Comorbidade Psiquiátrica: Fato ou Artefato?

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Declaração de Conflitos de Interesse

- De acordo com a Norma 1595/2000 do Conselho Federal de Medicina e a Resolução RDC 102/2000 da Agência Nacional de Vigilância Sanitária declaro que:
  - Sou Diretor Médico do Laboratório Roche no Brasil

Agenda

- Concepts
- Diagnosing mental illness
- Comorbidity is fashionable
- Discussion

Definition

- The term ‘comorbidity’ was introduced in medicine by Feinstein (1970) to denote those cases in which a ‘distinct additional clinical entity’ occurred during the clinical course of a patient having an index disease

The concept of syndrome in psychiatry

- *Several interrelated symptoms showing a stable, characteristic structure and a peculiar prognosis*
- A pathognomonic cluster of symptoms allows clinicians to distinguish different syndromes
- If a syndrome corresponds to a natural entity, than we should find a natural boundary or a discontinuity between this condition and its clinical “neighbors”
- Therefore, mixed conditions can exist, but they have to be less common than the pure syndromal form

CNS and biological processes

- CNS complexity and variation in structure/function result from genetic diversity and environmental exposures during development
- Basic biological processes vs. psychiatric symptoms/signs: much more frequently many-to-many than one-to-one
- Psychiatric disorders as a stable network of causes that interact across levels – the most realistic avenue to ground diagnoses in aetiology

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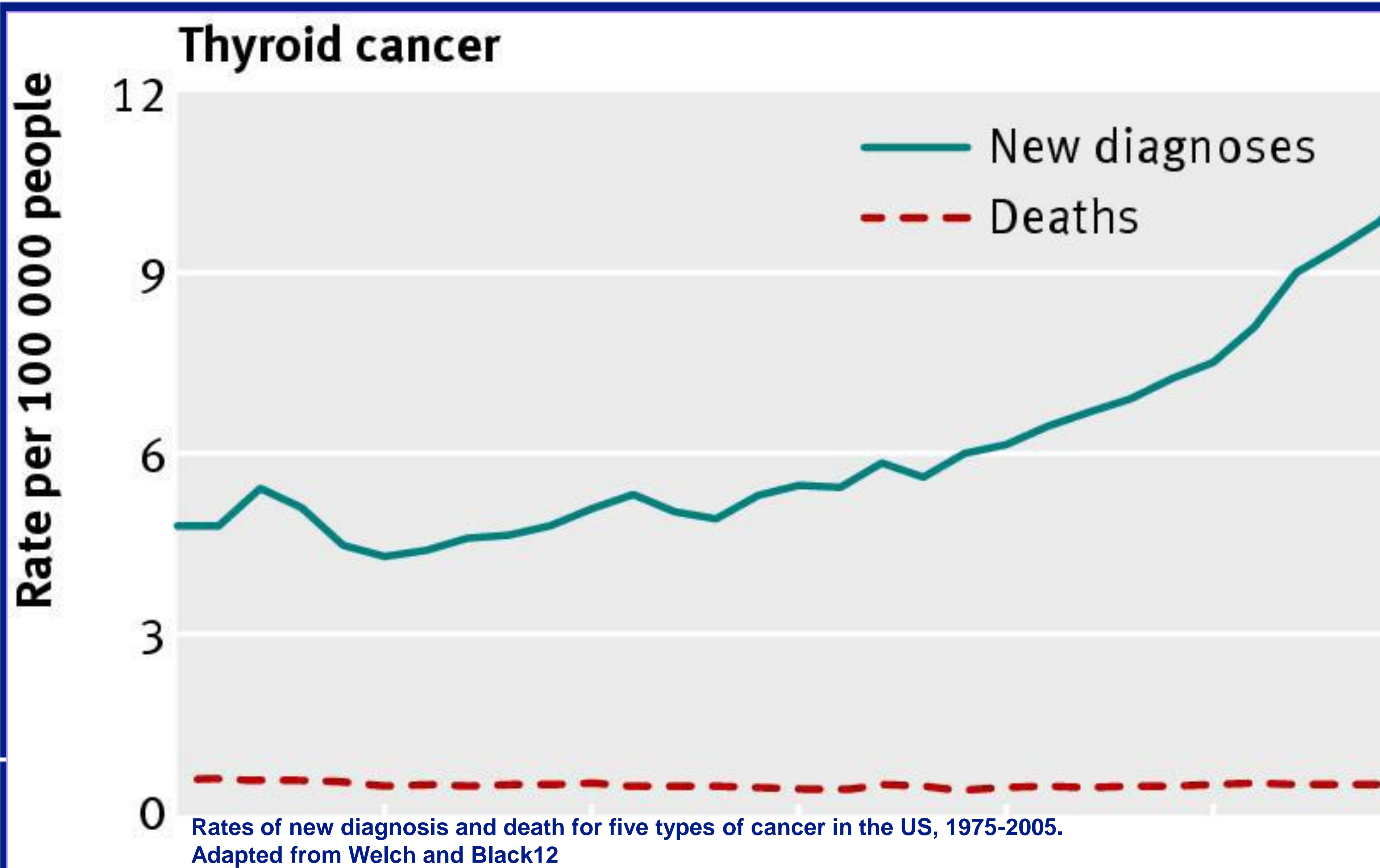
Preventing overdiagnosis: how to stop harming the healthy



Rates of new diagnosis and death for five types of cancer in the US, 1975-2005. Adapted from Welch and Black12

Nosology vs. statistical classification

- Nosology: uses scientific methods to arrive at a classification of psychiatric disorders and is concerned with the validity of its entities
- Statistical classification: aims to attain the widest compliance in spite of differences in the theoretical orientation of its users. It must therefore be atheoretical, and must represent a widely negotiated agreement between its future users

Nosology: Kraepelin (1899)

- Dementia praecox as a disorder of intellectual functioning, deteriorating course with a poor prognosis in terms of a deficit syndrome
- Manic depressive illness: primarily described as a disorder of affects or mood, course of acute exacerbations followed by complete remissions with no lasting deterioration of intellectual functioning

Statistical: DSM-IV and ICD-10

- Diagnostic categories defined descriptively in terms of symptoms observed to co-vary in individuals
- Optional severity dimensions
- Cross-cutting dimension for assessment of functioning
- *Assumption: as in general medicine, the phenomenon of symptom co-variation was an indication that their presentation could be explained by a common underlying etiology and pathophysiology and that, over time, these etiological factors would be elucidated…*

...however, 40 years later...

- No laboratory marker has been shown to be diagnostically useful for making any DSM diagnosis
- Other evidence suggesting that the current classification lacks validity include
  - high rates of diagnostic comorbidity
  - lack of treatment specificity for the diagnostic categories
  - evidence that distinct syndromes share a genetic basis
  - high rates not otherwise specified (NOS)
  - *Continued use of the current diagnostic paradigm might impede future research efforts*

“…the classes thus formed represent the result of an idealising abstraction and selection process. They do not correspond with entities that really exist, but are theoretical terms or constructs and therefore depend on the respective theoretical position…”

Moller HJ. Eur Arch Psychiatry Clin Neurosci (2008)

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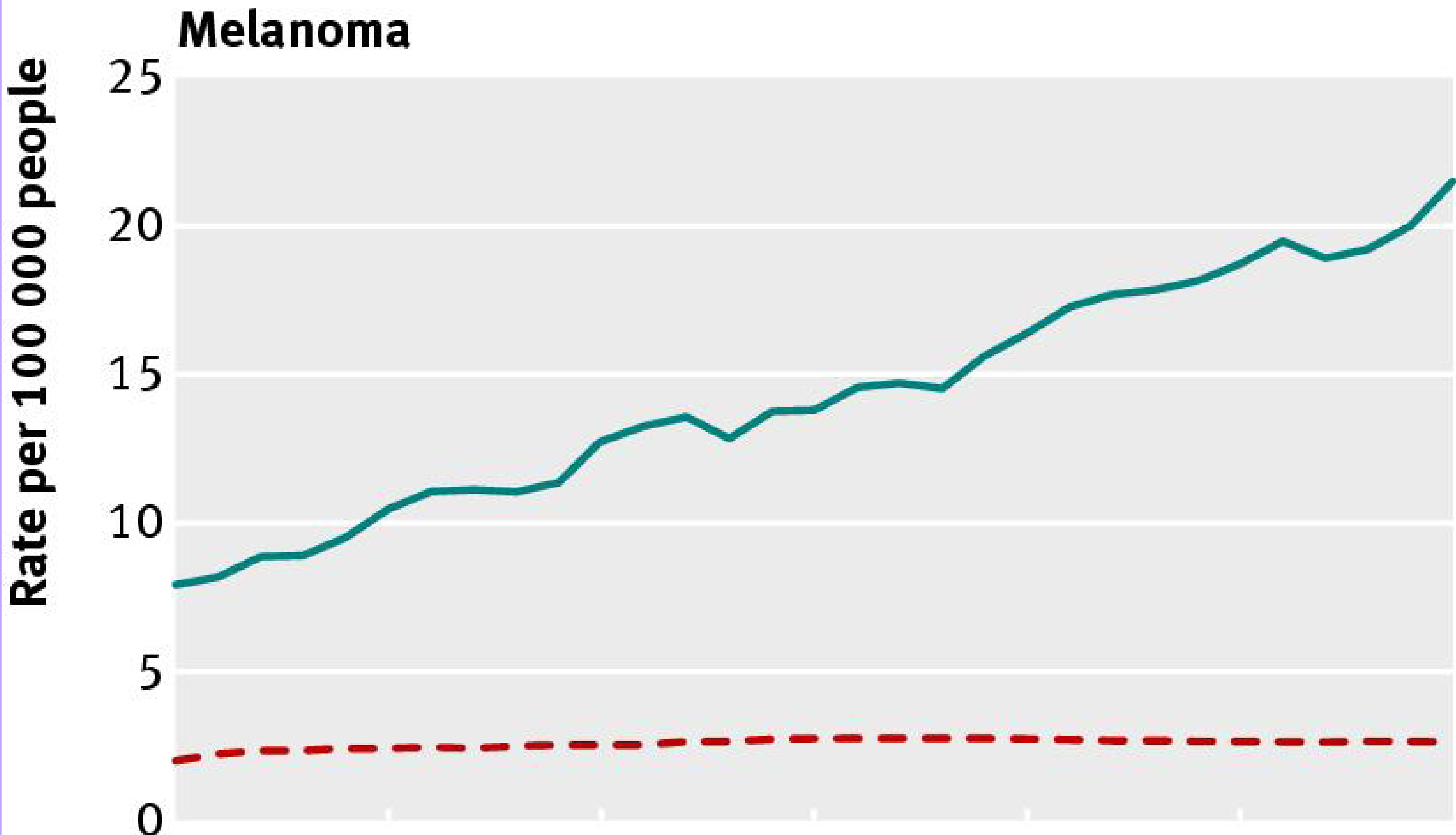

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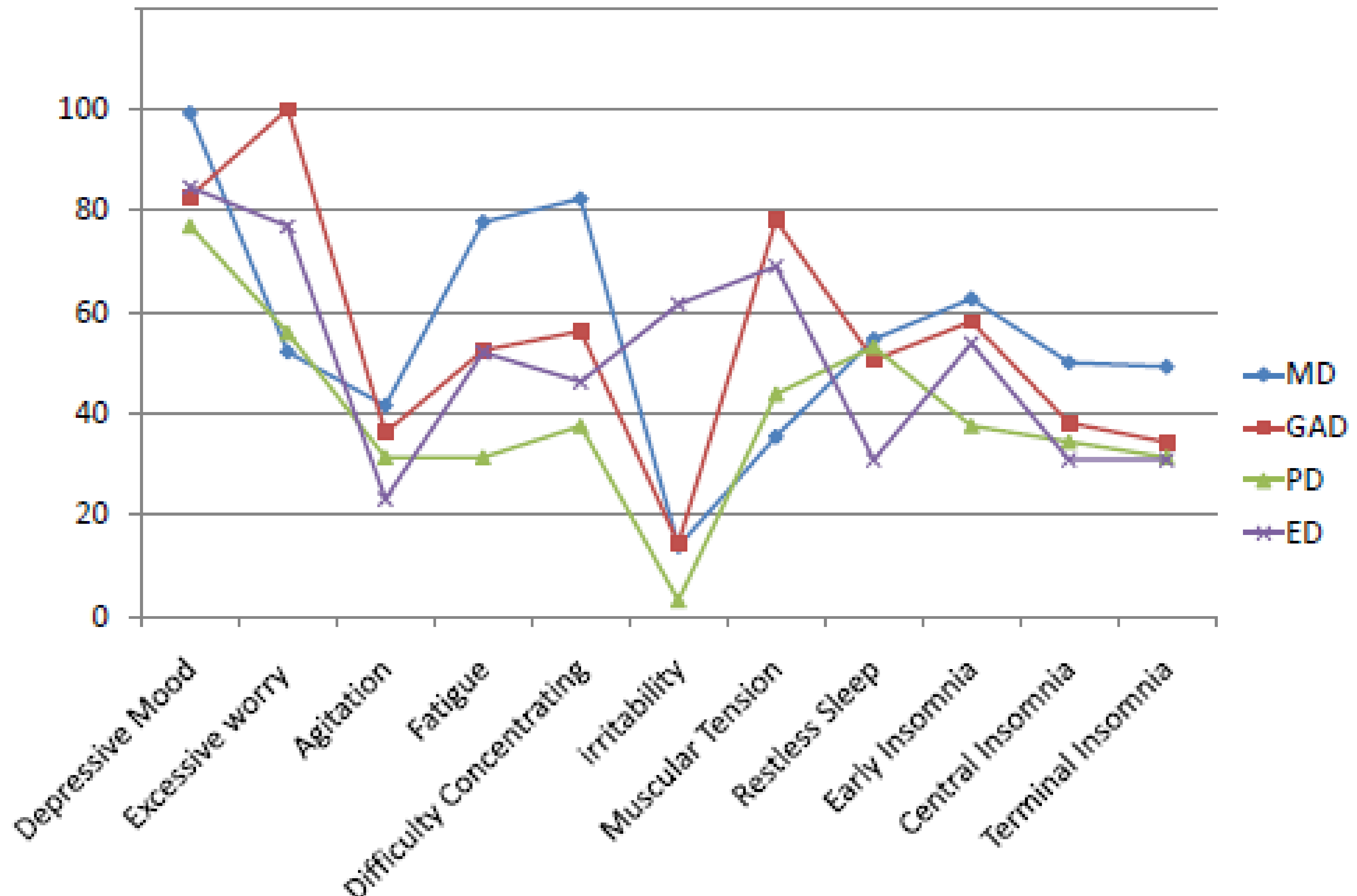
Comorbidity is highly prevalent

- US NCS (Kessler, 1994): 51% of patients with a diagnosis of MDD had at least one 'comorbid' anxiety disorder and only 26% of them had no concomitant mental disorder
- Early Developmental Stages of Psychopathology Study (Wittchen et al, 1998): 48.6% and 34.8%
- Australian National Survey of Mental Health and Well-Being (Andrews et al, 2002): 21% of people fulfilling DSM–IV criteria for any mental disorder met the criteria for three or more 'comorbid' disorders

ICD-10, DSM-IV & psychiatric comorbidity

- Proliferation of diagnosis categories
- Reduced number of hierarchical rules
- Tendency to psychopathological oversimplification
- *The use of multiple diagnosis in the same patient may prevent a holistic approach to the individual case and encorauge na unwarranted use of polypharmacy*

Occurrence of specific symptoms across different diagnoses



Comorbidity: Psychopathology

- The nature of psychopathology is intrinsically composite and changeable, and that what is currently conceptualised as the co-occurrence of multiple disorders could be better reformulated as the complexity of many psychiatric conditions (with increasing complexity being an obvious predictor of greater severity, disability and service utilisation)

Comorbidity: Psychodinamic

- The interaction of congenital predisposition, individual experiences and the type and success of defence mechanisms employed may generate <u>an infinite variety of combinations of symptoms and signs</u>

Comorbidity: Psychobiologic

- ‘Noxious stimuli . . . perturb a variety of neuronal circuits . . .The extent to which the various neuronal circuits will be involved varies individually, and consequently psychiatric conditions will lack symptomatic consistency and predictability’ (van Praag, 1996)

Comorbidity: Evolutionary

- Mental disorders are the expression of preformed response patterns shared by all humans, which may be activated simultaneously or successively in the same individual by noxae of various nature

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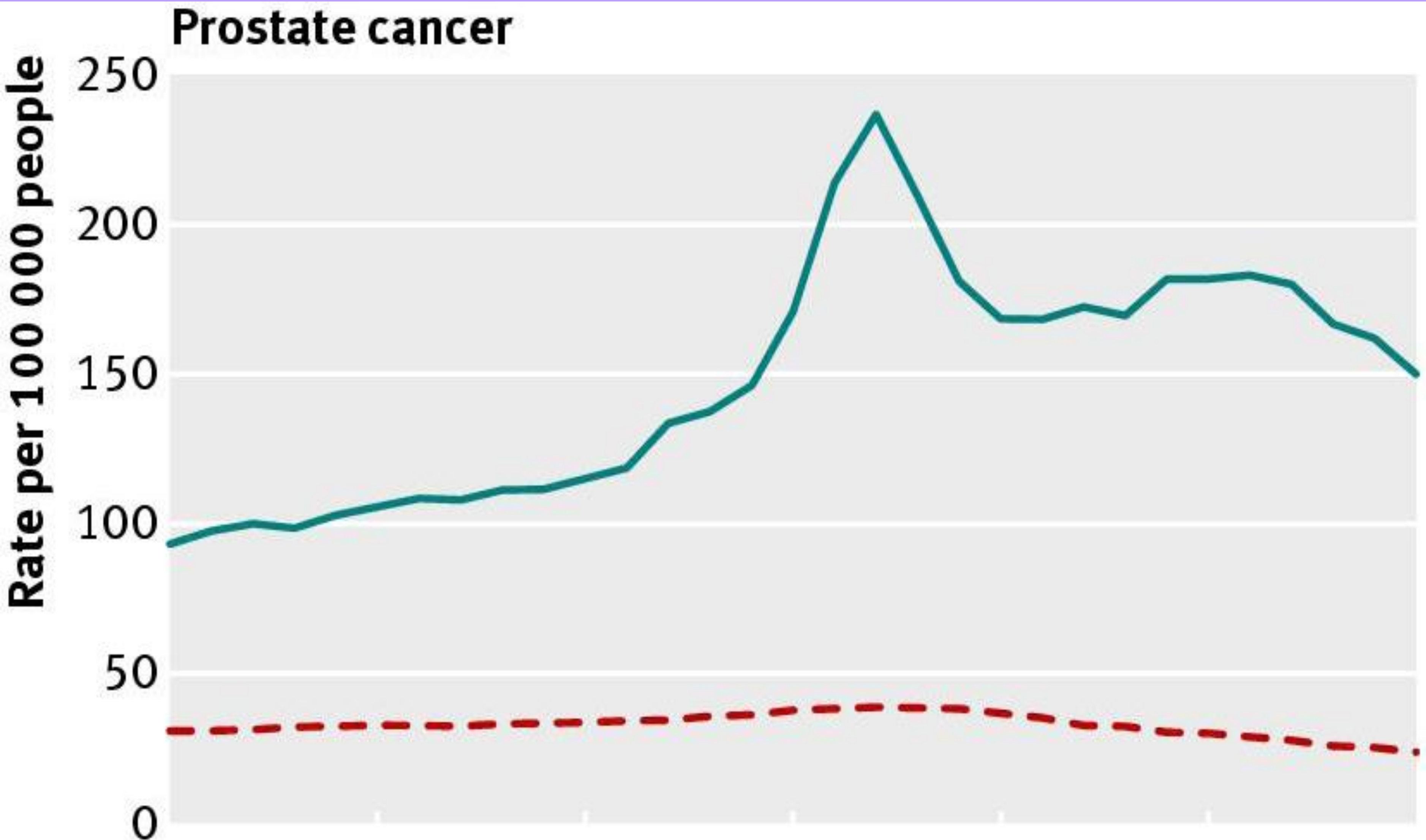

‘The use of imprecise language may lead to correspondingly imprecise thinking’ (Lilienfeld et al, 1994)

1. Psychopharmacological decision-making and psychiatric classification

1. *Nosological* e.g. treatment of schizophrenia with antipsychotics (supposed main mechanism: antidopaminergic)
2. *Syndromatological* e.g. treatment of psychotic symptoms with antipsychotics, treatment of depressive symptoms in the context of schizophrenia with antidepressants
3. *Transnosological* (*trans-syndromal*?) Antidepressants (especially SSRIs) not only for the treatment of depressive but also anxiety disorders (supposed main mechanism: serotonergic/noradrenergic)
4. *Based on pharmacological mechanisms* e.g. second generation antipsychotics with their broad spectrum of pharmacological mechanisms can be used

- To treat schizophrenia (antidopaminergic action: D2/D3 blockade)
- To treat depression (serotonergic action: 5HT2 blockade, 5HT1 agonism)
- To treat anxiety disorders? (serotonergic action)

2. An useful classification of mental disorders must enable:

a) Optimal prognoses about the spontaneous course and therapeutic response

b) Conclusions to be drawn about possible causal factors

c) Individual cases to be assigned reliably to classes or types

- *The better a classification of mental disorders fulfills these criteria, the better is it suited to everyday clinical practice*

3. Heads-up: current systems do not facilitate innovation

- The current nosographic system prevents psychiatry from benefiting of the significant technological progress that has led the rest of medical sciences to important clinical achievements in the last 20 years
- In the future, psychiatry will be probably able to find new and more specific markers and instruments

4. On the need of biomarkers

- Toxicity
- Patients
- Disease
- Efficacy

Back-up

What is the DSM method for revising psychiatric nosology?

- ‘Iterative model’: incremental changes made while retaining the fundamental assumptions of the existing model
- ‘paradigm shift model’: the underlying paradigm is discarded in favor of a fundamentally new approach
- *DSM–III (1980): “DSM–III is only one still frame in the ongoing process of attempting to better understand mental disorders.” DSM–III–R represents another still frame.’ (p. xvii).8*

4. On the need of an aetiologically based paradigm

- Research advances support psychiatry's view of mental illness as neurobiologically based diseases
- *However, not a single DSM category is defined in terms of brain processes*
- It might be only a matter of time until advances allow for the arrival of the necessary major neurobiological breakthroughs
- Clear molecular and/or neurobiological mechanisms will allow the development of a 'real' aetiologically based nosological system
  - *Challenge: most psychiatric disorders are inherently multifactorial*

Jaspers (1913)

- ‘True diseases’ (such as general paresis), which have clear boundaries among themselves and with normality
- ‘Circles’ (such as manic–depressive insanity and schizophrenia), which have clear boundaries with normality but not among themselves
- ‘Types’ (such as neuroses and abnormal personalities), which do not have clear boundaries either among themselves or with normality