Why DSM is false

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Disclosure

- Director, Translational Medicine-Neuroscience, Novartis Institutes for Biomedical Research
- The views expressed here are my own and not that of my employers.

Sources

- Hannah Decker, The Making of DSM-III
- Edward Shorter, Before Prozac
- Nassir Ghaemi, On Depression
- www.psychiatryletter.org

Our best drugs are our oldest drugs

- Antipsychotics: Clozapine (1970s Europe)
- "Mood stabilizers": Lithium (1970 US)
- Antidepressants: ECT (1930s), Amphetamines (1930s), Tranylcypromine (1960), Amitrityline (1961)
- Anxiolytics: Benzodiazepines (1950s)
- "Stimulants": Amphetamines (1930s)

- Newer drugs, like SRIs or anticonvulsants or newer antipsychotics, are more tolerable in some ways, but equally or less effective

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What changed?

- Drug development process 1950s-1970s
  - No FDA regulation for efficacy until 1962
  - Mainstream American psychiatry was psychoanalytic: Ignored drugs and minimized importance of diagnosis
  - All advances happened in central European pharmaceutical companies – not US
- Drug development process 1970s- current
  - Heavy FDA regulation
  - Mainstream American psychiatry became more biologica: extensive use of drugs; huge power of DSM-III to 5
  - Major psychotropic drugs produced by US pharmaceutical companies

Mainstream American psychiatry

- Before 1970s
  - Mainly psychoanalytic
  - Little attention to diagnosis
  - Drugs viewed as symptomatic and superficial
- After 1970s
  - More biological (biopsychosocial model published 1977)
  - Huge attention to diagnosis (DSM-III 1980)
  - Drugs viewed as more than just symptomatic
    - Some deeper cure
      - Acute depressive or manic episode completely goes away
      - Patients with schizophrenia able to leave state hospitals after decades

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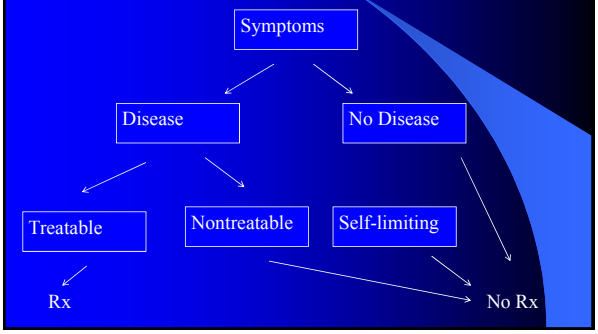
SN Ghaemi, Mood Disorders: A Practical Guide

Hippocratic Practice



MF Gliatto, SN Caroff, Neurosyphilis: A history and clinical review, Psychiatric Annals, 2001, 31: 153-161

Syphilis

- Bleeding
- Mercury
  - Islamic sources used for yaws and leprosy
  - Salves, pills, gums, fumigations, enemas
  - Produces sweating, diarrhea, salivation
- Toxic
  - Gum ulceration, tooth loss
  - psychosis
- 1909 – Ehrlich – arsphenamine (magic bullet)
- 1927 – Nobel prize to Wagner-Jauregg – malaria fever therapy

History of DSM-III

- Science
  - 4 validators of diagnosis
  - Diagnostic reliability and hoped for validity
  - Biological research
- Practice
  - Drugs that seemed specific to illness
- Politics/Economics
  - Compromise between psychoanalysts and psychopharmacologists
  - Biopsychosocial model

E Shorter, Before Prozac, 2009, Oxford University Press

Validators of Diagnosis: No Gold Standard

- Phenomenology
  - cross-sectional symptoms
  - DSM-IV criteria
- Family History - genetics
- Course
  - Age of onset, # episodes, outcome
- Treatment Effects
  - substitute for biological markers
    - Can be nonspecific

Modified from Robins and Guze 1970

Goodwin and Guze's *Psychiatric Diagnosis*: 10 Diagnoses

- Affective Disorders
  - Bipolar and major depressive
- Schizophrenic Disorders
- Panic disorder
- Obsessive compulsive disorder
- Phobic disorders
- Alcoholism
- Drug Dependence
- Sociopathy
- Brain syndrome
  - Dementia, Delirium, Epilepsies
- Anorexia Nervosa

1st edition, 1974

Research Diagnostic Criteria: 22 diagnoses – Part I

- Schizophrenia
  - 6 subtypes
- Schizoaffective disorder
  - Manic/depressed
- Depressive syndrome superimposed on residual schizophrenia
- Manic/hypomanic disorder
- Bipolar with mania (type I)
- Bipolar with hypomania (rype II)
- Major depressive disorder
  - Primary, secondary, recurrent unipolar, psychotic, incapacitating, agitated, retarded, endogenous, situtaitonal, simple, predominant mood
- Minor depressive disorder – with significant anxiety
- Intermittent depressive disorder

R Spitzer et al, Arch Gen Psychiatry, 1978, 35: 773-782

Research Diagnostic Criteria: 22 diagnoses - Part II

- Panic disorder
- Generalized anxiety disorder – with significant depression
- Cyclothymic personality
- Labile personality
- Briquet's disorder (somatization)
- Antisocial personality
- Alcoholism
- Drug use disorder
- OCD
- Phobic disorder
- Unspecified functional psychosis
- Other psychiatric disorder
- Schizotypal features
- Currently not mentally ill
- Never mentally ill

R Spitzer et al, Arch Gen Psychiatry, 1978, 35: 773-782

"Disorder"

- Severe symptoms plus functional impairment
- Clinical pictures – *Zustandbilden*
- Disease processes - *Krankheitprozesen*

E Boestroem, Zustandbild und Krankheit in der Psichatrie, Klinische Wochenschrift. 1923. 37/38: 1728-1731

Heirarchy of Diagnosis

- Mood Disorders
  - Bipolar
  - Unipolar
- Psychotic Disorders
  - Schizoaffective
  - Schizophrenia
- Anxiety Disorders
- Other
  - Personality Disorders
  - ADHD

PG Surtees, RE Kendell. Br J Psych, 1979, 135:438-443

The philosophy of DSM-III and IV (and 5)

- "Pragmatism"
  - What do the DSM committees think is the best outcome?
    - Outcome ≠ Treatment benefit
    - Outcome = benefit for the profession, for society
    - Reliability does not lead to validity
- Postmodernism
  - All diagnoses are arbitrary
    - There is no "Truth"
    - Diseases either don't exist or are unknown
  - Science is arbitrary
  - Don't believe the experts

SN Ghaemi, Couch-pragmatism, Psychiatric Times, November 2010

DSM-postmodernism

- Science relies on the truth of our diagnoses
- DSM diagnoses are *consciously invented* to guess at the best clinical outcomes, not reality of diagnoses
- Science is *blocked* by our diagnostic system
  - Our current system guarantees no or very little progress
    - Biological research
    - Genetic research
    - Treatment research
- Result: By being "pragmatic", DSM produces poor practical results

Reliability and Validity

- Reliability
  - "Dictionary"
  - Reification into "Bible"
  - Fails: DSM-5 MDD kappa 0.25 worse than 1980
- Validity
  - Rejected by "pragmatism"
  - Disproven
    - NIMH decision to reject DSM diagnoses in 2013

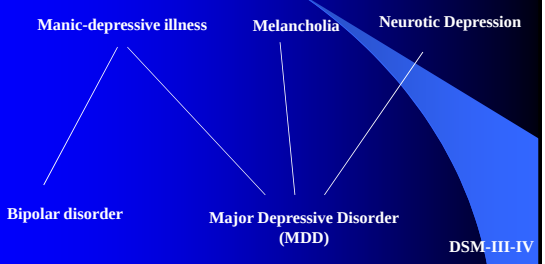
Sisyphus Problem

- DSM-Conservatism
  - Began with DSM-IV
- Raising the scientific threshold to higher and higher levels
  - Jules Angst's Zurich cohort study and the radical change from MDI to bipolar/MDD
- Dooms any claim to improving validity over time

Examples: DSM-5

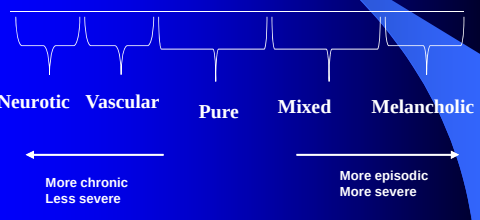
- MDI vs MDD
  - Jules Angst
    - Zurich Cohort
  - Duration of hypomania
    - 4 days versus 2 days
- Personality traits versus "disorders"
- Prodromal schizophrenia
- DMDD

Manic Depressive Illness vs Bipolar/MDD



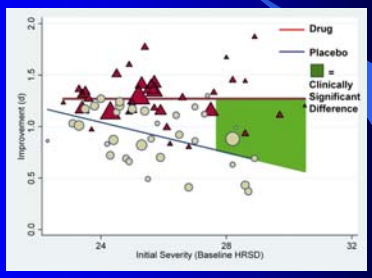
The MDD Spectrum

SN Ghaemi, PA Vohringer, D Vergne:
The varieties of depressive experience: Diagnosing depression
Psychiatric Clinics of North America, 2012



Ghaemi SN, Vohringer PA, Vergne D. Psych Clinics North Am 2012;35(1):73-86.

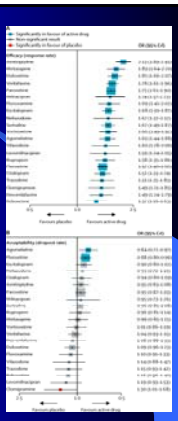
AD meta-analysis: Don't work?



Kirsch et al, PLOS Med, 2008

Lancet: ADs work!

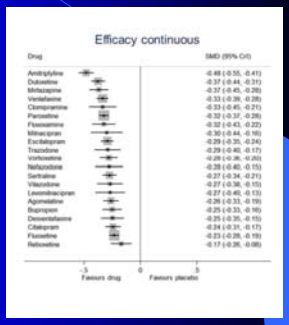
- **522 RCTs**
- **21 antidepressants vs placebo**
- **116 K patients**
- **"Our study brings together the best available evidence to inform and guide doctors and patients in their treatment decisions," said Cipriani in a press release.**



A Cipriani et al: The Lancet 2018 391, 1357-1366

Lancet: ADs work!

- p 150 of 290 page online appendix
- Cohen's d standardized effect size 0.25-0.5 small
- 0.5-0.75 medium
- >0.75 large



A Cipriani et al: The Lancet 2018 391, 1357-1366

STARD

AJ Rush et al, Acute and longer-term outcomes in depressed outpatients…: A STAR*D report. American Journal of Psychiatry. 2006 Nov;163(11):1905-17.

SN Ghaemi, Why antidepressants are not antidepressants, Bipolar Disorders, 2008, 10: 957-968

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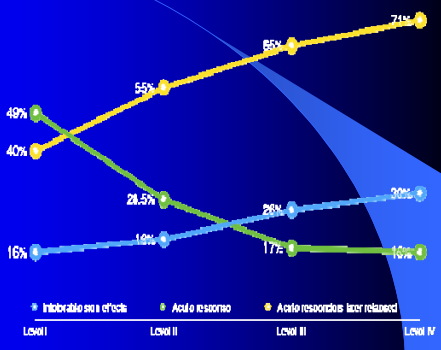
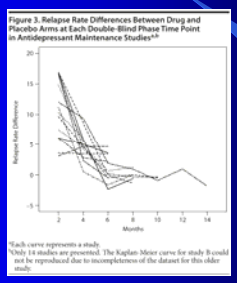


Not disease-modifying: FDA meta-analysis of all maintenance RCTs – ADs MDD



S Borges et al, J Clin Psychiatry 2014; 75: 205-214

Solutions

- New Research Diagnostic Criteria
  - Clinical and honest, unlike DSM
  - Not only brain based NIMH RDoC
- Rely on scientific research
- Rely on clinical judgment

Themes

- Postmodernist conceptual assumptions
  - DSM is a social construction
- Reliability and Validity
- Sisyphus Problem
  - Pragmatic failure of "pragmatism"
- Dooming of psychiatric research