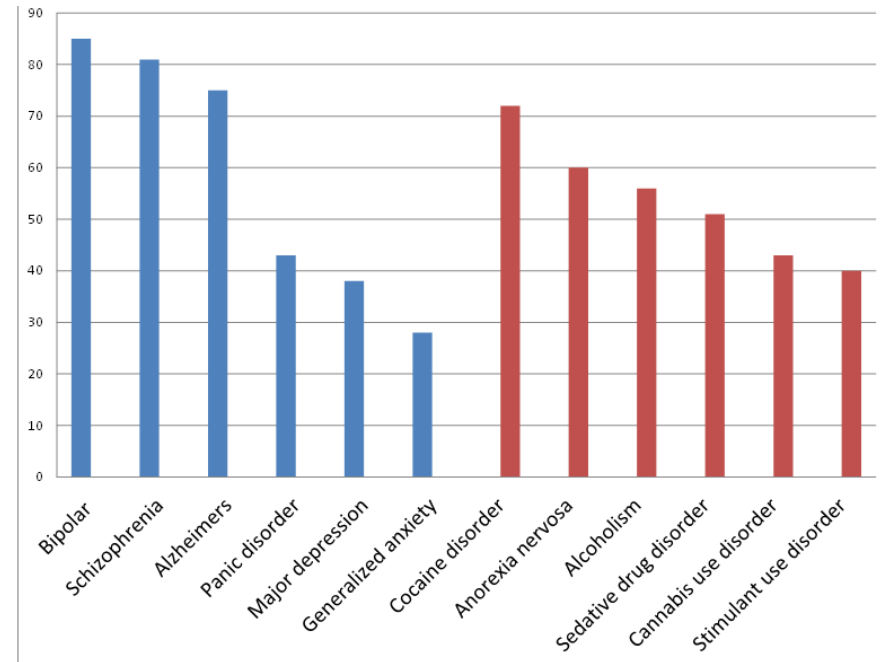
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# BD I: Etiopathogenesis

- Vulnerability
  - Predisposition to develop a MD by genetic and environmental factors, whose interaction determines the expression of the MD
- 1. Genetic factors: Heritability
  - Estimated heritability: 85% (0.73 – 0.93) (McGuffin et al, 2003)
  - Small number of genes of modest effect

First degree relative	10 times more risk
Dizygotic twins	Concordance: 10-20%
Monozygotic twins	Concordance: 40-70%

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# BD I: Etiopathogenesis

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## 2. Environmental factors

- Substance abuse
- Childhood abuse and trauma (earlier onset, greater comorbidity)
- Adverse life events: smaller role than in unipolar depression
- Lifestyle incongruent with sleep/wake rhythm



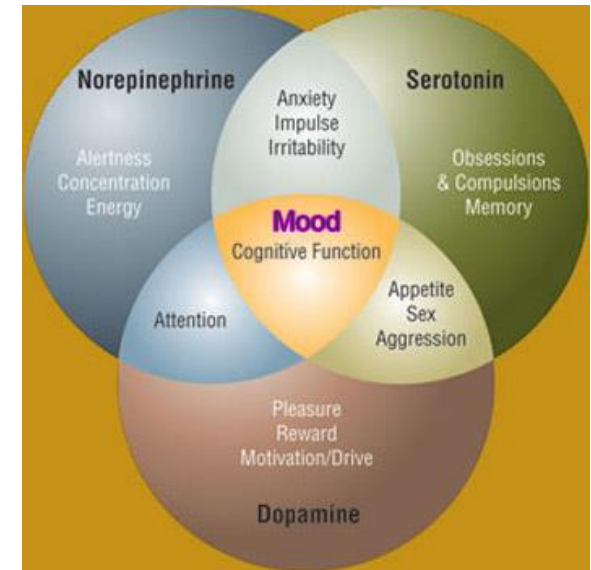
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# BD I: Etiopathogenesis

- Neurotransmitters
  - Bipolar depression
    - DA and NA hypoactivity (5-HT less significant than in unipolar depression)
  - Bipolar mania
    - DA and NA hyperactivity
    - Excitatory amino acids (glutamate, aspartate, cysteine, homocysteine)
- Neuroendocrine factors (HPA axis, thyroid)
- Neuroimaging
  - Global grey matter loss and enlarged brain ventricles
    - Prefrontal cortex and insula (BD I > BD II, also in MDD)
  - Abnormalities in white matter connectivity (BD > MDD)
    - Deep white matter hyperintensities

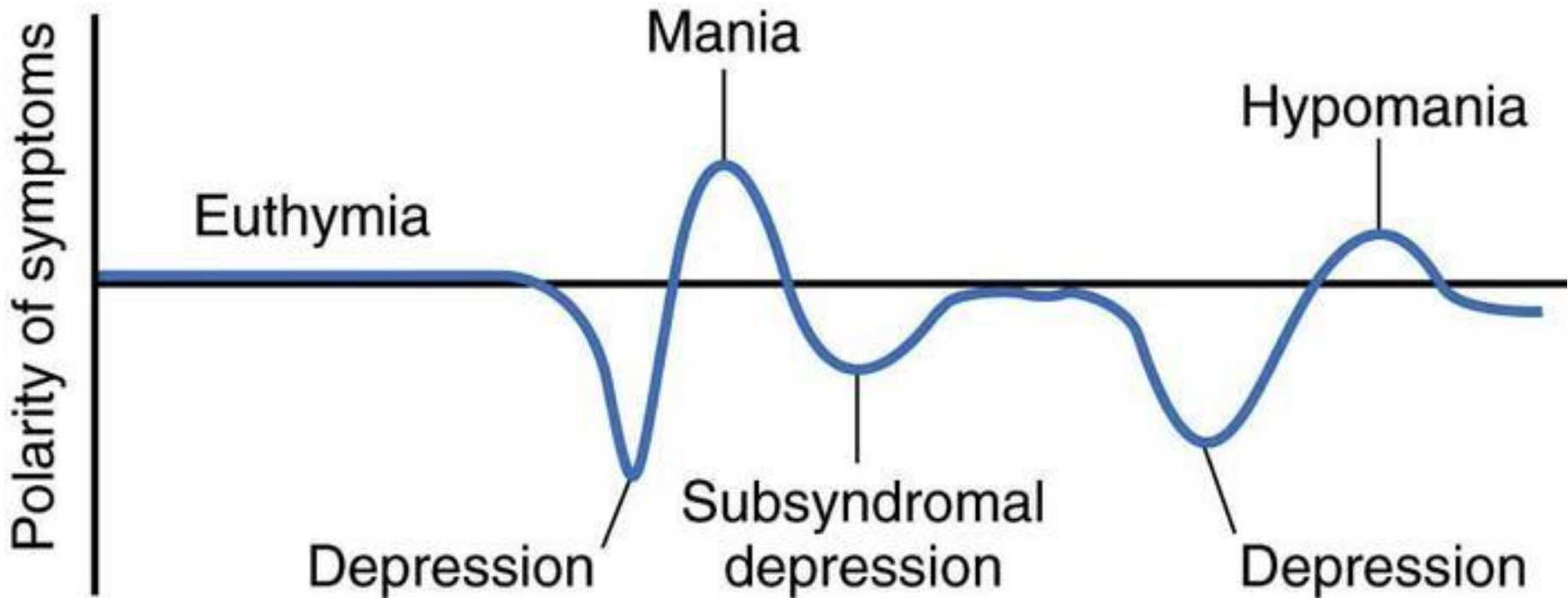


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# BD: Clinical characteristics



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# BD: Clinical characteristics

## Episode subtype

### Major depressive episode

A. At least 2 weeks,  $\geq 2$

- Depressed mood (in children irritability)
- Marked loss of interest or pleasure
- Decreased energy or increased fatiguability

B.  $\geq 2$

- Loss of confidence and self-esteem
- Unreasonable feelings of self-reproach or excessive and inappropriate guilt
- Recurrent thoughts of death or suicide, or any suicidal behaviour
- Complaints or evidence of diminished ability to think or concentrate, indecisiveness or vacillation
- Change in psychomotor activity, with agitation or retardation
- Sleep disturbance of any type
- Change in appetite with weight change

### Manic / Hypomanic episode

A. The mood is predominantly elevated, expansive or irritable (for at least a week – unless hospitalized- / 4 days)

B.  $\geq 3$  (4 if the mood is merely irritable):

- Increased activity / physical restlessness
- Increased talkativeness (pressure of speech)
- Flight of ideas or the subjective experience of thoughts racing
- Loss of normal social inhibitions
- Decreased need for sleep
- Inflated self-esteem or grandiosity
- Distractibility or constant changes in plans
- Behaviour foolhardy
- Marked sexual energy or sexual indiscretions

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(Severe) MANIA: delusions, hallucinations

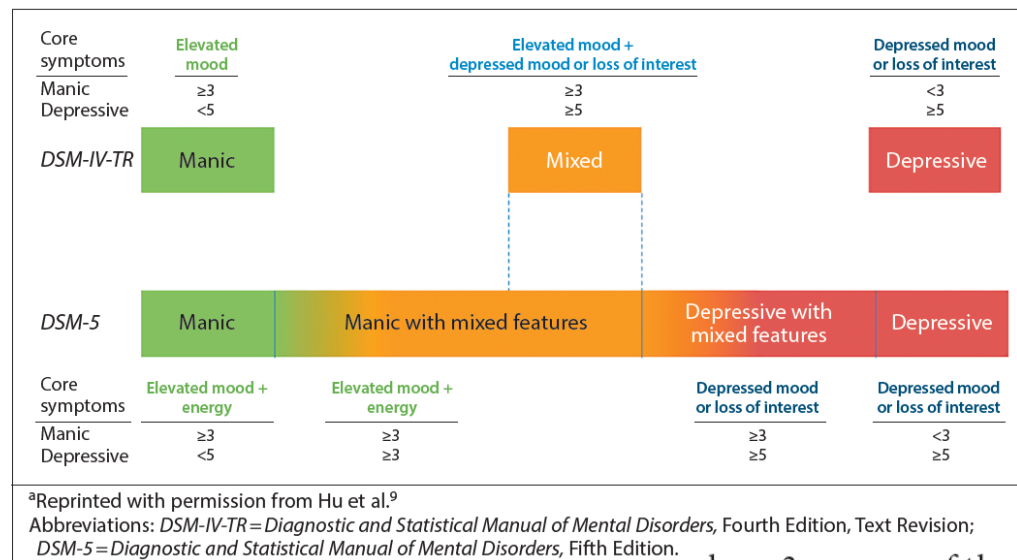


# BD: Clinical characteristics

## Episode subtype: Mixed episode

- Current episode: either a mixture / rapid alternation (within a few hours) of hypomanic, manic and depressive symptoms
- Manic and depressive symptoms prominent most of the time for at least 2 wks
- At least 1 well authenticated hypomanic/manic, depressive, mixed episode in the past

Figure 1. Conceptualization of Bipolar Mixed States in *DSM-IV-TR*<sup>5</sup> Versus *DSM-5*<sup>8</sup> Editions<sup>a</sup>



have at least 3 of the following 6 depressive symptoms:  
 (1) prominent dysphoria or depressed mood, (2) psychomotor retardation, (3) feelings of worthlessness or excessive guilt, (4) diminished interest or pleasure in almost all activities, (5) fatigue or loss of energy, or (6) recurrent thoughts of death.<sup>8</sup>

have 3 or more of the following symptoms of mania/hypomania: (1) elevated or expansive mood, (2) inflated self-esteem or grandiosity, (3) increased talkativeness or pressured speech, (4) flight of ideas or racing thoughts, (5) increase in energy or goal-directed activity, (6) increased or excessive involvement in risky behavior, or (7) decreased need for sleep.<sup>8</sup>

# BD: Clinical characteristics

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- Cognitive impairment
  - Widespread impairments in global cognition and in multiple cognitive domains (in acutely symptomatic and euthymic patients)
  - BD I  $\approx$  BD II
  - Domains
    - **Verbal memory**
    - Processing speed
    - Executive functioning

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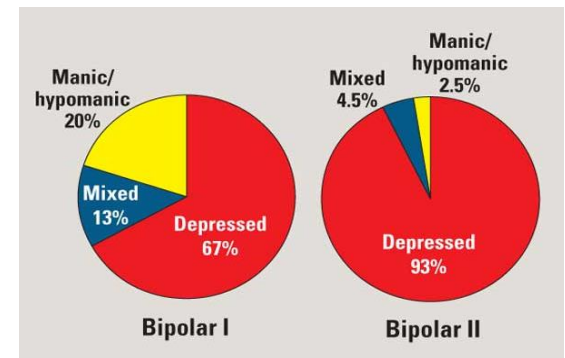


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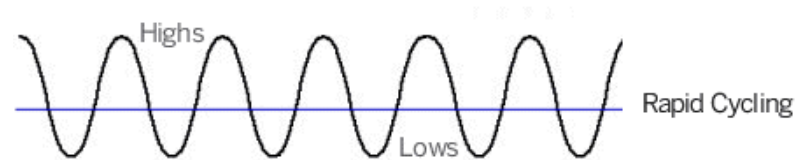
# BD: Subtypes

Episode subtype	BD I	BD II	Cyclothymia (2 years)	BD NOS
Major depressive episode			Subsyndromic sx Subsyndromic symptoms: sx are not sufficient to meet criteria for major depression, mania or a mixed episode	Subsyndromic sx
Manic episode				
Hypomanic episode				Subsyndromic sx
Mixed episode				

- **BD I**
  - DSM: 1 or more manic or mixed episodes
  - ICD: 1 major depressive + 1 manic episode
- **Rapid cycling (any BD type)**
  - 4 or more episodes / yr
  - More frequent in women
  - More resistant to treatment

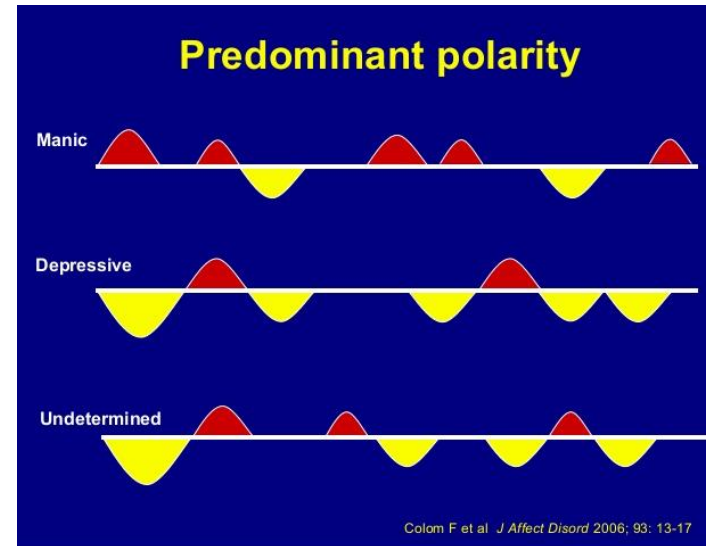


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# BD: Subtypes

- Predominant polarity (PP): roughly 50% of patients
  - Depressive predominant polarity (DPP)
    - The most prevalent
    - Higher number of suicidal attempts
    - Poor prognosis
    - Poor response to treatment
      - “Hidden bipolar”
  - Manic or hypomanic PP (MPP)
    - Younger age at onset
    - History of substance abuse



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# BD: Differential diagnosis

- Unipolar depression: consider Bipolar depression if **≥5 of the following**

<b>Symptoms</b>	Hypersomnia and/or delayed sleep phase
	Increased appetite / Weight increase
	Other atypical depressive sx
	Psychomotor retardation
	Psychotic sx / Excessive and inappropriate guilt
	Emotional lability / Irritability
	Melancholia
<b>Course of illness</b>	Early onset (first episode <25 a)
	Onset of depression in autumn
	History of child abuse or other stressors
	Past or current anxiety or substance use disorders
<b>Family history</b>	Positive for BD
<b>Treatment response</b>	More treatment-refractory
	Risk of affective switching secondary to treatment
<b>Risk of suicidal behaviours</b>	



# Bipolar vs Unipolar depression

Figure 3. Age at Onset of Bipolar Disorder Versus Major Depressive Disorder<sup>a</sup>

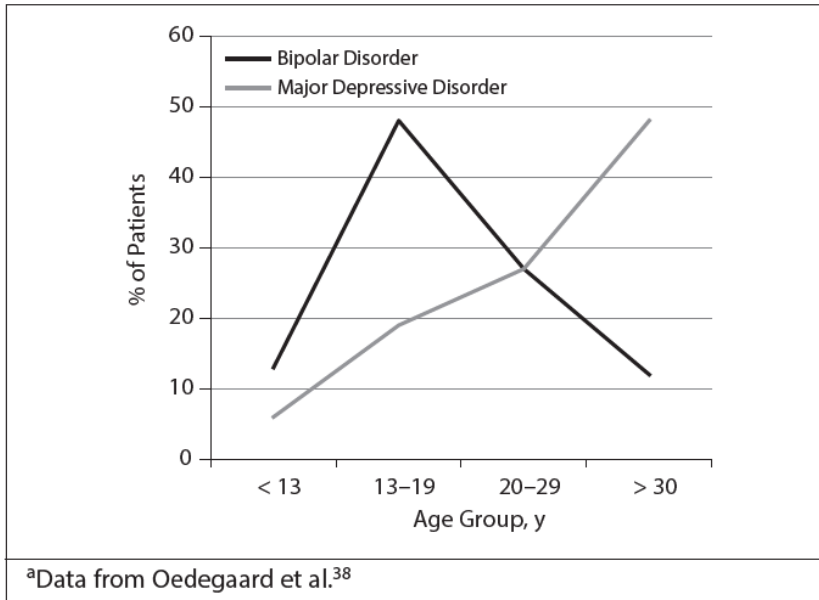
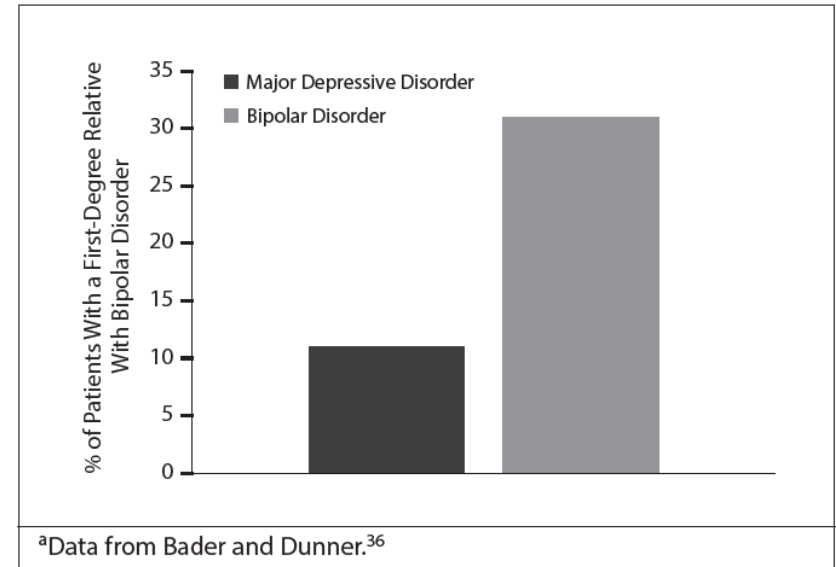


Figure 4. Bipolar Disorder Among First-Degree Relatives in Patients With Major Depressive Disorder Versus Bipolar Disorders<sup>a</sup>



> likelihood of onset with depression



# BD: Differential diagnosis

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2/3 of patients shows at least one Axis I / II comorbidity

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- Anxiety disorders
  - 75-90% of patients with BD I has comorbid clinical anxiety
  - Panic and Generalized anxiety disorders
- Substance use disorders
  - Frequently comorbid
  - Alcohol, cannabis, cocaine, extasis and anphetamines
  - En relación con elevación del humor y alivio de la ansiedad
  - SUD: multiple drugs abuse / BD: 1 ó 2 (alcohol, cocaine)
- Borderline personality disorder
  - Mood instability, impulsivity, substance abuse, chaotic relationships
  - Comorbid in the 20-30% of patients with BD
  - Infrequently euphoria



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# BD: Differential diagnosis

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- Schizophrenia
  - First episodes
  - Family history of schizophrenia, premorbid adjustment, bizarre psychotic symptoms, lack of persistent mood symptoms
  - Longitudinal observation
- Somatic illnesses
  - Parietal lobe infarction (depression and mania)
  - Hyperthyroidism (mania), Hypothyroidism (depression)
  - Temporal lobe epilepsy
  - Cancer
  - Drugs: corticosteroids, opiate derivatives, ..



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