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La centralità del paziente nel trattamento del disturbo bipolare

Prof. Luigi Janiri

Università Cattolica S. Cuore

Una mente inquieta

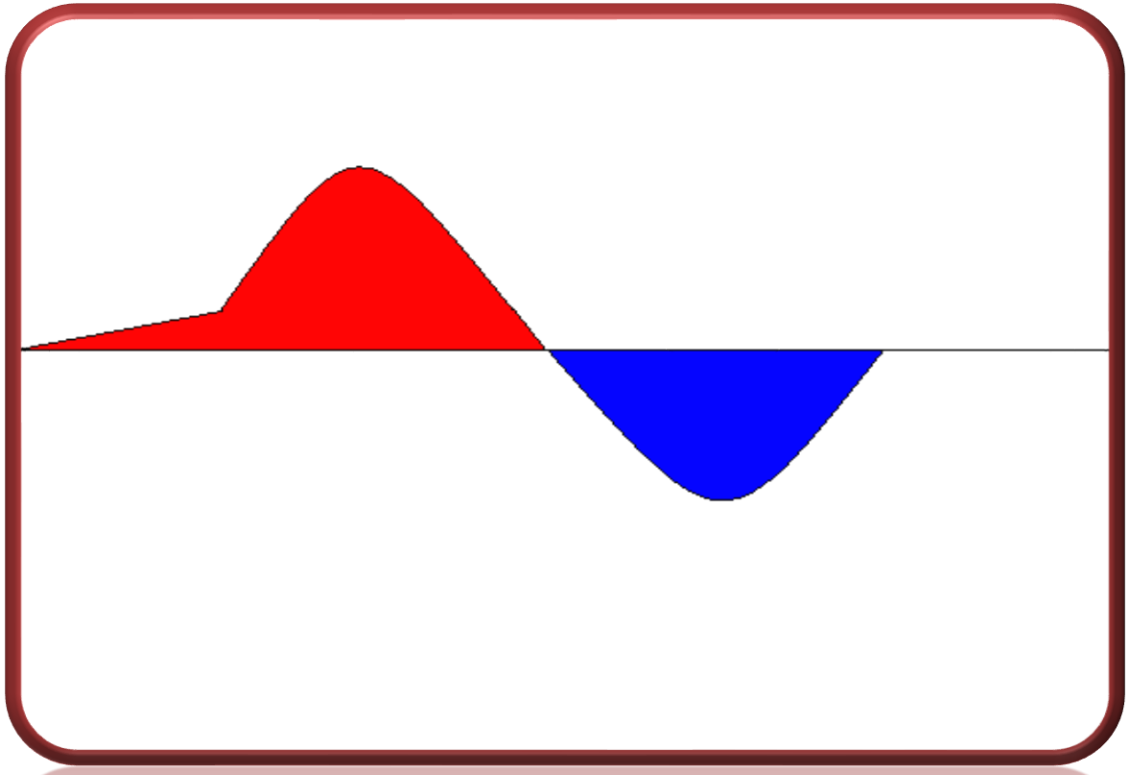
Kay Redfield Jamison

It is not a gentle or easy disease

“I have had manic-depressive illness, also known as bipolar disorder, since I was 18 years old. It is an illness that ensures that those who have it will experience a frightening, chaotic and emotional ride. It is not a gentle or easy disease.”

Kay Redfield Jamison (2014). “An Unquiet Mind: A memoir of moods and madness”,

Il disturbo bipolare è una patologia cronica caratterizzata dalla ricorrenza di sintomi maniacali, ipomaniacali e depressivi, alternati ad intervalli liberi e asintomatici.



DSM 5

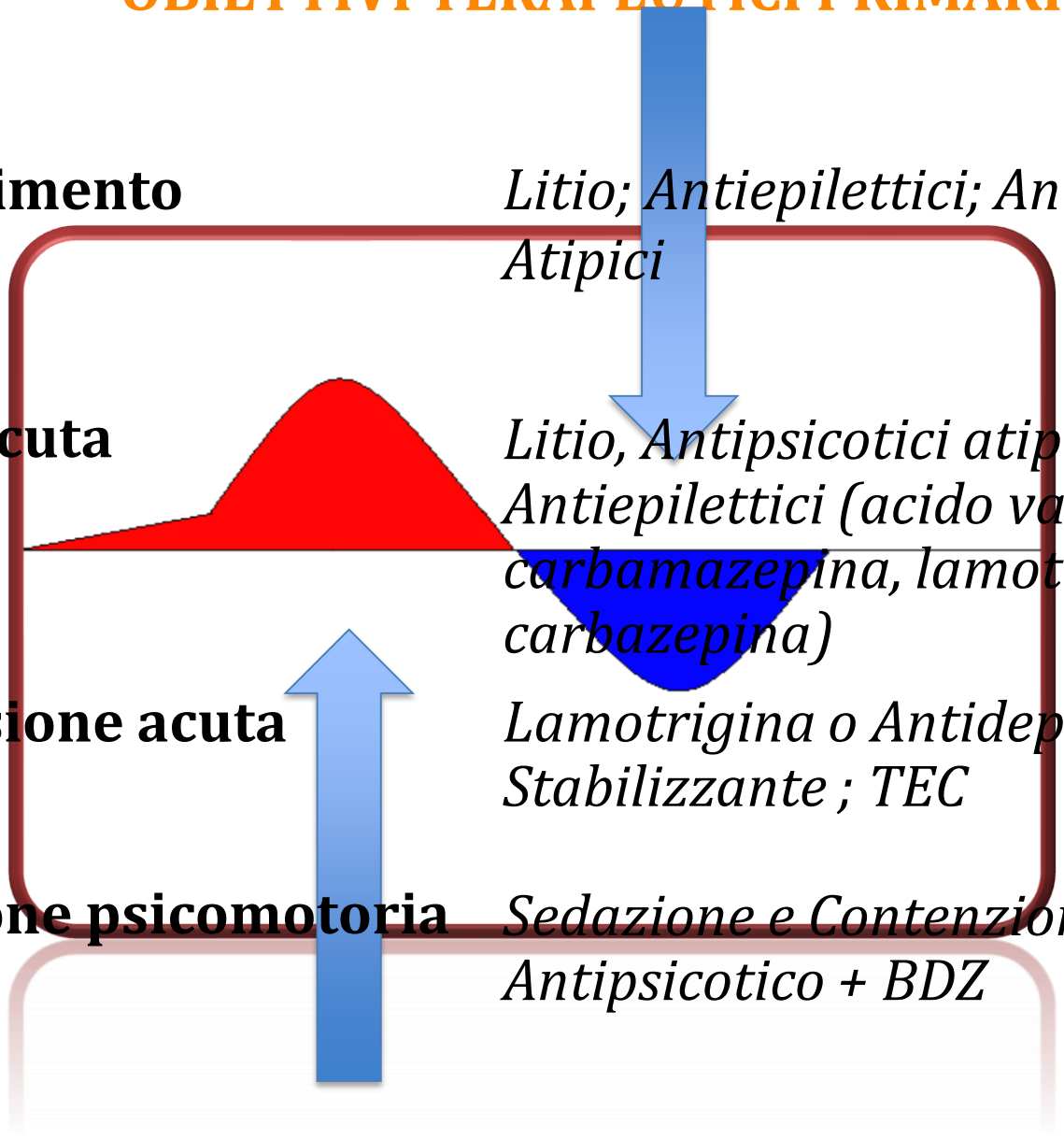
- **Disturbo Bipolare I**: caratterizzato dall'alternarsi di fasi depressive e maniacali o dalla sola presenza di ricorrenti episodi
- **Disturbo Bipolare II**: caratte
  ipomaniacali; in anamnesi
  episodio depressivo.
- **Disturbo Ciclotimic**
  ipomaniacali che no
  sintomi depressivi
  sintomi, nei due an
- **Disturbo Schizoaf**
  qualche momento, s
  concomitanza a sint

Specificatori:

- Con ansia
- Con caratteristiche miste
- Con cicli rapidi
- Con caratteristiche melanconiche
- Con caratteristiche atipiche
- Con caratteristiche psicotiche
- Con catatonia
- Con esordio nel peripartum
- Con andamento stagionale

indotto da sostanze/farmaci

OBIETTIVI TERAPEUTICI PRIMARI



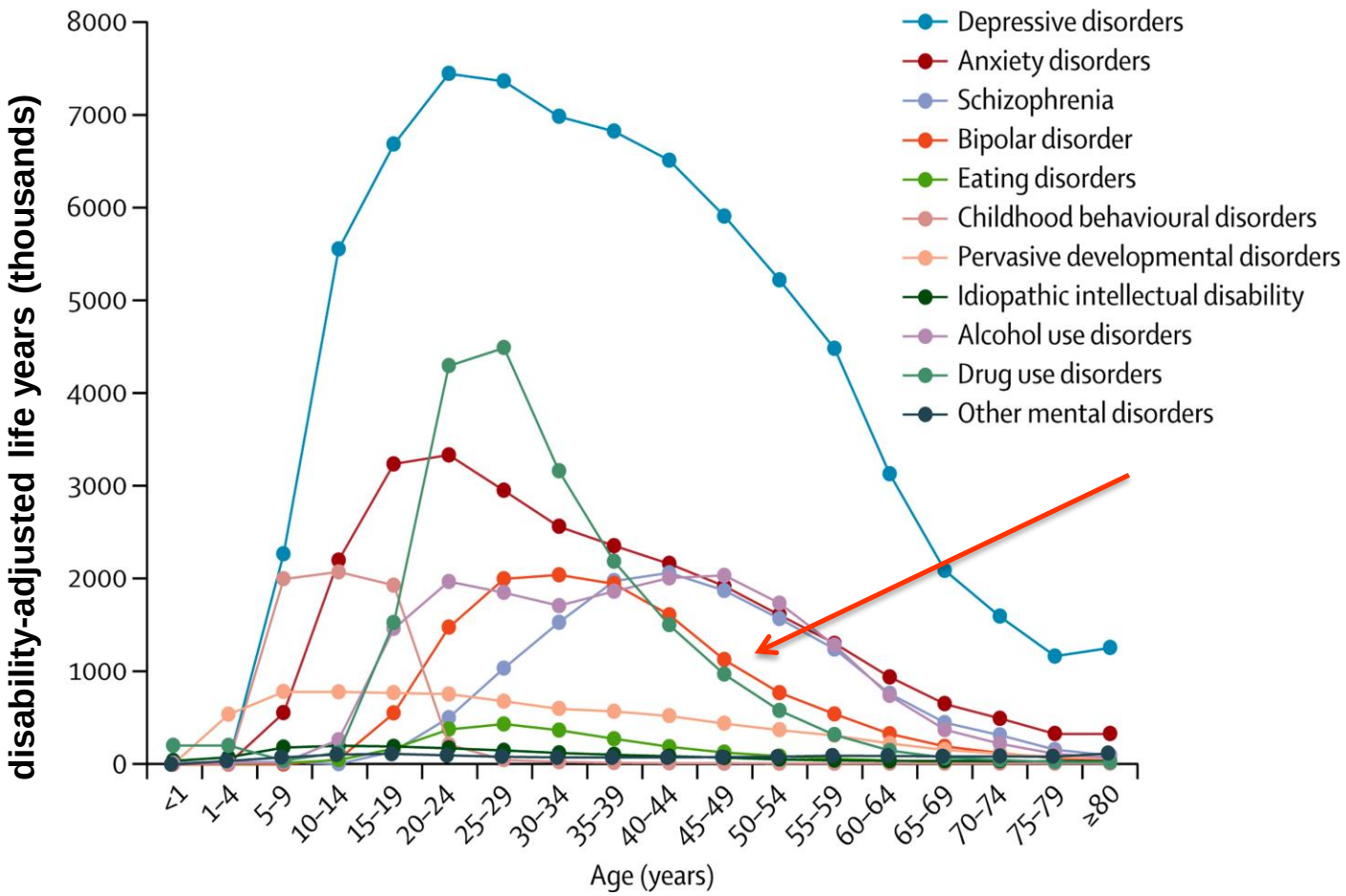
Mantenimento — *Litio; Antiepilettici; Antipsicotici Atipici*

Mania acuta — *Litio, Antipsicotici atipici, Antiepilettici (acido valproico, carbamazepina, lamotrigina, ox-carbazepina)*

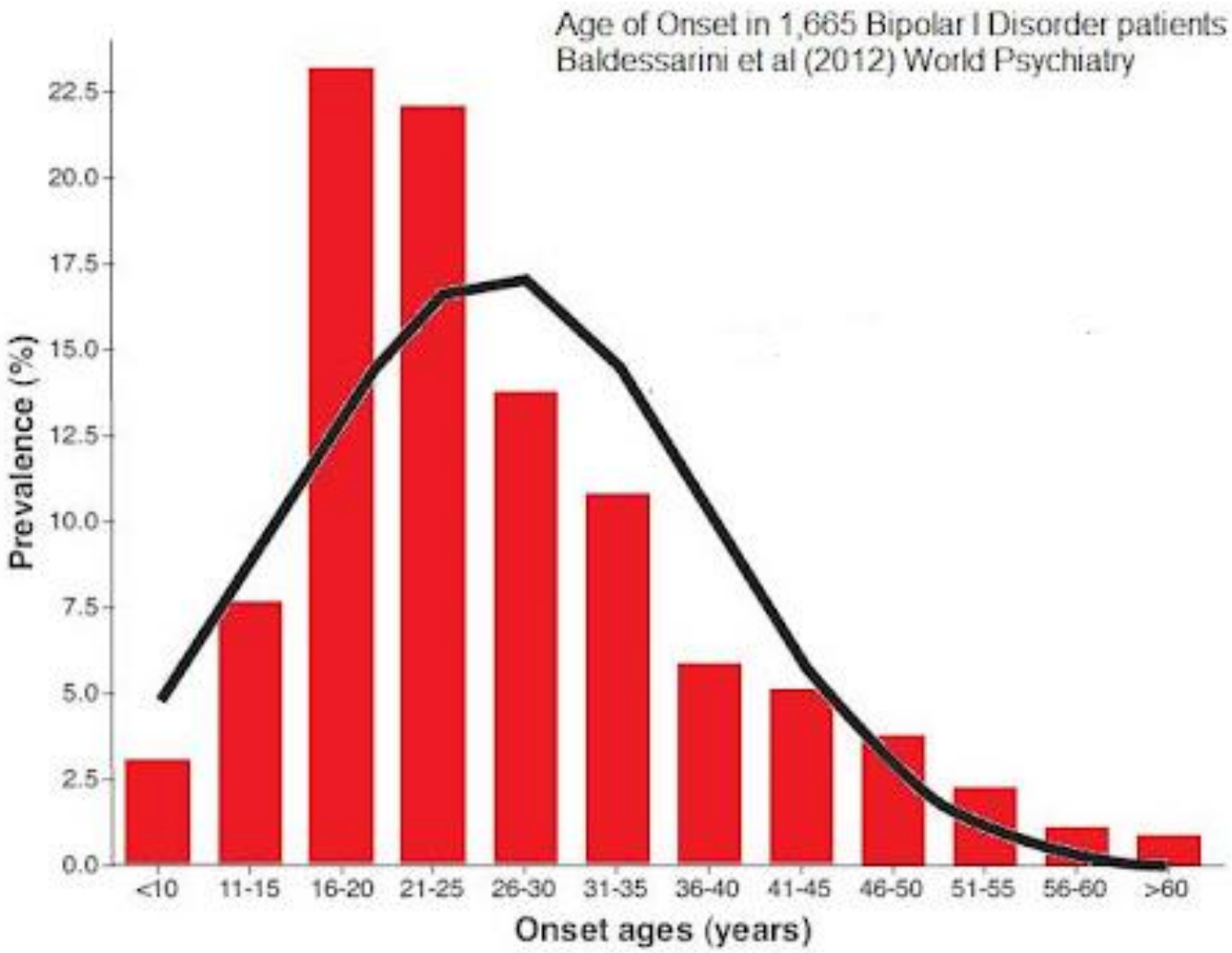
Depressione acuta — *Lamotrigina o Antidepressivo + Stabilizzante ; TEC*

Agitazione psicomotoria — *Sedazione e Contenzione: Antipsicotico + BDZ*

Global burden of disease attributable to mental and substance use disorders: findings from the Global Burden of Disease Study 2010 (Whiteford et al. Lancet 2013)



Depressive disorders account for 40.5% of DALYs; anxiety disorders accounting for 14.6% , illicit drug use disorders for 10.9%, alcohol use disorders for 9.6%, schizophrenia for 7.4%, bipolar disorder for 7.0%, pervasive developmental disorders for 4.2%, childhood behavioural disorders for 3.4%, and eating disorders for 1.2%. DALYs varied by age and sex, with the highest proportion of total DALYs occurring in people aged 10–29 years.


Age of Onset in 1,665 Bipolar I Disorder patients
Baldessarini et al (2012) World Psychiatry
Prevalence (%)
22.5
20.0
17.5
15.0
12.5
10.0
7.5
5.0
2.5
0.0
<10
11-15
16-20
21-25
26-30
31-35
36-40
41-45
46-50
51-55
56-60
>60
Onset ages (years)

MIGLIORE STRATEGIA di intervento nel disturbo bipolare:

DIMINUZIONE

✧numero

✧durata

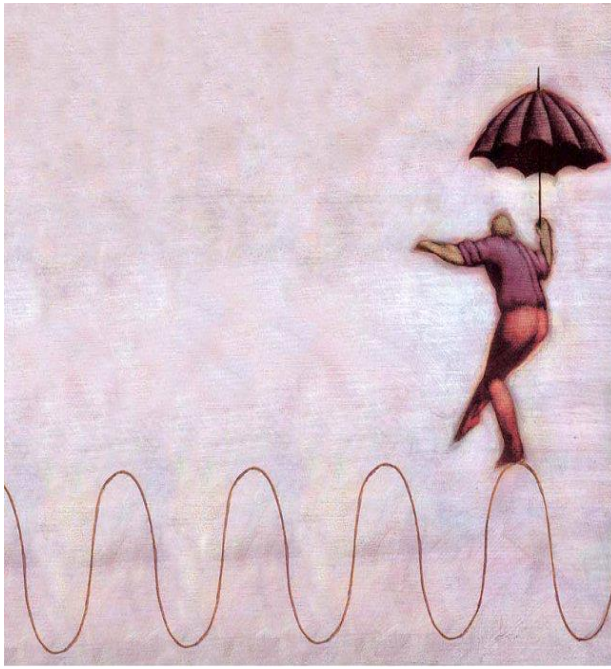
✧gravità

DEGLI EPISODI

Vieta et al., Nature Reviews 2018

LAVORARE SUL DECORSO

LAVORARE SUL TEMPO



Time will pass

Time will pass; these mood will pass; and I will, eventually, be myself again.

Kay Redfield Jamison (2014). “An Unquiet Mind: A memoir of moods and madness”,

TIME

Alice: “How long is forever?”
White Rabbit: “Sometimes, just one second”.

Lewis Carrol

Lavorare sul tempo….

Il litio

This lithium that you gave to me, and which I have been taking for a month, does not do anything to me. I sleep better, I do not quarrel with my wife, I go to work quietly in the morning, I do not have moments of despair, I do not visit pornographic websites at night and I do not crave for cocaine. But I do feel like it does not anything to me.

A patient

Lithium, the forgotten drug

- Psychiatrists' preference for having a medicine that is simple to use, not potentially toxic, possibly transnosographic and which does not require frequent physical and laboratory tests
- Introduction of new effective drugs supported by strong economic interests
- Different effects of lithium in the bipolar spectrum

Mario Maj

Lithium

Guidelines of the British Association for Psychopharmacology

“The strongest evidence among medicines that are often referred to as mood stabilisers for bipolar I disorder is still for lithium.”

Goodwin et al. Guidelines of the British Association for Psychopharmacology. J Psychopharmacol 2016; 30: 495–553

Prescribing trend in Bipolar Disorder: 1995-2009

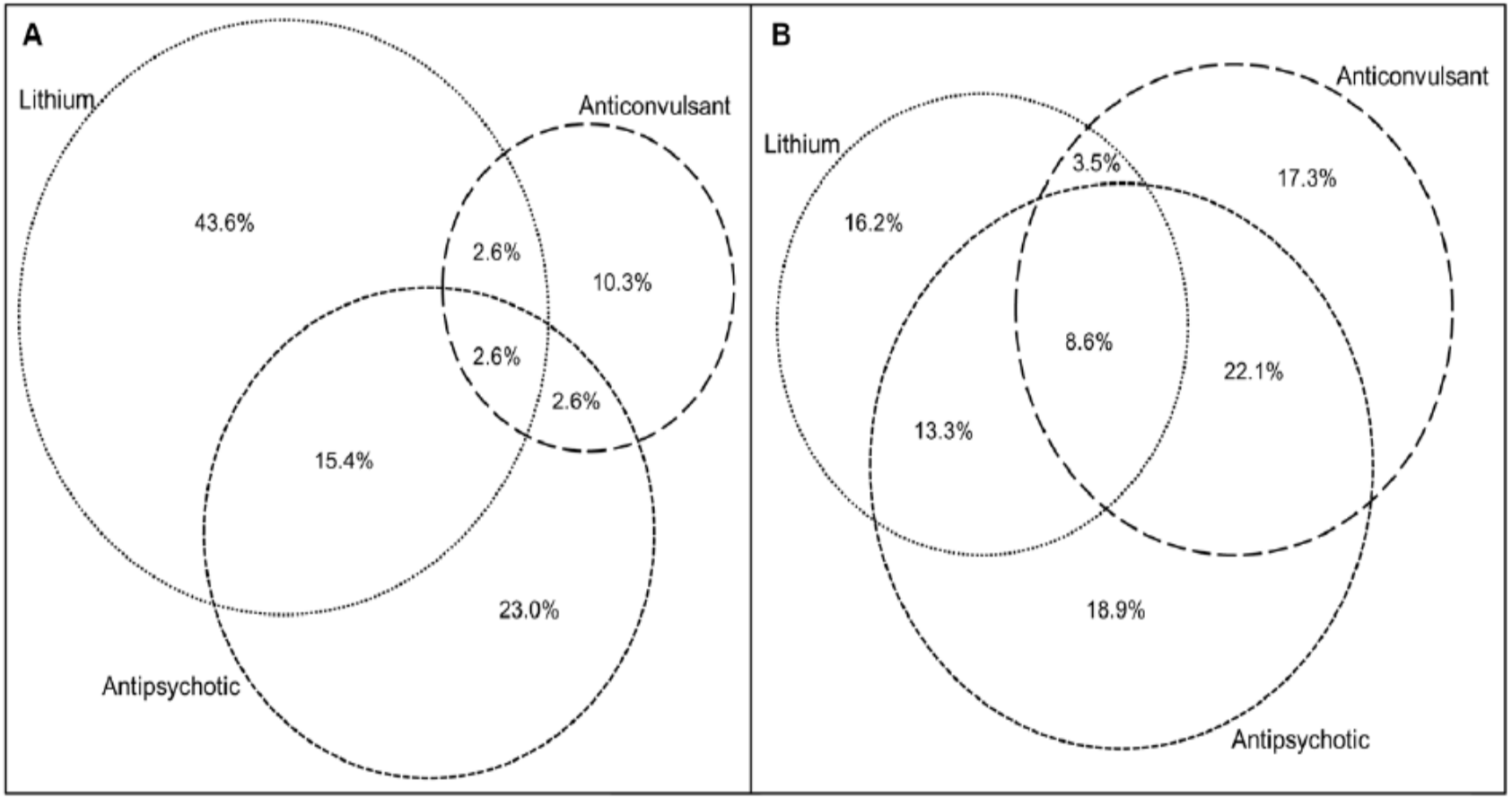


Figure 6. Percentage of treated individuals by medication group in A) 1995 and B) 2009*.

Hayes et al., 2011

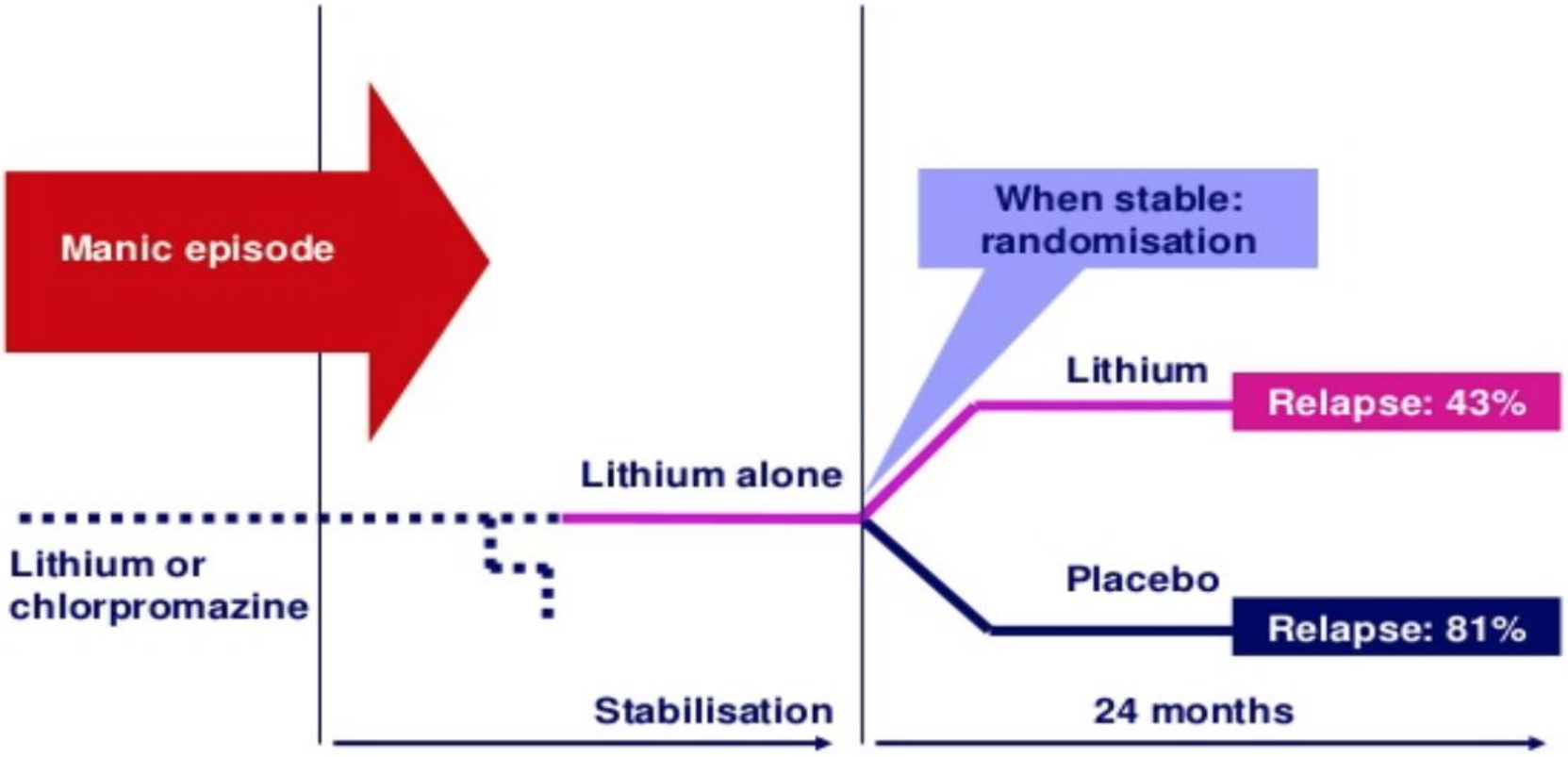
Use of lithium

- Treatment of Mania
- Prophylaxis of recurrences
- Prevention of suicide
- Neuroprotection

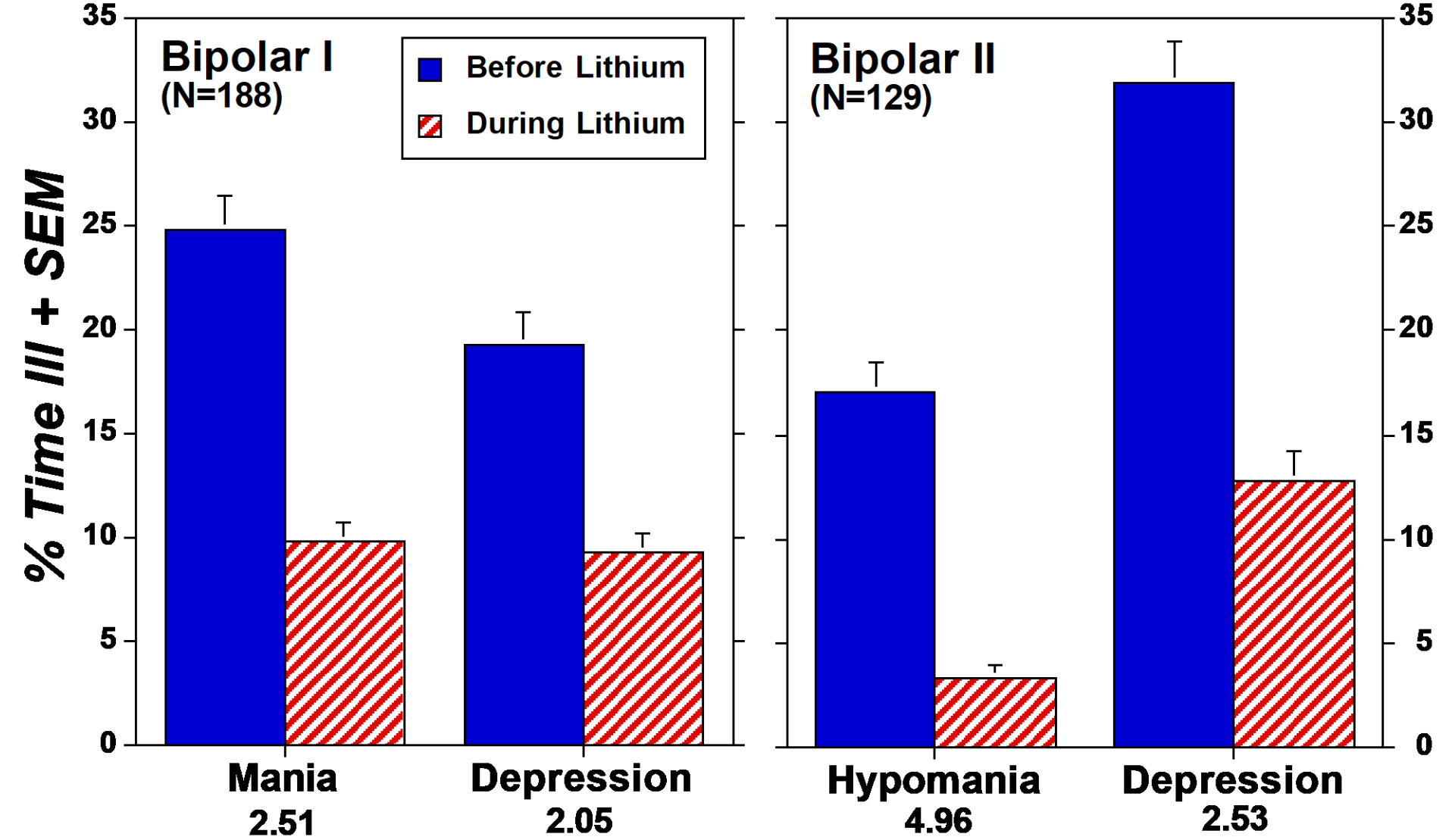
Use of lithium

- Treatment of Mania
- Prophylaxis of recurrences
- Predictor of phase change
- Prevention of suicide
- Neuroprotection

The current knowledge about Li solidly supports its usefulness during all phases of bipolar illness and its specific effectiveness on suicidal prevention



Prien et al Arch Gen Psychiatry. 1973 Mar;28(3):337-41



Illness Phase & Treatment-Benefit Ratio

[From Tondo et al.: Br J Psychiatry 2001; 178 (S-40): 184–190]

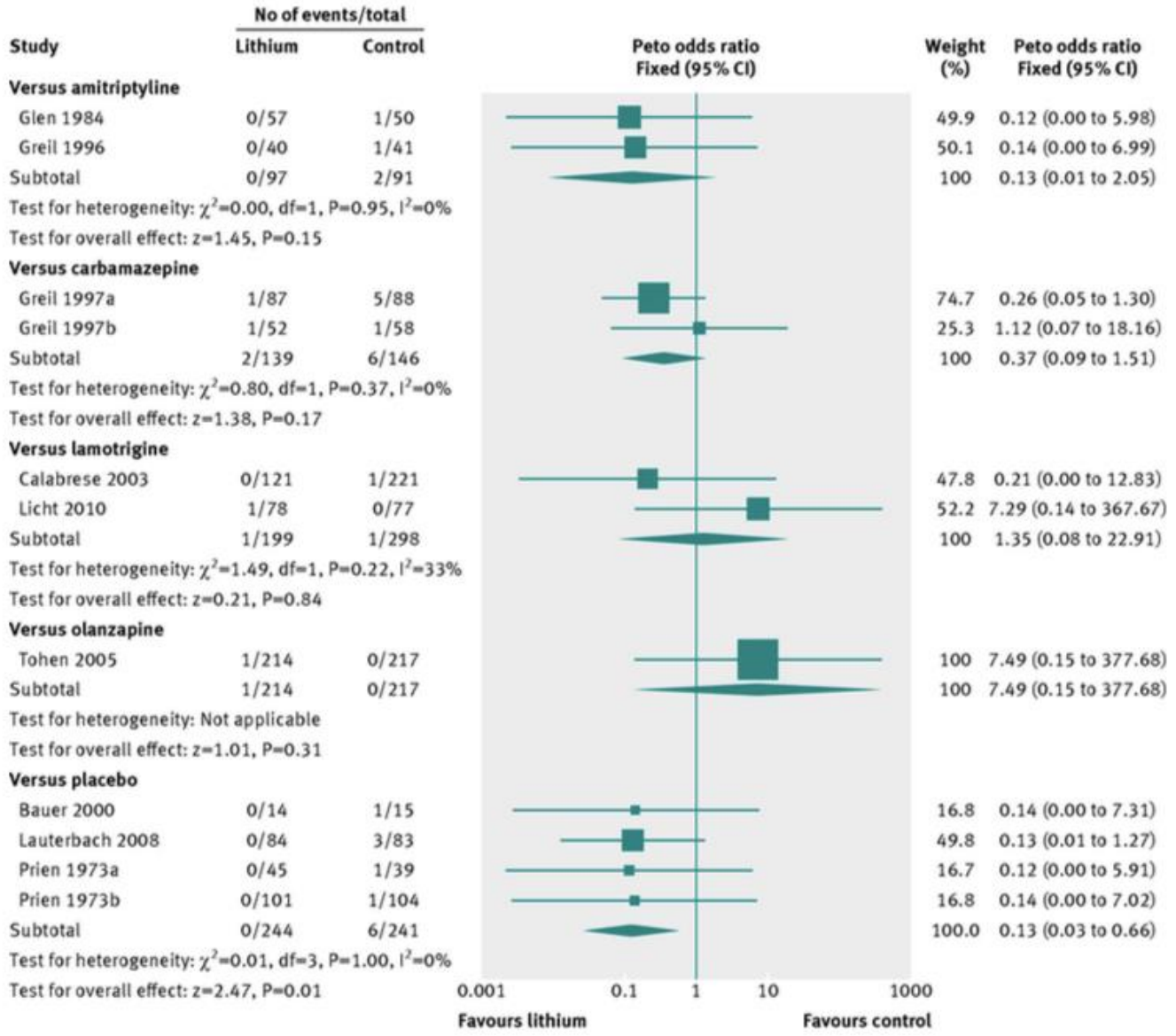
Medications with the highest SMD

1. **Interferon for chronic hepatitis C** **2.27**
2. **Proton pump inhibitors for reflux esophagitis** **1.39**
3. **Lithium for prophylaxis of bipolar disorder** **1.12**
4. **Metformin for diabetes** **0.87**
5. **Methotrexate for rheumatoid arthritis** **0.86**

Leucht et al, 2012

Use of lithium

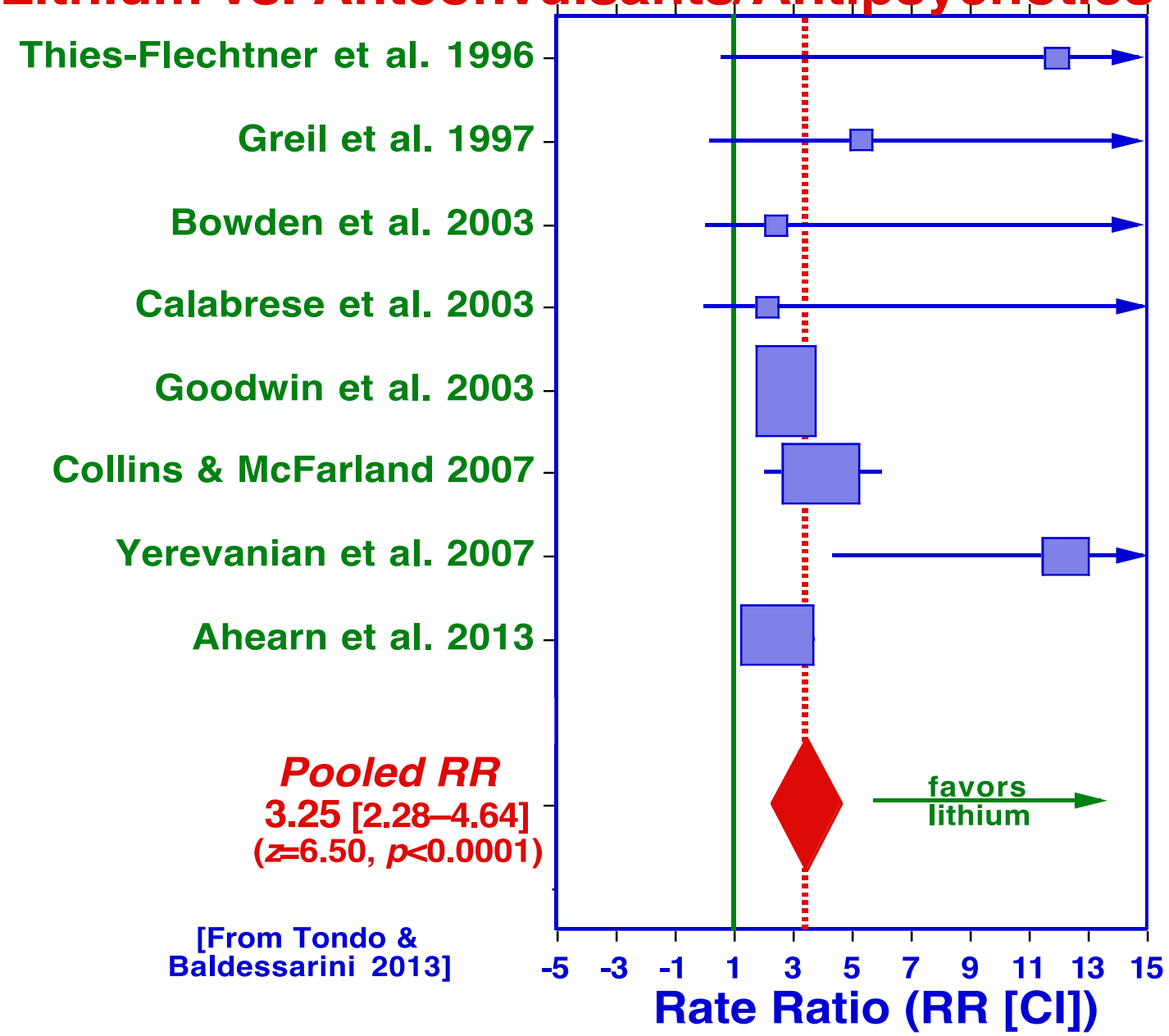
- Treatment of Mania
- Prophylaxis of recurrences
- Predictor of phase change
- **Prevention of suicide**
- Neuroprotection



Lithium is more effective than placebo in reducing the number of suicides (odds ratio 0.13, 95% confidence interval 0.03 to 0.66)

Cipriani ei al, BMJ 2013

Suicidal Acts in Bipolar Disorder:
Lithium vs. Antconvulsants/Antipsychotics

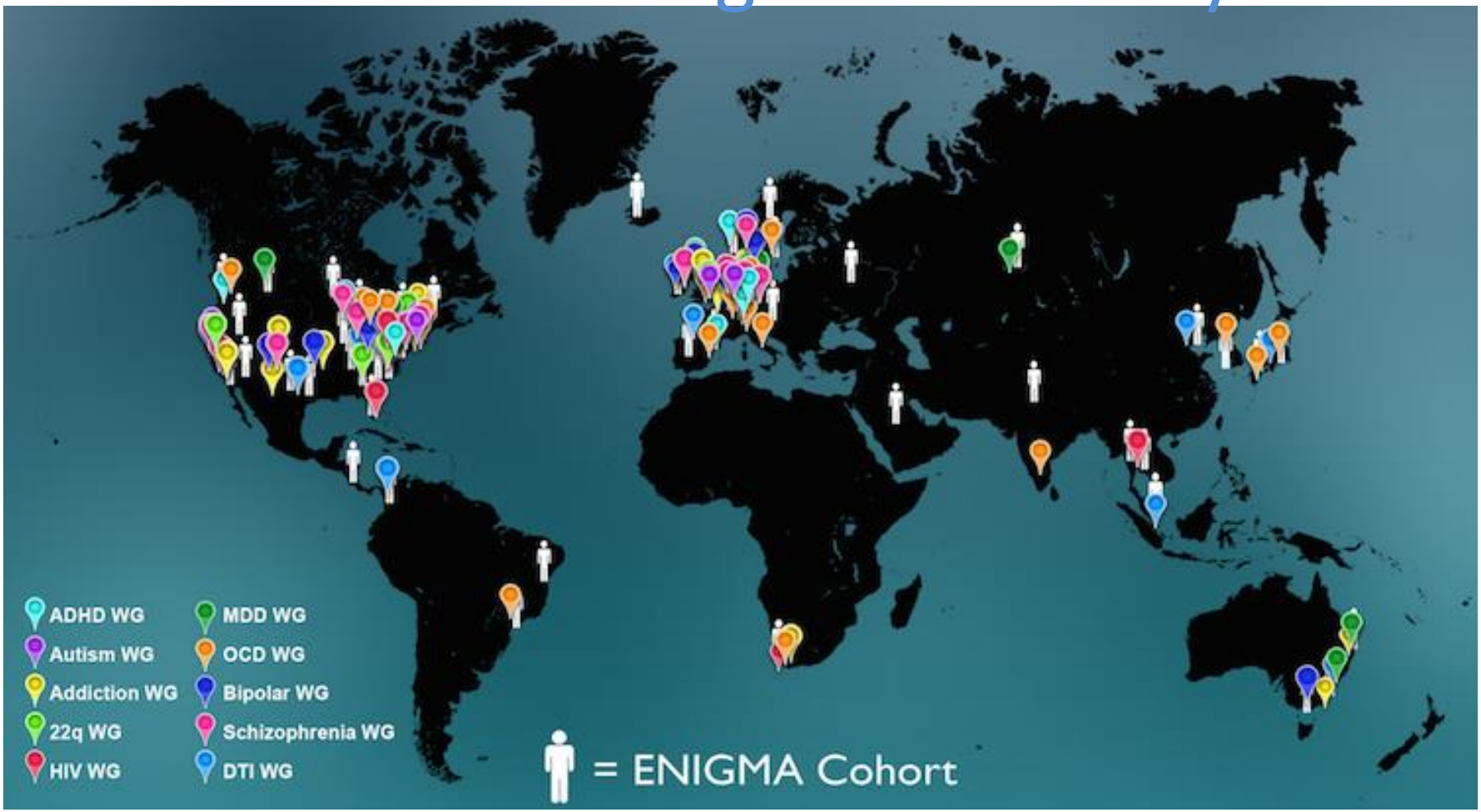


[From Tondo & Baldessarini 2013]

Use of lithium

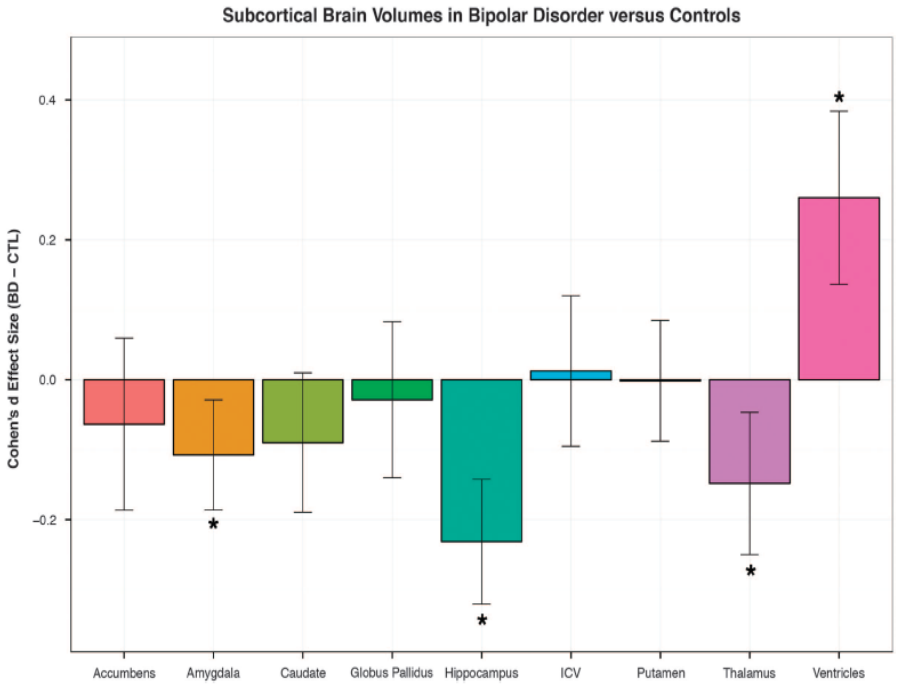
- Treatment of Mania
- Prophylaxis of recurrences
- Predictor of phase change
- Prevention of suicide
- **Neuroprotection**

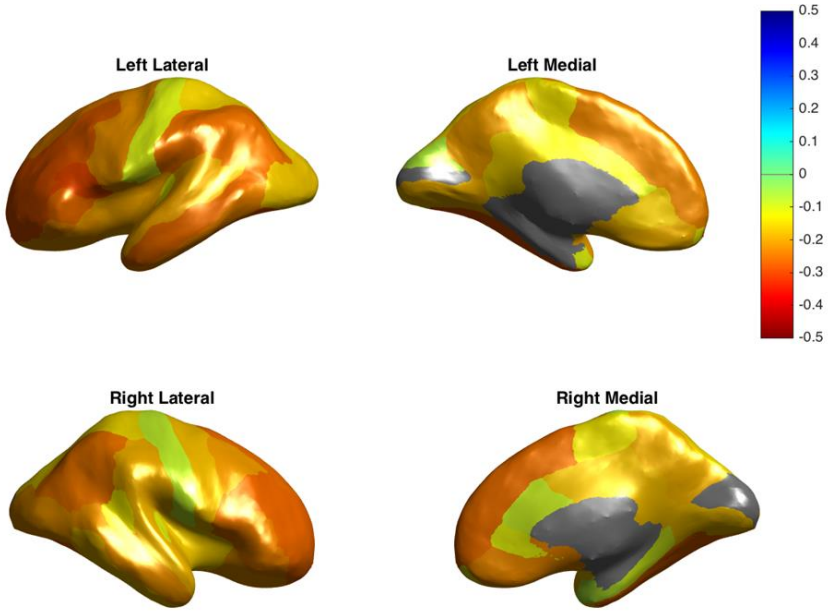
ENIGMA: Enhancing Neuroimaging Genetics Through Meta-Analysis



ENIGMA: Bipolar Disorder

Brain Structural Changes in 2260 BD patients compared to 3819 healthy controls



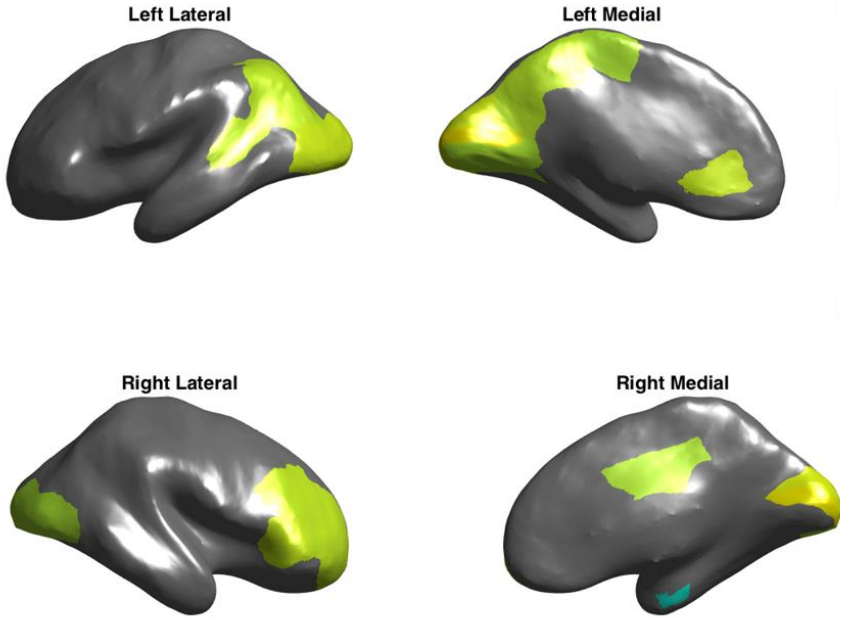


Cortical gray matter was thinner in frontal, inferior temporal and inferior parietal regions of both brain hemispheres; strongest effects on the inferior frontal gyrus (Cohen's d = -0.29; P = 3.98×10^{-26} middle frontal cortex (d = -0.28; P = 1.71×10^{-2}3) and left fusiform gyrus (d = -0.28; P = 2.65×10^{-23}) and insula esp. in younger patients (d=-0.18; p=0.0002)

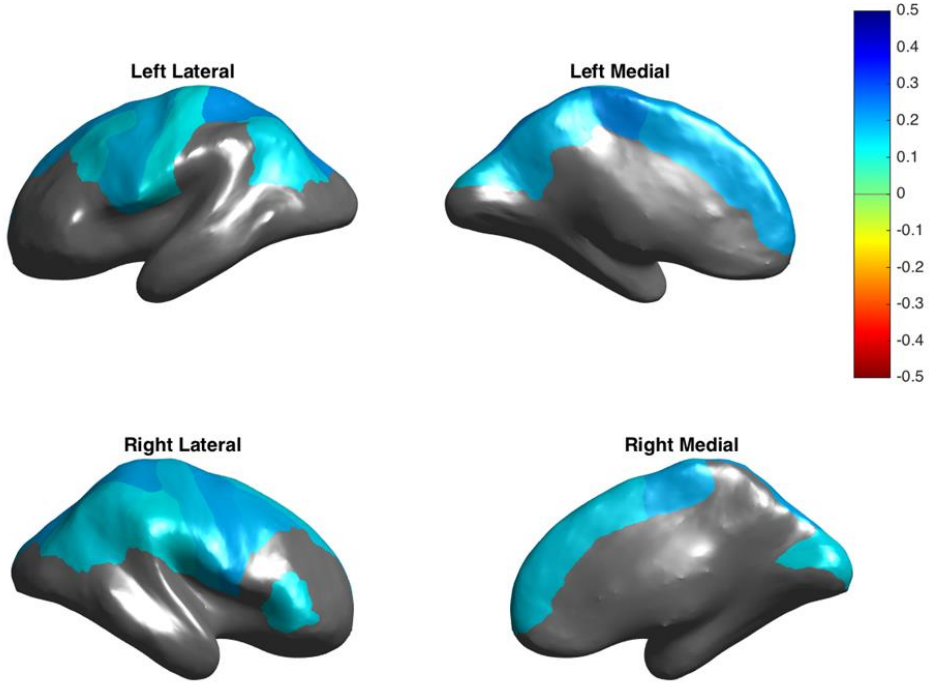
Hibar et al. Mol Psychiatry. 2016
Hibar et al. Mol Psychiatry, 2017

ENIGMA: Bipolar Disorder

Duration of Illness



Effect of Lithium Treatment



Hibar et al. Mol Psychiatry. 2017

WHO CAN NOT OR DO NOT WANT TO USE LITHIUM MUST NOT TAKE CARE OF BIPOLAR PATIENTS.

Frederick K. Goodwin

Lavorare sul tempo….

Interventi di psicoeducazione

Criticità nel decorso

- ✓ **VULNERABILITA' AGLI STRESS**
- ✓ **STILI DI VITA A RISCHIO (instabilità ritmi circadiani, abuso sostanze etc.)**
- ✓ **RECIDIVE**
- ✓ **DURATA DEGLI INTERVALLI LIBERI**
- ✓ **SINTOMI SUB-SINDROMICI INTEREPISODICI**
- ✓ **DETERIORAMENTO DEL FUNZIONAMENTO (cognitivo e psicosociale)**
- ✓ **CICLI RAPIDI**
- ✓ **MORTALITA'**

FALLIMENTI TERAPEUTICI

-SCARSA ADERENZA

- RITMI BIOLOGICI IRREGOLARI

- ABUSO DI SOSTANZE

- DESIDERABILITÀ IPOMANIA

È evidente un notevole divario tra l'efficacia dei trattamenti in acuto e l'esito terapeutico a lungo termine nei pazienti bipolari

Un po' di storia….

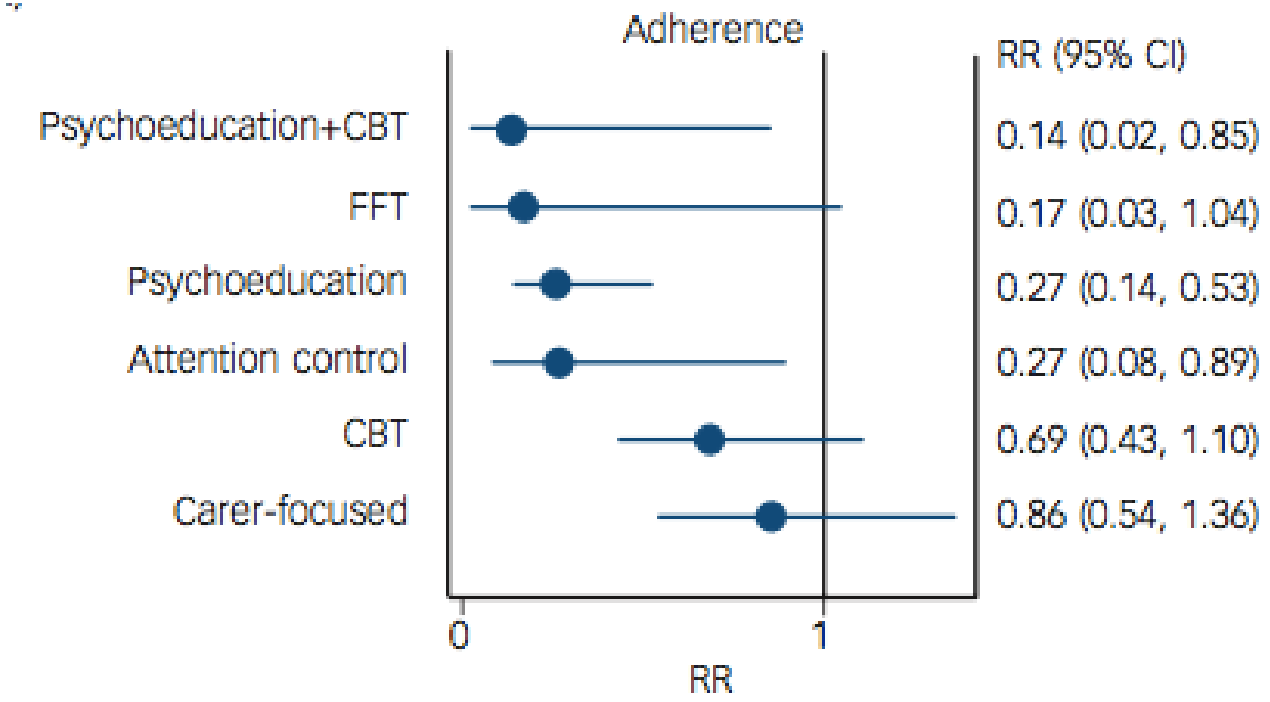
- ✓ **Peet et al. 1991 → programma educativo per pz trattati con Litio.**
- ✓ **Perry et al. 1999 → primi studi clinici controllati, randomizzati. Dimostrazione efficacia psicoterapia individuale nella riduzione recidive maniacali.**
- ✓ **van Gent EM et al. 1988 e Clarkin JF 1998 → primi interventi psicoeducativi poco strutturati**
- ✓ **Bauer MS et al 1996 → interventi focalizzati sulla capacità di gestione della malattia atto a diminuire numero ricoveri**
- ✓ **Colom et al 2003 → Primo studio clinico randomizzato condotto in cieco per dimos trattamer BPII**

ORIGINAL ARTICLE

A Randomized Trial on the Efficacy of Group Psychoeducation in the Prophylaxis of Recurrences in Bipolar Patients Whose Disease Is in Remission

Francesco Colom, PhD; Eduard Vieta, MD, PhD; Anabel Martínez-Arán, PhD; María Reinares; José Manuel Goikolea; Antonio Benabarre, MD; Carla Torrent; Mercè Comes; Barbara Corbella; Gemma Parramon; Josep Corominas, MD, PhD

Le evidenze oggi



The most recent meta-analysis on the topic showed that Psychoeducation alone and in combination with cognitive–behavioural therapy (CBT) significantly reduced medication non-adherence.

Chatterton et al, 2017 The British journal of psychiatry

I will, eventually, be myself again.

"Which of my feelings are real? Which of the me's is me? The wild, impulsive, chaotic, energetic, and crazy one? Or the shy, withdrawn, desperate, suicidal, doomed, and tired one? Probably a bit of both, hopefully much that is neither."

Time will pass; these mood will pass; and I will, eventually, be myself again.

Kay Redfield Jamison (2014). "An Unquiet Mind: A memoir of moods and madness",